Long-term Efficacy and Safety of Etrasimod for Ulcerative Colitis: Results from the Open-label Extension of the OASIS Study

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Abstract

Objectives: To evaluate the efficacy and safety of etrasimod, a novel oral, selective, sphingosine 1-phosphate receptor 1, 4, and 5 (S1P1, S1P4, S1P5) modulator in development for treatment of immune and inflammatory-mediated diseases, in the open-label extension (OLE) of the double-blind (DB) OASIS study (NCT02447302). Safety was evaluated by treatment-emergent adverse events (TEAEs) and other studies (NCT02536404); subsequently evaluated, for an additional 34 weeks, the safety and efficacy of etrasimod in achieving and maintaining clinical response and/or remission in patients who completed OASIS.

Methods

- During the 12-week DB OASIS study, patients were treated once daily with etrasimod 1 mg, etrasimod 2 mg, or placebo.
- Patients who completed the DB study were eligible to enroll in the OLE and receive etrasimod 2 mg once daily for up to an additional 34 weeks, irrespective of their response or treatment during the DB study (Figure 1).
- A few patients (n = 6) received placebo during the OLE and were included in the safety, but not the efficacy, analyses.
- Efficacy was summarized in the evaluable cohort, which included patients who received etrasimod 2 mg throughout the OLE. The modified intention-to-treat (mITT) population included patients with the required assessments.
- Endpoints were:
  - Clinical response (Mayo Clinic endoscopic score < 1 with absence of friability), rectal bleeding (RB) score ≤ 1, and stool frequency (SF) score ≤ 1 with ≤ 1 point decrease from baseline at DB end of treatment (EOT).
  - Clinical response (improvement in RB score ≤ 1, or RB score of ≤ 1 at EOT), and endoscopic improvement, defined as Mayo Clinic endoscopic score ≤ 1 or maintenance of endoscopic improvement at EOT.
  - Safety was evaluated by treatment-emergent adverse events (TEAEs) and treatment-emergent serious adverse events (SAEs).

Conclusions

- Clinical response, clinical remission, or endoscopic improvement observed with etrasimod 2 mg at week 12 was sustained or improved up to week 46 in most patients participating in the OLE.
- Etrasimod demonstrated a favourable safety profile, with most TEAEs of mild to moderate severity; no new safety findings were reported.

References


Acknowledgments

Supported by Arena Pharmaceuticals, Inc. (San Diego, CA, USA); Lisa Baker, PhD, on behalf of Arena Pharmaceuticals, Inc., and Precision IBD, Inc. (Bedford Park, IL, USA); grandparents writing support from armed forces by AstraZeneca; Grandfather, Johannes Verheijen, Etsch Verheijen, Netherlands.

Declaration of Conflicting Interests

No financial support or honoraria are required or received from any company, except Arena Pharmaceuticals. All authors have completed a full disclosure statement, and all authors have no competing interests.

Abbreviations

- DB: Double-blind
- OLE: Open-label extension
- mITT: Modified intention-to-treat
- EOT: End of treatment
- SG: Statistical group
- LP: Liopron Pharmaceuticals
- SABA: Sulfasalazine
- UC: Ulcerative colitis

Results

- Among patients achieving clinical response, clinical remission, or endoscopic improvements at Week 12, treatment effects were maintained at EOT in the majority of patients (Figure 3).
- The overall group is patients who received any treatment during the DB study and the OLE (placebo, etrasimod 1 mg, or etrasimod 2 mg) during the DB period. The 6 patients who received placebo during the DB period are not shown. (placebo, etrasimod 1 mg, or etrasimod 2 mg) during the DB period. The 6 patients who received placebo during the DB period are not shown.

Table 2. Summary of Adverse Events During the OLE in Patients Receiving Etrasimod 2 mg in the OLE Safety Population

<table>
<thead>
<tr>
<th>Group</th>
<th>N (%)</th>
<th>Placebo</th>
<th>Etrasimod 1 mg</th>
<th>Etrasimod 2 mg</th>
<th>Overall N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with ≥ 1 TEAEs, n (%)</td>
<td>31 (36)</td>
<td>25 (60)</td>
<td>25 (66)</td>
<td>17 (53)</td>
<td>67 (60)</td>
</tr>
<tr>
<td>Number of TEAEs</td>
<td>115</td>
<td>85</td>
<td>56</td>
<td>252</td>
<td></td>
</tr>
<tr>
<td>Patients with ≥ 3 SAEs, n (%)</td>
<td>10</td>
<td>4 (10)</td>
<td>0</td>
<td>3 (9)</td>
<td>7 (6)</td>
</tr>
<tr>
<td>Number of SAEs</td>
<td>33</td>
<td>11</td>
<td>0</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Patients discontinued due to TEAE, n (%)</td>
<td>4 (10)</td>
<td>2 (5)</td>
<td>4 (13)</td>
<td>10 (9)</td>
<td></td>
</tr>
</tbody>
</table>

- Patients with TEAEs of moderate/severe: 0.48/12 | 45/613 | 31/38/16 | 401/49/10

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