Poster B0387

Baseline Demographics and Disease Characteristics of Patients with Ulcerative Colitis Who Responded to Vedolizumab at Week 6

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Background

- The gut-selective anti-lymphocyte trafficking α4β7 integrin antagonist, vedolizumab, is effective in the treatment of moderately to severely active ulcerative colitis (UC).[1] However, therapy does not elicit a response in some patients[2]
- Identifying patient-specific characteristics that are associated with early response to vedolizumab treatment may aid the positioning of drugs in the therapeutic algorithm for UC
- Previous studies of response to biologics have been limited by their often low numbers of included patients[3]

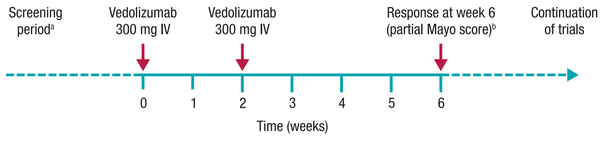
Aim

- The aim of these analyses was to identify baseline demographic, medical, phenotypic, and laboratory variables associated with early response to vedolizumab by combining data from four clinical trials

Methods

- This was a post hoc analysis that pooled data from four phase 3 and 4 clinical trials that evaluated the efficacy of vedolizumab: ENTERPRET, GEMINI 1, VARSITY, and VISIBLE 1
- All four trials enrolled adult patients with moderate to severe UC who had experienced inadequate response or loss of response to conventional therapies or anti-tumor necrosis factor α (TNFα) treatment
- Patients were included in the analysis if they received vedolizumab 300 mg intravenously at weeks 0 and 2 as part of the trial (**Figure 1**)
- Collected variables included patient demographics, UC phenotype and disease characteristics, concomitant medications (immunomodulators and corticosteroids), and disease activity
  - Disease activity was measured using the complete and partial Mayo scores, and categorized as mild, moderate, or severe
- The primary outcome of this post hoc analysis was clinical response at week 6, which was defined as a decrease in partial Mayo score of at least 2 points and at least 25% from baseline, with a decrease in rectal bleeding sub-score of at least 1 or an absolute rectal bleeding sub-score of 1 or less
- Patient characteristics were pooled from all four trials and analyzed using descriptive statistics, with mean or median values calculated for continuous variables, and the number and proportion reported for categorical variables
- For selected characteristics of interest, univariable analysis and calculation of odds ratios (ORs) were used to determine the likelihood of clinical response to vedolizumab at week 6

Figure 1. Study design



IV, intravenous.
[a]ENTERPRET, 4 weeks; GEMINI 1, 3 weeks; VARSITY, ≤ 3 weeks; VISIBLE 1, 4 weeks. [b]Decrease in partial Mayo score of ≥ 2 points and ≥ 25% from baseline, with a decrease in rectal bleeding sub-score of ≥ 1 or an absolute rectal bleeding sub-score of ≤ 1.

Results

- Of the 1,183 pooled patients, 783 (66.2%) had a response to vedolizumab at week 6 (**Table 1**)
- When comparing the proportions of responders and nonresponders, there was no significant difference associated with response to vedolizumab for the majority of patient characteristics

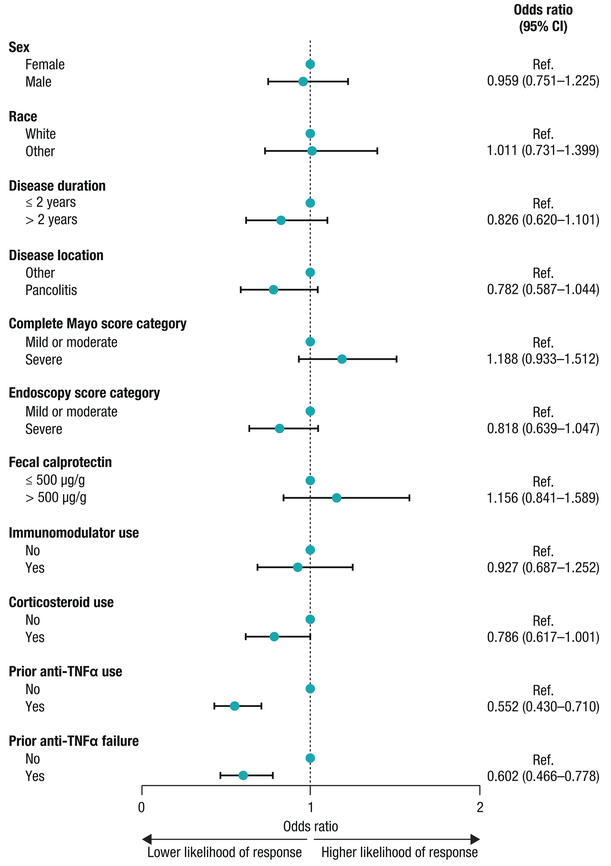
Table 1. Baseline demographics and disease characteristics for week 6 responders and nonresponders

Demographic or characteristic	Responder N = 783	Nonresponder N = 400	*p* value
Sex, male, N (%)	456 (58.2)	237 (59.3)	0.76
Race, N (%)			0.93[a]
White	655 (83.7)	334 (83.5)	
Black or African American	17 (2.2)	16 (4.0)	
Asian	99 (12.6)	49 (12.3)	
Other	12 (1.5)	1 (0.3)	
Duration of disease, years, mean (SD)	7.5 (7.0)	7.1 (7.0)	0.40
Disease location,[b] N (%)			0.10[c]
Pancolitis	191 (24.4)	131 (32.8)	
Proctosigmoiditis	67 (8.6)	43 (10.8)	
Left-sided colitis	220 (28.1)	96 (24.0)	
Extensive colitis	41 (5.2)	37 (9.3)	
Missing	264 (33.7)	93 (23.3)	
Complete Mayo score, median	9	9	
Complete Mayo score, categories, N (%)			0.17[d]
Mild (score < 6)	9 (1.1)	9 (2.3)	
Moderate (score 6–8)	333 (42.5)	183 (45.8)	
Severe (score 9–12)	440 (56.2)	208 (52.0)	
Missing	1 (0.1)	0	
Mayo endoscopic sub-score, categories, N (%)			0.12
Moderate (score 2)	333 (42.5)	151 (37.8)	
Severe (score 3)	449 (57.3)	249 (62.3)	
Missing	1 (0.1)	0	
Fecal calprotectin, µg/g, mean (SD)	2,853.7 (4,105.8)	3,315.4 (6,184.2)	0.19
Immunomodulator use,[e] N (%)			0.64
Yes	202 (25.8)	91 (22.8)	
No	450 (57.5)	188 (47.0)	
Missing	131 (16.7)	121 (30.3)	
Oral corticosteroid use, N (%)			0.06
Yes	393 (50.2)	225 (56.3)	
No	389 (49.7)	175 (43.8)	
Missing	1 (0.1)	0	
Prior anti-TNFα use, N (%)			< 0.0001
Yes	227 (29.0)	170 (42.5)	
No	556 (71.0)	230 (57.5)	
Prior anti-TNFα failure, N (%)			< 0.0001
Yes	211 (26.9)	152 (38.0)	
No	572 (73.1)	248 (62.0)	

Data are pooled from the ENTERPRET, GEMINI 1, VARSITY, and VISIBLE 1 trials.
SD, standard deviation; TNFα, tumor necrosis factor α.
[a]Comparison of White vs other races. [b]Disease location was not recorded in the VARSITY trial. [c]Comparison of pancolitis vs other locations. [d]Comparison of severe vs mild and moderate disease. [e]Immunomodulator use was not recorded in the ENTERPRET trial.

- Disease duration was similar in responders and nonresponders (7.5 years vs 7.1 years) (**Table 1**)
- Similar proportions of responders and nonresponders were receiving immunomodulators (25.8% vs 22.8%) or oral corticosteroids (50.2% vs 56.3%) (**Table 1**)
- Disease location was not associated with response to vedolizumab; patients with pancolitis were as likely to respond as patients with less-extensive disease (OR, 0.782; 95% confidence interval [CI], 0.587–1.044; univariate analysis, $p = 0.10$) (**Figure 2**). Disease location was analyzed for three trials; these data were not available for VARSITY

Figure 2. Likelihood of response to vedolizumab at week 6 for selected patient demographics and baseline clinical characteristics



Data are pooled from ENTERPRET, GEMINI 1, VARSITY, and VISIBLE 1 trials, except for disease location and immunomodulator use, because these data were not available for VARSITY and ENTERPRET, respectively.
CI, confidence interval; Ref., reference; TNFα, tumor necrosis factor α.

- Disease severity at baseline was not associated with response; the odds of responding to vedolizumab were similar for patients with severe disease and those with mild or moderate disease based on complete Mayo score (OR, 1.188; 95% CI, 0.933–1.512; univariate analysis, $p = 0.17$) (**Figure 2**)
- Patients who had experienced previous failure or inadequate response to anti-TNFα treatment were significantly less likely to respond to vedolizumab at week 6 than those who had not experienced anti-TNFα treatment failure (OR, 0.602; 95% CI, 0.466–0.778; univariate analysis, $p < 0.0001$) (**Figure 2**)

Summary and Conclusions

- **In this analysis of pooled clinical trial data, most demographics and baseline disease characteristics were similar between the groups of patients who responded or did not respond to vedolizumab at week 6**
- **The only variables that were significantly associated with nonresponse to vedolizumab on univariable analysis were prior anti-TNFα treatment use or failure**
- **This post hoc analysis suggests that vedolizumab is effective for the treatment of patients with UC across a range of demographics and baseline disease characteristics, including those with severe disease activity**

References

1. Rubin DT, et al. *Am J Gastroenterol.* 2019;114:384-413.
2. Feagan BG, et al. *N Engl J Med.* 2013;369:699-710.
3. Gisbert JP, Chaparro M. *J Crohns Colitis.* 2020;14:694-709.

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Disclosures

Andres Yarur: served as a consultant for Arena Pharmaceuticals, Bristol Myers Squibb, Prometheus Laboratories, and Takeda. Vipul Jairath: served as an advisory board consultant for AbbVie, Alimentiv Inc., Arena Pharmaceuticals, Asahi Kasei Pharma, Asieris, Bristol Myers Squibb, Celltrion Healthcare, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead, GlaxoSmithKline, Janssen, Lilly, Merck, Mylan, Pandion, PendoPharm, Pfizer, Protagonist Therapeutics, Reistone Biopharma, Roche, Sandoz, Second Genome, Takeda, Teva, and TopiVert, and received speaker's fees from AbbVie, Ferring, Galapagos, Janssen, Pfizer, Shire, and Takeda. Edward V Loftus Jr: served as a consultant for AbbVie, Amgen, Arena Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Calibr, Celgene, Celltrion Healthcare, Genentech, Gilead, Gossamer Bio, Iterative Scopes, Janssen, Lilly, Morphic, Ono Pharma, Pfizer, Protagonist, Scipher Medicine, Surrozen, Sun Pharma, Takeda, and UCB, and received research support from AbbVie, Amgen, Bristol Myers Squibb, Celgene, Genentech, Gilead, Gossamer Bio, Janssen, Pfizer, Receptos, Robarts Clinical Trials, Takeda, Theravance, and UCB. Bruce E Sands: served as a consultant for AbbVie, Abivax, Alimentiv, Allergan, Amgen, Arena Pharmaceuticals, AstraZeneca, Bacainn Therapeutics, Baxalta Bioscience India, Boehringer Ingelheim, Boston Pharmaceuticals, Calibr, Capella BioScience, Celgene, Celltrion Healthcare, ClostraBio, F. Hoffmann-La Roche, Galapagos, Gilead, Gossamer Bio, Immunic, InDex Pharmaceuticals, Innovation Pharmaceuticals, Ironwood Pharmaceuticals, Janssen, Johnson & Johnson, Lilly, Morphic Therapeutic, Oppilan Pharma, OSE Immunotherapeutics, Otsuka, Pfizer, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, RedHill Biopharma, Rheos Medicines, Salix Pharmaceuticals, Seres Therapeutics, Shire, Surrozen, Takeda, Target RWE, Theravance Biopharma R&D, USWM Enterprises, and Vivelix Pharmaceuticals. Sharif Uddin and Rana M Qasim Khan: employees of Takeda Pharmaceuticals U.S.A., Inc., and hold stock or stock options.

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