

Bilag til Medicinrådets vurdering af sacituzumab govitecan til behandling af ikke-resektabel eller metastatisk ER+/HER2- negativ brystkræft

Vers. 1.0



Bilagsoversigt

1. Ansøgers notat til Rådet vedr. sacituzumab
2. Forhandlingsnotat fra Amgros vedr. sacituzumab
3. Ansøgers endelige ansøgning vedr. sacituzumab

Til Medicinrådet,

Gilead takker for et godt samarbejde og gode faglige diskussioner undervejs i processen med Trodelvy® til HR+ og HER2-NEG mBC. Medicinrådet og Gilead er enige om, at patientpopulationen for indikationen er meget lille (cirka 15 patienter per år) og kendetegnes ved, at patienterne ikke har haft reel mulighed for behandling med en ADC tidligere.

Gilead har afventet med at indsende ansøgningen til Medicinrådet til begge vores 2 fase III studier havde indsamlet de endelige resultater for Overall Survival (OS) og vi derfor kunne præsentere Medicinrådet for en opdateret meta-analyse og en sundhedsøkonomisk model med mindst mulig usikker. Dette arbejde er udført udelukkende til brug for Medicinrådet, da Gilead har vurderet, at dette var nødvendigt for at opnå en anbefaling fra Medicinrådet. Ansøgning komplimenteres af et Dansk RWE studie iværksat af Gilead. Vi hæfter os ved, at *"Medicinrådet vurderer, at den poolede analyse af TROPiCS-02- og EVER-132-002-studierne kan ligge til grund for vurderingen, da studiepopulationerne er tilstrækkelig sammenlignelige med hinanden og med en dansk population"*

Vi opfatter således den kliniske del af vurderingsrapporten som en afbalanceret og grundig gennemgang af den samlede kliniske evidens med en anerkendelse af effekten af Trodelvy® i denne afgrænsede patientpopulation.

Desværre afspejler den sundhedsøkonomiske evaluering ikke dette, af to årsager.

Årsag nr. 1: Ekstrapoleringer/fremskrivning af overlevelse:

Medicinrådet har så pessimistiske fremskrivninger, at de underestimerer den faktisk observerede overlevelse for TPC i analysen udført af DBCG i det danske RWE studie.

Vi mener, at tabel 18 og 19 i vurderingsrapporten understreger, at der bør sættes spørgsmålstejn ved kurvernes kliniske troværdighed, da den inkrementelle QALY gevinst i Progressed Disease stadiet er negativ. Omsat til et klinisk argument betyder dette, at man antager, at **patienter behandlet med Trodelvy® vil dø hurtigere efter progression end patienter behandlet med TPC.**

Medicinrådets to kurvevalg bevirker i øvrigt, at de to overlevelseskurver krydser hinanden. Dette betyder, at fra det tidspunkt hvor kurverne krydser, vil flere være døde i Trodelvy® armen sammenlignet med TPC armen. Det på trods af, at Trodelvy® kurven har ligget væsentligt over TPC armen frem til dette tidspunkt.

Gilead er bekymret for, om Fagudvalget er blevet oplyst om, hvilke kliniske antagelser man skal acceptere for at opnå en fremskrivning, der sigter efter, at ingen, eller meget få, patienter er i live efter 5 år, og om de i givet fald er enige i disse antagelser

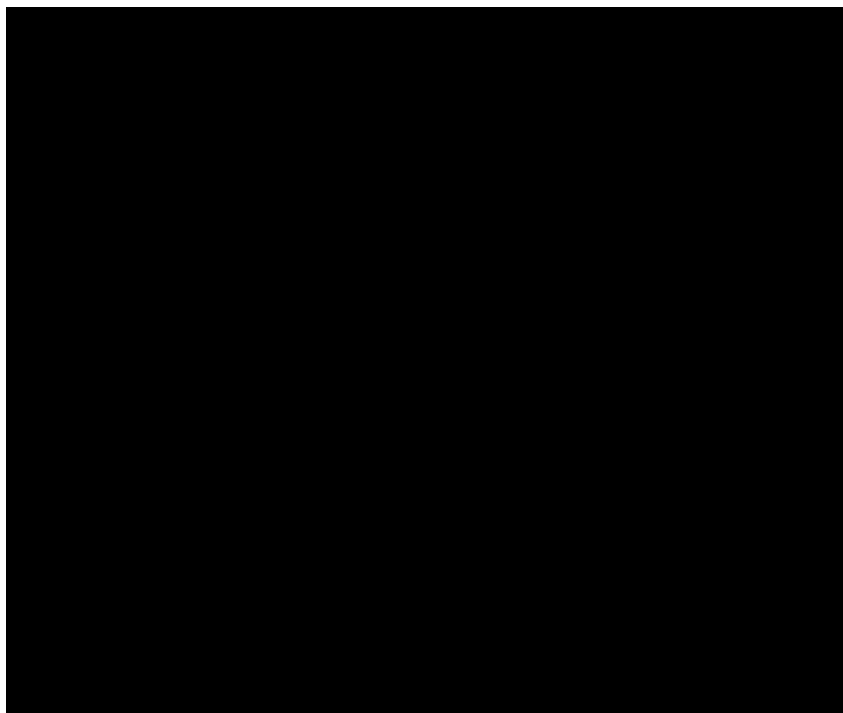
Årsag nr. 2: Fase III data fra EVER-132-002 ekskluderes i scenarie 2

Medicinrådet beskriver, at data fra EVER-132-002 ” *bidrager med usikkerhed vedrørende størrelsen af OS-gevinsten*”.

En skærende kontrast til HTA myndigheden i Sverige, TLV, som bedømmer ” *att osäkerheten avseende den kliniska effekten är låg, då den relativa effekten baseras på poolad analys av två randomiserade, direkt jämförande, fas III-kliniska studier*”.

Medicinrådet forklarer, at det er fordi kun TROPiCS-02 har været indsendt til EMA. Som læser må vi således konkludere, at data som Medicinrådet finder ” *tilstrækkelig sammenlignelig.. ... med en dansk population*” kan ekskluderes, hvis de ikke er vurderet af EMA. Gilead er i tvivl om, hvad denne praksis vil betyde for fremtidige ansøgninger til Medicinrådet. Betyder det, at vi og andre ansøgere i fremtiden ikke skal basere ansøgninger på mest mulig tilgængelig evidens, hvis denne ikke har været indsendt til EMA?

I Norge og Finland har man, som i Medicinrådets scenarie 2, alene vurderet sundhedsøkonomien ud fra TROPiCS-02 studiet, og ikke inkluderet data fra fase III studiet EVER-132-002. Deres adgangssituation adskiller sig fra resten af Europas adgang til Trodelvy® for HR+ indikationen:



Gilead er derfor bekymret for, om eksklusion af EVER-132-002 i scenarie 2 og italesættelsen af scenarierne som ” *lige klinisk plausibel*” vil føre til misforståelser og en deraf afledt underestimering af effekt og manglende anbefaling til følge.

Gilead henstiller derfor til, at scenarie 2 fjernes, da eksklusion af relevant data (EVER-132-002) ikke er en evidensbaseret tilgang til vurdering af nye lægemidler og nye indikationer og kan føre til manglende adgang til behandling for danske patienter.

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Forhandlingsnotat

02.10.2026
LSC/DBS

Dato for vurdering i Medicinrådet	28.10.2026
Leverandør	Gilead Sciences
Lægemiddel	Trodelvy (Sacituzumab govitecan)
Ansøgt indikation	Monoterapi til behandling af voksne patienter med ikke-resektabel eller metastatisk hormonreceptor (HR)-positiv, HER2-negativ brystkræft, som har fået endokrinbaseret behandling og mindst to yderligere systemiske behandlinger ved fremskreden sygdom
Nyt lægemiddel / indikationsudvidelse	Indikationsudvidelse

Prisinformation

Amgros har følgende pris på Trodelvy:

Tabel 1: Aftalepris

Lægemiddel	Styrke (pakning)	AIP (DKK)	Nuværende SAIP (DKK)	Nuværende rabat ift. AIP
Trodelvy	200 mg (1 stk.)	6.538,99		

Aftaleforhold

Amgros har en eksisterende aftale på Trodelvy. Aftalen gælder til den 30.09.2027 med mulighed for at forlænge i 12 måneder. Der er inkluderet mulighed for prisregulering i aftalen.

Informationer fra forhandlingen

Konkurrencesituationen

Patienterne behandles i dag individuelt med endokrin behandling og efterfølgende bl.a. kemoterapi eller trastuzumab deruxtecan afhængigt af sygdomsforløb og patientkarakteristika. I 4. linje er kemoterapi standardbehandling, og Trodelvy vil udgøre en ny behandlingsmulighed i 4 linje.

Tabel 2 viser de årlige lægemiddeludgifter ved behandling med Trodelvy. Lægemiddeludgifter til kemoterapi er ikke medtaget i tabel 2.

Tabel 2: Lægemiddeludgifter pr. patient

Lægemiddel	Styrke (pakning)	Dosering	Pris pr. pakning (SAIP, DKK)	Lægemiddeludgift pr. år (SAIP, DKK)
Trodelvy	200 mg (1 stk.)	10 mg/kg*, ** på dag 1 og dag 8 af en 21-dages behandlingsserie		

*Gennemsnitsvægt 71 kg, jf. Medicinrådets vurdering af sacituzumab govitecan til behandling af ikke-resektabel eller metastatisk ER+/HER2-negativ brystkræft

**Der regnes med hele hætteglas

Status fra andre lande

Tabel 3: Status fra andre lande

Land	Status	Link
Norge	Ikke anbefalet	Link til vurdering
Sverige	Anbefalet	Link til vurdering
England	Anbefalet	Link til vurdering

Opsummering

Amgros har en eksisterende aftale på Trodelvy der gælder indtil 30.09.2027.

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Application for the assessment of Trodelvy[®] for the treatment of adult patients with unresectable or metastatic hormone receptor-positive (HR+), human epidermal growth factor receptor 2 (HER2)-negative breast cancer who have received endocrine-based therapy, and at least two additional systemic therapies in the advanced setting



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Abbreviations

Abbreviation	Description
ADC	Antibody-drug conjugates



AE	Adverse events
AIC	Akaike information criteria
BC	Breast Cancer
BIC	Bayesian information criteria
BICR	Blinded independent central review
BSA	Body surface area
CEM	Cost effectiveness model
CI	Confidence interval
CR	Complete response
CT	Computer Tomography
CTCAE	Common Terminology Criteria for Adverse Events
DBCG	Danish Breast Cancer group
DCO	Data cut-offs
DMC	Danish Medicines Council
DOR	Duration of Response
ECS	Expert consensus statements
EORTC	European Organization for the Research and Treatment of Cancer
EOT	End of therapy
EPAR	European Public Assessment Report
ER	Expressing estrogen receptor
ET	Endocrine Therapy
HR	Hormone receptor
HRQoL	Health-related quality of life
IHC	Immunohistochemistry
IPD	Individual patient data



IRC	Independent review committee
ISH	<i>In situ</i> hybridisation
ITT	Intention-to-Treat
KM	Kaplan-Meier
LIR	Local investigator review
LS	Least squares
mBC	Metastatic breast cancer
MMRM	Mixed model repeated measure
ORR	Objective response rate
OS	Overall survival
OWSA	One-way sensitivity analysis
PD	Progressed disease
PF	Progression-free
PFS	Progression-free survival
PO	Peroral
PR	Progesterone receptor
PSA	Probabilistic sensitivity analyses
PSM	Partitioned survival model
QOL	Quality of life
RDI	Relative dose intensity
RECIST	Response Evaluation Criteria in Solid Tumors version 1.1
RWE	Real world evidence
SAE	Serious adverse events
SG	Sacituzumab govitecan
SLR	Systematic literature review
SmPC	Summary of product characteristics



TPC	Treatment of physician's choice
TTD	Time to treatment discontinuation
VAS	Visual Analogue scale

1. Information on the drug

Drug information

Trade name	Trodelvy®
Generic name	Sacituzumab govitecan (SG)
Indication as formulated by the European Medicines Agency (EMA)	SG as monotherapy is indicated for the treatment of adult patients with unresectable or metastatic hormone receptor-positive (HR+), human epidermal growth factor receptor 2 (HER2)-negative breast cancer who have received endocrine-based therapy, and at least two additional systemic therapies in the advanced setting (EMA, 2021).
Marketing Authorization Holder in Denmark	Gilead Sciences
ATC code	L01FX06
Combination therapy and/or concurrent treatment	No
Expected date of EU approval (marketing authorisation)	The commission decision was issued on 26 July 2023 for the type II variation, extension of indication (EMA, 2025c).
Has the drug received a conditional marketing authorisation?	No
Has the drug been in 'accelerated' assessment' at EMA?	No
Does the drug have orphan drug designation?	No
Other indications approved by the EMA	Yes, the initial market authorisation was issued on 22 November 2021 (EMA procedure number EMA/623887/2021) for SG as monotherapy for the treatment of adult patients with unresectable or metastatic triple-negative breast cancer (mTNBC)



	who have received two or more prior systemic therapies, including at least one of them for advanced disease.
Other indications that have been evaluated by the Danish Medicines Council	Yes, the DMC recommended SG as the standard treatment on the 21st of May 2025 as monotherapy for adult patients with unresectable or mTNBC who have received two or more prior systemic therapies, including at least one for advanced disease (Medicinrådet, 2025c).
Joint Nordic Assessment (JNHB): Is current treatment practice comparable across the Nordic countries (DK, FI, IS, NO, SE)?	No
Joint Nordic Assessment (JNHB): Is the drug suitable for a joint Nordic assessment?	No, a joint Nordic assessment is not relevant as assessments in the other Nordic countries are finalised. SG is already recommended for the HR+ indication in Sweden and Iceland.
Has a joint European assessment (JCA) been carried out via the EU HTA Regulation?	No
Delivery	BEGR
Packaging – types, sizes/number of units and concentrations	200 mg powder, for concentrate for solution for infusion. Each pack contains one vial.

2. Summary table

Overview	
Indication relevant to the assessment	As monotherapy for the treatment of adult patients with unresectable or metastatic HR+, HER2-negative breast cancer who have received endocrine-based therapy, and at least two additional systemic therapies in the advanced setting (EMA, 2021)
Dosage regimen and administration route	The recommended dose of SG is 10 mg/kg administered as an intravenous infusion once weekly on Day 1 and Day 8 of 21-



	day treatment cycles. Treatment should be continued until disease progression or unacceptable toxicity (EMA, 2021).
Comparator selection	The relevant comparator for SG is that used in the pivotal TROPiCS-02 and EVER-132-002 studies, namely the physician's choice of single-agent chemotherapy (eribulin, vinorelbine, capecitabine, or gemcitabine), referred to as treatment of physician's choice (TPC). This (single-agent chemotherapies) reflects current Danish clinical practice, based on DBCG guidelines (DBCG, 2024), for patients with ER+/HER2-negative metastatic breast cancer (mBC) who have received prior endocrine-based therapy and at least two additional systemic regimens in the advanced setting. There is no preferred specific chemotherapy in later treatment lines (DBCG, 2024).
Prognosis with current standard treatment (comparator(s))	Median overall survival in mBC varies over molecular subtypes, and the prognosis for patients with HR+/HER2-negative mBC remains poor once endocrine-based therapy and targeted options have been exhausted. For patients treated in later lines with single-agent chemotherapy, the median overall survival decreases with each line of therapy and is between 7 and 24 months (DCBG, 2024; Waks et al., 2022). Danish real-world data for this specific patient group, collected by DBCG, showed a median OS of 13.3 months in third line, and 10.2 months in fourth line (Dahl et al., 2025), which is consistent with data from the EVER-132-002 TPC arms (12.3 months) (Xu et al., 2024) and TROPiCS-02 (11.2 months) (Rugo et al., 2023), respectively. Moreover, previous DMC assessments (e.g. for CDK4/6 inhibitors and trastuzumab deruxtecan) confirm that disease progression in the mBC setting is continuous and associated with declining quality of life and limited survival benefit from further chemotherapy, underscoring the high unmet medical need (Medicinerådet, 2023b, 2025b).
Type of documentation for the clinical evaluation	Head-to-head pooled analysis of TROPiCS-02 (NCT03901339) and EVER-132-002 (NCT04639986)
Main outcomes including at least one outcome for health-related quality of life (difference/improvement compared to comparator(s))	For efficacy, the results from the meta-analysis for prior CDK4/6 inhibitor treated: The median OS was [REDACTED] months [95% CI [REDACTED]] for SG and [REDACTED] months [95% [REDACTED]] for TPC, difference: [REDACTED] months (HR [REDACTED] [95% CI: [REDACTED]]) The median PFS was 4.7 months [95% CI: 4.1, 5.7] for SG and 3.7 months [95% CI: 2.8, 4.2] for TPC, difference: 1.0 month (HR 0.65 [95% CI: 0.52, 0.81]) HRQoL measurements from TROPiCS-02, mean change from baseline EQ-5D-5L index score, average (SE): SG: 0.87 (0.054), TPC: 0.54 (0.138), difference: 0.248 (95% CI: -0.071, 0.568)



Serious adverse events for the intervention and comparator	There were no serious adverse events with a frequency $\geq 5\%$ in any treatment arm. The most common treatment-related adverse events were neutropenia, leukopenia, anaemia, diarrhoea, fatigue, febrile neutropenia, and hypokalaemia. These were included in the cost-effectiveness analysis.
Type of health economic analysis	Cost-utility analysis
Health economic model	Three-state partitioned survival model
Outcomes and sources for extrapolating patient transitions	Progression-free survival (pooled meta-analysis of TROPiCS-02 and EVER-132-002, prior CDK4/6i treated patients) Overall survival (pooled meta-analysis of TROPiCS-02 and EVER-132-002, prior CDK4/6i treated patients))
Instrument and sources for health-related quality of life	EQ-5D-5L (TROPiCS-02 and EVER-132-002), Danish EQ-5D index scores (utility scores), and EQ-VAS. The utility scores over time were broadly similar between the treatment arms.
Life years gained (discounted, corrected for half-cycle and background mortality)	0.42
QALYs gained (discounted, corrected for half-cycle and background mortality)	0.35
ICER (DKK/QALY) (discounted, corrected for half-cycle and background mortality)	951,460 DKK/QALY
Applicant's assessment of uncertainty	Main uncertainty: Choice of extrapolation of OS



3. Patient population, intervention, choice of comparator(s) and outcome(s)

3.1 Patient population

3.1.1 The disease

Breast cancer is the most frequent cancer among Danish women (Medicinrådet, 2023b), with approximately 4,900 new cases annually (DCBG, 2024). Around 6% present with metastatic disease at diagnosis, and 15% to 20% of early-stage tumours will develop metastases within ten years. This corresponds to approximately 1,000 new cases of metastatic breast cancer (mBC) per year in Denmark (DCBG, 2024). Tissue biopsy is recommended for pathological evaluation, including an assessment of hormone receptor (HR) and Human Epidermal Growth Factor Receptor 2 (HER2) status, and can be divided into four subtypes (Medicinrådet, 2023b). Among the subtypes, HR-positive (HR+), which includes tumours expressing oestrogen receptor (ER) and/or progesterone receptor (PR) in tumour cells (DCBG, 2024).

HR+ HER2-negative breast cancer is primarily driven by ER-mediated signalling, which promotes tumour cell proliferation and survival. In later lines of therapy, the disease is typically endocrine-refractory and driven by more aggressive biological behaviour. In Denmark, ER+ HER2-negative BC has been estimated to affect 3,300 patients per year (Medicinrådet, 2023b). As the expression of progesterone lacks clinical value in Denmark, it is not tested for, and HR+ breast cancer is referred to as ER-positive (ER+) breast cancer (Medicinrådet, 2023a).

HER2 status is determined by immunohistochemistry (IHC) and confirmed by *in situ* hybridisation (ISH) when required. Traditionally, HER2-positive breast cancer is defined as IHC 3+ or IHC 2+ with HER2 gene amplification by ISH, whereas tumours with IHC 0, IHC 1+, or IHC 2+/ISH-negative are considered HER2-negative (Wolff et al., 2018). Following the market authorisation in Europe for trastuzumab deruxtecan (T-DXd, Enhertu®) in HER2 low (EMA, 2022) and ultralow (EMA, 2025a) the clinical relevance of the HER2 expression spectrum has expanded.

The ESMO 2023 Expert Consensus (Tarantino et al., 2023) defines the expanded HER2 spectrum as:

- HER2-low: IHC 1+ and IHC 2+/ISH-negative
- HER2-ultralow: IHC0 with faint, incomplete membrane staining in ≤10 % of tumour cells (sometimes described as 'IHC >0 and ≤10 %')
- HER2-negative/HER2-null: IHC0 with no membranous staining in any tumour cells.



The prognosis for mBC is poor, and the disease is considered incurable, although treatments can extend survival and improve health-related quality of life (HRQoL) (DCBG, 2024). Individuals with mBC represent a highly heterogeneous group, with some experiencing a rapidly progressive disease despite treatment, with limited QoL, whereas others can live for many years with controlled disease and a maintained HRQoL (DCBG, 2024). The median overall survival (mOS) for ER+/HER2-normal is 43 months (95% CI, 42.5–44.5) (DCBG, 2024). After progression on endocrine therapy + CDK4/6 inhibitors, outcomes are highly variable and driven by disease burden and biology (DCBG, 2024).

A Danish real-world evidence study from the Danish Breast Cancer group (DBCG) included individuals with ER+/HER2-negative mBC treated with a CDK4/6 inhibitor and endocrine therapy in 1st or 2nd line. These patients, initiating a 3rd line therapy, represent a population that is heavily pretreated, typically older (median age 68 years) and with the majority having visceral involvement (83%) and ≥3 metastatic sites involved (60%).

The prognosis for these patients is particularly poor, the mOS is approximately 13 months (95% CI: 12.3-14.5) (Dahl et al., 2025), decreasing to 10.2 months and 8.3 months in next lines of therapy. Median progression-free survival (mPFS) across lines is four to five months, indicating limited durability of the current available treatments in Denmark and a rapid disease progression for these patients.

3.1.2 Selected patient population

The relevant population for sacituzumab govitecan (SG, Trodelvy®) includes adult patients with unresectable or metastatic HR+, HER2-negative breast cancer who have received endocrine-based therapy, and at least two additional systemic therapies in the advanced setting. This includes all HER2-negative patients, defined as IHC0 and IHC 1+ and IHC 2+/ISH-negative, who are not well-suited for treatment with T-DXd, given the Danish Medicines Council (DMC) restriction to not sequence SG and T-DXd (Medicinrådet, 2025b).

When calculating eligible patients for SG, given the nature of the disease and the poor general condition of the population, only incidence is relevant. It has previously been estimated that 275 individuals with ER+ HER2-negative mBC have endocrine-resistant tumours and are eligible for a single-agent chemotherapy (Medicinrådet, 2025b). Of those, 205 individuals are eligible for an additional line of therapy, 135 are expected to have HER2-low disease, of which 110 are expected to get T-DXd. The rest (205 minus 135), approximately 70 patients, are considered to have IHC0 tumours (Medicinrådet, 2025b).

Based on experience with SG in Sweden for HR+ mBC, it is estimated that approximately 15-20 patients annually are eligible for SG each year including IHC0 and selected patients with IHC 1+ and IHC 2+/ISH-negative disease who are ineligible for HER2-targeted antibody-drug conjugates (ADC) therapy (due to contraindication or intolerance).



Figure 1. Selected patient population

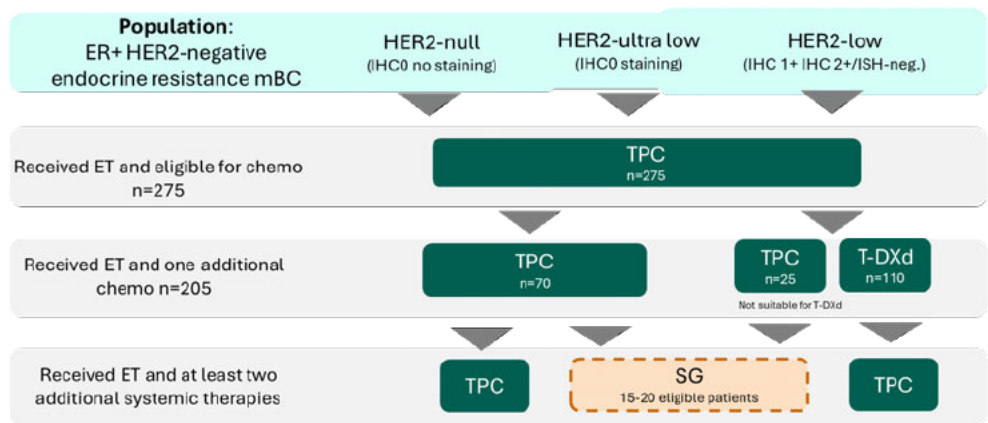


Table 1. Expected number of patients and patient uptake when implementing the intervention

Year	Year 1	Year 2	Year 3	Year 4	Year 5
Expected number of patients	15	15	15	15	15
Patient uptake	50%	100%	100 %	100%	100%

3.2 Intervention

Sacituzumab govitecan (ATC code: L01FX17) is a Trop-2-directed ADC that binds to Trop-2-expressing cancer cells and is internalised, resulting in the subsequent release of SN-38 from a hydrolysable linker. SN-38 interacts with topoisomerase I and prevents re-ligation of topoisomerase I-induced single-strand breaks. The resulting DNA damage leads to apoptosis and cell death.

An overview is given in Table 2, and an overview of the study intervention and the health economic model is shown in Table 3.

As management of adverse reactions may require temporary interruption, dose reduction, or treatment discontinuation of SG, individual patient-level data from TROPiCS-02 have been used in the model to derive dosing, including patient weight. Relative dose intensity (RDI) was assumed based on clinical experts' opinion and a previous DMC assessment of SG (Gilead, 2026a, 2026b, 2026c; Medicinrådet, 2022), and it is described in more detail in Section 11.1.1. The RDI from the trial was not used because it was not considered representative of Danish clinical practice, since patients are expected to be more frail, and therefore a lower RDI compared to the trial seems reasonable. Dose delays as observed in the study have been applied. Therefore, the dose distribution is implemented directly within the model and forms the basis for calculating drug costs. As a result, a separate aggregated table of dose distribution has not been included.



When applying the dose in the CE-model, European patients from TROPiCS-02 were used to directly incorporate the observed dosing patterns in the study, including RDI based on clinical experts' opinions (Gilead, 2026a, 2026b, 2026c) and dose delays from the clinical trials. While minor differences in patient characteristics (e.g. weight distribution) may occur, these are not expected to have a meaningful impact on effectiveness or safety. Any potential differences are expected to have a limited impact on drug costs.

Table 2. Overview of the intervention

Therapeutic indication relevant to the assessment	As monotherapy for the treatment of adult patients with unresectable or metastatic HR+, HER2-negative breast cancer who have received endocrine-based therapy, and at least two additional systemic therapies in the advanced setting.
Generic name	Sacituzumab govitecan
ATC code	L01FX06
Mechanism of action	SG is a Trop-2-directed ADC, that binds to Trop-2-expressing cancer cells and is internalised with the subsequent release of SN-38 from a hydrolysable linker (EMA, 2025b). SN-38 interacts with topoisomerase I and prevents re-ligation of topoisomerase I-induced single strand breaks. The resulting DNA damage leads to apoptosis and cell death (EMA, 2025b).
Administration method	Intravenous infusion
Packaging type, pack sizes, shelf life and strengths	One vial of powder contains 200 mg SG. After reconstitution, one mL of solution contains 10 mg sacituzumab govitecan. Unopened vials has a shelf life of 3 years
Package size(s)	1 vial (200 mg)
If vials: Can these be shared?	Yes
Pre-medication: Should pre-medication be administered? Which one?	Prior to each dose, treatment for the prevention of infusion-related reactions and prevention of chemotherapy-induced nausea and vomiting is recommended.
Co-administration: Should the drug be administered with other drugs? Which ones?	N/A



Need for diagnostics, monitoring or other tests (e.g., companion diagnostics)

Patients are monitored for any reactions during the infusion and for at least 30 minutes afterwards.
Assessment of HR and HER2 status is standard and done in earlier lines of therapy.

Table 3. The intervention in the study and the health economic model

	TROPICS-02	EVER-132-002 (ITT)	Health economic model
Dosage and frequency [if weight-based, please state weight in brackets and any criteria for transition to flat-dose]	10 mg/kg (mean weight: 68.3 kg) administered on Day 1 and Day 8 of 21-day treatment cycles.	10 mg/kg (mean weight: 59.5 kg) administered on Day 1 and Day 8 of 21-day treatment cycles.	10 mg/kg (weight: 66.4 kg based on European patient distribution in TROPiCS-02) administered on Day 1 and Day 8 of 21-day treatment cycles.
Average dose	█ mg per administration █ mg/kg per administration (calculated as mean cumulative dose/mean number of doses) x mean bodyweight in kg █ mg/kg	█ mg per administration █ mg/kg per administration (calculated as mean cumulative dose/mean number of doses) x mean bodyweight in kg █ mg/kg	█ administration with 50% vial sharing assumed in the base case. Calculated based on the required posology, assumed RDI in Danish clinical practice and the European patient weight distribution in TROPiCS-02, including drug waste and dose delay.
Criteria for treatment discontinuation	Until disease progression or unacceptable toxicity.	Until disease progression or unacceptable toxicity.	Until disease progression or unacceptable toxicity.
Treatment duration	Mean: █ months Median: 4.11 months	Mean: █ months Median: 5.95 months	Mean: █ months Median: 4.13 months
Dose adjustment: Report if/how dose adjustment is made	Protocol-defined dose reductions were permitted RDI: █ RDI was calculated as cumulative dosage	Protocol-defined dose reductions were permitted RDI: █ RDI was calculated as cumulative dosage	RDI: 83.0*% Assumed to represent the Danish clinical practice, validated by clinical experts (Gilead, 2026a, 2026b, 2026c).



	TROPiCS-02	EVER-132-002 (ITT)	Health economic model
	received/ total assigned dosage x 100	received/ total assigned dosage x 100	
Dose pause: Specify if/how pause (treatment interruption) is performed	Dose delays were allowed as per protocol The actual mean dose received was █████ mg/kg per administration vs protocol 10 mg/kg per administration	Dose delays were allowed as per protocol The actual mean dose received was █████ mg/kg per administration vs protocol 10 mg/kg per administration	Dose delay factor: █████ % A dose delay factor was applied, calculated as the actual dose of the pooled meta-analysis of TROPiCS-02 and EVER-132-002 dataset/total dose per protocol

Note: * The RDI value is derived to yield a specific relative dose of 75%. Details of this calculation are presented in Section 11.1.1

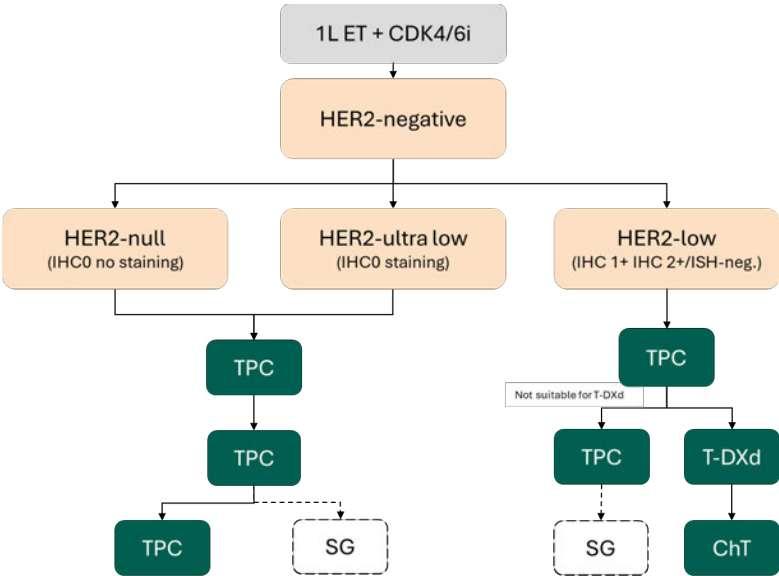
3.2.1 The intervention in the context of Danish clinical practice

The expected placement of SG is presented in Figure 2. Treatment patterns in the Danish clinical practice, based on the DBCG data from (Dahl et al., 2025), indicates that patients are treated sequentially with single-agent chemotherapies, but that there is no single standard regimen preferred. The relevant Danish population (see section 3.1.2) will be a subgroup of heavily pretreated individuals, as described by Dahl and colleagues (Dahl et al., 2025). Since the recommendation of T-DXd as a standard treatment for individuals with mBC and HER2-low tumours after one systemic treatment in the metastatic setting, coupled with the recommendation **not** to sequence SG and T-DXd (Medicinrådet, 2025b), SG is expected to be used for:

- Patients with ER+ HER2-negative (IHC0) metastatic breast cancer, and
- Selected patients with HER2-low (IHC 1+ and IHC 2+/ISH-negative) disease who are ineligible for HER2-targeted ADC therapy (due to contraindication or intolerance).



Figure 2. The expected placement of SG



Abbreviations: 1L, First-line; ET, Endocrine therapy; CDK4/6i, Cyclin-dependent kinases 4 and 6 inhibitor; HER2, Human epidermal growth factor receptor 2; IHC, Immunohistochemistry; ; T-DXd, TPC, Treatment of physician's choice; Trastuzumab deruxtecan; SG, Sacituzumab govitecan

3.2.2 ATMP

N/A

3.3 Selection of comparator(s)

The relevant comparator is the treatment of physicians' choice (TPC), of single-agent chemotherapy. The DBCG guidelines recommend sequential treatment with single-agent chemotherapy (in this application, referred to as TPC), with each line of chemotherapy continued until progression or unacceptable toxicity. The DBCG do not specify a preferred single-agent chemotherapy, and TPC options in Denmark may include capecitabine, vinorelbine, eribulin, gemcitabine, and carboplatin (DBCG, 2024), reflecting the TPC used in the TROPiCS-02 and EVER-132-002 trials.

These single-agent chemotherapies were confirmed to be representative of Danish clinical practice by Danish clinical experts (Gilead, 2026a, 2026b, 2026c). In addition, Danish real-world evidence from DBCG (Dahl et al., 2025) further demonstrates that these agents, alongside other single-agent chemotherapies (taxanes and anthracyclines), are routinely used in later lines of therapy without a fixed sequence.

Details of the respective treatments reflecting the TPC in Denmark and how these were used in the study and applied in the health economic model are presented below from Table 4 to Table 11.

Similar to SG, as adverse reactions may require temporary interruption, dose reduction, or treatment discontinuation of the respective TPC, individual patient-level data from TROPiCS-02 have been used in the model to derive dosing, including patient weight and



dose delays. For RDI, since the trial data were not considered representative for Danish clinical practice, the same RDI derived for SG was applied to all TPC treatments. Further details are given in Section 11.1.1. The dose distribution is implemented directly within the model and forms the basis for calculating drug costs.

The CE-model used the demography of European patients from TROPiCS-02 and incorporates observed dosing patterns, including RDI based on clinical experts' opinions (Gilead, 2026a, 2026b, 2026c) and dose delay from clinical trials. This is considered representative of Danish clinical practice. While minor differences in patient characteristics (e.g. weight distribution) may occur, these are not expected to have a meaningful impact on effectiveness or safety. Any potential differences are expected to have only a limited impact on drug costs.

Table 4. Comparator overview - Eribulin

Therapeutic indication relevant to the assessment	Treatment of adult patients with locally advanced or mBC who have progressed after at least one chemotherapeutic regimen for advanced disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting unless patients were not suitable for these treatments.
Generic name	Eribulin
ATC code	L01XX41
Mechanism of action	Eribulin exerts its effects via a tubulin-based antimitotic mechanism leading to G2/M cell-cycle block, disruption of mitotic spindles, and, ultimately, apoptotic cell death after prolonged and irreversible mitotic blockage.
Administration method	Intravenous infusion
Packaging type, pack sizes, shelf life and strengths	0.44 mg/ml in vials size 2 ml. Unopened vials have a shelf life of 2 years.
Package size(s)	Eribulin 0.44 mg/ml solution for injection. Each package contains a single vial of 2 ml solution.
If vials: Can these be shared?	Yes
Pre-medication: Should pre-medication be administered? Which one?	N/A
Co-administration: Should the drug be administered with other drugs? Which ones?	Antiemetic prophylaxis, including corticosteroids, should be considered since patients may experience nausea and vomiting.



Need for diagnostics, monitoring or other tests (e.g., companion diagnostics)

Monitoring of complete blood count, signs of peripheral motor and sensory neuropathy.

Source: EMA (EMA)

Table 5. Comparator (Eribulin) in the study and the health economic model

	TROPiCS-02	EVER-132-002 (ITT)	Health economic model
Dosage and frequency [if weight-based, please state weight in brackets and any criteria for transition to flat-dose]	1.23 mg/m ² (Mean BSA: 1.7) on Days 1 and 8 of a 21-day cycle	1.23 mg/m ² (Mean BSA: 1.6) on Days 1 and 8 of a 21-day cycle	1.23 mg/m ² (BSA: 1.7 based on European patient distribution in TROPiCS-0272) on Days 1 and 8 of a 21-day cycle
Average dose	2.11 mg per administration 1.24 mg/m ² (calculated as mean cumulative dose/mean number of doses) x mean BSA $15.57/12.57 = 1.24\text{mg/m}^2$	2.08 mg per administration 1.30 mg/m ² (calculated as mean cumulative dose/mean number of doses) x mean BSA $19.71 / 15.11 = 1.30\text{mg/m}^2$	1.95 mg per administration, with 1.58 mg administered to the patients and 0.37 mg assumed as waste. Calculated based on the required posology, assumed RDI in Danish clinical practice and European patients' weight distribution from TROPiCS-02, including drug waste.
Criteria for treatment discontinuation	Until disease progression or unacceptable toxicity	Until disease progression or unacceptable toxicity	Until disease progression or unacceptable toxicity.
Treatment duration	Mean: 4.39 months Median: 3.37 months	Mean: 5.29 months Median: 3.91 months	Mean TPC basket: 3.6 months Median TPC basket: 2.5 months
Dose adjustment: Report if/how dose adjustment is made	Protocol-defined dose reductions were permitted RDI: 89.9%	Protocol-defined dose reductions were permitted RDI: 93.3%	RDI: 83.0*% Assumed to represent the Danish clinical practice, validated by clinical experts



	TROPiCS-02	EVER-132-002 (ITT)	Health economic model
	RDI was calculated as cumulative dosage received/ total assigned dosage x 100	RDI was calculated as cumulative dosage received/ total assigned dosage x 100	(Gilead, 2026a, 2026b, 2026c).
Dose pause: Specify if/how pause (treatment interruption) is performed	Dose delays were allowed as per protocol The actual mean dose received was 1.24 mg/m² per administration vs protocol 1.23 mg/m² per administration.	Dose delays were allowed as per protocol The actual mean dose received was 1.30 mg/m² per administration vs protocol 1.23 mg/m² per administration.	Dose delay factor: 90.3% A dose delay factor was applied in the CEM, calculated as the actual dose of the pooled meta-analysis of TROPiCS-02 and EVER-132-002/total dose per protocol

* The RDI value is assumed to be the same as the intervention. Details of this calculation are described in Section 11.1.1.

Table 6. Comparator overview - Capecitabine

Therapeutic indication relevant to the assessment	As monotherapy for the treatment of patients with locally advanced or mBC after failure of taxanes and an anthracycline containing chemotherapy regimen or for whom further anthracycline therapy is not indicated.
Generic name	Capecitabine
ATC code	L01BC06
Mechanism of action	Capecitabine is a non-cytotoxic fluoropyrimidine carbamate, which functions as an orally administered precursor of the cytotoxic moiety 5-fluorouracil (5-FU).
Administration method	Oral use
Packaging type, pack sizes, shelf life and strengths	150 mg x 60 film-coated tablets and 500 mg x 120 film-coated tablets. Shelf life is 2 years.
Package size(s)	Capecitabine is available as film-coated tablets (150 mg x 60 tablets and 500 mg x 120 tablets).
If vials: Can these be shared?	N/A



Pre-medication: Should pre-medication be administered? Which one? N/A

Co-administration: Should the drug be administered with other drugs? Which ones? N/A

Need for diagnostics, monitoring or other tests (e.g., companion diagnostics) N/A

Source: EMA (EMA)

Table 7. Comparator (capecitabine) in the study and the health economic model

	TROPiCS-02	EVER-132-002 (ITT)	Health economic model
Dosage and frequency [if weight-based, please state weight in brackets and any criteria for transition to flat-dose]	1,000-1,250 mg/m ² (Mean BSA: 1.7) PO twice daily on Days 1-14 of a 21-day cycle	1,000-1,250 mg/m ² (Mean BSA: 1.6) PO twice daily on Days 1-14 of a 21-day cycle	1,000-1,250 mg/m ² (BSA: 1.7 based on European patient distribution in TROPiCS-02) PO twice daily on Days 1-14 of a 21-day cycle
Average dose	1,645 mg per administration (3,290 mg per day) 967.68mg/m ² per administration (calculated as mean cumulative dose/mean number of doses) x mean BSA $193,673.35/200.14 = 967.68 \text{ mg/m}^2$	1,589 mg per administration (3,117 mg per day) 992.87 mg/m ² per administration (calculated as mean cumulative dose/mean number of doses) x mean BSA $209,408.01/226.91 = 992.87 \text{ mg/m}^2$	1508.13 mg per administration (1455.44 mg to patients and 52.69 mg assumed to be lost to waste). Calculated based on the required posology, assumed RDI in Danish clinical practice and European patients' in TROPiCS-02 BSA, including drug waste and dose delay.
Criteria for treatment discontinuation	Until disease progression or unacceptable toxicity.	Until disease progression or unacceptable toxicity.	Until disease progression or unacceptable toxicity.
Treatment duration	Mean: 4.8 months Median: 4.5 month	Mean: 5.3 months Median: 4.9 months	Mean TPC basket: 3.6 months Median TPC basket: 2.5 months



	TROPiCS-02	EVER-132-002 (ITT)	Health economic model
Dose adjustment: Report if/how dose adjustment is made	Protocol-defined dose reductions were permitted RDI: 85.7% RDI was calculated as cumulative dosage received/ total assigned dosage x 100	Protocol-defined dose reductions were permitted RDI: 92.7% RDI was calculated as cumulative dosage received/ total assigned dosage x 100	RDI: 83.0%* Assumed to represent the Danish clinical practice, validated by clinical experts (Gilead, 2026a, 2026b, 2026c)
Dose pause: Specify if/how pause (treatment interruption) is performed	Dose delays were allowed as per protocol The actual mean dose was 967.68 mg/m ² per administration vs protocol 1,000-1,250 mg/m ² per administration	Dose delays were allowed as per protocol The actual mean dose was 992.87 mg/m ² vs protocol 1,000-1,250 mg/m ² per administration	Dose delay factor: 90.9% A dose delay factor was applied in the CEM, calculated as the actual dose of the pooled meta-analysis of TROPiCS-02 and EVER-132-002/total dose per protocol

* The RDI value is assumed to be the same as the intervention. Details of this calculation are described in Section 11.1.1.1.

Table 8. Comparator overview - Vinorelbine

Therapeutic indication relevant to the assessment	Intravenous infusion: Treatment of mBC (stage 4) in which chemotherapy with anthracycline and taxane has failed or is inadequate. Oral administration: Advanced breast cancer stage 3 and 4 relapsing after or refractory to an anthracycline containing regimen.
Generic name	Vinorelbine
ATC code	L01CA04
Mechanism of action	Vinorelbine inhibits tubulin polymerisation and binds preferentially to mitotic microtubules, only affecting axonal microtubules at high concentrations; it blocks mitosis in phase G2-M, causing cell death in interphase or at the following mitosis.



Administration method	Intravenous infusion or oral administration
Packaging type, pack sizes, shelf life and strengths	Intravenous administration: 10mg/ml in vial sizes 1 ml (10 mg) and 5 ml (50 mg). Unopened vials have a shelf life of 3 years. Oral administration: 1 x 20 mg, 1 x 30 mg and 1x 80 mg film-coated soft capsules, shelf life 3 years.
Package size(s)	Intravenous administration: Vinorelbine is available as a 10 mg/ml infusion solution (1 ml and 5 ml) Oral administration: Vinorelbine is available as soft capsules (20, 30, and 80 mg).
If vials: Can these be shared?	Yes
Pre-medication: Should pre-medication be administered? Which one?	N/A
Co-administration: Should the drug be administered with other drugs? Which ones?	An intravenous infusion should always be followed by at least 250 ml of normal saline to flush the vein.
Need for diagnostics, monitoring or other tests (e.g., companion diagnostics)	N/A

Source: Lægemiddelstyrelsen (Lægemiddelstyrelsen/, 2024)

Table 9. Comparator (vinorelbine) in the study and the health economic model

	TROPiCS-02	EVER-132-002 (ITT)	Health economic model
Dosage and frequency [if weight-based, please state weight in brackets and any criteria for transition to flat-dose]	25 mg/m ² (Mean BSA: 1.7) IV Day 1 weekly	25 mg/m ² (Mean BSA: 1.6) IV on Day 1 weekly	60 mg/m ² (BSA: 1.7) PO once per week for 3 weeks, then 80 mg/m ² (BSA: 1.7) PO once per week
Average dose	39.2 mg per IV administration 23.1 mg/m ² per IV administration (calculated as mean cumulative)	35.8 mg per administration 22.4 mg/m ² per IV administration (calculated as mean cumulative)	83.83 mg PO per administration for the first 3 weeks, with 73.54 mg administered to patients and 10.29 mg



	TROPiCS-02	EVER-132-002 (ITT)	Health economic model
	dose/mean number of doses)	dose/mean number of doses)	assumed to be wasted.
	171.53/7.43 = 23.1 mg/m ²	151.97/6.79= 22.4 mg/m ²	137.71 mg PO per administration over the following weeks, with 98.05 mg administered to patients and 39.66 mg assumed to be wasted (oral medicine). Calculated based on the required posology, assumed RDI in Danish clinical practice and European patient BSA distribution from TROPiCS-02, drug waste and dose delay.
Criteria for treatment discontinuation	Until disease progression or unacceptable toxicity	Until disease progression or unacceptable toxicity	Until disease progression or unacceptable toxicity.
Treatment duration	Mean: 1.9 months Median: 1.2 months	Mean: 1.7 months Median: 1.4 months	Mean TPC basket: 3.6 months Median TPC basket: 2.5 months
Dose adjustment: Report if/how dose adjustment is made	Protocol-defined dose reductions were permitted RDI: 90.0% RDI was calculated as cumulative dosage received/ total assigned dosage x 100	Protocol-defined dose reductions were permitted RDI: 84.6% RDI was calculated as cumulative dosage received/ total assigned dosage x 100	RDI: 83.0%* Assumed to represent the Danish clinical practice, validated by clinical experts (Gilead, 2026a, 2026b, 2026c)
Dose pause: Specify if/how pause (treatment interruption) is performed	Dose delays were allowed as per protocol The actual mean dose received was 23.1 mg/m ² per administration vs protocol 25 mg/m ² per administration.	Dose delays were allowed as per protocol The actual mean dose received was 22.4 mg/m ² per administrations protocol 25 mg/m ² per administration.	Dose delay factor: 86.1% A dose delay factor was applied in the CEM, calculated as the actual dose of the pooled meta-analysis of TROPiCS-02 and



TROPiCS-02	EVER-132-002 (ITT)	Health economic model
		EVER-132-002/total dose per protocol.

* The RDI value is assumed to be the same as the intervention. Details of this calculation are described in Section 11.1.1.1.

Table 10. Comparator overview - Gemcitabine

Therapeutic indication relevant to the assessment	Treatment of unresectable, locally recurrent or metastatic breast cancer who have relapsed following adjuvant/neoadjuvant chemotherapy. Prior chemotherapy should have included an anthracycline unless clinically contraindicated.
Generic name	Gemcitabine
ATC code	L01BC05
Mechanism of action	Gemcitabine (dFdC), which is a pyrimidine antimetabolite, is metabolised intracellularly by nucleoside kinase to the active diphosphate (dFdCDP) and triphosphate (dFdCTP) nucleosides. The cytotoxic effect of gemcitabine is due to inhibition of DNA synthesis by two mechanisms of action by dFdCDP and dFdCTP. First, dFdCDP inhibits ribonucleotide reductase, which is uniquely responsible for catalysing the reactions that produce deoxynucleoside triphosphates (dCTP) for DNA synthesis. Inhibition of this enzyme by dFdCDP reduces the concentration of deoxynucleosides in general and, in particular, dCTP. Second, dFdCTP competes with dCTP for incorporation into DNA (self-potential). After incorporation into DNA, gemcitabine appears to induce programmed cell death, known as apoptosis.
Administration method	Intravenous infusion
Packaging type, pack sizes, shelf life and strengths	10 mg/ml in vial sizes 120 ml, 140 ml, 160 ml, 180 ml, 200 ml and 220 ml. 38 mg/ml in vial sizes 26.3 ml (1g) and 52.6 ml (2g), 40 mg/ml in vial sizes 25 ml and 50 ml, shelf life 2 years.
Package size(s)	Gemcitabine concentrate for solution for infusion, single dose vials are available in the strengths 10 mg/ml (120 ml, 140 ml, 160 ml, 180 ml, 200 ml, and



220 ml), 38 mg/ml (26.3 ml and 52.6 ml) and 40 mg/ml (25 ml and 50 ml).

If vials: Can these be shared?	Yes
Pre-medication: Should pre-medication be administered? Which one?	NA
Co-administration: Should the drug be administered with other drugs? Which ones?	Could be used with cisplatin or carboplatin
Need for diagnostics, monitoring or other tests (e.g., companion diagnostics)	All patients should be monitored for platelet and granulocyte counts prior to each dose. The total number of granulocytes must be at least $1\,500 \times 10^6/l$ and platelet count $100,000 \times 10^6/l$ before starting a treatment cycle.

Source: Lægemiddelstyrelsen (Lægemiddelstyrelsen, 2024)

Table 11. Comparator (gemcitabine) in the study and the health economic model

	TROPiCS-02	EVER-132-002 (ITT)	Health economic model
Dosage and frequency [if weight-based, please state weight in brackets and any criteria for transition to flat-dose]	800-1,200 mg/m ² (Mean BSA: 1.7) on Days 1, 8, and 15 of a 28-day cycle	800-1,200 mg/m ² (Mean BSA: 1.6) on Days 1, 8, and 15 of a 28-day cycle	1,000 mg/m ² (BSA: 1.7) on Days 1, 8 and 15 of a 28-day cycle.
Average dose	1,555.25 mg per administration 914.85 mg/m ² per administration (calculated as mean cumulative dose/mean number of doses) $8,782.62/9.60 = 914.85$ mg/m ²	1553.60 mg per administration 971.01 mg/m ² per administration (calculated as mean cumulative dose/mean number of doses) $10,438.31/10.75 = 971.01$ mg/m ²	1981.20 mg per administration, with 1,195.44 mg administered to patients and 785.76 mg assumed to go to waste. Calculated based on the required posology, RDI and European patient BSA distribution, including drug waste and dose delay.
Criteria for treatment discontinuation	Until disease progression or	Until disease progression or unacceptable toxicity.	Until disease progression or unacceptable toxicity.



	TROPiCS-02	EVER-132-002 (ITT)	Health economic model
	unacceptable toxicity.		
Treatment duration	Mean: 2.9 months Median: 1.5 months	Mean: 3.1 months Median: 2.3 months	Mean TPC basket: 3.6 months Median TPC basket: 2.5 months
Dose adjustment: Report if/how dose adjustment is made	Protocol-defined dose reductions were permitted RDI: 83.8% RDI was calculated as cumulative dosage received/ total assigned dosage x 100	Protocol-defined dose reductions were permitted RDI: 96.5% RDI was calculated as cumulative dosage received/ total assigned dosage x 100	RDI: 83.0%* Assumed to represent the Danish clinical practice, validated by clinical experts (Gilead, 2026a, 2026b, 2026c)
Dose pause: Specify if/how pause (treatment interruption) is performed	Dose delays were allowed as per protocol The actual dose received was 914.85mg/m ² per administration vs protocol 800-1,200 mg/m ² per administration.	Dose delays were allowed as per protocol The actual dose received was 971.01 mg/m ² per administration vs protocol 800-1,200 mg/m ² per administration.	Dose delay factor: 84.0% A dose delay factor was applied in the CEM, calculated as the actual dose of the pooled meta-analysis of TROPiCS-02 and EVER-132-002/total dose per protocol.

* The RDI value is assumed to be the same as the intervention. Details of this calculation are described in Section 11.1.1.

3.4 Subsequent treatment

Patients in Danish clinical practice are expected to be treated with subsequent lines of treatment after treatment with SG and TPC.

Subsequent treatments were included in the analysis as a one-off cost at progression. The proportion from each arm receiving subsequent therapy is applied directly by using



the actual treatment usage and duration, from TROPiCS-02 adjusted to only include the treatments used and their composition in Denmark by Dahl et al., and clinical experts (Gilead, 2026a, 2026b, 2026c).

Treatment duration was based on the observed treatment duration in TROPiCS-02, and it was equated for both arms based on the TPC arms, to reflect Danish clinical practice under the assumption that upon progression, both patients will receive the same treatment lines from Dahl et al (Dahl et al., 2025).

The subsequent treatment share was calculated as follows:

Subsequent treatments reported to be used in more than 3% of patients in at least one treatment arm in TROPiCS-02 were considered. These were: capecitabine, carboplatin, cyclophosphamide, doxorubicin, alpelisib, fulvestrant, epirubicin, etoposide, everolimus, exemestane, trastuzumab deruxtecan, eribulin, gemcitabine, paclitaxel, Trodelvy® , vinorelbine, fluorouracil, methotrexate, abemaciclib and docetaxel.

The treatments listed in Dahl et al. for the 5th lines were the following:

5th line treatment:

- ET (Endocrine therapy): 23%
- Capecitabine: 9%
- Taxane: 12%
- Eribulin: 17%
- Vinorelbine: 9.10%
- Anthracycline: 8.30%
- Gemcitabine: 1.20%
- Other chemo: 3.20%
- Other: 9.70%
- No treatment: 7.10%

The treatment types and shares from Dahl et al. were redistributed according to the following rules:

- Values from “ET” and “Other” were distributed equally across all the other treatments
- No treatment was excluded from the total

This yields the following distribution:

- Capecitabine: 13.57%
- Taxane: 16.67%
- Eribulin: 21.67%
- Vinorelbine: 13.77%
- Anthracycline: 12.97%
- Gemcitabine: 5.87%
- Other chemo: 7.87%



Then, these treatments from Dahl et al. were allocated to the available TROPiCS-02 treatments using the following rules:

- Capecitabine, gemcitabine, eribulin and vinorelbine were directly assigned,
- Carboplatin and cyclophosphamide were assigned the share from 'Other chemo' equally; fluorouracil and methotrexate were removed for simplicity under the assumption that carboplatin and cyclophosphamide would better represent later chemotherapies lines in this population.
- Doxorubicin was assigned the share from Anthracycline
- Paclitaxel was assigned the share from the taxane, and docetaxel was excluded for simplicity.

The remaining treatments from TROPiCS-02 were not considered.

The final results for both treatment arms are thus the following:

- Capecitabine: 13.57%
- Carboplatin: 3.94%
- Cyclophosphamide: 3.94%
- Doxorubicin: 12.97%
- Eribulin: 21.67%
- Gemcitabine: 5.87%
- Paclitaxel: 16.67%
- Vinorelbine: 13.77%

Table 12. Assumptions regarding subsequent treatment in the health economic analysis

Subsequent treatment	SG %	TPC %	Average treatment duration including source	Dosage (Dose, frequency and form of administration including source)	Any assumptions regarding dose adjustment and pause including source
Capecitabine	13.57%	13.57%	40.6 weeks Source: TROPiCS-02	TROPiCS-02 protocol: 1,125 mg/m ² administered in a 21-day cycle, administered orally twice daily for 2 weeks followed by 1-week rest period.	RDI: 83.0%* Dose delay: 90.9% Source: Assumption based on clinical experts, Danish clinical practice (Gilead, 2026a, 2026b, 2026c) and



Subsequent treatment	SG %	TPC %	Average treatment duration including source	Dosage (Dose, frequency and form of administration including source)	Any assumptions regarding dose adjustment and pause including source
					TROPiCS-02 and EVER-132-002.
Carboplatin	3.94%	3.94%	13.5 weeks Source: TROPiCS-02	SmPC: 400 mg/m ² , given as an intravenous infusion once every four weeks.	83.0%* RDI and no dose delay is assumed.
Cyclophosphamide	3.94%	3.94%	20.9 weeks Source: TROPiCS-02	SmPC: 1400 mg/m ² once every 21 days	83.0%* RDI and no dose delay is assumed.
Doxorubicin	12.97%	12.97%	17.0 weeks Source: TROPiCS-02	SmPC: a dose of 60 - 75 mg/m ² body surface area is recommended every three weeks when doxorubicin is used as a single agent.	83.0%* RDI and no dose delay is assumed.
Eribulin	21.67%	21.67%	23.0 weeks Source: TROPiCS-02	TROPiCS-02 protocol: Eribulin was administered IV at dose 1.23 mg/m ² at European sites on Days 1 and 8 of a 21-day cycle	RDI: 83.0%* Dose delay: 90.3% Source: Assumption based on clinical experts, Danish clinical practice (Gilead, 2026a, 2026b, 2026c) and TROPiCS-02 and EVER-132-002.



Subsequent treatment	SG %	TPC %	Average treatment duration including source	Dosage (Dose, frequency and form of administration including source)	Any assumptions regarding dose adjustment and pause including source
Gemcitabine	5.87%	5.87%	22.0 weeks Source: TROPiCS-02	TROPiCS-02 protocol: 1,000 mg/m ² was administered IV on Days 1, 8, and 15 of a 28-day cycle.	RDI: 83.0%* Dose delay: 83.9% Source: Assumption based on clinical experts, Danish clinical practice (Gilead, 2026a, 2026b, 2026c) and TROPiCS-02 and EVER-132-002.
Paclitaxel	16.67%	16.67%	23.4 weeks Source: TROPiCS-02	SmPC: Second-line chemotherapy of breast carcinoma: The recommended dose of paclitaxel is 175 mg/m ² administered intravenously with a 3-week interval between courses.	83.0%* RDI and no dose delay is assumed.
Vinorelbine	13.77%	13.77%	12.9 weeks Source: TROPiCS-02	TROPiCS-02 protocol: 80 mg/m ² once weekly, oral administration	RDI: 83.0%* Dose delay: 86.1% Source: Assumption based on clinical experts, Danish clinical practice (Gilead, 2026a, 2026b, 2026c) and TROPiCS-02



Subsequent treatment	SG %	TPC %	Average treatment duration including source	Dosage (Dose, frequency and form of administration including source)	Any assumptions regarding dose adjustment and pause including source
					and EVER-132-002.

* The RDI value is assumed to be the same as the intervention. Details of this calculation are described in Section 11.1.1.1.

3.5 Relevant outcomes

3.5.1 Definition of outcomes

The health economic analysis for this assessment compares SG to TPC. This comparison is based on a pooled analysis of the pivotal clinical trials TROPiCS-02 and prior CDK4/6i treated patients from EVER132-002. The efficacy outcomes (OS and PFS) were based on the following data cut-offs (DCO):

- TROPiCS-02: DCO December 1, 2022 for OS and PFS
- EVER-132-002: DCO December 12, 2024 for OS
- EVER-132-002: DCO April 30, 2023 for PFS (latest available)

The efficacy outcomes (PFS and OS) were used to compare SG and TPC (Table 13).

Table 13. Outcomes

Outcome	Follow-up time	Definition
Progression-free survival	Not available.	PFS was defined as the time from the date of randomisation to the date of the first documentation of disease progression or death (whichever occurred first). PFS was measured by BICR using RECIST 1.1 and estimated using Kaplan-Meier.
Overall survival (OS)	The median survival follow-up durations in TROPiCS-02 were 18.6 and 15.1 months for the SG and TPC groups, respectively. In EVER-132-002 the median survival follow-up times were	OS was defined as the time from the date of randomisation to the date of death from any cause. OS was estimated using Kaplan-Meier estimate.



Outcome	Follow-up time	Definition
	14.39 months for SG and 10.97 for TPC.	

3.5.2 Relevance of outcomes

N/A

3.5.3 The validity of outcomes

According to Danish clinical practice, the goal of systemic treatment of metastatic or advanced BC is to prevent disease progression by reducing the spread of the disease, relieving symptoms, and prolonging the survival of the patients (DCBG, 2024). The most persuasive outcomes to demonstrate efficacy in anticancer trials are OS, PFS, and patient-reported outcomes (EMA, 2020). PFS and OS were the main endpoints in TROPiCS-02 and EVER-132-002 and are used in the health economic analysis for SG.

4. Health economic analysis

4.1 Basic assumptions

Basic assumptions used in the health economic analysis are described in Table 14.

Table 14. Basic assumptions in the health economic analysis

Assumption regarding	Assumption	Justification
Patient population	Adult patients with unresectable or metastatic hormone receptor-positive (HR+), human epidermal growth factor receptor 2 (HER2)-negative breast cancer who have received endocrine-based therapy, and at least two additional systemic therapies in the advanced setting.	The population expected to be treated in Denmark.
Intervention	SG	The technology being assessed.
Comparator(s)	Treatment of the physician's choice (eribulin, capecitabine, vinorelbine, gemcitabine)	According to national treatment guidelines (DCBG, 2024). Validated by a Danish clinical experts (Gilead, 2026a, 2026b, 2026c).



Assumption regarding	Assumption	Justification
Clinical outcomes	OS and PFS	PFS and OS are used to calculate patients' time in each health state over time, based on the projections. These are directly informed by the clinical trial data.
Analysis type	Cost-utility analysis	In line with the DMC guidelines.
Model type	Three-state partitioned survival model	To accurately describe the progression of the disease.
Average age at entry into the model	56.4 years	Mean age from TROPiCS-02 - European subgroup, assumed to be representative of the Danish patient population.
Time horizon	Lifetime (30 years)	To capture all health benefits and costs, in line with the prognosis of this population and previous assessments by the DMC (Medicinrådet, 2025c).
Cycle length	7 days	To accommodate varying drug administration frequencies.
Half-cycle correction	Yes	DMC guidelines.

4.2 Model type and model structure

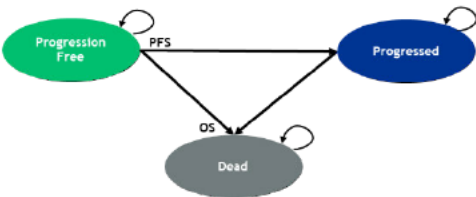
The health economic analysis was conducted using a partitioned survival model (PSM). In this modelling framework, the proportion of patients occupying each health state at each time point is determined directly from survival estimates, rather than through explicit modelling of transitions between health states. Figure 3 shows the three health states included in the model: progression-free (PF), progressed disease (PD), and death.

The proportion of patients in the PF state is derived from the PFS curve, and the proportion alive is derived from the OS curve. The proportion in the PD state is estimated as the difference between OS and PFS, while the proportion in the death state is estimated as one minus OS.

Using this approach, the model captures disease progression, survival, and the accumulation of costs and health outcomes over the analysis' time horizon.



Figure 3 Model structure



Abbreviations: OS: Overall survival; PFS: Progression-free survival

The survival curves from the trials are constrained in the following way:

- The risk of death cannot be lower than the all-cause mortality of the general population in Denmark during each model cycle.
- PFS is constrained by OS, such that the number of individuals who are PF cannot exceed the total number of individuals alive at any point in time.

Time on treatment is modelled independently from PFS, allowing patients to discontinue treatment despite not having progressed, e.g., due to tolerability issues or patient preference. Costs were assigned to each health state, and utilities were applied according to disease status and the type of treatment received, while the same utility was used for both treatment arms in case of progression. Cost and utility data were summed per treatment arm over the time horizon, enabling the calculation of differences in accumulated costs and effectiveness between model arms.

The modelling approach is flexible and adequately quantifies the primary objectives for treating individuals with HR+/HER2- mBC, particularly because it is not necessary to model multiple lines of subsequent therapy given the limited treatment options in this setting. The clinical efficacy is informed by two pooled meta-analyses of the two main studies, TROPiCS-02 and EVER-132-002 (Gilead, 2026b; Rugo et al., 2023; Xu et al., 2024), with a total population of 704 patients. Table 15 summarises the model structure.

Table 15. Choice of health economic analysis, model and model structure

Health economic analysis	Model type	Model structure	Assumptions
Cost-utility analysis	Partitioned survival model (PSM)	Three health states: PFS and OS, and the absorbing death state.	No assumptions concerning cure, waning effect, or use of surrogate outcomes



5. Literature overview

5.1 Literature used to assess clinical efficacy and safety

The clinical efficacy and safety of SG versus TPC was obtained from a pooled dataset of TROPiCS-02 (ITT population) and EVER-132-002 prior CDK4/6 treated subjects. The results from the meta-analysis have been published by Glutz et al 2025. To estimate OS, a later DCO (December 12, 2024) was used for EVER-132-002, the pooled analysis was updated for OS using this later DCO (Gilead data on file). For safety outcomes, the pooled analysis for the safety populations was used (Gilead data on file) (Table 16).

Table 16. Relevant literature included in the assessment of efficacy and safety

Reference	Study name	NCT number	Study dates (Start date and expected end date, data cut-off and expected data cut-offs)	Used when comparing
Gluz, et al. (2025) Efficacy of sacituzumab govitecan versus treatment of physician’s choice in previously treated HR+ and HER2– mBC: a meta-analysis of TROPiCS-02 and EVER-132-002 trials." Therapeutic Advances in Medical Oncology 17 (2025): 7588359251320285. (Gluz et al., 2025)	A meta-analysis of TROPiCS-02 and EVER-132-002 trials.	NCT03901339 & NCT04639986	TROPiCS-02 Start: 2019-05-08 Completion: 2023-10-20 DCO: 2022-12-01 EVER-132-002 Start: 2019-05-08 Completion: 2023-10-20 DCO: 2023-04-30	PFS for SG versus TPC in patients with prior CDK4/6



Reference	Study name	NCT number	Study dates (Start date and expected end date, data cut-off and expected data cut-offs)	Used when comparing
Gilead Data on file (2024) Meta-analysis report, TRODELVY® (SACITUZUMAB GOVITECAN-HZIY) HR+/HER2- Metastatic Breast Cancer, Data on file - December 2024 DCO.	A meta-analysis of TROPiCS-02 and EVER-132-002 trials.	NCT03901339 & NCT04639986	TROPiCS-02 Start: 2019-05-08 Completion: 2023-10-20 DCO: 2022-12-01 EVER-132-002 Start: 2019-05-08 Completion: 2023-10-20 DCO: 2023-04-30	PFS for SG versus TPC in patients with prior CDK4/6i
Gilead Data on file (2026) Meta-analysis report, TRODELVY® (SACITUZUMAB GOVITECAN-HZIY) HR+/HER2- Metastatic Breast Cancer, Data on file - December 2024 DCO.	A meta-analysis of TROPiCS-02 and EVER-132-002 trials.	NCT03901339 & NCT04639986	TROPiCS-02 Start: 2019-05-08 Completion: 2023-10-20 DCO: 2022-12-01 EVER-132-002 Start: 2019-05-08 Completion: 2023-10-20 DCO: 2024-12-12	OS for SG versus TPC in patients with prior CDK4/6i



Reference	Study name	NCT number	Study dates (Start date and expected end date, data cut-off and expected data cut-offs)	Used when comparing
Gilead Data on file 2022 EVER-132-002 CSR Final analysis	Pooled Adverse Events from TROPiCS-02 and EVER-132-002 trials.	NCT03901339 & NCT04639986	TROPiCS-02 Start: 2019-05-08 Completion: 2023-10-20 DCO: 2022-12-01	Safety versus TPC in patients with prior CDK4/6i
Gilead Data on file 2025 TROPiCS-02 CSR Final analysis			EVER-132-002 Start: 2019-05-08 Completion: 2023-10-20 DCO: 2024-12-12	



5.2 Literature used to assess health-related quality of life

The health-related quality of life (HRQoL) was obtained from the pooled analysis from TROPiCS-02 (DCO December 1, 2022) and the prior CDK4/6i treated from EVER-132-002 (DCO December 12, 2024).

Table 17. Relevant literature included in the assessment of health-related quality of life

Reference	Instrument and purpose	Identification method (documented in appendix)	Used in paragraph
Gilead Data on File 2026. Utility Analyses Pooled (Denmark Tariffs)	EQ-5D-5L index scores derived using the Danish value set	Sourced directly from the relevant trials	Section 10
Gilead Data on File 2026 HRQoL EVER-132-002 Final analysis	EQ-5D-5L Pattern of Missing Data and Completion and Summary Statistics EQ 5D-5L Index Score and EQ-VAS	Sourced directly from the relevant trials	Section 10
Gilead Data on File 2026 HRQoL TROPiC-02 Final analysis	EQ-5D-5L Pattern of Missing Data and Completion and Summary Statistics EQ 5D-5L Index Score and EQ-VAS	Sourced directly from the relevant trials	Section 10



5.3 Literature used for input into the health economic model

The clinical inputs in the health economic model were obtained from the pooled analysis of TROPiCS-02 and EVER-132-002 (see previous section). Unit costs have been sourced from publicly available Danish literature, which ensures that the model is applicable to the Danish healthcare setting. The literature used for inputs in the economic model are listed in Table 18.

Table 18. Relevant literature used in the health economic model

Reference (Full citation including reference number)	Input/estimate	Identification method (documented in appendix)	Used in paragraph
Publicly available data	Medicine costs, medicine administration, monitoring and patient costs, management of adverse events costs	Sourced from medicinpriser.dk (medicinpriser.dk, 2026), Catalogue for estimating unit costs (Værdisætning af enhedsomkostninger (Medicinrådet, 2023c)), Danish DRG costs from Sundhedsdatastyrelsen (Sundhedsdatastyrelsen, 2026)	Section 11



6. Clinical studies

6.1 SG compared to TPC for adult patients with unresectable or metastatic HR+, HER2-negative breast cancer

Table 19. Overview of study characteristics for all studies included in the comparison

Study name, NCT number (reference)	Study design	Duration of study	Patient population	Intervention	Comparator	Outcomes and follow-up time
TROPiCS-02 NCT03901339	An international, multicentre, randomised, open-label, phase III trial. Enrolled patients were randomly assigned in a 1:1 ratio to receive SG or single-agent chemotherapy. No crossover was allowed. Study has been completed	Start date: 2019-05-08 Study completion: 2023-10-20 DCO: 2022-12-01	Adults with HR-positive HER2-negative metastatic breast cancer who have failed at least two prior chemotherapy regimens.	SG administered as 10 mg/kg via intravenous (IV) injection administered on Day 1 and Day 8 of a 21-day cycle (n = 272)	Single-agent standard of care chemotherapy as specified prior to randomisation by the investigator (eribulin 1.4 [North American sites] or 1.23 [European sites] mg/m ² IV on days 1 and 8 of a 21-day cycle; vinorelbine 25 mg/m ² IV on day 1 weekly; gemcitabine 800 to 1,200 mg/m ² IV on days 1, 8, and 15 of a 28-day cycle; capecitabine 1,000 to 1,250 mg/m ² orally twice daily on days 1 through 14 of a 21-day cycle) (n = 271)	Primary outcome: PFS as determined by BICR using RECIST v1.1 (Up to 42.8 months) Secondary outcomes: OS (Up to 42.8 months) ORR as determined by BICR and LIR using RECIST v1.1 (Up to 42.8 months) DOR as determined by BICR and LIR using RECIST v1.1 (Up to 42.8 months) CBR as determined by BICR and LIR using RECIST v1.1 (Up to 42.8 months) PFS as determined by LIR using RECIST v1.1



Study name, NCT number (reference)	Study design	Duration of study	Patient population	Intervention	Comparator	Outcomes and follow-up time
						TTD in global health status/QOL, pain, and fatigue domains of EORTC QLQ-C30 (Up to 37.8 months)
						Safety and tolerability (Up to 43.4 months)
EVER-132-002 NCT04639986 Xu, B., et al. "Sacituzumab govitecan in HR+ HER2–metastatic breast cancer: the randomized phase 3 EVER-132-002 trial." Nature Medicine 30.12 (2024): 3709–3716	An international, multicentre, randomised, open-label, phase III trial. Enrolled patients were randomly assigned in a 1:1 ratio to receive SG or single-agent chemotherapy. No crossover was allowed. Study has been completed.	Start date: 2020-11-23 Study completion: 2025-12 DCO: 2023-04-30 DCO: 2024-12-12	Adults with HR-positive HER2-negative metastatic breast cancer who have failed at least two prior chemotherapy regimens.	Sacituzumab govitecan administered as 10 mg/kg via intravenous (IV) injection administered on Day 1 and Day 8 of a 21-day cycle (n=166)	Single-agent standard of care chemotherapy as specified prior to randomisation by the investigator (eribulin 1.4 or 1.23 mg/m ² IV on days 1 and 8 of a 21-day cycle; vinorelbine 25 mg/m ² IV on day 1 weekly; gemcitabine 800 to 1,200 mg/m ² IV on days 1, 8, and 15 of a 28-day cycle; capecitabine 1,000 to 1,250 mg/m ² orally twice daily on days 1 through 14 of a 21-day cycle) (n = 165)	Primary endpoint PFS determined according to RECIST v1.1 by and IRC Secondary endpoint: OS ORR by an IRC DOR by an IRC CBR by and IRC Safety and tolerability HRQOL, EORTC QLQ-C30, EQ-5D-5L, and 9 events from PRO-CTCAE PK profile of SG in participants with HR+/HER2–metastatic breast cancer



6.1.1 Comparability of studies

TROPiCS-02 and EVER-132-002 are both international, multicentre, open-label, randomised, phase III trials. The health economic analysis of this application is based on a pooled analysis of the data of both these trials, which was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses of Individual Participant Data (PRISMA-IPD) guidelines (Gluz et al., 2025; Stewart, 2015) and assessed for bias according to the Cochrane Handbook for Systematic Reviews of Interventions (Gluz et al., 2025; Higgins, 2019). The primary rationale for conducting a pooled Individual Participant Data (IPD) meta-analysis of TROPiCS-02 and EVER-132-002, rather than relying solely on TROPiCS-02, is to increase statistical power and precision in estimating the treatment effect of SG versus TPC. An increased number of events will also enable better estimation of survival model parameters, reducing uncertainty in survival extrapolation.

In order to confirm that the trials were sufficiently similar, a feasibility assessment of the meta-analytic framework was conducted by evaluating the availability of evidence and heterogeneity of prognostic factors at trial and patient levels, as well as the approaches to meta-analyse the effect sizes of SG versus TPC from the TROPiCS-02 and EVER132-002 trials. The feasibility assessment included the identification of heterogeneous variables using regression methods and seeking clinician feedback, an assessment of statistical heterogeneity, and meta-analytic model selection based on outcome type and heterogeneity assessment (Gluz et al., 2025). The feasibility assessment confirmed the validity of pooling data from the TROPiCS-02 and EVER-132-002 trials, which were sufficiently similar in design and patient characteristics (Gluz et al., 2025).

6.1.1.1 Comparability of patients across studies

Table 20 presents the relevant baseline characteristics across treatment arms for both clinical trials. A total of 543 (SG: n = 272, TPC: n = 271) and 331 (SG: n = 166, TPC: n = 165) patients were enrolled and randomised in TROPiCS-02 and EVER-132-002.

Baseline parameters across trials were generally similar, with the main differences being the region of origin. Variability in patient geography and patient ethnicity could potentially introduce unmeasured confounding. However, previous studies in breast cancer have found race to have no effect on survival when controlling for clinical and sociodemographic factors (Chu et al., 2010; Komenaka et al., 2010). Including the Asian population from EVER-132-002 in this assessment is therefore reasonable. This is aligned with DMCs approach in previous assessments of pharmaceuticals within breast cancer, where Asian populations have been included in the overall assessment of all previous breast cancer assessments.

Demographic characteristics and prior treatment histories were otherwise similar between treatment arms and across trials. Almost all patients were female; the mean age was comparable across both trials, with the majority of the population younger than 65, an Eastern Cooperative Oncology Group performance status (ECOG PS) of 1, and



having previously received more than one prior line of chemotherapy in the metastatic setting.

Table 20. Baseline characteristics of patients in included studies for the comparative analysis of efficacy and safety

	TROPiCS-02		EVER-132-002	EVER 132-002 Prior CDK4/6i treated		
	SG (N=272)	TPC (N=271)	SG (N=166)	TPC (N=165)	SG (N=81)	TPC (N=80)
Median age, years (range)	57.0 (29–86)	55.0 (27–78)	52.5 (32–72)	51.7 (28–79)	51.0 (33–72)	50.0 (28–78)
Female, n (%)	270 (99.3%)	268 (98.9%)	166 (100.0%)	163 (98.8%)	81 (100%)	79 (98.8%)
Median baseline weight, kg	67.0	64.9	60.2	58.9	59.0	57.0
Race or ethnic group, n (%)						
White	184 (67.6%)	178 (65.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Black	8 (2.9%)	13 (4.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Asian	11 (4.0%)	5 (1.8%)	166 (100%)	165 (100%)	81 (100%)	80 (100%)
Other/Not reported	69 (25.4%)	75 (27.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Baseline ECOG, n (%)						
0	115 (42.3%)	126 (46.5%)	33 (19.9%)	41 (24.8%)	20 (24.7%)	21 (26.3%)
1	157 (57.7%)	145 (53.5%)	133 (80.1%)	124 (75.2%)	61 (75.3%)	59 (73.8%)
Liver metastases, n (%)	229 (84.2%)	237 (87.5%)	115 (69.3%)	119 (72.1%)	61 (75.3%)	64 (80.0%)
De novo metastatic	78 (29%)	60 (22%)	27 (16.3%)	30 (18.2%)	n.a.	n.a.



	TROPiCS-02		EVER-132-002	EVER 132-002 Prior CDK4/6i treated		
	SG (N=272)	TPC (N=271)	SG (N=166)	TPC (N=165)	SG (N=81)	TPC (N=80)
breast cancer, n (%)						
Median time from first metastasis to randomisation, months (range)	48.5 (1.2–243.8)	46.6 (3.0–248.8)	39.1 (1.4–156.2)	36.9 (0.8–171.0)	41.3 (6.3–139.7)	39.8 (0.8–119.9)
Prior chemotherapy in (neo)adjuvant setting, n (%)	173 (63.6%)	184 (67.9%)	120 (72.3%)	118 (71.5%)	51 (63.0%)	58 (72.5%)
Prior endocrine therapy use in the metastatic setting ≥6 months, n (%)	235 (86.4%)	234 (86.3%)	131 (78.9%)	126 (76.4%)	70 (86.4%)	70 (87.5%)
Prior CDK4/6i in metastatic setting, n (%)						
Yes	267 (98.2%)	270 (99.6%)	81 (48.8%)	80 (48.5%)	81 (100%)	80 (100%)
≤12 months	161 (59.2%)	166 (61.3%)	56 (33.7%)	53 (32.1%)	56 (69.1%)	53 (66.3%)
>12 months	106 (39.0%)	102 (37.6%)	25 (15.1%)	27 (16.4%)	25 (30.9%)	27 (33.8%)
Unknown	5 (1.8%)	3 (1.1%)	0 (0.0%)	1 (0.6%)	0 (0.0%)	0 (0.0%)
No	5 (1.8%)	1 (0.4%)	85 (51.2%)	84 (50.9%)	0 (0.0%)	0 (0.0%)
Prior chemotherapy regimens in the metastatic setting, n (%)						
0	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)



	TROPiCS-02		EVER-132-002	EVER 132-002 Prior CDK4/6i treated		
	SG (N=272)	TPC (N=271)	SG (N=166)	TPC (N=165)	SG (N=81)	TPC (N=80)
1	8 (2.9%)	2 (0.7%)	10 (6.0%)	8 (4.8%)	3 (3.7%)	3 (3.8%)
2	104 (38.2%)	118 (43.5%)	91 (54.8%)	90 (54.5%)	47 (58.0%)	46 (57.5%)
3	96 (35.3%)	93 (34.3%)	47 (28.3%)	48 (29.1%)	22 (27.2%)	21 (26.3%)
4	57 (21.0%)	56 (20.7%)	18 (10.8%)	19 (11.5%)	9 (11.1%)	10 (12.5%)
>4	6 (2.2%)	2 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Median prior systemic chemotherapy regimens, n (range)	4.0 (1–9)	4.0 (2–7)	3.0 (2–7)	3.0 (2–6)	3.0 (2–5)	3.0 (2–6)
Median prior systemic anticancer regimens, n (range)	7.0 (3–17)	7.0 (3–16)	6.0 (2–11)	6.0 (2–11)	6.0 (3–11)	6.0 (3–11)

Source: Data on file (Gilead Sciences 2022, 2023)

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

In this line of treatment, the eligible patient population in Danish clinical practice is expected to be pre-treated with CDK4/6 inhibitors (Gilead, 2026a, 2026b, 2026c). This was an inclusion criterion for TROPiCS-02 enrolment, but only 49% of patients in EVER-132-002 received CDK4/6 inhibitors. Therefore, to inform the clinical efficacy of the submission, only the patients pre-treated with CDK4/6 inhibitors were considered from the EVER trial. For baseline characteristics, the European patient subgroup from TROPiCS-02 was used in the submission. This was believed to increase the comparability between the study and Danish clinical practice, and the characteristics were confirmed to be largely representative by clinical experts (Gilead, 2026a, 2026b, 2026c)

Table 21. Characteristics of the relevant Danish population and input parameters in the health economic model



	Danish population (source)	Study population	Health economic model (source)
Age (Mean)	65** (Dahl et al., 2025)	TROPiCS-02 (European subgroup): 56.4 EVER-132-002: 52.1	56.4 (TROPiCS-02 (European subgroup))
Sex	99%* (DBCG, 2024)	TROPiCS-02 (European subgroup): 99.1% EVER-132-002: 99.4%	99%* (TROPiCS-02 (European subgroup))
Body weight	71 kg (Medicinrådet, 2025b)	TROPiCS-02 (European subgroup): 66.5 kg EVER-132-002: 59.5 kg	66.5 kg (TROPiCS-02 (European subgroup))
BSA, mean (std)	1.671 (0.171) (Medicinrådet, 2025a)	TROPiCS-02 (European subgroup): 1.7 (0.18) EVER-132-002: 1.6 (0.13)	1.72 (0.17) (TROPiCS- 02 (European subgroup))

*All BC types

**Median – mean values not reported.

6.1.3 Analysis method

For both clinical trials, all efficacy analyses were conducted based on the Intention-to-Treat (ITT) Population, which was defined as all participants who were randomised, regardless of whether they received study treatment or not.

For TROPiCS-02 (Tolaney et al., 2023), PFS was defined as the time from date of randomisation to the first observation of documented disease progression based on RECIST v1.1 or death due to any cause, whichever came first. The primary analysis of PFS was based on BICR. The primary analysis of PFS for comparison between the SG and TPC groups was performed using a stratified log-rank test with the stratification factors employed in randomisation: prior chemotherapy regimens for treatment of metastatic disease (2 or 3/4 lines), visceral metastasis (yes or no), and endocrine therapy in the metastatic setting for at least 6 months (yes or no). The estimates of hazard ratio (HR) and its 95% confidence interval (CI) were based on a stratified Cox proportional-hazards model with treatment group as the only covariate, stratified by the same factors employed in randomisation. The test comparing the treatment groups was performed using a 2-sided alpha level of 0.05. PFS was plotted over time using Kaplan-Meier (KM) curves. Median PFS was derived from KM estimates, and its associated 95% CI was calculated using the Brookmeyer and Crowley method with log-log transformation. Further details are described in section 6.1.4.1.



OS was defined as the time from randomisation into the study to death from any cause. OS was analysed using the same method as for the primary PFS analysis. As the OS was significant at the IA2 analysis ($P = 0.0200$) and was less than the P value boundary prespecified by multiplicity control based on the Lan DeMets-Pocock approach, no further statistical testing was deemed necessary. Further details are described in section 6.1.4.2.

For EVER-132-002 (Xu et al., 2024), the primary analysis of PFS per BICR for comparison between the SG and TPC groups was performed on the ITT population using a stratified log-rank test with the stratification factors employed in randomisation. The HR and its associated 95% CI were estimated using a stratified Cox proportional-hazards model with treatment group as the only covariate, stratified by the stratification factors employed in randomisation. The test comparing the treatment groups was performed using a 2-sided alpha level of 0.05. Progression-free survival was plotted over time using KM curves. Median PFS was derived from KM estimates, and its associated 95% CI was calculated using the Brookmeyer and Crowley method with log-log transformation. The PFS rates at 3, 6, 9, 12, and 18 months after randomisation were derived from KM estimates. PFS details are described in section 6.1.4.1.

OS was analysed in the ITT Population using the same method as for the primary analysis of PFS. The OS rates at 12, 18, and 24 months after randomisation were derived from KM estimates. Further details are mentioned in section 6.1.5.1.2. The efficacy endpoints used to inform the submission were derived from a meta-analysis with pooled data from both clinical trials. This is described in section 7.1.

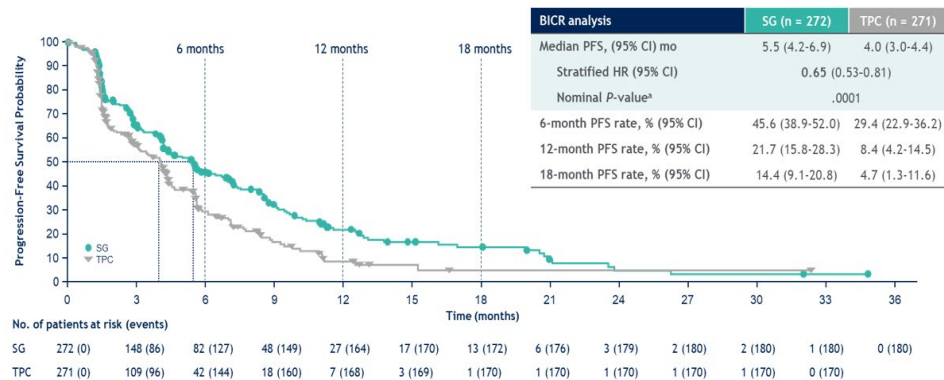
6.1.4 Effect – results per study TROPiCS-02

6.1.4.1 Progression-free survival

PFS was the primary endpoint of the trial, which was met. Patients treated with SG demonstrated a statistically significant improvement in PFS compared to patients treated with TPC. The patients treated with SG experienced a median PFS improvement of 5.5 months (95% CI: 4.2, 6.9), compared to 4.0 months (95% CI: 3.0, 4.4) in the patients treated with TPC (HR: 0.65; 95% CI: 0.53, 0.81; nominal $P = 0.0001$) (Tolaney et al., 2023). SG demonstrated a median improvement in PFS of 1.5 months, with a 35% reduction in risk of progression or death. The PFS rates at 6 months, 12 months, and 18 months, were 45.6% (95% CI: 38.9%–52.0%), 21.7% (95% CI: 15.8%–28.3%), and 14.4% (95% CI: 9.1%–20.8%) respectively for SG (Tolaney et al., 2023). The corresponding PFS 6-month, 12-month, and 18-month PFS rates for TPC were 29.4% (95% CI: 22.9%–36.2%), 8.4% (95% CI: 4.2%–14.5%), and 4.7% (95% CI: 1.3%–11.6%) (Tolaney et al., 2023). There were 180 PFS events (66.2%) in patients treated with SG and 170 (62.7%) among those treated with TPC (Gilead Sciences 2022).



Figure 4 TROPiCS-02 Kaplan-Meier plots of progression-free survival

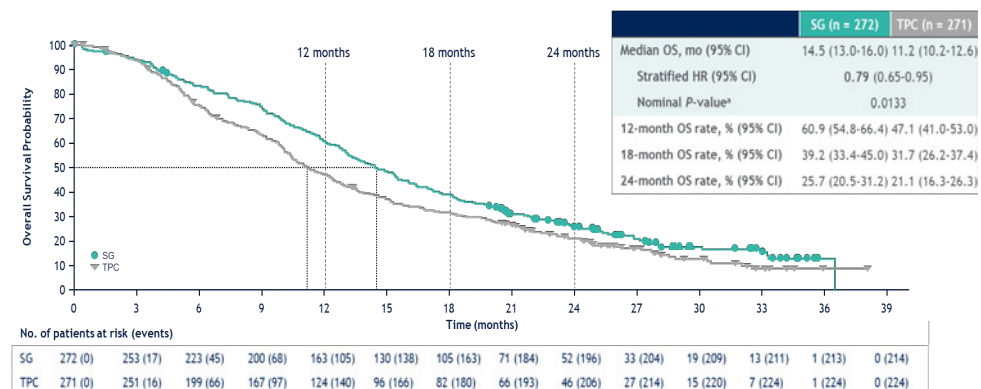


Source: (Tolaney et al., 2023)

6.1.4.2 Overall survival

In the latest data cutoff (1st of December 2022), SG demonstrated a statistically significant improvement in OS. The SG group had a median OS of 14.5 months (95% CI: 13.0, 16.0), compared to 11.2 months (95% CI: 10.2, 12.6) the TPC group (HR: 0.788; 95% CI: 0.652, 0.952; nominal P = 0.0133) (Tolaney et al., 2023). SG demonstrated a median 3.3-month improvement in OS with a 21% reduction in risk of death (Tolaney et al., 2023). The OS rates at 12 months, 18 months, and 24 months were 60.9% (95% CI: 54.8%–66.4%), 39.2% (95% CI: 33.4%–45.0%), and 25.7% (95% CI: 20.5%–31.2%) for patients treated with SG (Tolaney et al., 2023). The corresponding 12-month, 18-month, and 24-month OS rates for those treated with TPC were 47.1% (95% CI: 41.0%–53.0%), 31.7% (95% CI: 26.2%–37.4%), and 21.1% (95% CI: 16.3%–26.3%) (Tolaney et al., 2023). There were 214 (78.7%) patients with OS events in the SG-treated group, and 224 (82.7%) patients with OS events in the TPC-treated group (Gilead, 2024c).

Figure 5 TROPiCS-02 Kaplan-Meier plots of overall survival



Source: (Tolaney et al., 2023)



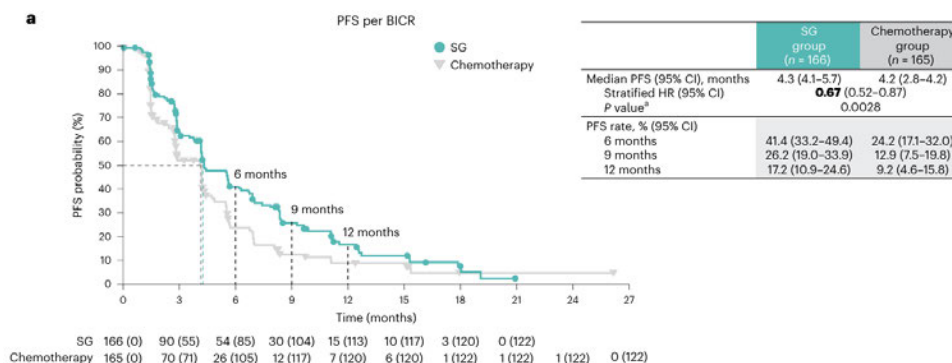
6.1.5 Effect – results per study EVER-132-002

6.1.5.1 Progression-free survival

6.1.5.1.1 ITT patient population

The primary endpoint of statistical improvement in PFS was met. The PFS for the SG group was 4.3 months (95% CI: 4.1, 5.7) and 4.2 months (95% CI: 2.8, 4.2) for the TPC group, with a 33% reduction in risk of disease progression or death (HR: 0.67; 95% CI: 0.52, 0.87; $P = 0.0028$) (Xu et al., 2024). The PFS rates at months 6 and 12 were 41.4% (95% CI: 33.2%, 49.4%) and 17.2% (10.9%, 24.6%), respectively for patients treated with SG (Xu et al., 2024). In comparison, the 6-month and 12-month PFS rates for patients given TPC were 24.2% (95% CI: 17.1%, 32.0%) and 9.2% (4.6%, 15.8%), respectively (Xu et al., 2024).

Figure 6 EVER-132-002 Kaplan-Meier PFS plots, ITT patient population



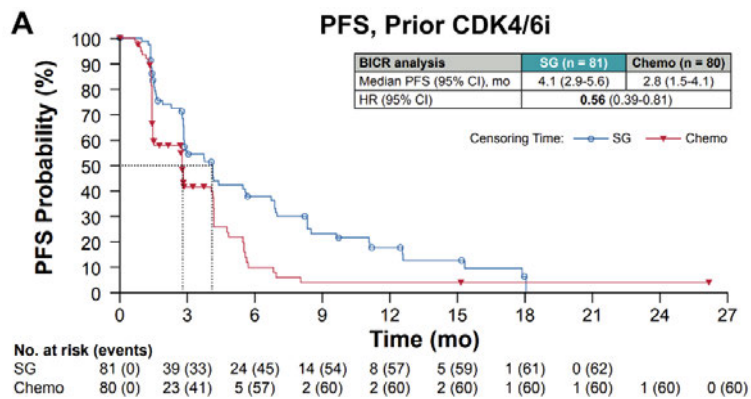
Source: (Xu et al., 2024)

6.1.5.1.2 Prior CDK4/6i patient population

A statistical improvement in PFS was also observed in the patient group previously treated with CDK4/6 inhibitors. The median PFS for the SG-treated patients was 4.1 months (95% CI: 2.9, 5.6) and 2.8 months (95% CI: 1.5, 4.1) for the TPC-treated patients, with a 44% reduction in risk of disease progression or death (HR: 0.56; 95% CI: 0.39, 0.81) (Xu et al., 2024). The PFS rates at 6 months, 9 months, and 12 months, were 37.8% (95% CI: 26.6%–49.0%), 23.3% (95% CI: 13.9%–34.0%), and 17.7% (95% CI: 9.4%–28.1%) respectively for SG. The corresponding 6-month, 9-month, and 12-month PFS rates for TPC were 9.9% (95% CI: 3.7%–19.7%), 4.0% (95% CI: 0.7%–11.9%), and 4.0% (95% CI: 0.7%–11.9%). The group of patients treated with SG experienced 62 PFS events (76.5%), and the TPC-treated patients had 60 events (75.0%) (Gilead Sciences 2023).



Figure 7. EVER-132-002 Kaplan Meier PFS plots, prior CDK4/6i treated patient population



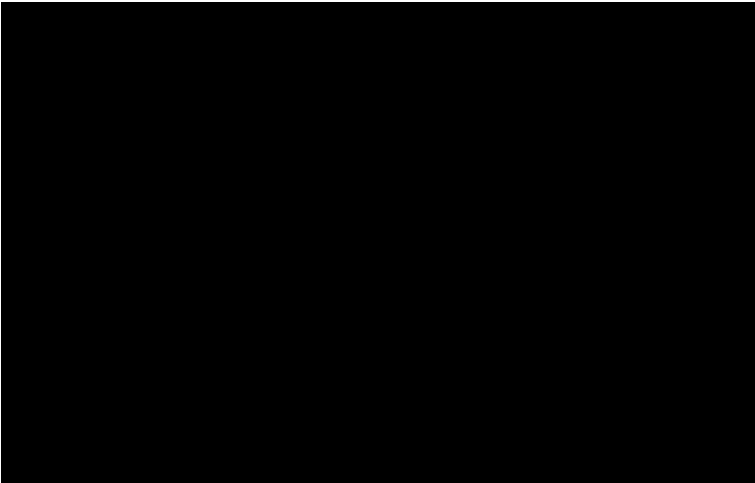
Source: (Sohn et al., 2025)

6.1.5.2 Overall survival

6.1.5.2.1 ITT patient population

SG demonstrated an improvement in OS in the latest data cutoff (12 December 2024). Patients treated with SG experienced a median survival of [REDACTED] (95% CI: [REDACTED]) months, while patients treated with TPC had a median survival of [REDACTED] months (95% CI: 13.4, 19.0), resulting in a hazard ratio of [REDACTED] (95% CI: [REDACTED]).

Figure 8. EVER-132-002 Kaplan Meier OS plots, ITT patient population



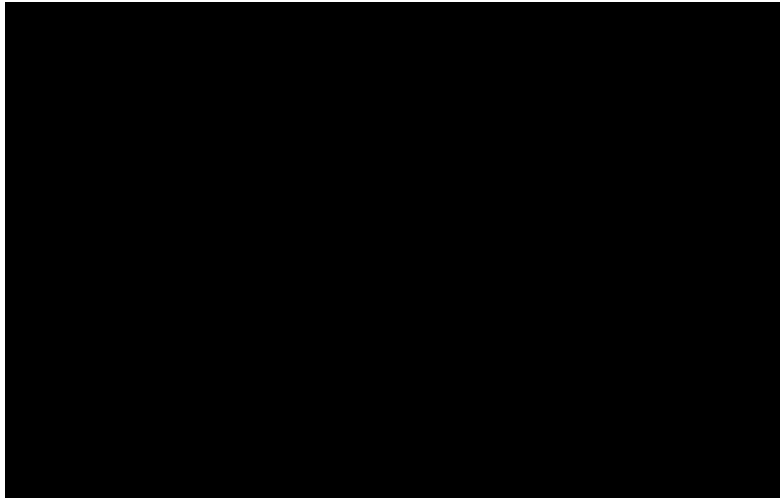
Source: Data on file (Gilead, 2025)

6.1.5.2.2 Prior CDK4/6i treated patient population

In a subgroup analysis of patients who had previously been treated with CDK4/6 inhibitors in the latest data cutoff (12 December 2024), the SG-arm had a statistically significant improved survival, with a median OS of [REDACTED] months (95% CI: [REDACTED]) compared to the median OS of [REDACTED] months (95% CI: [REDACTED]) in the TPC-arm. There were 60 OS events (74.1%) in the SG arm and 68 (85.0%) in the TPC arm (Gilead, 2024b).



Figure 9. EVER-132-002 Kaplan Meier OS plots, prior CDK4/6i treated patient population



Source: Data on file (Gilead, 2026e)

7. Comparative analyses

7.1 Method of analysis

To combine the relevant clinical evidence from the two head-to-head studies of Trdelvy® against TPC in HR+ HER2- mBC, TROPiCS-02 and EVER-132-002 (Rugo et al., 2023; Xu et al., 2024), a meta-analysis was performed (Gilead, 2024a; Gluz et al., 2025).

Meta-analysis involves combining effect size estimates from individual studies to estimate an overall effect size. When conducting meta-analysis through Individual Participant Data (IPD), diverse methodologies are accessible, such as the one-stage, two-stage, and propensity score matching approaches. A one-stage IPD meta-analysis involves pooling and analysing the raw data from multiple studies simultaneously in a single integrated statistical model. By combining all individual participant data in a single analysis, a one-stage approach leads to increased statistical power and precision in estimating treatment effects. The one-stage approach was the primary analysis method used for the relevant efficacy outcomes: OS, PFS and ORR (Gilead, 2024a; Gluz et al., 2025). OS data were updated with the latest available data cut (Gilead, 2026d).

To perform the analysis, IPD were collected from both studies, comprising raw patient-level information, patient attributes, event occurrence times, and event status. The data were then cleaned and harmonised to ensure consistency and data format compatibility. (Gilead, 2024a).

The IPD from both studies was consolidated into one unified dataset, with details about the source study retained. A Cox proportional hazards regression model was applied to the merged dataset. The model analysed time-to-event data and estimated the HR for the treatment effect while considering covariates. Relevant clinical and statistical covariates were adjusted in the Cox model to control for potential confounding factors



(Gilead, 2024a). These were ECOG PS, target/nontarget liver lesions, mean disease duration, prior chemo regimen, TROP-2 expression and TPC distribution (Gilead, 2024a). All efficacy results presented and used in the health economic analysis are from the pooled prior CDK 4/6 inhibitor-treated population to better represent the Danish-eligible patients in both trials. The HR and 95% CI for survival outcomes such as OS and PFS were estimated for using a stratified Cox proportional hazards regression analysis.

7.2 Results from the comparative analysis

Table 22 presents a summary of the efficacy results for OS and PFS from the meta-analysis of the HR+/HER2-negative mBC patients with prior CDK4/6 inhibitor treatment,

Table 22. Results from the comparative analysis of SG vs. TPC for HR+ HER2- mBC, prior CDK4/6 inhibitors

Outcome	SG (N= 351)	TPC (N=353)	Result
OS – Prior CDK4/6 inhibitor treated	Median OS: [REDACTED] months [95% CI: [REDACTED]]	Median OS: [REDACTED] months [95% CI: [REDACTED]]	Difference: [REDACTED] months, HR: [REDACTED] [95%CI: [REDACTED]]
PFS – Prior CDK4/6 inhibitor treated	Median PFS: 4.7 months [95% CI: 4.1, 5.7]	Median PFS: 3.7 months [95% CI: 2.8, 4.2]	Difference: 1.0 month, HR 0.65 [95% CI: 0.52, 0.81]

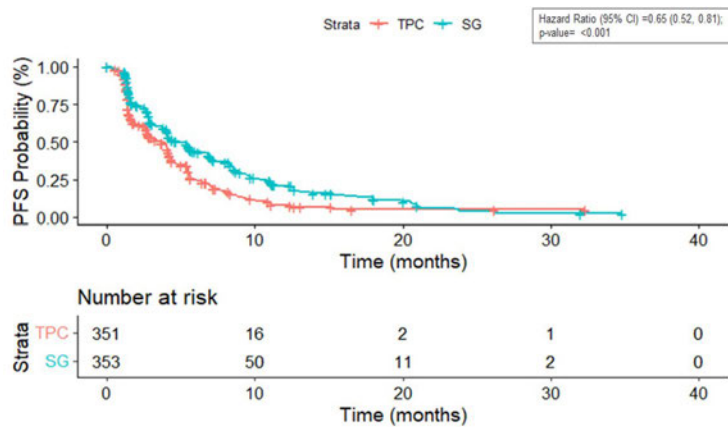
Abbreviations: CI: Confidence interval; HR; Hazard ratio; OS: Overall survival; PFS: Progression free survival; RR: Rate ratio; SG: Trodelvy®; TPC: Treatment of physician choice.

7.3 Effect – results per PFS

Among the HR+/HER2-negative mBC patients with prior CDK4/6 inhibitor treatment, a statistically significantly better PFS was observed with SG compared to TPC using the base-case, one-stage method adjusted for both statistical and clinical covariates (median PFS, 4.70 months [95% CI: 4.10, 5.70] vs. 3.70 months [95% CI: 2.80, 4.20]; HR 0.65 [95% CI: 0.52, 0.81], $p<0.001$) as shown in Figure 10. The PFS rates at 6 months, 9 months, and 12 months, were 43.8% (95% CI: 38.0%–49.4%), 30.0% (95% CI: 24.5%–35.7%), and 20.8% (95% CI: 15.8%–26.3%) respectively for SG. The corresponding 6-month, 9-month, and 12-month PFS rates for TPC were 24.8% (95% CI: 19.4%–30.5%), 13.5% (95% CI: 9.1%–18.8%), and 7.6% (95% CI: 4.2%–12.5%). There was a total of 472 PFS events in the pooled analysis. 230 events in the TPC arm and 242 events in the SG arm (Gilead, 2024a; Gluz et al., 2025).



Figure 10 PFS KM in patients who were previously treated with CDK4/6i, one-stage model



Abbreviations: CI: Confidence interval; PFS: Progression free survival; SG: Trodelvy®; TPC: Treatment of physician choice.

7.4 Effect – results per OS

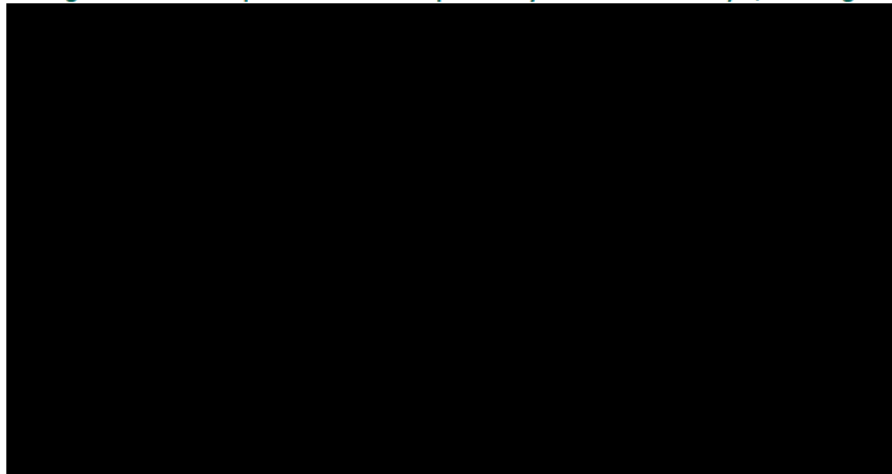
Among the HR+/HER2- MBC patients with prior CDK4/6 inhibitor treatment, a statistically significantly better overall survival was observed with SG compared to TPC using the base-case, one-stage method, adjusted for both statistical and clinical covariates (median OS: [redacted] months [95% CI: [redacted]] vs. [redacted] months [95% CI: [redacted]]); HR: [redacted] [95% CI: [redacted]] as shown in Figure 11. This pooled HR is considered the most robust and precise estimate of the treatment effect for the population of interest (prior CDK4/6i treated), as it is based on a larger sample size and was adjusted for relevant clinical and statistical covariates (ECOG PS, liver lesions, disease duration, prior chemo regimen, TROP-2 expression, and TPC distribution).

Increasing the variability of patients in the health economic model (e.g., ECOG status, de novo disease, previous treatments) is probably more representative of Danish patients than relying solely on the TROPICS-02 population. Further, the pooling was restricted to patients previously treated with a CDK4/6 inhibitor to better reflect Danish clinical practice. The DMC methods guide recommends using all relevant high-quality evidence when the patient populations are sufficiently similar, as confirmed by the feasibility assessment.

The OS rates at 12 months, 24 months, and 36 months, were 63.2% (95% CI: 57.9%–68.0%), 29.2% (95% CI: 24.4%–34.2%), and 15.5% (95% CI: 11.1%–20.6%) respectively for SG. The corresponding 12-month, 24-month, and 36-month OS rates for TPC were 48.5% (95% CI: 43.1%–53.7%), 21.1% (95% CI: 16.8%–25.7%), and 7.8% (95% CI: 4.4%–12.5%). There were a total of 566 OS events in the pooled analysis. 292 events in the TPC arm and 274 events in the SG arm.



Figure 11 OS KM in patients who were previously treated with CDK4/6i, one-stage model



Abbreviations: CI: Confidence interval; OS: overall survival; SG: Trodelyv®; TPC: Treatment of physician choice

8. Safety

The following section includes the safety results from the pooled data of TROPiC-02 and EVER-132-002 safety populations. The safety populations were defined as all participants in the ITT populations who received at least 1 dose of study drug, and included N=433, 268 (98.5%) from TROPiCS-02 and 165 (99.4%) from EVER-132-002 in the SG arm and N=413, 249 (91.9%) from TROPiCS-02 and 164 (99.4%) from EVER-132-002 in the TPC arm. An overview of safety events from the pooled data is presented in Table 23.

Table 23. Overview of adverse events - pooled TROPiCS-02 (DCO: 01 December 2022) and EVER-132-002 (DCO: 12 December 2024)

	SG (N = 433)	TPC (N =413)	Difference , % points	Difference , RR (95% CI)
All adverse events (AE), n (%)	433 (100.0%)	403 (97.6%)	2.42 (0.94, 3.90)	1.025 (1.009, 1.041)
Serious AE (SAE), n (%) 1	112 (25.9%)	80 (19.4%)	6.50 (0.88, 12.12)	1.335 (1.037, 1.720)
AE grade ≥ 3, n (%) 2	334 (77.1%)	263 (63.7%)	13.46 (7.36, 19.56)	1.211 (1.108, 1.324)
Dose reduction due to AE, n (%)	133 (30.7%)	135 (32.7%)	-1.97 (-8.24, 4.30)	0.940 (0.771, 1.145)
Treatment discontinuation due to AE, n (%)	24 (5.5%)	17 (3.9%)	1.58 (-1.22, 4.38)	1.347 (0.734, 2.470)

AE = adverse event; CI = confidence interval; RR = risk ratio; SAE = serious adverse event. 1 See ICH definition. 2 CTCAE v. 5.0 is preferred. Note: The population in the pooled analysis are based on the safety population from TROPiCS-02 SG: N=268; TPC: 249 and EVER-132-002 SG: N=156; TPC=152 * A serious adverse event is an event or reaction that at any dose results in death, is life-threatening, requires hospitalisation or prolongation of



existing hospitalisation, results in persistent or significant disability or incapacity, or results in a congenital anomaly or birth defect (see the [ICH's complete definition](#)). ** Includes the proportion (%) of ITT with the event (SG: N=438; TPC: N=436)

Table 24 presents all adverse events with a frequency of $\geq 10\%$, as well as adverse events of grade ≥ 3 that occurred in $\geq 3\%$ in either of the treatment arms. The presented proportion of patients is the pooled result of TROPiCS-02 and EVER-132-002. An AE was included if it occurred at a relevant frequency ($\geq 10\%$ or $\geq 3\%$) in either treatment arm of either trial. Finally, a list of all serious adverse events that are provided in Appendix F.

Table 24. Proportion of patients with adverse events - pooled TROPiCS-02 (DCO: 01 December 2022) and EVER-132-002 (DCO: 12 December 2024)

	SG (N = 433)		TPC (N = 413)	
	All ¹	Grade ≥ 3 or SAE ²	All ¹	Grade ≥ 3 or SAE ²
Neutropenia	325 (75.1%)	254 (58.7%)	273 (66.1%)	198 (47.9%)
Nausea	244 (56.4%)	-	147 (35.6%)	-
Anaemia	167 (38.6%)	50 (11.5%)	208 (50.4%)	18 (4.4%)
Alopecia	174 (40.2%)	-	169 (40.9%)	-
Diarrhoea	223 (51.5%)	38 (8.8%)	106 (25.7%)	3 (0.7%)
Leukopenia	63 (14.5%)	92 (21.2%)	217 (52.5%)	75 (18.2%)
Fatigue	187 (43.2%)	28 (6.5%)	86 (20.8%)	12 (2.9%)
Constipation	154 (35.6%)	-	99 (24.0%)	-
Decreased appetite	109 (25.2%)	-	118 (28.6%)	-
Vomiting	103 (23.8%)	-	87 (21.1%)	-
Aspartate aminotransferase increased	77 (17.8%)	-	112 (27.1%)	-
Alanine aminotransferase increased	67 (15.5%)	-	114 (27.6%)	-
Asthenia	112 (25.9%)	-	39 (9.4%)	-
Thrombocytopenia	58 (13.4%)	8 (1.8%)	91 (22.0%)	17 (4.1%)
Abdominal pain	87 (20.1%)	-	53 (12.8%)	-
Pyrexia	84 (19.4%)	-	49 (11.9%)	-



Blood alkaline phosphatase increased	52 (12.0%)	-	74 (17.9%)	-
Lymphopenia	61 (14.1%)	20 (4.6%)	58 (14.0%)	13 (3.1%)
Headache	80 (18.5%)	-	30 (7.3%)	-
Dyspnoea	88 (20.3%)	-	22 (5.3%)	-
Hypokalaemia	38 (8.8%)	22 (5.1%)	68 (16.5%)	6 (1.5%)
Back pain	67 (15.5%)	-	34 (8.2%)	-
Hyperglycaemia	26 (6.0%)	-	66 (16.0%)	-
Hypoalbuminaemia	19 (4.4%)	-	71 (17.2%)	-
Gamma-glutamyl transferase increased	20 (4.6%)	-	69 (16.7%)	-
Cough	51 (11.8%)	-	38 (9.2%)	-
Arthralgia	70 (16.2%)	-	12 (2.9%)	-
Urinary tract infection	50 (11.5%)	-	28 (6.8%)	-
Insomnia	29 (6.7%)	-	48 (11.6%)	-
Blood lactate dehydrogenase increased	22 (5.1%)	-	54 (13.1%)	-
Upper abdominal pain	41 (9.5%)	-	28 (6.8%)	-
Weight decreased	29 (6.7%)	-	32 (7.7%)	-
Hyponatraemia	10 (2.3%)	-	48 (11.6%)	-
Pruritus	38 (8.8%)	-	17 (4.1%)	-
Upper respiratory tract infection	11 (2.5%)	-	43 (10.4%)	-
Blood bilirubin increased	22 (5.1%)	-	31 (7.5%)	-
Hypocalcaemia	5 (1.2%)	-	44 (10.7%)	-
Malaise	9 (2.1%)	-	40 (9.7%)	-
Dizziness	19 (4.4%)	-	28 (6.8%)	-
Hyperuricaemia	1 (0.2%)	-	36 (8.7%)	-



Hypoaesthesia	5 (1.2%)	-	29 (7.0%)	-
Febrile neutropenia	-	25 (5.8%)	-	18 (4.4%)

SAE = serious adverse event; 1 List all adverse events with a frequency of $\geq 10\%$. 2 Report SAEs if adverse events are not CTCAE graded and indicate events with a frequency of $\geq 3\%$ in either arm.

9. Extrapolation of patient transitions

9.1 Clinical data for extrapolation of patient transitions

The clinical outcomes extrapolated in the analysis were PFS, OS and time to treatment discontinuation (TTD). All endpoints were derived from the pooled analysis of TROPICS-02 and prior CDK4/6 inhibitor-treated patients from EVER 132-002.

The extrapolation of OS and TTD used the latest available data cut (Gilead, 2026d), while the PFS was based on a previous data cut (Gilead, 2024a; Gluz et al., 2025), as it was not collected further, given its maturity, with PFS estimating less than 10% survival in both arms at the end of the observed period. Standard parametric survival models were fitted independently to each clinical outcome (Medicinnrådet, 2021; Nicholas Latimer, 2013), and for each clinical outcome, both treatment arms were fitted with the same model, in line with NICE TSD 14 guidelines (Nicholas Latimer, 2013). Given that both modelled treatment arms comprise chemotherapy-based regimens, it was considered clinically appropriate to apply the same parametric distribution to both arms. This approach preserves consistency in the assumed long-term disease process and avoids introducing artificial differences in survival behaviour that are not supported by the treatment mechanism or clinical evidence.

Applying different distributions by arm would imply that the treatments produce fundamentally different long-term hazard patterns. Such an assumption may be reasonable where there is a mechanistically distinct intervention, for example, immunotherapy with potential delayed or durable effects; however, this rationale does not apply here because both arms are, in essence, chemotherapy. Therefore, a common distribution across arms is the more parsimonious and clinically coherent approach, with treatment differences captured through the observed between-arm survival effect rather than through unrelated extrapolation shapes. For all endpoints, survival was constrained by the general background mortality.

9.2 Extrapolation using parametric extrapolation models

9.2.1 Extrapolation of PFS

An overview of assumptions for the extrapolation of PFS is presented in Table 25.



Table 25. Overview of assumptions regarding extrapolation of PFS

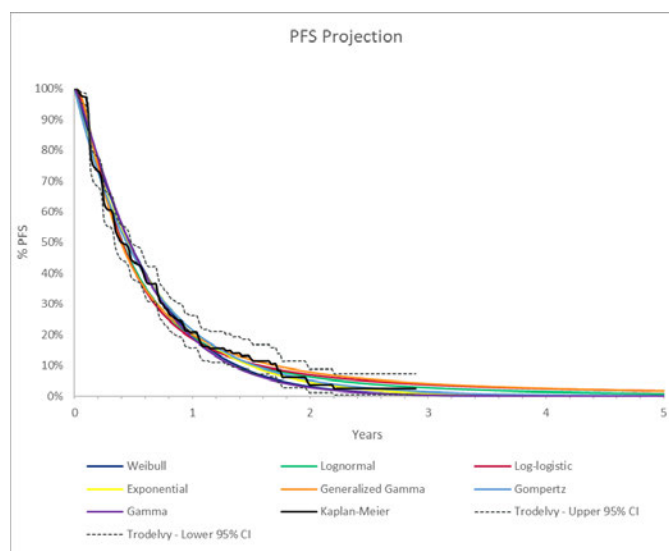
Method/approach	Description/assumption
Data	Meta-analysis of the pooled population from TROPiCS-02 and EVER-132-002 CDK4/6i experienced population
Selected distribution	SG: lognormal TPC: lognormal
Models investigated	The seven standard survival models were fitted to the meta-analysis data: exponential, Weibull, Gompertz, log-logistic, lognormal, gamma and generalised gamma
<i>Assumptions</i>	
Proportional hazards between intervention and comparator	No
Flexible parametric models	No
Cure point and/or share	No
Treatment waning	No
Any other assumptions	No
<i>Internal validity</i>	
Distribution with the best AIC fit	SG: generalised gamma TPC: generalised gamma
Distribution with the best BIC fit	SG: lognormal TPC: lognormal
Distribution(s) with best visual fit on probability scale (e.g., Kaplan-Meier data)	SG: lognormal TPC: lognormal
Distribution(s) with best visual fit according to evaluation of smoothed hazards	SG: lognormal TPC: lognormal
<i>External validity</i>	
References for validating external validity	Danish clinical practice (Dahl et al., 2025).
Distribution with highest external validity	SG: Not available TPC: lognormal



Following NICE TSD 14 (Nicholas Latimer, 2013) and DMC guidelines (Medicinnrådet, 2021), the lognormal distribution was selected as the base case model for both arms. Considering the number of events, 68% (242/353) and 65% (230/351) of patients experienced an event with SG and TPC, respectively. The parametric models were fitted independently, in line with DMC recommendations (Medicinnrådet, 2021). Moreover, the proportional hazard assumption was not valid. A detailed justification for the choice of extrapolated models, based on internal and external validity as outlined by DMC guidelines (Medicinnrådet, 2021), is provided in the Appendix (E.1.1). The choice of extrapolation models for the PFS has a minor impact on the analysis outcomes, as the different distributions yield similar PFS estimates within the respective treatment arms.

In Figure 12 and Figure 13, extrapolated data for all model candidates are shown together with the observed KM data, adjusted for background mortality, for SG and TPC, respectively. Figure 14 shows both treatment arms extrapolated with the chosen lognormal distributions, with the observed KM data, adjusted for background mortality.

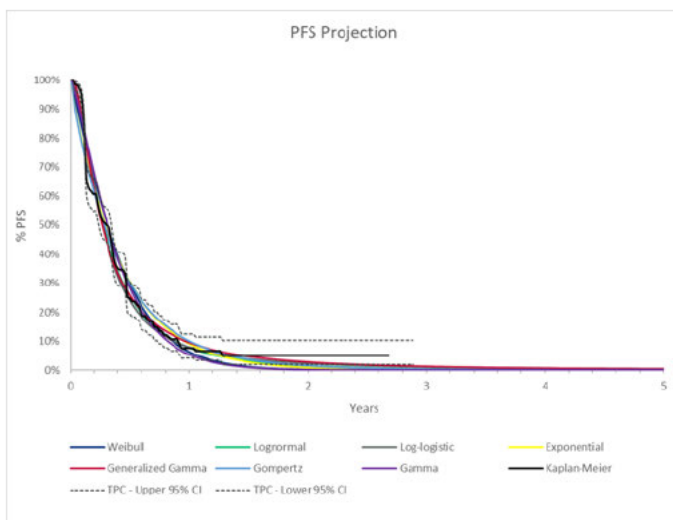
Figure 12 PFS extrapolation and KM data – SG



Abbreviations: CI: Confidence interval.

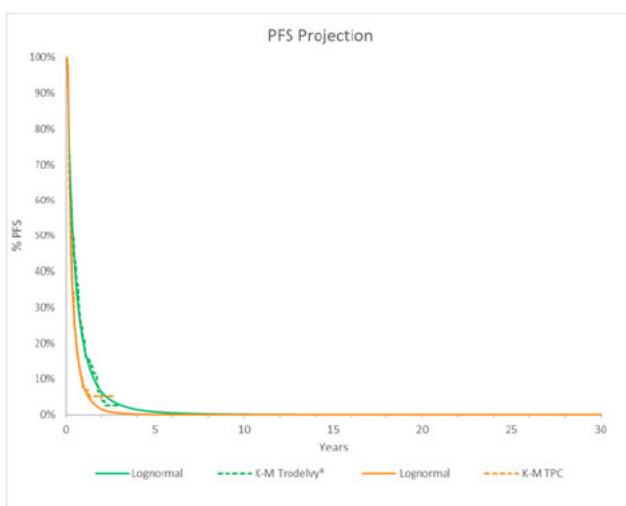


Figure 13 PFS extrapolation and KM data - TPC



Abbreviations: CI: Confidence interval; TPC: Treatment of physician choice.

Figure 14 PFS extrapolation for SG and TPC, lognormal distributions



Abbreviations: KM: Kaplan-Meier; TPC: Treatment of physician choice.

9.2.2 Extrapolation of OS

An overview of assumptions for the extrapolation of OS is presented in Table 26.

Table 26 Overview of assumptions regarding extrapolation of OS

Method/approach	Description/assumption
Data	Meta-analysis of the pooled population from TROPiCS-02 and EVER-132-002 prior CDK4/6i treated
Selected distribution	SG: log-logistic TPC: log-logistic



Method/approach	Description/assumption
Models investigated	The seven standard survival models were fitted to the meta-analysis data: exponential, Weibull, Gompertz, log-logistic, lognormal, gamma and generalised gamma
<i>Assumptions</i>	
Proportional hazards between intervention and comparator	No
Flexible parametric models	No
Cure point and/or share	No
Treatment waning	No
Any other assumptions	No
<i>Internal validity</i>	
Distribution with best AIC fit	SG: gamma TPC: log-logistic
Distribution with best BIC fit	SG: gamma TPC: log-logistic
Distribution(s) with best visual fit on probability scale (e.g., Kaplan-Meier data)	SG: log-logistic TPC: log-logistic
Distribution(s) with best visual fit according to evaluation of smoothed hazards	SG: generalised gamma TPC: log-logistic
<i>External validity</i>	
References for validating external validity	Danish clinical practice (Dahl et al., 2025)
Distribution with highest external validity	SG: Not available TPC: log-logistic

The OS data were mature, and the extrapolation choice was based on NICE TSD 14 (Nicholas Latimer, 2013) and DMC guidelines (Medicinerådet, 2021). Around [REDACTED] experienced an event with TPC compared with [REDACTED] SG. The seven standard parametric models were fitted independently, in line with DMC recommendations (Medicinerådet, 2021), and the proportional hazard assumption was tested as shown in the Appendix (E.1.2). Based on the available evidence, it was decided to reject the proportional hazards assumption. The chosen distributions for both arms

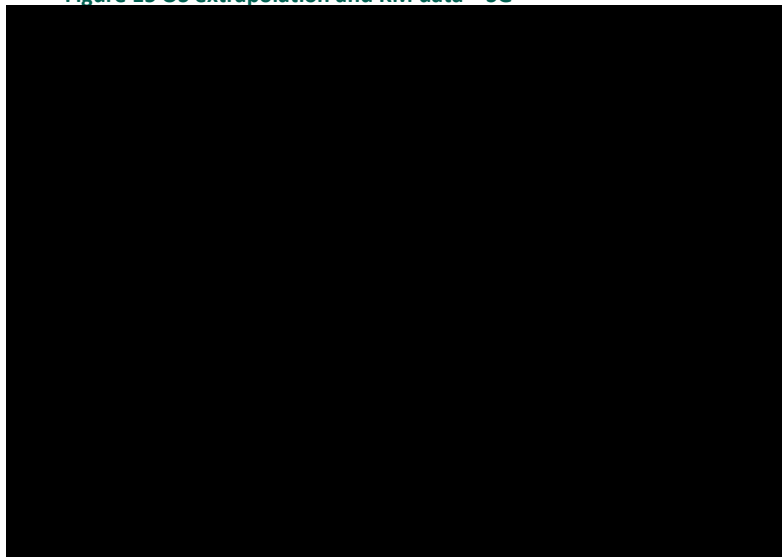


were log-logistic. The choice of model selection is explained in detail in the Appendix (E.1.2), and it was informed by the shape of the hazard, the maturity of the data, clinical plausibility, the visual fit and the goodness-of-fit statistics.

According to NICE TSD 14 guidelines (Nicholas Latimer, 2013), fitting different types of parametric model to different treatment arms require substantial justification, as different models allow very different shaped distributions. Therefore, in selecting the models, priority was given to the TPC arm due to the higher number of events (83%) and a better fit with the external clinical data. In particular, the conservative distributions of SG, predicting lower OS rates than those shown in the RW study (Dahl et al., 2025) at 5 years were excluded. Those patients will experience progression and receive subsequent therapies, which are aligned with the ones patients received in Denmark (Dahl et al., 2025). It was therefore deemed clinically implausible that these patients will survive less than their real-world evidence (RWE) counterpart.

In Figure 15 and Figure 16, extrapolated data for all model candidates are shown together with the observed KM data, adjusted for background mortality, for SG and TPC, respectively. Figure 17 shows both treatment arms extrapolated using the chosen log-logistic distributions, based on the observed KM data, adjusted for background mortality.

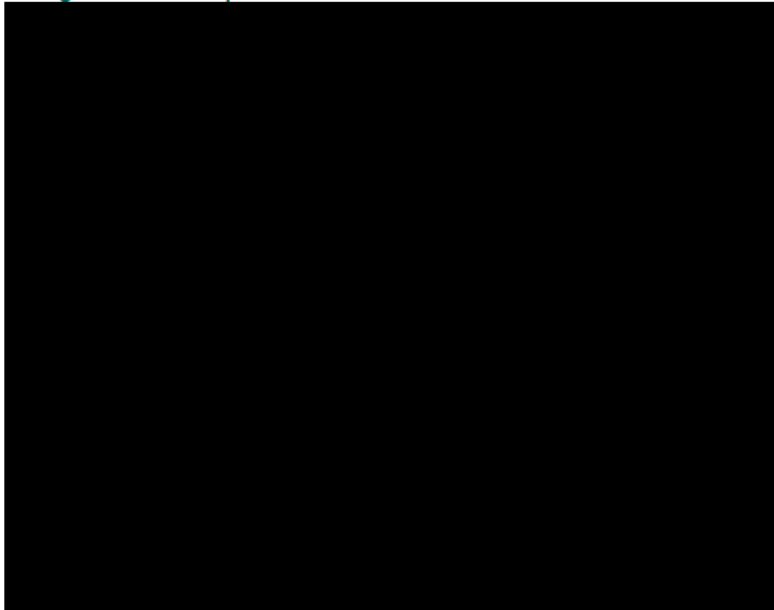
Figure 15 OS extrapolation and KM data – SG



Abbreviations: CI: Confidence interval.

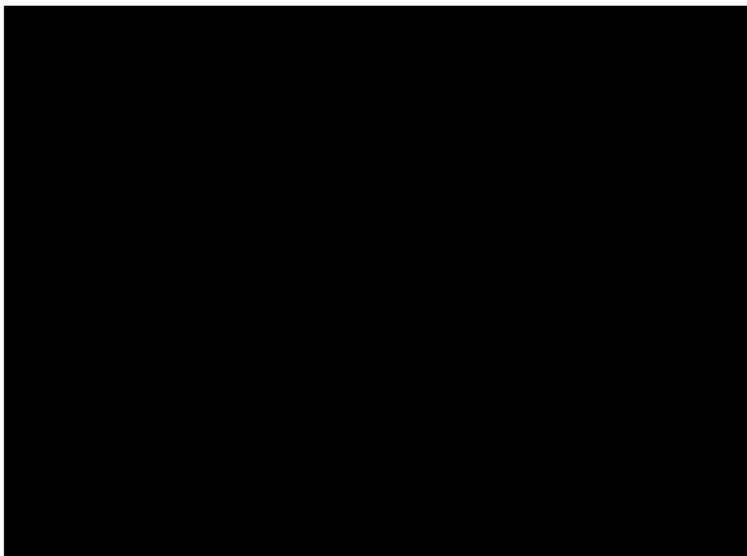


Figure 16 OS extrapolation and KM data - TPC



Abbreviations: CI: Confidence interval; TPC: Treatment of physician choice.

Figure 17 OS extrapolation for SG and TPC, log-logistic distributions



Abbreviations: KM: Kaplan-Meier; TPC: Treatment of physician choice.

9.2.3 Extrapolation of TTD

An overview of assumptions for the extrapolation of TTD is presented in Table 27.

Table 27 Overview of assumptions regarding extrapolation of TTD

Method/approach	Description/assumption
Data	Meta-analysis of the pooled population from TROPiCS-02 and EVER-132-002 CDK4/6i experienced population



Method/approach	Description/assumption
Selected distribution	SG: exponential TPC: exponential
Models investigated	The seven standard survival models were fitted to the meta-analysis data: exponential, Weibull, Gompertz, log-logistic, lognormal, gamma and generalised gamma
<i>Assumptions</i>	
Proportional hazards between intervention and comparator	No
Flexible parametric models	No
Cure point and/or share	No
Treatment waning	No
Any other assumptions	No
<i>Internal validity</i>	
Distribution with best AIC fit	SG: exponential TPC: exponential
Distribution with best BIC fit	SG: exponential TPC: exponential
Distribution(s) with best visual fit on probability scale (e.g., Kaplan-Meier data)	SG: exponential TPC: exponential
Distribution(s) with best visual fit according to evaluation of smoothed hazards	SG: exponential TPC: exponential
<i>External validity</i>	
References for validating external validity	Not available
Distribution with highest external validity	Not available

In the latest available data cut (Gilead, 2026d), the TTD KM curves were complete, with 100% of patients experiencing an event. Extrapolation models were fitted to represent the underlying TTD distribution. This methodology was preferred over the KM curves. Even when the Kaplan–Meier curve is mature or complete, fitting a parametric survival

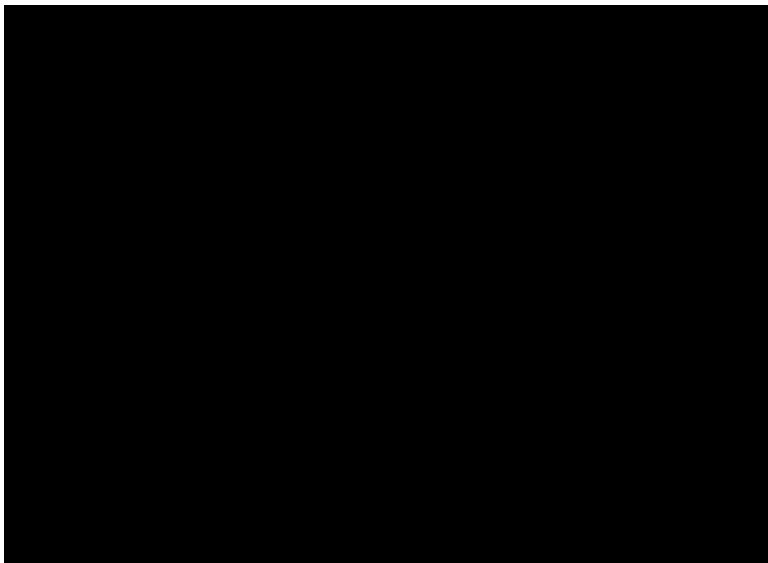


distribution is appropriate because the observed KM can be viewed as a single realisation from an underlying stochastic survival process. Parametric models provide a coherent framework for extrapolating beyond the observed follow-up period while accounting for uncertainty in the estimated survival parameters. In addition, they are particularly useful in probabilistic sensitivity analyses, where parameter uncertainty can be propagated through repeated sampling from the fitted survival distribution, without relying on bootstrapping.

Extrapolation was assessed primarily using goodness-of-fit statistics, and both arms were extrapolated using the exponential models (Nicholas Latimer, 2013). With respect to TTD, the choice of extrapolation has a minimal impact on the overall model results. Further details are discussed in Appendix E.1.3. The best fitting distribution considering hazard shape, goodness-of-fit and visual fit was the exponential model for both arms. The difference between using the complete KM and the extrapolated model is minimal.

In Figure 18 and Figure 19, the extrapolations for all models are shown together with the observed KM data, adjusted for background mortality for SG and TPC, respectively. Figure 20 shows both treatment arms extrapolated with the chosen exponential distributions, with the observed KM data, adjusted for background mortality.

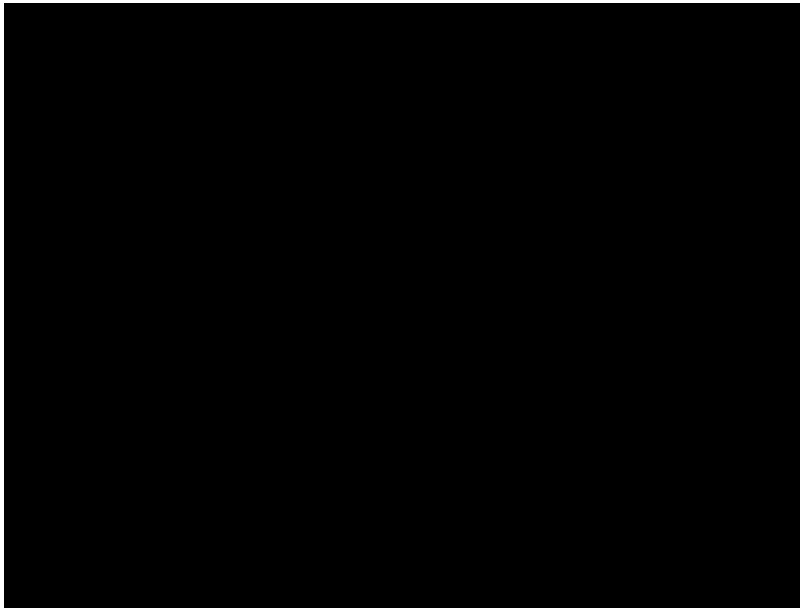
Figure 18 TTD extrapolation and KM data – SG



Abbreviations: CI: Confidence interval.

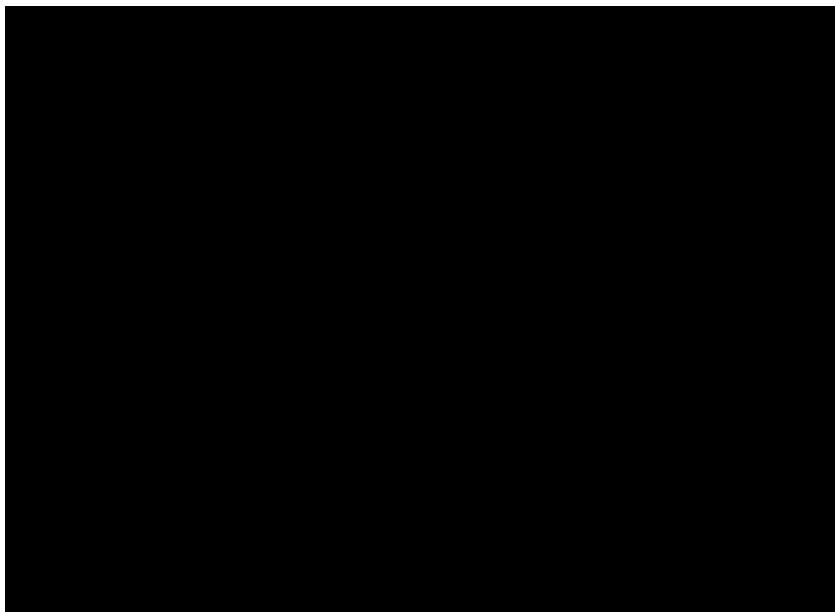


Figure 19 TTD extrapolation and KM data - TPC



Abbreviations: CI: Confidence interval; TPC: Treatment of physician choice.

Figure 20 TTD extrapolation for SG and TPC, exponential distributions



Abbreviations: KM: Kaplan-Meier; TPC: Treatment of physician choice.

9.3 Extrapolation using transition probabilities N/A

Table 28. Transition probabilities in the health economic model N/A



From health state	To health state	Transition probability, including calculation	Assumption	Reference
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Table 29. Transition matrix for [intervention/comparator] N/A

Off/On	State A	State B	State C	...
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9.4 Summary and validity of extrapolated patient transitions

Table 30 presents the average life-years and treatment duration calculated by the model for both SG and TPC. Treatment with SG is on average longer, lasting approximately an additional 2.24 months compared to TPC. It also generates 0.52 additional life years, calculated as undiscounted and adjusted by background mortality and half-cycle correction, most of which are accrued during the progressed survival. Figure 21 and Figure 22 show the patients' flows through the model time horizon for SG and TPC, respectively.

Table 30. Modelled averages in years, undiscounted estimates, half-cycle corrected and adjusted for background mortality

	SG	TPC	Difference
Total life years	2.06	1.58	0.48
Life years in Progress free - PFS	0.72	0.44	0.28
Life years in Progressed - PD	1.34	1.15	0.20
Duration of treatment (Mean - years)	0.52	0.30	0.22



Figure 21 Patient flow – SG

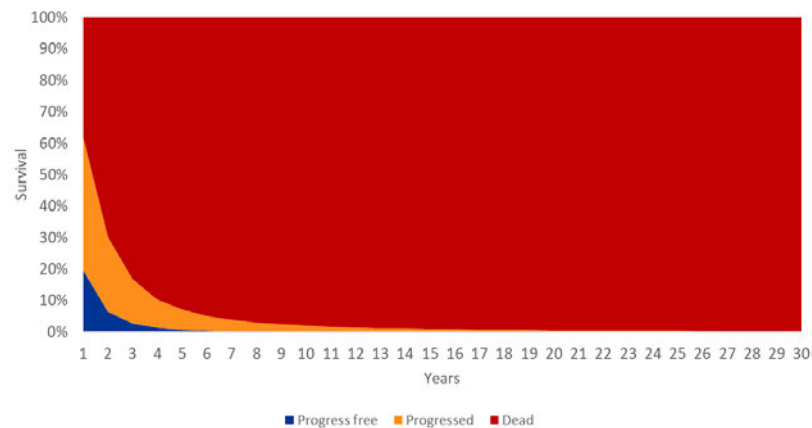
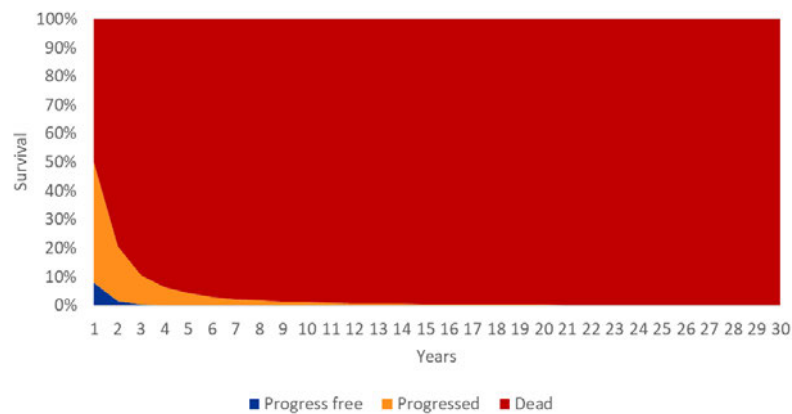


Figure 22 Patient flow - TPC



Abbreviations: TPC: Treatment of physician choice.

10. Health-related quality of life

10.1 Overview

To assess and compare the impact of treatment on Health-Related Quality of Life (HRQoL) between treatment arms in TROPiCS-02 and EVER 132-002, the European Organisation for the Research and Treatment of Cancer (EORTC) quality of life (QOL) questionnaire version 30 (QLQ-C30) and the European Quality of Life (EuroQOL) EQ-5D-5L instruments were used. The EQ-5D-5L health status instrument was the relevant instrument included in this assessment (Table 31). The EQ-5D-5L instrument has two parts: a descriptive system with which patients rate the severity of their experience across 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) on 5 levels of severity. A utility value for each health state was assigned on the basis of a set of preference weights (tariffs) elicited from the general



population specific to Denmark, and the EQ-5D visual analogue scale (EQ-VAS) for patients to self-rate their health state.

Table 31. Overview of included instruments for health-related quality of life

Instrument	Median follow-up time and data cut	Application	Source	Reference to description
EQ-5D-5L	Data cut: 01 December 2022	QoL	TROPiCS-02	Section 10.2.1
EQ-5D-5L	Data cut: 12 December 2024	QoL	EVER-132-002	Section 10.2.1
EQ-VAS	Data cut: 01 December 2022	QoL	TROPiCS-02	Section 10.2.1
EQ-VAS	Data cut: 12 December 2024	QoL	EVER-132-002	Section 10.2.1.3

Table 32. Basis for estimating utility values

Instrument	Preference weights	Source	Short description
EQ-5D-5L	DK	Pooled data from TROPiCS-02 and EVER-132-002.	Pooled analysis from EVER and TROPiCS-02, the same studies that inform clinical efficacy and safety

10.2 Instruments

10.2.1 EQ-5D-5L

10.2.1.1 Study design and instrument – EQ-5D

EQ-5D-5L dimension scores, EQ-5D-5L summary index and EQ-VAS were summarised descriptively for each visit. Change from baseline EQ-5D-5L summary index and EQ-VAS was analysed using a mixed model repeated measure (MMRM).

Change from baseline values at each time point was fitted to a mixed-effects model including subjects as a random effect, baseline score, treatment, baseline-by-treatment interaction, and randomisation stratification factors as fixed effects, and time point as a within-subject effect. An unstructured covariate matrix was used. Comparisons between the treatment arms were made using least squares (LS) means, LS differences, 95% CIs, and p-values. To derive the EQ-5D-5L summary index, the health state values were converted to EQ-5D-5L index values using the Danish-specific value sets.



10.2.1.2 Data collection – EQ-5D

The EQ-5D-5L and EQ-VAS evaluable population was defined as all participants in the ITT population who had an evaluable assessment of EQ-5D at baseline and at least 1 evaluable assessment at post-baseline visits.

An evaluable assessment at a given visit was defined as at least 1 of the 5 dimensions of the EQ-5D-5L or VAS score being non-missing at that scheduled visit.

The EQ-5D evaluable population from TROPiCS-02 included 445 (82.0%) subjects, 238 (87.5%) in the SG arm and 207 (76.45) in the TPC arm. The EQ-5D evaluable population from EVER-132-002 included 318 (96.1%) subjects, 161 (97.0%) in the SG arm and 157 (95.2%) in the TPC arm, however, only observations from patients previously treated with CDK4/6 inhibitors were included in the analysis.

In the TROPiCS-02 trial, HRQoL was assessed at Baseline (prior to the first dose of study drug), on Day 1 of each subsequent cycle, at the time of withdrawal, and at the Off-Treatment Visit. In addition, QoL was assessed every 60 days during the follow-up period and at the time of PFS2.

In the EVER-132-002 study, HRQoL was evaluated on the first day of each treatment cycle, at each tumour assessment visit, and at the end-of-treatment visit.

In Table 33-Table 36, all time points, except “END OF TREATMENT” and “LONG TERM FOLLOW-UP”, were collected for patients who were progression-free at the time point. The drop in number of responses is due to patients progressing over time.

Table 33. Overview of responses intervention (TROPiCS-02)

Time	Number of patients “at risk”* at time t (expected number of responses) N	Number of responses at time t N	Proportion of responses out of the number of patients “at risk” at time t** %	Proportion of responses out of the number of patients at randomisation*** %
BASELINE	272	250	91.9%	91.9%
CYCLE 2 DAY 1	266	222	83.5%	81.6%
CYCLE 3 DAY 1	264	180	68.2%	66.2%
CYCLE 4 DAY 1	261	165	63.2%	60.7%
CYCLE 5 DAY 1	258	141	54.7%	51.8%
CYCLE 6 DAY 1	253	137	54.2%	50.4%
CYCLE 7 DAY 1	247	118	47.8%	43.4%



Time	Number of patients "at risk" * at time t (expected number of responses) N	Number of responses at time t N	Proportion of responses out of the number of patients "at risk" at time t ** %	Proportion of responses out of the number of patients at randomisation *** %
CYCLE 8 DAY 1	237	111	46.8%	40.8%
CYCLE 9 DAY 1	227	89	39.2%	32.7%
CYCLE 10 DAY 1	223	83	37.2%	30.5%
CYCLE 11 DAY 1	215	71	33%	26.1%
CYCLE 12 DAY 1	210	64	30.5%	23.5%
CYCLE 13 DAY 1	206	54	26.2%	19.9%
CYCLE 14 DAY 1	198	50	25.3%	18.4%
CYCLE 15 DAY 1	190	45	23.7%	16.5%
CYCLE 16 DAY 1	180	39	21.7%	14.3%
CYCLE 17 DAY 1	174	38	21.8%	14.0%
CYCLE 18 DAY 1	168	31	18.5%	11.4%
CYCLE 19 DAY 1	159	26	16.4%	9.6%
CYCLE 20 DAY 1	147	25	17%	9.2%
CYCLE 21 DAY 1	141	24	17%	8.8%
CYCLE 22 DAY 1	132	23	17.4%	8.5%
CYCLE 23 DAY 1	128	19	14.8%	7.0%
CYCLE 24 DAY 1	120	17	14.2%	6.3%
CYCLE 25 DAY 1	113	16	14.2%	5.9%
CYCLE 26 DAY 1	108	15	13.9%	5.5%
CYCLE 27 DAY 1	102	15	14.7%	5.5%
CYCLE 28 DAY 1	97	11	11.3%	4.0%
CYCLE 29 DAY 1	95	11	11.6%	4.0%



Time	Number of patients "at risk" * at time t (expected number of responses) N	Number of responses at time t N	Proportion of responses out of the number of patients "at risk" at time t ** %	Proportion of responses out of the number of patients at randomisation *** %
CYCLE 30 DAY 1	91	11	12.1%	4.0%
CYCLE 31 DAY 1	75	8	10.7%	2.9%
CYCLE 32 DAY 1	72	8	11.1%	2.9%
CYCLE 33 DAY 1	67	7	10.4%	2.6%
CYCLE 34 DAY 1	65	8	12.3%	2.9%
CYCLE 35 DAY 1	58	8	13.8%	2.9%
CYCLE 36 DAY 1	53	9	17%	3.3%
CYCLE 37 DAY 1	47	9	19.1%	3.3%
CYCLE 38 DAY 1	43	6	14%	2.2%
CYCLE 39 DAY 1	38	6	15.8%	2.2%
CYCLE 40 DAY 1	29	4	13.8%	1.5%
CYCLE 41 DAY 1	26	5	19.2%	1.8%
CYCLE 42 DAY 1	22	4	18.2%	1.5%
CYCLE 43 DAY 1	20	4	20%	1.5%
CYCLE 44 DAY 1	18	3	16.7%	1.1%
CYCLE 45 DAY 1	18	3	16.7%	1.1%
CYCLE 46 DAY 1	14	2	14.3%	0.7%
CYCLE 47 DAY 1	10	2	20%	0.7%
CYCLE 48 DAY 1	8	2	25%	0.7%
CYCLE 49 DAY 1	5	2	40%	0.7%
CYCLE 50 DAY 1	4	2	50%	0.7%
CYCLE 51 DAY 1	3	2	66.7%	0.7%



Time	Number of patients "at risk" * at time t (expected number of responses) N	Number of responses at time t N	Proportion of responses out of the number of patients "at risk" at time t ** %	Proportion of responses out of the number of patients at randomisation *** %
CYCLE 52 DAY 1	2	2	100%	0.7%
CYCLE 53 DAY 1	2	2	100%	0.7%
CYCLE 55 DAY 1	1	1	100%	0.4%
CYCLE 56 DAY 1	1	1	100%	0.4%
END OF TREATMENT	217	193	88.9%	71.0%
LONG TERM FOLLOW-UP	16	15	93.8%	5.9%

* Number of patients "at risk": Patients who have not died or been censored before time t , and who are therefore expected to complete the questionnaire. Patients who have discontinued treatment must be counted. . **Proportion of responses out of patients "at risk" at time t = number of responses at time t /number of patients "at risk" at time t . ***Proportion of responses since randomization = number of responses at time t /number of patients at randomisation.

Table 34. Overview of responses comparator (TROPiCS-02)

Time	Number of patients "at risk" * at time t (expected number of responses) N	Number of responses at time t N	Proportion of responses out of the number of patients "at risk" at time t ** %	Proportion of responses out of the number of patients at randomisation *** %
BASELINE	271	234	86.3%	86.3%
CYCLE 2 DAY 1	267	193	72.3%	71.2%
CYCLE 3 DAY 1	266	133	50%	49.1%
CYCLE 4 DAY 1	260	118	45.4%	43.5%
CYCLE 5 DAY 1	255	97	38%	35.8%
CYCLE 6 DAY 1	250	82	32.8%	30.3%
CYCLE 7 DAY 1	236	62	26.3%	22.9%
CYCLE 8 DAY 1	228	55	24.1%	20.3%



Time	Number of patients "at risk" * at time t (expected number of responses) N	Number of responses at time t N	Proportion of responses out of the number of patients "at risk" at time t ** %	Proportion of responses out of the number of patients at randomisation *** %
CYCLE 9 DAY 1	211	46	21.8%	17.0%
CYCLE 10 DAY 1	199	34	17.1%	12.5%
CYCLE 11 DAY 1	188	27	14.4%	10.0%
CYCLE 12 DAY 1	179	22	12.3%	8.1%
CYCLE 13 DAY 1	174	17	9.8%	6.3%
CYCLE 14 DAY 1	166	14	8.4%	5.2%
CYCLE 15 DAY 1	159	15	9.4%	5.5%
CYCLE 16 DAY 1	143	12	8.4%	4.4%
CYCLE 17 DAY 1	133	8	6%	3.0%
CYCLE 18 DAY 1	126	8	6.3%	3.0%
CYCLE 19 DAY 1	117	7	6%	2.6%
CYCLE 20 DAY 1	111	5	4.5%	1.8%
CYCLE 21 DAY 1	102	5	4.9%	1.8%
CYCLE 22 DAY 1	100	5	5%	1.8%
CYCLE 23 DAY 1	93	5	5.4%	1.8%
CYCLE 24 DAY 1	89	4	4.5%	1.5%
CYCLE 25 DAY 1	87	3	3.4%	1.1%
CYCLE 26 DAY 1	83	3	3.6%	1.1%
CYCLE 27 DAY 1	81	2	2.5%	0.7%
CYCLE 28 DAY 1	77	2	2.6%	0.7%
CYCLE 29 DAY 1	76	2	2.6%	0.7%
CYCLE 30 DAY 1	71	1	1.4%	0.4%



Time	Number of patients "at risk" * at time t (expected number of responses) N	Number of responses at time t N	Proportion of responses out of the number of patients "at risk" at time t ** %	Proportion of responses out of the number of patients at randomisation *** %
CYCLE 31 DAY 1	68	1	1.5%	0.4%
CYCLE 32 DAY 1	60	1	1.7%	0.4%
CYCLE 33 DAY 1	54	1	1.9%	0.4%
CYCLE 34 DAY 1	51	0	0%	0.0%
CYCLE 35 DAY 1	46	0	0%	0.0%
CYCLE 36 DAY 1	44	0	0%	0.0%
CYCLE 37 DAY 1	37	0	0%	0.0%
CYCLE 38 DAY 1	34	0	0%	0.0%
CYCLE 39 DAY 1	29	0	0%	0.0%
CYCLE 40 DAY 1	24	0	0%	0.0%
CYCLE 41 DAY 1	18	0	0%	0.0%
CYCLE 42 DAY 1	16	0	0%	0.0%
CYCLE 43 DAY 1	15	0	0%	0.0%
CYCLE 44 DAY 1	13	0	0%	0.0%
CYCLE 45 DAY 1	12	0	0%	0.0%
CYCLE 46 DAY 1	7	0	0%	0.0%
CYCLE 47 DAY 1	4	0	0%	0.0%
CYCLE 48 DAY 1	4	0	0%	0.0%
CYCLE 49 DAY 1	2	0	0%	0.0%
CYCLE 50 DAY 1	2	0	0%	0.0%
CYCLE 51 DAY 1	1	0	0%	0.0%
CYCLE 52 DAY 1	1	0	0%	0.0%



Time	Number of patients "at risk" * at time t (expected number of responses) N	Number of responses at time t N	Proportion of responses out of the number of patients "at risk" at time t ** %	Proportion of responses out of the number of patients at randomisation *** %
CYCLE 53 DAY 1	1	0	0%	0.0%
CYCLE 55 DAY 1	0	0	0%	0.0%
CYCLE 56 DAY 1	0	0	0%	0.0%
END OF TREATMENT	198	169	85.4%	62.4%
LONG TERM FOLLOW-UP	15	15	100%	5.5%

* Number of patients "at risk": Patients who have not died or been censored before time t, and who are therefore expected to complete the questionnaire. Patients who have discontinued treatment must be counted. **Proportion of responses out of patients "at risk" at time t = number of responses at time t/number of patients "at risk" at time t. ***Proportion of responses since randomization = number of responses at time t/number of patients at randomisation.

Table 35. Overview of responses intervention (EVER-132-002)

Time	Number of patients "at risk" * at time t (expected number of responses) N	Number of responses at time t N	Proportion of responses out of the number of patients "at risk" at time t ** %	Proportion of responses out of the number of patients at randomisation *** %
BASELINE	81	80	98.8%	98.8%
WEEK 4	81	39	48.1%	48.1%
WEEK 7	81	61	75.3%	75.3%
WEEK 10	79	36	45.6%	44.4%
WEEK 13	78	51	65.4%	63.0%
WEEK 16	77	24	31.2%	29.6%
WEEK 19	77	41	53.2%	50.6%
WEEK 22	77	17	22.1%	21.0%
WEEK 25	77	37	48.1%	45.7%



Time	Number of patients "at risk" * at time t (expected number of responses) N	Number of responses at time t N	Proportion of responses out of the number of patients "at risk" at time t ** %	Proportion of responses out of the number of patients at randomisation *** %
WEEK 28	75	12	16%	14.8%
WEEK 31	71	31	43.7%	38.3%
WEEK 34	70	8	11.4%	9.9%
WEEK 37	66	27	40.9%	33.3%
WEEK 40	64	5	7.8%	6.2%
WEEK 43	62	20	32.3%	24.7%
WEEK 46	59	1	1.7%	1.2%
WEEK 49	59	15	25.4%	18.5%
WEEK 52	56	0	0%	0.0%
WEEK 55	56	12	21.4%	14.8%
WEEK 58	53	0	0%	0.0%
WEEK 61	53	1	1.9%	1.2%
WEEK 67	45	9	20%	11.1%
WEEK 70	45	1	2.2%	1.2%
WEEK 79	40	3	7.5%	3.7%
WEEK 91	37	1	2.7%	1.2%
WEEK 94	35	1	2.9%	1.2%
WEEK 103	29	1	3.4%	1.2%
WEEK 115	23	0	0%	0.0%
END OF TREATMENT	65	57	87.7%	70.4%

* Number of patients "at risk": Patients who have not died or been censored before time t, and who are therefore expected to complete the questionnaire. Patients who have discontinued treatment must be counted. **Proportion of responses out of patients "at risk" at time t = number of responses at time t/number of patients "at risk" at time t. ***Proportion of responses since randomization = number of responses at time t/number of patients at randomisation.



Table 36. Overview of responses comparator (EVER-132-002)

Time	Number of patients "at risk" * at time t (expected number of responses) N	Number of responses at time t N	Proportion of responses out of the number of patients "at risk" at time t ** %	Proportion of responses out of the number of patients at randomisation *** %
BASELINE	80	78	97.5%	97.5%
WEEK 4	79	37	46.8%	46.3%
WEEK 7	76	52	68.4%	65.0%
WEEK 10	76	22	28.9%	27.5%
WEEK 13	75	37	49.3%	46.3%
WEEK 16	73	12	16.4%	15.0%
WEEK 19	71	25	35.2%	31.3%
WEEK 22	70	2	2.9%	2.5%
WEEK 25	68	15	22.1%	18.8%
WEEK 28	67	1	1.5%	1.3%
WEEK 31	65	9	13.8%	11.3%
WEEK 34	61	1	1.6%	1.3%
WEEK 37	57	6	10.5%	7.5%
WEEK 40	55	1	1.8%	1.3%
WEEK 43	52	3	5.8%	3.8%
WEEK 46	51	1	2%	1.3%
WEEK 49	46	2	4.3%	2.5%
WEEK 52	41	1	2.4%	1.3%
WEEK 55	40	2	5%	2.5%
WEEK 58	35	1	2.9%	1.3%
WEEK 61	35	0	0%	0.0%



Time	Number of patients "at risk" * at time t (expected number of responses) N	Number of responses at time t N	Proportion of responses out of the number of patients "at risk" at time t ** %	Proportion of responses out of the number of patients at randomisation *** %
WEEK 67	32	2	6.2%	2.5%
WEEK 70	32	0	0%	0.0%
WEEK 79	28	1	3.6%	1.3%
WEEK 91	22	1	4.5%	1.3%
WEEK 94	22	0	0%	0.0%
WEEK 103	16	1	6.2%	1.3%
WEEK 115	12	1	8.3%	1.3%
END OF TREATMENT	66	62	93.9%	77.5%

* Number of patients "at risk": Patients who have not died or been censored before time t, and who are therefore expected to complete the questionnaire. Patients who have discontinued treatment must be counted. **Proportion of responses out of patients "at risk" at time t = number of responses at time t/number of patients "at risk" at time t.***Proportion of responses since randomization = number of responses at time t/number of patients at randomisation.

Table 37. Overview of responses by health state – SG in TROPiCS-02

Health state	Number of responses in health state N	Number of patients who have provided at least one response in the health state N
Progression free	1717	Not available
Progressed	366	Not available

Table 38. Overview of responses by health state – TPC in TROPiCS-02

Health state	Number of responses in health state N	Number of patients who have provided at least one response in the health state N
Progression free	989	Not available
Progressed	241	Not available



Table 39. Overview of responses by health state – SG in EVER-132-002

Health state	Number of responses in health state N	Number of patients who have provided at least one response in the health state N
Progression free	Not available	Not available
Progressed	Not available	Not available

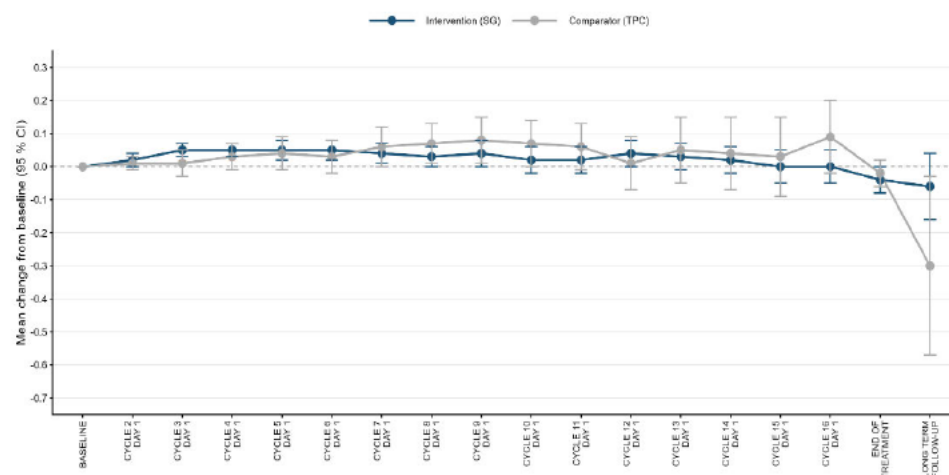
Table 40. Overview of responses by health state – TPC in EVER-132-002

Health state	Number of responses in health state N	Number of patients who have provided at least one response in the health state N
Progression free	Not available	Not available
Progressed	Not available	Not available

10.2.1.3 Results EQ-5D

Table 41 and Table 43 include the results at baseline and at the relevant data collection timepoints for the EQ-5D-5L index. The EQ-5D VAS score for the two trials are presented in Table 42 and Table 44. The mean changes from baseline are illustrated in Figure 23 and Figure 25 through the different data collection time points for both intervention and comparator in both trials.

Figure 23. EQ-5D-5L change over time - TROPiCS-02





No. Of patients

SG	233	210	166	154	129	125	108	102	80	76	65	58	48	45	40	35	179	13
TPC	205	181	124	108	88	77	59	54	45	33	26	21	16	13	14	11	156	15

Table 41. Results for EQ-5D-5L – TROPiCS-02

Time	SG	TPC	Difference
	Average (SE)	Average (SE)	Difference (95%CI)
Baseline	0.8 (0.013)	0.79 (0.014)	-
CYCLE 2 DAY 1	0.82 (0.014)	0.81 (0.015)	0.003 (-0.028, 0.034)
CYCLE 3 DAY 1	0.86 (0.012)	0.82 (0.02)	0.038 (-0.008, 0.083)
CYCLE 4 DAY 1	0.86 (0.013)	0.83 (0.019)	0.017 (-0.03, 0.063)
CYCLE 5 DAY 1	0.85 (0.017)	0.83 (0.021)	0.009 (-0.045, 0.063)
CYCLE 6 DAY 1	0.86 (0.015)	0.81 (0.022)	0.022 (-0.03, 0.074)
CYCLE 7 DAY 1	0.85 (0.018)	0.84 (0.023)	-0.025 (-0.086, 0.036)
CYCLE 8 DAY 1	0.85 (0.02)	0.85 (0.022)	-0.044 (-0.102, 0.013)
CYCLE 9 DAY 1	0.85 (0.022)	0.85 (0.022)	-0.046 (-0.117, 0.024)
CYCLE 10 DAY 1	0.84 (0.023)	0.83 (0.027)	-0.044 (-0.118, 0.03)
CYCLE 11 DAY 1	0.83 (0.025)	0.88 (0.019)	-0.04 (-0.115, 0.035)
CYCLE 12 DAY 1	0.86 (0.022)	0.85 (0.026)	0.024 (-0.058, 0.105)
CYCLE 13 DAY 1	0.85 (0.027)	0.88 (0.019)	-0.026 (-0.118, 0.066)
CYCLE 14 DAY 1	0.84 (0.03)	0.86 (0.036)	-0.018 (-0.115, 0.078)
CYCLE 15 DAY 1	0.82 (0.033)	0.84 (0.03)	-0.035 (-0.144, 0.074)
CYCLE 16 DAY 1	0.83 (0.038)	0.87 (0.032)	-0.087 (-0.206, 0.032)
END OF TREATMENT	0.77 (0.021)	0.78 (0.018)	-0.027 (-0.078, 0.023)
LONG TERM FOLLOW-UP	0.87 (0.054)	0.54 (0.138)	0.248 (-0.071, 0.568)



Figure 24. EQ-5D VAS change over time - TROPiCS-02

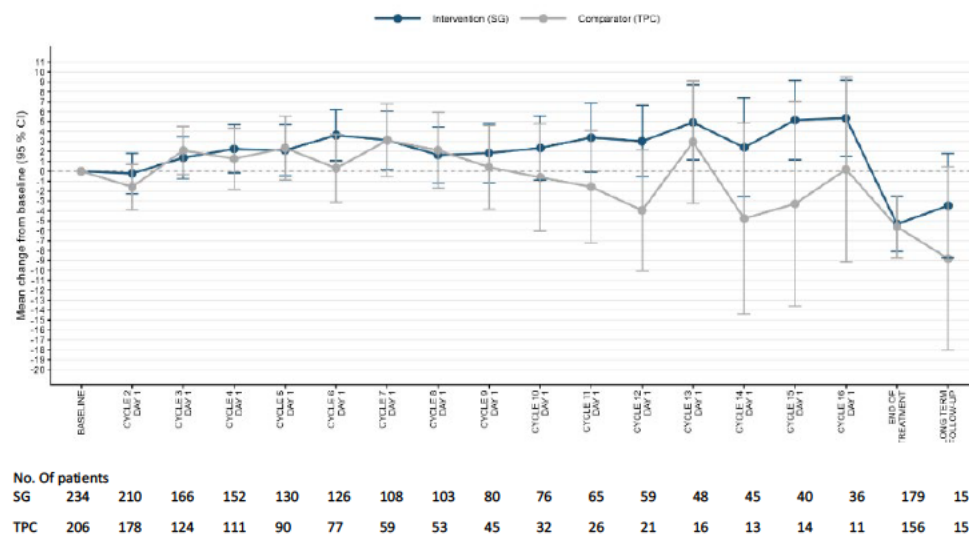


Table 42. Results for EQ-5D VAS – TROPiCS-02

Time	SG	TPC	Difference
	Average (SE)	Average (SE)	Difference (95%CI)
Baseline	69.56 (1.244)	68.04 (1.409)	-
CYCLE 2 DAY 1	70.49 (1.314)	67.94 (1.435)	1.362 (-1.718, 4.442)
CYCLE 3 DAY 1	72.46 (1.38)	71.76 (1.524)	-0.733 (-3.973, 2.507)
CYCLE 4 DAY 1	73.35 (1.476)	70.75 (1.767)	0.985 (-2.921, 4.891)
CYCLE 5 DAY 1	72.9 (1.621)	71.94 (1.86)	-0.234 (-4.364, 3.896)
CYCLE 6 DAY 1	75.2 (1.442)	70.36 (2.064)	3.34 (-0.958, 7.639)
CYCLE 7 DAY 1	73.95 (1.737)	74.93 (2.21)	0.03 (-4.83, 4.891)
CYCLE 8 DAY 1	73.01 (1.775)	74.72 (2.371)	-0.48 (-5.35, 4.391)
CYCLE 9 DAY 1	73.54 (1.945)	73.36 (2.456)	1.433 (-3.723, 6.589)
CYCLE 10 DAY 1	72.67 (1.886)	70.5 (2.979)	2.963 (-3.247, 9.173)
CYCLE 11 DAY 1	73.75 (2.028)	76.35 (2.767)	4.968 (-1.7, 11.635)
CYCLE 12 DAY 1	73.27 (2.357)	75.38 (3.136)	6.97 (-0.212, 14.151)
CYCLE 13 DAY 1	74.46 (2.389)	77.81 (3.161)	1.977 (-5.642, 9.596)



Time	SG	TPC	Difference
CYCLE 14 DAY 1	71.4 (3.014)	69.31 (4.848)	7.156 (-3.719, 18.03)
CYCLE 15 DAY 1	73.53 (2.53)	69.79 (4.409)	8.44 (-0.921, 17.8)
CYCLE 16 DAY 1	74.17 (3.062)	72.73 (4.491)	5.161 (-3.745, 14.067)
END OF TREATMENT	65.45 (1.591)	64.28 (1.731)	0.267 (-3.944, 4.478)
LONG TERM FOLLOW-UP	71.53 (5.516)	67.87 (6.308)	5.333 (-5.79, 16.456)

Figure 25. EQ-5D-5L change over time - EVER-132-002

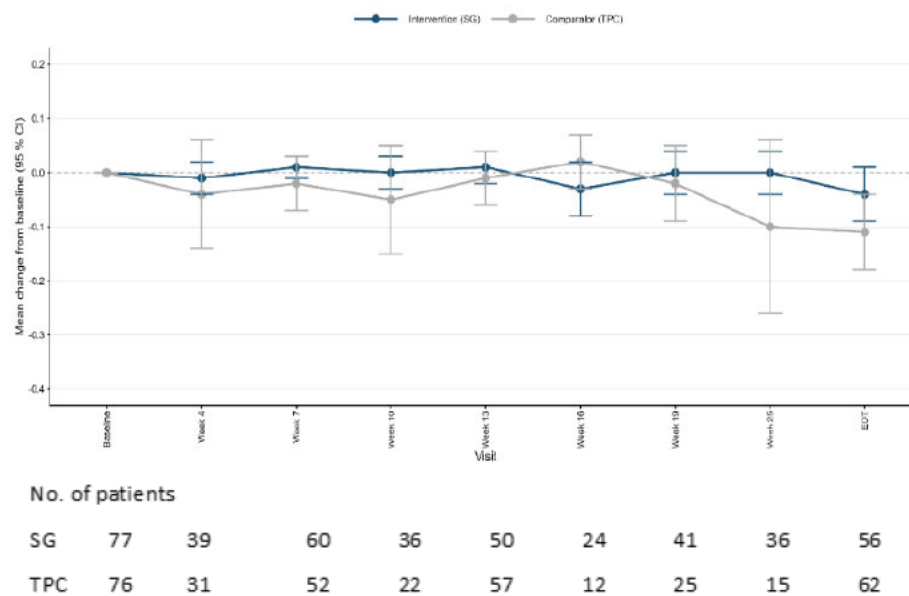


Table 43. Results for EQ-5D-5L – EVER-132-002

Time	SG	TPC	Difference
	Average (SE)	Average (SE)	Difference (95%CI)
Baseline	0.89 (0.014)	0.83 (0.021)	-
WEEK 4	0.88 (0.029)	0.79 (0.05)	0.03 (-0.075, 0.135)
WEEK 7	0.89 (0.012)	0.82 (0.03)	0.03 (-0.024, 0.084)
WEEK 10	0.89 (0.017)	0.82 (0.046)	0.048 (-0.06, 0.156)



Time	SG	TPC	Difference
WEEK 13	0.9 (0.013)	0.88 (0.022)	0.023 (-0.034, 0.08)
WEEK 16	0.86 (0.024)	0.86 (0.037)	-0.045 (-0.122, 0.032)
WEEK 19	0.89 (0.016)	0.84 (0.037)	0.014 (-0.072, 0.1)
WEEK 25	0.89 (0.02)	0.75 (0.07)	0.099 (-0.083, 0.282)
END OF TREATMENT	0.85 (0.024)	0.71 (0.038)	0.076 (-0.007, 0.16)

Figure 26. EQ-5D VAS change over time - EVER-132-002

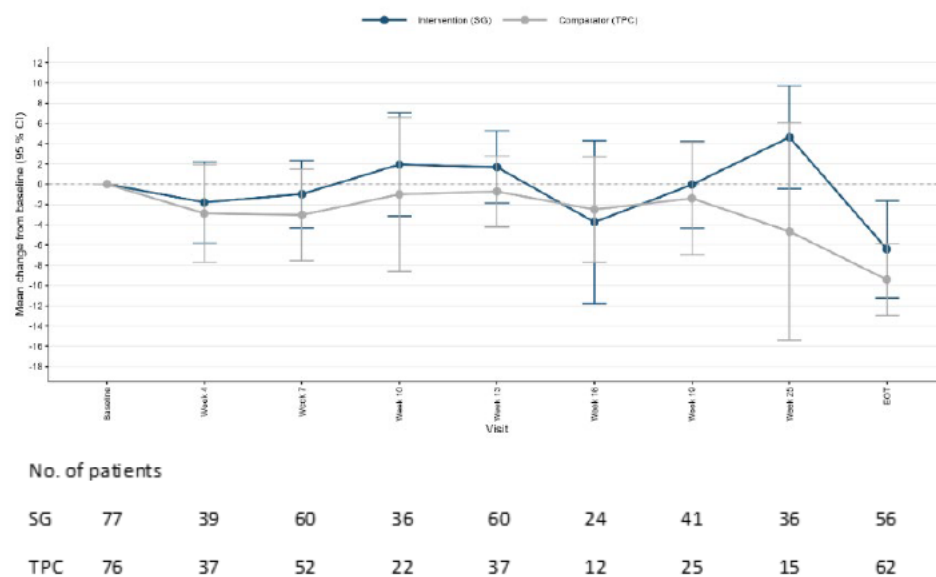


Table 44. Results for EQ-5D VAS – EVER-132-002

Time	SG	TPC	Difference
	Average (SE)	Average (SE)	Difference (95%CI)
Baseline	77.95 (1.762)	75.39 (1.955)	-
WEEK 4	76.54 (2.637)	72.51 (3.008)	1.097 (-5.277, 7.471)
WEEK 7	76.72 (2.022)	73.4 (2.324)	2.055 (-3.615, 7.725)
WEEK 10	76.39 (2.772)	74.23 (4.047)	2.944 (-6.513, 12.401)
WEEK 13	78.76 (1.989)	80.08 (2.217)	2.41 (-2.637, 7.457)
WEEK 16	72.5 (4.288)	74.17 (3.835)	-1.25 (-11.182, 8.682)



Time	SG	TPC	Difference
WEEK 19	76.88 (2.029)	76.2 (3.018)	1.351 (-5.845, 8.547)
WEEK 25	81.69 (2.232)	75.33 (3.142)	9.306 (-3.341, 21.952)
END OF TREATMENT	71.75 (2.578)	65.4 (2.512)	3.007 (-3.024, 9.038)

The mean utility in the SG arm at baseline was 0.8 (SE=0.013) in TROPiCS-02 and 0.89 (SE=0.014) in EVER-132-002. The mean utility at the following scheduled cycle visits was consistently higher than at baseline in TROPiCS-02 and broadly equivalent to that observed at baseline in EVER-132-002. More specifically, there was an initial increase in mean utility at Cycles 2 and 3 in TROPiCS-02, which remained constant through Cycle 15. At Cycle 15, only 40 patients had scheduled cycle visits from the initial group of 234 patients at baseline; the mean utility at this point was thus obtained from 17% of patients, and the decreasing sample size over time led to increasingly wider SEs. Finally, the mean utility at the end of therapy (EOT) visit was 0.77 (SE=0.022) and 0.85 (SE=0.024) in TROPiCS-02 and EVER-132-002, respectively, both lower than the mean utility measured at baseline.

In the TPC treatment arm, the mean utility at baseline was 0.79 (SE = 0.014) in TROPiCS-02 and 0.83 (SE = 0.021) in EVER-132-002. The mean utility increased slowly from Cycle 2 to Cycle 9 in TROPiCS-02, whereas it decreased over the same cycles in EVER-132-002. After Cycle 9, utility began to fluctuate. However, mean utility was obtained from 22% of patients, and the decreasing sample size over time led to increasingly wider SEs. Beyond Cycle 16, data were available for approximately 5% of patients, explaining the high volatility of mean estimates. The mean utility value in EVER-132-002 fluctuated across cycles, which could be explained by variability in the number of scheduled visits. The mean utility at the EOT visit was 0.78 (SE=0.018) in TROPiCS-02 and 0.71 (SE=0.038) in EVER-132-002, respectively, both lower than most utilities measured at any scheduled cycle visit or at baseline.

Comparing the SG and TPC treatment arms, SG patients remained on treatment substantially longer than TPC patients. In general, mean utility at scheduled cycle visits was higher in the SG treatment arm than in the TPC treatment arm in EVER-132-002, and higher in the SG arm than in the TPC arm in TROPiCS-02 through Cycle 7. From Cycle 7 onward, the trend is unclear. Utility fluctuates in both arms because of the decreasing number of observations. The difference between SG patients and TPC patients at the EOT visit was minimal.

10.3 Utility values

10.3.1 Dataset(s)

Pooled EQ-5D-5L values collected from TROPiCS-02 and EVER-132-002 (CDK4/6i pre-treated subpopulation) form the basis for calculating utility values used in the model.

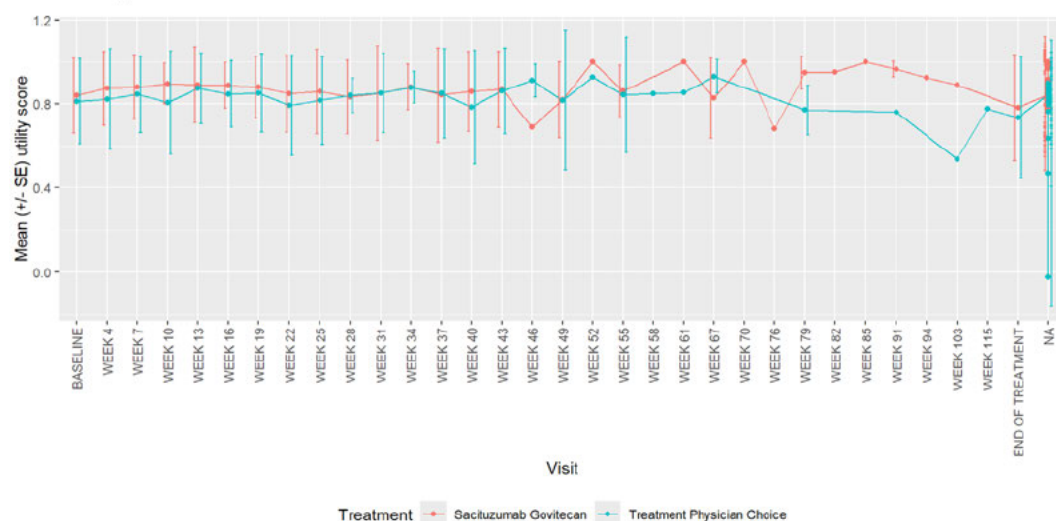


Age adjustment has been performed according to national guidelines and Danish preference weights (Jensen et al. , 2021) have been used to derive Danish EQ-5D-5L index scores.

In Figure 27 the change EQ-5D-5L in utility score over time for the pooled analysis is presented.

Figure 27 Change over time EQ-5D-5L DK pooled analysis

Plot Utility over Time



10.3.2 Calculation of utility values

EQ-5D-5L utility scores from all visits were analysed in the base case using a multivariate mixed-effects linear regression model with a random intercept for each patient to account for the clustering of multiple observations. Utility values were applied to each health state in the model to capture HRQoL associated with treatment and disease outcomes. Specifically, the analysis base case assigns utility values to the health state PF by treatment and a single utility value to PD, applicable to all treatments, assuming that HRQoL after progression does not differ by initial treatment received. The rationale for different PF utility values by treatment arm is the statistically significant difference in HRQoL observed between the two arms in the pooled TROPiCS-02 and EVER-132-002 regression models, see Table 45. Additionally, as the effects of adverse reactions on HRQoL are captured, using different PF utility values by treatment arm reflects the different toxicity profiles across treatment arms. The model was adjusted for baseline utility (centred on the mean utility in the eligible population) to account for between-patient differences in baseline utility.

Table 45. Results of the mixed-effects linear regression used in the base case analysis

Term	Value	SE	p-value
Intercept	0.7965833	0.0097350	0.0000000



EQ-5D-5L utility score at baseline (centred)	0.6799819	0.0251076	0.0000000
Progression status by treatment (SG PF vs. PD)	0.0420385	0.0068099	0.0000000
Progression Status by Treatment (TPC PF vs. PD)	0.0252201	0.0078521	0.0013305
*Adverse Event Grade 3+ (Yes vs. No)	-0.0072927	0.0101541	0.4729142

Abbreviations: EQ-5D-5L, EuroQol five-dimension five-level; PD, Progressed disease; PF, Progression-free; SE, Standard error; TPC, Treatment of physician's choice

*Currently experiencing an adverse event at the time of the questionnaire

10.3.3 Adverse events, comorbidity, and other state-specific adjustments to the utility values

Disutilities for adverse reactions were not used in the base-case analysis, as the HRQoL data from TROPiCS-02 and EVER-132-002 capture the effects of adverse reactions on HRQoL.

10.3.4 Results for utility values

Table 46. Utility values used in the health economic model

	Utility value [95% CI]	Instrument, preference weight	Source and reference
Main analysis			
Progression-free – SG*	0.831 (0.818–0.844)	EQ-5D-5L, Danish preference weights	Pooled TROPiCS-02 and EVER-132-002 (CDK4/6i pre-treated), Section 10.3.2
Progression-free – TPC*	0.815 (0.800–0.830)	EQ-5D-5L, Danish preference weights	Pooled TROPiCS-02 and EVER-132-002 (CDK4/6i pre-treated), Section 10.3.2
Progressed – All treatments**	0.797 (0.778–0.816)	EQ-5D-5L, Danish preference weights	Pooled TROPiCS-02 and EVER-132-002 (CDK4/6i pre-treated), Section 10.3.2

* The variance and resulting standard error were calculated using the model variance-covariance matrix. The the CI was calculated using the normal approximation.

** Calculated from the regression coefficient and its standard error using the normal approximation



11. Cost calculations

11.1 Drug costs

11.1.1 Drug costs for intervention and comparator

The dosages of SG and TPC are described in Sections 3.2 and 3.2.2. The dose distributions were based on the individual European patients in TROPiCS-02, as these are assumed to be most representative of Danish patients. For each treatment, the posology is used to calculate the required dose and the associated price per mg. A RDI value of 83% is assumed to reflect the Danish clinical practice, since patients are expected to be frail and receive less active substance in later lines. This assumption was validated by Danish clinical experts (Gilead, 2026a, 2026b). The 83% RDI was used to obtain a final approximate relative dose of 75% of the required dose of SG when dose delay is taken into account. The 75% relative dose is based on a previous assumption proposed by the DMC (Medicinrådet, 2022). To ensure a fair and consistent comparison within the model, the same 83% RDI value is applied to all treatments, including the comparator (TPC) and any subsequent therapies. This prevents introducing bias by applying different intensity assumptions to different treatment arms.

The weighted average based on the patient's weight (or BSA) distribution is used to calculate the cost per dose. Separately, a dose delay as mentioned above, which accounts for any interruptions in administration, is applied for each treatment.

Based on co-medication use in the TROPiCS-02 trial, immunostimulants with granulocyte colony-stimulating factor (G-CSF), filgrastim, were included in the analysis as prophylaxis for neutropenia. The recommended dose of filgrastim is 0.5 million units (μg)/kg/day (5 μg /kg/day). Daily dosing with filgrastim should continue until the neutrophil count has recovered to the normal range. Following established chemotherapy for solid tumours, the treatment duration required to fulfil these criteria is expected to be up to 14 days. Therefore, in the model, it is administered 14 times (once per day).

The same proportion of G-CSF use was applied to both arms because clinical practice typically applies G-CSF prophylaxis based on neutropenia risk rather than on the specific regimen. This conservative, evidence-based assumption avoids penalising SG and aligns the economic analysis with real-world prescribing patterns. The proportion was based on the use in the SG arm in TROPiCS-02 (35.4%).

Further, vial sharing is assumed to be 50% for SG. This is considered appropriate in this setting, as it is expected to reduce drug wastage in routine clinical practice for a costly drug. Although the eligible patient population for SG in this indication is relatively small, treatment is likely to be centralised, increasing the likelihood that patients can be scheduled and treated to enable vial sharing.



In addition, SG is already indicated and used in Denmark, meaning that vial sharing may reasonably occur under real-world conditions among different patients treated in the same clinics.

For TPC regimens, vial sharing is not assumed, as they involve a mix of treatments and routes of administration (oral and IV). This assumption was confirmed by Danish clinicians (Gilead, 2026a, 2026b).

11.1.2 Drug costs for subsequent treatment

Subsequent treatments are described in Section 3.4. The same rationale used to calculate drug costs for the intervention and comparator is applied to the subsequent treatments. The distribution of subsequent therapies per treatment arm is presented in Appendix C.

11.2 Hospital costs

11.2.1 Administration

Table 47 presents the cost used for treatment administration.

Table 47. Assumptions regarding administrative costs

Route of administration	Diagnosis and procedure codes*	DRG group	Unit cost, DKK
IV chemotherapy	DC509M (A) BWAA62 (P)	09MA98: 1 dagsgruppe, pat. mindst 7 år	1,625
Management of special oral chemotherapy for malignant disease	N/A	N/A	No cost is assumed for oral treatments

*Include other patient information if relevant for the selection of DRG group; A = action diagnosis

11.2.2 Disease management

Table 48 presents the assumptions used regarding disease management.

Table 48. Assumptions regarding costs for disease management

Activity/Pathway	Frequency	Duration	Diagnosis and procedure codes*	DRG group	Unit cost
Oncologist visit - PFS	Every 20 weeks (0.05)	Until disease progression	DC509M (A)	09MA98: 1- dagsgruppe,	1,625



Activity/Pathway	Frequency	Duration	Diagnosis and procedure codes*	DRG group	Unit cost
	per model cycle)			pat. mindst 7 år	
Oncologist visit - PD	Every 10 weeks (0.1 per model cycle)	Until death	DC509M (A)	09MA98: 1-dagsgruppe, pat. mindst 7 år	1,625
Renal function	Approximately once every month (0.2 per model cycle)	Until disease progression	N/A	N/A	Assumed to be included in cost of specialist visit

*Include other patient information if relevant to the selection of DRG group; A = action diagnosis; P = procedure. PF: Progress free, PD: progressed.

11.2.3 Treatment monitoring

No additional treatment monitoring costs were included for anything but CT scans, based on disease management assumptions – see Table 48.

Table 49. Assumptions regarding costs for treatment monitoring

Activity/Pathway	Frequency	Duration	Diagnosis and procedure codes*	DRG group	Unit cost
CT scan - PF	Once every four months (0.06 per model cycle)	Until disease progression	DC509M (A) UXCC75 (P) UXCD00 (P)	30PR06: CT-scanning, kompliceret	2,861
CT scan - PD	Once every two months (0.13 per model cycle)	Model time horizon	DC509M (A) UXCC75 (P) UXCD00 (P)	30PR06: CT-scanning, kompliceret	2,861
Full blood count	Approximately once every month (0.2 per model cycle)	Until disease progression	N/A	N/A	Assumed to be included in cost of specialist visit
Liver function	Approximately once every	Until disease progression	N/A	N/A	Assumed to be



	month (0.2 per model cycle)				included in cost of specialist visit
Renal function	Approximately once every month (0.2 per model cycle)	Until disease progression	N/A	N/A	Assumed to be included in cost of specialist visit

*Include other patient information if relevant to the selection of DRG group; A = action diagnosis; P = procedure.

11.2.4 Management of adverse events

AEs' costs have been accounted for only for those at or above grade 3 and only if the difference between intervention and comparator was $\geq 3\%$. The assumptions concerning AEs are shown in Table 50. AEs costs are included as a one-off cost at the beginning of the treatment cycle.

Table 50. Assumptions regarding costs for management of adverse events

Adverse event	Proportion		Diagnosis codes*	DRG group	Unit cost
	SG	TPC			
Outpatient visit due to anaemia	11.5%	4.36%	DD649 (A) and DC509M (B), duration < 12 hours (short)	16MA98 1-dagsgruppe, pat. mindst 7 år	2,195
Outpatient visit due to asthenia/fatigue	6.47%	2.91%	DT983D5 (A) and DC509M (B), duration < 12 hours (short)	21MA98 1-dagsgruppe, pat. mindst 7 år	1,975
Outpatient visit due to diarrhoea	8.78%	0.73%	DK529B1 (A) and DC509M (B), duration < 12 hours (short)	06MA98 1-dagsgruppe, pat. mindst 7 år	1,729
Outpatient visit due to leukopenia	21.25%	18.16%	DD728H (A) and DC509M (B), duration < 12 hours (short)	16MA98 1-dagsgruppe, pat. mindst 7 år	2,195



Adverse event	Proportion		Diagnosis codes*	DRG group	Unit cost
	SG	TPC			
Admission due to neutropenia /low neutrophil count	58.66%	47.94%	DD709A (A) and DC509M (B), duration < 12 hours (short)	16MA03 Granulog trombocytopeni	2,195
Admission due to febrile neutropenia	5.77%	4.36%	DT888N (A) and DC509M (B), duration ≥ 12 hours (long)	16MA03 Granulog trombocytopeni	40,195
Outpatient visit due to hypokalaemia	5.08%	1.45%	DD976 (A) and DC509M (B), duration < 12 hours (short)	10MA06 1-dagsgruppe, pat. mindst 7 år	2,150
Outpatient visit due to thrombocytopenia	1.85%	4.12%	DD696 (A) and DC509M (B), duration < 12 hours (short)	16MA98 1-dagsgruppe, pat. mindst 7 år	2,195
Outpatient visit due to lymphopenia	4.62%	3.15%	DD728D (A) and DC509M (B), duration < 12 hours (short)	16MA98 1-dagsgruppe, pat. mindst 7 år	2,195

*Include relevant procedure codes and other patient information if relevant for the selection of DRG group; A = action diagnosis; B = secondary diagnosis.

11.2.5 Other hospital costs

N/A

11.3 Patient costs

Patient and travel time were calculated for the oncologist visits and CT-scans. The non-medical costs were applied based on the time spent on disease management and scans. Doctor visits and CT-scans were assumed to take 60 and 30 minutes, respectively.

In both the progression-free and the progressed health state, 100% of patients were assumed to incur non-medical costs.

Further, patient and travel time associated with IV administration was accounted for in the intervention and comparator arms, as per the respective summary of product characteristics (SmPCs). The unit cost for patient time (200 DKK) and the travel cost (150 DKK) were both sourced from the recommended DMC sources (Medicinrådet, 2026a).



For transport cost, in addition to the travel cost, 90 minutes of patient time are also charged (Medicinrådet, 2026a). Transport costs are charged each time patients require IV administration. The costs and assumptions used in the model are described in Table 51.

Table 51. Assumptions regarding patient time

Activity	Frequency of activity	Time spent on activity	Transport time	Note
Intravenous administration of SG	Twice in a three-week cycle	1.14 hours	1.5 hour	Transport time is accounted for as the travel cost of 150 DKK, with an additional 300 DKK for patient time
Intravenous administration of TPC - Eribulin	Twice in a three-week cycle	0.083 hours	1.5 hour	Transport time is accounted for as the travel cost of 150 DKK, with an additional 300 DKK for patient time
Intravenous administration of TPC - Gemcitabine	Thrice in a three-week cycle	0.5 hours	1.5 hour	Transport time is accounted for as the travel cost of 150 DKK, with an additional 300 DKK for patient time
Visit to the oncologist	Once every 10 weeks for the PD patients; Once every 20 weeks for the PFS patients	1 hour	1.5 hour	Transport time is accounted for as the travel cost of 150 DKK, with an additional 300 DKK for patient time
CT scan	Once every 2 months when PF,	0.5	1.5 hour	Transport time is accounted for



Activity	Frequency of activity	Time spent on activity	Transport time	Note
	once every 4 months when PD.			as the travel cost of 150 DKK, with an additional 300 DKK for patient time

11.4 Other costs

N/A

12. Results

Table 52 shows the results of the base-case analysis of SG compared with TPC. Treatment with SG is associated with an incremental cost of 330,984 DKK, driven by the drug cost, and incremental QALYs of 0.35. The ICER is DKK 951,460 per QALY.

Table 52. Results, discounted estimates, half-cycle corrected (where relevant) and adjusted for background mortality

	SG	TPC	Difference
Drug costs	326,122 kr	34,360 kr	291,762 kr
Drug costs for subsequent treatment	23,567 kr	26,910 kr	-3,342 kr
Administration	26,946 kr	11,017 kr	15,929 kr
Disease management	13,229 kr	10,840 kr	2,390 kr
Treatment monitoring	26,783 kr	21,945 kr	4,838 kr
Management of adverse events	4,857 kr	3,560 kr	1,297 kr
Patient costs	26,607 kr	13,463 kr	13,144 kr
Other costs, e.g., co-medication	11,772 kr	6,804 kr	4,967 kr
Total costs	459,883 kr	128,899 kr	330,984 kr
Life years in PFS	0.703	0.434	0.269
Life years in PD	1.209	1.062	0.147



	SG	TPC	Difference
Total life years	1.912	1.495	0.416
QALYs in PFS	0.584	0.353	0.231
QALYs in PD	0.962	0.845	0.117
QALY loss in AEs	0.000	0.000	0.000
Total QALYs	1.546	1.198	0.348
Incremental costs per life year gained			794,925 kr
Incremental costs per QALY gained (ICER)			951,460 kr

Table 53. Results per drug if combination treatments (more than one drug) N/A

Drug costs

12.1 Sensitivity analyses

One-way sensitivity analysis (OWSA) and probabilistic sensitivity analysis (PSA) were performed. The OWSA presents relevant cases with their associated incremental costs and QALYs, while the PSA simultaneously varies multiple inputs to assess parametric uncertainty.

12.1.1 Deterministic sensitivity analyses

Various OWSA analyses were conducted to assess the impact of deviations from the base case. The results are shown in Table 54.

Table 54. Results of deterministic sensitivity analyses

Deterministic sensitivity analysis	Incremental costs (DKK)	Incremental QALYs	ICER
Mean age - Increased to 65 years old	330,958	0.346	957,241
Mean weight - increased to 70 kg	339,210	0.348	975,107
Discount - Cost: 0%, Benefits: 0%	334,982	0.396	845,475

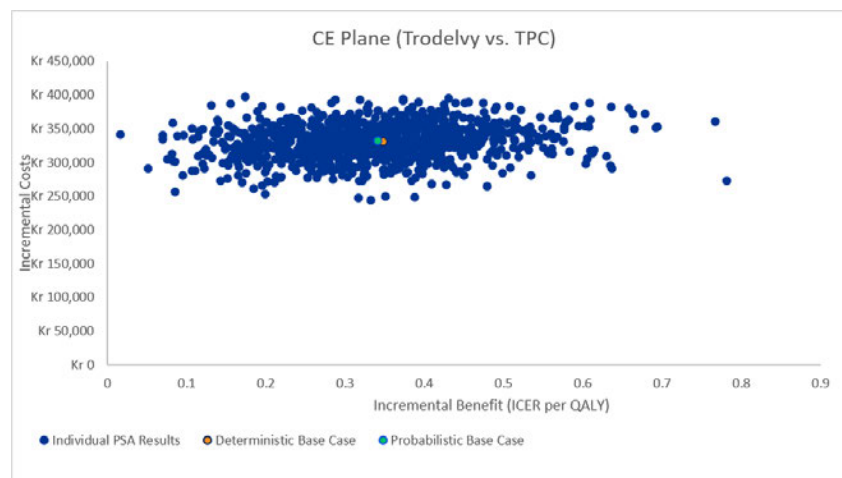


Discount - Cost: 5%, Benefits: 5%	329,517	0.332	992,423
Extrapolation OS: SG: Gamma, TPC: Gamma	326,638	0.255	1,281,643
Utilities - Not treatment specific, with AEs disutilities included	330,984	0.340	974,881

12.1.2 Probabilistic sensitivity analyses (PSA)

The PSA was performed following the DMC guidelines (Medicinerådet, 2026b). A Monte Carlo simulation with 1,000 runs was conducted to assess the impact of parameter uncertainty. The average probabilistic ICER was Kr 971,535, which is very close to the deterministic result. In Figure 28, Figure 29 and Figure 30, the scatter plot and cost effectiveness plane, the cost effectiveness acceptability curve, and the convergence plot are shown. In the scatter plot, all simulations cluster in the north-east quadrant except for one case. All results suggest that SG will generate higher incremental cost and incremental QALY gains compared to treatment with TPC.

Figure 28 Scatter plot – cost-effectiveness plane of SG vs TPC



Note: Since the deterministic result is very close to the probabilistic case, the two points overlap slightly in the graphical representation of the cost-effectiveness plane.



Figure 29 Cost-effectiveness acceptability curve

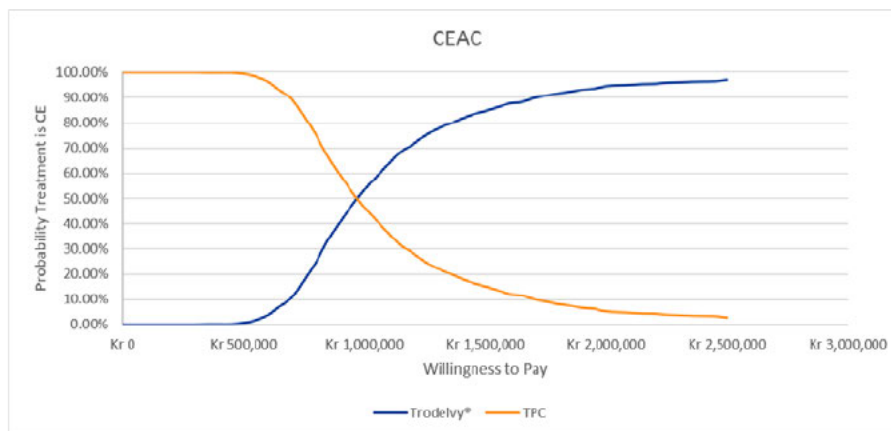
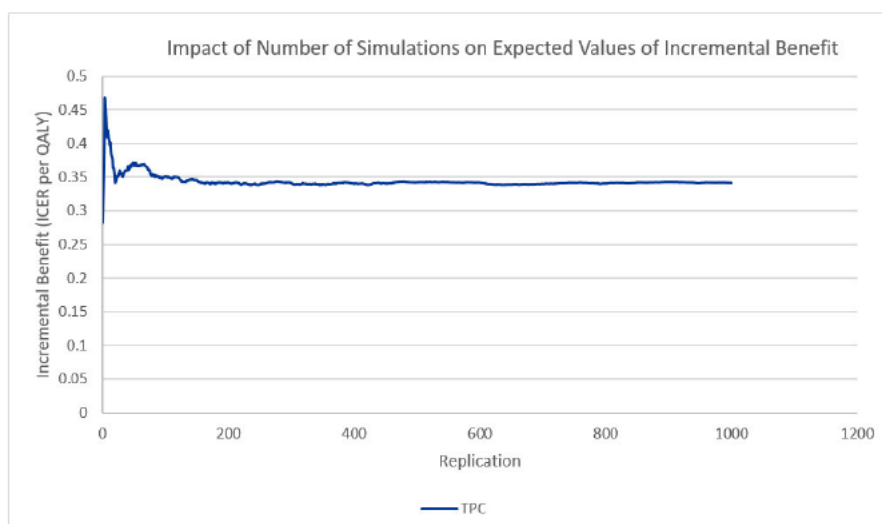


Figure 30 Convergence plot



13. Budget impact analysis

The budget impact of the introduction of SG is shown in Table 55, as prescribed with DMC guidelines. The calculations are based on the expected number of patients and patient uptake described in Section 3.1.2. Results are shown in millions of DKK.

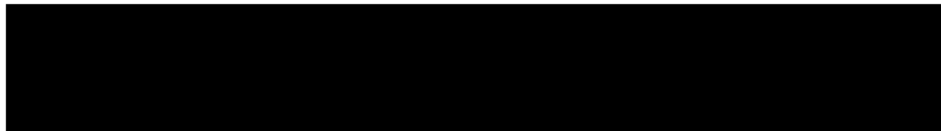
Table 55. Budget impact (non-discounted estimates), DKK 1m

	Year 1	Year 2	Year 3	Year 4	Year 5
Regional costs of recommendation					
Drug costs	2.4	4.6	4.9	4.9	4.9
Other regional hospital costs	1.0	1.3	1.4	1.5	1.5



	Year 1	Year 2	Year 3	Year 4	Year 5
Total by recommendation	3.4	5.9	6.3	6.4	6.5
Regional costs of non-recommendation					
Drug costs	0.5	0.5	0.5	0.5	0.5
Other regional hospital costs	0.9	1.1	1.1	1.2	1.2
Total for non-recommendation	1.4	1.6	1.6	1.7	1.7
Total budget impact	2.0	4.3	4.7	4.7	4.8

14. List of experts





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Appendix A. Study characteristics

Table 56. Main characteristics of included studies

TROPiCS-02		NCT number: 03901339
Purpose	The primary objective of the study was to assess and compare the efficacy and safety of SG versus treatment of physician's choice (TPC) in participants with hormonal receptor-positive (HR+) human epidermal growth factor receptor 2 (HER2-) negative metastatic breast cancer (MBC).	
Publications – title, author, journal, year	Overall survival with sacituzumab govitecan in hormone receptor-positive and human epidermal growth factor receptor 2-negative metastatic breast cancer (TROPiCS-02): a randomised, open-label, multicentre, phase 3 trial, Hugo et al., The Lancet, 2023.	
Study type and design	Open-label, multicentre, randomised, phase 3 trial, Patients were randomly assigned 1:1 to receive SG or chemotherapy.	
Number of trial participants (N)	543	
Primary inclusion criteria	• Documented evidence of HER2-negative/HR-positive mBC • Refractory of at least 2, but no more than 4, prior systemic chemotherapy regimens • Eligible for at least one of the TPC chemotherapy options • Documented disease progression after most recent therapy	
Primary exclusion criteria	• Previous treatment with topoisomerase 1 Inhibitors • History of significant cardiovascular disease or ECG abnormality • Medically unfit to receive SG	
Intervention	Patients (272) received 10 mg/kg via intravenous (IV) injection administered on Day 1 and Day 8 of a 21-day cycle.	
Comparator(s)	Patients (271) received treatment of physician's choice, which included Eribulin: 1.4 mg/m² for North American sites, 1.23 mg/m² for European sites) via IV on Days 1 and 8 of a 21-day cycle Capecitabine: 1000-1250 mg/m² orally twice daily for 2 weeks followed by a 1-week rest period given as a 21-day cycle Gemcitabine: 800-1200 mg/m² via IV on Days 1, 8, and 15 of each 28-day cycle or per institution Vinorelbine: 25 mg/m² via IV on Day 1 weekly cycle per institution	



TROPiCS-02		NCT number: 03901339
Follow-up time	The median survival follow-up durations of 14.39 and 10.97 months for the SG and TPC groups, respectively.	
Is the study used in the health economic model?	Yes	
Primary, secondary and exploratory endpoints	Outcomes included in this application: The primary endpoint was progression-free survival (PFS) by blinded independent central review (BICR) assessment using response evaluation criteria in solid tumours version 1.1 (RECIST 1.1). Secondary endpoint was overall survival (OS), defined as time from randomisation to the date of death. OS was estimated using Kaplan Meier estimate. Health-related quality of life (HRQoL) was measured by EORTC QLQ-C30.	
Analysis method	Efficacy analyses were conducted based on the Intent-to-Treat (ITT) Population, which was defined as all participants who were randomised, regardless of whether they received study treatment or not. PFS and OS were derived from Kaplan-Meier estimates. The primary analyses of PFS and OS for comparison between the SG and TPC groups were performed using a stratified log-rank test with stratification factors. The estimates of the hazard ratio (HR) and its 95% CI were based on a stratified Cox proportional-hazards model.	
Subgroup analyses	N/A	
Other relevant information	N/A	

Table 57 Main characteristics of included studies

EVER-132-002		NCT number: 03901339
Purpose	The purpose of the study was to compare the study drug, SG, versus doctors' treatment of choice in participants with HR+/HER2- metastatic breast cancer (MBC) who have failed at least 2 prior chemotherapy regimens.	
Publications – title, author, journal, year	Sacituzumab govitecan in HR+ HER2– metastatic breast cancer: the randomized phase 3 EVER-132-002 trial, Xu et al., Nature Medicine, 2024	



Study type and design	Open-label, multicentre, randomised, phase 3 trial, Patients were randomly assigned 1:1 to receive SG or chemotherapy.
Number of trial participants (N)	331
Primary inclusion criteria	• Documented evidence of HER2-negative/HR-positive mBC • Refractory of at least 2, but no more than 4, prior systemic chemotherapy regimens • Eligible for at least one of the TPC chemotherapy options • Documented disease progression after most recent therapy
Primary exclusion criteria	• Previous treatment with topoisomerase 1 Inhibitors • Known brain metastases • Medically unfit to receive either study treatment
Intervention	Patients (166) received 10 mg/kg via intravenous (IV) injection administered on Day 1 and Day 8 of a 21-day cycle.
Comparator(s)	Patients (165) received treatment of physician's choice, which included Eribulin: 1.4 mg/m² or 1.23 mg/m² via IV on Days 1 and 8 of a 21-day cycle Capecitabine (1000 to 1250 mg/m² twice daily on Days 1 to 14 of a 21-day cycle) Gemcitabine: 800-1200 mg/m² via IV on Days 1, 8, and 15 of each 28-day cycle Vinorelbine: 25 mg/m² via IV on Day 1 weekly
Follow-up time	The median follow-up duration in the ITT Population was 17.0 months (range: 0.1-45.7). The median survival follow-up durations were 18.6 and 15.1 months for the SG and TPC groups, respectively.
Is the study used in the health economic model?	Yes
Primary, secondary and exploratory endpoints	Outcomes included in this application: The primary endpoint was progression-free survival (PFS), disease progression was determined according to response evaluation criteria in solid tumours version 1.1 (RECIST 1.1) by independent reviewing committee (IRC). Secondary endpoint was overall survival (OS), defined as time from randomisation to the date of death. OS was estimated using Kaplan Meier estimate. Health-related quality of life (HRQoL) was measured by EORTC QLQ-C30.
Analysis method	Efficacy analyses were conducted based on the Intent-to-Treat (ITT) Population, which was defined as all participants who were

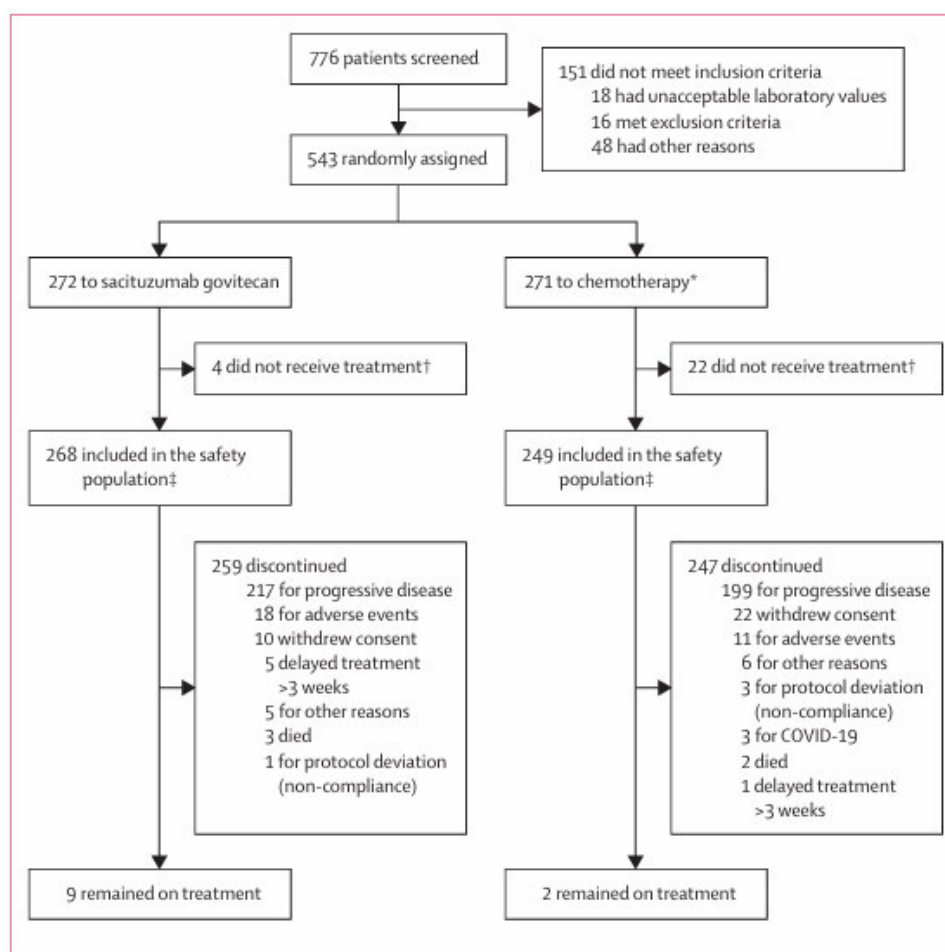


randomised, regardless of whether they received study treatment or not. PFS and OS were derived from Kaplan-Meier estimates. The primary analyses of PFS and OS for comparison between the SG and TPC groups were performed using a stratified log-rank test with stratification factors. The estimates of the hazard ratio (HR) and its 95% CI were based on a stratified Cox proportional-hazards model.

Subgroup analyses N/A

Other relevant information N/A

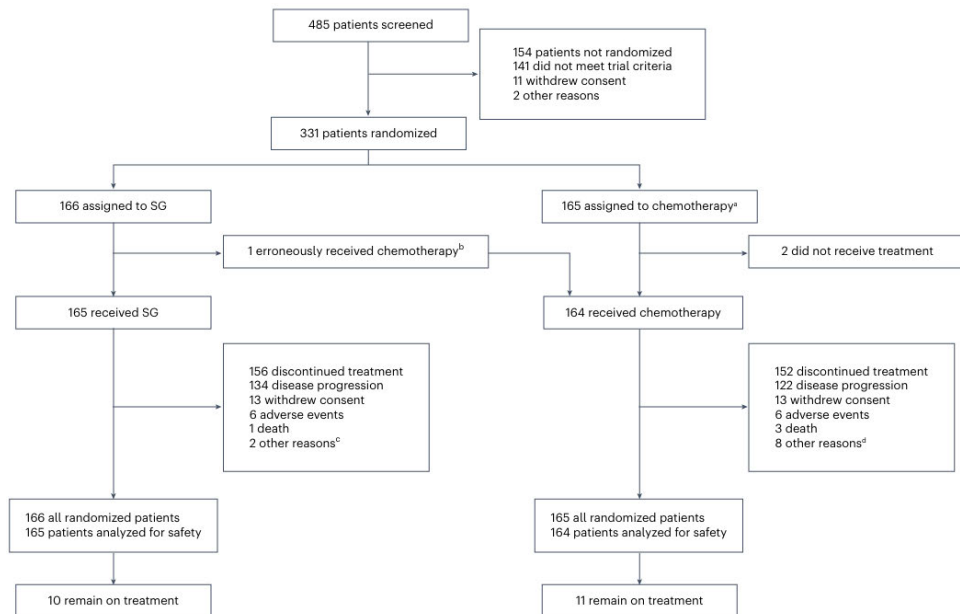
Figure 31 Patient flow TROPiCS-02



Source: (Rugo et al., 2023)



Figure 32 Patient flow EVER-132-002



Source: (Xu et al., 2024)



Appendix B. Results regarding effectiveness per study

Table 58. Results per study

Results of TROPiCS-02 (NCT03901339)										
				Estimated absolute difference in effect			Estimated relative difference in effect			Analysis methods
Outcome	Study arm	N	Result (CI)	Difference	95% CI	P- value	Difference	95% CI	P- value	References
Median progression-free survival (time point)	SG	272	5.5 months (95% CI: 4.2, 6.9)	1.5 months			HR: 0.65	0.53, 0.81	0.0001	Median PFS was from KM estimate. The CI for the median was computed using the Brookmeyer-Crowley method. Stratified log-rank test and stratified Cox regression adjusted for stratification factors: prior chemotherapy regimens for treatment of metastatic disease, visceral metastasis, and endocrine therapy in the metastatic setting for at least 6 months.
	TPC	271	4.0 months (95% CI: 3.0, 4.4)							



Results of TROPiCS-02 (NCT03901339)										
			Estimated absolute difference in effect			Estimated relative difference in effect			Analysis methods	References
Outcome	Study arm	N	Result (CI)	Difference	95% CI	P- value	Difference	95% CI	P- value	
Median overall survival (time point)	SG	272	14.5 months (95% CI: 13.0, 16.0)	3.3 months			HR: 0.79	0.65, 0.95	0.0133	Median OS was from KM estimate. The CI for the median was computed using the Brookmeyer-Crowley method. Stratified log-rank test and stratified Cox regression adjusted for stratification factors: prior chemotherapy regimens for treatment of metastatic disease, visceral metastasis, and endocrine therapy in the metastatic setting for at least 6 months.
	TPC	271	11.2 months (95% CI 10.2, 12.6)							
Objective response rate (ORR)	SG	272	21% (16.3%, 26.3%)	7%			Odds ratio: 1.66	1.06, 2.61	0.027	ORR was analysed and compared between treatment groups using the Cochran Mantel-Haenszel method stratified by the factors used in randomisation. Two-sided 95% CIs were
	TPC	271	14% (10.1%, 18.7%)							



Results of TROPiCS-02 (NCT03901339)										
				Estimated absolute difference in effect			Estimated relative difference in effect			Analysis methods
Outcome	Study arm	N	Result (CI)	Difference	95% CI	P- value	Difference	95% CI	P- value	References
Clinical Benefit Rate (CBR)	SG	272	34% (28.2%, 39.8%)	12%			Odds ratio: 1.80	1.23, 2.63	0.0025	calculated using the Clopper-Pearson exact method.
	TPC	271	22% (17.3%, 27.6%)							CBR was defined as the proportion of participants who had a best confirmed response of CR, PR, or durable SD with duration of ≥ 6 months. CBR was analysed and compared between treatment groups using the Cochran Mantel-Haenszel method stratified by the factors used in randomisation. Two-sided 95% CIs were calculated using the Clopper-Pearson exact method.



Results of TROPiCS-02 (NCT03901339)										
				Estimated absolute difference in effect			Estimated relative difference in effect			Analysis methods
Outcome	Study arm	N	Result (CI)	Difference	95% CI	P- value	Difference	95% CI	P- value	References
Median Duration of Response (DOR)	SG	272	8.1 (6.7, 8.9) months	2.5 months			N/A	N/A	N/A	Median DOR was from KM estimate. The CI for the median was computed using the Brookmeyer-Crowley method. Analyses of DOR were conducted for participants who experienced a best overall response of CR or PR per BICR. Duration of response was defined as the number of months from the date of initial response to the date of the event defined as the first documented progression per RECIST v1.1 or death due to any cause, whichever occurred earlier.
	TPC	271	5.6 s (3.8, 7.9) month							



Results of EVER-132-002 (NCT04639986)										
Outcome	Study arm	N	Result (CI)	Estimated absolute difference in effect			Estimated relative difference in effect			Analysis methods
				Difference	95% CI	P- value	Difference	95% CI	P- value	
Median progression-free survival, overall patient population (Apr2023)	SG	166	4.3 months (95% CI: 4.1, 5.7)	0.1 months			HR: 0.671	0.517, 0.870	0.0028	Median survival is based on the Kaplan-Meier estimator. HR is based on a Cox proportional hazards model adjusting for the variables used for stratification for randomization and study arm.
	TPC	165	4.2 months (95% CI: 2.8, 4.2)							
Median progression-free survival, prior CDK4/6 inhibitor patient population (Apr2023)	SG	81	4.1 months (95% CI: 2.9, 5.6)	1.3 months			HR: 0.56	0.39, 0.81		Median survival is based on the Kaplan-Meier estimator. HR is based on a Cox proportional hazards model adjusting for the variables used for stratification for randomization and study arm.
	TPC	80	2.8 months (95% CI: 1.5, 4.1)							



Results of EVER-132-002 (NCT04639986)

Outcome	Study arm	N	Result (CI)	Estimated absolute difference in effect			Estimated relative difference in effect			Analysis methods	References
				Difference	95% CI	P- value	Difference	95% CI	P- value		
Median overall survival, overall patient population (Dec2024)	SG	166	████ months (95% CI: █████)				HR: █████	████	████	Survival rates are based on the Kaplan-Meier estimator. HR is based on a Cox proportional hazards model adjusting for stratification and study arm.	
	TPC	165	████ months (95% CI: █████)								
Median overall survival, prior CDK4/6 inhibitor patient population (Dec2024)	SG	81	████ months (95% CI: █████)				HR: █████	████		Survival rates are based on the Kaplan-Meier estimator. HR is based on a Cox proportional hazards model adjusting for stratification and study arm.	
	TPC	80	████ months (95% CI: █████)								



Appendix C. Subsequent treatment

Table 59 shows the distribution of subsequent treatments used in the model based on Dahl et al (Dahl et al., 2025) patients and the available treatment in TROPiCS-02, while Table 60 shows the distribution calculated from the original study. Treatments from the RWE study which were not available in TROPiCS-02, or not relevant for the indication (Dahl et al., 2025; Gilead, 2026a, 2026b, 2026c), such as ET or unspecified treatments, were excluded from the model, and their share was evenly distributed among the available treatments. Further, the shares redistributed from Dahl account for patients who progressed but received no further systemic treatment. The subsequent treatment received in the model is assumed not to be mutually exclusive; patients may have received multiple treatment lines.

Table 59 Subsequent treatment distribution - Model

Treatment arm	Capecitabine	Carboplatin	Cyclophosphamide	Doxorubicin	Eribulin	Gemcitabine	Paclitaxel	Vinorelbine
SG	13.57%	3.94%	3.94%	12.97%	21.67%	5.87%	16.67%	13.77%
TPC	13.57%	3.94%	3.94%	12.97%	21.67%	5.87%	16.67%	13.77%

Table 60. Subsequent treatments in Dahl et al – 5th line

ET	Capecitabine	Taxane*	Eribulin	Vinorelbine	Anthracycline*	Gemcitabine	Other chemotherapies*	Other	No treatment
23.00%	8.90%	12.00%	17.00%	9.10%	8.30%	1.20%	3.20%	9.70%	7.10%

Notes: * Taxane was assumed to be paclitaxel, anthracycline was assumed to be doxorubicin and the other chemotherapies were split equally between carboplatin and cyclophosphamide. Other treatments, no treatment, and ET were distributed equally across the rest of the available treatments found in TROPiCS-02.



Table 61 Subsequent treatments TROPICS-02

Drug name	SG (N=268)	TPC (N=249)	Total (N=517)
At least one subsequent anti-cancer therapy	190 (70.9%)	153 (61.4%)	343 (66.3%)
Eribulin	76 (28.4%)	23 (9.2%)	99 (19.1%)
Gemcitabine	55 (20.5%)	36 (14.5%)	91 (17.6%)
Carboplatin	40 (14.9%)	40 (16.1%)	80 (15.5%)
Cyclophosphamide	33 (12.3%)	40 (16.1%)	73 (14.1%)
Paclitaxel	24 (9.0%)	25 (10.0%)	49 (9.5%)
Vinorelbine	29 (10.8%)	20 (8.0%)	49 (9.5%)
Fulvestrant	20 (7.5%)	19 (7.6%)	39 (7.5%)
Capecitabine	22 (8.2%)	15 (6.0%)	37 (7.2%)
Pegylated liposomal doxorubicin hydrochloride	20 (7.5%)	17 (6.8%)	37 (7.2%)
Vinorelbine tartrate	11 (4.1%)	26 (10.4%)	37 (7.2%)
Doxorubicin	16 (6.0%)	18 (7.2%)	34 (6.6%)
Everolimus	12 (4.5%)	19 (7.6%)	31 (6.0%)
Fluorouracil	14 (5.2%)	17 (6.8%)	31 (6.0%)
Exemestane	10 (3.7%)	16 (6.4%)	26 (5.0%)
Liposomal doxorubicin	12 (4.5%)	14 (5.6%)	26 (5.0%)
Methotrexate	11 (4.1%)	12 (4.8%)	23 (4.4%)
Alpelisib	12 (4.5%)	9 (3.6%)	21 (4.1%)
Epirubicin	5 (1.9%)	14 (5.6%)	19 (3.7%)
Abemaciclib	9 (3.4%)	9 (3.6%)	18 (3.5%)
Etoposide	4 (1.5%)	12 (4.8%)	16 (3.1%)
Sacituzumab govitecan	1 (0.4%)	15 (6.0%)	16 (3.1%)
Docetaxel	7 (2.6%)	8 (3.2%)	15 (2.9%)
Pembrolizumab	8 (3.0%)	7 (2.8%)	15 (2.9%)
Trastuzumab deruxtecan	4 (1.5%)	11 (4.4%)	15 (2.9%)
Gemcitabine hydrochloride	7 (2.6%)	7 (2.8%)	14 (2.7%)



Paclitaxel nanoparticle albumin-bound	6 (2.2%)	4 (1.6%)	10 (1.9%)
Eribulin mesilate	7 (2.6%)	2 (0.8%)	2 (0.8%)
Letrozole	5 (1.9%)	4 (1.6%)	9 (1.7%)
Tamoxifen	5 (1.9%)	3 (1.2%)	8 (1.5%)
Doxorubicin hydrochloride	5 (1.9%)	2 (0.8%)	7 (1.4%)
Investigational drug	5 (1.9%)	2 (0.8%)	7 (1.4%)
Olaparib	4 (1.5%)	3 (1.2%)	7 (1.4%)
Radiotherapy	6 (2.2%)	1 (0.4%)	7 (1.4%)
Ixabepilone	2 (0.7%)	4 (1.6%)	6 (1.2%)
Vincristine	5 (1.9%)	1 (0.4%)	6 (1.2%)
Anastrozole	5 (1.9%)	0	5 (1.0%)
Mitomycin	1 (0.4%)	4 (1.6%)	5 (1.0%)
Other therapeutic products	2 (0.7%)	3 (1.2%)	5 (1.0%)
Trastuzumab	0	5 (2.0%)	5 (1.0%)
Irinotecan	1 (0.4%)	3 (1.2%)	4 (0.8%)
Balixafortide	1 (0.4%)	2 (0.8%)	3 (0.6%)
Liposomal doxorubicin hydrochloride	1 (0.4%)	2 (0.8%)	3 (0.6%)
Neratinib	0	3 (1.2%)	3 (0.6%)
Talimogene laherparepvec	1 (0.4%)	2 (0.8%)	3 (0.6%)
Bevacizumab	1 (0.4%)	1 (0.4%)	2 (0.4%)
Cisplatin	1 (0.4%)	1 (0.4%)	2 (0.4%)
Folinic acid	0	2 (0.8%)	2 (0.4%)
Inavolisib	1 (0.4%)	1 (0.4%)	2 (0.4%)
Orin 1001	2 (0.7%)	0	2 (0.4%)
Pertuzumab	0	2 (0.8%)	2 (0.4%)
Ribociclib	1 (0.4%)	1 (0.4%)	2 (0.4%)
Sacituzumab govitecan hziy	0	2 (0.8%)	2 (0.4%)
Trastuzumab deruxtecan nxki	2 (0.7%)	0	2 (0.4%)
Trastuzumab emtansine	0	2 (0.8%)	2 (0.4%)
9 ing 41	0	1 (0.4%)	1 (0.2%)
Abbv 155	0	1 (0.4%)	1 (0.2%)
Antineoplastic agents	1 (0.4%)	0	1 (0.2%)



Atezolizumab	0	1 (0.4%)	1 (0.2%)
Denosumab	1 (0.4%)	0	1 (0.2%)
Dexamethasone	0	1 (0.4%)	1 (0.2%)
Df 1001	1 (0.4%)	0	1 (0.2%)
Enzalutamide	1 (0.4%)	0	1 (0.2%)
Ferumoxytol	0	1 (0.4%)	1 (0.2%)
Gedatolisib	0	1 (0.4%)	1 (0.2%)
Gemcitabine;vinorelbine	0	1 (0.4%)	1 (0.2%)
Idarubicin	1 (0.4%)	0	1 (0.2%)
Investigational antineoplastic drugs	1 (0.4%)	0	1 (0.2%)
Megestrol	0	1 (0.4%)	1 (0.2%)
Megestrol acetate	1 (0.4%)	0	1 (0.2%)
Methotrexate sodium	1 (0.4%)	0	1 (0.2%)
Mgd 013	1 (0.4%)	0	1 (0.2%)
Milademetan	0	1 (0.4%)	1 (0.2%)
Neratinib maleate	0	1 (0.4%)	1 (0.2%)
Niraparib	1 (0.4%)	0	1 (0.2%)
Nivolumab	0	1 (0.4%)	1 (0.2%)
Other protein kinase inhibitors	0	1 (0.4%)	1 (0.2%)
Oxandrolone	0	1 (0.4%)	1 (0.2%)
Palbociclib	0	1 (0.4%)	1 (0.2%)
Pazopanib	0	1 (0.4%)	1 (0.2%)
Pegylated liposomal doxorubicin	1 (0.4%)	0	1 (0.2%)
Pen 866	1 (0.4%)	0	1 (0.2%)
Spartalizumab	1 (0.4%)	0	1 (0.2%)
Taxanes	0	1 (0.4%)	1 (0.2%)
Trabectedin	0	1 (0.4%)	1 (0.2%)
Trastuzumab anns	0	1 (0.4%)	1 (0.2%)
Vaccines	0	1 (0.4%)	1 (0.2%)
Vinblastine	0	1 (0.4%)	1 (0.2%)
Vincristine sulfate	0	1 (0.4%)	1 (0.2%)
Zoledronic acid	1 (0.4%)	0	1 (0.2%)



Zotatifin	0	1 (0.4%)	1 (0.2%)
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Table 62 Subsequent treatments EVER-132-002

Drug Name	SG (N=165)	TPC (N=164)	Total (N=329)
At least one subsequent anti-cancer therapy	137 (83.0)	137 (83.5%)	274 (83.3%)
Abemaciclib	31 (18.8%)	42 (25.6%)	73 (22.2%)
Eribulin	30 (18.2%)	7 (4.3%)	37 (11.2%)
Eribulin mesilate	32 (19.4%)	4 (2.4%)	36 (10.9%)
Fulvestrant	32 (19.4%)	39 (23.8%)	71 (21.6%)
Gemcitabine	18 (10.9%)	23 (14.0%)	41 (12.5%)
Gemcitabine hydrochloride	20 (12.1%)	21 (12.8%)	41 (12.5%)
Exemestane	24 (14.5%)	25 (15.2%)	49 (14.9%)
Cisplatin	22 (13.3%)	27 (16.5%)	49 (14.9%)
Bevacizumab	27 (16.4%)	22 (13.4%)	49 (14.9%)
Capecitabine	27 (16.4%)	23 (14.0%)	50 (15.2%)
Doxorubicin	4 (2.4%)	12 (7.3%)	16 (4.9%)
Dalpiciclib isethionate	13 (7.9%)	4 (2.4%)	17 (5.2%)
Trastuzumab deruxtecan	13 (7.9%)	12 (7.3%)	25 (7.6%)
Catequentinib hydrochloride	14 (8.5%)	11 (6.7%)	25 (7.6%)
Vinorelbine tartrate	15 (9.1%)	23 (14.0%)	38 (11.6%)
Vinorelbine	13 (7.9%)	13 (7.9%)	26 (7.9%)
Everolimus	10 (6.1%)	16 (9.8%)	26 (7.9%)
Paclitaxel nanoparticle albumin-bound	15 (9.1%)	11 (6.7%)	26 (7.9%)
Paclitaxel	11 (6.7%)	17 (10.4%)	28 (8.5%)
Letrozole	10 (6.1%)	13 (7.9%)	23 (7.0%)
Carboplatin	23 (13.9%)	10 (6.1%)	33 (10.0%)
Disitamab vedotin	11 (6.7%)	9 (5.5%)	20 (6.1%)
Palbociclib	5 (3.0%)	9 (5.5%)	14 (4.3%)



Anastrozole	5 (3.0%)	4 (2.4%)	9 (2.7%)
Docetaxel	4 (2.4%)	5 (3.0%)	9 (2.7%)
Lobaplatin	6 (3.6%)	3 (1.8%)	9 (2.7%)
Ribociclib	3 (1.8%)	4 (2.4%)	7 (2.1%)
Liposomal doxorubicin hydrochloride	5 (3.0%)	2 (1.2%)	7 (2.1%)
Goserelin acetate	6 (3.6%)	6 (3.7%)	12 (3.6%)
Etoposide	6 (3.6%)	6 (3.7%)	12 (3.6%)
Catequentinib	5 (3.0%)	5 (3.0%)	10 (3.0%)
Dalpiciclib	2 (1.2%)	4 (2.4%)	6 (1.8%)
Toremifene	2 (1.2%)	4 (2.4%)	6 (1.8%)
Toremifene citrate	2 (1.2%)	4 (2.4%)	6 (1.8%)
Chidamide	6 (3.6%)	0	6 (1.8%)
Camrelizumab	4 (2.4%)	2 (1.2%)	6 (1.8%)
Leuprorelin acetate	3 (1.8%)	4 (2.4%)	7 (2.1%)
Liposomal doxorubicin	3 (1.8%)	3 (1.8%)	6 (1.8%)
Albumin human;paclitaxel	2 (1.2%)	5 (3.0%)	7 (2.1%)
Tislelizumab	2 (1.2%)	3 (1.8%)	5 (1.5%)
Investigational drug (targeted therapy)	3 (1.8%)	1 (0.6%)	4 (1.2%)
Bb 1701	3 (1.8%)	1 (0.6%)	4 (1.2%)
Mrg 002	3 (1.8%)	1 (0.6%)	4 (1.2%)
Shr a1811	0	4 (2.4%)	4 (1.2%)
Megestrol acetate	0	4 (2.4%)	4 (1.2%)
Investigational drug (cdk4/6)	2 (1.2%)	2 (1.2%)	4 (1.2%)
Toripalimab	3 (1.8%)	1 (0.6%)	4 (1.2%)
Goserelin	2 (1.2%)	2 (1.2%)	4 (1.2%)
Epirubicin hydrochloride	2 (1.2%)	2 (1.2%)	4 (1.2%)
Epirubicin	1 (0.6%)	2 (1.2%)	3 (0.9%)
Doxorubicin hydrochloride	1 (0.6%)	2 (1.2%)	3 (0.9%)
Tamoxifen	3 (1.8%)	0	3 (0.9%)



Tamoxifen citrate	1 (0.6%)	2 (1.2%)	3 (0.9%)
Medroxyprogesterone acetate	2 (1.2%)	1 (0.6%)	3 (0.9%)
Leuporelin	1 (0.6%)	2 (1.2%)	3 (0.9%)
Investigational drug (hormonal therapy)	2 (1.2%)	1 (0.6%)	3 (0.9%)
Cyclophosphamide;panax ginseng total ginsenoside extract	2 (1.2%)	1 (0.6%)	3 (0.9%)
Tegafur;uracil	1 (0.6%)	2 (1.2%)	3 (0.9%)
Rivoceranib mesylate	2 (1.2%)	1 (0.6%)	3 (0.9%)
Investigational drug (adc)	1 (0.6%)	1 (0.6%)	2 (0.6%)
Sacituzumab govitecan	0	2 (1.2%)	2 (0.6%)
Pf 07220060	2 (1.2%)	0	2 (0.6%)
Ribociclib succinate	0	2 (1.2%)	2 (0.6%)
Investigational drug (immunotherapy)	2 (1.2%)	0	2 (0.6%)
Pembrolizumab	1 (0.6%)	1 (0.6%)	2 (0.6%)
Calcium folinate	0	2 (1.2%)	2 (0.6%)
Fluorouracil;folinic acid;oxaliplatin	1 (0.6%)	1 (0.6%)	2 (0.6%)
Gimeracil;oteracil potassium;tegafur	1 (0.6%)	1 (0.6%)	2 (0.6%)
Trastuzumab	2 (1.2%)	0	2 (0.6%)
Olaparib	1 (0.6%)	1 (0.6%)	2 (0.6%)
Tqb 3823	1 (0.6%)	1 (0.6%)	2 (0.6%)
Pirarubicin hydrochloride	1 (0.6%)	1 (0.6%)	2 (0.6%)
Azd 8205	0	1 (0.6%)	1 (0.3%)
Bat 8006	0	1 (0.6%)	1 (0.3%)
Bl m02d1	0	1 (0.6%)	1 (0.3%)
Datopotamab deruxtecan	0	1 (0.6%)	1 (0.3%)
Other monoclonal antibodies and antibody drug conjugates	0	1 (0.6%)	1 (0.3%)



Skb 264	0	1 (0.6%)	1 (0.3%)
Mitoxantrone hydrochloride liposomal	0	1 (0.6%)	1 (0.3%)
Nedaplatin	1 (0.6%)	0	1 (0.3%)
Oxaliplatin	0	1 (0.6%)	1 (0.3%)
Paclitaxel liposome	1 (0.6%)	2 (1.2%)	3 (0.9%)
Ixabepilone	1 (0.6%)	0	1 (0.3%)
Pemetrexed disodium	0	1 (0.6%)	1 (0.3%)
Tegafur	1 (0.6%)	0	1 (0.3%)
Temozolomide	1 (0.6%)	0	1 (0.3%)
Thiotepa	1 (0.6%)	0	1 (0.3%)
Bicalutamide	1 (0.6%)	0	1 (0.3%)
Scr 6852	1 (0.6%)	0	1 (0.3%)
Tqb 3915	0	1 (0.6%)	1 (0.3%)
Antineoplastic agents (immunotherapy)	0	1 (0.6%)	1 (0.3%)
Inbrx 106	0	1 (0.6%)	1 (0.3%)
Pd-1/pdl-1 (programmed cell death protein 1/death ligand 1) inhibitors	1 (0.6%)	0	1 (0.3%)
Investigational drug (investigational therapy)	2 (1.2%)	3 (1.8%)	5 (1.5%)
Other therapeutic products	1 (0.6%)	0	1 (0.3%)
Alectinib hydrochloride	0	1 (0.6%)	1 (0.3%)
Antineoplastic agents (targeted therapy)	1 (0.6%)	0	1 (0.3%)
Cetuximab	1 (0.6%)	0	1 (0.3%)
Pf 07104091	0	1 (0.6%)	1 (0.3%)
Pt (0506)101	1 (0.6%)	0	1 (0.3%)
Rivoceranib	1 (0.6%)	0	1 (0.3%)
Tqb 3728	0	1 (0.6%)	1 (0.3%)



Vascular endothelial growth factor inhibitors	1 (0.6%)	0	1 (0.3%)
Fluzoparib	0	1 (0.6%)	1 (0.3%)
Investigational drug (parp)	0	1 (0.6%)	1 (0.3%)
Venadaparib	0	1 (0.6%)	1 (0.3%)
Alpelisib	0	1 (0.6%)	1 (0.3%)
Inavolisib	1 (0.6%)	0	1 (0.3%)



Appendix D. Comparative analyses

Table 63 shows the relevant endpoint used in the meta-analysis as described in Section 7.

Table 63. Comparative analysis of studies comparing SG with TPC for patients with HR+/HER2- mBC

Outcome	Studies included in the analysis	Absolute difference			Relative difference			Analysis method	Are results used in the health economic analysis?
		Difference	CI	P-value	Difference	CI	P-value		
Median OS	TROPiCS-02 EVER-132-002, prior CDK4/6i population		N/A	N/A	HR			In the one-stage model, pooled HRs and CIs were calculated using Cox regression, stratified by statistically significant and clinically recommended stratification factors.	Yes
Median PFS	TROPiCS-02 EVER-132-002, prior CDK4/6i population	1.0	N/A	N/A	HR: 0.65	0.52-0.81	0.001	In the one-stage model, pooled HRs and CIs were calculated using Cox regression, stratified by statistically significant and clinically recommended stratification factors.	Yes



Appendix E. Extrapolation of patient transitions

E.1 Parametric extrapolation models

E.1.1 Extrapolation of PFS

The PFS curves were mature, with more than 60% of the patients experiencing an event by the end of the follow-up. Following guidance from the DMC and NICE DSU guidance (Nicholas Latimer, 2013), the seven standard survival parametric curves were fitted, and statistical fit was evaluated using the Akaike information criteria (AIC) and the Bayesian information criteria (BIC). Judging by the shape of the diagnostic plots, as discussed in section E.1.1.1, the evidence supporting the proportional hazards assumption was not deemed sufficient. Therefore, the models were fit independently, and following NICE TSD 14 guidelines, both treatment arms were fitted with the same model (Nicholas Latimer, 2013). Using the available evidence from Dahl et al., 2025 (Dahl et al., 2025) and based on the goodness-of-fit criteria, the lognormal distribution was selected to extrapolate the PFS for both treatment arms. As discussed in section 9 the same distribution was used for both arms; given that both modelled treatment arms comprise chemotherapy-based regimens, it was considered clinically appropriate to apply the same parametric distribution to both arms.

Lognormal models had good relative statistical fit for both treatment arms, good visual fit, and were aligned with the hazard shape.

E.1.1.1 Log-cumulative hazard plots and residual plots - PFS

Figure 33, Figure 34 and Figure 35 show the diagnostic plots for PFS, using the pooled meta-analysis data. In the Schoenfeld residual graph, a non-constant trend is evident. Furthermore, in the log-cumulative hazard plot, the two treatment arms cross. Therefore, the proportional hazards assumption was not utilised in the modelling approach.



Figure 33. PFS Pooled meta-analysis, Schoenfeld residuals

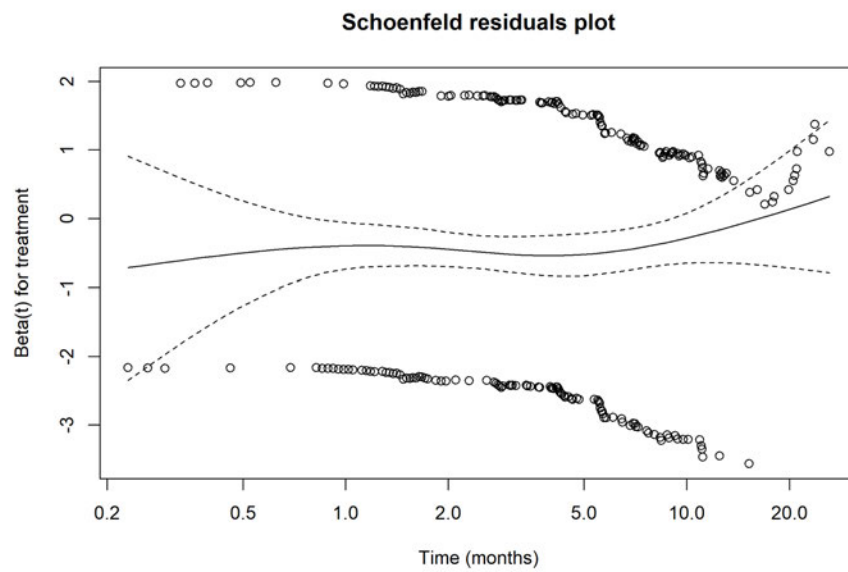


Figure 34 PFS Pooled meta-analysis, log-cumulative hazard plot

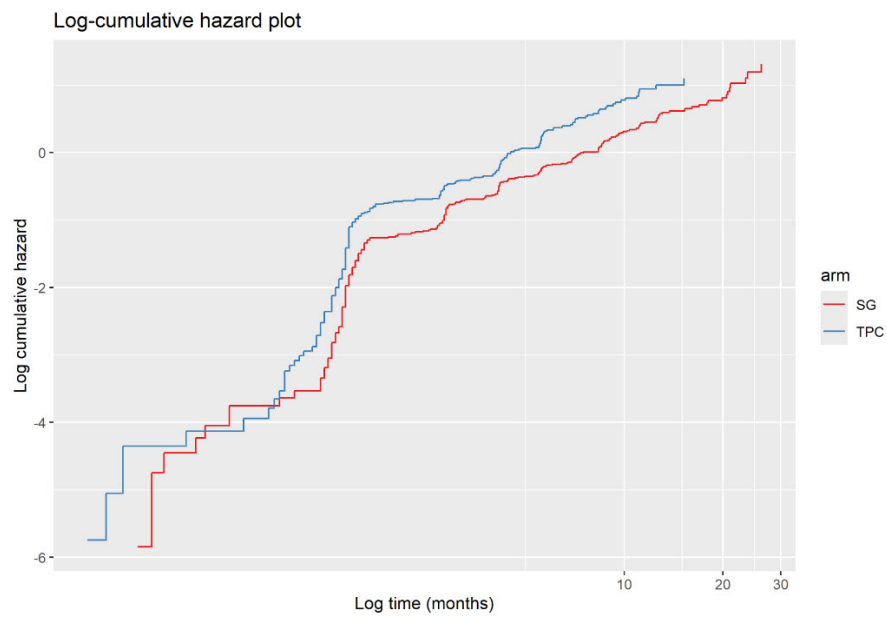
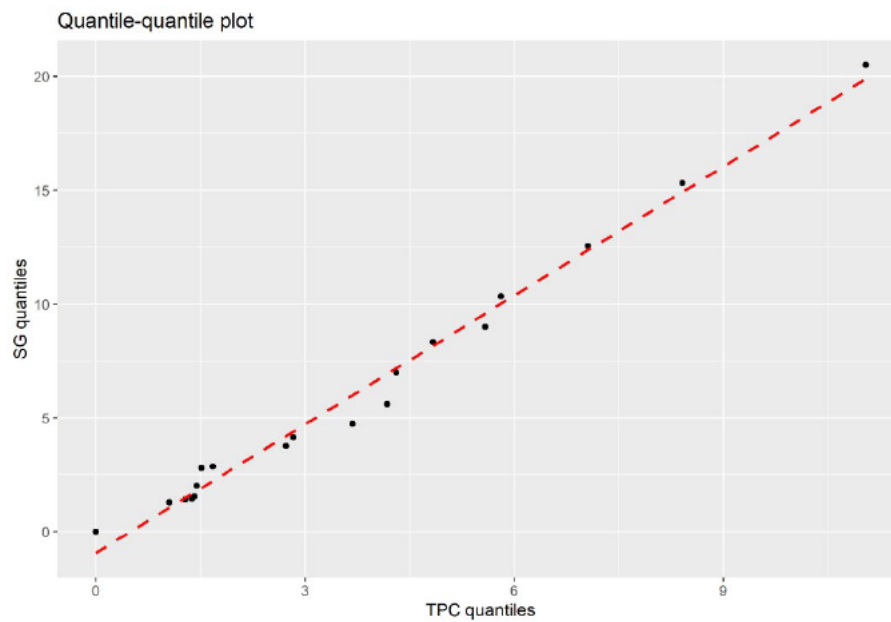




Figure 35 PFS Pooled meta-analysis, Q-Q plot



E.1.1.2 Internal validity

E.1.1.2.1 Assessment of statistical and visual fit (AIC and BIC) - PFS

Visual fit was assessed by comparing the shapes of the parametric models with the observed KM curves. Clinical plausibility was evaluated by comparing the shape of the hazard function with the smoothed hazards from the clinical trial data.

For SG, the lognormal had one of the best visual fits to the KM curve. Gamma and Weibull had the worst visual fit. Based on the AIC and BIC, only generalised gamma (global BIC minima) and the lognormal (global AIC minima) are plausible selections. Since the two have ΔAIC and ΔBIC values under 4, they are equally plausible candidates based on the data alone (Burnham & Anderson, 2004). However, the lognormal provides the best overall statistical fit, as indicated by the AIC and BIC. The remaining five models have high ΔAIC and ΔBIC values, i.e., are less supported by the evidence. SG's goodness-of-fit statistics with the relative ΔAIC and ΔBIC are shown in Table 64.

Table 64 PFS Goodness-of-fit statistics SG

Distribution	AIC	BIC	ΔAIC	ΔBIC	Combined
Generalised Gamma	1439.733	1451.332	0.00	3.80	3.80
Lognormal	1439.801	1447.534	0.07	0.00	0.07
Log-logistic	1451.858	1459.591	12.13	12.06	24.18
Gamma	1470.238	1477.971	30.50	30.44	60.94



Weibull	1475.414	1483.147	35.68	35.61	71.29
Exponential	1477.765	1481.632	38.03	34.10	72.13
Gompertz	1479.486	1487.219	39.75	39.68	79.44

For TPC, the lognormal was considered to have the best visual fit, whereas log-logistic and generalised gamma showed the worst fit to the KM curve. According to AIC, the generalised gamma and log-normal have the best statistical fit, both being equivalent ($\Delta AIC < 3$), while the other five distributions have $\Delta AIC > 7$. For BIC, lognormal and generalised gamma again have the best fit. TPC's goodness-of-fit statistics with the relative ΔAIC and ΔBIC are shown in Table 65.

Table 65 PFS Goodness-of-fit statistics TPC

Distribution	AIC	BIC	ΔAIC	ΔBIC	Combined Δ
Generalised Gamma	1143.336	1154.919	0.00	1.76	1.76
Lognormal	1145.433	1153.155	2.10	0.00	2.10
Log-logistic	1152.350	1160.071	9.01	6.92	15.93
Gamma	1184.429	1192.150	41.09	39.00	80.09
Weibull	1196.173	1203.895	52.84	50.74	103.58
Exponential	1205.117	1208.978	61.78	55.82	117.60
Gompertz	1206.231	1213.953	62.89	60.80	123.69

E.1.1.2.2 Assessment of smoothed hazard functions - PFS

The smoothed hazards for SG and TPC are shown in Figure 36-Figure 49 compared to each survival model. The estimated hazards in the clinical trial show an upward trend toward the end of the trial period, reflecting that only a few subjects remain at risk. In both treatment arms, the observed hazard is non-monotonic.

For SG, the lognormal distribution closely matches the hazard shape in the first period, whereas a substantial deviation is observed in the last period, a pattern common across all models considered due to the lack of patients at risk. The log-logistic, gamma, and generalised gamma also exhibit hazards similar to the observed trial hazard.



Figure 36 Smoothed hazard, PFS, SG - Exponential

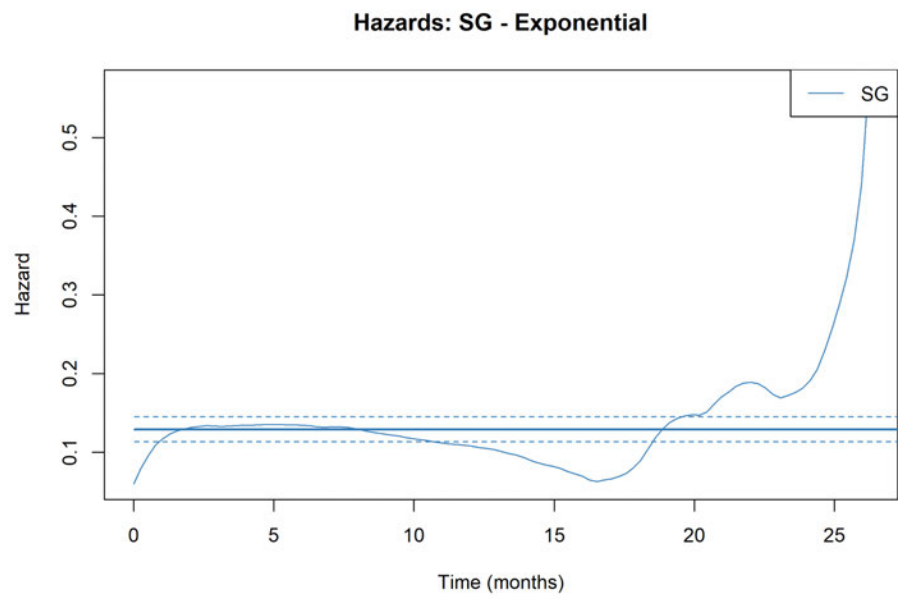


Figure 37 Smoothed hazard, PFS, SG - Weibull

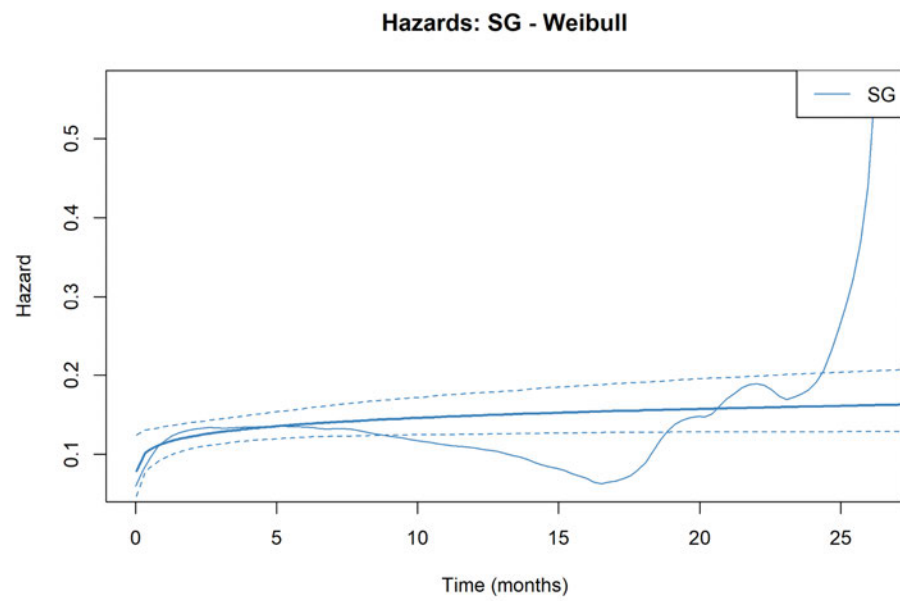




Figure 38 Smoothed hazard, PFS, SG - Gompertz

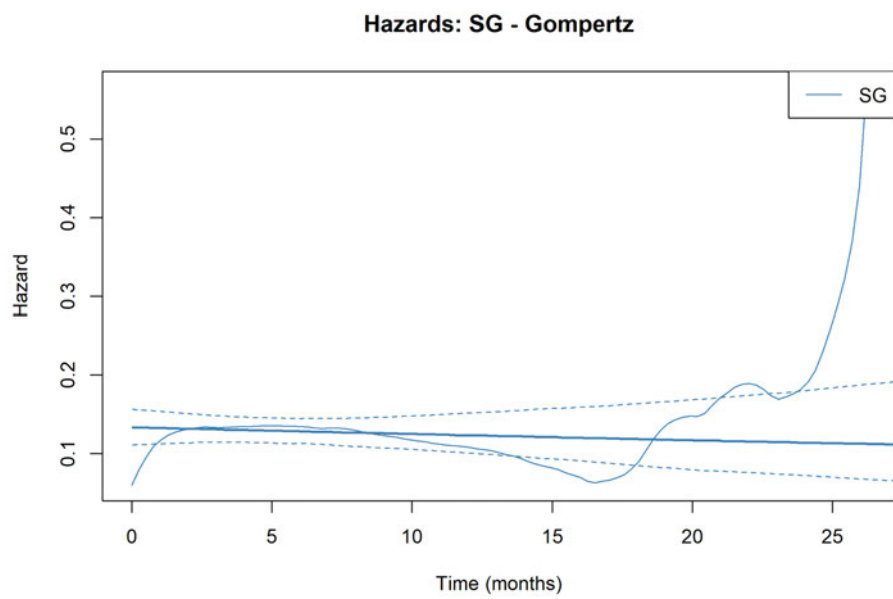


Figure 39 Smoothed hazard, PFS, SG - Gamma

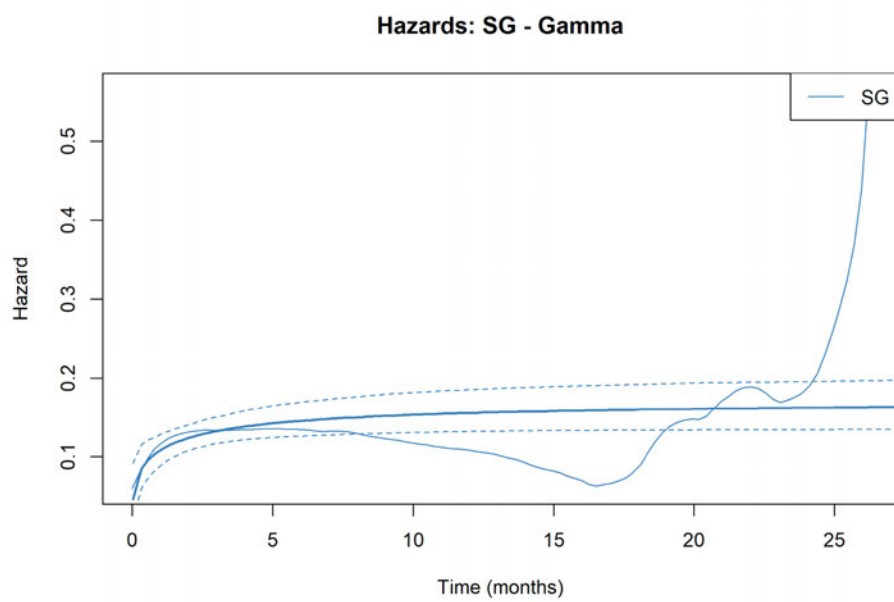




Figure 40 Smoothed hazard, PFS, SG - Lognormal

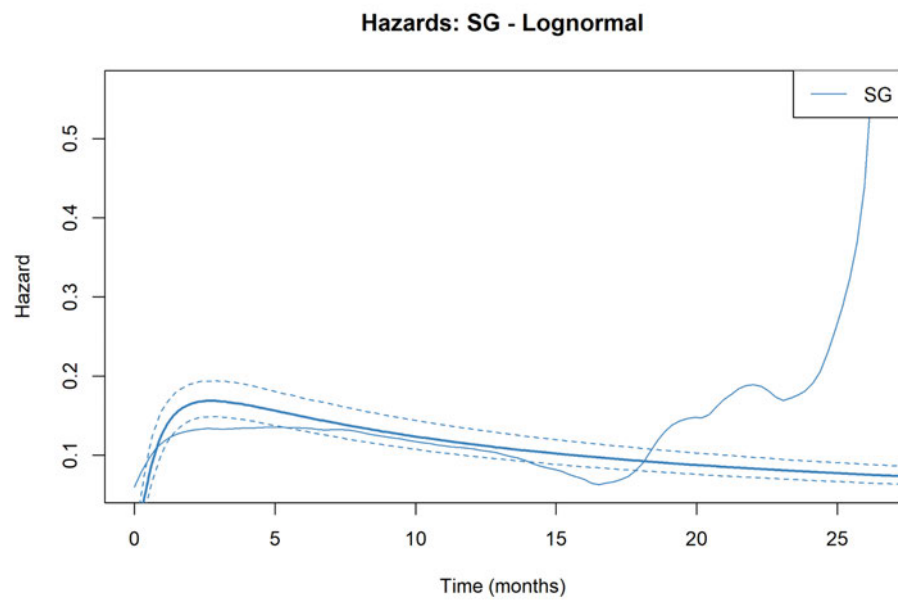


Figure 41 Smoothed hazard, PFS, SG – log-logistic

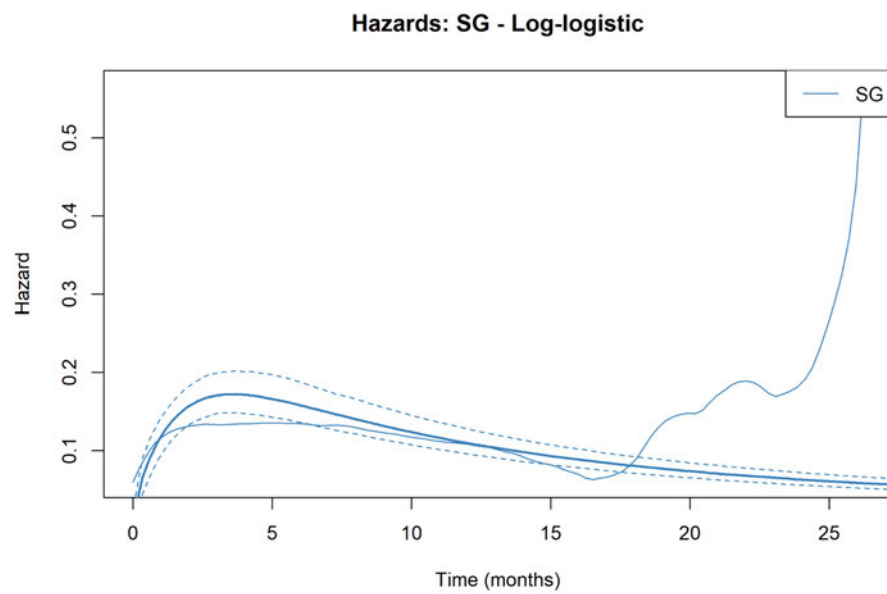




Figure 42 Smoothed hazard, PFS, SG – Generalised gamma

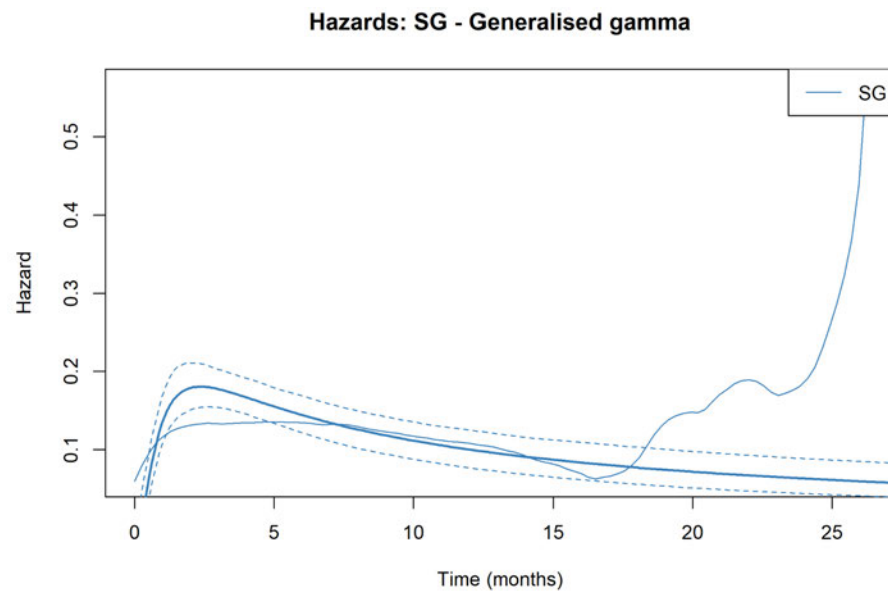


Figure 43 Smoothed hazard, PFS, TPC – Exponential

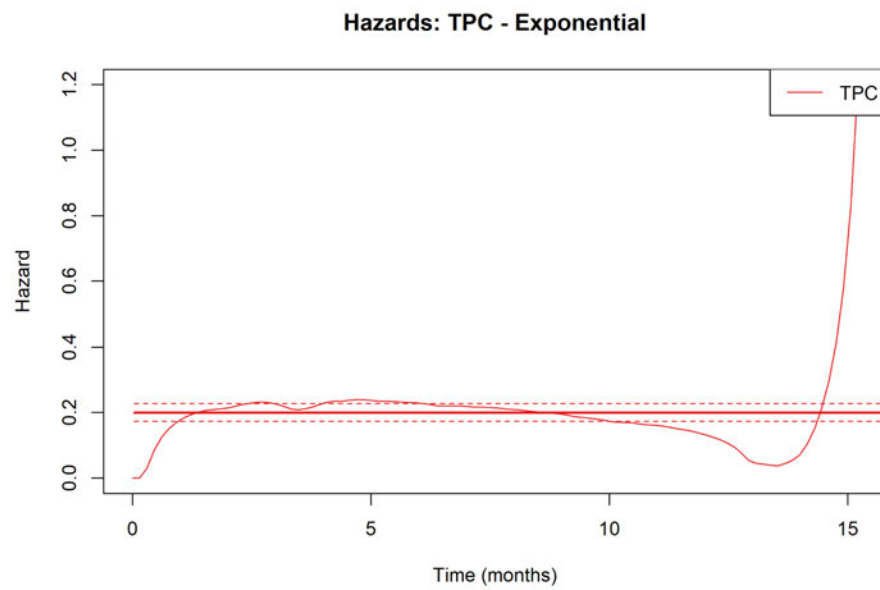




Figure 44 Smoothed hazard, PFS, TPC – Weibull

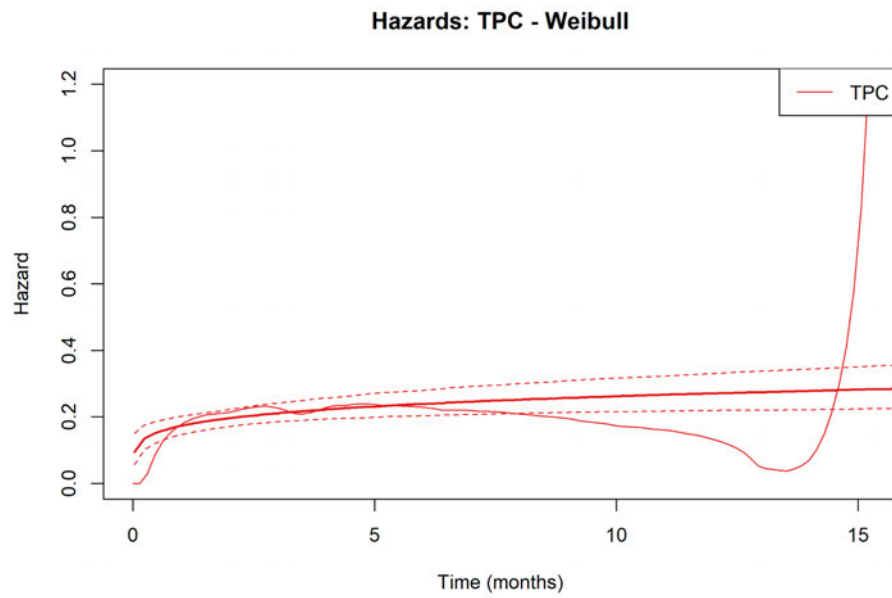


Figure 45 Smoothed hazard, PFS, TPC – Gompertz

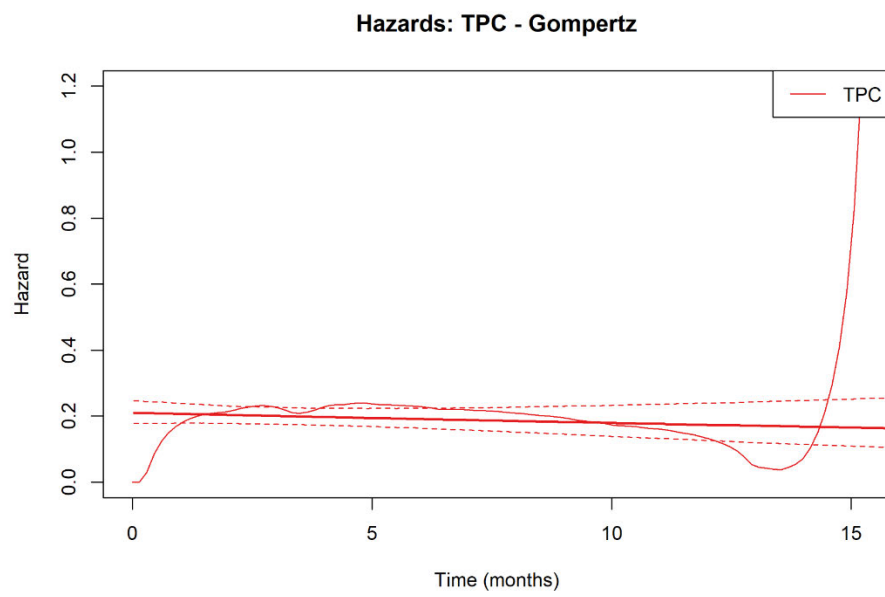




Figure 46 Smoothed hazard, PFS, TPC – Gamma

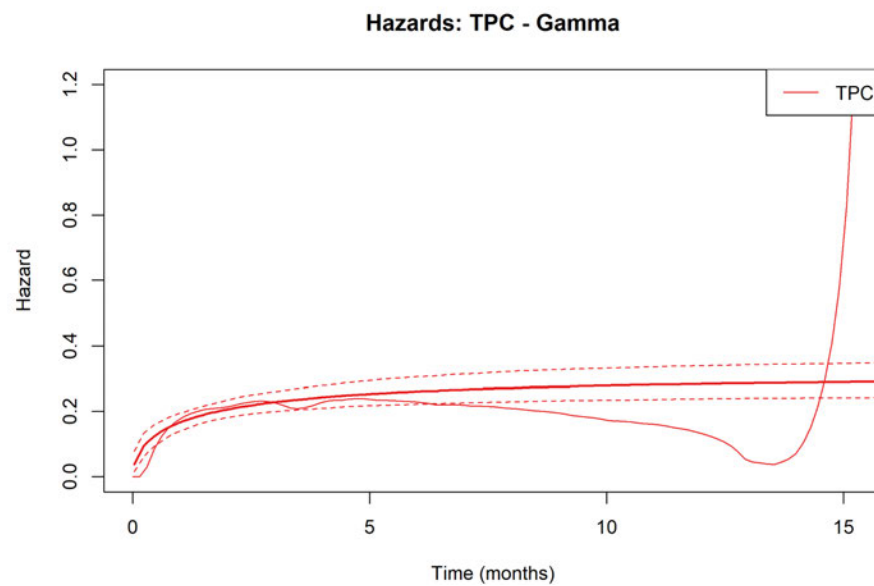


Figure 47 Smoothed hazard, PFS, TPC – Lognormal

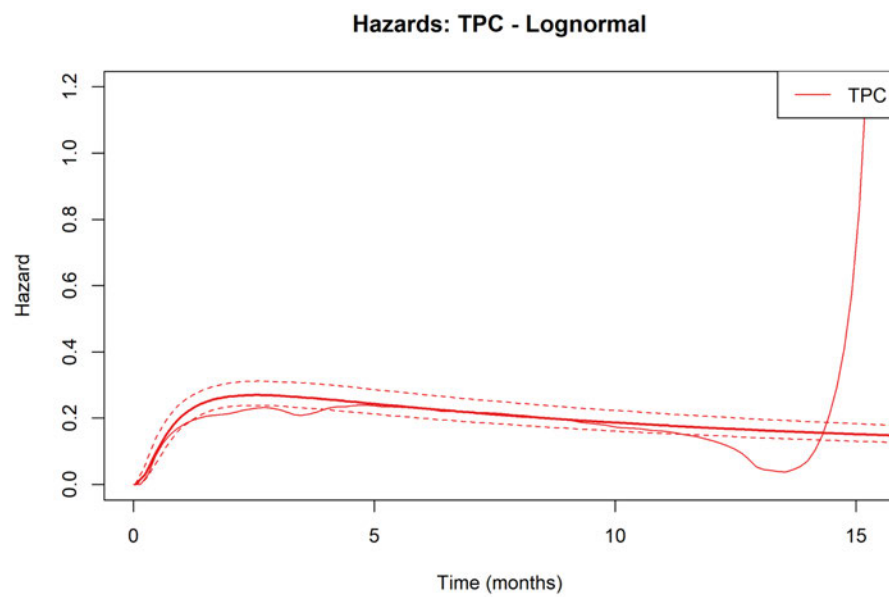




Figure 48 Smoothed hazard, PFS, TPC – Log-logistic

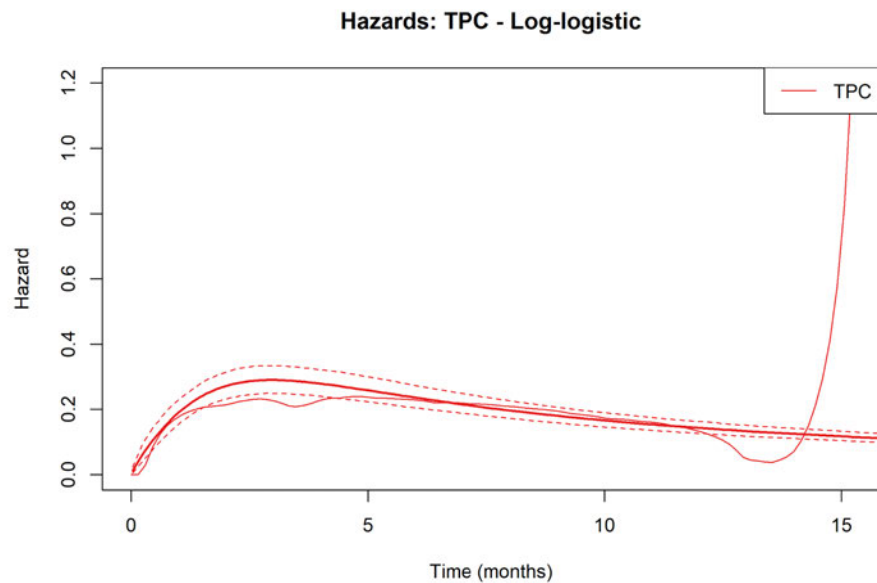
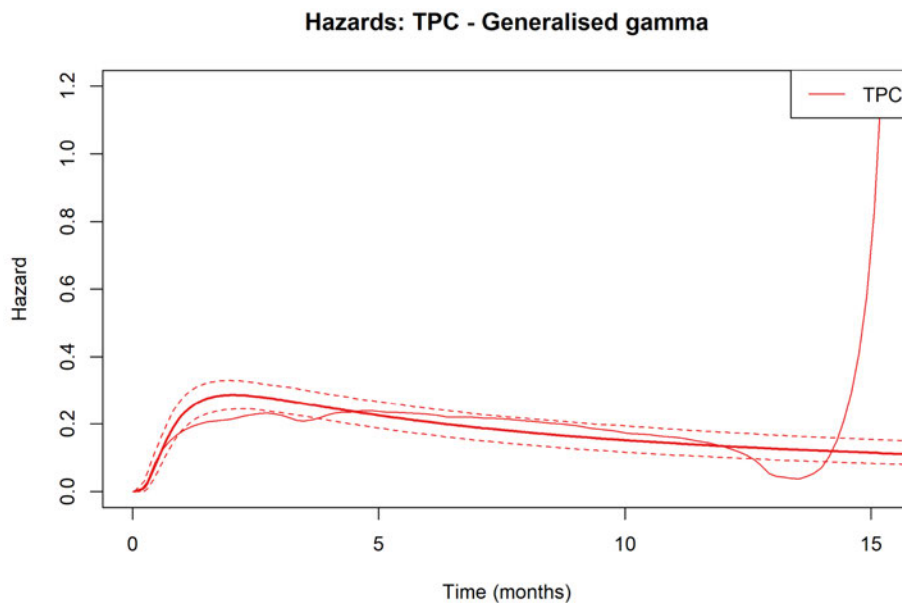


Figure 49 Smoothed hazard, PFS, TPC – Generalised gamma



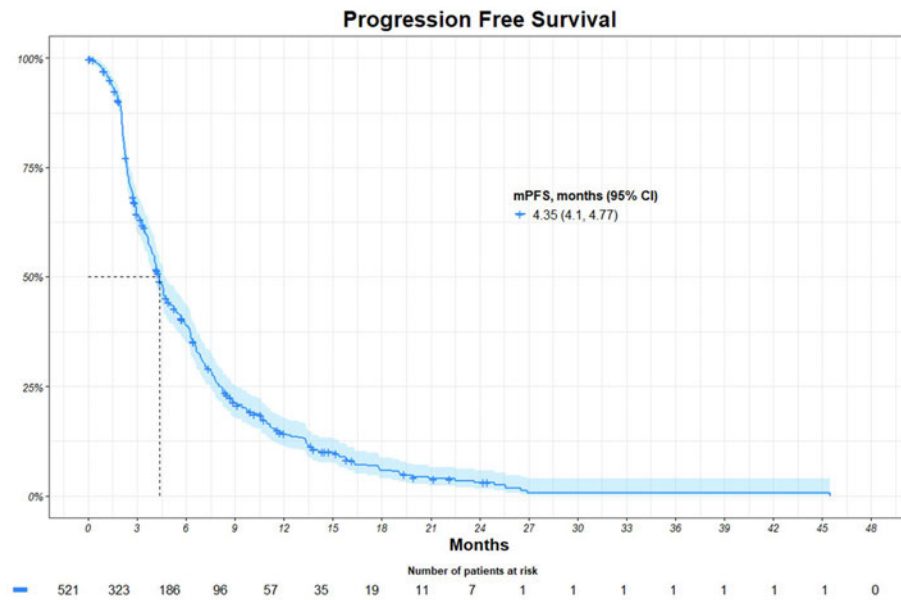
E.1.1.3 External validity

While the PFS data for the SG arm could not be directly compared with external clinical data due to insufficient data, the TPC extrapolations were tested against Danish clinical practice (Dahl et al., 2025). The study of late-stage treatment of heavily pretreated advanced ER+, HER2- breast cancer patients in Denmark who have initiated CDK4/6i treatment in the 1st or 2nd line of treatment from 2017 to 2021. The relevant survival outcomes and treatment patterns were described in the 3rd, 4th and 5th lines of treatment. Given the indication for SG in the current application, both the 4th and 5th lines were deemed relevant for comparison with TPC's predicted PFS. PFS 4th- and 5th-



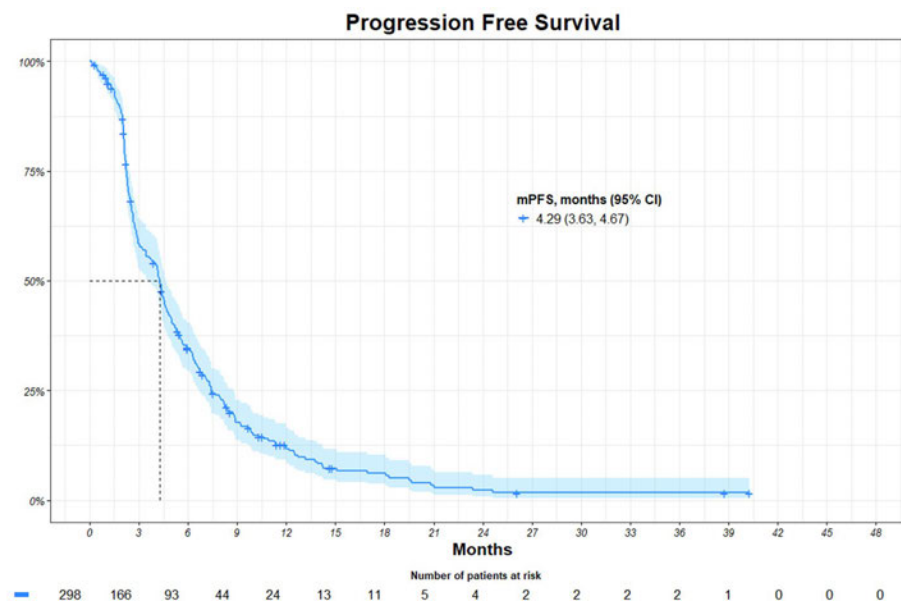
line KM curves from Dahl (Dahl et al., 2025) are shown in Figure 50 and Figure 51, respectively.

Figure 50 PFS 4th line – Dahl et al., 2025



465 patients experienced an event. 56 (10.7%) of patients were censored.

Figure 51 PFS 5th line – Dahl et al., 2025



264 patients experienced an event. 34 (11.4%) of patients were censored.

The available predicted PFS shares from the 4th and 5th lines are compared with the model extrapolations in Table 66. The generalised gamma, lognormal, and log-logistic



distributions, which show both good statistical and visual fit, predict PFS rates similar to those reported by Dahl and colleagues. However, both the log-logistic and the generalised gamma predict a share of long-term PFS which is not observed in the RW. Therefore, the log-normal was deemed the best-fitting model.

Table 66 TPC predicted PFS extrapolations – landmarks

Extrapolation	Year 1	Year 2	Year 3	Year 4	Year 5	Year 10	Year 15	Year 20
PFS – Overall patient 4 th line, n= 761 (Dahl et al., 2025)	11.90%	2.75%	1.22%	0.00%*	N/A	N/A	N/A	N/A
PFS - Overall patient 5 th line, n= 493 (Dahl et al., 2025)	9.96%	2.27%	1.60%	N/A	N/A	N/A	N/A	N/A
Weibull	6.65%	0.21%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
Lognormal	8.07%	1.51%	0.45%	0.17%	0.07%	0.00%	0.00%	0.00%
Log-logistic	8.15%	2.36%	1.12%	0.66%	0.44%	0.12%	0.06%	0.00%
Exponential	9.50%	0.88%	0.08%	0.01%	0.00%	0.00%	0.00%	0.00%
Generalised Gamma	9.76%	2.85%	1.26%	0.68%	0.42%	0.08%	0.03%	0.00%
Gompertz	10.37%	1.55%	0.32%	0.09%	0.03%	0.00%	0.00%	0.00%
Gamma	5.68%	0.17%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%

Notes: *KM was recorded until 45.5 months for PFS 4th line and 40.2 months for PFS 5th line.



For reference, SG predicted PFS shares of SG are listed in Table 67. In both arms, most patients are expected to experience progression by year 1, regardless of the model selected.

Table 67 SG predicted PFS extrapolations – landmarks

Extrapolation	Year 1	Year 2	Year 3	Year 4	Year 5	Year 10	Year 15	Year 20
PFS – Overall patient 4 th line, n= 761 (Dahl et al., 2025)	11.90%	2.75%	1.22%	0.00%*	N/A	N/A	N/A	N/A
PFS - Overall patient 5 th line, n= 493 (Dahl et al., 2025)	9.96%	2.27%	1.60%	N/A	N/A	N/A	N/A	N/A
Weibull	20.07%	3.13%	0.44%	0.06%	0.01%	0.00%	0.00%	0.00%
Lognormal	19.44%	6.31%	2.74%	1.40%	0.79%	0.10%	0.03%	0.00%
Log-logistic	18.76%	7.00%	3.76%	2.39%	1.68%	0.55%	0.29%	0.00%
Exponential	21.42%	4.59%	0.98%	0.21%	0.05%	0.00%	0.00%	0.00%
Generalised Gamma	20.18%	7.87%	4.13%	2.51%	1.67%	0.42%	0.18%	0.00%
Gompertz	21.58%	5.23%	1.41%	0.42%	0.14%	0.00%	0.00%	0.00%
Gamma	19.12%	2.83%	0.40%	0.05%	0.01%	0.00%	0.00%	0.00%

Notes: *KM was recorded until 45.5 months for PFS 4th line and 40.2 months for PFS 5th line.



E.1.1.4 Other assumptions

N/A

E.1.2 Extrapolations of OS

Using the same procedure as PFS (section E.1.1), OS was extrapolated. OS was mature, with most patients experiencing an event by the end of the follow-up, [REDACTED] for TPC and [REDACTED] for SG, respectively. The shape of the diagnostic plots, as shown in the section E.1.2.1 does not rule out the proportional hazards assumption. However, it is unlikely that a constant treatment effect will be observed over the analysis's time horizon. Therefore, survival models were fit independently, consistent with the methodology used for PFS extrapolation. Using the available evidence from Dahl et al., 2025 (Dahl et al., 2025) and based on the goodness-of-fit criteria, the log-logistic model was chosen to extrapolate OS for both treatment arms.

In line with NICE TSD 14 (Nicholas Latimer, 2013), and as for PFS, the same distribution was used for both arms; given that both modelled treatment arms comprise chemotherapy-based regimens, it was considered clinically appropriate to apply the same parametric distribution to both arms. In selecting the model, priority was given to TPC due to the higher number of events [REDACTED] for Trodelvy®). Furthermore, extrapolations of SG were ruled out if they predicted significantly lower OS than the share observed in the RW study (Dahl et al., 2025). The rationale behind this is that, based on the pivotal trials, SG was predicted to have both a better PFS and OS compared to the chemotherapy used in Danish clinical practice (Dahl et al., 2025). It was therefore deemed clinically implausible that these patients would have a worse survival than their RWE counterparts.

The log-logistic model was the stronger candidate for TPC, providing the best statistical fit, a good visual fit to the KM data, and a plausible smoothed hazard.

E.1.2.1 Log-cumulative hazard plots and residual plots - OS

Figure 52, Figure 53, and Figure 54 show the diagnostic plots for OS, using the latest available data cut from the pooled meta-analysis. In the Schoenfeld residual graph, the residuals show a slight downward trend towards the end of the trial. Furthermore, in the log-cumulative hazard plot, the two treatment arms cross, but they remain relatively parallel thereafter. Due to inconclusive evidence and the low likelihood of a constant treatment effect, the proportional hazards assumption was not used, and models were fit independently.



Figure 52 OS Pooled meta-analysis, Schoenfeld residuals

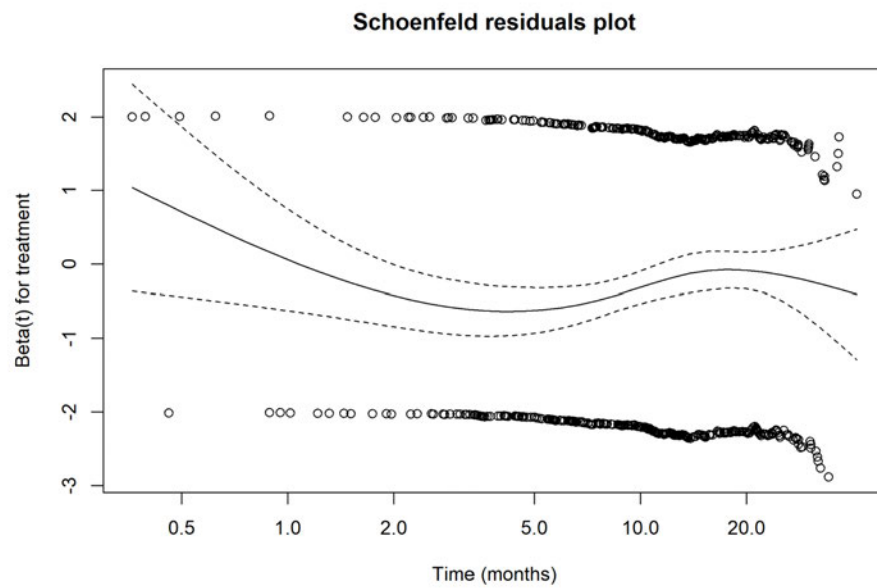


Figure 53 OS Pooled meta-analysis, Log-cumulative hazard plot

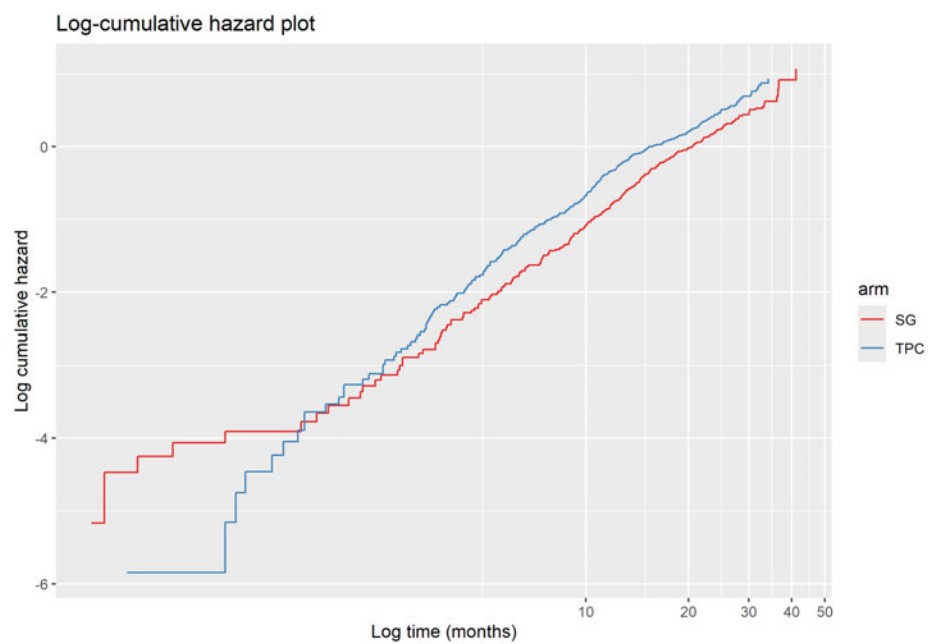
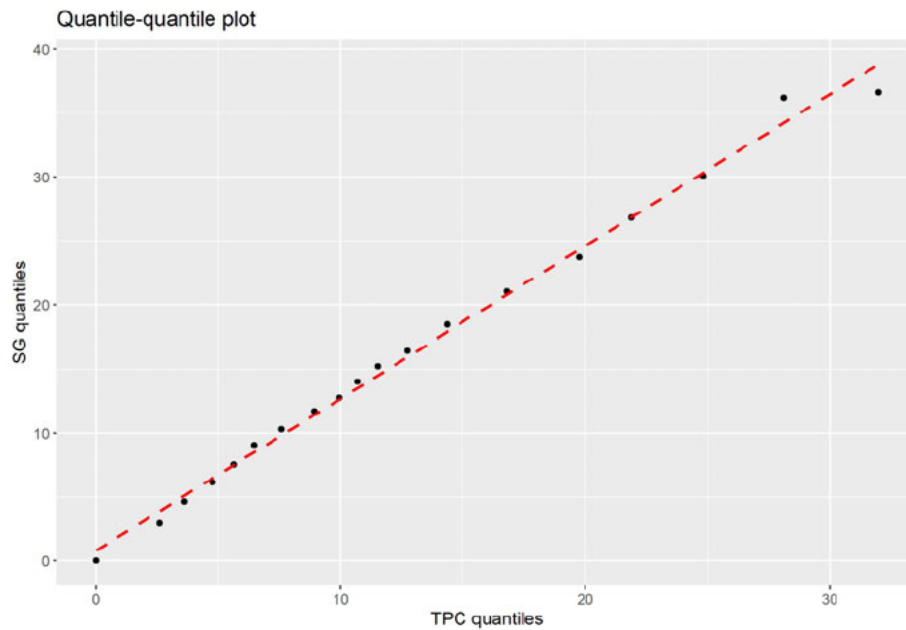




Figure 54 Pooled meta-analysis, Q-Q plot



E.1.2.2 Internal validity

E.1.2.2.1 Assessment of statistical and visual fit (AIC and BIC) - OS

Visual fit was assessed by evaluating the shape of the parametric and observed KM curves. Clinical plausibility was evaluated by comparing the shape of the hazard function with the smoothed hazards from the clinical trial data.

For SG, the best visual fit functions are log-logistic, gamma, generalised gamma, and Weibull, with very similar visual fits to the KM curve. Exponential and lognormal models did not have a good visual fit. Based on the AIC, the gamma is the global minimum, while Weibull and generalised gamma may also be considered supported by the evidence ($\Delta\text{AIC} < 4$). The log-logistic is a close second best ($\Delta\text{AIC} < 5$). All the other models have ΔAIC above 10. The result is consistent for BIC, with the gamma model having the lowest value and Weibull a close second ($\Delta\text{BIC} < 4$). Generalised gamma and log-logistic remain suitable candidates (ΔAIC close to 5). SG's goodness-of-fit statistics with the relative ΔAIC and ΔBIC are shown in Table 68.

Table 68 OS Goodness-of-fit statistics SG

Distribution	AIC	BIC	ΔAIC	ΔBIC	Combined Δ
Gamma	2181.58	2189.32	0.00	0.00	0.00
Weibull	2181.85	2189.59	0.27	0.27	0.54
Generalised Gamma	2183.24	2194.84	1.66	5.53	7.19



Log-logistic	2186.53	2194.26	4.95	4.95	9.89
Gompertz	2196.14	2203.87	14.55	14.55	29.10
Lognormal	2213.06	2220.79	31.47	31.47	62.95
Exponential	2219.77	2223.64	38.18	34.32	72.50

For TPC, the best visual-fit models were generalised gamma, log-logistic, and lognormal. Goodness-of-fit statistics are shown in Table 69. The log-logistic model was the global minimum for both AIC and BIC. Generalised gamma, lognormal, and gamma models were suitable candidates, with both Δ AIC and Δ BIC under 5. The other models exhibited relatively poor statistical fit.

Table 69 OS Goodness-of-fit statistics TPC

Distribution	AIC	BIC	Δ AIC	Δ BIC	Combined
Log-logistic	2179.34	2187.06	0.00	0.00	0.00
Generalised Gamma	2179.63	2191.22	0.29	4.15	4.44
Lognormal	2182.21	2189.93	2.87	2.87	5.73
Gamma	2183.16	2190.88	3.82	3.82	7.63
Weibull	2190.29	2198.01	10.95	10.95	21.89
Gompertz	2212.07	2219.79	32.73	32.73	65.45
Exponential	2224.79	2228.65	45.45	41.59	87.03

E.1.2.2.2 Assessment of smoothed hazard functions – OS

The smoothed hazards for SG and TPC in OS are shown in Figure 55 to Figure 61, and in Figure 62 to Figure 68, respectively, comparing each survival model to the estimated smoothed hazard from the clinical trial. For both treatment arms, the non-parametric hazards show an upward trend at the end of the trial period, an artefact due to fewer subjects at risk. For SG, the observed hazard is monotonic, while TPC shows a non-monotonic shape with a turning point around 15 months.

For SG, among the best-fitting distributions, Weibull, gamma, log-logistic, and generalised gamma show very similar patterns up to 30 months, closely following the non-parametric hazard. Among the best-fit models for TPC, gamma, log-logistic, lognormal, and generalised gamma, provided a reasonably good fit during the first 20 months of the non-parametric hazards.



Figure 55 Smoothed hazard, OS, SG - Exponential

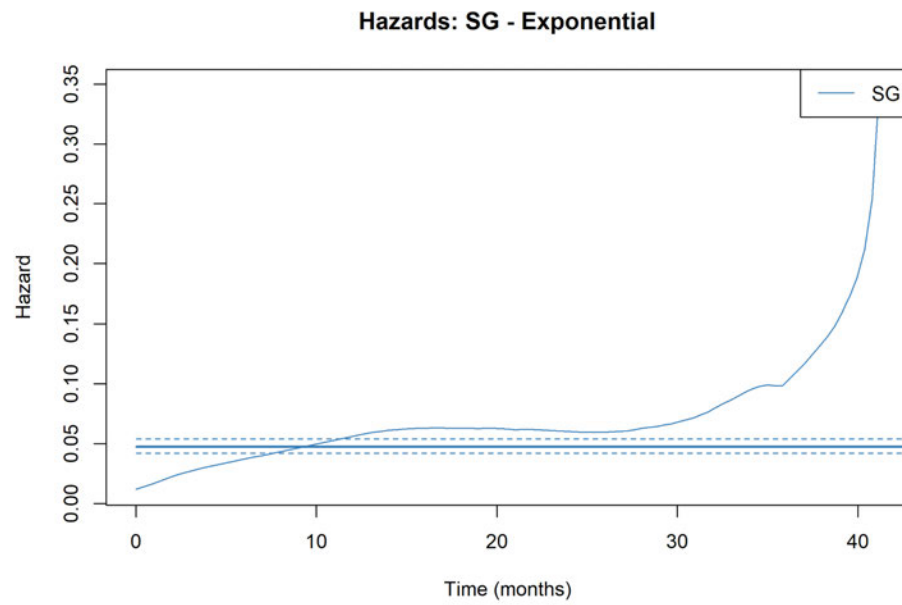


Figure 56 Smoothed hazard, OS, SG - Weibull

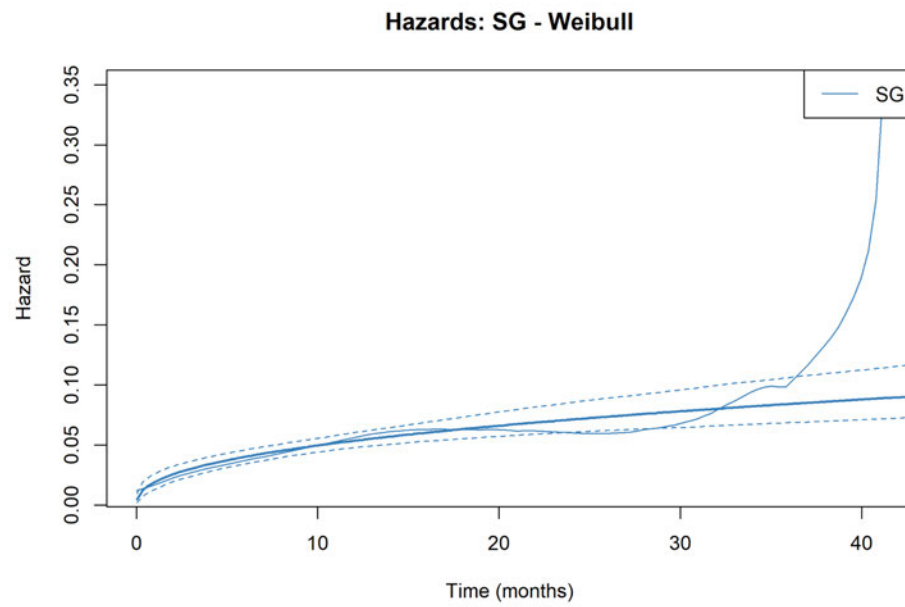




Figure 57 Smoothed hazard, OS, SG - Gompertz

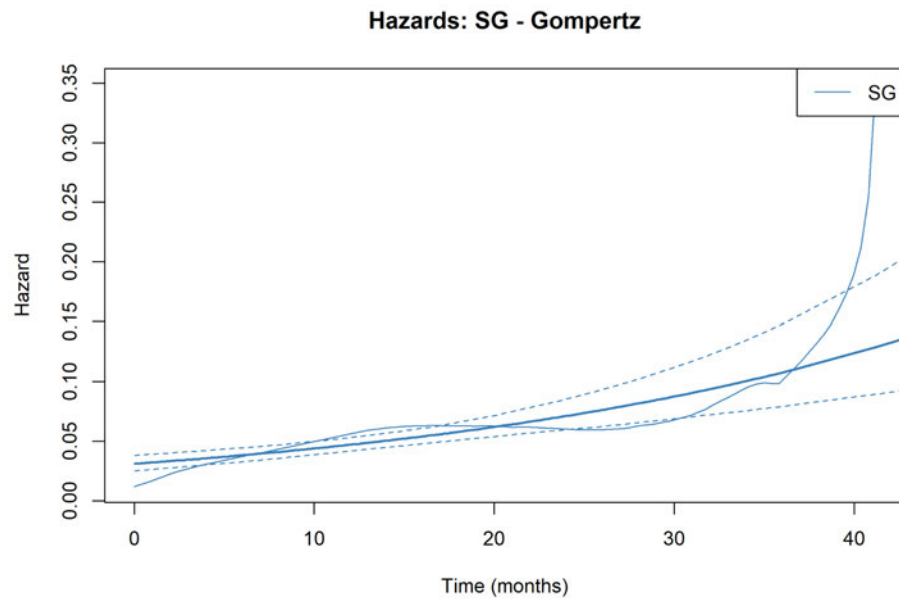


Figure 58 Smoothed hazard, OS, SG - Gamma

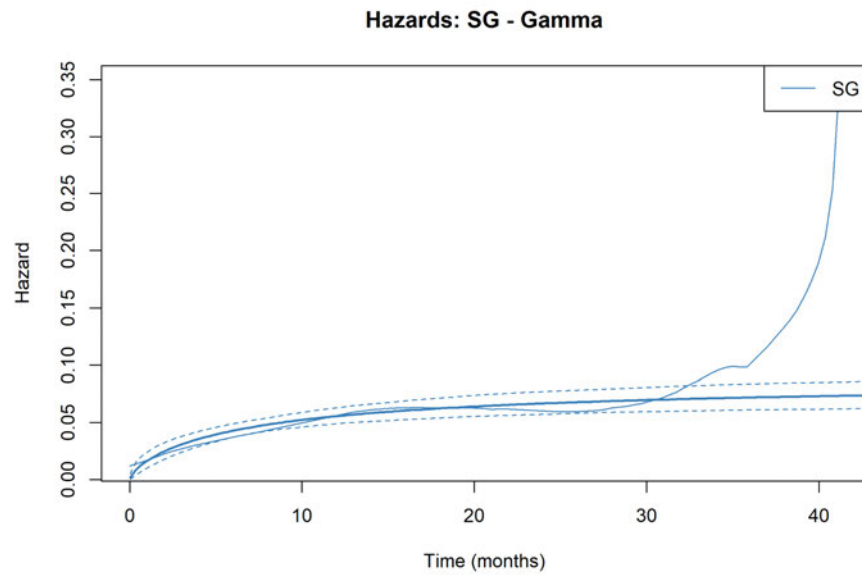




Figure 59 Smoothed hazard, OS, SG - Lognormal

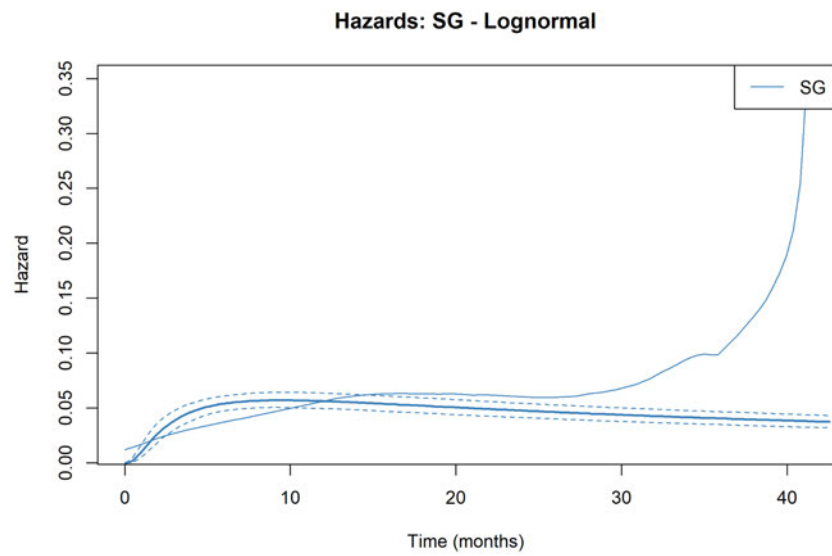


Figure 60 Smoothed hazard, OS, SG - Log-logistic

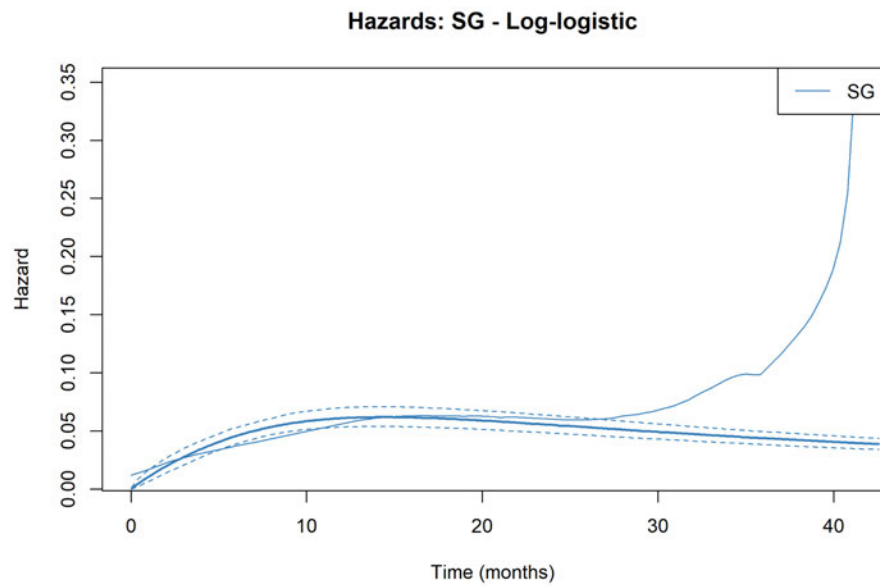




Figure 61 Smoothed hazard, OS, SG - Generalised gamma

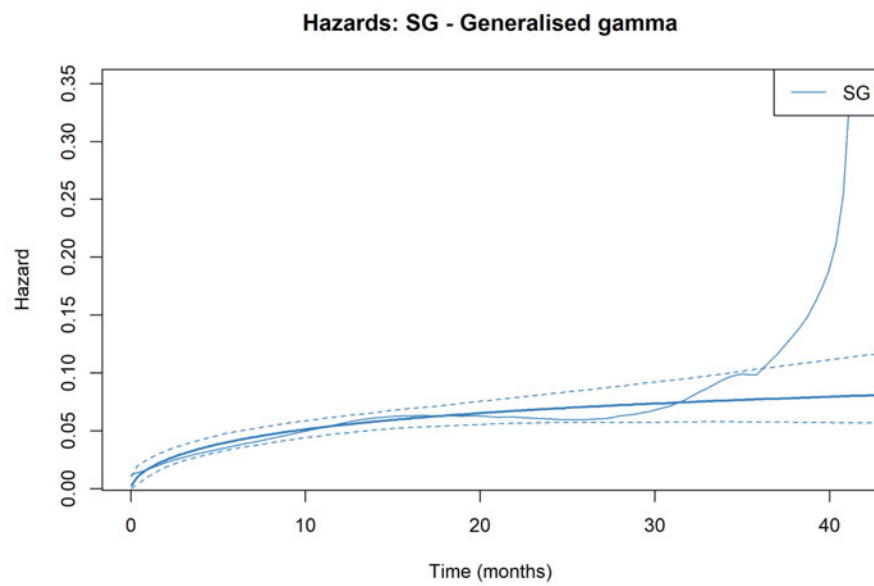


Figure 62 Smoothed hazard, OS, TPC - Exponential

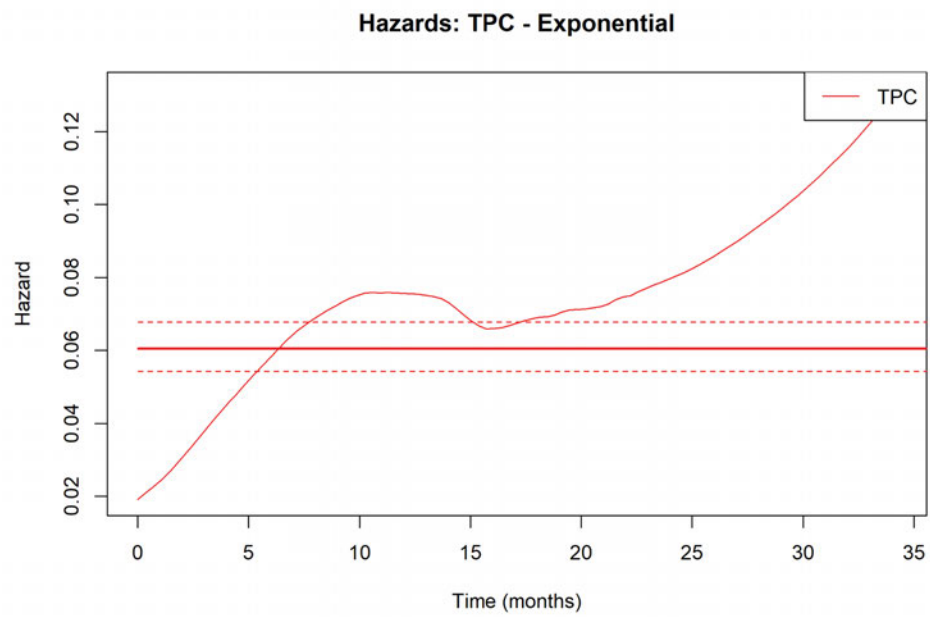




Figure 63 Smoothed hazard, OS, TPC - Weibull

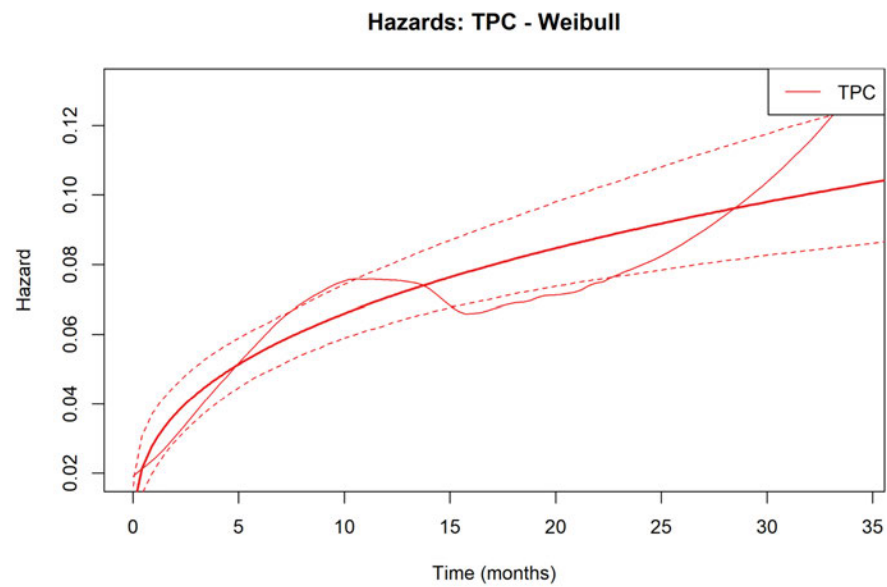


Figure 64 Smoothed hazard, OS, TPC - Gompertz

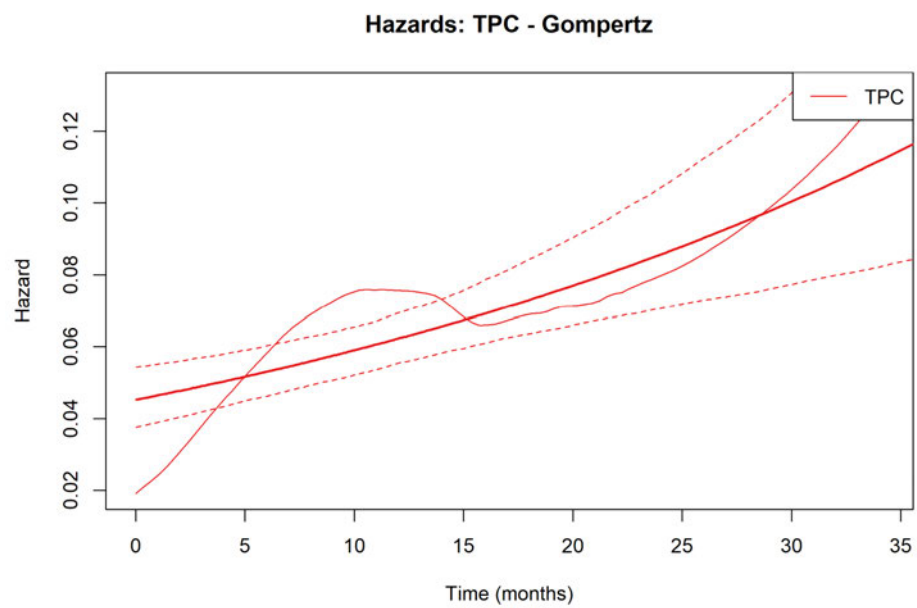




Figure 65 Smoothed hazard, OS, TPC - Gamma

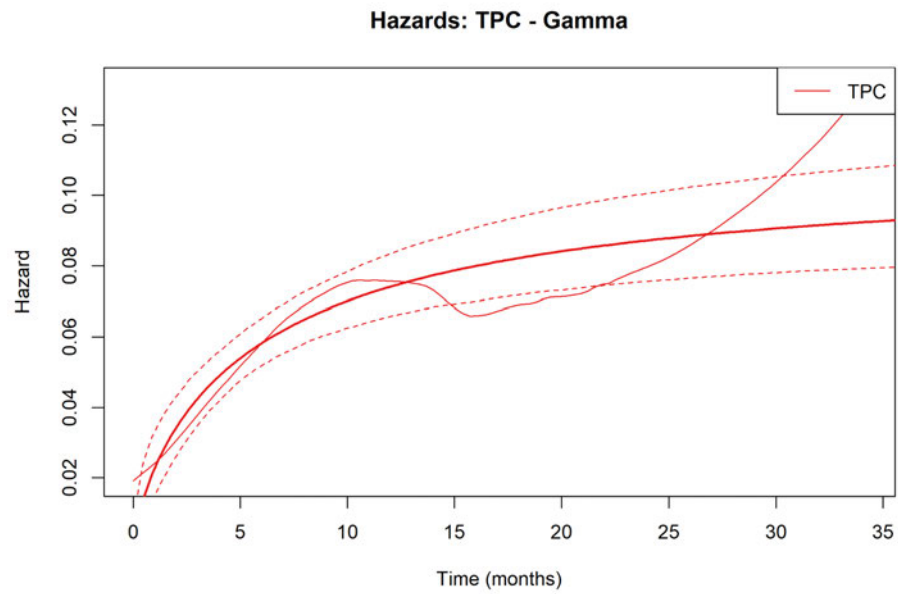


Figure 66 Smoothed hazard, OS, TPC - Lognormal

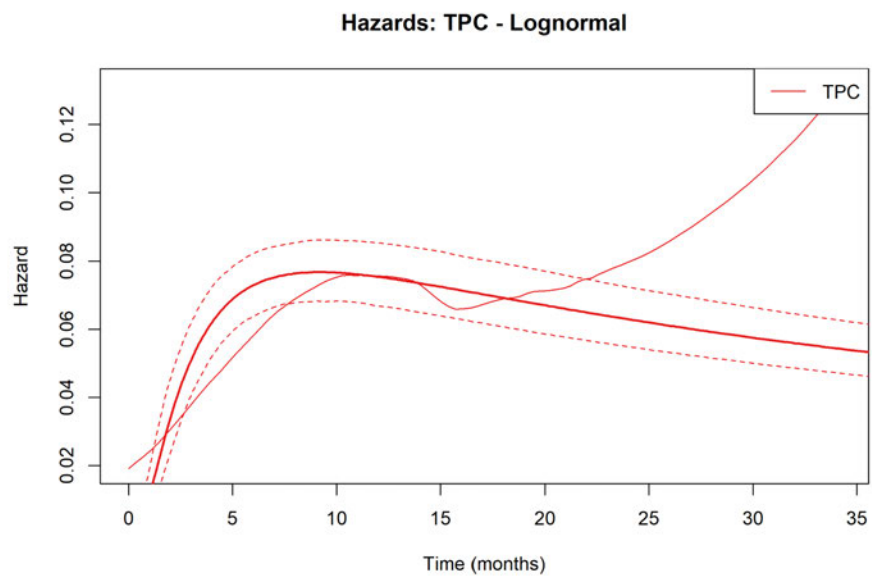




Figure 67 Smoothed hazard, OS, TPC – Log-logistic

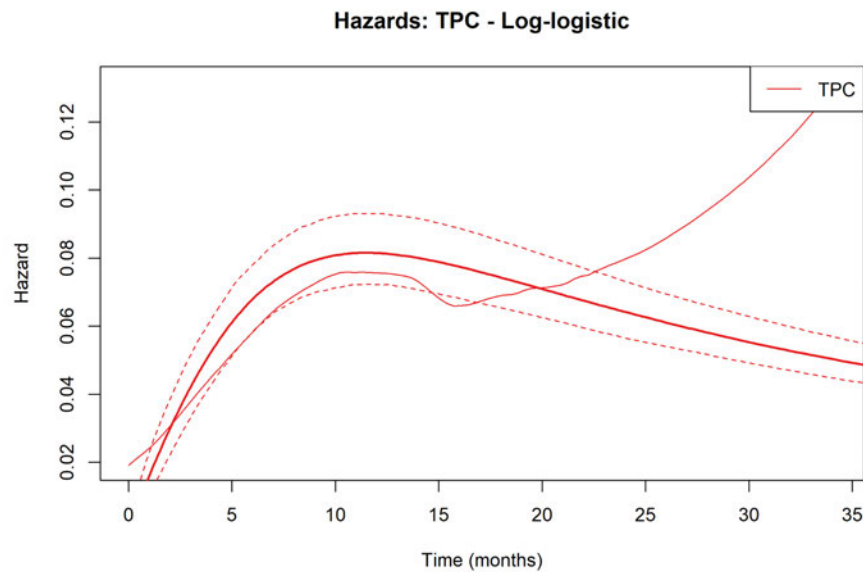
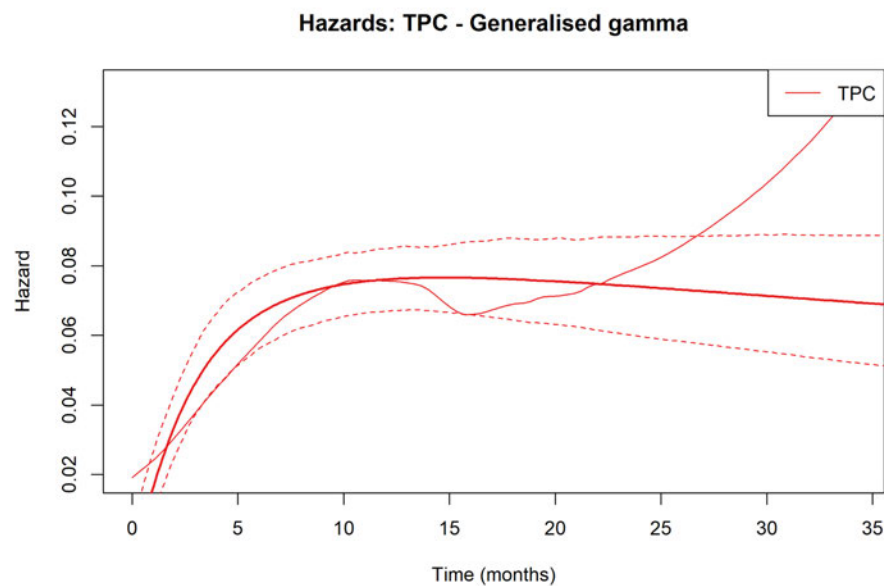


Figure 68 Smoothed hazard, OS, TPC – Generalised gamma

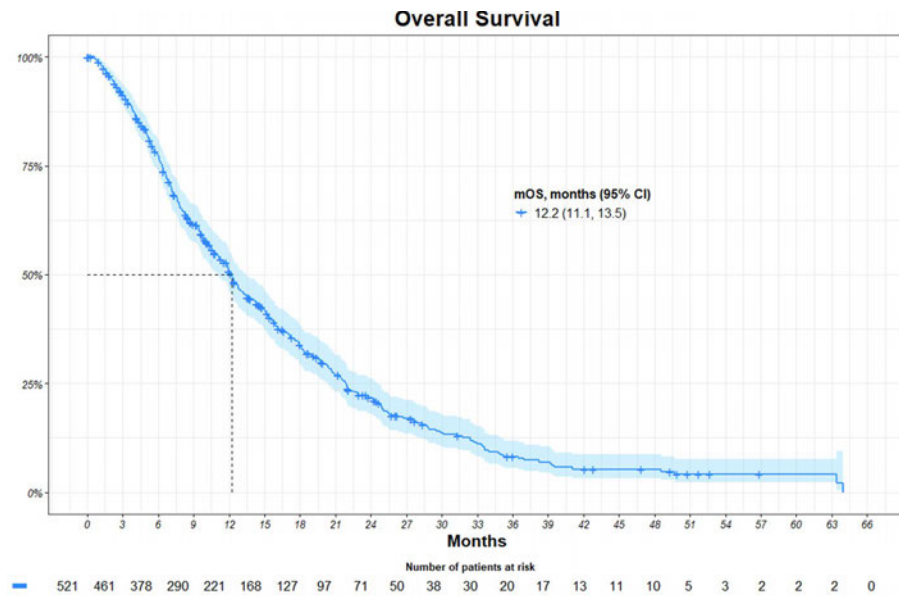


E.1.2.3 External validity

TPC extrapolated survival shares were tested against Danish clinical practice (Dahl et al., 2025). The study described late-stage treatment of heavily pretreated advanced ER+, HER2- breast cancer patients in Denmark who have initiated CDK4/6i treatment in the 1st or 2nd line of treatment from 2017 to 2021. The relevant survival outcomes and treatment patterns were described in the 3rd, 4th and 5th lines of treatment. OS 4th- and 5th-line KM curves from Dahl (Dahl et al., 2025) are shown in Figure 69 and Figure 70, respectively.

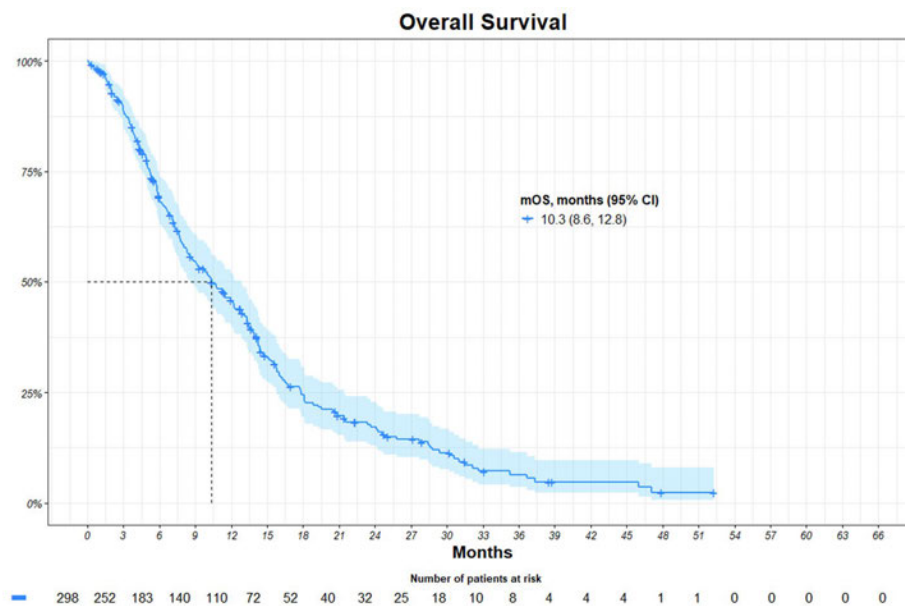


Figure 69 OS 4th line – Dahl et al., 2025



402 patients experienced an event. 119 (22.8%) of patients were censored.

Figure 70 OS 5th line – Dahl et al., 2025



231 patients experienced an event. 67 (22.5%) of patients were censored.

Given the indication for SG in the current application, both the 4th and 5th lines were deemed relevant for comparison with TPC's predicted OS. The available predicted OS shares from the 4th and 5th lines are compared with the model extrapolations in Table 70.



Table 70 TPC predicted OS extrapolations – landmarks

Extrapolation	Year 1	Year 2	Year 3	Year 4	Year 5	Year 10	Year 15	Year 20
OS – Overall patient 4 th line, n= 761 (Dahl et al., 2025)	43.64%	19.11%	8.02%	4.76%	2.90%	N/A	N/A	N/A
OS - Overall patient 5 th line, n= 493 (Dahl et al., 2025)	37.78%	12.79%	5.69%	2.86%	0.74%*	N/A	N/A	N/A
Weibull	54.29%	20.63%	6.42%	1.72%	0.40%	0.00%	0.00%	0.00%
Lognormal	49.37%	21.53%	10.77%	5.96%	3.55%	0.50%	0.12%	0.04%
Log-logistic	50.15%	20.66%	10.59%	6.35%	4.21%	1.13%	0.52%	0.30%
Exponential	48.88%	23.73%	11.52%	5.59%	2.71%	0.07%	0.00%	0.00%
Generalised Gamma	51.13%	20.66%	8.79%	3.98%	1.90%	0.08%	0.01%	0.00%
Gompertz	53.29%	22.28%	6.72%	1.29%	0.13%	0.00%	0.00%	0.00%
Gamma	53.49%	20.19%	6.86%	2.21%	0.69%	0.00%	0.00%	0.00%

Note: *Last endpoint for KM OS 5th line is at 52.3 months.

Compared with the available data, the extrapolated TPC shares show relatively consistent predictions across the distributions, although the predicted values are closer to the 4th-line than to 5th-line. However, a few extrapolations predict lower OS survival compared to the RWE after year 3, such as the gamma and Weibull models. The log-



logistic model fits the RWE of 4th-line patients while preserving some long-term survivors, as confirmed through clinical interviews (Gilead, 2026a, 2026b, 2026c). It was therefore considered the best model to align with the external data.

For reference, SG predicted OS shares are listed in Table 71. Compared with the RWE, a few models predict lower survival rates at year 5, such as Weibull, gamma, Gompertz and generalised gamma. Only the log-logistic and lognormal models predict small shares of long-term survivors, in line with the estimates of clinical experts (Gilead, 2026a, 2026b, 2026c) and the TPC arm.

Table 71 SG predicted OS extrapolations – landmarks

Extrapolation	Year 1	Year 2	Year 3	Year 4	Year 5	Year 10	Year 15	Year 20
OS – Overall patient 4 th line, n= 761 (Dahl et al., 2025)	43.64%	19.11%	8.02%	4.76%	2.90%	0.00%	0.00%	0.00%
OS - Overall patient 5 th line, n= 493 (Dahl et al., 2025)	37.78%	12.79%	5.69%	2.86%	0.74%	0.00%	0.00%	0.00%
Weibull								
Lognormal								
Log-logistic								
Exponential								
Generalised Gamma								
Gompertz								



Gamma



E.1.3 Extrapolations of TTD

The TTD curves were complete. In accordance with guidance from the DMC and NICE TSD 14 guidance (Nicholas Latimer, 2013), standard survival parametric curves were fitted, and a measure of statistical fit was evaluated through AIC and BIC criteria. Given the completion of the TTD curves, more attention was given to the goodness-of-fit for the model selection. To maintain consistency with the other extrapolated endpoints, models were fit independently. Extrapolations were applied to the data, which was preferred over using the KM curves, a trial-specific, non-parametric step function reflecting the structure and events of the pooled trials. Nevertheless, the difference between the selected models and the KM curves is minimal.

E.1.3.1 Log-cumulative hazard plots and residual plots - TTD

Figure 71 to Figure 73 show the diagnostic plots for TTD. In the Schoenfeld residual graph, a clear downward trend is evident, with some residuals showing on the line. However, in the log-cumulative hazard plot, the two treatment arms do not cross and remain parallel. Therefore, the proportional hazards assumption could not be entirely ruled out, but it was preferred to fit models independently in line with DMC recommendations.

Figure 71 TTD Pooled meta-analysis, Schoenfeld residuals

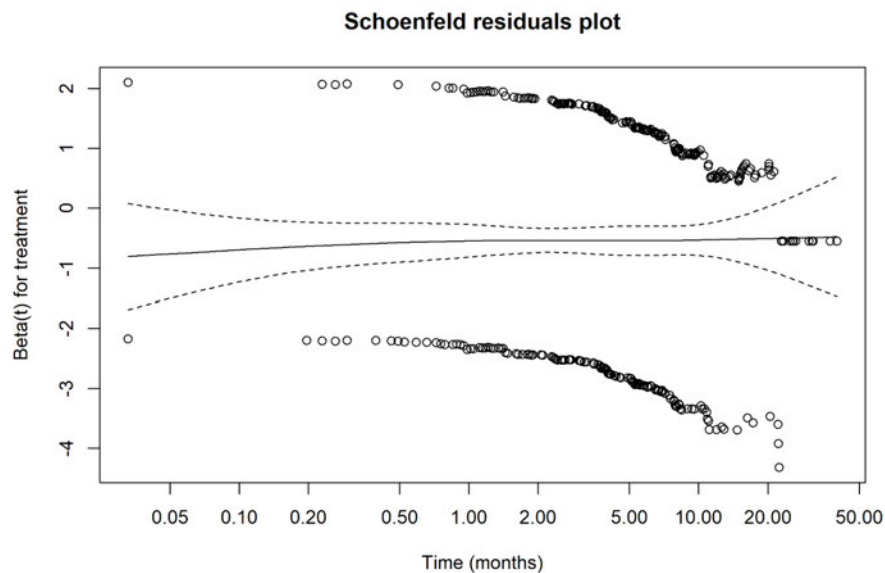




Figure 72 TTD Pooled meta-analysis, Log-cumulative hazard plot

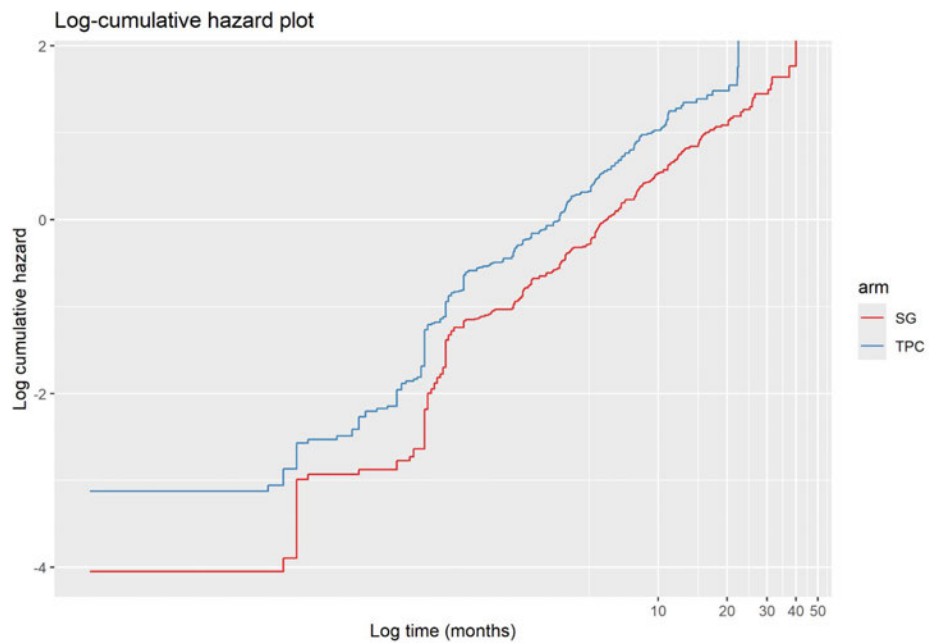
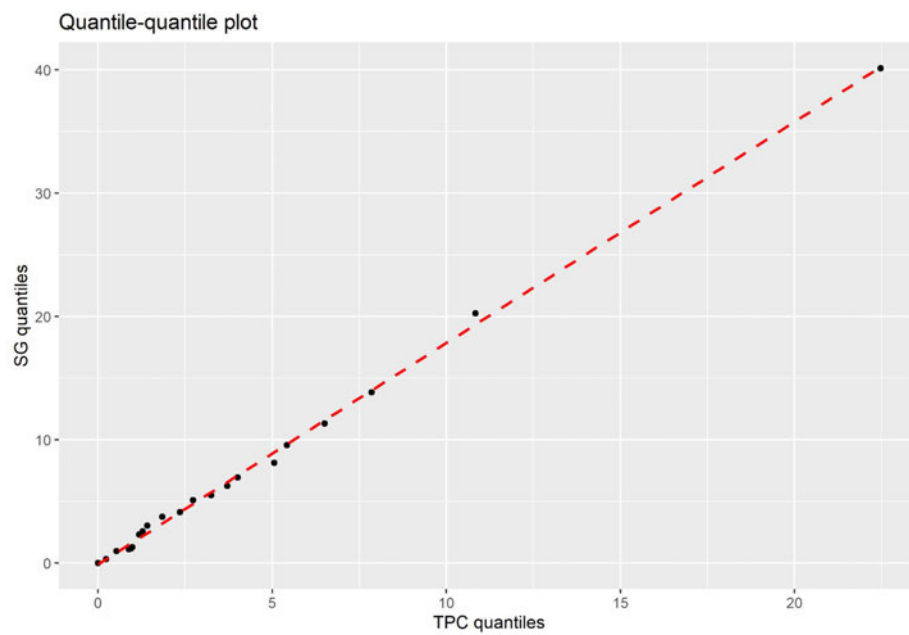


Figure 73 TTD Pooled meta-analysis, Q-Q plot



E.1.3.2 Internal validity

E.1.3.2.1 Assessment of statistical and visual fit (AIC and BIC) – TTD

Visual fit was assessed by evaluating the shape of the parametric and observed KM curves. Clinical plausibility was evaluated by comparing the shape of the hazard function with the smoothed hazards from the clinical trial data.



For SG TTD, most curves have a good visual fit, with only marginal differences among them, except for the lognormal and log-logistic. Based on both AIC and BIC, the exponential model is the best candidate, while gamma, Weibull and Gompertz remain suitable alternatives. SG's goodness-of-fit statistics with the relative Δ AIC and Δ BIC are shown in Table 72.

Table 72 TTD goodness-of-fit statistics – SG

Distribution	AIC	BIC	Δ AIC	Δ BIC	Combined Δ
Exponential	1956.32	1960.17	0.00	0.00	0.00
Gompertz	1957.86	1965.55	1.54	5.39	6.93
Gamma	1958.20	1965.90	1.88	5.73	7.62
Weibull	1958.32	1966.02	2.00	5.85	7.85
Generalized Gamma	1958.50	1970.05	2.18	9.88	12.06
Log-logistic	1986.09	1993.79	29.77	33.62	63.39
Lognormal	2003.21	2010.91	46.90	50.75	97.64

For TPC, all models closely matched the KM shape, except the lognormal. Concerning goodness-of-fit statistics, the results are shown in Table 73. The exponential model was the global minimum for both AIC and BIC. Weibull, Gompertz and gamma models were suitable candidates, with both Δ AIC and Δ BIC below 6. The other models exhibited poor fit.

Table 73 TTD goodness-of-fit statistics – TPC

Distribution	AIC	BIC	Δ AIC	Δ BIC	Combined
Exponential	1468.62	1472.40	0.00	0.00	0.00
Gompertz	1469.96	1477.54	1.34	5.13	6.48
Weibull	1470.60	1478.17	1.98	5.77	7.75
Gamma	1470.61	1478.19	2.00	5.78	7.78
Generalized Gamma	1472.09	1483.46	3.48	11.05	14.53
Log-logistic	1500.27	1507.85	31.66	35.44	67.10
Lognormal	1531.12	1538.70	62.50	66.29	128.80



E.1.3.2.2 Assessment of smoothed hazard functions - TTD

The smoothed hazards for SG and TPC in TTD are shown in Figure 74 to Figure 80, and in Figure 81 to Figure 87, respectively, compared with the non-parametric smoothed hazard from the clinical trial. For both treatment arms, the hazards show an upward trend toward the end of the trial period due to a few subjects remaining at risk. However, for both arms, the smoothed hazard is flat before month 30. Therefore, given the goodness-of-fit statistics, both arms were extrapolated using the exponential model, which aligns well with the observed hazard shapes prior to the final period.

Figure 74 Smoothed hazard, TTD, SG - Exponential

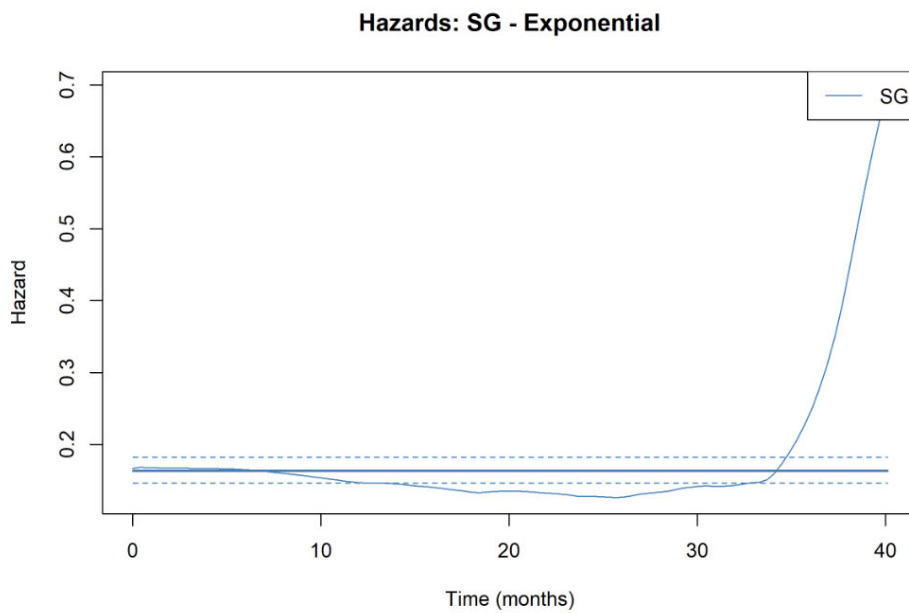


Figure 75 Smoothed hazard, TTD, SG - Weibull

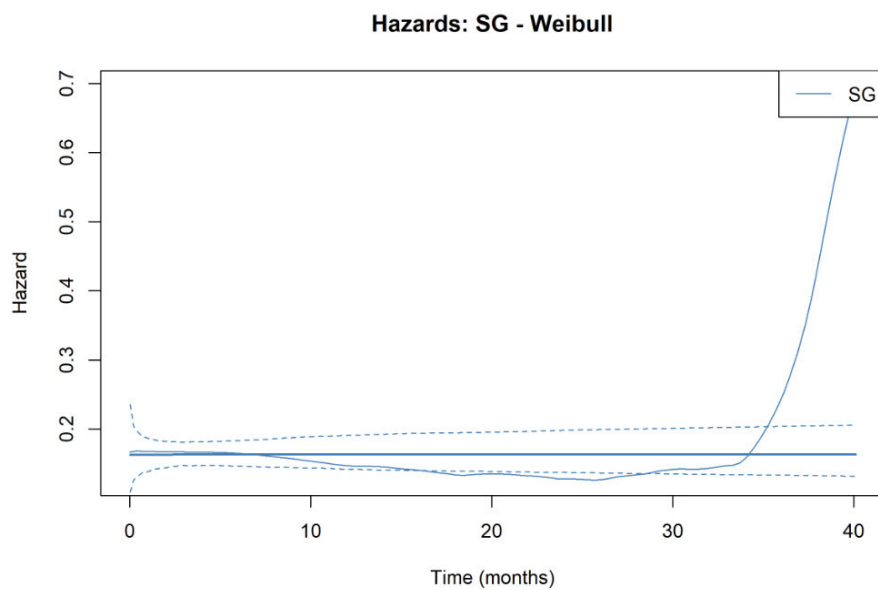




Figure 76 Smoothed hazard, TTD, SG - Gompertz

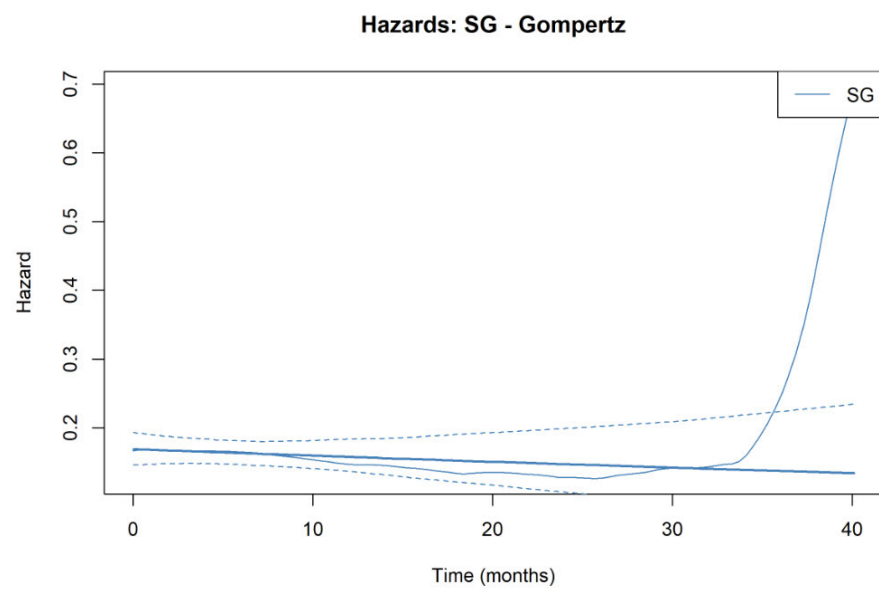


Figure 77 Smoothed hazard, TTD, SG - Gamma

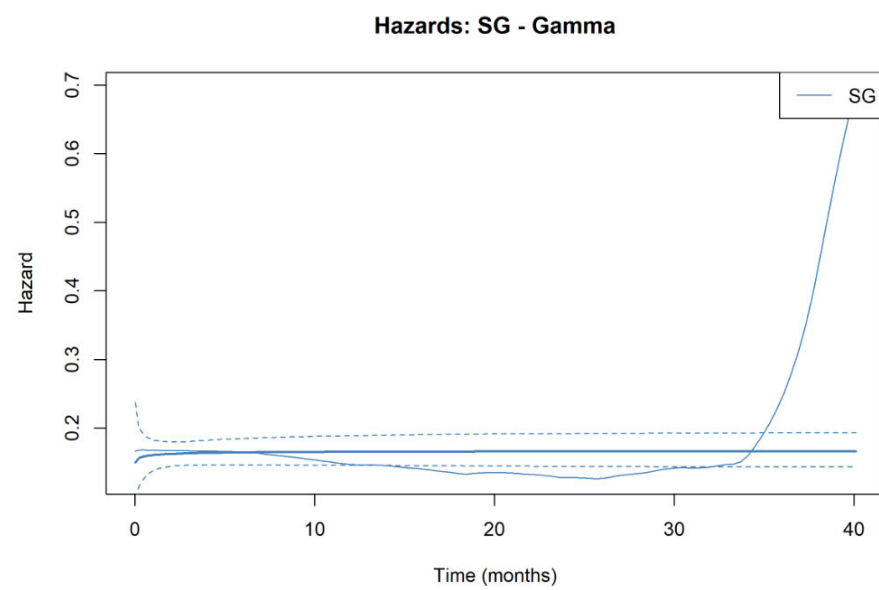




Figure 78 Smoothed hazard, TTD, SG - Lognormal

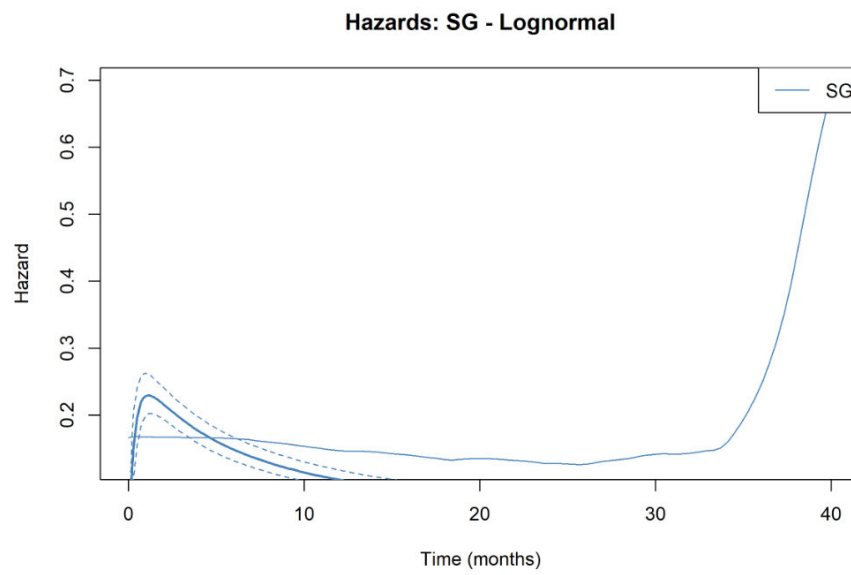


Figure 79 Smoothed hazard, TTD, SG - Log-logistic

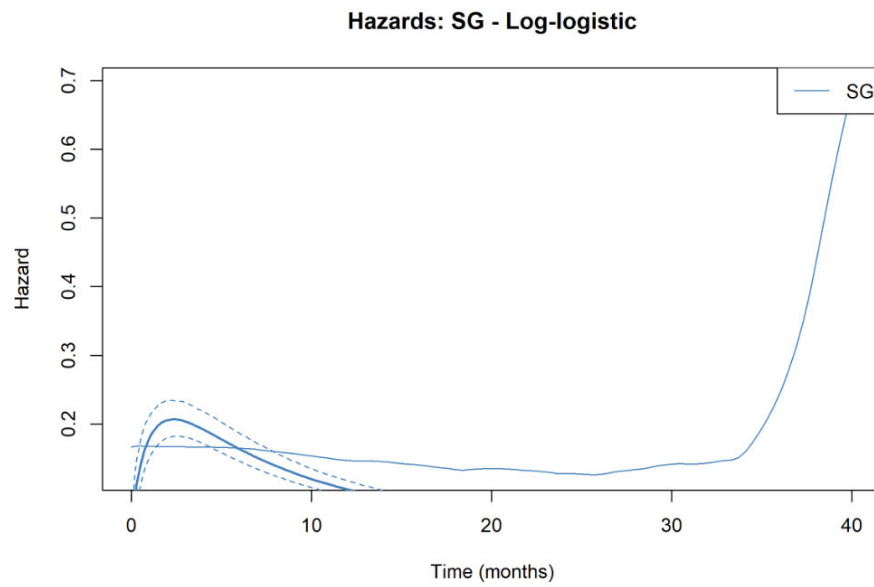




Figure 80 Smoothed hazard, TTD, SG - Generalised gamma

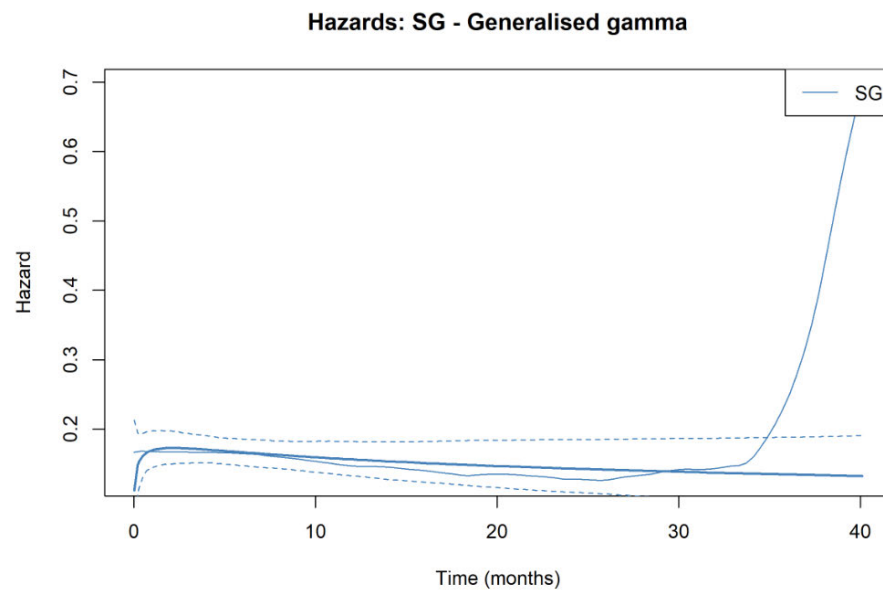


Figure 81 Smoothed hazard, TTD, TPC - Exponential

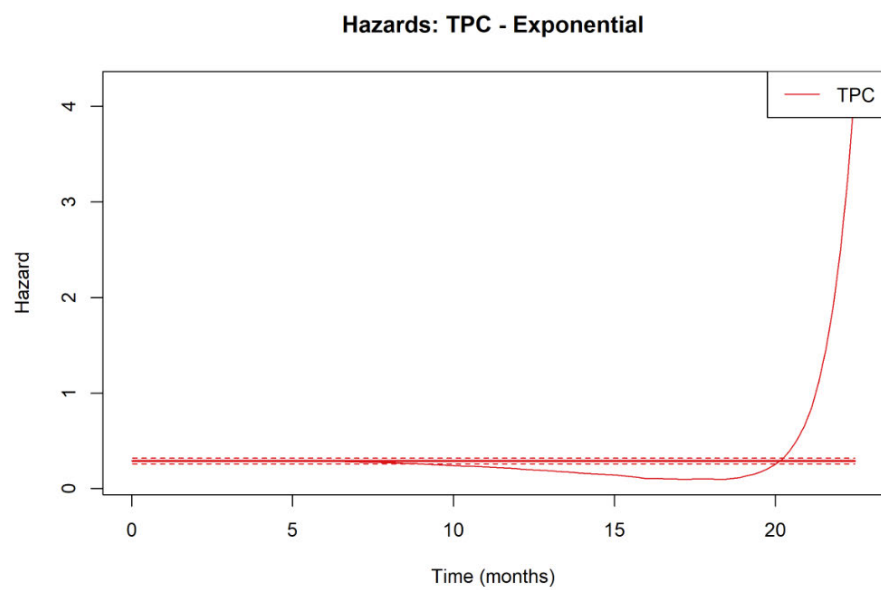




Figure 82 Smoothed hazard, TTD, TPC - Weibull

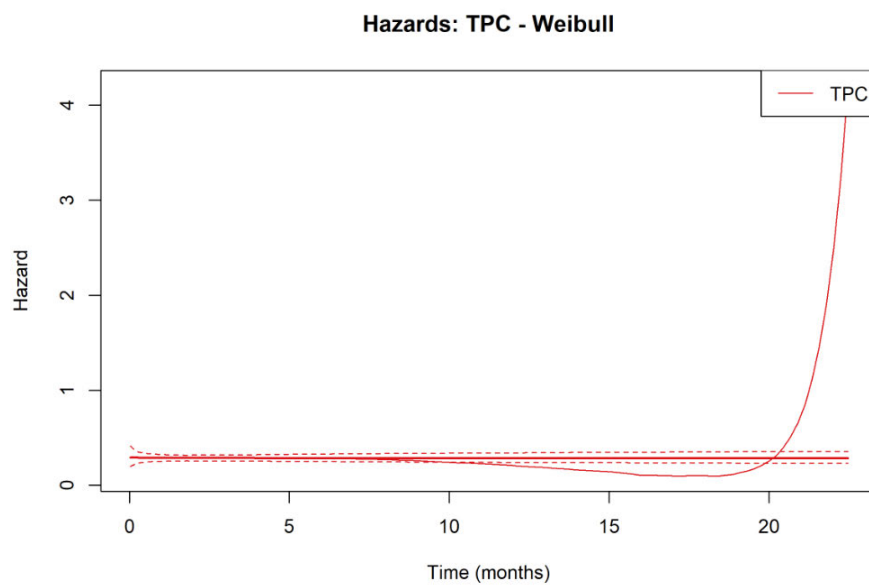


Figure 83 Smoothed hazard, TTD, TPC - Gompertz

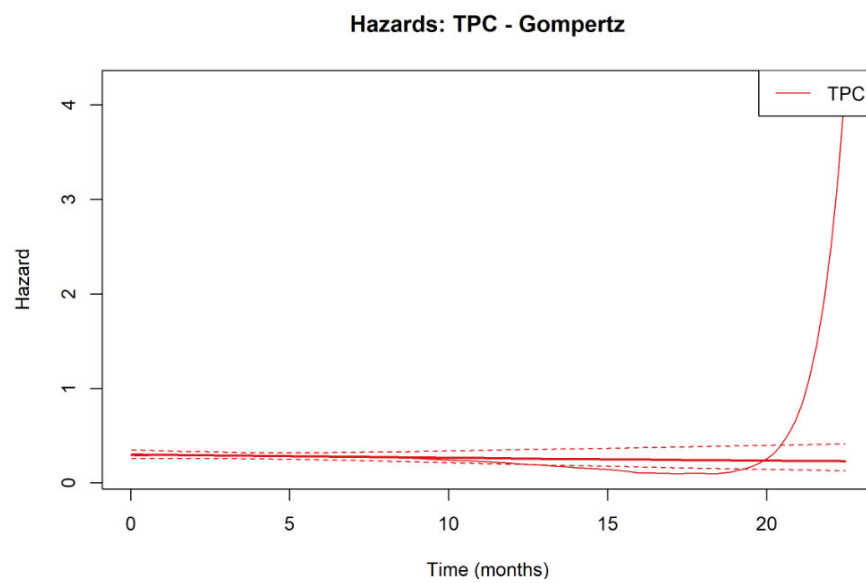




Figure 84 Smoothed hazard, TTD, TPC - Gamma

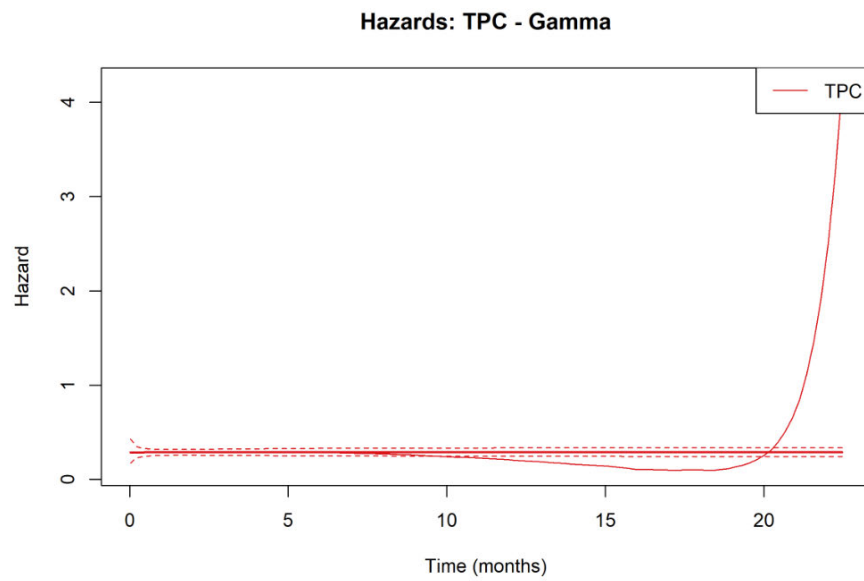


Figure 85 Smoothed hazard, TTD, TPC - Lognormal

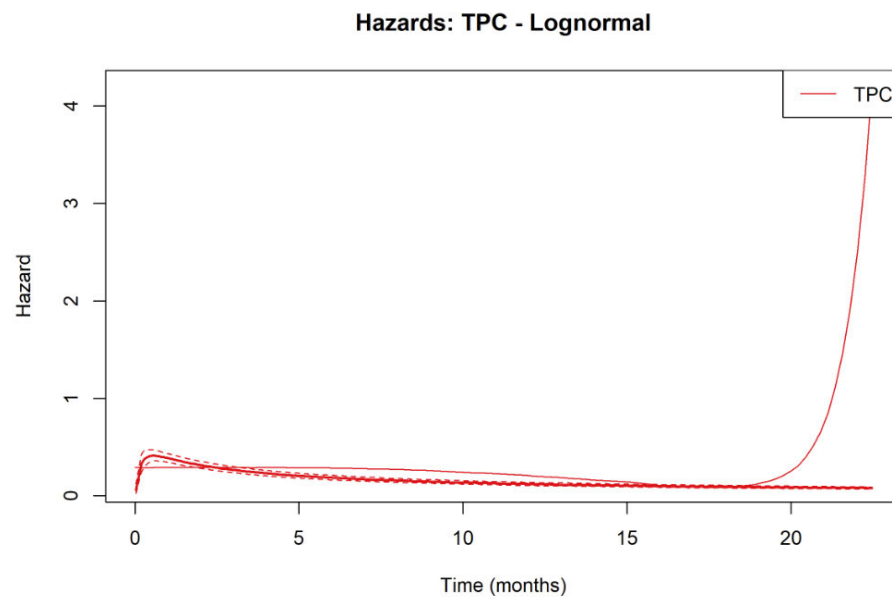




Figure 86 Smoothed hazard, TTD, TPC - Log-logistic

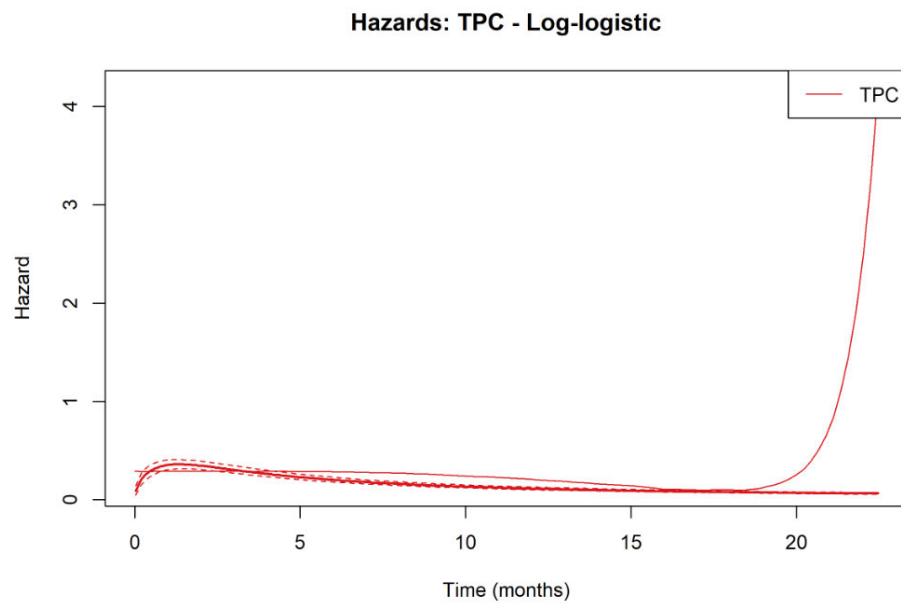
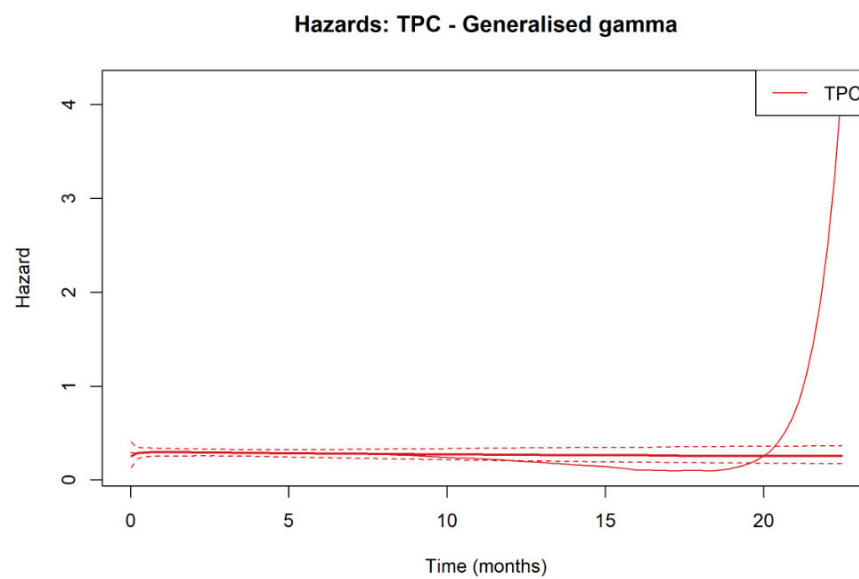


Figure 87 Smoothed hazard, TTD, TPC – Generalised gamma



E.1.3.3 External validity

External validity was not evaluated for TTD due to a lack of data.

E.2 Transition probabilities N/A

E.2.1 Internal validity

E.2.2 External validity



E.2.3 Other assumptions

Appendix F. Serious adverse events

Table 74. Treatment Emergent Serious Adverse Events - Safety population pooled analysis

System organ class preferred term	SG N=433	TPC N=413
Subjects with any treatment emergent SAE	112 (25.87%)	80 (19.37%)
Blood and lymphatic system disorders	37 (8.55%)	27 (6.54%)
Febrile neutropenia	18 (4.16%)	13 (3.15%)
Neutropenia	15 (3.46%)	9 (2.18%)
Anaemia	4 (0.92%)	2 (0.48%)
Thrombocytopenia	3 (0.69%)	3 (0.73%)
Leukopenia	1 (0.23%)	0 (0.00%)
Thrombocytosis	0 (0.00%)	1 (0.24%)
Lymphopenia	1 (0.23%)	0 (0.00%)
Myelosuppression	1 (0.23%)	0 (0.00%)
Cardiac disorders	5 (1.15%)	2 (0.48%)
Myocardial infarction	1 (0.23%)	1 (0.24%)
Arrhythmia	2 (0.46%)	0 (0.00%)
Cardiac failure	0 (0.00%)	1 (0.24%)
Myocardial ischaemia	1 (0.23%)	0 (0.00%)
Left ventricular dysfunction	1 (0.23%)	0 (0.00%)
Endocrine disorders	1 (0.23%)	0 (0.00%)
Secondary adrenocortical insufficiency	1 (0.23%)	0 (0.00%)
Eye disorders	1 (0.23%)	0 (0.00%)



Blepharospasm	1 (0.23%)	0 (0.00%)
Gastrointestinal disorders	40 (9.24%)	15 (3.63%)
Diarrhoea	17 (3.93%)	1 (0.24%)
Nausea	2 (0.46%)	5 (1.21%)
Vomiting	6 (1.39%)	2 (0.48%)
Abdominal pain	8 (1.85%)	3 (0.73%)
Colitis	4 (0.92%)	1 (0.24%)
Neutropenic colitis	5 (1.15%)	0 (0.00%)
Enteritis	1 (0.23%)	1 (0.24%)
Ascites	1 (0.23%)	2 (0.48%)
Gastroesophageal reflux disease	1 (0.23%)	0 (0.00%)
Impaired gastric emptying	1 (0.23%)	0 (0.00%)
Large intestine perforation	1 (0.23%)	0 (0.00%)
Stomatitis	1 (0.23%)	1 (0.24%)
Abdominal distension	1 (0.23%)	0 (0.00%)
Constipation	0 (0.00%)	1 (0.24%)
Haemorrhoids	1 (0.23%)	0 (0.00%)
Ileus	1 (0.23%)	0 (0.00%)
Intestinal obstruction	1 (0.23%)	0 (0.00%)
Pancreatitis	0 (0.00%)	1 (0.24%)
General disorders and administration site conditions	10 (2.31%)	8 (1.94%)
Pyrexia	4 (0.92%)	4 (0.97%)
Fatigue	2 (0.46%)	1 (0.24%)
General physical health deterioration	1 (0.23%)	1 (0.24%)
Asthenia	1 (0.23%)	1 (0.24%)



Mucosal inflammation	1 (0.23%)	0 (0.00%)
Oedema peripheral	0 (0.00%)	1 (0.24%)
Pain	1 (0.23%)	0 (0.00%)
Malaise	0 (0.00%)	1 (0.24%)
Hepatobiliary disorders	3 (0.69%)	0 (0.00%)
Cholangitis	1 (0.23%)	0 (0.00%)
Cholangitis acute	1 (0.23%)	0 (0.00%)
Hyperbilirubinaemia	1 (0.23%)	0 (0.00%)
Hepatic cyst	1 (0.23%)	0 (0.00%)
Infections and infestations	37 (8.55%)	16 (3.87%)
Pneumonia	6 (1.39%)	7 (1.69%)
Urinary tract infection	4 (0.92%)	2 (0.48%)
Sepsis	4 (0.92%)	1 (0.24%)
COVID-19 pneumonia	2 (0.46%)	1 (0.24%)
Pyelonephritis	2 (0.46%)	1 (0.24%)
Septic shock	3 (0.69%)	0 (0.00%)
Anal abscess	0 (0.00%)	1 (0.24%)
COVID-19	4 (0.92%)	0 (0.00%)
Clostridium difficile colitis	1 (0.23%)	0 (0.00%)
Clostridium difficile infection	1 (0.23%)	0 (0.00%)
Device related infection	1 (0.23%)	0 (0.00%)
Diverticulitis	1 (0.23%)	0 (0.00%)
Escherichia bacteraemia	1 (0.23%)	0 (0.00%)
Herpes zoster disseminated	2 (0.46%)	0 (0.00%)
Lower respiratory tract infection viral	1 (0.23%)	0 (0.00%)
Mastitis	0 (0.00%)	1 (0.24%)



Peritonitis	2 (0.46%)	0 (0.00%)
Pneumocystis jirovecii infection	1 (0.23%)	0 (0.00%)
Tooth abscess	0 (0.00%)	1 (0.24%)
Urosepsis	1 (0.23%)	0 (0.00%)
Vascular device infection	1 (0.23%)	0 (0.00%)
Wound infection	1 (0.23%)	0 (0.00%)
Enterocolitis infectious	1 (0.23%)	0 (0.00%)
Febrile infection	1 (0.23%)	0 (0.00%)
Localised infection	0 (0.00%)	1 (0.24%)
Periodontitis	0 (0.00%)	1 (0.24%)
Upper respiratory tract infection	1 (0.23%)	0 (0.00%)
Injury, poisoning and procedural complications	3 (0.69%)	4 (0.97%)
Compression fracture	0 (0.00%)	1 (0.24%)
Fall	0 (0.00%)	1 (0.24%)
Femoral neck fracture	0 (0.00%)	1 (0.24%)
Femur fracture	1 (0.23%)	0 (0.00%)
Pelvic fracture	1 (0.23%)	0 (0.00%)
Procedural pneumothorax	0 (0.00%)	1 (0.24%)
Tibia fracture	1 (0.23%)	0 (0.00%)
Thoracic vertebral fracture	0 (0.00%)	1 (0.24%)
Investigations	4 (0.92%)	2 (0.48%)
Blood glucose decreased	1 (0.23%)	0 (0.00%)
Liver function test increased	1 (0.23%)	0 (0.00%)
Alanine aminotransferase increased	1 (0.23%)	2 (0.48%)
Aspartate aminotransferase increased	0 (0.00%)	2 (0.48%)
Blood bilirubin increased	1 (0.23%)	0 (0.00%)



Metabolism and nutrition disorders	6 (1.39%)	4 (0.97%)
Dehydration	2 (0.46%)	2 (0.48%)
Hypercalcaemia	2 (0.46%)	1 (0.24%)
Decreased appetite	1 (0.23%)	0 (0.00%)
Hyperkalaemia	1 (0.23%)	0 (0.00%)
Hypokalaemia	0 (0.00%)	1 (0.24%)
Musculoskeletal and connective tissue disorders	5 (1.15%)	5 (1.21%)
Arthralgia	1 (0.23%)	1 (0.24%)
Muscular weakness	0 (0.00%)	2 (0.48%)
Osteonecrosis of jaw	1 (0.23%)	0 (0.00%)
Bone pain	3 (0.69%)	0 (0.00%)
Back pain	0 (0.00%)	3 (0.73%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (0.23%)	0 (0.00%)
Tumour pain	1 (0.23%)	0 (0.00%)
Nervous system disorders	3 (0.69%)	4 (0.97%)
Headache	0 (0.00%)	2 (0.48%)
Cerebral haemorrhage	1 (0.23%)	0 (0.00%)
Cerebral ischaemia	1 (0.23%)	0 (0.00%)
Dizziness	0 (0.00%)	1 (0.24%)
Epilepsy	0 (0.00%)	1 (0.24%)
Nervous system disorder	1 (0.23%)	0 (0.00%)
Neuropathy peripheral	1 (0.23%)	0 (0.00%)
Transient ischaemic attack	1 (0.23%)	0 (0.00%)
Spinal cord compression	1 (0.23%)	0 (0.00%)
Product issues	1 (0.23%)	0 (0.00%)



Device leakage	1 (0.23%)	0 (0.00%)
Psychiatric disorders	1 (0.23%)	2 (0.48%)
Confusional state	0 (0.00%)	2 (0.48%)
Depression	1 (0.23%)	0 (0.00%)
Renal and urinary disorders	4 (0.92%)	2 (0.48%)
Acute kidney injury	3 (0.69%)	1 (0.24%)
Hydronephrosis	1 (0.23%)	0 (0.00%)
Nephrolithiasis	1 (0.23%)	0 (0.00%)
Urinary tract obstruction	0 (0.00%)	1 (0.24%)
Respiratory, thoracic and mediastinal disorders	11 (2.54%)	12 (2.91%)
Dyspnoea	2 (0.46%)	4 (0.97%)
Pleural effusion	4 (0.92%)	6 (1.45%)
Respiratory failure	1 (0.23%)	1 (0.24%)
Cough	1 (0.23%)	1 (0.24%)
Pneumothorax	1 (0.23%)	0 (0.00%)
Pulmonary embolism	1 (0.23%)	0 (0.00%)
Asphyxia	0 (0.00%)	1 (0.24%)
Interstitial lung disease	1 (0.23%)	0 (0.00%)
Skin and subcutaneous tissue disorders	1 (0.23%)	0 (0.00%)
Palmar-plantar erythrodysaesthesia syndrome	1 (0.23%)	0 (0.00%)
Vascular disorders	6 (1.39%)	2 (0.48%)
Embolism	2 (0.46%)	0 (0.00%)
Haematoma	1 (0.23%)	1 (0.24%)
Hypotension	1 (0.23%)	1 (0.24%)
Hypertension	2 (0.46%)	0 (0.00%)

Note: The population in the pooled analysis are based on the safety population from TROPiCS-02 SG: N=268; TPC: 249 and EVER-132-002 SG: N=156; TPC=152



Appendix G. Health-related quality of life N/A

The appendix is not applicable as all domains are in line with the guidelines, as described in section 10.

G.1 Data collection – overview of responses

[If a JCA has been performed, please refer to the relevant sections of the JCA report.]

G.2 Reporting of domains

[For each measurement, frequencies and proportions are presented for each domain and each level. The development over time (and possibly across treatment arms) is presented in figures.

If a JCA has been performed, reference is made to the relevant sections of the JCA report.]

G.3 Mapping

[Description of mapping study.]

G.4 Calculation of utility values

[Applicant must describe and justify how the utility values for the individual health states are calculated, including all necessary formulas to calculate the final utility values. The description should cover the choice of regression model, choice of explanatory variables, presentation of the final model and regression results (parameter estimates, standard errors and confidence intervals), validation of the final model, uncertainties and sensitivity analyses.]



Appendix H. Literature searches for the clinical assessment N/A

H.1 Effect and safety of intervention and comparators

[Describe the literature search, including purpose and search strategy. Explain the concepts used, any search filters and limitations.

Insert tables with databases and other sources used. Name, platform/website and date(s) of the searches must be provided. See examples of tables below.]

Example of table. Bibliographic databases

Database	Platform/Website	Date of search
PubMed/Medline	Ovid/https://pubmed.ncbi.nlm.nih.gov	dd.mm.yyyy
Embase	Ovid/www.embase.com	dd.mm.yyyy

Example of table. Other sources

Source	Website	Search strategy/ keywords used	Date of search
NICE	www.nice.org.uk	'non-small cell lung cancer'	dd.mm.yyyy

[The searches must be documented with search strings line by line, including the number of hits. They can be inserted into tables in this section or submitted as supplementary attachments in any format (e.g. Word or PDF).]

H.2 Systematic selection of studies and references

[Describe the selection process, including number of reviewers, and how disagreements were resolved.

Complete Table 75. with inclusion and exclusion criteria (PICOS) or replace with a corresponding table. If a broader systematic literature review (SLR) is used, it must be stated whether there are changes in the criteria for Danish conditions, e.g. in relation to



(smaller) population or (fewer) comparators.

Table 75 must be populated with studies/references that are included in the assessment, and Table 76 for the studies/references that are excluded. These must also be submitted in supplementary annexes.]

Table 75. Inclusion and exclusion criteria [must be deleted/replaced]

Clinical effect	Inclusion criteria	Exclusion criteria	Change, local adaptation
Population			
Intervention			
Comparators			
Outcome			
Study design/ publication type			
Limitations, e.g. language			

[Complete the PRISMA diagram below or replace with an equivalent one. If a broader SLR is used, the boxes for 'Local adaptation' must indicate how many studies/publications are transferred to and omitted from the Danish assessment.]

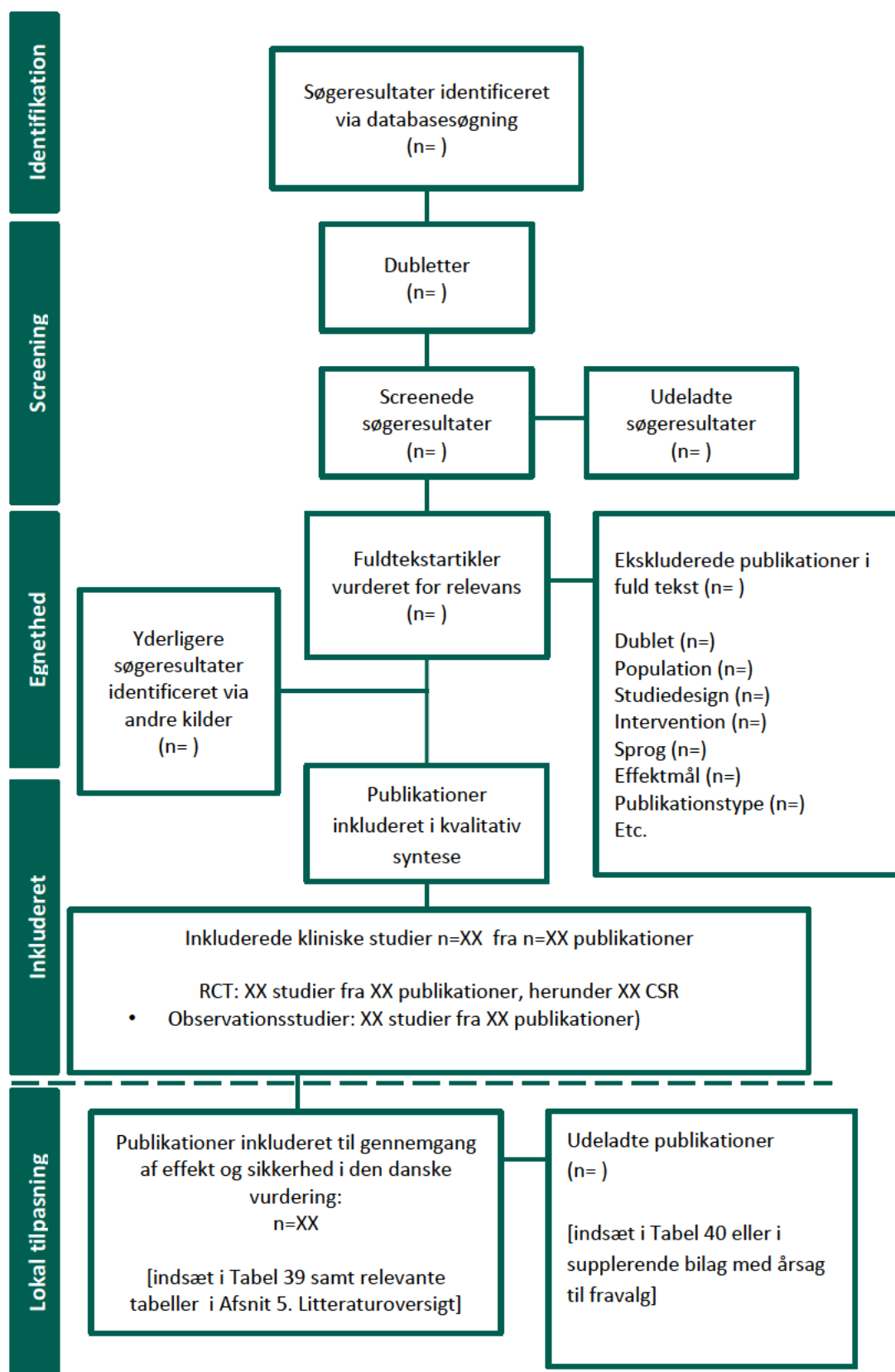




Table 76. Studies/references included in the Danish assessment

Study	Reference(s)
Study 1	
Study 2	

Table 77. Excluded studies/references [may alternatively be submitted as a supplementary appendix]

Study	Reference(s)
Study 1	
Study 2	

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

N/A

I.1 Systematic search

[Follow instructions/structure for appendix H. The tables can be copy-pasted as needed.]

I.2 Focused search

[Describe the purpose of the search and which sources were used, as well as the date of execution. The search must be documented/described to the fullest extent possible, including the search technique and keywords used, and criteria for relevance assessment.

Insert a table with identified references, and transfer the references included in the assessment to the relevant table in the Literature overview section.]



Appendix J. Literature searches for supplementary input to the health economic model N/A

J.1 Systematic search

N/A

J.2 Focused search

N/A

Appendix K. Reasons for confidential information

Table 78. Justifications regarding confidential information

Parameter	Justification
List of experts	Name, job title, and workplace of clinical experts
OS from EVER-132-002 Dec2024 DCO	The information has been redacted because it constitutes confidential business information not publicly available. The redacted data form part of Gilead’s proprietary analyses and commercial strategy. Public disclosure or release of the information in question would enable third parties to infer commercially sensitive parameters (including pricing strategy, patient estimates, or model assumptions), thereby weakening the company’s competitive position in the market. Disclosure would therefore cause significant commercial and financial harm to Gilead by placing competitors in a more advantageous position in current and future negotiations. Under Section 30(2) of the Public Access Act, the data should therefore not be subject to disclosure.
Dose delay SG	
RDI and Mean dose SG	
TTD	
OS data from EVER-132-002	Unpublished data.



Parameter	Justification
OS data from the pooled analysis	Unpublished data.
Extrapolation of OS	The extrapolation of OS is considered to be commercially sensitive.
Extrapolation of TTD	The extrapolation of TTD is considered to be commercially sensitive.
Average dose of SG	The average dose of SG is unpublished and was derived from patient-level data.

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