

Cost-effectiveness of a Circulating Tumor Fraction Molecular Biomarker for Treatment Response Monitoring

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INTRODUCTION

Clinical validation studies have demonstrated that molecular biomarkers quantifying ctDNA changes in circulating tumor fraction (TF) predict survival outcomes and may be used for treatment response monitoring (TRM). While clinical utility studies to determine the impact on outcomes of molecular biomarker-driven treatment decisions versus standard of care imaging are ongoing, cost-effectiveness has not been evaluated. Here, we simulate the clinical utility and evaluate the cost-effectiveness of a molecular biomarker, Tempus xM, used for TRM.

METHODS

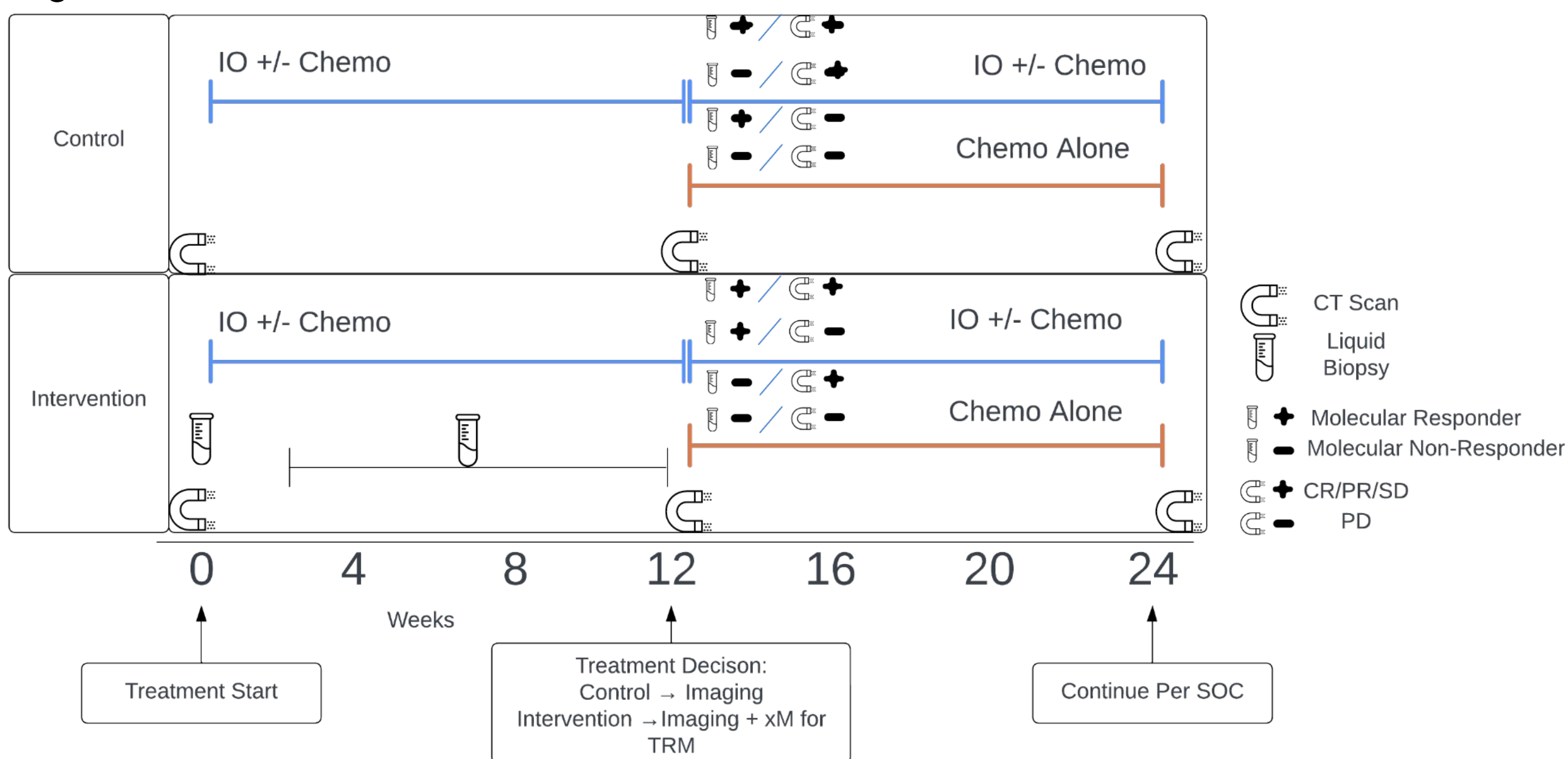
xM quantifies changes in TF from baseline and on-treatment liquid biopsies and classifies patients as molecular responders ($\geq 50\%$ reduction in circulating tumor fraction) and molecular non-responders.

We used a patient-level Markov simulation to compare xM-guided treatment (intervention) to diagnostic imaging-guided treatment (control) over 24 weeks of therapy. In both arms xM and imaging is assessed at 12 weeks and treatment decisions are made based on xM (intervention) or diagnostic imaging (control), (Figure 1). We assume non-responders discontinue ICIs and switch to CT and responders remain on ICIs. Appropriate therapy was defined as treatment decisions concordant with xM results. Costs of xM, imaging and therapies were calculated from Medicare's perspective in 2023 USD. Control patients do not accrue the cost of xM. Costs per week of inappropriate therapy were calculated.

Imaging and xM concordance was based on a retrospective, real-world (RW) study of 51 patients tested with xM that also received rw-imaging treated with immune checkpoint inhibitors (ICIs) +/- chemotherapy (CT). Patients were evaluable if rw-imaging occurred within 3-18 weeks of ICI start and on-treatment liquid biopsy was within 3-26 weeks of ICI start.

Parameter values are shown in Table 1. Sensitivity analyses were conducted, where we varied parameters within +/-20% of their base value.

Figure 1: Simulation Framework



SUMMARY

- We simulated the clinical utility and cost-effectiveness of xM for TRM, a circulating tumor fraction molecular biomarker for treatment response monitoring of immunotherapy
- This model demonstrates that xM for TRM guided treatment is cost-saving compared to imaging alone during 24 weeks of therapy, saving ~\$4,400 & preventing 4.1 weeks of inappropriate ICI treatment compared to imaging alone

RESULTS

- xM-Guided treatment saved ~\$4,400, and prevented 4.1 weeks of inappropriate treatment compared to imaging alone (Figure 2)
- xM-Guided treatment resulted in an incremental cost savings of \$1,057.87 per week of inappropriate therapy avoided
- Outcomes were most sensitive to shift in scan timelines, proportional cost of chemotherapy, and the proportion of scan responders who are xM non-responders (Figure 3)

Table 1: Input Parameters, Sensitivity Range, and Incremental Costs

Parameter	Base Value (Sensitivity Range)	Sources
xM True Positivity	0.98 (0.96 - 1)	Assumption
xM True Negativity	0.97 (0.96 - 1)	Assumption
Cost of xM	\$2,000 (\$1,000 - \$3,000)	Internal Data
Cost of Immunotherapy	\$180,187 (\$144,149.6 - \$216,224.4)	Jansen et al. 2023. DOI: https://doi.org/10.1016/j.jval.2023.08.010
Proportional Cost of Chemotherapy	0.01 (0.01 - 0.5)	Jansen et al. 2023. DOI: https://doi.org/10.1016/j.jval.2023.08.010
Week Earlier of Scan if xM Non-Responder	0 (0 - 4)	Assumption
Proportion of Scan Responders who are xM Non-Responders	0.255 (0.204 - 0.306)	Iams et al. 2024. Relationship Between Dynamic Changes in Circulating Tumor Fraction and Real-World Imaging with Real-World Survival in Patients with Solid Tumors Treated with Immunotherapy. Abstract 3046
Proportion of Scan Non-Responders who are xM Responders	0.098 (0.078 - 0.118)	Iams et al. 2024. Relationship Between Dynamic Changes in Circulating Tumor Fraction and Real-World Imaging with Real-World Survival in Patients with Solid Tumors Treated with Immunotherapy. Abstract 3046

Figure 2: xM for TRM is cost-effective compared to standard of care

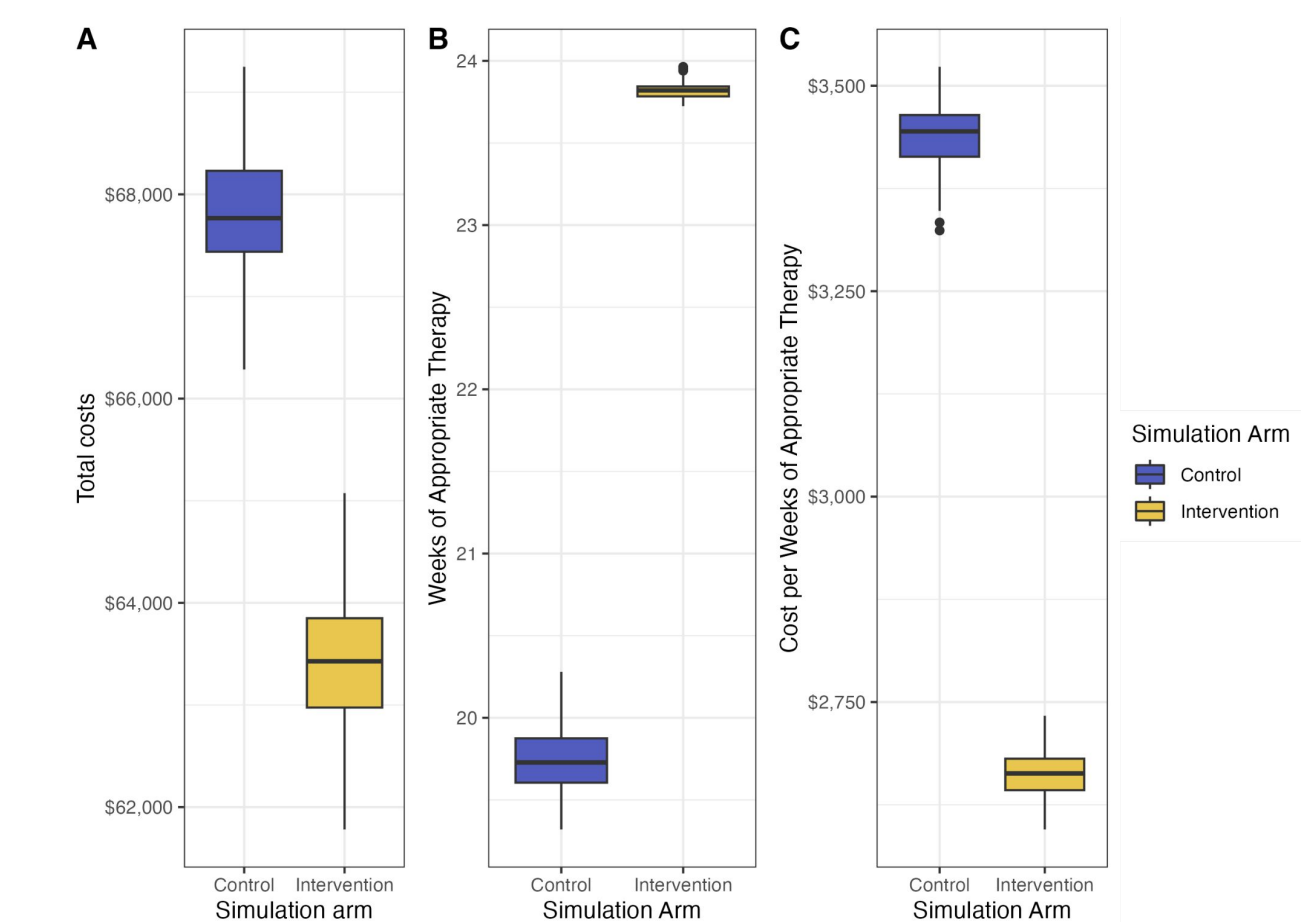


Figure 2. Box and whisker plots of A: Total Costs, B: Weeks of Appropriate Therapy, and C: Costs per Week of Appropriate Therapy in the control and intervention groups

Figure 3: Cost savings is robust to parameter sensitivity analysis

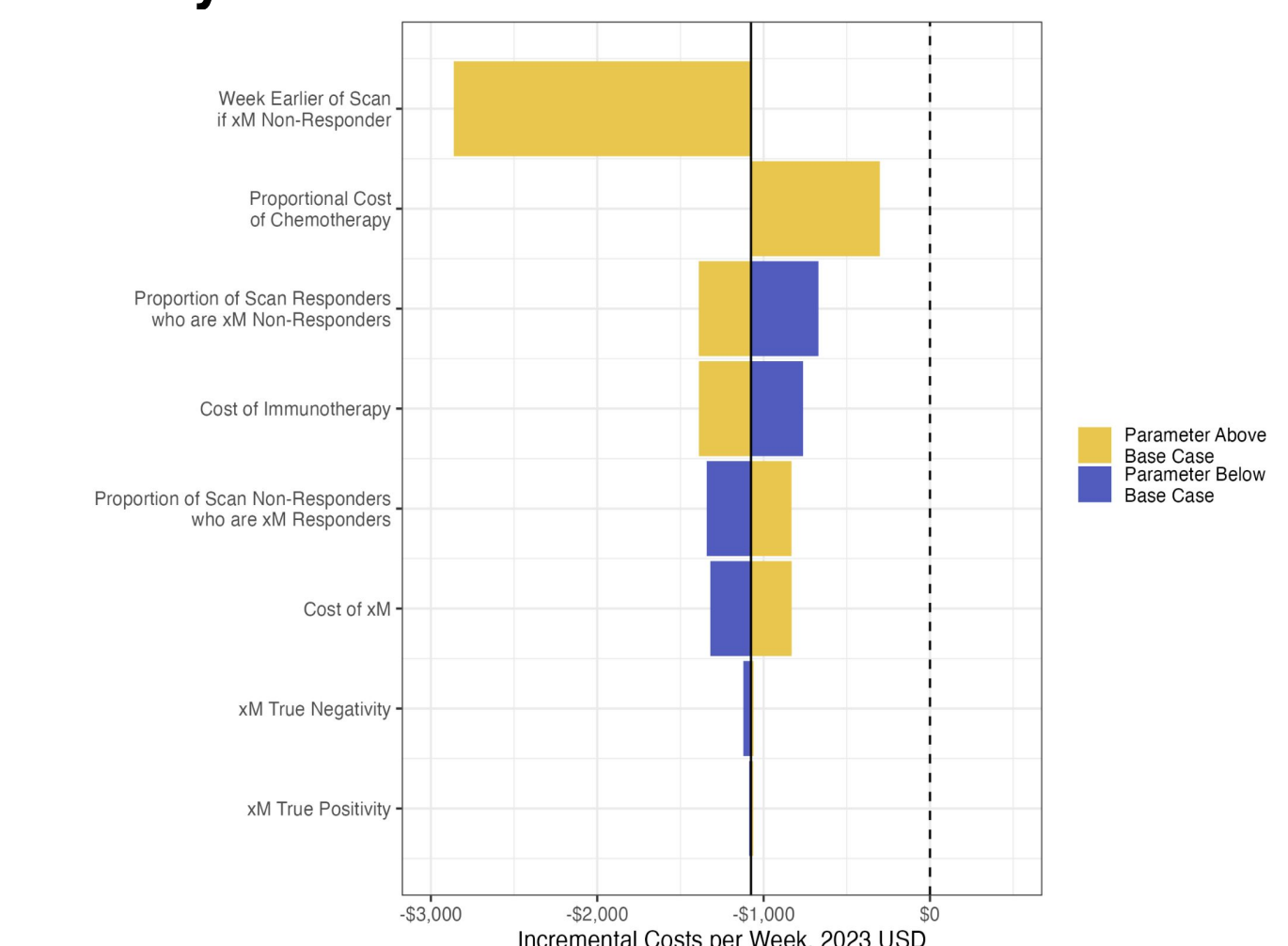


Figure 3. Sensitivity analysis highlighting the impact of input parameters on incremental costs per week. Dashed line indicates the transition from cost-saving to cost-increasing.

ACKNOWLEDGMENTS

We thank Amrita A. Iyer, Ph.D from the Tempus Science Communications team for poster development.