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When the tail wags the dog II:

how much of a mature overall-survival benefit still rests on assumption (TROPION-Breast02)

WHY THIS CASE STUDY

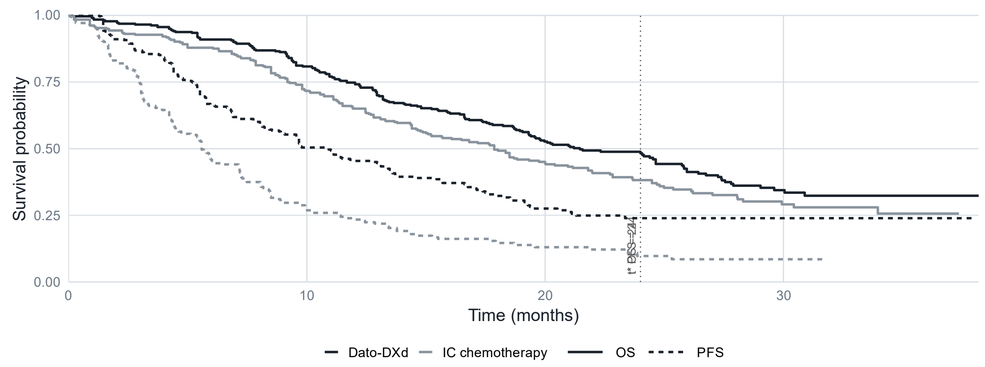
TROPION-Breast02 is the case that tests whether maturity is enough. Both overall-survival medians were reached, and the effect is statistically significant; by 24 months 47.7% and 54.5% of patients had died and the curves had fallen to 0.48 and 0.38. Reaching the median tells you the curves have descended through the middle. It says nothing about the tail, and the tail is where the mean lives.

BACKGROUND

Cost-effectiveness models in oncology are driven by extrapolated survival curves, and almost nobody reports how much of the modelled lifetime benefit was seen in the trial and how much was assumed beyond it. We introduced a new framework at ISPOR Philadelphia this year we called *When the tail wags the dog* [1] and in this series we apply the framework to five recent oncology trials each representing a different survival pattern. For each case study we report the share of the incremental gain arising after the data end, where in time that gain sits, and what changes when general-population mortality is placed underneath the extrapolation (relative survival [2]).

TROPION-Breast02

- Previously untreated inoperable or metastatic triple-negative breast cancer in patients not candidates for immunotherapy; median age 56 years, over 99% female.
- **Datopotamab deruxtecan** against **investigator's choice chemotherapy**.
- **Overall survival** — published hazard ratio 0.79 (95.01% CI 0.64–0.98), medians 23.7 against 18.7 months. 168 and 181 deaths among 323 and 321 patients.
- **Progression-free survival** — published hazard ratio 0.57 (99% CI 0.44–0.73), medians 10.8 against 5.6 months. 199 and 209 progression events in the same patients.
- The contrast is the whole case study: a mature, significant overall-survival benefit whose lifetime magnitude is still mostly assumed.
- Dent R, et al. *Ann Oncol* 2026;37(8):1066–1080. PMID 41937088.



Kaplan–Meier curves are reconstructed from the published figures [3,4]; all trial results quoted are as reported.

METHODS

Extrapolation

Pseudo-individual patient data were reconstructed from the published Kaplan–Meier curves [3,4]. Eight distributions were fitted jointly — one shared distribution with a treatment covariate on the location parameter and ancillary parameters common to both arms, so the two arms share a hazard shape and differ by a single treatment parameter — over a 40-year horizon [1]. All-cause fits are unconstrained; relative-survival fits model the excess hazard over ONS UK population mortality [2,5]. The median age and sex of the trial population, given in the case study above, index that life table, so the extrapolation sits above the mortality a general-population cohort of the same age and sex would experience.

t* separates the observed period from the extrapolated one and is not simply the maximum trial follow-up. Instead it is a judgement call, made from a reading of the reverse Kaplan–Meier curve for censoring [1]: it marks the end of reliable follow-up, before the risk sets are spent and before the two arms' censoring patterns diverge. t* is marked on the reconstructed Kaplan–Meier curves above.

Fits are compared on the Akaike and Bayesian information criteria (AIC and BIC), the standard fit statistics for choosing between parametric survival models. Both are reported for all eight distributions on each basis.

Transparency statistics

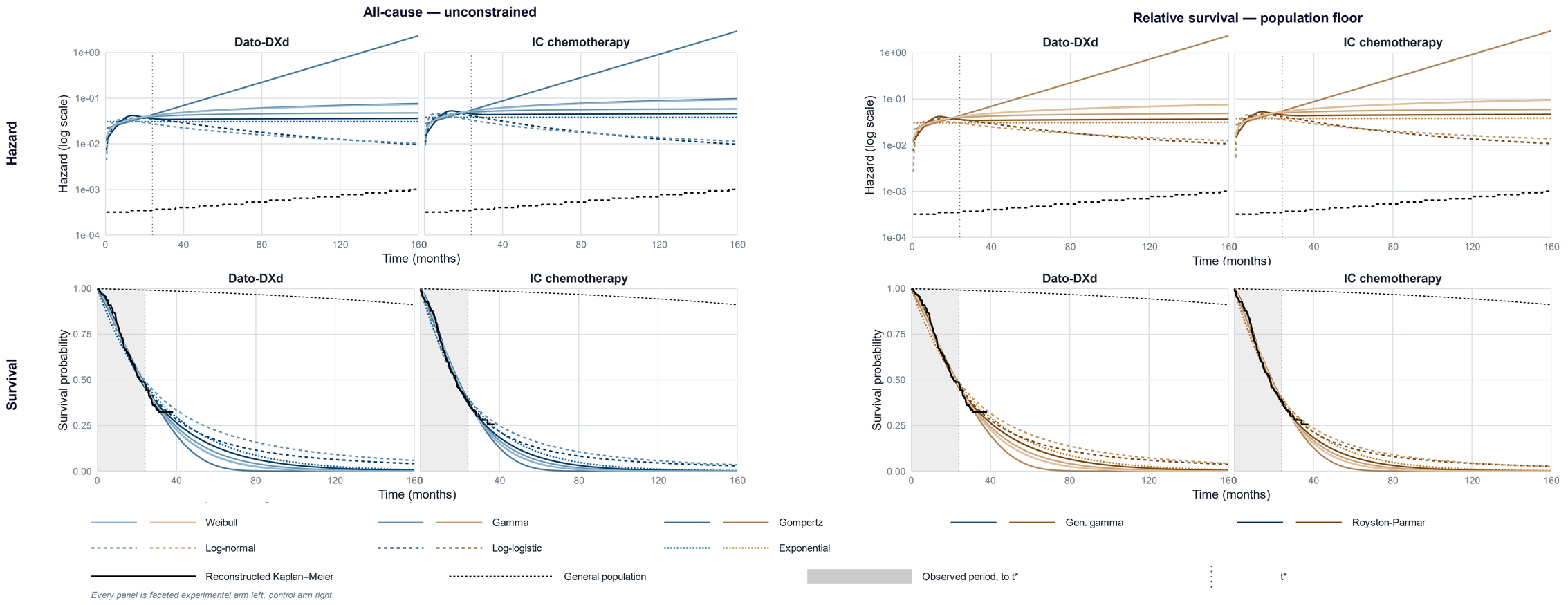
The area under each survival curve up to t* is the Restricted Mean Survival Time (RMST) and the period beyond t* is the Extrapolated Mean Survival Time (EMST). Added together they give the Unrestricted Mean Survival Time (UMST), which is the quantity that is compared between arms in an HTA / cost-effectiveness analysis:

- **ΔUMST** = ΔRMST + ΔEMST

From these quantities we form two transparency statistics [1]:

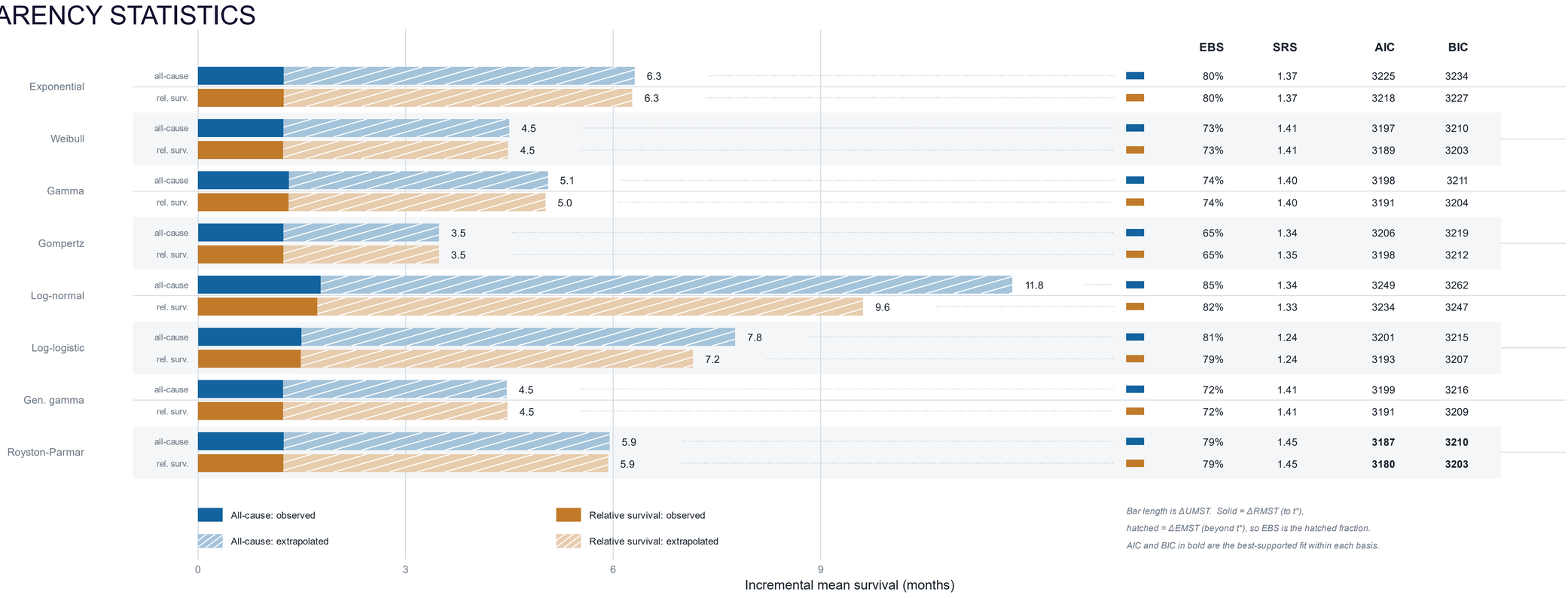
- **EBS** = ΔEMST / ΔUMST — the share of the incremental gain arising beyond the observed data.
- **SRS** = $(EMST_T/EMST_C) / (RMST_T/RMST_C)$ — above 1, the gain is concentrated in the extrapolated tail.

THE EXTRAPOLATION



Every panel is faceted experimental arm left, control arm right.

TRANSPARENCY STATISTICS



Bar length is ΔUMST. Solid = ΔRMST (to t), hatched = ΔEMST (beyond t*), so EBS is the hatched fraction. AIC and BIC in bold are the best-supported fit within each basis.*

CONCLUSION

Even where median survival is reached, most of the modelled lifetime gain is beyond the data.

Both information criteria select the Royston-Parmar spline. Its lifetime gain is 5.9 months. EBS puts 79% of that gain after the data end, and across the eight distributions EBS runs 65–82% on gains of 3–10 months, with SRS of 1.2–1.5 placing the advantage modestly in the tail. The selection is weaker than it looks: BIC separates the Royston-Parmar spline from the Weibull by 0.3 units, and the fit that tracks the observed curves most closely is the log-logistic, at 7.2 months. The population-mortality floor moves only the two long-tailed fits and leaves the other six unchanged — costless here rather than decisive, because disease-specific mortality dominates background mortality over this horizon.

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REFERENCES

1. Briggs A, Lin Z, Hill A, Fenwick EA. When the tail wags the dog: rethinking partitioned survival modelling in oncology (MSR215). *Value in Health*. 2026;29(6 Suppl):S342. https://www.valueinhealthjournal.com/article/S1098-3015(26)01852-8/fulltext
2. Rutherford MJ, Lambert PC, Sweeting MJ, Pennington B, Crowther MJ, Abrams KR, Latimer NR. *NICE DSU Technical Support Document 21: Flexible methods for survival analysis*. Sheffield: NICE Decision Support Unit; 2020 (updated 2022). https://sheffield.ac.uk/nice-dsu/tsds/flexible-methods-survival-analysis
3. Zhang JZ, Rios JD, Pechlivanoglou T, Yang A, Zhang Q, Deris D, Cromwell I, Pechlivanoglou P. SurvdigitizeR: an algorithm for automated survival curve digitization. *BMC Med Res Methodol*. 2024;24:147. doi:10.1186/s12874-024-02273-8. PMID 39003440
4. Guyot P, Ades AE, Ouwens MJNM, Welton NJ. Enhanced secondary analysis of survival data: reconstructing the data from published Kaplan–Meier survival curves. *BMC Med Res Methodol*. 2012;12:9. doi:10.1186/1471-2288-12-9. PMID 22297116
5. Office for National Statistics. *National life tables – life expectancy in the UK: 2021 to 2023*. Newport: ONS; 18 March 2025. https://www.ons.gov.uk/releases/nationallifetablelifeexpectancyintheuk20212023
6. Dent R, Shao Z, Schmid P, et al. *Ann Oncol*. 2026;37(8):1066–1080. doi:10.1016/j.annonc.2026.03.008. PMID 41937088

DISCLOSURES

The analysis was conducted by Occam Research Ltd as relationship investment; no trial-sponsor funding. Public data only. AI-assisted content disclosable per ISPOR policy: scaffolding and drafting assistance were used, and all analysis and outputs were validated by the authors.