Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the treatment of patients with moderate to severe psoriasis with randomized withdrawal and retreatment: Results from the phase III, double-blind, placebo- and active comparator–controlled VOYAGE 2 trial

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Background: Phase II data suggested that guselkumab, an anti-interleukin-23 monoclonal antibody, was efficacious in psoriasis.

Objective: We sought to assess efficacy and safety of guselkumab in moderate to severe psoriasis versus placebo and adalimumab, including interrupted treatment and switching adalimumab nonresponders to guselkumab.

Methods: Patients were randomized to guselkumab 100 mg (weeks 0 and 4, then every 8 weeks; n = 496); placebo → guselkumab (weeks 0, 4, and 12 then guselkumab at weeks 16 and 20; n = 248); or adalimumab (80 mg week 0, then 40 mg week 1, and every 2 weeks through week 23; n = 248). At week 28, guselkumab 90% or greater improvement in Psoriasis Area and Severity Index (PASI) score from baseline (PASI 90) responders were rerandomized to guselkumab or placebo with guselkumab after loss of response.

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Placebo→guselkumab responders and adalimumab responders received placebo, then guselkumab after loss of response. Nonresponders received guselkumab.

Results: At week 16, more patients receiving guselkumab achieved an Investigator Global Assessment (IGA) score 0/1 (cleared/minimal) (84.1% vs 8.5%) and PASI 90 (70.0% vs 2.4%) versus placebo (coprimary end points). Guselkumab was superior to adalimumab at week 16 (IGA score 0/1, 75% or greater improvement in PASI score from baseline, and PASI 90) and week 24 (IGA score 0/1 and 0, PASI 90, 100% improvement in PASI score from baseline) ($P < .001$). From weeks 28 to 48, better persistence of response was observed in guselkumab maintenance versus withdrawal groups ($P < .001$). Of adalimumab nonresponders who switched to guselkumab, 66.1% achieved PASI 90 at week 48. Guselkumab improved patient-reported outcomes. Adverse events were comparable among groups.

Limitations: One-year follow-up limits retreatment data.

Conclusions: Guselkumab is a highly effective, well-tolerated, maintenance therapy, including in adalimumab nonresponders. (J Am Acad Dermatol 2017;76:418-31.)

Key words: adalimumab; efficacy; guselkumab; interleukin-23; psoriasis; safety; switching; VOYAGE 1; VOYAGE 2.

Psoriasis is a chronic immune-mediated inflammatory disease. Although therapeutic options have progressively expanded for moderate to severe psoriasis, new unmet needs have emerged.[1,2] Standards for treatment goals have escalated; patients often desire complete skin clearance[3,4] and improved long-term efficacy.[5,6] In addition, as new therapeutic options become available, more information is needed about interruption of and transition between treatments.

CAPSULE SUMMARY

- Guselkumab effectively treated moderate to severe psoriasis in the phase II X-PLORE study.
- Phase III VOYAGE 2 confirmed VOYAGE 1 results and demonstrated benefits of maintenance versus withdrawal therapy, and effective treatment with guselkumab among adalimumab nonresponders.
- Data addressing treatment interruption and switching patients from adalimumab to this new, more effective agent are useful for guiding treatment decisions.

Recent studies of biologics for psoriasis treatment demonstrated substantial efficacy by selectively blocking the interleukin (IL)-23 or IL-17 pathways, both central to psoriasis pathogenesis.[7-14] Current findings show that selective inhibition of IL-23 alone results in clinical response and molecular improvements in the skin.[7,9,12,13]

Guselkumab (CNTO 1959; Janssen Research & Development, LLC, Spring House, PA) is a fully human IgG1 lambda monoclonal antibody that binds IL-23 and blocks binding and signaling through its receptor. High levels of efficacy were suggested in phase I[13] and phase II[7] studies. To confirm the therapeutic potential of guselkumab, the phase III VOYAGE 1[15] and VOYAGE 2 studies assessed the efficacy and safety of guselkumab versus placebo and adalimumab. VOYAGE 1 assessed continuous 1-year treatment, and VOYAGE 2 evaluated the efficacy and safety of interrupted treatment, as treatment gaps frequently occur in clinical practice.[16-19] In addition, VOYAGE 2 assessed the transition from adalimumab to guselkumab, providing clinically relevant information about patients who switch biologics.

METHODS

Patients

Adults (aged ≥18 years) with moderate to severe plaque-type psoriasis were eligible. Major inclusion/exclusion criteria are summarized in VOYAGE 1 (NCT02207231).[15] The study protocol was approved by investigational review boards at each site, and written informed consent was provided by all patients.

Study design

VOYAGE 2 was a phase III, multicenter, randomized, double-blind, placebo- and adalimumab comparator–controlled study (NCT02207244) conducted in 115 global sites from November 2014 to May 2016. The study consisted of a placebo-controlled period (weeks 0-16), an active comparator–controlled period (weeks 0-28),

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