Efficacy and Safety of Mirikizumab After 52-Weeks Maintenance Treatment in Patients with Moderate-to-Severe Crohn’s Disease

Bruce E. Sands1, William Sandborn2, Laurent Peyrin-Biroulet3, Peter Higgins4, Fumihito Hira5, Vipul Jairath6, Geert D’Haens7, Maria Abreu8, Ruth Belin9, Elisa Gomez Valderas9, Debra Miller10, April Naegele11, Vipin Arora12, Paul Pollack12, Jay Tuttle12, Toshifumi Hibi11

1Cahn School of Medicine at Mount Sinai, NY, USA; 2University of California San Diego, CA, USA; 3University Hospital of Nancy, Vandoeuvre-les-Nancy, France; 4University of Michigan, MI, USA; 5Fukuoka University, Fukuoka, Japan; 6University of Miami, FL, USA; 7Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands; 8University of Miami School of Medicine, FL, USA; 9Eli Lilly and Company, IN, USA; 10Kitsato Institute, Tokyo, Japan

BACKGROUND
- The interleukin (IL)-23/Th17 pathway has a significant role in the pathogenesis of Crohn’s disease (CD) with various anti-IL-23 antibodies having shown efficacy in treating CD.
- Mirikizumab (miri) is a humanized immunoglobulin G4 (IgG4)—variant monoclonal antibody that binds to the p19 subunit of IL-23.
- Phase 2 studies of miri have shown efficacy in treating ulcerative colitis1,2,3,4, and Crohn’s disease leading to further development in ongoing Phase 3 studies in CD.
- We previously reported the safety and efficacy of miri after 12-Week induction therapy in a Phase 2, multicenter, randomized, parallel-arm, double-blind, placebo (PBO)-controlled trial (NCT02891265) in patients with moderate-to-severely active CD.
- Maintenance Week 52 results are reported here.

KEY RESULTS

Efficacy Endpoints Definition
- **Endoscopic Response and Remission**
  - Endoscopic Remission
    - Stool frequency ≤2.5 and abdominal pain ≤1 and no worse than baseline
  - Endoscopic Improvement (≥1 point reduction in SES-CD score)
- **CD Activity Index (CDAI)**
  - CDAI <150
  - 50% reduction from baseline in CDAI

Methods
- Patients who entered maintenance (Period 2) are included in the analysis.
- Due to small sample size, no formal statistical comparisons were reported here.
- Of patients with response/remission at W12, the percent of patients with non-responders at W12 was calculated.

Objective and Endpoints
- **Inclusion**
  - Diagnosis of CD for ≥3 months before baseline (Week 0, randomization)
  - Active CD defined as stool frequency ≥4 and/or abdominal pain ≥2 at baseline
  - SES-CD ≥2 (centrally read) for subjects with ileal/ileocolic or ≥4 for subjects with isolated ileal disease
  - Prior treatment for CD: failure/intolerance to conventional immunosuppressants (≤3 line)
  - Previous exposure to any biologic therapy targeting IL-23/Th17

Exclusion
- Strictures, stenoses, any other manifestation which might require surgery
- Bowel resection, diversion, or placement of a stoma
- Previous exposure to any biologic therapy targeting IL-23/Th17

Enrollment Criteria
- **Randomized Maintenance Group**
  - W12 induction: NISTRA/CCP/SCCP ≥1
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Patient Disposition after W12 induction period
- **Non-Responders and Placebo**
  - Endoscopic Improvement
  - Percent of patients with response/remission at W52

RESULTS

Baseline Demographics and Disease Characteristics
- **At screening (W-4 to 0)**
  - Age, years: 48 (13.5), 37.8 (11.9), 38.6 (12.8), 15.91 (11.2)
  - Male, %: 51.6 (23.8), 32.3 (26.9), 17.0 (24.9), 38.1 (11.1)
  - Disease Duration, years: 7.6 (8.4), 6.8 (8.3), 10.1 (3.7), 10.0 (3.8)
  - Disease Location, %
    - Ileal
    - 40.6 (44.0), 9.9 (16.7), 16 (37.1)
    - Ileocolonic
    - 18.6 (24.2), 8.8 (25.7)
    - Colon/Loss to follow-up
      - SES-CD: 14.9 (17.6), 14.3 (17.7), 11.2 (5.0), 12.0 (9.4)
    - Endoscopic Response
      - 7.3 (6.9), 7.3 (5.5), 6.6 (3.6), 6.5 (11.5)
    - CDAI: 393 (84.7), 327 (95.9), 281 (90.3), 286 (91.5)

Durations of Efficacy
- **Durations of Efficacy Endpoints at Week 52**

Safety - week 52
- No serious infections, no deaths, no serious AEs

DISCLOSURES
- The study was previously presented at United European Gastroenterology Week - 28th Annual Conference; Virtual; October 11 – 13, 2020.
- These Phase 2 data support continued characterization of miri efficacy and safety in the ongoing VIVID-1 Phase 3 program (NCT03926130).

REFERENCES
- CDAI ≥100 or CDAI <150
- Immunosuppressant use, %

CONCLUSIONS
- Miri treatment demonstrated durable endoscopic and symptomatic efficacy after 52 weeks in patients with Crohn’s disease.
- The proportion of patients who had response/remission at Week 12 was maintained or improved at Week 52 across multiple parameters (endoscopic, PRO, CDAI).
- Among patients who did not have endoscopic improvement after 12 weeks of miri treatment, continued treatment with miri led to additional patients achieving endoscopic response/remission at week 52.
- The safety profile of miri treatment was consistent with the anti-il-23/Th17 class, with no new discontinuations in the re-randomized maintenance group due to adverse events.

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