Correlation of Fecal Calprotectin and C-Reactive Protein Concentrations With Clinical Outcomes and Endoscopic Disease Activity in Patients With Ulcerative Colitis Receiving Induction Therapy With Etrasimod


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Introduction

Surrogate biomarkers of disease activity in ulcerative colitis are needed to assess responses to treatment. 

Shepingone-1-phosphate (S1P) receptor modulators lead to reduced inflammation and induction of clinical remission in patients with ulcerative colitis.

Etrasimod (APD334), a once-daily, oral, selective S1P receptor modulator, showed efficacy in patients with moderately to severely active ulcerative colitis in the randomized, double-blind, placebo-controlled, phase 2 OASIS study.

This post hoc analysis of the phase 2 OASIS study assessed the utility of fecal calprotectin and C-reactive protein as surrogate biomarkers for assessing efficacy in patients receiving etrasimod.

Methods

Post hoc Study Design

Patients enrolled in the phase 2 OASIS study (ClinicalTrials.gov identifier, NCT02447302): - were aged 18-80 years - had moderate to severe ulcerative colitis (3-component modified Mayo Clinic score [MCS] of 4-8) with endoscopic subscore ≥2 and rectal bleeding score ≥1 - had prior inadequate response or loss of response or intolerance to at least one conventional agent, anti-tumor necrosis factor-α (TNF-α) agent, or anti-integrin agent

Patients were randomized to receive oral etrasimod 1 mg, etrasimod 2 mg, or placebo, all once daily for 12 weeks.

Fecal calprotectin and C-reactive protein were measured at baseline and weeks 4, 8, and 12 from stool and blood samples, respectively.

Clinical and endoscopic outcomes were evaluated at baseline and week 12 using MCS:

The modified MCS (range 0-9) included endoscopic, rectal bleeding, and stool frequency scores.

Remission was defined as an endoscopic subscore ≤1 (with absence of friability), rectal bleeding and stool frequency scores ≤1, and a stool frequency decrease from baseline of ≥1 stool per day.

Statistical Analyses

The effect of treatment with etrasimod versus placebo at each time point and over the 12 weeks was analyzed with a mixed model for repeated measures of log-transformed biomarker values (1-sided P-values) with current oral corticosteroid use, prior exposure to TNF-α antagonists, treatment, week, and treatment-by-week interaction as factors and baseline value as a covariate.

Comparisons between those who achieved remission by study week and those who did not were assessed by a Wilcoxon rank-sum test (2-sided P-values).

Analysis of correlation between modified MCS, endoscopic subscore, C-reactive protein, and fecal calprotectin was conducted using the Spearman’s rank coefficient (2-sided P-values).

Results

Table 1. Baseline Patient Demographics and Disease Characteristics

| Age, mean ± SD, years | 44.8 ± 14.9 | 43.2 ± 12.2 | 40.4 ± 12.4 |
| Sex, male, n (%) | 32 (59.3) | 30 (57.7) | 27 (54.0) |
| Race, white, n (%) | 51 (94.4) | 48 (92.3) | 49 (98.0) |
| Weight, mean ± SD, kg | 75.8 ± 16.2 | 73.7 ± 13.4 | 70.4 ± 16.7 |
| Duration of UC, mean ± SD, years | 8.6 ± 7.2 | 7.0 ± 6.1 | 6.2 ± 4.7 |
| Disease location, n (%) | Proctosigmoiditis | 34 (63.0) | 34 (65.4) | 30 (60.0) |
| Pancolitis | 23 (42.6) | 20 (38.5) | 14 (28.0) |
| Current oral corticosteroid use, n (%) | 16 (29.6) | 13 (25.0) | 18 (36.0) |
| Duration of oral corticosteroid use, median (range), weeks | 31.4 | 26.1 | 25.7 |
| Total MCS, mean ± SD | 8.7 ± 1.7 | 8.6 ± 1.4 | 8.9 ± 1.5 |
| Modified MCS, mean ± SD | 6.5 ± 1.5 | 6.5 ± 1.2 | 6.6 ± 1.2 |
| CRP, median (range), mg/L | 0.31 (0.19-10) | 0.21 (0.25-20) | 0.29 (76-90) |
| Fecal calprotectin, median (µg/g) | 1429 | 1210 | 1449 |

Figure 1. (A) Fecal Calprotectin and (B) C-Reactive Protein Levels Over Time in Patients Treated With Etrasimod 2 mg by Clinical Remission Status at Week 12

Figure 2. (A) Fecal Calprotectin and (B) C-Reactive Protein Levels Over Time in Patients Treated With Etrasimod 2 mg by Clinical Remission Status at Week 12

Conclusions

Patients who received etrasimod 2 mg exhibited significant decreases in both fecal calprotectin and C-reactive protein versus placebo.

Fecal calprotectin and C-reactive protein were reliable biomarkers of clinical and endoscopic responses in patients with ulcerative colitis enrolled in the OASIS trials.

Disclosures

The authors report no relevant conflicts of interest.

References


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