#P1378

Failure of Vedolizumab as First Line Biologic Does Not Decrease Response Rate of Second Line Therapy

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Background

Vedolizumab (VDZ) is an anti-α4β7 integrin monoclonal antibody approved for the treatment of Crohn's disease (CD) and ulcerative colitis (UC). It is clear from multiple clinical trials that patients who have failed anti-TNF therapy have a significantly diminished response to a second line biologic.[1-4] It is unclear if this remains true for patients who fail vedolizumab as first line therapy.

Aim

To assess the clinical response of IBD pts treated with an anti-TNF agent following failure of VDZ as a first-line biologic.

Methods

We reviewed all biologic-naïve IBD pts who were started on VDZ treatment in a large, multicenter, gastroenterology private practice from the drug approval date through March, 2018.

- Data collected included demographics, disease characteristics, prior and concurrent therapy, and disease activity scores.
- Disease activity was retrospectively assessed utilizing the Harvey Bradshaw Index (HBI) in CD pts and the partial Mayo score (pMayo) in UC pts.

Pts who discontinued VDZ were then further analyzed for:

- Time to discontinuation and subsequent reasons
- Therapy received following VDZ discontinuation.

Outcomes were assessed for those pts who received a 2nd line agent following VDZ and included:

- Disease activity at VDZ discontinuation, initiation of 2nd line therapy, and 3 months post 2nd line intervention.
- Clinical response at 3 months, defined as any decline in disease activity score.
- Clinical remission at 3 months was defined as HBI <5 or pMayo score <2.
- Steroid reduction and change in biomarkers at 3 months.

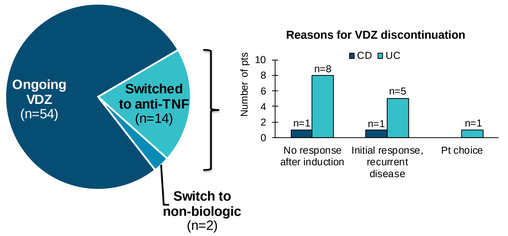
Data analysis included descriptive statistics on the patient population, response to VDZ, discontinuation of VDZ, and clinical outcome upon switching to an anti-TNF agent. The Kaplan Meier Log Rank test was used to assess the association between diagnosis and time to discontinuation of VDZ. Changes in clinical indicators (steroid use, ESR, CRP) were assessed using the n-1 chi square test for equivalence of proportions and the Wilcoxon signed rank test.

Demographics

Characteristics	CD (n=11)	UC (n=59)	Total (n=70)
Gender, n (%)			
Male	4 (36)	31 (53)	35 (50)
Age			
Mean yrs (range)	58 (24-86)	48 (20-82)	49 (20-86)
Disease Duration			
Median yrs (IQR)	12 (4-28)	9 (2-16)	9 (2-16)
Prior IBD Characteristics, n (%)			
Extraintestinal manifestations (EIMs)	4 (36)	10 (17)	14 (20)
Perianal disease	3 (27)	0	7 (10)
Concurrent Medications, n (%)			
5-Aminosalicylate	3 (27)	35 (59)	38 (54)
Corticosteroid	4 (36)	11 (19)	29 (41)
Immunomodulator	1 (9)	25 (42)	12 (17)

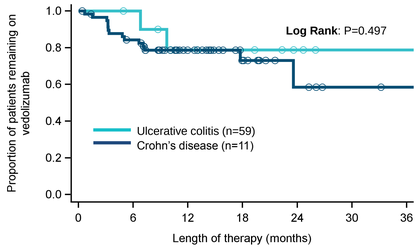
Results

VDZ Discontinuations



- VDZ was discontinued in 16/70 pts (23%).
- Upon VDZ discontinuation 14/16 pts (88%) were switched to an anti-TNF agent.
- 2 pts were not treated with a 2nd line agent (1 with surgery due to progressive disease and 1 stepped down to 5-ASA due to pt choice).

Time to Discontinuation of VDZ



- VDZ discontinuation occurred at a median length of therapy of 21 weeks.
- 6 pts (38%) discontinued VDZ within 14 weeks, 8 pts (50%) between 14 and 52 weeks, and 2 pts (12%) following 1 year of VDZ therapy.
- There was no difference in time to VDZ discontinuation by diagnosis (P=0.497).

2nd Line Treatment Following VDZ Discontinuation

Treatment Characteristics	CD (n=2)	UC (n=12)	Total (n=14)
Adalimumab			
Dosage (mg)*	40 (-)	-	-
Infliximab			
Dosage (mg)*	-	475 (200-700)	-
All Therapies			
Mean time from VDZ discontinuation to initiation, wks (range)	8 (4-12)	9 (3-24)	9 (3-24)
Concurrent Medications, n (%)			
5-Aminosalicylates	-	5 (42)	5 (36)
Corticosteroids	1 (50)	10 (83)	11 (79)
Immunomodulators	1 (50)	4 (33)	5 (36)

*Initially, ADA was administered every other week and IFX at 0,2, and 4 weeks then 8 wk

- No pt had a dose escalation within 3 mo of ADA or IFX initiation.
- Significantly more patients received concurrent steroids (71% vs. 41%) in the group failing VDZ treated with a 2nd line biologic than those who did not fail VDZ (P=0.041).

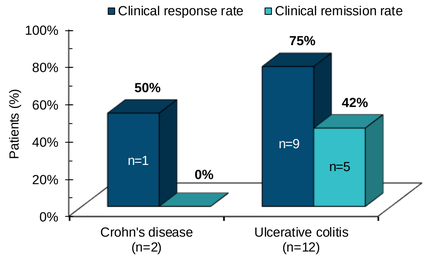
3-Month Change in Disease Activity

Disease activity score	Prior to VDZ	Initiation of anti-TNF	3-Month of anti-TNF	% Score Decrease with anti-TNF
UC pts Initiated on IFX (n=12)				
pMayo, mean	5.3	3.9	2.4	38
Stool frequency	2.5	1.8	1.3	28
Rectal bleeding	0.8	0.7	0.2	71
Physician global assessment	2	1.4	1	29
CD pts Initiated on ADA (n=2)				
HBI, mean	5.5	7.5	5	33
General well-being	1	1.5	0.5	67
Abdominal pain	2	1	0	100
Liquid stool frequency	1.5	3.5	3	14
Abdominal mass	0	0	0	no change

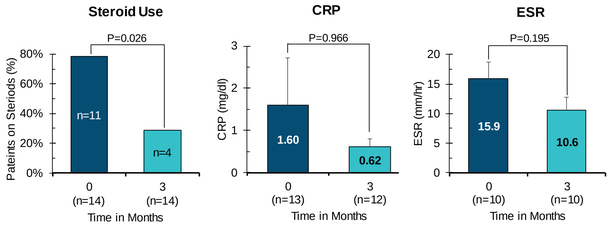
Abbreviations: CD: Crohn's disease; UC: ulcerative colitis; HBI: Harvey-Bradshaw Index; pMayo: partial Mayo Score; ADA: adalimumab; IFX: infliximab; pts: patients; VDZ: vedolizumab; TNF: tumor necrosis factor.

- UC pts experienced a 38% reduction in the pMayo score primarily due to the decline in rectal bleeding.
- The overall reduction in disease activity in CD and UC pts were comparable (38 vs 33%).

3-Month Clinical Response Rate



3-Month Changes in Steroid Use and Biomarkers



- Steroid use, ESR, and CRP declined by 50, 33, 61%, respectively, at 3 mo.

Discussion

- Of the 70 pts who received VDZ as first line therapy for IBD, 16 (23%) required 2nd line therapy.
- 18% (2/11) of CD patients and 24% (14/59) of UC patients discontinued VDZ.
- Median length of time to VDZ discontinuation was 21 weeks. Discontinuation occurred for:
  - Primary non-response in 9 (56%).
  - Secondary non-response in 6 (38%).
- Of the 16 VDZ failures, 14 (88%) initiated anti-TNF biologic therapy following VDZ.
- The 2 CD patients initiated ADA and the 12 UC patients initiated IFX.
- The group failing VDZ treated with an anti-TNF had a significantly higher use of concurrent steroids (P=0.041).
- One of the 2 CD pts treated with ADA had a reduction of disease activity but not clinical remission at 3 months.
- 9/12 (75%) of the UC pts had reduced disease activity, with 5 (42%) in clinical remission at 3 months.
- Change in steroid use declined significantly at 3-months (P=0.026). Improvements were seen in ESR and CRP, although not significant.
- The study is limited by small sample size.

Conclusion

- These observations suggest that failure of VDZ as first line therapy does not appear to diminish the response to anti-TNF agents as 2nd line therapy.
- These interesting data warrant continued study with a larger sample and longer follow-up time in order to confirm initial findings.

References

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