Medicinrådet

Bilag til Medicinrådets vurdering af selinexor, bortezomib og dexamethason til behandling af patienter med knoglemarvskræft som har fået mindst én tidligere behandling

Patienter, som er refraktære overfor lenalidomid og ikke kan behandles med anti-CD38-antistof

Vers. 1.0

Bilagsoversigt

1. Ansøgers notat til Rådet vedr. selinexor, bortezomib og dexamethason
2. Forhandlingsnotat fra Amgros vedr. selinexor, bortezomib og dexamethason
3. Ansøgers endelige ansøgning vedr. selinexor, bortezomib og dexamethason

Menarini Stemline response to DMC assessment of selinexor in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy and are refractory to lenalidomide and where an anti-CD38 antibody is not appropriate

2nd October 2025

Menarini Stemline would like to thank DMC for the fair assessment and for its collaboration during the assessment process for what is our first submission to the DMC.

Menarini Stemline has submitted documentation for selinexor in combination with bortezomib and dexamethasone (SelBorDex) for the treatment of adult patients with relapsed refractory multiple myeloma (MM) who have received at least one prior therapy and are refractory to lenalidomide and where an anti-CD38 antibody is not appropriate.

The application concerns a patient population with a very high disease severity, a poor prognosis and in need of well documented, effective and tolerable treatment options.

Despite advances in treatment, MM remains incurable in the majority of patients; most patients relapse on treatment and require multiple lines of treatment. As patients pass through each line of treatment, their fitness and general health decline, and their symptom burden increases. Chance of survival worsens with each progressive line of treatment leading to attrition, with the time to relapse with triplet regimens being longer than doublet regimens. Early treatment with a range of combination treatments with different mechanisms of action (MoA) is therefore valuable in prolonging survival for this hard-to-treat patient population.

As a first in class treatment, selinexor as part of the combination of SelBorDex provides a new triplet combination, with the new mode of action for patients, which is a key factor when choosing therapy beyond the first line setting.

The treatment landscape is changing currently. Recently, DaraLenDex was recommended for use in the front-line setting in Denmark. This means that patients now have the potential to be both lenalidomide refractory and *also* unsuitable for an anti-CD38 antibody before initiating 2nd line therapy. Therefore, there is now an even bigger unmet need for patients who are lenalidomide refractory and anti-CD38 antibody refractory after first relapse.

Hence, with increasing use of daratumumab and lenalidomide early in the course of disease there is a need for a triplet combination beyond first line therapy which provides the opportunity to treat with a new mechanism of action for a population of patients who are anti-CD38 antibody and lenalidomide exposed/refractory. A recommendation of SelBorDex will thus permit a double drug class switch in these patients.

In this treatment setting, selinexor offers a treatment with a new mechanism of action that has not been used in previous lines, which is to be considered optimal. In addition, Selinexor has the benefit of being an oral treatment, which reduces the burden for the patients and also for the Danish health care system.

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03.10.2025

LSC/DBS

Forhandlingsnotat

Dato for behandling i Medicinrådet	29.10.2025
Leverandør	Menarini Stemline
Lægemiddel	Nexpovio (selinexor)
Ansøgt indikation	Selinexor i kombination med bortezomib og dexamethason er indiceret til behandling af voksne patienter med myelomatose, som har fået mindst én tidligere behandling. Ansøgningen er afgrænset til patienter, der er refraktære overfor lenalidomid, og som ikke kan behandles med anti-CD38 antistof.
Nyt lægemiddel / indikationsudvidelse	Nyt lægemiddel

Prisinformation

Amgros har forhandlet følgende pris på Nexpovio (selinexor):

Tabel 1: Forhandlingsresultat

Lægemiddel	Styrke (pakningsstørrelse)	AIP (DKK)	Forhandlet SAIP (DKK)	Forhandlet rabat ift. AIP
Nexpovio	20 mg x 20 stk.	56.665,60	[redacted]	[redacted]

Prisen er betinget af Medicinrådets anbefaling.

Det betyder, at hvis Medicinrådet ikke anbefaler Nexpovio indkøbes det til AIP.

Aftaleforhold

[redacted]

Konkurrencesituationen

Der findes flere behandlingsalternativer til patientgruppen, og der er flere nye behandlinger under vurdering i Medicinrådet. Ifølge Medicinrådets lægemiddelrekommandation vedr. myelomatose er nuværende standardbehandling til patientpopulationen carfilzomib i kombination med dexamethason (CarDex) eller pomalidomid i kombination med bortezomib og dexamethason (PomBorDex).

Tabel 2 viser den årlige lægemiddeludgift for Nexpovio i relation til CarDex og PomBorDex.

Tabel 2: Sammenligning af lægemiddeludgifter pr. patient

Lægemiddel	Styrke (paknings-størrelse)	Dosering	Pris pr. pakning (SAIP, DKK)	Lægemiddeludgift pr. år (SAIP, DKK)
Nexpovio + BorDex				[redacted]
Nexpovio	20 mg, 20 stk.	100 mg (p.o.) en gang om ugen	[redacted]	[redacted]
Bortezomib "Stada"*	2,5 mg/ml, 1,4 ml. hætteglas	1,3 mg/m^2 (s.c.) én gang om ugen i 4 uger, herefter 1 uges pause	[redacted]	[redacted]
Dexamethason "Krka"	4 mg, 20 stk. tabletter	20 mg (p.o.) to gange ugentligt	[redacted]	[redacted]
PomBorDex				[redacted]
Pomalidomid "Sandoz"	4 mg, 21 stk. kapsler	4 mg (p.o.) én gang dagligt på dag 1 til 14, efterfulgt af en uges pause.	[redacted]	[redacted]
Bortezomib "Stada"*	2,5 mg/ml, 1,4 ml. hætteglas	1,3 mg/m^2 (s.c.) én gang om ugen i 4 uger, herefter 1 uges pause	[redacted]	[redacted]
Dexamethason "Krka"	4 mg, 20 stk. tabletter	20 mg (p.o.) to gange ugentligt	[redacted]	[redacted]
CarDex				[redacted]

Kyprolis	30 mg, 1 stk. hætteglas	20 mg/m^2 (i.v.) på dag 1, 2, og derefter 56 mg/m^2 (i.v.) på dag 8, 9, 15 og 16, og efterfølgende cyklusser. I en 28-dages cyklus.	[redacted]	[redacted]
Dexamethason "Krka"	4 mg, 20 stk. tabletter	20 mg (p.o.) to gange ugentligt	[redacted]	[redacted]

*BSA = 1,85 m^2, baseret på BOSTON-studiet

[redacted]

Status fra andre lande

Tabel 3: Status fra andre lande

Land	Status	Kommentar	Link
Norge	Ikke anbefalet	Bestillerforum har afbestilt evalueringen	Link til vurderingen
England	Anbefaling		Link til anbefaling
Sverige	Anbefaling		Link til anbefaling

Opsummering

[redacted]

Application for the assessment of selinexor in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy and are refractory to lenalidomide and where an anti-CD38 antibody is not appropriate

Color scheme for text highlighting	
Color of highlighted text	**Definition of highlighted text**
	Confidential information
[Other]	[Definition of color-code]

Contact information

Contact information	
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Abbreviations

Abbreviation	Definition
1L	First line
2L	Second line
3L	Third line
3L+	Third line or later
AE	Adverse event
ASCT	Autologous stem cell transplant
BIW	Twice weekly
CI	Confidence interval
CNS	Central nervous system
DaraRd	Daratumumab + lenalidomide + dexamethasone
DaraVd	Daratumumab + bortezomib + dexamethasone
DCO	Data cut-off
DMC	Danish Medicines Council
ECOG	Eastern Cooperative Oncology Group
EloRd	Elotuzumab + lenalidomide + dexamethasone
EORTC	European Organization Research and Treatment of Cancer
HDT	High dose therapy
HR	Hazard ratio
HRQoL	Health-related quality of life
IMWG	International Myeloma Working Group
IQR	Interquartile range
IRC	Independent review Committee
ITT	Intention-to-treat
IxaRd	Ixazomib + lenalidomide + dexamethasone
Kd	Carfilzomib + dexamethasone
KRd	Carfilzomib + lenalidomide + dexamethasone
mg	Milligrams
MGUS	Monoclonal gammopathy of unknown significance
min	Minute
mL	Millilitres
MM	Multiple myeloma
MoA	Mechanism of Action

MyPOS	Myeloma Patient Outcome Scale
N/A	Not applicable
NE	Not estimable
NMA	Network meta-analysis
ORR	Overall response rate
OS	Overall survival
Pd	Pomalidomide + dexamethasone
PFS	Progression-free survival
PI	Protease-inhibitor
PVd	Pomalidomide + bortezomib + dexamethasone
QLQ-C30	Quality of Life Questionnaire-30
QLQ-CIPN20	Quality of Life– Chemotherapy-Induced Peripheral Neuropathy questionnaire
QW	Once weekly
Rd	Lenalidomide + dexamethasone
R-ISS	Revised international staging system
RRMM	Relapsed or refractory multiple myeloma
SC	Subcutaneous
SCT	Stem cell transplantation
SVd	Selinexor + bortezomib + dexamethasone
TOT	Time on treatment
TSP	Tumour suppressor protein
Vd	Bortezomib + dexamethasone
VRd	Bortezomib + lenalidomide + dexamethasone
XPO-1	Exportin 1

1. Regulatory information on the medicine

Overview of the medicine	
Proprietary name	Nexpovio®
Generic name	Selinexor
Therapeutic indication as defined by EMA	Selinexor is indicated in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.
Marketing authorization holder in Denmark	Stemline Therapeutics BV e
ATC code	L01XX66
Combination therapy and/or co-medication	Selinexor is given in combination with bortezomib and dexamethasone
(Expected) Date of EC approval	18 July 2022
Has the medicine received a conditional marketing authorization?	The marketing authorization for selinexor was initially conditional; however full, unconditional, marketing authorization was granted by the European Commission on 18-07-2022
Accelerated assessment in the European Medicines Agency (EMA)	No
Orphan drug designation (include date)	No
Other therapeutic indications approved by EMA	Selinexor is also indicated in combination with dexamethasone for the treatment of multiple myeloma in adult patients who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, two immunomodulatory agents and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.
Other indications that have been evaluated by the DMC (yes/no)	An application regarding selinexor in combination with dexamethasone for the treatment of multiple myeloma in adult patients who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, two immunomodulatory agents and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy will also be submitted to the DMC in August 2024

Joint Nordic assessment (JNHB)	Are the current treatment practices similar across the Nordic countries (DK, FI, IS, NO, SE)? No Is the product suitable for a joint Nordic assessment? No If no, why not? Due to differences in reimbursed treatments in the treatment pathway and therefore a difference in comparators e.g. DRd – daratumumab, lenalidomide and dexamethasone
Dispensing group	BEGR
Packaging – types, sizes/number of units and concentrations	8 x 20mg tablets 12 x 20mg tablets 16 x 20mg tablets 20 x 20mg tablets

2. Summary table

Provide the summary in the table below, maximum 2 pages.

Summary	
Therapeutic indication relevant for the assessment	*Based on the current reimbursed treatment pathway in Denmark, selinexor in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy and are refractory to lenalidomide and where an anti-CD38 antibody is not appropriate.* In Europe, selinexor in combination with bortezomib and dexamethasone (SVd) is approved for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.[1] Based on clinician feedback, selinexor will be used in patients who are refractory to lenalidomide based on its novel mode of action and efficacy in a post-hoc analysis of the BOSTON study and where an anti-CD38 is not appropriate.
Dosage regiment and administration	The recommended selinexor, bortezomib and dexamethasone doses based on a 35-day cycle are as follows:[1] • Selinexor 100 mg taken orally once weekly on Day 1 of each week. The dose of selinexor should not exceed 70 mg/m2 per dose. • Bortezomib 1.3 mg/m2 administered subcutaneously (SC) once weekly on Day 1 of each week for 4 weeks followed by 1 week off. • Dexamethasone 20 mg taken orally twice weekly on Days 1 and 2 of each week.

Choice of comparator	• Based on the treatment guideline for MM published by the DMC[2], the relevant comparators in 2L+ (for lenalidomide-refractory patients) and where an anti-CD38 antibody is not appropriate are:
	  ○ Carfilzomib in combination with dexamethasone (Kd)
	  ○ Pomalidomide in combination with bortezomib and dexamethasone (PVd)
	• Based on clinical feedback it is anticipated that SVd will be used as an alternative to Kd in the treatment pathway

Prognosis with current treatment (comparator)	According to the Danish treatment guidelines, median survival for newly diagnosed patients that are candidates for high-dose therapy (HDT) and stem-cell transplantation (SCT) is approximately seven years, while newly-diagnosed patients that are not candidates to HDT/SCT have a median survival of approximately three years.[3] To the best of our knowledge, data on the prognosis of Danish lenalidomide-refractory patients in 2L+ is not available; however, a 2016 study, examining real-world data from Belgium, France, Germany, Italy, Spain, Switzerland, and the UK, found that MM patients receiving treatment in 2L had a median time to progression (TTP) of 13 months, with patients in 3L and 4L having a median TTP of 7 and 5 months, respectively.[4]
Type of evidence for the clinical evaluation	The comparative evidence against the relevant comparators is obtained from a frequentist random-effects network meta-analysis (NMA) including the BOSTON[5], ENDEAVOR[6], and OPTIMISMM[7] trials.
Most important efficacy endpoints (Difference/gain compared to comparator)	The observed effect of SVd versus Vd in the lenalidomide-refractory subpopulation in the BOSTON trial (adjusted for treatment switching) is presented below: **Overall survival (OS)** SVd median OS, months (95% CI): 26.7 (16.92, NE) Vd median OS, months (95% CI): 18.6 (13.95 to 29.01) Hazard ratio (95% CI): 0.53 (0.30 to 0.95) **Progression-free survival (PFS)** SVd median OS, months (95% CI): 10.2 (5.8, NE) Vd median OS, months (95% CI): 7.1 (3.5 to 9.8) Hazard ratio (95% CI): 0.52 (0.31 to 0.88) **Comparative efficacy** While several outcomes are included in the DMC treatment guideline, the ENDEAVOR[6] and OPTIMISMM[7] trials only reported OS and PFS in a way that allowed for inclusion in the NMA. The comparative efficacy of SVd versus Kd and PVd is provided below. **OS:**

	SVd versus Kd; Hazard ratio (HR): 0.62 (95% confidence interval [CI]: 0.31 to 1.22, p-value = 0.1648) SVd versus PVd; Hazard ratio (HR): 0.60 (95% confidence interval [CI]: 0.31 to 1.13, p-value = 0.1127) **PFS:** SVd versus Kd; Hazard ratio (HR): 0.65 (95% confidence interval [CI]: 0.35 to 1.20, p-value = 0.1735) SVd versus PVd; Hazard ratio (HR): 0.80 (95% confidence interval [CI]: 0.45 to 1.43, p-value = 0.4556) As shown above, while SVd is numerically superior to both comparators for both OS and PFS, the differences are not statistically significant.
Most important serious adverse events for the intervention and comparator	The only serious adverse events occurring in more than 5% of patients in the included trial was pneumonia (occurring in 14.9% of patients in the SVd arm and 13.2% in the bortezomib + dexamethasone [Vd] arm in BOSTON).[8] In the health-economic model, adverse events of grade 3-4 that occurred in more than 5% of patients in the BOSTON trial are included, these are shown in Table 36.
Impact on health-related quality of life	**Clinical documentation**: In BOSTON, health-related quality of life (HRQoL) was measured using EORTC QLQ-C30. Both treatment arms (SVd and Vd) showed a similar reduction in the EORTC QLQ-C30 global health status score at end of treatment, reflecting improved quality of life in both the overall and lenalidomide-refractory population. Health economic model: Not applicable.
Type of economic analysis that is submitted	Cost-minimisation analysis using a partitioned survival model.
Data sources used to model the clinical effects	BOSTON clinical trial data for the lenalidomide refractory patients
Data sources used to model the health-related quality of life	Not applicable.
Life years gained	Not applicable
QALYs gained	Not applicable
Incremental costs	DKK -235,606 versus Kd DKK 168,772 versus PVd
ICER (DKK/QALY)	Not applicable

Uncertainty associated with the ICER estimate	The main parameters driving the incremental cost were time-on-treatment (ToT) and OS.					
Number of eligible patients in Denmark	**Year**	**2019**	**2020**	**2021**	**2022**	**2023**
	Incidence in Denmark	N/A	400[b]	370 [b]	396 [b]	397 [b]
	Prevalence in Denmark	3,106[a]	3,332 [a]	3,577 [a]	N/A	3,470 [a]
Budget impact (in year 5)	DKK 9,624,905					

Abbreviations: N/A, Not applicable.

Notes: *Estimated using the incidence from 2021 and population sizes from 2022 and 2023. [a]From Nordcan. [b] From Dansk Myelomatose Database

Sources: Nordcan[9] and Dansk Myelomatose Databse[10]

3. The patient population, intervention, choice of comparator(s) and relevant outcomes

3.1 The medical condition

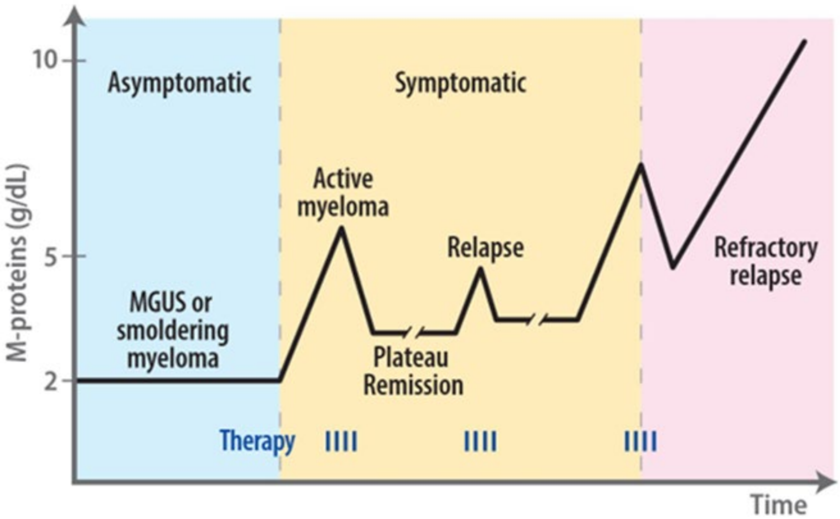
Multiple myeloma is a rare, clonal B-cell malignant neoplasm, characterised by accumulation of abnormal clonal plasma cells (myeloma cells) in the bone marrow microenvironment.[11] MM can be caused by several genetic plasma cell abnormalities which modify the expression of adhesion molecules on the cell surface, and the cellular response to growth stimuli within the bone marrow, promoting cell growth, survival, and migration.[12,13] Malignant plasma cell clones make an excess of a specific immunoglobulin (which comprises two heavy chains and two light chains), and also an excess of additional light chains, paraproteins which are detectable in the blood and useful in both the diagnosis and monitoring of MM.[14]

Symptomatic or active MM typically presents with symptoms referred to as CRAB and differentiates itself from monoclonal gammopathy of unknown significance (MGUS) and smouldering myeloma.[14,15] The acronym CRAB summarises the most typical clinical manifestations of MM, these being hypercalcaemia, renal failure, anaemia, and bone disease. As the bone marrow becomes filled with malignant plasma cells, the ability of haematopoietic stem cells to produce new blood cells is diminished, which can lead to anaemia, neutropenia, thrombocytopenia, and immune paresis with resulting infection. Cytokines released by tumour cells stimulate osteoclast mediated bone resorption causing hypercalcaemia, bone pain, and increased risk of fracture. Renal failure can result from the toxic effects of the paraproteins mentioned above on the renal glomeruli and tubules, as well as direct toxicity from hypercalcaemia. Hypercalcaemia can also lead to gastrointestinal symptoms such as thirst, nausea, and constipation, as well as neurological effects including confusion, drowsiness, and neuropathy.[14-19]

In the plasma cells of MM patients, levels of exportin 1 (XPO-1), a key nuclear export receptor, are higher than in healthy people.[11,20] When XPO-1 is overexpressed, tumour suppressor proteins are exported and lose their anti-neoplasm functionality. This leads to erroneous growth signalling and oncogenic cell expansion. High XPO-1 levels are associated with poor disease prognosis and resistance to chemotherapies.[11,20]

Despite advances in treatment, MM remains incurable in the majority of patients; most patients relapse on treatment and require multiple lines of treatment.[21] The typical pattern of disease progression for MM patients is presented in Figure 1. As patients pass through each line of treatment, their fitness and general health decline, and their symptom burden increases. Chance of survival worsens with each progressive line of treatment leading to attrition, with the time to relapse with triplet regimens being longer than doublet regimens.[4,22-25] Early treatment with a range of combination treatments with different mechanisms of action (MoA) is therefore valuable in prolonging survival.

Figure 1. Graphical representation of MM disease progression phases



Abbreviations: MGUS, monoclonal gammopathy of undetermined significance
Source: Durie et al. 2018 (International Myeloma Foundation)[21]

In a survey of UK MM patients, published in 2016, 557 patients were asked to complete the Myeloma Patient Outcome Scale (MyPOS), a myeloma specific quality of life (QOL) questionnaire consisting of 30 questions. The included patients reported a mean of 7.2 symptoms (median: 7, range: 0-15), with the most burdensome symptoms (scored by patients as severe or overwhelming) being fatigue (scored as overwhelming by 21.9%), pain (13.8%), and tingling in the hands or feet (10.2%).[26]

The UK survey included newly diagnosed, treatment-free, and relapsed/progressed patients; out of these the relapsed/progressed patients had the highest mean number of symptoms and the highest mean total MyPOS score.[26] Regression analysis showed that the patients QLQ-C30 global score was associated with pain, weakness/lack of energy, anxiety, depression, and poor mobility. Similarly, the EQ5D index score was associated with pain, depression, having an Eastern Cooperative Oncology Group (ECOG) performance status of 3 or 4, and poor mobility.[26]

3.2 Patient population

Multiple Myeloma is the second most common haematological cancer in Denmark, and in 2020, the DMC estimated that 1,800 patients are living with MM in Denmark. [27]The DMC reported the median age at diagnosis as 71 years and stated that 20% of newly diagnosed patients have asymptomatic, smouldering multiple myeloma.[27]

According to Nordcan statistics, the crude incidence rate of multiple myeloma in Denmark was 10.8 per 100.000 in 2021, amounting to 632 newly diagnosed patients considering a population size of 5,850,189 in 2021.[9] However, the incidence reported by Nordcan is somewhat higher, than what was estimated by the DMC in the background materials for the treatment guideline for multiple myeloma[3] – this may be partly caused by inclusion of other types of myeloma (e.g., smouldering MM) in Nordcan. The Danish Myeloma Database (DaMyDa) reports yearly incidence for multiple myeloma specifically for the years 2020-2023 in their yearly report for 2023[10]. The incidence according of multiple myeloma in Denmark according to DaMyDa statistics are presented in Table 1. The DaMyDa yearly report also reports prevalence for 2023; however, no prevalence estimates for previous years are presented – therefore the prevalence for 2019-2021 is obtained from Nordcan. With a population size in Denmark of 5,932,654 per January 1st 2023[28], an incidence of 397 corresponds to a crude incidence rate of 6.69 per 100,000.

The prevalence presented in Table 1 is the total prevalence, i.e., all people alive who have had a diagnosis of MM.[9] The numbers are somewhat higher than the 1,800 people living with MM reported by the DMC; based on the numbers available from Nordcan, one possible explanation is that the numbers reported by the DMC are 5-year prevalence, where only patients who have had a MM diagnosis within the last 5-years are counted. The prevalence for 2022 and 2023 has not been estimated.

Table 1. Incidence and prevalence in the past 5 years

Year	2019	2020	2021	2022	2023
Incidence in Denmark	N/A	400 [b]	370 [b]	396[b]	397[b]
Prevalence in Denmark	3,106[a]	3,332[a]	3,577[a]	N/A	3470[b]
Global prevalence	N/A	N/A	N/A	N/A	N/A

Abbreviations: N/A, Not applicable.

Notes: *Estimated using the incidence from 2021 and population sizes from 2022 and 2023. [a]From Nordcan. [b]From Dansk Myelomatose Database

Sources: Nordcan[9] and Dansk Myelomatose Databse[10]

This application concerns MM patients in 2L+ who are refractory to lenalidomide and ineligible for an anti-CD38 monoclonal antibody. In Europe around 95% of those diagnosed with MM receive 1L treatment, of which 61% receive 2L treatment, around 38% receive 3L, and around 15% reach 4L[4]. In Denmark, an estimated 399 people will be diagnosed with MM in 2024. Thus, approximately 259 patients will be eligible for 2L+ treatment. As patients will be eligible for SVd once in the treatment pathway once, there is therefore a maximum eligible patient population of 259 patients. In the DMC guideline for MM, it is stated that approximately 70% of lenalidomide-refractory patients in 2L should receive DaraVd, with PVd and Kd being considered for the remaining 30%. Based on feedback from the DMC, out of all the patients eligible for treatment between 2L to 4L, approximately 16% of these patients will be eligible for treatment with SVd at one point in the pathway.

Based on clinical feedback SVd is expected to mainly replace Kd in the treatment pathway, while PVd is expected to be replaced in a lower grade. Based on this SVd is expected to have a market share no higher than 65% within the next 5 years (17 patients by year 5, see Table 55).

Table 2 reports the estimated number of patients in Denmark who are eligible for SVd treatment in the coming five years.

Table 2. Estimated number of patients eligible for treatment

Year	2024	2025	2026	2027	2028
Estimated population in Denmark	5,961,249	5,984,461	5,966,968	5,981,620	5,996,169
Estimated MM incidence	399	400	399	400	401
Estimated 2L+ population	259	260	260	260	261
Number of patients in Denmark who are eligible for treatment with SVd in the coming years	42	42	42	42	42

Abbreviations: 2L+, Second line plus; MM, Multiple myeloma.

Notes: The estimated MM incidence is calculated using the estimated population in Denmark and the 20213 MM incidence from DaMyBa. The estimated 2L population is calculated using the European treatment percentage.

Source: Danish Myeloma Database[10], Statistics Denmark [28] and Yong 2016[4].

3.3 Current treatment options

The choice of treatment for patients with MM is complicated and depends on many factors, including age and general health. After 1st line treatment, the key driver of treatment decisions is refractoriness to previous treatments, and due to the clonal nature of the disease a change in the mode of action in the next line of therapy is considered key[29]. Current treatment options, as described by the DMC[2], are outlined below.

1L treatment

Current 1L treatment options depend on whether the patient is a candidate for high-dose chemotherapy (HDT) with stem cell transplantation (SCT) or not. This depends on the patient's age and physical and mental health.

In the first line, newly diagnosed patients who are candidates for HDT are generally offered induction therapy with bortezomib + lenalidomide + dexamethasone (VRd), cyclophosphamide and peripheral stem cell harvest, HDT with melphalan and stem cell support and post-HDT maintenance therapy with lenalidomide. Consolidation therapy (repeat HDT with VRd or lenalidomide + dexamethasone [Rd]) can be considered.

For patients that are not eligible for HDT and SCT, approximately 60% should be treated with either VRd or daratumumab + bortezomib + melphalan + prednisone, with VRd being the first choice. For the remaining 40%, Rd should be considered.

2L treatment

In 2L, treatments are chosen based on treatments received in 1L, refractory status, and patient characteristics important for eligibility. In the DMC treatment guidelines[2], treatment regimens are presented for two broad categories:

Patients that are sensitive to lenalidomide:

For patients in 2L that are sensitive to lenalidomide, the first-choice regimen is daratumumab + lenalidomide + dexamethasone (DaraRd), which should be used for approximately 70%. For patients for whom daratumumab is contraindicated, elotuzumab + lenalidomide + dexamethasone (EloRd) and carfilzomib + lenalidomide + dexamethasone (KRd) can be considered, with EloRd being the first choice. For patients ineligible to the regimens described above, ixazomib + lenalidomide + dexamethasone (IxaRd), daratumumab + bortezomib + dexamethasone (DaraVd), PVd, and Kd can be considered.[2]

Patients that are lenalidomide-refractory and sensitive to daratumumab:

For patients in 2L that are refractory to lenalidomide but sensitive to daratumumab, the first-choice regimen is DaraVd, which should be used for approximately 70% of the population. For the remaining 30%, PVd and Kd can be considered. It is not entirely clear which characteristics would make patients in this category ineligible to DaraVd and thus relevant for PVd and Kd, but it is likely that these would be patients refractory to lenalidomide and ineligible for daratumumab.[2]

Additionally, patients that received HDT and SCT in 1L and who achieved long remission (defined as longer than three years for patients in maintenance treatment, and longer than one and a half year for patients without maintenance treatment), can be offered repeat HDT and SCT.[2]

3L treatment

For 3L treatment, the DMC guidelines states that treatment regimens recommended in second line can be used in third and later lines, if the patient can tolerate and is not refractory to the medicines included.[2]

For those patients for whom regimens recommended in 2L are not appropriate, PVd, pomalidomide + dexamethasone (Pd), and Kd are recommended. It is explicitly stated that these regimens are not considered equivalent, and that treatment should be chosen considering refractoriness, toxicity, comorbidities, and patient preferences.[2]

4L+ treatment

For fourth and subsequent lines the DMC guidelines recommend choosing between pomalidomide- and carfilzomib containing regimens as described for 3L treatment, considering refractoriness and other factors described above.[2]

Additionally, in February 2024, the DMC recommended teclistamab for patients with relapsed and refractory MM, who have received at least three prior treatments, including an immunomodulatory agent (IMiD), a protease-inhibitor (PI), and an anti-CD38 antibody, who progressed during their last treatment.[30]

The full treatment pathway from diagnosis is visualised in Appendix K.

3.4 The intervention

The intervention, SVd, is described in Table 3 below.

Table 3. The intervention

Overview of intervention	
Therapeutic indication relevant for the assessment	*Selinexor in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy, and who are refractory to lenalidomide and where an anti-CD38 antibody is inappropriate.* In Europe, selinexor in combination with bortezomib and dexamethasone (SVd) is approved for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.[1] However, based on clinician feedback, SVd will be used in patients refractory to lenalidomide and where an anti-CD38 monoclonal antibody is inappropriate in the 2L to 4L setting. It is expected mainly to replace the use of Kd. Thus, the relevant indication for the assessment is as provided above.
Method of administration	**Selinexor**: Oral administration **Bortezomib:** Subcutaneous administration **Dexamethasone**: Oral administration
Dosing	The recommended selinexor, bortezomib and dexamethasone doses based on a 35-day cycle are as follows:[1] • Selinexor 100 mg taken orally once weekly on Day 1 of each week. The dose of selinexor should not exceed 70 mg/ m2 per dose. • Bortezomib 1.3 mg/m2 administered subcutaneously once weekly on Day 1 of each week for 4 weeks followed by 1 week off. • Dexamethasone 20 mg taken orally twice weekly on Days 1 and 2 of each week.
Dosing in the health economic model (including relative dose intensity)	The relative dose intensity used for the SVd regime was 88.90% for selinexor, 99% for bortezomib and 100% for dexamethasone, based on the median RDI observed in BOSTON trial.

Should the medicine be administered with other medicines?	Yes, combination treatment with bortezomib and dexamethasone
Treatment duration / criteria for end of treatment	Treatment with selinexor combined with bortezomib and dexamethasone should be continued until disease progression or unacceptable toxicity.[1]
Necessary monitoring, both during administration and during the treatment period	Selinexor can cause weight loss and anorexia. Patients should have their body weight, nutritional status and volume checked at baseline, during treatment, and as clinically indicated.[1] Selinexor can cause hyponatraemia. Patients should have their sodium levels checked at baseline, during treatment, and as clinically indicated.[1]
Need for diagnostics or other tests (e.g. companion diagnostics). How are these included in the model?	N/A
Package size(s)	8 x 20mg tablets 12 x 20mg tablets 16 x 20mg tablets 20 x 20mg tablets

Selinexor is an oral, bioavailable, first-in class, selective inhibitor of nuclear export compound that specifically blocks activity of XPO-1 which is involved in cytoplasmic translocation of tumour suppressor proteins (TSPs).[31,32] Nuclear export of these TSPs leads to their inactivation which allows malignant cells to evade apoptosis and to proliferate. XPO-1 is often overexpressed in MM cells; binding of selinexor to XPO-1 results in nuclear localisation of TSPs maintaining their proapoptotic function, resulting in apoptosis of myeloma cells.[33,34]

As a first in class treatment selinexor as part of the combination of SVd provides a new triplet combination, with the new mode of action for patients, which is a key factor when choosing therapy beyond the first line setting. In PI naïve patients it provides an opportunity for a double class switch. The combination of selinexor, dexamethasone and bortezomib demonstrated synergistic cytotoxic effects in multiple myeloma in vitro and increased antitumour activity in murine xenograft multiple myeloma models in vivo, including those resistant to proteasome inhibitors.[1]

Selinexor was initially granted a conditional marketing authorization, with the condition being that data from an updated data cut-off (DCO) from the BOSTON trial (February 2021 DCO).[35] This information was submitted on April 7th, 2022; and the marketing authorisation was changed to a non-conditional marketing authorisation on July 18th, 2022.[36]

3.4.1 The intervention in relation to Danish clinical practice

Based on clinician feedback and the post HOC analysis of the BOSTON study, SVd will be positioned in the lenalidomide refractory population, where an anti-CD38 antibody is not appropriate. It is expected to mainly replace Kd in the treatment pathway as offers the option of a triplet therapy in the lenalidomide refractory population. This is also reflected in guidelines published by the European Hematological Association (EMA) and the European Society for Medical Oncology (ESMO), where, although SVd had not received EMA approval at the time of publishing, SVd is discussed as an option for patients previously treated with lenalidomide and/or daratumumab.[37]

In Denmark, DaraRd is reimbursed in 2L and all treatments that are listed in the "Use" category in the treatment guideline contain either lenalidomide or daratumumab as part of their regimen. However, for lenalidomide-refractory patients in 2L, Kd and PVd are listed in the "consider" category, indicating that there are some 2L patients are not eligible for an anti-CD38 antibody – for these patients SVd can be considered an alternative to Kd and PVd.

Additionally, Kd, Pd, and PVd, are all listed in the "use" category for patients that have received two or more prior treatments (3L+); however, it is noted that the treatments are not considered clinically equivalent and that treatments should be chosen based on refractory status to previous treatments, comorbidities, safety, and patient preferences.[2] As triplet therapies are now used in preference to doublets, Pd would primarily be used for patients that cannot tolerate bortezomib and therefore are ineligible to PVd treatment; as SVd also contains bortezomib these patients would also be ineligible to SVd treatment.

In appendix 1 of the DMC treatment guideline, it is clarified that the patients eligible for Kd or PVd in 3L+, will be refractory to both daratumumab and lenalidomide.[2]

Based on the above, the appropriate position for SVd in the Danish treatment pathway is for lenalidomide refractory patients in 2L+, who are ineligible for an anti-CD38 antibody making Kd and PVd the relevant comparators.

3.5 Choice of comparator(s)

Based on the treatment guideline for MM published by the DMC[2] and the rationale described in 3.4.1, the relevant comparators for lenalidomide refractory patients who are ineligible for an anti-CD38 antibody in 2L+ are Kd and PVd. The chosen comparators are described in Table 4 and Table 5. As both Kd and PVd are combination treatments including dexamethasone, dexamethasone is described separately in Table 6.

Table 4. Overview of comparator: Kd

Overview of comparator	
Generic name	• Carfilzomib • Dexamethasone
ATC code	• L01XG02 (carfilzomib) • H02AB02 (dexamethasone)
Mechanism of action	Carfilzomib is a tetrapeptide epoxyketone proteasome inhibitor that selectively and irreversibly binds to the N terminal threonine containing active sites of the 20S proteasome, the proteolytic core particle within the 26S proteasome, and displays little to no activity against other protease classes. Carfilzomib had antiproliferative and proapoptotic activities in preclinical models in haematologic tumours.
Method of administration	• Carfilzomib is administered intravenously as a 30-minute infusion on two consecutive days. • Dexamethasone is administered orally
Dosing	When combined with dexamethasone, carfilzomib is administered each week for three weeks (days 1, 2, 8, 9, 15, and 16) followed by a 12-day rest period (days 17 to 28). Each 28-day period is considered one treatment cycle. Carfilzomib is administered at a starting dose of 20 mg/ m^2 (maximum dose 44 mg) in cycle 1 on days 1 and 2. If tolerated, the dose should be increased on day 8 of cycle 1 to 56 mg/ m^2 (maximum dose 123 mg). When carfilzomib is combined with dexamethasone alone, dexamethasone is administered as 20 mg on days 1, 2, 8, 9, 15, 16, 22, and 23 of the 28-day cycles. Dexamethasone should be administered 30 minutes to 4 hours before carfilzomib.
Dosing in the health economic model (including relative dose intensity)	Carfilzomib is administered intravenously as a 30-minute infusion on two consecutive days, each week for three weeks (days 1, 2, 8, 9, 15, and 16) followed by a 12-day rest period (days 17 to 28) as shown in table 2. Each 28-day period is considered one treatment cycle. Carfilzomib is administered at a starting dose of 20 mg/m2 (maximum dose 44 mg) in cycle 1 on days 1 and 2. If tolerated, the dose should be increased on day 8 of cycle 1 to 56 mg/m2 (maximum dose 123 mg). Dexamethasone is administered as 20 mg on days 1, 2, 8, 9, 15, 16, 22, and 23 of the 28-day cycles. RDI of 91% was applied for carfilzomib and 100% for dexamethasone.
Should the medicine be administered with other medicines?	Yes. Kd is a combination treatment including carfilzomib and dexamethasone.
Treatment duration/ criteria for end of treatment	Treatment may be continued until disease progression or until unacceptable toxicity occurs.
Need for diagnostics or other tests (i.e. companion diagnostics)	No.

Package size(s)	Carfilzomib: 1 unit of 10 mg, 1 unit of 30 mg, 1 unit of 60 mg Dexamethasone: See Table 6.

Abbreviations: Kd, Carfilzomib + dexamethasone; mg, Milligrams.

Source: Kyprolis – Summary of Product Characteristics[38]

Table 5. Overview of comparator: PVd

Overview of comparator	
Generic name	• Pomalidomide • Bortezomib • Dexamethasone
ATC code	• L04AX06 (pomalidomide) • L01XG01 (bortezomib) • H02AB02 (dexamethasone)
Mechanism of action	Pomalidomide has direct anti-myeloma tumoricidal activity, immunomodulatory activities and inhibits stromal cell support for multiple myeloma tumour cell growth. Specifically, pomalidomide inhibits proliferation and induces apoptosis of haematopoietic tumour cells. Additionally, pomalidomide inhibits the proliferation of lenalidomide-resistant multiple myeloma cell lines and synergises with dexamethasone in both lenalidomide-sensitive and lenalidomide-resistant cell lines to induce tumour cell apoptosis. Pomalidomide enhances T cell- and natural killer (NK) cell-mediated immunity and inhibits production of pro-inflammatory cytokines (e.g., TNF-α and IL-6) by monocytes. Pomalidomide also inhibits angiogenesis by blocking the migration and adhesion of endothelial cells. Bortezomib is a proteasome inhibitor. It is specifically designed to inhibit the chymotrypsin-like activity of the 26S proteasome in mammalian cells. The 26S proteasome is a large protein complex that degrades ubiquitinated proteins. The ubiquitin-proteasome pathway plays an essential role in regulating the turnover of specific proteins, thereby maintaining homeostasis within cells. Inhibition of the 26S proteasome prevents this targeted proteolysis and affects multiple signalling cascades within the cell, ultimately resulting in cancer cell death.
Method of administration	• Pomalidomide is administered orally • Bortezomib is administered intravenously or subcutaneously • Dexamethasone is administered orally
Dosing	The recommended starting dose of pomalidomide is 4 mg taken orally once daily on Days 1 to 14 of repeated 21-day cycles. Pomalidomide is administered in combination with bortezomib and dexamethasone. The recommended starting dose of bortezomib is 1.3 mg/ m^2 intravenous or subcutaneous once daily, on days 1, 4, 8, and 11 of cycle 1-8 and on days 1 and 8 from cycle 9 and onwards. The recommended dose of dexamethasone is 20 mg taken orally once daily, on days 1, 2, 4, 5, 8, 9, 11, and 12 of cycle 1-8 and on days 1, 2, 8, and 9 from cycle 9 and onwards.
Dosing in the health economic model	PVd was dosed according to the SmPC. Pomalidomide is dosed as 4 mg taken orally once daily on Days 1 to 14 of repeated 21-day cycles.

(including relative dose intensity)	Bortezomib is administrated as 1.3mg/m2 on day 1, 4, 8, and 11, during the first eight 21-day cycles, while bortezomib is only administrated on day 1 and 8 from cycle 9 and onwards. Dexamethasone is taken on two days in a row starting on the days when bortezomib is administrated. RDI of 85% is applied for pomalidomide, 80% for bortezomib, and 100% for dexamethasone.
Should the medicine be administered with other medicines?	Yes. PVd is a combination treatment including pomalidomide, bortezomib, and dexamethasone
Treatment duration/ criteria for end of treatment	Treatment may be continued until disease progression or until unacceptable toxicity occurs.
Need for diagnostics or other tests (i.e. companion diagnostics)	No.
Package size(s)	Pomalidomide: 14 units of 1 mg, 14 units of 2 mg, 14 units of 3 mg, 14 units of 4 mg, 21 units of 1 mg, 21 units of 2 mg, 21 units of 3 mg, 21 units of 4 mg. Bortezomib: 1.4 ml of 2.5 mg/ml, 1 unit of 3.5 mg. Dexamethasone: See Table 6.

Abbreviations: PVd, Pomalidomide + bortezomib + dexamethasone; mg, Milligrams.

Source: Imnovid – Summary of Product Characteristics[1,38].

Table 6. Overview of comparator component: Dexamethasone

Overview of comparator	
Generic name	Dexamethasone
ATC code	H02AB02
Mechanism of action	Dexamethasone is a highly potent and long-acting glucocorticoid which causes apoptosis in MM cells. In MM, dexamethasone inhibits the expression of cytokines (e.g. interleukin-6 (IL-6)). In MM patients, most bone marrow plasma cells produce IL-6 and cells proliferate at a significantly higher level than normal plasma cells. Therefore, inhibition of IL-6 in MM dramatically reduces cell growth.[39] Dexamethasone has a biological half-life of 36-54 hours and is therefore suitable in conditions where continuous action of glucocorticoids is required.
Method of administration	Dexamethasone is administered orally or intravenously.
Dosing	Dosing depends on coadministration. Specific information on dosing is provided in Table 4 and Table 5.
Dosing in the health economic model (including relative dose intensity)	Dosing depends on coadministration. Specific information on dosing in the health economic model is provided in Table 4 and Table 5.

Should the medicine be administered with other medicines?	Yes. For more information, see Table 4 and Table 5.
Treatment duration/ criteria for end of treatment	Treatment may be continued until disease progression or until unacceptable toxicity occurs.
Need for diagnostics or other tests (i.e. companion diagnostics)	N/A
Package size(s)	20 units of 1 mg, 100 units of 1 mg, 20 units of 4 mg, 100 units of 4 mg, 10 units of 40 mg.

Source: Danish Medicines Agency [40]

3.6 Cost-effectiveness of the comparator(s)

The comparators are included in the DMC treatment guideline for MM[2], and have thus been evaluated by the DMC.

3.7 Relevant efficacy outcomes

3.7.1 Definition of efficacy outcomes included in the application

The efficacy outcomes considered relevant and necessary to evaluate the effect of SVd in lenalidomide-refractory MM patients in 2L+ are OS, PFS and HRQoL. An overview of the relevant efficacy outcomes as described in the included trials is presented in Table 7.

Table 7. Efficacy outcome measures relevant for the application

Outcome measure	Time point*	Definition	How was the measure investigated/method of data collection
OS BOSTON	Maximum duration of 75 months	Time from date of randomization to the date of death or censored date, whichever occurred first.	Overall survival was calculated from date of randomization to date of death. Patients without events were censored at the date of study discontinuation or date of last participating visit, whichever occurred first. Missing data was handled by censoring.
OS ENDEAVOR	Up to 54 weeks	Time from randomization to the date of death (whatever the cause).	OS was calculated from date of randomization to date of death. Participants who were alive or lost to follow-up as of the data analysis cut-off date were censored at the patient's date of last contact (last

			known to be alive). Missing data was handled by censoring.
OS OPTIMISMM	Up to approximately 65 months	Time from randomization to death from any cause.	OS is calculated as the time from randomization to death from any cause. Missing data was handled by censoring patients with missing data.
PFS BOSTON	Up to 32 months	Time from date of randomization until the first date of IRC-confirmed PD, per IMWG response criteria, or death due to any cause, whichever occurs first.	An Independent Review Committee (IRC) was formed to review the MM disease assessment data for this study to independently assess disease response and the time of PD. The IRC reviewed all medical data that was used for the final analysis of PFS. Missing data was handled by censoring patients with missing data.
PFS ENDEAVOR	30 months	Progression-free survival (PFS) was defined as the time from randomization to the earlier of disease progression or death due to any cause.	Participants were evaluated for PD according to the International Myeloma Working Group-Uniform Response Criteria (IMWG-URC) as assessed by an IRC. Missing data was handled by censoring patients with missing data.
PFS OPTIMISMM	Up to approximately 42 months	Time between the randomization and progressive disease (PD) or death.	PFS was assessed by the Independent Response Adjudication Committee (IRAC). Missing data was handled by censoring patients with missing data.
HRQoL BOSTON	Up to 526 days	HRQoL absolute values as measured by the EORTC-QLQ-C30.	The actual value and change from baseline before initiating a new MM treatment were summarized using descriptive statistics over time for each of the 5 functional scales, 3 symptom scales, the global health status/QoL scale, and 6 single items. Scale scores were calculated only if at least half of the items from the subscale are answered. Missing data were handled as described in the EORTC QLQ-C30 scoring manual.

Abbreviations: HRQoL, Health-related quality of life; OS, overall survival; PFS, progression free survival

Validity of outcomes

The presented efficacy outcomes (OS, PFS and HRQoL measured by EORTC-QLQ-C30) were chosen based on the background materials for the DMC MM treatment guideline [3] in which these outcomes are described as ‘critical’ or ‘important’.

In the BOSTON trial, HRQoL was measured using the following instruments: 1) the EORTC Core Quality of Life (QLQ-C30) instrument for measuring QoL in cancer patients, 2) the EORTC Core Quality of Life Chemotherapy-Induced Peripheral Neuropathy (QLQ-CIPN20) and 3) the European Quality of Life 5 Dimension 5 Level (EQ-5D-5L). As only HRQoL measured by the EORTC QLQ-C30 is listed as 'important' by the DMC[3], only EORTC QLQ-C30-results are reported as a clinical efficacy outcome in this submission.

4. Health economic analysis

The chosen health economic analysis is a cost-minimization analysis. Initially, this submission was expected to follow the direct placement into treatment guideline-trace; however, the DMC requested the company to conduct a cost-minimization analysis following a dialogue meeting. As a result of this, the simplest approach was to adapt the global cost-effectiveness partitioned-survival model into a local cost-minimisation model. The choice of the cost-minimization analysis is based on the results of an NMA showing numerically superior differences in favour of SVd in efficacy outcomes compared to PVd and Kd, but no statistical differences. These data are presented in section 7.

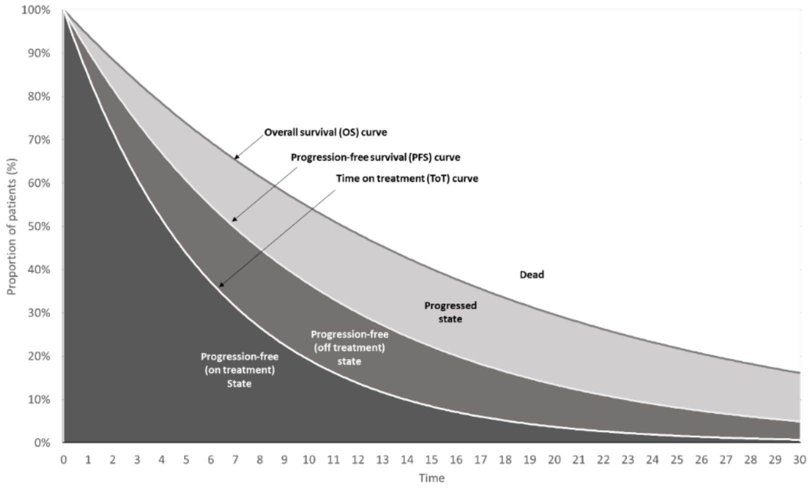
Due to the complex and ever evolving treatment landscape within MM, it is often the case that any differences in relative treatment effects produced from NMA's are not statistically significant within this disease area. Therefore, the cost-minimisation approach might underestimate the clinical benefits of SVd. However, as a conservative approach, no difference in treatment efficacy was assumed in the health economic model, thus, applying a cost-minimisation framework. The approach to this was to set all HRs in the economic model to 1 in order to assume equal efficacy.

4.1 Model structure

A standard partitioned survival model (PSM) structure was identified as being most suitable for this evaluation. The PSM structure, illustrated in Figure 2, is a well-established modelling approach for the health economic analysis of oncology therapies. Like state transition approaches (the most frequently used alternative), the PSMs typically categories patients into three main health states: progression-free, progressed, and dead. In this model, the progression-free health state was subdivided in the model according to whether patients are on or off treatment to incorporate assumptions that not all patients will be treated until disease progression.

The PSM distribute patients directly from the area between overall survival (OS) and progression-free survival (PFS) curves, as illustrated in Figure 2. As discussed in NICE TSD 19,[41] this is a particular advantage for analyses of the type considered for SVd where indirect comparisons are required against comparator treatments for which patient data are not available. Kaplan-Meier curves for OS and PFS, both common and widely reported endpoints in published literature, alongside summary patient data are sufficient for informing relative estimates without the need for transition probabilities to be estimated.

Figure 2. Illustration of partitioned survival model structure



4.2 Model features

The cost-minimization model uses the PSM structure to account for patient health state membership. The economic evaluation considers the cost of selinexor in combination with bortezomib and dexamethasone (SVd) and comparators for multiple myeloma (MM) patients that have received at least one prior line of therapy and are refractory to a lenalidomide. The main model features are presented in Table 8.

Table 8. Features of the economic model

Model features	Description	Justification
Patient population	Multiple myeloma patients that have received at least one prior line of therapy and are refractory to a lenalidomide and where the use of an anti-CD38 antibody is inappropriate	Based on clinical expert feedback, this is the relevant position for SVd
Perspective	Limited societal perspective	According to DMC guidelines
Time horizon	Lifetime (35 years)	To capture all health benefits and costs in line with DMC guidelines.
Cycle length	1 week	To capture treatment cycles
Half-cycle correction	Yes	To account for events and transitions can occur at any point during the cycle
Discount rate	3.5 %	The DMC applies a discount rate of 3.5 % for all years
Intervention	Selinexor + bortezomib + dexamethasone	Intervention of interest

Comparator(s)	1) Carfilzomib + dexamethasone 2) Pomalidomide + bortezomib + dexamethasone	According to national treatment guidelines. Validated by Danish clinical expert
Outcomes used to model	OS, PFS, and ToT	To account for the PSM model setup. Not used to account for efficacy, but only to account for health state membership

Abbreviations: DMC, Danish Medicines Council; OS, overall survival; PFS, progression-free survival; ToT, time on treatment; SVd, selinexor + bortezomib + dexamethasone.

5. Overview of literature

5.1 Literature used for the clinical assessment

To identify evidence of the clinical efficacy and safety of selinexor and relevant comparator treatments for RRMM patients, a systematic literature review (SLR) was conducted to support this company submission for SVd, as well as the simultaneous company submission of selinexor in combination with dexamethasone versus comparators, for the treatment of MM in adult patients who are penta-refractory, and who have demonstrated disease progression on the last therapy. The SLR research question related to the scope of this submission is:

What is the relative clinical efficacy and safety of selinexor in combination with bortezomib and dexamethasone versus comparators, for the treatment of adult patients with RRMM who have received one or two prior lines of therapy?

The SLR was undertaken according to the principles of systematic reviewing published in the Cochrane Handbook and the NICE Methodology Process and Methods guide.[42,43] The SLR search strategy and study selection methods are described in Appendix H.[44]

An overview of the literature used in the clinical assessment is provided in Table 9.

Table 9. Relevant literature included in the assessment of efficacy and safety

Reference (Full citation incl. reference number)	Trial name	NCT identifier	Dates of study* (Start and expected completion date, data cut-off and expected data cut-offs)	Used in comparison of
Menarini Stemline. (2021). Clinical Study Report KCP-330-023: A PHASE 3 RANDOMIZED, CONTROLLED, OPEN-LABEL STUDY OF SELINEXOR, BORTEZOMIB, AND DEXAMETHASONE (SVd) VERSUS BORTEZOMIB AND DEXAMETHASONE (Vd) IN PATIENTS WITH RELAPSED OR REFRACTORY MULTIPLE MYELOMA (RRMM).[45] Clinicaltrials.gov. (2023). Bortezomib, Selinexor, and Dexamethasone in Patients With Multiple Myeloma (BOSTON). https://clinicaltrials.gov/study/NCT03110562[46]	BOSTON	NCT03110562	Study start date: 24/05/17 Primary completion date: 18/02/20 Study completion date (estimated): 01/09/23 Data cut-off: Updated analysis - 15/02/21	SVd vs. Vd for RRMM in adult patients who have received 1 to 3 prior anti-MM regimens.
Dimopoulos, M. A., Moreau, P., Palumbo, A., Joshua, D., Pour, L., Hajek, R., Facon, T., Ludwig, H., Oriol, A., Goldschmidt, H., Rosinol, L., Straub, J., Suvorov, A., Araujo, C., Rimashevskaya, E., Pika, T., Gaidano, G., Weisel, K., Goranova-Marinova, V., . . . Investigators, E. (2016). Carfilzomib and dexamethasone versus bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma (ENDEAVOR): a randomised, phase 3, open-label, multicentre study. Lancet Oncol, 17(1), 27-38. https://doi.org/10.1016/S1470-2045(15)00464-7 [6] Orlowski, R. Z., Moreau, P., Niesvizky, R., Ludwig, H., Oriol, A., Chng, W. J., Goldschmidt, H., Yang, Z., Kimball, A. S., & Dimopoulos, M. (2019). Carfilzomib-Dexamethasone Versus Bortezomib-Dexamethasone in Relapsed or Refractory Multiple Myeloma: Updated Overall Survival, Safety, and Subgroups. Clin Lymphoma Myeloma Leuk, 19(8), 522-530 e521. https://doi.org/10.1016/j.clml.2019.04.018 [47] Clinicaltrials.gov. (2022). Phase 3 Study With Carfilzomib and Dexamethasone Versus Bortezomib and Dexamethasone for Relapsed Multiple Myeloma Patients (ENDEAVOR). https://www.clinicaltrials.gov/study/NCT01568866 [48]	ENDEAVOR	NCT01568866	Study start date: 20/06/12 Primary completion date: 10/11/14 Study completion date: 05/02/18	Kd vs. Vd for relapsed MM in adult patients who have received 1 to 3 prior anti-MM regimens.
Richardson, P. G., Oriol, A., Beksac, M., Liberati, A. M., Galli, M., Schjesvold, F., Lindsay, J., Weisel, K., White, D., Facon, T., San Miguel, J., Sunami, K., O'Gorman, P., Sonneveld, P., Robak, P., Semochkin, S., Schey, S., Yu, X., Doerr, T., . . . investigators, O. t. (2019). Pomalidomide, bortezomib, and dexamethasone for patients with relapsed or refractory multiple myeloma previously treated with lenalidomide (OPTIMISMM): a randomised, open-label, phase 3 trial. Lancet Oncol, 20(6), 781-794. https://doi.org/10.1016/S1470-2045(19)30152-4 [7]	OPTIMISMM	NCT01734928	Study start date: 07/01/13 Primary completion date: 09/05/22	PVd vs. Vd for RRMM in adult patients who have received 1 to 3 prior anti- MM regimens.

Clinicaltrials.gov. (2023). Safety and Efficacy of Pomalidomide, Bortezomib and Low-dose Dexamethasone in Subjects With Relapsed or Refractory Multiple Myeloma (OPTIMISMM). https://clinicaltrials.gov/study/NCT01734928 [49]	Study completion date: 13/05/22

Abbreviations: Kd, Carfilzomib + dexamethasone; MM, Multiple myeloma; PVd, Pomalidomide + bortezomib + dexamethasone; RRMM, Relapsed or refractory multiple myeloma; SVd, Selinexor + bortezomib + dexamethasone; Vd, Bortezomib + dexamethasone.
Notes: * Unless otherwise stated, dates of study are actual.

5.2 Literature used for the assessment of health-related quality of life

Not applicable.

5.3 Literature used for inputs for the health economic model

In Table 10, list the literature used for input to the economic model is presented. The literature searches were presented in Appendix J.

Table 10. Relevant literature used for input to the health economic model

Reference (Full citation incl. reference number)	Input/estimate	Method of identification	Reference to where in the application the data is described/applied
NICE submission for DaraVd TA573, superseded by TA897.[50]	Assumptions on subsequent treatment length	Systematic literature review	Section 11.6
Lau, I. J., Smith, D., Aitchison, R., Blesing, N., Roberts, P., Peniket, A., Yong, K., Rabin, N., & Ramasamy, K. (2015). Bendamustine in combination with thalidomide and dexamethasone is a viable salvage option in myeloma relapsed and/or refractory to bortezomib and lenalidomide. Annals of hematology, 94(4), 643–649. https://doi.org/10.1007/s00277-014-2238-2[51]	bendamustine + thalidomide + dexamethasone (BTD) regimen dosing schedule	Systematic literature review	Section 11.6

6. Efficacy

6.1 Efficacy of SVd compared to Kd and PVd for adult patients with multiple myeloma who have received two or more prior treatments

6.1.1 Relevant studies

In this application, subgroup analyses of lenalidomide-refractory subpopulations, as well as results from the ITT population, will be presented. An overview of the relevant studies for evaluating the efficacy of SVd compared to Kd and PVd in lenalidomide-refractory MM patients in 2L+ is presented in Table 11. All included studies are described in detail in Appendix A.

Table 11. Overview of study design for studies included in the comparison

Trial name, NCT-number (reference)	Study design	Study duration	Patient population	Intervention	Comparator	Outcomes and follow-up period *
BOSTON (NCT03110562)	A Phase 3, 2-arm, randomized, active comparator-controlled, open-label, multicenter study of SVd vs. Vd.	See Table 9	Adult patients with RRMM who had received at least one prior therapy (2L+) and were refractory to lenalidomide. The BOSTON trial included patients with one to three prior lines of therapy, regardless of refractory status; however, as this submission is for lenalidomide-refractory patients who have received one or more prior treatments, the lenalidomide-refractory subgroup of the BOSTON trial is used.	SVd (35-day cycles): • Selinexor 100mg orally (5 tables of 20mg each) on Days 1, 8, 15, 22 and 29 of each 35-day cycle • Bortezomib 1.3mg/m2 subcutaneously on Days 1, 8, 15, and 22 of each 35-day cycle • Dexamethasone 20mg orally on Days 1, 2, 8, 9, 15, 16, 22, 23, 29, and 30 of each 35-day cycle	Vd (Cycles 1 through 8; 21-day cycles): • Bortezomib will be given at a dose of 1.3 mg/m2 SC on Days 1, 4, 8, and 11 of each 21-day cycle for the first 8 cycles. • Dexamethasone will be given as an oral 20-mg dose on Days 1, 2, 4, 5, 8, 9, 11, and 12 of each 21-day cycle for the first 8 cycles. Vd (Cycles ≥9; 35-day cycles) • Bortezomib will be given at a dose of 1.3 mg/m2 SC on Days 1, 8, 15, and 22 of each 35-day cycle. • Dexamethasone will be given as an oral 20 mg dose on Days 1, 2, 8, 9, 15, 16, 22, 23, 29, and 30 of each 35-day cycle.	The following outcomes from the BOSTON trial are listed in the DMC treatment guideline: Primary endpoint • PFS assessed by IRC (Follow-up: up to 32 months) Secondary endpoints • OS (Follow-up: up to 75 months) • Adverse events (Follow-up: from randomization to 30 days after last dose of treatment) • Discontinuations due to adverse events (Follow-up: from randomization to 30 days after last dose of treatment) Exploratory endpoints • HRQoL measured with EORTC QLQ-C30 (Follow up: until end of treatment)
ENDEAVOR (NCT01568866)	A Phase 3, 2-arm, randomized, active	See Table 9	Adult patients with RRMM, who have had at least one prior line of therapy and who are	Carfilzomib plus dexamethasone: Participants received 20 mg/m² carfilzomib	Bortezomib plus dexamethasone: Participants received bortezomib 1.3 mg/m² administered IV or subcutaneously (SC) on Days 1, 4,	The following outcomes from the ENDEAVOR trial are listed in the DMC treatment guideline: Primary endpoint

	comparator-controlled, open-label, multicenter study of Kd vs. Vd.		refractory to lenalidomide The ENDEAVOR trial included patients with one to three prior lines of therapy; however, as this submission is for lenalidomide-refractory patients in 2L+, only the subgroup listed above is included.	administered by intravenous (IV) infusion on Days 1 and 2 of Cycle 1, followed by 56 mg/m² on Days 8, 9, 15, and 16 of Cycle 1 and for each 28-day cycle thereafter. Additionally, participants received 20 mg dexamethasone on Days 1, 2, 8, 9, 15, 16, 22, and 23 of each 28 day cycle.	8, and 11 of a 21-day cycle plus dexamethasone 20 mg administered on Days 1, 2, 4, 5, 8, 9, 11, and 12 of each 21-day cycle.	• PFS assessed by IRC (Follow-up: from randomization until 10-11-2014) Secondary endpoints • OS (Follow-up: from randomization until 03-01-2017) • Discontinuation due to adverse events (Follow-up: from randomization until 03-01-2017 • Adverse events (Follow-up: from randomization until 03-01-2017)
OPTIMISMM (NCT01734928)	A phase 3, multicenter, randomized, open-label study of PVd vs. Vd.	See Table 9	Adult patients with RRMM, who have had at least one prior line of therapy and who are refractory to lenalidomide The OPTIMISMM trial included patients with one to three prior lines of therapy; however, as this submission is for lenalidomide-refractory patients in 2L+, only the subgroup listed above is included.	Pomalidomide, Bortezomib and Low Dose Dexamethasone: 4 mg of Pomalidomide will be taken orally on Days 1-14 of a 21-day cycle along with 1.3 mg/m2 of Bortezomib administered subcutaneously on Days 1, 4, 8 and 11 of 21 days for cycles 1 -8 and on days 1, 8 of 21 days for cycle 9 and onward until disease progression, and Dexamethasone 20 mg/day [≤ 75 years old] or 10 mg/day [> 75 years old] orally on days 1, 2, 4, 5, 8, 9, 11, 12 of 21 days for cycles 1-8 and on days 1, 2,8, 9 of 21 days for cycles	Bortezomib and Low Dose Dexamethasone: 1.3 mg/m2 of Bortezomib will be administered subcutaneously on Days 1, 4, 8 and 11 of 21 days for cycles 1 -8 and on Days 1, 8 of 21 days for cycle 9 and onward until disease progression along with Dexamethasone 20 mg/day [≤ 75 years old]or 10 mg/day [> 75 years old] orally on days 1, 2, 4, 5, 8, 9, 11, 12 of 21 days for cycles 1-8 and on Days 1, 2, 8, 9 of 21 days for cycles 9 and onward until disease progression.	The following outcomes from the OPTIMISMM trial are listed in the DMC treatment guideline: Primary endpoint: • PFS assessed by IRC (Follow-up: from randomization until to progressive disease or death during the IRC assessment period (approximately 42 months) Secondary endpoints: • OS (Follow-up: from randomization until death, up to approximately 65 months) • Discontinuation due to adverse events (Follow-up: from randomization until end of treatment) • Adverse events (Follow-up: from first dose to 28 days after the last dose [up to approximately 44 months])

		9 and onward until disease progression	

Abbreviations: Kd, Carfilzomib + dexamethasone, mg, miligram; OS, Overall survival; PFS, progression-free survival; PVd, pomalidomide + bortezomib + dexamethasone; SVd, selinexor + bortezomib + dexamethasone, Vd, bortezomib + dexamethasone
Notes: * Only relevant outcomes are presented, i.e. outcomes listed in the DMC treatment guideline.

6.1.2 Comparability of studies

The three included studies (BOSTON, ENDEAVOR, and OPTIMISSM) are all phase 3, randomised, open-label, Vd-controlled studies. All three studies included MM patients that had received one to three prior lines of therapy, and all reported OS and PFS for lenalidomide-refractory patients separately[5,7,52].

The median follow-up for both the intention-to-treat (ITT) and lenalidomide-refractory populations in the included trials is provided in Table 12.

Table 12. Median follow up in the trials included in the comparative analysis (ITT and lenalidomide-refractory populations)

<table>
<tr><th>Population</th><th>Trial</th><th colspan="2">Median follow-up (months)</th></tr>
<tr><td rowspan="3">ITT population</td><td>BOSTON</td><td>OS:
SVd: 28.71
Vd: 28.65</td><td>PFS:
SVd: 13.5
Vd: 24.5</td></tr>
<tr><td>ENDEAVOR</td><td>OS:
Kd: 44.3
Vd: 43.7</td><td>PFS:
Kd: 11.9
Vd: 11.1</td></tr>
<tr><td>OPTIMISMM</td><td>OS:
PVd and Vd: 64.5</td><td>PFS:
PVd: 15.9
Vd: 15.9</td></tr>
<tr><td rowspan="3">Lenalidomide-refractory population</td><td>BOSTON</td><td colspan="2">SVd: 28.2
Vd: 27.1</td></tr>
<tr><td>ENDEAVOR</td><td colspan="2">Kd: Not reported
Vd: Not reported</td></tr>
<tr><td>OPTIMISMM</td><td colspan="2">PVd: Not reported
Vd: Not reported</td></tr>
</table>

Abbreviations: ITT, Intention-to-treat; Kd, Carfilzomib + dexamethasone; OS, Overall survival; PFS, Progression-free survival; SVd, Selinexor + bortezomib + dexamethasone; Vd, Bortezomib + dexamethasone.

In the ITT population, BOSTON, ENDEAVOR and OPTMISMM had relatively similar follow-up times for PFS; whereas the median follow-up for OS was longer in the ENDEAVOR and OPTIMISMM trials. Median follow-up times for the lenalidomide-refractory populations were not reported for the ENDEAVOR and OPTIMISMM trials.

Overall, the included trials were considered sufficiently similar to allow for inclusion in an indirect treatment comparison.

6.1.2.1 Comparability of patients across studies

The baseline characteristics of the ITT populations included in BOSTON, ENDEAVOR, and OPTIMISMM are shown in Table 13.

Table 13. Baseline characteristics of patients in studies included for the comparative analysis of efficacy and safety - ITT Population

	BOSTON[5]		ENDEAVOR[52]		OPTIMISMM[7]	
	SVd (n=195)	Vd (n=207)	Kd (n=464)	Vd (n=465)	PVd (n=281)	Vd (n=278)
Age, median (IQR)	66 (59-72)	67 (61-74)	65 (35-89)	65 (30-88)	67 (60-73)	68 (59-73)
Age, ≥ 65 years, n (%)	109 (56%)	132 (64%)	*223 (48%)[a]*	*210 (45%)[a]*	123 (44%)	120 (43%)
Male gender, n (%)	115 (59%)	115 (56%)	240 (52%)	229 (49%)	155 (55%)	147 (53%)
Time since diagnosis, median (IQR)	3.8 (2.5 – 5.4)	3.6 (2.1 – 5.6)	Not reported	Not reported	4.0 (2.6 – 6.5)	4.3 (2.5 – 6.4)
Previous HDT/ASCT, %	76 (39%)	63 (30%)	266 (57%)	272 (58%)	161 (57%)	163 (59%)
≥2 prior lines of therapy, %	96 (49%)	108 (52%)	232 (50%)	232 (50%)	170 (60%)	163 (59%)
Prior lenalidomide treatment, %	77 (39%)	77 (37%)	177 (38%)	177 (38%)	281 (100%)	278 (100%)
Refractory to lenalidomide, %	53 (27%)	53 (26)	113 (29%)	122 (26%)	200 (71%)	191 (69%)
ECOG performance score, n (%)						
0 1 2	69 (35%) 106 (54%) 20 (10%)	77 (37%) 114 (55%) 16 (8%)	221 (48%) 211 (45%) 32 (7%)	232 (50%) 203 (44%) 30 (6%)	149 (53%) 121 (43%) 11 (4%)	137 (49%) 119 (43%) 22 (8%)
High-risk cytogenics, %	97 (50%)	95 (46%)	97 (21%)	113 (24%)	61 (22%)	49 (18%)
Creatinin clearance ≥ 60mL / min, %	139 (71%)	136 (66%)	*379 (82%)[b]*	*366 (79)[b]*	190 (68%)	202 (73%)

[a]In ENDEAVOR, only the proportion above 65 years of age (>65) was reported
[b]In ENDEAVOR, only the proportion of patients with creatinine clearance ≥50mL/min was reported

In the ITT populations, the proportion of patients that had received prior ASCT was substantially lower in BOSTON than in ENDEAVOR and OPTIMISSM. Additionally, patients in BOSTON had slightly higher ECOG scores compared to ENDEAVOR and OPTIMISMM.

Finally, the proportion of patients with high-risk cytogenetics is higher in BOSTON than in the comparator trials. Overall, the baseline characteristics presented in Table 13 indicate that the patients included in BOSTON had more severe disease, and thus a worse prognosis, than those included in ENDEAVOR and OPTIMISSM, making the results of an unadjusted indirect comparison (such as an NMA) a conservative approach.

Baseline characteristics for the lenalidomide-refractory subpopulation in BOSTON are shown in Table 14; however, for the ENDEAVOR and OPTIMISMM trials, baseline characteristics in this population were not reported.

Table 14. Baseline characteristics of patients in studies included for the comparative analysis of efficacy and safety – Lenalidomide-refractory population

	BOSTON[5]		ENDEAVOR[52]		OPTIMISMM[7]	
	SVd (n=53)	Vd (n=53)	Kd (n=)	Vd (n=)	PVd (n=)	Vd (n=)
Age, median (IQR)	65 (40-87)	66 (45-85)	Not reported	Not reported	Not reported	Not reported
Age, ≥ 65 years, n (%)	Not available	Not available	Not reported	Not reported	Not reported	Not reported
Male gender, n (%)	37 (69.8%)	29 (54.7)	Not reported	Not reported	Not reported	Not reported
Time since diagnosis, median (IQR)	3.69 (0.9-12.0)	3.48 (0.4-13.4)	Not reported	Not reported	Not reported	Not reported
Previous HDT/ASCT, %	23 (43.3%)	20 (37.7%)	Not reported	Not reported	Not reported	Not reported
≥2 prior lines of therapy, %	37 (69.8%)	39 (73.6%)	Not reported	Not reported	Not reported	Not reported
ECOG performance score, n (%)						
0 1 2	23 (43.4%) 26 (49.1%) 4 (7.6%)	20 (37.7%) 29 (54.6%) 4 (7.6%)	Not reported	Not reported	Not reported	Not reported
High-risk cytogenics, %	29 (54.7%)	16 (30.2%)	Not reported	Not reported	Not reported	Not reported
Creatinin clearance ≥ 60mL / min, %	39 (73.6%)	34 (64.1%)	Not reported	Not reported	Not reported	Not reported

Abbreviations: ASCT, Autologous stem cell transplant; ECOG, Eastern Cooperative Oncology Group; HDT, High-dose therapy; IQR, Interquartile range; Kd, Carfilzomib + dexamethasone; mL, Millilitres; min, Minute; PVd, Pomalidomide + bortezomib + dexamethasone; SVd, Selinexor + bortezomib + dexamethasone; Vd, Bortezomib + dexamethasone.

As baseline characteristics for the lenalidomide-refractory subpopulation were not reported for the OPTIMISMM and ENDEAVOR trials, it is not possible to directly compare with the lenalidomide-refractory subpopulation. Thus, it is assumed that like in the ITT population, the lenalidomide-refractory patients in BOSTON had more severe disease than the corresponding patients in the ENDEAVOR and OPTIMISMM trials, while acknowledging the uncertainty related to this assumption.

6.1.3 Comparability of the study population(s) with Danish patients eligible for treatment

Overall, the study populations are considered reasonably similar to Danish patients eligible for treatment, although data on Danish patient characteristics in 2L and later is sparse. In the background materials to the DMC treatment guideline, it is noted that the median age at diagnosis is 71 years old[3], meaning that patients in 2L and later, would likely be older than this, although older patients have a worse prognosis, which might lead to somewhat lower age in subsequent lines. This was acknowledged by the DMC assessment of ciltacabtagene autolecel for MM patients in 4L+, that had been exposed to an IMiD, a PI, and an anti-CD38-antibody, where it was stated that the median age of Danish MM patients reaching 4L may be higher than 68 years. However, the DMC also noted that elderly and frail patients may not reach later lines of treatment[53].

In Denmark, MM is more common in men than women[3], which aligns well with the gender distribution in the included studies.

Table 15. Characteristics in the relevant Danish population and in the health economic model

	Value in Danish population (reference)	Value used in health economic model (reference if relevant)
Age	Median age at diagnosis: 71 years[3]	65.56[8]
Gender	Slightly more common in men than women[3]	62% male[46]

6.1.4 Efficacy – results per BOSTON

As presented in Table 11, three relevant efficacy outcomes (i.e. results listed in the DMC treatment guideline[3]) were identified in the BOSTON trial; namely OS, PFS and HRQoL. This section presents the results relating to these outcomes as well as discontinuation due to any reason.

All results in the following sections are based on an updated analysis based on the data cut-off date of February 15th, 2021. This analysis was requested by the Committee for Medicinal Products for Human Use (CHMP) and superseded the primary analysis for the BOSTON trial with a data cut-off date of February 18th, 2020. Although the updated analysis is non-inferential, and the P-values were therefore nominal, it presents data based on longer follow-up than the primary analysis; therefore, results from the updated analysis are presented below.

A tabular presentation of the relevant efficacy outcomes is presented in Appendix B.

6.1.4.1 Overall survival

In the ITT population, 74 (36%) patients from the Vd arm crossed over after confirmed PD to receive a regimen that included selinexor (SVdX or SdX), with patients able to tolerate bortezomib receiving SVd, whereas patients in the Vd arm who had significant tolerability issues with bortezomib (patients who were unable to tolerate continue bortezomib treatments due to Grade >2 peripheral neuropathy or Grade ≥2 peripheral neuropathy with pain) crossed over to SdX treatment. Therefore OS data presented are adjusted for crossover (a switch-adjusted HR was calculated for OS to account for crossover, using a two-stage estimation method).[8] Details on the cross-over adjustment, including information on the patients that crossed over, is available in Appendix L.

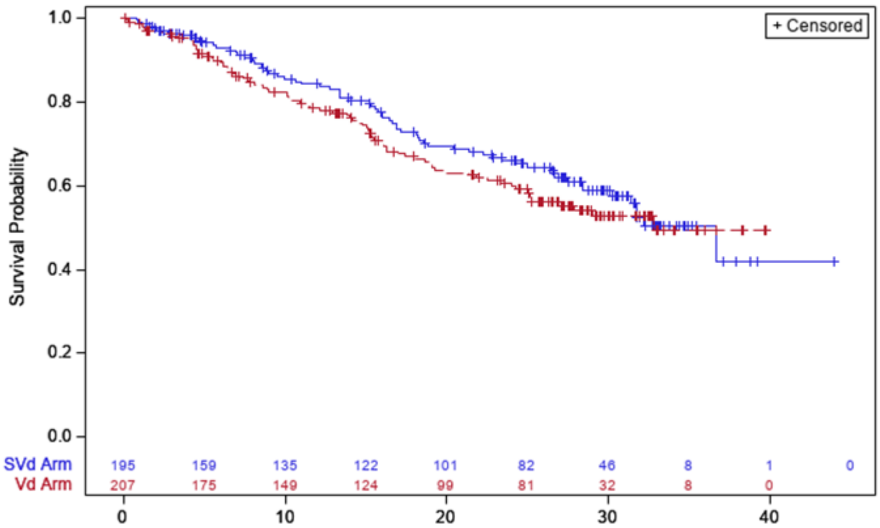
At the time of the updated analysis cut-off date, in the overall population, the median OS was 36.67 (95% CI: 30.19, NE) months in the SVd arm and 32.76 (95% CI: 25.11, NE) months in the Vd arm, a median improvement of approximately 4 months in patients treated with selinexor (Table 16, Figure 3). In the lenalidomide-refractory population, median OS was significantly improved in the SVd arm compared with the Vd arm (26.7 months versus 18.6 months, HR = 0.53, 95% CI: 0.30 to 0.95; P = 0.015) (Table 16, Figure 4). These data continue to support the therapeutic value of selinexor.[45]

Table 16. OS by treatment arm (BOSTON ITT and lenalidomide-refractory population)

	ITT population		Lenalidomide-refractory population (post-hoc analysis)	
	SVd (n = 195)	Vd (n=207)	SVd (n = 53)	Vd (n = 53)
Median follow-up, months (95% CI)	28.71 (27.24, 29.90)	28.65 (27.63, 29.67)	28.2 (23.36 to 33.08)	27.1 (21.65 to 34.1)
Median OS (without crossover adjustment), months (95% CI)	36.67 (30.19, NE)	32.76 (27.83, NE)	26.68 (16.92, NE)	19.61 (14.42, 29.11)
Median OS[a], months (95% CI)	36.7 (30.2, NE)	32.8 (25.1, NE)	26.7 (16.92, NE)	18.6 (13.95 to 29.01)
One-sided P-value[b,c]	0.147		0.015	
Hazard ratio[b,c,d] (95% CI)	0.84 (0.60 to 1.17)		0.53 (0.30 to 0.95)	
Deaths, n (%)	68 (34.9)	80 (38.6)	23 (43.4)	29 (54.7)
Patients censored, n (%)	127 (65.1)	127 (61.4)	30 (56.6)	24 (45.3)

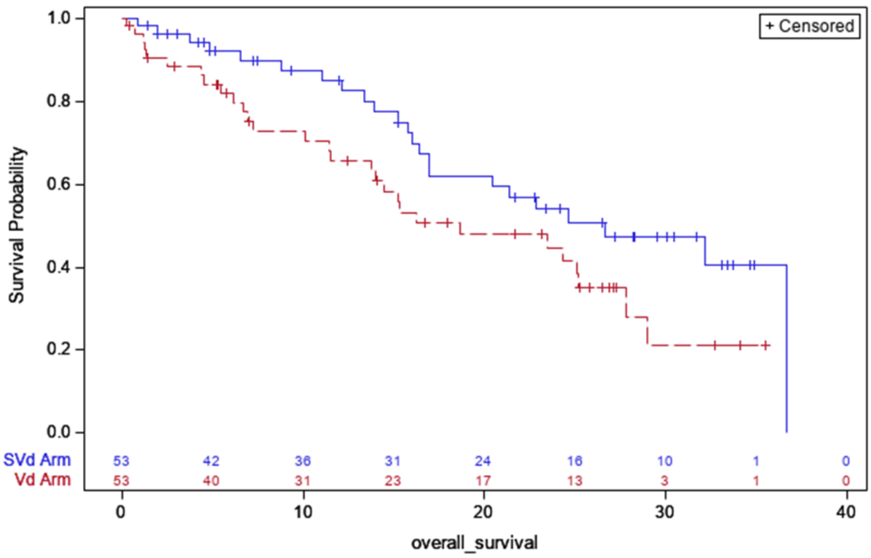
Abbreviations: BICR, independent review committee; CI, confidence interval; INV, investigator; ITT, intent-to-treat population; n, number of patients; NE, not estimable; PFS, progression-free survival; SVd, selinexor + bortezomib + dexamethasone; Vd, bortezomib + dexamethasone.
Notes: Results are based on the updated analysis (February 15th, 2021).
[a] OS adjusted for crossover
[b] Calculated by Stratified Log-rank Test
[c] Stratified for prior PI therapies, number of prior anti-MM regimens, and R-ISS stage at study entry
[d] Based on stratified Cox Proportional Hazard model with Efron's Method of handling ties
Source: Mateos et al 2024. [54]

Figure 3. Kaplan-Meier curve of OS in the ITT population of BOSTON



Source: Data on file[45].

Figure 4. Kaplan-Meier curve of OS in the lenalidomide-refractory population of BOSTON



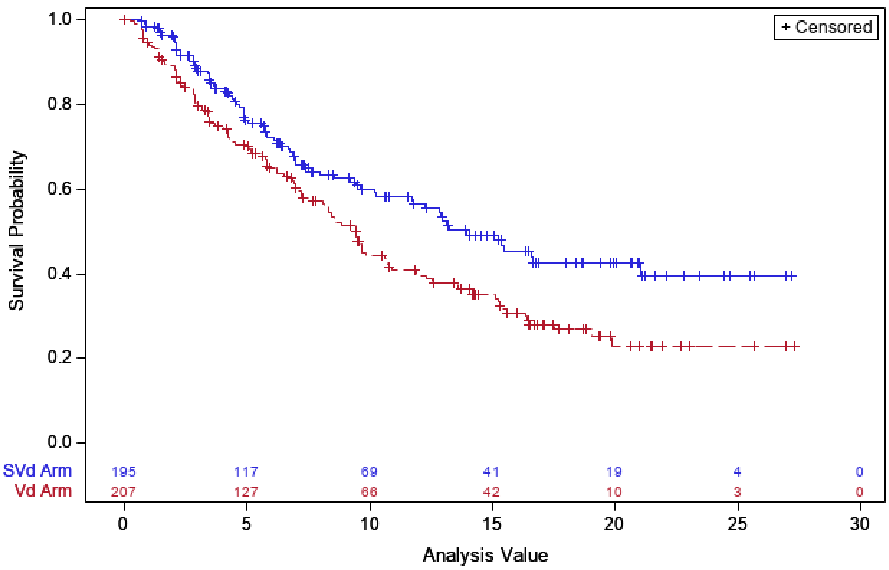
Source: Mateos et al 2024. [54]

6.1.4.2 Progression-free survival

In the updated analysis (15th February 2021) for the overall population, the median BICR-assessed progression-free survival (PFS) was significantly improved in the SVd arm compared to the Vd arm (13.2 months versus 9.5 months; HR=0.71, 95% CI: 0.54 to 0.93; P=0.006). In the post-hoc analysis in the lenalidomide-refractory subgroup, median PFS was also significantly improved in the SVd arm compared to the Vd arm (10.2 months versus 7.1 months; HR=0.52, 95% CI: 0.31 to 0.88; P=0.006) (Table 17).[54]

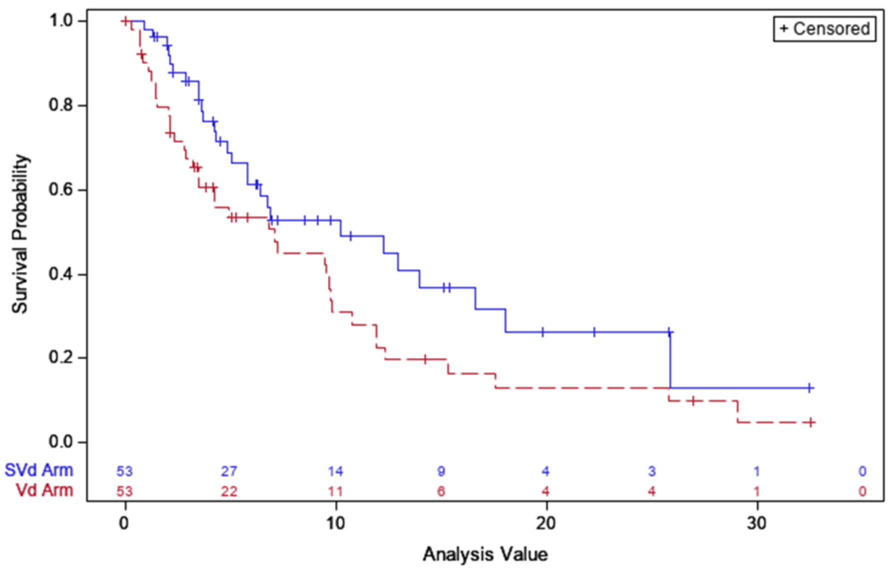
The Kaplan-Meier curves for BICR-assessed PFS in the ITT population and the lenalidomide-refractory subpopulation are shown in Figure 5 and Figure 6 respectively.

Figure 5. Kaplan-Meier curve of BICR-assessed PFS in the ITT population of BOSTON



Source: Data on file. [45]

Figure 6. Kaplan-Meier curve of BICR-assessed PFS in the lenalidomide refractory population of BOSTON



Source: Mateos et al 2024. [54]

Table 17. PFS based on BICR assessment by treatment arm (BOSTON ITT and lenalidomide-refractory population)

	ITT population		Lenalidomide-refractory population (post-hoc analysis)	
	SVd (n = 195)	Vd (n=207)	SVd (n = 53)	Vd (n = 53)
Median follow-up time, months (95% CI)	13.47 (10.64 to 24.87)	24.48 (21.16 to 29.17)	28.2 (23.36 to 33.08)	27.1 (21.65 to 34.1)
Median PFS, months (95% CI)	13.2 (11.7 to 23.4)	9.5 (8.1 to 10.8)	10.2 (5.8, NE)	7.1 (3.5 to 9.8)
One-sided P-value[a]	0.006		0.012	
Hazard ratio[a,b,c] (95% CI)	0.71 (0.54 to 0.93)		0.52 (0.31 to 0.88)	
Patients with events, n (%)	92 (47.2)	137 (66.2)	27 (50.9)	38 (71.7)
Patients censored, n (%)	103 (52.8)	70 (33.8)	26 (49.1)	15 (28.3)

Abbreviations: BICR, independent review committee; CI, confidence interval; INV, investigator; ITT, intent-to-treat population; n, number of patients; NE, not estimable; PFS, progression-free survival; SVd, selinexor + bortezomib + dexamethasone; Vd, bortezomib + dexamethasone.

Notes: Results are based on the updated analysis (February 15th, 2021).
[a] Calculated by Stratified Log-rank Test
[b] Stratified for prior PI therapies, number of prior anti-MM regimens, and R-ISS stage at study entry
[c] Based on stratified Cox Proportional Hazard model with Efron's Method of handling ties
Source: Mateos et al 2024[54]

6.1.4.3 HRQoL

HRQoL was measured in BOSTON using the EORTC QLQ-CIPN20 measure (secondary endpoint), EORTC QLQ-C30 measure, and EQ-5D-5L (exploratory endpoints).[8,45] As per the DMC treatment guideline[3], only HRQoL measured using the EORTC QLQ-C30 is considered relevant to this submission. However, results from the EORTC QLQ-CIPN20 and EQ-5D-5L measures are also presented in Table 19 and Table 20.

EORTC QLQ-C30

The EORTC QLQ-C30 was an exploratory endpoint only in the BOSTON trial. The change from baseline to end of treatment data at the time of the updated analysis for global health status are summarised in Table 18. Both treatment arms showed a similar reduction in the EORTC QLQ-C30 global health status score at end of treatment, reflecting improved quality of life in both the overall and lenalidomide-refractory population.[45]

Table 18. Change from baseline in EORTC QLQ-C30 Global Health Status in BOSTON

	ITT Population		Lenalidomide-refractory population (post-hoc analysis)	
	SVd (n = 195)	Vd (n=207)	SVd (n = 53)	Vd (n = 53)
Rate of change (weekly mean change)				

Estimated rate of change	-0.0482	-0.0159	-0.0415	-0.1533
Estimated mean treatment difference (SE)	-0.0323 (0.0339)		0.1138 (0.124)	
95% CI of mean treatment difference	-0.0998 to 0.0352		-0.1522 to 0.3798	
P-value	0.5249		0.3742	

Abbreviations: CI, confidence interval; SE, standard error; SVd, selinexor + bortezomib + dexamethasone
Notes: Results are based on the updated analysis (February 15th, 2021).
Source: Data on file[45].

Table 19. Linear mixed effect model for change from baseline in EORTC QLQ-CIPN20 scores in the overall and lenalidomide refractory population of BOSTON

	ITT Population		Lenalidomide-refractory population (post-hoc analysis)	
	SVd (n=195)	Vd (n =207)	SVd (n=53)	Vd (n=53)
EORTC QLQ-CIPN20 sensory system				
Rate of change (weekly mean change)				
Estimated rate of change	0.0378	0.1660	0.0123	0.1474
Estimated mean treatment difference (SE)	-0.1282 (0.0335)		-0.1351 (0.0709)	
95% CI of mean treatment difference	-0.1952 to -0.0613		-0.2892 to 0.0191	
P-value	0.0003		0.0805	
EORTC QLQ-CIPN20 motor system				
Rate of change (weekly mean change)				
Estimated rate of change	0.0938	0.1559	0.0422	0.2118
Estimated mean treatment difference (SE)	-0.0621 (0.0381)		-0.1696 (0.0701)	
95% CI of mean treatment difference	-0.1375to 0.0134		-0.3245 to -0.0191	
P-value	0.1058		0.0347	

EORTC QLQ-CIPN20 autonomic system				
Rate of change (weekly mean change)				
Estimated rate of change	0.1056	0.0688	0.1572	0.1406
Estimated mean treatment difference (SE)	0.0368 (0.0501)		0.0167 (0.1316)	
95% CI of mean treatment difference	-0.0631 to 0.1366		-0.2542 to 0.2875	
P-value	0.4654		0.9002	

Abbreviations: CI, confidence interval; SE, standard error; SVd, selinexor + bortezomib + dexamethasone

Source: Data on file.[55]

Table 20. Change from baseline in EQ-5D-5L Global Health Status in BOSTON

	ITT Population		Lenalidomide-refractory population (post-hoc analysis)	
	SVd (n=195)	Vd (n =207)	SVd (n=53)	Vd (n=53)
Rate of change (weekly mean change)				
Estimated rate of change	-0.0008	-0.0008	-0.0006	-0.0012
Estimated mean treatment difference (SE)	0.0001 (0.0003)		0.0006 (0.0009)	
95% CI of mean treatment difference	-0.0006 to 0.0007		-0.0012 to 0.0025	
P-value	0.8654		0.4751	

Abbreviations: CI, confidence interval; SE, standard error; SVd, selinexor + bortezomib + dexamethasone

Source: Data on file.[55]

6.1.4.4 Discontinuation

As of the data cut-off date for the updated analysis, of the 399 patients who were dosed in the study, 362 (90.7%) patients had discontinued study treatment (174 [89.2%]) in the SVd arm and 188 [92.2%] in the Vd arm with 37 (9.3%) patients continuing to receive the study treatment (21 [10.8%] in the SVd arm and 16 [7.8%] in the Vd arm)[45]. Reasons for discontinuation in the BOSTON trial are presented in Table 21.

Table 21. Treatment discontinuation in the BOSTON trial

Reason for discontinued treatment	SVd Arm (N=195) n (%)	Vd Arm (N=204) n (%)	Total (N=399)* n (%)
Disease Progression	76 (36.0%)	118 (57.8%)	194 (48.6%)
Withdrawal by Patient	37 (19.0%)	21 (10.3%)	58 (14.5%)
Adverse Event**	33 (16.9%)	26 (12.7%)	59 (14.8%)
Death	14 (7.2%)	14 (6.9%)	28 (7.0%)
Lost to Follow-up	3 (1.5%)	2 (1.0%)	5 (1.3%)
Protocol deviation	1 (0.5%)	2 (1.0%)	3 (0.8%)
Physician decision	10 (5.1%)	5 (2.5%)	15 (3.8%)
Total	174 (89.2%)	188 (92.2%)	362 (90.7%)

Abbreviations: SVd, Selinexor + bortezomib + dexamethasone; Vd, Bortezomib + dexamethasone.
Notes: * Three patients were randomized but did not receive any dose of study drug due to withdrawal of consent, death or AE. The presented percentages are calculated from the number of patients who received the study drug.
** Includes toxicity to study drug.
Source: Data on file[45].

6.1.5 Efficacy – results per ENDEAVOR

As presented in Table 11, two relevant efficacy outcomes (i.e. results listed in the DMC treatment guideline) were identified for the lenalidomide-refractory subpopulation in the ENDEAVOR trial; OS and PFS. This section presents the results relating to these outcomes as well as discontinuation due to any reason. A tabular presentation of the relevant efficacy outcomes is presented in Appendix B.

6.1.5.1 Overall survival

OS results are based on an updated analysis with a data cut-off date of July 19th, 2017. This analysis superseded the primary analysis for the ENDEAVOR OS analysis with a data cut-off date of January 3rd, 2017.

Median OS was estimated using the KM method. CIs for the median were estimated using the method by Klein and Moeschberger with log-log transformation. For the comparison of OS between treatment groups HRs and corresponding 95% CIs were estimated using stratified or unstratified Cox proportional hazards models for the primary ITT population and subgroup OS analyses, respectively. The results for OS are shown in Table 22.

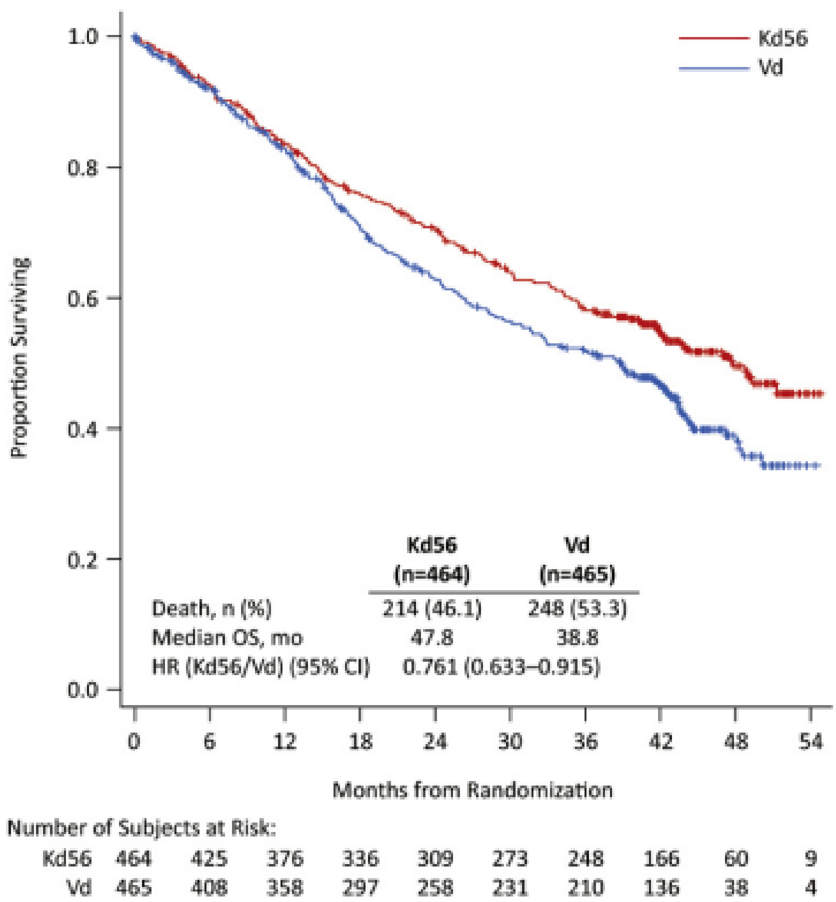
Table 22. OS results from ENDEAVOR[47]

	ITT population		Lenalidomide-refractory population (post-hoc analysis)	
	Kd (n=464)	Vd (n=465)	Kd (n =113)	Vd (n=122)
Median follow-up, months	44.3	43.7	Not reported	Not reported

Median OS, months (95% CI)	47.8 (41.9, NE)	38.8 (31.7, 42.7)	29.9 (Not reported)	21.4 (Not reported)
One-sided P-value	0.0017		Not reported	
Hazard ratio (95% CI)	0.76 (0.63, 0.92)		0.86 (0.62, 1.18)	

KM curves for OS in the ITT population are shown in Figure 7 and KM curves for OS in the lenalidomide-refractory population are shown in Figure 8.

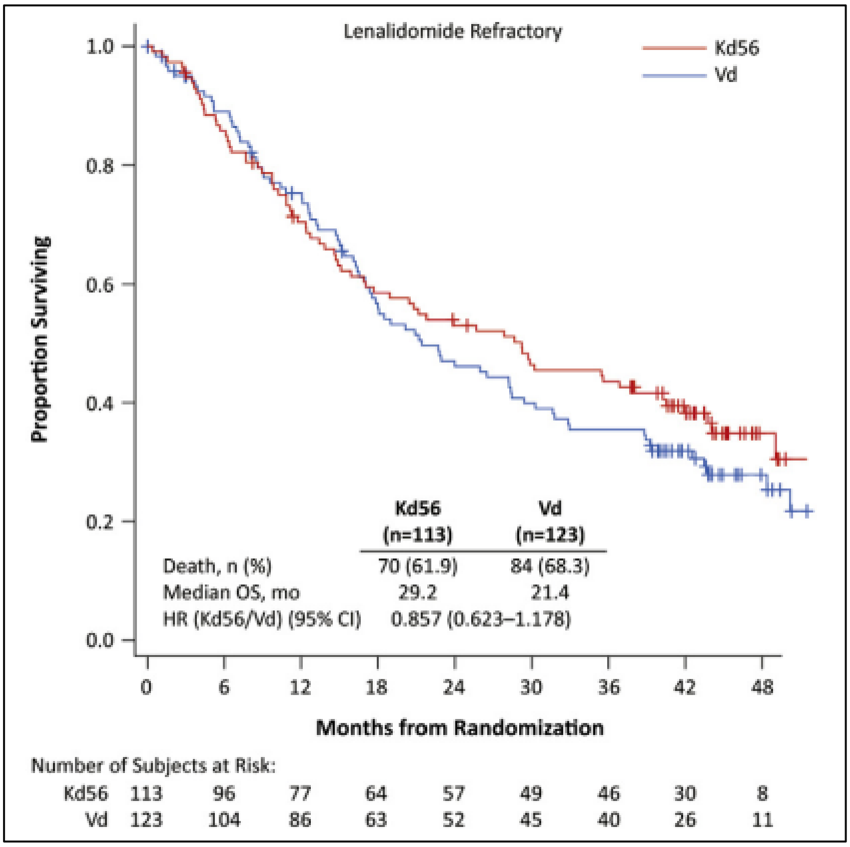
Figure 7. Kaplan-Meier curve of OS in the ITT population of ENDEAVOR



Abbreviations: CI, Confidence interval; HR, Hazard ratio; ITT, Intention-to-treat; Kd, Carfilzomib + dexamethasone; mo, Months; OS, Overall survival; Vd, Bortezomib + dexamethasone.

Source: Orlowski et al. [47]

Figure 8. Kaplan-Meier curve of OS in the lenalidomide-refractory population of ENDEAVOR



Abbreviations: CI, Confidence interval; HR, Hazard ratio; Kd, Carfilzomib + dexamethasone; mo, Months; OS, Overall survival; Vd, Bortezomib + dexamethasone.
Source: Orlowski et al. [47]

6.1.5.2 Progression-free survival

The final PFS results were reported in the first interim analysis of ENDEAVOR (data cut-off November 10th, 2014). PFS was compared between treatment groups using a log-rank test and the corresponding hazard ratio (HR) was estimated using a Cox regression model.

The results for PFS are shown in Table 23.

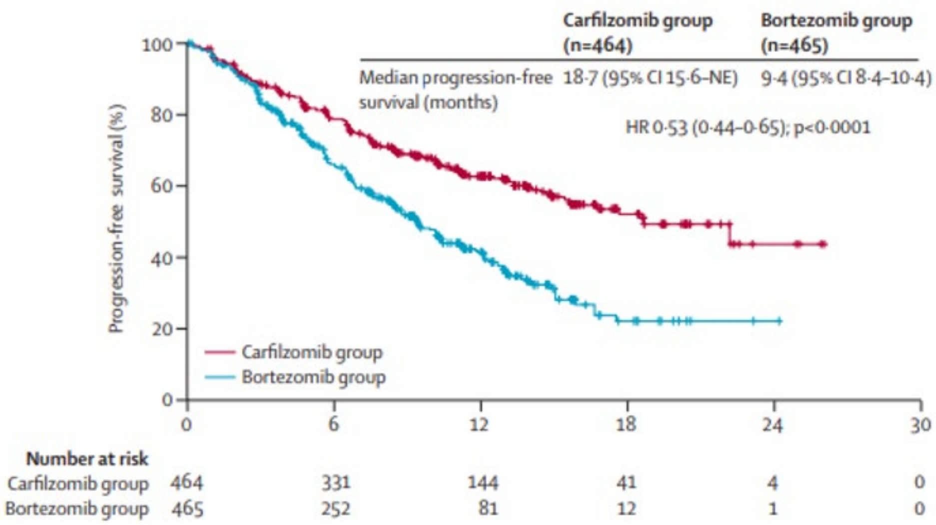
Table 23. PFS results from ENDEAVOR[6]

	ITT population		Lenalidomide-refractory population (post-hoc analysis)	
	Kd (n=464)	Vd (n=465)	Kd (n =113)	Vd (n=122)
Median follow-up, months	11.9	11.1	Not reported	Not reported
Median PFS, months (95% CI)	18.7 (15.6, NE)	9.4 (8.4, 10.4)	8.6 (6.61 to 11.25)	6.6 (5.23 to 7.53)

One-sided P-value	<0.0001	Not reported
Hazard ratio (95% CI)	0.53 (0.44, 0.65)	0.80 (0.57, 1.11)

Additionally, the number of deaths and/or disease progressions in the Kd vs. the Vd group are reported in Figure 10 and Figure 11 for the ITT and the lenalidomide-refractory population, respectively.

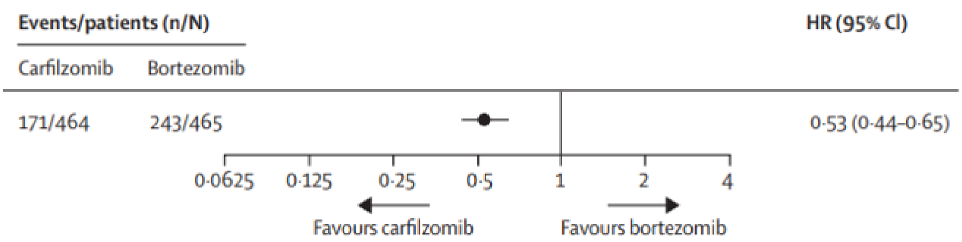
Figure 9. Kaplan-Meier curve of PFS in the ITT population of ENDEAVOR



Abbreviations: CI, Confidence interval; HR, Hazard ratio; ITT, Intention-to-treat; NE, Not estimable; PFS, Progression-free survival.

Source: Dimopoulous et al. [6]

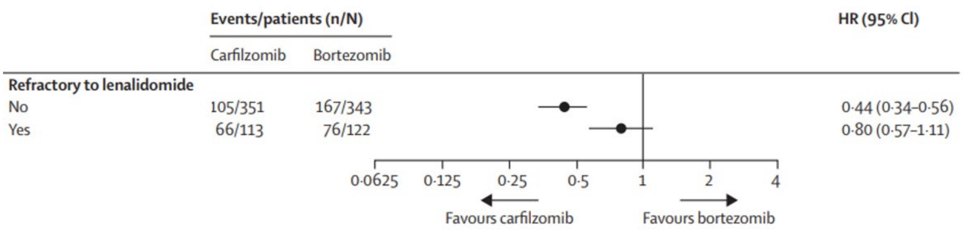
Figure 10. PFS in the ITT population (ENDEAVOR)



Abbreviations: CI, Confidence interval; HR, Hazard ratio; ITT, Intention-to-treat; PFS, Progression-free survival.

Source: Dimopoulous et al. [6]

Figure 11. PFS in the lenalidomide-refractory population (ENDEAVOR)



Abbreviations: CI, Confidence interval; HR, Hazard ratio; PFS, Progression-free survival.

Source: Dimopoulous et al. [6]

6.1.5.3 Discontinuation

Of the 929 patients who were randomly assigned in the study, 919 were dosed with a study drug (463 in the Kd arm and 456 in the Vd arm). Of these, 614 discontinued treatment (263 in the Kd arm and 351 in the Vd arm)[6]. Reasons for discontinuation in the ENDEAVOR trial are presented in Table 24.

Table 24. Treatment discontinuation in the ENDEAVOR trial

Reason for discontinued treatment	Kd Arm (N=463)*	Vd Arm (N=456)*	Total (N=919)*
Disease Progression	117 (25.3%)	168 (36.8%)	285 (31%)
Adverse Event	65 (14.0%)	73 (16%)	138 (15%)
Patient request	40 (8.6%)	45 (9.9%)	85 (9.2%)
Investigator decision	18 (3.9%)	35 (7.7%)	53 (5.8%)
Death	13 (2.8%)	9 (2%)	22 (2.4%)
Withdrawal of consent	6 (1.3%)	19 (4.2%)	25 (2.7%)
Non-compliance	4 (0.8%)	1 (0.2%)	5 (0.5%)
Lost to follow-up	0	1 (0.2%)	1 (0.1%)
Total	263 (56.8%)	351 (77%)	614 (66.8%)

Abbreviations: AE, Adverse event; Kd, Carfilzomib + dexamethasone; Vd, Bortezomib + dexamethasone.

Notes: * Number of patients who received a study drug.

Source: Data on file[45].

6.1.6 Efficacy – results per OPTIMISMM

Between Jan 7, 2013, and May 15, 2017, 559 patients were enrolled into the OPTIMISMM trial. Out of these, 331 patients (70%) were lenalidomide-refractory.

6.1.6.1 Overall survival

Final data on overall survival in OPTIMISMM was presented at the 2023 IMS conference.[56] The available results are shown in Table 25.

Table 25. OS Results from OPTIMISMM[56]

	ITT population		Lenalidomide-refractory population (post-hoc analysis)	
	PVd (n=281)	Vd (n=278)	PVd (n =113)	Vd (n=122)
Median follow-up, months	64.5		Not reported	
Median OS, months (95% CI)	35.6 (Not reported	31.6 (Not reported	Not reported	Not reported
One-sided P-value	0.571		Not reported	
Hazard ratio (95% CI)	0.94 (0.77 to 1.15)		0.89 (0.71 to 1.12)	

6.1.6.2 Progression-free survival

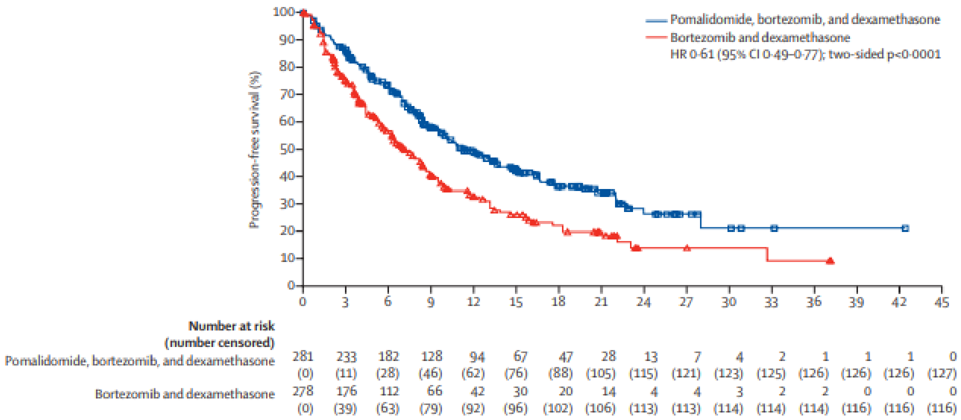
Progression-free survival data was obtained from the primary publication of OPTIMISMM, published in 2019.[7] The results are shown in Table 26.

Table 26. PFS Results from OPTIMISMM[7]

	ITT population		Lenalidomide-refractory population (post-hoc analysis)	
	PVd (n=281)	Vd (n=278)	PVd (n =113)	Vd (n=122)
Median follow-up, months	15.9		Not reported	
Median PFS, months (95% CI)	11.20 (9.66, 13.73)	7.10 (5.88, 8.84)	9.53 (8.05, 11.30)	5.59 (4.44, 7.00)
One-sided P-value	0.0001		0.0008	
Hazard ratio (95% CI)	0.61 (0.49 to 0.77)		0.65 (0.50 to 0.84)	

Kaplan-Meier curves of PFS in the ITT and lenalidomide-refractory populations are shown in Figure 12 and Figure 13.

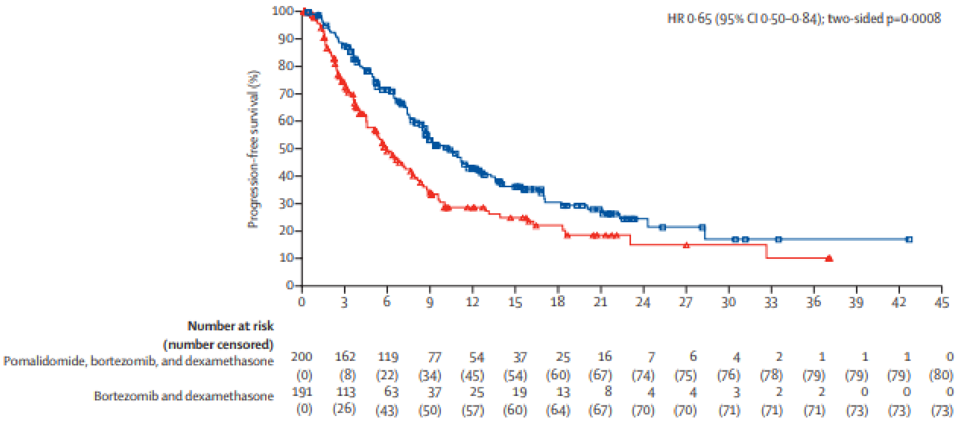
Figure 12. Kaplan-Meier curve of PFS in the ITT population of OPTIMISMM



Abbreviations: CI, Confidence interval; HR, Hazard ratio; ITT, Intention-to-treat; PFS, Progression-free survival

Source: Richardson et al. [7]

Figure 13. Kaplan-Meier curve of PFS in the lenalidomide refractory population of OPTIMISMM



Abbreviations: CI, Confidence interval; HR, Hazard ratio; PFS, Progression-free survival
Source: Richardson et al. [7]

6.1.6.3 Discontinuation

Of the 559 patients who were randomly assigned in the study, 548 were dosed with a study drug (278 in the PVd arm and 270 in the Vd arm). Of these, 410 discontinued treatment (185 in the PVd arm and 225 in the Vd arm)[6]. Reasons for treatment discontinuation in the ENDEAVOR trial are presented in Table 27.

Table 27. Treatment discontinuation in the OPTIMISMM trial

Reason for discontinued treatment	PVd Arm (N=281)*	Vd Arm (N=278)*	Total (N=559)*
Disease Progression	110 (39.1%)	131 (47.1%)	241 (43.1%)
Adverse Event	30 (10.7%)	49 (17.6%)	79 (14.1%)
Death	18 (6.4%)	9 (3.2%)	27 (4.8%)

Withdrawal of consent	21 (7.5%)	21 (7.6%)	42 (7.5%)
Lost to follow-up	0 (0%)	2 (0.7%)	2 (0.4%)
Other	6 (2.1%)	13 (4.7%)	19 (3.4%)
Total	185 (65.8%)	225 (80.9%)	410 (73.3%)

7. Comparative analyses of efficacy

7.1.1 Differences in definitions of outcomes between studies

The only relevant outcomes reported for the lenalidomide-refractory population in ENDEAVOR and OPTIMISMM were OS and PFS; and thus, these are the only outcomes included.

No substantial differences in the definition of OS or PFS were identified, with OS being defined as time from randomization to death and PFS being defined as time from randomization to progression or death. In all trials, PFS was assessed by an IRC.

7.1.2 Method of synthesis

For both PFS and OS, hazard ratios of SVd, Kd, and PVd against Vd in the lenalidomide-refractory population were extracted. These were then combined using frequent NMA methodology, using the *netmeta* package in the freely available software R.

The methods used for the NMA are briefly described here; details on the methods of synthesis are provided in Appendix C.

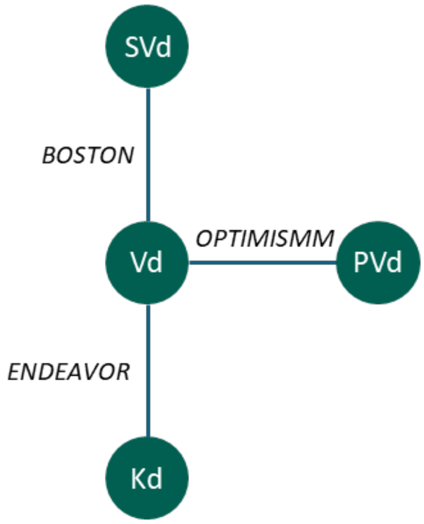
The *netmeta* package adopts the approach proposed by Rücker, which relies on graph-theoretical methods[57]. To fit the fixed and random effect models, treatment estimates and corresponding standard errors of all pairwise comparisons must be available. As is common in meta-analysis, standard errors are assumed to be known and fixed[58].

A random-effects model can be defined by assuming a common heterogeneity variance, τ^2, for each pairwise treatment comparison; the random-effects model is then fitted by adding this estimate of τ^2 to the variance of each comparison. The default estimator for τ^2 in the *netmeta* package is a special case of the generalised DerSimonian-Laird estimate[58].

Global inconsistency (i.e., between-design heterogeneity) can be estimated based on a full-design-by-treatment interaction random effects model; local inconsistency in each treatment comparison separately can be evaluated by separating indirect from direct evidence and test them against each other. A *z* test of the difference between direct and indirect estimate indicates potential evidence for inconsistency for each comparison in the network[58].

As the conducted NMA included only one study per comparison, there was no within-comparison heterogeneity, meaning that fixed- and random effect models provided exactly similar estimates. Similarly, as the network graph (shown in Figure 14) contained no closed loops (and thus no NMA estimates were informed by different designs), no inconsistency was observed.

Figure 14. Network graph for frequentist NMA of SVd versus Kd and PVd



7.1.3 Results from the comparative analysis

The results of the NMA of SVd versus Kd and PVd for lenalidomide-refractory MM patients in 2L+ are shown in Table 28. Forest plots of Vd, Kd, and PVd versus SVd for OS and PFS are shown in Figure 15 and Figure 16 respectively.

Table 28. Results from the comparative analysis of SVd vs. Kd and PVd for lenalidomide-refractory MM patients in 2L+

Outcome measure	BOSTON (SVd = 53 Vd = 53)	ENDEAVOR[47] (Kd = 113 Vd = 123)	OPTIMISMM (PVd = 200 Vd = 191)	NMA Results (random-effects, frequentist NMA)
OS	SVd median OS: 26.68 months 95% CI: 16.92, not estimable Vd median OS: 18.65 months 95% CI: 13.95 to 29.01 SVd v. Vd HR: 0.53 95% CI: 0.29 to 0.96	Kd median OS: 29.2 months 95% CI: Not reported Vd median OS: 21.4 months 95% CI: Not reported Kd v. Vd HR: 0.857 95% CI: 0.623 to 1.178	PVd median OS: Not reported 95% CI: Not reported Vd median OS: Not reported 95% CI: Not reported PVd v. Vd HR: 0.89 95% CI: 0.71 to 1.12	SVd v. Kd HR: 0.62 95% CI: 0.31 to 1.22 SVd v. PVd HR: 0.60 95% CI: 0.31 to 1.13
PFS	SVd median PFS: 10.18 months 95% CI: 5.8, not estimable	Kd median PFS: 8.6 95% CI: 6.61 to 11.25	PVd median PFS: 9.53 months 95% CI: 8.05 to 11.30	SVd v. Kd HR: 0.65 95% CI: 0.35 to 1.21

Vd median PFS: 7.06 months 95% CI: 3.5 to 9.8 SVd v. Vd HR: 0.52 95% CI: 0.31 to 0.88	Vd median PFS: 6.6 95% CI: 5.23 to 7.53 Kd v. Vd HR: 0.80 95% CI: 0.57 to 1.11	Vd median PFS: 5.59 months 95% CI: 4.44 to 7.00 PVd v. Vd HR: 0.65 95% CI: 0.50 to 0.84	SVd v. PVd HR: 0.80 95% CI: 0.45 to 1.43

Abbreviations: CI, Confidence interval; HR, Hazard ratio; Kd, Carfilzomib + dexamethasone; OS, Overall survival; PFS, Progression-free survival; PVd, Pomalidomide + bortezomib + dexamethasone; SVd, Selinexor + bortezomib + dexamethasone; Vd, Bortezomib + dexamethasone.

Figure 15. Forest plot of SVd versus Vd, Kd, and PVd in lenalidomide-refractory patients in 2L+; Overall survival

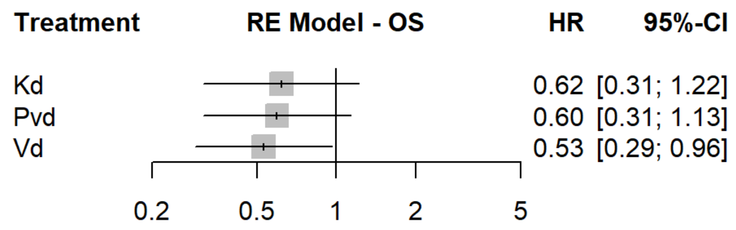
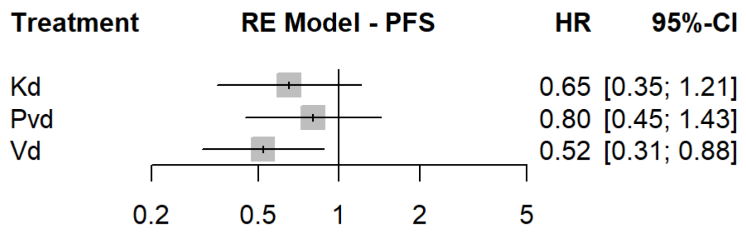


Figure 16. Forest plot of SVd versus Vd, Kd, and PVd in lenalidomide-refractory patients in 2L+; Progression-free survival



Kaplan-Meier curves from the individual studies (BOSTON, ENDEAVOR and OPTIMISMM) are presented in sections 6.1.4 to 6.1.6.

7.1.4 Results per [outcome measure]

See above

8. Modelling of efficacy in the health economic analysis

While the model is a cost-minimization model, the health state membership is based on clinical efficacy data and the parametric curves extrapolated from based on the data from the BOSTON trial lenalidomide refractory patients. This is presented below.

8.1 Presentation of efficacy data from the clinical documentation used in the model

PFS, OS and ToT endpoints corresponding to patients treated with SVd were derived from patient-level data for lenalidomide refractory patients from the February 15th, 2021 data cut of the BOSTON trial. Survival model were chosen based on the NICE DSU technical support document 14.[59]

8.1.1 Extrapolation of efficacy data

In order to estimate the cost of SVd and comparators, parametric curves were fitted for each endpoint, both independently (i.e., only to the SVd arm of the trial), and jointly (dependent curves fitted to both SVd and Vd arms, with the calculation of a treatment arm coefficient to capture differences between the two). Each approach has its advantages: the jointly fitted estimates draw on a greater pool of evidence, informed by approximately twice the number of observations, but assumes proportional hazards between the two arms. Independent curve fitting avoids the undue influence of the comparator arm on estimates, and does not rely on the proportional hazards' assumption, but incurs greater uncertainty associated with sample size.

Proportional hazards assessments were conducted for each set of analyses, and results from both dependent- and independently fitted models are presented in scenario analyses (section 12.2.1.1). Although, Vd is not included as a comparator in the submission, given the role of Vd as a 'bridging' arm between SVd and comparators, dependent fitted curves were prioritized in the base case to preserve estimated relativities between SVd and Vd unless clear violations of proportional hazards were violated. In cases where Schoenfeld residual tests suggested a potential violation, a visual assessment was made of log-cumulative and Schoenfeld residual plots, the results of proportional assessments in larger BOSTON populations were considered (to determine whether sample size was a likely factor) and the consistency of extrapolations using both approaches was compared against with landmark estimates from clinical experts to assess face validity.

For the dependent curves' estimation of overall survival, it was necessary to adjust for the crossover of patients from the Vd to SVd arm in the BOSTON trial prior to curve fitting. This was carried out using a two-stage-estimation (TSE) approach, aligned with the company submission to EMA and the HTA submission to NICE, and in accordance with NICE guidance.[60] According to this approach, disease progression (as a precursor to treatment switching) is used as a secondary baseline timepoint, to differentiate between pre- and post-progression survival rates. This allowed for the influence of treatment switching to be accounted for, controlling for prognostic factors at baseline and at progression.[60] Adjusted OS estimates with re-censoring (to avoid bias from informative censoring introduced by the methodology) are implemented in the base case, with results using unadjusted OS and adjusted OS without re-censoring explored as model scenarios.

Seven parametric models (exponential, Weibull, Gompertz, log-normal, log-logistic, gamma and generalised gamma) were fitted to data for each endpoint. Appropriate curve selection was determined according to statistical and visual goodness of fit and the clinical plausibility of extrapolations as determined by myeloma experts during an expert Advisory Board held in May 2023.[61] Expert clinical and health economic input was sought at the same time regarding the need for more flexible (spline or piecewise) extrapolation approaches. To keep the mortality risk of eligible patients equivalent to or greater than the general population in all model cycles, all outcomes (OS, PFS, and TTD) were capped by general mortality using Danish life tables.

Due to the cost-minimization approach, the selected extrapolated curves were applied for SVd, PVd, and Kd, equal to a hazard ratio of 1.

8.1.1.1 Extrapolation of overall survival

The approach to modelling of OS is presented in Table 29. The time-to-event data along with the base-case extrapolations are presented in Figure 17.

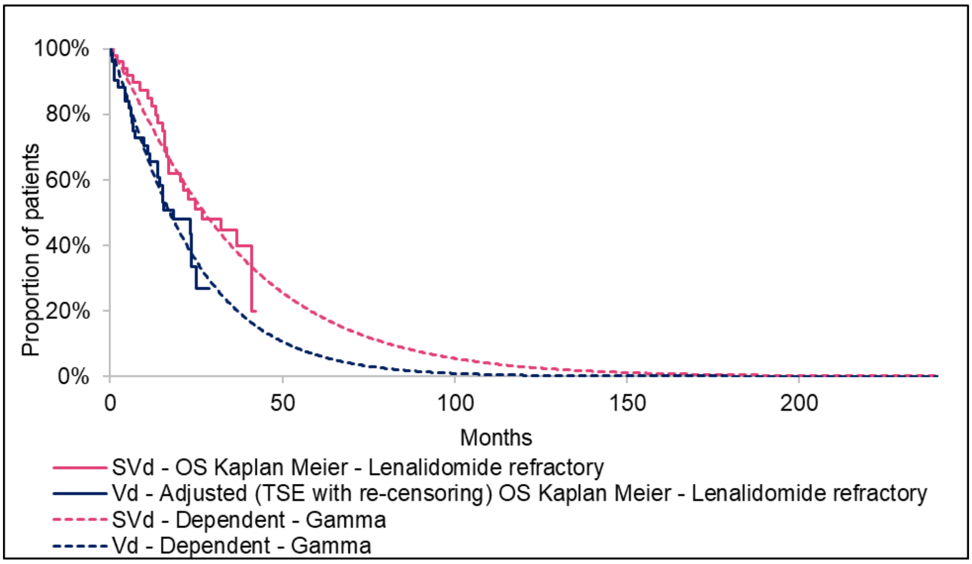
From a statistical standpoint, the Gompertz curve was the best fitting in terms of combined AIC, while the exponential curve had the best BIC fitting. AIC and BIC measures showed little numerical difference between curves.

Table 29. Summary of assumptions associated with extrapolation of overall survival

Method/approach	Description/assumption
Data input	BOSTON clinical trial lenalidomide refractory data.
Model	The seven standard parametric curves
Assumption of proportional hazards between intervention and comparator	Yes. Assumption of proportional hazards assumed to hold.
Function with best AIC fit	Dependent model: Gompertz
Function with best BIC fit	Dependent model: Exponential
Function with best visual fit	Dependent model: Gamma
Function with best fit according to evaluation of smoothed hazard assumptions	Dependent model: Gamma
Validation of selected extrapolated curves (external evidence)	Clinical advisory board.
Function with the best fit according to external evidence	Dependent model: Gamma

Selected parametric function in base case analysis	Dependent model: Gamma
Adjustment of background mortality with data from Statistics Denmark	OS capped by Danish general mortality.
Adjustment for treatment switching/cross-over	Yes.
Assumptions of waning effect	No.
Assumptions of cure point	No.

Figure 17. Time-to-event data along with extrapolation of overall survival



8.1.1.2 Extrapolation of progression-free survival

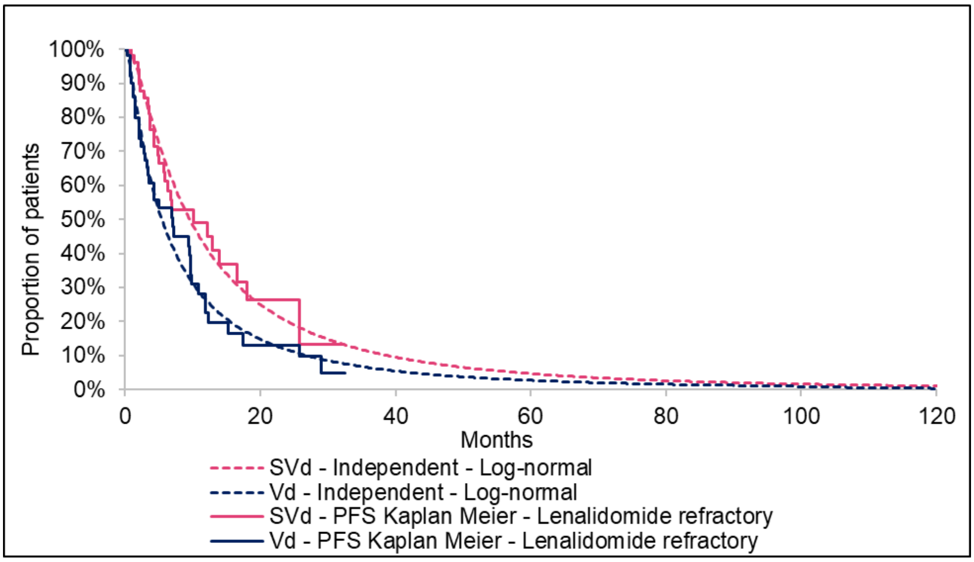
The approach to modelling of PFS is presented in Table 30. The time-to-event data along with the base-case extrapolations are presented in Figure 18.

For the PFS extrapolation, the proportional hazards assumption did not hold based on testing, and therefore independent log-normal models were chosen. Log-normal provided the best statistical fit for SVd both in terms of AIC and BIC, and was not found clinical implausible.

Table 30. Summary of assumptions associated with extrapolation of progression-free survival

Method/approach	Description/assumption
Data input	BOSTON clinical trial lenalidomide refractory data.
Model	The seven standard parametric curves
Assumption of proportional hazards between intervention and comparator	No. Proportional hazards assumption was violated.
Function with best AIC fit	SVd: Log-normal Vd: Log-normal
Function with best BIC fit	SVd: Log-normal Vd: Exponential
Function with best visual fit	SVd: Log-normal Vd: Log-normal
Function with best fit according to evaluation of smoothed hazard assumptions	SVd: Log-normal Vd: Log-normal
Validation of selected extrapolated curves (external evidence)	Clinical advisory board.
Function with the best fit according to external evidence	SVd: Log-normal Vd: Log-normal
Selected parametric function in base case analysis	SVd: Log-normal Vd: Log-normal
Adjustment of background mortality with data from Statistics Denmark	OS was capped by general mortality.
Adjustment for treatment switching/cross-over	No.
Assumptions of waning effect	No.
Assumptions of cure point	No.

Figure 18. Time-to-event data along with extrapolation of progression-free survival



8.1.1.3 Extrapolation of time-on-treatment

The approach to modelling of ToT is presented in Table 31. The time-to-event data along with the base-case extrapolations are presented in Figure 19.

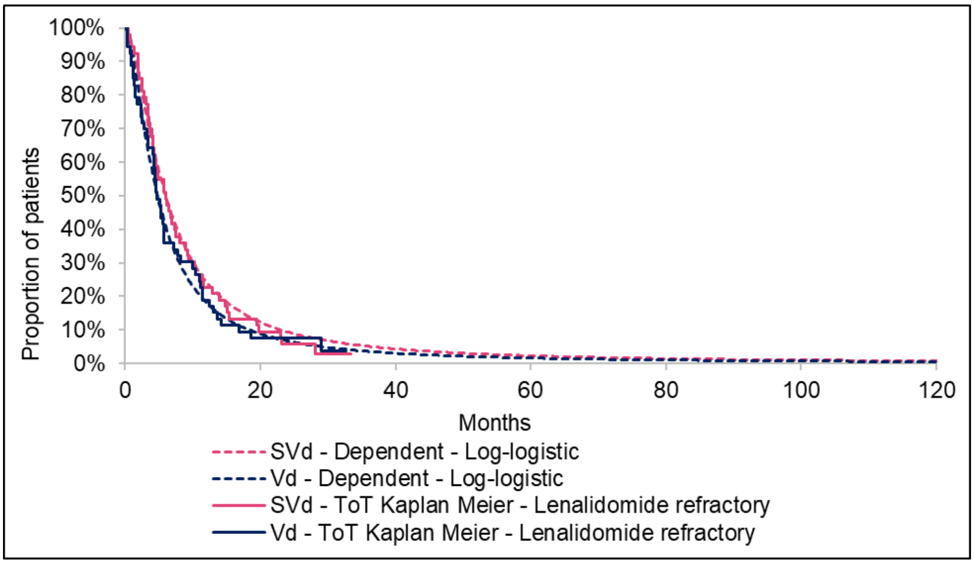
The proportional hazards assumption was assumed to hold for ToT. The log-logistic curve provided the best statistical fit based on both AIC and BIC, and was not found clinically implausible.

Table 31. Summary of assumptions associated with extrapolation of time-on-treatment

Method/approach	Description/assumption
Data input	BOSTON clinical trial lenalidomide refractory data.
Model	The seven standard parametric curves
Assumption of proportional hazards between intervention and comparator	Yes. Assumption of proportional hazards assumed to hold.
Function with best AIC fit	Dependent model: Log-logistic
Function with best BIC fit	Dependent model: Log-logistic
Function with best visual fit	Dependent model: Log-logistic

Function with best fit according to evaluation of smoothed hazard assumptions	Dependent model: Log-logistic
Validation of selected extrapolated curves (external evidence)	Clinical advisory board.
Function with the best fit according to external evidence	Dependent model: Log-logistic
Selected parametric function in base case analysis	Dependent model: Log-logistic
Adjustment of background mortality with data from Statistics Denmark	N/a
Adjustment for treatment switching/cross-over	No.
Assumptions of waning effect	No.
Assumptions of cure point	No.

Figure 19. Time-to-event data along with extrapolation of time-on-treatment



8.1.2 Calculation of transition probabilities

Not applicable.

8.2 Presentation of efficacy data from additional documentation

Not applicable.

8.3 Modelling effects of subsequent treatments

Effects of subsequent treatments were not included in the health economic model.

8.4 Other assumptions regarding efficacy in the model

Not applicable.

8.5 Overview of modelled average treatment length and time in model health state

The main efficacy parameters predicting the cost of SVd, Kd, and PVd are the OS along with ToT. The modelled and observed OS and ToT are presented in Table 32. As requested by the DMC on 20th Nov 2024, the PFS values were added in Table 32.

Table 32. Estimates in the model

	Modelled average OS (reference in Excel)	Modelled median OS (reference in Excel)	Observed median OS from relevant study
SVd	36.89	27.60	26.70
Kd	36.89	27.60	Not relevant
PVd	36.89	27.60	Not relevant
	Modelled average ToT (reference in Excel)	**Modelled median ToT (reference in Excel)**	**Observed median ToT from relevant study**
SVd	11.44	6.21	6.05
Kd	11.44	6.21	Not relevant
PVd	11.44	6.21	Not relevant
	Modelled average PFS (reference in Excel)	**Modelled median PFS (reference in Excel)**	**Observed median PFS from relevant study**
SVd	17.30	9.66	10.18
Kd	17.30	9.66	Not relevant
PVd	17.30	9.66	Not relevant

The modelled average treatment length and time in model health state are presented in Table 33. The health state occupation was based on OS, PFS, and ToT curves, and the health state occupation is equal for SVd and comparators, due to the cost-minimization format, assuming equal relative efficacy.

Table 33. Overview of modelled average treatment length and time in model health state, undiscounted and not adjusted for half cycle correction

Treatment	Treatment length months	Progression free months	Progressed disease months
SVd	11.44	17.30	19.59
Kd	11.44	17.30	19.59

PVd	11.44	17.30	19.59

9. Safety

9.1 Safety data from the clinical documentation

In all three trials included in the clinical documentation, the safety population was defined as patients that had received at least one dose of study drug. Safety results are shown for the overall populations, rather than the lenalidomide-refractory subpopulations as clinical expert feedback stated that there is no clinical reason to assume the safety data for lenalidomide-refractory patients would differ from that of the whole BOSTON safety population.

Safety data from BOSTON, ENDEAVOR, and OPTIMISMM is presented in Table 34.

Table 34. Overview of safety events in BOSTON, ENDEAVOR, and OPTIMISMM.

	BOSTON (Updated analysis)		ENDEAVOR		OPTIMISMM	
	SVd (n = 195)	Vd (n = 204)	Kd (n = 463)	Vd (n = 456)	PVd (n = 278)	Vd (n = 270)
Number of adverse events, n	Not available	Not available	Not reported	Not reported	Not reported	Not reported
Number and proportion of patients with ≥1 adverse events, n (%)	194 (99.5%)	198 (97.1%)	455 (98.3%)	447 (98.7%)	Not reported	Not reported
Number of serious adverse events*, n	Not available	Not available	Not reported	Not reported	Not reported	Not reported
Number and proportion of patients with ≥ 1 serious adverse events*, n (%)	106 (54.4%)	79 (38.7%)	224 (48.4%)	162 (35.%)	177 (63.7%)	193 (44.1%)
Number of CTCAE grade ≥ 3 events, n	Not available	Not available	Not reported	Not reported	Not reported	Not reported
Number and proportion of patients with ≥ 1 CTCAE grade ≥ 3 events[§], n (%)	153 (78.5%)	115 (56.4%)	Not reported	Not reported	Not reported	Not reported
Number of adverse reactions, n	Not available	Not available	Not reported	Not reported	Not reported	Not reported
Number and proportion of patients with ≥ 1 adverse reactions, n (%)	187 (95.9%)	167 (81.9%)	Not reported	Not reported	Not reported	Not reported
Number and proportion of patients who had a dose reduction, n (%)	141 (72.3%)	106 (52.0%)	106 (23%)	218 (48%)	200 (72%)	139 (51%)

Number and proportion of patients who discontinue treatment regardless of reason, n (%)	174 (89.2%)	188 (92.2%)	263 (56.8%)	351 (77.0%)	185 (66.6%)	225 (80.9%)
Number and proportion of patients who discontinue treatment due to adverse events, n (%)	41 (21.0%)	34 (16.7%)	65 (14.0%)	73 (16.0%)	30 (10.8%)	49 (17.6%)

Sources: BOSTON, Clinical Study Report[45], ENDEAVOR, clinicaltrials.gov and Dimopoulos 2016[6], OPTIMISMM, clinicaltrials.gov and Richardson 2019[7]
Time-point: BOSTON, From date of randomization up to 30 days after last dose of treatment (up to 32 months); ENDEAVOR, From the first dose of study drug up to 30 days after the last dose of study drug as of the data cut-off date of 03 January 2017; OPTIMISMM, up to approximately 44 months.

The only serious adverse event observed in any of the included trials with a frequency of more than 5% in any of the treatment arms was pneumonia (Table 35). All observed serious adverse events observed in the included trials are presented in Appendix E.

Table 35. Serious adverse events

Adverse events	BOSTON (Updated analysis)		ENDEAVOR		OPTIMISMM	
	SVd (n = 195)	Vd (n = 204)	Kd (n = 456)	Vd (n = 463)	PVd (n = 278)	Vd (n = 270)
Pneumonia, n (%)	29 (14.9%)	27 (13.2%)	42 (9.2%)	39 (8.4%)	34 (12.2%)	17 (6.3%)

Sources: BOSTON, Clinical Study Report[45], ENDEAVOR, clinicaltrials.gov and Dimopoulos 2016[6], OPTIMISMM, clinicaltrials.gov and Richardson 2019[7]
Time-point: BOSTON, From date of randomization up to 30 days after last dose of treatment (up to 32 months); ENDEAVOR, From the first dose of study drug up to 30 days after the last dose of study drug as of the data cut-off date of 03 January 2017; OPTIMISMM, up to approximately 44 months.

The model includes estimates of the costs and disutilities associated with Grade 3-4 adverse events that were reported in 5% or more of patients in the BOSTON SVd arm as a conservative approach. Adverse event rates for SVd were taken from the BOSTON trial. Adverse event rates for Kd were taken from the ENDEAVOUR study, while the adverse event rates for PVd were taken from OPTIMISMM. The rates applied in the model are presented in Table 36.

Table 36. Adverse events used in the health economic model

Adverse events	SVd	Kd	PVd	
	N (Weekly rate) used in the model	N (Weekly rate) used in the model	N (Weekly rate) used in the model	Source and justification
Adverse event, n (%)				
Anaemia	32 (0.1314%))	80 (0.0897%)	38 (0.1975%)	BOSTON[8], ENDEAVOUR[52], OPTIMISMM[7]. Grade 3-4 adverse events that were reported in 5% or more of patients in the BOSTON SVd arm
Asthenia	16 (0.0657%)	NR	8 (0.0416%)	
Cataract	22 (0.0903%)	NR	NR	
Diarrhoea	13 (0.0534%)	19 (0.0213%)	20 (0.1040%)	
Fatigue	26 (0.1067%)	32 (0.0359%)	23 (0.1196%)	
Febrile neutropenia	1 (0.0041%)	NR	NR	
Hypertension	8 (0.0329%)	69 (0.0773%)	NR	
Hypophosphataemia	11 (0.0452%)	NR	17 (0.0884%)	
Leukopenia	1 (0.0041%)	NR	NR	
Lymphopenia	7 (0.0288%)	NR	NR	
Lower respiratory tract infection	4 (0.0164%)	NR	NR	
Nausea	15 (0.0616%)	NR	1 (0.0052%)	
Neutropenia	18 (0.0739%)	12 (0.0135%)	116 (0.6017%)	
Hyperglycaemia	4 (0.0164%)	NR	25 (0.1300%)	
Peripheral neuropathy	9 (0.0370%)	11 (0.0123%)	23 (0.1196%)	

Pneumonia	28 0.1150%)	NR	31 (0.1612%)
Thrombocytopenia	79 0.3240%)	58 0.0650%)	76 (0.3946%)

9.2 Safety data from external literature applied in the health economic model

Not applicable. All safety data applied in the model are presented in section 9.1.

10. Documentation of health-related quality of life (HRQoL)

Not applicable.

10.1 Presentation of the health-related quality of life [make a subsection for each of the applied HRQoL instruments]

Not applicable.

10.1.1 Study design and measuring instrument

Not applicable.

10.1.2 Data collection

Not applicable.

10.1.3 HRQoL results

Not applicable.

10.2 Health state utility values (HSUVs) used in the health economic model

Not applicable.

10.2.1 HSUV calculation

Not applicable.

10.2.1.1 Mapping

Not applicable.

10.2.2 Disutility calculation

Not applicable.

10.2.3 HSUV results

Not appliacable.

10.3 Health state utility values measured in other trials than the clinical trials forming the basis for relative efficacy

Not applicable.

10.3.1 Study design

Not applicable.

10.3.2 Data collection

Not applicable.

10.3.3 HRQoL Results

Not applicable.

10.3.4 HSUV and disutility results

Not applicable.

11. Resource use and associated costs

11.1 Medicine costs - intervention and comparator

Selinexor was administered in the BOSTON trial as an oral 100mg dose (up to a maximum 70mg per m^2), equating to five tablets of 20mg. Selinexor was taken once per week (five times per 35-day cycle). Bortezomib was administered subcutaneously at a dose of 1.3mg/m^2 once weekly on Day 1 for 4 weeks followed by 1 week off; and dexamethasone was administered as a fixed oral 20mg dose twice weekly (10 days of each 35-day cycle).[62]

The acquisition cost for selinexor is DKK 62,119.00 per 20 units of 20mg tablets at list price. The dosing regimen of SVd applied in the CEM reflects the SmPC for selinexor and is aligned with the BOSTON clinical trial, whereby selinexor is costed at a dose of 100mg (five tablets of 20mg) on Days 1, 8, 15, 22 and 29 of each 35-day cycle; bortezomib is costed at a dose of 1.3mg/m^2 on days 1, 8, 15 and 22 of each 35-day cycle and dexamethasone is costed at a dose of 20mg on Days 1, 2, 8, 9, 15, 16, 22, 23, 29 and 30 of each 35-day cycle.[8,62] The median RDI applied for each components are derived from the BOSTON trial.[45] This is presented in Table 37.

Kd was dosed according to the SmPC. Carfilzomib is administered intravenously as a 30-minute infusion on two consecutive days, each week for three weeks (days 1, 2, 8, 9, 15, and 16) followed by a 12-day rest period (days 17 to 28) as shown in table 2. Each 28-day period is considered one treatment cycle. Carfilzomib is administered at a starting dose of 20 mg/m2 (maximum dose 44 mg) in cycle 1 on days 1 and 2. If tolerated, the dose should be increased on day 8 of cycle 1 to 56 mg/m2 (maximum dose 123 mg). dexamethasone is administered as 20 mg on days 1, 2, 8, 9, 15, 16, 22, and 23 of the 28-day cycles. The RDI applied reflect the median RDI reported for the carfilzomib group in ENDEAVOR.[63] This is presented in Table 38.

PVd was dosed according to the SmPC. Pomalidomide is dosed as 4 mg taken orally once daily on Days 1 to 14 of repeated 21-day cycles. Bortezomib is administrated as 1.3mg/m^2 on day 1, 4, 8, and 11, during the first eight 21-day cycles, while bortezomib is only administrated on day 1 and 8 from cycle 9 and onwards. Dexamethasone is taken on two days in a row starting on the days where bortezomib is administrated. The RDI applied reflect the median RDI reported for the carfilzomib group in OPTIMISMM.[7]
This is presented in Table 39.

Table 37. Dosing of the selinexor + bortezomib + dexamethasone regimen

Medicine	Dose	Relative dose intensity	Frequency	Vial sharing
Selinexor	100 mg	88.90%	Five times per 35-day cycle	No
Bortezomib	1.30 mg/m^2	99.00%	Four times per 35-day cycle	No
Dexamethasone	20 mg	100.00%	10 times per 35-day cycle	No

Table 38. Dosing of the carfilzomib + dexamethasone regimen

Medicine	Dose	Relative dose intensity	Frequency	Vial sharing
Carfilzomib	20 mg/m^2	91.0%	Two consecutive days, each week for three weeks	No
	56 mg/m^2	91.0%	Two consecutive days, each week for three weeks	No
Dexamethasone	20 mg	100.0%	2 times a week (days 1, 2, 8, 9, 15, 16, 22, 23)	No

Table 39. Dosing of the pomalidomide + bortezomib + dexamethasone regimen

Medicine	Dose	Relative dose intensity	Frequency	Vial sharing
Pomalidomide	4 mg	85.0%	Once daily on Days 1 to 14 of repeated 21-day cycles.	No
Bortezomib	1.30 mg/m^2	80.0%	On day 1, 4, 8, and 11 during the first eight 21-day dosing cycles.	No
	1.30 mg/m^2	80.0%	On day 1 and 8 from dosing cycle 9 and onwards	No
Dexamethasone	20 mg	100.0%	Four times a week (days 1, 2, 4, 5, 8, 9, 11, and 12) for cycles 1-8 Twice a week (days 1, 2, 8, 9) for cycle 9 onward	No

Medicine costs were sourced from medicinpriser.dk. The prices were sources in March 2024. If multiple packages were available, the package providing the cheapest cost per mg were used. The prices are presented in Table 40.

Table 40. Medicine costs

Medicine	ATC	Strength	Units per pack	AIP (DKK)	Administration type
Selinexor	L01XX66	20.0 mg	20	62,119.00	Oral
Bortezomib	L01XG01	3.5 mg	1	1,850.00	SC or IV
Dexamethasone	H02AB02	4.0 mg	100	599.00	Oral
Carfilzomib	L01XG02	30.0 mg	1	3,738.23	IV
Pomalidomide	L04AX06	4.0 mg	14	34,449.46	Oral

11.2 Medicine costs – co-administration

Nausea is a common side effect of Selinexor, oral ondansetron is administered to all patients in the cost effectiveness analysis to manage the effects of nausea. Therefore, the cost of ondansetron was added to the SVd regimen. A pack of ondansetron (100 units of 8 mg) costs DKK 160.00.

Table 41. Dosing of ondansetron used for the SVd regimen.

Medicine	Dose	Relative dose intensity	Frequency	Vial sharing
Ondansetron	8 mg	100.00%	87.5 times per 35-day cycle	No

11.3 Administration costs

The cost of administration was included in the model by using the DRG 2024 tariffs. Oral administration was assumed not to result in any cost. The costs of intravenous and subcutaneous infusions are presented in Table 42.

Table 42. Administration costs used in the model

Administration type	Frequency	Unit cost [DKK]	DRG code	Reference
Intravenous infusion	Frequency per dosing as seen in Table 37, Table 38 and Table 39	1989.00	17MA98	DRG 2024
Subcutaneous infusion	Frequency per dosing as seen in Table 37, Table 38 and Table 39	1989.00	17MA98	DRG 2024

11.4 Disease management costs

The relevant resource use for disease management was identified in past MM submissions. Routine health state costs included haematologist clinical visits, full blood counts, biochemistry, protein electrophoresis, immunoglobulin, urinary light chain excretion, red blood cell transfusions and platelet transfusions. As a conservative assumption, given existing limited data to stratify between health states, health state resource use costs are assumed to be equal between health states. The costs of the disease management activities were based on DRG 2024 tariffs and the labportal.dk cost of tests. The resource use frequencies were applied from the NICE TA897 (formerly TA573). The frequencies were reported as resource use per week, which is also applied in the model, but for the purpose of the DMC template, the frequencies are approximated in non-numerical format below in Table 43.

Table 43. Disease management costs used in the model

Activity	Frequency	Unit cost [DKK]	DRG code	Reference
Haematologist clinical visit	Once a month (0.23 per week)	DKK 1,989.00	17MA98	DRG 2024

Activity	Frequency	Unit cost [DKK]	DRG code	Reference
Full blood count	Once a month (0.21 per week)	DKK 46.00	N/a	https://labportal.rh.dk/LabPortal.asp NPU17580 (Leukocytetypes), NPU02902 (neutrofilocytes), and NPU02319 (Haemaglobin + thrombocytes).
Biochemistry	Once a month (0.19 per week)	DKK 104.00	N/a	https://labportal.rh.dk/LabPortal.asp - Klorid;P, Kalium;P, Natrium;P,.(NPU01536, NPU03230,
Protein electrophoresis	Once every two months (0.13 per week)	DKK 14.00	N/a	NPU03429
Immunoglobulin	Once every two months (0.12 per week)	DKK 83.00	N/a	https://labportal.rh.dk/LabPortal.asp Albumin;P,.(NPU19673)
Urinary light chain excretion	Once every three months (0.05 per week)	DKK 901.00	N/a	https://labportal.rh.dk/LabPortal.asp (NPU19825, NPU19795, NPU19814) Immunoglobulin M;P, Immunoglobulin A;P, Immunoglobulin G;P

11.5 Costs associated with management of adverse events

The frequencies of the adverse events included as input in the model, are presented in section 9. As described in section 9, the adverse event costs are applied as weekly probabilities. The costs of adverse events are estimated using the DRG 2024 tariff system. The estimated costs of adverse events are presented in Table 44.

Table 44. Cost associated with management of adverse events

	DRG code	Unit cost/DRG tariff
Anaemia	16MA98: MDC16 1-dagsgruppe, pat. mindst 7 år, Diagnosis: DD592: Hæmolytisk ikke-autoimmun anæmi forårsaget af lægemiddel	DKK 2,111.00
Asthenia	23MA03: Symptomer og fund, u. kompl. bidiag., Diagnosis: DR539A: Udmattelse	DKK 5,103.00
Cataract	02MA01: Øvrige kontakter ved øjensygdomme, Diagnose: DH269 Grå stær UNS	DKK 1,068.00
Diarrhoea	06MA11: Malabsorption og betændelse i spiserør, mave og tarm, pat. mindst 18 år, u. kompl. bidiag., Diagnosis: DK529B: Ikke-infektiøs diaré UNS	DKK 7,818.00
Fatigue	23MA03: Symptomer og fund, u. kompl. bidiag., Diagnosis: DR539A: Udmattelse	DKK 5,103.00
Febrile neutropenia	16MA98: MDC16 1-dagsgruppe, pat. mindst 7 år, Diagnosis: DD709A: Neutropeni og agranulocytose forårsaget af lægemiddel	DKK 2,111.00
Hypertension	05MA98: MDC05 1-dagsgruppe, pat. mindst 7 år, Diagnosis: DI109: Essentiel hypertension	DKK 1,183.00
Hypophosphataemia	10MA98: MDC10 1-dagsgruppe, pat. mindst 7 år, Diagnosis: DE833A: Hypofosfatæmi	DKK 1,847.00
Leukopenia	16MA98: MDC16 1-dagsgruppe, pat. mindst 7 år, Diagnosis: DD728H: Leukopeni	DKK 2,111.00
Lymphopenia	16MA98: MDC16 1-dagsgruppe, pat. mindst 7 år, Diagnosis: DD728D: Lymfopeni	DKK 2,111.00
Lower respiratory tract infection	04MA98: MDC04 1-dagsgruppe, pat. mindst 7 år, Diagnosis: DJ189: Pneumoni UNS	DKK 1,311.00
Nausea	DRG 2024, 06MA11: Malabsorption og betændelse i spiserør, mave og tarm, pat. mindst 18 år, u. kompl. bidiag., Diagnosis: DR119C: Opkastning	DKK 7,818.00
Neutropenia	DRG 2024, 16MA98: MDC16 1-dagsgruppe, pat. mindst 7 år, Diagnosis: DD709A: Neutropeni og agranulocytose forårsaget af lægemiddel	DKK 2,111.00

	DRG code	Unit cost/DRG tariff
Hyperglycaemia	DRG 2024, 10MA98: MDC10 1-dagsgruppe, pat. mindst 7 år, Diagnosis: DE162: Hypoglykæmi UNS	DKK 1,847.00
Peripheral neuropathy	DRG 2024, 21MA98: MDC21 1-dagsgruppe, pat. Mindst 7 år: Diagnosis: DT983DD: Følgetilstand med neuropati efter kræftbehandling	DKK 1,582.00
Pneumonia	DRG 2024, 04MA98: MDC04 1-dagsgruppe, pat. mindst 7 år, Diagnosis: DJ189: Pneumoni UNS	DKK 1,311.00
Thrombocytopenia	DRG 2024, 16MA98: MDC16 1-dagsgruppe, pat. mindst 7 år, Diagnosis: DD696: Trombocytopeni UNS	DKK 2,111.00

11.6 Subsequent treatment costs

The BOSTON clinical trial lenalidomide-refractory population was used to determine the number of patients receiving subsequent therapies in the model: 48 patients were recorded as receiving subsequent treatment and 62 patients progressed across the trial follow-up. Therefore, 77.4% (48/62) of patients are assumed to receive subsequent treatment in the cost effectiveness analysis. The types of treatments received as subsequent therapies were derived from the distribution of subsequent therapies recorded in BOSTON clinical trial data, with those unavailable in the Denmark excluded and the remainder rescaled to achieve an equivalent overall level of receipt (Table 45). Rules were also applied to ensure that treatments received at model baseline would not be received again subsequently (i.e. patients receiving Kd in 2L will not receive Kd in subsequent treatments). As the model tries to reflect a MM patient population refractory to lenalidomide and anti-CD38 antibodies, the daratumumab-based regimens were also excluded from the subsequent treatments.

The proportion of subsequent treatments exceeds 100% as it accounts for multiple lines of therapy. Data from the BOSTON trial underline the significant unmet need among patients with RRMM, where lenalidomide-refractory patients are often prescribed lenalidomide in subsequent lines of treatment due to limited alternative options. The occurrence of this practice within the controlled environment of a clinical trial further reinforces its likelihood in Danish clinical practice. However, in response to queries raised by the DMC on December 19, 2024, a scenario analysis was conducted to evaluate the impact of excluding lenalidomide combinations from subsequent treatment options. In this scenario, the treatment distribution was reweighted across the remaining alternatives to reflect this adjustment.

Subsequent therapy costs are applied to patients following progression in the base case, with a scenario analysis to assess the impact of assuming subsequent therapies are used at the point of discontinuation (i.e., prior to progression, if the initial treatment ended earlier due to toxicity).

Table 45 Distribution of subsequent treatments

Treatment	Base case			Scenario analysis (no lenalidomide)		
	N of patients	Proportion (SVd and PVd)	Proportion (Kd)	N of patients	Proportion (SVd and PVd)	Proportion (Kd)
Chemotherapy	**8.00**	16.7%	18.81	**12.67**	26.4%	31.91%
Elo	**2.00**	4.2%	4.70	**6.67**	13.9%	16.79%
EloTd	**6.00**	12.5%	14.11%	**10.67**	22.2%	26.87%
IsaPd	**2.00**	4.2%	4.70%	**6.67**	13.9%	16.79
Kd	**9.00**	18.8%	0.00%	**13.67**	28.5%	0.00%
KRd	**11.00**	22.9%	25.86%	**0.00**	00.0%	0.00%
Pd	**24.00**	30.0%	56.43%	**28.67**	59.7%	72.22%
Rd	**13.00**	27.1%	30.57%	**0.00**	00.0%	0.00%
VRd	**4.00**	8.3%	9.40%	**0.00**	00.0%	0.00%
Total	**79.00**	164.58%		**79**	00.0%	0.00%

Abbreviations: Elo, Elotuzumab; EloTd, Elotuzumab, Thalidomide and Dexamethasone; IsaPd, Isatuxumab, Pomalidomide and Dexamethasone; Kd, Carfilzomib and Dexamethasone; KRd, Carfilzomib, lenalidomide and Dexamethasone, Pd, Pomalidomide and Dexamethasone, Rd, Lenalidomide and Dexamethasone; VRd, Bortezomib, lenalidomide and dexamethasone
Source: Data on file.[55]

The duration of each subsequent therapy is assumed to be nine months, aligning with the NICE submission for DVd (TA573, superseded by TA897).[50] This assumption allows for weighted average weekly costs to be estimated for treatments in which dosing schedules and costs varied across cycles. Where chemotherapy is received as a subsequent therapy, costs are based on a bendamustine + thalidomide + dexamethasone (BTD) regimen; the dosing schedule aligns with Lau *et al*. 2015[51]. Relative dose intensity for each regimen was based on the clinical trials, in which the regimen was identified. Subsequent treatment cost did not alter the results of the analysis significantly, however, following consultation with the DMC, the subsequent treatment costs were still applied in the model.

Table 46. Medicine costs of subsequent treatments

Medicine		Strength	Package size	Pharmacy purchase price [DKK]	Relative dose intensity	Average duration of treatment
Chemotherapy	Bendamustine	2.5 mg/ml	200 ml	1,100.00	100%	39.13 weeks
	Thalidomide	50 mg	28 units	2,081.52	100%	
	Dexamethasone	4 mg	100 units	599.00	100%	
Elotuzumab	Elotuzumab	300 mg	1 unit	6,442.24	100%	39.13 weeks
EloTd	Elotuzumab	300 mg	1 unit	6,442.24	100%	39.13 weeks
	Thalidomide	50 mg	28 units	2,081.52	100%	
	Dexamethasone	4 mg	100 units	599.00	100%	
IsaPd	Isatuximab	20 mg	25 units	18,877.23	91.1%	39.13 weeks
	Pomalidomide	4 mg	14 units	34,449.46	81.9%	
	Dexamethasone	4 mg	100 units	599.00	85.2%	
Kd	Carfilzomib	30 mg	1 unit	3,738.23	91.0%	39.13 weeks
	Dexamethasone	4 mg	100 units	599.00	100%	
KRd	Carfilzomib	30 mg	1 unit	3,738.23	94.0%	39.13 weeks
	Lenalidomide	25 mg	21 units	20,000.00	100%	
	Dexamethasone	4 mg	100 units	599.00	100%	

Medicine		Strength	Package size	Pharmacy purchase price [DKK]	Relative dose intensity	Average duration of treatment
Pd	Pomalidomide	4 mg	14 units	34,449.46	90%	39.13 weeks
	Dexamethasone	4 mg	100 units	599.00	100%	
Rd	Lenalidomide	25 mg	21 units	20,000.00	100%	39.13 weeks
	Dexamethasone	4 mg	100 units	599.00	100%	
VRd	Bortezomib	3.50 mg	1 unit	1,850.00	100%	39.13 weeks
	Lenalidomide	25 mg	21 units	20,000.00	100%	
	Dexamethasone	4 mg	100 units	599.00	100%	

11.7 Patient costs

The unit costs from DMC's catalogue of unit costs were applied in the model, with a patient hour being costed as DKK 188.00. A per kilometre cost of DKK 3.79 were applied for transportation assuming 2x20 km per visit. The visit was assumed to last 3 hours. The activity assumption is presented in Table 47.

Table 47. Patient costs used in the model

Activity	Time spent [minutes, hours, days]
Hospital visit	3 hours

11.8 Other costs (e.g. costs for home care nurses, out-patient rehabilitation and palliative care cost)

Not applicable.

12. Results

12.1 Base case overview

An overview of the base case including the central aspects of the analysis is presented in Table 48.

Table 48. Base case overview

Feature	Description
Comparators	Carfilzomib + dexamethasone Pomalidomide + bortezomib + dexamethasone
Type of model	Partitioned-survival model
Time horizon	35 years (life time)
Treatment line	Treatment of patients with *at least one prior therapy and are refractory to lenalidomide and where an anti-CD38 antibody is not appropriate*
Measurement and valuation of health effects	Excluded due to cost-minimization format
Costs included	Medicine costs Hospital costs

	Costs of adverse events Patient costs
Dosage of medicine	Based on SmPCs. Dosage of bortezomib and carfilzomib was based on average body surface area. Remaining medicines were fixed dosage.
Average time on treatment	SVd: 11.44 months Kd: 11.44 months PVd: 11.44 months
Parametric function for PFS	SVd: Independent log-normal Comparators applied same efficacy
Parametric function for OS	SVd: Dependent gamma Comparators applied same efficacy
Inclusion of waste	Wastage included.
Average time in model health state	Health state occupation was the same for SVd, Kd, and PVd: Treatment length: 11.44 months Progression free: 17.30 months Progressed disease: 19.59 months

12.1.1 Base case results

The base case results were present for the comparison versus Kd in Table 49, while the results for the comparison versus PVd are presented in Table 50

Table 49. Base case results versus Kd, discounted estimates

	SVd	Kd	Difference
Drug costs	DKK 811,791.90	DKK 1,053,012.67	-DKK 241,220.77
Admin costs	DKK 75,549.76	DKK 141,655.79	-DKK 66,106.04
Adverse events	DKK 1,623.07	DKK 383.19	DKK 1,239.88
Resource use - PF	DKK 42,237.25	DKK 42,237.25	DKK 0.00
Resource use - PD	DKK 46,097.37	DKK 46,097.37	DKK 0.00
Subsequent therapies	DKK 580,752.40	DKK 510,271.92	DKK 70,480.48
Patient time and transport cost	DKK 19,289.78	DKK 19,289.78	DKK 0.00

Total costs	**DKK 1,577,341.52**	**DKK 1,812,947.98**	**-DKK 235,606.45**

Table 50. Base case results versus PVd, discounted estimates

	SVd	PVd	Difference
Drug costs	DKK 811,791.90	DKK 629,779.21	DKK 182,012.69
Administration costs	DKK 75,549.76	DKK 88,064.34	-DKK 12,514.58
Adverse events	DKK 1,623.07	DKK 2,349.67	-DKK 726.60
Resource use - PF	DKK 42,237.25	DKK 42,237.25	DKK 0.00
Resource use - PD	DKK 46,097.37	DKK 46,097.37	DKK 0.00
Subsequent therapies	DKK 580,752.40	DKK 580,752.40	DKK 0.00
Patient time and transport cost	DKK 19,289.78	DKK 19,289.78	DKK 0.00
Total costs	**DKK 1,577,341.52**	**DKK 1,408,570.45**	**DKK 168,771.52**

12.2 Sensitivity analyses

12.2.1 Deterministic sensitivity analyses

The deterministic sensitivity analyses were done by varying one parameter at a time to its lower and upper bound. For parameters without published sensitivity estimates, an uncertainty of 10% was assumed. The results obtained from deterministic one-way sensitivity analyses versus Kd are presented in Table 51, and illustrated as a tornado diagram Figure 20. The deterministic one-way sensitivity analyses versus PVd are presented in Table 52 and Figure 23.

Table 51. One-way sensitivity analyses results versus Kd

	Lower bound parameter	Upper bound parameter	Incr cost lower bound (DKK)	Incr cost upper bound (DKK)	Difference (DKK)
ToT Parametric Curves	Multivariant normal	Multivariant normal	-213,794.44	-273,738.73	59,944.29
Duration of subsequent therapy - Kd	31.46	46.80	-261,781.72	-209,695.00	52,086.72

IV administration (subsequent)	1,599.16	2,378.84	-210,797.72	-260,415.18	49,617.46
SC administration	1,599.16	2,378.84	-250,413.93	-220,798.97	29,614.96
OS Parametric Curves	Multivariant normal	Multivariant normal	-239,773.02	-224,586.93	15,186.09
Duration of subsequent therapy - Pd	31.46	46.80	-231,105.15	-240,107.75	9,002.60
Duration of subsequent therapy - KRd	31.46	46.80	-232,545.13	-238,667.78	6,122.66
PFS Parametric Curves	Multivariant normal	Multivariant normal	-241,373.21	-235,355.06	6,018.15
Duration of subsequent therapy - EloTd	31.46	46.80	-234,617.70	-236,595.21	1,977.50
Duration of subsequent therapy - Rd	31.46	46.80	-234,655.87	-236,557.03	1,901.16

Figure 20. Tornado diagram for the one-way sensitivity analyses versus Kd

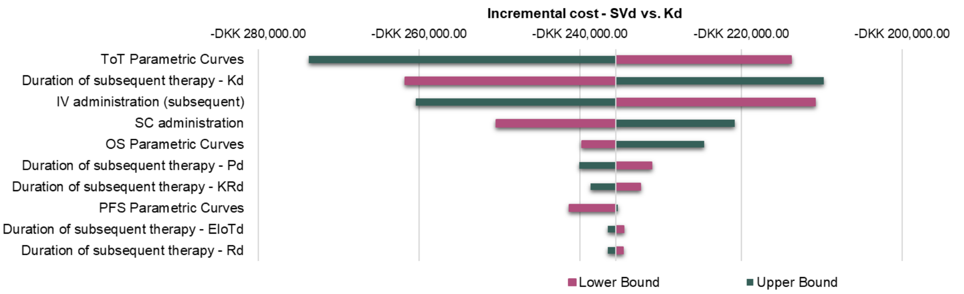
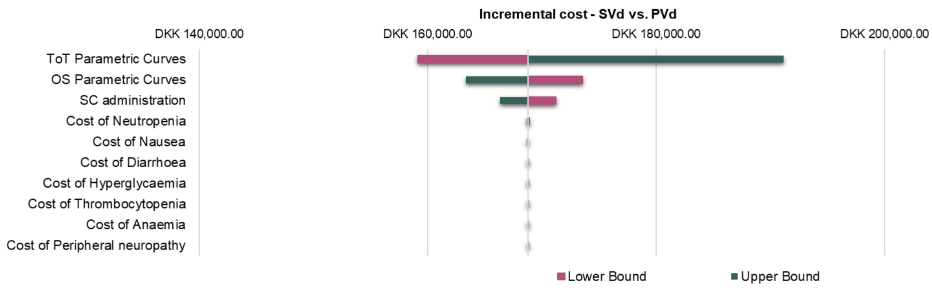


Table 52. One-way sensitivity analyses results versus PVd

	Lower bound parameter	Upper bound parameter	ICER lower bound (DKK)	ICER upper bound (DKK)	Difference (DKK)
ToT Parametric Curves	Multivariant normal	Multivariant normal	159,165.97	191,163.08	31,997.11
OS Parametric Curves	Multivariant normal	Multivariant normal	173,553.55	163,336.40	10,217.15

SC administration	1,599.16	2,378.84	171,224.32	166,318.69	4,905.63
Cost of Neutropenia	1,697.25	2,524.75	168,874.12	168,668.89	205.22
Cost of Nausea	6,285.70	9,350.30	168,730.90	168,812.11	81.21
Cost of Diarrhoea	6,285.70	9,350.30	168,807.95	168,735.06	72.89
Cost of Hyperglycaemia	1,484.99	2,209.01	168,790.82	168,752.19	38.63
Cost of Thrombocytopenia	1,697.25	2,524.75	168,785.24	168,757.77	27.47
Cost of Anaemia	1,697.25	2,524.75	168,784.37	168,758.65	25.72
Cost of Peripheral neuropathy	1,271.93	1,892.07	168,783.54	168,759.47	24.08

Figure 21. Tornado diagram for the one-way sensitivity analyses versus PVd



12.2.1.1 Scenario analysis

A series of scenarios were also conducted in order to test essential parameters. This included time horizon, discounting, curve selection and cost assumptions. PFS was not presented in scenario analysis due to the low impact of PFS on the results. Results are presented in Table 53.

Table 53. Scenario analyses

	Change Kd	Change PVd	Reason / Rational / Source	Incremental cost versus Kd (DKK)	Incremental cost versus PVd (DKK)
Base case	-			-235,606	168,772
Time horizon 5 years	-5.73%	-10.73%		-222,109	150,668

Time horizon 10 years	-3.13%	-3.40%	Impact of shorter time horizon	-228,231	163,028
0% discounting	3.54%	6.21%	Impact of discounting	-243,953	179,254
6% discounting	-1.90%	-3.52%		-231,140	162,829
Crossover adjustment: unadjusted	0.15%	0.09%	Impact of adjustments	-235,963	168,918
Crossover adjustment: adjusted without re-censoring	0.03%	0.02%		-235,673	168,799
Overall survival curves:					
Independent curves - exponential SVd	1.40%	1.25%	Curves selection	-238,905	170,886
Independent curves - Weibull SVd	-4.86%	-3.56%		-224,156	162,759
Independent curves - log-normal SVd	4.98%	1.65%		-247,332	171,558
Independent curves - log-logistic SVd	4.49%	1.65%		-246,174	171,557
Independent curves - Gompertz SVd	-11.54%	-9.47%		-208,419	152,796
Independent curves - generalised gamma SVd	-8.58%	-6.79%		-215,394	157,304
Independent curves - gamma SVd	-2.28%	-1.48%		-230,235	166,278
Dependent curves - exponential	-2.28%	1.25%		-230,235	170,886

Dependent curves - Weibull	-2.28%	-0.96%		-230,235	167,146
Dependent curves - log-normal	-2.28%	1.65%		-230,235	171,558
Dependent curves - log-logistic	-2.28%	1.65%		-230,235	171,558
Dependent curves - Gompertz	-2.28%	-7.93%		-230,235	155,388
Dependent curves - generalised gamma	-2.28%	-11.67%		-230,235	149,072
Time on treatment curves					
Independent curves - exponential SVd	-24.72%	-22.35%	Curve selection	-177,368	131,056
Independent curves - Weibull SVd	-25.06%	-24.03%		-176,561	128,216
Independent curves - log-normal SVd	-20.36%	-18.05%		-187,640	138,301
Independent curves - log-logistic SVd	-12.95%	-12.83%		-205,102	147,125
Independent curves - Gompertz SVd	-24.98%	-22.71%		-176,752	130,450
Independent curves - generalised gamma SVd	-23.46%	-21.65%		-180,333	132,239
Independent curves - gamma SVd	-23.46%	-21.65%		-180,333	132,239
Dependent curves - exponential	-24.72%	-22.35%		-177,368	131,056
Dependent curves - Weibull	-25.11%	-23.17%		-176,437	129,675

Dependent curves - log-normal	-5.92%	-4.41%		-221,664	161,333
Dependent curves - Gompertz	0.00%	0.00%		-235,606	168,772
Dependent curves - generalised gamma	-21.42%	-18.70%		-185,144	137,208
Dependent curves - gamma	-16.46%	-23.55%		-196,834	143,059
Exclude wastage	-77.95%	8.54%	Drug cost assumptions	-51,957	183,186
Exclude RDI	0.11%	0.00%		-235,863	168,772

12.2.2 Probabilistic sensitivity analyses

A PSA was conducted to estimate the total parameter uncertainty. The PSA contains all relevant parameters that are subject to uncertainty. The parameters were assigned the appropriate distributions. Sensitivity estimates were added from the reference if available. For parameters without published sensitivity estimates, an uncertainty of 10% was assumed. The full parameter list can be identified in Appendix G.

As the cost-minimization analysis did not include efficacy outcomes, the PSA only presented the impact of the uncertainty on the total cost. Therefore, the PSA results were presented as a convergence plot of incremental cost (Figure 22 and Figure 23).

As requested by the DMC on 20th Nov 2024, a strip chart showing the probabilistic incremental costs for Kd and PVd was added in Figure 24.

The average incremental cost result in the probabilistic analysis was DKK -242,495.55 versus Kd and DKK 172,215.09 versus PVd. The PSA results aligned overall with the deterministic results (DKK -235,606.45 versus Kd and DKK 168,771.51 versus PVd).

Figure 22. Convergence of incremental cost – SVd versus Kd

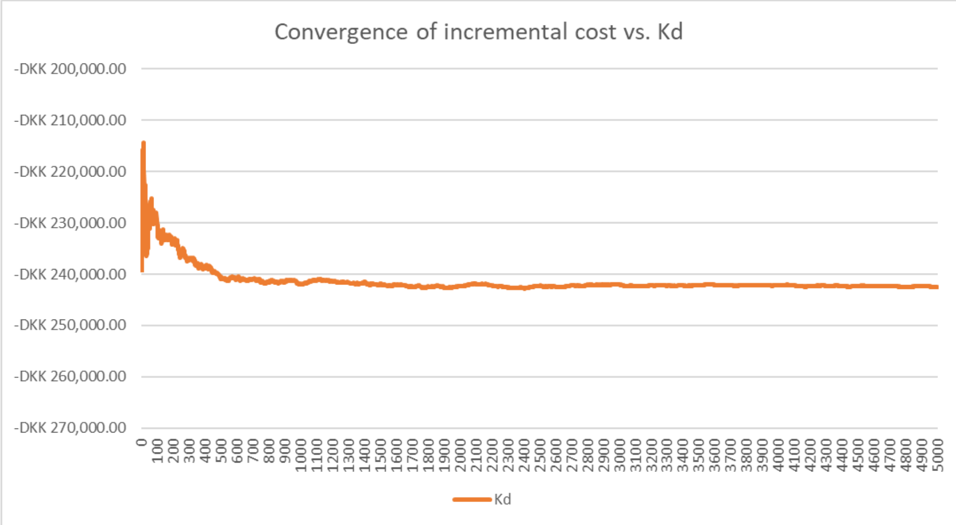


Figure 23. Convergence of incremental cost – SVd versus PVd

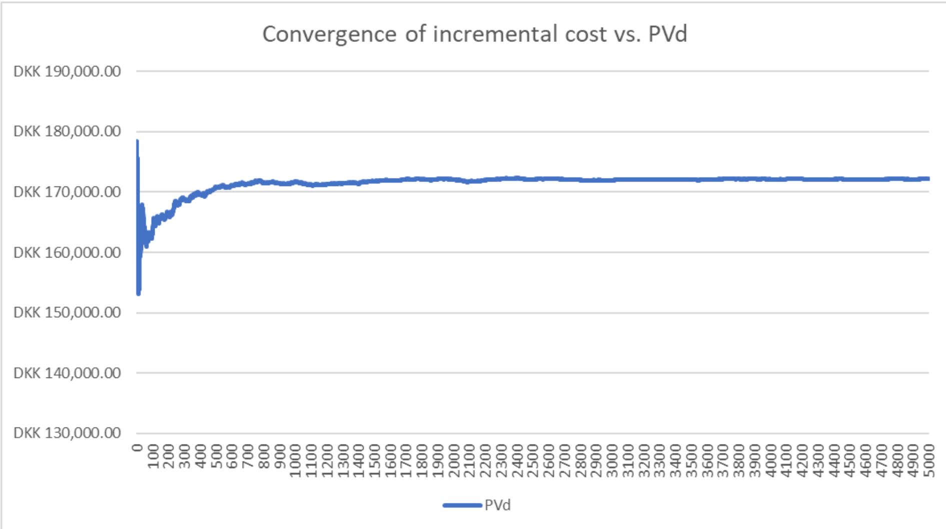
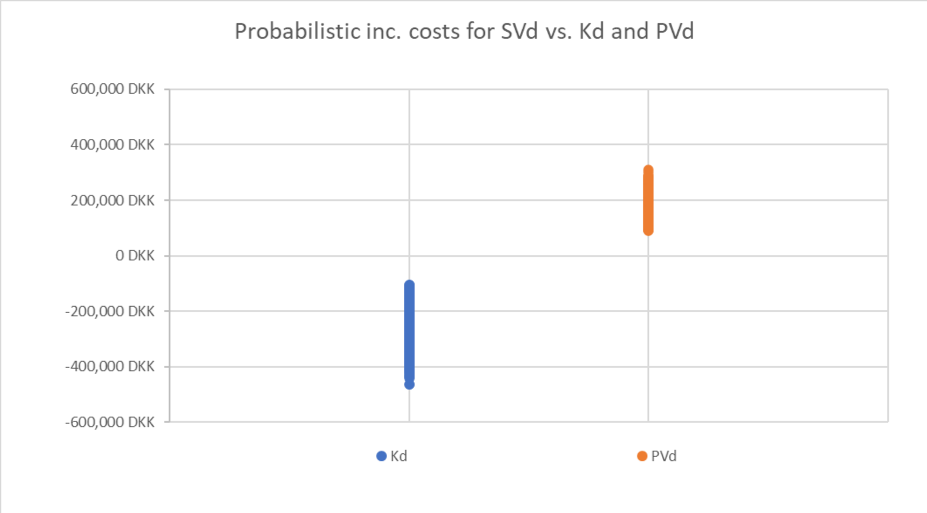


Figure 24. Probabilistic incremental costs for SVd vs Kd and PVd



12.2.3 Scenario analysis performed following DMC comments

As requested by the DMC on 20th Nov 2024, a scenario was conducted testing the use of PFS curve for SVd to estimate treatment costs "assuming PFS is censored out by toxicity".

Following the comments received on 19th December 2024, an additional scenario was added testing the exclusion of lenalidomide as subsequent treatment option

The use of TTD to estimate treatment length precisely reflect clinical data, as in BOSTON patients would receive treatment until PD was confirmed, investigator or patient decision to discontinue study treatment, pregnancy, unacceptable AEs or toxicity that could not be managed by supportive care, withdrawal of consent, death, or Sponsor decision to terminate the study. This is expected to be reflective in the Danish clinical practice. In the treatment of myeloma, both in clinical practice and in clinical trials patients may discontinue treatment despite having had an initial response and therefore it cannot be assumed patients have progressed at the time of treatment discontinuation and that TTD matches PFS. Therefore, using PFS as a proxy for treatment length results in loss of information and in a less accurate estimates of the expected clinical practice.

Assuming TTD=PFS results in higher savings for SVd vs Kd (incremental cost of -235,606 in the base case and -392,618 in the scenario) while increases the incremental cost of SVd vs PVd (168,772 in the base case vs 275,989 in the scenario)

Excluding lenalidomide from the subsequent treatment decreases the cost savings for SVd vs Kd (incremental cost of -235,606 in the base case and -206,168 in the scenario) and does not vary the incremental results vs PVd, as the analysis includes the same cost of subsequent treatments for SVd and Kd.

Table 54. Scenario analysis (TTD=PFS)

	Total cost	Incremental cost
Scenario with TTD=PFS		

SVd	2,025,202	-
Kd	2,417,820	-392,618
PVd	1,749,213	275,989
Scenario with no lenalidomide as subsequent treatment		
SVd	1,647,863	-
Kd	1,854,032	-206,168
PVd	1,479,092	168,772

13. Budget impact analysis

A budget impact model was constructed to outline the budgetary consequences of recommending SVd in Denmark. The cost input in the budget impact analysis originates from the cost-analysis, excluding discounting and patient costs.

Number of patients (including assumptions of market share)

The expected number of eligible patients are presented in section 3.2. As such, the budget impact model assumed 42 patients per year. It is assumed that the market share for Kd and PVd is split equally (i.e. 50% each). In the scenario where SVd is implemented, it is expected that SVd will have a market share of 30% in year 1, 50% in year 2, 60% in year 3 and 65% in year 4 and year 5. It is assumed that SVd's market share will come from the patients that are currently being treated with Kd and PVd. As such, in the scenario where SVd is recommended, Kd is assumed to have a market share of 35% in year 1, 25% in year 2, 15% in year 3 and 10% in year 4 and year 5, while PVd is assumed to have a market share of 35% in year 1 and 25% onwards.

Table 55. Number of new patients expected to be treated over the next five-year period if the medicine is introduced (adjusted for market share)

	Year 1	Year 2	Year 3	Year 4	Year 5
			Recommendation		
SVd	13	21	25	27	27
Kd	15	11	6	4	4
PVd	15	11	11	11	11
			Non-recommendation		
SVd	0	0	0	0	0

Kd	21	21	21	21	21
PVd	21	21	21	21	21

Budget impact

Table 56. Expected budget impact of recommending the medicine for the indication

	Year 1 (DKK)	Year 2 (DKK)	Year 3 (DKK)	Year 4 (DKK)	Year 5 (DKK)
The medicine under consideration is recommended	20,582,646	32,478,253	37,697,648	41,301,410	44,109,322
The medicine under consideration is NOT recommended	17,563,631	24,795,468	29,288,018	32,347,071	34,484,417
Budget impact of the recommendation	3,019,015	7,682,785	8,409,630	8,954,339	9,624,905

14. List of experts

Not applicable.

15. References

1. European Medicines Agency. Nexpovio - Summary of Product Characteristics. 2021.
2. Medicinraadet. Medicinrådets lægemiddelrekommandation og behandlingsvejledning vedrørende lægemidler til knoglemarvskræft (myelomatose) (version 1.11). 2024.
3. Medicinraadet. Baggrund for Medicinrådets behandlingsvejledning vedrørende lægemidler til knoglemarvskræft (myelomatose). 2020.
4. Yong K, Delforge M, Driessen C, et al. Multiple myeloma: patient outcomes in real-world practice. *Br J Haematol* 2016; **175**(2): 252-64.
5. Grosicki S, Simonova M, Spicka I, et al. Once-per-week selinexor, bortezomib, and dexamethasone versus twice-per-week bortezomib and dexamethasone in patients with multiple myeloma (BOSTON): a randomised, open-label, phase 3 trial. *Lancet* 2020; **396**(10262): 1563-73.
6. Dimopoulos MA, Moreau P, Palumbo A, et al. Carfilzomib and dexamethasone versus bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma (ENDEAVOR): a randomised, phase 3, open-label, multicentre study. *Lancet Oncol* 2016; **17**(1): 27-38.
7. Richardson PG, Oriol A, Beksac M, et al. Pomalidomide, bortezomib, and dexamethasone for patients with relapsed or refractory multiple myeloma previously treated with lenalidomide (OPTIMISMM): a randomised, open-label, phase 3 trial. *Lancet Oncol* 2019; **20**(6): 781-94.
8. Karyopharm Therapeutics Inc. Clinical Study Report (KCP-330-023), 2021.
9. Association of the Nordic Cancer Registries. Nordcan 2.0 - Multiple Myeloma. 2024. https://nordcan.iarc.fr/en/dataviz/tables?cancers=380.
10. Dansk Myelomatose Studie Gruppe. Dansk Myelomatose Database (DaMyDa) - Årsrapport 2023. 2024.
11. Gandhi UH, Senapedis W, Baloglu E, et al. Clinical Implications of Targeting XPO1-mediated Nuclear Export in Multiple Myeloma. *Clin Lymphoma Myeloma Leuk* 2018; **18**(5): 335-45.
12. Palumbo A, Anderson K. Multiple myeloma. *N Engl J Med* 2011; **364**(11): 1046-60.
13. Palumbo A, Bringhen S, Mateos MV, et al. Geriatric assessment predicts survival and toxicities in elderly myeloma patients: an International Myeloma Working Group report. *Blood* 2015; **125**(13): 2068-74.
14. Rajkumar SV, Kumar S. Multiple Myeloma: Diagnosis and Treatment. *Mayo Clin Proc* 2016; **91**(1): 101-19.
15. Sive J, Cuthill K, Hunter H, et al. Guidelines on the diagnosis, investigation and initial treatment of myeloma: a British Society for Haematology/UK Myeloma Forum Guideline. *Br J Haematol* 2021; **193**(2): 245-68.
16. Ocio EM, Montes-Gaisán C, Bustamante G, et al. Clinical and Sociodemographic Characteristics of Patients With Relapsed and/or Refractory Multiple Myeloma and Their influence on Treatment in the Real-World Setting in Spain: The CharisMMa Study. *Clin Lymphoma Myeloma Leuk* 2022; **22**(4): e241-e9.
17. Ramsenthaler C, Kane P, Gao W, et al. Prevalence of symptoms in patients with multiple myeloma: a systematic review and meta-analysis. *Eur J Haematol* 2016; **97**(5): 416-29.
18. Seesaghur A, Petruski-Ivleva N, Banks VL, et al. Clinical features and diagnosis of multiple myeloma: a population-based cohort study in primary care. *BMJ Open* 2021; **11**(10): e052759.
19. Sverrisdóttir IS, Rögnvaldsson S, Thorsteinsdottir S, et al. Comorbidities in multiple myeloma and implications on survival: A population-based study. *Eur J Haematol* 2021; **106**(6): 774-82.

20. Benkova K, Mihalyova J, Hajek R, Jelinek T. Selinexor, selective inhibitor of nuclear export: Unselective bullet for blood cancers. *Blood Reviews* 2021; **46**: 100758.
21. International Myeloma Foundation (Durie B, . Concise Review of the Disease and Treatment Options: Multiple Myeloma, 2018.
22. Rajkumar SV. Multiple myeloma: 2020 update on diagnosis, risk-stratification and management. *American journal of hematology* 2020; **95**(5): 548-67.
23. Verelst S, Blommestein H, De Groot S, et al. Long-term Outcomes in Patients With Multiple Myeloma: A Retrospective Analysis of the Dutch Population-based HAematological Registry for Observational Studies (PHAROS). *HemaSphere* 2018; **2**(4): e45.
24. Hájek R, Jarkovsky J, Maisnar V, et al. Real-world Outcomes of Multiple Myeloma: Retrospective Analysis of the Czech Registry of Monoclonal Gammopathies. *Clin Lymphoma Myeloma Leuk* 2018; **18**(6): e219-e40.
25. Willson J, Bruno A, Opalinska J, et al. Current real-world treatment patterns and outcomes in patients with relapsed/refractory multiple myeloma. *Journal of Clinical Oncology* 2018; **36**(15_suppl): e20038-e.
26. Ramsenthaler C, Osborne TR, Gao W, et al. The impact of disease-related symptoms and palliative care concerns on health-related quality of life in multiple myeloma: a multi-centre study. *BMC Cancer* 2016; **16**: 427.
27. Medicinraadet. Baggrund for Medicinrådets behandlingsvejledning vedrørende lægemidler til knoglemarvskræft

(myelomatose). 2020.
28. Danmarks Statistik. BEFOLK2: Befolkningen 1. januar efter køn og alder. 2024. https://www.statistikbanken.dk/BEFOLK2.
29. Kræftens Bekæmpelse. Første behandlingsvalg ved myelomatose. 2021. https://www.cancer.dk/myelomatose-knoglemarvskraeft/behandling/rettet-mod-myelomatosecellerne/foerste-behandlingsvalg/.
30. Medicinraadet. Medicinrådets anbefaling vedr. teclistamab til knoglemarvskræft, vers. 1.0. 2024.
31. Talati C, Sweet K. Nuclear transport inhibition in acute myeloid leukemia: recent advances and future perspectives. *International Journal of Hematologic Oncology* 2018; **7**(3): IJH04.
32. Peterson TJ, Orozco J, Buege M. Selinexor: A First-in-Class Nuclear Export Inhibitor for Management of Multiply Relapsed Multiple Myeloma. *The Annals of pharmacotherapy* 2020; **54**(6): 577-82.
33. Mo CC, Jagannath S, Chari A, et al. Selinexor for the treatment of patients with previously treated multiple myeloma. *Expert Rev Hematol* 2021; **14**(8): 697-706.
34. Richard S, Jagannath S. Targeting Nuclear Export Proteins in Multiple Myeloma Therapy. *BioDrugs : clinical immunotherapeutics, biopharmaceuticals and gene therapy* 2022; **36**(1): 13-25.
35. European Medicines Agency. Assessment report - Nexpovio - Procedure No. EMEA/H/C/005127/0000. 2021.
36. European Commission. COMMISSION IMPLEMENTING DECISION of 18.7.2022 - granting marketing authorisation under Regulation (EC) No 726/2004 of the European Parliament and of the Council for "NEXPOVIO - selinexor", a medicinal product for human use and repealing Decision C(2021)2299(final). 2022.
37. Dimopoulos MA, Moreau P, Terpos E, et al. Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up(dagger). *Ann Oncol* 2021; **32**(3): 309-22.
38. European Medicines Agency. Imnovid - Summary of Product Characteristics. 2023.
39. Rosenberg AS. From mechanism to resistance - changes in the use of dexamethasone in the treatment of multiple myeloma. *Leuk Lymphoma* 2023; **64**(2): 283-91.

40. Danish Medicines Agency. Produktresumé for Dexamethason "2care4", tabletter (2care4), 2023.
41. Woods B, Sideris E, Palmer S, Latimer N, Soares M. NICE DSU TSD 19: Partitioned Survival Analysis as a decision modelling tool2nd June 2017, 2017. http://nicedsu.org.uk/wp-content/uploads/2017/06/Partitioned-Survival-Analysis-final-report.pdf (accessed.
42. Higgins JPT, Thomas J, Chandler J, et al. Cochrane Handbook for Systematic Reviews of Interventions (version 6.0), Updated July 2019.
43. National Institute for Health and Care Excellence (NICE). PMG36: NICE health technology evaluations: the manual, 2022.
44. Tolley Health Economics Ltd. Selinexor versus comparators for the treatment of RRMM: a clinical systematic review, 2023.
45. Menarini Stemline. Clinical Study Report KCP-330-023: A PHASE 3 RANDOMIZED, CONTROLLED, OPEN-LABEL STUDY OF SELINEXOR, BORTEZOMIB, AND DEXAMETHASONE (SVd) VERSUS BORTEZOMIB AND DEXAMETHASONE (Vd) IN PATIENTS WITH RELAPSED OR REFRACTORY MULTIPLE MYELOMA (RRMM), 2021.
46. Clinicaltrials.gov. Bortezomib, Selinexor, and Dexamethasone in Patients With Multiple Myeloma (BOSTON). 2023. https://clinicaltrials.gov/study/NCT031105622023).
47. Orlowski RZ, Moreau P, Niesvizky R, et al. Carfilzomib-Dexamethasone Versus Bortezomib-Dexamethasone in Relapsed or Refractory Multiple Myeloma: Updated Overall Survival, Safety, and Subgroups. *Clin Lymphoma Myeloma Leuk* 2019; **19**(8): 522-30 e1.
48. Clinicaltrials.gov. Phase 3 Study With Carfilzomib and Dexamethasone Versus Bortezomib and Dexamethasone for Relapsed Multiple Myeloma Patients (ENDEAVOR). 2022. https://www.clinicaltrials.gov/study/NCT01568866.
49. Clinicaltrials.gov. Safety and Efficacy of Pomalidomide, Bortezomib and Low-dose Dexamethasone in Subjects With Relapsed or Refractory Multiple Myeloma (OPTIMISMM). 2023. https://clinicaltrials.gov/study/NCT01734928.
50. National Institute for Health and Care Excellence (NICE). TA897: Daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma. 2023. https://www.nice.org.uk/guidance/ta897.
51. Lau IJ, Smith D, Aitchison R, et al. Bendamustine in combination with thalidomide and dexamethasone is a viable salvage option in myeloma relapsed and/or refractory to bortezomib and lenalidomide. *Ann Hematol* 2015; **94**(4): 643-9.
52. Dimopoulos MA, Moreau P, Palumbo A, et al. Carfilzomib and dexamethasone versus bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma (ENDEAVOR): a randomised, phase 3, open-label, multicentre study. *The Lancet Oncology* 2016; **17**(1): 27-38.
53. Medicinraadet. Medicinrådets anbefaling vedr. ciltacabtagene autoleucel til behandling af patienter med knoglemarvskræft, som har fået mindst tre tidligere terapier. 2024.
54. Mateos MV, Engelhardt M, Leleu X, et al. Impact of prior treatment on selinexor, bortezomib, dexamethasone outcomes in patients with relapsed/refractory multiple myeloma: Extended follow-up subgroup analysis of the BOSTON trial. *Eur J Haematol* 2024; **113**(2): 242-52.
55. Menarini Stemline. Data on file, 2023.
56. Beksac M, Richardson P, Oriol A, et al. OA-44 Pomalidomide, bortezomib, and dexamethasone vs bortezomib and dexamethasone in relapsed or refractory multiple myeloma (OPTIMISMM): final survival outcomes from a randomized, open-label, phase 3 trial. *Clinical Lymphoma Myeloma and Leukemia* 2023; **23**: S27-S8.
57. Rucker G. Network meta-analysis, electrical networks and graph theory. *Res Synth Methods* 2012; **3**(4): 312-24.

58. Balduzzi S, Rücker G, Nikolakopoulou A, et al. netmeta: An R Package for Network Meta-Analysis Using Frequentist Methods. *Journal of Statistical Software* 2023; **106**(2).
59. Latimer N. NICE DSU TECHNICAL SUPPORT DOCUMENT 14: SURVIVAL ANALYSIS FOR ECONOMIC EVALUATIONS ALONGSIDE CLINICAL TRIALS - EXTRAPOLATION WITH PATIENT-LEVEL DATA: DECISION SUPPORT UNIT - NICE DSU - School of Health and Related Research, University of Sheffield, UK, 2011.
60. Latimer NR, Abrams KR, Lambert PC, et al. Adjusting for treatment switching in randomised controlled trials - A simulation study and a simplified two-stage method. *Stat Methods Med Res* 2017; **26**(2): 724-51.
61. Tolley Health Economics. Selinexor HE Advisory Board Report. 2023.
62. Medicines and Healthcare products Regulatory Agency (MHRA). Summary of Product Characteristics: Nexpovio, 2023.
63. Dimopoulos MA, Goldschmidt H, Niesvizky R, et al. Carfilzomib or bortezomib in relapsed or refractory multiple myeloma (ENDEAVOR): an interim overall survival analysis of an open-label, randomised, phase 3 trial. *The lancet oncology* 2017; **18**(10): 1327-37.
64. National Institute for Health and Care Excellence. Developing NICE guidelines: the manual: - 5 Identifying the evidence: literature searching and evidence submission, 2014.
65. McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement. *J Clin Epidemiol* 2016; **75**: 40-6.
66. Centre for Reviews and Dissemination (CRD). Systematic reviews: CRD's guidance for undertaking reviews in health care.: University of York, 2009.
67. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015; **4**(1).
68. McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement. *Journal of Clinical Epidemiology* 2016; **75**: 40-6.
69. Cooper C, Booth A, Varley-Campbell J, Britten N, Garside R. Defining the process to literature searching in systematic reviews: a literature review of guidance and supporting studies. *BMC Medical Research Methodology* 2018; **18**(1): 85.
70. Piechotta V, Jakob T, Langer P, et al. Multiple drug combinations of bortezomib, lenalidomide, and thalidomide for first-line treatment in adults with transplant-ineligible multiple myeloma: a network meta-analysis. *The Cochrane database of systematic reviews* 2019; (11).
71. He Y, Wheatley K, Clark O, Glasmacher A, Ross H, Djulbegovic B. Early versus deferred treatment for early stage multiple myeloma. *The Cochrane database of systematic reviews* 2003; (1).
72. Kahale LA, Matar CF, Tsolakian I, et al. Antithrombotic therapy for ambulatory patients with multiple myeloma receiving immunomodulatory agents. *The Cochrane database of systematic reviews* 2021; **9**(9).
73. Glanville J. The ISSG search filters resource. *J Euro Assoc Health Info Libs,* 2006; **2**(2): 14-6.
74. Suzy Paisley, Andrew Booth, Shaila Mensinkai. Chapter 12: Health-related Quality of Life Studies; 2005.
75. Kvam AK, Waage A. Health-related quality of life in patients with multiple myeloma - does it matter? *Haematologica* 2015; **100**(6): 704-5.
76. Sonneveld P, Verelst SG, Lewis P, et al. Review of health-related quality of life data in multiple myeloma patients treated with novel agents. *Leukemia* 2013; **27**(10): 1959-69.

77. Paul Levay. Systematic searching in Ovid Embase: understanding the MEDLINE document collection and identifying conference records. 2022. http://medrxiv.org/content/early/2022/04/27/2022.04.23.22274201.abstract.

Appendix A. Main characteristics of studies included

Table 57. Main characteristics of BOSTON

Trial name: BOSTON	NCT number: NCT03110562
Objective	To compare the efficacy and HRQoL and assess the safety of SVd versus Vd in adult patients with RRMM who have received 1 to 3 prior anti-MM regimens
Publications – title, author, journal, year	Auner, H. W.; Gavriatopoulou, M.; Delimpasi, S.; Simonova, M.; Spicka, I.; Pour, L.; Dimopoulos, M. A.; Kriachok, I.; Pylypenko, H.; Leleu, X.; Doronin, V.; Usenko, G.; Hajek, R.; Benjamin, R.; Dolai, T. K.; Sinha, D. K.; Venner, C. P.; Garg, M.; Stevens, D. A.; Quach, H.; Jagannath, S.; Moreau, P.; Levy, M.; Badros, A.; Anderson, L. D., Jr.; Bahlis, N. J.; Facon, T.; Mateos, M. V.; Cavo, M.; Chai, Y.; Arazy, M.; Shah, J.; Shacham, S.; Kauffman, M. G.; Richardson, P. G.; Grosicki, S.. Effect of age and frailty on the efficacy and tolerability of once-weekly selinexor, bortezomib, and dexamethasone in previously treated multiple myeloma. 2021. American Journal of Hematology. 96:6 (708-718). Benjamin, R.; Garg, M.; Basu, S.; Chai, Y.; DeCastro, A.; Boulhabel, F.; Shah, J.; Auner, H.. Outcomes of Patients (pts) with Previously Treated Multiple Myeloma (MM) from European Countries and the United Kingdom, Treated with Selinexor, Bortezomib and Dexamethasone (XVd) Versus Bortezomib and Dexamethasone (Vd): A Post Hoc Analysis from the . 2022. British Journal of Haematology. 197(SUPPL 1): (127-128). Dolph, M.; Tremblay, G.; Leong, H.. Cost Effectiveness of Triplet Selinexor-Bortezomib-Dexamethasone (XVd) in Previously Treated Multiple Myeloma (MM) Based on Results from the Phase III BOSTON Trial. 2021. PharmacoEconomics. 39:11 (1309-1325). EUCTR, B. E.. Bortezomib, Selinexor and Dexamethasone in Patients with Multiple Myeloma. 2017. https://trialsearch.who.int/Trial2.aspx?TrialID=EUCTR2016-003957-14-BE. Facon, T.; Auner, H.; Gavriatopoulou, M.; Delimpasi, S.; Simonova, M.; Spicka, I.; Pour, L.; Dimopoulos, M.; Kriachok, I.; Pylypenko, H.; et al.. Survival among older patients with previously treated multiple myeloma treated with selinexor, bortezomib, and dexamethasone (xvd) in the boston study. 2021. Hemasphere. 5:SUPPL 2 (458). Facon, T; Auner, H; Gavriatopoulou, M; Delimpasi, S; Simonova, M; Spicka, I; Pour, L; Dimopoulos, M; Kriachok, I; Pylypenko, H; Leleu, X; Quach, H; Benjamin, R; Dolai, T; Sinha, D; Garg, M; Stevens, D; Shah, J; Richardson, P; Grosicki, S. EP976: survival among older patients with previously treated

multiple myeloma treated with selinexor, bortezomib, and dexamethasone (xvd) in the boston study. 2021.

Facon, T.; Auner, H. W.; Gavriatopoulou, M.; Delimpasi, S.; Simonova, M.; Spicka, I.; Pour, L.; Dimopoulos, M. A.; Kriachok, I.; Pylypenko, H.; et al. Survival among older patients with previously treated multiple myeloma treated with selinexor, bortezomib, and dexamethasone (XVd) in the BOSTON study. 2021. Journal of clinical oncology. 39:15.

Grosicki, S.; Simonova, M.; Spicka, I.; Pour, L.; Kriachok, I.; Gavriatopoulou, M.; Pylypenko, H.; Auner, H. W.; Leleu, X.; Doronin, V.; et al. Once-per-week selinexor, bortezomib, and dexamethasone versus twice-per-week bortezomib and dexamethasone in patients with multiple myeloma (BOSTON): a randomised, open-label, phase 3 trial. 2020. Lancet (london, england). 396:10262 (1563-1573).

Jagannath, S.; Facon, T.; Badros, A. Z.; Levy, M.; Moreau, P.; Delimpasi, S.; Simonova, M.; Spicka, I.; Kriachok, I.; Gavriatopoulou, M.; Pylypenko, H.; Auner, H. W.; Leleu, X.; Doronin, V.; Usenko, G.; Hajek, R.; Benjamin, R.; Dolai, T. K.; Sinha, D. K.; Venner, C. P.; Garg, M.; Mesa, M. G.; Jurczyszyn, A.; Robak, T.; Galli, M.; Wallington-Beddoe, C. T.; Radinoff, A.; Salogub, G.; Stevens, D.; Basu, S.; Liberati, A. M.; Quach, H.; Marinova, V. S. G.; Bila, J. S.; Katodritou, E.; DeCastro, A.; Chai, Y.; Van Domelen, D. R.; Mishal, M.; Bentur, O. S.; Shah, J.; Shacham, S.; Kauffman, M. G.; Grosicki, S.; Richardson, P. G.. Clinical outcomes in patients (pts) with dose reduction of selinexor in combination with bortezomib, and dexamethasone (XVD) in previously treated multiple myeloma from the Boston study. 2021. Blood. 138(SUPPL 1): (3793).

Leleu, X.; Mateos, M. V.; Jagannath, S.; Delimpasi, S.; Simonova, M.; Spicka, I.; Pour, L.; Kriachok, I.; Gavriatopoulou, M.; Dimopoulos, M.; et al. Efficacy and safety of selinexor, bortezomib, and dexamethasone based on refractory status to lenalidomide in patients with previously treated multiple myeloma: a post-hoc analysis of the boston study. 2021. Hemasphere. 5: SUPPL 2 (456-457).

Leleu, X.; Mateos, M. V.; Jagannath, S.; Delimpasi, S.; Simonova, M.; Spicka, I.; Pour, L.; Kriachok, I.; Gavriatopoulou, M.; Dimopoulos, M. A.; et al. Effects of refractory status to lenalidomide on safety and efficacy of selinexor, bortezomib, and dexamethasone (XVd) versus bortezomib and dexamethasone (Vd) in patients with previously treated multiple myeloma. 2021. Journal of clinical oncology. 39:15.

Leleu, X; Mateos, M; Jagannath, S; Delimpasi, S; Simonova, M; Spicka, I; Pour, L; Kriachok, I; Gavriatopoulou, M; Dimopoulos, M; Pylypenko, H; Auner, H; Benjamin, R; Venner, C; Garg, M; DeCastro, A; Chai, Y; Shah, J; Grosicki, S; Richardson, P. EP974: efficacy and safety of selinexor, bortezomib, and dexamethasone based on refractory status to lenalidomide in patients with previously treated multiple myeloma: a post-hoc analysis of the boston study. 2021.

Mateos, M. V.; Engelhardt, M.; Leleu, X.; Mesa, M. G.; Auner, H.W.; Cavo, M.; Dimopoulos, M.A.; Bianco, M.; Merlo, G.M.; La Porte, C.; Moreau P. P886: efficacy, survival and safety of selinexor, bortezomib and dexamethasone (SVd) in patients with lenalidomide-refractory multiple myeloma: subgroup data from the BOSTON trial. 2023.

Mateos, M.M.; Engelhardt, M.; Leleu, X.; Mesa, M.G.; Auner, H.W.; Cavo, M.; Dimopoulos, M.A.; Bianco, M.; Merlo, G.M.; La Porte, C.; Moreau, P. P917:

selinexor, bortezomib, and dexamethasone in patients with previously treated multiple myeloma: updated results of BOSTON trial by prior therapies. 2023.

Mateos, M. V.; Engelhardt, M.; Leleu, X.; Mesa, M. G.; Cavo, M.; Dimopoulos, M.; Bianco, M.; Merlo, G. M.; La Porte, C.; Moreau, P. Selinexor, bortezomib, and dexamethasone in patients with previously treated multiple myeloma (MM): Updated results of BOSTON trial by prior therapies. 2023. Oncology Research and Treatment. 46:Supplement 5 (176).

Mateos, M. V.; Engelhardt, M.; Leleu, X.; Mesa, M. G.; Cavo, M.; Dimopoulos, M.; Bianco, M.; Merlo, G. M.; La Porte, C.; Moreau, P. Eftcacy, survival and safety of selinexor, bortezomib and dexamethasone (SVd) in patients with lenalidomiderefractory multiple myeloma: Subgroup data from the BOSTON Trial. 2023. Oncology Research and Treatment. 46:Supplement 5 (235).

NCT. Bortezomib, Selinexor, and Dexamethasone in Patients With Multiple Myeloma. 2017. https://clinicaltrials.gov/show/ NCT03110562.

Reuben B, Mamta Garg Supratik Basu Yi Chai Andrew DeCastro Faouzia Boulhabel Jatin Shah Holger Auner. BSH22-PO81 | Outcomes of Patients (pts) with Previously Treated Multiple Myeloma (MM) from European Countries and the United Kingdom, Treated with Selinexor, Bortezomib and Dexamethasone (XVd) Versus Bortezomib and Dexamethasone (Vd): A Post Hoc Analysis. 2022.

Richard, S.; Chari, A.; Delimpasi, S.; Simonova, M.; Spicka, I.; Pour, L.; Kriachok, I.; Dimopoulos, M. A.; Pylypenko, H.; Auner, H. W.; et al.. Selinexor, bortezomib, and dexamethasone versus bortezomib and dexamethasone in previously treated multiple myeloma: outcomes by cytogenetic risk. 2021. American journal of hematology. 96:9 (1120-1130).

Thierry F, Holger W. Auner Maria Gavriatopoulou Sosana Delimpasi Maryana Simonova Ivan Spicka LudÄ›k Pour Meletios A. Dimopoulos Iryna Kriachok Halyna Pylypenko Xavier Leleu Hang Quach Benjamin Reuben Tuphan Kanti Dolai Dinesh Kumar Sinha Mamta Garg Don A. Stevens Jatin J. Shah Paul G. Richardson Sebastian Grosicki. 8019: Survival among older patients with previously treated multiple myeloma treated with selinexor, bortezomib, and dexamethasone (XVd) in the BOSTON study. 2021.

EUCTR2016-003957-14-HU. Bortezomib, Selinexor and Dexamethasone in Patients with Multiple Myeloma.

White, D.; Chen, C.; Baljevic, M.; Tuchman, S.; Bahlis, N. J.; Schiller, G. J.; Lipe, B.; Kotb, R.; Sutherland, H. J.; Madan, S.; Sebag, M.; Lentzsch, S.; Callander, N. S.; Biran, N.; Venner, C. P.; LeBlanc, R.; Rossi, A. C.; Zhou, T.; Gasparetto, C.. Oral selinexor, pomalidomide, and dexamethasone (XPd) at recommended phase 2 dose in relapsed refractory multiple myeloma (MM). 2021. Journal of Clinical Oncology. Conference: Annual Meeting of the American Society of Clinical Oncology, ASCO. 39:15.

Xavier Leleu, Maria-Victoria Mateos Sundar Jagannath Sosana Delimpasi Maryana Simonova Ivan Spicka LudÄ›k Pour Iryna Kriachok Maria Gavriatopoulou Meletios A. Dimopoulos Halyna Pylypenko Holger W. Auner Benjamin Reuben Vadim Doronin Christopher P. Venner Mamta Garg Andrew DeCastro Jatin J. Shah Sebastian Grosicki Paul G. Richardson. 8024: Effects of refractory status to lenalidomide on safety and efficacy of selinexor, bortezomib, and dexamethasone (XVd) versus bortezomib and

	dexamethasone (Vd) in patients with previously treated multiple myeloma. 2021. Ctri. Study of Selinexor, Bortezomib, AND Dexamethasone Versus Bortezomib and Dexamethasone In Patients With Relapsed Or Refractory Multiple Myeloma. 2017. https://trialsearch.who.int/Trial2.aspx?TrialID=CTRI/2017/11/010561.
Study type and design	A Phase 3, 2-arm, randomized, active comparator-controlled, open-label, multicenter study. Enrolled patients were randomly assigned 1:1 to either SVd of Vd using interactive response technology and stratified by previous proteasome inhibitor therapy, lines of treatment, and MM stage. Crossover from the Vd Arm to a treatment that includes selinexor (i.e., SVdX or SdX) was allowed at the point of IRC-confirmed objective disease progression per the IMWG criteria for patients in the Vd Arm. The study is completed, and results were first posted in 2020.
Sample size (n)	SVd Arm: 195 Vd Arm: 207
Main inclusion criteria	Patients were eligible if they were aged 18 years or older, had measurable myeloma according to the IMWG criteria18 with documented evidence of progressive disease on or after their most recent treatment regimen, and had previously received treatment with at least one, but no more than three, different regimens for MM. Patients who had previously received proteasome inhibitors (alone or as part of a combination treatment) were required to have had at least a partial response to the therapy and at least a 6-month interval since their last proteasome inhibitor therapy, with no history of discontinuation of bortezomib due to grade 3 or higher toxicity. Patients were also required to have an ECOG performance status score of 0–2, and adequate hepatic, renal, and haematopoietic function.
Main exclusion criteria	Patients were excluded if they had systemic light-chain amyloidosis, CNS involvement, or grade 2 painful or grade 2 or higher peripheral neuropathy.
Intervention	SVd (195): Participants received a fixed oral dose of 100 mg selinexor tablets (5 tablets of 20 mg each) QW on Days 1, 8, 15, 22, and 29 of each 35-day cycle, along with SC injection of 1.3 mg/m^2 bortezomib QW on Days 1, 8, 15, and 22 of each 35-day cycle, and an oral dose of 20 mg of dexamethasone BIW on Days 1, 2, 8, 9, 15, 16, 22, 23, 29, and 30 of each 35-day cycle until PD confirmed by the IRC, investigator or participant decision to discontinue study treatment, pregnancy, unacceptable AEs or toxicity that could not be managed by supportive care, withdrawal of consent, death, or sponsor decision to terminate the study.
Comparator(s)	Vd (207): Participants received SC injection of 1.3 mg/m^2 bortezomib QW on Days 1, 4, 8, and 11 of each 21-day cycle for the first 8 cycles, followed by greater than or equal to (>=) 9 cycles on Days 1, 8, 15, and 22 of each 35-day cycle, and received oral dose of 20 mg dexamethasone BIW on Days 1, 2, 4, 5, 8, 9, 11, and 12 of each 21-day cycle for the first 8 cycles and for cycles >= 9 on Days 1, 2, 8, 9, 15, 16, 22, 23, 29, and 30 of each 35-day cycle until PD

	confirmed by the IRC, investigator or participant decision to discontinue study treatment, pregnancy, unacceptable AEs or toxicity that could not be managed by supportive care, withdrawal of consent, death, or sponsor decision to terminate the study.
Follow-up time	Median follow-up durations were 13.2 months [IQR 6.2–19.8] for the SVd group and 16.5 months [9.4–19.8] for the Vd group.
Is the study used in the health economic model?	Yes.
Primary, secondary and exploratory endpoints	**Endpoints included in this application:** The primary endpoint was PFS defined as time from randomisation until the first disease progression (determined by the independent review committee) per IMWG response criteria, or until death from any cause in the intention-to-treat population. Prespecified secondary endpoints included OS and safety and tolerability of study treatment;. **Other endpoints:** Overall response rate, duration of response, PFS on the subsequent line of therapy; time to next anti-MM treatment; time to response; incidence of any grade 2 or higher peripheral neuropathy events; and patient-reported peripheral neuropathy as measured by the Quality of Life– Chemotherapy-Induced Peripheral Neuropathy questionnaire (QLQ-CIPN20) from the EORTC were included as secondary endpoints in the study, but results are not included in this application.
Method of analysis	The ITT population included all enrolled patients who met all eligibility criteria and was used for the primary efficacy analysis. The safety population included all patients who received at least one dose of study treatment. PFS was compared between the SVd group and the Vd group with a stratified log-rank test. HRs and corresponding 95% CIs were estimated with use of a stratified Cox proportional hazards model, with treatment as the single covariate. A stratified Cochran-Mantel-Haenszel χ^2 test was used to test differences in ORRs between the two groups. One-sided p values are presented for efficacy endpoints.
Subgroup analyses	The data presented in this submission is based on the post-hoc subpopulation of lenalidomide-refractory patients. Progression-free survival was analysed on the following pre-specified subgroups: • Previous proteasome inhibitor therapy (Yes, No) • Previous lines of anti-multiple myeloma therapy (One, Two, Three, Two or more) • Previous stem-cell transplantation (Yes, No) • Previous therapy (Bortezomib, Carfilzomib, Daratumumab, Lenalidomide)

- Baseline R-ISS stage (I-II, I, II, III)
- High-risk cytogenetic abnormalities (del(17p), t(4;14), t(14;16), del(17p) or t(4;14) or t(14;16), 1q21 amplification, Any of the above)
- Estimated creatinine clearance (mL/min) (30–60, >60)
- Baseline ECOG score (0, 1, 2)
- Age (years) (<65, ≥65)
- Frailty (Frail, Non-frail)
- Sex (Male, Female)
- Race (White, Others combined)
- Hispanic or Latino ethnicity (Yes, No)
- Region (1, 2, 3, 4)

PFS was compared between the groups with a stratified log-rank test. All subgroup analyses were done in the ITT population.

The sample size was designed to have 80% power to detect a median time to PFS of 13.5 months for patients treated with SVd versus 9.4 months for patients treated with Vd, using a onesided α of 0.025, 15-month accrual, 18-month follow-up, and a 1:1 allocation to the two treatment groups, allowing for an interim analysis of progression-free survival for futility or superiority.

Other relevant information	

Abbreviations: AE, Adverse event; BIW, Twice weekly; CI, Confidence interval; CNS, Central nervous system; ECOG, Eastern Cooperative Oncology Group; EORTC, European Organization Research and Treatment of Cancer; HR, Hazard ratio; HRQoL, Health-related quality of life; IMWG, International Myeloma Working Group; IRC, Independent Review Committee; ITT, Intention-to-treat; mg, Milligrams; MM, Multiple myeloma; ORR, Overall response rate; OS, Overall survival; PD, Progressive disease; PFS, Progression-free survival; QW, Once weekly; R-ISS, Revised international staging system; RRMM, Relapsed or refractory multiple myeloma; SC, Subcutaneous; SVd, Selinexor + bortezomib + dexamethasone; Vd, Bortezomib + dexamethasone.

Table 58. Main characteristics of ENDEAVOR

Trial name: ENDEAVOR	NCT number: NCT01568866
Objective	The primary objective of this study was to compare progression-free survival in patients with multiple myeloma who relapsed after 1 to 3 prior therapies treated with carfilzomib plus dexamethasone or bortezomib plus dexamethasone
Publications – title, author, journal, year	Chng, W. J.; Goldschmidt, H.; Dimopoulos, M. A.; Moreau, P.; Joshua, D.; Palumbo, A.; Facon, T.; Ludwig, H.; Pour, L.; Niesvizky, R.; et al. Carfilzomib-dexamethasone vs bortezomib-dexamethasone in relapsed or refractory multiple myeloma by cytogenetic risk in the phase 3 study ENDEAVOR. 2017. Leukemia. 31:6 (1368--1374). Dimopoulos, M. A.; Goldschmidt, H.; Niesvizky, R.; Joshua, D.; Chng, W. J.; Oriol, A.; Orlowski, R. Z.; Ludwig, H.; Facon, T.; Hajek, R.; et al.. Carfilzomib or bortezomib in relapsed or

refractory multiple myeloma (ENDEAVOR): an interim overall survival analysis of an open-label, randomised, phase 3 trial. 2017. The lancet. Oncology. 18:10 (1327-1337).

Dimopoulos, M. A.; Moreau, P.; Palumbo, A.; Joshua, D.; Pour, L.; HÃ¡jek, R.; Facon, T.; Ludwig, H.; Oriol, A.; Goldschmidt, H.; et al. Carfilzomib and dexamethasone versus bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma (ENDEAVOR): a randomised, phase 3, open-label, multicentre study. 2016. The lancet. Oncology. 17:1 (27-38).

EUCTR, C. Z. A Randomized, Open-label, Phase 3 Study of Carfilzomib Plus Dexamethasone vs Bortezomib Plus Dexamethasone in Patients With Relapsed Multiple Myeloma. 2012. https://trialsearch.who.int/Trial2.aspx?TrialID=EUCTR2012-000128-16-CZ.

Goldschmidt, H.; Moreau, P.; Ludwig, H.; Niesvizky, R.; Chng, W. J.; Joshua, D.; Weisel, K.; Spencer, A.; Orlowski, R. Z.; Feng, S.; et al. Carfilzomib-dexamethasone versus subcutaneous or intravenous bortezomib in relapsed or refractory multiple myeloma: secondary analysis of the phase 3 ENDEAVOR study. 2018. Leukemia & lymphoma. 59: (1364-1374).

EUCTR2012-000128-16-DE. A Clinical Study to Test the Effectiveness of Carfilzomib Plus Dexamethasone Versus Bortezomib Plus Dexamethasone in Patients with Multiple Myeloma (Bone Marrow Cancer).

Ludwig, H.; Moreau, P.; Dimopoulos, M. A.; Mateos, M. V.; Kaiser, M.; Hajek, R.; Feng, S.; Cocks, K.; Buchanan, J.; Weisel, K.. Health-related quality of life in the ENDEAVOR study: carfilzomib-dexamethasone vs bortezomib-dexamethasone in relapsed/refractory multiple myeloma. 2019. Blood cancer journal. 9:3 (23).

Moreau, P.; Joshua, D.; Chng, W. J.; Palumbo, A.; Goldschmidt, H.; HÃ¡jek, R.; Facon, T.; Ludwig, H.; Pour, L.; Niesvizky, R.; et al.. Impact of prior treatment on patients with relapsed multiple myeloma treated with carfilzomib and dexamethasone vs bortezomib and dexamethasone in the phase 3 ENDEAVOR study. 2017. Leukemia. 31:1 (115-122).

Anonymous. Correction: carfilzomib or bortezomib in relapsed or refractory multiple myeloma (ENDEAVOR): an interim overall survival analysis of an open-label, randomised, phase 3 trial (The Lancet Oncology (2017) 18(10) (1327-1337) (S1470204517305788) (10.1016/S1470. 2017. Lancet oncology. 18:10 (e562).

NCT. Phase 3 Study With Carfilzomib and Dexamethasone Versus Bortezomib and Dexamethasone for Relapsed Multiple Myeloma Patients. 2012. https://clinicaltrials.gov/show/NCT01568866.

Orlowski, R. Z.; Moreau, P.; Niesvizky, R.; Ludwig, H.; Oriol, A.; Chng, W. J.; Goldschmidt, H.; Yang, Z.; Kimball, A. S.;

	Dimopoulos, M.. Carfilzomib-Dexamethasone Versus Bortezomib-Dexamethasone in Relapsed or Refractory Multiple Myeloma: updated Overall Survival, Safety, and Subgroups. 2019. Clinical lymphoma, myeloma & leukemia. 19:8 (522-530.e1).
Study type and design	A phase 3, multicenter, randomized, open-label study. Enrolled patients were randomly assigned 1:1 using a blocked randomisation scheme (block size of four) to receive carfilzomib with dexamethasone (carfilzomib group) or bortezomib with dexamethasone (bortezomib group). Randomisation was stratified by previous proteasome inhibitor therapy, previous lines of treatment, International Staging System stage, and planned route of bortezomib administration if randomly assigned to bortezomib with dexamethasone The study is completed, and results were first posted in 2016.
Sample size (n)	Bortezomib + DEX: 465 Carfilzomib + DEX: 464
Main inclusion criteria	Patients aged 18 years or older with RRMM, measurable disease (i.e., serum M-protein of at least 5 g/L or urine M-protein of at least 200 mg/24 h; or in patients without detectable serum or urine M-protein, serum free light chain of at least 100 mg/L [involved light chain] and an abnormal serum κ:λ ratio), ECOG performance status of 0 to 2, one to three previous treatments, and at least a partial response to at least one previous treatment were eligible.
Main exclusion criteria	1. Multiple Myeloma of IgM subtype. 2. Glucocorticoid therapy (prednisone > 30 mg/day or equivalent) within 14 days prior to randomization. 3. POEMS syndrome. 4. Plasma cell leukemia or circulating plasma cells ≥ 2 × 10^9/L. 5. Waldenstrom's Macroglobulinemia. 6. Patients with known amyloidosis. 7. Chemotherapy with approved or investigational anticancer therapeutics within 21 days prior to randomization. 8. Patients randomized or previously randomized in any other Onyx-Sponsored Phase 3 trial. 9. Focal radiation therapy within 7 days prior to randomization. Radiation therapy to an extended field involving a significant volume of bone marrow within 21 days prior to randomization (i.e., prior

radiation must have been to less than 30% of the bone marrow).

10. Immunotherapy within 21 days prior to randomization.

11. Major surgery (excluding kyphoplasty) within 28 days prior to randomization.

12. Active congestive heart failure (NYHA Class III to IV), symptomatic ischemia, or conduction abnormalities uncontrolled by conventional intervention. Myocardial infarction within four months prior to randomization.

13. Acute active infection requiring systemic antibiotics, antiviral (except antiviral therapy directed at hepatitis B) or antifungal agents within 14 days prior to randomization.

14. Known HIV seropositive, hepatitis C infection, and/or hepatitis B (except for patients with hepatitis B surface antigen [SAg] or core antibody receiving and responding to antiviral therapy directed at hepatitis B: these patients are allowed).

15. Patients with known cirrhosis.

16. Second malignancy within the past 3 years except:
    - adequately treated basal cell or squamous cell skin cancer
    - carcinoma in situ of the cervix
    - prostate cancer < Gleason score 6 with stable prostate-specific antigen (PSA) over 12 months
    - breast carcinoma in situ with full surgical resection
    - treated medullary or papillary thyroid cancer
    - Patients with myelodysplastic syndrome.

17. Significant neuropathy (Grades 3 to 4, or Grade 2 with pain) within 14 days prior to randomization.

18. Female patients who are pregnant or lactating.

19. Known history of allergy to Captisol (a cyclodextrin derivative used to solubilize carfilzomib).

20. Patients with hypersensitivity to carfilzomib, Velcade, boron, or mannitol.

21. Patients with contraindication to dexamethasone.

22. Contraindication to any of the required concomitant drugs or supportive treatments, including

	hypersensitivity to antiviral drugs, or intolerance to hydration due to preexisting pulmonary or cardiac impairment. 23. Ongoing graft-vs-host disease. 24. Patients with pleural effusions requiring thoracentesis or ascites requiring paracentesis within 14 days prior to randomization.
Intervention	Carfilzomib + DEX (464): Participants received 20 mg/m² carfilzomib administered by intravenous (IV) infusion on Days 1 and 2 of Cycle 1, followed by 56 mg/m² on Days 8, 9, 15, and 16 of Cycle 1 and for each 28-day cycle thereafter. Additionally, participants received 20 mg dexamethasone on Days 1, 2, 8, 9, 15, 16, 22, and 23 of each 28-day cycle.
Comparator(s)	Bortezomib + DEX (465): Participants received bortezomib 1.3 mg/m² administered IV or subcutaneously (SC) on Days 1, 4, 8, and 11 of a 21-day cycle plus dexamethasone 20 mg administered on Days 1, 2, 4, 5, 8, 9, 11, and 12 of each 21-day cycle.
Follow-up time	Median follow-up was 11.9 months (IQR 9.3–16.1) in the carfilzomib group and 11.1 months (8.2–14.3) in the bortezomib group.
Is the study used in the health economic model?	Yes.
Primary, secondary and exploratory endpoints	**Endpoints included in this application:** The primary endpoint was progression-free survival based on the independent review committee's disease outcome assessments, defined as the time from randomisation until disease progression or death due to any cause, whichever occurred first. Secondary endpoints included overall survival (defined as the time from randomisation to death due to any cause). **Other endpoints:** Overall response (partial response or better), duration of response (calculated for patients who achieved a partial response or better; for such patients, duration of response was defined as the time from first evidence of a partial response or better to confirmation of disease progression or death from any cause), incidence of grade 2 or higher peripheral neuropathy events, incidence of significant reduction in LVEF, CFB in right ventricular Fractional Area Change (FAC) and CFB in Pulmonary Artery Systolic Pressure (PASP) were included as secondary outcomes but are not included in this application.
Method of analysis	Progression-free survival and overall survival were compared between treatment groups using a log-rank test and the corresponding hazard ratio (HR) was estimated using a Cox

	regression model. An interim analysis was scheduled after about 395 events had occurred (75% of the required total). The objective of the planned interim analysis was to monitor differences between treatment groups for evidence of substantial benefit of carfilzomib and dexamethasone versus bortezomib and dexamethasone. An O'Brien-Fleming stopping boundary for efficacy was calculated with the use of a Lan-DeMets alpha-spending function so that the overall type I error was less than or equal to 0·05 (two-sided). Duration of response was summarised descriptively using the Kaplan-Meier method. Efficacy assessments were based on the ITT population (consisting of all randomly assigned patients). The overall response was compared between groups using a Mantel-Haenszel test, and the associated odds ratio (OR) and 95% CI were estimated. A Pearson χ^2 test was used to compare the incidence of grade 2 or higher peripheral neuropathy between treatment groups, and the OR and 95% CI were estimated. For the echocardiogram substudy, we used a mixed model for repeated measures under the assumption of missing-at random to estimate longitudinal differences between the treatment groups in the reduction of left ventricular ejection fraction and right ventricular function. For the distribution of time-to-event endpoints, the medians and 95% CIs were estimated using the Kaplan-Meier point estimates. For median follow-up data, the IQR was calculated. All reported p values are two-sided. SAS software version 9.3 was used for the statistical analyses.
Subgroup analyses	Data presented in the application is based on the subpopulation of lenalidomide refractory patients. In total, 526 events (disease progression or death) were needed to provide 90% power to detect a 25% reduction in the risk of disease progression or death (HR 0.75) at a two-sided significance level of 0.05. Progression-free survival was analysed on the following pre-specified subgroups: • Age (<65, 65-74, ≥75) • Sex (male, female) • Race (White, Asian, other) • Geographical region (Eastern Europe, Western Europe, North America, Asia-Pacific) • ECOG performance status (0, 1, ≥2) • Previous peripheral neuropathy (no, yes) • ISS stage (I, II or III) • Risk group by FISH (High risk, Standard risk, Unknown, Missing)

	• Number of previous regimens (1, 2–3*) • Previous stem cell transplant (No, Yes) • Previous bortezomib (No, Yes) • Previous immunomodulatory agent (No, Yes) • Previous immunomodulatory agent and bortezomib (No, Yes) • Previous lenalidomide (No, Yes) • Previous thalidomide (No, Yes) • Refractory to bortezomib (No, Yes) • Refractory to lenalidomide (No, Yes) Progression-free survival was compared between treatment groups using a log-rank test and the corresponding hazard ratio (HR) was estimated using a Cox regression model.
Other relevant information	

Table 59. Main characteristics of OPTIMISMM

Trial name: OPTIMISMM	NCT number: NCT01734928
Objective	To compare the efficacy and safety of pomalidomide, bortezomib and low-dose dexamethasone versus bortezomib and low-dose dexamethasone in subjects with relapsed or refractory multiple myeloma.
Publications – title, author, journal, year	NCT. Safety and Efficacy of Pomalidomide, Bortezomib and Low-dose Dexamethasone in Subjects With Relapsed or Refractory Multiple Myeloma. 2012. https://clinicaltrials.gov/show/ NCT01734928. Richardson, P. G.; Oriol, A.; Beksac, M.; Liberati, A. M.; Galli, M.; Schjesvold, F.; Lindsay, J.; Weisel, K.; White, D.; Facon, T.; et al.. Pomalidomide, bortezomib, and dexamethasone for patients with relapsed or refractory multiple myeloma previously treated with lenalidomide (OPTIMISMM): a randomised, open-label, phase 3 trial. 2019. The lancet. Oncology. 20:6 (781-794). Richardson, P. G.; Schjesvold, F.; Weisel, K.; Moreau, P.; Anderson, L. D., Jr.; White, D.; Rodriguez-Otero, P.; Sonneveld, P.; Engelhardt, M.; Jenner, M.; Corso, A.; Durig, J.; Pavic, M.; Salomo, M.; Beksac, M.; Oriol, A.; Lindsay, J.; Liberati, A. M.; Galli, M.; Robak, P.; Larocca, A.; Yagci, M.; Vural, F.; Kanate, A. S.; Jiang, R.; Grote, L.; Peluso, T.; Dimopoulos, M.. Pomalidomide, bortezomib, and dexamethasone at first relapse in lenalidomide-pretreated myeloma: A subanalysis of OPTIMISMM by clinical characteristics. 2022. European Journal of Haematology. 108:1 (73-83). Weisel, K.; Dimopoulos, M.; Moreau, P.; Yagci, M.; Larocca, A.; Kanate, A. S.; Vural, F.; Cascavilla, N.; Basu, S.; Johnson, P.; Byeff, P.; Hus, M.; Rodriguez-Otero, P.; Muelduer, E.; Anttila, P.; Hayden, P. J.; Krauth, M. T.;

Lucio, P.; Ben-Yehuda, D.; Mendeleeva, L.; Guo, S.; Yu, X.; Grote, L.; Biyukov, T.; Dhanasiri, S.; Richardson, P.. Health-related quality-of-life results from the phase 3 OPTIMISMM study: pomalidomide, bortezomib, and low-dose dexamethasone versus bortezomib and low-dose dexamethasone in relapsed or refractory multiple myeloma. 2020. Leukemia & Lymphoma. 61:8 (1850-1859).

Weisel, K; Dimopoulos, M; Oriol, A; Beksac, M; Schjesvold, F; Liberati, A; Lindsay, J; White, D; Miguel, J; Moreau, P; Larry D..; Lorocca, A; Robak, P; Vogel, P; Jiang, R; Grote, L; Peluso, T; Richardson, P. EP988: pomalidomide, bortezomib, and dexamethasone after 1 prior line of therapy in relapsed or refractory multiple myeloma: a safety subanalysis of the phase 3 OPTIMISMM trial. 2021.

2014-000268-17. A Phase 3, Multicenter, Randomized, Open-Label Study to Compare the Efficacy and Safety of Pomalidomide, Bortezomib and Low-Dose Dexamethasone Versus Bortezomib and Low-Dose Dexamethasone in Subjec.

Weisel, K.; Dimopoulos, M.; Oriol, A.; Beksac, M.; Schjesvold, F.; Liberati, A. M.; Lindsay, J.; White, D.; San-Miguel, J.; Moreau, P.; Anderson, L. D.; Lorocca, A.; Robak, P.; Vogel, P.; Jiang, R.; Grote, L.; Peluso, T.; Richardson, P.. Pomalidomide (POM), bortezomib (BORT), and dexamethasone (DEX) after 1 prior line of therapy in relapsed or refractory multiple myeloma (RRMM): a safety subanalysis of the phase 3 OPTIMISMM trial. 2022. Oncology Research and Treatment. 45(Supplement 3): (165).

Weisel, K.; Dimopoulos, M. A.; Oriol, A.; Beksac, M.; Dimopoulos, F.; Liberati, A. M.; Lindsay, J.; White, D.; San-Miguel, J. F.; Moreau, P.; et al.. P-224: pomalidomide, bortezomib, and dexamethasone after 1 prior line of therapy in relapsed or refractory multiple myeloma (RRMM): a safety subanalysis of the phase 3 OPTIMISMM trial. 2021. Clinical lymphoma, myeloma & leukemia. 21: (S163).

Dimopoulos, M.; Weisel, K.; Moreau, P.; Anderson, L. D., Jr.; White, D.; San-Miguel, J.; Sonneveld, P.; Engelhardt, M.; Jenner, M.; Corso, A.; Durig, J.; Pavic, M.; Salomo, M.; Casal, E.; Srinivasan, S.; Yu, X.; Nguyen, T. V.; Biyukov, T.; Peluso, T.; Richardson, P.. Pomalidomide, bortezomib, and dexamethasone for multiple myeloma previously treated with lenalidomide (OPTIMISMM): outcomes by prior treatment at first relapse. 2021. Leukemia. 35:6 (1722-1731).

Beksaç, M.; Richardson, P.; Oriol, A.; Lindsay, J.; Schjesvold, F.; Galli, M.; Yağcı, M.; Larocca, A.; Weisel, K.; Yu, X.; Donahue, C.; Acosta, J.; Peluso, T.; Dimopoulos, T. Pomalidomide, bortezomib, and dexamethasone versus bortezomib and dexamethasone in relapsed or refractory multiple myeloma (OPTIMISMM): final survival outcomes from a randomized, open-label, phase 3 trial. 2023. IMS conference.

Weisel, K.; Dimopoulos, M.; Oriol, A.; Beksac, M.; Schjesvold, F.; Liberati, A. M.; Lindsay, J.; White, D.; San Miguel, J.; Moreau, P.; et al. OPTIMISMM Subanalyse: sicherheit von Pomalidomid (POM), Bortezomib (BORT) und Dexamethason (DEX) (PVd) Behandlung (Tx) nach einer vorherigen Therapielinie (LoT) bei Patienten (pts) mit rezidiviertem oder refraktÃ¤rem multiplen Myelom (RRMM). 2022. Oncology research and treatment. 45: (283).

Study type and design	A phase 3, multicenter, randomized, open-label study. Enrolled patients were randomly assigned 1:1 to either pomalidomide, bortezomib and low dose dexamethasone (experimental arm) or bortezomib and low dose dexamethasone (comparator arm), using a permutated blocked design in blocks of four, stratified according to age, number of previous regimens, and concentration of β2 microglobulin at screening. The study is completed, and results were first posted in 2019.
Sample size (n)	Pomalidomide, bortezomib and low dose dexamethasone (experimental arm): 281 Bortezomib and low dose dexamethasone (comparator arm): 278
Main inclusion criteria	• Must be ≥ 18 years at the time of signing informed consent. • Must have documented diagnosis of multiple myeloma and have measureable disease by serum and urine protein electrophoresis. • Must have had at least 1 but no greater than 3 prior anti-myeloma regimens. • Must have documented disease progression during or after their last anti-myeloma therapy. • All subjects must have received prior treatment with a lenalidomide containing regimen for at least 2 consecutive cycles.
Main exclusion criteria	• Documented progressive disease during therapy or within 60 days of the last dose of a bortezomib-containing therapy under the 1.3 mg/m^2 dose twice weekly dosing schedule. • Peripheral neuropathy Grade 3, Grade 4 or Grade 2 with pain within 14 days prior to randomization. • Non-secretory multiple myeloma. • Subjects with severe renal impairment requiring dialysis. • Previous therapy with pomalidomide.
Intervention	Pomalidomide, bortezomib and low dose dexamethasone (n = 281): 4 mg of pomalidomide will be taken orally on days 1-14 of a 21-day cycle along with 1.3 mg/m2 of bortezomib administered subcutaneously on days 1, 4, 8 and 11 of 21 days for cycles 1 -8 and on days 1, 8 of 21 days for cycle 9 and onward until disease progression, and dexamethasone 20 mg/day [≤ 75 years old] or 10 mg/day [> 75 years old] orally on days 1, 2, 4, 5, 8, 9, 11, 12 of 21 days for cycles 1-8 and on days 1, 2,8, 9 of 21 days for cycles 9 and onward until disease progression.
Comparator(s)	Bortezomib and low dose dexamethasone (n = 278): 1.3 mg/m2 of Bortezomib will be administered subcutaneously on Days 1, 4, 8 and 11 of 21 days for cycles 1 -8 and on Days 1, 8 of 21 days for cycle 9 and onward until disease progression along with Dexamethasone 20 mg/day [≤ 75 years old]or 10 mg/day [> 75 years old] orally on days 1, 2, 4, 5, 8, 9, 11, 12 of 21

	days for cycles 1-8 and on Days 1, 2, 8, 9 of 21 days for cycles 9 and onward until disease progression.
Follow-up time	Median follow-up was 15.9 months (IQR 9.9-21.7).
Is the study used in the health economic model?	Yes.
Primary, secondary and exploratory endpoints	**Endpoints included in this application:** The primary endpoint was progression-free survival in the intention-to-treat population, as assessed by Independent Response Adjudication Committee (IRAC). Secondary endpoints included overall survivalnumber of patients with grade 3-4 treatment emergent adverse events and number of patients with grade 5 treatment emergent adverse events. **Other endpoints:** Overall response rate by IRAC and duration of response by IRAC, were included as secondary outcomes, but are not included in this submission.
Method of analysis	We estimated the analysis of progression-free survival would provide 80% power to detect a hazard ratio (HR) of 0.73 for disease progression or death with pomalidomide, bortezomib, and dexamethasone. Efficacy analyses included one interim analysis for futility (at approximately 50% of progression-free survival events) and one final analysis for progression-free survival. Using a two-sided significance level of 5%, with one interim analysis for futility only at 50% of events, we initially estimated that 381 events would be needed to detect a 33% increase in median progression-free survival in patients assigned pomalidomide, bortezomib, and dexamethasone (12 months) versus bortezomib and dexamethasone (9 months), with 80% power. Primary, secondary, and prespecified exploratory analyses were done in the intention-to-treat population, which included all patients who were randomly assigned. Safety assessments were done in the safety population, which included all patients who received at least one dose of study medication. The intention-to-treat population, efficacy-assessable population (which included all patients who received at least one dose of study medication and had a baseline and at least one post-baseline efficacy assessment), and all efficacy analyses except for duration of response were adjusted by stratification factors (age, number of previous regimens, and concentration of β2 microglobulin at screening). However, subgroup analyses for efficacy endpoints were not adjusted by stratification factors. Th Kaplan-Meier method was used to estimate progression-free survival. The treatment effect (measured by HR and 95% CI) was estimated using a stratified Cox proportional hazards model. A stratified Cochran-Mantel-Haenszel test was used to compare responses. The observed change in HRQOL score from baseline was calculated using a mixed-model repeated measure approach, using baseline covariates where appropriate to estimate the least square means (95% CI and p value) for changes from baseline across all scheduled

	visits (excluding the visit at the end of treatment) and on day 1 of cycles five, nine, 19, and 25 within each treatment group, as well as the difference in the least square means between treatment groups. SAS software (version 9.2) was used for the statistical analysis.
Subgroup analyses	Progression-free survival was analysed on the following pre-specified subgroups: • Age (≤75, >75, ≤65, >65) • Baseline ECOG performance status (0, 1 or 2) • High-risk cytogenetics (yes, no) • Previous lines of treatment (1, >1, 2, >2) • ISS stage at study entry (I, II, III) • Previous stem-cell transplantation (yes, no) • Baseline creatinine clearance (mL/min) (<60, ≥60) • Refractory to lenalidomide in the last lenalidomide-containing regimen (non-refractory to lenalidomide in the last lenalidomide-containing regimen, refractory to last previous treatment, previous exposure to proteasome inhibitors) All subgroup analyses were done in the ITT population. Progression-free survival was estimated using the Kaplan-Maier method.
Other relevant information	

Appendix B. Efficacy results per study

B.1.1 Results per BOSTON

In the following tables relevant efficacy results (i.e. results listed in the DMC treatment guideline) from the BOSTON, ENDEAVOR and OPTIMISMM trials are presented.

Table 60. Results per study (BOSTON) – Lenalidomide-refractory subpopulation

Results of BOSTON (NCT03110562)											
				Estimated absolute difference in effect			Estimated relative difference in effect			Description of methods used for estimation	References
Outcome	Study arm	N	Result (CI)	Difference	95% CI	*P* value	Difference	95% CI	*P* value		
Median OS, months (DCO: 15/02/2021)	SVd	53	26.82 (16.92, NE)	8.17	Not calculated	Not calculated	HR: 0.531	0.297 to 0.949	0.030	The median survival is based on the Kaplan-Meier estimator. The HR is based on a stratified Cox proportional hazards model with Efron's method of handling ties with stratification for prior PI therapies, number of prior anti-MM regimens, and R-ISS stage at screening	Data on file[45]
	Vd	53	18.65 (13.95 to 29.01)								Data on file[45]
Median PFS, months (DCO: 15/02/2021)	SVd	53	10.18 (5.8, NE)	3.12	Not calculated	Not calculated	HR: 0.521	0.310 to 0.877	0.012	The median survival is based on the Kaplan-Meier estimator. The HR is based on a stratified Cox proportional hazards model with Efron's method of handling ties with stratification for prior PI therapies, number of prior anti-MM regimens, and R-ISS stage at screening	Data on file[45]
	Vd	53	7.06 (3.5 to 9.8)								Data on file[45]
HRQoL measured with EORTC QLQ-C30 Global Health Status, estimated	SVd	53	-0.0415	0.1138	0.1522 to 0.3798	0.3742	N/A	N/A	N/A	The estimated weekly mean change was obtained using linear regression	Data on file[45]
	Vd	53	-0.1533								Data on file[45]

Outcome	Study arm	N	Result (CI)	Difference	95% CI	P value	Difference	95% CI	P value	Description of methods used for estimation	References
weekly mean change (Follow up: until end of treatment)											
EORTC QLQ-CIPN20 sensory system, weekly mean change	SVd	53	0.0123	-0.1351	-0.2892 to 0.0191	0.0805	N/A	N/A	N/A		Data on file[45]
	Vd	53	0.1474								
EORTC QLQ-CIPN20 motor system, weekly mean change	SVd	53	0.0422	-0.1696	-0.3245 to -0.0191	0.0347	N/A	N/A	N/A		Data on file[45]
	Vd	53	0.2118								
EORTC QLQ-CIPN20 autonomic system, weekly mean change	SVd	53	0.1572	0.0167	-0.2542 to 0.2875	0.9002	N/A	N/A	N/A		Data on file[45]
	Vd	53	0.1406								
EQ-5D-5L, weekly mean change	SVd	53	-0.0006	0.0006	-0.0012 to 0.0025	0.4751	N/A	N/A	N/A		Data on file[45]
	Vd	53	-0.0012								

Abbreviations: CI, Confidence interval; DCO, Data cut-off; EORTC, European Organization for Research and Treatment of Cancer; HR, Hazard ratio; HRQoL, Health-related quality of life; MM, Multiple myeloma; N/A, Not applicable; NE, Not estimable; OS, Overall survival; PFS, Progression-free survival; PI, Protease Inhibitor; QLQ-C30, Quality of Life Questionnaire-30; R-ISS, Revised international staging system; SVd, Selinexor + bortezomib + dexamethasone; Vd, Bortezomib + dexamethasone.

Table 61. Results per study (BOSTON) – ITT population

Results of BOSTON (NCT03110562)											
				Estimated absolute difference in effect			Estimated relative difference in effect			Description of methods used for estimation	References
Outcome	Study arm	N	Result (CI)	Difference	95% CI	*P* value	Difference	95% CI	*P* value		

Median OS, months (DCO: 15/02/2021)	SVd	195	36.7 (30.2, NE)	3.9	Not calculated	Not calculated	HR: 0.84	0.60 to 1.17	0.147	The median survival is based on the Kaplan-Meier estimator. The HR is based on a stratified Cox proportional hazards model with Efron's method of handling ties with stratification for prior PI therapies, number of prior anti-MM regimens, and R-ISS stage at screening	Data on file[45]
	Vd	207	32.8 (25.1, NE)								Data on file[45]
Median PFS, months (DCO: 15/02/2021)	SVd	195	13.2 (11.7, 23.4)	3.7	Not calculated	Not calculated	HR: 0.71	0.54 to 0.93	0.006	The median survival is based on the Kaplan-Meier estimator. The HR is based on a stratified Cox proportional hazards model with Efron's method of handling ties with stratification for prior PI therapies, number of prior anti-MM regimens, and R-ISS stage at screening	Data on file[45]
	Vd	207	9.5 (8.1 to 10.8)								Data on file[45]
HRQoL measured with EORTC QLQ-C30 Global Health Status, estimated weekly mean change (Follow up: until end of treatment)	SVd	195	-0.0482	-0.0323	-0.0998 to 0.0352	0.5249	N/A	N/A	N/A	The estimated weekly mean change was obtained using linear regression	Data on file[45]
	Vd	207	-0.049								Data on file[45]
EORTC QLQ-CIPN20 sensory system, weekly mean change	SVd	195	0.0378	-0.1282	-0.1952 to -0.0613	0.0003	N/A	N/A	N/A		Data on file[45]
	Vd	207	0.1660								
EORTC QLQ-CIPN20 motor system, weekly mean change	SVd	195	0.0938	-0.0621	-0.1375 to -0.0134	0.1058	N/A	N/A	N/A		Data on file[45]
	Vd	207	0.1559								
EORTC QLQ-CIPN20	SVd	195	0.1056	0.0368	-0.0631 to 0.1366	0.4654	N/A	N/A	N/A		Data on file[45]
	Vd	207	0.0688								

autonomic system, weekly mean change											
EQ-5D-5L, weekly mean change	SVd	195	-0.0008	0.0001	-0.0006 to 0.0007	0.8654	N/A	N/A	N/A		Data on file[45]
	Vd	207	-0.0008								

Abbreviations: CI, Confidence interval; DCO, Data cut-off; EORTC, European Organization for Research and Treatment of Cancer; HR, Hazard ratio; HRQoL, Health-related quality of life; MM, Multiple myeloma; N/A, Not applicable; NE, Not estimable; OS, Overall survival; PFS, Progression-free survival; PI, Protease Inhibitor; QLQ-C30, Quality of Life Questionnaire-30; R-ISS, Revised international staging system; SVd, Selinexor + bortezomib + dexamethasone; Vd, Bortezomib + dexamethasone.

B.1.2 Results per ENDEAVOR

Table 62. Results per study (ENDEAVOR) – Lenalidomide-refractory subpopulation.

Results of ENDEAVOR											
				Estimated absolute difference in effect			Estimated relative difference in effect			Description of methods used for estimation	References
Outcome	Study arm	N	Result (CI)	Difference	95% CI	*P* value	Difference	95% CI	*P* value		
Median OS, months	Kd	113	29.2 months 95% CI: Not reported	7.8	Not calculated	Not calculated	HR: 0.857	0.623 to 1.178	Not reported	Progression-free survival and overall survival were compared between treatment groups using a log-rank test and the corresponding hazard ratio (HR) was estimated using a Cox regression model	Dimoupoulos et al 2016[6]
	Vd	123	21.4 months 95% CI: Not reported								
Median PFS, months	Kd	113	8.6 (6.61 to 11.25)	2.0	Not calculated	Not calculated	HR: 0.80	0.57 to 1.11	Not calculated	For the distribution of time-to-event endpoints, the medians and 95% CIs were estimated using the Kaplan-Meier point estimates	Orlowski et al. 2019[47]
	Vd	53	6.6 (5.23 to 7.53)								

Abbreviations: CI, Confidence interval; DCO, Data cut-off; HR, Hazard ratio; Kd, Carfilzomib + dexamethasone; OS, Overall survival; PFS, Progression-free survival; Vd, Bortezomib + dexamethasone.

Table 63. Results per study (ENDEAVOR) – ITT population.

Results of ENDEAVOR												
				Estimated absolute difference in effect			Estimated relative difference in effect			Description of methods used for estimation	References
Outcome	Study arm	N	Result (CI)	Difference	95% CI	*P* value	Difference	95% CI	*P* value		
Median OS, months	Kd	464	47.8 (41.9, NE)	9.0	Not calculated	Not calculated	HR: 0.76	0.63 to 0.92	0.0017	Progression-free survival and overall survival were compared between treatment groups using a log-rank test and the corresponding hazard ratio (HR) was estimated using a Cox regression model For the distribution of time-to-event endpoints, the medians and 95% CIs were estimated using the Kaplan-Meier point estimates	Dimoupoulos et al 2016[6]
	Vd	465	38.8 (31.7, 42.7)								
Median PFS, months	Kd	464	18.7 (15.6 to NE)	9.7	Not calculated	Not calculated	HR: 0.53	0.4 to 0.65	<0.0001		Orlowski et al. 2019[47]
	Vd	465	9.4 (8.4 to 10.4)								

Abbreviations: CI, Confidence interval; DCO, Data cut-off; HR, Hazard ratio; Kd, Carfilzomib + dexamethasone; OS, Overall survival; PFS, Progression-free survival; Vd, Bortezomib + dexamethasone.

B.1.3 Results per OPTIMISMM

Table 64. Results per study (OPTIMISMM) – Lenalidomide-refractory population

Results of OPTIMISMM (NCT01734928)			
	Estimated absolute difference in effect	Estimated relative difference in effect	Description of methods used for estimation	References

Outcome	Study arm	N	Result (CI)	Difference	95% CI	*P* value	Difference	95% CI	*P* value		
Median OS, months	PVd	200	Not reported	N/A	N/A	N/A	HR: 0.89	0.71 to 1.12	Not calculated	Not reported	Beksac et al. 2023[56]
	Vd	191	Not reported								
Median PFS, months	PVd	200	9.53 (8.05 to 11.30)	3.94	Not calculated	Not calculated	HR: 0.65	0.50 to 0.84	Not calculated	Th Kaplan-Meier method was used to estimate progression-free survival. The treatment effect (measured by HR and 95% CI) was estimated using a stratified Cox proportional hazards model.	Richardson et al. 2019[7]
	Vd	191	5.59 (4.44 to 7.00)								

Abbreviations: CI, Confidence interval; DCO, Data cut-off; HR, Hazard ratio; OS, Overall survival; PFS, Progression-free survival; PPd, Pomalidomide + bortezomib + dexamethasone; Vd, Bortezomib + dexamethasone.

Table 65. Results per study (OPTIMISMM) – Lenalidomide-refractory population

Results of OPTIMISMM (NCT01734928)											
				Estimated absolute difference in effect			Estimated relative difference in effect			Description of methods used for estimation	References

Outcome	Study arm	N	Result (CI)	Difference	95% CI	*P* value	Difference	95% CI	*P* value		
Median OS, months	PVd	281	35.6 (not reported)	4.0	N/A	N/A	HR: 0.94	0.77 to 1.15	0.571	Not reported	Beksac et al. 2023[56]
	Vd	278	31.6 (not reported)								
Median PFS, months	PVd	281	11.20 (9.66 to 13.73)	4.10	Not calculated	Not calculated	HR: 0.61	0.49 to 0.77	0.0001	Th Kaplan-Meier method was used to estimate progression-free survival. The treatment effect (measured by HR and 95% CI) was estimated using a stratified Cox proportional hazards model.	Richardson et al. 2019[7]
	Vd	278	7.10 (5.88 to 8.84)								

Abbreviations: CI, Confidence interval; DCO, Data cut-off; HR, Hazard ratio; OS, Overall survival; PFS, Progression-free survival; PPd, Pomalidomide + bortezomib + dexamethasone; Vd, Bortezomib + dexamethasone.

Appendix C. Comparative analysis of efficacy

To facilitate a comparison of SVd versus Kd and PVd, an indirect treatment comparison was carried out. As all trials shared a common comparator (Vd), and trials were considered sufficiently similar to allow for indirect treatment comparison without population adjustment, a frequentist NMA was chosen as the appropriate method for indirect comparison.

This application includes three studies reporting efficacy data for either SVd, Kd, or PVd for the treatment of relapsed or refractory multiple myeloma in lenalidomide-refractory patients: the BOSTON, ENDEAVOR, and OPTIMISMM trials. A description of the trial design and methods is provided in Appendix A.

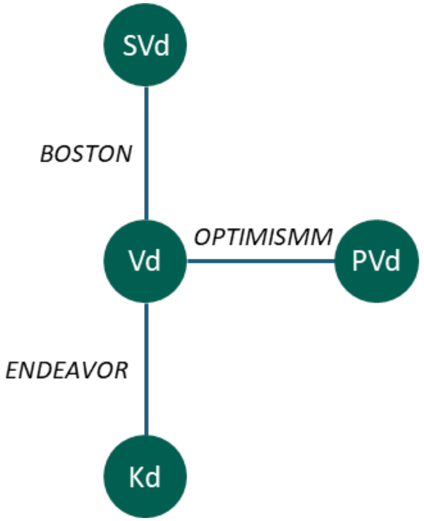
C.1 Method of synthesis

The included studies were combined using frequentist NMA methodology as implemented in the *netmeta* package for R[58]. The detailed methods of the frequentist NMA are described in the paper accompanying the R package (Balduzzi et al. 2023) and will not be described in detail here.

The *netmeta* package adopts the approach proposed by Rücker, which relies on graph-theoretical methods[57]. As all outcomes included in the NMA were time-to-event outcomes, random-effect models were fitted with the *netmeta* package, using HRs as the summary measure. The pooling of study-specific estimates was done using the inverse-variance method, where more weight is given to studies with larger sample sizes and more precise estimates. For the random-effects model, the direct treatment estimates are based on the common between-study variance τ^2 from the network meta-analysis. The default estimator for τ^2 in the *netmeta* package, is a special case of the generalised DerSimonian-Laird estimate[58].

Within-design heterogeneity (i.e., heterogeneity between studies examining the same treatments, e.g., nirsevimab versus placebo) can be assessed using τ^2. Between-design heterogeneity can only be assessed when “closed loops” exist in the treatment network, i.e., when at least one comparison is informed by both direct and indirect evidence. As the treatment network employed here (shown in Figure 25) only contains one trial for each comparison and no closed loops, neither within- or between-design heterogeneity was assessed.

Figure 25. Network graph for frequentist NMA of SVd versus Kd and PVd



C.2 Results of NMA – Lenalidomide refractory population

C.2.1 Overall survival

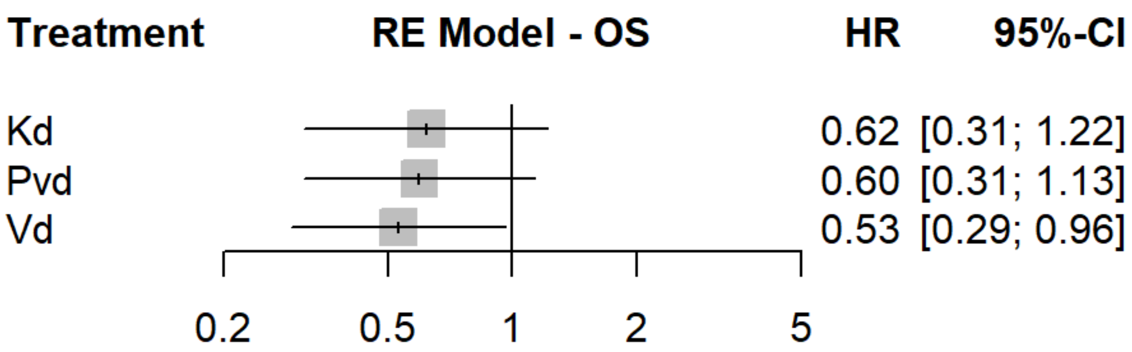
The results of the frequentist NMA, for the outcome of overall survival, are displayed in Table 66 and Figure 26.

Table 66. NMA results – Overall survival in the lenalidomide-refractory population

	SVd (BOSTON)	Kd (ENDEAVOR)	PVd (OPTMISMM)	Vd
SVd (BOSTON)	N/A	HR: 0.62 (95% CI: 0.31 to 1.22)	HR: 0.60 (95% CI: 0.31 to 1.13)	HR: 0.53 (95% CI: 0.29 to 0.96)
Kd (ENDEAVOR)	HR: 1.62 (95% CI: 0.82 to 3.19)	N/A	HR: 0.96 (95% CI: 0.65 to 1.42)	HR: 0.86 (95% CI: 0.62 to 1.18)
PVd (OPTMISMM)	HR: 1.68 (95% CI: 0.89 to 3.19)	HR: 1.04 (95% CI: 0.70 to 1.54)	N/A	HR: 0.89 (95% CI: 0.71 to 1.12)
Vd	HR: 1.89 (95% CI: 1.04 to 3.43)	HR: 1.17 (95% CI: 0.85 to 1.60)	HR: 1.12 (95% CI: 0.89 to 1.60)	N/A

Notes: The hazard ratios presented above can be interpreted in the following way: The treatment in the row is the reference treatment and the treatment in the column is the comparator, i.e., SVd versus Kd results in a HR of 0.62, whereas Kd versus SVd results in a HR of 1.62

Figure 26. Forest plot of the NMA for overall survival in the lenalidomide-refractory population (reference treatment: SVd)



As shown above, SVd was statistically significantly superior to Vd, and numerically superior to Kd and PVd for OS with hazard ratios of 0.53 (95% CI: 0.29 to 0.96), 0.60 (95% CI: 0.31 to 1.13), and 0.62 (95% CI: 0.31 to 1.22)

As described above, due to the structure of the treatment network, neither within- or between-design heterogeneity was present.

C.2.2 Progression-free survival

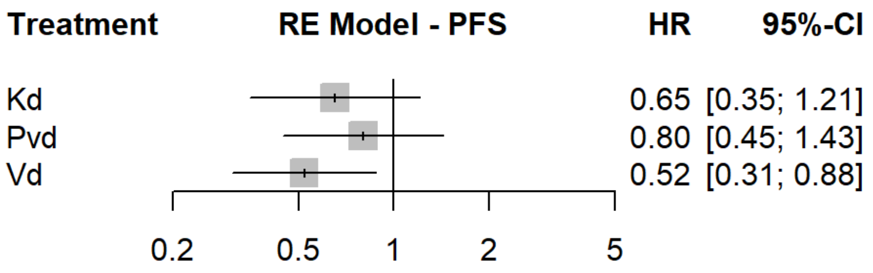
The results of the frequentist NMA, for the outcome of progression survival, are displayed in Table 67 and Figure 27.

Table 67. NMA results – Progression-free survival in the lenalidomide-refractory population

	SVd (BOSTON)	Kd (ENDEAVOR)	PVd (OPTMISMM)	Vd
SVd (BOSTON)	N/A	HR: 0.65 (95% CI: 0.35 to 1.21)	HR: 0.80 (95% CI: 0.45 to 1.43)	HR: 0.52 (95% CI: 0.31 to 0.88)
Kd (ENDEAVOR)	HR: 1.54 (95% CI: 0.83 to 2.85)	N/A	HR: 1.23 (95% CI: 0.81 to 1.88)	HR: 0.80 (95% CI: 0.57 to 1.12)
PVd (OPTMISMM)	HR: 1.25 (95% CI: 0.70 to 2.23)	HR: 0.81 (95% CI: 0.53 to 1.24)	N/A	HR: 0.65 (95% CI: 0.50 to 0.84)
Vd	HR: 1.92 (95% CI: 1.14 to 3.23)	HR: 1.25 (95% CI: 0.90 to 1.74)	HR: 1.54 (95% CI: 1.19 to 1.99)	N/A

Notes: The hazard ratios presented above can be interpreted in the following way: The treatment in the row is the reference treatment and the treatment in the column is the comparator, i.e., SVd versus Kd results in a HR of 0.65, whereas Kd versus SVd results in a HR of 1.54

Figure 27. Forest plot of the NMA for progression-free survival in the lenalidomide-refractory population (reference treatment: SVd)



As for OS, SVd was statistically significantly superior to Vd, and numerically superior to Kd and PVd for PFS with hazard ratios of 0.52 (95% CI: 0.31 to 0.88), 0.80 (95% CI: 0.45 to 1.43), and 0.65 (95% CI: 0.35 to 1.21)

As described above, due to the structure of the treatment network, neither within- or between-design heterogeneity was present.

C.3 Results of NMA – ITT population

C.3.1 Overall survival

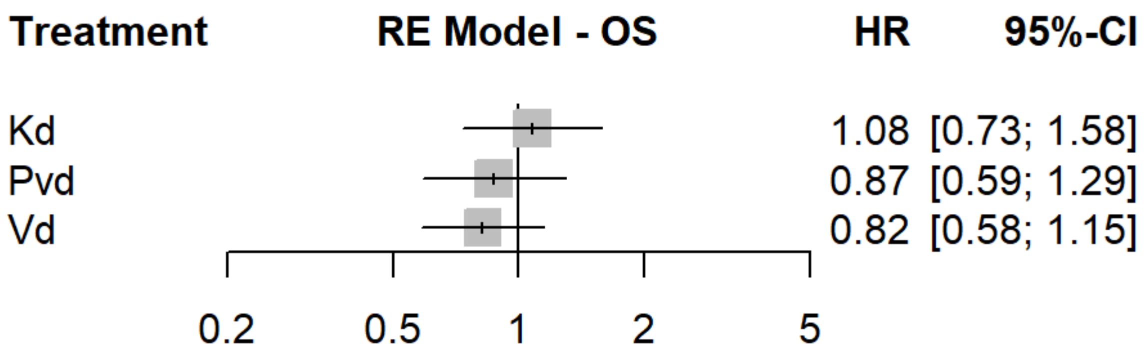
The results of the frequentist NMA, for the outcome of overall survival, are displayed in Table 68 and Figure 28.

Table 68. Overall survival in the ITT population

	SVd (BOSTON)	Kd (ENDEAVOR)	PVd (OPTMISMM)	Vd
SVd (BOSTON)	N/A	HR: 1.08 (95% CI: 0.73 to 1.58)	HR: 0.87 (95% CI: 0.62 to 1.29)	HR: 0.82 (95% CI: 0.58 to 1.15)
Kd (ENDEAVOR)	HR: 0.93 (95% CI: 0.63 to 1.36)	N/A	HR: 0.81 (95% CI: 0.62 to 1.06)	HR: 0.76 (95% CI: 0.63 to 0.91)
PVd (OPTMISMM)	HR: 1.15 (95% CI: 0.77 to 1.70)	HR: 1.23 (95% CI: 0.94 to 1.62)	N/A	HR: 0.94 (95% CI: 0.77 to 1.15)
Vd	HR: 1.22 (95% CI: 0.87 to 1.71)	HR: 1.31 (95% CI: 1.09 to 1.58)	HR: 1.06 (95% CI: 0.87 to 1.30)	N/A

Notes: The hazard ratios presented above can be interpreted in the following way: The treatment in the row is the reference treatment and the treatment in the column is the comparator, i.e., SVd versus Kd results in a HR of 1.08, whereas Kd versus SVd results in a HR of 0.93

Figure 28. Forest plot of the NMA for overall survival in the ITT population (reference treatment: SVd)



As shown above, in the ITT population SVd was numerically superior to Vd and PVd, and numerically inferior to Kd for OS

As in the lenalidomide refractory population, due to the structure of the treatment network, neither within- or between-design heterogeneity was present.

C.3.2 Progression-free survival

The results of the frequentist NMA, for the outcome of progression survival in the ITT population, are displayed in Table 69 and Figure 29

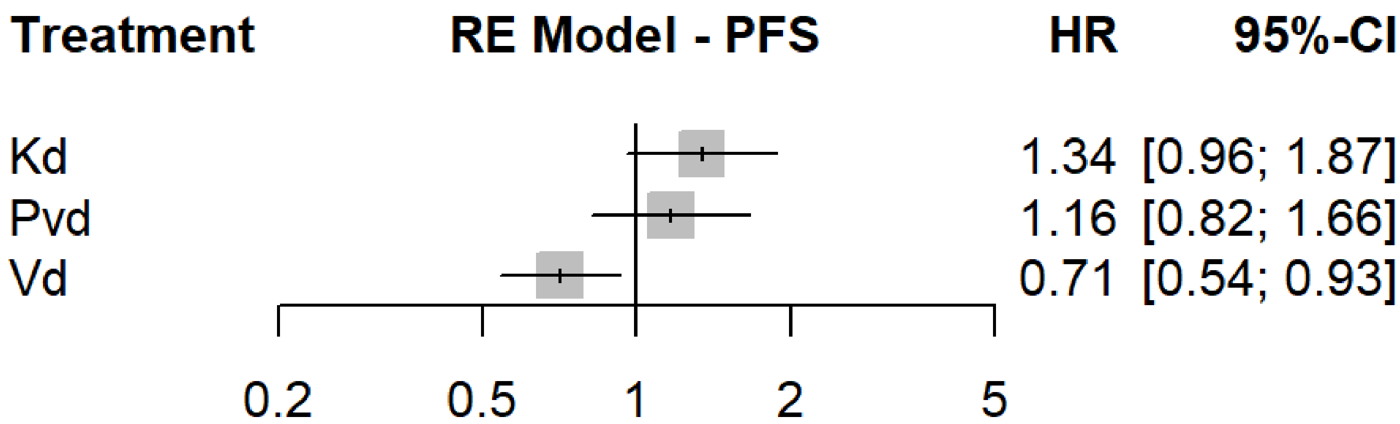
Table 69. Progression-free survival in the ITT population

	SVd (BOSTON)	Kd (ENDEAVOR)	PVd (OPTMISMM)	Vd
SVd (BOSTON)	N/A	HR: 1.34 (95% CI: 0.96 to 1.87)	HR: 1.16 (95% CI: 0.82 to 1.166)	HR: 0.71 (95% CI: 0.54 to 0.93)

Kd (ENDEAVOR)	HR: 0.75 (95% CI: 0.53 to 1.04)	N/A	HR: 0.87 (95% CI: 0.64 to 1.17)	HR: 0.53 (95% CI: 0.44 to 0.64)
PVd (OPTMISMM)	HR: 0.86 (95% CI: 0.60 to 1.22)	HR: 1.15 (95% CI: 0.85 to 1.55)	N/A	HR: 0.61 (95% CI: 0.49 to 0.76)
Vd	HR: 1.41 (95% CI: 1.07 to 1.84)	HR: 1.89 (95% CI: 1.55 to 2.29)	HR: 1.64 (95% CI: 1.30 to 2.05)	N/A

Notes: The hazard ratios presented above can be interpreted in the following way: The treatment in the row is the reference treatment and the treatment in the column is the comparator, i.e., SVd versus Kd results in a HR of 1.34, whereas Kd versus SVd results in a HR of 0.75

Figure 29. Forest plot of the NMA for progression-free survival in the ITT population (reference treatment: SVd)



For progression-free survival in the ITT population, SVd was numerically superior to Vd, and numerically inferior to Kd and PVd.

As in the other analyses, due to the structure of the treatment network, neither within- or between-design heterogeneity was present.

Appendix D. Extrapolation

D.1 Extrapolation of overall survival

D.1.1 Data input

The data derived from patient-level data from the February 15th, 2021 data cut of the BOSTON clinical trial lenalidomide-refractory patients. Survival model were chosen based on the NICE DSU technical support document 14.[59] The Kaplan Meier curves for OS was used. Both OS for SVd and Vd was analysed, in order to be able to test for proportional hazards assumption.

D.1.2 Model

For each endpoint, parametric curves were fitted both independently (i.e., only to the SVd arm of the trial), and jointly (dependent curves fitted to both SVd and Vd arms, with the calculation of a treatment arm coefficient to capture differences between the two). Each approach has its advantages: the jointly fitted estimates draw on a greater pool of evidence, informed by approximately twice the number of observations, but assumes proportional hazards between the two arms. Independent curve fitting avoids the undue influence of the comparator arm on estimates, and does not rely on the proportional hazards' assumption, but incurs greater uncertainty associated with sample size.

D.1.3 Proportional hazards

Based on the results of the proportional hazards testing, the proportional hazard assumption was assumed to hold between the SVd and Vd treatment arms using the adjusted OS (with re-censoring) data in the lenalidomide refractory population. Therefore, the base case uses a single model to extrapolate outcomes with a covariate estimating the treatment effect i.e., dependent parametric curves. The Schoenfeld residuals and log-cumulative hazard plots are available in Figure 30 and Figure 31. The Grambsch and Therneau test found proportional hazards may hold between the treatment arms with a p-value=0.06.

Figure 30. Schoenfeld plot for the overall survival

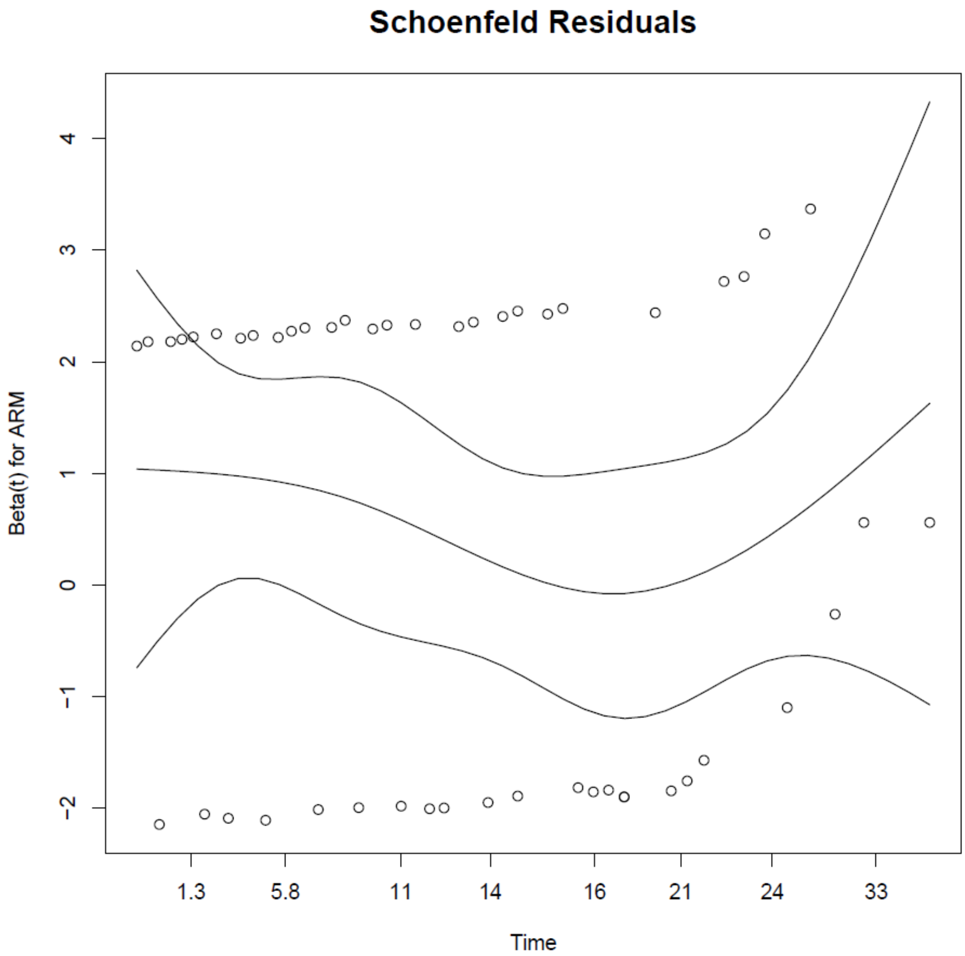
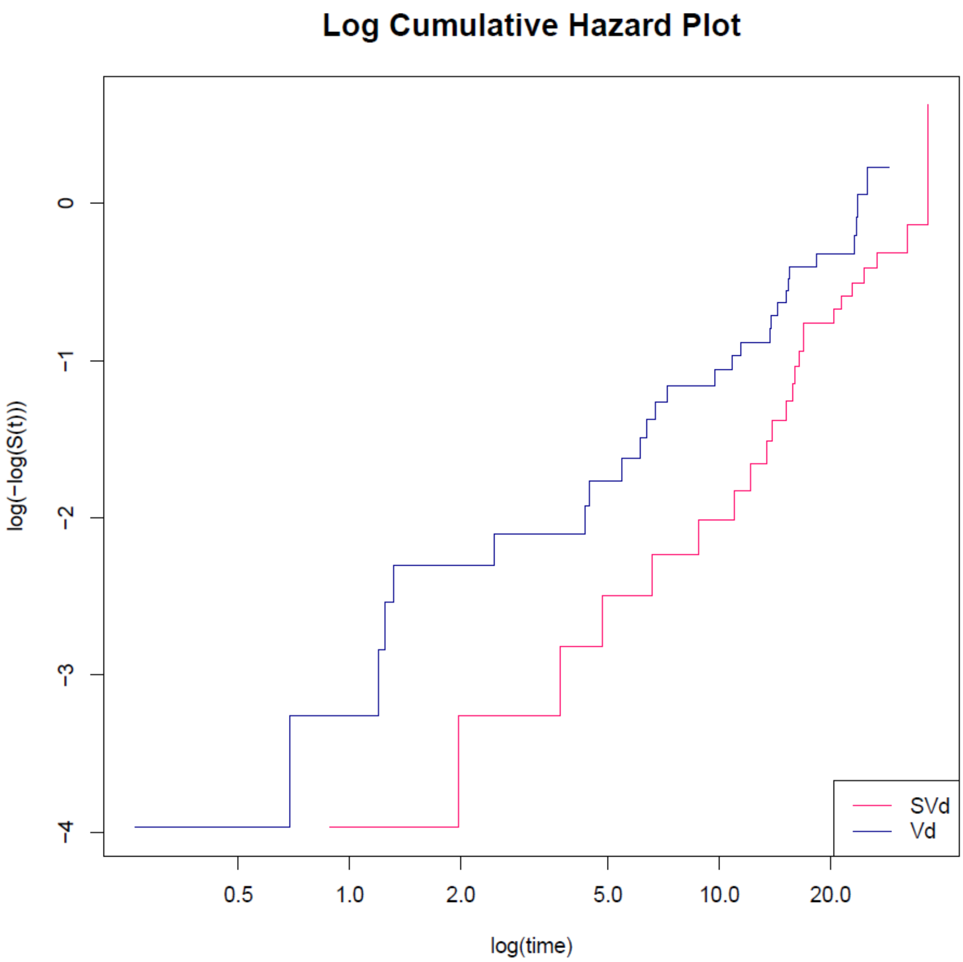


Figure 31. Log cumulative hazard plot for overall survival



D.1.4 Evaluation of statistical fit (AIC and BIC)

The AIC and BIC for the dependent model is presented in Table 70.

Table 70. AIC and BIC for dependent OS parametric functions

Function	AIC	BIC
Exponential	449	454
Weibull	449	457
Lognormal	455	463
Loglogistic	451	459
Gompertz	447	455

Generalised Gamma	450	460
Gamma	449	457

D.1.5 Evaluation of visual fit

The SVd OS curves are presented in Figure 32. In general, the gamma, Weibull, and exponential curves have a decent visual fit. Generalized gamma and Gompertz seem to underestimate survival, while log-logistic and log-normal have longer tails, risking overestimating survival. As requested by the DMC on 20th Nov 2024, the Vd OS curves are presented in Figure 33. However, Vd is not a comparator and therefore OS extrapolations have no impact on the model.

Figure 32. Overall survival curves for SVd lenalidomide refractory patients

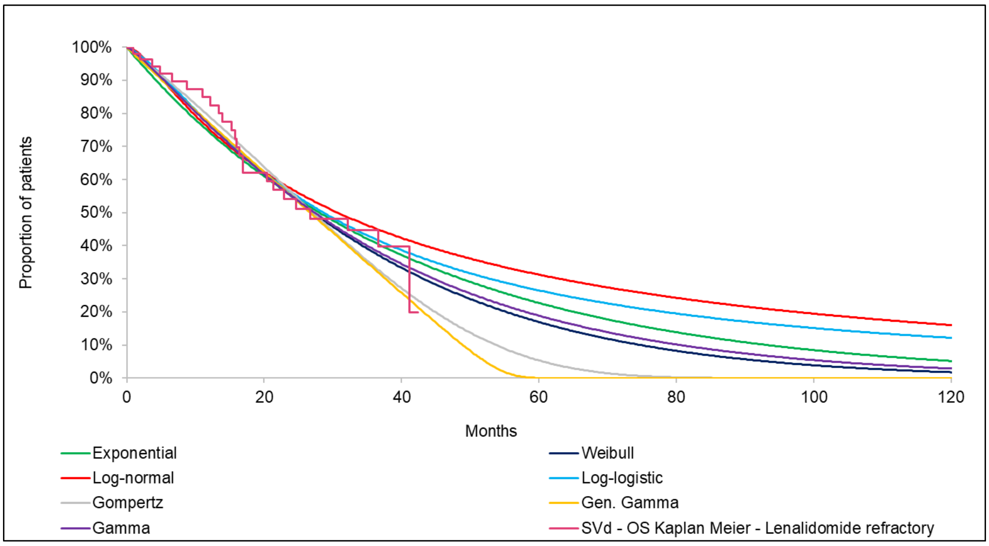
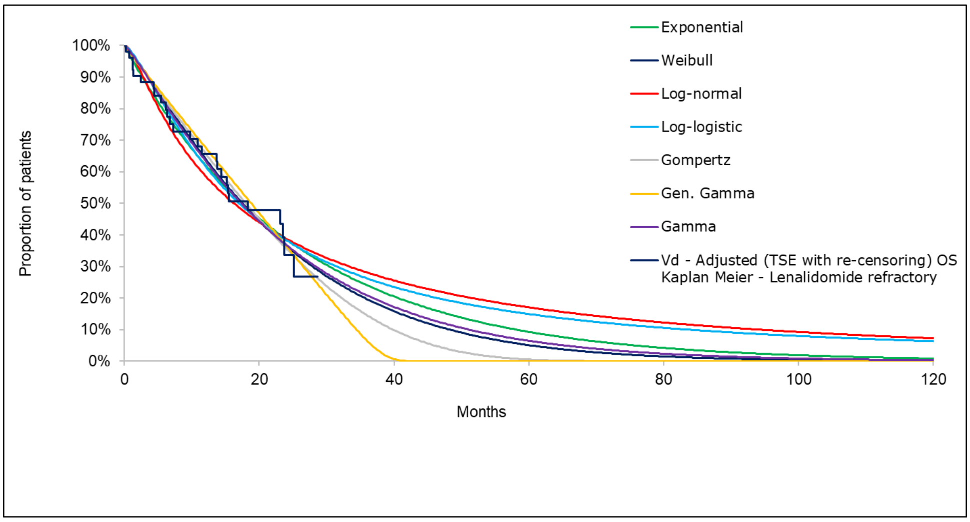


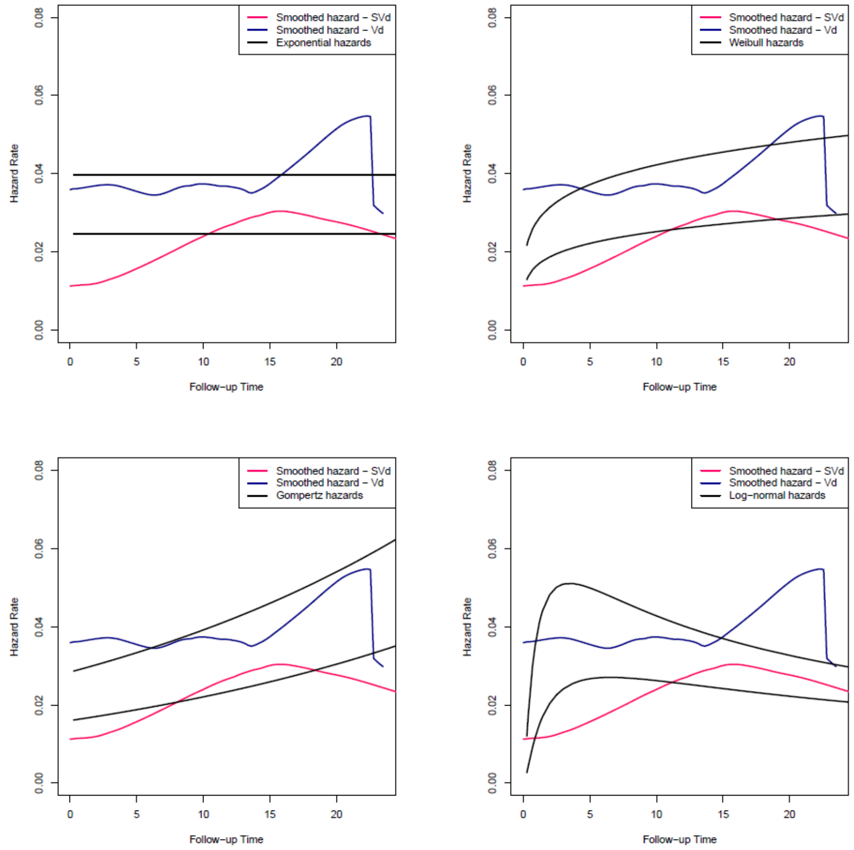
Figure 33. Overall survival curves for Vd lenalidomide refractory patients

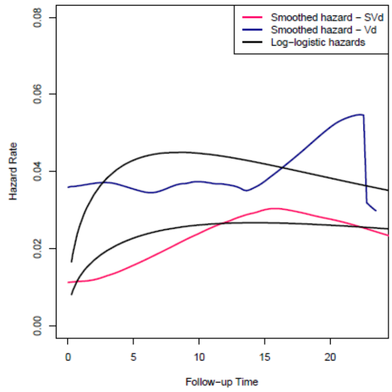


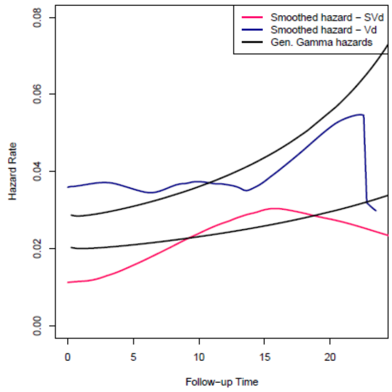
D.1.6 Evaluation of hazard functions

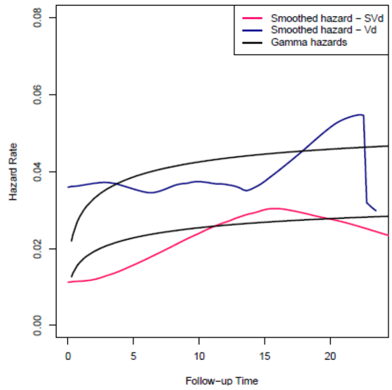
The hazard functions are presented in Figure 41. While none of the functions seems to have a perfect fit to the smoothed hazard function, it is seen that for SVd the log-logistic and gamma functions have the best fit to the smoothed hazard functions.

Figure 34. Hazard plots for dependent overall survival functions









D.1.7 Validation and discussion of extrapolated curves

Log-normal and log-logistic curves were excluded based on extrapolated 10-year survival rates in excess of more than 10% of the patient population. Further, the 10-year survival rate of 0% estimated using the Gompertz was considered likely to be a too pessimistic extrapolation for a 2L only setting, given that expected range of 1-10% survival at 10 years elicited from clinical experts was provided in the context of a combined 2L and 3L patient population. Of the remaining curves considered (gamma, generalised gamma and Weibull), the gamma was best fitting and selected in the base case, with an extrapolated estimate of 3% survival at 10 years.

D.1.8 Adjustment of background mortality

The OS was adjusted for background mortality using the general mortality provided in the from “Key figures including general mortality within the Danish population” Excel file.

D.1.9 Adjustment for treatment switching/cross-over

In the base case, the adjusted OS with re-censoring was used. Analyses were conducted on unadjusted OS data and OS data adjusted for crossover from the Vd arm to selinexor using the two-stage estimation (TSE) approach with and without re-censoring. The TSE is the only approach considered to adjust for treatment crossover.

D.1.10 Waning effect

Not applicable.

D.1.11 Cure-point

Not applicable.

D.2 Extrapolation of progression-free survival

D.2.1 Data input

The data derived from patient-level data from the February 15th, 2021 data cut of the BOSTON clinical trial lenalidomide-refractory patients. Survival model were chosen based on the NICE DSU technical support document 14.[59] The Kaplan Meier curves for PFS was used. Both PFS for SVd and Vd was analysed, in order to be able to test for proportional hazards assumption.

D.2.2 Model

For each endpoint, parametric curves were fitted both independently (i.e., only to the SVd arm of the trial), and jointly (dependent curves fitted to both SVd and Vd arms, with the calculation of a treatment arm coefficient to capture differences between the two). Each approach has its advantages: the jointly fitted estimates draw on a greater pool of evidence, informed by approximately twice the number of observations, but assumes proportional hazards between the two arms. Independent curve fitting avoids the undue influence of the comparator arm on estimates, and does not rely on the proportional hazards' assumption, but incurs greater uncertainty associated with sample size

D.2.3 Proportional hazards

For the PFS extrapolation, the proportional hazards assumption did not hold based on testing, and therefore independent log-normal models were chosen, as illustrated in Figure 35. It is also seen in the log-cumulative hazard plot in Figure 36, that the curves are crossing, indicating that proportional hazards are unlikely to hold. In addition, the Grambsch and Therneau test found proportional hazards may be unlikely to hold between the treatment arms with a p-value<0.05.

Figure 35. Schoenfeld plot for the progression-free survival

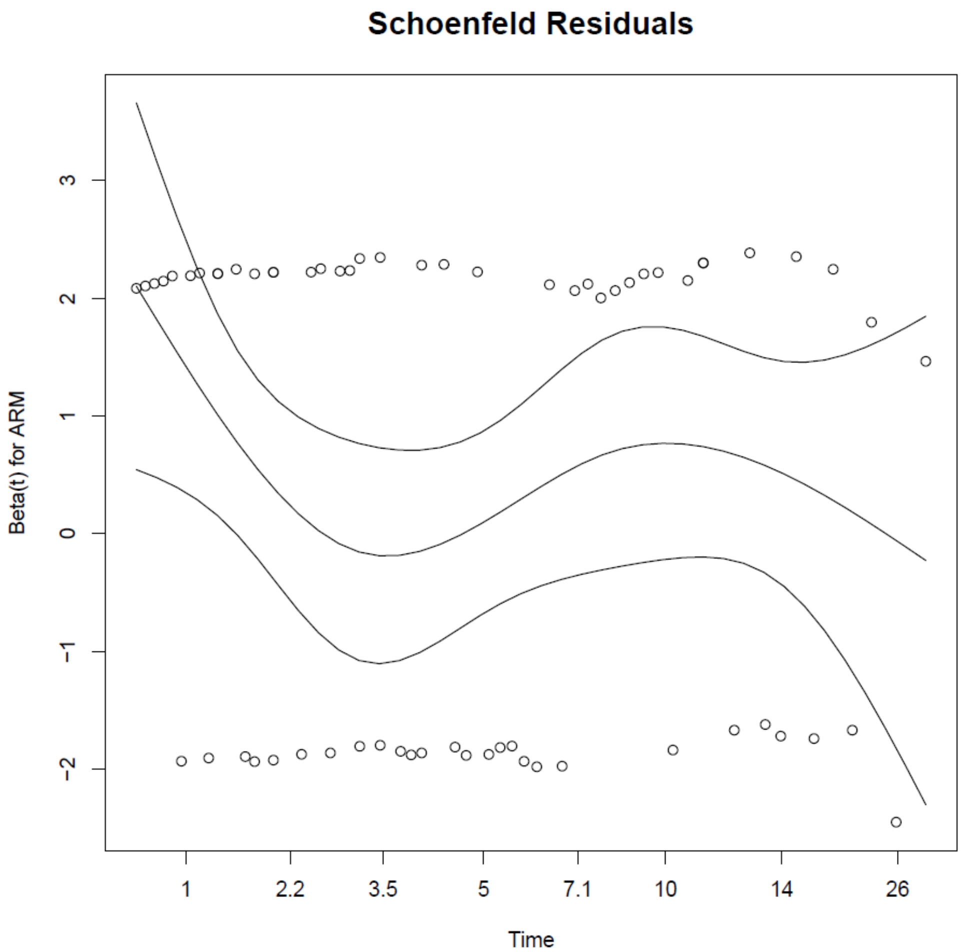
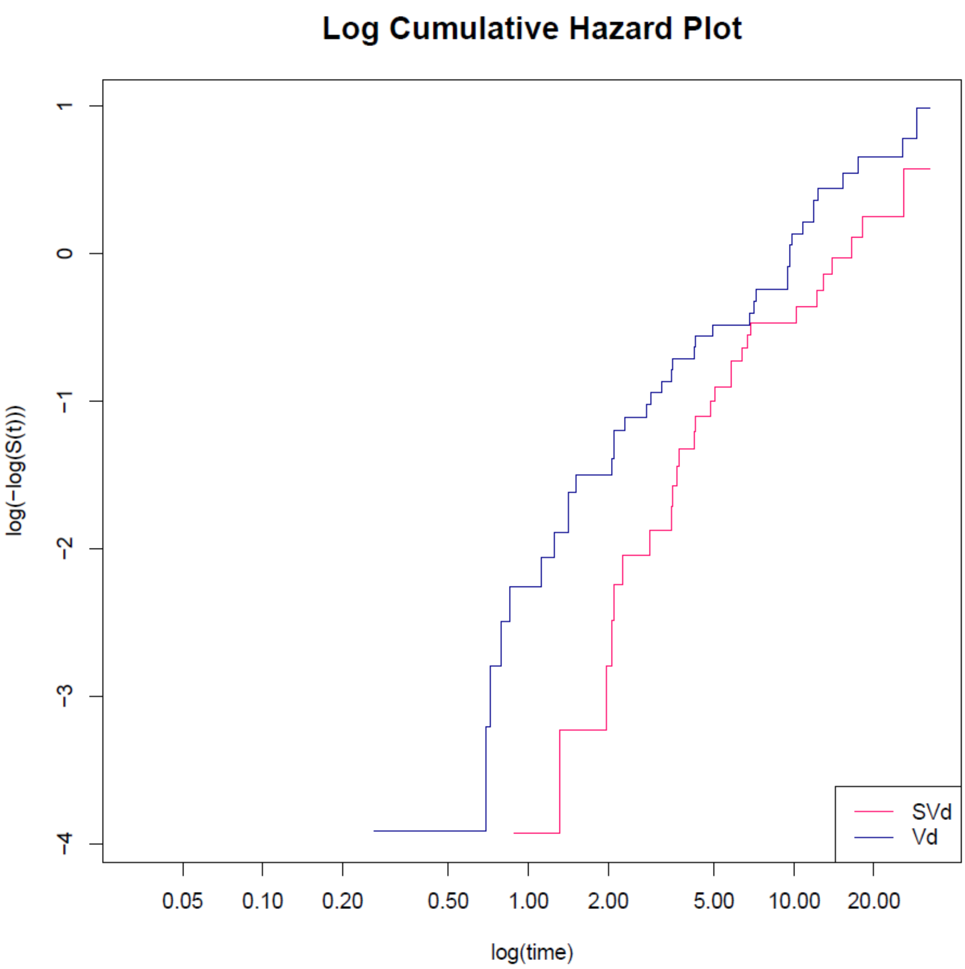


Figure 36. Log cumulative hazard plot for progression free survival



D.2.4 Evaluation of statistical fit (AIC and BIC)

The AIC and BIC for the independent model is presented in Table 71.

Table 71. AIC and BIC from independent parametric models – PFS BICR – lenalidomide refractory

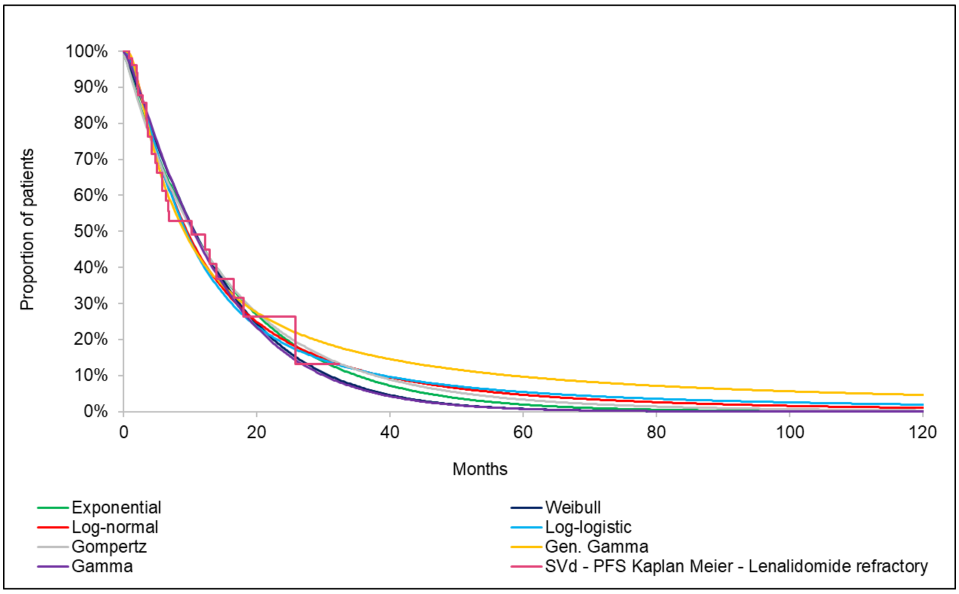
	SVd		Vd	
	AIC	BIC	AIC	BIC
Exponential	203	205	249	251
Weibull	204	208	251	254
Lognormal	200	204	248	252
Loglogistic	201	205	249	253
Gompertz	205	209	250	254

Generalised Gamma	201	207	250	256
Gamma	204	208	251	255

D.2.5 Evaluation of visual fit

As seen in Figure 37, Weibull and gamma curves seems to underestimate the PFS, while generalized gamma seem to overestimate PFS. Remaining curves seem to have a good visual fit.

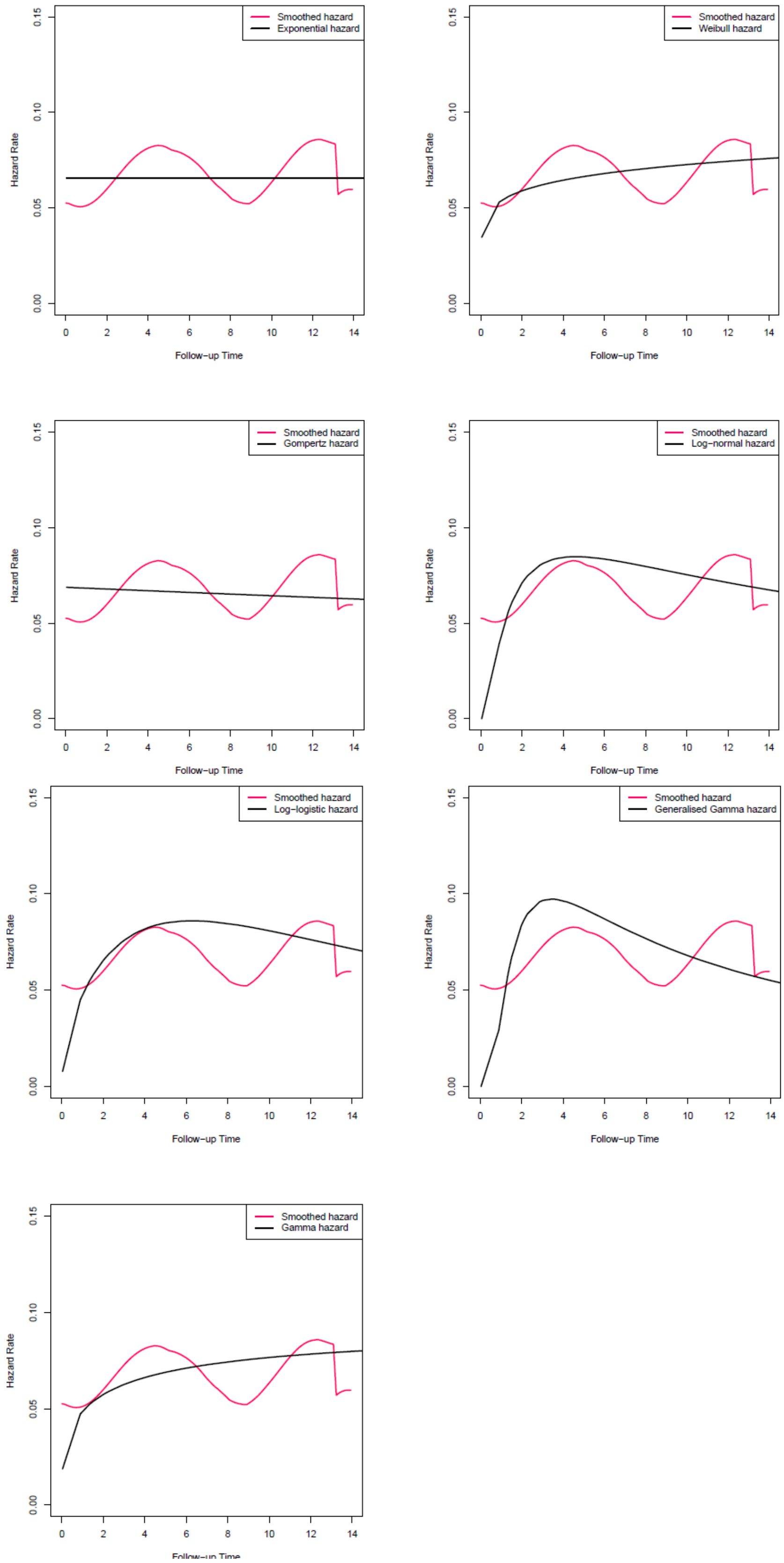
Figure 37. Progression-free survival curves for SVd lenalidomide refractory patients



D.2.6 Evaluation of hazard functions

As seen in Figure 38, the smoothed hazard function is entails variations of hazard, which is mostly seen in the log-logistic, generalized gamma and gamma functions, as such these seem to have the best fit to the smoothed hazard function.

Figure 38. Hazard plots for independent progression-free survival functions



D.2.7 Validation and discussion of extrapolated curves

Log-normal provided the best statistical fit for SVd both in terms of AIC and BIC, and was not found clinical implausible.

D.2.8 Adjustment of background mortality

PFS not adjusted. OS was capped by Danish general mortality based on the DMC's excel file.

D.2.9 Adjustment for treatment switching/cross-over

Not applicable.

D.2.10 Waning effect

Not applicable.

D.2.11 Cure-point

Not applicable.

D.3 Extrapolation of time on treatment

D.3.1 Data input

The data derived from patient-level data from the February 15th, 2021 data cut of the BOSTON clinical trial lenalidomide-refractory patients. Survival model were chosen based on the NICE DSU technical support document 14.[59] The Kaplan Meier curves for ToT was used. Both ToT for SVd and Vd was analysed, in order to be able to test for proportional hazards assumption.

D.3.2 Model

For each endpoint, parametric curves were fitted both independently (i.e., only to the SVd arm of the trial), and jointly (dependent curves fitted to both SVd and Vd arms, with the calculation of a treatment arm coefficient to capture differences between the two). Each approach has its advantages: the jointly fitted estimates draw on a greater pool of evidence, informed by approximately twice the number of observations, but assumes proportional hazards between the two arms. Independent curve fitting avoids the undue influence of the comparator arm on estimates, and does not rely on the proportional hazards' assumption, but incurs greater uncertainty associated with sample size.

D.3.3 Proportional hazards

Based on the results of the proportional hazards testing, the proportional hazard assumption was assumed to hold between the SVd and Vd treatment arms using the ToT) data in the lenalidomide refractory population. Therefore, the base case uses a single model to extrapolate outcomes with a covariate estimating the treatment effect i.e., dependent parametric curves. The Schoenfeld residuals and log-cumulative hazard plots are available in Figure 39 and Figure 40. The Grambsch and Therneau test found that the proportional hazards assumption may hold between the treatment arms with a p-value=0.532.

Figure 39. Schoenfeld plot for the time on treatment

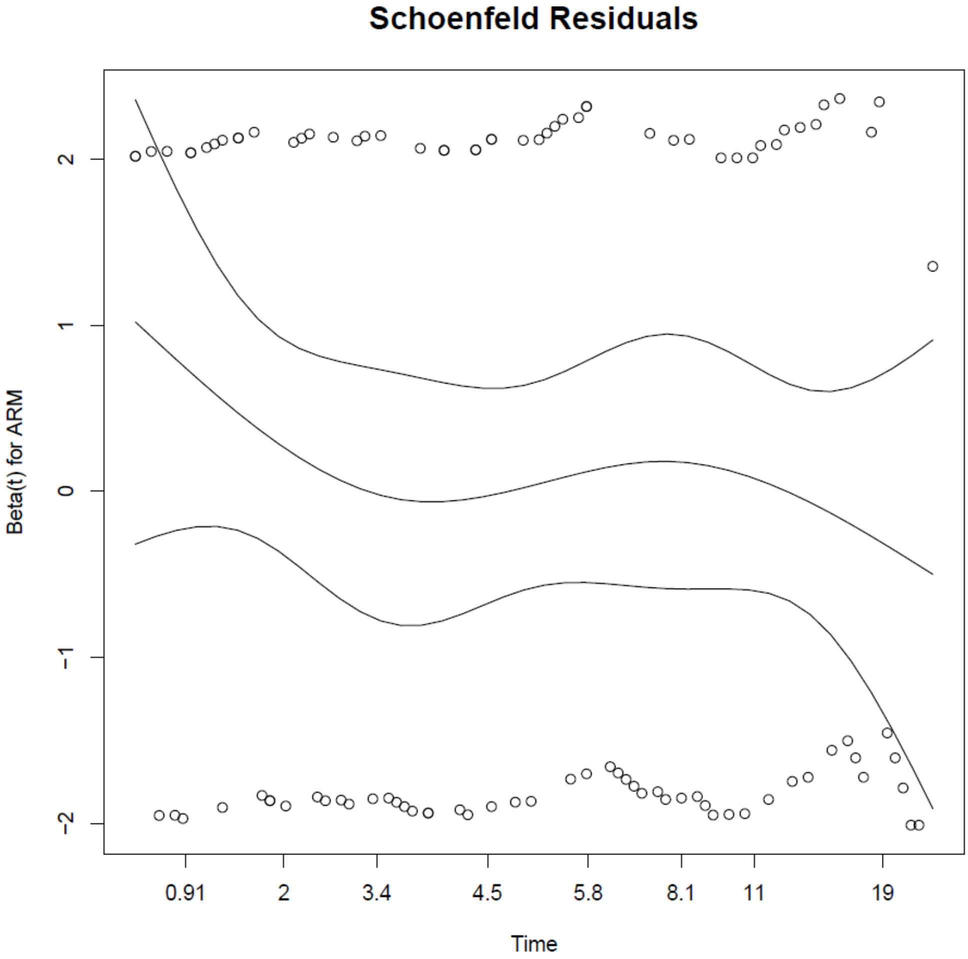
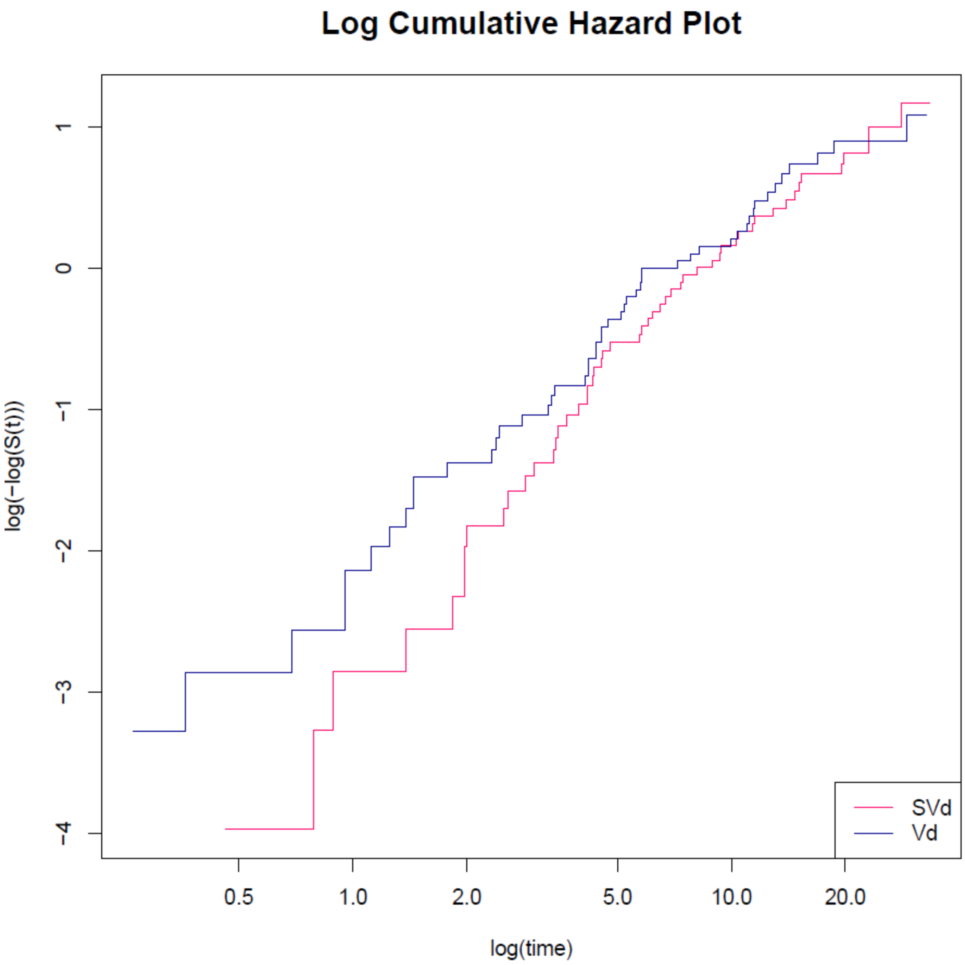


Figure 40. Log cumulative hazard plot for time on treatment



D.3.4 Evaluation of statistical fit (AIC and BIC)

The AIC and BIC for the dependent model is presented in Table 72.

Table 72. AIC and BIC from dependent parametric models - ToT – lenalidomide refractory

Function	AIC	BIC
Exponential	637	642
Weibull	638	646
Lognormal	633	641
Loglogistic	632	640
Gompertz	638	646

Generalised Gamma	634	645
Gamma	637	645

D.3.5 Evaluation of visual fit

Overall, all curves seem to have a decent visual fit, as seem om Figure 41. As requested by the DMC on 20th Nov 2024, the Vd OS curves are presented in Figure 42. However, Vd is not a comparator and therefore OS extrapolations have no impact on the model.

Figure 41. Time on treatment curves for SVd lenalidomide refractory patients

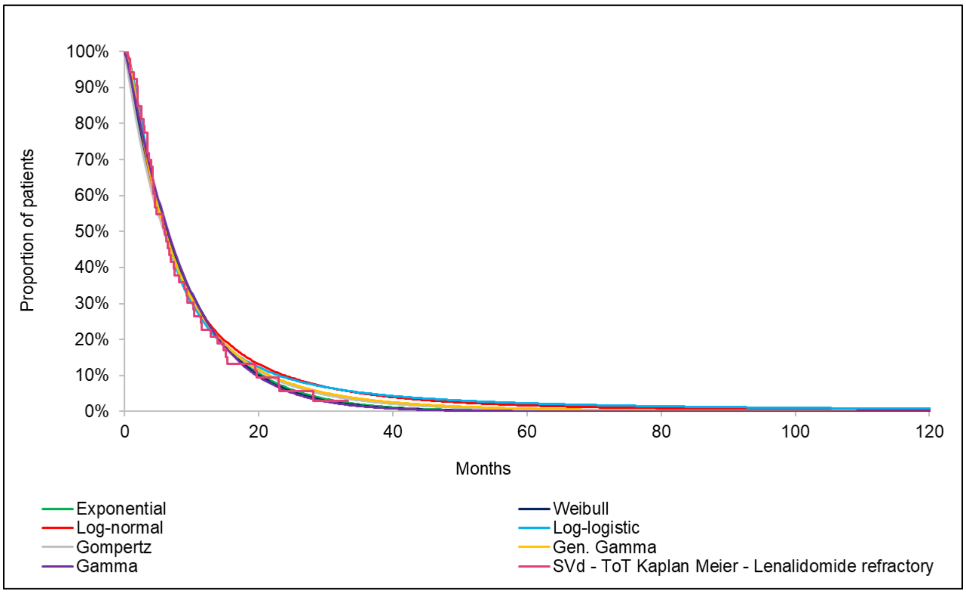
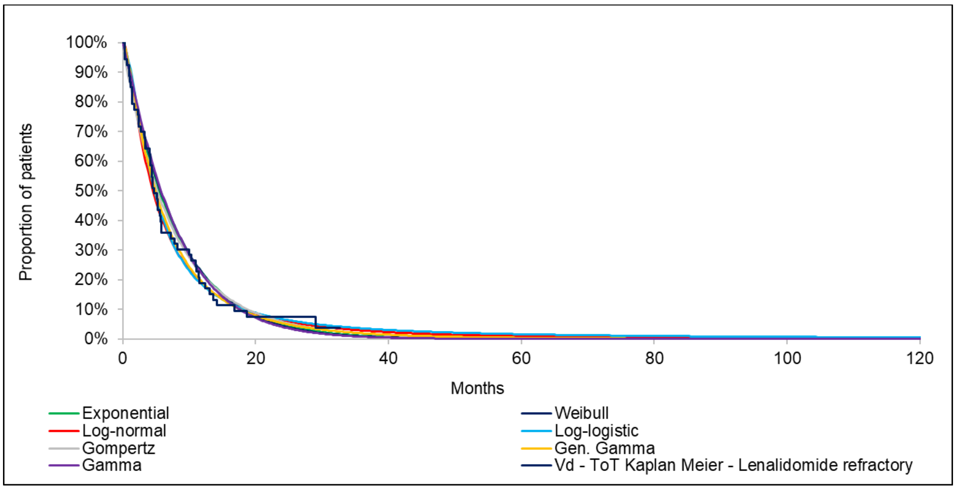


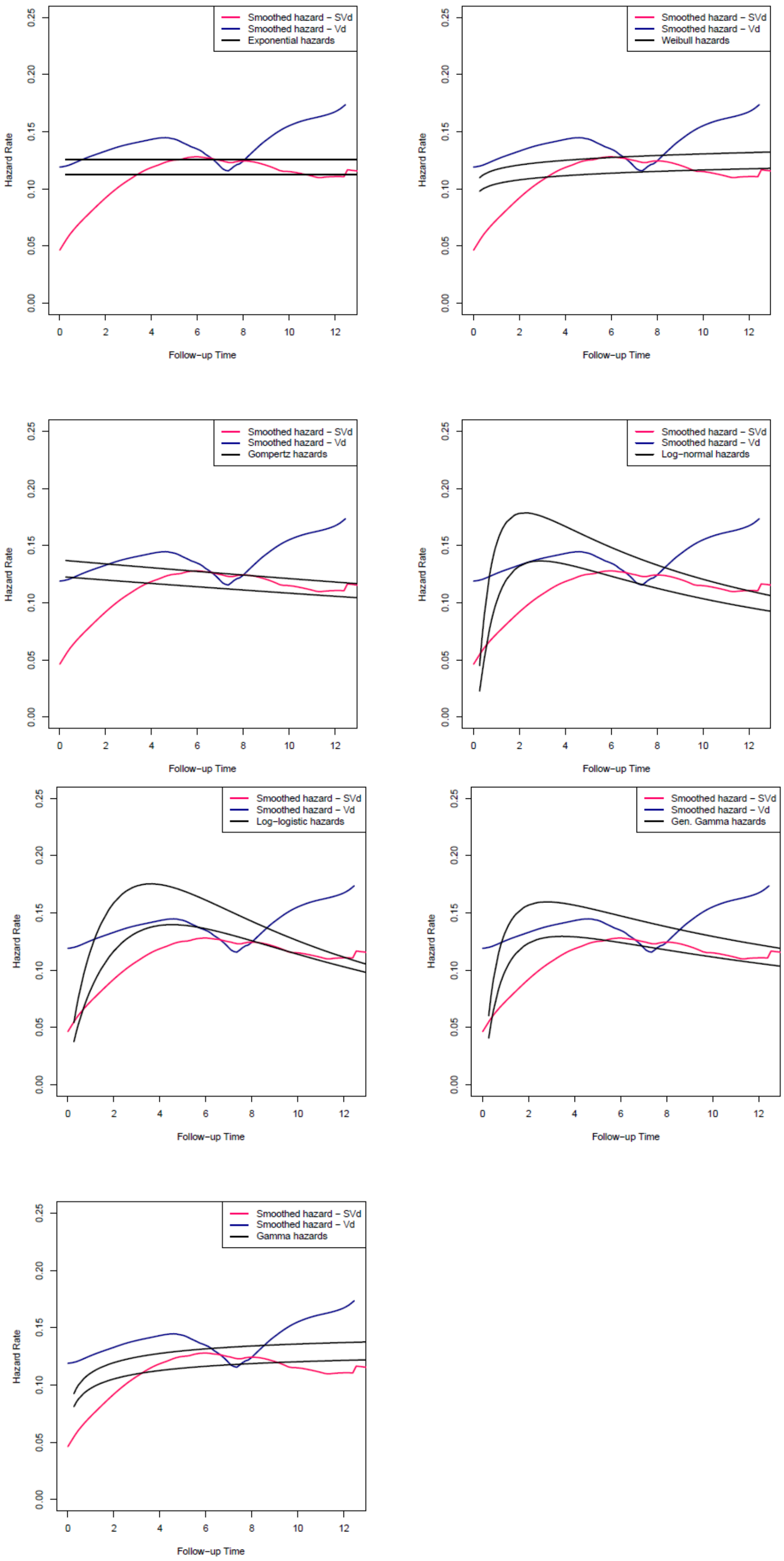
Figure 42. Time on treatment curves for Vd lenalidomide refractory patients



D.3.6 Evaluation of hazard functions

The hazard functions for the dependent models are presented in Figure 43. The log-logistic and generalized gamma functions seemed to have the best fit.

Figure 43. Hazard plots for independent time on treatment functions



D.3.7 Validation and discussion of extrapolated curves

The log-logistic curve provided the best statistical fit based on both AIC and BIC, and was not found clinically implausible.

D.3.8 Adjustment of background mortality

Not applicable.

D.3.9 Adjustment for treatment switching/cross-over

Not applicable.

D.3.10 Waning effect

Not applicable.

D.3.11 Cure-point

Not applicable.

Appendix E. Serious adverse events

Table 73. Serious adverse events observed in BOSTON, ENDEAVOR, and OPTIMISMM

Adverse event	SVd (n = 195)	Vd (n = 204)	Vd (n=456)	Kd (n=463)	PVd (n=278)	Vd (n=270
Blood and lympathic system disorders						
Anaemia	5 (2.56%)	3 (1.47%)	1 (0.22%)	4 (0.86%)	4 (1.44%)	5 (1.85%)
Thrombocytopenia	3 (1.54%)	1 (0.49%)	6 (1.32%)	4 (0.86%)	2 (0.72%)	3 (1.11%)
Febrile neutropenia	1 (0.51%)	1 (0.49%)	3 (0.66%)	3 (0.65%)	5 (1.8%)	1 (0.37%)
Neutropenia	1 (0.51%)	0 (0%)	0 (0%)	1 (0.22%)	1 (0.36%)	0 (0%)
Haemorrhagic anaemia	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
Plasmacytosis	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
Thrombotic microangiopathy	0 (0%)	0 (0%)	0 (0%)	2 (0.43%)	0 (0%)	0 (0%)
Thrombotic thrompocytopenic purpura	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)

Hyperviscosity syndrome	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (1.11%)
Lymphopenia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Cardiac disorders						
Atrial fibrillation	4 (2.05%)	2 (0.98%)	4 (0.88%)	6 (1.3%)	9 (3.24%)	2 (0.74%)
Cardiac failure congestive	1 (0.51%)	1 (0.49%)	0 (0%)	1 (0.22%)	3 (1.08%)	2 (0.74%)
Myocardial infarction	1 (0.51%)	1 (0.49%)	2 (0.44%)	5 (1.08%)	1 (0.36%)	1 (0.37%)
Acute myocardial infarction	0 (0%)	1 (0.49%)	2 (0.44%)	1 (0.22%)	1 (0.36%)	1 (0.37%)
Angina pectoris	0 (0%)	1 (0.49%)	0 (0%)	3 (0.65%)	1 (0.36%)	0 (0%)
Atrioventricular block	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Bradycardia	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Cardiac arrest	1 (0.51%)	0 (0%)	1 (0.22%)	2 (0.43%)	2 (0.72%)	0 (0%)
Cardiac failure	0 (0%)	1 (0.49%)	3 (0.66%)	9 (1.94%)	3 (1.08%)	2 (0.74%)

Cardio-respiratory arrest	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Cardiomyopathy	0 (0%)	1 (0.49%)	0 (0%)	2 (0.43%)	0 (0%)	0 (0%)
Cardiovascular disorder	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Left ventricular dysfunction	1 (0.51%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	1 (0.37%)
Left ventricular failure	0 (0%)	1 (0.49%)	1 (0.22%)	0 (0%)	0 (0%)	1 (0.37%)
Myocardial ischaemia	0 (0%)	1 (0.49%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Sinus tachycardia	1 (0.51%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
Ventricular arrhythmia	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Acute coronary syndrome	0 (0%)	0 (0%)	0 (0%)	2 (0.43%)	2 (0.72%)	0 (0%)
Acute left ventricular failure	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
Aortic valve incompetence	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
Atrial flutter	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	2 (0.72%)	1 (0.37%)

Bifascicular block	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
Cardiac failure acute	0 (0%)	0 (0%)	1 (0.22%)	2 (0.43%)	0 (0%)	0 (0%)
Cardiac hypertrophy	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
Pericardial effusion	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	1 (0.37%)
Pleuropericarditis	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
Right ventricular failure	0 (0%)	0 (0%)	1 (0.22%)	1 (0.22%)	0 (0%)	0 (0%)
Stress cardiomyopathy	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
Supraventricular tachycardia	0 (0%)	0 (0%)	0 (0%)	2 (0.43%)	0 (0%)	1 (0.37%)
Angina unstable	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.72%)	0 (0%)
Atrial thrombosis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Atrioventricular block complete	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Atrioventricular block second degree	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Bundle branch block left	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)

Coronary artery disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.72%)	0 (0%)
Pericarditis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Restrictive cardiomyopathy	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Sinus bradycardia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Sinus node dysfunction	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.72%)	0 (0%)
Ear and labyrinth disorders						
Hearing imparied	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
Vertigo	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Endocrine disorders						
Inappropriate antidiuretic hormone secretion	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
Hyperthyroidism	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Eye disorders						
Cataract	4 (2.05%)	0 (0%)	1 (0.22%)	0 (0%)	1 (0.36%)	0 (0%)

Retinal tear	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
Retinal detachment	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Retinal vein thrmbosis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Gastrointestinal disorders						
Diarrhoea	7 (3.59%)	0 (0%)	11 (2.41%)	5 (1.08%)	5 (1.8%)	6 (2.22%)
Vomiting	7 (3.59%)	0 (0%)	2 (0.44%)	5 (1.08%)	1 (0.36%)	3 (1.11%)
Nausea	4 (2.05%)	0 (0%)	3 (0.66%)	2 (0.43%)	1 (0.36%)	3 (1.11%)
Constipation	1 (0.51%)	2 (0.98%)	2 (0.44%)	1 (0.22%)	2 (0.72%)	2 (0.74%)
Abdominal pain	0 (0%)	2 (0.98%)	2 (0.44%)	2 (0.43%)	2 (0.72%)	1 (0.37%)
Colitis	1 (0.51%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
Colitis ischaemic	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Dyspepsia	0 (0%)	1 (0.49%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Lower gastrointestinal haemorrhage	1 (0.51%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	1 (0.37%)

Abdominal distension	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
Abdominal pain upper	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	1 (0.36%)	0 (0%)
Abdominal strangulated hernia	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
Diverticulum	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
Enterocolitis	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	1 (0.36%)	0 (0%)
Gastric haemorrhage	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	1 (0.36%)	0 (0%)
Gastrointestinal disorder	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
GASTROINTESTINAL HAEMORRHAGE	0 (0%)	0 (0%)	2 (0.44%)	1 (0.22%)	0 (0%)	1 (0.37%)
ILEUS	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	1 (0.36%)	1 (0.37%)
ILEUS PARALYTIC	0 (0%)	0 (0%)	3 (0.66%)	0 (0%)	0 (0%)	0 (0%)
INTESTINAL OBSTRUCTION	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	1 (0.36%)	0 (0%)
INTESTINAL POLYP HAEMORRHAGE	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
LARGE INTESTINE PERFORATION	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)

MELAENA	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
PANCREATITIS	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
PARAESTHESIA ORAL	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
SMALL INTESTINAL OBSTRUCTION	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
SUBILEUS	0 (0%)	0 (0%)	1 (0.22%)	1 (0.22%)	0 (0%)	0 (0%)
Abdominal pain upper	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.72%)	0 (0%)
Colonic fistula	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Food poisoning	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Gastric ulcer haemorrhage	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Gastric volvulus	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Haemorrhoidal haemorrhage	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	1 (0.37%)
Pancreatitis acute	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Parotid gland enlargement	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)

Retroperitoneal haematoma	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Retroperitoneal haemorrhage	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Umbilical hernia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Upper gastrointestinal haemorrhage	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
General disorders						
Asthenia	2 (1.03%)	2 (0.98%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
Pyrexia	3 (1.54%)	1 (0.49%)	3 (0.66%)	19 (4.1%)	12 (4.32%)	5 (1.85%)
Fatigue	2 (1.03%)	1 (0.49%)	1 (0.22%)	3 (0.65%)	1 (0.36%)	0 (0%)
General physical health deterioration	3 (1.54%)	0 (0%)	1 (0.22%)	3 (0.65%)	5 (1.8%)	9 (3.33%)
Chest pain	1 (0.51%)	1 (0.49%)	1 (0.22%)	3 (0.65%)	0 (0%)	0 (0%)
Death	1 (0.51%)	0 (0%)	0 (0%)	1 (0.22%)	4 (1.44%)	0 (0%)

Multiple organ dysfunction syndrome	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Non-cardiac chest pain	1 (0.51%)	0 (0%)	0 (0%)	1 (0.22%)	3 (1.08%)	2 (0.74%)
CARDIAC DEATH	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
DEVICE OCCLUSION	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
DISEASE PROGRESSION	0 (0%)	0 (0%)	6 (1.32%)	8 (1.73%)	0 (0%)	0 (0%)
GENERALISED OEDEMA	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
HYPERPYREXIA	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
HYPERTHERMIA	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
MALAISE	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	2 (0.74%)
OEDEMA PERIPHERAL	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
PAIN	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	1 (0.36%)	1 (0.37%)
SUDDEN DEATH	0 (0%)	0 (0%)	1 (0.22%)	3 (0.65%)	0 (0%)	0 (0%)

THROMBOSIS IN DEVICE	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
Gait disturbance	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.74%)
Influenza like illness	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Non-cardiac chest pain	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (1.08%)	2 (0.74%)
Systemic inflammatory response syndrome	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Hepatobiliary disorders						
Cholecystitis acute	1 (0.51%)	0 (0%)	1 (0.22%)	0 (0%)	1 (0.36%)	0 (0%)
Cholelithiasis	1 (0.51%)	0 (0%)	2 (0.44%)	0 (0%)	1 (0.36%)	0 (0%)
Hepatic cirrhosis	0 (0%)	1 (0.49%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Liver disorder	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
BILE DUCT STONE	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
HEPATIC FAILURE	0 (0%)	0 (0%)	0 (0%)	2 (0.43%)	0 (0%)	0 (0%)
HEPATOCELLULAR INJURY	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)

JAUNDICE CHOLESTATIC	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
Cholecystitis chronic	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Hepatitis acute	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Hepatotoxicity	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Hyperbilirubinaemia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Immune system disorders						
HYPERSENSITIVITY	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
HYPOGAMMAGLOBULINAEMIA	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
Infections and infestations						
Pneumonia	23 (11.79%)	24 (11.76%)	42 (9.21%)	39 (8.42%)	34 (12.23%)	17 (6.3%)
Lower respiratory tract infection	4 (2.05%)	3 (1.47%)	5 (1.1%)	7 (1.51%)	10 (3.6%)	5 (1.85%)
Bronchitis	3 (1.54%)	2 (0.98%)	2 (0.44%)	8 (1.73%)	3 (1.08%)	2 (0.74%)

Gastroenteritis	4 (2.05%)	1 (0.49%)	4 (0.88%)	5 (1.08%)	0 (0%)	1 (0.37%)
Influenza	3 (1.54%)	1 (0.49%)	4 (0.88%)	5 (1.08%)	10 (3.6%)	4 (1.48%)
Septic shock	4 (2.05%)	0 (0%)	3 (0.66%)	4 (0.86%)	6 (2.16%)	0 (0%)
Upper respiratory tract infection	3 (1.54%)	1 (0.49%)	3 (0.66%)	7 (1.51%)	3 (1.08%)	3 (1.11%)
Urinary tract infection	4 (2.05%)	0 (0%)	4 (0.88%)	6 (1.3%)	3 (1.08%)	0 (0%)
Respiratory syncytial virus infection	2 (1.03%)	1 (0.49%)	2 (0.44%)	0 (0%)	2 (0.72%)	0 (0%)
Urosepsis	3 (1.54%)	0 (0%)	3 (0.66%)	0 (0%)	1 (0.36%)	2 (0.74%)
Cellulitis	1 (0.51%)	1 (0.49%)	1 (0.22%)	3 (0.65%)	2 (0.72%)	1 (0.37%)
Clostridium difficile colitis	0 (0%)	2 (0.98%)	0 (0%)	0 (0%)	4 (1.44%)	0 (0%)
Infection	1 (0.51%)	1 (0.49%)	0 (0%)	4 (0.86%)	3 (1.08%)	1 (0.37%)
Pneumonia pneumococcal	2 (1.03%)	0 (0%)	1 (0.22%)	1 (0.22%)	1 (0.36%)	2 (0.74%)

Staphylococcal sepsis	1 (0.51%)	1 (0.49%)	0 (0%)	0 (0%)	1 (0.36%)	1 (0.37%)
Chest wall abscess	0 (0%)	1 (0.49%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Clostridium difficile infection	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Corona virus infection	1 (0.51%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
Escherichia bacteraemia	1 (0.51%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	1 (0.37%)
Gangrene	0 (0%)	1 (0.49%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Gastroenteritis norovirus	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
H1N1 influenza	0 (0%)	1 (0.49%)	0 (0%)	1 (0.22%)	1 (0.36%)	1 (0.37%)
Laryngitis	0 (0%)	1 (0.49%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Meningitis tuberculous	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Orchitis	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pneumonia bacterial	1 (0.51%)	0 (0%)	1 (0.22%)	1 (0.22%)	2 (0.72%)	1 (0.37%)

Pneumonia fungal	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pneumonia influenzal	1 (0.51%)	0 (0%)	0 (0%)	1 (0.22%)	2 (0.72%)	0 (0%)
Pneumonia parainfluenzae viral	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Pneumonia respiratory syncytial viral	0 (0%)	1 (0.49%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Pulmonary sepsis	0 (0%)	1 (0.49%)	1 (0.22%)	0 (0%)	2 (0.72%)	0 (0%)
Sepsis	1 (0.51%)	0 (0%)	4 (0.88%)	7 (1.51%)	5 (1.8%)	1 (0.37%)
ABDOMINAL INFECTION	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
ABSCESS LIMB	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	1 (0.36%)	0 (0%)
ACUTE SINUSITIS	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
APPENDICITIS	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
BACTERAEMIA	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
BACTERIAL DIARRHOEA	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)

BACTERIAL INFECTION	0 (0%)	0 (0%)	2 (0.44%)	1 (0.22%)	0 (0%)	0 (0%)
BREAST ABSCESS	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
BRONCHIOLITIS	0 (0%)	0 (0%)	0 (0%)	2 (0.43%)	1 (0.36%)	0 (0%)
BRONCHOPNEUMONIA	0 (0%)	0 (0%)	1 (0.22%)	7 (1.51%)	0 (0%)	0 (0%)
BRONCHOPULMONARY ASPERGILLOSIS	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	1 (0.37%)
BURSITIS INFECTIVE	0 (0%)	0 (0%)	1 (0.22%)	1 (0.22%)	0 (0%)	0 (0%)
CATHETER SITE INFECTION	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	1 (0.36%)	0 (0%)
CLOSTRIDIAL INFECTION	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
CLOSTRIDIUM DIFFICILE SEPSIS	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
DEVICE RELATED INFECTION	0 (0%)	0 (0%)	0 (0%)	2 (0.43%)	0 (0%)	1 (0.37%)
DIVERTICULITIS	0 (0%)	0 (0%)	0 (0%)	3 (0.65%)	1 (0.36%)	0 (0%)
ENCEPHALITIC INFECTION	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
ENCEPHALITIS HERPES	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)

ENTERITIS INFECTIOUS	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
ERYSIPELAS	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	2 (0.72%)	0 (0%)
ESCHERICHIA URINARY TRACT INFECTION	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	3 (1.08%)	1 (0.37%)
FEBRILE INFECTION	0 (0%)	0 (0%)	0 (0%)	2 (0.43%)	0 (0%)	0 (0%)
GASTROENTERITIS VIRAL	0 (0%)	0 (0%)	1 (0.22%)	1 (0.22%)	0 (0%)	0 (0%)
HAEMOPHILUS SEPSIS	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	1 (0.37%)
HERPES ZOSTER	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
INFECTIOUS PLEURAL EFFUSION	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
INFECTIVE EXACERBATION OF CHRONIC OBSTRUCTIVE AIRWAYS DISEASE	0 (0%)	0 (0%)	1 (0.22%)	1 (0.22%)	0 (0%)	0 (0%)
LISTERIOSIS	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
LOBAR PNEUMONIA	0 (0%)	0 (0%)	1 (0.22%)	2 (0.43%)	0 (0%)	0 (0%)
LOWER RESPIRATORY TRACT INFECTION VIRAL	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
LUNG INFECTION	0 (0%)	0 (0%)	3 (0.66%)	5 (1.08%)	2 (0.72%)	2 (0.74%)

NECROTISING ULCERATIVE PERIODONTITIS	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
ORAL FUNGAL INFECTION	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
OSTEOMYELITIS	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	1 (0.36%)	0 (0%)
PARAINFLUENZAE VIRUS INFECTION	0 (0%)	0 (0%)	0 (0%)	2 (0.43%)	0 (0%)	0 (0%)
PHARYNGITIS	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	1 (0.36%)	0 (0%)
PNEUMOCOCCAL INFECTION	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
PNEUMOCYSTIS JIROVECI PNEUMONIA	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	1 (0.36%)	0 (0%)
PNEUMONIA MORAXELLA	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	1 (0.36%)	0 (0%)
PSEUDOMEMBRANOUS COLITIS	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
RESPIRATORY TRACT INFECTION	0 (0%)	0 (0%)	5 (1.1%)	10 (2.16%)	5 (1.8%)	0 (0%)
RESPIRATORY TRACT INFECTION VIRAL	0 (0%)	0 (0%)	1 (0.22%)	2 (0.43%)	1 (0.36%)	0 (0%)
SINUSITIS	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	2 (0.72%)	0 (0%)
STREPTOCOCCAL BACTERAEMIA	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)

TRACHEOBRONCHITIS	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
VIRAL INFECTION	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
VIRAL UPPER RESPIRATORY TRACT INFECTION	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
Acute hepatitis B	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Atypical pneumonia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Bacterial sepsis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Bronchitis bacterial	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Bronchitis pneumococcal	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Endocarditis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Enterobacter pneumonia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	1 (0.37%)
Enterococcal sepsis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Epididymitis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Escherichia sepsis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	1 (0.37%)

Gastroenteritis salmonella	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.72%)	0 (0%)
Herpes oesophagitis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Herpes zoster	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Hordeolum	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Leishmaniasis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Localised infection	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Mastoiditis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Meningitis listeria	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Meningococcal infection	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Muscle abscess	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Neutropenic sepsis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Oesophageal candidiasis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Periorbital cellulitis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)

Pharyngotonsillitis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Pneumococcal sepsis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Pneumonia haemophilus	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Pneumonia legionella	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.72%)	0 (0%)
Pneumonia staphylococcal	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.72%)	0 (0%)
Pneumonia streptococcal	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	2 (0.74%)
Respiratory syncytial virus bronchiolitis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Respiratory tract infection bacterial	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Rhinovirus infection	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Skin infection	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.72%)	0 (0%)
Staphylococcal bacteraemia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Streptococcal sepsis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Urinary tract infection bacterial	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	1 (0.37%)

Urinary tract infection staphylococcal	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Injury, poisoning and procedural complications						
Femur fracture	2 (1.03%)	1 (0.49%)	1 (0.22%)	0 (0%)	1 (0.36%)	3 (1.11%)
Fall	2 (1.03%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Cervical vertebral fracture	0 (0%)	1 (0.49%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Femoral neck fracture	0 (0%)	1 (0.49%)	1 (0.22%)	0 (0%)	1 (0.36%)	0 (0%)
Hip fracture	1 (0.51%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
Injury	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Overdose	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Pelvic fracture	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Postoperative respiratory failure	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Rib fracture	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	1 (0.37%)

Subdural haemorrhage	0 (0%)	1 (0.49%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
CHEST INJURY	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
COMPRESSION FRACTURE	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
FACIAL BONES FRACTURE	0 (0%)	0 (0%)	1 (0.22%)	1 (0.22%)	0 (0%)	0 (0%)
FOOT FRACTURE	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
FRACTURE	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
HEAD INJURY	0 (0%)	0 (0%)	1 (0.22%)	1 (0.22%)	0 (0%)	1 (0.37%)
HUMERUS FRACTURE	0 (0%)	0 (0%)	0 (0%)	3 (0.65%)	2 (0.72%)	1 (0.37%)
INFUSION RELATED REACTION	0 (0%)	0 (0%)	0 (0%)	3 (0.65%)	1 (0.36%)	0 (0%)
LIGAMENT SPRAIN	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
OPEN WOUND	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)

PUBIS FRACTURE	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
SPINAL COMPRESSION FRACTURE	0 (0%)	0 (0%)	1 (0.22%)	1 (0.22%)	0 (0%)	0 (0%)
ULNA FRACTURE	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
UPPER LIMB FRACTURE	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
Post procedural haemorrhage	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Spinal fracture	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Subcutaneous haematoma	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Investigations						
Blood glucose abnormal	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
ALANINE AMINOTRANSFERASE INCREASED	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	1 (0.36%)	0 (0%)
ASPARTATE AMINOTRANSFERASE INCREASED	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	1 (0.36%)	0 (0%)

BLOOD CORTISOL DECREASED	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
BLOOD CREATININE INCREASED	0 (0%)	0 (0%)	0 (0%)	2 (0.43%)	1 (0.36%)	1 (0.37%)
INFLUENZA B VIRUS TEST POSITIVE	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
LYMPHOCYTE COUNT DECREASED	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
PLATELET COUNT DECREASED	0 (0%)	0 (0%)	3 (0.66%)	2 (0.43%)	0 (0%)	0 (0%)
TROPONIN T INCREASED	0 (0%)	0 (0%)	1 (0.22%)	1 (0.22%)	0 (0%)	0 (0%)
Blood alkaline phosphatase increased	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Chest X-ray abnormal	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Coronavirus test positive	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
General physical condition abnormal	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
International normalised ratio increased	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Neutrophil count decreased	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Metabolism and nutrition disorders						

Dehydration	3 (1.54%)	0 (0%)	3 (0.66%)	0 (0%)	3 (1.08%)	2 (0.74%)
Hypokalaemia	1 (0.51%)	1 (0.49%)	1 (0.22%)	1 (0.22%)	0 (0%)	0 (0%)
Cachexia	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Decreased appetite	1 (0.51%)	0 (0%)	2 (0.44%)	0 (0%)	0 (0%)	0 (0%)
Hyperkalaemia	0 (0%)	1 (0.49%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Tumour lysis syndrome	0 (0%)	1 (0.49%)	0 (0%)	1 (0.22%)	1 (0.36%)	0 (0%)
DIABETES MELLITUS	0 (0%)	0 (0%)	1 (0.22%)	2 (0.43%)	0 (0%)	1 (0.37%)
DIABETES MELLITUS INADEQUATE CONTROL	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
HYPERCALCAEMIA	0 (0%)	0 (0%)	5 (1.1%)	0 (0%)	1 (0.36%)	0 (0%)
HYPERGLYCAEMIA	0 (0%)	0 (0%)	1 (0.22%)	4 (0.86%)	3 (1.08%)	1 (0.37%)
HYPOGLYCAEMIA	0 (0%)	0 (0%)	0 (0%)	3 (0.65%)	2 (0.72%)	0 (0%)
HYPONATRAEMIA	0 (0%)	0 (0%)	1 (0.22%)	2 (0.43%)	2 (0.72%)	0 (0%)
HYPOVOLAEMIA	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	1 (0.36%)	0 (0%)

Hypoalbuminaemia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Hypomagnesaemia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Malnutrition	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Metabolic acidosis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Type 2 diabetes mellitus	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Musculoskeletal and connective tissue disorders						
Bone pain	1 (0.51%)	1 (0.49%)	0 (0%)	4 (0.86%)	1 (0.36%)	1 (0.37%)
Back pain	0 (0%)	1 (0.49%)	3 (0.66%)	6 (1.3%)	3 (1.08%)	1 (0.37%)
Mobility decreased	1 (0.51%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
Osteoarthritis	1 (0.51%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
Osteochondrosis	0 (0%)	1 (0.49%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Spinal pain	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
ARTHRALGIA	0 (0%)	0 (0%)	3 (0.66%)	1 (0.22%)	1 (0.36%)	0 (0%)

FLANK PAIN	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
INTERVERTEBRAL DISC PROTRUSION	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
LUMBAR SPINAL STENOSIS	0 (0%)	0 (0%)	1 (0.22%)	2 (0.43%)	0 (0%)	0 (0%)
MUSCULAR WEAKNESS	0 (0%)	0 (0%)	1 (0.22%)	1 (0.22%)	1 (0.36%)	1 (0.37%)
MUSCULOSKELETAL CHEST PAIN	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	1 (0.36%)	0 (0%)
MUSCULOSKELETAL PAIN	0 (0%)	0 (0%)	1 (0.22%)	1 (0.22%)	0 (0%)	1 (0.37%)
MYALGIA	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
OSTEONECROSIS OF JAW	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
PAIN IN EXTREMITY	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	2 (0.74%)
PATHOLOGICAL FRACTURE	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	2 (0.72%)	0 (0%)
RHABDOMYOLYSIS	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
Arthritis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Cervical spinal stenosis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)

Osteorrhagia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
Myelodysplastic syndrome	0 (0%)	1 (0.49%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Ovarian neoplasm	0 (0%)	1 (0.49%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pancreatic carcinoma metastatic	0 (0%)	1 (0.49%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
ACUTE MYELOID LEUKAEMIA	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
BASAL CELL CARCINOMA	0 (0%)	0 (0%)	0 (0%)	2 (0.43%)	6 (2.16%)	1 (0.37%)
BLADDER TRANSITIONAL CELL CARCINOMA	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
CANCER PAIN	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
CARCINOMA IN SITU	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
COLON CANCER	0 (0%)	0 (0%)	1 (0.22%)	1 (0.22%)	0 (0%)	0 (0%)

MENINGEAL NEOPLASM	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
METASTASES TO SPINE	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
MULTIPLE MYELOMA	0 (0%)	0 (0%)	1 (0.22%)	5 (1.08%)	0 (0%)	0 (0%)
OESOPHAGEAL SQUAMOUS CELL CARCINOMA	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
PLASMACYTOMA	0 (0%)	0 (0%)	0 (0%)	5 (1.08%)	1 (0.36%)	1 (0.37%)
PLEURAL MESOTHELIOMA	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
RECTAL CANCER	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
SQUAMOUS CELL CARCINOMA	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	1 (0.36%)	1 (0.37%)
TONGUE NEOPLASM MALIGNANT STAGE UNSPECIFIED	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
Acute lymphocytic leukaemia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Basosquamous carcinoma	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)

Bowen's disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.72%)	0 (0%)
Bronchial carcinoma	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Keratoacanthoma	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Metastases to meninges	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Plasma cell leukaemia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Porocarcinoma	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Prostate cancer	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Renal cell carcinoma	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Scrotal cancer	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Squamous cell carcinoma of skin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4 (1.44%)	2 (0.74%)
Nervous system disorders						

Cerebral infarction	0 (0%)	2 (0.98%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Neuropathy peripheral	0 (0%)	2 (0.98%)	2 (0.44%)	1 (0.22%)	0 (0%)	0 (0%)
Syncope	1 (0.51%)	1 (0.49%)	4 (0.88%)	1 (0.22%)	6 (2.16%)	5 (1.85%)
Transient ischaemic attack	1 (0.51%)	1 (0.49%)	2 (0.44%)	0 (0%)	1 (0.36%)	0 (0%)
Brain oedema	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Carotid artery aneurysm	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Cerebral haemorrhage	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Cerebral ischaemia	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Dementia Alzheimer's type	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Encephalopathy	1 (0.51%)	0 (0%)	0 (0%)	1 (0.22%)	1 (0.36%)	0 (0%)
Hepatic encephalopathy	0 (0%)	1 (0.49%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Ischaemic stroke	0 (0%)	1 (0.49%)	0 (0%)	3 (0.65%)	0 (0%)	1 (0.37%)

Metabolic encephalopathy	1 (0.51%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
Neuralgia	0 (0%)	1 (0.49%)	1 (0.22%)	1 (0.22%)	0 (0%)	0 (0%)
Paraesthesia	0 (0%)	1 (0.49%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Presyncope	0 (0%)	1 (0.49%)	0 (0%)	0 (0%)	1 (0.36%)	1 (0.37%)
Vascular dementia	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
ACQUIRED EPILEPTIC APHASIA	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
CENTRAL NERVOUS SYSTEM LESION	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
CEREBROVASCULAR ACCIDENT	0 (0%)	0 (0%)	0 (0%)	4 (0.86%)	2 (0.72%)	0 (0%)
COGNITIVE DISORDER	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	1 (0.36%)	1 (0.37%)
CONVULSION	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
DEPRESSED LEVEL OF CONSCIOUSNESS	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	1 (0.37%)
DIZZINESS	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	1 (0.37%)

HEADACHE	0 (0%)	0 (0%)	0 (0%)	2 (0.43%)	0 (0%)	0 (0%)
HYPERCAPNIC COMA	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
HYPERTENSIVE ENCEPHALOPATHY	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
LETHARGY	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
LOSS OF CONSCIOUSNESS	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	1 (0.37%)
PARAPARESIS	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	1 (0.36%)	0 (0%)
PARAPLEGIA	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	1 (0.36%)	0 (0%)
POLYNEUROPATHY	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME	0 (0%)	0 (0%)	0 (0%)	2 (0.43%)	0 (0%)	0 (0%)
RADICULITIS BRACHIAL	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
RADICULOPATHY	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
SCIATICA	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
SPINAL CORD COMPRESSION	0 (0%)	0 (0%)	2 (0.44%)	4 (0.86%)	1 (0.36%)	2 (0.74%)

Altered state of consciousness	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Amnesia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Aphasia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Disturbance in attention	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Dizziness	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Epilepsy	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Generalised tonic-clonic seizure	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Guillain-Barre syndrome	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Hypoxic-ischaemic encephalopathy	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Ischaemic cerebral infarction	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Lumbar radiculopathy	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Motor dysfunction	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Nerve root compression	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)

Peripheral motor neuropathy	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Peripheral sensory neuropathy	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Trigeminal neuralgia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Pregnancy, puerpium and perinatal conditions						
Pregnancy	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Psychiatric disorders						
Affect lability	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Mixed anxiety and depressive disorder	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Personality change	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Reactive psychosis	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
COMPLETED SUICIDE	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
CONFUSIONAL STATE	0 (0%)	0 (0%)	4 (0.88%)	4 (0.86%)	1 (0.36%)	0 (0%)

DEPRESSION	0 (0%)	0 (0%)	1 (0.22%)	1 (0.22%)	1 (0.36%)	0 (0%)
DYSTHYMIC DISORDER	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
MENTAL DISORDER	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
PSYCHOTIC DISORDER	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
Anxiety	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Mental status changes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)
Renal and urinary disorders						
Acute kidney injury	4 (2.05%)	2 (0.98%)	0 (0%)	0 (0%)	8 (2.88%)	6 (2.22%)
Haematuria	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
ALBUMINURIA	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
ANURIA	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	1 (0.36%)	0 (0%)
NEPHROPATHY	0 (0%)	0 (0%)	1 (0.22%)	1 (0.22%)	0 (0%)	0 (0%)
NEPHROTIC SYNDROME	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)

PROTEINURIA	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
RENAL FAILURE	0 (0%)	0 (0%)	0 (0%)	5 (1.08%)	0 (0%)	0 (0%)
RENAL FAILURE ACUTE	0 (0%)	0 (0%)	7 (1.54%)	11 (2.38%)	0 (0%)	0 (0%)
RENAL IMPAIRMENT	0 (0%)	0 (0%)	2 (0.44%)	1 (0.22%)	0 (0%)	0 (0%)
URINARY RETENTION	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	1 (0.36%)	0 (0%)
PROSTATOMEGALY	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
UTERINE HAEMORRHAGE	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
Chronic kidney disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Nephrolithiasis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Renal colic	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Urinary bladder haemorrhage	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Reproductive system and breast disorder						
Pelvic prolapse	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Respiratory, thoracic and mediastinal disorders

Chronic obstructive pulmonary disease	1 (0.51%)	2 (0.98%)	1 (0.22%)	2 (0.43%)	0 (0%)	1 (0.37%)
Dyspnoea	2 (1.03%)	1 (0.49%)	1 (0.22%)	18 (3.89%)	4 (1.44%)	1 (0.37%)
Epistaxis	3 (1.54%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pulmonary embolism	2 (1.03%)	1 (0.49%)	3 (0.66%)	10 (2.16%)	9 (3.24%)	1 (0.37%)
Pulmonary oedema	1 (0.51%)	1 (0.49%)	1 (0.22%)	2 (0.43%)	0 (0%)	0 (0%)
Acute respiratory failure	1 (0.51%)	0 (0%)	1 (0.22%)	0 (0%)	3 (1.08%)	0 (0%)
Bronchiectasis	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Bronchospasm	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pneumonitis	1 (0.51%)	0 (0%)	1 (0.22%)	2 (0.43%)	0 (0%)	1 (0.37%)
ACUTE PULMONARY OEDEMA	0 (0%)	0 (0%)	1 (0.22%)	3 (0.65%)	1 (0.36%)	0 (0%)

ACUTE RESPIRATORY DISTRESS SYNDROME	0 (0%)	0 (0%)	1 (0.22%)	1 (0.22%)	0 (0%)	0 (0%)
ASTHMA	0 (0%)	0 (0%)	1 (0.22%)	3 (0.65%)	0 (0%)	0 (0%)
BRONCHOPNEUMOPATHY	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
EPISTAXIS	0 (0%)	0 (0%)	1 (0.22%)	1 (0.22%)	0 (0%)	0 (0%)
HYPOXIA	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	2 (0.72%)	1 (0.37%)
INTERSTITIAL LUNG DISEASE	0 (0%)	0 (0%)	0 (0%)	2 (0.43%)	0 (0%)	1 (0.37%)
LUNG DISORDER	0 (0%)	0 (0%)	1 (0.22%)	3 (0.65%)	0 (0%)	0 (0%)
PLEURAL EFFUSION	0 (0%)	0 (0%)	1 (0.22%)	2 (0.43%)	3 (1.08%)	3 (1.11%)
PULMONARY ARTERIAL HYPERTENSION	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
PULMONARY HYPERTENSION	0 (0%)	0 (0%)	0 (0%)	3 (0.65%)	0 (0%)	0 (0%)
RESPIRATORY FAILURE	0 (0%)	0 (0%)	0 (0%)	4 (0.86%)	2 (0.72%)	2 (0.74%)
Dyspnoea exertional	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Haemothorax	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.37%)

Hypoxia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.72%)	1 (0.37%)
Pleural effusion	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (1.08%)	3 (1.11%)
Respiratory acidosis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Respiratory alkalosis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Skin and subcutaneous tissue disorders						
DRUG ERUPTION	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
ECZEMA	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
ERYTHEMA MULTIFORME	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
PRURITUS GENERALISED	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
PURPURA	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
Rash	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Skin disorder	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)
Surgical and medical procedures						

COLOSTOMY CLOSURE	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
HAEMORRHOID OPERATION	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
REMOVAL OF INTERNAL FIXATION	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)
Vascular disorders						
Deep vein thrombosis	1 (0.51%)	2 (0.98%)	3 (0.66%)	5 (1.08%)	4 (1.44%)	4 (1.48%)
Blood pressure fluctuation	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Circulatory collapse	0 (0%)	1 (0.49%)	1 (0.22%)	1 (0.22%)	0 (0%)	1 (0.37%)
Embolism	0 (0%)	1 (0.49%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Hypotension	1 (0.51%)	0 (0%)	4 (0.88%)	1 (0.22%)	3 (1.08%)	1 (0.37%)
Orthostatic hypotension	0 (0%)	1 (0.49%)	4 (0.88%)	0 (0%)	0 (0%)	0 (0%)
Peripheral ischaemia	0 (0%)	1 (0.49%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Shock haemorrhagic	1 (0.51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

AORTIC ANEURYSM	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
AORTIC EMBOLUS	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
HAEMATOMA	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
HYPERTENSION	0 (0%)	0 (0%)	0 (0%)	3 (0.65%)	1 (0.36%)	0 (0%)
HYPERTENSIVE CRISIS	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
MALIGNANT HYPERTENSION	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	0 (0%)	0 (0%)	0 (0%)	2 (0.43%)	1 (0.36%)	0 (0%)
THROMBOPHLEBITIS	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
VENA CAVA THROMBOSIS	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
VENOUS THROMBOSIS LIMB	0 (0%)	0 (0%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)
Orthostatic hypotension	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	1 (0.37%)

Peripheral arterial occlusive disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.36%)	0 (0%)

Appendix F. Health-related quality of life

Not applicable.

Appendix G. Probabilistic sensitivity analyses

The full input parameter set is presented in Table 74. The results are presented in section 12.2.2.

Table 74. Input list for the PSA

Input parameter	Point estimate	Lower bound	Upper bound	Probability distribution
Age at baseline - Lenalidomide refractory	65.56	64.63	65.50	Normal
Proportion male at baseline - Lenalidomide refractory	0.62	0.57	0.66	Beta
ECOG score at baseline - Lenalidomide refractory	0.67	0.61	0.68	Normal
EQ-5D-3L at baseline - Lenalidomide refractory	0.72	0.71	0.73	Beta
Weight - Lenalidomide refractory	76.80	75.33	76.49	Normal
BSA - Lenalidomide refractory	1.85	1.83	1.84	Normal
Proportion high-risk cytogenetics - Lenalidomide refractory	0.49	0.44	0.48	Beta
ECOG = 1 - Lenalidomide refractory	0.52	0.47	0.50	Beta
ECOG = 2 - Lenalidomide refractory	0.08	0.05	0.05	Beta
R-ISS = 2 - Lenalidomide refractory	0.58	0.54	0.56	Beta
R-ISS = 3 - Lenalidomide refractory	0.10	0.08	0.10	Beta
Proportion prior SCT - Lenalidomide refractory	0.41	0.36	0.43	Beta
Time since diagnosis - Lenalidomide refractory	4.05	3.73	4.06	Normal
OS Parametric Curves	NA	NA	NA	Multivariate normal
PFS Parametric Curves	NA	NA	NA	Multivariate normal

ToT Parametric Curves	NA	NA	NA	Multivariate normal
Oral administration	0.00	0.00	0.00	Normal
SC administration	1989.00	1599.16	1945.74	Normal
IV administration (first)	1989.00	1599.16	1662.56	Normal
IV administration (subsequent)	1989.00	1599.16	1949.78	Normal
Progression-free resource use (weekly)	595.63	478.89	715.83	Normal
Progressed disease resource use (weekly)	595.63	478.89	662.44	Normal
Cost of Anaemia	2111.00	1697.25	2060.56	Normal
Cost of Asthenia	5103.00	5103.00	5103.00	Normal
Cost of Cataract	1068.00	858.68	1034.06	Normal
Cost of Diarrhoea	7818.00	6285.70	7127.89	Normal
Cost of Fatigue	5103.00	5103.00	5103.00	Normal
Cost of Febrile neutropenia	2111.00	1697.25	1968.01	Normal
Cost of Hypertension	1183.00	951.14	1159.58	Normal
Cost of Hypophosphataemia	1847.00	1484.99	1666.59	Normal
Cost of Leukopenia	2111.00	1697.25	2164.41	Normal
Cost of Lymphopenia	2111.00	1697.25	2059.97	Normal
Cost of Lower respiratory tract infection	1311.00	1054.05	1283.68	Normal
Cost of Nausea	7818.00	6285.70	7367.10	Normal
Cost of Neutropenia	2111.00	1697.25	2416.35	Normal
Cost of Hyperglycaemia	1847.00	1484.99	1953.55	Normal
Cost of Peripheral neuropathy	1582.00	1271.93	1517.66	Normal
Cost of Pneumonia	1311.00	1054.05	1249.11	Normal
Cost of Thrombocytopenia	2111.00	1697.25	1927.27	Normal
Cost of end-of-life care	0.00	0.00	0.00	Fixed

Societal perspective - travel costs (pre-progression)	0.35	0.28	0.35	Normal
Societal perspective - travel costs (progressed disease)	0.35	0.28	0.37	Normal
Societal perspective - productivity costs per death	0.00	0.00	0.00	Normal
PFS Hazard ratio - Kd vs. SVd	1.00	1.00	1.00	Fixed
PFS Hazard ratio - PVd vs. SVd	1.00	1.00	1.00	Fixed
OS Hazard ratio - Kd vs. SVd	1.00	1.00	1.00	Fixed
OS Hazard ratio - PVd vs. SVd	1.00	1.00	1.00	Fixed
Cost per pack - Selinexor	62119.00	62119.00	62119.00	Fixed
Cost per pack - Bortezomib SC	1850.00	1850.00	1850.00	Fixed
Cost per pack - Bortezomib IV	1850.00	1850.00	1850.00	Fixed
Cost per pack - Oral Dexamethasone	599.00	599.00	599.00	Fixed
Cost per pack - Oral Ondansetron	160.00	160.00	160.00	Fixed
Cost per pack - SC Daratumumab	36418.71	36418.71	36418.71	Fixed
Cost per pack - IV Daratumumab	11754.23	11754.23	11754.23	Fixed
Cost per pack - Carfilzomib	3738.23	3738.23	3738.23	Fixed
Cost per pack - pomalidomide	34449.46	34449.46	34449.46	Fixed
Cost per pack - lenalidomide	20000.00	20000.00	20000.00	Fixed
Cost per pack - elotuzumab	6442.24	6442.24	6442.24	Fixed
Cost per pack - isatuximab	18877.23	18877.23	18877.23	Fixed
Cost per pack - ixazomib	44626.56	44626.56	44626.56	Fixed
Cost per pack - panobinostat	29725.33	29725.33	29725.33	Fixed

Cost per pack - venetoclax	453.35	453.35	453.35	Fixed
Dose intensity - SVd - Selinexor	0.89	0.88	0.89	Beta
Dose intensity - SVd - Bortezomib	0.99	0.97	0.99	Beta
Dose intensity - SVd - Dexamethasone	1.00	1.00	1.00	Beta
Dose intensity - SVd - Ondansetron	1.00	1.00	1.00	Beta
Dose intensity - Vd - Bortezomib	1.00	1.00	1.00	Beta
Dose intensity - Vd - Dexamethasone	1.00	1.00	1.00	Beta
Dose intensity - DaraKd - Daratumumab	0.96	0.65	0.87	Beta
Dose intensity - DaraKd - Carfilzomib	0.91	0.67	0.93	Beta
Dose intensity - DaraKd - Dexamethasone	0.91	0.67	0.99	Beta
Dose intensity - DaraPd - Daratumumab	0.94	0.66	0.97	Beta
Dose intensity - DaraPd - Pomalidomide	0.74	0.58	0.76	Beta
Dose intensity - DaraPd - Dexamethasone	0.83	0.64	0.84	Beta
Dose intensity - DaraRd - Daratumumab	1.00	1.00	1.00	Beta
Dose intensity - DaraRd - Lenalidomide	0.85	0.65	0.97	Beta
Dose intensity - DaraRd - Dexamethasone	1.00	1.00	1.00	Beta
Dose intensity - DaraVd - Daratumumab	0.99	0.99	0.99	Beta
Dose intensity - DaraVd - Bortezomib	0.87	0.66	0.97	Beta
Dose intensity - DaraVd - Dexamethasone	0.98	0.75	1.00	Beta
Dose intensity - EloPd - Elotuzumab	1.00	1.00	1.00	Beta
Dose intensity - EloPd - Pomalidomide	1.00	1.00	1.00	Beta
Dose intensity - EloPd - Dexamethasone	1.00	1.00	1.00	Beta
Dose intensity - EloRd - Elotuzumab	1.00	1.00	1.00	Beta
Dose intensity - EloRd - Lenalidomide	1.00	1.00	1.00	Beta
Dose intensity - EloRd - Dexamethasone	1.00	1.00	1.00	Beta
Dose intensity - IsaKd - Isatuximab	0.94	0.66	0.83	Beta

Dose intensity - IsaKd - Carfilzomib	0.91	0.67	0.80	Beta
Dose intensity - IsaKd - Dexamethasone	0.85	0.65	0.88	Beta
Dose intensity - IsaPd - Isatuximab	0.91	0.67	0.73	Beta
Dose intensity - IsaPd - Pomalidomide	0.82	0.63	0.84	Beta
Dose intensity - IsaPd - Dexamethasone	0.85	0.65	0.89	Beta
Dose intensity - IxaRd - Ixazomib	0.97	0.66	1.00	Beta
Dose intensity - IxaRd - Lenalidomide	0.94	0.66	1.00	Beta
Dose intensity - IxaRd - Dexamethasone	0.92	0.66	1.00	Beta
Dose intensity - Kd - Carfilzomib	0.91	0.90	0.91	Beta
Dose intensity - Kd - Dexamethasone	1.00	1.00	1.00	Beta
Dose intensity - KRd - Carfilzomib	0.94	0.66	0.99	Beta
Dose intensity - KRd - Lenalidomide	1.00	1.00	1.00	Beta
Dose intensity - KRd - Dexamethasone	1.00	1.00	1.00	Beta
Dose intensity - PanoVd - Panobinostat	0.81	0.63	0.84	Beta
Dose intensity - PanoVd - Bortezomib	0.76	0.59	0.79	Beta
Dose intensity - PanoVd - Dexamethasone	0.88	0.66	0.80	Beta
Dose intensity - Pd - Pomalidomide	0.90	0.67	0.98	Beta
Dose intensity - Pd - Dexamethasone	1.00	1.00	1.00	Beta
Dose intensity - PVd - Pomalidomide	0.85	0.84	0.85	Beta
Dose intensity - PVd - Bortezomib	0.80	0.79	0.81	Beta
Dose intensity - PVd - Dexamethasone	1.00	1.00	1.00	Beta
Dose intensity - Rd - Lenalidomide	1.00	1.00	1.00	Beta
Dose intensity - Rd - Dexamethasone	1.00	1.00	1.00	Beta
Dose intensity - VenVd - Venetoclax	1.00	1.00	1.00	Beta
Dose intensity - VenVd - Bortezomib	1.00	1.00	1.00	Beta

Dose intensity - VenVd - Dexamethasone	1.00	1.00	1.00	Beta
Duration of subsequent therapy - Chemotherapy	39.13	31.46	34.32	Normal
Duration of subsequent therapy - Dara monotherapy	39.13	31.46	36.95	Normal
Duration of subsequent therapy - DaraKd	39.13	31.46	29.46	Normal
Duration of subsequent therapy - DaraPd	39.13	31.46	42.72	Normal
Duration of subsequent therapy - DaraRd	39.13	31.46	42.69	Normal
Duration of subsequent therapy - DaraVd	39.13	31.46	38.25	Normal
Duration of subsequent therapy - Elo	39.13	31.46	39.54	Normal
Duration of subsequent therapy - EloPd	39.13	31.46	36.95	Normal
Duration of subsequent therapy - EloRd	39.13	31.46	44.67	Normal
Duration of subsequent therapy - EloTd	39.13	31.46	39.49	Normal
Duration of subsequent therapy - IsaPd	39.13	31.46	36.98	Normal
Duration of subsequent therapy - IxaRd	39.13	31.46	37.81	Normal
Duration of subsequent therapy - Kd	39.13	31.46	44.25	Normal
Duration of subsequent therapy - KRd	39.13	31.46	35.81	Normal
Duration of subsequent therapy - PanoVd	39.13	31.46	41.65	Normal
Duration of subsequent therapy - Pd	39.13	31.46	39.42	Normal
Duration of subsequent therapy - Rd	39.13	31.46	41.68	Normal
Duration of subsequent therapy - Td	39.13	31.46	34.32	Normal
Duration of subsequent therapy - Vd	39.13	31.46	42.69	Normal
Duration of subsequent therapy - VRd	39.13	31.46	34.60	Normal
Proportion of patients receiving subsequent therapy	0.77	0.77	0.77	Beta
Cost of BTD	1304.11	1048.51	1260.46	Normal
Cost of Td	2261.22	1818.03	2559.09	Normal

Cost of VRd	6245.49	5021.40	5731.47	Normal
Cost of EloTd	10464.10	8413.17	10747.79	Normal

Appendix H. Literature searches for the clinical assessment

H.1 Efficacy and safety of the intervention and comparator(s)

H.1.1 Objective

Two SLR's were conducted to support this submission for selinexor; One primary SLR with searches conducted in February 2023, and an SLR update, with searches conducted in December 2023. The SLR's were conducted to identify evidence of the clinical efficacy and safety of selinexor in combination with bortezomib and dexamethasone (SVd) as well as selinexor in combination with dexamethasone only (Sd) for the treatment of patients with RRMM.

The SLR's answer the following two research questions, the first of which relates to the scope of this submission:

1. What is the relative clinical efficacy and safety of selinexor in combination with bortezomib and dexamethasone versus comparators, for the treatment of adult patients with RRMM who have received one or two prior lines of therapy?
2. What is the relative clinical efficacy and safety of selinexor in combination with dexamethasone versus comparators, for the treatment of MM in adult patients who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, two immunomodulatory agents and an anti-CD38 monoclonal antibody (penta-refractory), and who have demonstrated disease progression on the last therapy?

H.1.2 Methods

The SLR's were undertaken according to the principles of systematic reviewing published in the Cochrane Handbook[42], and the NICE Methodology Process and Methods guide[64].

H.1.3 Information sources

The search strategy included searching of bibliographic databases, trial registers, key regulatory and HTA websites, and conference proceedings, each of which is detailed below.

H.1.3.1 Bibliographic databases

All bibliographic databases searched as part of the primary SLR are listed in Table 75.

Table 75. Bibliographic databases included in the literature search (primary search)

Database	Platform/source	Relevant period for the search	Date of search completion
Embase	Embase.com	1980 to 2023 Week 05	05.02.2023
Medline	PubMed	1946 to present	05.02.2023
CDSR	Cochrane Library	Issue 2 of 12, February 2023	05.02.2023
CENTRAL	Cochrane Library	Issue 2 of 12, February 2023	05.02.2023
DARE	CRD	Inception to March 2015	05.02.2023
HTA	CRD	Inception to March 2018	05.02.2023
NHS EED	CRD	Inception to March 15	05.02.2023

Abbreviations: CDSR, Cochrane Database of Systematic Reviews; CENTRAL, Cochrane Central Register of Clinical Trials; CRD, Center for Reviews and Dissemination; DARE, Database of Abstracts of Reviews of Effects; HTA, Health Technology Assessment; NHS EED, National Health Service Economic Evaluation Database.

All bibliographic databases searched as part of the updated SLR are listed in Table 76.

Table 76. Bibliographic databases included in the literature search (updated search)

Database	Platform/source	Relevant period for the search	Date of search completion
Embase	Ovid	1980 to 2023 December 11	12.12.2023
Medline	Ovid	1946 to December 07 2023	12.12.2023
CDSR	Wiley	Inception to December 2023	12.12.2023
CENTRAL	Wiley	Inception to November 2023	12.12.2023

Abbreviations: CDSR, Cochrane Database of Systematic Reviews; CENTRAL, Cochrane Central Register of Clinical Trials; CRD, Center for Reviews and Dissemination; DARE, Database of Abstracts of Reviews of Effects; HTA, Health Technology Assessment; NHS EED, National Health Service Economic Evaluation Database.
Note: CRD DARE, CRD HTA and NHS EED were not searched in the SLR update, as no new records were added to any of the databases

The detailed search strategies for bibliographic databases (both primary and updated searches) are provided in sections H.1.4.1 - H.1.4.6 further below.

H.1.3.2 Trial registers

All trial registers searched as part of the SLR are listed in Table 77. The detailed search strategies for trial registers are provided in sections H.1.4.7 - H.1.4.9 further below.

Table 77. Trial registers included in the literature search (primary and updated search)

Database	Platform/source	Relevant period for the search	Date of search completion
US NIH registry & results database	www.clinicaltrials.gov	-	05.02.2023 and 12.12.23

WHO ICTRP registry	www.trialsearch.who.int	-	05.02.2023 and 12.12.23
EMA EUCTR	www.clinicaltrialregister.eu	-	05.02.2023 and 13.12.23

Abbreviations: NIH, National Institutes of Health; WHO, World Health Organization; ICTRP, International Clinical Trials Registry Platform; EMA, European Medicines Agency; EUCTR, The EU Clinical Trials Register.

H.1.3.3 Key regulatory and HTA websites

The regulatory and HTA websites searched as part of the SLR are provided in Table 78.

In all regulatory and HTA websites, the term 'Multiple Myeloma' was searched. The results were refined through visual inspection, downloading any items which adhered to the inclusion criteria for the review. Where eligibility was unclear, the item was downloaded for further screening.

A cascading approach to searching was used. The first time a guidance or a potentially eligible record was identified, it was recorded and downloaded. If the guidance was identified again, by another search, the search was not recorded. This approach de-duplicated as the searching evolved. For the updated search, searches were limited back to the date of the last search.

Table 78. Key regulatory and HTA websites

Source name	Location/source	Search strategy	Date of search
NICE	www.nice.org.uk	Multiple Myeloma	5 Feb 2023 and December 2023
SMC	www.scottishmedicines.org.uk/	Multiple Myeloma	5 Feb 2023 and December 2023
NIHRIO tech briefings		Multiple Myeloma	5 Feb 2023 and December 2023
EMA	www.ema.europa.eu	Multiple Myeloma	5 Feb 2023 and December 2023
MHRA	www.gov.uk	Multiple Myeloma	5 Feb 2023 and December 2023
TLV	www.tlv.se	Multiple Myeloma	5 Feb 2023 and December 2023
NIPH	www.fhi.no/en/	Multiple Myeloma	5 Feb 2023 and December 2023
DTC		Multiple Myeloma	5 Feb 2023 and December 2023
FIMEA	www.fimea.fi/etusivu	Multiple Myeloma	5 Feb 2023 and December 2023
NCPE	www.ncpe.ie/	Multiple Myeloma	5 Feb 2023 and December 2023

RIZIV-INAMI	www.inami.fgov.be/	Multiple Myeloma	5 Feb 2023 and December 2023
ZIN	www.zorginstituutnederland.nl/	Multiple Myeloma	5 Feb 2023 and December 2023

Abbreviations: NICE, National Institute for Health and Care Excellence; SMC, Scottish Medicines Consortium; NIHRIO, National Institute for Health and Care Research Innovation Observatory; EMA, European Medicines Agency; MHRA, Medicines and Healthcare products Regulatory Agency; TLV, Tandvårds- & läkemedelsförmånsverket; NIPH, Norwegian Institute of Public Health; DTC, Danish Treatment Council; FIMEA, Finnish Medicines Agency; NCPE, National Centre for Pharmacoeconomics - Ireland; RIZIV-INAMI, Rijksinstituut voor Ziekte- en Invaliditeitsverzekering; ZIN, Zorginstituut Nederland.

H.1.3.4 Conference proceedings

The sources searched for conference proceedings are provided in Table 79. Embase and CPCI-s were searched using search strategies provided in sections H.1.4.1 and H.1.4.11. The individual conferences listed below were hand-searched.

Table 79. Conference material included in the literature search

Conference	Source of abstracts	Search strategy	Words/terms searched	Date of search
Embase (Ovid)	www.embase.com	1980 to 2023 Week 05	See section H.1.4.1	4 Feb 2023 and December 2023
CPCI-S (Clarivate)	www.webofscience.com	1990-Current	See section H.1.4.11	5 Feb 2023 and December 2023
ASCO	www.old-prod.asco.org	N/A	N/A	5 Feb 2023 and December 2023
Handsearching ASH	www.hematology.org	N/A	N/A	5 Feb 2023 and December 2023
BSH	www.b-s-h.org.uk	N/A	N/A	5 Feb 2023 and December 2023
COMy	www.comylive.cme	N/A	N/A	5 Feb 2023 and December 2023
EHA	www.ehaweb.org	N/A	N/A	5 Feb 2023 and December 2023
EMN	www.myeloma-europe.org	N/A	N/A	5 Feb 2023 and December 2023
ESMO	www.esmo.org	N/A	N/A	5 Feb 2023 and December 2023
IMS	www.myelomasociety.org	N/A	N/A	5 Feb 2023 and December 2023

Abbreviations: CPCI-S, Conference Proceedings Citation Index – Science; ASCO, American Society of Clinical Oncology; ASH, American Society of Hematology; BSH, British Society for Haematology; COMy, Controversies in Multiple Myeloma; EHA, European Hematology Association; EMN, European Myeloma Network; ESMO, European Society for Medical Oncology; IMS, International Myeloma Society; N/A = Not applicable.

H.1.4 Search strategies

The SLR search strategy was developed by a trained information scientist and checked by the research team using the PRESS checklist.[65] The search strategies applied are detailed in the tables below.

H.1.4.1 Embase

The Embase database was searched through Ovid.com. In the primary search, the database was searched from 1980 to Week 5, 2023. In the updated search, the database was searched from 1974 to 2023 December 11. The searches were carried out on February 5th, 2023, and December 12th, 2023, respectively. The detailed search strategies and results are provided in Table 80 and Table 81.

Table 80. Search strategy table for Embase (primary search)

No.	Query	Results
1	exp *multiple myeloma/	54598
2	(myelom* or ((Penta or triple-class) adj1 refractory)).ti,ab,kw,kf,ot.	111816
3	kahler*.ti,ab,kw,kf,ot.	188
4	*plasmacytoma/	5642
5	(plasm?cytom* or plasm?zytom* or plasma cytoma* or plasma zytoma*).ti,ab,kw,kf,ot.	8922
6	(plasm* adj3 (neoplas* or leukaem* or leukem* or tumor* or tumour* or dyscrasia)).ti,ab,kw,kf,ot.	19426
7	((plasmacytic* or plasmocytic* or plasmocyte*) adj1 (leukem* or leukaem*)).ti,ab,kw,kf,ot.	37
8	(myelomatoses or myelomatosis).ti,ab,kw,kf.	365
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	132932
10	selinexor/	1430
11	(selinexor* or nexpovio* or xpovio* or "ATG 010" or ATG010 or "ATG-010" or "KPT 330" or KPT330 or "KPT-330" or "ONO 7705" or ONO7705 or "ONO-7705" or 31TZ62FO8F or "1393477-72-9").ti,ab,kw,kf,ot.	1106
12	bortezomib/	37690
13	(bortezomib* or velcade* or "BXCL 101" or BXCL101 or "BXCL-101" or "LDP 341" or LDP341 or "LDP-341" or "mg 341" or mg341 or "mg-341" or "PS 341" or PS341 or "PS-341" or "jnj 26866138" or jnj26866138 or "jnj-26866138" or 69G8BD63PP or "179324-69-7").ti,ab,kw,kf,ot.	23552
14	dexamethasone/	172546
15	(Dexamethason* or Dexam?thason* or "aeroseb dex*" or "aeroseb–d*" or "aeroseb–dex*" or "Apo Dexam?thason*" or "Apo-Dexamethason*" or "bisu ds*" or "dacortina fuerte*" or "dacortine fuerte*" or "de–sone la*" or "dexa cortisyl*" or "dexa dabrosan*" or "dexa korti*" or "dexa scherosan*" or "dexa scherozon*" or "dexa scherozone*" or "dexa–p*" or "dexacen 4*" or "dexacen–4*" or "dexpak taperpak*" or "ex s1*" or "fluormethyl prednisolone*" or "isopto dex*" or "isopto maxidex*" or "isopto–dex*" or "lokalison f*" or "methazon ion*" or "methazone ion*" or "metisone lafi*" or "oftan–dexa*" or "predni f tablinen*" or "predni–f*" or "prednisolone f*" or Adrecort* or Adrenocot* or Aflucoson* or Alfalyl* or Anaflogistico* or Aphtasolon* or Apo	93079

	Dexam?thason* or Apo-Dexamethason* or Arcodexan* or Artrosone* or Auxiron* or Azium* or Baycadron* or Bidexol* or Calonat* or Cebedex* or Cetadexon* or Colofoam* or Corsona* or Corsone* or Cortastat* or Cortidex* or Cortidexason* or Cortidrona* or Cortidrone* or Cortisumman* or Dalalone* or Danasone* or Decacortin* or Decadeltosona* or Decadeltosone* or Decaderm* or Decadion* or Decadran* or Decadron* or Decadronal* or Decadrone* or Decaesadril* or Decagel* or Decaject* or Decalix* or Decamethasone* or Decasone* or Decaspray* or Decasterolone* or Decdan* or Decilone* or Decofluor* or Dectancyl* or Dekacort* or Delladec* or Deltafluoren* or Deltafluorene* or Dergramin* or Deronil* or Desacort* or Desacortone* or Desadrene* or Desalark* or Desameton* or Desametone* or Desigdron* or Dexachel* or Dexacort* or Dexacortal* or Dexacorten* or Dexacortin* or Dexacortisyl* or Dexadabroson* or Dexadecadrol* or Dexadrol* or Dexagel* or Dexagen* or Dexahelvacort* or Dexakorti* or Dexalien* or Dexalocal* or Dexame* or Dexamecortin* or Dexameson* or Dexamesone* or Dexametason* or Dexameth* or Dexamethasone* or Dexamethasone* or Dexamethasone* or Dexamethasone* or Dexamethazon* or Dexamethonium* or Dexamonozon* or Dexan* or Dexane* or Dexano* or Dexapot* or Dexascheroson* or Dexascherozon* or Dexascherozone* or Dexason* or Dexasone* or Dexinoral* or Dexionil* or Dexmethsone* or Dexona* or Dexone* or Dextelan* or Dextenza* or Dextrasone* or Dexycu* or Dezone* or Dibasona* or Esacortene* or Exadion* or Exadione* or Firmalone* or Fluormethylprednisolon* or Fluormethylprednisolone* or Fluormone* or Fluorocort* or Fluorodelta* or Fluoromethylprednisolone* or Fortecortin* or Gammacorten* or Gammacortene* or Grosodexon* or Grosodexone* or Hemady* or Hexadecadiol* or Hexadiol* or Hexadrol* or Isnacort* or Isoptodex* or Isoptomaxidex* or Loverine* or Luxazone* or Marvidione* or Maxidex* or Mediamethasone* or Megacortin* or Mephameson* or Mephamesone* or Metasolon* or Metasolone* or Methazonion* or Methazonione* or Mexasone* or Millicorten* or Millicortenol* or Mymethasone* or Neoforderx* or Neofordex* or Nisomethasona* or Novocort* or Opticorten* or Opticortinol* or Oradexan* or Oradexon* or Oradexone* or Orgadrone* or Ozurdex* or Pidexon* or Policort* or Posurdex* or Prodexona* or Prodexone* or Sanamethasone* or Santenson* or Santeson* or Sawasone* or Solurex* or Spoloven* or Sterasone* or Thilodexine* or Triamcimetil* or Vexamet* or Visumetazone* or Visumethazone* or "isv 305" or isv305 or "isv-305" or "mk 125" or mk125 or "mk-125" or "nsc 34521" or nsc34521 or "nsc-34521" or "oto 104" or oto104 or "oto-104" or "sk 0503" or sk0503 or "sk-0503" or "spt 2101" or spt2101 or "spt-2101" or 7S5I7G3JQL or "50-02-2").ti,ab,kw,kf,ot.	
16	lenalidomide/	25117
17	(lenalidomid* or "apo-lenalidomide" or ladevina* or revlimid* or "CC 5013" or CC5013 or "CC-5013" or "CDC 501" or CDC501 or "CDC-501" or "ENMD 0997" or ENMD0997 or "ENMD-0997" or "imid 3" or imid3 or "imid-3" or "SYP 1512" or SYP1512 or "SYP-1512" or F0P408N6V4 or "191732-72-6").ti,ab,kw,kf,ot.	16040
18	carfilzomib/	6347
19	(carfilzomib* or kyprolis* or "ono 7057" or ono7057 or "ono-7057" or "PR 171" or PR171 or "PR-171" or 72X6E3J5AR or "868540-17-4").ti,ab,kw,kf,ot.	4047
20	panobinostat/	4850

21	(panobinostat* or farydak* or "lbh 589*" or lbh589* or "lbh-589*" or "mtx 110" or mtx110 or "mtx-110" or 9647FM7Y3Z or "404950-80-7").ti,ab,kw,kf,ot.	2316
22	daratumumab/	5554
23	(daratumumab* or dalinvi* or darasarex* or darzalex* or Faspro* or "hlx 15" or hlx15 or "hlx-15" or "HuMax-CD 38" or "JNJ-54767414" or 4Z63YK6E0E or "945721-28-8").ti,ab,kw,kf,ot.	3909
24	pomalidomide/	5086
25	(pomalidomid* or actimid* or imnovid* or pomalyst* or "CC 4047" or CC4047 or "CC-4047" or "cdc 394" or cdc394 or "cdc-394" or D2UX06XLB5 or "19171-19-8").ti,ab,kw,kf,ot.	3253
26	ixazomib/	2346
27	(Ixazomib* or ninlaro* or "MLN 2238" or MLN2238 or "MLN-2238" or "MLN 9708" or MLN9708 or "MLN-9708" or 71050168A2 or "1072833-77-2").ti,ab,kw,kf,ot.	1550
28	belantamab/	53
29	(belantamab* or BLENREP or "gsk 2857914" or gsk2857914 or "gsk-2857914" or "GSK 2857916" or GSK2857916 or "GSK-2857916" or "WHO 10754" or WHO10754 or "WHO-10754" or DB1041CXDG or "2050232-20-5" or "2061894−48−0").ti,ab,kw,kf,ot.	333
30	ciltacabtagene autoleucel/	185
31	(ciltacabtagen* or carvykti* or "jnj 4528" or jnj4528 or "jnj-4528" or "JNJ 68284528" or JNJ68284528 or "JNJ-68284528" or "LCAR B38M" or LCARB38M or "LCAR-B38M" or 0L1F17908Q).ti,ab,kw,kf,ot.	151
32	elotuzumab/	1652
33	(elotuzumab* or empliciti* or "BMS 901608" or BMS901608 or "BMS-901608" or "PDL 063" or PDL063 or "PDL-063" or huluc63 or 1351PE5UGS or "915296-00-3").ti,ab,kw,kf,ot.	915
34	idecabtagene vicleucel/	327
35	(idecabtagen* or abecma* or "BB 2121" or BB2121 or "BB-2121" or "id cel" or idecel or "ide−cel" or 8PX1X7UG4D).ti,ab,kw,kf,ot.	212
36	isatuximab/	839
37	(isatuximab* or sarclisa* or "Hu 38SB19" or Hu38SB19 or "Hu-38SB19" or "SAR 650984" or SAR650984 or "SAR-650984" or R30772KCU0 or "1461640-62-9").ti,ab,kw,kf,ot.	533
38	melphalan flufenamide/	175
39	(melphalan* or melflufen* or pepaxti* or pepaxto* or ygalo* or "j 1" or j1 or "ck 1535" or ck1535 or "ck-1535" or F70C5K4786 or "380449-51-4" or "380449−54−7").ti,ab,kw,kf,ot.	19282
40	teclistamab/	130
41	(teclistamab* or tecvayli* or "JNJ 64007957" or JNJ64007957 or "JNJ-64007957" or "jnj 7957" or jnj7957 or "jnj-7957" or 54534MX6Z9 or "2119595-80-9").ti,ab,kw,kf,ot.	68
42	venetoclax/	8549
43	(venetoclax* or venclexta* or "a 11954250" or a11954250 or "ABT 199" or ABT199 or "ABT-199" or "GDC 0199" or GDC0199 or GDC-0199 or "RG	6590

	7601" or RG7601 or "RG-7601" or "ro 5537382" or ro5537382 or N54AIC43PW or "1257044-40-8").ti,ab,kw,kf,ot.	
44	Cyclophosphamide/	229549
45	(Cyclophosphamid* or Alkyroxan* or Carloxan* or Ciclofosfamida* or Ciclolen* or Cicloxal* or Clafen* or "cyclo−cell*" or Cycloblastin* or Cycloblastin* or "cyclofos amide*" or Cyclofosfamid* or Cyclofosfamid* or Cyclophar* or Cyclophosphamid* or Cyclophosphamid* or Cyclophosphamid* or Cyclophosphan* or Cyclophosphan* or Cyclostin* or Cyclostin* or Cycloxan* or Cyphos* or Cyrevia* or Cytophosphan* or Cytophosphan* or Cytophosphan* or cytoxan lyophilized* or Cytoxan* or Endoxan* or Endoxon* or Enduxan* or "endocyclo phosphat*" or Genoxal* or Ledoxan* or Ledoxina* or "lyophilized Cytoxan*" or Mitoxan* or Neosan* or Neosar* or Noristan* or Procytox* or Procytoxide* or Semdoxan* or Sendoxan* or Syklofosfamid* or "b 518" or "b518" or "b-518" or "nsc 26271" or "nsc-26271" or "nsc26271" or "nsc 2671" or "nsc2671 pr nsc-2671" or 6UXW23996M or "50-18-0").ti,ab,kw,kf,ot.	92178
46	chemo*.af.	1675536
47	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46	1982059
48	(Randomized Controlled Trial or Controlled Clinical Trial or Pragmatic Clinical Trial or Equivalence Trial or Clinical Trial, Phase III).pt.	0
49	Randomized Controlled Trial/	755138
50	exp Randomized Controlled Trials as Topic/	246980
51	"Randomized Controlled Trial (topic)"/	246872
52	Controlled Clinical Trial/	467822
53	exp Controlled Clinical Trials as Topic/	256400
54	"Controlled Clinical Trial (topic)"/	13233
55	Randomization/	97448
56	Random Allocation/	93577
57	Double-Blind Method/	176829
58	Double Blind Procedure/	201726
59	Double-Blind Studies/	162253
60	Single-Blind Method/	47675
61	Single Blind Procedure/	49742
62	Single-Blind Studies/	49742
63	Placebos/	324924
64	Placebo/	381700
65	Control Groups/	110772
66	Control Group/	110772
67	(random* or sham or placebo*).ti,ab,hw,kf,kw.	2434550
68	((singl* or doubl*) adj (blind* or dumm* or mask* or arm or arms)).ti,ab,hw,kf,kw.	370032

69	((tripl* or trebl*) adj (blind* or dumm* or mask*)).ti,ab,hw,kf,kw.	1972
70	(control* adj3 (study or studies or trial* or group*)).ti,ab,kf,kw.	1650007
71	(Nonrandom* or non random* or non-random* or quasi-random* or quasirandom*).ti,ab,hw,kf,kw.	67069
72	allocated.ti,ab,hw.	104620
73	((open label or open-label) adj5 (study or studies or trial* or extension)).ti,ab,hw,kf,kw.	85734
74	((sub* and (group adj2 anal*)) or (subgroup adj2 anal*)).ti,ab,kw,kf.	113006
75	((equivalence or superiority or non-inferiority or noninferiority) adj3 (study or studies or trial*)).ti,ab,hw,kf,kw.	17377
76	(pragmatic study or pragmatic studies).ti,ab,hw,kf,kw.	851
77	((pragmatic or practical) adj3 trial*).ti,ab,hw,kf,kw.	8153
78	((quasiexperimental or quasi-experimental) adj3 (study or studies or trial*)).ti,ab,hw,kf,kw.	18259
79	("Phase 3*" or "phase3*" or "phase III*" or P3* or "PIII*" or "Phase 2*" or "phase2*" or "phase II*" or P2* or "PII*").ti,ab,kw,kf.	596041
80	(trial or trail).ti,ab,kw,kf.	1108589
81	48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80	4394242
82	Clinical study/	117016
83	Case control study/	198089
84	Family study/	25666
85	Longitudinal study/	183606
86	Retrospective study/	1376303
87	Prospective study/	834133
88	Randomized controlled trials/	246872
89	87 not 88	823878
90	Cohort analysis/	959124
91	(Cohort adj (study or studies)).mp.	448732
92	(Case control adj (study or studies)).tw.	162882
93	(follow up adj (study or studies)).tw.	69214
94	(observational adj (study or studies)).tw.	239673
95	(epidemiologic$ adj (study or studies)).tw.	117597
96	(cross sectional adj (study or studies)).tw.	318450
97	82 or 83 or 84 or 85 or 86 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96	3667254
98	"systematic review"/	405604
99	(Systematic* adj2 Review*).ti,ab,kw,kf,ot.	367074
100	Meta-Analysis/	275276
101	(meta anal* or (MAIC or (indirect* adj3 comparison*))).ti,ab,kw,kf.	337490

102	98 or 99 or 100 or 101	667819
103	81 or 97 or 102	7528631
104	9 and 47 and 103	21680
105	(conference abstract* or conference review or conference paper or conference proceeding).db,pt,su.	5445560
106	104 not 105	9546

Table 81. Search strategy table for Embase (updated search)

#	Searches	Results
1	exp *multiple myeloma/	60017
2	(myelom* or ((Penta or triple-class) adj1 refractory)).ti,ab,kw,kf,ot.	121148
3	kahler*.ti,ab,kw,kf,ot.	259
4	*plasmacytoma/	6246
5	(plasm?cytom* or plasm?zytom* or plasma cytoma* or plasma zytoma*).ti,ab,kw,kf,ot.	10052
6	(plasm* adj3 (neoplas* or leukaem* or leukem* or tumor* or tumour* or dyscrasia)).ti,ab,kw,kf,ot.	21076
7	((plasmacytic* or plasmocytic* or plasmocyte*) adj1 (leukem* or leukaem*)).ti,ab,kw,kf,ot.	45
8	(myelomatoses or myelomatosis).ti,ab,kw,kf.	529
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	144742
10	selinexor/	1719
11	(selinexor* or nexpovio* or xpovio* or "ATG 010" or ATG010 or "ATG-010" or "KPT 330" or KPT330 or "KPT-330" or "ONO 7705" or ONO7705 or "ONO-7705" or 31TZ62FO8F or "1393477-72-9").ti,ab,kw,kf,ot.	1250
12	bortezomib/	40465
13	(bortezomib* or velcade* or "BXCL 101" or BXCL101 or "BXCL-101" or "LDP 341" or LDP341 or "LDP-341" or "mg 341" or mg341 or "mg-341" or "PS 341" or PS341 or "PS-341" or "jnj 26866138" or jnj26866138 or "jnj-26866138" or 69G8BD63PP or "179324-69-7").ti,ab,kw,kf,ot.	24553
14	dexamethasone/	191815
15	(Dexamethason* or Dexam?thason* or "aeroseb dex*" or "aeroseb—d*" or "aeroseb—dex*" or "Apo Dexam?thason*" or "Apo-Dexamethason*" or "bisu ds*" or "dacortina fuerte*" or "dacortine fuerte*" or "de—sone la*" or "dexa cortisyl*" or "dexa dabrosan*" or "dexa korti*" or "dexa scherosan*" or "dexa scherozon*" or "dexa scherozone*" or "dexa—p*" or "dexacen 4*" or "dexacen—4*" or "dexpak taperpak*" or "ex s1*" or "fluormethyl prednisolone*" or "isopto dex*" or "isopto maxidex*" or "isopto—dex*" or "lokalison f*" or "methazon ion*" or "methazone ion*" or "metisone lafi*" or "oftan—dexa*" or "predni f tablinen*" or "predni—f*" or "prednisolone f*" or Adrecort* or Adrenocot* or Aflucoson* or Alfalyl* or Anaflogistico* or Aphtasolon* or Apo Dexam?thason* or Apo-Dexamethason* or Arcodexan* or Artrosone* or Auxiron* or Azium* or Baycadron* or Bidexol* or Calonat* or Cebedex* or Cetadexon* or Colofoam* or Corsona* or Corsone* or Cortastat* or Cortidex* or Cortidexason* or Cortidrona* or Cortidrone* or	100490

	Cortisumman* or Dalalone* or Danasone* or Decacortin* or Decadeltosona* or Decadeltosone* or Decaderm* or Decadion* or Decadran* or Decadron* or Decadronal* or Decadrone* or Decaesadril* or Decagel* or Decaject* or Decalix* or Decamethasone* or Decasone* or Decaspray* or Decasterolone* or Decdan* or Decilone* or Decofluor* or Dectancyl* or Dekacort* or Delladec* or Deltafluoren* or Deltafluorene* or Dergramin* or Deronil* or Desacort* or Desacortone* or Desadrene* or Desalark* or Desameton* or Desametone* or Desigdron* or Dexachel* or Dexacort* or Dexacortal* or Dexacorten* or Dexacortin* or Dexacortisyl* or Dexadabroson* or Dexadecadrol* or Dexadrol* or Dexagel* or Dexagen* or Dexahelvacort* or Dexakorti* or Dexalien* or Dexalocal* or Dexame* or Dexamecortin* or Dexameson* or Dexamesone* or Dexametason* or Dexameth* or Dexamethasone* or Dexamethasone* or Dexamethasone* or Dexamethasone* or Dexamethazon* or Dexamethonium* or Dexamonozon* or Dexan* or Dexane* or Dexano* or Dexapot* or Dexascheroson* or Dexascherozon* or Dexascherozone* or Dexason* or Dexasone* or Dexinoral* or Dexionil* or Dexmethsone* or Dexona* or Dexone* or Dextelan* or Dextenza* or Dextrasone* or Dexycu* or Dezone* or Dibasona* or Esacortene* or Exadion* or Exadione* or Firmalone* or Fluormethylprednisolon* or Fluormethylprednisolone* or Fluormone* or Fluorocort* or Fluorodelta* or Fluoromethylprednisolone* or Fortecortin* or Gammacorten* or Gammacortene* or Grosodexon* or Grosodexone* or Hemady* or Hexadecadiol* or Hexadiol* or Hexadrol* or Isnacort* or Isoptodex* or Isoptomaxidex* or Loverine* or Luxazone* or Marvidione* or Maxidex* or Mediamethasone* or Megacortin* or Mephameson* or Mephamesone* or Metasolon* or Metasolone* or Methazonion* or Methazonione* or Mexasone* or Millicorten* or Millicortenol* or Mymethasone* or Neoforderx* or Neofordex* or Nisomethasona* or Novocort* or Opticorten* or Opticortinol* or Oradexan* or Oradexon* or Oradexone* or Orgadrone* or Ozurdex* or Pidexon* or Policort* or Posurdex* or Prodexona* or Prodexone* or Sanamethasone* or Santenson* or Santeson* or Sawasone* or Solurex* or Spoloven* or Sterasone* or Thilodexine* or Triamcimetil* or Vexamet* or Visumetazone* or Visumethazone* or "isv 305" or isv305 or "isv-305" or "mk 125" or mk125 or "mk-125" or "nsc 34521" or nsc34521 or "nsc-34521" or "oto 104" or oto104 or "oto-104" or "sk 0503" or sk0503 or "sk-0503" or "spt 2101" or spt2101 or "spt-2101" or 7S5I7G3JQL or "50-02-2").ti,ab,kw,kf,ot.	
16	lenalidomide/	27493
17	(lenalidomid* or "apo-lenalidomide" or ladevina* or revlimid* or "CC 5013" or CC5013 or "CC-5013" or "CDC 501" or CDC501 or "CDC-501" or "ENMD 0997" or ENMD0997 or "ENMD-0997" or "imid 3" or imid3 or "imid-3" or "SYP 1512" or SYP1512 or "SYP-1512" or F0P408N6V4 or "191732-72-6").ti,ab,kw,kf,ot.	16956
18	carfilzomib/	7251
19	(carfilzomib* or kyprolis* or "ono 7057" or ono7057 or "ono-7057" or "PR 171" or PR171 or "PR-171" or 72X6E3J5AR or "868540-17-4").ti,ab,kw,kf,ot.	4381
20	panobinostat/	5256
21	(panobinostat* or farydak* or "lbh 589*" or lbh589* or "lbh-589*" or "mtx 110" or mtx110 or "mtx-110" or 9647FM7Y3Z or "404950-80-7").ti,ab,kw,kf,ot.	2387
22	daratumumab/	6861

23	(daratumumab* or dalinvi* or darasarex* or darzalex* or Faspro* or "hlx 15" or hlx15 or "hlx-15" or "HuMax-CD 38" or "JNJ-54767414" or 4Z63YK6E0E or "945721-28-8").ti,ab,kw,kf,ot.	4592
24	pomalidomide/	5818
25	(pomalidomid* or actimid* or imnovid* or pomalyst* or "CC 4047" or CC4047 or "CC-4047" or "cdc 394" or cdc394 or "cdc-394" or D2UX06XLB5 or "19171-19-8").ti,ab,kw,kf,ot.	3501
26	ixazomib/	2769
27	(Ixazomib* or ninlaro* or "MLN 2238" or MLN2238 or "MLN-2238" or "MLN 9708" or MLN9708 or "MLN-9708" or 71050168A2 or "1072833-77-2").ti,ab,kw,kf,ot.	1666
28	belantamab/	83
29	(belantamab* or BLENREP or "gsk 2857914" or gsk2857914 or "gsk-2857914" or "GSK 2857916" or GSK2857916 or "GSK-2857916" or "WHO 10754" or WHO10754 or "WHO-10754" or DB1041CXDG or "2050232-20-5" or "2061894—48—0").ti,ab,kw,kf,ot.	420
30	ciltacabtagene autoleucel/	353
31	(ciltacabtagen* or carvykti* or "jnj 4528" or jnj4528 or "jnj-4528" or "JNJ 68284528" or JNJ68284528 or "JNJ-68284528" or "LCAR B38M" or LCARB38M or "LCAR-B38M" or 0L1F17908Q).ti,ab,kw,kf,ot.	222
32	elotuzumab/	1853
33	(elotuzumab* or empliciti* or "BMS 901608" or BMS901608 or "BMS-901608" or "PDL 063" or PDL063 or "PDL-063" or huluc63 or 1351PE5UGS or "915296-00-3").ti,ab,kw,kf,ot.	958
34	idecabtagene vicleucel/	583
35	(idecabtagen* or abecma* or "BB 2121" or BB2121 or "BB-2121" or "id cel" or idecel or "ide—cel" or 8PX1X7UG4D).ti,ab,kw,kf,ot.	328
36	isatuximab/	1072
37	(isatuximab* or sarclisa* or "Hu 38SB19" or Hu38SB19 or "Hu-38SB19" or "SAR 650984" or SAR650984 or "SAR-650984" or R30772KCU0 or "1461640-62-9").ti,ab,kw,kf,ot.	618
38	melphalan flufenamide/	208
39	(melphalan* or melflufen* or pepaxti* or pepaxto* or ygalo* or "j 1" or j1 or "ck 1535" or ck1535 or "ck-1535" or F70C5K4786 or "380449-51-4" or "380449—54—7").ti,ab,kw,kf,ot.	20287
40	teclistamab/	274
41	(teclistamab* or tecvayli* or "JNJ 64007957" or JNJ64007957 or "JNJ-64007957" or "jnj 7957" or jnj7957 or "jnj-7957" or 54534MX6Z9 or "2119595-80-9").ti,ab,kw,kf,ot.	153
42	venetoclax/	10782
43	(venetoclax* or venclexta* or "a 11954250" or a11954250 or "ABT 199" or ABT199 or "ABT-199" or "GDC 0199" or GDC0199 or GDC-0199 or "RG 7601" or RG7601 or "RG-7601" or "ro 5537382" or ro5537382 or N54AIC43PW or "1257044-40-8").ti,ab,kw,kf,ot.	7959
44	Cyclophosphamide/	252547
45	(Cyclophosphamid* or Alkyroxan* or Carloxan* or Ciclofosfamida* or Ciclolen* or Cicloxal* or Clafen* or "cyclo—cell*" or Cycloblastin* or	100334

	Cycloblastin* or "cyclofos amide*" or Cyclofosfamid* or Cyclofosfamid* or Cyclophar* or Cyclophosphamid* or Cyclophosphamid* or Cyclophosphamid* or Cyclophosphan* or Cyclophosphan* or Cyclostin* or Cyclostin* or Cycloxan* or Cyphos* or Cyrevia* or Cytophosphan* or Cytophosphan* or Cytophosphan* or cytoxan lyophilized* or Cytoxan* or Endoxan* or Endoxon* or Enduxan* or "endocyclo phosphat*" or Genoxal* or Ledoxan* or Ledoxina* or "lyophilized Cytoxan*" or Mitoxan* or Neosan* or Neosar* or Noristan* or Procytox* or Procytoxide* or Semdoxan* or Sendoxan* or Syklofosfamid* or "b 518" or "b518" or "b-518" or "nsc 26271" or "nsc-26271" or "nsc26271" or "nsc 2671" or "nsc2671 pr nsc-2671" or 6UXW23996M or "50-18-0").ti,ab,kw,kf,ot.	
46	chemo*.af.	1805136
47	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46	2144885
48	(Randomized Controlled Trial or Controlled Clinical Trial or Pragmatic Clinical Trial or Equivalence Trial or Clinical Trial, Phase III).pt.	0
49	Randomized Controlled Trial/	797291
50	exp Randomized Controlled Trials as Topic/	266447
51	"Randomized Controlled Trial (topic)"/	266322
52	Controlled Clinical Trial/	471699
53	exp Controlled Clinical Trials as Topic/	275891
54	"Controlled Clinical Trial (topic)"/	13458
55	Randomization/	98893
56	Random Allocation/	92557
57	Double-Blind Method/	188602
58	Double Blind Procedure/	213603
59	Double-Blind Studies/	171048
60	Single-Blind Method/	50689
61	Single Blind Procedure/	52757
62	Single-Blind Studies/	52757
63	Placebos/	349389
64	Placebo/	406338
65	Control Groups/	110700
66	Control Group/	110700
67	(random* or sham or placebo*).ti,ab,hw,kf,kw.	2598304
68	((singl* or doubl*) adj (blind* or dumm* or mask* or arm or arms)).ti,ab,hw,kf,kw.	395945
69	((tripl* or trebl*) adj (blind* or dumm* or mask*)).ti,ab,hw,kf,kw.	2250
70	(control* adj3 (study or studies or trial* or group*)).ti,ab,kf,kw.	1758351
71	(Nonrandom* or non random* or non-random* or quasi-random* or quasirandom*).ti,ab,hw,kf,kw.	71680
72	allocated.ti,ab,hw.	111630

73	((open label or open-label) adj5 (study or studies or trial* or extension)).ti,ab,hw,kf,kw.	91323
74	((sub* and (group adj2 anal*)) or (subgroup adj2 anal*)).ti,ab,kw,kf.	124639
75	((equivalence or superiority or non-inferiority or noninferiority) adj3 (study or studies or trial*)).ti,ab,hw,kf,kw.	18938
76	(pragmatic study or pragmatic studies).ti,ab,hw,kf,kw.	971
77	((pragmatic or practical) adj3 trial*).ti,ab,hw,kf,kw.	9016
78	((quasiexperimental or quasi-experimental) adj3 (study or studies or trial*)).ti,ab,hw,kf,kw.	20437
79	("Phase 3*" or "phase3*" or "phase III*" or P3* or "PIII*" or "Phase 2*" or "phase2*" or "phase II*" or P2* or "PII*").ti,ab,kw,kf.	625399
80	(trial or trail).ti,ab,kw,kf.	1185813
81	48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80	4683536
82	Clinical study/	164923
83	Case control study/	210458
84	Family study/	25758
85	Longitudinal study/	202187
86	Retrospective study/	1532796
87	Prospective study/	896067
88	Randomized controlled trials/	266322
89	87 not 88	885141
90	Cohort analysis/	1087442
91	(Cohort adj (study or studies)).mp.	490497
92	(Case control adj (study or studies)).tw.	171308
93	(follow up adj (study or studies)).tw.	74737
94	(observational adj (study or studies)).tw.	263123
95	(epidemiologic$ adj (study or studies)).tw.	123715
96	(cross sectional adj (study or studies)).tw.	354595
97	82 or 83 or 84 or 85 or 86 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96	4049767
98	"systematic review"/	443879
99	(Systematic* adj2 Review*).ti,ab,kw,kf,ot.	407515
100	Meta-Analysis/	299684
101	(meta anal* or (MAIC or (indirect* adj3 comparison*))).ti,ab,kw,kf.	369796
102	98 or 99 or 100 or 101	727221
103	81 or 97 or 102	8151588
104	9 and 47 and 103	23592
105	(conference abstract* or conference review or conference paper or conference proceeding).db,pt,su.	5771584

106	104 not 105	10495
107	(2023* or 2024*).yr.	1785467
108	106 and 107	885

H.1.4.2 MEDLINE

The MEDLINE database was searched through Ovid.com. The database was searched from 1946 to present in both the primary and updated search. The searches were carried out on February 5th, 2023, and December 12th, 2023, respectively. The detailed search strategies and results are provided in Table 82 and Table 83.

Table 82. Search strategy table for MEDLINE (primary search)

No.	Query	Results
1	exp Multiple Myeloma/	46760
2	(myelom* or ((Penta or triple-class) adj1 refractory)).ti,ab,kw,kf,ot.	72631
3	kahler*.ti,ab,kw,kf,ot.	368
4	Plasmacytoma/	8845
5	(plasm?cytom* or plasm?zytom* or plasma cytoma* or plasma zytoma*).ti,ab,kw,kf,ot.	8514
6	(plasm* adj3 (neoplas* or leukaem* or leukem* or tumor* or tumour* or dyscrasia)).ti,ab,kw,kf,ot.	13381
7	((plasmacytic* or plasmocytic* or plasmocyte*) adj1 (leukem* or leukaem*)).ti,ab,kw,kf,ot.	42
8	(myelomatoses or myelomatosis).ti,ab,kw,kf.	781
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	96482
10	(selinexor* or nexpovio* or xpovio* or "ATG 010" or ATG010 or "ATG-010" or "KPT 330" or KPT330 or "KPT-330" or "ONO 7705" or ONO7705 or "ONO-7705" or 31TZ62FO8F or "1393477-72-9").ti,ab,kw,kf,ot.	391
11	Bortezomib/	6733
12	(bortezomib* or velcade* or "BXCL 101" or BXCL101 or "BXCL-101" or "LDP 341" or LDP341 or "LDP-341" or "mg 341" or mg341 or "mg-341" or "PS 341" or PS341 or "PS-341" or "jnj 26866138" or jnj26866138 or "jnj-26866138" or 69G8BD63PP or "179324-69-7").ti,ab,kw,kf,ot.	9890
13	Dexamethasone/	55136
14	(Dexamethason* or Dexam?thason* or "aeroseb dex*" or "aeroseb–d*" or "aeroseb–dex*" or "Apo Dexam?thason*" or "Apo-Dexamethason*" or "bisu ds*" or "dacortina fuerte*" or "dacortine fuerte*" or "de–sone la*" or "dexa cortisyl*" or "dexa dabrosan*" or "dexa korti*" or "dexascherosan*" or "dexa scherozon*" or "dexa scherozone*" or "dexa–p*" or "dexacen 4*" or "dexacen–4*" or "dexpak taperpak*" or "ex s1*" or "fluormethyl prednisolone*" or "isopto dex*" or "isopto maxidex*" or "isopto–dex*" or "lokalison f*" or "methazon ion*" or "methazone ion*" or "metisone lafi*" or "oftan–dexa*" or "predni f tablinen*" or "predni–f*" or "prednisolone f*" or Adrecort* or Adrenocot* or Aflucoson* or Alfalyl* or Anaflogistico* or Aphtasolon* or Apo Dexam?thason* or Apo-Dexamethason* or Arcodexan* or Artrosone* or Auxiron* or Azium* or Baycadron* or Bidexol* or Calonat*	66639

	or Cebedex* or Cetadexon* or Colofoam* or Corsona* or Corsone* or Cortastat* or Cortidex* or Cortidexason* or Cortidrona* or Cortidrone* or Cortisumman* or Dalalone* or Danasone* or Decacortin* or Decadeltosona* or Decadeltosone* or Decaderm* or Decadion* or Decadran* or Decadron* or Decadronal* or Decadrone* or Decaesadril* or Decagel* or Decaject* or Decalix* or Decamethasone* or Decasone* or Decaspray* or Decasterolone* or Decdan* or Decilone* or Decofluor* or Dectancyl* or Dekacort* or Delladec* or Deltafluoren* or Deltafluorene* or Dergramin* or Deronil* or Desacort* or Desacortone* or Desadrene* or Desalark* or Desameton* or Desametone* or Desigdron* or Dexachel* or Dexacort* or Dexacortal* or Dexacorten* or Dexacortin* or Dexacortisyl* or Dexadabroson* or Dexadecadrol* or Dexadrol* or Dexagel* or Dexagen* or Dexahelvacort* or Dexakorti* or Dexalien* or Dexalocal* or Dexame* or Dexamecortin* or Dexameson* or Dexamesone* or Dexametason* or Dexameth* or Dexamethasone* or Dexamethasone* or Dexamethasone* or Dexamethasone* or Dexamethazon* or Dexamethonium* or Dexamonozon* or Dexan* or Dexane* or Dexano* or Dexapot* or Dexascheroson* or Dexascherozon* or Dexascherozone* or Dexason* or Dexasone* or Dexinoral* or Dexionil* or Dexmethsone* or Dexona* or Dexone* or Dextelan* or Dextenza* or Dextrasone* or Dexycu* or Dezone* or Dibasona* or Esacortene* or Exadion* or Exadione* or Firmalone* or Fluormethylprednisolon* or Fluormethylprednisolone* or Fluormone* or Fluorocort* or Fluorodelta* or Fluoromethylprednisolone* or Fortecortin* or Gammacorten* or Gammacortene* or Grosodexon* or Grosodexone* or Hemady* or Hexadecadiol* or Hexadiol* or Hexadrol* or Isnacort* or Isoptodex* or Isoptomaxidex* or Loverine* or Luxazone* or Marvidione* or Maxidex* or Mediamethasone* or Megacortin* or Mephameson* or Mephamesone* or Metasolon* or Metasolone* or Methazonion* or Methazonione* or Mexasone* or Millicorten* or Millicortenol* or Mymethasone* or Neoforderx* or Neofordex* or Nisomethasona* or Novocort* or Opticorten* or Opticortinol* or Oradexan* or Oradexon* or Oradexone* or Orgadrone* or Ozurdex* or Pidexon* or Policort* or Posurdex* or Prodexona* or Prodexone* or Sanamethasone* or Santenson* or Santeson* or Sawasone* or Solurex* or Spoloven* or Sterasone* or Thilodexine* or Triamcimetil* or Vexamet* or Visumetazone* or Visumethazone* or "isv 305" or isv305 or "isv-305" or "mk 125" or mk125 or "mk-125" or "nsc 34521" or nsc34521 or "nsc-34521" or "oto 104" or oto104 or "oto-104" or "sk 0503" or sk0503 or "sk-0503" or "spt 2101" or spt2101 or "spt-2101" or 7S5I7G3JQL or "50-02-2").ti,ab,kw,kf,ot.	
15	Lenalidomide/	3407
16	(lenalidomid* or "apo-lenalidomide" or ladevina* or revlimid* or "CC 5013" or CC5013 or "CC-5013" or "CDC 501" or CDC501 or "CDC-501" or "ENMD 0997" or ENMD0997 or "ENMD-0997" or "imid 3" or imid3 or "imid-3" or "SYP 1512" or SYP1512 or "SYP-1512" or F0P408N6V4 or "191732-72-6").ti,ab,kw,kf,ot.	5341
17	(carfilzomib* or kyprolis* or "ono 7057" or ono7057 or "ono-7057" or "PR 171" or PR171 or "PR-171" or 72X6E3J5AR or "868540-17-4").ti,ab,kw,kf,ot.	1351
18	Panobinostat/	621
19	(panobinostat* or farydak* or "lbh 589*" or lbh589* or "lbh-589*" or "mtx 110" or mtx110 or "mtx-110" or 9647FM7Y3Z or "404950-80-7").ti,ab,kw,kf,ot.	1027

20	(daratumumab* or dalinvi* or darasarex* or darzalex* or Faspro* or "hlx 15" or hlx15 or "hlx-15" or "HuMax-CD 38" or "JNJ-54767414" or 4Z63YK6E0E or "945721-28-8").ti,ab,kw,kf,ot.	1271
21	(pomalidomid* or actimid* or imnovid* or pomalyst* or "CC 4047" or CC4047 or "CC-4047" or "cdc 394" or cdc394 or "cdc-394" or D2UX06XLB5 or "19171-19-8").ti,ab,kw,kf,ot.	1012
22	(Ixazomib* or ninlaro* or "MLN 2238" or MLN2238 or "MLN-2238" or "MLN 9708" or MLN9708 or "MLN-9708" or 71050168A2 or "1072833-77-2").ti,ab,kw,kf,ot.	531
23	(belantamab* or BLENREP or "gsk 2857914" or gsk2857914 or "gsk-2857914" or "GSK 2857916" or GSK2857916 or "GSK-2857916" or "WHO 10754" or WHO10754 or "WHO-10754" or DB1041CXDG or "2050232-20-5" or "2061894−48−0").ti,ab,kw,kf,ot.	110
24	(ciltacabtagen* or carvykti* or "jnj 4528" or jnj4528 or "jnj-4528" or "JNJ 68284528" or JNJ68284528 or "JNJ-68284528" or "LCAR B38M" or LCARB38M or "LCAR-B38M" or 0L1F17908Q).ti,ab,kw,kf,ot.	41
25	(elotuzumab* or empliciti* or "BMS 901608" or BMS901608 or "BMS-901608" or "PDL 063" or PDL063 or "PDL-063" or huluc63 or 1351PE5UGS or "915296-00-3").ti,ab,kw,kf,ot.	349
26	(idecabtagen* or abecma* or "BB 2121" or BB2121 or "BB-2121" or "id cel" or idecel or "ide−cel" or 8PX1X7UG4D).ti,ab,kw,kf,ot.	60
27	(isatuximab* or sarclisa* or "Hu 38SB19" or Hu38SB19 or "Hu-38SB19" or "SAR 650984" or SAR650984 or "SAR-650984" or R30772KCU0 or "1461640-62-9").ti,ab,kw,kf,ot.	204
28	(melphalan* or melflufen* or pepaxti* or pepaxto* or ygalo* or "j 1" or j1 or "ck 1535" or ck1535 or "ck-1535" or F70C5K4786 or "380449-51-4" or "380449−54−7").ti,ab,kw,kf,ot.	11661
29	Cyclophosphamide/	52905
30	(teclistamab* or tecvayli* or "JNJ 64007957" or JNJ64007957 or "JNJ-64007957" or "jnj 7957" or jnj7957 or "jnj-7957" or 54534MX6Z9 or "2119595-80-9").ti,ab,kw,kf,ot.	20
31	(venetoclax* or venclexta* or "a 11954250" or a11954250 or "ABT 199" or ABT199 or "ABT-199" or "GDC 0199" or GDC0199 or GDC-0199 or "RG 7601" or RG7601 or "RG-7601" or "ro 5537382" or ro5537382 or N54AIC43PW or "1257044-40-8").ti,ab,kw,kf,ot.	2354
32	(Cyclophosphamid* or Alkyroxan* or Carloxan* or Ciclofosfamida* or Ciclolen* or Cicloxal* or Clafen* or "cyclo−cell*" or Cycloblastin* or Cycloblastin* or "cyclofos amide*" or Cyclofosfamid* or Cyclofosfamid* or Cyclophar* or Cyclophosphamid* or Cyclophosphamid* or Cyclophosphamid* or Cyclophosphan* or Cyclophosphan* or Cyclostin* or Cyclostin* or Cycloxan* or Cyphos* or Cyrevia* or Cytophosphan* or Cytophosphan* or Cytophosphan* or cytoxan lyophilized* or Cytoxan* or Endoxan* or Endoxon* or Enduxan* or "endocyclo phosphat*" or Genoxal* or Ledoxan* or Ledoxina* or "lyophilized Cytoxan*" or Mitoxan* or Neosan* or Neosar* or Noristan* or Procytox* or Procytoxide* or Semdoxan* or Sendoxan* or Syklofosfamid* or "b 518" or "b518" or "b-518" or "nsc 26271" or "nsc-26271" or "nsc26271" or "nsc 2671" or "nsc2671 pr nsc-2671" or 6UXW23996M or "50-18-0").ti,ab,kw,kf,ot.	60017
33	chemo*.af.	1029673

34	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33	1158380
35	(Randomized Controlled Trial or Controlled Clinical Trial or Pragmatic Clinical Trial or Equivalence Trial or Clinical Trial, Phase III).pt.	681034
36	Randomized Controlled Trial/	585934
37	exp Randomized Controlled Trials as Topic/	164077
38	"Randomized Controlled Trial (topic)"/	0
39	Controlled Clinical Trial/	95177
40	exp Controlled Clinical Trials as Topic/	169779
41	"Controlled Clinical Trial (topic)"/	0
42	Randomization/	106905
43	Random Allocation/	106905
44	Double-Blind Method/	174201
45	Double Blind Procedure/	0
46	Double-Blind Studies/	174201
47	Single-Blind Method/	32466
48	Single Blind Procedure/	0
49	Single-Blind Studies/	32466
50	Placebos/	35925
51	Placebo/	0
52	Control Groups/	1902
53	Control Group/	1902
54	(random* or sham or placebo*).ti,ab,hw,kf,kw.	1749896
55	((singl* or doubl*) adj (blind* or dumm* or mask* or arm or arms)).ti,ab,hw,kf,kw.	273917
56	((tripl* or trebl*) adj (blind* or dumm* or mask*)).ti,ab,hw,kf,kw.	1492
57	(control* adj3 (study or studies or trial* or group*)).ti,ab,kf,kw.	1176704
58	(Nonrandom* or non random* or non-random* or quasi-random* or quasirandom*).ti,ab,hw,kf,kw.	52251
59	allocated.ti,ab,hw.	80290
60	((open label or open-label) adj5 (study or studies or trial* or extension)).ti,ab,hw,kf,kw.	43379
61	((sub* and (group adj2 anal*)) or (subgroup adj2 anal*)).ti,ab,kw,kf.	72790
62	((equivalence or superiority or non-inferiority or noninferiority) adj3 (study or studies or trial*)).ti,ab,hw,kf,kw.	11351
63	(pragmatic study or pragmatic studies).ti,ab,hw,kf,kw.	558
64	((pragmatic or practical) adj3 trial*).ti,ab,hw,kf,kw.	7282
65	((quasiexperimental or quasi-experimental) adj3 (study or studies or trial*)).ti,ab,hw,kf,kw.	11217
66	("Phase 3*" or "phase3*" or "phase III*" or P3* or "PIII*" or "Phase 2*" or "phase2*" or "phase II*" or P2* or "PII*").ti,ab,kw,kf.	380198

67	(trial or trail).ti,ab,kw,kf.	751593
68	35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67	3085995
69	Epidemiologic studies/	9249
70	exp case control studies/	1387971
71	exp cohort studies/	2442964
72	Case control.tw.	147995
73	(cohort adj (study or studies)).tw.	291522
74	Cohort analy$.tw.	10937
75	(Follow up adj (study or studies)).tw.	54825
76	(observational adj (study or studies)).tw.	149425
77	Longitudinal.tw.	304624
78	Retrospective.tw.	696733
79	Cross sectional.tw.	479440
80	Cross-sectional studies/	455141
81	69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80	3654578
82	"systematic review"/	218901
83	(Systematic* adj2 Review*).ti,ab,kw,kf,ot.	285105
84	Meta-Analysis/	175009
85	(meta anal* or (MAIC or (indirect* adj3 comparison*))).ti,ab,kw,kf.	254049
86	82 or 83 or 84 or 85	435445
87	68 or 81 or 86	6182289
88	9 and 34 and 87	7611

Table 83. Search strategy table for MEDLINE (updated search)

No.	Query	Results
1	exp Multiple Myeloma/	48299
2	(myelom* or ((Penta or triple-class) adj1 refractory)).ti,ab,kw,kf,ot.	76197
3	kahler*.ti,ab,kw,kf,ot.	377
4	Plasmacytoma/	8896
5	(plasm?cytom* or plasm?zytom* or plasma cytoma* or plasma zytoma*).ti,ab,kw,kf,ot.	8716
6	(plasm* adj3 (neoplas* or leukaem* or leukem* or tumor* or tumour* or dyscrasia)).ti,ab,kw,kf,ot.	14040
7	((plasmacytic* or plasmocytic* or plasmocyte*) adj1 (leukem* or leukaem*)).ti,ab,kw,kf,ot.	43
8	(myelomatoses or myelomatosis).ti,ab,kw,kf.	784
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	100687

10	(selinexor* or nexpovio* or xpovio* or "ATG 010" or ATG010 or "ATG-010" or "KPT 330" or KPT330 or "KPT-330" or "ONO 7705" or ONO7705 or "ONO-7705" or 31TZ62FO8F or "1393477-72-9").ti,ab,kw,kf,ot.	474
11	Bortezomib/	6952
12	(bortezomib* or velcade* or "BXCL 101" or BXCL101 or "BXCL-101" or "LDP 341" or LDP341 or "LDP-341" or "mg 341" or mg341 or "mg-341" or "PS 341" or PS341 or "PS-341" or "jnj 26866138" or jnj26866138 or "jnj-26866138" or 69G8BD63PP or "179324-69-7").ti,ab,kw,kf,ot.	10447
13	Dexamethasone/	55991
14	(Dexamethason* or Dexam?thason* or "aeroseb dex*" or "aeroseb−d*" or "aeroseb−dex*" or "Apo Dexam?thason*" or "Apo-Dexamethason*" or "bisu ds*" or "dacortina fuerte*" or "dacortine fuerte*" or "de−sone la*" or "dexa cortisyl*" or "dexa dabrosan*" or "dexa korti*" or "dexa scherosan*" or "dexa scherozon*" or "dexa scherozone*" or "dexa−p*" or "dexacen 4*" or "dexacen−4*" or "dexpak taperpak*" or "ex s1*" or "fluormethyl prednisolone*" or "isopto dex*" or "isopto maxidex*" or "isopto−dex*" or "lokalison f*" or "methazon ion*" or "methazone ion*" or "metisone lafi*" or "oftan−dexa*" or "predni f tablinen*" or "predni−f*" or "prednisolone f*" or Adrecort* or Adrenocot* or Aflucoson* or Alfalyl* or Anaflogistico* or Aphtasolon* or Apo Dexam?thason* or Apo-Dexamethason* or Arcodexan* or Artrosone* or Auxiron* or Azium* or Baycadron* or Bidexol* or Calonat* or Cebedex* or Cetadexon* or Colofoam* or Corsona* or Corsone* or Cortastat* or Cortidex* or Cortidexason* or Cortidrona* or Cortidrone* or Cortisumman* or Dalalone* or Danasone* or Decacortin* or Decadeltosona* or Decadeltosone* or Decaderm* or Decadion* or Decadran* or Decadron* or Decadronal* or Decadrone* or Decaesadril* or Decagel* or Decaject* or Decalix* or Decamethasone* or Decasone* or Decaspray* or Decasterolone* or Decdan* or Decilone* or Decofluor* or Dectancyl* or Dekacort* or Delladec* or Deltafluoren* or Deltafluorene* or Dergramin* or Deronil* or Desacort* or Desacortone* or Desadrene* or Desalark* or Desameton* or Desametone* or Desigdron* or Dexachel* or Dexacort* or Dexacortal* or Dexacorten* or Dexacortin* or Dexacortisyl* or Dexadabroson* or Dexadecadrol* or Dexadrol* or Dexagel* or Dexagen* or Dexahelvacort* or Dexakorti* or Dexalien* or Dexalocal* or Dexame* or Dexamecortin* or Dexameson* or Dexamesone* or Dexametason* or Dexameth* or Dexamethasone* or Dexamethasone* or Dexamethasone* or Dexamethasone* or Dexamethazon* or Dexamethonium* or Dexamonozon* or Dexan* or Dexane* or Dexano* or Dexapot* or Dexascheroson* or Dexascherozon* or Dexascherozone* or Dexason* or Dexasone* or Dexinoral* or Dexionil* or Dexmethsone* or Dexona* or Dexone* or Dextelan* or Dextenza* or Dextrasone* or Dexycu* or Dezone* or Dibasona* or Esacortene* or Exadion* or Exadione* or Firmalone* or Fluormethylprednisolon* or Fluormethylprednisolone* or Fluormone* or Fluorocort* or Fluorodelta* or Fluoromethylprednisolone* or Fortecortin* or Gammacorten* or Gammacortene* or Grosodexon* or Grosodexone* or Hemady* or Hexadecadiol* or Hexadiol* or Hexadrol* or Isnacort* or Isoptodex* or Isoptomaxidex* or Loverine* or Luxazone* or Marvidione* or Maxidex* or Mediamethasone* or Megacortin* or Mephameson* or Mephamesone* or Metasolon* or Metasolone* or Methazonion* or Methazonione* or Mexasone* or Millicorten* or Millicortenol* or Mymethasone* or Neoforderx* or Neofordex* or Nisomethasona* or Novocort* or Opticorten* or Opticortinol* or Oradexan* or Oradexon* or Oradexone* or Orgadrone* or Ozurdex* or Pidexon* or Policort* or Posurdex* or Prodexona* or Prodexone* or Sanamethasone* or Santenson* or Santeson* or Sawasone* or Solurex*	69412

	or Spoloven* or Sterasone* or Thilodexine* or Triamcimetil* or Vexamet* or Visumetazone* or Visumethazone* or "isv 305" or isv305 or "isv-305" or "mk 125" or mk125 or "mk-125" or "nsc 34521" or nsc34521 or "nsc-34521" or "oto 104" or oto104 or "oto-104" or "sk 0503" or sk0503 or "sk-0503" or "spt 2101" or spt2101 or "spt-2101" or 7S5I7G3JQL or "50-02-2").ti,ab,kw,kf,ot.	
15	Lenalidomide/	3595
16	(lenalidomid* or "apo-lenalidomide" or ladevina* or revlimid* or "CC 5013" or CC5013 or "CC-5013" or "CDC 501" or CDC501 or "CDC-501" or "ENMD 0997" or ENMD0997 or "ENMD-0997" or "imid 3" or imid3 or "imid-3" or "SYP 1512" or SYP1512 or "SYP-1512" or F0P408N6V4 or "191732-72-6").ti,ab,kw,kf,ot.	5750
17	(carfilzomib* or kyprolis* or "ono 7057" or ono7057 or "ono-7057" or "PR 171" or PR171 or "PR-171" or 72X6E3J5AR or "868540-17-4").ti,ab,kw,kf,ot.	1503
18	Panobinostat/	637
19	(panobinostat* or farydak* or "lbh 589*" or lbh589* or "lbh-589*" or "mtx 110" or mtx110 or "mtx-110" or 9647FM7Y3Z or "404950-80-7").ti,ab,kw,kf,ot.	1094
20	(daratumumab* or dalinvi* or darasarex* or darzalex* or Faspro* or "hlx 15" or hlx15 or "hlx-15" or "HuMax-CD 38" or "JNJ-54767414" or 4Z63YK6E0E or "945721-28-8").ti,ab,kw,kf,ot.	1519
21	(pomalidomid* or actimid* or imnovid* or pomalyst* or "CC 4047" or CC4047 or "CC-4047" or "cdc 394" or cdc394 or "cdc-394" or D2UX06XLB5 or "19171-19-8").ti,ab,kw,kf,ot.	1124
22	(Ixazomib* or ninlaro* or "MLN 2238" or MLN2238 or "MLN-2238" or "MLN 9708" or MLN9708 or "MLN-9708" or 71050168A2 or "1072833-77-2").ti,ab,kw,kf,ot.	594
23	(belantamab* or BLENREP or "gsk 2857914" or gsk2857914 or "gsk-2857914" or "GSK 2857916" or GSK2857916 or "GSK-2857916" or "WHO 10754" or WHO10754 or "WHO-10754" or DB1041CXDG or "2050232-20-5" or "2061894−48−0").ti,ab,kw,kf,ot.	155
24	(ciltacabtagen* or carvykti* or "jnj 4528" or jnj4528 or "jnj-4528" or "JNJ 68284528" or JNJ68284528 or "JNJ-68284528" or "LCAR B38M" or LCARB38M or "LCAR-B38M" or 0L1F17908Q).ti,ab,kw,kf,ot.	75
25	(elotuzumab* or empliciti* or "BMS 901608" or BMS901608 or "BMS-901608" or "PDL 063" or PDL063 or "PDL-063" or huluc63 or 1351PE5UGS or "915296-00-3").ti,ab,kw,kf,ot.	377
26	(idecabtagen* or abecma* or "BB 2121" or BB2121 or "BB-2121" or "id cel" or idecel or "ide−cel" or 8PX1X7UG4D).ti,ab,kw,kf,ot.	105
27	(isatuximab* or sarclisa* or "Hu 38SB19" or Hu38SB19 or "Hu-38SB19" or "SAR 650984" or SAR650984 or "SAR-650984" or R30772KCU0 or "1461640-62-9").ti,ab,kw,kf,ot.	243
28	(melphalan* or melflufen* or pepaxti* or pepaxto* or ygalo* or "j 1" or j1 or "ck 1535" or ck1535 or "ck-1535" or F70C5K4786 or "380449-51-4" or "380449−54−7").ti,ab,kw,kf,ot.	12044
29	Cyclophosphamide/	53619
30	(teclistamab* or tecvayli* or "JNJ 64007957" or JNJ64007957 or "JNJ-64007957" or "jnj 7957" or jnj7957 or "jnj-7957" or 54534MX6Z9 or "2119595-80-9").ti,ab,kw,kf,ot.	66

31	(venetoclax* or venclexta* or "a 11954250" or a11954250 or "ABT 199" or ABT199 or "ABT-199" or "GDC 0199" or GDC0199 or GDC-0199 or "RG 7601" or RG7601 or "RG-7601" or "ro 5537382" or ro5537382 or N54AIC43PW or "1257044-40-8").ti,ab,kw,kf,ot.	2973
32	(Cyclophosphamid* or Alkyroxan* or Carloxan* or Ciclofosfamida* or Ciclolen* or Cicloxal* or Clafen* or "cyclo−cell*" or Cycloblastin* or Cycloblastin* or "cyclofos amide*" or Cyclofosfamid* or Cyclofosfamid* or Cyclophar* or Cyclophosphamid* or Cyclophosphamid* or Cyclophosphamid* or Cyclophosphan* or Cyclophosphan* or Cyclostin* or Cyclostin* or Cycloxan* or Cyphos* or Cyrevia* or Cytophosphan* or Cytophosphan* or Cytophosphan* or cytoxan lyophilized* or Cytoxan* or Endoxan* or Endoxon* or Enduxan* or "endocyclo phosphat*" or Genoxal* or Ledoxan* or Ledoxina* or "lyophilized Cytoxan*" or Mitoxan* or Neosan* or Neosar* or Noristan* or Procytox* or Procytoxide* or Semdoxan* or Sendoxan* or Syklofosfamid* or "b 518" or "b518" or "b-518" or "nsc 26271" or "nsc-26271" or "nsc26271" or "nsc 2671" or "nsc2671 pr nsc-2671" or 6UXW23996M or "50-18-0").ti,ab,kw,kf,ot.	62092
33	chemo*.af.	1084889
34	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33	1218630
35	(Randomized Controlled Trial or Controlled Clinical Trial or Pragmatic Clinical Trial or Equivalence Trial or Clinical Trial, Phase III).pt.	700093
36	Randomized Controlled Trial/	604459
37	exp Randomized Controlled Trials as Topic/	169449
38	"Randomized Controlled Trial (topic)"/	0
39	Controlled Clinical Trial/	95475
40	exp Controlled Clinical Trials as Topic/	175162
41	"Controlled Clinical Trial (topic)"/	0
42	Randomization/	107044
43	Random Allocation/	107044
44	Double-Blind Method/	176845
45	Double Blind Procedure/	0
46	Double-Blind Studies/	176845
47	Single-Blind Method/	33083
48	Single Blind Procedure/	0
49	Single-Blind Studies/	33083
50	Placebos/	35934
51	Placebo/	0
52	Control Groups/	2061
53	Control Group/	2061
54	(random* or sham or placebo*).ti,ab,hw,kf,kw.	1860379
55	((singl* or doubl*) adj (blind* or dumm* or mask* or arm or arms)).ti,ab,hw,kf,kw.	285390
56	((tripl* or trebl*) adj (blind* or dumm* or mask*)).ti,ab,hw,kf,kw.	1716

57	(control* adj3 (study or studies or trial* or group*)).ti,ab,kf,kw.	1261769
58	(Nonrandom* or non random* or non-random* or quasi-random* or quasirandom*).ti,ab,hw,kf,kw.	56377
59	allocated.ti,ab,hw.	86433
60	((open label or open-label) adj5 (study or studies or trial* or extension)).ti,ab,hw,kf,kw.	47037
61	((sub* and (group adj2 anal*)) or (subgroup adj2 anal*)).ti,ab,kw,kf.	83640
62	((equivalence or superiority or non-inferiority or noninferiority) adj3 (study or studies or trial*)).ti,ab,hw,kf,kw.	12733
63	(pragmatic study or pragmatic studies).ti,ab,hw,kf,kw.	629
64	((pragmatic or practical) adj3 trial*).ti,ab,hw,kf,kw.	8044
65	((quasiexperimental or quasi-experimental) adj3 (study or studies or trial*)).ti,ab,hw,kf,kw.	12995
66	("Phase 3*" or "phase3*" or "phase III*" or P3* or "PIII*" or "Phase 2*" or "phase2*" or "phase II*" or P2* or "PII*").ti,ab,kw,kf.	399711
67	(trial or trail).ti,ab,kw,kf.	812157
54	or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67	3281134
69	Epidemiologic studies/	9440
70	exp case control studies/	1464085
71	exp cohort studies/	2548195
72	Case control.tw.	158081
73	(cohort adj (study or studies)).tw.	333065
74	Cohort analy$.tw.	12416
75	(Follow up adj (study or studies)).tw.	57216
76	(observational adj (study or studies)).tw.	169566
77	Longitudinal.tw.	333586
78	Retrospective.tw.	776903
79	Cross sectional.tw.	536913
80	Cross-sectional studies/	485615
81	69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80	3893342
82	"systematic review"/	246662
83	(Systematic* adj2 Review*).ti,ab,kw,kf,ot.	334927
84	Meta-Analysis/	191123
85	(meta anal* or (MAIC or (indirect* adj3 comparison*))).ti,ab,kw,kf.	291375
86	82 or 83 or 84 or 85	497150
87	68 or 81 or 86	6597367
88	9 and 34 and 87	8106
89	(2023* or 2024*).dt,dp,ed,ep,yr.	1711835
90	88 and 89	548

H.1.4.3 CDSR and CENTRAL

The Cochrane Database of Systematic Reviews (CDSR) and CENTRAL were searched through the Cochrane Library. In the primary search, the databases were searched from inception to February 2023. In the updated search, the databases were searched from February 1st, 2023, to December 12th, 2023. The searches were carried out on February 5th, 2023, and December 12th, 2023, respectively. The detailed search strategies and results are provided in Table 84 and Table 85.

Table 84. Search strategy table for CDSR and CENTRAL (primary search)

No.	Query	Results
1	MeSH descriptor: [Multiple Myeloma] explode all trees	2095
2	(myelom* or ((Penta or triple-class) NEAR/1 refractory)):ti,ab,kw	6986
3	kahler*:ti,ab,kw	21
4	MeSH descriptor: [Plasmacytoma] this term only	91
5	(plasm?cytom* or plasm?zytom* or plasma cytoma* or plasma zytoma*):ti,ab,kw	323
6	(plasm* NEAR/3 (neoplas* or leukaem* or leukem* or tumor* or tumour* or dyscrasia)):ti,ab,kw	1358
7	((plasmacytic* or plasmocytic* or plasmocyte*) NEAR/1 (leukem* or leukaem*)):ti,ab,kw	1
8	(myelomatoses or myelomatosis):ti,ab,kw	34
9	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8	7754
10	(selinexor* or nexpovio* or xpovio* or "ATG 010" or ATG010 or "ATG-010" or "KPT 330" or KPT330 or "KPT-330" or "ONO 7705" or ONO7705 or "ONO-7705" or 31TZ62FO8F or "1393477-72-9"):ti,ab,kw	149
11	MeSH descriptor: [Bortezomib] this term only	609
12	(bortezomib* or velcade* or "BXCL 101" or BXCL101 or "BXCL-101" or "LDP 341" or LDP341 or "LDP-341" or "mg 341" or mg341 or "mg-341" or "PS 341" or PS341 or "PS-341" or "jnj 26866138" or jnj26866138 or "jnj-26866138" or 69G8BD63PP or "179324-69-7"):ti,ab,kw	2375
13	MeSH descriptor: [Dexamethasone] this term only	5476
14	(Dexamethason* or Dexam?thason* or "aeroseb dex*" or "aeroseb–d*" or "aeroseb–dex*" or "Apo Dexam?thason*" or "Apo-Dexamethason*" or "bisu ds*" or "dacortina fuerte*" or "dacortine fuerte*" or "de–sone la*" or "dexa cortisyl*" or "dexa dabrosan*" or "dexa korti*" or "dexa scherosan*" or "dexa scherozon*" or "dexa scherozone*" or "dexa–p*" or "dexacen 4*" or "dexacen–4*" or "dexpak taperpak*" or "ex s1*" or "fluormethyl prednisolone*" or "isopto dex*" or "isopto maxidex*" or "isopto–dex*" or "lokalison f*" or "methazon ion*" or "methazone ion*" or "metisone lafi*" or "oftan–dexa*" or "predni f tablinen*" or "predni–f*" or "prednisolone f*" or Adrecort* or Adrenocot* or Aflucoson* or Alfalyl* or Anaflogistico* or Aphtasolon* or Apo Dexam?thason* or Apo-Dexamethason* or Arcodexan* or Artrosone* or Auxiron* or Azium* or Baycadron* or Bidexol* or Calonat* or Cebedex* or Cetadexon* or Colofoam* or Corsona* or Corsone* or Cortastat* or	14612

	Cortidex* or Cortidexason* or Cortidrona* or Cortidrone* or Cortisumman* or Dalalone* or Danasone* or Decacortin* or Decadeltosona* or Decadeltosone* or Decaderm* or Decadion* or Decadran* or Decadron* or Decadronal* or Decadrone* or Decaesadril* or Decagel* or Decaject* or Decalix* or Decamethasone* or Decasone* or Decaspray* or Decasterolone* or Decdan* or Decilone* or Decofluor* or Dectancyl* or Dekacort* or Delladec* or Deltafluoren* or Deltafluorene* or Dergramin* or Deronil* or Desacort* or Desacortone* or Desadrene* or Desalark* or Desameton* or Desametone* or Desigdron* or Dexachel* or Dexacort* or Dexacortal* or Dexacorten* or Dexacortin* or Dexacortisyl* or Dexadabroson* or Dexadecadrol* or Dexadrol* or Dexagel* or Dexagen* or Dexahelvacort* or Dexakorti* or Dexalien* or Dexalocal* or Dexame* or Dexamecortin* or Dexameson* or Dexamesone* or Dexametason* or Dexameth* or Dexamethasone* or Dexamethasone* or Dexamethasone* or Dexamethasone* or Dexamethazon* or Dexamethonium* or Dexamonozon* or Dexan* or Dexane* or Dexano* or Dexapot* or Dexascheroson* or Dexascherozon* or Dexascherozone* or Dexason* or Dexasone* or Dexinoral* or Dexionil* or Dexmethsone* or Dexona* or Dexone* or Dextelan* or Dextenza* or Dextrasone* or Dexycu* or Dezone* or Dibasona* or Esacortene* or Exadion* or Exadione* or Firmalone* or Fluormethylprednisolon* or Fluormethylprednisolone* or Fluormone* or Fluorocort* or Fluorodelta* or Fluoromethylprednisolone* or Fortecortin* or Gammacorten* or Gammacortene* or Grosodexon* or Grosodexone* or Hemady* or Hexadecadiol* or Hexadiol* or Hexadrol* or Isnacort* or Isoptodex* or Isoptomaxidex* or Loverine* or Luxazone* or Marvidione* or Maxidex* or Mediamethasone* or Megacortin* or Mephameson* or Mephamesone* or Metasolon* or Metasolone* or Methazonion* or Methazonione* or Mexasone* or Millicorten* or Millicortenol* or Mymethasone* or Neoforderx* or Neofordex* or Nisomethasona* or Novocort* or Opticorten* or Opticortinol* or Oradexan* or Oradexon* or Oradexone* or Orgadrone* or Ozurdex* or Pidexon* or Policort* or Posurdex* or Prodexona* or Prodexone* or Sanamethasone* or Santenson* or Santeson* or Sawasone* or Solurex* or Spoloven* or Sterasone* or Thilodexine* or Triamcimetil* or Vexamet* or Visumetazone* or Visumethazone* or "isv 305" or isv305 or "isv-305" or "mk 125" or mk125 or "mk-125" or "nsc 34521" or nsc34521 or "nsc-34521" or "oto 104" or oto104 or "oto-104" or "sk 0503" or sk0503 or "sk-0503" or "spt 2101" or spt2101 or "spt-2101" or 7S5I7G3JQL or "50-02-2"):ti,ab,kw	
15	MeSH descriptor: [Lenalidomide] this term only	550
16	(lenalidomid* or "apo-lenalidomide" or ladevina* or revlimid* or "CC 5013" or CC5013 or "CC-5013" or "CDC 501" or CDC501 or "CDC-501" or "ENMD 0997" or ENMD0997 or "ENMD-0997" or "imid 3" or imid3 or "imid-3" or "SYP 1512" or SYP1512 or "SYP-1512" or F0P408N6V4 or "191732-72-6"):ti,ab,kw	2519
17	(carfilzomib* or kyprolis* or "ono 7057" or ono7057 or "ono-7057" or "PR 171" or PR171 or "PR-171" or 72X6E3J5AR or "868540-17-4"):ti,ab,kw	506
18	MeSH descriptor: [Panobinostat] this term only	33
19	(panobinostat* or farydak* or "lbh 589*" or lbh589* or "lbh-589*" or "mtx 110" or mtx110 or "mtx-110" or 9647FM7Y3Z or "404950-80-7"):ti,ab,kw	119
20	(daratumumab* or dalinvi* or darasarex* or darzalex* or Faspro* or "hlx 15" or hlx15 or "hlx-15" or "HuMax-CD 38" or "JNJ-54767414" or 4Z63YK6E0E or "945721-28-8"):ti,ab,kw	544

21	(pomalidomid* or actimid* or imnovid* or pomalyst* or "CC 4047" or CC4047 or "CC-4047" or "cdc 394" or cdc394 or "cdc-394" or D2UX06XLB5 or "19171-19-8"):ti,ab,kw	476
22	(Ixazomib* or ninlaro* or "MLN 2238" or MLN2238 or "MLN-2238" or "MLN 9708" or MLN9708 or "MLN-9708" or 71050168A2 or "1072833-77-2"):ti,ab,kw	251
23	(belantamab* or BLENREP or "gsk 2857914" or gsk2857914 or "gsk-2857914" or "GSK 2857916" or GSK2857916 or "GSK-2857916" or "WHO 10754" or WHO10754 or "WHO-10754" or DB1041CXDG or "2050232-20-5" or "2061894−48−0"):ti,ab,kw	66
24	(ciltacabtagen* or carvykti* or "jnj 4528" or jnj4528 or "jnj-4528" or "JNJ 68284528" or JNJ68284528 or "JNJ-68284528" or "LCAR B38M" or LCARB38M or "LCAR-B38M" or 0L1F17908Q):ti,ab,kw	10
25	(elotuzumab* or empliciti* or "BMS 901608" or BMS901608 or "BMS-901608" or "PDL 063" or PDL063 or "PDL-063" or huluc63 or 1351PE5UGS or "915296-00-3"):ti,ab,kw	142
26	(idecabtagen* or abecma* or "BB 2121" or BB2121 or "BB-2121" or "id cel" or idecel or "ide−cel" or 8PX1X7UG4D):ti,ab,kw	8
27	(isatuximab* or sarclisa* or "Hu 38SB19" or Hu38SB19 or "Hu-38SB19" or "SAR 650984" or SAR650984 or "SAR-650984" or R30772KCU0 or "1461640-62-9"):ti,ab,kw	163
28	(melphalan* or melflufen* or pepaxti* or pepaxto* or ygalo* or "j 1" or j1 or "ck 1535" or ck1535 or "ck-1535" or F70C5K4786 or "380449-51-4" or "380449−54−7"):ti,ab,kw	5283
29	MeSH descriptor: [Cyclophosphamide] this term only	5679
30	(teclistamab* or tecvayli* or "JNJ 64007957" or JNJ64007957 or "JNJ-64007957" or "jnj 7957" or jnj7957 or "jnj-7957" or 54534MX6Z9 or "2119595-80-9"):ti,ab,kw	11
31	(venetoclax* or venclexta* or "a 11954250" or a11954250 or "ABT 199" or ABT199 or "ABT-199" or "GDC 0199" or GDC0199 or GDC-0199 or "RG 7601" or RG7601 or "RG-7601" or "ro 5537382" or ro5537382 or N54AIC43PW or "1257044-40-8"):ti,ab,kw	542
32	(Cyclophosphamid* or Alkyroxan* or Carloxan* or Ciclofosfamida* or Ciclolen* or Cicloxal* or Clafen* or "cyclo−cell*" or Cycloblastin* or Cycloblastin* or "cyclofos amide*" or Cyclofosfamid* or Cyclofosfamid* or Cyclophar* or Cyclophosphamid* or Cyclophosphamid* or Cyclophosphamid* or Cyclophosphan* or Cyclophosphan* or Cyclostin* or Cyclostin* or Cycloxan* or Cyphos* or Cyrevia* or Cytophosphan* or Cytophosphan* or Cytophosphan* or cytoxan lyophilized* or Cytoxan* or Endoxan* or Endoxon* or Enduxan* or "endocyclo phosphat*" or Genoxal* or Ledoxan* or Ledoxina* or "lyophilized Cytoxan*" or Mitoxan* or Neosan* or Neosar* or Noristan* or Procytox* or Procytoxide* or Semdoxan* or Sendoxan* or Syklofosfamid* or "b 518" or "b518" or "b-518" or "nsc 26271" or "nsc-26271" or "nsc26271" or "nsc 2671" or "nsc2671 pr nsc-2671" or 6UXW23996M or "50-18-0"):ti,ab,kw	14365
33	chemo*:ti,ab,kw	103980
34	#10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33	124933
35	#9 AND #34	5201

Table 85. Search strategy table for CDSR and CENTRAL (updated search)

#	Search term	Hits
#1	MeSH descriptor: [Multiple Myeloma] explode all trees	2802
#2	(myelom* or ((Penta or triple-class) NEAR/1 refractory)):ti,ab,kw	7250
#3	kahler*:ti,ab,kw	22
#4	MeSH descriptor: [Plasmacytoma] this term only	148
#5	(plasm?cytom* or plasm?zytom* or plasma cytoma* or plasma zytoma*):ti,ab,kw	328
#6	(plasm* NEAR/3 (neoplas* or leukaem* or leukem* or tumor* or tumour* or dyscrasia)):ti,ab,kw	1426
#7	((plasmacytic* or plasmocytic* or plasmocyte*) NEAR/1 (leukem* or leukaem*)):ti,ab,kw	1
#8	(myelomatoses or myelomatosis):ti,ab,kw	34
#9	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8	8048
#10	(selinexor* or nexpovio* or xpovio* or "ATG 010" or ATG010 or "ATG-010" or "KPT 330" or KPT330 or "KPT-330" or "ONO 7705" or ONO7705 or "ONO-7705" or 31TZ62FO8F or "1393477-72-9"):ti,ab,kw	155
#11	MeSH descriptor: [Bortezomib] this term only	623
#12	(bortezomib* or velcade* or "BXCL 101" or BXCL101 or "BXCL-101" or "LDP 341" or LDP341 or "LDP-341" or "mg 341" or mg341 or "mg-341" or "PS 341" or PS341 or "PS-341" or "jnj 26866138" or jnj26866138 or "jnj-26866138" or 69G8BD63PP or "179324-69-7"):ti,ab,kw	2442
#13	MeSH descriptor: [Dexamethasone] this term only	5687
#14	(Dexamethason* or Dexam?thason* or aeroseb dex* or aeroseb—d* or aeroseb—dex* or Apo Dexam?thason* or Apo-Dexamethason* or bisu ds* or dacortina fuerte* or dacortine fuerte* or de—sone la* or dexa cortisyl* or dexa dabrosan* or dexa korti* or dexa scherosan* or dexa scherozon* or dexa scherozone* or dexa—p* or dexacen 4* or dexacen—4* or dexpak taperpak* or ex s1* or fluormethyl prednisolone* or isopto dex* or isopto maxidex* or isopto—dex* or lokalison f* or methazon ion* or methazone ion* or metisone lafi* or oftan—dexa* or predni f tablinen* or predni—f* or prednisolone f* or Adrecort* or Adrenocot* or Aflucoson* or Alfalyl* or Anaflogistico* or Aphtasolon* or Apo Dexam?thason* or Apo-Dexamethason* or Arcodexan* or Artrosone* or Auxiron* or Azium* or Baycadron* or Bidexol* or Calonat* or Cebedex* or Cetadexon* or Colofoam* or Corsona* or Corsone* or Cortastat* or Cortidex* or Cortidexason* or Cortidrona* or Cortidrone* or Cortisumman* or Dalalone* or Danasone* or Decacortin* or Decadeltosona* or Decadeltosone* or Decaderm* or Decadion* or Decadran* or Decadron* or Decadronal* or Decadrone* or Decaesadril* or Decagel* or Decaject* or Decalix* or Decamethasone* or Decasone* or Decaspray* or Decasterolone* or Decdan* or Decilone* or Decofluor* or Dectancyl* or Dekacort* or Delladec* or Deltafluoren* or Deltafluorene* or Dergramin* or Deronil* or Desacort* or Desacortone* or Desadrene* or Desalark* or Desameton* or Desametone* or Desigdron* or Dexachel* or Dexacort* or Dexacortal*	22759

	or Dexacorten* or Dexacortin* or Dexacortisyl* or Dexadabroson* or Dexadecadrol* or Dexadrol* or Dexagel* or Dexagen* or Dexahelvacort* or Dexakorti* or Dexalien* or Dexalocal* or Dexame* or Dexamecortin* or Dexameson* or Dexamesone* or Dexametason* or Dexameth* or Dexamethasone* or Dexamethasone* or Dexamethasone* or Dexamethasone* or Dexamethazon* or Dexamethonium* or Dexamonozon* or Dexan* or Dexane* or Dexano* or Dexapot* or Dexascheroson* or Dexascherozon* or Dexascherozone* or Dexason* or Dexasone* or Dexinoral* or Dexionil* or Dexmethsone* or Dexona* or Dexone* or Dextelan* or Dextenza* or Dextrasone* or Dexycu* or Dezone* or Dibasona* or Esacortene* or Exadion* or Exadione* or Firmalone* or Fluormethylprednisolon* or Fluormethylprednisolone* or Fluormone* or Fluorocort* or Fluorodelta* or Fluoromethylprednisolone* or Fortecortin* or Gammacorten* or Gammacortene* or Grosodexon* or Grosodexone* or Hemady* or Hexadecadiol* or Hexadiol* or Hexadrol* or Isnacort* or Isoptodex* or Isoptomaxidex* or Loverine* or Luxazone* or Marvidione* or Maxidex* or Mediamethasone* or Megacortin* or Mephameson* or Mephamesone* or Metasolon* or Metasolone* or Methazonion* or Methazonione* or Mexasone* or Millicorten* or Millicortenol* or Mymethasone* or Neoforderx* or Neofordex* or Nisomethasona* or Novocort* or Opticorten* or Opticortinol* or Oradexan* or Oradexon* or Oradexone* or Orgadrone* or Ozurdex* or Pidexon* or Policort* or Posurdex* or Prodexona* or Prodexone* or Sanamethasone* or Santenson* or Santeson* or Sawasone* or Solurex* or Spoloven* or Sterasone* or Thilodexine* or Triamcimetil* or Vexamet* or Visumetazone* or Visumethazone* or "isv 305" or isv305 or "isv-305" or "mk 125" or mk125 or "mk-125" or "nsc 34521" or nsc34521 or "nsc-34521" or "oto 104" or oto104 or "oto-104" or "sk 0503" or sk0503 or "sk-0503" or "spt 2101" or spt2101 or "spt-2101" or 7S5I7G3JQL or "50-02-2"):ti,ab,kw	
#15	MeSH descriptor: [Lenalidomide] this term only	583
#16	(lenalidomid* or "apo-lenalidomide" or ladevina* or revlimid* or "CC 5013" or CC5013 or "CC-5013" or "CDC 501" or CDC501 or "CDC-501" or "ENMD 0997" or ENMD0997 or "ENMD-0997" or "imid 3" or imid3 or "imid-3" or "SYP 1512" or SYP1512 or "SYP-1512" or F0P408N6V4 or "191732-72-6"):ti,ab,kw	2636
#17	(carfilzomib* or kyprolis* or "ono 7057" or ono7057 or "ono-7057" or "PR 171" or PR171 or "PR-171" or 72X6E3J5AR or "868540-17-4"):ti,ab,kw	537
#18	MeSH descriptor: [Panobinostat] this term only	33
#19	(panobinostat* or farydak* or lbh 589* or lbh589* or lbh-589* or "mtx 110" or mtx110 or "mtx-110" or 9647FM7Y3Z or "404950-80-7"):ti,ab,kw	119
#20	(daratumumab* or dalinvi* or darasarex* or darzalex* or Faspro* or "hlx 15" or hlx15 or "hlx-15" or "HuMax-CD 38" or "JNJ-54767414" or 4Z63YK6E0E or "945721-28-8"):ti,ab,kw	597
#21	(pomalidomid* or actimid* or imnovid* or pomalyst* or "CC 4047" or CC4047 or "CC-4047" or "cdc 394" or cdc394 or "cdc-394" or D2UX06XLB5 or "19171-19-8"):ti,ab,kw	503

#22	(Ixazomib* or ninlaro* or "MLN 2238" or MLN2238 or "MLN-2238" or "MLN 9708" or MLN9708 or "MLN-9708" or 71050168A2 or "1072833-77-2"):ti,ab,kw	266
#23	(belantamab* or BLENREP or "gsk 2857914" or gsk2857914 or "gsk-2857914" or "GSK 2857916" or GSK2857916 or "GSK-2857916" or "WHO 10754" or WHO10754 or "WHO-10754" or DB1041CXDG or "2050232-20-5" or "2061894—48—0"):ti,ab,kw	81
#24	(ciltacabtagen* or carvykti* or "jnj 4528" or jnj4528 or "jnj-4528" or "JNJ 68284528" or JNJ68284528 or "JNJ-68284528" or "LCAR B38M" or LCARB38M or "LCAR-B38M" or 0L1F17908Q):ti,ab,kw	14
#25	(elotuzumab* or empliciti* or "BMS 901608" or BMS901608 or "BMS-901608" or "PDL 063" or PDL063 or "PDL-063" or huluc63 or 1351PE5UGS or "915296-00-3"):ti,ab,kw	151
#26	(idecabtagen* or abecma* or "BB 2121" or BB2121 or "BB-2121" or "id cel" or idecel or "ide—cel" or 8PX1X7UG4D):ti,ab,kw	15
#27	(isatuximab* or sarclisa* or "Hu 38SB19" or Hu38SB19 or "Hu-38SB19" or "SAR 650984" or SAR650984 or "SAR-650984" or R30772KCU0 or "1461640-62-9"):ti,ab,kw	178
#28	(melphalan* or melflufen* or pepaxti* or pepaxto* or ygalo* or "j 1" or j1 or "ck 1535" or ck1535 or "ck-1535" or F70C5K4786 or "380449-51-4" or "380449—54—7"):ti,ab,kw	5533
#29	MeSH descriptor: [Cyclophosphamide] this term only	5762
#30	(teclistamab* or tecvayli* or "JNJ 64007957" or JNJ64007957 or "JNJ-64007957" or "jnj 7957" or jnj7957 or "jnj-7957" or 54534MX6Z9 or "2119595-80-9"):ti,ab,kw	16
#31	(venetoclax* or venclexta* or "a 11954250" or a11954250 or "ABT 199" or ABT199 or "ABT-199" or "GDC 0199" or GDC0199 or GDC-0199 or "RG 7601" or RG7601 or "RG-7601" or "ro 5537382" or ro5537382 or N54AIC43PW or "1257044-40-8"):ti,ab,kw	615
#32	(Cyclophosphamid* or Alkyroxan* or Carloxan* or Ciclofosfamida* or Ciclolen* or Cicloxal* or Clafen* or cyclo—cell* or Cycloblastin* or Cycloblastin* or cyclofos amide* or Cyclofosfamid* or Cyclofosfamid* or Cyclophar* or Cyclophosphamid* or Cyclophosphamid* or Cyclophosphamid* or Cyclophosphan* or Cyclophosphan* or Cyclostin* or Cyclostin* or Cycloxan* or Cyphos* or Cyrevia* or Cytophosphan* or Cytophosphan* or Cytophosphan* or cytoxan lyophilized* or Cytoxan* or Endoxan* or Endoxon* or Enduxan* or endocyclo phosphat* or Genoxal* or Ledoxan* or Ledoxina* or lyophilized Cytoxan* or Mitoxan* or Neosan* or Neosar* or Noristan* or Procytox* or Procytoxide* or Semdoxan* or Sendoxan* or Syklofosfamid* or "b 518" or "b518" or "b-518" or "nsc 26271" or "nsc-26271" or "nsc26271" or "nsc 2671" or "nsc2671 pr nsc-2671" or 6UXW23996M or "50-18-0"):ti,ab,kw	14703
#33	chemo*:ti,ab,kw	109222
#34	#10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33	137425
#35	#9 AND #34	5391

H.1.4.4 Database of Abstract of Reviews of Effects

The Database of Abstracts of Reviews of Effects (DARE) was searched through the CRD website. The database was searched from inception until the last update (March 31st, 2015). The detailed search strategy and results can be seen in Table 86.

Table 86. Search strategy table for DARE

No.	Query	Results
1	(Multiple Myeloma OR RRMM OR ((relapsed OR refractory OR triple class OR penta OR doublet or triplet) AND (Myeloma)) OR Kahler OR Plasmacytoma OR (plasma cell AND (neoplasm OR cancer OR dyscrasia)))	92

H.1.4.5 HTA Database

The CRD HTA database was searched through the CRD website. The database was searched from inception until the last update (March 31st, 2018). The detailed search strategy and results can be seen in Table 87.

Table 87. Search strategy table for HTA Database

No.	Query	Results
1	(Multiple Myeloma OR RRMM OR ((relapsed OR refractory OR triple class OR penta OR doublet or triplet) AND (Myeloma)) OR Kahler OR Plasmacytoma OR (plasma cell AND (neoplasm OR cancer OR dyscrasia)))	223

H.1.4.6 NHS Economic Evaluations Database

The CRD NHS Economic Evaluations Database was searched through the CRD website. The database was searched from inception until the last update (March 31st, 2015). The detailed search strategy and results can be seen in Table 88.

Table 88. Search strategy table for NHS EED

No.	Query	Results
1	(Multiple Myeloma OR RRMM OR ((relapsed OR refractory OR triple class OR penta OR doublet or triplet) AND (Myeloma)) OR Kahler OR Plasmacytoma OR (plasma cell AND (neoplasm OR cancer OR dyscrasia)))	162

H.1.4.7 Clinicaltrials.gov

The search strategies used in clinicaltrials.gov are provided in Table 89.

Table 89. Search strategy table for Clinicaltrials.gov

No.	Query	Results

1	(Multiple Myeloma OR RRMM OR ((relapsed OR refractory OR triple class OR penta OR doublet or triplet) AND (Myeloma)) OR Kahler OR Plasmacytoma OR (plasma cell AND (neoplasm OR cancer OR dyscrasia)))	5590

H.1.4.8 WHO ICTRP

The search strategies used in WHO ICTRP are provided in Table 90.

Table 90. Search strategy table for WHO ICTRP

No.	Query	Results
1	(Multiple Myeloma OR RRMM OR ((relapsed OR refractory OR triple class OR penta OR doublet or triplet) AND (Myeloma)) OR Kahler OR Plasmacytoma OR (plasma cell AND (neoplasm OR cancer OR dyscrasia)))	4214

Abbreviations: WHO ICTRP = World Health Organization International Clinical Trial Registry Platform.

H.1.4.9 EMA EUCTR

The search strategy used in clinicaltrials.gov and the ICTRP was not applicable in EUCTR, as the search yielded 175 pages of results and the interface was limited to downloads at one page at a time (with no ability to enlarge the number of records per page, or to select all records). Since EUCTR content is captured by ICTRP and Cochrane CENTRAL – where a more sensitive search had already been undertaken - this search focused on condition and combination terms. The searches were carried out on February 5th, 2023, and December 13th, 2023, respectively. The search strategies used in EMA EUCTR are provided in Table 91 and Table 92.

Table 91. Search strategy table for EMA EUCTR (primary search)

No.	Query	Results
1	((multiple myeloma) AND (selinexor AND bortezomib AND dexamethasone))	6
2	((multiple myeloma) AND (selinexor AND dexamethasone))	7
3	((multiple myeloma) AND (belantamab mafodotin))	16
4	((multiple myeloma) AND (bortezomib monotherapy))	9
5	((multiple myeloma) AND (bortezomib AND dexamethasone))	163
6	((multiple myeloma) AND (carfilzomib AND dexamethasone))	62
7	((multiple myeloma) AND (carfilzomib AND lenalidomide AND dexamethasone))	46
8	((multiple myeloma) AND (ciltacabtagene autoleucel))	5
9	((multiple myeloma) AND (cyclophosphamide))	61
10	((multiple myeloma) AND (daratumumab monotherapy))	12
11	((multiple myeloma) AND (daratumumab AND bortezomib AND dexamethasone))	37
12	((multiple myeloma) AND (daratumumab AND carfilzomib AND dexamethasone))	18

13	((multiple myeloma) AND (daratumumab AND lenalidomide AND dexamethasone))	41
14	((multiple myeloma) AND (daratumumab AND pomalidomide AND dexamethasone))	22
15	((multiple myeloma) AND (elotuzumab AND lenalidomide AND dexamethasone))	10
16	((multiple myeloma) AND (elotuzumab AND pomalidomide AND dexamethasone))	5
17	((multiple myeloma) AND (Idecabtagene vicleucel))	4
18	((multiple myeloma) AND (Isatuximab AND carfilzomib AND dexamethasone))	9
19	((multiple myeloma) AND (Isatuximab AND pomalidomide AND dexamethasone))	8
20	((multiple myeloma) AND (Ixazomib AND lenalidomide AND dexamethasone))	21
21	((multiple myeloma) AND (lenalidomide AND dexamethasone))	178
22	((multiple myeloma) AND (melphalan flufenamide AND dexamethasone))	6
23	((multiple myeloma) AND (panobinostat AND bortezomib AND dexamethasone))	6
24	((multiple myeloma) AND (pomalidomide AND dexamethasone))	62
25	((multiple myeloma) AND (pomalidomide AND bortezomib AND dexamethasone))	34
26	((multiple myeloma) AND (pomalidomide AND cyclophosphamide AND dexamethasone))	7
27	((multiple myeloma) AND (teclistamab))	7
28	((multiple myeloma) AND (venetoclax AND bortezomib AND dexamethasone))	3

Table 92. Search strategy table for EMA EUCTR (updated search)

No.	Query	Results
1	((multiple myeloma) AND (selinexor AND bortezomib AND dexamethasone))	0
2	((multiple myeloma) AND (selinexor AND dexamethasone))	0
3	((multiple myeloma) AND (belantamab mafodotin))	1
4	((multiple myeloma) AND (bortezomib monotherapy))	0
5	((multiple myeloma) AND (bortezomib AND dexamethasone))	3
6	((multiple myeloma) AND (carfilzomib AND dexamethasone))	0
7	((multiple myeloma) AND (carfilzomib AND lenalidomide AND dexamethasone))	0
8	((multiple myeloma) AND (ciltacabtagene autoleucel))	0

9	((multiple myeloma) AND (cyclophosphamide))	0
10	((multiple myeloma) AND (daratumumab monotherapy))	0
11	((multiple myeloma) AND (daratumumab AND bortezomib AND dexamethasone))	0
12	((multiple myeloma) AND (daratumumab AND carfilzomib AND dexamethasone))	0
13	((multiple myeloma) AND (daratumumab AND lenalidomide AND dexamethasone))	1
14	((multiple myeloma) AND (daratumumab AND pomalidomide AND dexamethasone))	0
15	((multiple myeloma) AND (elotuzumab AND lenalidomide AND dexamethasone))	0
16	((multiple myeloma) AND (elotuzumab AND pomalidomide AND dexamethasone))	0
17	((multiple myeloma) AND (Idecabtagene vicleucel))	0
18	((multiple myeloma) AND (Isatuximab AND carfilzomib AND dexamethasone))	0
19	((multiple myeloma) AND (Isatuximab AND pomalidomide AND dexamethasone))	0
20	((multiple myeloma) AND (Ixazomib AND lenalidomide AND dexamethasone))	0
21	((multiple myeloma) AND (lenalidomide AND dexamethasone))	3
22	((multiple myeloma) AND (melphalan flufenamide AND dexamethasone))	0
23	((multiple myeloma) AND (panobinostat AND bortezomib AND dexamethasone))	0
24	((multiple myeloma) AND (pomalidomide AND dexamethasone))	0
25	((multiple myeloma) AND (pomalidomide AND bortezomib AND dexamethasone))	0
26	((multiple myeloma) AND (pomalidomide AND cyclophosphamide AND dexamethasone))	0
27	((multiple myeloma) AND (teclistamab))	0
28	((multiple myeloma) AND (venetoclax AND bortezomib AND dexamethasone))	0
Total		8 – duplicates = 4

Notes: In the updated search, the 'select date range' was to limit results to Feb 01 to Dec 13.

H.1.4.10 Embase (conference proceedings)

The detailed search strategy for conference proceedings through Embase (Ovid.com) is detailed in Table 93.

Table 93. Search strategy table for Embase (conference proceedings)

No.	Query	Results
1	exp *multiple myeloma/	54598

2	(myelom* or ((Penta or triple-class) adj1 refractory)).ti,ab,kw,kf,ot.	111816
3	kahler*.ti,ab,kw,kf,ot.	188
4	*plasmacytoma/	5642
5	(plasm?cytom* or plasm?zytom* or plasma cytoma* or plasma zytoma*).ti,ab,kw,kf,ot.	8922
6	(plasm* adj3 (neoplas* or leukaem* or leukem* or tumor* or tumour* or dyscrasia)).ti,ab,kw,kf,ot.	19426
7	((plasmacytic* or plasmocytic* or plasmocyte*) adj1 (leukem* or leukaem*)).ti,ab,kw,kf,ot.	37
8	(myelomatoses or myelomatosis).ti,ab,kw,kf.	365
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	132932
10	selinexor/	1430
11	(selinexor* or nexpovio* or xpovio* or "ATG 010" or ATG010 or "ATG-010" or "KPT 330" or KPT330 or "KPT-330" or "ONO 7705" or ONO7705 or "ONO-7705" or 31TZ62FO8F or "1393477-72-9").ti,ab,kw,kf,ot.	1106
12	bortezomib/	37690
13	(bortezomib* or velcade* or "BXCL 101" or BXCL101 or "BXCL-101" or "LDP 341" or LDP341 or "LDP-341" or "mg 341" or mg341 or "mg-341" or "PS 341" or PS341 or "PS-341" or "jnj 26866138" or jnj26866138 or "jnj-26866138" or 69G8BD63PP or "179324-69-7").ti,ab,kw,kf,ot.	23552
14	dexamethasone/	172546
15	(Dexamethason* or Dexam?thason* or "aeroseb dex*" or "aeroseb−d*" or "aeroseb−dex*" or "Apo Dexam?thason*" or "Apo-Dexamethason*" or "bisu ds*" or "dacortina fuerte*" or "dacortine fuerte*" or "de−sone la*" or "dexa cortisyl*" or "dexa dabrosan*" or "dexa korti*" or "dexa scherosan*" or "dexa scherozon*" or "dexa scherozone*" or "dexa−p*" or "dexacen 4*" or "dexacen−4*" or "dexpak taperpak*" or "ex s1*" or "fluormethyl prednisolone*" or "isopto dex*" or "isopto maxidex*" or "isopto−dex*" or "lokalison f*" or "methazon ion*" or "methazone ion*" or "metisone lafi*" or "oftan−dexa*" or "predni f tablinen*" or "predni−f*" or "prednisolone f*" or Adrecort* or Adrenocot* or Aflucoson* or Alfalyl* or Anaflogistico* or Aphtasolon* or Apo Dexam?thason* or Apo-Dexamethason* or Arcodexan* or Artrosone* or Auxiron* or Azium* or Baycadron* or Bidexol* or Calonat* or Cebedex* or Cetadexon* or Colofoam* or Corsona* or Corsone* or Cortastat* or Cortidex* or Cortidexason* or Cortidrona* or Cortidrone* or Cortisumman* or Dalalone* or Danasone* or Decacortin* or Decadeltosona* or Decadeltosone* or Decaderm* or Decadion* or Decadran* or Decadron* or Decadronal* or Decadrone* or Decaesadril* or Decagel* or Decaject* or Decalix* or Decamethasone* or Decasone* or Decaspray* or Decasterolone* or Decdan* or Decilone* or Decofluor* or Dectancyl* or Dekacort* or Delladec* or Deltafluoren* or Deltafluorene* or Dergramin* or Deronil* or Desacort* or Desacortone* or Desadrene* or Desalark* or Desameton* or Desametone* or Desigdron* or Dexachel* or Dexacort* or Dexacortal* or Dexacorten* or Dexacortin* or Dexacortisyl* or Dexadabroson* or Dexadecadrol* or Dexadrol* or Dexagel* or Dexagen* or Dexahelvacort* or Dexakorti* or Dexalien* or Dexalocal* or Dexame* or Dexamecortin* or Dexameson* or Dexamesone* or Dexametason* or Dexameth* or Dexamethasone* or Dexamethasone* or Dexamethasone* or Dexamethasone* or Dexamethazon* or Dexamethonium* or Dexamonozon* or Dexan* or Dexane* or Dexano* or Dexapot* or Dexascheroson* or Dexascherozon*	93079

	or Dexascherozone* or Dexason* or Dexasone* or Dexinoral* or Dexionil* or Dexmethsone* or Dexona* or Dexone* or Dextelan* or Dextenza* or Dextrasone* or Dexycu* or Dezone* or Dibasona* or Esacortene* or Exadion* or Exadione* or Firmalone* or Fluormethylprednisolon* or Fluormethylprednisolone* or Fluormone* or Fluorocort* or Fluorodelta* or Fluoromethylprednisolone* or Fortecortin* or Gammacorten* or Gammacortene* or Grosodexon* or Grosodexone* or Hemady* or Hexadecadiol* or Hexadiol* or Hexadrol* or Isnacort* or Isoptodex* or Isoptomaxidex* or Loverine* or Luxazone* or Marvidione* or Maxidex* or Mediamethasone* or Megacortin* or Mephameson* or Mephamesone* or Metasolon* or Metasolone* or Methazonion* or Methazonione* or Mexasone* or Millicorten* or Millicortenol* or Mymethasone* or Neoforderx* or Neofordex* or Nisomethasona* or Novocort* or Opticorten* or Opticortinol* or Oradexan* or Oradexon* or Oradexone* or Orgadrone* or Ozurdex* or Pidexon* or Policort* or Posurdex* or Prodexona* or Prodexone* or Sanamethasone* or Santenson* or Santeson* or Sawasone* or Solurex* or Spoloven* or Sterasone* or Thilodexine* or Triamcimetil* or Vexamet* or Visumetazone* or Visumethazone* or "isv 305" or isv305 or "isv-305" or "mk 125" or mk125 or "mk-125" or "nsc 34521" or nsc34521 or "nsc-34521" or "oto 104" or oto104 or "oto-104" or "sk 0503" or sk0503 or "sk-0503" or "spt 2101" or spt2101 or "spt-2101" or 7S5I7G3JQL or "50-02-2").ti,ab,kw,kf,ot.	
16	lenalidomide/	25117
17	(lenalidomid* or "apo-lenalidomide" or ladevina* or revlimid* or "CC 5013" or CC5013 or "CC-5013" or "CDC 501" or CDC501 or "CDC-501" or "ENMD 0997" or ENMD0997 or "ENMD-0997" or "imid 3" or imid3 or "imid-3" or "SYP 1512" or SYP1512 or "SYP-1512" or F0P408N6V4 or "191732-72-6").ti,ab,kw,kf,ot.	16040
18	carfilzomib/	6347
19	(carfilzomib* or kyprolis* or "ono 7057" or ono7057 or "ono-7057" or "PR 171" or PR171 or "PR-171" or 72X6E3J5AR or "868540-17-4").ti,ab,kw,kf,ot.	4047
20	panobinostat/	4850
21	(panobinostat* or farydak* or "lbh 589*" or lbh589* or "lbh-589*" or "mtx 110" or mtx110 or "mtx-110" or 9647FM7Y3Z or "404950-80-7").ti,ab,kw,kf,ot.	2316
22	daratumumab/	5554
23	(daratumumab* or dalinvi* or darasarex* or darzalex* or Faspro* or "hlx 15" or hlx15 or "hlx-15" or "HuMax-CD 38" or "JNJ-54767414" or 4Z63YK6E0E or "945721-28-8").ti,ab,kw,kf,ot.	3909
24	pomalidomide/	5086
25	(pomalidomid* or actimid* or imnovid* or pomalyst* or "CC 4047" or CC4047 or "CC-4047" or "cdc 394" or cdc394 or "cdc-394" or D2UX06XLB5 or "19171-19-8").ti,ab,kw,kf,ot.	3253
26	ixazomib/	2346
27	(Ixazomib* or ninlaro* or "MLN 2238" or MLN2238 or "MLN-2238" or "MLN 9708" or MLN9708 or "MLN-9708" or 71050168A2 or "1072833-77-2").ti,ab,kw,kf,ot.	1550
28	belantamab/	53

29	(belantamab* or BLENREP or "gsk 2857914" or gsk2857914 or "gsk-2857914" or "GSK 2857916" or GSK2857916 or "GSK-2857916" or "WHO 10754" or WHO10754 or "WHO-10754" or DB1041CXDG or "2050232-20-5" or "2061894−48−0").ti,ab,kw,kf,ot.	333
30	ciltacabtagene autoleucel/	185
31	(ciltacabtagen* or carvykti* or "jnj 4528" or jnj4528 or "jnj-4528" or "JNJ 68284528" or JNJ68284528 or "JNJ-68284528" or "LCAR B38M" or LCARB38M or "LCAR-B38M" or 0L1F17908Q).ti,ab,kw,kf,ot.	151
32	elotuzumab/	1652
33	(elotuzumab* or empliciti* or "BMS 901608" or BMS901608 or "BMS-901608" or "PDL 063" or PDL063 or "PDL-063" or huluc63 or 1351PE5UGS or "915296-00-3").ti,ab,kw,kf,ot.	915
34	idecabtagene vicleucel/	327
35	(idecabtagen* or abecma* or "BB 2121" or BB2121 or "BB-2121" or "id cel" or idecel or "ide−cel" or 8PX1X7UG4D).ti,ab,kw,kf,ot.	212
36	isatuximab/	839
37	(isatuximab* or sarclisa* or "Hu 38SB19" or Hu38SB19 or "Hu-38SB19" or "SAR 650984" or SAR650984 or "SAR-650984" or R30772KCU0 or "1461640-62-9").ti,ab,kw,kf,ot.	533
38	melphalan flufenamide/	175
39	(melphalan* or melflufen* or pepaxti* or pepaxto* or ygalo* or "j 1" or j1 or "ck 1535" or ck1535 or "ck-1535" or F70C5K4786 or "380449-51-4" or "380449−54−7").ti,ab,kw,kf,ot.	19282
40	teclistamab/	130
41	(teclistamab* or tecvayli* or "JNJ 64007957" or JNJ64007957 or "JNJ-64007957" or "jnj 7957" or jnj7957 or "jnj-7957" or 54534MX6Z9 or "2119595-80-9").ti,ab,kw,kf,ot.	68
42	venetoclax/	8549
43	(venetoclax* or venclexta* or "a 11954250" or a11954250 or "ABT 199" or ABT199 or "ABT-199" or "GDC 0199" or GDC0199 or GDC-0199 or "RG 7601" or RG7601 or "RG-7601" or "ro 5537382" or ro5537382 or N54AIC43PW or "1257044-40-8").ti,ab,kw,kf,ot.	6590
44	Cyclophosphamide/	229549
45	(Cyclophosphamid* or Alkyroxan* or Carloxan* or Ciclofosfamida* or Ciclolen* or Cicloxal* or Clafen* or "cyclo−cell*" or Cycloblastin* or Cycloblastin* or "cyclofos amide*" or Cyclofosfamid* or Cyclofosfamid* or Cyclophar* or Cyclophosphamid* or Cyclophosphamid* or Cyclophosphamid* or Cyclophosphan* or Cyclophosphan* or Cyclostin* or Cyclostin* or Cycloxan* or Cyphos* or Cyrevia* or Cytophosphan* or Cytophosphan* or Cytophosphan* or cytoxan lyophilized* or Cytoxan* or Endoxan* or Endoxon* or Enduxan* or "endocyclo phosphat*" or Genoxal* or Ledoxan* or Ledoxina* or "lyophilized Cytoxan*" or Mitoxan* or Neosan* or Neosar* or Noristan* or Procytox* or Procytoxide* or Semdoxan* or Sendoxan* or Syklofosfamid* or "b 518" or "b518" or "b-518" or "nsc 26271" or "nsc-26271" or "nsc26271" or "nsc 2671" or "nsc2671 pr nsc-2671" or 6UXW23996M or "50-18-0").ti,ab,kw,kf,ot.	92178
46	chemo*.af.	1675536

47	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46	1982059
48	(Randomized Controlled Trial or Controlled Clinical Trial or Pragmatic Clinical Trial or Equivalence Trial or Clinical Trial, Phase III).pt.	0
49	Randomized Controlled Trial/	755138
50	exp Randomized Controlled Trials as Topic/	246980
51	"Randomized Controlled Trial (topic)"/	246872
52	Controlled Clinical Trial/	467822
53	exp Controlled Clinical Trials as Topic/	256400
54	"Controlled Clinical Trial (topic)"/	13233
55	Randomization/	97448
56	Random Allocation/	93577
57	Double-Blind Method/	176829
58	Double Blind Procedure/	201726
59	Double-Blind Studies/	162253
60	Single-Blind Method/	47675
61	Single Blind Procedure/	49742
62	Single-Blind Studies/	49742
63	Placebos/	324924
64	Placebo/	381700
65	Control Groups/	110772
66	Control Group/	110772
67	(random* or sham or placebo*).ti,ab,hw,kf,kw.	2434550
68	((singl* or doubl*) adj (blind* or dumm* or mask* or arm or arms)).ti,ab,hw,kf,kw.	370032
69	((tripl* or trebl*) adj (blind* or dumm* or mask*)).ti,ab,hw,kf,kw.	1972
70	(control* adj3 (study or studies or trial* or group*)).ti,ab,kf,kw.	1650007
71	(Nonrandom* or non random* or non-random* or quasi-random* or quasirandom*).ti,ab,hw,kf,kw.	67069
72	allocated.ti,ab,hw.	104620
73	((open label or open-label) adj5 (study or studies or trial* or extension)).ti,ab,hw,kf,kw.	85734
74	((sub* and (group adj2 anal*)) or (subgroup adj2 anal*)).ti,ab,kw,kf.	113006
75	((equivalence or superiority or non-inferiority or noninferiority) adj3 (study or studies or trial*)).ti,ab,hw,kf,kw.	17377
76	(pragmatic study or pragmatic studies).ti,ab,hw,kf,kw.	851
77	((pragmatic or practical) adj3 trial*).ti,ab,hw,kf,kw.	8153
78	((quasiexperimental or quasi-experimental) adj3 (study or studies or trial*)).ti,ab,hw,kf,kw.	18259

79	("Phase 3*" or "phase3*" or "phase III*" or P3* or "PIII*" or "Phase 2*" or "phase2*" or "phase II*" or P2* or "PII*").ti,ab,kw,kf.	596041
80	(trial or trail).ti,ab,kw,kf.	1108589
81	48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80	4394242
82	Clinical study/	117016
83	Case control study/	198089
84	Family study/	25666
85	Longitudinal study/	183606
86	Retrospective study/	1376303
87	Prospective study/	834133
88	Randomized controlled trials/	246872
89	87 not 88	823878
90	Cohort analysis/	959124
91	(Cohort adj (study or studies)).mp.	448732
92	(Case control adj (study or studies)).tw.	162882
93	(follow up adj (study or studies)).tw.	69214
94	(observational adj (study or studies)).tw.	239673
95	(epidemiologic$ adj (study or studies)).tw.	117597
96	(cross sectional adj (study or studies)).tw.	318450
97	82 or 83 or 84 or 85 or 86 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96	3667254
98	"systematic review"/	405604
99	(Systematic* adj2 Review*).ti,ab,kw,kf,ot.	367074
100	Meta-Analysis/	275276
101	(meta anal* or (MAIC or (indirect* adj3 comparison*))).ti,ab,kw,kf.	337490
102	98 or 99 or 100 or 101	667819
103	81 or 97 or 102	7528631
104	9 and 47 and 103	21680
105	(conference abstract* or conference review or conference paper or conference proceeding).db,pt,su.	5445560
106	104 and 105	12134
107	(2021* or 2022* or 2023*).yr.	3715827
108	106 and 107	1932

H.1.4.11 CPCI-S

The detailed search strategy for conference proceedings through CPCI-S (Clarivate) is detailed in Table 94.

Table 94. Search strategy table for CPCI-S

No.	Query	Results
1	"Multiple Myeloma" (Topic)	13,559
2	(myelom* or ((Penta or triple-class) NEAR/1 refractory)) (Topic)	18,271
3	TS=((kahler* or plasmcytom* or plasma cytoma* or plasma zytoma* or myelomatoses or myelomatosis))	551
4	(plasm* NEAR/3 (neoplas* or leukaem* or leukem* or tumor* or tumour* or dyscrasia)) (Topic)	1,210
5	#1 OR #2 OR #3 OR #4 OR #5	3
6	#1 OR #2 OR #3 OR #4 OR #5 and 2023 or 2022 or 2021 (Publication Years)	369

H.1.4.12 Key regulatory and HTA websites

A summary of results of the web searching across both the primary and the updated search is provided in Table 95.

Table 95. Summary results of web searching (primary and updated search)

Database or resource	N (primary)	N (updated)
NICE	32	6
SMC	33	2
NIRHIO tech briefings	19	1
EMA	27	0
MHRA	0	5
TLV	0	0
NIPH	1	1
DTC	8	0
FIMEA	8	0
NCPE	15	4
RIZIV-INAMI	0	1
ZIN	2	0
Total	145	20

Abbreviations: DTC, Danish Treatment Council; EMA, European Medicines Agency; FIMEA, Finnish Medicines Agency and Food Authority; MHRA, Medicines and Healthcare Products Regulator Agency; NCPE, National Centre for Pharmacoeconomics; NIPH, Norwegian Institute of Public Health; NIRIO, National Institute for Health Research Innovation Observatory; RIZIV-INAMI, National institute for sickness and disability insurance; SMC, Scottish Medicines Consortium; TLV, Dental and Pharmaceutical Benefits Agency (Tandvårds- och läkemedelsförmånsverket); ZIN, National Health Care Institute (Zorginstituut Nederland).

H.1.4.13 Conference proceedings

A summary of results of the conference searching across both the primary and the updated search is provided in Table 96.

Table 96. Summary results of conference searching (primary and updated search)

Conference searching	N (primary)	N (updated)
Embase search	1932	423
CPCI-S Search	369	357
ASCO	94	93
Handsearching ASH	759	263
BSH	39	21
COMy	Access not achieved – could not search	client providing
EHA	232	125
EMN	0	0
ESMO	11	1
IMS	Access not achieved – could not search	client providing
Total	3436	1283

H.1.5 Systematic selection of studies

H.1.5.1 Eligibility criteria

H.1.5.1.1 Global SLR

For the global SLR, during primary screening, titles and abstracts of identified records were assessed against the population, intervention, comparator, outcomes and study design (PICOS) criteria, detailed in Table 97 to select those addressing the SLR eligibility criteria. This assessment was undertaken by at least two reviewers independently, using the Covidence online screening tool. Electronic or paper copies of potentially relevant full papers meeting the SLR inclusion criteria were then obtained for secondary screening and assessed in detail for relevance to the eligibility criteria by two reviewers independently, and final selection of studies was made to inform the SLR. Where researchers disagreed regarding the inclusion or exclusion of a record at either primary or secondary screening, a third reviewer joined discussions where reasons for disagreement were discussed until a consensus was reached.

Eligible studies were data extracted initially by one reviewer, with a second carrying out a cell-by-cell data quality check. Where more than one publication of a study existed (e.g., a conference abstract and a paper published in a peer-reviewed journal), reports were grouped together and the primary publication was used in synthesis, and supplemented by additional records where relevant outcomes were only published in earlier versions. Any discrepancy between published versions were highlighted.

During data extraction, researchers conducted quality assessment of each included study using the NICE checklist for RCTs (adapted from CRD guidance) and NICE checklist for non-RCTs (adapted from CASP) as appropriate[64]. Quality assessment was used to provide an assessment of the risk of bias for each included study and was not used to exclude eligible studies.[43] Quality assessment was used to provide an assessment of the risk of bias for each included study and was not used to exclude eligible studies.

The PICO(s) and inclusion and exclusion criteria used for the global SLR are provided in Table 97.

Table 97. Inclusion and exclusion criteria used for assessment of studies

Clinical effectiveness	Inclusion criteria	Exclusion criteria
Population	Adults (≥18 years) with RRMM with ≥1 prior line of therapy	Newly diagnosed/ untreated MM
Intervention	**Selinexor + bortezomib + dexamethasone*** Selinexor + dexamethasone Belantamab mafodotin Best supportive careb Bortezomib monotherapy Bortezomib + dexamethasone **Carfilzomib + dexamethasone*** Carfilzomib + lenalidomide + dexamethasone Ciltacabtagene autoleucel Conventional chemotherapy (e.g., cyclo) b Daratumumab monotherapy Daratumumab + bortezomib + dexamethasone Daratumumab + carfilzomib + dexamethasone Daratumumab + lenalidomide + dexamethasone Daratumumab + pomalidomide + dexamethasone Elotuzumab + lenalidomide + dexamethasone Elotuzumab + pomalidomide + dexamethasone Idecabtagene vicleucel Isatuximab + carfilzomib + dexamethasone Isatuximab + pomalidomide + dexamethasone Ixazomib + lenalidomide + dexamethasone Lenalidomide + dexamethasone Melphalan flufenamide + dexamethasone Panobinostat + bortezomib + dexamethasone Pomalidomide + dexamethasone **Pomalidomide + bortezomib + dexamethasone***	Any intervention, or combinations of interventions, that are not listed for inclusion

	Pomalidomide + cyclophosphamide + dexamethasone Teclistamab Venetoclax + bortezomib + dexamethasone	
Comparators	Trials that include a comparator of any type (including but not limited to the interventions listed above), including placebo, or with no comparator	
Outcomes	Survival and response: ORR, DoR, BOR, PFS, EFS, OS, CBR, TTR, TTP, TTNT, ToT Safety and tolerability: TEAEs, STEAEs, TEAES leading to discontinuation/ dose reduction, TRAEs, serious TRAES, deaths HRQoL: EQ-5D, EORTC QLQ-C30, EORTC QLQ-MY20, EORTC QLQ CIPN20; FACT-G, FACT-MM.	
Study design/publication type	RCTs Single-arm non-RCTs Open-label extension trials Retrospective and prospective observational studies Peer review publications Abstracts and conference presentations Guidelines Trial protocols Systematic reviews HTA/ regulatory guidance documents Horizon scanning documents	Phase I trials In vitro and animal studies Pharmacokinetics Pharmacodynamics Non-systematic reviews Opinion pieces Editorials Letters Reports Press releases Case series studies Case reports
Language restrictions	No language restrictions [a]	
Publication year	No date limits applied with the exception of conference abstracts, which are limited to those published 2021 to present [b]	

Abbreviations: BOR, best overall response; CBR, clinical benefit rate; DoR, duration of response; EFS, event free survival; EORTC-QLQ-30; European Organisation For Research And Treatment Of Cancer Quality of life questionnaire – 30; EORTC-QLQ CIPN20, European Organisation For Research And Treatment Of Cancer Quality of life questionnaire – Chemotherapy-Induced Peripheral Neuropathy Module; EORTC-QLQ-MY20, European Organisation For Research And Treatment Of Cancer Quality of life questionnaire multiple myeloma module; EQ-5D, EuroQol-5 dimension; FACT-G; FuNCTional Assessment of Cancer Therapy – General; FACT-MM, FuNCTional Assessment of Cancer Therapy - Multiple Myeloma; HRQoL, health-related quality of life; HTA, health technology appraisal; MM, multiple myeloma; ORR, overall response rate; OS, overall survival; PFS, progression free survival; PICOS, population, intervention, comparator, outcomes, study design; RCT, randomised controlled trial; RRMM, relapsed and/ or refractory multiple myeloma; STEAE, serious treatment emergent adverse event; TEAE, treatment emergent adverse event; TOT, time on treatment; TRAE, treatment-related adverse event; TTNT, time to next treatment; TTP, time to progression; TTR, time to response.
Notes: [a] Records will be translated to judge eligibility. Where this is not possible, records will be detailed in the report. [b] Trials of BSC and conventional chemotherapy will only be eligible in population 2.
*Studies examining treatments marked with bold and an asterisk were included in the Danish adaptation of the SLR (see also Table 98)

H.1.5.1.2 Local adaptation

The search strategy was developed as part of a global SLR, and thus includes interventions not relevant in the Danish setting. For the adaptation to the Danish setting, all included studies were screened again using the criteria provided in Table 98, and studies included in the global SLR not includable in the Danish adaptation were excluded at the full-text screening stage.

The PICO(s) and inclusion and exclusion criteria were adapted to the Danish setting by restricting to relevant interventions (SVd and Kd); all other criteria were kept the same.

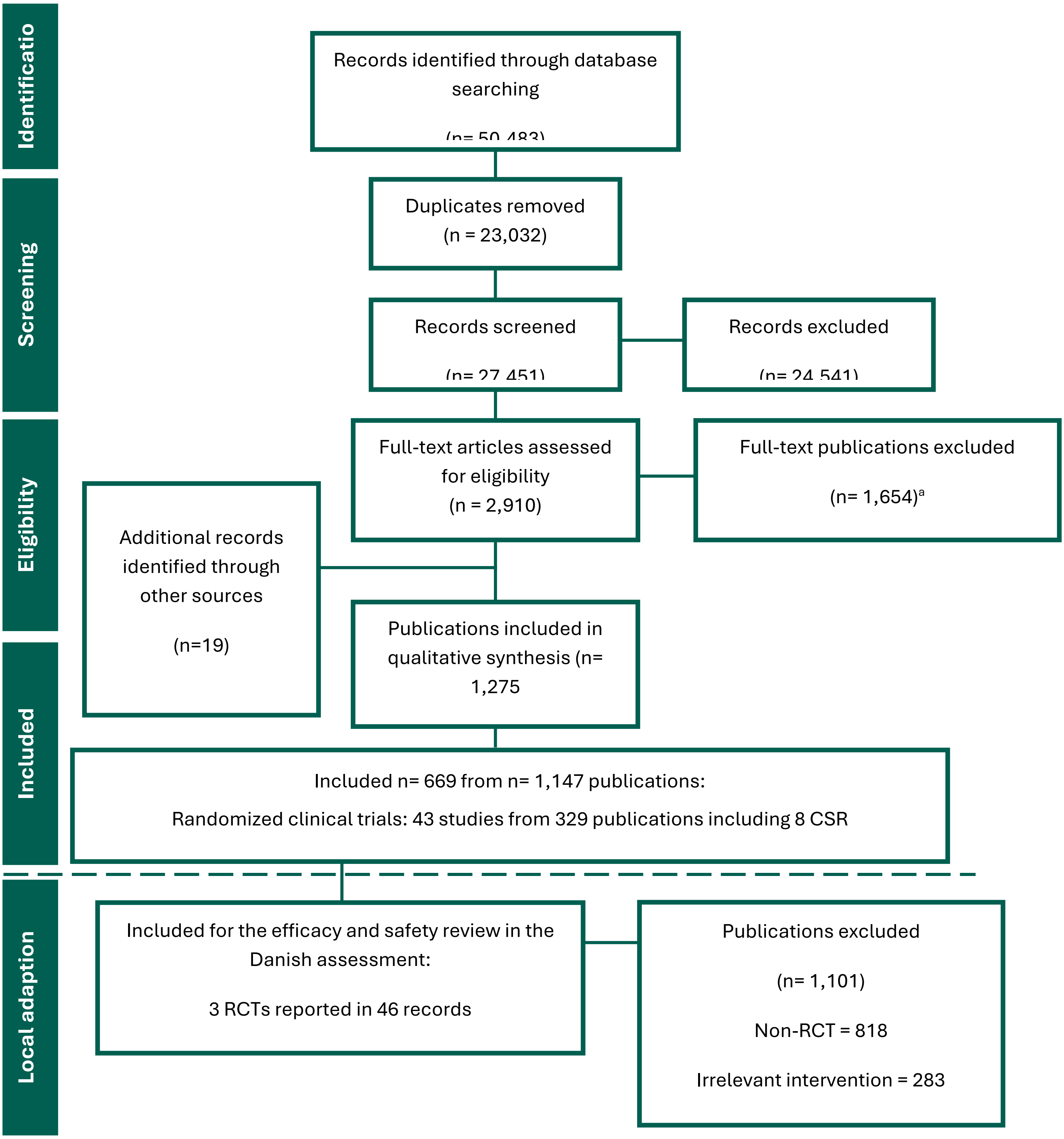
Table 98. Inclusion and exclusion criteria used for assessment of studies (Danish adaptation)

Clinical effectiveness	Inclusion criteria	Exclusion criteria
Population	Adults (≥18 years) with RRMM with ≥1 prior line of therapy	Newly diagnosed/ untreated MM
Intervention	Selinexor + bortezomib + dexamethasone Carfilzomib + dexamethasone Pomalidomide + bortezomib + dexamethasone	Any intervention, or combinations of interventions, that are not listed for inclusion
Comparators	Trials that include a comparator of any type (including but not limited to the interventions listed above), including placebo, or with no comparator	
Outcomes	Survival and response: ORR, DoR, BOR, PFS, EFS, OS, CBR, TTR, TTP, TTNT, ToT Safety and tolerability: TEAEs, STEAEs, TEAES leading to discontinuation/ dose reduction, TRAEs, serious TRAES, deaths HRQoL: EQ-5D, EORTC QLQ-C30, EORTC QLQ-MY20, EORTC QLQ CIPN20; FACT-G, FACT-MM.	
Study design/publication type	RCTs Single-arm non-RCTs Open-label extension trials Retrospective and prospective observational studies Peer review publications Abstracts and conference presentations Guidelines Trial protocols Systematic reviews HTA/ regulatory guidance documents Horizon scanning documents	Phase I trials In vitro and animal studies Pharmacokinetics Pharmacodynamics Non-systematic reviews Opinion pieces Editorials Letters Reports Press releases Case series studies Case reports
Language restrictions	No language restrictions [a]	
Publication year	No date limits applied with the exception of conference abstracts, which are limited to those published 2021 to present [b]	

H.1.5.2 Studies included in the SLR

The flow of studies of the global SLR is described across the primary and the updated search simultaneously. Following removal of duplicates, 27,451 records were eligible for primary screening, of which 24,541 records were excluded and 2,910 were taken forward to secondary screening. Following secondary screening 1,147 records were eligible for inclusion in this review with an additional 19 records identified from handsearching, and data on file from the company. The results of the study selection process for the global SLR as well as the local adaptation are summarised in Figure 44, according to the PRISMA guidance.

Figure 44. PRISMA flowchart for the SLR - Primary and updated SLR combined



Abbreviations: CSR, Clinical study report; SLR, systematic literature review
[a]Exclusion reasons: Abstract pre-2021, n=389; abstract only with insufficient information, n=177; eligible patients NR separately n=45; No eligible interventions, n=216; Ineligible outcomes of eligible trial, n=22; Ineligible population, n=172; Ineligible publication type, n=225; Ineligible study design, n=193; Ineligible subgroup of eligible trial, n=89; Insufficient information, n=3; No eligible outcomes, n=56; Unable to locate record, n=62; Unable to translate, n=5.
[c]Between the date of the original searches and the update searches, six studies that were previously yet to

report, published outcome data. On this basis 20 records associated with these studies have moved from the "studies yet to report" records number to the "records for inclusion" records number

Of the 1,147 records included in the SLR, 1,101 were excluded from the Danish adaptation, either due to not describing a RCT (n = 818) or because they only examined interventions not relevant for this application (n = 283).

46 records describing the BOSTON (n=24), ENDEAVOR (n=11), and OPTIMISMM (n=11) trials were included. These records are provided in Table 99.

Table 99. Records included in the Danish adaptation of the global SLR

Trial	Included records
BOSTON	Auner, H. W.; Gavriatopoulou, M.; Delimpasi, S.; Simonova, M.; Spicka, I.; Pour, L.; Dimopoulos, M. A.; Kriachok, I.; Pylypenko, H.; Leleu, X.; Doronin, V.; Usenko, G.; Hajek, R.; Benjamin, R.; Dolai, T. K.; Sinha, D. K.; Venner, C. P.; Garg, M.; Stevens, D. A.; Quach, H.; Jagannath, S.; Moreau, P.; Levy, M.; Badros, A.; Anderson, L. D., Jr.; Bahlis, N. J.; Facon, T.; Mateos, M. V.; Cavo, M.; Chai, Y.; Arazy, M.; Shah, J.; Shacham, S.; Kauffman, M. G.; Richardson, P. G.; Grosicki, S.. Effect of age and frailty on the efficacy and tolerability of once-weekly selinexor, bortezomib, and dexamethasone in previously treated multiple myeloma. 2021. American Journal of Hematology. 96:6 (708-718).
	Benjamin, R.; Garg, M.; Basu, S.; Chai, Y.; DeCastro, A.; Boulhabel, F.; Shah, J.; Auner, H.. Outcomes of Patients (pts) with Previously Treated Multiple Myeloma (MM) from European Countries and the United Kingdom, Treated with Selinexor, Bortezomib and Dexamethasone (XVd) Versus Bortezomib and Dexamethasone (Vd): A Post Hoc Analysis from the . 2022. British Journal of Haematology. 197(SUPPL 1): (127-128).
	Dolph, M.; Tremblay, G.; Leong, H.. Cost Effectiveness of Triplet Selinexor-Bortezomib-Dexamethasone (XVd) in Previously Treated Multiple Myeloma (MM) Based on Results from the Phase III BOSTON Trial. 2021. PharmacoEconomics. 39:11 (1309-1325).
	EUCTR, B. E.. Bortezomib, Selinexor and Dexamethasone in Patients with Multiple Myeloma. 2017. https://trialsearch.who.int/Trial2.aspx?TrialID=EUCTR2016-003957-14-BE.
	Facon, T.; Auner, H.; Gavriatopoulou, M.; Delimpasi, S.; Simonova, M.; Spicka, I.; Pour, L.; Dimopoulos, M.; Kriachok, I.; Pylypenko, H.; et al.. Survival among older patients with previously treated multiple myeloma treated with selinexor, bortezomib, and dexamethasone (xvd) in the boston study. 2021. Hemasphere. 5:SUPPL 2 (458).
	Facon, T; Auner, H; Gavriatopoulou, M; Delimpasi, S; Simonova, M; Spicka, I; Pour, L; Dimopoulos, M; Kriachok, I; Pylypenko, H; Leleu, X; Quach, H; Benjamin, R; Dolai, T; Sinha, D; Garg, M; Stevens, D; Shah, J; Richardson, P;

Grosicki, S. EP976: survival among older patients with previously treated multiple myeloma treated with selinexor, bortezomib, and dexamethasone (xvd) in the boston study. 2021.

Facon, T.; Auner, H. W.; Gavriatopoulou, M.; Delimpasi, S.; Simonova, M.; Spicka, I.; Pour, L.; Dimopoulos, M. A.; Kriachok, I.; Pylypenko, H.; et al. Survival among older patients with previously treated multiple myeloma treated with selinexor, bortezomib, and dexamethasone (XVd) in the BOSTON study. 2021. Journal of clinical oncology. 39:15.

Grosicki, S.; Simonova, M.; Spicka, I.; Pour, L.; Kriachok, I.; Gavriatopoulou, M.; Pylypenko, H.; Auner, H. W.; Leleu, X.; Doronin, V.; et al. Once-per-week selinexor, bortezomib, and dexamethasone versus twice-per-week bortezomib and dexamethasone in patients with multiple myeloma (BOSTON): a randomised, open-label, phase 3 trial. 2020. Lancet (london, england). 396:10262 (1563-1573).

Jagannath, S.; Facon, T.; Badros, A. Z.; Levy, M.; Moreau, P.; Delimpasi, S.; Simonova, M.; Spicka, I.; Kriachok, I.; Gavriatopoulou, M.; Pylypenko, H.; Auner, H. W.; Leleu, X.; Doronin, V.; Usenko, G.; Hajek, R.; Benjamin, R.; Dolai, T. K.; Sinha, D. K.; Venner, C. P.; Garg, M.; Mesa, M. G.; Jurczyszyn, A.; Robak, T.; Galli, M.; Wallington-Beddoe, C. T.; Radinoff, A.; Salogub, G.; Stevens, D.; Basu, S.; Liberati, A. M.; Quach, H.; Marinova, V. S. G.; Bila, J. S.; Katodritou, E.; DeCastro, A.; Chai, Y.; Van Domelen, D. R.; Mishal, M.; Bentur, O. S.; Shah, J.; Shacham, S.; Kauffman, M. G.; Grosicki, S.; Richardson, P. G.. Clinical outcomes in patients (pts) with dose reduction of selinexor in combination with bortezomib, and dexamethasone (XVD) in previously treated multiple myeloma from the Boston study. 2021. Blood. 138(SUPPL 1): (3793).

Leleu, X.; Mateos, M. V.; Jagannath, S.; Delimpasi, S.; Simonova, M.; Spicka, I.; Pour, L.; Kriachok, I.; Gavriatopoulou, M.; Dimopoulos, M.; et al. Efficacy and safety of selinexor, bortezomib, and dexamethasone based on refractory status to lenalidomide in patients with previously treated multiple myeloma: a post-hoc analysis of the boston study. 2021. Hemasphere. 5: SUPPL 2 (456-457).

Leleu, X.; Mateos, M. V.; Jagannath, S.; Delimpasi, S.; Simonova, M.; Spicka, I.; Pour, L.; Kriachok, I.; Gavriatopoulou, M.; Dimopoulos, M. A.; et al. Effects of refractory status to lenalidomide on safety and efficacy of selinexor, bortezomib, and dexamethasone (XVd) versus bortezomib and dexamethasone (Vd) in patients with previously treated multiple myeloma. 2021. Journal of clinical oncology. 39:15.

Leleu, X; Mateos, M; Jagannath, S; Delimpasi, S; Simonova, M; Spicka, I; Pour, L; Kriachok, I; Gavriatopoulou, M; Dimopoulos, M; Pylypenko, H; Auner, H; Benjamin, R; Venner, C; Garg, M; DeCastro, A; Chai, Y; Shah, J; Grosicki, S; Richardson, P. EP974: efficacy and safety of selinexor, bortezomib, and dexamethasone based on refractory status to lenalidomide in patients with previously treated multiple myeloma: a post-hoc analysis of the boston study. 2021.

Mateos, M. V.; Engelhardt, M.; Leleu, X.; Mesa, M. G.; Auner, H.W.; Cavo, M.; Dimopoulos, M.A.; Bianco, M.; Merlo, G.M.; La Porte, C.; Moreau P. P886: efficacy, survival and safety of selinexor, bortezomib and dexamethasone (SVd) in patients with lenalidomide-refractory multiple myeloma: subgroup data from the BOSTON trial. 2023.

Mateos, M.M.; Engelhardt, M.; Leleu, X.; Mesa, M.G.; Auner, H.W.; Cavo, M.; Dimopoulos, M.A.; Bianco, M.; Merlo, G.M.; La Porte, C.; Moreau, P. P917: selinexor, bortezomib, and dexamethasone in patients with previously treated multiple myeloma: updated results of BOSTON trial by prior therapies. 2023.

Mateos, M. V.; Engelhardt, M.; Leleu, X.; Mesa, M. G.; Cavo, M.; Dimopoulos, M.; Bianco, M.; Merlo, G. M.; La Porte, C.; Moreau, P. Selinexor, bortezomib, and dexamethasone in patients with previously treated multiple myeloma (MM): Updated results of BOSTON trial by prior therapies. 2023. Oncology Research and Treatment. 46:Supplement 5 (176).

Mateos, M. V.; Engelhardt, M.; Leleu, X.; Mesa, M. G.; Cavo, M.; Dimopoulos, M.; Bianco, M.; Merlo, G. M.; La Porte, C.; Moreau, P. Eftcacy, survival and safety of selinexor, bortezomib and dexamethasone (SVd) in patients with lenalidomiderefractory multiple myeloma: Subgroup data from the BOSTON Trial. 2023. Oncology Research and Treatment. 46:Supplement 5 (235).

NCT. Bortezomib, Selinexor, and Dexamethasone in Patients With Multiple Myeloma. 2017. https://clinicaltrials.gov/show/ NCT03110562.

Reuben B, Mamta Garg Supratik Basu Yi Chai Andrew DeCastro Faouzia Boulhabel Jatin Shah Holger Auner. BSH22-PO81 | Outcomes of Patients (pts) with Previously Treated Multiple Myeloma (MM) from European Countries and the United Kingdom, Treated with Selinexor, Bortezomib and Dexamethasone (XVd) Versus Bortezomib and Dexamethasone (Vd): A Post Hoc Analysis. 2022.

Richard, S.; Chari, A.; Delimpasi, S.; Simonova, M.; Spicka, I.; Pour, L.; Kriachok, I.; Dimopoulos, M. A.; Pylypenko, H.; Auner, H. W.; et al.. Selinexor, bortezomib, and dexamethasone versus bortezomib and dexamethasone in previously treated multiple myeloma: outcomes by cytogenetic risk. 2021. American journal of hematology. 96:9 (1120-1130).

Thierry F, Holger W. Auner Maria Gavriatopoulou Sosana Delimpasi Maryana Simonova Ivan Spicka LudÄ›k Pour Meletios A. Dimopoulos Iryna Kriachok Halyna Pylypenko Xavier Leleu Hang Quach Benjamin Reuben Tuphan Kanti Dolai Dinesh Kumar Sinha Mamta Garg Don A. Stevens Jatin J. Shah Paul G. Richardson Sebastian Grosicki. 8019: Survival among older patients with previously treated multiple myeloma treated with selinexor, bortezomib, and dexamethasone (XVd) in the BOSTON study. 2021.

EUCTR2016-003957-14-HU. Bortezomib, Selinexor and Dexamethasone in Patients with Multiple Myeloma.

	White, D.; Chen, C.; Baljevic, M.; Tuchman, S.; Bahlis, N. J.; Schiller, G. J.; Lipe, B.; Kotb, R.; Sutherland, H. J.; Madan, S.; Sebag, M.; Lentzsch, S.; Callander, N. S.; Biran, N.; Venner, C. P.; LeBlanc, R.; Rossi, A. C.; Zhou, T.; Gasparetto, C.. Oral selinexor, pomalidomide, and dexamethasone (XPd) at recommended phase 2 dose in relapsed refractory multiple myeloma (MM). 2021. Journal of Clinical Oncology. Conference: Annual Meeting of the American Society of Clinical Oncology, ASCO. 39:15.
	Xavier Leleu, Maria-Victoria Mateos Sundar Jagannath Sosana Delimpasi Maryana Simonova Ivan Spicka LudÄ›k Pour Iryna Kriachok Maria Gavriatopoulou Meletios A. Dimopoulos Halyna Pylypenko Holger W. Auner Benjamin Reuben Vadim Doronin Christopher P. Venner Mamta Garg Andrew DeCastro Jatin J. Shah Sebastian Grosicki Paul G. Richardson. 8024: Effects of refractory status to lenalidomide on safety and efficacy of selinexor, bortezomib, and dexamethasone (XVd) versus bortezomib and dexamethasone (Vd) in patients with previously treated multiple myeloma. 2021.
	Ctri. Study of Selinexor, Bortezomib, AND Dexamethasone Versus Bortezomib and Dexamethasone In Patients With Relapsed Or Refractory Multiple Myeloma. 2017. https://trialsearch.who.int/Trial2.aspx?TrialID=CTRI/2017/11/010561.
ENDEAVOR	Chng, W. J.; Goldschmidt, H.; Dimopoulos, M. A.; Moreau, P.; Joshua, D.; Palumbo, A.; Facon, T.; Ludwig, H.; Pour, L.; Niesvizky, R.; et al. Carfilzomib-dexamethasone vs bortezomib-dexamethasone in relapsed or refractory multiple myeloma by cytogenetic risk in the phase 3 study ENDEAVOR. 2017. Leukemia. 31:6 (1368--1374).
	Dimopoulos, M. A.; Goldschmidt, H.; Niesvizky, R.; Joshua, D.; Chng, W. J.; Oriol, A.; Orlowski, R. Z.; Ludwig, H.; Facon, T.; Hajek, R.; et al.. Carfilzomib or bortezomib in relapsed or refractory multiple myeloma (ENDEAVOR): an interim overall survival analysis of an open-label, randomised, phase 3 trial. 2017. The lancet. Oncology. 18:10 (1327-1337).
	Dimopoulos, M. A.; Moreau, P.; Palumbo, A.; Joshua, D.; Pour, L.; HÃ¡jek, R.; Facon, T.; Ludwig, H.; Oriol, A.; Goldschmidt, H.; et al. Carfilzomib and dexamethasone versus bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma (ENDEAVOR): a randomised, phase 3, open-label, multicentre study. 2016. The lancet. Oncology. 17:1 (27-38).
	EUCTR, C. Z. A Randomized, Open-label, Phase 3 Study of Carfilzomib Plus Dexamethasone vs Bortezomib Plus Dexamethasone in Patients With Relapsed Multiple Myeloma. 2012. https://trialsearch.who.int/Trial2.aspx?TrialID= EUCTR2012-000128-16-CZ.
	Goldschmidt, H.; Moreau, P.; Ludwig, H.; Niesvizky, R.; Chng, W. J.; Joshua, D.; Weisel, K.; Spencer, A.; Orlowski, R. Z.; Feng, S.; et al. Carfilzomib-dexamethasone versus subcutaneous or intravenous bortezomib in relapsed or refractory multiple myeloma: secondary analysis of the phase 3 ENDEAVOR study. 2018. Leukemia & lymphoma. 59: (1364-1374).

	EUCTR2012-000128-16-DE. A Clinical Study to Test the Effectiveness of Carfilzomib Plus Dexamethasone Versus Bortezomib Plus Dexamethasone in Patients with Multiple Myeloma (Bone Marrow Cancer).
	Ludwig, H.; Moreau, P.; Dimopoulos, M. A.; Mateos, M. V.; Kaiser, M.; Hajek, R.; Feng, S.; Cocks, K.; Buchanan, J.; Weisel, K.. Health-related quality of life in the ENDEAVOR study: carfilzomib-dexamethasone vs bortezomib-dexamethasone in relapsed/refractory multiple myeloma. 2019. Blood cancer journal. 9:3 (23).
	Moreau, P.; Joshua, D.; Chng, W. J.; Palumbo, A.; Goldschmidt, H.; HÃ¡jek, R.; Facon, T.; Ludwig, H.; Pour, L.; Niesvizky, R.; et al.. Impact of prior treatment on patients with relapsed multiple myeloma treated with carfilzomib and dexamethasone vs bortezomib and dexamethasone in the phase 3 ENDEAVOR study. 2017. Leukemia. 31:1 (115-122).
	Anonymous. Correction: carfilzomib or bortezomib in relapsed or refractory multiple myeloma (ENDEAVOR): an interim overall survival analysis of an open-label, randomised, phase 3 trial (The Lancet Oncology (2017) 18(10) (1327-1337) (S1470204517305788) (10.1016/S1470. 2017. Lancet oncology. 18:10 (e562).
	NCT. Phase 3 Study With Carfilzomib and Dexamethasone Versus Bortezomib and Dexamethasone for Relapsed Multiple Myeloma Patients. 2012. https://clinicaltrials.gov/show/ NCT01568866.
	Orlowski, R. Z.; Moreau, P.; Niesvizky, R.; Ludwig, H.; Oriol, A.; Chng, W. J.; Goldschmidt, H.; Yang, Z.; Kimball, A. S.; Dimopoulos, M.. Carfilzomib-Dexamethasone Versus Bortezomib-Dexamethasone in Relapsed or Refractory Multiple Myeloma: updated Overall Survival, Safety, and Subgroups. 2019. Clinical lymphoma, myeloma & leukemia. 19:8 (522-530.e1).
OPTIMISMM	NCT. Safety and Efficacy of Pomalidomide, Bortezomib and Low-dose Dexamethasone in Subjects With Relapsed or Refractory Multiple Myeloma. 2012. https://clinicaltrials.gov/show/ NCT01734928.
	Richardson, P. G.; Oriol, A.; Beksac, M.; Liberati, A. M.; Galli, M.; Schjesvold, F.; Lindsay, J.; Weisel, K.; White, D.; Facon, T.; et al.. Pomalidomide, bortezomib, and dexamethasone for patients with relapsed or refractory multiple myeloma previously treated with lenalidomide (OPTIMISMM): a randomised, open-label, phase 3 trial. 2019. The lancet. Oncology. 20:6 (781-794).
	Richardson, P. G.; Schjesvold, F.; Weisel, K.; Moreau, P.; Anderson, L. D., Jr.; White, D.; Rodriguez-Otero, P.; Sonneveld, P.; Engelhardt, M.; Jenner, M.; Corso, A.; Durig, J.; Pavic, M.; Salomo, M.; Beksac, M.; Oriol, A.; Lindsay, J.; Liberati, A. M.; Galli, M.; Robak, P.; Larocca, A.; Yagci, M.; Vural, F.; Kanate, A. S.; Jiang, R.; Grote, L.; Peluso, T.; Dimopoulos, M.. Pomalidomide, bortezomib, and dexamethasone at first relapse in lenalidomide-pretreated myeloma: A

subanalysis of OPTIMISMM by clinical characteristics. 2022. European Journal of Haematology. 108:1 (73-83).

Weisel, K.; Dimopoulos, M.; Moreau, P.; Yagci, M.; Larocca, A.; Kanate, A. S.; Vural, F.; Cascavilla, N.; Basu, S.; Johnson, P.; Byeff, P.; Hus, M.; Rodriguez-Otero, P.; Muelduer, E.; Anttila, P.; Hayden, P. J.; Krauth, M. T.; Lucio, P.; Ben-Yehuda, D.; Mendeleeva, L.; Guo, S.; Yu, X.; Grote, L.; Biyukov, T.; Dhanasiri, S.; Richardson, P.. Health-related quality-of-life results from the phase 3 OPTIMISMM study: pomalidomide, bortezomib, and low-dose dexamethasone versus bortezomib and low-dose dexamethasone in relapsed or refractory multiple myeloma. 2020. Leukemia & Lymphoma. 61:8 (1850-1859).

Weisel, K; Dimopoulos, M; Oriol, A; Beksac, M; Schjesvold, F; Liberati, A; Lindsay, J; White, D; Miguel, J; Moreau, P; Larry D..; Lorocca, A; Robak, P; Vogel, P; Jiang, R; Grote, L; Peluso, T; Richardson, P. EP988: pomalidomide, bortezomib, and dexamethasone after 1 prior line of therapy in relapsed or refractory multiple myeloma: a safety subanalysis of the phase 3 OPTIMISMM trial. 2021.

2014-000268-17. A Phase 3, Multicenter, Randomized, Open-Label Study to Compare the Efficacy and Safety of Pomalidomide, Bortezomib and Low-Dose Dexamethasone Versus Bortezomib and Low-Dose Dexamethasone in Subjec.

Weisel, K.; Dimopoulos, M.; Oriol, A.; Beksac, M.; Schjesvold, F.; Liberati, A. M.; Lindsay, J.; White, D.; San-Miguel, J.; Moreau, P.; Anderson, L. D.; Lorocca, A.; Robak, P.; Vogel, P.; Jiang, R.; Grote, L.; Peluso, T.; Richardson, P.. Pomalidomide (POM), bortezomib (BORT), and dexamethasone (DEX) after 1 prior line of therapy in relapsed or refractory multiple myeloma (RRMM): a safety subanalysis of the phase 3 OPTIMISMM trial. 2022. Oncology Research and Treatment. 45(Supplement 3): (165).

Weisel, K.; Dimopoulos, M. A.; Oriol, A.; Beksac, M.; Dimopoulos, F.; Liberati, A. M.; Lindsay, J.; White, D.; San-Miguel, J. F.; Moreau, P.; et al.. P-224: pomalidomide, bortezomib, and dexamethasone after 1 prior line of therapy in relapsed or refractory multiple myeloma (RRMM): a safety subanalysis of the phase 3 OPTIMISMM trial. 2021. Clinical lymphoma, myeloma & leukemia. 21: (S163).

Dimopoulos, M.; Weisel, K.; Moreau, P.; Anderson, L. D., Jr.; White, D.; San-Miguel, J.; Sonneveld, P.; Engelhardt, M.; Jenner, M.; Corso, A.; Durig, J.; Pavic, M.; Salomo, M.; Casal, E.; Srinivasan, S.; Yu, X.; Nguyen, T. V.; Biyukov, T.; Peluso, T.; Richardson, P.. Pomalidomide, bortezomib, and dexamethasone for multiple myeloma previously treated with lenalidomide (OPTIMISMM): outcomes by prior treatment at first relapse. 2021. Leukemia. 35:6 (1722-1731).

Beksaç, M.; Richardson, P.; Oriol, A.; Lindsay, J.; Schjesvold, F.; Galli, M.; Yağcı, M.; Larocca, A.; Weisel, K.; Yu, X.; Donahue, C.; Acosta, J.; Peluso, T.; Dimopoulos, T. 95. 2023. IMS conference.

Weisel, K.; Dimopoulos, M.; Oriol, A.; Beksac, M.; Schjesvold, F.; Liberati, A. M.; Lindsay, J.; White, D.; San Miguel, J.; Moreau, P.; et al. OPTIMISMM Subanalyse: sicherheit von Pomalidomid (POM), Bortezomib (BORT) und Dexamethason (DEX) (PVd) Behandlung (Tx) nach einer vorherigen Therapielinie (LoT) bei Patienten (pts) mit rezidiviertem oder refraktÃ¤rem multiplen Myelom (RRMM). 2022. Oncology research and treatment. 45: (283).

H.1.6 Excluded full text references

As a very high number of records were excluded at the full-text screening stage (1,654 in the global SLR and an additional 1,101 for the Danish adaptation), these are not shown here, but are available upon request.

H.1.7 Quality assessment

The literature search conducted was very extensive, with very broad search strategies and a high number of searched databases. Additionally, a wide range of web sources and conferences were searched. Study selection was done independently by two reviewers at all stages. The sparsity of data on penta-refractory MM patients can be considered a limitation; however, every effort was taken to identify any potentially relevant studies.

H.1.8 Unpublished data

The only non-published data included in this application is from the clinical study reports and internal safety analyses from the BOSTON trial, and of such is of high quality.

Additionally, the results of the frequentist NMA conducted for this application have not been published. No publication of these results is planned.

Appendix I. Literature searches for health-related quality of life

Not applicable.

I.1 Health-related quality-of-life search

Not applicable.

Table 100. Bibliographic databases included in the literature search

Database	Platform	Relevant period for the search	Date of search completion
			dd.mm.yyyy
			dd.mm.yyyy
			dd.mm.yyyy

Abbreviations:

Table 101. Other sources included in the literature search

Source name	Location/source	Search strategy	Date of search
			dd.mm.yyyy
			dd.mm.yyyy

Table 102. Conference material included in the literature search

Conference	Source of abstracts	Search strategy	Words/terms searched	Date of search

I.1.1 Search strategies

Not applicable.

Table 103. Search strategy for [name of database]

No.	Query	Results
#1		88244

I.1.2 Quality assessment and generalizability of estimates

Not applicable.

I.1.3 Unpublished data

Not applicable.

Appendix J. Literature searches for input to the health economic model

J.1 External literature for input to the health economic model

The literature searches for input to the health economic model was performed as part of an economic SLR. This SLR, including objective, methods, information sources and search strategies, is presented below here.

J.1.1 Systematic search for health economic inputs

J.1.1.1 Objective

An economic systematic literature review (SLR) was conducted to identify published evidence of cost-effectiveness, costs, resource use, and HRQoL/ utility evidence for the treatment of patients with RRMM. The SLR had two research questions, the second of which relates to the scope of this submission:

The research questions for this review were:

- What is the cost-effectiveness of selinexor compared to comparator interventions in adult patients with RRMM, who have received one or two prior lines of therapy (2L or 3L)?
- What is the cost-effectiveness of selinexor compared to comparator interventions in adult patients with RRMM, who have received greater than four prior therapies, and whose disease is refractory to at least two proteasome inhibitors, two immunomodulatory agents and an anti-CD38 monoclonal antibody (penta-refractory), and who have demonstrated disease progression on the last therapy?

J.1.1.2 Methods

This systematic review was undertaken according to the principles of systematic reviewing published in the Cochrane Handbook,[42] the Centre for Reviews and Dissemination (CRD),[66] the NICE manual for health technology evaluations,[43] and in line with the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (PRISMA-P) checklist.[67]

J.1.1.3 Information sources

J.1.1.3.1 Bibliographic databases

The bibliographic databases searched across all three economic SLR components (cost-effectiveness studies, health-related quality of life studies, and cost and/ or healthcare resource use studies) are presented in Table 100. The search strategies for each bibliographic database are provided in J.1.2.1

Table 104. Bibliographic databases included in the literature search

Database	Platform	Relevant period for the search	Date of search completion
MEDLINE ALL	Ovid	1946 to present	28.05.2024
Embase	Ovid	1980 to 2023 Week 05	28.05.2024
Econlit	EbscoHost	1886-Current	28.05.2024
Cochrane: CDSR	Wiley	Issue 2 of 12, February 2023	28.05.2024
Cochrane: CENTRAL	Wiley	Issue 2 of 12, February 2023	28.05.2024
University of York, CRD DARE*	https://www.crd.york.ac.uk/CRDWeb/HomePage.asp	N/A	28.05.2024
CRD HTA*	https://www.crd.york.ac.uk/CRDWeb/HomePage.asp	N/A	28.05.2024
CRD NHS EED*	https://www.crd.york.ac.uk/CRDWeb/HomePage.asp	N/A	28.05.2024

Abbreviations: CDSR = Cochrane Database of Systematic Reviews; CENTRAL = Cochrane Central Register of Controlled Trials; CRD = Centre for Reviews and Dissemination; DARE = Database of Abstracts and Review of Effects; HTA = Health Technology Assessment; N/A = Not applicable; NHS EED = NHS Economic Evaluation Database.

J.1.1.3.2 Conference proceedings

The conference proceedings presented in Table 105 were searched. The search strategies for conference proceedings are detailed in Section J.1.2.2

Table 105. Conference searches

Conference	Conference website	Date of search
Embase	N/a	28.05.2024
International Society for Pharmacoeconomics and Outcomes (ISPOR) [Europe & US]	https://www.ispor.org/	28.05.2024
Health Economists' Study Group (HESG)	https://hesg.org.uk/	28.05.2024
Health Technology Assessment International (HTAi)	https://htai.org/	28.05.2024

American Society of Clinical Oncology (ASCO)	https://www.asco.org/	28.05.2024
American Society of Hematology (ASH)	https://www.hematology.org/	28.05.2024
Controversies in Multiple Myeloma (COMy)	https://comylive.cme-congresses.com/	28.05.2024
British Society of Haematology (BSH)	https://b-s-h.org.uk/	28.05.2024
European Hematology Association (EHA)	https://ehaweb.org/	28.05.2024
European Society of Medical Oncology (ESMO)	https://www.esmo.org/	28.05.2024
International Myeloma Society (IMS) and annual events	https://www.myelomasociety.org/	28.05.2024

Abbreviations: N/A = Not applicable.

The annual conference meetings searched as part of the conference searches, or those conferences noted as upcoming, are presented in Table 106.

Table 106. Conferences by year

Conference	2021	2022	2023
ISPOR Annual Meeting	ISPOR Europe 30 November – 3 December, Virtual ISPOR 2021 17-20 May, Virtual	ISPOR Europe 6-9 November, Vienna, Austria ISPOR 2022 16-18 May 2022, Washington, DC, USA	ISPOR Europe 12-15 November 2023, Copenhagen, Denmark ISPOR 2023 7-10 May, Boston, MA, USA
HESG Meeting	Winter 2021, 6-8 January, London (Virtual) Summer 2021, 30 June – 2 July, Cambridge (Virtual)	Winter 2022, 5-7 January, Leeds Summer 2022, 22-24 June, Sheffield	Winter 2023, 11-13 January, Manchester Summer 2023, 21-23 June, Oxford
HTAi Annual Meeting	19-23 June, Manchester (Virtual)	25-29 June, Utrecht, Netherlands	24-28 June, Adelaide, Australia
ASCO Annual Meeting	4-8 June, Virtual	3-7 June, Chicago, IL, USA	2-6 June, Chicago, IL, USA

Conference	2021	2022	2023
ASH Annual Meeting & Exposition	11-14 December, Atlanta, GA	10-13 December, New Orleans, LA, USA	TBC
EHA Congress	9-17 June, Virtual	9-12 June, Vienna, Austria and virtually (hybrid)	8-11 June, Frankfurt Germany 14-16 June Virtual
ESMO	16-21 September, Virtual	9-13 September, Paris France	20-24 October, Madrid, Spain
IMS annual events	18th International Myeloma Workshop 8-11 September, Vienna, Austria	19th International Myeloma Society Annual Meeting 25-27 August, Los Angeles, California, USA	20th Annual Meeting and Exposition 27-30 September, Athens, Greece
COMy Congress	7th World Congress 7-9 May, virtual meeting	8th World Congress 12-15 May, Paris (& virtual)	9th World Congress 11-14 May, Paris (& virtual)
BSH Annual Scientific Meeting	25-28 April, Virtual	3-5 April, Manchester, UK	23-25 April, Birmingham, UK

Abbreviations: ASCO = American Society of Clinical Oncology; ASH = American Society of Hematology; BSH = British Society for Haematology; COMy = Controversies in Multiple Myeloma; EHA = European Hematology Association; ESMO = European Society of Medical Oncology; HESG = Health Economists' Study Group; HTAi = Health Technology Assessment International; IMS = International Myeloma Society; ISPOR = International Society for Pharmacoeconomics and Outcomes Research; TBC = to be confirmed; UK = United Kingdom; USA = United States of America.

J.1.1.3.3 Key regulatory and HTA websites

The key regulatory and HTA websites presented in Table 107 were searched. The detailed search strategy is presented in Section J.1.2.3.

Additional methods to identify relevant evidence included searching the reference lists of SLR records and relevant studies identified by the economic SLR bibliographic searches.

Economic records identified in the clinical review were cross-checked with records identified in the searches from this review, and any eligible records included.

Table 107. Key regulatory and HTA websites included in the literature search

Source name	Location/source	Date of search
National Institute for Health and Care Excellence (NICE)	https://www.nice.org.uk/	28.05.2024
Scottish Medicines Consortium (SMC)	https://www.scottishmedicines.org.uk/	28.05.2024
National Institute for Health and Care Research Innovation Observatory (NIHRIO) tech briefings	https://www.io.nihr.ac.uk/	28.05.2024
European Medicines Agency (EMA)	https://www.ema.europa.eu/en	28.05.2024
Medicines and Healthcare products Regulatory Agency (MHRA)	https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency	28.05.2024
Dental and Pharmaceutical Benefits Agency (Tandvårds- och läkemedelsförmånsverket; TLV) (Sweden)	https://www.tlv.se/	28.05.2024
Norwegian Institute of Public Health (NIPH) (Norway)	https://www.fhi.no/en/	28.05.2024
Danish Medicines Council (DMC) (Denmark)	https://medicinraadet.dk/om-os/in-english	28.05.2024
Finnish Medicines Agency (Fimea) (Finland)	https://www.fimea.fi/web/en	28.05.2024
National Centre for Pharmacoeconomics (NCPE) (Ireland)	https://www.ncpe.ie/	28.05.2024
National Institute for Health and Disability Insurance (RIZIV-INAMI) (Belgium)	http://www.inami.fgov.be/	28.05.2024
National Health Care Institute (Zorginstituut Nederland, ZiN) (Netherlands)	https://english.zorginstituutnederland.nl/	28.05.2024
EconPapers within Research Papers in Economics	http://repec.org/	28.05.2024
University of Sheffield ScHARRHUD utility database	http://www.scharrhud.org/	28.05.2024

Source name	Location/source	Date of search
EuroQoL website	https://euroqol.org/	28.05.2024
Tufts CEA registry	https://cevr.tuftsmedicalcenter.org/databases/cea-registry	28.05.2024

J.1.2 Search strategies

One set of searches were designed to meet the needs all three components of the SLR: economic evaluations, healthcare costs and resource use, and HRQoL (including utilities). The aim of this search was to identify studies reporting economic evaluations or evaluations of cost effectiveness, as well as studies reporting burden of illness (including quality of life), in patients living with RRMM.

The SLR search strategy was developed by a trained information scientist and checked by the research team using the PRESS checklist.[68] The search strategy included searching of bibliographic databases, key regulatory and HTA websites, and conference proceedings, each of which is detailed separately below.

J.1.2.1 Bibliographic database searches

Table 108. Search strategy for MEDLINE

Search strategy	Search narrative
1 exp Multiple Myeloma/ (46704) 2 (myelom* or ((Penta or triple-class) adj1 refractory)).ti,ab,kw,kf,ot. (72554) 3 kahler*.ti,ab,kw,kf,ot. (368) 4 Plasmacytoma/ (8842) 5 (plasm?cytom* or plasm?zytom* or plasma cytoma* or plasma zytoma*).ti,ab,kw,kf,ot. (8509) 6 (plasm* adj3 (neoplas* or leukaem* or leukem* or tumor* or tumour* or dyscrasia)).ti,ab,kw,kf,ot. (13365) 7 ((plasmacytic* or plasmocytic* or plasmocyte*) adj1 (leukem* or leukaem*)).ti,ab,kw,kf,ot. (42) 8 (myelomatoses or myelomatosis).ti,ab,kw,kf. (781)	Condition search terms: The search does not limit by treatment line despite our research objective being >1 prior line. This seeks to minimise the risk of missing studies that are in scope for our review but do not mention treatment line. We use a combination of controlled indexing terms (in this example, Medical Subject Headings or MeSH) and free-text search terms.[69] Line 1 is the MeSH term for Multiple Myeloma (the / indicates that this is a controlled indexing term). We have 'exploded' this indexing term (represented by exp) to capture not only studies indexed as Multiple Myeloma but also to capture the other

9 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 (96388)	relevant sub indexing term, Leukemia, Plasma Cell.
	
	Our free-text search lines have been developed to cross-check the indexing terms and these terms are searched in the following fields:
	
	ti = title;
	
	ab = abstract;
	
	kw = keyword;
	
	kf = author selected keyword; and
	
	ot = original title.
	
	Within free-text, we harness the functionality of the Ovid database, namely truncation, proximity/adjacency markers, and wildcards.
	
	Truncation is represented by * (it can also be represented by $ in Ovid databases). Truncation searches for the root word and alternate word endings. For example, line 6: tumour searches not only for tumour but also tumours.
	
	Adjacency is represented by adj, for example in line 6 we search for plasma adjacent by two words to tumour. For instance, plasma cell tumour. Adj searches in either order, so in Line 2 we would identity triple class refractory OR refractory (triple class).
	
	We use a wild card marker indicated by ?. This searches for alternate spellings of words, for instance UK or US spelling variants.
	
	The condition search terms complete at Line 9. Here all search terms are combined using the Boolean connector OR.
	
	We compared our condition search structure and terms to Cochrane reviews in a similar population and found general agreement with this structure and approach.[70-72]

10 economics/ (27492) 11 exp "Costs and Cost Analysis"/ (262388) 12 economics, dental/ (1920) 13 exp Economics, Hospital/ or Financial management, hospital/ (32943) 14 Economics, Medical/ (9237) 15 economics, nursing/ (4013) 16 economics, pharmaceutical/ (3093) 17 (economic* or cost or costs or costly or costing or expense or expenses or price or prices or pricing or pharmacoeconomic* or CEA or CUA or CBA or CMA or ICER or ICUR).ti,ab,kw,kf. (1081179) 18 exp "fees and charges"/ (31293) 19 exp budgets/ (14072) 20 (resource*1 and (allocation or utili* or usage or use*1)).ti,ab,kw,kf. (245854) 21 (expenditure* not energy).ti,ab,kw,kf. (35705) 22 (value adj1 money).ti,ab,kw,kf. (43) 23 (budget* or fiscal or funding or financial or finance*).ti,ab,kw,kf. (221524) 24 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 (1545997)	Search filter for economic or cost evaluations: We use the CRD NHS EED search filter. The filter is available from The InterTASC Information Specialists' Sub-Group Search Filter Resource.[73]
25 (15D or 15-D or 15 dimension).ti,ab,kw,kf. (5952) 26 (eq-5d or eq5d or eq-5 or eq5 or EQ-5D-Y or euro qual or euro qual or euro qual5d or euroqual5d or euro qol or euroqol or euro qol5d or euroqol5d or euro quol or euroquol or euro quol5d or euroquol5d or eur qol or eurqol or eurqol5d or eur qol5d or eur?qul or eur?qul5d or euro$ quality of life or european qol or EQ-5D-3L).ti,ab,ot,hw,kw,kf. (15916) 27 (sf6 or sf 6 or SF-6D or short form 6 or short-form 6 or short-form six or shortform 6 or sf six or sfsix or shortform six or short form six).ti,ab,ot,hw,kw,kf. (3278)	Quality of life and burden of Illness: We have adopted the Paisley and Booth filter for Quality of life and incorporated burden of illness search terms.[74] This filter has been developed by the research team over time and it has been regularly compared to relevant search filters available on the ISSG search filter resource.[73] We have included a sub quality of life search at Line 53. This incorporates condition specific questionnaires. This line was developed by scoping relevant

28 (sf8 or sf 8 or sf-8 or short form 8 or shortform 8 or sf eight or sfeight or shortform eight or shortform eight).ti,ab,ot,hw,kw,kf. (715) 29 (sf10 or sf 10 or short form 10 or short-form 10 or short-form ten or shortform 10 or sf ten or sften or shortform ten or short form ten).ti,ab,ot,hw,kw,kf. (155) 30 (sf12 or sf 12 or short form 12 or short-form 12 or short-form twelve or shortform 12 or sf twelve of sftwelve or shortform twelve or short form twelve).ti,ab,ot,hw,kw,kf. (7274) 31 (sf16 or sf 16 or short form 16 or short-form 16 or short-form sixteen or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).ti,ab,ot,hw,kw,kf. (38) 32 (sf20 or sf 20 or short form 20 or short-form 20 or short-form twenty or shortform 20 or sf twenty of sftwenty or shortform twenty of short form twenty).ti,ab,ot,hw,kw,kf. (435) 33 (sf36 or sf 36 or short form 36 or short-form 36 or short-form thirty six or shortform 36 or sf thirtysix or sf thirty six or shortform thirstysix or shortform thirty six or short form thirty six or short form thirtysix or short form thirty six).ti,ab,ot,hw,kw,kf. (29606) 34 (health utilities index* or (hui or hui1 or hui2 or hui3 or hui4 or hui-4 or hui-1 or hui-2 or hui-3)).ti,ab,ot,hw,kw,kf. (2159) 35 ("time trade off" or "time tradeoff" or "time trade-off" or TTO).ti,ab,ot,hw,kw,kf. (2231) 36 (standard gamble* or SG).ti,ab,ot,hw,kw,kf. (13465) 37 ("discrete choice" or DCE).ti,ab,ot,hw,kw,kf. (9462) 38 (AQoL or "Assessment of Quality of Life").ti,ab,ot,hw,kw,kf. (2235) 39 Quality-Adjusted Life Years/ (15372) 40 (HRQoL or HRQL or HQL or HQOL or H QoL or hr QoL or QoL or (quality adj3 life) or quality time or HYE or HYES or (health* adj3 equivalent*)).ti,ab,ot,hw,kw,kf. (436691) 41 quality of life/ (258423) 42 value of life/ (5800)	reviews of condition specific instruments.[75,76]

43 uncertainty/ (17049)

44 (Disability adjusted life or Disability-adjusted life or health adjusted life or health-adjusted life or "years of healthy life" or healthy years equivalent or "years of potential life lost" or "years of healthlife lost").ti,ab,ot,kw,kf. (5691)

45 (HSUV* or health state* value* or health state* preference* or HSPV*).ti,ab,ot,kw,kf. (511)

46 (uncertain* or wellbeing or "well being" or "quality of wellbeing" or "index of wellbeing" or "index of well being" or rosser or "willingness to pay" or "Quality of Well-Being" or QWB).ti,ab,kw,kf. (340037) 47 (utility* or disutili*).ti,ab,kw,kf. (246484)

48 (illness state*1 or health state* or health status or Quality adjusted life year* or QALY or QALD or DALY* or HALY* or YHL or HYES or YPLL or YHLL or qale or qtime or AQoL* or life year* or ICER or "incremental cost").ti,ab,ot,hw,kw,kf. (213805)

49 (burden and (disease or illness or caregiver or home)).ti,ab,kw,kf. (128677)

50 (lost adj2 (productivity or work or employment or earnings)).ti,ab,kw,kf. (3282)

51 (Work* adj2 (productivity or employment or disability or missed)).ti,ab,kw,kf. (10548)

52 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 (1264513)

53 (EORTC QLQ-MY20 or EORTC-QLQ-C30 or QLQ-C30 or QLQ-MY24 or QLQ-MY20 or QLQ-CIPN20 or FACT-Multiple Myeloma or FACT-MM or FACIT-Fatigue or FACT-NTx or FACT- BMT or FACT-An or "Functional Assessment of Cancer Therapy – General" or "FACT-G" or SEIQoL-DW or MDASI-MM or MyPOS or HPRSS).ti,ab,kw,kf. (7320)

54 52 or 53 (1265441)

55 24 or 54 (2601625) 56 9 and 55 (5737)	At Line 55 we combine the search for economics/costs (Line 24) with the search for health related quality of life/burden of illness (line 54). We then combine these filters with the condition terms at Line 9.

	We have not limited this search by language, date, or publication type (other than where specified above).

Table 109. Search strategy for Embase

No.	Query	Results
1	exp Multiple Myeloma/	102915
2	(myelom* or ((Penta or triple-class) adj1 refractory)).ti,ab,kw,kf,ot.	124976
3	kahler*.ti,ab,kw,kf,ot.	261
4	Plasmacytoma/	14271
5	(plasm?cytom* or plasm?zytom* or plasma cytoma* or plasma zytoma*).ti,ab,kw,kf,ot.	10257
6	(plasm* adj3 (neoplas* or leukaem* or leukem* or tumor* or tumour* or dyscrasia)).ti,ab,kw,kf,ot.	21703
7	((plasmacytic* or plasmocytic* or plasmocyte*) adj1 (leukem* or leukaem*)).ti,ab,kw,kf,ot.	46
8	(myelomatoses or myelomatosis).ti,ab,kw,kf.	531
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	170247
10	Health Economics/	36509
11	exp Economic Evaluation/	368630
12	exp Health Care Cost/	353192
13	pharmacoeconomics/	13019
14	Economics, Medical/	35512
15	economics, nursing/	34582
16	economics, pharmaceutical/	13019
17	(economic* or cost or costs or costly or costing or expense or expenses or price or prices or pricing or pharmacoeconomic* or CEA or CUA or CBA or CMA or ICER or ICUR).ti,ab,kw,kf.	1554408

No.	Query	Results
18	exp fee/	45143
19	exp budget/	34690
20	(resource*1 and (allocation or utili* or usage or use*1)).ti,ab,kw,kf.	381472
21	(expenditure* not energy).ti,ab,kw,kf.	53611
22	(value adj1 money).ti,ab,kw,kf.	46
23	(budget* or fiscal or funding or financial or finance*).ti,ab,kw,kf.	375083
24	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23	2364055
25	(15D or 15-D or 15 dimension).ti,ab,kw,kf.	7942
26	(eq-5d or eq5d or eq-5 or eq5 or EQ-5D-Y or euro qual or euroqual or euro qual5d or euroqual5d or euro qol or euroqol or euro qol5d or euroqol5d or euro quol or euroquol or euro quol5d or euroquol5d or eur qol or eurqol or eur qol5d or eur qol5d or eur?qul or eur?qul5d or euro$ quality of life or european qol or EQ-5D-3L).ti,ab,ot,hw,kw,kf.	37944
27	(sf6 or sf 6 or SF-6D or short form 6 or short-form 6 or short-form six or shortform 6 or sf six or sfsix or shortform six or short form six).ti,ab,ot,hw,kw,kf.	4710
28	(sf8 or sf 8 or sf-8 or short form 8 or shortform 8 or sf eight or sfeight or shortform eight or shortform eight).ti,ab,ot,hw,kw,kf.	1474
29	(sf10 or sf 10 or short form 10 or short-form 10 or short-form ten or shortform 10 or sf ten or sften or shortform ten or short form ten).ti,ab,ot,hw,kw,kf.	271
30	(sf12 or sf 12 or short form 12 or short-form 12 or short-form twelve or shortform 12 or sf twelve of sftwelve or shortform twelve or short form twelve).ti,ab,ot,hw,kw,kf.	15976
31	(sf16 or sf 16 or short form 16 or short-form 16 or short-form sixteen or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).ti,ab,ot,hw,kw,kf.	75
32	(sf20 or sf 20 or short form 20 or short-form 20 or short-form twenty or shortform 20 or sf twenty of sftwenty or shortform twenty of short form twenty).ti,ab,ot,hw,kw,kf.	621
33	(sf36 or sf 36 or short form 36 or short-form 36 or short-form thirty six or shortform 36 or sf thirtysix or sf thirty six or shortform thirstysix or shortform	63164

No.	Query	Results
	thirty six or short form thirty six or short form thirtysix or short form thirty six).ti,ab,ot,hw,kw,kf.	
34	(health utilities index* or (hui or hui1 or hui2 or hui3 or hui4 or hui-4 or hui-1 or hui-2 or hui-3)).ti,ab,ot,hw,kw,kf.	4682
35	("time trade off" or "time tradeoff" or "time trade-off" or TTO).ti,ab,ot,hw,kw,kf.	3739
36	(standard gamble* or SG).ti,ab,ot,hw,kw,kf.	23181
37	("discrete choice" or DCE).ti,ab,ot,hw,kw,kf.	15778
38	(AQoL or "Assessment of Quality of Life").ti,ab,ot,hw,kw,kf.	4029
39	*quality adjusted life year/	1986
40	(HRQoL or HRQL or HQL or HQOL or H QoL or hr QoL or QoL or (quality adj3 life) or quality time or HYE or HYES or (health* adj3 equivalent*)).ti,ab,ot,hw,kw,kf.	873150
41	*"quality of life"/	145786
42	*socioeconomics/	24801
43	*uncertainty/	9082
44	(Disability adjusted life or Disability-adjusted life or health adjusted life or health-adjusted life or "years of healthy life" or healthy years equivalent or "years of potential life lost" or "years of healthlife lost").ti,ab,ot,kw,kf.	8475
45	(HSUV* or health state* value* or health state* preference* or HSPV*).ti,ab,ot,kw,kf.	882
46	(uncertain* or wellbeing or "well being" or "quality of wellbeing" or "index of wellbeing" or "index of well being" or rosser or "willingness to pay" or "Quality of Well-Being" or QWB).ti,ab,kw,kf.	505662
47	(utility* or disutili*).ti,ab,kw,kf.	387593
48	(illness state*1 or health state* or health status or Quality adjusted life year* or QALY or QALD or DALY* or HALY* or YHL or HYES or YPLL or YHLL or qale or qtime or AQoL* or life year* or ICER or "incremental cost").ti,ab,ot,hw,kw,kf.	272282
49	(burden and (disease or illness or caregiver or home)).ti,ab,kw,kf.	247639

No.	Query	Results
50	(lost adj2 (productivity or work or employment or earnings)).ti,ab,kw,kf.	5302
51	(Work* adj2 (productivity or employment or disability or missed)).ti,ab,kw,kf.	18479
52	25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51	2125718
53	(EORTC QLQ-MY20 or EORTC-QLQ-C30 or QLQ-C30 or QLQ-MY24 or QLQ-MY20 or QLQ-CIPN20 or FACT-Multiple Myeloma or FACT-MM or FACIT-Fatigue or FACT-NTx or FACT- BMT or FACT-An or "Functional Assessment of Cancer Therapy – General" or "FACT-G" or SEIQoL-DW or MDASI-MM or MyPOS or HPRSS).ti,ab,kw,kf.	17061
54	52 or 53	2127461
55	24 or 54	4120601
56	9 and 55	20875
57	(conference abstract* or conference review or conference paper or conference proceeding).db,pt,su.	5955309
58	56 not 57	9736
59	(2023* or 2024*).yr.	2618719
60	58 and 59	1155

Notes: The structure and filters used here are the same as for MEDLINE. We have removed conferences proceedings from the searching using the guidance of Levay[77]. Conferences are searched separately for this review.

Table 110. Search strategy for EconLit

No.	Query	Search narrative	Results
1	TI ((Multiple Myeloma OR RRMM OR ((relapsed OR refractory OR triple class OR penta OR doublet or triplet) AND (Myeloma)) OR Kahler OR Plasmacytoma OR (plasma cell AND (neoplasm OR cancer OR dyscrasia)))) OR AB ((Multiple Myeloma OR RRMM OR ((relapsed OR refractory OR triple class OR penta OR doublet or triplet) AND (Myeloma)) OR Kahler OR Plasmacytoma OR (plasma cell AND (neoplasm OR cancer OR dyscrasia))))	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	2

Table 111. Cochrane CDSR and CENTRAL search strategy

No.	Query	Results
#1	MeSH descriptor: [Multiple Myeloma] explode all trees	2454
#2	(myelom* or ((Penta or triple-class) NEAR/1 refractory)):ti,ab,kw	7572
#3	kahler*:ti,ab,kw	22
#4	MeSH descriptor: [Plasmacytoma] this term only	86
#5	(plasm?cytom* or plasm?zytom* or plasma cytoma* or plasma zytoma*):ti,ab,kw	335
#6	(plasm* NEAR/3 (neoplas* or leukaem* or leukem* or tumor* or tumour* or dyscrasia)):ti,ab,kw	1481
#7	((plasmacytic* or plasmocytic* or plasmocyte*) NEAR/1 (leukem* or leukaem*)):ti,ab,kw	1
#8	(myelomatoses or myelomatosis):ti,ab,kw	34
#9	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8	8410
#10	MeSH descriptor: [Economics] this term only	59
#11	MeSH descriptor: [Costs and Cost Analysis] explode all trees	16495
#12	MeSH descriptor: [Economics, Hospital] this term only	36
#13	MeSH descriptor: [Financial Management, Hospital] this term only	2
#14	MeSH descriptor: [Economics, Medical] this term only	35
#15	MeSH descriptor: [Economics, Nursing] this term only	14
#16	MeSH descriptor: [Economics, Pharmaceutical] this term only	138
#17	(economic* or cost or costs or costly or costing or expense or expenses or price or prices or pricing or pharmacoeconomic* or CEA or CUA or CBA or CMA or ICER or ICUR):ti,ab,kw	112345
#18	MeSH descriptor: [Fees and Charges] explode all trees	345
#19	MeSH descriptor: [Budgets] explode all trees	66

#20	(resource* and (allocation or utili* or usage or use*)):ti,ab,kw	23277
#21	(expenditure* not energy):ti,ab,kw	2557
#22	(value NEAR/1 money):ti,ab,kw	6
#23	(budget* or fiscal or funding or financial or finance*):ti,ab,kw	33336
#24	#10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23	150699
#25	(15D or "15-D" or 15 dimension):ti,ab,kw	2106
#26	("eq-5d" or eq5d or "eq-5" or eq5 or "EQ-5D-Y" or euro qual or euro qual or euro qual5d or euroqual5d or euro qol or euroqol or euro qol5d or euroqol5d or euro quol or euroquol or euro quol5d or euroquol5d or eur qol or eurqol or eurqol5d or eur qol5d or euro* quality of life or european qol or "EQ-5D-3L"):ti,ab,kw	22870
#27	(sf6 or sf 6 or "SF-6D" or short form 6 or "short- form 6" or "short-form six" or shortform 6 or sf six or sfsix or shortform six or short form six):ti,ab,kw	21526
#28	(sf8 or sf 8 or "sf-8" or short form 8 or shortform 8 or sf eight or sfeight or shortform eight or shortform eight):ti,ab,kw	14055
#29	(sf10 or sf 10 or short form 10 or "short-form 10" or "short-form ten" or shortform 10 or sf ten or sften or shortform ten or short form ten):ti,ab,kw	12511
#30	(sf12 or sf 12 or short form 12 or "short-form 12" or "short-form twelve" or shortform 12 or sf twelve of sftwelve or shortform twelve or short form twelve):ti,ab,kw	17859
#31	(sf16 or sf 16 or short form 16 or "short-form 16" or "short-form sixteen" or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen):ti,ab,kw	5500
#32	(sf20 or sf 20 or short form 20 or "short-form 20" or "short-form twenty" or shortform 20 or sf twenty of sftwenty or shortform twenty of short form twenty):ti,ab,kw	8787
#33	(sf36 or sf 36 or short form 36 or "short-form 36" or "short-form thirty six" or shortform 36 or sf thirtysix or sf thirty six or shortform thirstysix or shortform thirty six or short form thirty six or short form thirtysix or short form thirty six):ti,ab,kw	20601
#34	(health utilities index* or (hui or hui1 or hui2 or hui3 or hui4 or "hui-4" or "hui-1" or "hui-2" or "hui-3" or "hui-4")):ti,ab,kw	600

#35	("time trade off" or "time tradeoff" or "time trade-off" or TTO):ti,ab,kw	329
#36	(standard gamble* or SG):ti,ab,kw	2120
#37	("discrete choice" or DCE):ti,ab,kw	643
#38	(AQoL or "Assessment of Quality of Life"):ti,ab,kw	1115
#39	MeSH descriptor: [Quality-Adjusted Life Years] this term only	2346
#40	(HRQoL or HRQL or HQL or HQOL or H QoL or hr QoL or QoL or (quality NEAR/3 life) or quality time or HYE or HYES or (health* NEAR/3 equivalent*)):ti,ab,kw	198863
#41	MeSH descriptor: [Quality of Life] this term only	43850
#42	MeSH descriptor: [Value of Life] this term only	49
#43	MeSH descriptor: [Uncertainty] this term only	385
#44	(Disability adjusted life or "Disability-adjusted life" or health adjusted life or "health-adjusted life" or "years of healthy life" or healthy years equivalent or "years of potential life lost" or "years of healthlife lost"):ti,ab,kw	11179
#45	(HSUV* or health state* value* or health state* preference* or HSPV*):ti,ab,kw	5797
#46	(uncertain* or wellbeing or "well being" or "quality of wellbeing" or "index of wellbeing" or "index of well being" or rosser or "willingness to pay" or "Quality of Well-Being" or QWB):ti,ab,kw	43826
#47	(utility* or disutili*):ti,ab,kw	19418
#48	(illness state* or health state* or health status or Quality adjusted life year* or QALY or QALD or DALY* or HALY* or YHL or HYES or YPLL or YHLL or qale or qtime or AQoL* or life year* or ICER or "incremental cost"):ti,ab,kw	178607
#49	(burden and (disease or illness or caregiver or home)):ti,ab,kw	19331
#50	(lost NEAR/2 (productivity or work or employment or earnings)):ti,ab,kw	715
#51	(Work* NEAR/2 (productivity or employment or disability or missed)):ti,ab,kw	2586
#52	("EORTC QLQ-MY20" or "EORTC-QLQ-C30" or "QLQ-C30" or "QLQ-MY24" or "QLQ-MY20" or "QLQ- CIPN20" or "FACT-Multiple Myeloma" or "FACT-MM" or "FACIT-Fatigue" or "FACT-NTx" or "FACT- BMT" or "FACT-An" or "Functional Assessment of Cancer Therapy – General" or "FACT-G" or "SEIQoL-DW" or "MDASI-MM" or MyPOS or HPRSS):ti,ab,kw	19058

#53	#25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52	358694
#54	#24 or #53	444990
#55	#9 AND #54	2107

Abbreviations: CDSR = Cochrane Database of Systematic Reviews; CENTRAL = Cochrane Central Register of Controlled Trials.

Notes: It was not feasible to search at the level of the condition (only) as the search results were too large (n=8410 in this update). We filtered this search to identify any Cochrane review which included resource or health related quality of life outcomes. Whilst resource use outcomes are rare in Cochrane reviews, we aimed to identify any data systematically and to report this transparently. Search = 2107. 20 = CDSR (of which 2 were in date range for this update), 2086 = Trials (CENTRAL) and 1 = Editorial.

J.1.2.2 Conference searches

Searches of clinical and economic conference proceedings were conducted for proceedings taking place during 2021 to 2022, and 2023 when the conference occurred prior to the search date. Upcoming 2023 conferences, held later in the year, were included when they occurred during the life cycle of the review, with any relevant records identified that met the PICOS criteria included as grey literature records. Detailed search strategies for conference searches are presented in the tables below.

Table 112. Conference search strategy for Embase

No.	Query	Results
1	exp Multiple Myeloma/	102915
2	(myelom* or ((Penta or triple-class) adj1 refractory)).ti,ab,kw,kf,ot.	124976
3	kahler*.ti,ab,kw,kf,ot.	261
4	Plasmacytoma/	14271
5	(plasm?cytom* or plasm?zytom* or plasma cytoma* or plasma zytoma*).ti,ab,kw,kf,ot.	10257
6	(plasm* adj3 (neoplas* or leukaem* or leukem* or tumor* or tumour* or dyscrasia)).ti,ab,kw,kf,ot.	21703
7	((plasmacytic* or plasmocytic* or plasmocyte*) adj1 (leukem* or leukaem*)).ti,ab,kw,kf,ot.	46
8	(myelomatoses or myelomatosis).ti,ab,kw,kf.	531
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	170247
10	Health Economics/	36509
11	exp Economic Evaluation/	368630

12	exp Health Care Cost/	353192
13	pharmacoeconomics/	13019
14	Economics, Medical/	35512
15	economics, nursing/	34582
16	economics, pharmaceutical/	13019
17	(economic* or cost or costs or costly or costing or expense or expenses or price or prices or pricing or pharmacoeconomic* or CEA or CUA or CBA or CMA or ICER or ICUR).ti,ab,kw,kf.	1554408
18	exp fee/	45143
19	exp budget/	34690
20	(resource*1 and (allocation or utili* or usage or use*1)).ti,ab,kw,kf.	381472
21	(expenditure* not energy).ti,ab,kw,kf.	53611
22	(value adj1 money).ti,ab,kw,kf.	46
23	(budget* or fiscal or funding or financial or finance*).ti,ab,kw,kf.	375083
24	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23	2364055
25	(15D or 15-D or 15 dimension).ti,ab,kw,kf.	7942
26	(eq-5d or eq5d or eq-5 or eq5 or EQ-5D-Y or euro qual or euroqual or euro qual5d or euroqual5d or euro qol or euroqol or euro qol5d or euroqol5d or euro quol or euroquol or euro quol5d or euroquol5d or eur qol or eurqol or eur qol5d or eur qol5d or eur?qul or eur?qul5d or euro$ quality of life or european qol or EQ-5D-3L).ti,ab,ot,hw,kw,kf.	37944
27	(sf6 or sf 6 or SF-6D or short form 6 or short-form 6 or short-form six or shortform 6 or sf six or sfsix or shortform six or short form six).ti,ab,ot,hw,kw,kf.	4710
28	(sf8 or sf 8 or sf-8 or short form 8 or shortform 8 or sf eight or sfeight or shortform eight or shortform eight).ti,ab,ot,hw,kw,kf.	1474
29	(sf10 or sf 10 or short form 10 or short-form 10 or short-form ten or shortform 10 or sf ten or sften or shortform ten or short form ten).ti,ab,ot,hw,kw,kf.	271
30	(sf12 or sf 12 or short form 12 or short-form 12 or short-form twelve or shortform 12 or sf twelve of sftwelve or shortform twelve or short form twelve).ti,ab,ot,hw,kw,kf.	15976
31	(sf16 or sf 16 or short form 16 or short-form 16 or short-form sixteen or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).ti,ab,ot,hw,kw,kf.	75
32	(sf20 or sf 20 or short form 20 or short-form 20 or short-form twenty or shortform 20 or sf twenty of sftwenty or shortform twenty of short form twenty).ti,ab,ot,hw,kw,kf.	621
33	(sf36 or sf 36 or short form 36 or short-form 36 or short-form thirty six or shortform 36 or sf thirtysix or sf thirty six or shortform thirstysix or shortform thirty six or short form thirty six or short form thirtysix or short form thirty six).ti,ab,ot,hw,kw,kf.	63164

34	(health utilities index* or (hui or hui1 or hui2 or hui3 or hui4 or hui-4 or hui-1 or hui-2 or hui-3)).ti,ab,ot,hw,kw,kf.	4682
35	("time trade off" or "time tradeoff" or "time trade-off" or TTO).ti,ab,ot,hw,kw,kf.	3739
36	(standard gamble* or SG).ti,ab,ot,hw,kw,kf.	23181
37	("discrete choice" or DCE).ti,ab,ot,hw,kw,kf.	15778
38	(AQoL or "Assessment of Quality of Life").ti,ab,ot,hw,kw,kf.	4029
39	*quality adjusted life year/	1986
40	(HRQoL or HRQL or HQL or HQOL or H QoL or hr QoL or QoL or (quality adj3 life) or quality time or HYE or HYES or (health* adj3 equivalent*)).ti,ab,ot,hw,kw,kf.	873150
41	*"quality of life"/	145786
42	*socioeconomics/	24801
43	*uncertainty/	9082
44	(Disability adjusted life or Disability-adjusted life or health adjusted life or health-adjusted life or "years of healthy life" or healthy years equivalent or "years of potential life lost" or "years of healthlife lost").ti,ab,ot,kw,kf.	8475
45	(HSUV* or health state* value* or health state* preference* or HSPV*).ti,ab,ot,kw,kf.	882
46	(uncertain* or wellbeing or "well being" or "quality of wellbeing" or "index of wellbeing" or "index of well being" or rosser or "willingness to pay" or "Quality of Well-Being" or QWB).ti,ab,kw,kf.	505662
47	(utility* or disutili*).ti,ab,kw,kf.	387593
48	(illness state*1 or health state* or health status or Quality adjusted life year* or QALY or QALD or DALY* or HALY* or YHL or HYES or YPLL or YHLL or qale or qtime or AQoL* or life year* or ICER or "incremental cost").ti,ab,ot,hw,kw,kf.	272282
49	(burden and (disease or illness or caregiver or home)).ti,ab,kw,kf.	247639
50	(lost adj2 (productivity or work or employment or earnings)).ti,ab,kw,kf.	5302
51	(Work* adj2 (productivity or employment or disability or missed)).ti,ab,kw,kf.	18479
52	25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51	2125718
53	(EORTC QLQ-MY20 or EORTC-QLQ-C30 or QLQ-C30 or QLQ-MY24 or QLQ-MY20 or QLQ-CIPN20 or FACT-Multiple Myeloma or FACT-MM or FACIT-Fatigue or FACT-NTx or FACT- BMT or FACT-An or "Functional Assessment of Cancer Therapy – General" or "FACT-G" or SEIQoL-DW or MDASI-MM or MyPOS or HPRSS).ti,ab,kw,kf.	17061
54	52 or 53	2127461
55	24 or 54	4120601
56	9 and 55	20875
57	(conference abstract* or conference review or conference paper or conference proceeding).db,pt,su.	5955309

58	56 and 57	11139
59	(2023* or 2024*).yr.	2618719
60	58 and 59	875

Table 113. Conference search strategy for ISPOR

No.	Search strategy	Results
N/A	Searches were made of the database using Multiple Myeloma and RRMM.	87

Abbreviations: ISPOR = International Society for Pharmacoeconomics and Outcomes; N/A = Not applicable.

Searched via: https://www.ispor.org/heor-resources/presentations-database/search

Table 114. Conference search strategy for HESG

No.	Search strategy	Results
N/A	The abstract books for the twice-yearly meetings were downloaded from the conference website. The abstracts books were hand searched for abstracts at the level of the condition.	0

Abbreviations: HESG = Health Economists' Study Group; N/A = Not applicable.

Searched via: https://hesg.org.uk/

Table 115. Conference search strategy for ASCO

Year	Search strategy	Results
2021	We searched ASCO Annual meetings via the ASCO abstract presentation database/interface. We limited our searches to: Annual Meetings, by years 2021-2023 inclusive, and Media: Abstracts or Posters.	38
2022		56
2023		93
2024		106

Abbreviations: ASCO = American Society of Clinical Oncology; N/A = Not applicable.

Searched via: https://meetings.asco.org/abstracts-presentations

Table 116. Conference search strategy for ASH

Year	Search strategy	Results
2021	https://ashpublications.org/blood/issue/138/Supplement%201	454
2022	https://ashpublications.org/blood/issue/140/Supplement%201	305
2023	https://ashpublications.org/blood/issue/140/Supplement%201	263

Abbreviations: ASH = American Society of Hematology; N/A = Not applicable.

Searched via: https://ashpublications.org/blood/issue/138/Supplement%201 (2021) and https://ashpublications.org/blood/issue/140/Supplement%201 (2022)

Table 117. Conference search strategy for EHA

Year	Search strategy	Results
2021	N/A	114

Year	Search strategy	Results
2022		118
2023		125
2024		10

Abbreviations: EHA = European Hematology Association; N/A = Not applicable.

*Searched via: https://library.ehaweb.org/eha/?menu=16&browseby=9&sortby=1&trend=4016#!*menu=16*browseby=9*sortby=1*trend=4016*

Table 118. Conference search strategy for ESMO

Year	Search strategy	Results
2021	https://oncologypro.esmo.org/meeting-resources/esmo-congress	4
2022		7
2023		1

Abbreviations: ESMO = European Society of Medical Oncology; N/A = Not applicable.

*Searched via: https://library.ehaweb.org/eha/?menu=16&browseby=9&sortby=1&trend=4016#!*menu=16*browseby=9*sortby=1*trend=4016*

Table 119. Conference search strategy for CPCI-S

No.	Query	Results
1	"Multiple Myeloma" (Topic)	15,856
2	(myelom* or ((Penta or triple-class) NEAR/1 refractory)) (Topic)	20,947
3	TS=((kahler* or plasmcytom* or plasma cytoma* or plasma zytoma* or myelomatoses or myelomatosis))	551
4	(plasm* NEAR/3 (neoplas* or leukaem* or leukem* or tumor* or tumour* or dyscrasia)) (Topic)	1,382
5	#1 OR #2 OR #3 OR #4	22, 712
6	#1 OR #2 OR #3 OR #4 and 2023 or 2024 (Publication Years)	1,309

Abbreviations: CPI-S = Conference Proceedings Citation Index – Science; N/A = Not applicable.

Searched via: Database search via Clarivate (1990-current).

Table 120. Conference search strategy for BSH

Year	Search strategy	Results
2021	https://onlinelibrary.wiley.com/toc/13652141/2021/193/S1	19
2022		20
2023		21

Abbreviations: BSH = British Society of Haematology; N/A = Not applicable.

Searched via: https://onlinelibrary.wiley.com/toc/13652141/2021/193/S1 (2021) and https://onlinelibrary.wiley.com/toc/13652141/2022/197/S1 (2022)

J.1.2.3 Web searches

The number of records identified for each HTA country-specific site are presented in Table 121. Websites were searched using the term 'Multiple Myeloma' with searches of EMA based on intervention name only, and MHRA, RIZIV-INAMI and Tufts CEA websites searched using the term 'Multiple Myeloma' alongside intervention names. The searcher was based in London when undertaking these searches. We used a cascading approach to searching. The first time we identified guidance or a potentially eligible record, we recorded it and we downloaded it. If the guidance was identified again, by another search, we did not record the search. This approach de-duplicated as the searching evolved.

Table 121. Web searching

Source name	Location/source	Results original	Results updated	Date of search
National Institute for Health and Care Excellence (NICE)	https://www.nice.org.uk/	32	10	28.05.2024
Scottish Medicines Consortium (SMC)	https://www.scottishmedicines.org.uk/	33	6	28.05.2024
National Institute for Health and Care Research Innovation Observatory (NIHRIO) tech briefings	https://www.io.nihr.ac.uk/	19	1	28.05.2024
European Medicines Agency (EMA)	https://www.ema.europa.eu/en	27	Not searched in this update	28.05.2024
Medicines and Healthcare products Regulatory Agency (MHRA)	https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency	0	Not searched in this update	28.05.2024
Dental and Pharmaceutical Benefits Agency (Tandvårds- och läkemedelsförmånsverket; TLV) (Sweden)	https://www.tlv.se/	0	1	28.05.2024
Norwegian Institute of Public Health (NIPH) (Norway)	https://www.fhi.no/en/	1	0	28.05.2024
Danish Medicines Council (DMC)/ Danish Treatment Council (DTC) (Denmark)	https://medicinraadet.dk/om-os/in-english	8	0	28.05.2024
Finnish Medicines Agency (Fimea) (Finland)	https://www.fimea.fi/web/en	8	0	28.05.2024
National Centre for Pharmacoeconomics (NCPE) (Ireland)	https://www.ncpe.ie/	15	5	28.05.2024

Source name	Location/source	Results original	Results updated	Date of search
National Institute for Health and Disability Insurance (RIZIV-INAMI) (Belgium)	http://www.inami.fgov.be/	0	0	28.05.2024
National Health Care Institute (Zorginstituut Nederland, ZiN) (Netherlands)	https://english.zorginstituutnederland.nl/	2	0	28.05.2024
EconPapers within Research Papers in Economics	http://repec.org/	3	5	28.05.2024
University of Sheffield ScHARRHUD utility database	http://www.scharrhud.org/	0	Not searched in this update	28.05.2024
EuroQoL website	https://euroqol.org/	0	0	28.05.2024
Tufts CEA registry	https://cevr.tuftsmedicalcenter.org/databases/cea-registry		0	28.05.2024

*Notes: * Number of records identified matching eligibility criteria*

J.1.2.4 Study selection

During primary screening, titles and abstracts of identified records were assessed against the population, intervention, comparator, outcomes and study design (PICOS) criteria, detailed in Table 122, to select those addressing the SLR eligibility criteria. This assessment was undertaken by two reviewers independently, using the Covidence online screening tool. Electronic or paper copies of potentially relevant full papers meeting the SLR inclusion criteria were then obtained for secondary screening and assessed in detail for relevance to the eligibility criteria by two reviewers independently, and final selection of studies was made to inform the SLR. Where researchers disagreed regarding the inclusion or exclusion of a record at either primary or secondary screening, a third reviewer joined discussions where reasons for disagreement were discussed until a consensus was reached.

Eligible studies were data extracted initially by one reviewer, with a second carrying out a cell-by-cell data check. Where more than one publication of a study existed (e.g., a conference abstract and a paper published in a peer-reviewed journal), the primary publication was used in synthesis, and supplemented by additional records where relevant outcomes were only published in earlier versions. Any discrepancies between published versions were highlighted in the data extraction form.

During data extraction, researchers conducted quality assessment of each included study using specific checklists relevant to each economic data component (economic evaluations, HRQoL, and cost and/ or resource use). Quality assessment was used to provide an assessment of the risk of bias for each study included to contribute to the evaluation of the overall strength of evidence.

Table 122. Eligibility criteria

Criterion	Inclusion criteria	Exclusion
Population(s)	Adult (≥18 years) with previously treated RRMM i.e., with ≥1 prior line of therapy (2L+)[a]	Newly diagnosed/ untreated MM/ mixed MM populations that include newly diagnosed patients where treatment line was not reported separately or where newly diagnosed participants form ≥10% of the trial population.
Intervention/ Comparators	Systemic therapies	Non-systemic therapies, surgery (e.g., for bone metastasis), or stem cell/ bone marrow transplant
Outcomes	**Economic evaluations:** Total costs Costs per outcome (e.g., treatment, benefit) QALYs LYs ICER ICUR Budget impact per population **Healthcare costs/ resource use:** Treatment costs Unit costs Costs of adverse events Direct costs of inpatient and outpatient services Indirect costs (e.g., carer burden, travel) Frequency of resource use, (e.g., hospitalisation/ inpatient days, accident and emergency visits, outpatient visits) Outpatient and inpatient healthcare resource utilisation Work productivity, travel, employment, and work disability **HRQoL (patient and carer):** Any HRQoL outcomes (from generic or condition-specific measures) reporting utilities, disutilities or HRQoL scores.	
Study design	**Economic evaluations:** CEA CUA Cost-minimisation analysis (CMA) [Cost-comparison analysis]	Case series Case reports Animal studies Studies/ trials with <20 participants

	Cost-consequence analysis (CCA) Cost-benefit analysis (CBA) Cost-offset analysis (COA) Budget impact analysis (BIA) **Healthcare costs/ resource use and HRQoL (patient and carer):** Economic evaluations (as above) Randomised and non-randomised (comparative) clinical trials Non-comparative single-arm studies Early access treatment protocol (EAP) studies Patient chart reviews Patient and disease registry studies Claims data analyses.	
Publication types	Full-text peer reviewed publications Conference abstracts, posters and oral presentations (2021+) HTA documents Guidance documents Horizon scanning documents Trial protocols Systematic reviews[b]	Non-systematic reviews Letters Editorials Commentaries Opinion pieces Press releases
Limits	**Economic evaluations:** No restriction **Healthcare costs/ resource use:** 2013 to present [limited to previous 10 full years to capture most up-to-date cost data] **HRQoL (patient and carer):** No restriction **Country:** No restriction[c] **Language:** No restriction[d]	

Abbreviations: BIA, budget impact analysis; CBA, cost-benefit analysis; CCA, cost-consequence analysis; CEA, cost-effectiveness analysis; CMA, cost-minimisation analysis; COA, cost-offset analysis; CUA, cost-utility analysis; EAP, early access treatment protocol; HRQoL, health-related quality of life; HTA, Health technology assessment; ICER, incremental cost-effectiveness ratio; ICUR, incremental cost-utility ratio; LY, life year; MM, multiple myeloma; PICOS, population, intervention, comparators, outcomes, study design; QALYs, quality-adjusted life years; RRMM, relapsed and/ or refractory multiple myeloma.

[a] *Evidence across all lines of therapy were eligible for inclusion. Studies including data in patients with one or two prior therapies (2L-3L) and at least four prior lines of therapy (5L+) or penta-refractory MM (the two populations of interest) were prioritised in an evidence hierarchy assessment, followed by studies that provide economic evidence in other lines of therapy (e.g., 4L)*

[b] *Systematic reviews included for reference-tracking and were not eligible for full data extraction.*

c No records were excluded based on country but in data synthesis records were prioritised in an evidence hierarchy assessment

[d] *Records will be translated using Google translate to judge eligibility.*

Primary screening

Titles and abstracts of identified records will be assessed to select those addressing the systematic review eligibility criteria. This assessment will be undertaken by at least two reviewers, independently (RH, LS, DP, JNL), using the Covidence online screening tool. If there is uncertainty about the relevance of a record based on the abstract, it will be included, and a full copy of the publication will be obtained.

Secondary screening

Electronic or paper copies of potentially relevant full papers meeting the PICOS inclusion criteria will be obtained. Tolley Health Economics Ltd will obtain articles for full-text screening by first checking which are available free of charge, and then will work with Menarini to obtain articles via their in-house library.

Once full text studies are obtained, they will be independently assessed in detail for relevance to the eligibility criteria by at least two researchers (RH, LS, DP, JNL), and final selection of studies will be made to inform the review. Where researchers disagree regarding the inclusion or exclusion of a record, they will discuss reasons for disagreement. If consensus is not reached, then a third researcher will be involved to make a decision.

At the end of the selection process a list of included and excluded studies identified through the searches will be produced. Reasons for exclusion will be provided for all studies excluded during full text review and a PRISMA flow diagram will be completed.36

During primary and secondary screening, records will be tagged in Covidence to streamline evidence categorisation. The following tags have been pre-defined to ensure consistency amongst reviewers, however additional tags may be added during screening, and each record may be tagged with more than one tag.

• Type of evidence: Economic evaluation, Resource use, HRQoL, Societal costs/ RU

• Location: England, UK, European, USA, Asia, Scotland.

• Indication: Triple-exposed, Quad-exposed, Penta-exposed, Mixed exposure, Triple class refractory, Quad-refractory, Penta-refractory, Mixed refractory, 2L+ (BOSTON indication) relevant, 5L+ (STORM indication) relevant, Full popn. eligible, Subgroup-only eligible.

• HRQoL measure: EORTC QLQ-CR29, EORTC QLQ-CR38, EORTC QLQ-C30, EQ-5D (unspecified), EQ-5D-3L, EQ-5D-5L, Utility values, TTO, Standard gamble, Mapping algorithm, SF36, SF6D, Utility values (mapped), FACT, FACT-G, FACT-An, FACT-BMT, FACT-MM, FACT-NTx, MyPOS, FACIT-EORTC QLQ-MY20, EORTC QLQ-CIPN20, Health state utility values, Treatment related utility values.

• Economic evidence: ICER, QALY, DALY, HALY, CUA, CEA, CMA, CCA, HYE, LYG, Costs per outcome, Budget impact, CBA, COA, Economic Model, Markov model, PSM, Decision tree, Cohort model -other, DES.

• Costs: Costs >10 years old (<2013)

• Other: Clinical, Abstract only, Abstract pre-2021, Poster, Systematic review, review, Technology appraisal.

J.1.2.4.1 All cost-effectiveness studies

Following removal of duplicates, 5,077 records were eligible for primary screening of title/ abstract, of which 3,558 records were excluded and 243 were taken forward to secondary screening. An additional 16 records were identified in grey literature searching via methods such as reference tracking and additional HTA website searching. In total, 358 records were eligible for inclusion in this review following secondary screening. The PRISMA diagram details the number of records identified (Figure 45).

The SLR identified 103 records as eligible for inclusion (**Table** 123), in the whole RRMM population, across at least one of the three economic SLR components, as per the PICOS criteria. The 140 records excluded at secondary (full-text) screening, are listed by exclusion (Table 124).

Table 123. Included records in the economic SLR

Title	Authors	Year	Journal
Correction to Lancet Haematol 2024; 11: e216â€“27 (The Lancet Haematology (2024) 11(3) (e216â€“e227), (S235230262400005X), (10.1016/S2352-3026(24)00005-X))		2024	The lancet haematology
Healthcare Resource Utilization and Economic Burden of Cytokine Release Syndrome and Neurotoxicity in Patients with Relapsed and Refractory Multiple Myeloma (RRMM) Receiving Idecabtagene Vicleucel in Earlier-Line Settings in the KarMMa-3 Clinical Trial	Ailawadhi, S.; McGarvey, N.; Imanak, K.; Mirza, S.; Patwardhan, P.	2023	Blood
Erratum: Comparison of health care costs and resource utilization for commonly used proteasome inhibitor-immunomodulatory drug-based triplet regiments for the management of patients with relapsed/refractory multiple myeloma in the United States (Journal	Anonymous	2023	Journal of Managed Care and Specialty Pharmacy
The EASEMENT study: A multicentre, observational, cross-sectional study to evaluate patient preferences, treatment satisfaction, quality of life, and healthcare resource use in patients with multiple myeloma receiving injectable-containing or fully oral t	Ayto, R.; Annibali, O.; Biedermann, P.; Roset, M.; Sanchez, E.; Kotb, R.	2024	European Journal of Haematology
Real-world utilization and healthcare costs for multiple myeloma: A retrospective analysis of patients in Singapore	Bayani, D. B.; Lin, Y. C.; Ooi, M. G.; Tso, A. C. Y.; Wee, H. L.	2023	EJHaem
Assessing the Treatment Pattern, Health Care Resource Utilisation, and Economic Burden of Multiple Myeloma in France	Bessou, Antoine; Colin, Xavier; De Nascimento, Julie; Sopwith, Will;	2023	European Journal of

Using the Systeme National des Donnees de Sante (SNDS) Database: A Retrospective Cohort Study	Ferrante, Shannon; Gorsh, Boris		Health Economics
EE403 Budget Impact of Selinexor Combination Regimens in Previously Treated Multiple Myeloma	Carter JA1, Ijioma S2, Ray D3	2024	
Patient-Reported Outcomes Among Patients with Triple-Class Refractory Multiple Myeloma in Real-World Clinical Practice: A Prospective, Multi-Site Observational Study	Charalampous, Charalampos; Kumar, Shaji Kunnathu; Parrondo, Ricardo; Chhabra, Saurabh; Duh, Mei Sheng; Bobbili, Priyanka; Wang, Aolin; Chen, Jingyi; Mohan, Manasi; Hlavacek, Patrick; Ren, Jinma; Schepart, Alex; Nador, Guido; DiBonaventura, Marco	2023	Blood
EE660 Real-World Economic Burden and Healthcare Resource Utilization (HCRU) Among Patients with Triple-Class Exposed Relapsed/Refractory Multiple Myeloma (RRMM) in the United States	Chari, A.; Lin, X.; Ammann, E.; Matt, K.; Potluri, R.; Nair, S.	2023	Value in Health
Systematic literature review of health economic models developed for multiple myeloma to support future analyses	Choon-Quinones, M.; Zelei, T.; Nemeth, B.; Toth, M.; Jia, X. Y.; Barnett, M.; Keown, P.; Durie, B.; Harousseau, J. L.; Hose, D.; Kalo, Z.	2023	Journal of Medical Economics
RWD157 Assessment of Real-World Treatment Patterns and Healthcare Resource Utilization (HCRU) in Patients with Lenalidomide-Refractory Relapsed/Refractory Multiple Myeloma (RRMM) from the US Optum Database	Costa, L.; Nair, S.; Lin, X.; O'Hara, M.; Slavcev, M.; Marshall, A.; Potluri, R.; Tyagi, R.; Hashmi, H.	2023	Value in Health
An Investigation into the Relationship Between Choice of Model Structure and How to Adjust for Subsequent Therapies Using a Case Study in Oncology	Cranmer, H. L.; Shields, G. E.; Bullement, A.	2023	Applied Health Economics & Health Policy
A Study Comparing Talquetamab Plus Pomalidomide, Talquetamab Plus Teclistamab, and Elotuzumab, Pomalidomide, and Dexamethasone or Pomalidomide, Bortezomib, and Dexamethasone in Participants with Relapsed or Refractory Myeloma who Have Received an Anti-CD3	Ctri	2024	https://trialsearch.who.int/Trial2.aspx?TrialID=CTRI/2024/02/063266
Assessment of the psychometric properties of the Spanish version of EORTC QLQ-MY20 and evaluation of health-related quality of Life outcomes in patients with relapsed and/or refractory multiple myeloma in the real-world setting in Spain: results from the	Dachs, L. R.; Gaisan, C. M.; Bustamante, G.; Lopez, S. G.; Garcia, E. G.; Persona, E. P.; Gonzalez-Calle, V.; Auzmendi, M. S.; Perez, J. M. A.; Gonzalez	2023	Leukemia and Lymphoma

	Montes, Y.; Rios Tamayo, R.; de Miguel Llorente, D.; Bernal, L. P.; Mayol, A. S.; Caro, C. C.; Grande, M.; Fernandez-Nistal, A.; Naves, A.; Miguel, E. M. O. S.		
Whether and How Disutilities of Adverse Events were Used in the Economic Evaluation of Drug Therapy for Cancer Treatment	Dai, Z.; Chang, F.; Wang, L.; He, J.; Shi, P.; Zhang, H.; Lu, Y.	2023	PharmacoEconomics
Real-World Study of Patients with Triple-Class Exposed Relapsed/Refractory Multiple Myeloma: Analysis across a Spectrum of Advanced Disease Stage Medicare Patients in the United States	Delea, T.; Moynahan, A.; Ge, W.; Song, X.; Kroog, G. S.; Noguera-Troise, I.; Rodriguez Lorenc, K.; Ma, Q.	2023	Blood
Health-related quality of life in patients with triple-class exposed relapsed and refractory multiple myeloma treated with idecabtagene vicleucel or standard regimens: patient-reported outcomes from the phase 3, randomised, open-label KarMMa-3 clinical tr	Delforge, M.; Patel, K.; Eliason, L.; Dhanda, D.; Shi, L.; Guo, S.; Marshall, T. S.; Arnulf, B.; Cavo, M.; Nooka, A.; et al.	2024	The Lancet. Haematology
Health related quality of life (HRQoL) in patients with triple-class-exposed relapsed/ refractory multiple myeloma (TCE RRMM) treated with idecabtagene vicleucel (ide-cel) versus standard regimens: patient-reported outcomes (PROs) from KarMMa-3 phase 3 ra	Delforge, M.; Patel, K. K.; Eliason, L.; Dhanda, D.; Shi, L.; Guo, S.; Marshall, T.; Arnulf, B.; Cavo, M.; Nooka, A. K.; et al.	2023	Journal of clinical oncology
Effects of Idecabtagene Vicleucel (Ide-Cel) Versus Standard Regimens on Health-Related Quality of Life (HRQoL) in Patients with Relapsed/Refractory Multiple Myeloma (RRMM) Who Had Received 2-4 Prior Regimens: Updated Results from the Phase 3 KarMMa-3 Tri	Delforge, M.; Patel, K. K.; Eliason, L.; Dhanda, D.; Shi, L.; Guo, S.; Marshall, T. S.; Arnulf, B.; Cavo, M.; Nooka, A. K.; Manier, S.; Callander, N. S.; Giralt, S. A.; Einsele, H.; Ailawadhi, S.; Popa-McKiver, M.; Cook, M.; Otero, P. R.	2023	Blood
Effects of Idecabtagene Vicleucel (Ide-Cel) Versus Standard Regimens on Health-Related Quality of Life (HRQoL) in Patients with Triple-Class-Exposed (TCE) Relapsed/Refractory Multiple Myeloma (RRMM) Who Received at Least 3 Lines of Prior Antimyeloma Regim	Delforge, M.; Patel, K. K.; Eliason, L.; Dhanda, D.; Shi, L.; Guo, S.; Marshall, T. S.; Arnulf, B.; Cavo, M.; Nooka, A. K.; Manier, S.; Callander, N. S.; Giralt, S. A.; Einsele, H.; Ailawadhi, S.; Popa-McKiver, M.; Cook, M.; Rodriguez Otero, P.	2023	Blood
Patient reported outcomes in Triple Class Exposed, Relapsed/ Refractory Multiple Myeloma (TCE RRMM) patients in KarMMa 3 trial (Phase 3 RCT):	Einsele, H.; Delforge, M.; Patel, K.; Eliason, L.; Dhanda, D.; Shi, L.; Guo,	2023	Oncology research and treatment

idecabtagene Vicleucel (ide-cel) versus standard regimens	S.; Marshall, T.; Arnulf, B.; Cavo, M.; et al.		
EE260 Cost-Effectiveness Analysis of Daratumumab Triplet Therapy Vs Carfilzomib Duplet Therapy in Patients with Relapsed or Refractory Multiple Myeloma in Egypt from Payer Perspective	Elsisi, G.; Elattar, M.; Eldesouky, N.	2023	Value in Health
Impact of Disease Progression, Line of Therapy, and Response on Health-Related Quality of Life in Multiple Myeloma: A Systematic Literature Review	Fonseca, R.; Tran, D.; Laidlaw, A.; Rosta, E.; Rai, M.; Duran, J.; Ammann, E. M.	2023	Clinical lymphoma, myeloma & leukemia
Costs of plasmocytic myeloma therapy in the drug programme at a Regional Oncology Centre in Poland	Futyma, K.; Sliwczynski, A.; Halka, J.; Brzozowska, M.	2023	Annals of Agricultural & Environmental Medicine
Health-related quality of life among patients with multiple myeloma treated with CAR-T therapy	Gagnon, S. J.; Nooka, A. K.	2023	Journal of Clinical Oncology
EE335 Burden of Disease in Patients Who Are Eligible for Bcma-Targeted Immunotherapy for Multiple Myeloma: A Retrospective Claims Database Analysis	Giri S1, Lin D2, Dixon R3, Kim N2, Fowler J2, Barron J3, Tan H3, Nguyen C3, Asefaha F3, Vojjala S3, Min E2, Wu B2	2024	
EE531 Resource Optimization for Greek NHS Hospitals from the Use of Daratumumab SC for Multiple Myeloma	Golnas, P.; Kontogiorgos, I.; Golna, C.; Konstantopoulou, T.; Christodoulou, T. K.; Souliotis, K.	2023	Value in Health
Cost-effectiveness and budget impact analysis of Daratumumab, Lenalidomide and dexamethasone for relapsed-refractory multiple myeloma	Goudarzi, Z.; Shahtaheri, R. S.; Najafpour, Z.; Hamedifar, H.; Ebrahimi, H.	2024	Cost Effectiveness & Resource Allocation
The Impact of Outpatient versus Inpatient Administration of CAR-T Therapies on Clinical, Economic, and Humanistic Outcomes in Patients with Hematological Cancer: A Systematic Literature Review	Hansen, D. K.; Liu, Y. H.; Ranjan, S.; Bhandari, H.; Potluri, R.; McFarland, L.; De Braganca, K. C.; Huo, S.	2023	Cancers
Cost per Responder Analysis of Patients with Lenalidomide-Refractory Multiple Myeloma Who Received Cilta-Cel from the Cartitude-4 Trial	Hansen, D. K.; Lu, X.; Castaneda, O.; Sorensen, S.; Usmani, S. Z.; Zhang, E.; Huo, S.; Jagannath, S.	2023	Blood
Cost per Responder Analysis of Patients with Lenalidomide-Refractory Multiple Myeloma Who Received Cilta-Cel from the Cartitude-4 Trial	Hansen, D. K.; Lu, X.; Castaneda, O.; Sorensen, S.; Usmani, S. Z.; Zhang, E.; Huo, S.; Jagannath, S.	2024	Transplantation and Cellular Therapy
HTA18 Challenges of Identifying Health Utility Data for Patients With Penta-Refractory Multiple Myeloma to Inform HTA Reimbursement Discussion for Newer Treatment Options	Hibbs, R.; Bianco, M.; Noble-Longster, J.; Stainer, L.; Cooper, C.; Strickson, A. J.	2023	Value in Health

Health-Related Quality of Life (HRQoL) Among Patients with Triple-Class Exposed Relapsed/Refractory Multiple Myeloma (RRMM) Treated with Linvoseltamab in Linker-MM1: Interim Assessment up to 36 Weeks of Treatment	Hoffman, James E.; Bumma, Naresh; Richter, Joshua; Dhodapkar, Madhav V.; Lee, Hans C.; Suvannasankha, Attaya; Houde, Christiane A.; Maly, Joseph J.; Shah, Mansi R.; Baz, Rachid; Namburi, Swathi; Wu, Ka Lung; Pianko, Matthew; Ye, Jing Christine; Lentzsch, Suzanne; Silbermann, Rebecca; Min, Chang-Ki; Vekemans, Marie-Christiane; Munder, Markus; Byun, Ja Min; Lopez, JoaquÃn MartÃ-nez; DeVeaux, Michelle; Ivanescu, Cristina; Rodriguez Lorenc, Karen; Kroog, Glenn S.; Houvras, Yariv; Inocencio, Timothy J.; Chi, Lei; Harnett, James; Ma, Qiufei; Jagannath, Sundar	2023	Blood
Evaluating process utilities for the treatment burden of chemotherapy in multiple myeloma in Japan: a time trade-off valuation study	Ishida, T.; Nakakoji, M.; Murata, T.; Matsuyama, F.; Iida, S.	2023	Journal of Medical Economics
A clinical study to compare teclistamab monotherapy versus pomalidomide, bortezomib, dexamethasone (PVd) or carfilzomib, dexamethasone (Kd) in participants with relapsed or refractory multiple myeloma who have received 1 to 3 prior lines of therapy, inclu	Isrctn	2023	https://trialsearch.who.int/Trial2.aspx?TrialID=ISRCTN80324107
A study comparing talquetamab plus pomalidomide, talquetamab plus teclistamab, and elotuzumab, pomalidomide, and dexamethasone or pomalidomide, bortezomib, and dexamethasone in participants with relapsed or refractory myeloma who have received an Anti-CD3	Isrctn	2023	https://trialsearch.who.int/Trial2.aspx?TrialID=ISRCTN74178658
Component Costs of CAR-T Therapy in Addition to Treatment Acquisition Costs in Patients with Multiple Myeloma	Jagannath, S.; Joseph, N.; Crivera, C.; Kharat, A.; Jackson, C. C.; Valluri, S.; Cost, P.; Phelps, H.; Slowik, R.; Klein, T.; Smolen, L.; Yu, X.; Cohen, A. D.	2023	Oncology & Therapy
Healthcare Resource Utilization and Costs Among Patients With Relapsed/	Jagannath, S.; Kharat, A.; Fu, A.; Huo, S.; Kohli,	2023	Clinical Lymphoma,

Refractory Multiple Myeloma Treated With Chimeric Antigen Receptor-T (CAR-T) Cell Therapy	M.; Adams, S.; Umeh, E.; Foster, M.		Myeloma and Leukemia
e23185 Assessment of health-related quality of life (HRQoL) in triple-classâ€"exposed patients with relapsed or refractory multiple myeloma (RRMM) treated with linvoseltamab in the LINKER-MM1 trial.	James E. Hoffman, Naresh Bumma, Joshua Ryan Richter, Madhav V. Dhodapkar, Hans C. Lee, Attaya Suvannasankha, Jeffrey A. Zonder, Joseph J. Maly, Mansi R. Shah, Rachid C. Baz, Michelle DeVeaux, Cristina Ivanescu, Karen Rodriguez-Lorenc, Glenn Scott Kroog, Yariv J. Houvras, Timothy J Inocencio, Lei Chi, James Harnett, Qiufei Ma, Sundar Jagannath	2024	
P2300 ASSESSMENT OF HEALTH-RELATED QUALITY OF LIFE IN TRIPLE-CLASS EXPOSED PATIENTS WITH RELAPSED OR REFRACTORY MULTIPLE MYELOMA (RRMM) TREATED WITH LINVOSELTAMAB IN THE LINKER-MM1 TRIAL	James E. Hoffman, Naresh Bumma, Joshua Richter, Madhav Dhodapkar, Hans Lee, Attaya Suvannasankha, Jeffrey Zonder, Joseph J. Maly, Mansi R. Shah, Rachid Baz, Michelle DeVeaux, Cristina Ivanescu, Cristina Karen Rodriguez Lorenc, Glenn Kroog, Yariv Houvras, Timothy Inocencio, Lei Chi, James Harnett, Qiufei Ma, Sundar Jagannath	2024	
Cost-effectiveness of idecabtagene vicleucel compared with conventional care in triple-class exposed relapsed/refractory multiple myeloma patients in Canada and France	Karampampa, K.; Zhang, W.; Venkatachalam, M.; Cotte, F. E.; Dhanda, D.	2023	Journal of Medical Economics
Daratumumab in Indian patients with relapsed and refractory multiple myeloma: a prospective, multicenter, phase IV study	Kumar, L.; Melinkeri, S.; Ganesan, P.; Kumar, J.; Biswas, G.; Kilara, N.; Pathalingappa, H.; Prasad, S. V. S. S.; Jain, M.; Mishra, S. K.; Prasad, S.; Boyella, P. K.; Sahoo, R. K.; Bondarde, S.; Shah, S.; Rege, M.; Deb, U.; Korde, T.; Dixit, J.	2024	Future Oncology
Second Line Therapy in Multiple Myeloma: A SEER Medicare Analysis	LeBlanc, M. R.; Zhou, X.; Baggett, C. D.; Tuchman, S. A.; Jensen, C. E.; Lichtman, E. I.; Rubinstein, S. M.	2024	Clinical lymphoma, myeloma & leukemia

Treatment Patterns, Survival, Quality of Life, and Healthcare Resource Use Among Patients With Triple-Class Refractory Multiple Myeloma in US Clinical Practice: Findings From the Connect MM Disease Registry	Lee, H. C.; Ramasamy, K.; Weisel, K.; Abonour, R.; Hardin, J. W.; Rifkin, R. M.; Ailawadhi, S.; Terebelo, H. R.; Durie, B. G. M.; Tang, D.; Joshi, P.; Liu, L.; Jou, Y. M.; Che, M.; Hernandez, G.; Narang, M.; Toomey, K.; Gasparetto, C.; Wagner, L. I.; Jagannath, S.	2023	Clinical lymphoma, myeloma & leukemia
EE496 Cost of Anti-CD38 Monoclonal Antibodies in Combination With Carfilzomib and Dexamethasone for Relapsed Refractory Multiple Myeloma	Lin P1, Petitjean A2, Drea E3, Lin F4	2024	
Teclistamab Improves Patient-Reported Symptoms and Health-Related Quality of Life in Relapsed or Refractory Multiple Myeloma: Results From the Phase II MajesTEC-1 Study	Martin, T. G.; Moreau, P.; Usmani, S. Z.; Garfall, A.; Mateos, M. V.; San-Miguel, J. F.; Oriol, A.; Nooka, A. K.; Rosinol, L.; Chari, A.; Karlin, L.; Krishnan, A.; Bahlis, N.; Popat, R.; Besemer, B.; Martinez-Lopez, J.; Delforge, M.; Trancucci, D.; Pei, L.; Kobos, R.; Fastenau, J.; Gries, K. S.; van de Donk, Nwcj	2024	Clinical lymphoma, myeloma & leukemia
Real-world treatment patterns, healthcare resource use and disease burden in patients with multiple myeloma in Europe	Martinez-Lopez, J.; Bailey, A.; Lambert, A.; Luke, E.; Ribbands, A.; Erler-Yates, N.; Valluri, S.; Haefliger, B.; Gay, F.	2023	Future Oncology
Adjusted comparison of outcomes between patients from CARTITUDE-1 versus multiple myeloma patients with prior exposure to proteasome inhibitors, immunomodulatory drugs and anti-CD38 antibody from the prospective, multinational LocoMMotion study of real-wo	Mateos, M. V.; Weisel, K.; Martin, T.; Berdeja, J. G.; Jakubowiak, A.; Stewart, A. K.; Jagannath, S.; Lin, Y.; Diels, J.; Ghilotti, F.; Thilakarathne, P.; Perualila, N. J.; Cabrieto, J.; Haefliger, B.; Erler-Yates, N.; Hague, C.; Jackson, C. C.; Schecter, J. M.; Strulev, V.; Nesheiwat, T.; Pacaud, L.; Einsele, H.; Moreau, P.	2023	Haematologica
EE162 Healthcare Resource Utilization and 2022 Cost Update of Cytokine Release Syndrome and Neurotoxicity in Patients with Relapsed/Refractory Multiple Myeloma (RRMM) Receiving Idecabtagene Vicleucel (IDE-CEL, BB2121) in KarMMa	McGarvey, N.; Imanak, K.; Carattini, T.; Ung, B.; Campbell, T. B.; Gitlin, M.; Patwardhan, P.	2023	Value in Health

Post-infusion Costs Associated with Idecabtagene Vicleucel Treatment for Patients with Relapsed/Refractory Multiple Myeloma in the KarMMa Trial	McGarvey, N.; Ung, B.; Carattini, T.; Imanak, K.; Lee, A.; Campbell, T. B.; Patwardhan, P.	2023	Advances in Therapy
Treatment Pattern, Healthcare Resource Utilization and Symptom Burden Among Patients with Triple Class Exposed Multiple Myeloma: A Population-Based Cohort Study	Mian, H.; Seow, H.; Pond, G. R.; Gayowsky, A.; Foley, R.; Balistky, A.; Ebraheem, M.; Cipkar, C.; Sapru, H.; Mohyuddin, G. R.; Hadidi, S. A.; Visram, A.	2024	Clinical lymphoma, myeloma & leukemia
Patient-Reported Outcomes in the Phase 3 CARTITUDE-4 Study of Ciltacabtagene Autoleucel Vs Standard of Care in Patients with Lenalidomide-Refractory Multiple Myeloma after 1-3 Lines of Therapy	Mina, R.; Mylin, A. K.; Yokoyama, H.; Magen, H.; Alsdorf, W.; Minnema, M. C.; Shune, L.; Isufi, I.; Harrison, S. J.; Shah, U. A.; et al.	2023	Blood
Impact of elranatamab on quality of life: Patient-reported outcomes from MagnetisMM-3	Mohty, M.; Bahlis, N. J.; Nooka, A. K.; DiBonaventura, M.; Ren, J.; Conte, U.	2024	British Journal of Haematology
Patient-reported frailty phenotype (PRFP) vs. International Myeloma Working Group frailty index (IMWG FI) proxy: A comparison between two approaches to measuring frailty	Murugappan, M. N.; King-Kallimanis, B. L.; Bhatnagar, V.; Kanapuru, B.; Farley, J. F.; Seifert, R. D.; Stenehjem, D. D.; Chen, T. Y.; Horodniceanu, E. G.; Kluetz, P. G.	2024	Journal of Geriatric Oncology
Carfilzomib (in combination with daratumumab and dexamethasone)	NCPE	2024	
Elranatamab	NCPE	2024	
Talquetamab	NCPE	2024	
Teclistamab	NCPE	2024	
Psychosocial Mobile Application (THRIVE-M) for Patients With Multiple Myeloma	Nct	2023	https://clinicaltrials.gov/ct2/show/NCT06073353
TA970 Selinexor with dexamethasone for treating relapsed or refractory multiple myeloma after 4 or more treatments	NICE	2024	
TA974 Selinexor with bortezomib and dexamethasone for previously treated multiple myeloma	NICE	2024	
Single-agent belantamab mafodotin in patients with relapsed/refractory multiple myeloma: Final analysis of the DREAMM-2 trial	Nooka, A. K.; Cohen, A. D.; Lee, H. C.; Badros, A.; Suvannasankha, A.; Callander, N.; Abdallah, A. O.; Trudel, S.; Chari, A.; Libby, E. N.; Chaudhry, M.; Hultcrantz, M.; Kortum,	2023	Cancer

	K. M.; Popat, R.; Sborov, D.; Hakim, S.; Lewis, E.; Gorsh, B.; Bhushan, B.; McKeown, A.; Gupta, I.; Opalinska, J.; Richardson, P. G.; Lonial, S.		
Real-World Health Care Services Utilization Associated With the Management of Patients With Relapsed and Refractory Multiple Myeloma in Spain: The CharisMMa Study	Ocio, E. M.; Montes-Gaisan, C.; Bustamante, G.; Garzon, S.; Gonzalez, E.; Perez-Persona, E.; Gonzalez-Calle, V.; Sirvent, M.; Arguinano, J. M.; Gonzalez, Y.; Rios, R.; de Miguel, D.; Grande, M.; Fernandez-Nistal, A.; Naves, A.; Rosinol, L.	2023	Clinical lymphoma, myeloma & leukemia
The impact of current therapeutic options on the health-related quality of life of patients with relapse/refractory multiple myeloma: a systematic review of clinical studies	Ojo, A. S.; Araoye, M. O.; Ali, A.; Sarma, R.	2024	Journal of cancer survivorship : research and practice
Patient-Reported Outcomes among Multiple Myeloma Patients Treated with Standard of Care Idecabtagene Vicleucel	Oswald, L. B.; Gudenkauf, L. M.; Li, X.; De Avila, G.; Peres, L. C.; Kirtane, K.; Gonzalez, B. D.; Hoogland, A. I.; Nguyen, O.; Rodriguez, Y.; Baz, R. C.; Shain, K. H.; Alsina, M.; Locke, F. L.; Freeman, C.; Castaneda Puglianini, O.; Nishihori, T.; Liu, H.; Blue, B.; Grajales-Cruz, A.; Jim, H. S. L.; Hansen, D. K.	2023	Cancers
Real-World Treatment Patterns, Outcomes, Health Care Resource Utilization and Cost Burden of Multiple Myeloma in South Korea Using the National Claims Data	Park, Y.; Park, S. S.; Yoon, S.; Jeong, J.; Lee, D.; Kim, K.	2023	Blood
PCR73 Sensitivity of EQ-5D to Assess Health-Related Quality of Life (HRQoL) for Triple-Class Exposed (TCE) Relapsed/Refractory Multiple Myeloma (RRMM): karMMa-3 Case Study Exploring EQ-5D Mapped from Disease-Specific Instruments	Paul, E.; McLoone, D.; Eliason, L.; Karampampa, K.; Pepper, A. N.; Cope, S.; Dhanda, D.	2023	Value in health
Facility-Related Healthcare Resource Utilization (HCRU) for Patients Treated with Idecabtagene Vicleucel (Ide-Cel, bb2121) in a Real-World (RW) Setting: A Single-Center Experience	Peres, Lauren C.; Patwardhan, Pallavi; Huggar, David; De Avila, Gabriel; Oswald, Laura B.; Grajales-Cruz, Ariel F.; Blue, Brandon; Abraham Miranda,	2023	Blood

	Julieta; Reid, Kayla; Liu, Hien; Nishihori, Taiga; Shain, Kenneth H.; Baz, Rachid; Alsina, Melissa; Castaneda, Omar; Locke, Frederick L.; Freeman, Ciara Louise L.; Tiwana, Simrandeep; Botros, Afraim; Hansen, Doris K.		
Is it a chimera? A systematic review of the economic evaluations of CAR-T cell therapy - an update	Petrou, P.	2023	Expert Review of Pharmacoeconomics & Outcomes Research
Patient-Reported Outcomes With Belantamab Mafodotin Treatment in Patients With Triple-Class Refractory Multiple Myeloma	Popat, Rakesh; Lonial, Sagar; Voorhees, Peterm; Esposti, Simonadegli; Gorsh, Boris; Gupta, I. R. A.; Opalinska, Joanna; Sapra, Sandhya; Piontek, Trisha; Zangdong, H. E.; et al.	2023	JADPRO: journal of the advanced practitioner in oncology
Improved efficiency of daratumumab treatment of multiple myeloma adopting the subcutaneous route: A micro-costing analysis in three Italian hematology centers	Pradelli, L.; Massaia, M.; Todisco, E.; Gherlinzoni, F.; Furlan, A.; La Targia, M.; Grande, E.; Tripoli, I. E.; Occhipinti, F.; Comello, F.; Iannello, F.; Bellucci, S.	2023	Cancer Medicine
Real-world patient-reported outcomes and concordance between patient and physician reporting of side effects across lines of therapy in multiple myeloma within the USA	Ribbands, A.; Boytsov, N.; Bailey, A.; Gorsh, B.; Luke, E.; Lambert, A.	2023	Supportive Care in Cancer
P43 Cost-Effectiveness of Talquetamab-tgvs Vs Idecabtagene Vicleucel for Triple-Class Exposed Relapsed or Refractory Multiple Myelom	Rong R, Tang T, Shi L	2024	
Comparison of health care costs and resource utilization for commonly used proteasome inhibitor-immunomodulatory drug-based triplet regimens for the management of patients with relapsed/refractory multiple myeloma in the United States	Sanchez, L.; Chari, A.; Cheng, M.; Cherepanov, D.; DerSarkissian, M.; Huang, F.; Stull, D. M.; Dabora, J.; Young, M.; Noga, S. J.; Pi, S.; Zhang, M.; Banatwala, A.; Duh, M. S.; Ailawadhi, S.	2023	Journal of Managed Care & Specialty Pharmacy
Symptoms, Functioning, and Health-Related Quality of Life in Patients with Relapsed/Refractory Multiple Myeloma Treated with Talquetamab: Updated Patient-Reported Outcomes from the Phase 1/2 MonumenTAL-1 Study	Schinke, Carolina; Touzeau, Cyrille; Oriol, Albert; Mateos, MarÃa-Victoria; Stevens, Don A.; Rasche, Leo; Qin, Xiang; Kato, Kelly; Ming, Timothy; Katz, Eva G.;	2023	Blood

	Gries, Katharine S.; Campagna, Michela; Masterson, Tara J.; Hilder, Brandi W.; Tolbert, Jaszianne; Renaud, Thomas; Heuck, Christoph; Moreau, Philippe; San-Miguel, JesÃºs; RodrÃguez Otero, Paula; Chari, Ajai		
Patient-Reported Outcomes (Pro) in Relapsed/ Refractory Multiple Myeloma (Rrmm) Treated with Melflufen and Dexamethasone (Dex) or Pomalidomide (Pom) and Dex: Analyses from the Phase 3 Ocean Study	Schjesvold, F.; Ludwig, H.; Delimpasi, S.; Robak, P.; Mateos, M.; Sandberg, A.; Thuresson, M.; Norin, S.; Richardson, P.; Sonneveld, P.	2023	HemaSphere
Treatment sequences and drug costs from diagnosis to death in multiple myeloma	Seefat, M. R.; Cucchi, D. G. J.; Groen, K.; Donker, M. L.; van der Hem, K. G.; Westerman, M.; Gerrits, A. M.; Beeker, A.; van de Donk, Nwcj; Blommestein, H. M.; Zweegman, S.	2024	European Journal of Haematology
EE14 Cost of Care Comparison of Elranatamab-bcmm and Teclistamab-cqyv in Adult Patients with Relapsed or Refractory Multiple Myeloma (RRMM)	Shah B1, Sandin R2, Liu Y3, Hu Y4, Schepart A5, Hughes D6, Hart J7, Hlavacek P7	2024	
EE428 Budget Impact of Elranatamab-bcmm in Patients with Relapsed or Refractory Multiple Myeloma (RRMM) in the United States	Shah B1, Sandin R2, Liu Y3, Hu Y4, Schepart A5, Hughes D6, Hart J7, Hlavacek P5	2024	
teclistamab (Tecvayli)	SMC2668	2024	
elranatamab (Elrexfio)	SMC2669	2024	
selinexor (Nexpovio)	SMC2673		
Clinical Outcomes of Autologous Hematopoietic Stem Cell Transplant in Multiple Myeloma Patients: A 5-year Experience from a Single Centre in North India	Sood, N.; Tiwari, A. K.; Pabbi, S.; Dikshit, R.; Singh, P.; Ramaswami, A.; Gautam, D.; Singh, M. K.	2023	South Asian Journal of Cancer
HTA82 Adjusting Utilities Using Age and Time-to-Death Decrements in Cost-Effectiveness Analyses: A Case Study in Relapsed and/or Refractory Multiple Myeloma	Su W1, Clayson M2	2024	
Current Health State Affected Patient Preferences More Than Disease Status: A Discrete Choice Experiment in Multiple Myeloma	Tervonen, T.; Duenas, A.; Collacott, H.; Lam, A.; Gries, K. S.; Carson, R.; Trevor, N.; Krucien, N.; He, J.	2023	Value in Health
Health-Related Quality of Life in Patients with Relapsed/Refractory Multiple	Van De Donk, N.; Rasche, L.; Touzeau, C.;	2023	HemaSphere

Myeloma Treated with Talquetamab, a G Protein-Coupled Receptor Family C Group 5 Member D X Cd3 Bispecific Antibody, from Monumental-1	Chari, A.; Schinke, C.; Minnema, M.; Berdeja, J.; Oriol, A.; Rodriguez-Otero, P.; Askari, E.; Mateos, M.; Costa, L.; Caers, J.; Krishnan, A.; Vishwamitra, D.; Ma, J.; Qin, X.; Gries, K. S.; Kato, K.; Campagna, M.; Masterson, T.; Hilder, B.; Tolbert, J.; Renaud, T.; Goldberg, J.; Heuck, C.; Moreau, P.; San-Miguel, J.		
Treatment Patterns and Healthcare Resource Utilization Among Patients with Triple Class Exposed Multiple Myeloma: A Population-Based Cohort Study	Visram, A.; Seow, H.; Pond, G.; Gayowsky, A.; McCurdy, A.; Cipkar, C.; Sapru, H.; Kouroukis, C. T.; Aljama, M.; Ebraheem, M.; Foley, S. R.; Mian, H.	2023	Blood
Evaluation of Outpatient Administration of Ciltacabtagene Autoleucel in Relapsed/Refractory Multiple Myeloma: Single Center Experience	Waqar, S. H. B.; Hansen, D. K.; Freeman, C. L.; De Avila, G.; Harvey, K.; Grajales, A.; Blue, B.; Liu, H.; Baz, R.; Alsina, M.; Shain, K.; Jain, M. D.; Locke, F. L.; Castaneda, O.; Nishihori, T.	2024	Transplantation and Cellular Therapy
Impact of Elotuzumab Plus Pomalidomide/Dexamethasone on Health-related Quality of Life for Patients With Relapsed/Refractory Multiple Myeloma: Final Data From the Phase 2 ELOQUENT-3 Trial	Weisel, K.; Dimopoulos, M. A.; San-Miguel, J.; Paner, A.; Engelhardt, M.; Taylor, F.; Lord-Bessen, J.; Yip, C.; Greenwood, M.; Tang, J.; Cavo, M.	2023	HemaSphere
Patient (pt)-reported outcomes in pts with relapsed/ refractory multiple myeloma (RRMM) treated with belantamab mafodotin (belamaf) vs pomalidomide/low dose dexamethasone (Pd) in the phase III, open-label, randomized, multicenter DREAMM-3 study	Weisel, K.; Hungria, V.; Currie, B.; Perera, S.; Sule, N.; He, W.; McKeown, A.; Sapra, S.; Li, M.; Barale, S.; Boyle, J.; McPoyle, K.; Dimopoulos, M. A.	2023	Oncology Research and Treatment
Cost effectiveness analysis of CAR-T cell therapy for patients with relapsed/refractory multiple myeloma in China	Wu, W.; Ding, S.; Mingming, Z.; Yuping, Z.; Sun, X.; Zhao, Z.; Yang, Y.; Hu, Y.; Dong, H.	2023	Journal of Medical Economics
Cost-Effectiveness of Anti-BCMA Chimeric Antigen Receptor T Cell Therapy in Relapsed/Refractory Multiple Myeloma	Yamamoto, C.; Minakata, D.; Yokoyama, D.; Furuki, S.; Noguchi, A.; Koyama, S.; Oyama, T.; Murahashi, R.; Nakashima, H.; Ikeda, T.; Kawaguchi, S. I.; Hyodo, K.; Toda, Y.;	2024	Transplantation and Cellular Therapy

	Ito, S.; Nagayama, T.; Umino, K.; Morita, K.; Ashizawa, M.; Ueda, M.; Hatano, K.; Sato, K.; Ohmine, K.; Fujiwara, S. I.; Kanda, Y.		
Health care resource utilization and costs among patients with multiple myeloma with exposure to double-class or triple-class multiple myeloma treatments: A retrospective US claims database analysis	Yang, J.; Boytsov, N.; Carlson, J. J.; Barthold, D.	2023	Journal of Managed Care & Specialty Pharmacy
P905: PATIENT REPORTED OUTCOMES IN TRIPLE CLASS EXPOSED, RELAPSED/REFRACTORY MULTIPLE MYELOMA (TCE RRMM) PATIENTS IN KARMMA 3 TRIAL (PHASE 3 RCT): IDECABTAGENE VICLEUCEL (IDE-CEL) VERSUS STANDARD REGIMENS	Michel Delforge, Krina Patel, Laurie Eliason, Devender Dhanda, Ling Shi, Shien Guo, Thomas Marshall, Bertrand Arnulf, Michele Cavo, Ajay Nooka, Salomon Manier, Natalie Callander, Sergio Giralt, Hermann Einsele, Sikander Ailawadhi, Mihaela Popa McKiver, Mark Cook, Paula RodrÃguez-Otero	2023	
P964: PATIENT (PT)-REPORTED OUTCOMES IN PTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM) TREATED WITH BELANTAMAB MAFODOTIN (BELAMAF) VS POMALIDOMIDE/LOW DOSE DEXAMETHASONE (PD) IN THE DREAMM-3 STUDY	Vania Hungria, Katja Weisel, Brooke Currie, Sue Perera, Neal Sule, Wei He, Astrid McKeown, Sandhya Sapra, Linda Nelsen, Mary Li, Sophie Barale, Julia Boyle, Kaytlyn McPoyle, Meletios A. Dimopoulos	2023	
P979: PATIENT-REPORTED OUTCOMES FOR TECLISTAMAB VERSUS REAL-WORLD PHYSICIANâ€™S CHOICE OF THERAPY IN THE LOCOMMOTION STUDY IN PATIENTS WITH TRIPLE-CLASS EXPOSED RELAPSED/REFRACTORY MULTIPLE MYELOMA	Philippe Moreau, Niels W.C.J. van de Donk, Michel Delforge, Hermann Einsele, Valerio De Stefano, Aurore Perrot, Britta Besemer, Charlotte Pawlyn, Lionel Karlin, Salomon Manier, Xavier Leleu, Pushpike Thilakarathne, Joris Diels, Katharine Gries, Nichola Erler-Yates, Kirsten van Nimwegen, RaÃºl Morano, Vadim Strulev, Imene Haddad, Rachel Kobos, Jennifer SMIT, Alexander Marshall, Mary Slavcev, Maria-Victoria Mateos, Katja Weisel	2023	

TA897: Daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma	NICE		
TA870: Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma	NICE		
Elranatamab for treating relapsed or refractory multiple myeloma after 3 therapies [ID4026]	NICE		
SMC2597: belantamab mafodotin (Blenrep)	SMC		
SMC2669: elranatamab (Elrexfio)	SMC		
SMC2668: teclistamab (Tecvayli)	SMC		
The cost of multiple myeloma and its complications: a single-center study from Oran, Algeria	Haouatti, F.; Belhadj, I. K.; Goumidi, A.; Yafour, N.; Houari, T.	2024	Annales Pharmaceutiques Françaises

Table 124. Excluded records by reason for SLR of economic evidence

Title	Authors	Year	Journal
PCR239 Quality of Life (QOL) Instruments Used in Clinicaltrials.gov-Indexed Trials of Gene-Modified Cell Therapy (GMCT) in Patients With Multiple Myeloma (MM)	Cadarette, S.; Arregui Rementeria, M.; Gomez Espinosa, E.; Stewart, F.; Brisibe, T.; Devani, D.; Kistler, K.; Oladapo, T.; Rangi, N. D.; Wissinger, E.	2023	Value in Health
Trends in Medicare Spending on Multiple Myeloma Drugs, 2013 to 2021	Cliff, E. R. S.; McGuire, M.; Mohyuddin, G. R.; Kesselheim, A. S.; Feldman, W. B.	2023	Blood
RWD85 A Systematic Literature Review on the Use of Real-World Evidence in NICE Technology Appraisals Indicated for Multiple Myeloma	Dempsey, J.; Tsang, C.; Duffield, C.	2023	Value in Health
The role of private insurance characteristics in the out-of-pocket costs of patients with multiple myeloma	Gasoyan, H.; Rothberg, M. B.	2023	Journal of Clinical Oncology
Efficacy of Isatuximab Combination Regimens in Patients with Relapsed and Refractory Multiple Myeloma: A Systematic Review and Meta-Analysis of Phase III Randomized Controlled Trials	Htut, T. W.; Phyu, E. M.; Win, M. A.; Thein, K. Z.	2023	Blood
Patient-Reported Outcomes in Patients With Relapsed or Refractory Multiple Myeloma (RRMM) Treated With Belantamab Mafodotin (Belamaf) Versus Pomalidomide Plus Low-Dose Dexamethasone (Pd) in the DREAMM-3 Study	Hungria, V.; Weisel, K.; Currie, B.; Perera, S.; Sule, N.; He, W.; Davy, K.; McKeown, A.; Sapra, S.; Nelsen, L.; et al.	2023	Clinical lymphoma, myeloma & leukemia

HPR106 Pricing of New Oncology Products in the US and Key European Markets	K, Kloc	2024	
HTA158 Exploring Efficiency of Living Systematic Literature Review (SLR) Tool for Submissions of Clinical Evidence to National Institute for Health and Care Excellence (NICE) by Combining Interventional and Real-World Evidence (RWE)	Liu, R.; Agranat, J.; Rizzo, M.; Forsythe, A.	2023	Value in Health
e24029 Trends in hospice utilization and place of death preferences in multiple myeloma-related deaths from 2003 to 2020: Analysis of CDC Wonder database.	Muhammad Salman Faisal, Mahnoor Sukaina, Rahul Mishra, Atulya Aman Khosla, Nitya Batra, Madhan Srinivasan Kumar, Noha Soror, Zain Ishtiaq Ahmad, Karan Jatwani, Faiz Anwer	2024	
Health-Related Quality of Life in Patient/Primary Caregiver Dyads in the Hematopoietic Stem Cell Transplantation Setting: 6-Month Follow up Data from the We'Re in This Together Study	Munshi, P. N.; Fall-Dickson, J.; Assarsson, J.; Beheshtian, S.; Lobo, T.; Chicaiza, A.; Yang, F.; Donato, M. L.; Kaur, S.; Suh, H.; Mathurin, A.; Wang, S.; Ahn, J.; Graves, K.	2023	Transplantation and Cellular Therapy
A phase 3, two-stage, randomized study of mezigdomide, carfilzomib, and dexamethasone (MeziKd) versus carfilzomib and dexamethasone (Kd) in relapsed/refractory multiple myeloma (RRMM): SUCCESSOR-2	Richardson, P. G.; Amatangelo, M.; Berenson, J. R.; Cerchione, C.; Dimopoulos, M. A.; Hansen, C. T.; Hwang, S. J.; Koo, P.; Kuroda, J.; Oriol, A.; et al.	2023	Journal of clinical oncology
Real-World Treatment Outcomes of Teclistamab Under an Outpatient Model for Step-up Dosing Administration	Sandahl, T. B.; Soefje, S. A.; Calay, E. S.; Lin, Y.; Fonseca, R.; Ailawadhi, S.; Parrondo, R.; Lin, D.; Wu, B.; Silvert, E.; Kim, N.; Carpenter, C.; Wagner, T. E.; Fowler, J.; Hester, L.; Marshall, A.; Stoy, P.; Gifkins, D.; Kumar, S. K.	2023	Blood
Real-World Treatment Sequences and Costs of 96 Patients with Multiple Myeloma from Diagnosis to Death	Seefat, M. R.; Cucchi, D. G. J.; Groen, K.; Donker, M. L.; Van Der Hem, K. G.; Westerman, M.; Gerrits, A. M.; Beeker, A.; Van De Donk, N.; Blommestein, H. M.; Zweegman, S.	2023	HemaSphere
7543 Patient-reported outcomes (PROs) from the DREAMM-7 randomized phase 3	Vania Hungria, Pawel Robak, Marek Hus,	2024	

study comparing belantamab mafodotin, bortezomib, and dexamethasone (BVd) vs daratumumab, bortezomib, and dexamethasone (DVd) in patients with relapsed/refractory multiple myeloma	Chengcheng Fu, Vera Zherebtsova, Christopher Ward, Ana Carolina de Almeida, P. Joy Ho, Roman Hajek, Claudio Cerchione, Nicholas Pirooz, Astrid McKeown, Hena Baig, Lydia Eccersley, Farrah Pompilus, Simon McNamara, Chee Paul Lin, Sumita Roy-Ghanta, Joanna Opalinska, Maria-Victoria Mateos		
HTA16 Summary of Economic Evaluations on Onco-Hematology in France By the Has: What Did We Learn?	Boussahoua, M.; Sambuc, C.; Tehard, B.; Chevalier, J.; Midy, F.; Roze, S.	2023	Value in Health
PCR209 Joint Modeling of Progression-Free Survival (PFS) and Patient-Reported Symptoms Among Relapsed/Refractory Multiple Myeloma (RRMM) Patients	Knop S1, Einsele H2, Dhanda D3, Marshall T3, Eliason L3, McLoone D4, Caisip C4, Chen J4, Boehm D3, Dhamane AD3, Ramasamy K5, Cope S6, Towle K4	2024	
Idecabtagene Vicleucel (ideâ€‘cel) Versus Standard Regimens in Patients With Tripleâ€‘Classâ€"Exposed (TCE) Relapsed and Refractory Multiple Myeloma (RRMM): karMMaâ€‘3, a Phase III Randomized Controlled Trial (RCT)	Giralt, S.; Ailawadhi, S.; Arnulf, B.; Patel, K.; Cavo, M.; Nooka, A. K.; Manier, S.; Callander, N.; Costa, L. J.; Vij, R.; et al.	2023	Clinical lymphoma, myeloma & leukemia
SINGLE-AGENT BELANTAMAB MAFODOTIN IN PATIENTS WITH RELAPSED OR REFRACTORY MULTIPLE MYELOMA: FINAL ANALYSIS OF THE DREAMM-2 TRIAL	Nooka, A.; Cohen, A.; Lee, H.; Badros, A.; Suvannasankha, A.; Callander, N.; Abdallah, A.; Trudel, S.; Chari, A.; Libby, E.; et al.	2023	Hemasphere
Idecabtagene Vicleucel (ide-cel) Versus Standard (std) Regimens in Patients (pts) with Triple-Class-Exposed (TCE) Relapsed and Refractory Multiple Myeloma (RRMM): Updated Analysis from KarMMa-3	Otero, P. R.; Ailawadhi, S.; Arnulf, B.; Patel, K. K.; Cavo, M.; Nooka, A. K.; Manier, S.; Callander, N. S.; Costa, L.; Vij, R.; Bahlis, N. J.; Moreau, P.; Solomon, S. R.; Abrahamsen, I. W.; Baz, R.; Broijl, A.; Chen, C.; Jagannath, S.; Raje, N. S.; Scheid, C.; Delforge, M.; Benjamin, R.; Pabst, T.; Iida, S.; Berdeja, J. G.; Truppel-Hartmann, A.; Bhatnagar, R.; Wu, F.; Piasecki, J.; Eliason, L.; Dhanda, D.; Felten, J.; Caia, A.; Cook, M.; Popa-McKiver, M.; Giralt, S. A.	2023	Blood

COST-EFFECTIVENESS OF EARLY VERSUS DELAYED AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT) FOR MULTIPLE MYELOMA (MM)	Kelkar, A.; Midha, S.; Richardson, P.; Anderson, K.; Munshi, N.; Laubach, J.; Ghobrial, I.; Mo, C.; Nadeem, O.; Cliff, E.; Abel, G.; Soiffer, R.; Cutler, C.	2023	Bone Marrow Transplantatio n
EE185 Direct Medical Costs of Multiple Myeloma in Chinese Urban Population: A Nationwide Real-World Study (2012-2016)	(2012-2016), Direct Medical Costs of Multiple Myeloma in Chinese Urban Population: A Nationwide Real-World Study	2024	
Single-agent belantamab mafodotin in patients with relapsed/refractory multiple myeloma: Final analysis of the DREAMM-2 trial	Ramasamy, K.; Nooka, A.; Cohen, A.; Lee, H.; Badros, A.; Suvannasankha, A.; Callander, N.; Abdallah, A. O.; Trudel, S.; Chari, A.; Libby, E.; Chaudhry, M.; Hultcrantz, M.; Kortum, K. M.; Richardson, P.; Popat, R.; Sborov, D.; Hakim, S.; Lewis, E.; Bhushan, B.; Gorsh, B.; Gupta, I.; Opalinska, J.; Lonial, S.	2023	British Journal of Haematology
Association of Selinexor Dose Reductions With Clinical Outcomes in the BOSTON Study	Jagannath, S.; Delimpasi, S.; Grosicki, S.; Van Domelen, D. R.; Bentur, O. S.; Spicka, I.; Dimopoulos, M. A.	2023	Clinical lymphoma, myeloma & leukemia
HPR51 Better Safe Than Sorry? Identification of Drug Combinations for Targeted Price Regulation in German Claims Data	Witte, J.; Gensorowsky, D.; Fritz, M.; Schoenfeldt, F.	2023	Value in Health
Immediate inpatient toxicities associated with CAR T-cell therapy: Real world data from a national inpatient sample	Singh, V.; Al-alwan, A.; Sirpal, V.; Khalid, F.; Gupta, R.; Eltoukhy, H.	2023	Journal of Clinical Oncology
Outcomes Among Hospitalized Patients with Relapsing Multiple Myeloma Utilizing Palliative Care: A United States Population-Based Cohort Study	Arya, Y.; Syal, A.; Casipit, B. A.; Dourado, C.; Mayo, R. J.; Heller, G.	2023	Blood
P25 Association between Adherence to Lenalidomide and Patient-Reported Outcomes in Patients with Multiple Myeloma: A Systematic Literature Search	Ramasamy K1, von Lilienfeld-Toal M2, Maisel C3, Gustavsson B4, BÃ¤ck K5, Glasmacher A6, Leleu X7	2023	
P1978: PATIENT-REPORTED OUTCOMES FROM THE RANDOMIZED PHASE 3 CANOVA STUDY OF VENETOCLAX-DEXAMETHASONE VS POMALIDOMIDE-DEXAMETHASONE IN PATIENTS WITH T(11;14)-POSITIVE	Maria-Victoria Mateos, Meral Beksac, Meletios A. Dimopoulos, Moshe E. Gatt, Francesca Gay, Jae-Cheol Jo, Prashant Kapoor, K Martin	2024	

RELAPSED/REFRACTORY MULTIPLE MYELOMA	Kortum, Silvia Ling, Chandramouli Nagarajan, Kenshi Suzuki, lugui qiu, Eirini Katodritou, Krina Patel, Maika Onishi, Nabanita Mukherjee, Edyta Dobkowska, Allicia Girvan, Emma Arriola, Orlando F. Bueno, Nizar J Bahlis, Shinsuke Iida, Philippe Moreau, Jason Valent, Rakesh Popat		
P945 PATIENT-REPORTED OUTCOMES FROM DREAMM-7 A RANDOMIZED PHASE 3 STUDY OF BELANTAMAB MAFODOTIN, BORTEZOMIB + DEXAMETHASONE (DEX) VS DARATUMUMAB, BORTEZOMIB + DEX IN RELAPSED/REFRACTORY MULTIPLE MYELOMA	Vania Hungria, Pawel Robak, Marek Hus, Chengcheng Fu, Vera Zherebtsova, Christopher Ward, Ana Carolina Almeida, P. Joy Ho, Roman HÃijek, Claudio Cerchione, Nick Pirooz, Astrid McKeown, Hena Baig, Lydia Eccersley, Farrah Pompilus, Simon McNamara, Chee Paul Lin, Sumita Roy-Ghanta, Joanna Opalinska, Maria-Victoria Mateos	2024	
Quality of Life Assessment & Out-of-Pocket Expenditure in Multiple Myeloma: An Observational Study	Pohregaonkar, S.; Akshaykumar, A.; Pohregaonkar, A. S.; Kadam, G.; Talekar, R. S.; Shah, P.	2023	International Journal of Pharmaceutical and Clinical Research
HTA80 Impact of Restricted EU Market Access Decisions on Patient Access To Medicines in Multiple Myeloma	Alleman C1, Katsikostas-Michopoulos G2, Fora B3, Azough A4, Griffin A4, Hickson S5, Rollmann D5, Mckendrick J6	2024	
Treatment Patterns and Outcomes in Patients with Multiple Myeloma Who Received Ixazomib and in Patients with Triple-Class Refractory Multiple Myeloma: A Retrospective, Observational, Real-World Historical Database Analysis Study from China	An, Gang; Li, Lin; Liu, Sha; Qiu, Lugui	2023	Blood
Evaluating Patient-Reported Outcomes and Wearable Data Among Individuals with Relapsed/Refractory Multiple Myeloma	Banerjee, R.; Brassil, K.; Grossfeld, T.; Barr, A.; Cowan, A. J.	2023	Blood
A real-world study of belantamab mafodotin in a heavily pretreated population of multiple myeloma patients	Bird, S.; Bishop, E.; Panopoulou, K.; Saso, R.; Mir, F.; Stern, S.; Kaiser, M.; Boyd, K.; Pawlyn, C.	2023	British Journal of Haematology

Analysis of patient-reported experiences up to 2 years after receiving idecabtagene vicleucel (ide-cel, bb2121) for relapsed or refractory multiple myeloma: Longitudinal findings from the phase 2 KarMMa trial	Delforge, M.; Otero, P. R.; Shah, N.; Moshkovich, O.; Braverman, J.; Dhanda, D. S.; Lanar, S.; Devlen, J.; Miera, M.; Gerould, H.; Campbell, T. B.; Munshi, N. C.	2023	Leukemia Research
Multiple Myeloma Treatment-Related Decision-Making and Preferences of Patients and Care Partners in the United States	Flora, D. R.; Byrd, R.; Platt, D.; Hlavacek, P.; Goldman, E. H.; Cappelleri, J. C.; Kennedy, C. T.; LeBlanc, T. W.	2023	Blood
Identifying Causes of Unscheduled Healthcare Interactions and Changes to Patient Disposition in Individuals Receiving Outpatient Commercial Bispecific Antibody Therapy in Relapsed/Refractory Multiple Myeloma (RRMM)	Howard, A. J.; Shekarkhand, T.; Hamadeh, I. S.; Wang, A.; Patel, D.; Tan, C.; Hultcrantz, M.; Mailankody, S.; Hassoun, H.; Shah, U. A.; Korde, N.; Maclachlan, K. H.; Landau, H.; Scordo, M.; Shah, G. L.; Lahoud, O. B.; Giralt, S. A.; Chung, D.; Lesokhin, A.; Usmani, S. Z.; Firestone, R.	2023	Blood
e19524 Exploring gender-based decision-making differences among patients with relapsed/refractory multiple myeloma.	Mary Arnett, Karla Mariana Castro BÃ³rquez, Jorge Arturo Hurtado MartÃnez, Andrea Isabel Robles Espinoza, Patricia Alejandra Flores PÃ©rez, Andrea Jimena Cuevas Vicencio, Felipe Flores Quiroz, Rachel M. Jensen, Robert Z. Orlowski, Julie Strain, Laura L. Iadeluca, Rachel Solomon, Virginie Delwart, Cynthia Chmielewski, Jennifer M. Ahlstrom, Jay R Hydren	2024	
A Phase 3, Two-Stage, Randomized Study of Mezigdomide, Carfilzomib, and Dexamethasone (Mezikd) Versus Carfilzomib and Dexamethasone (Kd) in Relapsed/Refractory Multiple Myeloma (Rrmm): Successor-2	Md, P. G. R.; Phd, M. A.; Md, J. R. B.; Phd, C. C. M.; Md, M. A. D.; Md, C. T. H.; Phd, J. K. M.; Phd, A. O. M.; Phd, R. Z. O. M.; Hq, M.; Md, M. S. R.; Phd, A. R. M.; Md, D. W.; Phd, Z. Z.; Phd, V. H. M.	2023	Hematology, Transfusion and Cell Therapy
Real-World Treatment Patterns and Clinical Outcomes Among Triple-Class	Mian, H.; Harper, J. S.; Le, H. H.; Fu, A. Z.; Patel,	2023	Blood

Exposed and B- Cell Maturation Antigen (BCMA) Exposed Multiple Myeloma Patients	S. N.; Zhang, X. K.; Fonseca, R.		
TA968 Melphalan flufenamide with dexamethasone for treating relapsed or refractory multiple myeloma (terminated appraisal)	NICE	2024	
Elranatamab monotherapy or with daratumumab for previously treated relapsed or refractory multiple myeloma	NIHRIO	2024	
Personal Financial Burdens of Multiple Myeloma: A Deep Dive into the Patient's Journey Using Qualitative Interview	Park, Y.; Cho, J.; Kim, S.; Kim, K.; Yoon, S. E.; Kang, D.; Bang, G.; Kim, N.; Park, J. H.; Kim, S. J.	2023	Blood
A Phase III, Two-Stage, Randomized Study of Mezigdomide, Bortezomib, and Dexamethasone (MeziVd) Versus Pomalidomide, Bortezomib, and Dexamethasone (PVd) in Relapsed/ Refractory Multiple Myeloma (RRMM): SUCCESSOR-1	Richardson, P. G.; Badelita, S. N.; Besemer, B.; Boudreault, J. S.; Byun, J. M.; Cerchione, C.; Gatt, M. E.; Gibbs, S.; Koroda, J.; Martinez-Lopez, J.; et al.	2023	Clinical lymphoma, myeloma & leukemia
TPS7576 Evaluation of elranatamab vs EPd, PVd, or Kd in patients with relapsed or refractory multiple myeloma and prior anti-CD38â€“directed therapy: MagnetisMM-32.	Steven Robert Schuster, Satoshi Ito, Margaret Hoyle, Anne Yver, Fangxin Hong, Gregory Finn	2024	
MajesTEC-9: A randomized phase 3 study of teclistamab versus pomalidomide, bortezomib, and dexamethasone or carfilzomib and dexamethasone in patients with relapsed/refractory multiple myeloma	Touzeau, C.; Hungria, V. T. M.; Bhutani, D.; Landgren, O.; Vieyra, D.; Guo, Y.; Verona, R.; Miao, X.; Qi, M.; Watkins, L.; Shah, P.; Chastain, K.; Quach, H.	2023	Journal of Clinical Oncology
P886: EFFICACY, SURVIVAL AND SAFETY OF SELINEXOR, BORTEZOMIB AND DEXAMETHASONE (SVD) IN PATIENTS WITH LENALIDOMIDE-REFRACTORY MULTIPLE MYELOMA: SUBGROUP DATA FROM THE BOSTON TRIAL	Maria-Victoria Mateos, Monika Engelhardt, Xavier Leleu, Mercedes Gironella Mesa, Holger W. Auner, Michele Cavo, Meletios A. Dimopoulos, Martina Bianco, Giovanni Marino Merlo, Charles la Porte, Philippe Moreau	2023	
P904: LOCOMMOTION: A PROSPECTIVE, OBSERVATIONAL, MULTINATIONAL STUDY OF REAL-LIFE CURRENT STANDARDS OF CARE IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMAâ€“ FINAL ANALYSIS AT 2-YEAR FOLLOW-UP	Philippe Moreau, Katja Weisel, Valerio De Stefano, Hartmut Goldschmidt, Michel Delforge, Mohamad Mohty, Joanne Lindsey-Hill, Dominik Dytfeld, Emanuele Angelucci, Laure Vincent, Aurore Perrot, Reuben Benjamin, Niels W.C.J.	2023	

	van de Donk, Enrique Ocio, Ester in 't Groen-Damen, Tito Roccia, Jordan Schecter, Imene Haddad, Vadim Strulev, Lada Mitchell, Jozefien Buyze, Silva Saarinen, Octavio Costa Filho, Hermann Einsele, Maria-Victoria Mateos		
P922: ADJUSTED COMPARISONS OF CILTACABTAGENE AUTOLEUCEL WITH THERAPIES FROM REAL-WORLD CLINICAL PRACTICE: TWO-YEAR FOLLOW-UP ANALYSES FROM CARTITUDE-1 AND THE PROSPECTIVE LOCOMMOTION STUDY	Maria-Victoria Mateos, Katja Weisel, Tom Martin, Jesus Berdeja, Andrzej Jakubowiak, Keith Stewart, Sundar Jagannath, Yi Lin, Joris Diels, Francesca Ghilotti, Pushpike Thilakarathne, Nolen Perualila, Jedelyn Cabrieto, Nichola Erler-Yates, Carolyn C Jackson, Jordan Schecter, Vadim Strulev, Imene Haddad, Octavio Costa Filho, Lida Pacaud, Hermann Einsele, Philippe Moreau	2023	
P927: ACTUAL USAGE OF CURRENT SYSTEMIC TREATMENTS AND INFLUENCE OF KEY DRIVERS FOR MULTIPLE MYELOMA IN THE FIRST 2 LINES OF THERAPY. DATA FROM	Nicolas Blin, Siegfried Ertl, Elodie Schneider, Christine Mai	2023	
EXCALIBER-RRMM: A phase 3, two-stage study of iberdomide, daratumumab, and dexamethasone (IberDd) versus daratumumab, bortezomib, and dexamethasone (DVd) in patients (pts) with relapsed/refractory multiple myeloma (RRMM)	Lonial, Sagar; Quach, Hang; Dimopoulos, Meletios A.; RodrÃguez-Otero, Paula; Berdeja, Jesus G.; Richardson, Paul G.; Kyada, Margee; Chu, Shuyu; Chen, Min; Abad, Patricia C.; Morando, Juliane; van de Donk, Niels W. C. J.	2023	Journal of Clinical Oncology
Open label single arm study to assess the implementation of home based daratumumab administration in patients being treated for multiple myeloma	Binder, Adam F.; Martinez-Outschoorn, Ubaldo E.; Wilde, Lindsay; Kasner, Margaret T.; Keiffer, Gina; Filicko-O'Hara, Joanne E.; Bi, Xia; Gergis, Usama; Rising, Kristin; Porcu, Pierluigi	2023	Journal of Clinical Oncology
Patient and Caregiver Experience Decision Factors in Treatment Decision Making: Results of a Systematic Literature Review of Multiple Myeloma Decision Aids	Choon-Quinones, M.; Hose, D.; Kalo, Z.; Zelei, T.; Harousseau, J. L.;	2023	Value in Health

	Durie, B.; Keown, P.; Barnett, M.; Jakab, I.		
Benefits of switching from intravenous to subcutaneous daratumumab: Perspectives from UK healthcare providers	Cook, G.; Ashcroft, J.; Fernandez, M.; Henshaw, S.; Khalaf, Z.; Pratt, G.; Tailor, A.; Rabin, N.	2023	Frontiers in Oncology
Treatment patterns of triple-class refractory (TCR) multiple myeloma (MM) across the United States (US), Canada, and western Europe: A real-world observational chart review study	Goyal, R. K.; Frugier, G.; Rombi, J.; Esterberg, L.; Davis, K. L.; Hlavacek, P.; Ren, J. M.; Schepart, A.; Aydin, D.; DiBonaventura, M.	2023	Journal of Clinical Oncology
Real-world treatment patterns of triple-class refractory (TCR) multiple myeloma (MM) across the United States (US), Canada, and western Europe: A retrospective chart study	Guillaume, X.; Horchi, D.; Gomez, J.; Hlavacek, P.; Ren, J. M.; Schepart, A.; Aydin, D.; DiBonaventura, M.	2023	Journal of Clinical Oncology
EE73 Ocean (OP-103): Patients with Relapsed/Refractory Multiple Myeloma Treated with Melflufen Plus Dexamethasone or Pomalidomide Plus Dexamethasone - a Resource Utilization Analysis of Adverse Events Leading to Hospitalizations	Hellem Schjesvold F1, Ludwig H2, Delimpasi S3, Robak P4, Mateos MV5, Sandberg A6, ObermÃ¼ller J6, Norin S6, Richardson PG7, Sonneveld P8	2023	
Unscheduled healthcare interactions in multiple myeloma patients receiving T cell redirection therapies	Howard, A. J.; Concepcion, I.; Wang, A. X.; Hamadeh, I. S.; Hultcrantz, M. L.; Mailankody, S.; Tan, C. R.; Korde, N.; Lesokhin, A. M.; Hassoun, H.; Shah, U. A.; Maclachlan, K. H.; Rajeeve, S.; Landau, H. J.; Scordo, M.; Shah, G. L.; Lahoud, O. B.; Chung, D. J.; Giralt, S. A.; Usmani, S. Z.; Firestone, R. S.	2024	Blood Advances
HSD57 Treatment Patterns and Healthcare Resource Utilization in Patients with Relapsed/Refractory Multiple Myeloma (RRMM) on Second and Third Line (2L/3L) Therapy, Classified By Urbanicity and Ethnicity	Molinari, A.; Boytsov, N.; Tkacz, J.; Wang, P. F.; Perera, S.; Norris, K.; Landi, S.; Gorsh, B.	2023	Value in Health
CO120 Real-World Effectiveness of Monoclonal Antibodies for Patients with Multiple Myeloma: A Systematic Literature Review	Lai JH, Kenawy AS, Aiyeolemi AA, Russo AJ, Sohn TJ, Chen S, Rascati KL, AvanceÃ±a A	2023	
OUTCOMES OF IDECABTAGENE VICLEUCEL IN RELAPSED AND REFRACTORY MULTIPLE MYELOMA PREVIOUSLY TREATED WITH BELANTAMAB MAFODOTIN	Melody, M.; Przybylski, D.; Robinson, A.; Lin, A.; Gordon, L.; Adekola, K.; Singhal, S.; Mehta, J.; Moreira, J.	2023	Bone Marrow Transplantatio n

PCR134 Psychometric Properties of the Multiple Myeloma Symptom and Impact Questionnaire (MySIm-Q) in Patients with Relapsed/Refractory Multiple Myeloma (MM): Analysis of Phase 2 CARTITUDE-2 Study Cohorts A, B, and C	Mateos MV1, Cohen AD2, Cohen YC3, Agha M4, San-Miguel J5, Richard S6, van de Donk NWCJ7, De Champlain A8, Katz EG8, Iaconangelo C9, De Braganca KC10, Schecter JM10, Varsos H10, Corsale C10, Deraedt W11, Koneru M12, Costa Filho O12, Akram M12, Gries KS8	2024	
Measuring Frailty Using Patient-Reported Outcomes (PRO) Data: A Feasibility Study in Patients with Multiple Myeloma	Murugappan, M. N.; King-Kallimanis, B. L.; Bhatnagar, V.; Kanapuru, B.; Farley, J. F.; Seifert, R. D.; Stenehjem, D. D.; Chen, T. Y.; Horodniceanu, E. G.; Kluetz, P. G.	2023	Quality of Life Research
Patient (pt) Experiences of Receiving Idecabtagene Vicleucel (Ide-Cel, bb2121) Versus Standard (Std) Regimens for the Treatment (Tx) of Relapsed/Refractory Multiple Myeloma (RRMM) in the Randomized, Controlled KarMMa-3 Clinical Trial: Analysis of Longitud	Rodriguez Otero, P.; Patel, K. K.; Raje, N. S.; Moshkovich, O.; Gerould, H.; Devlen, J.; Dhanda, D.; Eliason, L.; Cook, M.; Popa-McKiver, M.; Manier, S.	2023	Blood
Efficacy and safety of elranatamab in patients with relapsed/refractory multiple myeloma (RRMM) and prior B-cell maturation antigen (BCMA)-directed therapies: A pooled analysis from MagnetisMM studies	Nooka, A. K.; Lesokhin, A. M.; Mohty, M.; Niesvizky, R.; Maisel, C.; Arnulf, B.; Larson, S. M.; Yanovsky, A. V.; Leleu, X. P.; Karlin, L.; Vesole, D. H.; Bahlis, N. J.; de Larrea, C. F.; Raje, N. S.; Leip, E.; Conte, U.; Elmeliegy, M.; Viqueira, A.; Manier, S.	2023	Journal of Clinical Oncology
Epidemiology and Predictors of 30-Day Readmission in CAR-T Cell Therapy Recipients	Sharma, A.; Singh, V.; Deol, A.	2023	Transplantation and Cellular Therapy
Drug Expenditure, Price, and Utilization in US Medicaid: A Trend Analysis for New Multiple Myeloma Medications from 2016 to 2022	Alrasheed, M.; Alsuhibani, A.; Balkhi, B.; Guo, J. J.	2023	Healthcare
Exploring Symptom Burden, Treatment Bother, Physical Function, and Quality of Life By Frailty Status in Patients with Multiple Myeloma	Coombs, N. C.; Beamon, E.; Rusli, E.; Wujcik, D.; Galaznik, A.; Jamy, O.	2023	Blood
A patient survey indicates quality of life and progression-free survival as equally important outcome measures in multiple myeloma clinical trials	Fleischer, A.; Zapf, L.; Allgaier, J.; Jordan, K.; Gelbrich, G.; Pryss, R.; Schobel, J.; Bittrich, M.; Einsele, H.; Kortum, M.;	2023	Journal of Cancer Research and Clinical Oncology

	Maatouk, I.; Weinhold, N.; Rasche, L.		
EPH236 Hospitalizations Related to Cytopenias Among the Multiple Myeloma Adult Inpatient Population in the United States	Gorbatov, M.; Lee, A.; Imanak, K.; Gitlin, M.; McGarvey, N.	2023	Value in Health
RWD20 Health Care Resource Utilization Patterns in Finnish Multiple Myeloma Patients: A Population-Based Cohort Study	Metsa, R.; Kosunen, M.; Ruotsalainen, J.; Purmonen, T.; Raittinen, P.; Kallio, A.	2023	Value in Health
P1671: CARFILZOMIB-DEXAMETHASONE MAINTENANCE HAMPERS RECOVERY AFTER SALVAGE AUTOLOGOUS STEM CELL TRANSPLANTATION IN PATIENTS WITH MULTIPLE MYELOMA	Lene Kongsgaard Nielsen, Fredrik Schjesvold, SÃ¶ren MÃ¶ller, Nina Guldbrandsen, Markus Hansson, Kari Remes, Valdas PeÄeliÅ«nas, Henrik Gregersen, Madeleine King, Niels Abildgaard	2023	
Financial Toxicity and Time Toxicity in Multiple Myeloma: Prevalence, Predictors, and Impact on QOL	Banerjee, R.; Cowan, A. J.; Chavez-Ortega, M.; Carpenter, P. A.; Ueda Oshima, M.; Salit, R. B.; Vo, P. T.; Lee, C. J.; Mehta, R. S.; Kuderer, N. M.; Shankaran, V.; Lee, S. J.; Su, C. T.	2023	Blood
Changes in income and employment after diagnosis among patients with multiple myeloma in The Netherlands	Bennink, C.; Brink, M.; Duijts, S. F. A.; Scheurer, H.; Sonneveld, P.; Blommestein, H. M.	2024	Clinical lymphoma, myeloma & leukemia
Health-related quality of life and quality-adjusted progression free survival for carfilzomib and dexamethasone maintenance following salvage autologous stem-cell transplantation in patients with multiple myeloma: a randomized phase 2 trial by the Nordic	Nielsen, L. K.; Schjesvold, F.; Moller, S.; Guldbrandsen, N.; Hansson, M.; Remes, K.; Peceliunas, V.; Abildgaard, N.; Gregersen, H.; King, M. T.	2024	Journal of patient-reported outcomes
Financial Toxicity, Time Toxicity, and Quality of Life in Multiple Myeloma	Banerjee, R.; Cowan, A. J.; Ortega, M.; Missimer, C.; Carpenter, P. A.; Oshima, M. U.; Salit, R. B.; Vo, P. T.; Lee, C. J.; Mehta, R. S.; Kuderer, N. M.; Shankaran, V.; Lee, S. J.; Su, C. T.	2024	Clinical lymphoma, myeloma & leukemia
Patient-Reported Outcomes in Long-Term Survivors of Autologous Hematopoietic Cell Transplantation in Multiple Myeloma	Chakraborty, R.; Yi, J.; Rybicki, L.; Preussler, J.; Deol, A.; Loren, A.; Savani, B.; Jim, H. S. L.; Cerny, J.; Reynolds, J.; Whitten, J.; Wingard, J. R.; McGuirk, J. P.;	2023	Transplantatio n and Cellular Therapy

	Uberti, J.; Khera, N.; Stiff, P.; Jaglowski, S. M.; Hashmi, S.; Holtan, S. G.; Devine, S.; Hahn, T.; Whalen, V. L.; Saber, W.; Wood, W.; Baker, K. S.; Syrjala, K.; Majhail, N. S.		
Multiple Myeloma and DALY in the USA: Insights of the Global Burden of Disease	Cuartas, M.; Pan, C. W.	2023	Blood
Trajectories of quality of life recovery and symptom burden after autologous hematopoietic cell transplantation in multiple myeloma	D'Souza, A.; Brazauskas, R.; Stadtmauer, E. A.; Pasquini, M. C.; Hari, P.; Bashey, A.; Callander, N.; Devine, S.; Efebera, Y.; Ganguly, S.; et al.	2023	American journal of hematology
Health-related quality of life and use of medication with anticholinergic activity in patients with multiple myeloma	de Lima, M. S. R.; de Padua, C. A. M.; de Miranda Drummond, P. L.; Silveira, L. P.; Malta, J. S.; Dos Santos, R. M. M.; Reis, A. M. M.	2023	Supportive Care in Cancer
Health-related quality of life and its determinants among cancer patients: evidence from 12,148 patients of Indian database	Dixit, J.; Gupta, N.; Kataki, A.; Roy, P.; Mehra, N.; Kumar, L.; Singh, A.; Malhotra, P.; Gupta, D.; Goyal, A.; Rajsekar, K.; Krishnamurthy, M. N.; Gupta, S.; Prinja, S.	2024	Health & Quality of Life Outcomes
Patients' Perception of Usability and Utility of a Digital Health Tool for Electronic Patient-Reported Outcomes Monitoring in Real-Life Hematology Practice: Evidence from the Gimema-Alliance Platform	Efficace, F.; Luppi, M.; Potenza, L.; Sparano, F.; Caocci, G.; Fazio, F.; Breccia, M.; Petrucci, M. T.; Patriarca, A.; Baldi, T.; Santopietro, M.; Battistini, R.; Tafuri, A.; Margiotta Casaluci, G.; Colaci, E.; Giusti, D.; Pioli, V.; De Fabritiis, P.; Ardu, N. R.; Niscola, P.; Mulas, O.; Fozza, C.; Siragusa, S.; Mancuso, S.; Boggione, P.; De Paoli, L.; Leporace, A. P.; Bianchi, M. P.; Carmosino, I.; Cartoni, C.; Di Rocco, A.; Capodanno, I.; Pini, M.; Romano, A.; Fazi, P.; Vignetti, M.	2023	Blood
Changing Care Journey for Patients with Multiple Myeloma in the United States	Flora, D. R.; Byrd, R.; Platt, D.; Hlavacek, P.; Goldman, E. H.; Cappelleri, J. C.; Kennedy, C. T.; LeBlanc, T. W.	2023	Blood

Financial Burden Is Associated with Postponing Care and Decreasing Physical and Emotional Quality of Life Among Patients with Multiple Myeloma and Chronic Lymphocytic Leukemia	Fortune, Erica E.; Miller, Melissa F.; Kranzler, Elissa C.; Ackourey, Jemeille; Clark, Kelly; Badt, Heather; Bohannon, Linda; Cole, Craig E.; Leblanc, Thomas W.; Zaleta, Alexandra K.	2020	Blood
Quality of Life in Adult Patients with Hematological Malignancy- Treading a Road Less Travelled	Garg, A.; Nair, K.; Mukundan, M.; Kumar, P.; Purohit, A.	2023	Indian Journal of Hematology and Blood Transfusion
Association of measures of socioeconomic deprivation with healthcare utilization in elderly patients enrolled in SWOG cancer clinical trials	Hershman, D. L.; Vaidya, R.; Till, C.; Barlow, W. E.; LeBlanc, M. L.; Ramsey, S. D.; Unger, J. M.	2023	Journal of Clinical Oncology
Longitudinal patient-reported outcomes in patients receiving chimeric antigen receptor T-cell therapy	Johnson, P. C.; Dhawale, T.; Newcomb, R. A.; Amonoo, H. L.; Lavoie, M. W.; Vaughn, D.; Karpinski, K.; El-Jawahri, A.	2023	Blood Advances
SERIAL QUALITY OF LIFE EVALUATIONS OF MYELOMA PATIENTS TREATED WITH UPFRONT ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOLLOWED BY BORTEZOMIB MAINTENANCE	Lamore, K.; LeBlanc, R.; Roy, J.; Ahmad, I.; Ogez, D.	2023	Bone Marrow Transplantatio n
Patterns of follow-up care in adult blood cancer survivors-Prospective evaluation of health-related outcomes, resource use, and quality of life	Lax, H.; Baum, J.; Lehmann, N.; Merkel-Jens, A.; Beelen, D. W.; Jockel, K. H.; Duhrsen, U.	2024	Cancer Medicine
Impact of Geriatric Assessment and Management on Quality of Life, Unplanned Hospitalizations, Toxicity, and Survival for Older Adults With Cancer: the Randomized 5C Trial	Puts, M.; Alqurini, N.; Strohschein, F.; Koneru, R.; Szumacher, E.; Mariano, C.; Monette, J.; Hsu, T.; Brennenstuhl, S.; McLean, B.; et al.	2023	Journal of clinical oncology
Predictors of health-related quality of life of the patients treated for MM: the first study in the Palestinian healthcare system	Shawahna, R.; Amer, R.; Salameh, H.; Shawahna, A. R.; Aljondy, M.; Zain-Aldain, M.	2023	Annals of Hematology
Cost Analysis for Multiple Myeloma (MM) Patients Undergoing to First Autologous Hematopoietic Stem Cell Transplant at a Philanthropic Center in Sao Paulo, Brazil	Silva, C. C.; Malheiro, D. T.; Vogel, C.; Kerbauy, L. N.; Kerbauy, M. N.; Ribeiro, A. F.; Lopes, D. O.; Yamazaki Centrone, A. F.; Waisbeck, T. M.; Sa, G. R.; Silva Costa, C. D.; Arcuri, L. J.; Teich, V. D.; Hamerschlak, P. N.	2023	Transplantatio n and Cellular Therapy
EE148 The Institutional Level Impact of Additional Apheresis Days for Multiple	Skaar J1, Lessor J2	2024	

Myeloma Patients Undergoing Autologous Stem Cell Transplantation on Costs and Healthcare Resource Utilization			
e19528 Cost effective utilization of apheresis for stem cell transplantation in multiple myeloma.	Srinivas S. Devarakonda, Arti Vaishnav, Qiuhong Zhao, Naresh Bumma, Francesca Cottini, Nidhi Sharma, Elvira Umyarova, Ashley Elizabeth Rosko, Don M. Benson, Abdullah Mohammad Khan	2024	
Patient-reported symptoms and diagnostic journey in Multiple Myeloma	Vijjhalwar, R.; Song, K.; Shrestha, R.; Bowcock, S.; Sanchez-Santos, M. T.; Ramasamy, K.; Javaid, M. K.	2023	Frontiers in Oncology
Real-world evidence of multiple myeloma treated from 2013 to 2019 in the Hospital District of Helsinki and Uusimaa, Finland	Vikkula, J.; Uusi-Rauva, K.; Ranki, T.; Toppila, I.; Aalto-Setala, M.; Pousar, K.; Vassilev, L.; Porkka, K.; Silvennoinen, R.; Bruck, O.	2023	Future Oncology
Repetitive transcranial magnetic stimulation for chemotherapy-induced peripheral neuropathy in multiple myeloma: A pilot study	Yan, Z.; Cao, W.; Miao, L.; Li, J.; Wang, H.; Xu, D.; Yu, H.; Zhu, Y.	2023	SAGE Open Medicine
e19519 Hospitalizations for multiple myeloma in the United States from 2011 to 2019: An analysis of trends and disparities.	Zeeshan Solangi, Emeka Agudile, Arun Kumar, Ghulam Shah, Amirta Devi, Yusuf Yalcin, Ahda Solangi, Olga N. Kozyreva, Darren M. Evanchuk	2024	
Multiple myeloma patients undergoing chemotherapy: Which symptom clusters impact quality of life?	Zeng, L.; Huang, H.; Qirong, C.; Ruan, C.; Liu, Y.; An, W.; Guo, Q.; Zhou, J.	2023	Journal of Clinical Nursing
Caregiver Quality of Life: Satisfaction and Burnout	Blom, C.; Reis, A.; Lencastre, L.	2023	International Journal of Environmental Research and Public Health
Health-related quality of life in patients with multiple myeloma treated in the phase 3 ATLAS trial of post-transplant maintenance with carfilzomib, lenalidomide, dexamethasone or lenalidomide alone	Kubicki, T.; Jamroziak, K.; Robak, P.; Czyz, J.; Tyczynska, A.; Druzd-Sitek, A.; Giannopoulos, K.; Wrobel, T.; Nowicki, A.; Szczepaniak, T.; Lojko-Dankowska, A.; Matuszak, M.; Gil, L.; Pula, B.; Szukalski, L.; Konska, A.; Zaucha, J. M.; Walewski, J.; Mikulski, D.; Czabak, O.;	2024	Polish Archives Of Internal Medicine

	Robak, T.; Kruk-Kwapisz, D.; Derman, B. A.; Major, A.; Jakubowiak, A. J.; Dytfeld, D.		
P1680: HEALTH-RELATED QUALITY OF LIFE IN TRANSPLANT-INELIGIBLE REAL-LIFE MULTIPLE MYELOMA PATIENTS TREATED WITH FIXED-DURATION BORTEZOMIB-MELPHALAN-PREDNISONE VS. CONTINUOUS LENALIDOMIDE-DEXAMETHASONE	Mattia D'Agostino, Sara Bringhen, Nicola Giuliani, Elisabetta Antonioli, Renato Zambello, Francesco Cattel, Roberto Ria, Alessandro Allegra, Giovanna Leonardi, ANGELO BELOTTI, Piero Galieni, Gloria Margiotta-Casaluci, Maria Cantonetti, Valentina Cotugno, barbara gamberi, Fabrizio Pane, anna marina liberati, Patrizia Tosi, Maide Maria Cavalli, Donato Mannina, Giulia Benevolo, Silvia Mangiacavalli, Andrea Evangelista, Giovannino Ciccone, Mario Boccadoro, Benedetto Bruno, Alessandra Larocca	2023	
Health care costs among patients with hematologic malignancies receiving allogeneic transplants: a US payer perspective	Maziarz, R. T.; Gergis, U.; Edwards, M. L.; Song, Y.; Liu, Q.; Anderson, A.; Signorovitch, J.; Manghani, R.; Simantov, R.; Shin, H.; Sivaraman, S.	2024	Blood Advances
Healthcare Utilization Outcomes of Outpatient CAR-T Cell Therapy with Remote Patient Monitoring Program	Paludo, J.; Bansal, R.; Hathcock, M.; Pritchett, J. C.; De Menezes Silva Corraes, A.; Oyarzabal, B. A.; Harmsen, W. S.; Lunde, J. J.; Coffey, J. D.; Haugen, K. L.; Spychalla, M.; Khurana, A.; Alkhateeb, H.; Dingli, D.; Hayman, S. R.; Kapoor, P.; Gertz, M. A.; Wang, Y.; Binder, M.; Hampel, P. J.; Kenderian, S. S.; Kourelis, T.; Kumar, S. K.; Shah, M. V.; Siddiqui, M. A.; Warsame, R. M.; Villasboas, J. C.; Bennani, N. N.; Johnston, P. B.; Ansell, S. M.; Haddad, T. C.; Lin, Y.	2023	Blood

Effectiveness, Safety, and Cost Implications of Outpatient Autologous Hematopoietic Stem Cell Transplant for Multiple Myeloma	Marini, J.; Maldonado, A.; Weeda, E.; Neppalli, A.; Hashmi, H.; Edwards, K.	2023	Hematology/ Oncology and Stem Cell Therapy
Outpatient practice utilization for CAR-T and T cell engager in patients with lymphoma and multiple myeloma	Bansal, R.; Paludo, J.; Corraes, A. D. S.; Megan, S.; Khurana, A.; Hampel, P. J.; Durani, U.; Dingli, D.; Hayman, S. R.; Kapoor, P.; Wang, Y. C.; Binder, M.; Kourelis, T.; Kumar, S.; Warsame, R. M.; Bennani, N. N.; Gertz, M. A.; Johnston, P. B.; Ansell, S. M.; Lin, Y.	2023	Journal of Clinical Oncology
Health-Related Quality of Life in Multiple Myeloma Patients Treated with High- or Low-Dose Lenalidomide Maintenance Therapy after Autologous Stem Cell Transplantation-Results from the LenaMain Trial (NCT00891384)	Boquoi, A.; Giagounidis, A.; Goldschmidt, H.; Heinsch, M.; Rummel, M. J.; Kroger, N.; Mai, E. K.; Strapatsas, J.; Haas, R.; Kobbe, G.	2023	Cancers
Assessment of Multiple Myeloma-Related Burden on Caregivers - a Portuguese National Study	Costa, C. B.; Neves, M.; Roque, A. I.; Sarmento-Ribeiro, A. B.; Gerivaz, R.; Tome, A.; Afonso, S.; Santos, J. S.; Afonso, C.; Afonso, A. V.; Freitas, J.; Ramos, I.; Sousa, P.; Cesar, P.; Garrido, T.; Rochate, D.; Silveira, M. P.; Pestana, C.; Geraldes, C.; Bergantim, R.; Joao, C.	2023	Blood
A Randomized Controlled Trial of a Financial Navigation Program for Patients with Multiple Myeloma	Djulbegovic, M.; Doherty, M.; Fanslau, K.; Chen, K.; Girgis, S.; Joslyn, P.; Carney, S.; Mitchell, J.; Etzweiler, A.; Vogl, D. T.; Cohen, A. D.; Garfall, A. L.; Waxman, A.; Susanibar-Adaniya, S.; Frosch, Z. A.; Long, Q.; Glanz, K.; Stadtmauer, E. A.	2023	Blood
The impact of divergent forms of social support on health-related quality of life in patients with multiple myeloma and its precursor states	Greinacher, A.; Kuehl, R.; Mai, E. K.; Goldschmidt, H.; Wiskemann, J.; Fleischer, A.; Rasche, L.; Dapunt, U.; Maatouk, I.	2024	Journal of Cancer Research & Clinical Oncology
Health-Related Quality of Life (HRQoL) in Patients with Genetic Standard and High-Risk Disease at Trial Entry: A Cross-Sectional Analysis of RADAR (UK-MRA Myeloma XV)	Lecat, C. S.; Chant, A.; McCourt, O.; Meads, D.; Cicero, R.; Royle, K. L.; Bygrave, C.; Chantry, A.; Chapman, M. A.; Cook,	2023	Blood

	G.; Dawkins, B.; Drayson, M.; Jackson, G.; Jenner, M. W.; Kaiser, M. F.; Mehta, D.; Owen, R.; Popat, R.; Parrish, C.; Pratt, G.		
Psychometric Evaluation of the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30-Items and Myeloma 20-Item Module in Multiple Myeloma Patients	Romero, H.; Mazerolle, F.; Cherepanov, D.; Alin, T.; Jean-Pierre, P.; Regnault, A.	2023	Value in Health
Burden of multiple myeloma in China: an analysis of the Global Burden of Disease, Injuries, and Risk Factors Study 2019	Liu, J.; Liu, W.; Mi, L.; Cai, C.; Gong, T.; Ma, J.; Wang, L.	2023	Chinese Medical Journal
Psychometric properties of the Chilean version of the quality of life questionnaire for multiple myeloma	Lorca, L. A.; Sacomori, C.; Pena, C.; Barrera, C.; Salazar, M.; Leao, I.; Valladares, X.; Rojas, C.	2024	Revista Brasileira de Enfermagem
Patient-reported symptoms and diagnostic journey in multiple myeloma	Vijjhalwar, R.; Song, K.; Bowcock, S.; Ramasamy, K.; Javaid, K.	2023	British Journal of Haematology
P1675 QUALITY OF LIFE OF PORTUGUESE MULTIPLE MYELOMA PATIENTS AND ITS RELATIONSHIP WITH CAREGIVERS â€“ A NATIONAL STUDY	Adriana Roque, Carlos Costa, Manuel Neves, Ana Bela Sarmento-Ribeiro, Rita Gerivaz, Ana Luisa Tome, Helena Martins, Joana Ramos Vieira, Sofia Afonso, Joana Saraiva Santos, Celina Afonso, Ana Jorge, JosÃ© Freitas, InÃªs Ramos, PatrÃcia Sousa, Paula Cesar, Teresa Garrido, DINA SILVA, Maria Pedro Barata Valadao Silveira, Fernanda Trigo, Rui Bergantim, Cristina JoÃ£o, Catarina Isabel Batista Geraldes Santos	2024	
The effect of exercise interventions on quality of life in patients with multiple myeloma: a systematic review and meta-analysis of randomised controlled trials	Goodhew, R. E.; Edwards, B. A.	2023	Clinical & Experimental Medicine
The unknown impact of multiple myeloma: assessing the impact of financial well-being on quality of life of caregivers	Metin, T.; Ugur, O.; Ozdemir, S. C.; Gonderen, A.; Sunu, C.	2023	Supportive Care in Cancer
Global Burden and Trends of Multiple Myeloma in High-Income North America Countries between 1990-2019, with Projections of Deaths to 2040: A Benchmarking Analysis for the Global Burden of Disease Study 2019	Gadhiya, D.; Amin, V.; Kamani, Y.; Mahesh, G.; Kotak, K.; Ratheesh, R.; Desai, H. D.	2023	Blood

On-demand plerixafor added to high-dose cyclophosphamide and pegylated recombinant human granulocyte colony-stimulating factor in the mobilization of patients with multiple myeloma: a treatment with high effectiveness, convenient, and affordable cost	Hou, L. Q.; Liu, J. R.; Gu, J. L.; Chen, M. L.; Kuang, L. F.; Huang, B. H.; Zou, W. Y.; Li, J.	2023	Frontiers in Oncology
The economic impact of cancer mortality among working-age individuals in Brazil from 2001 to 2030	De Camargo Cancela, M.; Monteiro dos Santos, J. E.; Lopes de Souza, L. B.; Martins, L. F. L.; Bezerra de Souza, D. L.; Barchuk, A.; Hanly, P.; Sharp, L.; Soerjomataram, I.; Pearce, A.	2023	Cancer Epidemiology
Surveillance of Symptom Burden Using the Patient-Reported Outcome Version of the Common Terminology Criteria for Adverse Events in Patients With Various Types of Cancers During Chemoradiation Therapy: Real-World Study	Kang, D.; Kim, S.; Kim, H.; Lee, M.; Kong, S. Y.; Chang, Y. J.; Sim, S. H.; Kim, Y. J.; Cho, J.	2023	JMIR Public Health and Surveillance
An Economic Model to Establish the Costs Associated With Routes to Presentation for Patients With Multiple Myeloma in the United Kingdom	Porteous, A.; Gibson, S.; Eddowes, L. A.; Drayson, M.; Pratt, G.; Bowcock, S.; Willis, F.; Parkin, H.; Renwick, S.; Laketic-Ljubojevic, I.; Howell, D.; Smith, A.; Stern, S.	2023	Value in Health Regional Issues
Evolution of Pharmacological Treatments and Associated Costs for Multiple Myeloma in the Public Healthcare System of Catalonia: A Retrospective Observational Study	Garrido-Alejos, G.; Saborit-Canals, G.; Guarga, L.; de Pando, T.; Umbria, M.; Oriol, A.; Feliu, A.; Pontes, C.; Vallano, A.	2023	Cancers
Medicare characteristics, treatment, cost and survival in triple class exposed relapsed or refractory multiple myeloma	Hlavacek, P.; Schepart, A.; Silverstein, A. R.; Petrilla, A. A.; Johnson, W.; Schroeder, A.	2023	Future Oncology
Quality of Life and Prognostic Awareness in Caregivers of Patients Receiving Chimeric Antigen Receptor T Cell Therapy	Barata, A.; Dhawale, T.; Newcomb, R. A.; Amonoo, H. L.; Nelson, A. M.; Yang, D.; Karpinski, K.; Holmbeck, K.; Farnam, E.; Frigault, M.; Johnson, P. C.; El-Jawahri, A.	2024	Transplantatio n and Cellular Therapy
Subcutaneous Daratumumab Versus Intravenous Daratumumab for the Treatment of Patients with Multiple Myeloma: A Time, Motion and Cst Assessment Study in a General Hospital	Badibouidi, F.; Can-Kose, L.; Dupont, L.; Truttet, C.; Ait-Kac, F.	2023	European Journal of Oncology Pharmacy
Fair Allocation of Scarce CAR T-Cell Therapies for Relapsed/Refractory Multiple Myeloma	Derman, B. A.; Parker, W. F.	2023	Jama

Pharmacoeconomic issues in stem cell mobilization	Lazzaro, C.	2023	Transfusion and Apheresis Science
CAR-T therapy for multiple myeloma in China. Does it make sense financially?	Petrou, P.	2023	Journal of Medical Economics
Health-related quality of life in relapsed/refractory multiple myeloma treated with melflufen and dexamethasone: analyses from the phase III OCEAN study	Schjesvold, F. H.; Ludwig, H.; Delimpasi, S.; Robak, P.; Coriu, D.; Tomczak, W.; Pour, L.; Spicka, I.; Dimopoulos, M. A.; Masszi, T.; Chernova, N. G.; Sandberg, A.; Thuresson, M.; Norin, S.; Bakker, N. A.; Mateos, M. V.; Richardson, P. G.; Sonneveld, P.	2024	Haematologica
High Hospital-related Costs at the End-of-life in Patients With Multiple Myeloma: A Single-center Study	Bennink, C.; Westgeest, H.; Schoonen, D.; Boersen, F.; Sonneveld, P.; Hazelzet, J.; Blommestein, H.; Van Der Klift, M.	2023	HemaSphere
Clinical implications and insights from patient-reported outcome data in KarMMa-3	Chakraborty, R.	2024	The Lancet Haematology
An indirect treatment comparison of efficacy and health-related quality of life following treatment with idecabtagene vicleucel versus belantamab mafodotin in triple-class exposed relapsed/refractory patients with multiple myeloma	Rodriguez Otero, P.; Towle, K.; Cope, S.; Caisip, C.; Davies, F. E.; Delforge, M.; Weisel, K.; Marshall, T. S.; Karampampa, K.; Ayers, D.; Mojebi, A.; Braverman, J.; Farrell, J.; Dhanda, D.	2023	Leukemia & Lymphoma
Efficacy, safety, and cost of mobilization strategies in multiple myeloma: a prospective, observational study	Dhakal, B.; Zhang, M. J.; Burns, L. J.; Tang, X.; Meyer, C.; Mau, L. W.; Nooka, A. K.; Stadtmauer, E.; Micallef, I. N.; McGuirk, J.; Costa, L.; Juckett, M. B.; Shah, N.; Champlin, R. E.; Usmani, S. Z.; Farag, S. S.; Nishihori, T.; Roy, V.; Bodiford, A.; Barnes, Y. J.; Drea, E. J.; Hari, P.; Hamadani, M.	2023	Haematologica
Out-of-pocket costs of oral anticancer drugs for Medicare beneficiaries vary by strength and formulation	Gupta, A.; Arora, N.; Haque, W.; Hussaini, S. M. Q.; Sedhom, R.; Blaes, A. H.; Dusetzina, S. B.	2023	Journal of Geriatric Oncology

Alternate-day dosing of pomalidomide in relapsed/ refractory multiple myeloma: a multicenter, single-arm phase 2 trial	Zander, T.; Pabst, T.; Schar, S.; Aebi, S.; Mey, U.; Novak, U.; Lerch, E.; Rhyner Agocs, G.; Goede, J.; Maniecka, Z.; Hayoz, S.; Rufer, A.; Renner, C.; Driessen, C.	2023	Leukemia
Use of the European Organisation for Research and Treatment of Cancer multiple myeloma module (EORTC QLQ-MY20): a review of the literature 25 years after development	Forde, K.; Cocks, K.; Wells, J. R.; McMillan, I.; Kyriakou, C.	2023	Blood Cancer Journal
UK oncology approvals in 2022: global regulatory collaboration and new regulatory pathways deliver new anti-cancer therapies	Lythgoe, M. P.; Sullivan, R.; Blagden, S.	2023	The Lancet Oncology
Chemotherapy-Induced Peripheral Neuropathy Impacts Quality Of Life And Activities Of Daily Living Of Brazilian Multiple Myeloma Patients	de Miranda Drummond, P. L.; Dos Santos, R. M. M.; Silveira, L. P.; Malta, J. S.; Reis, A. M. M.; Costa, N. L.; de Paula, E. Silva R. O.; Fagundes, E. M.; de Padua, C. A. M.	2023	Current Drug Safety
Correction to Lancet Haematol 2024; 11: e216â€"27 (The Lancet Haematology (2024) 11(3) (e216â€"e227), (S235230262400005X), (10.1016/S2352-3026(24)00005-X))		2024	The lancet haematology
Healthcare Resource Utilization and Economic Burden of Cytokine Release Syndrome and Neurotoxicity in Patients with Relapsed and Refractory Multiple Myeloma (RRMM) Receiving Idecabtagene Vicleucel in Earlier-Line Settings in the KarMMa-3 Clinical Trial	Ailawadhi, S.; McGarvey, N.; Imanak, K.; Mirza, S.; Patwardhan, P.	2023	Blood
Erratum: Comparison of health care costs and resource utilization for commonly used proteasome inhibitor-immunomodulatory drug-based triplet regiments for the management of patients with relapsed/refractory multiple myeloma in the United States (Journal	Anonymous	2023	Journal of Managed Care and Specialty Pharmacy
The EASEMENT study: A multicentre, observational, cross-sectional study to evaluate patient preferences, treatment satisfaction, quality of life, and healthcare resource use in patients with multiple myeloma receiving injectable-containing or fully oral t	Ayto, R.; Annibali, O.; Biedermann, P.; Roset, M.; Sanchez, E.; Kotb, R.	2024	European Journal of Haematology
Real-world utilization and healthcare costs for multiple myeloma: A retrospective analysis of patients in Singapore	Bayani, D. B.; Lin, Y. C.; Ooi, M. G.; Tso, A. C. Y.; Wee, H. L.	2023	EJHaem

Assessing the Treatment Pattern, Health Care Resource Utilisation, and Economic Burden of Multiple Myeloma in France Using the Systeme National des Donnees de Sante (SNDS) Database: A Retrospective Cohort Study	Bessou, Antoine; Colin, Xavier; De Nascimento, Julie; Sopwith, Will; Ferrante, Shannon; Gorsh, Boris	2023	European Journal of Health Economics
EE403 Budget Impact of Selinexor Combination Regimens in Previously Treated Multiple Myeloma	Carter JA1, Ijioma S2, Ray D3	2024	
Patient-Reported Outcomes Among Patients with Triple-Class Refractory Multiple Myeloma in Real-World Clinical Practice: A Prospective, Multi-Site Observational Study	Charalampous, Charalampos; Kumar, Shaji Kunnathu; Parrondo, Ricardo; Chhabra, Saurabh; Duh, Mei Sheng; Bobbili, Priyanka; Wang, Aolin; Chen, Jingyi; Mohan, Manasi; Hlavacek, Patrick; Ren, Jinma; Schepart, Alex; Nador, Guido; DiBonaventura, Marco	2023	Blood
EE660 Real-World Economic Burden and Healthcare Resource Utilization (HCRU) Among Patients with Triple-Class Exposed Relapsed/Refractory Multiple Myeloma (RRMM) in the United States	Chari, A.; Lin, X.; Ammann, E.; Matt, K.; Potluri, R.; Nair, S.	2023	Value in Health
Systematic literature review of health economic models developed for multiple myeloma to support future analyses	Choon-Quinones, M.; Zelei, T.; Nemeth, B.; Toth, M.; Jia, X. Y.; Barnett, M.; Keown, P.; Durie, B.; Harousseau, J. L.; Hose, D.; Kalo, Z.	2023	Journal of Medical Economics
RWD157 Assessment of Real-World Treatment Patterns and Healthcare Resource Utilization (HCRU) in Patients with Lenalidomide-Refractory Relapsed/Refractory Multiple Myeloma (RRMM) from the US Optum Database	Costa, L.; Nair, S.; Lin, X.; O'Hara, M.; Slavcev, M.; Marshall, A.; Potluri, R.; Tyagi, R.; Hashmi, H.	2023	Value in Health
An Investigation into the Relationship Between Choice of Model Structure and How to Adjust for Subsequent Therapies Using a Case Study in Oncology	Cranmer, H. L.; Shields, G. E.; Bullement, A.	2023	Applied Health Economics & Health Policy
A Study Comparing Talquetamab Plus Pomalidomide, Talquetamab Plus Teclistamab, and Elotuzumab, Pomalidomide, and Dexamethasone or Pomalidomide, Bortezomib, and Dexamethasone in Participants with Relapsed or Refractory Myeloma who Have Received an Anti-CD3	Ctri	2024	https://trialsearch.who.int/Trial2.aspx?TrialID=CTRI/2024/02/063266
Assessment of the psychometric properties of the Spanish version of EORTC QLQ-MY20 and evaluation of health-related quality of Life outcomes in	Dachs, L. R.; Gaisan, C. M.; Bustamante, G.; Lopez, S. G.; Garcia, E. G.; Persona, E. P.;	2023	Leukemia and Lymphoma

patients with relapsed and/or refractory multiple myeloma in the real-world setting in Spain: results from the	Gonzalez-Calle, V.; Auzmendi, M. S.; Perez, J. M. A.; Gonzalez Montes, Y.; Rios Tamayo, R.; de Miguel Llorente, D.; Bernal, L. P.; Mayol, A. S.; Caro, C. C.; Grande, M.; Fernandez-Nistal, A.; Naves, A.; Miguel, E. M. O. S.		
Whether and How Disutilities of Adverse Events were Used in the Economic Evaluation of Drug Therapy for Cancer Treatment	Dai, Z.; Chang, F.; Wang, L.; He, J.; Shi, P.; Zhang, H.; Lu, Y.	2023	PharmacoEconomics
Real-World Study of Patients with Triple-Class Exposed Relapsed/Refractory Multiple Myeloma: Analysis across a Spectrum of Advanced Disease Stage Medicare Patients in the United States	Delea, T.; Moynahan, A.; Ge, W.; Song, X.; Kroog, G. S.; Noguera-Troise, I.; Rodriguez Lorenc, K.; Ma, Q.	2023	Blood
Health-related quality of life in patients with triple-class exposed relapsed and refractory multiple myeloma treated with idecabtagene vicleucel or standard regimens: patient-reported outcomes from the phase 3, randomised, open-label KarMMa-3 clinical tr	Delforge, M.; Patel, K.; Eliason, L.; Dhanda, D.; Shi, L.; Guo, S.; Marshall, T. S.; Arnulf, B.; Cavo, M.; Nooka, A.; et al.	2024	The Lancet. Haematology
Health related quality of life (HRQoL) in patients with triple-class-exposed relapsed/ refractory multiple myeloma (TCE RRMM) treated with idecabtagene vicleucel (ide-cel) versus standard regimens: patient-reported outcomes (PROs) from KarMMa-3 phase 3 ra	Delforge, M.; Patel, K. K.; Eliason, L.; Dhanda, D.; Shi, L.; Guo, S.; Marshall, T.; Arnulf, B.; Cavo, M.; Nooka, A. K.; et al.	2023	Journal of clinical oncology
Effects of Idecabtagene Vicleucel (Ide-Cel) Versus Standard Regimens on Health-Related Quality of Life (HRQoL) in Patients with Relapsed/Refractory Multiple Myeloma (RRMM) Who Had Received 2-4 Prior Regimens: Updated Results from the Phase 3 KarMMa-3 Tri	Delforge, M.; Patel, K. K.; Eliason, L.; Dhanda, D.; Shi, L.; Guo, S.; Marshall, T. S.; Arnulf, B.; Cavo, M.; Nooka, A. K.; Manier, S.; Callander, N. S.; Giralt, S. A.; Einsele, H.; Ailawadhi, S.; Popa-McKiver, M.; Cook, M.; Otero, P. R.	2023	Blood
Effects of Idecabtagene Vicleucel (Ide-Cel) Versus Standard Regimens on Health-Related Quality of Life (HRQoL) in Patients with Triple-Class-Exposed (TCE) Relapsed/Refractory Multiple Myeloma (RRMM) Who Received at Least 3 Lines of Prior Antimyeloma Regim	Delforge, M.; Patel, K. K.; Eliason, L.; Dhanda, D.; Shi, L.; Guo, S.; Marshall, T. S.; Arnulf, B.; Cavo, M.; Nooka, A. K.; Manier, S.; Callander, N. S.; Giralt, S. A.; Einsele, H.; Ailawadhi, S.; Popa-McKiver, M.; Cook, M.; Rodriguez Otero, P.	2023	Blood

Patient reported outcomes in Triple Class Exposed, Relapsed/ Refractory Multiple Myeloma (TCE RRMM) patients in KarMMa 3 trial (Phase 3 RCT): idecabtagene Vicleucel (ide-cel) versus standard regimens	Einsele, H.; Delforge, M.; Patel, K.; Eliason, L.; Dhanda, D.; Shi, L.; Guo, S.; Marshall, T.; Arnulf, B.; Cavo, M.; et al.	2023	Oncology research and treatment
EE260 Cost-Effectiveness Analysis of Daratumumab Triplet Therapy Vs Carfilzomib Duplet Therapy in Patients with Relapsed or Refractory Multiple Myeloma in Egypt from Payer Perspective	Elsisi, G.; Elattar, M.; Eldesouky, N.	2023	Value in Health
Impact of Disease Progression, Line of Therapy, and Response on Health-Related Quality of Life in Multiple Myeloma: A Systematic Literature Review	Fonseca, R.; Tran, D.; Laidlaw, A.; Rosta, E.; Rai, M.; Duran, J.; Ammann, E. M.	2023	Clinical lymphoma, myeloma & leukemia
Costs of plasmocytic myeloma therapy in the drug programme at a Regional Oncology Centre in Poland	Futyma, K.; Sliwczynski, A.; Halka, J.; Brzozowska, M.	2023	Annals of Agricultural & Environmental Medicine
Health-related quality of life among patients with multiple myeloma treated with CAR-T therapy	Gagnon, S. J.; Nooka, A. K.	2023	Journal of Clinical Oncology
EE335 Burden of Disease in Patients Who Are Eligible for Bcma-Targeted Immunotherapy for Multiple Myeloma: A Retrospective Claims Database Analysis	Giri S1, Lin D2, Dixon R3, Kim N2, Fowler J2, Barron J3, Tan H3, Nguyen C3, Asefaha F3, Vojjala S3, Min E2, Wu B2	2024	
EE531 Resource Optimization for Greek NHS Hospitals from the Use of Daratumumab SC for Multiple Myeloma	Golnas, P.; Kontogiorgos, I.; Golna, C.; Konstantopoulou, T.; Christodoulou, T. K.; Souliotis, K.	2023	Value in Health
Cost-effectiveness and budget impact analysis of Daratumumab, Lenalidomide and dexamethasone for relapsed-refractory multiple myeloma	Goudarzi, Z.; Shahtaheri, R. S.; Najafpour, Z.; Hamedifar, H.; Ebrahimi, H.	2024	Cost Effectiveness & Resource Allocation
The Impact of Outpatient versus Inpatient Administration of CAR-T Therapies on Clinical, Economic, and Humanistic Outcomes in Patients with Hematological Cancer: A Systematic Literature Review	Hansen, D. K.; Liu, Y. H.; Ranjan, S.; Bhandari, H.; Potluri, R.; McFarland, L.; De Braganca, K. C.; Huo, S.	2023	Cancers
Cost per Responder Analysis of Patients with Lenalidomide-Refractory Multiple Myeloma Who Received Cilta-Cel from the Cartitude-4 Trial	Hansen, D. K.; Lu, X.; Castaneda, O.; Sorensen, S.; Usmani, S. Z.; Zhang, E.; Huo, S.; Jagannath, S.	2023	Blood
Cost per Responder Analysis of Patients with Lenalidomide-Refractory Multiple Myeloma Who Received Cilta-Cel from the Cartitude-4 Trial	Hansen, D. K.; Lu, X.; Castaneda, O.; Sorensen, S.; Usmani, S. Z.; Zhang, E.; Huo, S.; Jagannath, S.	2024	Transplantation and Cellular Therapy

HTA18 Challenges of Identifying Health Utility Data for Patients With Penta-Refractory Multiple Myeloma to Inform HTA Reimbursement Discussion for Newer Treatment Options	Hibbs, R.; Bianco, M.; Noble-Longster, J.; Stainer, L.; Cooper, C.; Strickson, A. J.	2023	Value in Health
Health-Related Quality of Life (HRQoL) Among Patients with Triple-Class Exposed Relapsed/Refractory Multiple Myeloma (RRMM) Treated with Linvoseltamab in Linker-MM1: Interim Assessment up to 36 Weeks of Treatment	Hoffman, James E.; Bumma, Naresh; Richter, Joshua; Dhodapkar, Madhav V.; Lee, Hans C.; Suvannasankha, Attaya; Houde, Christiane A.; Maly, Joseph J.; Shah, Mansi R.; Baz, Rachid; Namburi, Swathi; Wu, Ka Lung; Pianko, Matthew; Ye, Jing Christine; Lentzsch, Suzanne; Silbermann, Rebecca; Min, Chang-Ki; Vekemans, Marie-Christiane; Munder, Markus; Byun, Ja Min; Lopez, JoaquÃn MartÃ-nez; DeVeaux, Michelle; Ivanescu, Cristina; Rodriguez Lorenc, Karen; Kroog, Glenn S.; Houvras, Yariv; Inocencio, Timothy J.; Chi, Lei; Harnett, James; Ma, Qiufei; Jagannath, Sundar	2023	Blood
Evaluating process utilities for the treatment burden of chemotherapy in multiple myeloma in Japan: a time trade-off valuation study	Ishida, T.; Nakakoji, M.; Murata, T.; Matsuyama, F.; Iida, S.	2023	Journal of Medical Economics
A clinical study to compare teclistamab monotherapy versus pomalidomide, bortezomib, dexamethasone (PVd) or carfilzomib, dexamethasone (Kd) in participants with relapsed or refractory multiple myeloma who have received 1 to 3 prior lines of therapy, inclu	Isrctn	2023	https://trialsearch.who.int/Trial2.aspx?TrialID=ISRCTN80324107
A study comparing talquetamab plus pomalidomide, talquetamab plus teclistamab, and elotuzumab, pomalidomide, and dexamethasone or pomalidomide, bortezomib, and dexamethasone in participants with relapsed or refractory myeloma who have received an Anti-CD3	Isrctn	2023	https://trialsearch.who.int/Trial2.aspx?TrialID=ISRCTN74178658
Component Costs of CAR-T Therapy in Addition to Treatment Acquisition Costs in Patients with Multiple Myeloma	Jagannath, S.; Joseph, N.; Crivera, C.; Kharat, A.; Jackson, C. C.; Valluri, S.; Cost, P.; Phelps, H.;	2023	Oncology & Therapy

	Slowik, R.; Klein, T.; Smolen, L.; Yu, X.; Cohen, A. D.		
Healthcare Resource Utilization and Costs Among Patients With Relapsed/ Refractory Multiple Myeloma Treated With Chimeric Antigen Receptor-T (CAR-T) Cell Therapy	Jagannath, S.; Kharat, A.; Fu, A.; Huo, S.; Kohli, M.; Adams, S.; Umeh, E.; Foster, M.	2023	Clinical Lymphoma, Myeloma and Leukemia
e23185 Assessment of health-related quality of life (HRQoL) in triple-classâ€"exposed patients with relapsed or refractory multiple myeloma (RRMM) treated with linvoseltamab in the LINKER-MM1 trial.	James E. Hoffman, Naresh Bumma, Joshua Ryan Richter, Madhav V. Dhodapkar, Hans C. Lee, Attaya Suvannasankha, Jeffrey A. Zonder, Joseph J. Maly, Mansi R. Shah, Rachid C. Baz, Michelle DeVeaux, Cristina Ivanescu, Karen Rodriguez-Lorenc, Glenn Scott Kroog, Yariv J. Houvras, Timothy J Inocencio, Lei Chi, James Harnett, Qiufei Ma, Sundar Jagannath	2024	
P2300 ASSESSMENT OF HEALTH-RELATED QUALITY OF LIFE IN TRIPLE-CLASS EXPOSED PATIENTS WITH RELAPSED OR REFRACTORY MULTIPLE MYELOMA (RRMM) TREATED WITH LINVOSELTAMAB IN THE LINKER-MM1 TRIAL	James E. Hoffman, Naresh Bumma, Joshua Richter, Madhav Dhodapkar, Hans Lee, Attaya Suvannasankha, Jeffrey Zonder, Joseph J. Maly, Mansi R. Shah, Rachid Baz, Michelle DeVeaux, Cristina Ivanescu, Cristina Karen Rodriguez Lorenc, Glenn Kroog, Yariv Houvras, Timothy Inocencio, Lei Chi, James Harnett, Qiufei Ma, Sundar Jagannath	2024	
Cost-effectiveness of idecabtagene vicleucel compared with conventional care in triple-class exposed relapsed/refractory multiple myeloma patients in Canada and France	Karampampa, K.; Zhang, W.; Venkatachalam, M.; Cotte, F. E.; Dhanda, D.	2023	Journal of Medical Economics
Daratumumab in Indian patients with relapsed and refractory multiple myeloma: a prospective, multicenter, phase IV study	Kumar, L.; Melinkeri, S.; Ganesan, P.; Kumar, J.; Biswas, G.; Kilara, N.; Pathalingappa, H.; Prasad, S. V. S. S.; Jain, M.; Mishra, S. K.; Prasad, S.; Boyella, P. K.; Sahoo, R. K.; Bondarde, S.; Shah, S.; Rege, M.; Deb, U.; Korde, T.; Dixit, J.	2024	Future Oncology

Second Line Therapy in Multiple Myeloma: A SEER Medicare Analysis	LeBlanc, M. R.; Zhou, X.; Baggett, C. D.; Tuchman, S. A.; Jensen, C. E.; Lichtman, E. I.; Rubinstein, S. M.	2024	Clinical lymphoma, myeloma & leukemia
Treatment Patterns, Survival, Quality of Life, and Healthcare Resource Use Among Patients With Triple-Class Refractory Multiple Myeloma in US Clinical Practice: Findings From the Connect MM Disease Registry	Lee, H. C.; Ramasamy, K.; Weisel, K.; Abonour, R.; Hardin, J. W.; Rifkin, R. M.; Ailawadhi, S.; Terebelo, H. R.; Durie, B. G. M.; Tang, D.; Joshi, P.; Liu, L.; Jou, Y. M.; Che, M.; Hernandez, G.; Narang, M.; Toomey, K.; Gasparetto, C.; Wagner, L. I.; Jagannath, S.	2023	Clinical lymphoma, myeloma & leukemia
EE496 Cost of Anti-CD38 Monoclonal Antibodies in Combination With Carfilzomib and Dexamethasone for Relapsed Refractory Multiple Myeloma	Lin P1, Petitjean A2, Drea E3, Lin F4	2024	
Teclistamab Improves Patient-Reported Symptoms and Health-Related Quality of Life in Relapsed or Refractory Multiple Myeloma: Results From the Phase II MajesTEC-1 Study	Martin, T. G.; Moreau, P.; Usmani, S. Z.; Garfall, A.; Mateos, M. V.; San-Miguel, J. F.; Oriol, A.; Nooka, A. K.; Rosinol, L.; Chari, A.; Karlin, L.; Krishnan, A.; Bahlis, N.; Popat, R.; Besemer, B.; Martinez-Lopez, J.; Delforge, M.; Trancucci, D.; Pei, L.; Kobos, R.; Fastenau, J.; Gries, K. S.; van de Donk, Nwcj	2024	Clinical lymphoma, myeloma & leukemia
Real-world treatment patterns, healthcare resource use and disease burden in patients with multiple myeloma in Europe	Martinez-Lopez, J.; Bailey, A.; Lambert, A.; Luke, E.; Ribbands, A.; Erler-Yates, N.; Valluri, S.; Haefliger, B.; Gay, F.	2023	Future Oncology
Adjusted comparison of outcomes between patients from CARTITUDE-1 versus multiple myeloma patients with prior exposure to proteasome inhibitors, immunomodulatory drugs and anti-CD38 antibody from the prospective, multinational LocoMMotion study of real-wo	Mateos, M. V.; Weisel, K.; Martin, T.; Berdeja, J. G.; Jakubowiak, A.; Stewart, A. K.; Jagannath, S.; Lin, Y.; Diels, J.; Ghilotti, F.; Thilakarathne, P.; Perualila, N. J.; Cabrieto, J.; Haefliger, B.; Erler-Yates, N.; Hague, C.; Jackson, C. C.; Schecter, J. M.; Strulev, V.; Nesheiwat, T.; Pacaud, L.; Einsele, H.; Moreau, P.	2023	Haematologica
EE162 Healthcare Resource Utilization and 2022 Cost Update of Cytokine Release Syndrome and Neurotoxicity in	McGarvey, N.; Imanak, K.; Carattini, T.; Ung, B.;	2023	Value in Health

Patients with Relapsed/Refractory Multiple Myeloma (RRMM) Receiving Idecabtagene Vicleucel (IDE-CEL, BB2121) in KarMMa	Campbell, T. B.; Gitlin, M.; Patwardhan, P.		
Post-infusion Costs Associated with Idecabtagene Vicleucel Treatment for Patients with Relapsed/Refractory Multiple Myeloma in the KarMMa Trial	McGarvey, N.; Ung, B.; Carattini, T.; Imanak, K.; Lee, A.; Campbell, T. B.; Patwardhan, P.	2023	Advances in Therapy
Treatment Pattern, Healthcare Resource Utilization and Symptom Burden Among Patients with Triple Class Exposed Multiple Myeloma: A Population-Based Cohort Study	Mian, H.; Seow, H.; Pond, G. R.; Gayowsky, A.; Foley, R.; Balistky, A.; Ebraheem, M.; Cipkar, C.; Sapru, H.; Mohyuddin, G. R.; Hadidi, S. A.; Visram, A.	2024	Clinical lymphoma, myeloma & leukemia
Patient-Reported Outcomes in the Phase 3 CARTITUDE-4 Study of Ciltacabtagene Autoleucel Vs Standard of Care in Patients with Lenalidomide-Refractory Multiple Myeloma after 1-3 Lines of Therapy	Mina, R.; Mylin, A. K.; Yokoyama, H.; Magen, H.; Alsdorf, W.; Minnema, M. C.; Shune, L.; Isufi, I.; Harrison, S. J.; Shah, U. A.; et al.	2023	Blood
Impact of elranatamab on quality of life: Patient-reported outcomes from MagnetisMM-3	Mohty, M.; Bahlis, N. J.; Nooka, A. K.; DiBonaventura, M.; Ren, J.; Conte, U.	2024	British Journal of Haematology
Patient-reported frailty phenotype (PRFP) vs. International Myeloma Working Group frailty index (IMWG FI) proxy: A comparison between two approaches to measuring frailty	Murugappan, M. N.; King-Kallimanis, B. L.; Bhatnagar, V.; Kanapuru, B.; Farley, J. F.; Seifert, R. D.; Stenehjem, D. D.; Chen, T. Y.; Horodniceanu, E. G.; Kluetz, P. G.	2024	Journal of Geriatric Oncology
Carfilzomib (in combination with daratumumab and dexamethasone)	NCPE	2024	
Elranatamab	NCPE	2024	
Talquetamab	NCPE	2024	
Teclistamab	NCPE	2024	
Psychosocial Mobile Application (THRIVE-M) for Patients With Multiple Myeloma	Nct	2023	https://clinicaltrials.gov/ct2/show/NCT06073353
TA970 Selinexor with dexamethasone for treating relapsed or refractory multiple myeloma after 4 or more treatments	NICE	2024	
TA974 Selinexor with bortezomib and dexamethasone for previously treated multiple myeloma	NICE	2024	
Single-agent belantamab mafodotin in patients with relapsed/refractory multiple myeloma: Final analysis of the DREAMM-2 trial	Nooka, A. K.; Cohen, A. D.; Lee, H. C.; Badros, A.; Suvannasankha, A.; Callander, N.; Abdallah,	2023	Cancer

	A. O.; Trudel, S.; Chari, A.; Libby, E. N.; Chaudhry, M.; Hultcrantz, M.; Kortum, K. M.; Popat, R.; Sborov, D.; Hakim, S.; Lewis, E.; Gorsh, B.; Bhushan, B.; McKeown, A.; Gupta, I.; Opalinska, J.; Richardson, P. G.; Lonial, S.		
Real-World Health Care Services Utilization Associated With the Management of Patients With Relapsed and Refractory Multiple Myeloma in Spain: The CharisMMa Study	Ocio, E. M.; Montes-Gaisan, C.; Bustamante, G.; Garzon, S.; Gonzalez, E.; Perez-Persona, E.; Gonzalez-Calle, V.; Sirvent, M.; Arguinano, J. M.; Gonzalez, Y.; Rios, R.; de Miguel, D.; Grande, M.; Fernandez-Nistal, A.; Naves, A.; Rosinol, L.	2023	Clinical lymphoma, myeloma & leukemia
The impact of current therapeutic options on the health-related quality of life of patients with relapse/refractory multiple myeloma: a systematic review of clinical studies	Ojo, A. S.; Araoye, M. O.; Ali, A.; Sarma, R.	2024	Journal of cancer survivorship : research and practice
Patient-Reported Outcomes among Multiple Myeloma Patients Treated with Standard of Care Idecabtagene Vicleucel	Oswald, L. B.; Gudenkauf, L. M.; Li, X.; De Avila, G.; Peres, L. C.; Kirtane, K.; Gonzalez, B. D.; Hoogland, A. I.; Nguyen, O.; Rodriguez, Y.; Baz, R. C.; Shain, K. H.; Alsina, M.; Locke, F. L.; Freeman, C.; Castaneda Puglianini, O.; Nishihori, T.; Liu, H.; Blue, B.; Grajales-Cruz, A.; Jim, H. S. L.; Hansen, D. K.	2023	Cancers
Real-World Treatment Patterns, Outcomes, Health Care Resource Utilization and Cost Burden of Multiple Myeloma in South Korea Using the National Claims Data	Park, Y.; Park, S. S.; Yoon, S.; Jeong, J.; Lee, D.; Kim, K.	2023	Blood
PCR73 Sensitivity of EQ-5D to Assess Health-Related Quality of Life (HRQoL) for Triple-Class Exposed (TCE) Relapsed/Refractory Multiple Myeloma (RRMM): karMMa-3 Case Study Exploring EQ-5D Mapped from Disease-Specific Instruments	Paul, E.; McLoone, D.; Eliason, L.; Karampampa, K.; Pepper, A. N.; Cope, S.; Dhanda, D.	2023	Value in health
Facility-Related Healthcare Resource Utilization (HCRU) for Patients Treated with Idecabtagene Vicleucel (Ide-Cel,	Peres, Lauren C.; Patwardhan, Pallavi; Huggar, David; De Avila,	2023	Blood

bb2121) in a Real-World (RW) Setting: A Single-Center Experience	Gabriel; Oswald, Laura B.; Grajales-Cruz, Ariel F.; Blue, Brandon; Abraham Miranda, Julieta; Reid, Kayla; Liu, Hien; Nishihori, Taiga; Shain, Kenneth H.; Baz, Rachid; Alsina, Melissa; Castaneda, Omar; Locke, Frederick L.; Freeman, Ciara Louise L.; Tiwana, Simrandeep; Botros, Afraim; Hansen, Doris K.		
Is it a chimera? A systematic review of the economic evaluations of CAR-T cell therapy - an update	Petrou, P.	2023	Expert Review of Pharmacoeconomics & Outcomes Research
Patient-Reported Outcomes With Belantamab Mafodotin Treatment in Patients With Triple-Class Refractory Multiple Myeloma	Popat, Rakesh; Lonial, Sagar; Voorhees, Peterm; Esposti, Simonadegli; Gorsh, Boris; Gupta, I. R. A.; Opalinska, Joanna; Sapra, Sandhya; Piontek, Trisha; Zangdong, H. E.; et al.	2023	JADPRO: journal of the advanced practitioner in oncology
Improved efficiency of daratumumab treatment of multiple myeloma adopting the subcutaneous route: A micro-costing analysis in three Italian hematology centers	Pradelli, L.; Massaia, M.; Todisco, E.; Gherlinzoni, F.; Furlan, A.; La Targia, M.; Grande, E.; Tripoli, I. E.; Occhipinti, F.; Comello, F.; Iannello, F.; Bellucci, S.	2023	Cancer Medicine
Real-world patient-reported outcomes and concordance between patient and physician reporting of side effects across lines of therapy in multiple myeloma within the USA	Ribbands, A.; Boytsov, N.; Bailey, A.; Gorsh, B.; Luke, E.; Lambert, A.	2023	Supportive Care in Cancer
P43 Cost-Effectiveness of Talquetamab-tgvs Vs Idecabtagene Vicleucel for Triple-Class Exposed Relapsed or Refractory Multiple Myelom	Rong R, Tang T, Shi L	2024	
Comparison of health care costs and resource utilization for commonly used proteasome inhibitor-immunomodulatory drug-based triplet regimens for the management of patients with relapsed/refractory multiple myeloma in the United States	Sanchez, L.; Chari, A.; Cheng, M.; Cherepanov, D.; DerSarkissian, M.; Huang, F.; Stull, D. M.; Dabora, J.; Young, M.; Noga, S. J.; Pi, S.; Zhang, M.; Banatwala, A.; Duh, M. S.; Ailawadhi, S.	2023	Journal of Managed Care & Specialty Pharmacy
Symptoms, Functioning, and Health-Related Quality of Life in Patients with Relapsed/Refractory Multiple Myeloma Treated with Talquetamab: Updated	Schinke, Carolina; Touzeau, Cyrille; Oriol, Albert; Mateos, MarÃa-Victoria; Stevens, Don	2023	Blood

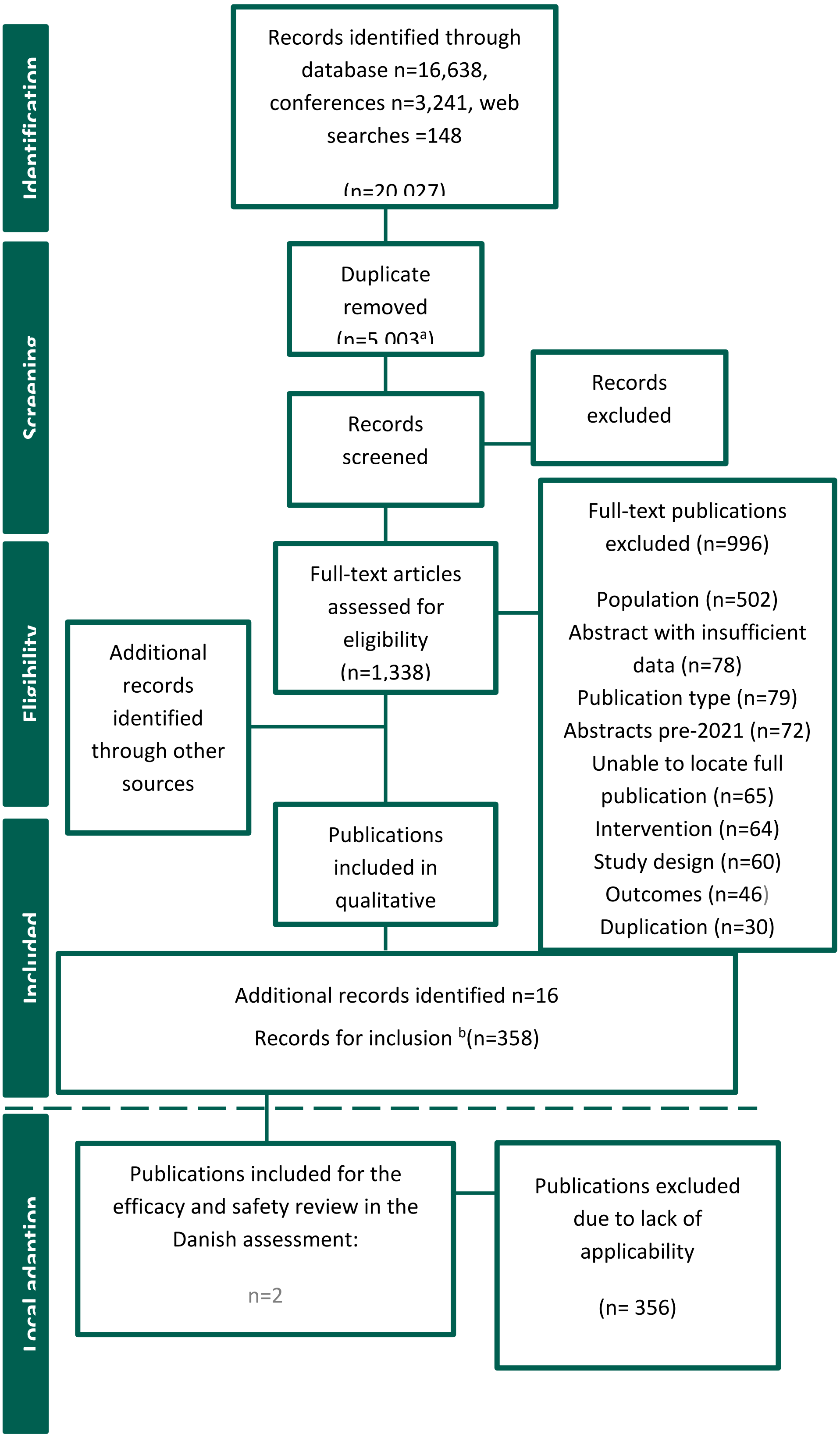
Patient-Reported Outcomes from the Phase 1/2 MonumenTAL-1 Study	A.; Rasche, Leo; Qin, Xiang; Kato, Kelly; Ming, Timothy; Katz, Eva G.; Gries, Katharine S.; Campagna, Michela; Masterson, Tara J.; Hilder, Brandi W.; Tolbert, Jaszianne; Renaud, Thomas; Heuck, Christoph; Moreau, Philippe; San-Miguel, JesÃºs; RodrÃguez Otero, Paula; Chari, Ajai		
Patient-Reported Outcomes (Pro) in Relapsed/ Refractory Multiple Myeloma (Rrmm) Treated with Melflufen and Dexamethasone (Dex) or Pomalidomide (Pom) and Dex: Analyses from the Phase 3 Ocean Study	Schjesvold, F.; Ludwig, H.; Delimpasi, S.; Robak, P.; Mateos, M.; Sandberg, A.; Thuresson, M.; Norin, S.; Richardson, P.; Sonneveld, P.	2023	HemaSphere
Treatment sequences and drug costs from diagnosis to death in multiple myeloma	Seefat, M. R.; Cucchi, D. G. J.; Groen, K.; Donker, M. L.; van der Hem, K. G.; Westerman, M.; Gerrits, A. M.; Beeker, A.; van de Donk, Nwcj; Blommestein, H. M.; Zweegman, S.	2024	European Journal of Haematology
EE14 Cost of Care Comparison of Elranatamab-bcmm and Teclistamab-cqyv in Adult Patients with Relapsed or Refractory Multiple Myeloma (RRMM)	Shah B1, Sandin R2, Liu Y3, Hu Y4, Schepart A5, Hughes D6, Hart J7, Hlavacek P7	2024	
EE428 Budget Impact of Elranatamab-bcmm in Patients with Relapsed or Refractory Multiple Myeloma (RRMM) in the United States	Shah B1, Sandin R2, Liu Y3, Hu Y4, Schepart A5, Hughes D6, Hart J7, Hlavacek P5	2024	
teclistamab (Tecvayli)	SMC2668	2024	
elranatamab (Elrexfio)	SMC2669	2024	
selinexor (Nexpovio)	SMC2673		
Clinical Outcomes of Autologous Hematopoietic Stem Cell Transplant in Multiple Myeloma Patients: A 5-year Experience from a Single Centre in North India	Sood, N.; Tiwari, A. K.; Pabbi, S.; Dikshit, R.; Singh, P.; Ramaswami, A.; Gautam, D.; Singh, M. K.	2023	South Asian Journal of Cancer
HTA82 Adjusting Utilities Using Age and Time-to-Death Decrements in Cost-Effectiveness Analyses: A Case Study in Relapsed and/or Refractory Multiple Myeloma	Su W1, Clayson M2	2024	
Current Health State Affected Patient Preferences More Than Disease Status: A Discrete Choice Experiment in Multiple Myeloma	Tervonen, T.; Duenas, A.; Collacott, H.; Lam, A.; Gries, K. S.; Carson, R.; Trevor, N.; Krucien, N.; He, J.	2023	Value in Health

Health-Related Quality of Life in Patients with Relapsed/Refractory Multiple Myeloma Treated with Talquetamab, a G Protein-Coupled Receptor Family C Group 5 Member D X Cd3 Bispecific Antibody, from Monumental-1	Van De Donk, N.; Rasche, L.; Touzeau, C.; Chari, A.; Schinke, C.; Minnema, M.; Berdeja, J.; Oriol, A.; Rodriguez-Otero, P.; Askari, E.; Mateos, M.; Costa, L.; Caers, J.; Krishnan, A.; Vishwamitra, D.; Ma, J.; Qin, X.; Gries, K. S.; Kato, K.; Campagna, M.; Masterson, T.; Hilder, B.; Tolbert, J.; Renaud, T.; Goldberg, J.; Heuck, C.; Moreau, P.; San-Miguel, J.	2023	HemaSphere
Treatment Patterns and Healthcare Resource Utilization Among Patients with Triple Class Exposed Multiple Myeloma: A Population-Based Cohort Study	Visram, A.; Seow, H.; Pond, G.; Gayowsky, A.; McCurdy, A.; Cipkar, C.; Sapru, H.; Kouroukis, C. T.; Aljama, M.; Ebraheem, M.; Foley, S. R.; Mian, H.	2023	Blood
Evaluation of Outpatient Administration of Ciltacabtagene Autoleucel in Relapsed/Refractory Multiple Myeloma: Single Center Experience	Waqar, S. H. B.; Hansen, D. K.; Freeman, C. L.; De Avila, G.; Harvey, K.; Grajales, A.; Blue, B.; Liu, H.; Baz, R.; Alsina, M.; Shain, K.; Jain, M. D.; Locke, F. L.; Castaneda, O.; Nishihori, T.	2024	Transplantation and Cellular Therapy
Impact of Elotuzumab Plus Pomalidomide/Dexamethasone on Health-related Quality of Life for Patients With Relapsed/Refractory Multiple Myeloma: Final Data From the Phase 2 ELOQUENT-3 Trial	Weisel, K.; Dimopoulos, M. A.; San-Miguel, J.; Paner, A.; Engelhardt, M.; Taylor, F.; Lord-Bessen, J.; Yip, C.; Greenwood, M.; Tang, J.; Cavo, M.	2023	HemaSphere
Patient (pt)-reported outcomes in pts with relapsed/ refractory multiple myeloma (RRMM) treated with belantamab mafodotin (belamaf) vs pomalidomide/low dose dexamethasone (Pd) in the phase III, open-label, randomized, multicenter DREAMM-3 study	Weisel, K.; Hungria, V.; Currie, B.; Perera, S.; Sule, N.; He, W.; McKeown, A.; Sapra, S.; Li, M.; Barale, S.; Boyle, J.; McPoyle, K.; Dimopoulos, M. A.	2023	Oncology Research and Treatment
Cost effectiveness analysis of CAR-T cell therapy for patients with relapsed/refractory multiple myeloma in China	Wu, W.; Ding, S.; Mingming, Z.; Yuping, Z.; Sun, X.; Zhao, Z.; Yang, Y.; Hu, Y.; Dong, H.	2023	Journal of Medical Economics
Cost-Effectiveness of Anti-BCMA Chimeric Antigen Receptor T Cell Therapy in Relapsed/Refractory Multiple Myeloma	Yamamoto, C.; Minakata, D.; Yokoyama, D.; Furuki, S.; Noguchi, A.; Koyama, S.; Oyama, T.; Murahashi, R.; Nakashima, H.; Ikeda,	2024	Transplantation and Cellular Therapy

	T.; Kawaguchi, S. I.; Hyodo, K.; Toda, Y.; Ito, S.; Nagayama, T.; Umino, K.; Morita, K.; Ashizawa, M.; Ueda, M.; Hatano, K.; Sato, K.; Ohmine, K.; Fujiwara, S. I.; Kanda, Y.		
Health care resource utilization and costs among patients with multiple myeloma with exposure to double-class or triple-class multiple myeloma treatments: A retrospective US claims database analysis	Yang, J.; Boytsov, N.; Carlson, J. J.; Barthold, D.	2023	Journal of Managed Care & Specialty Pharmacy
P905: PATIENT REPORTED OUTCOMES IN TRIPLE CLASS EXPOSED, RELAPSED/REFRACTORY MULTIPLE MYELOMA (TCE RRMM) PATIENTS IN KARMMA 3 TRIAL (PHASE 3 RCT): IDECABTAGENE VICLEUCEL (IDE-CEL) VERSUS STANDARD REGIMENS	Michel Delforge, Krina Patel, Laurie Eliason, Devender Dhanda, Ling Shi, Shien Guo, Thomas Marshall, Bertrand Arnulf, Michele Cavo, Ajay Nooka, Salomon Manier, Natalie Callander, Sergio Giralt, Hermann Einsele, Sikander Ailawadhi, Mihaela Popa McKiver, Mark Cook, Paula RodrÃguez-Otero	2023	
P964: PATIENT (PT)-REPORTED OUTCOMES IN PTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM) TREATED WITH BELANTAMAB MAFODOTIN (BELAMAF) VS POMALIDOMIDE/LOW DOSE DEXAMETHASONE (PD) IN THE DREAMM-3 STUDY	Vania Hungria, Katja Weisel, Brooke Currie, Sue Perera, Neal Sule, Wei He, Astrid McKeown, Sandhya Sapra, Linda Nelsen, Mary Li, Sophie Barale, Julia Boyle, Kaytlyn McPoyle, Meletios A. Dimopoulos	2023	
P979: PATIENT-REPORTED OUTCOMES FOR TECLISTAMAB VERSUS REAL-WORLD PHYSICIANâ€™S CHOICE OF THERAPY IN THE LOCOMMOTION STUDY IN PATIENTS WITH TRIPLE-CLASS EXPOSED RELAPSED/REFRACTORY MULTIPLE MYELOMA	Philippe Moreau, Niels W.C.J. van de Donk, Michel Delforge, Hermann Einsele, Valerio De Stefano, Aurore Perrot, Britta Besemer, Charlotte Pawlyn, Lionel Karlin, Salomon Manier, Xavier Leleu, Pushpike Thilakarathne, Joris Diels, Katharine Gries, Nichola Erler-Yates, Kirsten van Nimwegen, RaÃºl Morano, Vadim Strulev, Imene Haddad, Rachel Kobos, Jennifer SMIT, Alexander Marshall, Mary Slavcev,	2023	

	Maria-Victoria Mateos, Katja Weisel		
TA897: Daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma	NICE		
TA870: Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma	NICE		
Elranatamab for treating relapsed or refractory multiple myeloma after 3 therapies [ID4026]	NICE		
SMC2597: belantamab mafodotin (Blenrep)	SMC		
SMC2669: elranatamab (Elrexfio)	SMC		
SMC2668: teclistamab (Tecvayli)	SMC		
The cost of multiple myeloma and its complications: a single-center study from Oran, Algeria	Haouatti, F.; Belhadj, I. K.; Goumidi, A.; Yafour, N.; Houari, T.	2024	Annales Pharmaceutiques Françaises

Figure 45. PRISMA diagram of the study selection process



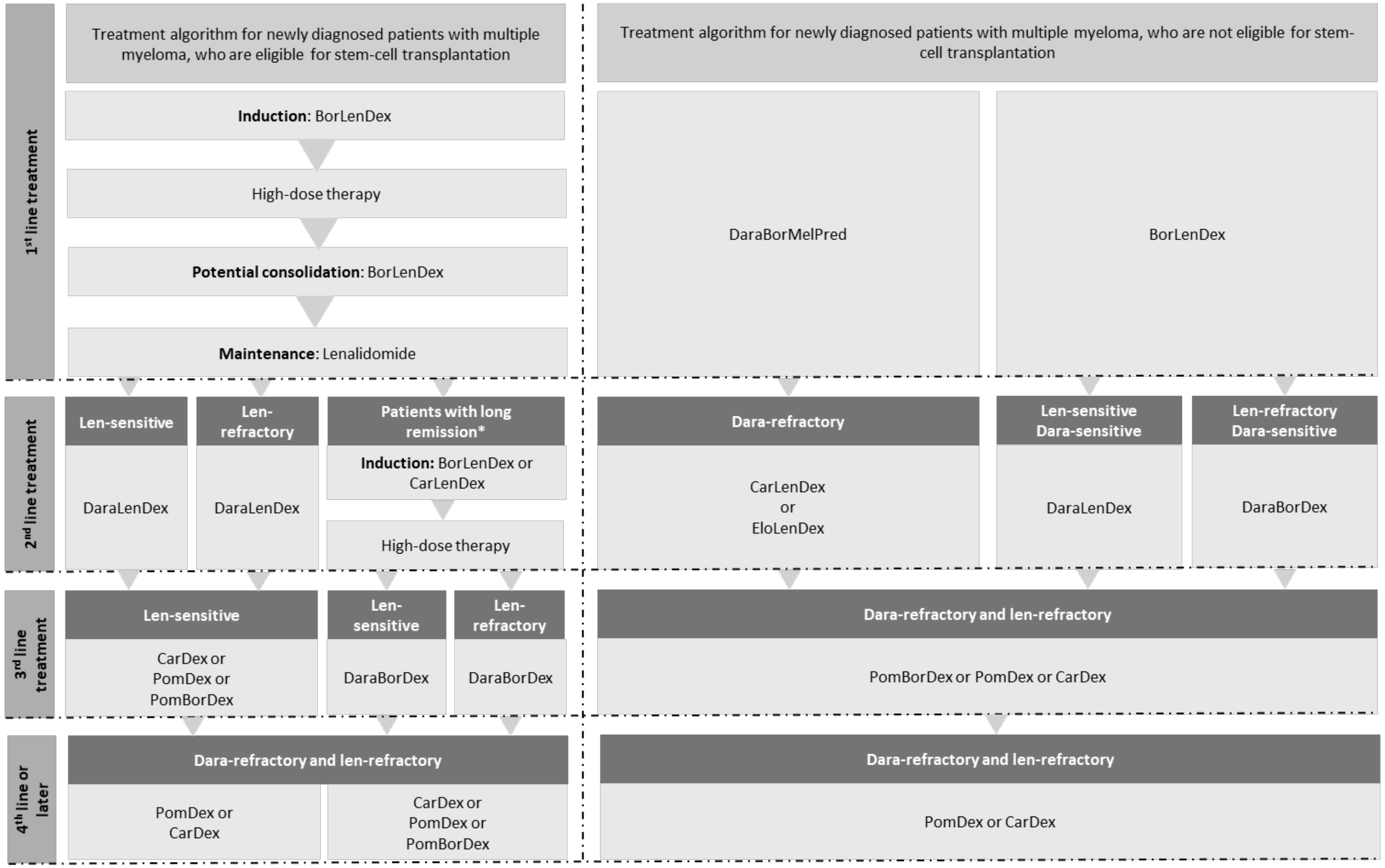
a de-duplication performed in EndNote and Covidence

b some records are data extracted for >1 economic SLR component

Appendix K. Treatment pathway for Multiple Myeloma in Denmark

The treatment pathway for multiple myeloma as described in version 1.3 of the DMC treatment guidelines is showing in Figure 46. It should be noted that in February 2024, the DMC recommended teclistamab for patients, that have received three or more prior treatments, including an IMiD, a PI, and a anti-CD38 antibody, and who have progressed on the last previous line of treatment[30]; however, teclistamab is not yet mentioned in the DMC treatment guidelines. However, this is not expected to have any influence on this submission.

Figure 46. Treatment algorithm for MM patients in Denmark, as per DMC treatment guidelines[2]



**For patients in maintenance treatment, long remission is > 3 years; without maintenance treatment long remission is > 1.5 year*

Appendix L. Adjustment for crossover from Vd to selinexor

The adjustment for crossover was done using two-stage estimation.

In the two-stage estimation, the time of disease progression was used as a secondary baseline for all Vd-treated patients, and post-progression survival was compared between switchers and non-switchers in the Vd arm, based on a Weibull accelerated failure time model, adjusting for prognostic characteristics measured at baseline and the time of disease progression. The following characteristics were adjusted for: age at enrolment (centered at the mean), number of ongoing medical history terms, number of adverse events of special interest, R-ISS stage, time of progression, physician experience with SVd, ECOG score, prior exposure, sensory component of the EORTC QLQ-CIPN20, and the number of prior anti-MM regimens. The acceleration factor obtained from the model was then used to adjust the observed survival times in Vd-switching patients to obtain counterfactual survival times[37].

A Cox proportional hazards regression model (stratified by R-ISS stage, prior PI therapy, and number of prior anti-MM regimens) was then fitted to the observed SVd arm survival times and the counterfactual Vd arm survival times to estimate a treatment switch-adjusted HR. The standard error of the log HR estimates was obtained from 2,000 bootstrap samples; hence, CI and p-value were based on a t-distribution using normal distribution theory method with the bootstrapped standard error. The possible artificial reduction of survival times when the goal of treatment is to extend survival times precluded re-censoring in the sensitivity analysis using a two-stage estimation method. Likewise, beside the relatively small number of deaths and sample size, the artificial censoring of death when deaths are, in fact, known to have occurred favored a two-stage estimation method over inverse probability of censoring weight.[37]

Crossover occurred at a median of 7.2 months, with a minimum of one month and a maximum 29 months. The reason of discontinuation of therapy in the comparator arm for all patients who crossed over was disease progression. Baseline and disease characteristics of the patients that crossed over are provided in Table 125.

Table 125. Baseline and disease characteristics for patients that crossed over from Vd to selinexor

	SVdX population (n = 63)	SVdX population (n = 11)
Age (years)		
Median	65.0	61.0
Mean (SD)	63.6 (9.81)	61.5 (8.78)
Range	38 to 85	48 to 81
Age category, n (%)		

18-50	7 (11.1%)	1 (9.1%)
51-64	22 (34.9%)	7 (63.6%)
65-74	26 (41.3%)	2 (18.2%)
>=75	8 (12.7%)	1 (9.1%)
Sex, n (%)		
Male	36 (57.1%)	7 (63.6%)
Female	27 (42.9%)	4 (36.4%)
Number of prior lines of MM therapy, n (%)		
2	25 (39.7%)	3 (27.3%)
3	20 (31.7%)	4 (36.4%)
4	18 (28.6%)	4 (36.4%)
Previously exposed, n (%)		
Carfilzomib	6 (9.5%)	1 (9.1%)
Ixazomib	0	0
Daratumumab	0	1 (9.1%)
Lenalidomide	28 (44.4%)	3 (27.3%)
Pomalidomide	5 (7.9%)	0
Prior stem cell transplant, n (%)		
Yes	23 (36.5%)	6 (54.5%)
Treatment free interval for patients with new MM treatment (days)		
Median	10	19
Mean (SD)	11.7 (8.05)	71.5 (132.80)
Min, Max	1 to 39	6 to 419

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