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ASIA EDITION

In a first ever head-to-head biologic clinical study in Ulcerative Colitis Takeda's Entyvio demonstrates superior results compared to Humira

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Vedolizumab superior to adalimumab in achieving clinical remission and mucosal healing at week 52 in patients with moderately to severely active ulcerative colitis

Takeda Pharmaceutical Company Limited has announced results from the Phase 3b head-to-head VARSITY study which demonstrated that the gut-selective biologic vedolizumab (Entyvio) was superior to the anti-tumor necrosis factor-alpha (anti-TNF?) biologic adalimumab (Humira) in achieving clinical remission in patients with moderately to severely active ulcerative colitis at week 52. Data showed that 31.3% (n=120/383) of patients receiving vedolizumab intravenous (IV) achieved the primary endpoint of clinical remission compared to 22.5% (n=87/386) of patients treated with adalimumab subcutaneous (SC) at week 52, with the difference being statistically significant (p=0.0061). These results were announced as an oral presentation (OP34) on Saturday March 9, 2019 from 09:40-09:50, at the 14th Congress of the European Crohn's and Colitis Organisation (ECCO) in Copenhagen, Denmark.

Furthermore, treatment with vedolizumab was associated with significantly higher rates of mucosal healing** at week 52, with 39.7% of patients receiving vedolizumab achieving mucosal healing compared to 27.7% treated with adalimumab (p=0.0005). A non-statistically significant difference in favor of adalimumab was seen in the percentage of patients using oral corticosteroids at baseline who discontinued corticosteroids and were in clinical remission*** at week 52. While the study was not powered to compare the safety of the two biologics, patients treated with vedolizumab (62.7%) had a lower rate of overall adverse events over 52 weeks than patients treated with adalimumab (69.2%), with a lower rate of infections reported in

patients treated with vedolizumab (33.5%) as compared to adalimumab (43.5%). The rate of serious adverse events was also lower in vedolizumab-treated patients than adalimumab (11.0% vs. 13.7% respectively).

“The VARSITY study addresses critical questions concerning the selection of biologic therapy in ulcerative colitis,” said Dr. Bruce E. Sands, primary investigator of the VARSITY study and Chief of the Dr. Henry D. Janowitz Division of Gastroenterology at Mount Sinai Hospital and the Icahn School of Medicine at Mount Sinai in New York. “The goal of treatment in ulcerative colitis is to achieve clinical remission and mucosal healing, and these results clearly highlight the benefits seen with vedolizumab versus adalimumab on these important outcomes. The results also showed lower rates of overall and serious adverse events including infections in patients treated with vedolizumab than adalimumab.”

“As the first clinical study to directly compare the efficacy and safety of two commonly used biologic therapies in patients with ulcerative colitis, VARSITY provides invaluable knowledge to help inform physicians’ treatment decisions when initiating biologic therapy,” said Jeff Bornstein, M.D., Executive Medical Director, Takeda. “This is also the first time we have seen a direct comparison between two medicines with distinct modes of action in ulcerative colitis, the gut-selective anti-alpha4beta7 integrin vedolizumab and the anti-TNF? adalimumab. This is an exciting time in the landscape of ulcerative colitis treatment, as head-to-head clinical data has not previously been available to guide treatment decisions around biologic therapies.”

VARSITY is a phase 3b, randomized, double-blind, double-dummy, multi-center, active-controlled study to evaluate the efficacy and safety of vedolizumab IV compared to adalimumab SC at week 52 in patients with moderately to severely active ulcerative colitis. The study randomized 769 patients (vedolizumab n=383 or adalimumab n=386), all of whom had inadequate response with, loss of response to, or intolerance to corticosteroids, immunomodulators, or one TNF?-antagonist other than adalimumab prior to being enrolled. Patients were randomized into one of two treatment groups, vedolizumab IV and placebo SC or adalimumab SC and placebo IV. Patients in the vedolizumab group were administered vedolizumab IV 300 mg at weeks 0, 2, 6 and every 8 weeks thereafter until week 46, along with placebo SC at week 0 and every 2 weeks until week 50. The adalimumab group were administered adalimumab SC 160 mg at week 0, 80 mg at week 2 and 40 mg every 2 weeks until week 50, along with placebo IV at weeks 0, 2, 6 and every 8 weeks thereafter until week 46. Dose escalation was not permitted in either treatment arm during the study.

* Primary endpoint: Clinical remission is defined as a complete Mayo score of ?2 points and no individual subscore ?1 point.2
** Secondary endpoint: Mucosal healing is defined as Mayo endoscopic subscore of ?1 point. Mayo score: instrument designed to measure disease activity of ulcerative colitis.2
*** Secondary endpoint: Corticosteroid-free clinical remission is defined as patients using oral corticosteroids at baseline (week 0) who have discontinued oral corticosteroids and are in clinical remission at week 52.2