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Comparisons of symptom-free and sign-free status among patients with moderate to severe plaque psoriasis treated with guselkumab or adalimumab: Results from VOYAGE 1

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Background and Objective: To evaluate differences in achieving patient-reported symptom-free and sign-free status between guselkumab (GUS)− and adalimumab (ADA)−treated patients in the VOYAGE 1 study.

Methods: Overall, 837 psoriasis patients were randomized to receive GUS for 48 wks (n = 329), ADA for 48 wks (n = 334), or placebo (n = 174). The PsO Symptom and Signs Diary (PSSD) was used to assess patient-reported symptoms (itch, burning, stinging, skin tightness, and pain) and patient-observable signs (skin dryness, cracking, scaling, shedding or flaking, redness, bleeding) using a 0-10 rating scale. Weekly average scores of the five symptoms and six signs assessed were used to derive symptom summary and sign summary scores (0-100), respectively. A score of 0 represents symptom-free or sign-free status. Outcomes for the GUS and ADA groups were compared at wk48.

Results: Compared with ADA, a greater proportion of GUS-treated patients achieved a PSSD symptom score of 0 (41.9% vs 23.1%, $P < .001$) or sign score of 0 (35.9% vs 18.6%, $P < .001$) at wk 48. A greater proportion of GUS-treated patients achieved a PSSD symptom score of 0 (53.2% vs 37.4%, $P < .001$) or sign score of 0 (49.2% vs 31.0%, $P < .001$) for at least 1 time point over 48 wks. GUS-treated patients experienced more symptom-free time (11.8 wks, 24.9% of treatment time) and sign-free time (9.3 wks, 19.9% of treatment time) over 48 wks compared with ADA-treated patients (6.5 wks, 13.8% of treatment time; 4.9 wks, 10.2% of treatment time, respectively).

Conclusions: Compared with ADA, GUS-treated patients were more likely to achieve symptom-free and sign-free status, and experience more symptom-free and sign-free time.

Commercial disclosure: This was sponsored by Janssen Research & Development.

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Maintenance of response through up to 4-years of continuous guselkumab treatment of psoriasis in the VOYAGE 2 phase 3 trial

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Introduction: Guselkumab (GUS) is a fully-human monoclonal antibody that binds and inhibits the p19 subunit of IL-23. In the VOYAGE 2 phase 3, randomized, double-blind, placebo/active comparator-controlled clinical trial of moderate to severe psoriasis (PsO), significantly greater proportions of GUS-treated patients achieved PASI90 response and Investigator Global Assessment (IGA) 0/1 scores vs placebo (PBO) at wk 16 vs adalimumab (ADA) at wk 24. Here, results following up to 4 years of continuous GUS treatment are presented.

Methods: Patients were randomized to GUS 100 mg (n = 496) at wks 0, 4, and 12, then every 8 wks (q8wk); PBO (n = 248) at wks 0, 4, and 12, followed by GUS 100 mg at wks 16, 20, then q8wk; or ADA 80 mg (n = 248) at wk 0, 40 mg at wk 1, then 40 mg q2wk until wk 23. Weeks 28-72 incorporated a randomized withdrawal study design. During the open-label period (wks 76-204), patients received GUS 100 mg q8wk. Physician and patient-reported outcomes were assessed. Efficacy was analyzed using pre-specified treatment failure rules beginning at wk 76 (patients were considered nonresponders after discontinuing due to lack of efficacy, worsening of PsO, or use of a prohibited treatment). Data were combined for patients randomized to GUS and for those originally randomized to PBO who later crossed over to GUS at wk 16 (GUS group).

Results: The proportions of patients in the GUS group who achieved designated clinical responses at wks 100 and 204, respectively, were: PASI90: 79.1%, 79.7%; PASI100: 48.4%, 51.0%; IGA 0/1: 83.1%, 81.9%; IGA 0: 52.7%, 52.7%; Dermatology Life Quality Index (DLQI) 0/1: 70.2%, 69.1%; Psoriasis Symptoms and Signs Diary (PSSD) symptom score 0: 5.7%, 39.7%; and PSSD sign score 0: 22.0%, 27.2%. No new safety signals were identified.

Conclusions: High levels of efficacy were maintained from wk 100 through wk 204 with continuous GUS treatment across multiple end points in the VOYAGE 2 study.GUS treatment was well tolerated.

Commercial disclosure: This study was sponsored by Janssen Research & Development.

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Identification of pathogenic variants in patients with melanoma who meet NCCN criteria for hereditary breast and ovarian cancer and Lynch syndrome testing

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Currently, CDKN2A and CDK4 have primarily been implicated in familial melanoma. However, pathogenic variants (PVs) in these genes only represent a small percentage of familial melanoma cases, indicating that other genes may be involved. By looking at the patient family history data of over 500,000 individuals tested with a pan-cancer panel because they met National Comprehensive Cancer Network (NCCN) hereditary breast and ovarian cancer and/or Lynch syndrome criteria, we identified 27,946 patients with a personal history of melanoma or first-degree relative with melanoma. Of these patients, 1932 (6.9%) patients carried a PV in a cancer predisposition gene, which was significantly higher than in individuals with no personal history of any cancer and no first-degree relative with melanoma (5.1%, $P < .0001$). These PVs were most commonly identified in CHEK2 (n = 356), BRCA2 (n = 313), ATM (n = 268), BRCA1 (n = 242), PALB2 (n = 137), and CDKN2A (n = 121). In this cohort, only one patient had a PV in CDK4. Of the 1520 patients first diagnosed with melanoma who went on to develop an additional primary cancer, 148 (9.7%) had a PV. These individuals went on to develop breast, colorectal, ovarian, or another cancer. Early identification of PV-carrying patients with melanoma would present the provider and patient with the opportunity to prevent the occurrence of a second primary cancer through increased surveillance or risk-reducing surgeries. Identification of patients with concerning family cancer histories eligible for hereditary cancer testing according to NCCN guidelines during dermatology appointments may lead to positive health outcomes by preventing future cancers.

Commercial disclosure: 100% sponsored by Myriad Genetics.

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Psoriasis area and severity index component improvements at week 48 in patients treated with guselkumab compared with secukinumab: Findings from the ECLIPSE study

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Background: Guselkumab (GUS), a fully human monoclonal antibody targeting interleukin-23, is approved to treat moderate to severe plaque psoriasis. In the ECLIPSE trial, GUS demonstrated a superior Psoriasis Area and Severity Index (PASI) 90 response compared with the interleukin-17A inhibitor secukinumab (SEC) at week 48. This subanalysis assessed PASI component responses at week 48.

Methods: ECLIPSE was a phase 3, randomized, multicenter, double-blind, active-comparator-controlled trial comparing GUS and SEC in patients with moderate to severe plaque psoriasis. Patients were randomized to receive subcutaneous injections of GUS 100 mg at weeks 0, 4, 12, and then every 8 weeks (n = 534) or SEC 300 mg at weeks 0, 1, 2, 3, 4, and then every 4 weeks (n = 514) both through week 44. For the purposes of this analysis, PASI component measures (induration, scaling, and erythema) were assessed at week 48.

Results: At week 48, numerically greater proportions of GUS patients achieved 100% improvement in induration (65.9% vs 53.3%), scaling (62.2% vs 50.6%), and erythema (60.5% vs 49.4%) than SEC patients. Similarly, a higher proportion of patients in the GUS group achieved ≥ 90% improvement in induration (84.3% vs 70.2%), scaling (84.8% vs 70.4%), and erythema (82.6% vs 69.5%) than patients in the SEC group. No unexpected safety findings were observed with GUS or SEC.

Conclusions: Overall, GUS demonstrated numerically greater levels of response in improving all PASI component measures (induration, scaling, and erythema) than SEC in patients with moderate to severe plaque psoriasis.

Commercial disclosure: This study was sponsored by Janssen Research & Development.