

COMPARISON OF 5-YEAR SURVIVAL AND ESTIMATED LIFE YEARS BETWEEN TWO DATA CUTS OF STUDY 309/KEYNOTE-775

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BACKGROUND

- The Study 309/KEYNOTE-775 trial was a Phase 3 trial, comparing the efficacy and safety of lenvatinib plus pembrolizumab (LEN+PEM) with treatment of physician's choice (TPC) (doxorubicin or paclitaxel) in adult women with advanced endometrial cancer who had disease progression after the receipt of at least one platinum-based therapy⁽¹⁾.
- A cost-effectiveness analysis (CEA) was conducted for the United States (US) and China⁽²⁾ that fitted parametric survival curves to overall survival (OS) data from the March 2022 data cut-off (DCO) of Study 309/KEYNOTE-775.
- The March 2022 DCO corresponded to the prespecified final OS analysis, which had a median follow-up of 18.7 months in the LEN+PEM arm and 12.2 months in the TPC arm.
- The OS hazard ratio (HR) for the all-comer population in this DCO was 0.65 (95% confidence interval [CI]: 0.55, 0.77) for LEN+PEM versus TPC.
- Updated results of Study 309/KEYNOTE-775 with a longer follow-up of approximately 5 years (February 2025 DCO) have recently been presented at the European Society for Medical Oncology (ESMO) Congress in 2025⁽³⁾ and reported in the Journal for ImmunoTherapy of Cancer⁽⁴⁾; the OS HR for the all-comer population was 0.66 (95% CI: 0.57, 0.77) for LEN+PEM versus TPC.

OBJECTIVE

- To compare estimates of 5-year survival and mean life years (LYs) between the final prespecified OS analysis (March 2022 DCO) and the 5-year follow-up (February 2025 DCO) of Study 309/KEYNOTE-775.
- This comparison investigates how longer trial follow-up impacts on previous estimates of both landmark survival at 5 years, and predictions of mean survival based on extrapolations of observed data.

METHODS

- Six parametric survival curves (exponential, generalized gamma, Gompertz, log-normal, log-logistic, Weibull) were fitted to OS data for each of the LEN+PEM and TPC arms, for each of the March 2022 and February 2025 DCOs.
 - Patient-level data were available for the 2022 DCO.
 - Recently published Kaplan-Meier (KM) data were digitized for the 2025 DCO using Engauge Digitizer Software; the Guyot algorithm⁽⁵⁾ was applied to generate pseudo-individual patient data.
- All parametric survival curves were considered for comparisons of 5-year survival and mean LYs between the two data cuts; when comparing incremental life years for LEN+PEM versus TPC between the two DCOs, the base-case survival curves from the previously published CEA were used (log-normal for LEN+PEM and log-logistic for TPC; selected based on statistical fit).
 - This approach was taken as the incremental life years are determined based on one of 36 combinations of survival distributions across LEN+PEM and TPC.
 - The same distributions were used for both DCOs to ensure comparability.
- Survival curves were plotted in Microsoft® Excel assuming a weekly cycle length, and survival was constrained such that the weekly probability of death could not fall below that of the age- and gender-matched general population, using life table data for England and Wales from the Office for National Statistics⁽⁶⁾.
 - The baseline age used to inform age- and gender-matched general population mortality estimates was 63.5 years (i.e. the mean baseline age of the all-comer population in the Study 309/KEYNOTE-775 trial).

RESULTS

- The OS extrapolations for the March 2022 DCO are presented in **Figure 1** and **Figure 2** for LEN+PEM and TPC, respectively.
- Corresponding extrapolations for the February 2025 DCO are presented in **Figure 3** and **Figure 4** for LEN+PEM and TPC, respectively.
- For each graph, the extrapolations are overlaid with the longest available KM curve for the relevant treatment arm (i.e. the KM data from the February 2025 DCO for LEN+PEM and TPC).

5-year survival

- 5-year survival estimates were informed by parametric models fitted to OS data from the March 2022 DCO and the observed KM data from the February 2025 DCO.
- Estimated 5-year survival for the 2022 DCO ranged between 10–17% for LEN+PEM, and 2–6% for TPC, across different distributions.
- Observed OS KM estimates at 5 years were higher than all predictions based on the March 2022 DCO: 20% for LEN+PEM and 7% for TPC.
- 5-year survival estimates for the 2022 and 2025 DCOs are shown in **Table 1** for LEN+PEM and TPC.

Table 1: 5-year survival estimates between the 2022 and 2025 DCO for LEN+PEM and TPC

Source of survival estimates	2022 DCO Exponential parametric model	2022 DCO Generalised Gamma parametric model	2022 DCO Gompertz parametric model	2022 DCO Log-logistic parametric model	2022 DCO Log-normal parametric model	2022 DCO Weibull parametric model	2025 KM data
LEN+PEM	12%	16%	13%	16%	17%	10%	20%
TPC	3%	5%	3%	6%	6%	2%	7%

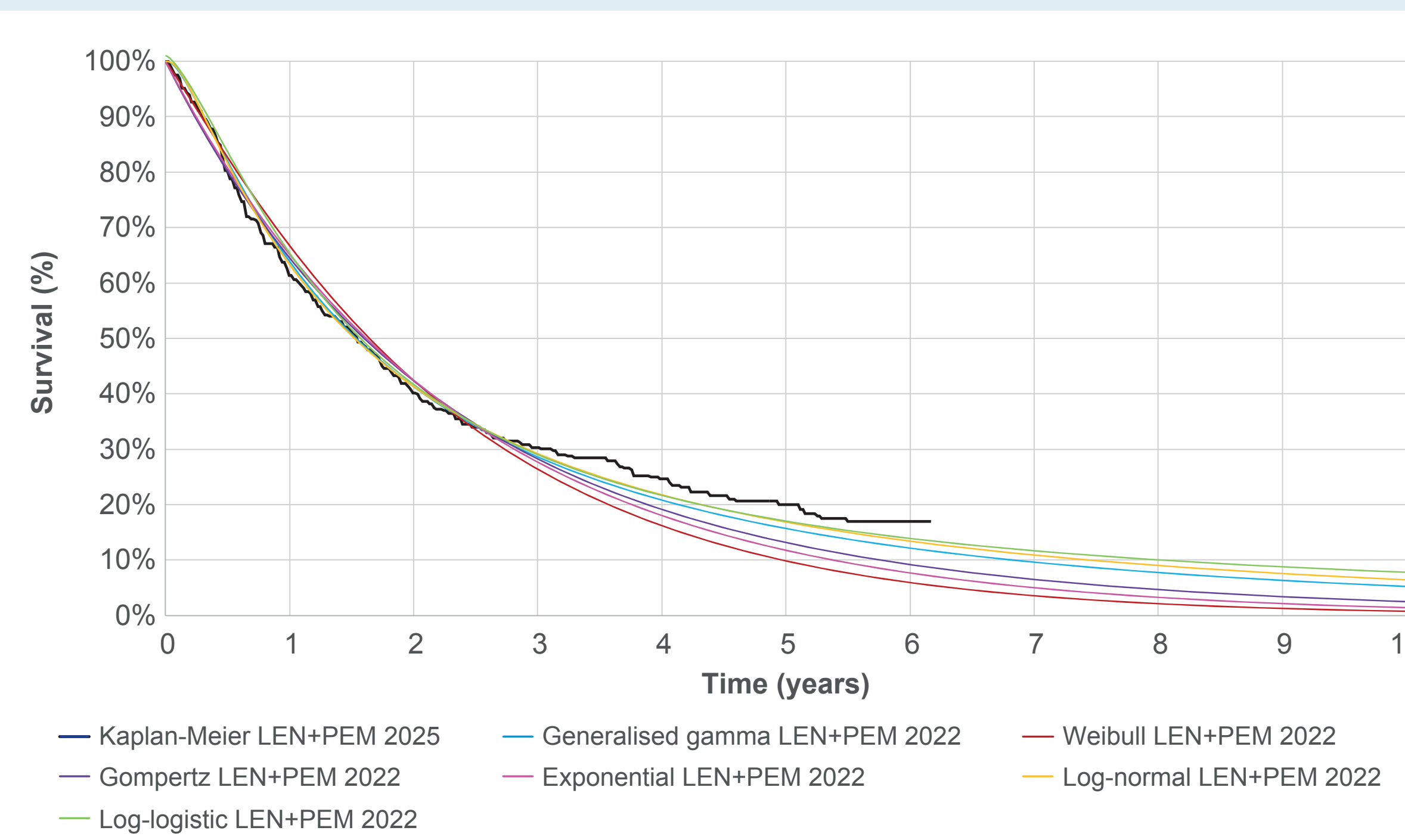
Abbreviations: DCO, data cut-off; KM, Kaplan Meier; LEN+PEM, lenvatinib plus pembrolizumab; TPC, treatment of physician's choice.

Table 2: Total LYs between the 2022 and 2025 DCO for LEN+PEM and TPC

Source of survival estimates	Exponential parametric model	Generalised Gamma parametric model	Gompertz parametric model	Log-logistic parametric model	Log-normal parametric model	Weibull parametric model
2022 DCO						
LEN+PEM	2.3	2.9	2.5	3.3	3.2	2.2
TPC	1.5	1.6	1.4	1.8	1.7	1.4
2025 DCO						
LEN+PEM	2.7	3.5	4.3	3.6	3.6	2.8
TPC	1.6	1.7	1.9	1.9	1.8	1.6

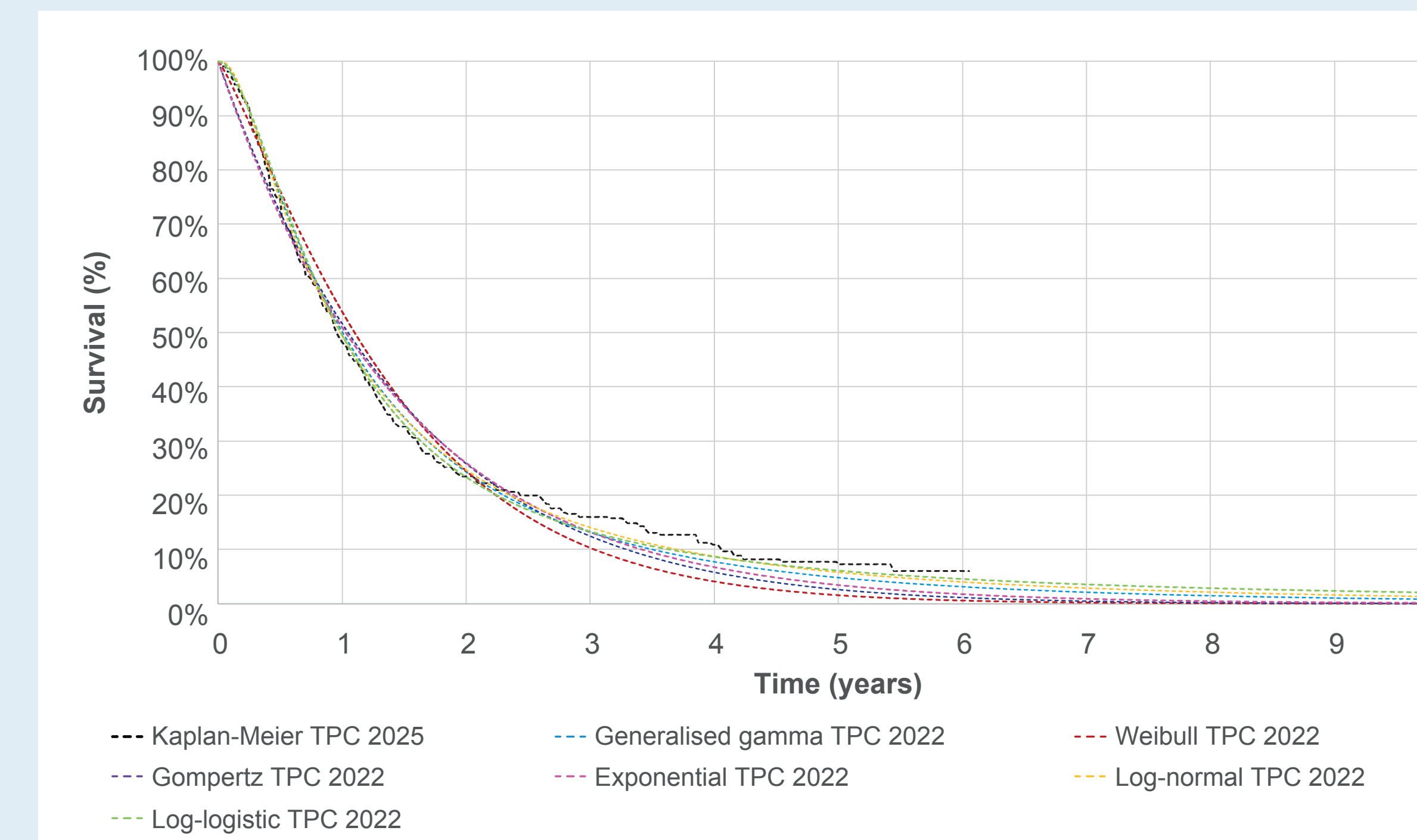
Abbreviations: DCO, data cut-off; LEN+PEM, lenvatinib plus pembrolizumab; LY, life year; TPC, treatment of physician's choice.

Figure 1: 2022 DCO parametric OS extrapolations and 2025 DCO KM curve for LEN+PEM



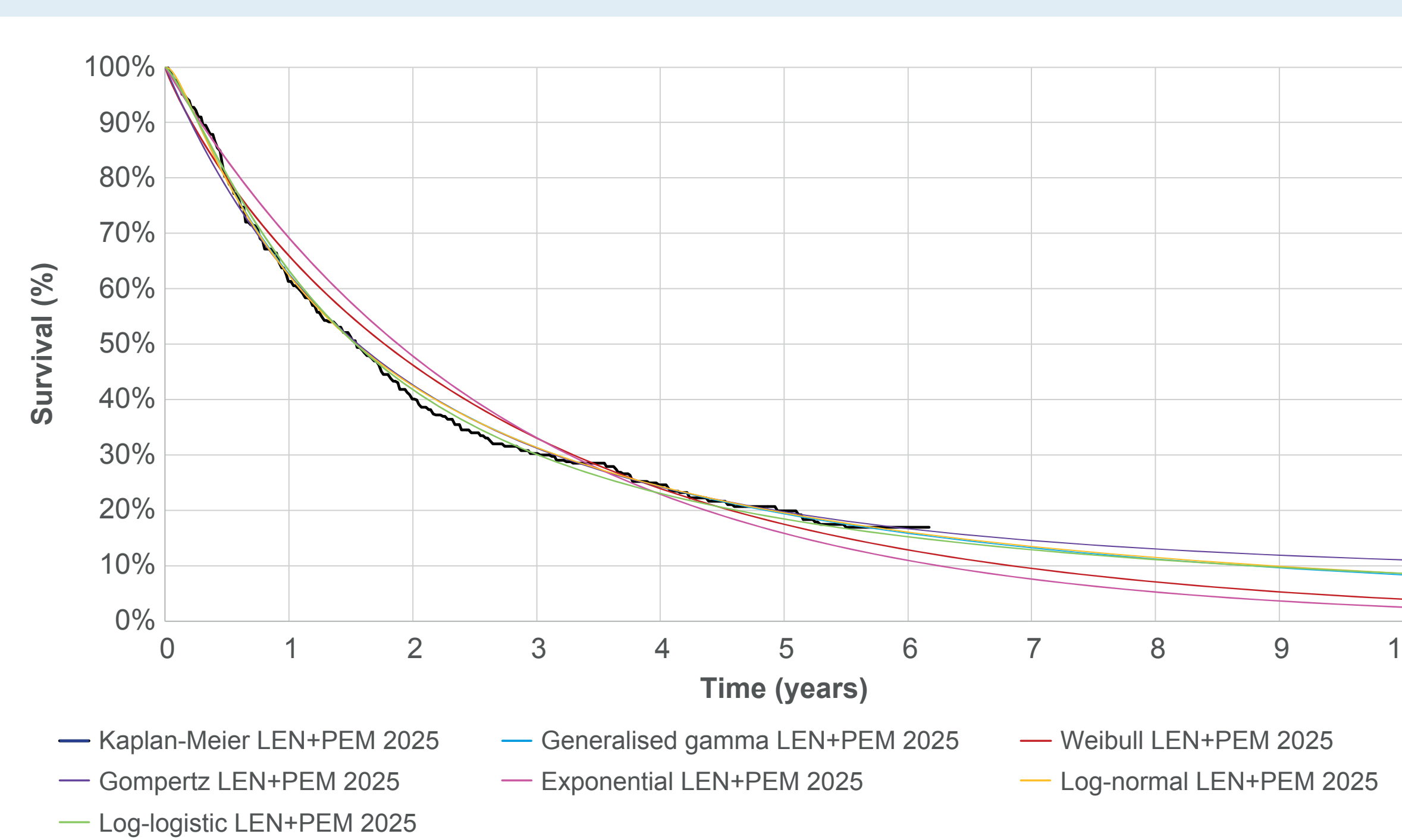
Abbreviations: DCO, data cut-off; KM, Kaplan Meier; LEN+PEM, lenvatinib plus pembrolizumab; OS, overall survival.

Figure 2: 2022 DCO parametric OS extrapolations and 2025 DCO KM curve for TPC



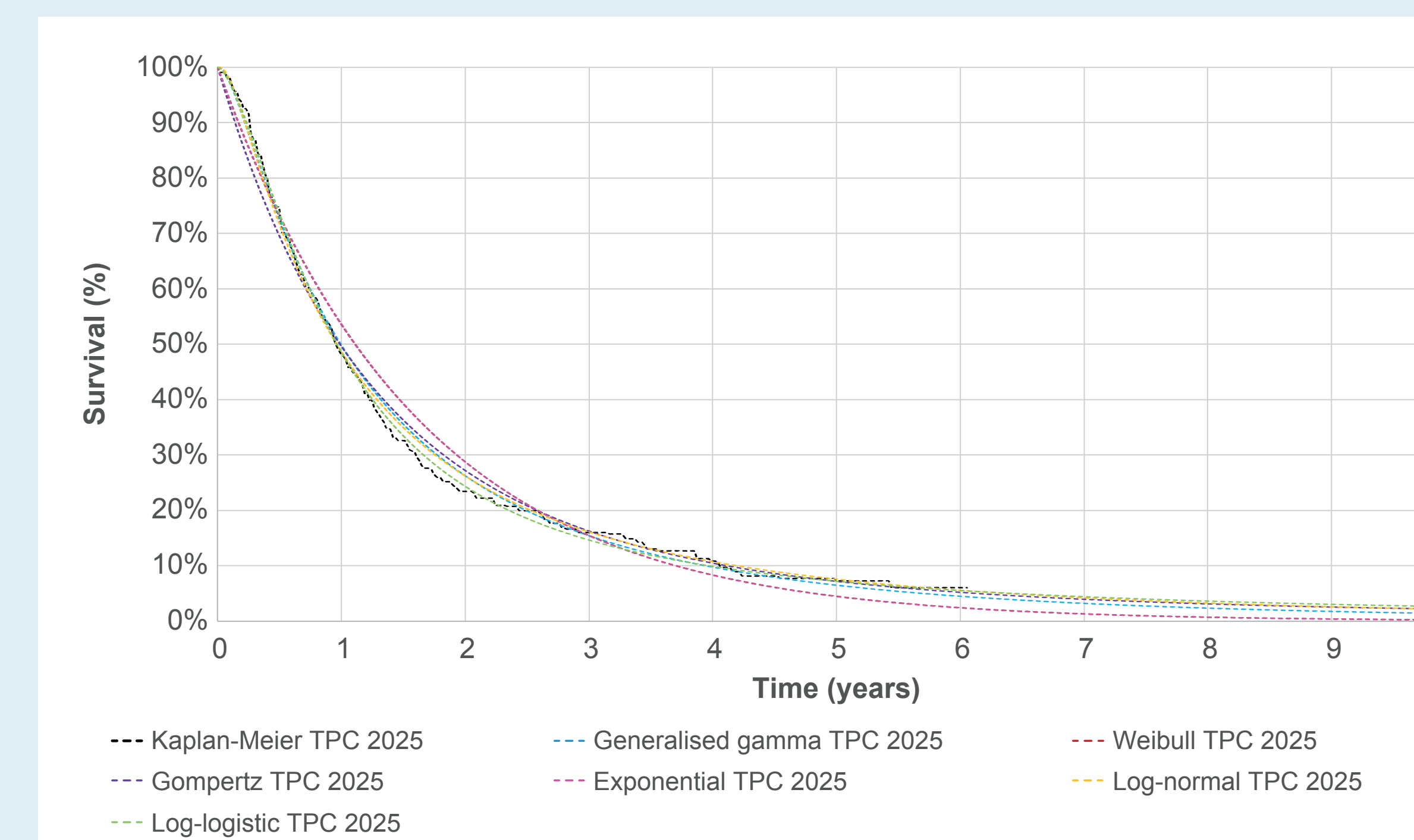
Abbreviations: DCO, data cut-off; KM, Kaplan Meier; OS, overall survival; TPC, treatment of physician's choice.

Figure 3: 2025 DCO parametric OS extrapolations and 2025 DCO KM curve for LEN+PEM



Abbreviations: DCO, data cut-off; KM, Kaplan Meier; LEN+PEM, lenvatinib plus pembrolizumab; OS, overall survival.

Figure 4: 2025 DCO parametric OS extrapolations and 2025 DCO KM curve for TPC



Abbreviations: DCO, data cut-off; KM, Kaplan Meier; OS, overall survival; TPC, treatment of physician's choice.

Estimated life years

- Total LYs across all six distributions increased from 2.2–3.3 for LEN+PEM and 1.4–1.8 for TPC using the 2022 DCO to 2.7–4.3 for LEN+PEM and 1.6–1.9 for TPC using the 2025 DCO.
- Using the log-normal distribution for LEN+PEM and the log-logistic distribution for TPC (chosen to align with selected distributions in the previously published CEA, which were based on statistical fit), incremental LYs were 1.4 for the 2022 DCO and 1.7 for the 2025 DCO.
- Total LYs for the two DCOs for LEN+PEM and TPC are presented in **Table 2**.

CONCLUSION

- Observed 5-year survival for LEN+PEM and TPC at the 2025 DCO exceeded estimates generated from 2022 DCO parametric curves using any of the six considered distributions.
- Incremental LYs increased between the two DCOs, while the OS HR remained consistent, suggesting no evidence of treatment effect waning for LEN+PEM versus TPC over 5 years.

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Disclosures

Qi Zhao and Carolyn Bodnar are employees of Eisai Inc. Iulia Dunnett, Elizabeth Hancock, and David Trueman are employees of Source Health Economics which received consultancy fees for analyses and medical writing services.

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