Vedolizumab efficacy exposure–response relationship for ulcerative colitis patients (GEMINI I) based on causal inference analysis

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Introduction

Vedolizumab (ADHERE) is a humanized monoclonal antibody targeting α4, a integrin that selectively blocks gut-specific lymphocyte trafficking. Vedolizumab (300 mg via intravenous infusion at Weeks 0, 2, and 6, and every 8 weeks thereafter) is licensed to treat ulcerative colitis (UC) and Crohn’s disease (CD). Greater proportions of patients achieved clinical remission and clinical response and lower partial Mayo scores for vedolizumab versus placebo. Clinical outcomes and patient-specific covariates are described in Figure 2.

Methods

• GEMINI I had 3 phases: randomized, double-blind, placebo-controlled trial investigating vedolizumab (300 mg) as induction therapy followed by maintenance therapy in patients with UC. For induction phase, higher total serum concentrations of anti-TNF agents are reported to correlate with clinical and endoscopic outcomes.

Results

• Exposure–response relationships for all exposure metrics and each outcome were evident in the quartile analyses of predicted vedolizumab trough concentrations and estimated vedolizumab clearance. The exposure–response relationships were more robust for Week 6 partial Mayo score and clinical response than for clinical remission.

Conclusions

• Higher trough concentrations and lower partial Mayo scores of vedolizumab were associated with better clinical outcomes, including higher rates of clinical response and improved partial Mayo score.

Figure 1. GEMINI I study design

Figure 2. Patient-specific covariates and clinical outcomes included in this analysis

Figure 3. Predicted vedolizumab trough concentrations and estimated vedolizumab clearance

Figure 4. Methodology for case-matching based on propensity score

Figure 5. Exposure-response relationships (patients with available data from 0 to 170 days)

References

2. C. Clinical response: adjusted data
3. B. Partial Mayo score†: unadjusted data
4. A. Partial Mayo score†: adjusted data

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