Missed Doses and Discontinuation of Infliximab in a Population-Based Cohort: Comparisons of Biosimilar and Originator Exposures

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Background

- In North America, biosimilars were approved only relatively recently, and real-world data are few.
- We described users of infliximab in the US, comparing patient tolerability of biosimilar and originator, in terms of missed doses and discontinuation.

Methods

- We used Marketscan® data (Jan-Dec. 2017) to identify adult (age>18) new users of infliximab biosimilar and originator, and switchers from originator to biosimilar.
- In new users, we assessed missed doses in both induction (among subjects with >2 months follow-up) and maintenance phases.
- 'Missed dose' was defined as any gap between infusions beyond recommended intervals (0, 2, and 6 weeks for induction and Q8 weekly for maintenance).
- Discontinuation (≥90-day gap between infusions without restarting therapy) during maintenance phase was also assessed.
- We used Cox regression to compare both times to first missed dose and complete discontinuation. We adjusted for age, sex, prior DMARDs, biologics, and prednisone, comorbidities (Charlson comorbidity index) and underlying disease (rheumatoid arthritis, RA, ankylosing spondylitis, AS, psoriasis/psoriatic arthritis, PsA, Inflammatory bowel disease, IBD).

Disclosures

CS Moura, None; **JR Curtis,** (AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB); **D Choquette,** (AbbVie, Amgen, BMS, Celgene, Eli-Lilly, Merck, Novartis, Pfizer, Sanofi-Genzyme); **G Boire,** (AbbVie, Amgen, BMS, Celgene, Eli-Lilly, Merck, Novartis, Pfizer); **VP Bykerk,** (AbbVie, Amgen, Brainstorm Therapeutics, BMS, Genentech, Gilead, NIH, Pfizer, Regeneron, Sanofi, Scipher, The Cedar Hill Foundation, UCB); **C Thorne,** (Amgen, AbbVie, CaREBiodam, Celgene, Centocor, Janssen, Eli-Lilly, Medexus/Medac, Merck, Novartis, Sandoz, Pfizer); **WP Maksymowych**, (AbbVie, Amgen, Boehringer, CARE Arthritis, Celgene, Eli Lilly, Janssen, Merck, Pfizer, Synarc, Sanofi, UCB Pharma); **PL Lakatos,** (Abbvie, Arena Pharmaceuticals, Celltrion, Falk Pharma GmbH, Ferring, Genetech, Janssen, Merck, MSD, Pfizer, Pharmacosmos, Roche, Shire, Takeda); **L Svenson,** None; **L Targownik,** None; **W Afif,** (Abbvie, Ferring, Janssen, Novartis, Pfizer, Prometheus, Takeda, Theradiag); **S Bernatsky,** None.

Results

- We identified 318 users of infliximab biosimilar, including 206 switchers from the originator (Table 1).
- For 92 new users of infliximab biosimilar with >2 months follow-up, the frequency of >1 missed dose in induction was 22%, similar to 25% in new users of originator. For patients completing induction, the adjusted hazard ratio (HR) showed a nonsignificant trend for longer time to first missing dose in maintenance (adjusted HR 0.33, 95% CI 0.08-1.30, Table 2).
- We were unable to determine if complete discontinuation differed in biosimilar vs originator (HR: 0.82; 95% CI: 0.11-6.02).

Table 1 – Baseline characteristics of infliximab initiators

Characteristic	Biosimilar (infliximab naïve, n=112)	Originator (infliximab naïve, n=3076)	Biosimilar (switchers from originator, n=206)
Female sex, N (%)	69 (61.6)	1848 (60.1)	128 (62.4)
Mean age (SD)	47.3 (15.8)	43.8 (14.9)	52.4 (16.5)
Mean age-adjusted CCI (SD)	1.9 (2.3)	1.4 (2.1)	1.8 (1.9)
Underlying disease[1] N (%)			
RA	39 (36.5)	638 (22.2)	69 (35.8)
AS	4 (3.7)	127 (4.4)	9 (4.7)
Psoriasis/PsA	15 (14.0)	300 (10.4)	28 (14.5)
IBD	49 (45.8)	1813 (63.0)	87 (45.1)
Ever DMARDs N (%)	53 (47.3)	1024 (33.3)	82 (39.8)
Ever prednisone N (%)	95 (84.8)	2424 (78.8)	131 (63.6)
Biologic use N (%)			
Adalimumab	32 (28.6)	796 (25.9)	13 (6.3)
Etanercept	11 (9.8)	218 (7.1)	3 (1.5)
Others[2]	8 (7.1)	216 (7.0)	5 (2.4)

[1]Based on the date of diagnosis closest to the start of treatment; 216 missing diagnosis.
[2]Including abatacept, golimumab, certolizumab, tocilizumab, and rituximab.
CCI: Charlson comorbidity index; RA: rheumatoid arthritis, AS: ankylosing spondylitis,
PsA: psoriatic arthritis, IBD: inflammatory bowel disease, including Crohn's disease and ulcerative colitis..

Table 2 – Factors associated with missed dose and discontinuation during the maintenance phase.

	HR (95% CI)	
Variable	Missed dose	Discontinuation
Infliximab biosimilar initiator	0.32 (0.18-3.07)	0.82 (0.11-6.02)
Female sex	1.13 (0.61-1.35)	0.77 (0.41-1.46)
Age	1.00 (0.98-1.01)	0.98 (0.96-1.01)
Age-adjusted CCI score	1.00 (1.07-1.27)	1.03 (0.85-1.26)
Underlying disease[1]		
RA	1.39 (0.88-2.20)	1.42 (0.32-6.21)
AS	1.10 (0.53-2.29)	0.89 (0.25-3.23)
Psoriasis/PsA	1.34 (0.83-2.17)	2.05 (0.78-5.33)
IBD	0.93 (0.63-1.35)	0.31 (0.31-1.64)
Past prednisone	0.98 (0.68-1.42)	0.59 (0.59-3.41)
Any prior biologic use	0.78 (0.58-1.06)	0.36 (0.36-1.37)

[1]IBD was the reference category.

Conclusions

- We documented low use of infliximab use in these US data during 2017; most infliximab biosimilar initiators are switchers from the originator. For previously infliximab-naïve patients, the frequency of >1 missed dose during infliximab induction phase was similar in originator and biosimilar new users.
- Additional analyses with more follow-up time may help determine if there are differences in persistence between biosimilars and their reference therapy.

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