CLINICAL UTILITY OF PRECISION-GUIDED TOOL FOR INFLIXIMAB DOSING DURING MAINTENANCE THERAPY OF INFLAMMATORY BOWEL DISEASE

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Introduction

A precision-guided dosing tool that uses Bayesian data assimilation was developed to forecast Infliximab (IFX) exposure. Our objective was to establish the utility of the tool in clinical decision making during IFX maintenance therapy when used reactively, to address inadequate disease control that results from suboptimal exposure, and proactively, to sustain exposure commensurate with disease remission in inflammatory bowel disease (IBD).

Methods

Blood specimens were collected, anytime 20 days after a prior infusion in a prospective study (EMPOWER). Pharmacokinetic (PK) testing was conducted at Prometheus Laboratories (San Diego, CA). Serum IFX, antibodies to IFX (ATI) and albumin concentrations were imputed with dosing regimen and weight in a Bayesian data assimilation tool to produce individualized PK profiles. Results consisted of forecasted IFX trough based on current dosing regimen, time to concentration below pre-specified thresholds (e.g., <10 µg/mL) and trough concentration at alternative dosing regimens. Physician's global assessment of disease activity was collected with the decision to change IFX based on PK test results. Statistical analysis consisted of Mann-Whitney and Fisher Exact test.

Results

- A total of 111 patients were assessed by 21 physicians. A change in IFX regimen was initiated in 51 patients (46%).
- Inadequate exposure and forecasted IFX levels < 10 µg/mL associated with dose intensification (76%, median IFX 6.3 µg/mL) (p<0.01)
- Forecasted IFX ≥ 10 µg/mL associated with a 4-fold higher likelihood of active disease (OR=4.1; 95%CI: 1.7-9.4) as compared to IFX levels < 10 µg/mL (p<0.01).
- Dose intensification using a 5 mg/kg every 4 weeks dosing regimen forecasted 2.3-fold higher IFX levels as compared to a 10 mg/kg every 8 weeks dosing regimen (median of 17.1 vs 7.4 µg/mL, respectively) (p<0.001).

Conclusions

Our study suggests that the precision-guided dosing tool provides clinical utility and helps with dose adjustments in both interval changes as well as dose intensification.

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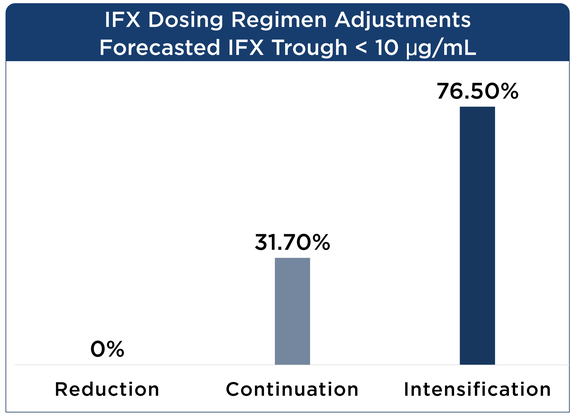

Forecasted IFX (µg/mL), active disease group (median, N=66)

	5 mg/kg	7.5 mg/kg	10 mg/kg
4 weeks	17.1	25.3	35.1
6 weeks	7.2	11.0	15.0
8 weeks	4.1	5.9	7.4

Forecasted IFX (µg/mL), disease remission group (median, N=45)

	5 mg/kg	7.5 mg/kg	10 mg/kg
4 weeks	23.6	34.7	48.6
6 weeks	11.2	16.6	22.2
8 weeks	6.0	8.5	11.8

Variable	IFX Dosing Regimen Adjustments			Overall Population
	Reduction N=17	Continuation N=60	Intensification N=34	N=111
Patient Characteristics				
Age (years)	16 (14-19)	32 (18-45)	32 (17-46)	26 (16-44)
Female (%, n/N)	44.1% (7/17)	43.3% (26/60)	44.1% (15/34)	43.2% (48/111)
CD/UC/Indeterminate	13/3/1	36/15/8	22/9/3	71/27/12
Weight (Kg)	64 (43-76)	71 (61-92)	69 (61-92)	70 (60-84)
Dose mg/Kg	10.0 (9.0-10.4)	8.2 (5.0-10.0)	5.5 (5.0-10.0)	8.0 (5.1-10.0)
Interdose interval (weeks)	6 (5-8)	8 (6-8)	8 (6-8)	8 (6-8)
PGA Remission Status, remission	70.6% (12/17)	41.7% (25/60)	23.5% (8/34)	40.5% (45/111)
Clinical PK Measurements				
Measured IFX levels (µg/mL)	23.3 (17.2-28.5)	12.9 (7.2-20.6)	8.0 (5.2-14.7)	12.5 (7.2-20.9)
ATI status (%, n/N)	0% (0/17)	10.0% (6/60)	11.8% (4/34)	9.0% (10/111)
Albumin (g/dL)	4.1 (4.0-4.3)	4.0 (3.6-4.2)	3.9 (3.7-4.2)	4.0 (3.7-4.2)
Clearance (L/day)	0.19 (0.15-0.22)	0.27 (0.20-0.33)	0.28 (0.22-0.35)	0.25 (0.19-0.31)
Time-to-Trough <10 µg/mL (weeks)	11 (10-12)	7 (6-9)	6 (4-7)	7 (6-9)
Forecasted Trough (µg/mL)	26.2 (20.1-34.5)	12.7 (8.6-17.6)	6.3 (3.1-9.4)	11.6 (6.5-19.5)
Forecasted Trough <10 µg/mL	0% (0/17)	31.7% (19/60)	76.5% (26/34)	40.5% (45/111)