The Cost-Effectiveness of Neoadjuvant FOLFIRINOX vs. Gemcitabine-based Chemoradiotherapy for Resectable and Borderline-Resectable Pancreatic Ductal Adenocarcinoma

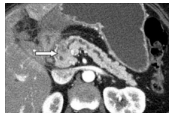
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BACKGROUND

The 2025 phase 3 PREOPANC-2 trial showed no significant survival improvement in treating patients with resectable or borderline-resectable pancreatic ductal adenocarcinoma (PDAC) with neoadjuvant FOLFIRINOX (FFX) vs. gemcitabine-based chemoradiotherapy (CRT), with both arms surviving approximately 21-22 months. Though the treatments appear clinically equivalent, it is unclear whether differences arise when considering toxicity and cost of treatment. Therefore, we created a decision tree to compare the risks and benefits of treating PDAC with FFX vs. CRT



OBJECTIVE

To understand the clinical impact of PREOPANC-2, a phase 3 trial comparing neoadjuvant FFX to neoadjuvant gemcitabine-based CRT for the treatment of resectable and borderline-resectable PDAC.

METHODS

We constructed a decision tree using utilities (**Table 1)** and costs per month (**Table 2)** from the literature, and probabilities directly from the PREOPANC-2 trial. Overall survival (OS) was defined as the time between randomization and death from any cause (including treatment); impact on quality of life was calculated in quality-adjusted life months (QALMs).

Table 1. Utility Values and Overall Survival (months)

Outcome	Utility	Overall Survival (months)
Progression-free survival (PFS), after resection	0.8	30
Metastatic or unresectable disease prior to surgery	0.73	8
Survival with progression after surgery (treatment-refractory)	0.58	3-6
Serious adverse events	0.526	3

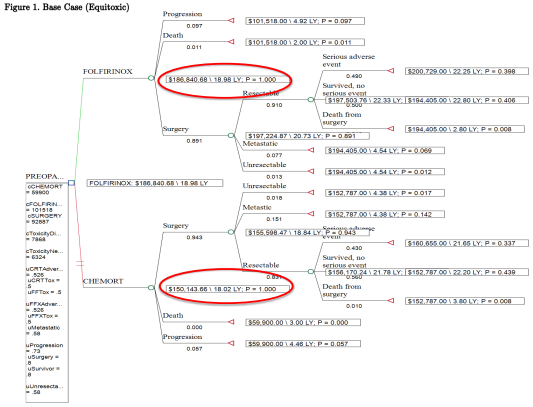
Table 2. Costs and Treatment Length (months)

Treatment	Costs	Length of treatment (months)
FOLFIRINOX (FFX)	$101,518	3
CRT	$59,900	6
Surgery	$99,157	1
Adverse events	Diarrhea treatment = $7,868 Neutropenia treatment = $6,324	3 (trial considered adverse events within 90 days)

RESULTS

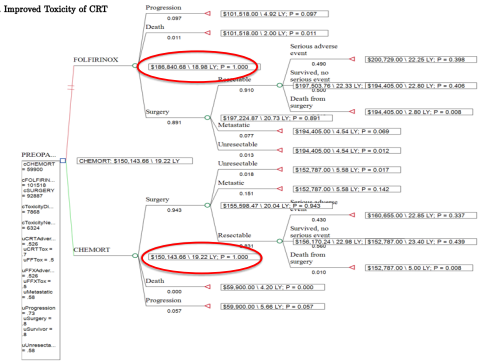
In our base case, assuming equal toxicity of FFX and CRT (utility of 0.5), FFX treatment resulted in more QALMs (18.98 vs 18.02) compared to CRT, but with an additional cost of $36,697.02

Figure 1. Base Case (Equitoxic)



If we improve the toxicity of CRT relative to FFX to a utility of 0.7, CRT is cheaper and results in more QALMs (19.22 vs. 18.98 QALMs, -$36,697.02)

Figure 2. Improved Toxicity of CRT



DISCUSSION

Treating PDAC with FFX vs CRT results in minimal differences in QALMs that are dependent on the toxicity of treatment. If considered equitoxic, though FFX results in slightly improved QALMs**, the cost exceeds most definitions of societal willingness-to-pay** ($440,364 per additional quality-adjusted life year, QALY). If the toxicity of CRT is considered significantly improved compared to FFX, **CRT becomes the dominant strategy.**

The difference in treatments amounts to a difference in toxicity and length, with FFX being shorter (3 months) but with harsher adverse effects, and CRT being longer (6 months), but more tolerable. When weighing in the exorbitant cost of FFX, it becomes clear that although CRT and FFX appear clinically equivalent, the more affordable and well-tolerated treatment (CRT) is the practical choice for majority of the population.

Project Limitations

- Our model used one fixed survival time for each outcome (e.g., 30 months after surgery), rather than the full range of survival times real patients have.
- Several quality-of-life scores and costs came from studies of patients with metastatic cancer or from Canada, not from the PREOPANC-2 patients.
- We counted only two side effects, diarrhea and neutropenia, and left out long-term problems such as the nerve damage FOLFIRINOX can cause.
- We counted only costs to the healthcare system, not costs to patients, such as the time and travel needed for 15 daily radiation treatments.

Future Directions

- When PREOPANC-2 publishes its quality-of-life surveys, we can use those patients' own scores instead of estimates from other studies.
- We plan to follow patients over their full lifetime, use U.S. Medicare costs, and test how our results change as costs and side effects vary.
- As new trials report, we can add other options, such as radiation given in fewer, higher-dose sessions, or FOLFIRINOX before and after surgery (PREOPANC-3).

CONCLUSIONS

Although PREOPANC-2 showed no significant survival difference in treating PDAC with neoadjuvant FFX vs. gemcitabine-based CRT, the cost of FFX exceeds most definitions of societal willingness-to-pay. When CRT toxicity is improved relative to FFX to reflect the harsh side-effects of FFX, CRT becomes the cheaper, preferred strategy.

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