Onset of Response with Infliximab vs. Vedolizumab in the Treatment of Bio-Naïve Inflammatory Bowel Disease

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Abstract

Introduction: Both infliximab (IFX) and vedolizumab (VDZ) are approved for the treatment of inflammatory bowel disease (IBD) in adults. Compared to IFX, VDZ is thought to have a slower onset of response. The purpose of this study was to characterize the incidence and timing of clinical remission 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. Primary endpoints were clinical remission rates at 6 months (mos), defined as pMayo less than 2 or mHBI less than 5, and time to remission represented by a Kaplan Meier curve. Patients in remission at baseline and those discontinuing therapy <6 mos were excluded from analyses.

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%. Thirty-three patients were excluded from efficacy analyses: 8 in remission at baseline, 25 discontinuing therapy <6 mos (16 IFX, 11 VDZ). Data are presented for the remaining 121 patients: IFX 60 (47 UC, 13 CD) and VDZ 61 (48 UC, 13 CD). Disease severity scores over 6 mos are depicted, with both IFX and VDZ demonstrating a rapid response by 2 weeks of treatment. Remission rates were similar among IFX and VDZ-treated UC patients (78.7% vs 64.6%, p=0.13), and significantly higher for IFX-treated CD patients (84.6% vs 46.2%, p=0.04). There was no difference in time to remission.

Discussion: We observed rapid onset of response and high remission rates among bio-naïve patients treated with both IFX and VDZ. While IFX-treated CD patients experienced significantly higher remission rates, our numbers were small. Importantly, time to remission did not differ between IFX and VDZ-treated patients. These data need to be verified in a larger cohort.

Background

While both infliximab (IFX) and vedolizumab (VDZ) can be positioned as first-line biologic therapy for inflammatory bowel disease (IBD) in adults, the onset of response with anti-integrin agents is thought to be slower in comparison to anti-TNF agents.[1-6] However, more recent post-hoc analyses of VDZ-treated ulcerative colitis (UC) and Crohn's disease (CD) patients from the GEMINI trials indicate significant clinical improvement as early as week 2 of therapy, particularly for those that were biologic-naïve.[7] Direct comparisons between IFX and VDZ remain limited.[8-9] The purpose of this study was to characterize the incidence and timing of clinical remission in a real-world setting using a case-matched cohort of bio-naïve IFX and VDZ IBD patients.

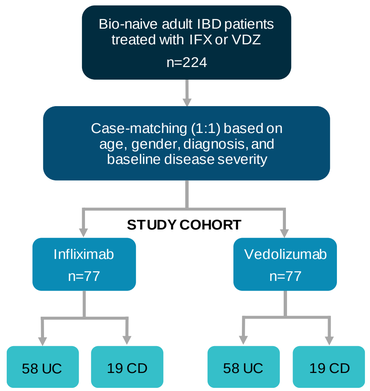
Methods

We conducted a retrospective review of all bio-naïve adult patients treated with IFX or VDZ for UC or CD at a large 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 corticosteroid use, and disease activity
- Disease activity was assessed using the partial Mayo (pMayo) for UC patients and the Harvey-Bradshaw Index (mHBI) for CD patients at the following time points: baseline, 2 weeks, 6 weeks, 14 weeks, and 6 months
- Primary efficacy endpoints were clinical remission rates at 6 months, and time to clinical remission
  - Clinical remission was defined by pMayo score <2 or mHBI score <5
  - Patients whose disease severity scores indicated remission at baseline and those discontinuing IFX or VDZ therapy <6 months were excluded from efficacy analyses
- 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. The Kaplan Meier Log Rank test was used to assess time to clinical remission.

Results

Patient Selection



Baseline Demographics

	Infliximab Cohort		Vedolizumab Cohort	
	UC n=58	CD n=19	UC n=58	CD n=19
Age (yrs), mean±SD	45±16.6	43±18.1	45±15.2	49±19.1
Male gender, n(%)	40 (69%)	6 (32%)	40 (69%)	7 (37%)
Disease duration (yrs), median (IQR)	2.2 (0.6-9.0)	0.4 (0.1-1.1)	6.6 (1.5-13.3)	1.3 (0.5-10.5)
pMayo at baseline, median (IQR)	6 (5-7)	-	6 (4-7)	-
mHBI at baseline, median (IQR)	-	7 (5.5-10)	-	7 (5-8)

- After case-matching, IFX and VDZ cohorts were similar with respect to age, gender, diagnosis, and baseline disease severity

Biologic Dosing

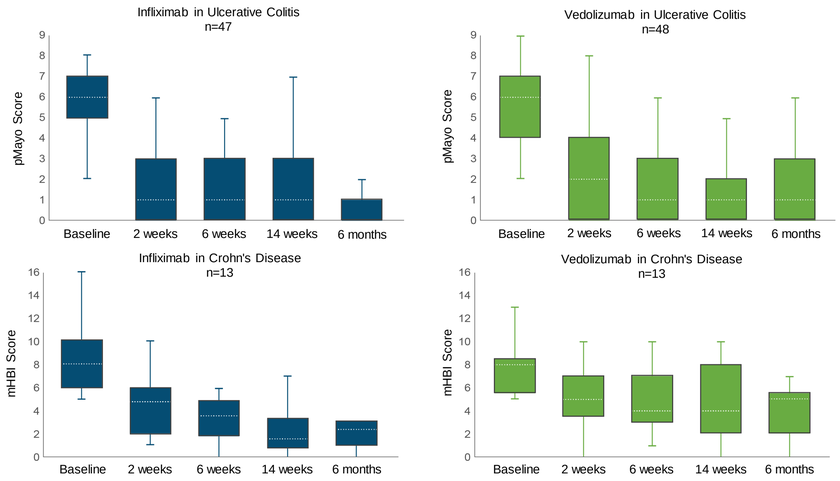
	Infliximab Cohort		Vedolizumab Cohort	
	UC n=58	CD n=19	UC n=58	CD n=19
Dose (mg), mean±SD	433±134	416±112	300 (-)	300 (-)
Dose (mg/kg), mean±SD	5.4±0.8	5.4±0.4	3.8±0.9	4.3±1.1
Dose escalation <6 months, n(%)	13 (22%)	6 (32%)	10 (17%)	1 (5%)
Time to dose escalation (months), mean±SD	4.3±0.8	4.4±1.5	4.6±0.6	4.6 (-)

- Standard initiation dosing of IFX and VDZ were prescribed
- 18 of 19 dose escalations in the IFX cohort were due to subtherapeutic drug levels. Only 6 of 11 dose escalations in the VDZ cohort were due to subtherapeutic drug levels. The remaining were for inadequate symptom control.

Concomitant Medication Use at Biologic Initiation

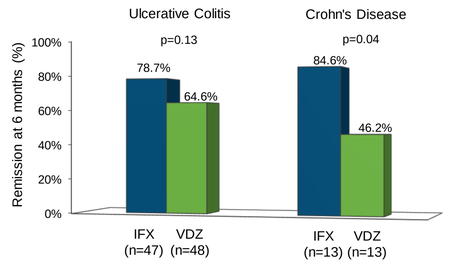
	Infliximab Cohort		Vedolizumab Cohort	
	UC n=58	CD n=19	UC n=58	CD n=19
Concomitant medications, n(%)	51 (88%)	14 (74%)	47 (81%)	14 (74%)
Steroids, n(%)	40 (69%)	13 (68%)	27 (47%)	11 (58%)
5-ASA, n(%)	31 (53%)	4 (21%)	30 (52%)	9 (47%)
Immunomodulator, n(%)	8 (14%)	2 (11%)	7 (12%)	2 (11%)
Multiple agents, n(%)	24 (41%)	4 (21%)	15 (26%)	7 (37%)

Infliximab vs. Vedolizumab: Disease Severity Scores at 6 months



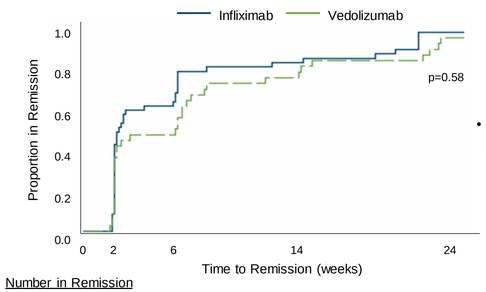
- 6 month efficacy data is presented for 121 of 154 patients. The following patients were excluded from analyses:
  - 8 with disease severity scores indicating remission at baseline
  - 25 that discontinued biologic therapy <6 months (16 IFX, 11 VDZ)
- Significant changes (p<0.05) in disease activity scores compared to baseline were observed as early as 2 weeks in both IFX and VDZ-treated IBD patients, with reductions maintained through 6 months

Infliximab vs. Vedolizumab: Remission Rates at 6 months



- Overall remission rates were 80% and 61% for IFX and VDZ-treated IBD patients, respectively
- Similar remission rates were achieved among IFX and VDZ-treated UC patients (78.7% vs. 64.6%, p=0.13)
- Significantly higher remission rates were observed in IFX-treated CD patients (84.6% vs. 46.2%, p=0.04)

Infliximab vs. Vedolizumab: Time to Remission

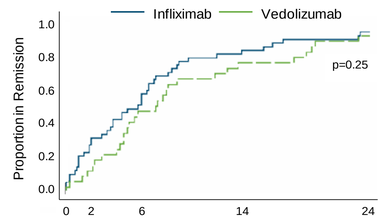


Number in Remission

Infliximab	31	34	37	48
Vedolizumab	17	28	29	37

- As depicted by the Kaplan Meier curve, there was no difference in time to remission (p=0.58)

Infliximab vs. Vedolizumab: Steroid Use at 6 months



- Similar proportions of patients were weaned off steroids by 6 months (IFX 83% vs. VDZ 74%, p=0.28)
- Additionally, there was no difference in time to steroid withdrawal following IFX or VDZ initiation (p=0.25)

Discussion

- We performed a case-matched comparison of clinical remission rates and time to remission in IFX and VDZ-treated IBD patients. To our knowledge, this is the first head-to-head study to investigate time to remission.
- Significant reductions in disease activity scores were observed as early as week 2 of therapy in both groups, and maintained through 6 months.
- Similar remission rates were achieved among IFX and VDZ-treated UC patients.
- Significantly higher remission rates were observed in IFX-treated CD patients. This finding is consistent with prior literature indicating more promising results for VDZ use in UC rather than CD.[10]
- It has been debated whether VDZ has a slower onset of action relative to other IBD agents.[3-4,7] In our case-matched cohort, we observed no difference in time to remission between IFX and VDZ.
- Similarly, proportions of patients weaned off concomitant steroids and time to steroid withdrawal was not different between IFX and VDZ-treated patients.

Conclusion

- In a case-matched retrospective review of infliximab and vedolizumab, remission rates were similar in UC patients and significantly higher in IFX-treated CD patients.
- We observed no difference in time to clinical remission.
- These data support the use of either agent for bio-naïve ulcerative colitis patients, though suggest that infliximab should remain first-line therapy for bio-naïve Crohn's disease patients.

References

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