https://doi.org/10.5217/ir.2020.00026 • Intest Res 2021;19(4):448-460

See "Efficacy and safety of a new vedolizumab subcutaneous formulation in Japanese patients with moderately to severely active ulcerative colitis" on page 448-460.

SUPPLEMENTARY MATERIAL

1. Subcutaneous Administration of Vedolizumab and Placebo

After receiving training from the health care provider (HCP; investigator or designee) on the proper SC injection technique and management of hypersensitivity reactions which may occur with the injection, patients or their caregivers injected vedolizumab subcutaneous (SC) or placebo SC under HCP supervision at clinic visits on Weeks 6 and 8. Blinding was maintained in the maintenance phase, and only the pharmacists at the study site were aware of treatment assignments.

During visits on Week 6 and 8, HCPs ensured proper injection technique prior to home dosing and observed for any potential hypersensitivity or injection site reactions associated with SC injection. Patients and caregivers could attend the clinic at Weeks 10 and 12 if further training was required. Patients or their caregivers also administered SC injections during the scheduled clinic visits at Weeks 14, 22, 30, 38, 46, and 50, under the supervision of the HCP, to allow continued observation of injection technique and adverse events (AEs); while all other scheduled SC injections occurred outside of the clinic. All intravenous (IV) infusions were administered by a HCP during clinic visits at Weeks 6, 14, 22, 30, 38, and 46. HCPs had appropriate monitoring and treatment for hypersensitivity reactions available for use following administration of study drug. Patients who experienced a severe hypersensitivity reaction associated with study drug administration were discontinued from the study.

Patients and their caregivers were instructed to inject SC doses into the thigh, abdomen, or upper arm, and to rotate the injection sites. Patients and their caregivers were instructed that the upper arm was to be used only when the caregiver administers the SC injection. For all SC dosing occurring outside of the clinic, patients received a phone call from their HCP within 24 hours prior to every injection to administer the progressive multifocal leukoencephalopathy (PML) subjective checklist and enquire about general health status and experience with prior injections. In accordance with the Risk Assessment and Management Plan for PML (RAMP), any positive PML subjective finding was evaluated via the physician administered PML objective checklist prior to the subject receiving the respective dose (refer to RAMP Site Staff Brochure). Patients also received a phone call from their HCP within 12 hours after the home injection at Weeks 10 and 12 to enquire about health status and experience with injection unless they attended the clinic on these days.

2. Corticosteroid Tapering Regimen

For prednisone at doses >10 mg/day (or equivalent), the dose was reduced at a rate of 5 mg/week until a 10 mg/day dose was reached. For prednisone at doses ≤10 mg/day (or equivalent) or a 10 mg/day dose (or equivalent) was achieved by tapering, the dose was reduced at a rate of 2.5 mg/week until discontinuation. For patients who could not tolerate the corticosteroid taper without recurrence of clinical symptoms, corticosteroids were increased up to the original dose at the start of induction therapy (without exceeding the baseline dose). In such cases, the tapering regimen was reinitiated within 2 weeks. Patients whose corticosteroid concentration consistently could not be tapered were withdrawn from the study.

3. Assessments

For disease activity assessment, baseline complete Mayo scores were obtained within 10 days prior to enrollment, using subject diary entries within the 10 days prior to enrollment and flexible sigmoidoscopy results obtained during the screening period. Sigmoidoscopy was conducted at Weeks 6 and 52 (or end-of-treatment visit), and a complete Mayo score was calculated for these visits for endpoint assessments. All endoscopies (Week 0, 6, and 52) were assessed centrally. Complete Mayo scores at Week 0, 6, and 52 were calculated by the investigator or designee, and the endoscopic component subscore was provided by the central reader.

4. Patient-Reported Outcomes

The Inflammatory Bowel Disease Questionnaire (IBDQ) is comprised of 32 questions that cover 4 domains of health-related quality of life, as follows: bowel symptoms (10 items), emotional function (12 items), social function (5 items), and

systemic function (5 items). Each question is rated on a scale of 1 to 7. A total IBDQ score is calculated by adding the scores from each domain (total IBDQ score ranging from 32 to 224). The EuroQol-5 Dimension visual analog scale score is a self-assessment questionnaire of overall health that uses a 20 cm visual, vertical scale, with a score ranging from 0 (worst) to 100 (best possible) health. The Work Productivity and Activity Impairment-Ulcerative Colitis (WPAI-UC) instrument consists of 4 metrics, as follows: absenteeism (percentage of work time missed owing to health-related issues in the past 7 days), presenteeism (percentage of impairment experienced owing to health-related issues while at work in the past 7 days), overall work productivity loss (an overall impairment estimate that is comprised of absenteeism and presenteeism), and activity impairment (percentage of impairment in daily activities owing to health-related issues in the past 7 days). Higher WPAI-UC percentages indicate greater impairment and lower productivity (i.e., worse outcomes).