

A Modular Oncology Reference Model for Early Economic Evaluation: A Case Study in EGFR-Mutated NSCLC

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Introduction

- Early health economic assessment of oncology treatments is increasingly required to inform pricing, evidence generation, and payer engagement, often before mature Phase 3 trial data are available.
- Early-phase oncology trials are frequently single-arm and immature, leading to repeated development of bespoke economic models - a process that is time-consuming, costly, and inconsistent across assets.
- A modular reference model with reusable structure and pluggable, indication-specific inputs can accelerate early-stage decision support while preserving methodological rigor.

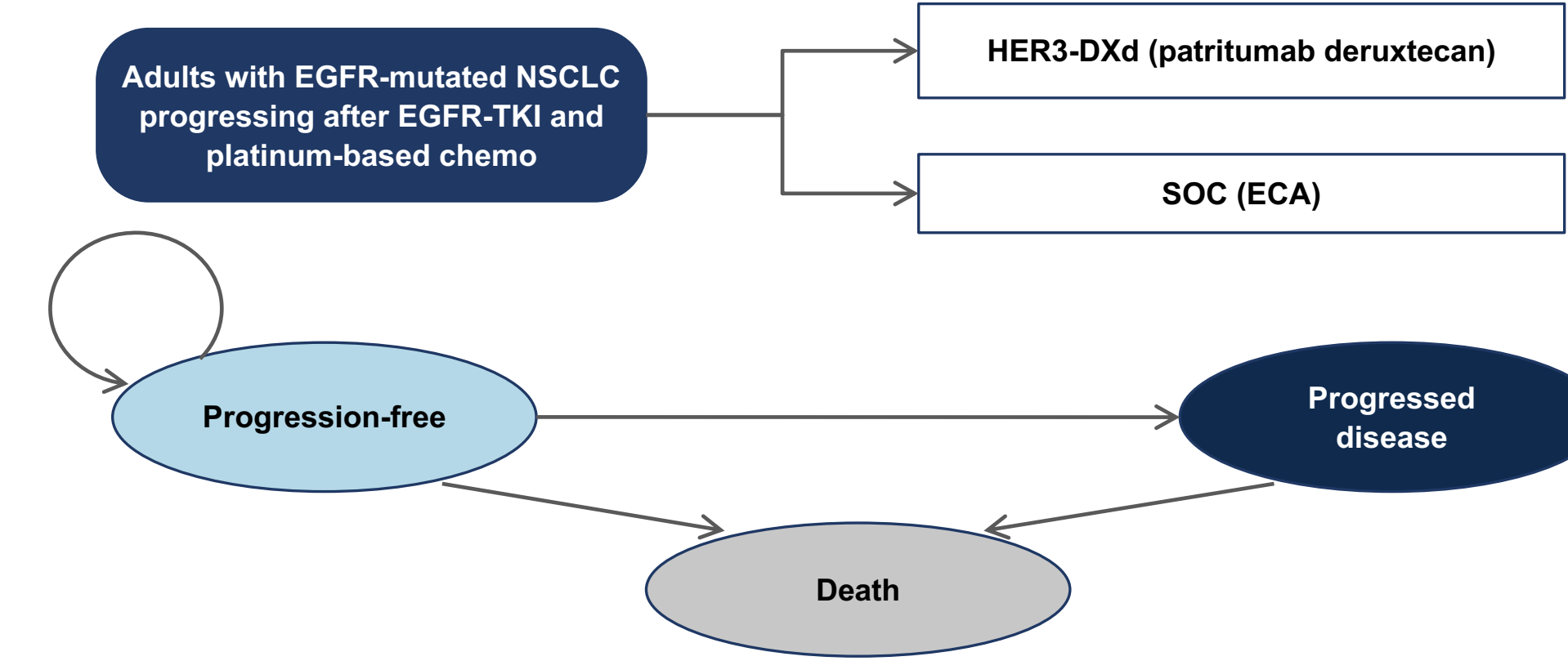
Objective

- Describe a modular oncology reference model for early economic evaluation and demonstrate its application via a HER3-DXd case study in EGFR-mutated NSCLC.

Methods

Modular reference model

- Partitioned survival framework with three health states (progression-free, progressed disease, death) relevant for end-of-life oncology treatments.



EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor; HER3-DXd, patritumab deruxtecan; SOC, standard of care.

- Modular efficacy, cost, and utility inputs.
- US healthcare-sector perspective; lifetime horizon; weekly cycles; 3% annual discount rate; no wastage assumed in base case.

Analyses

- **Validation:** model-derived PFS HR compared with HERTHENA-Lung02 Phase 3 trial.
- Value based price estimations using sensitivity analyses

Population, Intervention, Comparators, Outcomes (PICO)

- Adults with EGFR-mutated, locally advanced or metastatic NSCLC progressing after EGFR-TKI and platinum-based chemotherapy.
- **HER3-DXd:** OS / PFS from HERTHENA-Lung01 Phase 2 trial (NCT04619004).
- **External control arm (ECA):** real-world OS / PFS from de-identified EHR matched to trial population (PMID: 38958845).
- Outcomes: life-years (LYs), QALYs, incremental costs, ICER per QALY gained.

Key model inputs

- Drug acquisition cost for ECA regimen (per cycle) was estimated to be \$5,998
- HER3-DXd cost was tested using a range based on similar oncology products, varying the per vial cost between \$1,000 to \$3,000
- Health utility - progression-free varied from 0.804–0.86
- Health utility - progressed disease varied from 0.321–0.653

Results

Model validation

- Model-derived PFS HR (HER3-DXd vs ECA): **0.76** (computed from median PFS ratio).
- HERTHENA-Lung02 Phase 3 PFS HR: **0.77 (95% CI 0.63–0.94, P=0.011)**. Close concordance supports model validity (**Figure 1**).

Figure 1. PFS curves

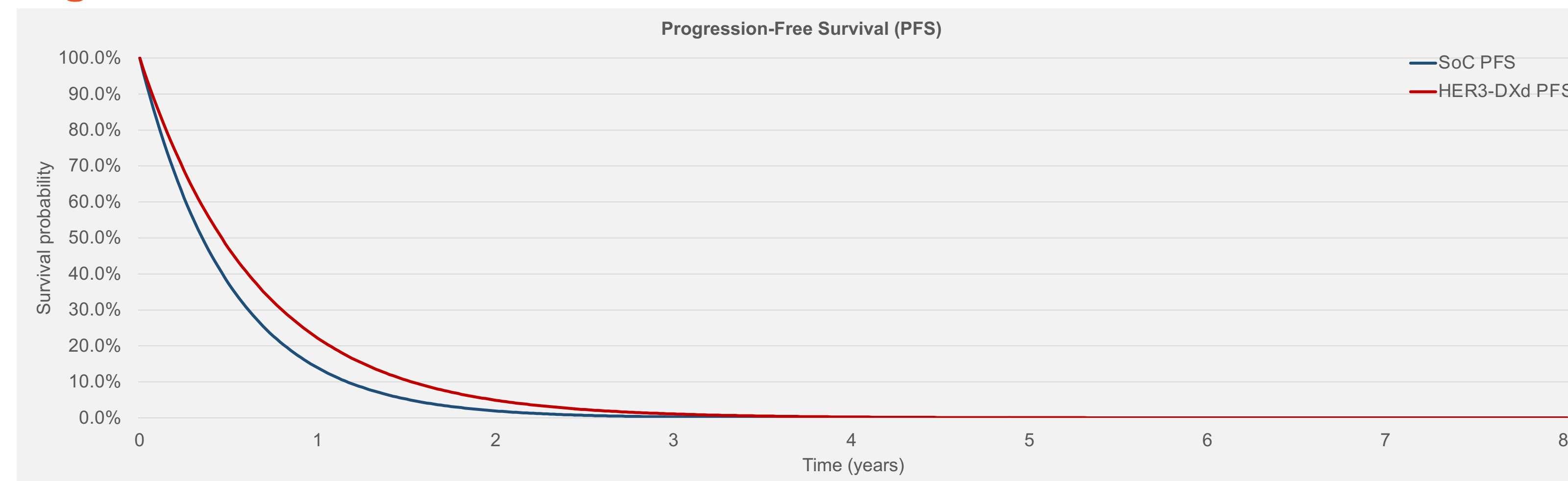
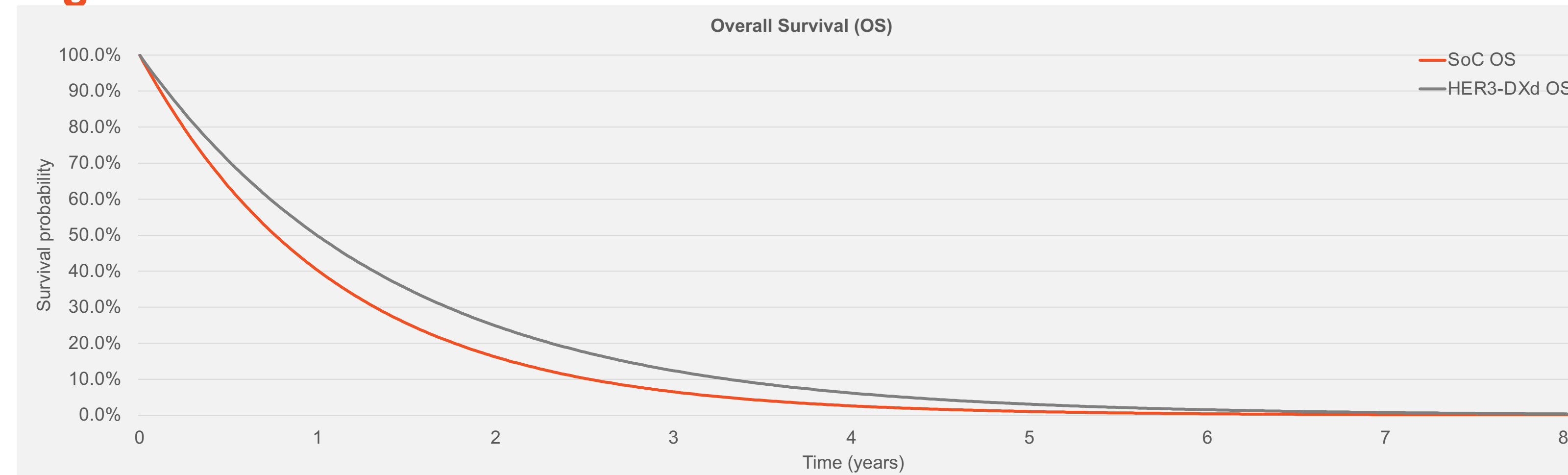


Figure 2. OS curves



Incremental clinical and economic outcomes (vs ECA)

- Median OS gain **+5.2 months**; PFS gain **+2.8 months** vs ECA (**Figures 1 and 2**).
- HER3-DXd adds **+0.31 LYs** and **+0.17 QALYs** per patient lifetime.
- Mean time on HER3-DXd was estimated to be 8.4 months (~12 cycles).
- Total incremental cost-effectiveness of HER3-DXd, based on assumed price range between \$1K–\$3K, varied between being dominant to \$378K/QALY.

Sensitivity analyses

- Key drivers of cost-effectiveness results were HER3-DXd cost and PF/PD utilities.
- When varying the HER3-DXd vial price between \$1K–\$3K, the model showed that HER3-DXd becomes cost saving at \$1,560/vial and remains cost-effective at \$2,140/vial, assuming a willingness to pay threshold of \$150K/QALY.

While HER3-DXd has not been eventually marketed, this case demonstrated the potential value of using our early oncology reference model in forecasting health and economic outcomes, identifying key model drivers, and informing value-based product pricing considerations.

Conclusions

- A modular oncology reference model combining a reusable partitioned-survival structure with indication-specific early-phase trial inputs and a real-world ECA enables timely, high-quality early economic evaluation.
- Validation against the HERTHENA-Lung02 Phase 3 trial (PFS HR **0.77**; model-derived **0.76**) supports the credibility of model outputs from early-phase data.
- AI-assisted data sourcing and parameterization architecture positions the platform for rapid, scalable deployment across future oncology assets.

Disclosures

This study was conducted by Genesis Research Group. Tingting Qu was an employee of Genesis Research Group. Marko Zivkovic, Aaron Crowley, and Agota Szende are employees of Genesis Research Group.

References

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