

SUPPLEMENTARY MATERIAL

Supplemental Methods: Study Design

The study design for LUCENT-1 and LUCENT-2 has been previously described.¹

Study Design Modifications for Japan: LUCENT-1 (Inclusion Criteria)

1. Adjustment to the duration of corticosteroid therapy from 2 weeks to 7 days to meet the definition of “corticosteroid-refractory colitis,” for consistency with clinical practice in Japan.
2. Adjustment to the dose of prednisone (from 10 mg/day to 5 mg/day) is required to meet the definition of “corticosteroid-dependent colitis,” for consistency with clinical practice in Japan.
3. Adjustment to the dose of azathioprine (≥ 1.5 mg/kg/day to ≥ 1.0 mg/kg/day) or 6-mercaptopurine (≥ 0.75 mg/kg/day to ≥ 0.5 mg/kg/day) required to meet the definition of “conventional failure” in order to be consistent with clinical practice in Japan, particularly with respect to lower-weight patients.

The following modifications were based on post-marketing findings in Japanese patients with rheumatoid arthritis who were receiving anti-tumor necrosis factor (TNF) agents,^{2,3} recommendations set by the Japan College of Rheumatology guidelines for TNF usage for patients with rheumatoid arthritis,¹ and possible safety issues of Japanese patients with general autoimmune disease who received immunomodulators or immunosuppressants.

4. Added testing of serum beta-D-glucan levels, a diagnostic test for *Pneumocystis jiroveci* pneumonia and invasive fungal infection during screening and at investigator discretion thereafter if pneumocystis pneumonia (PCP) is suspected during trial participation.
5. Added testing of serum KL-6 levels, a diagnostic test for interstitial lung disease, during screening and at investigator discretion thereafter if interstitial lung disease or PCP is suspected during trial participation.
6. Additional exclusion criteria for hepatitis B. Modified hepatitis B virus (HBV) DNA monitoring for patients with the following HBV serological pattern at baseline:
 - Negative for hepatitis B surface antigen (HBsAg⁻) and positive for anti-hepatitis B core antibody (anti-HBc⁺), with undetectable HBV DNA
 - Negative for HBsAg (HBsAg⁻) and positive for anti-hepatitis B surface antibody (anti-HBs⁺), with undetectable HBV DNA
 - Negative for HBsAg (HBsAg⁻) and positive for anti-HBc and anti-HBs, with undetectable HBV DNA

References

1. D'Haens G, Dubinsky M, Kobayashi T, et al. Mirikizumab as induction and maintenance therapy for ulcerative colitis. *N Engl J Med* 2023;388:2444-2455.
2. Takeuchi T, Tatsuki Y, Nogami Y, et al. Postmarketing surveillance of the safety profile of infliximab in 5000 Japanese patients with rheumatoid arthritis. *Ann Rheum Dis* 2008;67:189-194.
3. Koike T, Harigai M, Inokuma S, et al. Postmarketing surveillance of the safety and effectiveness of etanercept in Japan. *J Rheumatol* 2009;36:898-906.
4. Japan College of Rheumatology. The treatment guidelines of TNF-inhibitors for patients with rheumatoid arthritis [Internet]. c2017 [cited 2023 Nov 15]. http://www.ryumachi-jp.com/info/guideline_tnf.pdf

Graphical Plain Language Summary

INTESTINAL RESEARCH PEER-REVIEWED INFOGRAPHIC

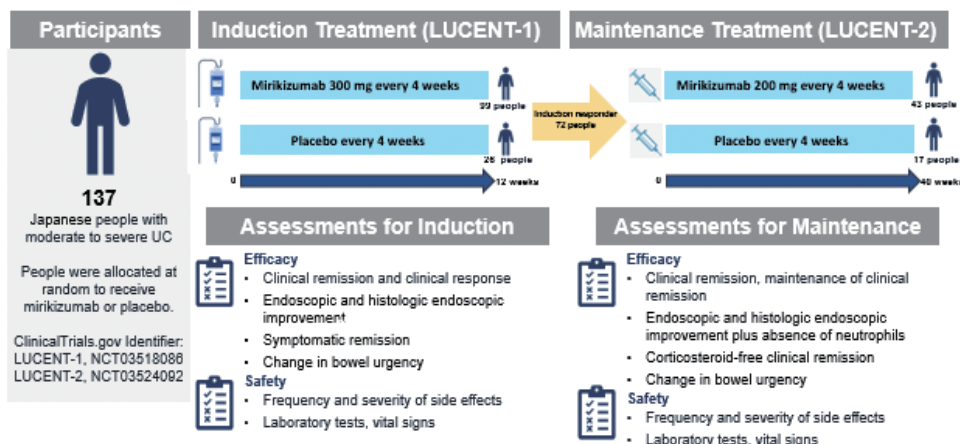
Mirikizumab as Induction and Maintenance Therapy for Japanese Patients with Ulcerative Colitis

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Why did we do this study?

- Ulcerative colitis (UC) is a long-term condition where the large intestine and rectum become inflamed and open sores or ulcers develop.
- Symptoms of UC may include abdominal pain, fatigue, diarrhea, bleeding, and bowel urgency.
- UC involves periods of 'relapse' when the inflammation in the bowel flares up, and periods of 'remission' when the inflammation calms down.
- There is no known cure for UC and treatments aim to treat relapses when they occur and help to maintain remission.
- Mirikizumab is a monoclonal antibody against the p19 subunit of interleukin 23 (IL-23).
- In recent global phase 3 studies (LUCENT-1 and LUCENT-2), mirikizumab was effective in inducing and maintaining clinical remission in patients with moderate to severe UC.
- In this analysis, we studied how effective and safe mirikizumab was for Japanese people with UC, a population where the incidence of UC has risen over the past 2 decades.

What did we do?



What did we learn?

- Induction**
- At week 12 of induction, the percentage of **clinical remission** was greater in the mirikizumab group compared with placebo (32.4% versus 2.9%).
 - The proportion of patients achieving **clinical response, endoscopic improvement, and histologic endoscopic improvement** were higher in the mirikizumab group versus placebo.
 - **Symptomatic remission** was greater in the mirikizumab group compared to placebo at week 4, and then from week 6 through to week 12.
 - Greater improvements in **bowel urgency** were observed in the mirikizumab group compared to placebo.
- Maintenance**
- At week 40 of maintenance, the percentage of **clinical remission** was greater in the mirikizumab group compared with placebo (48.9% versus 28.0%).
 - The proportion of patients achieving **corticosteroid-free clinical remission, maintenance of clinical remission, endoscopic and histologic-endoscopic mucosal improvement plus absence of neutrophils, and bowel urgency NRS 0 or 1** were greater in the mirikizumab group compared with placebo.
 - Improvements in **bowel urgency** were maintained, with greater reductions observed in the mirikizumab group compared with placebo at week 40.
 - Overall, findings in the Japanese population in the induction and maintenance studies were broadly consistent with previous findings in the overall population.
- Safety**
- Most adverse events of mirikizumab were mild or moderate in intensity. The most common adverse events were inflammation of the nose and throat (nasopharyngitis), headache, joint pain (arthralgia), and injection site pain (maintenance treatment only).

Mirikizumab is a potential treatment option for Japanese people with moderate to severe UC

This infographic represents the opinions of the authors. For full list of disclosures, including funding and author disclosure statements, please see full text online.