Real-World Comparison of Arthralgias with Infliximab vs. Vedolizumab in the Treatment of Bio-Naïve Inflammatory Bowel Disease

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Abstract

Background: Both infliximab (IFX) and vedolizumab (VDZ) are approved for the treatment of inflammatory bowel disease (IBD) in adults. VDZ is gut-specific and thought to be less effective in controlling extraintestinal manifestations than IFX. The purpose of this study was to compare the incidence and timing of arthralgias between IFX and VDZ.

Methods: We performed a retrospective cohort study of bio-naïve adult patients treated with IFX or VDZ for ulcerative colitis (UC) or Crohn's disease (CD) at a large multicenter gastroenterology private practice. Patients were case-matched 1:1 based on age, gender, diagnosis, and baseline disease severity using the partial Mayo (pMayo) for UC and the modified Harvey-Bradshaw Index (mHBI) for CD. Arthralgias were captured out to 12 months of therapy and classified as pre-existing or new-onset based on time to occurrence. Those with pre-existing arthralgias were excluded from new-onset arthralgias analyses. Rates of arthralgias and time to new-onset arthralgias were compared between IFX and VDZ patients.

Results: A total of 77 IFX (58 UC, 19 CD) and 77 VDZ (58 UC, 19 CD) case-matched pairs were generated. Baseline demographics were similar between IFX and VDZ groups: mean age 45±16.9 vs. 46±16.2, male gender 60% vs. 61%. Rates of pre-existing arthralgias were 13/77 (17%) and 12/77 (16%) in IFX and VDZ cohorts (p=0.83), respectively. Resolution of pre-existing arthralgias was also similar between groups (6/13 vs. 7/12, p=0.70). Of the remaining 64 IFX and 65 VDZ patients without arthralgias at baseline, 16 (25%) IFX patients and 17 (26%) VDZ patients experienced new-onset arthralgias (p=1.0). Median time to new-onset arthralgias was 5.0 (IQR 3.4-7.0) months in IFX patients, compared to 3.3 (IQR 1.4-5.3) months in VDZ patients (p=0.14). While VDZ patients appeared to develop new-onset arthralgias earlier, this was not significant (p=0.19). Of note, two IFX patients discontinued therapy due to suspected drug-induced lupus with arthralgias; there were no VDZ discontinuations due to arthralgias.

Conclusions: Our data suggests that resolution of pre-existing arthralgias and new-onset arthralgias are similar, despite the gut selectivity of VDZ compared to IFX. Additionally, there was no difference in overall time to new-onset arthralgias. These data need to be verified in a larger cohort.

Background

Arthralgias are reported in almost half of patients with inflammatory bowel disease (IBD) and can result is significant morbidity.[1] While both infliximab (IFX) and vedolizumab (VDZ) can be utilized as first-line therapy for IBD in adults, the gut-specific mechanism of VDZ is thought to limit its efficacy in preventing systemic extraintestinal manifestations such as arthralgias.[2-3] However, more recent post-hoc analyses of the GEMINI trials and observational studies suggest that VDZ is not associated with an increased risk of arthralgias.[4-6] To our knowledge, there has been no direct comparison of arthralgias between IFX and VDZ. The purpose of this study was to compare the incidence and timing of arthralgias in a real-world setting using a case-matched cohort of bio-naïve IFX and VDZ IBD patients.

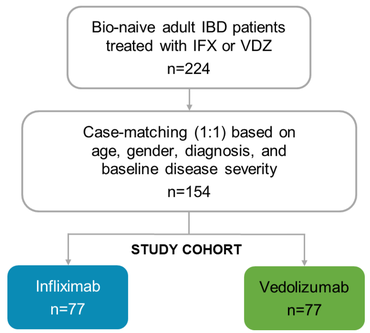
Methods

Retrospective review of all bio-naïve adult IBD patients treated with IFX or VDZ at a multicenter gastroenterology private practice. Patients were case-matched 1:1 based on age, gender, diagnosis, and baseline disease severity.

- Data collection included demographics, disease characteristics, IFX and VDZ biologic therapy, concomitant conventional agent use, and patient-reported arthralgias
- Arthralgias were captured out to 12 months of therapy and classified as pre-existing or new-onset based on time to occurrence
  - Those with pre-existing arthralgias were excluded from new-onset arthralgias analyses
- The influence of steroid weaning on new-onset arthralgias was also investigated
- Descriptive data were reported as frequencies and proportions for categorical variables, and as mean ± standard deviation (SD) or median (interquartile range, IQR) for continuous variables. Fisher's exact test was used for comparisons. Kaplan-Meier method was used for time-to-event analyses.

Results

Patient Selection



Baseline Demographics

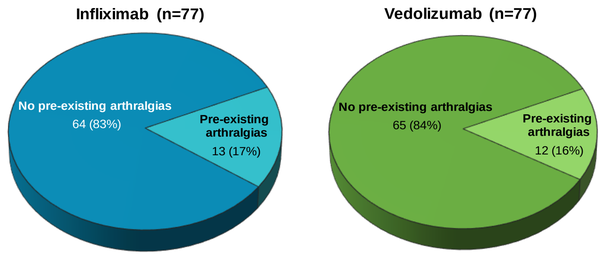
	Infliximab n=77	Vedolizumab n=77
Age in years, mean ± SD	45 ± 16.9	46 ± 16.2
Male gender, n (%)	46 (60%)	47 (61%)
Disease diagnosis, n (%)		
Ulcerative colitis	58 (75%)	58 (75%)
Crohn's disease	19 (25%)	19 (25%)
Disease duration in years, median (IQR)	1.7 (0.4-7.4)	4.6 (0.9-13.3)
Disease activity score at baseline		
pMayo, median (IQR)	6 (5-7)	6 (4-7)
mHBI, median (IQR)	7 (5.5-10)	7 (5-8)

Conventional Agents at Biologic Initiation

	Infliximab n=77	Vedolizumab n=77
Concomitant conventional agents, n (%)	65 (84%)	61 (79%)
Steroids	53 (69%)	38 (49%)
5-ASA	35 (45%)	39 (51%)
Immunomodulator	10 (13%)	8 (10%)
Multiple conventional agents, n (%)	28 (36%)	22 (29%)

- Over three-fourths of IFX and VDZ patients were on concomitant conventional agents at the time of biologic initiation

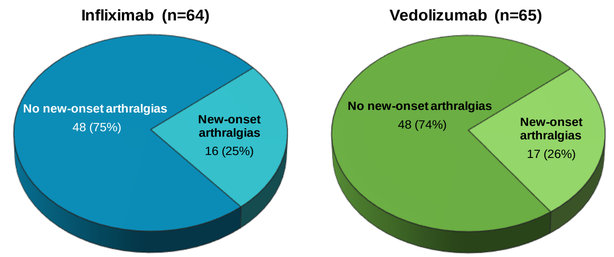
IFX vs. VDZ: Pre-Existing Arthralgias at Baseline



- 13 (17%) IFX and 12 (16%) VDZ patients had arthralgias at the time of biologic initiation
- Approximately half of patients with pre-existing arthralgias resolved (6/13 IFX and 7/12 VDZ patients, p=0.70) at median times of 2.3 (IQR 0.7-4.7) and 2.0 (IQR 0.5-5.1) months following biologic initiation, respectively

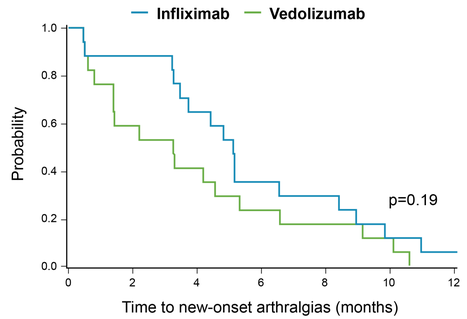
IFX vs. VDZ: New-Onset Arthralgias at 12 Months

- The remaining 64 IFX and 65 VDZ patients without pre-existing arthralgias were compared



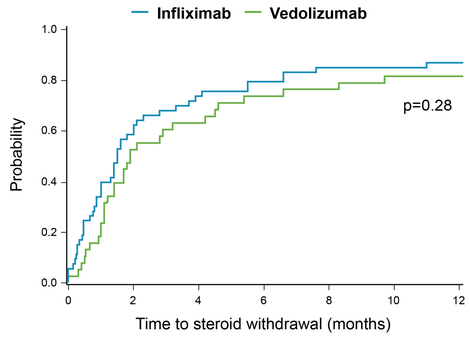
- There was no difference in the rate of new-onset arthralgias in IFX patients compared to VDZ patients (25% vs. 26%, p=1.0)

IFX vs. VDZ: Time to New-Onset Arthralgias



- Median time to new-onset arthralgias was 5.0 (IQR 3.4-7.0) months in IFX patients, compared to 3.3 (IQR 1.4-5.3) months in VDZ patients (p=0.14)
- While VDZ patients appeared to develop new-onset arthralgias earlier than IFX patients, this was not significant (p=0.19)

IFX vs. VDZ: Steroid Withdrawal at 12 Months



- Of 53 IFX and 38 VDZ patients on steroids at the time of biologic initiation, similar proportions were weaned off by 12 months [IFX 46 (87%) vs. VDZ 31 (82%), p=0.50]
- There was no difference in time to steroid withdrawal following biologic initiation

Discussion

- We performed a case-matched comparison of arthralgias in bio-naïve IFX and VDZ-treated IBD patients. To our knowledge, this is the first head-to-head study to investigate new-onset arthralgias and time to occurrence.
- Of 13 (17%) IFX and 12 (16%) VDZ patients with pre-existing arthralgias at the time of biologic initiation, rates of resolution and time to resolution were similar.
- The remaining 64 IFX and 65 VDZ patients without pre-existing arthralgias were compared with respect to new-onset arthralgias at 12 months and time to occurrence following biologic initiation.
  - We observed no difference in the rate of new-onset arthralgias between IFX and VDZ-treated patients at 12 months (25% vs. 26%, p=1.0).
  - There was also no difference in overall time to new-onset arthralgias between cohorts. VDZ patients reported symptoms earlier, but this was not significant. This may be attributable to VDZ's slower onset of action compared to IFX.
- Steroid withdrawal did not confound these findings.
  - Though more IFX patients were on steroids at the time of biologic initiation (IFX 69% vs. VDZ 49%), similar proportions were weaned off steroids by 12 months (87% vs. 82%, p=0.50) and there was no difference in the time to steroid withdrawal.

Conclusion

- In a case-matched retrospective review of infliximab and vedolizumab, rates of new-onset arthralgia were similar. Vedolizumab-treated patients experienced new-onset arthralgias earlier, though this was not statistically significant.
- Our data suggest that vedolizumab is as effective in controlling arthralgias as infliximab, despite its gut selectivity. These findings are consistent with post-hoc analyses of VDZ-treated patients in the GEMINI trial.[4]

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Disclosures

Dr. Ritter is a speaker and advisory board member with Janssen, and a speaker, advisory board member and grant recipient with Takeda. The other authors have no disclosures.