United States Rheumatology Practice-Based Real-World Evidence of Infusion Reactions in Rheumatoid Arthritis Patients Treated With Intravenous Golimumab or Infliximab: Impact of Prior Biologic Exposure and Methotrexate Utilization

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BACKGROUND

- AWARE (Comparative and Pragmatic Study of Golimumab [GLM] Intravenous [IV] Versus Infliximab [IFX] in Rheumatoid Arthritis [RA]) is an ongoing Phase 4 comparator study providing real-world assessment of GLM and IFX in patients with RA
- The primary endpoint of the AWARE study compares the proportion of GLM and IFX patients with an infusion reaction during the first 52 weeks of treatment
  - The study attained the primary endpoint (p<0.001) at a planned interim analysis when 833 patients had reached 52 weeks of treatment (or were discontinued)[1]
- Per protocol, at the baseline visit the AWARE study records whether enrolled patients have prior use of biologic medications and if there is concomitant use of methotrexate (MTX)
- AWARE affords the opportunity to assess the impact of prior exposure to biologic medications, medications used prior to infusion, or concomitant MTX on infusion reactions in a real-world rheumatology practice setting

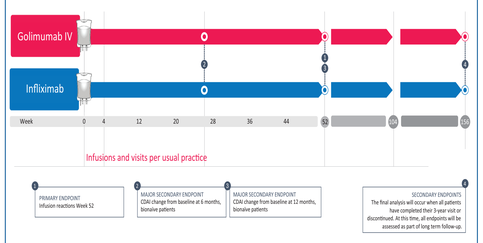
OBJECTIVE

- The objective of this analysis was to explore the effect of prior biologic exposure or concomitant MTX use on the incidence and management of infusion reactions among GLM-treated and IFX-treated patients

METHODS

- AWARE is a prospective, non-interventional, observational, multicenter (88 sites), 3-year study in the United States (Figure 1)
- A total of 1270 patients with RA were enrolled when initiating treatment with GLM or IFX
- The protocol did not restrict or introduce any medical interventions or medications (patients enrolled after the decision to treat with either GLM or IFX)
- Patients could not receive an investigational drug while enrolled in the study or be pregnant
- All treatment decisions including prescribed dose and dosing frequency were made at the discretion of the treating rheumatologist; patient visits occurred per usual clinical practice
- The sponsor did not provide study drug in the AWARE study
- An infusion reaction was defined as any adverse event that occurred during or within 1 hour after GLM or IFX infusion
- Information about infusion reactions including severity, seriousness, and medical management, was determined by the treating rheumatologist
- Use of prior biologic medications and concomitant use of MTX (at study baseline) was recorded
- Concomitant MTX use was defined as any dose of MTX on or after the baseline infusion of GLM
- Imputations were not performed on these AWARE data
- Data are shown as mean ± standard deviation (SD) or percentage of patients

Figure 1. Study Design



CDAI, clinical disease activity index; IV, intravenous

RESULTS

- The 52-week data set included 685 GLM-treated and 585 IFX-treated patients
- Demographics and disease characteristics between the treatment groups are presented in Table 1
  - Mean age and mean disease duration of GLM-treated patients were greater than IFX-treated patients by approximately 2 years
  - The proportion of non-bionaïve patients with prior exposure to ≥3 biologics was approximately 2-fold greater for GLM- vs IFX-treated patients
  - There was a higher proportion of bionaïve patients in the IFX-treated group than in the GLM-treated group
  - The proportion of concomitant MTX users were similar between GLM- and IFX-treated patients

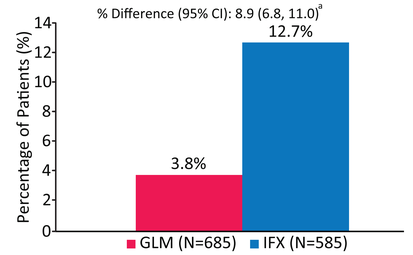
Table 1. Baseline Demographics and Disease Characteristics

	GLM (N=685)	IFX (N=585)
Age (years), mean (SD)	60.9 (13.4)	58.0 (12.9)
Female, n (%)	582 (85.0)	465 (79.5)
White, n (%)	599 (87.4)	496 (84.8)
Biologics bionaïve, n (%)	242 (35.3)	251 (42.9)
For non-bionaïve, prior exposure to biologics, n (%)		
1 prior biologic	198 (28.9)	184 (31.5)
2 prior biologics	107 (15.6)	87 (14.9)
≥3 prior biologics	138 (20.1)	63 (10.8)
Disease duration (years), mean (SD)	9.2 (10.0)	7.3 (9.7)
Concomitant MTX, n (%)	420 (61.3)	356 (60.9)
MTX dose, mean (SD)[a]	16.3 (10.7)	16.2 (7.0)

[a]MTX dose on/after baseline is the first MTX dose where MTX dose >0 mg and its start or stop date ≥ first study treatment date; GLM n=420, IFX n=356.
GLM, golimumab; IFX, infliximab; MTX, methotrexate; SD, standard deviation

- Overall, infusion reactions occurred more frequently in the IFX-treated group (12.7%) than among patients in the GLM-treated group (3.8%) (Figure 2)

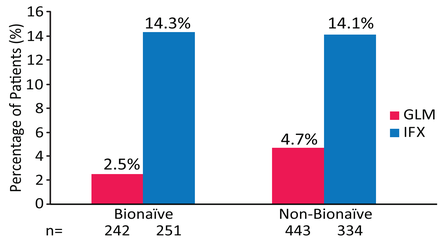
Figure 2. Primary Endpoint: Percentage of Patients With at Least One Infusion Reaction Through 52 Weeks of Treatment (or Discontinued)



[a]The confidence intervals are based on Wald method using inverse probability of treatment weighted propensity score.
CI, confidence interval; GLM, golimumab; IFX, infliximab

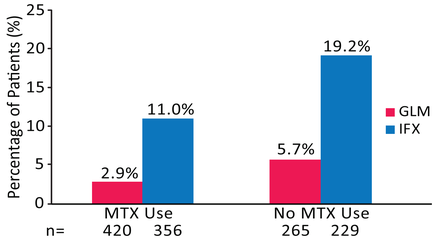
- The difference in infusion reaction rates between the IFX- and GLM-treated patients was also evident in subgroups of both bionaïve vs non-bionaïve patients (Figure 3), and in both MTX non-users vs MTX users (Figure 4)
- Infusion reactions accounted for 9.7% and 35.1% of discontinuations due to adverse events in GLM-treated and IFX-treated patients, respectively

Figure 3. Percentage of Patients With at Least One Infusion Reaction During Study by Prior Biologic Status



GLM, golimumab; IFX, infliximab

Figure 4. Percentage of Patients With at Least One Infusion Reaction During Study by Concomitant Methotrexate Use



GLM, golimumab; IFX, infliximab; MTX, methotrexate

Table 2. Number of Infusions With Pre-infusion Medication Used

	GLM (N=685)	IFX (N=585)
Patients with at least one pre-infusion medication used, n (%)	214 (31.2)	489 (83.6)
Total number of infusions	5609	5415
Infusions with pre-infusion medication used, n (%)	1272 (22.7)	3403 (62.8)
By bionaïve status, n/N (%)		
Infusions with pre-infusion medication from bionaïve patients	387/1922 (20.1)	1498/2512 (59.6)
Infusions with pre-infusion medication from non-bionaïve patients	885/3687 (24.0)	1905/2903 (65.6)
By MTX use, n/N (%)		
Infusions with pre-infusion medication from MTX users	867/3600 (24.1)	2198/3450 (63.7)
Infusions with pre-infusion medication from MTX non-users	405/2009 (20.2)	1205/1965 (61.3)
By medication type, n (%)		
Acetaminophen	945 (16.8)	2462 (45.5)
Diphenhydramine	229 (4.1)	1410 (26.0)
Loratadine	575 (10.3)	911 (16.8)
Cetirizine	216 (3.9)	638 (11.8)
Other	166 (3.0)	532 (9.8)
Methylprednisolone	120 (2.1)	373 (6.9)
Hydrocortisone	48 (0.9)	126 (2.3)
Prednisone	8 (0.1)	101 (1.9)

GLM, golimumab; IFX, infliximab; MTX, methotrexate

Table 3. Infusions With Medication Used for Infusion Reaction: Based on Prior Biologic Exposure and Concomitant Methotrexate Use

	GLM (N=685)	IFX (N=585)
Patients with at least one infusion reaction, n (%)[a]	27 (3.9)	83 (14.2)
Patients with at least one medication for infusion reaction, n (%)	15 (2.2)	64 (10.9)
Total number of infusions with infusion reaction	28	129
Total number of infusions with infusion reaction where medication status is known	28	129
Infusions with medication used for infusion reaction, n/N (%)	15/28 (53.6)	98/129 (76.0)
By bionaïve status, n/N (%)		
Infusions with medication, bionaïve patients	2/6 (33.3)	45/57 (78.9)
Infusions with medication, non-bionaïve patients	13/22 (59.1)	53/72 (73.6)
By MTX use, n/N (%)		
Infusions with medication, MTX users	7/12 (58.3)	59/76 (77.6)
Infusions with medication, MTX non-users	8/16 (50.0)	39/53 (73.6)

[a]Among patients who had at least one infusion reaction (ie, all patients with ≥1 infusion reactions in Week 52 dataset).
GLM, golimumab; IFX, infliximab; MTX, methotrexate

Table 4. Infusions With Medication Used for Infusion Reaction: Based on Medication Type

	GLM (N=685)	IFX (N=585)
Total number of infusions with infusion reaction where medication status is known	28	129
By Medication type, n (%)		
Diphenhydramine	8 (28.6)	53 (41.1)
Hydrocortisone	1 (3.6)	5 (3.9)
Methylprednisolone	4 (14.3)	30 (23.3)
Acetaminophen	5 (17.9)	9 (7.0)
Oxygen	3 (10.7)	4 (3.1)
Cetirizine	0 (0)	1 (0.8)
Other	9 (32.1)	60 (46.5)

GLM, golimumab; IFX, infliximab

Table 5. Number of Patients With Serious or Severe Infusion Reactions

	Patients with at least one serious infusion reaction		Patients with at least one severe infusion reaction	
	GLM (N=685)	IFX (N=585)	GLM (N=685)	IFX (N=585)
n (%)	0 (0)	2 (0.3)	1 (0.1)	4 (0.7)
By bionaïve status, n/N (%)				
Bionaïve patients	0/242 (0)	1/251 (0.4)	1/242 (0.4)	2/251 (0.8)
Non-bionaïve patients	0/443 (0)	1/334 (0.3)	0/443 (0)	2/334 (0.6)
By MTX use, n/N (%)				
MTX users	0/420 (0)	1/356 (0.3)	0/420 (0)	2/356 (0.6)
MTX non-users	0/265 (0)	1/229 (0.4)	1/265 (0.4)	2/229 (0.9)

GLM, golimumab; IFX, infliximab; MTX, methotrexate

CONCLUSIONS

- Whether bionaïve, non-bionaïve, concomitant MTX non-user, or concomitant MTX user at baseline, the incidence of infusion reactions was notably lower among GLM-treated patients than among IFX-treated patients
- Compared to GLM-treated patients, IFX-treated patients were more commonly administered both pre-infusion medications and also medications for an infusion reaction
- Serious infusion reactions did not occur among GLM-treated patients and were rare among IFX-treated patients
- Compared to GLM-treated patients, infusion reactions accounted for almost four times the number of discontinuations related to adverse events in IFX-treated patients

Reference: 1. Schwartzman S, et al. *CCR East.* 2019 (abstract).

Author Disclosures: S. Schwartzman, A. Broadwell, and A. Kivitz are advisors, investigators, and speakers for Janssen. S. Black, S. Xu, W. Langholff, and S. Kafka are employees of Janssen Scientific Affairs, LLC and Janssen Research & Development, LLC.

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