#P2139

Long-Term Safety Analysis of Vedolizumab for Treatment of Crohn's Disease and Ulcerative Colitis

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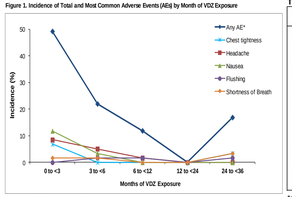
Abstract

Background: Vedolizumab (VDZ) was FDA approved in the US for treatment of Crohn's disease (CD) and ulcerative colitis (UC) in 2014. Several studies have reported the efficacy and safety of VDZ in real world settings; however, there is little information available on VDZ use over extended periods. This study reports on the safety of long-term VDZ therapy provided to patients in clinics associated with a large multicenter gastroenterology (GI) private practice.

Methods: A retrospective chart review was performed on (pts) treated with VDZ for ≥52 weeks of therapy from July 1, 2014 through March 31, 2017. Patient data collected included demographics, diagnosis, prior treatments, and VDZ dosing history and adverse events (AEs) with associated emergency department (ED) visits or hospitalizations. Regression analyses were performed with Odds Ratios (OR) to assess AE risk factors.

Results: A total of 69 pts (39 CD, 30 UC) were evaluated. Mean age was 44 years (range: 21-80) with 55% female. Pts received a median of 13 VDZ doses (range: 8-23) during the study period accounting for 1198 infusions with a median length of therapy of 87 weeks (range: 54-138). Three patients were biologic-naïve and all others had previous anti-TNF therapy prior to VDZ initiation. 20 pts (29%) reported 59 AEs, with 14 (70%) females, 15 (75%) with CD and 11 (55%) with concurrent oral IBD therapy. All were on previous anti-TNFs, 14/20 (70%) had previous surgeries and all AEs occurred in the first 52 wks of treatment in 17/20 (85%). Three of 14 pts who had VDZ dose escalation experienced AEs. Two pts developed upper respiratory tract infections during treatment. No pts discontinued VDZ due to AEs, although 1 pt had an ED visit and subsequent hospitalization due to therapy-related severe nausea and dehydration. Detailed AEs are described in Table 1. Overall incidence of common AEs by month of VDZ exposure is shown in Figure 1. Risk factors associated with development of AEs were previous IBD surgeries (OR=4.81, 95% CI=1.56-14.86, p=0.006) and diagnosis of CD (OR=3.12, 95% CI=0.98-9.94, p=0.05).

Figure 1. Incidence of Total and Most Common Adverse Events (AEs) by Month of VDZ Exposure



* represents 59 AEs experienced in 20 patients.

Table 1. VDZ Treatment-Related Adverse Events

Treatment-Related AE	Patients n, (%)
Chest tightness	5 (7.2)
Headache	4 (5.8)
Nausea	4 (5.8)
Flushing	3 (4.3)
Shortness of breath	3 (4.3)
Arthralgia	2 (2.9)
Cough	2 (2.9)
Nasopharyngitis	2 (2.9)
Pruritis/hives	2 (2.9)
Upper Respiratory Infection	2 (2.9)
Dehydration	1 (1.4)
Hypotension	1 (1.4)
Peripheral edema	1 (1.4)
Pleurisy	1 (1.4)
Pyrexia	1 (1.4)
Skin lesion	1 (1.4)
Vomiting	1 (1.4)

*, patients experienced ≥1 AE

Discussion: Limited data are available on the long-term use of VDZ in real world settings. We observed a low frequency of AEs with related hospitalizations and ED visits in moderate to severe IBD pts treated with long-term VDZ therapy. Previous IBD surgeries and diagnosis of CD were associated with a statistically significant increase in AEs.

Background

Vedolizumab (VDZ) is a gut-selective anti-α4β7 integrin antibody that is FDA-approved for the treatment of IBD. In pts who participated and received follow-up monitoring up to week 52 in the completed GEMINI 1 and 2 phase 3 trials, vedolizumab exposure was not associated with the occurrence of an AE (OR=1.23, 95% CI=0.96 to 1.58, p=0.107) [1-2]. Likewise, many observational studies have demonstrated that the benefits of VDZ far exceed its risks up to 1 year of VDZ exposure [3-4]. Currently, data in the literature are scarce regarding the real-world safety of VDZ beyond 52 weeks in a longitudinal cohort.

Aim:

- This study assessed the long-term safety of vedolizumab in a real-world private practice gastroenterology setting.

Methods

A multicenter, real-world, retrospective observational study was conducted in pts who had received therapy for at least 1 year.

Inclusion Criteria:

- IBD pts seen at Texas Digestive Disease Consultant (TDDC) clinics who received VDZ for ≥52 weeks between July 1, 2014 and March 31, 2017.

Data Collection:

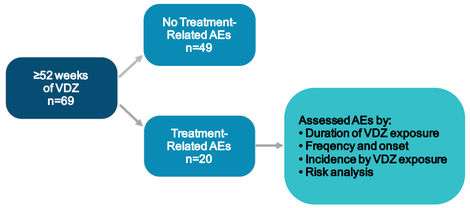
- Demographics, medication history, risk and prognostic factors, VDZ exposure by length of therapy, and dosage adjustments were collected for all pts.
- Treatment-related AEs, incidence of AEs, and clinical outcomes following the AEs were collected for pts who reported an AE.
  - Causality of AEs and clinical outcomes were assessed by the investigators.

Data analysis:

- Descriptive statistics were conducted to analyze the data in aggregate.
- Risk factors were determined using the Altman method including Odds Ratios (OR) and 95% confidence interval (CI) with a *p*-value <0.05 to be statistically significant [5].

Safety Cohort

Patient Flow Diagram



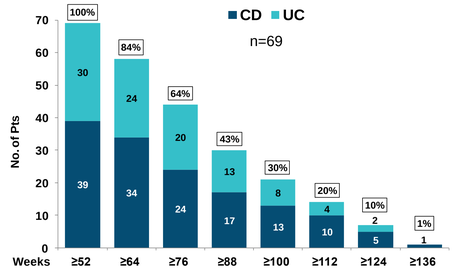
Demographics

Characteristics n=69	AEs n=20	No AEs n=49	*p*-value
Age, yrs			
Mean (range)	43 (22-71)	44 (21-80)	0.79
Gender, no. of pts (%)			
Female	14 (70)	24 (49)	0.79
IBD diagnosis, no. of pts (%)			
Crohn's Disease	15 (75)	24 (49)	0.05
Ulcerative Colitis	5 (25)	25 (51)	
Co-morbidities, no. of pts (%)			
≥1 diagnosis	17 (85)	32 (65)	0.10
Duration of disease, yrs			
Median (range)	11 (2-34)	8 (<1-42)	0.07
Duration of VDZ exposure, yrs			
Median wks (range)	90 (56-138)	83 (54-135)	0.36
Prior medications, no. of pts (%)			
TNFα inhibitors	20 (100)	46 (94)	0.27
Non-TNFα biologics	2 (10)	4 (8)	0.79
Concurrent medications, no. of pts (%)			
Immunomodulators	4 (20)	7 (14)	0.54
Corticosteriods	8 (40)	16 (33)	0.58

Statistics performed using Chi-squared and Mann-Whitney U test, with a $p<0.05$

VDZ Exposure

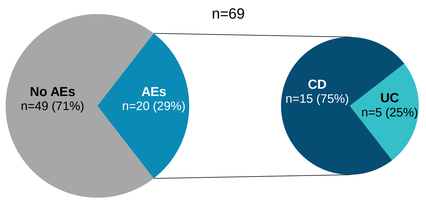
Duration of VDZ Exposure by Diagnosis



- The difference in the duration of VDZ exposure by IBD diagnosis was not significant (p=0.465).
- Median duration of VDZ use was 87 wks (56 to 138 wks).

Treatment-Related AEs

AE Experience in the Safety Cohort

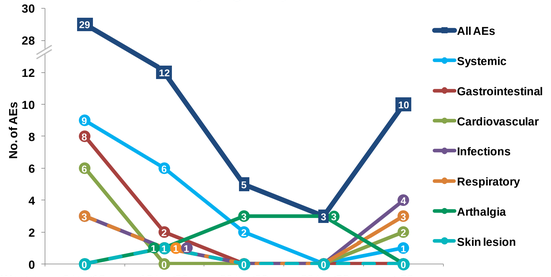


- 20 pts reported ≥1 AEs with 15/20 (75%) and 5/20 (25%) diagnosed with CD and UC, respectively.
  - 1 pt had an ED visit, hospitalization, and 2-week interruption in therapy due to 3 AEs.
- No pts discontinued VDZ due to an AE.

Frequency and Onset of AEs by Organ System

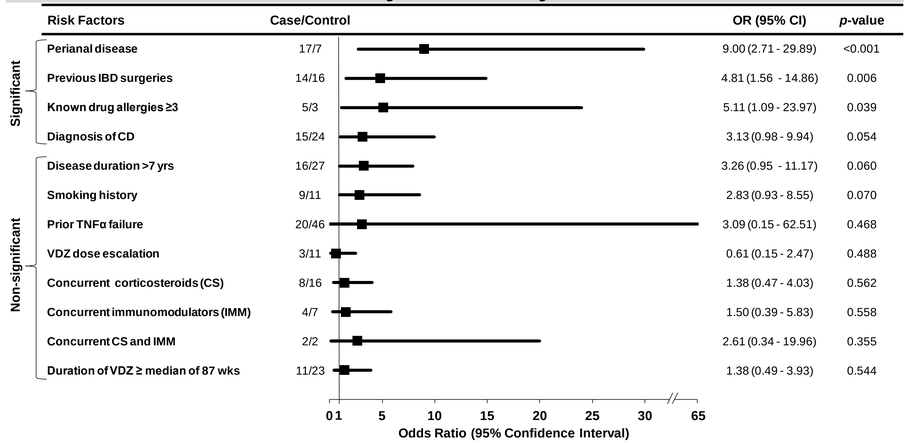
Organ System	Frequency		Onset
	No. of AEs	No. of Pt	Mean Wks (range)
Systemic	**31%**		
Headache	9	4	11 (0-30)
Pruritis/hives	4	2	65 (22-138)
Flushing	3	3	9 (2-14)
Dehydration	1	1	10
Pyrexia	1	1	10
Gastrointestinal	**17%**		
Nausea	9	4	7 (0-24)
Vomiting	1	1	10
Cardiovascular	**14%**		
Chest tightness	6	5	43 (0-138)
Hypotension	1	1	0
Peripheral edema	1	1	0
Infections	**14%**		
URI	6	2	82 (8-136)
Nasopharyngitis	2	2	3 (0-6)
Respiratory	**12%**		
Shortness of breath	4	3	68 (2-138)
Cough	2	2	72 (6-138)
Pleurisy	1	1	2.5
Others	**14%**		
Arthalgia	7	2	35 (24-38)
Skin lesion	1	1	14
Total	**59**	**36**	**32 (0-138)**

Time to Onset by Organ System and VDZ Exposure



- 29/59 (49%) AEs occurred during the first 3 months of therapy.

Safety Risk Analysis



Discussion

We evaluated VDZ treatment-related safety events in all pts who received ≥52 weeks of therapy within a large multicenter gastroenterology private practice.

- Demographic characteristics of pts who experienced an AE were similar to those who did not experience an AE. Likewise, duration of VDZ exposure by IBD diagnosis were similar across CD and UC.
- Pts received VDZ for a median duration of 87 wks, ranging from 52-138 wks.
- 29% pts reported at least 1 AE. Of those, 75% had CD.
  - 4 (5.7%) pts presented with 8 infections.
  - 49% of total AEs occurred within the first 3 months.
  - All cases of arthralgia occurred on or after 6 months of VDZ.
  - The incidence of AEs decreased from 49% to 5% during the first year of therapy followed by an increase to 17% after the first year.
- There were no VDZ discontinuations associated with AEs.
- An ED visit and hospitalization occurred in only 1 pt (1.4%).
- Safety risk factors that were associated with the occurrence of an AE were:
  - Perianal disease (p<0.001)
  - Previous IBD surgeries (p=0.006)
  - Know drug allergies ≥3 (p=0.039)
  - Diagnosis of CD (p=0.05).
- VDZ dose escalation and concurrent use of CS or IMM were not associated with an increase in AE occurrence.
- Incidence and specific AEs were comparable to other retrospective studies but lower than reported in VDZ clinical trials.
- Although retrospective, this real-world study represents a large cohort, providing safety data for pts who have received VDZ for greater than 52 weeks.

Conclusion

- Prolonged treatment of IBD with VDZ was associated with an exceptional safety profile.
- The majority of the AEs occurred early in treatment and again following the first year. None of these events resulted in discontinuation of VDZ.
- VDZ-related ED visits and hospitalizations were low.
- Larger real-world studies that go beyond one year of observations can further characterize the long-term safety profile of VDZ.

References

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