Cost-Effectiveness of a Novel Therapeutic Drug Monitoring Intervention in Adult Crohn's Disease Patients Initiating Infliximab Maintenance Therapy

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Introduction

Crohn's disease (CD) patients that lose response to biologics experience reduced quality of life (QoL) and costly hospitalizations. Precision-guided dosing provides clinicians with a comprehensive pharmacokinetic (PK) profile that allows for the next biologic dose to be personalized. We analyzed the cost-effectiveness of infliximab (IFX) Precision-guided dosing relative to two IFX dose intensification strategies (DIS).

Methods

We developed a hybrid (Markov and decision tree) model of CD patients who had a clinical response to IFX induction and entered IFX maintenance in "remission" or "mild symptoms" health states. The analysis took a US payer perspective, a time horizon of 2 years in the base case, and a cycle length of 4 weeks. There were 3 comparators for IFX dosing: Precision-guided dosing, dose intensification based on symptoms, inflammatory markers, and trough IFX concentration (DIS1), and IFX dose intensification based on symptoms alone (DIS2). Patients that failed IFX initiated ustekinumab (UST), followed by vedolizumab, and conventional therapy. Transition probabilities for IFX were estimated from real-world clinical PK data and interventional clinical trial (PMID: 34978325; 29317275) patient-level data. All other transition probabilities were derived from published randomized clinical trials and cost-effectiveness analyses. Utility values were sourced from previous health technology assessments. Direct costs included biologic acquisition and infusion, surgeries and procedures, conventional therapy, and lab testing. The primary outcomes were total discounted costs, total quality-adjusted life years (QALYs), and incremental cost-effectiveness ratios (ICERs). The robustness of results was assessed via one-way sensitivity, scenario, and probabilistic sensitivity analyses.

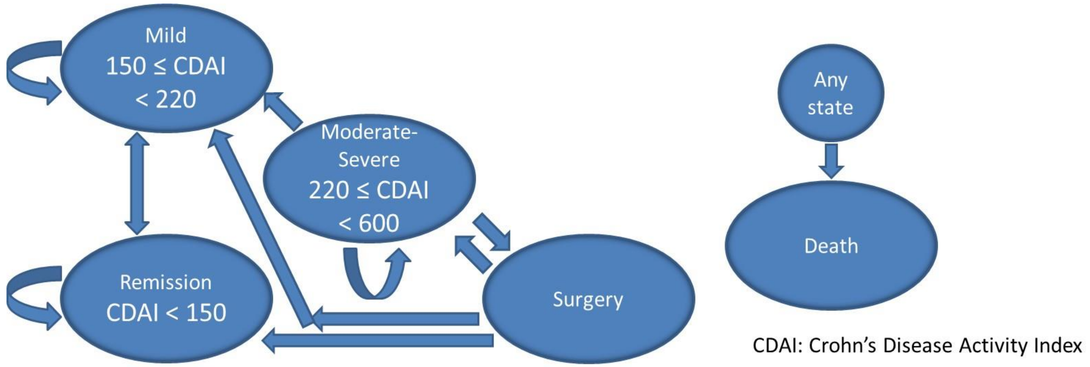

Figure 1: Multi-state Markov model for biologic maintenance phases. Infliximab induction responders enter the model as either Mild or Remission (50/50 split in the Base Case).

Results

2 YEAR HORIZON DISCOUNTED

DIS	Total QALYs	Total Costs	ICER Relative to			Incremental NMB vs DIS1			Incremental NMB vs DIS2		
			MIPD	DIS1	DIS2	WTP: $200K	WTP: $150K	WTP: $100K	WTP: $200K	WTP: $150K	WTP: $100K
MIPD*	1.572	$50,753	-	171,810	127,990	$989	-$765	-$2,519	$5,942	$1,816	-$2,310
DIS1†	1.537	$44,725	171,810	-	95,581	-	-	-	$4,953	$2,581	$210
DIS2‡	1.489	$40,191	127,990	95,581	-	-$4,953	-$2,581	-$210	-	-	-

*Model informed precision dosing with homogenous mobility shift assay (Prometheus Laboratories)
†Dose intensification based on a combination of symptoms, inflammatory markers and proactive therapeutic drug monitoring. Corresponds to cohorts 1 and 2 of the TAILORIX clinical trial.
‡Dose intensification reactive on symptoms only. Corresponds to cohort 3 of the TAILORIX clinical trial.
DIS: dose intensification strategy, ICER: incremental cost-effectiveness ratio, NMB: net monetary benefit, QALY: quality-adjusted life year, WTP: willingness to pay

Table 1: Base Case results, including total QALYs, total costs, incremental cost-effectiveness ratios, and net monetary benefits

Discussion

Precision-guided dosing provides substantial clinical and quality of life benefits relative to other dose intensification strategies by avoiding infliximab failure, reducing rates of surgery, and steadily maintaining CD remission.
Sensitivity analyses demonstrated that parameter uncertainty impacts cost-effectiveness results, with infliximab drug acquisition costs, PGD infliximab dosing interval, and PGD therapeutic drug monitoring being the primary cost drivers. The QALY estimates for DIS1 and DIS2 are likely to be significantly lower in a microsimulation that tracks individual patients over time where reduced remission utility post surgery or biologic failure is accounted for; therefore, these results are likely to be a conservative estimate of PGD cost-effectiveness relative to DIS1 and DIS2.

Conclusion

Precision-guided dosing is cost-effective relative to DIS1 and DIS2 at a WTP of $200,000 QALY.

Symbol Key

CD: Crohn's disease, CDAI: Crohn's disease activity index, CT: conventional therapy, DIS: dose intensification strategy, ICER: incremental cost-effectiveness ration, IFX: infliximab, M-S: moderate-severe, NMB: net monetary benefit, PGD: precision-guided dosing, PK: pharmacokinetic, PMPM: per member per month, QALY: quality-adjusted life year, QOL: quality of life, US: United States, UST: ustekinumab, VDZ: vedolizumab, WTP: willingness-to-pay

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