Latest Highlights on Biologic Treatments for Psoriasis and Psoriatic Arthritis from EADV 2020

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Meeting Summary

Recent studies have examined the potential efficacy and safety of treatments for psoriasis and psoriatic arthritis (PsA), including the monoclonal antibody guselkumab, which specifically binds to the p19 subunit of IL-23 (IL-23p19). The results of the Phase III VOYAGE 1, VOYAGE 2, DISCOVER-1,

and DISCOVER-2 trials with guselkumab showed that treatment was followed by sustained improvements in skin, joint, and soft tissue manifestations in adult patients with moderate-to-severe psoriasis and active PsA, with no new safety signals. The poster presentations in this review discussed the results of these trials at the 29th European Academy of Dermatology and Venereology (EADV) Virtual Congress.

Complete Skin Clearance Throughout 156 Consecutive Weeks of Guselkumab Treatment in Patients with Moderate-to-Severe Psoriasis: A Post Hoc Analysis of the VOYAGE 1 Trial

The VOYAGE 1 trial[1] was a placebo- and active-controlled Phase III study to evaluate long-term efficacy and safety of the IL-23p19 inhibitor guselkumab in patients with moderate-to-severe plaque psoriasis. The study demonstrated superior efficacy of guselkumab compared with the TNF inhibitor adalimumab through 48 weeks of therapy.[2] The trial consisted of an arm in which patients received guselkumab, an active comparator arm in which patients received adalimumab from Week 0 to Week 48, and a placebo arm in which patients who were randomised to placebo crossed over to guselkumab treatment at Week 16. After Week 16 or Week 48, all patients received guselkumab until the conclusion of the study.[1] The objective of this particular post hoc analysis was to examine the baseline clinical characteristics and demographics of patients who had achieved absolute Psoriasis Area and Severity Index (aPASI) scores of 0, indicating complete skin clearance, for at least 156 consecutive weeks.[1]

Data from 494 patients who had either received guselkumab from Week 0 or crossed over to guselkumab from placebo at Week 16 were combined, resulting in 178 patients with available aPASI data for at least 156 consecutive weeks. A total of 88 patients (17.8%) maintained an aPASI score of 0 over 3 years and were compared with 90 patients (18.2%) who did not achieve an aPASI score of 0 at any visit.

In the comparator group, median aPASI scores were 18.6 at baseline, 4.0 at Week 12, and 1.9 at Week 204, but median scores in the aPASI=0 group decreased from 18.3 at baseline to 0.0 at Week 12, maintained to Week 204. Notably, 51.1% of those patients achieved complete skin clearance by Week 12 of treatment and this proportion increased to 70.5% by Week 20.[1]

Patients in the aPASI=0 group had a numerically higher plasma concentration of guselkumab than those in the comparator group. Patients who achieved complete skin clearance also generally had more favourable baseline characteristics: they were younger, had a lower BMI, and had lower body weight. Importantly, they had less severe disease and a shorter disease duration. These results demonstrated the sustained response to biologic therapy using stringent aPASI=0 criteria for 156 consecutive weeks in patients with moderate-to-severe psoriasis.[1]

Long-Term Safety of Guselkumab in Patients with Moderate-to-Severe Plaque Psoriasis Through 4 Years of Continuous Follow-up in the VOYAGE 1 and 2 Trials

The cumulative safety experience with guselkumab was described using pooled data from the VOYAGE 1 and VOYAGE 2 trials through 4 years, to Week 204.[3] The safety outcomes evaluated included adverse events (AE), AE leading to discontinuation, serious AE, and other AE of special interest, such as serious infections, malignancies, and major adverse cardiovascular events (MACE). Three groups were included in the analysis: a guselkumab group, including patients who had received placebo and crossed over to guselkumab; a group of patients who had received adalimumab and crossed over to guselkumab; and a combined guselkumab group, which included all patients from the first two groups.[3]

Cumulative rates of AE, reported per 100 patient-years of follow-up, were generally comparable between groups, showing minor year-to-year variability without increasing trends. In

the guselkumab–adalimumab crossover and combined guselkumab groups, pooled AE rates that led to discontinuation per 100 patient-years of follow-up through Week 204 were 1.66, 1.48, and 1.62, respectively. Rates of special interest AE, including serious infections and MACE, were low. Malignancy rates in all groups were similar to the observed level in the general population in the USA. Furthermore, there were no reports of tuberculosis, anaphylactic or serum-sickness-like reactions, or inflammatory bowel disease in patients receiving guselkumab.[3]

Overall, the long-term safety profile of guselkumab remained favourable in patients with psoriasis, and AE rates were generally low and stable over a 4-year period during continuous guselkumab treatment.[3]

Guselkumab, an IL-23 Inhibitor that Specifically Binds to the IL-23 p19 Subunit, in Biologic-Naïve Patients with Active Psoriatic Arthritis: Composite Week 24 Efficacy of the Phase III, Randomised, Double-blind, Placebo-Controlled Studies

The DISCOVER-1 and DISCOVER-2 studies were multicentre, randomised, double-blind, placebo-controlled studies in patients with active PsA who were either biologic-naïve (both studies), or who had previously received a TNF inhibitor (DISCOVER-1).[4] In both studies, patients were randomised 1:1:1 to subcutaneous guselkumab 100 mg every 4 weeks (q4w); guselkumab 100 mg at Week 0, Week 4, then every 8 weeks (q8w); or placebo. Both trials included patients who had active PsA and active plaque psoriasis, nail changes, or a history of plaque psoriasis despite standard therapies. The pooled primary endpoint results for the American College of Rheumatology 20% (ACR 20) response at Week 24 showed a significantly better outcome in both guselkumab treatment arms (nominal $p<0.001$ for guselkumab versus placebo), with 28.0% for placebo-treated patients (n=261), 63.2% for the guselkumab 100 mg q8w (n=258) group, and 64.8% for patients who received guselkumab 100 mg q4w (n=273).[4] The analysis presented in this review assessed the composite joint and skin efficacy of guselkumab in the treatment of PsA separately for each study, using ACR 50 and PASI 100 scores at Week 24.[4]

The DISCOVER-1 analysis included 82 patients who received guselkumab 100 mg q8w, 89 who received guselkumab 100 mg q4w, and 78 who received placebo. ACR 50 and PASI 100 responses were achieved by 9.8% of patients who received the q8w dosage (8.7% difference; 95% confidence interval [CI]: 1.8–15.6) and 19.1% of patients who received the q4w dose of guselkumab (17.9% difference; 95% CI: 9.5–26.3), compared with 1.3% of patients who received placebo.[4]

The DISCOVER-2 analysis included 176 patients who received guselkumab 100 mg q8w, 184 who received guselkumab 100 mg q4w, and 183 who received placebo. ACR 50 and PASI 100 responses were achieved at Week 24 by 18.2% of patients who received the q8w dosage (17.4% difference; 95% CI: 11.7–23.0), and 21.7% of patients who received the q4w dose (21.2% difference; 95% CI: 15.2–27.1), compared with 0.5% of patients who received placebo.[4]

In conclusion, analysis of both studies demonstrated that in patients with active PsA, both the q4w and q8w doses of guselkumab demonstrated greater composite efficacy on joint improvement and complete skin clearance at Week 24 compared with placebo, regardless of prior biologic exposure.[4]

Efficacy and Safety of Guselkumab, a Monoclonal Antibody Specific to the p19 Subunit of IL-23, Through Week 52 of a Phase III, Randomised, Double-Blind, Placebo-Controlled Study Conducted in Biologic-Naïve Patients with Active Psoriatic Arthritis

The DISCOVER-2 study[5,6] revealed that, in addition to improving joint and skin signs and symptoms in biologic-naïve adults with active PsA, guselkumab significantly inhibited structural damage progression with the

100 mg q4w dosage. The results presented in this review reported on the efficacy and safety of guselkumab through Week 52 of treatment.[5]

ACR responses were measured in the modified intent-to-treat population, based on nonresponder imputation for missing data. Additional endpoints included improvements in physical function and health-related quality of life through Week 52.[5]

The analysis included a total of 712 out of 739 (96.3%) randomised and treated patients who continued the study agent at Week 24; 689 of 739 (93.2%) completed 52 weeks of treatment.[5]

Continued improvement with guselkumab treatment was seen in all three joint-treatment responses (ACR 20, 50, and 70) through Week 52. Of patients in the guselkumab q4w group, 70.6% achieved ACR 20 responses, as did 74.6% of patients in the q8w group. ACR 50 responses were achieved by 45.7% of patients in the q4w group and by 48.4% of patients in the q8w group. ACR 70 responses were achieved by 26.1% of patients in the q4w group and 27.8% of patients in the q8w group.[5]

Skin responses, including PASI 90 and PASI 100 scores, improved from Week 24 to 52 in patients with PsA who received guselkumab; this was also seen in the group that crossed over to guselkumab from placebo. Continued improvement in physical function and dactylitis and enthesitis outcomes, as well as a notable improvement in health-related quality of life were achieved from Week 24 to Week 52 in both active-treatment groups.[5]

Guselkumab treatment offered a favourable benefit–risk profile in patients with PsA, with no increases in serious infection rates, cases of tuberculosis or opportunistic infections, additional malignancies, MACE, or inflammatory bowel disease, consistent with the safety profile in psoriasis.[5]

Conclusions

When considered together, these results underscored the potential of specific IL-23 inhibition in psoriasis management; treatment with guselkumab resulted in high clinical response rates in PASI scores, which were maintained over 4 years of continuous treatment. These results suggested that psoriasis management goals may be shifting toward more stringent targets, such as the achievement of complete skin clearance. Furthermore, results from long-term safety analyses have revealed no new safety signals for guselkumab. Finally, IL-23 inhibition has also emerged as a promising target in PsA management, as demonstrated by the results of the DISCOVER-1 and DISCOVER-2 studies.

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