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Takeda announces results of Phase 3b VARSITY studies

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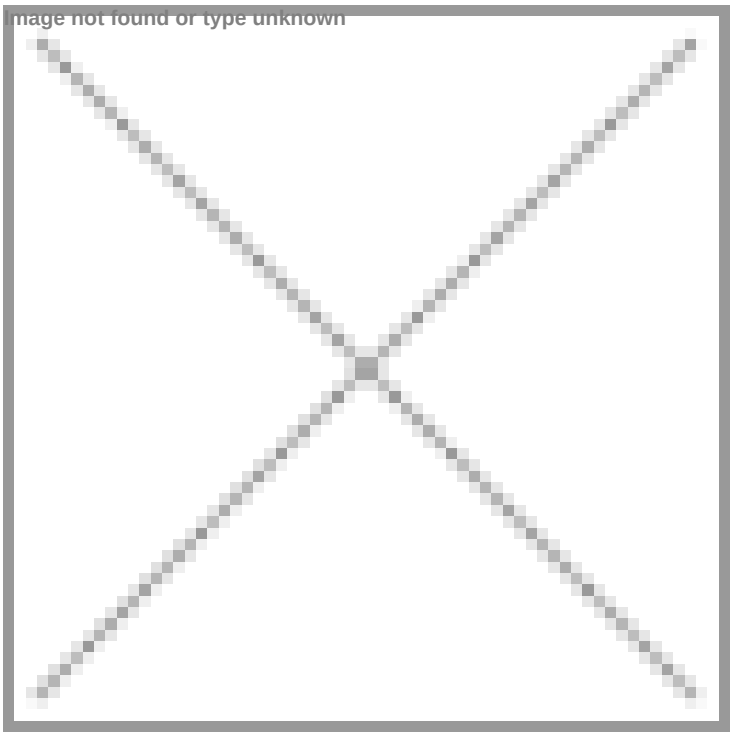
VARSITY is a Phase 3b, randomized, double-blind, double-dummy, multi-center, active-controlled study to evaluate the efficacy and safety of vedolizumab intravenous (IV) compared to adalimumab subcutaneous (SC) at week 52 in patients with moderately to severely active ulcerative colitis.



Takeda Pharmaceutical Company Limited has announced further 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* at week 52 in patients with moderately to severely active ulcerative colitis (UC).[1] New exploratory data showed that a greater proportion of patients receiving vedolizumab intravenous (IV) achieved clinical response** at week 14 compared to those treated with adalimumab subcutaneous (SC), 67.1% vs. 45.9% respectively. A separation between the treatment groups was seen as early as week 6, favoring vedolizumab. These results were announced in a Distinguished Abstract Plenary Lecture Presentation at the 2019 Digestive Disease Week (DDW) annual scientific meeting (May 18-21 in San Diego, CA), one of 18 Takeda sponsored vedolizumab abstracts accepted for presentation.[2]

Additional exploratory data on absence of active histologic disease were also presented at the meeting. Histologic disease activity is an endpoint assessing the degree of microscopic inflammation in the gut. Absence of active histologic disease is achieved when inflammation is less than a pre-defined severity threshold.[2,3,4]*** In the VARSITY study, consistent results were seen with vedolizumab treatment across both the Geboes Score (<3.2) and Robarts Histopathology Index (<5), with absence of active histologic disease achieved in 33.4% and 42.3% of patients treated with vedolizumab, respectively, compared with 13.7% and 25.6% of patients treated with adalimumab, respectively.[2]

“Exploratory data from the VARSITY study suggest that more patients experienced early symptomatic response and improvement of microscopic intestinal inflammation with vedolizumab as compared to adalimumab,” 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. “In clinical practice there is a need to balance early symptomatic improvement alongside the longer-term treatment goal of helping patients to achieve clinical remission, making these findings important to physicians.”

“Patients benefit from clinical trials that advance our understanding of the disease. The VARSITY study, a first-of-its-kind comparison of two biologics in ulcerative colitis, provides valuable information that can help inform treatment decisions, while also increasing our understanding of how these treatments are working at a microscopic level,” said Jeff Bornstein, M.D., Executive Medical Director, Takeda. “Data from the VARSITY study show consistent results for vedolizumab, supporting the use of this treatment as a first-line biologic therapy in ulcerative colitis.”

VARSITY is a Phase 3b, randomized, double-blind, double-dummy, multi-center, active-controlled study to evaluate the efficacy and safety of vedolizumab intravenous (IV) compared to adalimumab subcutaneous (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 tumor necrosis factor-alpha (TNF?)-antagonist other than adalimumab prior to being enrolled. Patients were randomized into one of two treatment groups, vedolizumab IV 300 mg and placebo SC or adalimumab SC 160 mg and placebo IV. Dose escalation was not permitted in either treatment arm during the study.[1,5]

At week 52, 31.3% (n=120/383) of patients receiving vedolizumab IV achieved the primary endpoint of clinical remission* compared to 22.5% (n=87/386) of patients treated with adalimumab SC, with the difference being statistically significant (p=0.0061). In addition, 39.7% of patients treated with vedolizumab achieved the secondary endpoint of mucosal healing± at week 52, compared to 27.7% receiving 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 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).[1]

- *Primary endpoint: Clinical remission is defined as a complete Mayo score of ?2 points and no individual subscore ?1 point.[5]
- **Exploratory endpoint: Clinical response is defined as a reduction in partial Mayo score of ?2 points and ?25% from baseline, with an accompanying decrease in rectal bleeding subscore of ?1 point or absolute rectal bleeding subscore of ?1 point. Patients with missing clinical response status were considered non-responders.
- *** Exploratory endpoint: Absence of active histologic disease is defined as a Geboes Score (<3.2) or Robarts Histopathology Index (<5).[2]
- ± Secondary endpoint: Mucosal healing is defined as Mayo endoscopic subscore of ?1 point. Mayo score: an instrument designed to measure disease activity of ulcerative colitis.[5]
- † 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.[5]

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