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Efficacy of Vedolizumab Maintenance Therapy With and Without Continued Immunosuppressant Use in GEMINI 1 and GEMINI 2


Introduction: In GEMINI 1 and GEMINI 2, vedolizumab (VDZ) was safe and effective in patients with ulcerative colitis (UC) or Crohn’s disease (CD), respectively, on stable doses of immunosuppressants 1.2. The effect of discontinuing immunosuppressants in patients who responded to VDZ induction therapy in these studies has not been characterized.

Methods: Patients who responded to VDZ at week 6 were re-randomized to placebo (VDZ/PBO) or VDZ every 4 weeks (VDZ/VDZ Q4W) or 8 weeks (VDZ/VDZ Q8W) for 46 weeks. At United States (US) sites, re-randomized patients discontinued immunosuppressant use at week 6. At non-US sites, patients could continue to use immunosuppressants; doses were to remain stable throughout the study unless the medication was discontinued because of a medication-related toxicity. Clinical efficacy, VDZ serum concentration, and immunogenicity via an enzyme-linked immunosorbent assay (ELISA) were evaluated post hoc in patients with baseline (week 0) immunosuppressant use stratified by region (US vs non-US).

Results: At week 52, rates of clinical remission, clinical response, mucosal healing (UC), and corticosteroid-free remission were numerically higher with VDZ, irrespective of baseline immunosuppressant use (Table). Mean trough concentrations were similar between US and non-US patients at week 46 (Table). The US and non-US sites had similar numbers of patients who were positive for anti-VDZ antibodies during VDZ maintenance therapy (Table).

Conclusion: Discontinuing immunosuppressants did not appear to substantially affect the clinical efficacy of VDZ maintenance therapy. Interpretation of these post hoc analyses is limited by the cross-regional comparison and the relatively small sample sizes.

[1862] Table 1. Maintenance VDZ With and Without Continued Immunosuppressant Use

<table>
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<tr>
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<th>US Patients (discontinued immunosuppressant)</th>
<th>Non-US Patients (discontinued immunosuppressant)</th>
<th>US Patients (continued immunosuppressant)</th>
<th>Non-US Patients (continued immunosuppressant)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VDZ/PBO at W6</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>0</td>
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<tr>
<td>VDZ/VDZ Q4W</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0</td>
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<tr>
<td>VDZ/VDZ Q8W</td>
<td>1</td>
<td>2</td>
<td>0</td>
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</table>

Efficacy endpoints: % difference from PBO (95% CI) at week 52
Clinical remission: 28.9% (−10.5, 63.3) 35.0% (−12.1, 68.6) 15.6% (−39.9, 63.8) 17.7% (0.2, 35.3)
Mucosal healing: 28.9% (−10.5, 63.3) 36.4% (−12.1, 68.6) N/A N/A
Corticosteroid-free remission: 30.8% (−35.0, 81.7) 28.0% (−15.8, 52.4) N/A 32.1% (7.2, 54.1)
Immunogenicity: No. of patients with at least one positive sample
VDZ/PBO 3 1 1 1
VDZ/VDZ 1 2 0 0
VDZ Concentration: Mean trough concentration at week 46 (μg/ml)
VDZ/PBO Q4W 13.0 (n=2) 10.7 (n=27) 9.4 (n=2) 11.8 (n=27)
VDZ/VDZ Q4W 39.0 (n=6) 44.1 (n=28) 38.8 (n=3) 31.7 (n=28)

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Initial Vitamin D Concentration Correlates With Disease Markers in Inflammatory Bowel Disease

Presidential Poster
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Introduction: Inflammatory bowel disease (IBD) includes Crohn’s disease (CD) and ulcerative colitis (UC), have a chronic relapsing and remitting course and can lead to hospitalizations, surgery, and decline in quality of life. There is a growing understanding of the complicated role that vitamin D plays in modulating the immune status in IBD. Studies have shown a high prevalence of vitamin D deficiency in IBD. In addition, vitamin D replacement has been shown to reduce the risk of disease relapse. The purpose of this study was to correlate the relationship of the initial serum vitamin D level on indices associated with IBD activity in a tertiary university hospital setting.

Methods: This was a retrospective study, where we used electronic medical record (EMR) to capture data for an academic medical center, including all gastroenterology clinic visits and outpatient lab values. Using the above-mentioned database, we identified 1863 patients with IBD over a 5 year period between 2013 and 2017. Patients with a 25(OH)D value above 50 were excluded from the analysis.

Results: There were 1408 patients (822 with CD and 586 with UC) over 4741 clinic visits. Based on our findings, there was a significant negative correlation between vitamin D concentration and C-reactive protein in CD (p ≤ 0.127, p = 0.01) and association in UC (p ≤ 0.118, p = 0.09). There was a positive correlation between vitamin D concentration with IBD in UC (r = 0.20, p = 0.04) but not CD (r = 0.09, p = 0.17). In CD, there was positive correlation 25(OH)D and other measures such as albumin, vitamin B12 and iron, with patients with a 25(OH)D value above 50 having the highest average values for each of those measures. There was also association between initial 25(OH)D levels and HBI in CD with improvement at higher concentrations of vitamin D ≥ 30 (p = 0.07).

Conclusion: Overall our data suggests that higher concentration of vitamin D in ambulatory patients with IBD were associated with improved disease markers. Our data suggest that, at a level above 50 to provide additional benefit over a level of 30. Further prospective randomized studies are necessary to confirm the appropriate level for vitamin D replacement in IBD.

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Fecal Lactoferrin (FLac) and Calprotectin (CAc) as Surrogate Markers of Mucosal Healing: Post-hoc Analysis from the PURSUIT SC Induction Study

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Introduction: Previously we reported greater improvement in both FLac/CAc levels in UC pts who showed clinical response/endoscopic healing in PURSUIT SC induction golimumab/GLM study.1 These post-hoc analyses assessed association of fecal inflammatory markers, FLac, with Mayo endoscopy subscores using data from this study.

Methods: The PH3 portion of PURSUIT-SC was a multicenter, rand, PBO-controlled, double-blind study to evaluate safety/efficacy of induction therapy with SC GLM. Pts with Mayo scores of 6-12 inclusive, including endoscopic subscore ≥2 were rand to PBO/FLAC/GLM 200mg/100mg, or GLM 400mg/200mg at Wk 0/8. Mucosal healing was assessed at Wk8 using Mayo endoscopy subscores. Stool samples were collected for FLac/CAc Wk0-Wk 8. Analyses for FLac/CAc concentrations were performed using validated methods. The area under a ROC curve(AUC)assessed the association of baseline/endoscopy FLac/CAc with Mayo endoscopy subscores of 0 (defining normal or inactive disease) subscores of 0 or 1 (defining endoscopic healing in this study) at Wk8. Various cut offs of FLac/CAc concentrations were explored to determine balance of sensitivity/specificity for endoscopic subscores of 0 or 0-1.

Results: Mayo endoscopy subscores of 0 or 1 were associated with lowest concentrations of FLac/CAc. Baseline FLac/CAc were poor predictors for endoscopic healing at Wk8(AUC= 0.63).

Conclusion: At Wk 8, FLac/CAc subscores were positively associated with levels of FLac/CAc. Cutoffs of FLac < 50 μg/ml & CAc < 250 mg/kg were found to offer the best area under ROC curve (AUC) at Wk8. Further validated sensitivity/specificity for normal/endoscopic disease activity. Overall these data suggest that fecal inflammatory marker levels might be useful surrogates for endoscopic improvement. Presented at ACG 2014.