#P189

Real World Evaluation of Prolonged Clinical Response with Vedolizumab in Crohn's Disease and Ulcerative Colitis Patients Treated in a Private Practice Setting

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Background

Vedolizumab (VDZ), a gut-selective anti-α4β7 integrin monoclonal antibody, was approved by the FDA in May 2014, for adult patients (pts) with moderate to severe Crohn's disease (CD) and ulcerative colitis (UC) [1]. When compared to other therapeutic agents for inflammatory bowel disease (IBD), VDZ is reported to take a notably longer time to induce a clinical response and achieve maximal efficacy than other therapeutic agents used for treatment of CD and UC. Studies indicate that there is a lag in response time following initiation of VDZ versus other agents [2,3,4].

Objective

Our objective was to observe prolonged clinical response to VDZ in IBD pts who achieved an initial clinical response in the first 6 months of treatment.

Methods

Study design

- Multicenter, real-world, retrospective observational study of IBD pts who achieved prolonged clinical response within 6 months (mo) of starting VDZ treatment (May 2014 and October 2015) with up to 24 months of available follow-up data.

Data collection

- Demographics, clinical characteristics, prior and concurrent therapies were collected for all pts.
- Labs and diagnostics, VDZ infusion history, treatment emergent adverse events (TEAEs) and clinical outcomes were collected.
- Prolonged clinical response was determined by presence of the following factors:
  - Physician global assessment of response
  - Continuation of therapy
  - Decrease in stool frequency
  - Decrease in abdominal pain
  - Where available:
    - Evidence of mucosal healing on colonoscopy
    - Absence of rectal bleeding, when noted
    - Absence of fecal incontinence
    - Absence of extraintestinal manifestations
- Assessment of response was conducted at 9, 12, 15, 18, 21, and 24 months post-VDZ initiation.

Data analysis

- Descriptive data statistics were analyzed in aggregate.
- The clinical response rate was calculated using the Kaplan-Meier method.
- Risk factors for VDZ non-response were determined using the Altman method including odds ratio (OR) and 95% confidence interval (CI) with a p value <0.05 to be statistically significant.

Results

Fig. 1. Patient Selection

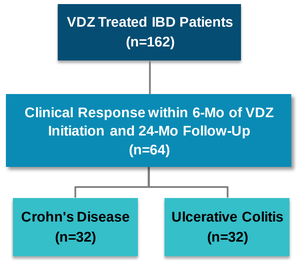


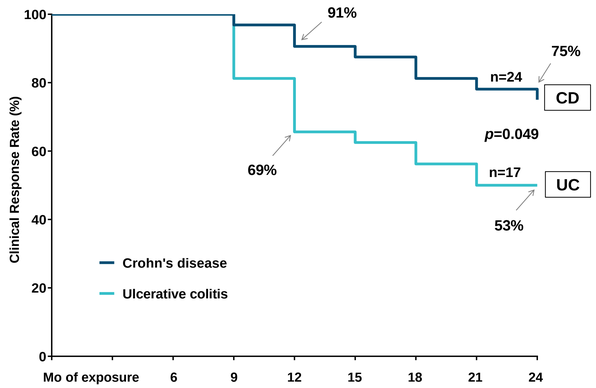
Table 1. Demographics and Baseline Characteristics

Patient Characteristics	CD (n=32)	UC (n=32)	Total (n=64)
Median age, years (IQR)	41 (16)	42 (21)	42 (20)
Gender, female, no. (%)	18 (56)	18 (56)	36 (56)
Median disease duration, years (IQR)	11 (8)	7 (7)	9 (9)
Current or former smoker, no. (%)	13 (41)	8 (25)	21 (33)
Prior surgical resection, no. (%)	23 (72)	5 (16)	28 (44)
Concomitant medication, no. (%)			
Corticosteroids	11 (34)	13 (41)	24 (38)
Immunomodulators	10 (31)	7 (22)	17 (27)
Prior anti-TNF therapies, no. (%)			
≥1	31 (97)	30 (94)	61 (95)
≥2	24 (75)	12 (38)	36 (56)
≥3	14 (44)	4 (13)	18 (28)

Table 2. VDZ Treatment Characteristics

Treatment Characteristics	CD (n=32)	UC (n=32)	Total (n=64)
Median VDZ duration, months (IQR)	27 (7)	23 (18)	26 (13)
Median no. of VDZ infusions (IQR)	15 (3)	14 (6)	14 (4)
Dose frequency, no of pts (%)			
Q4 weeks	2 (6)	5 (16)	7 (11)
Q6 weeks	3 (9)	1 (3)	4 (6)
Q7 weeks	1 (3)	0 (0)	1 (2)
Q8 weeks	26 (81)	26 (81)	52 (81)

Fig. 2. 24-Month Clinical Response Rate



CD (n)	32	31	29	28	26	25	24
UC (n)	32	26	22	21	19	17	17

- At 24 months, CD pts have significantly greater prolonged clinical response compared to UC pts (75% vs. 53%, *p*=0.049).

Table 3. Response Related to Prior Anti-TNF Use

Impact of Prior Anti-TNF Therapy on 24-Month Clinical Response (CR)							
No. of Prior Anti-TNFs	**Total No. of Pts**	**No. of CD Pts**			**No. of UC Pts**		
		CR	No CR	Time to Non-Response*	CR	No CR	Time to Non-Response*
1	25	5	2	13 mo (range 11-16)	8	10	10 mo (range 7-21)
≥2	36	19	5	18 mo (range 12-23)	8	4	12 mo (range 7-18)

*; Median time to non-response in months.

- The number of prior anti-TNF treatments did not significantly impact the 24 month response.
- Dosing frequency escalations did not impact prolonged clinical responses for either CD or UC.

Table 4. Changes in Corticosteroid Use

Impact of VDZ Therapy on Corticosteroid Use	CD (n=32)	UC (n=32)
Baseline corticosteroid use (no. of pts)	11	13
Steroid-free at 6-month	3 (27%)	5 (38%)
Steroid-free at 24-month	3 (27%)	7 (54%)
Corticosteroid added during VDZ therapy	1	0

Table 5. Treatment Emergent Adverse Events (TEAEs)

TEAE	CD (n=32)		UC (n=32)		Total
	No. of Pts (%)	No. of TEAEs (%)	No. of Pts (%)	No. of TEAEs (%)	No. of TEAEs (%)
6-24 Months on VDZ					
Arthalgia	1 (3)	3 (13)	1 (3)	4 (50)	7 (70)
Flushing	1 (3)	1 (4)	-	-	1 (10)
Headache	1 (3)	1 (4)	-	-	1 (10)
Nausea/vomiting	-	-	1 (3)	1 (12)	1 (10)
Total	**3**	**5**	**2**	**5**	**10**

- A total of 10 TEAEs occurred in 8% of pts (5/64) between 6 and 24 months.
- Most TEAEs occurred prior to 6 mo of VDZ (31 in 12 pts).
- None of the TEAEs led to VDZ discontinuation or hospitalization.

Table 6. Risk Analysis for Non-Response to VDZ

Risk Factor	CD		UC		Overall		
	OR	P Value	OR	P Value	OR	95% CI	P Value
Gender, female	0.20	0.08	1.33	0.69	0.41	0.14 to 1.17	0.10
Crohn's disease	-	-	-	-	0.38	0.13 to 1.09	0.07
Disease duration ≥5 years	2.33	0.47	0.20	0.80	1.81	0.59 to 5.57	0.30
Perianal disease	0.84	0.84	0.17	0.13	2.05	0.62 to 6.65	0.27
Extraintestinal manifestation	0.69	0.66	0.22	0.06	2.78	0.97 to 7.90	0.06

- Overall odds analysis used to predict potential risk factors associated with an unfavorable response to VDZ revealed no significant differences between both groups, VDZ responders (n=41) *vs.* non-responders (n=23).
- Similarly, odds analysis by IBD diagnosis revealed no significant differences between VDZ responders and non-responders.

Discussion

We evaluated clinical response in all pts treated within a large multicenter GI private practice who achieved prolonged clinical response to VDZ by 6 mo of starting therapy and with 2 years of available follow-up data.

- 64/162 IBD pts met the criteria for study inclusion at 6 months with 32 each diagnosed with CD and UC.
- 95% (61/64) of the study cohort were biologic-experienced with long-term disease. 38% of pts (24/64) were taking concomitant corticosteroids and 27% (17/64) were taking immunomodulators at VDZ. 19% (6/64) received a dose escalation of VDZ for therapy optimization.
- Overall prolonged clinical response at 24 months was seen in 64% (41/64). CD pts had a significantly higher response than UC pts, 75% (24/32) vs. 53% (17/32), *p*=0.049.
- 27% (3/11) of CD pts on concomitant corticosteroids at VDZ initiation were steroid-free at 6 and 24 months.
- 38% (5/13) of UC pts on concomitant corticosteroids at VDZ initiation were steroid-free at 6 months which increased to 54% (7/13) at 24 months.
- Multiple prior anti-TNF therapies and TEAEs did not impact persistence of response.
- No significant risk factors were determined for patients with a 24-month unfavorable response to VDZ, given the relatively small sample size in this study.

Conclusion

- The majority of IBD pts (64%) who achieved a response at 6 months, maintained the response at 24 months.
- Prolonged clinical response was greater in CD (75%) compared to UC (53%) pts with a third of pts steroid-free at the conclusion of the study.
- We did not identify any potential factors associated with pts who do not achieve prolonged response with VDZ.

References

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