INFLIXIMAB CLEARANCE AND EXPOSURE ARE COMPARABLE BETWEEN ORIGINATOR REMICADE AND BIOSIMILARS IN CLINICAL GASTROENTEROLOGY PRACTICE

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Introduction

Clearance is the key pharmacokinetic (PK) property of Infliximab (IFX) elimination from the body as a function of time (expressed as L/day) and is a poor prognostic factor associated with immunogenicity, suboptimal exposure and inadequate disease control.

Our objective was to compare IFX PK (as clearance) between Originator IFX and Biosimilars.

Methods

De-identified data were extracted from samples submitted for Originator (IFX, REMICADE®) or Biosimilars (RENFLEXIS®, IFX-abda and INFLECTRA®, IFX-dyyb) testing from a large commercial PK database (Prometheus Laboratories). Originator and Biosimilar testing were calibrated against WHO standard (NIBSC code: 16/170) with less than 3% difference in levels. Intra-day and interday coefficient of variation were below 5% and 10%, respectively. IFX levels, antibody-to-IFX (ATI) status (>3.1 U/mL), dosing and time of specimen collection relative to infusion were analyzed using nonlinear mixed effect models to estimate clearance. Statistical analysis consisted of Mann-Whitney and Fisher Exact test.

Results

- A total of 9,590 specimens from 7,551 patients (mean age 36 years, 48% female) who received a 5 or 10 mg/kg q8 weeks dosing were available for this analysis (714 Biosimilar specimens, 66.1% IFX-dyyb, 8,876 Originator).
- Overall, the PKs were comparable between Originator and Biosimilars, although a small trend toward higher clearance was observed in patients who received Biosimilars as compared to those who received Originator IFX (0.277±0.004 vs 0.262±0.001 L/day, respectively) (p<0.001).
- Higher ATI's were observed with Biosimilars vs Originator (19% [136/714] vs 15% [1320/8876], respectively) (p<0.001) as well as lower exposure (7.6±0.3 vs 8.5±0.1 µg/mL, respectively) (p<0.001). These differences were significant only among those who received 5 mg/Kg q8 weeks dosing.
- Clearance was 2-fold higher in the presence of ATI and resulted in 6-fold lower exposure for Originator (mean=1.5 vs 9.2 µg/mL) and Biosimilar (mean=1.5 vs 9.7 µg/mL) (p<0.001).

Table 1: Clearance (L/day) and IFX levels (µg/mL) by ATI status and IFX dosing schedules

	5 mg/kg q8 weeks	10 mg/kg q8 weeks	Overall
Clearance (L/day)			
ATI Negative	O: 0.223±0.001 (n=5,076) B: 0.232±0.004 (n=399) **Fold: 1.04; p=0.059**	O: 0.251±0.001 (n=2,480) B: 0.257±0.005 (n=179) **Fold: 1.02; p=0.176**	O: 0.232±0.001 (n=7556) B: 0.239±0.003 (n=578) **Fold: 1.03; p=0.033**
ATI Positive	O: 0.432±0.003 (n=1,015) B: 0.439±0.009 (n=115) **Fold: 1.02; p=0.196**	O: 0.443±0.006 (n=305) B: 0.428±0.028 (n=21) **Fold: 1.01; p=0.712**	O: 0.434±0.003 (n=1320) B: 0.437±0.009 (n=136) **Fold: 1.01; p=0.487**
Overall	O: 0.258±0.110 (n=6,091) B: 0.278±0.120 (n=514) **Fold: 1.08; p<0.01**	O: 0.272±0.097 (n=2785) B: 0.275±0.094 (n=200) **Fold: 1.01; p=0.375**	O: 0.262±0.001 (n=8876) B: 0.277±0.004 (n=714) **Fold: 1.06; p<0.001**
IFX (µg/mL)			
ATI Negative	O: 8.7±0.1 (n=5,076) B: 8.3±0.4 (n=399).95 **Fold: 0.95; p=0.538**	O: 11.6±0.2 (n=2,480) B: 10.7±0.6 (n=179) **Fold: 0.92; p=0.272**	O: 9.7±0.1 (n=7556) B: 9.2±0.3 (n=578) **Fold: 0.95; p=0.024**
ATI Positive	O: 1.3±0.1 (n=1,015) B: 1.2±0.2 (n=115) **Fold: 0.92; p=0.994**	O: 2.3±0.2 (n=305) B: 3.2±1.0 (n=21) **Fold: 1.4; p=0.626**	O: 1.5±0.1 (n=1320) B: 1.5±0.3 (n=136) **Fold: 1.00; p=0.818**
Overall	O: 7.5±0.1 (n=6,091) B: 6.7±0.3 (n=514) **Fold: 0.89; p<0.01**	O: 10.6±0.2 (n=2785) B: 9.9±0.6 (n=200) **Fold: 0.93; p=0.547**	O: 8.5±0.1 (n=8876) B: 7.6±0.3 (n=714) **Fold: 0.89; p<0.001**

O: Originator; B: Biosimilar. Results are expressed as Mean (SEM) with fold difference between B and O.

Conclusions

These data suggest that Originator and Biosimilars yield comparable exposure. The small detectable higher immunogenicity rate observed in the group of patients receiving Biosimilars could reflect longer duration of IFX treatment among those who switched from Originator to Biosimilar.

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