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Manuscript

Title Guselkumab Provides Sustained Domain-Specific and Comprehensive Efficacy Using Composite Indices in Patients With Active Psoriatic Arthritis

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ABSTRACT

Objectives: Evaluate the efficacy of guselkumab for the treatment of active psoriatic arthritis (PsA) utilizing composite indices.

Methods: Data were pooled from the Phase 3 DISCOVER-1 (N=381) and DISCOVER-2 (N=739) studies. In both studies, patients were randomized 1:1:1 to subcutaneous guselkumab 100 mg every 4 weeks (Q4W); guselkumab 100 mg at Week 0, Week 4, then Q8W; or placebo Q4W with crossover to guselkumab 100 mg Q4W at Week 24. Composite indices used to assess efficacy through Week 52 included Disease Activity Index for Psoriatic Arthritis (DAPSA), Psoriatic Arthritis Disease Activity Score (PASDAS), minimal disease activity (MDA), and very low disease activity (VLDA). Through Week 24, treatment failure rules were applied. Through Week 52, non-responder imputation was used for missing data.

Results: Greater proportions of guselkumab- than placebo-treated patients achieved DAPSA low disease activity (LDA) and remission, PASDAS LDA and VLDA, MDA, and VLDA at Week 24 versus placebo (all unadjusted $p<0.05$). At Week 52, in the guselkumab Q4W and Q8W groups, respectively, response rates were as follows: DAPSA LDA, 54.2% and 52.5%; DAPSA remission, 18.2% and 17.6%; PASDAS LDA, 45.3% and 41.9%; PASDAS VLDA, 16.9% and 19.5%; MDA, 35.9% and 30.7%; and VLDA, 13.1% and 14.4%. In the placebo-crossover-to-guselkumab group, response rates for all composite indices increased after patients switched to guselkumab, from Week 24 through Week 52.

Conclusion: Treatment with guselkumab provided robust and sustained benefits across multiple PsA domains through 1 year, indicating that guselkumab is an effective therapy for the diverse manifestations of PsA.

Trial registration: NCT03162796; NCT03158285

Key words: guselkumab, psoriatic arthritis, composite indices, remission, skin clearance, joint disease

KEY MESSAGES

- Composite indices combine physician-assessed and patient-reported measures to comprehensively evaluate outcomes across psoriatic arthritis domains.
- Assessments of guselkumab efficacy using composite indices showed significant, sustained achievement of low disease activity/remission.
- These results suggest that guselkumab is an effective treatment for diverse manifestations of psoriatic arthritis.

INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory disease characterized by several distinct clinical manifestations, including peripheral arthritis, axial disease, dactylitis, enthesitis, skin disease, and nail disease [1,2]. The initial presentation and disease course of PsA is remarkably heterogeneous, making diagnosis and treatment challenging. Most patients develop a range of both musculoskeletal and extra-articular disease manifestations, which respond differently to available therapies [2,3].

As a result of the multifaceted, systemic nature of PsA development and progression, treatment guidelines evolved to recommend a “treat-to-target” approach, with the goal of achieving remission or low disease activity (LDA) across all domains of disease [2,4,5]. The need to define thresholds for achievement of remission and LDA resulted in the development of several multidimensional indices [6,7], including the Disease Activity in Psoriatic Arthritis (DAPSA) [8], the Psoriatic Arthritis Disease Activity Score (PASDAS) [9,10], and minimal disease activity (MDA)/very low disease activity (VLDA) criteria [11,12]. These composite indices combine various physician-assessed and patient-reported outcome measures applicable to both PsA clinical trials and real-world clinical practice to comprehensively evaluate outcomes across PsA domains [6,7,13−16].

Guselkumab is a fully human monoclonal antibody that selectively and specifically binds and inhibits the p19 subunit of interleukin (IL)-23. Guselkumab is approved for the treatment of adults with moderate to severe plaque psoriasis and active PsA [17]. The safety and efficacy of guselkumab 100 mg administered every 4 weeks (Q4W) or every 8 weeks (Q8W) were evaluated in the DISCOVER-1 and DISCOVER-2 randomized, placebo-controlled, Phase 3 studies in patients with active PsA. In these studies, guselkumab Q4W and Q8W significantly improved signs and symptoms of PsA, including psoriasis-related skin symptoms, enthesitis,

dactylitis, physical function, and health-related quality of life, compared with placebo at Week 24 [18,19], with sustained improvements through 1 year [20,21]. In the current analyses, data were pooled from the DISCOVER-1 and DISCOVER-2 Phase 3 studies to assess guselkumab efficacy through 1 year utilizing various composite indices of PsA disease activity.

METHODS

Patients and study designs

DISCOVER-1 (NCT03162796) [18] and DISCOVER-2 (NCT03158285) [19] were similarly designed, randomized, placebo-controlled studies of guselkumab in patients with active PsA, diagnosed according to Classification Criteria for Psoriatic Arthritis (CASPAR) [22], who had an inadequate response or intolerance to nonbiologic disease-modifying anti-rheumatic drugs (DMARDs), apremilast, and/or nonsteroidal anti-inflammatory drugs (NSAIDs). In DISCOVER-1, active PsA was defined as ≥3 tender and ≥3 swollen joints and serum C-reactive protein (CRP) concentration ≥0.3 mg/dL. In DISCOVER-2, the definition of active PsA was more stringent, requiring ≥5 tender and ≥5 swollen joints and serum CRP concentration ≥0.6 mg/dL. In DISCOVER-1, prior treatment with 1 or 2 tumour necrosis factor-α inhibitors (TNFi) was permitted but was limited to approximately 30% of the study population [18], while all patients in DISCOVER-2 were biologic-naïve [19].

In both studies, patients were randomized in a 1:1:1 ratio to receive subcutaneous guselkumab 100 mg Q4W; guselkumab 100 mg at Week 0, Week 4, then Q8W; or placebo Q4W with crossover to guselkumab 100 mg Q4W at Week 24. Patients could continue stable baseline use of selected nonbiologic DMARDs, including methotrexate ≤25 mg/week, sulfasalazine ≤3 g/day, hydroxychloroquine ≤400 mg/day, or leflunomide ≤20 mg/day; oral corticosteroids (≤10 mg/day of prednisone or equivalent); and NSAIDs or other analgesics. At Week 16, patients with <5% improvement from baseline in both swollen joint count (SJC) and tender joint count (TJC) were

eligible for early escape and had the option to initiate or increase their dose of one selected nonbiologic DMARD, oral corticosteroids, NSAIDs, or other analgesics.

DISCOVER-1 and DISCOVER-2 were conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice. The study protocols were approved by governing ethics bodies. All participants provided written informed consent.

Assessments

The proportions of patients achieving DAPSA LDA, DAPSA remission, PASDAS LDA, PASDAS VLDA, MDA, and VLDA by visit were prespecified efficacy assessments in the DISCOVER-1 and DISCOVER-2 studies. The proportions of patients achieving clinical DAPSA (cDAPSA) LDA and remission were calculated post hoc for both studies. For the current analyses, data for these outcomes were pooled across the 2 studies and are also presented separately for each study.

DAPSA scores are calculated as the sum of TJC (range, 0-68), SJC (range, 0-66), patient pain assessment (0-10 cm visual analogue scale [VAS]), patient global assessment (PtGA) of arthritis activity (0-10 cm VAS), and CRP (mg/dL) [3,8]. cDAPSA is a modification of the DAPSA that excludes CRP [23]. Higher DAPSA and cDAPSA scores represent more severe disease activity. DAPSA LDA and remission are defined as scores of ≤14 and ≤4, respectively, and cDAPSA LDA and remission are defined as scores of ≤13 and ≤4, respectively [23]. Based on the measurement schedule for the individual assessments included, DAPSA and cDAPSA scores were determined at Weeks 4, 8, 12, 16, 20, 24, 28, 36, 44, and 52.

PASDAS scores are calculated based on a formula that includes physician global opinion of skin and joints (0-100 mm VAS), patient global opinion of skin and joints (0-100 mm VAS), 36-

item Short Form Health Survey physical component summary score (range, 0-100), SJC (0-66), TJC (0-68), Leeds Enthesitis Index (LEI) score (range, 0-6) [24], tender dactylitis count (range, 0-20), and CRP (mg/L). Total PASDAS scores range from 0 to 10, with higher scores representing more severe disease activity [9,10,12]. PASDAS LDA is defined as a score of ≤3.2, and PASDAS VLDA is defined as a score of ≤1.9 [12]. Based on the measurement schedule for the individual assessments included, PASDAS scores were calculated at Weeks 8, 16, 24, and 52.

Patients are considered to meet MDA or VLDA criteria, respectively, if they achieve 5 (MDA) or 7 (VLDA) of the following 7 outcomes: TJC ≤1, SJC ≤1, LEI ≤1, Psoriasis Area and Severity Index (PASI) score ≤1, patient pain VAS ≤15 mm (range, 0-100), PtGA of the maximum component of either psoriasis activity or PsA activity VAS ≤20 mm (range, 0-100), and Health Assessment Questionnaire-Disability Index (HAQ-DI) score ≤0.5 (range, 0-3) [3,11,12]. MDA and VLDA results were determined at Weeks 16, 24, and 52.

In DISCOVER-2, single radiographs of the hands (posteroanterior) and feet (anteroposterior) were obtained at Weeks 0, 24, and 52 (or at discontinuation if between Weeks 24 and 52; Reading Session 2) and scored by blinded central primary readers using the modified van der Heijde-Sharp score for PsA [25]. Mean changes in PsA-modified van der Heijde-Sharp score from Week 0 to Week 52 were compared for patients who did and did not achieve PASDAS LDA, DAPSA LDA, and MDA responses at Week 24 (all using observed data).

Statistical analyses

Through Week 24, data were imputed as non-response for patients meeting treatment failure criteria (i.e., discontinued study treatment, terminated study participation, initiated or increased their dose of nonbiologic DMARDs or oral corticosteroids, or initiated any protocol-prohibited

PsA treatments) and for patients with missing data (non-responder imputation). After Week 24, patients with missing data were considered to be non-responders (non-responder imputation), and treatment failure rules were not applied.

Comparisons between the guselkumab groups and the placebo group through Week 24 were performed using a Cochran-Mantel-Haenszel test stratified by randomization stratification factors (baseline use of nonbiologic DMARDs [yes/no] and prior exposure to TNFi [yes/no] in DISCOVER-1, and baseline use of nonbiologic DMARDs [yes/no] and most recent CRP value prior to randomization [<2.0 or ≥2.0 mg/dL] in DISCOVER-2). P-values were not adjusted for multiplicity. No treatment comparison was performed after Week 24.

RESULTS

Patient disposition and baseline characteristics

In these pooled analyses, 1120 patients were randomized and treated in the DISCOVER-1 (guselkumab Q4W, n=128; guselkumab Q8W, n=127; placebo, n=126) and DISCOVER-2 (guselkumab Q4W, n=245; guselkumab Q8W, n=248; placebo, n=246) studies. A total of 118 patients in DISCOVER-1 (10.5% of the pooled population) had prior exposure to 1 or 2 TNFi. In this pooled population, 351 (94%) patients randomized to guselkumab Q4W, 350 (93%) patients randomized to guselkumab Q8W, and 335 (90%) patients randomized to placebo who crossed over to guselkumab at Week 24 received study treatment through 1 year.

At baseline, pooled patient demographic and PsA disease characteristics were comparable across randomized treatment groups (Table 1). On average, patients had PsA for more than 5 years, with active skin disease (mean PASI score of 8.8-10.4), joint inflammation (mean SJC of 11.4-11.5, mean TJC of 19.9-21.0), and impaired physical function (mean HAQ-DI score of 1.2-1.3). More than 60% of patients presented with enthesitis, and more than 40% of patients

presented with dactylitis. Mean DAPSA (45.9-46.9), PASDAS (6.4-6.5), patient assessment of pain (6.1-6.2), and PtGA of disease activity (6.3-6.5) scores, and mean CRP concentrations (1.6-1.9 mg/dL) were consistent with highly active PsA.

Placebo-controlled period through Week 24

At Week 24, greater proportions of guselkumab- than placebo-treated patients achieved low levels of disease activity when assessed with DAPSA LDA (≤14), cDAPSA LDA (≤13), PASDAS LDA (≤3.2), and MDA (5 of 7 components) composite indices (Figure 1). Separation from placebo was observed in the guselkumab groups as early as Week 8 for achievement of DAPSA LDA, cDAPSA LDA, and PASDAS LDA and at Week 16 (earliest timepoint assessed) for MDA.

At Week 24, greater proportions of guselkumab- than placebo-treated patients achieved near or complete remission when assessed with DAPSA (≤4) and cDAPSA (≤4) remission, PASDAS VLDA (≤1.9), and VLDA (7 of 7 components) composite indices (Figure 2). Guselkumab-treated patients separated from the placebo group as early as Week 12 for DAPSA and cDAPSA remission, at Week 16 for PASDAS VLDA, and at Week 24 for VLDA.

In the pooled results, no notable differences in response rates were observed between the guselkumab Q4W and Q8W dosing regimens. Response trends were generally consistent in the individual DISCOVER-1 (biologic-naïve and TNFi-experienced patients) and DISCOVER-2 (biologic-naïve patients) studies (Supplementary Figures 1 and 2). However, response rates were higher in DISCOVER-1 than in DISCOVER-2 at Week 24 for both guselkumab dosing regimens (Q4W and Q8W) for DAPSA LDA, cDAPSA LDA, and PASDAS LDA, and for the guselkumab Q4W regimen for DAPSA remission, cDAPSA remission, PASDAS VLDA, and VLDA.

Active treatment period after Week 24 through Week 52

Among the guselkumab-randomized patients, response rates increased post-Week 24 through Week 52, with indications of the potential for higher response rates beyond Week 52 (i.e., no plateau was reached by Week 52 for PASDAS LDA/VLDA or MDA/VLDA). At Week 52, 54% (Q4W) and 52% (Q8W) of guselkumab-randomized patients achieved DAPSA LDA; 55% (Q4W) and 53% (Q8W) achieved cDAPSA LDA; 45% (Q4W) and 42% (Q8W) achieved PASDAS LDA, and 36% (Q4W) and 31% (Q8W) achieved MDA (Figure 1). For placebo-randomized patients who crossed over to guselkumab Q4W at Week 24, response rates for DAPSA LDA, cDAPSA LDA, PASDAS LDA, and MDA at Week 52 approached those achieved by guselkumab-randomized patients.

For the more stringent remission-related endpoints at Week 52, 18% (Q4W and Q8W) achieved DAPSA remission; 21% (Q4W and Q8W) achieved cDAPSA remission; 17% (Q4W) and 20% (Q8W) achieved PASDAS VLDA, and 13% (Q4W) and 14% (Q8W) achieved VLDA (Figure 2). Notably, VLDA was more difficult to attain than DAPSA remission and PASDAS remission when assessing longer-term treatment effect via these composite indices. In patients who crossed over from placebo to guselkumab Q4W at Week 24, substantial increases in composite response rates were seen by Week 52.

Across all composite indices, no notable differences in response rates were observed between the guselkumab Q4W and Q8W dosing regimens. Results were generally consistent in the individual DISCOVER-1 and DISCOVER-2 studies (Supplementary Figures 1 and 2). Differences in response rates between DISCOVER-1 and DISCOVER-2 were smaller at Week 52 than at Week 24, but DISCOVER-1 response rates remained notably higher in

patients randomized to guselkumab Q4W for DAPSA and cDAPSA LDA and remission, PASDAS LDA, and MDA (Supplementary Figures 1 and 2).

Maintenance of response

As shown in Figure 3, among guselkumab-treated patients who achieved low levels of disease activity at Week 24, nearly all maintained responses at Week 52 (PASDAS LDA: 88% Q4W and 91% Q8W; DAPSA LDA: 85% Q4W and 89% Q8W; MDA: 76% Q4W and 80% Q8W). Similarly, among guselkumab-treated patients who achieved remission/VLDA at Week 24, the majority maintained response at Week 52 (PASDAS VLDA: 82% Q4W and 90% Q8W; VLDA: 71% Q4W and 94% Q8W; DAPSA remission: 68% Q4W and 74% Q8W).

Association of radiographic progression at 1 year with composite efficacy responses at Week 24

In DISCOVER-2, patients who achieved PASDAS LDA, DAPSA LDA, and MDA at Week 24 had smaller mean changes in total PsA-modified van der Heijde-Sharp scores from Week 0 to Week 52 compared with patients who did not achieve these responses (Figure 4).

Assessment of residual disease based on components of MDA and VLDA

At Week 52, among guselkumab-randomized patients, a majority achieved ≤1 tender entheseal point (Q4W, 79%; Q8W, 77%), PASI score ≤1 (Q4W, 79%; Q8W, 73%), and SJC ≤1 (Q4W, 66%; Q8W, 61%) (Supplementary Figure 3). However, most patients continued to show signs of potential residual disease activity, as evidenced by lower rates achieving normalized physical function (HAQ-DI ≤0.5; Q4W, 44%; Q8W, 39%), PtGA ≤20 (Q4W, 39%; Q8W, 38%), TJC ≤1 (Q4W, 30%; Q8W, 33%), and pain ≤15 (Q4W, 32%; Q8W, 31%) (Figure 5).

DISCUSSION

Results of these pooled post hoc analyses from DISCOVER-1 and DISCOVER-2 showed that patients with active PsA who received guselkumab Q4W or Q8W achieved consistent and robust responses over placebo based on achievement of numerous composite measures of disease activity. Separation of guselkumab from placebo was observed as early as Week 8 for DAPSA LDA and PASDAS LDA. Among guselkumab-randomized patients, response rates for all composite indices continued to increase from baseline through Week 52. Furthermore, the majority of guselkumab-randomized patients who achieved responses at Week 24 had maintained or increased levels of response at Week 52, and in many cases slopes of the response curves suggest the potential for further improvement over time. Placebo-randomized patients who crossed over to guselkumab Q4W at Week 24 showed steady improvements in all composite indices, with response rates approaching those observed for guselkumab-randomized patients at Week 52.

Response trends were generally consistent when results from DISCOVER-1 and DISCOVER-2 were considered separately. However, across most composite indices, Week 24 response rates were higher in DISCOVER-1 than in DISCOVER-2, despite the fact that approximately 30% of patients in DISCOVER-1 had prior exposure to TNFi, and these TNFi-experienced patients had numerically lower MDA response rates compared with TNFi-naïve patients at Week 24 (17%-26% vs 32%-34%) [20]. The observed differences between studies may be related to differences in eligibility criteria requiring patients in DISCOVER-2 to have more severe disease (SJC and TJC ≥5, and CRP ≥0.6 mg/dL) at baseline than in DISCOVER-1 (SJC and TJC ≥3, and CRP ≥0.3 mg/dL).

In DISCOVER-2, composite measure responses at Week 24 were associated with reduced long-term radiographic progression based on smaller mean changes in total PsA-modified van

der Heijde-Sharp scores at Week 52. This finding suggests that early treatment with guselkumab may reduce the risk for permanent joint damage.

Pooled results showed that by Week 52, approximately one-third of all guselkumab-treated patients achieved the widely accepted treatment target of MDA. Evaluation of the proportions of patients achieving the individual MDA components showed particularly high and consistent response rates for objective measures, including resolution of enthesitis, swollen joints, and skin disease. Through Week 52, pain and TJC >1 – which would be expected to heavily influence the patient-reported outcomes of physical function (HAQ-DI) and PtGA – appeared to be the symptoms limiting achievement of MDA for many patients. However, the trajectory of responses for achievement of TJC ≤1, pain ≤15, and PtGA ≤20 suggest a possibility of increased response rates with continued treatment with guselkumab.

Our findings that disease activity based on TJC, pain, and PtGA measurements often limit the achievement of composite outcomes are generally consistent with published studies identifying pain, PtGA, skin disease, and tender joints as the most common unmet criteria in patients failing to achieve MDA/VLDA treatment targets [16,26,27]. However, in contrast to other studies [3,16,26], achievement of the skin disease criterion was not a limiting factor in attaining MDA/VLDA for most patients in DISCOVER-1 and DISCOVER-2. This finding is likely related to better efficacy of guselkumab (an IL-23 inhibitor) for the treatment of psoriasis compared with biologic DMARDs with different mechanisms of action (i.e., TNF, IL-17, or IL-12/23 inhibition) [28−33]. Specifically, in the DISCOVER studies, approximately 70% of guselkumab-randomized patients achieved PASI ≤1 at Week 24, and response rates increased to up to 79% by Week 52; in the placebo to guselkumab Q4W crossover group, the PASI ≤1 response rate increased from 27% at Week 24 to 74% at Week 52. These results are particularly noteworthy since these

analyses used the more stringent of two MDA definitions of skin response (i.e., PASI score ≤1 instead of body surface area of psoriasis ≤3%) [3,11,12].

Similarly, for DAPSA, high pain and PtGA parameters often limit the achievement of remission, even in patients without active joint inflammation [16,34]. For patients with established structural damage to affected joints before initiating treatment with guselkumab, achieving low levels of pain and satisfactory physical function and PtGA may not have been possible. Furthermore, recent studies indicate that substantial proportions of patients with PsA experience persistent, widespread pain despite effective control of inflammation with conventional or biologic DMARDs [34−36]. In one model of chronic pain, peripheral neurologic hypersensitivity develops following pathological changes in the central nervous system [35]. This altered pain perception in patients with PsA may lead to overestimation of joint tenderness and inflammatory activity [35]. Thus, achievement of low levels of pain may be especially difficult for some patients with PsA, and adjustment of treatment targets may be warranted (e.g., based on disease duration, amount of structural damage, or altered pain perception). Alternatively, centralized pain may develop in association with prevalent comorbidities, such as obstructive sleep apnoea, anxiety and/or depression, and deconditioned muscles and joints.

These analyses of the pooled DISCOVER-1 and DISCOVER-2 dataset provide a unique opportunity to demonstrate consistent and robust response rates with guselkumab versus placebo for several different composite measures, each with emphasis on different clinical outcomes. The DAPSA, which focuses mainly on measures of peripheral articular disease, does not include specific assessments of dactylitis, enthesitis, or skin disease, and requires laboratory testing to measure CRP levels [3,22,37−40]. In contrast to the DAPSA, the PASDAS and MDA assess multiple domains of articular and extra-articular disease activity [37,38]; therefore, these measures are more likely to be relevant as PsA treatment targets. In routine

clinical practice, MDA is used more often than the PASDAS because PASDAS scoring is complicated and not intuitive, limiting its use in real-world settings [7,13]. Overall, increased use of composite indices is important to promote recommended treat-to-target approaches, which may reduce the undertreatment of PsA and improve patient outcomes [38].

As with all controlled clinical trials, patients enrolled in the DISCOVER-1 and DISCOVER-2 studies were required to meet predefined selection criteria based on previous treatment and medical history. Additionally, while DAPSA LDA and remission, PASDAS LDA and VLDA, and MDA were prespecified secondary efficacy endpoints of the individual DISCOVER-1 and DISCOVER-2 studies, pooling the results across both studies was not prespecified and was performed post hoc to increase the sample size. Therefore, results from the current analyses may not be generalizable to all patients with PsA. However, consistent with results of these analyses, in a recent small real-world observational study in 24 patients with early PsA and severe skin disease, 75% (18/24) of patients achieved DAPSA LDA or remission after 6 months of guselkumab treatment; 17 of these patients completed 1 year of treatment, and all achieved DAPSA LDA (65% [11/17]) or remission (35% [6/17]) [41].

Comparison of the results from these analyses with other published studies is inherently limited. To date, few clinical studies have reported composite index results, and among published results, there are often differences in baseline disease and demographic characteristics, sample sizes, analysis methods (i.e., observed vs imputed data), and the composite endpoints reported [37,42-47]. However, results of analyses published to date suggest that composite indices can provide more comprehensive assessments of the range of PsA disease manifestations than conventional peripheral joint-based outcome measures (e.g., ACR20), and that treatment targets such as MDA, DAPSA LDA/remission, and PASDAS LDA/VLDA are achievable for many patients using currently available biologic or targeted synthetic therapies [37,42-47]. Thus,

composite indices may be useful in routine clinical practice and as key endpoints in future PsA clinical trials.

Taken together, results of these analyses indicate that patients with active PsA who receive treatment with guselkumab Q4W or Q8W can achieve robust and sustained low disease activity or remission, based on various composite indices that measure responses across domains including joint pain, swelling, stiffness, inflammation, and tenderness; and skin clearance. As such, guselkumab is a novel therapy for PsA that can provide effective treatment of the diverse manifestations of this disease.

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Data availability statement

The data sharing policy of Janssen Pharmaceutical Companies of Johnson & Johnson is available at https://www.janssen.com/clinical-trials/transparency. As noted on this site, requests for access to the study data can be submitted through Yale Open Data Access (YODA) Project site at http://yoda.yale.edu.

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FIGURE LEGENDS

Figure 1. Achievement of DAPSA LDA (A), cDAPSA LDA (B), PASDAS LDA (C), and MDA (D). Through Week 24, patients meeting treatment failure criteria or with missing data were considered non-responders. Treatment group comparisons through Week 24 were not adjusted for multiplicity of testing; all reported p-values are nominal. After Week 24 and through Week 52, patients with missing data were considered non-responders.
cDAPSA: clinical DAPSA (excludes C-reactive protein); DAPSA: Disease Activity in Psoriatic Arthritis; GUS: guselkumab; LDA: low disease activity; MDA: minimal disease activity; PASDAS: Psoriatic Arthritis Disease Activity Score; PBO: placebo; Q4W: every 4 weeks; Q8W: every 8 weeks.

Figure 2. Achievement of DAPSA remission (A), cDAPSA remission (B), PASDAS VLDA (C), and VLDA (D). Through Week 24, patients meeting treatment failure criteria or with missing data were considered non-responders. Treatment group comparisons through Week 24 were not adjusted for multiplicity of testing; all reported p-values are nominal. After Week 24 and through Week 52, patients with missing data were considered non-responders.
cDAPSA: clinical DAPSA (excludes C-reactive protein); DAPSA: Disease Activity in Psoriatic Arthritis; GUS: guselkumab; PASDAS: Psoriatic Arthritis Disease Activity Score; PBO: placebo; Q4W: every 4 weeks; Q8W: every 8 weeks; VLDA: very low disease activity.

Figure 3. Maintenance of PASDAS LDA, DAPSA LDA, and MDA (A), and PASDAS VLDA, VLDA, and DAPSA remission (B) at Week 52 among guselkumab-randomized patients with response at Week 24. N represents the total number of patients with response at Week 24. Through Week 24, patients meeting treatment failure criteria or with missing data were considered non-responders. After Week 24 and through Week 52, patients with missing data were considered non-responders.
DAPSA: Disease Activity Index for Psoriatic Arthritis; GUS: guselkumab; LDA: low disease activity; MDA: minimal disease activity; PASDAS: Psoriatic Arthritis Disease Activity Score; Q4W: every 4 weeks; Q8W: every 8 weeks; VLDA: very low disease activity.

Figure 4. Mean changes in PsA-modified total vdH-S score in DISCOVER-2 patients based on Week 24 PASDAS LDA, DAPSA LDA, and MDA response status. Evaluable patients had an observed change from baseline to Week 52 in PsA-modified vdH-S score and observed PASDAS, DAPSA, or MDA status, respectively, at Week 24.
DAPSA: Disease Activity Index for Psoriatic Arthritis; LDA: low disease activity; MDA: minimal disease activity; PASDAS: Psoriatic Arthritis Disease Activity Score; PsA: psoriatic arthritis; Q4W: every 4 weeks; Q8W: every 8 weeks; vdH-S: van der Heijde-Sharp.

Figure 5. Achievement of ≤1 tender joint (A), patient assessment of pain VAS ≤15 (B), HAQ-DI score ≤0.5 (C), and PtGA ≤20 (D). Through Week 24, patients meeting treatment failure criteria or with missing data were considered non-responders. Treatment group comparisons through Week 24 were not adjusted for multiplicity of testing; all reported p-values are nominal. After Week 24 and through Week 52, patients with missing data were considered non-responders.
GUS: guselkumab; HAQ-DI: Health Assessment Questionnaire-Disability Index; PBO: placebo; PtGA: patient global assessment of disease activity (arthritis and psoriasis); Q4W: every 4 weeks; Q8W: every 8 weeks; VAS: visual analog scale.

TABLES

Table 1. Baseline characteristics for randomized and treated patients in DISCOVER-1 and DISCOVER-2

	DISCOVER-1 and DISCOVER-2		
	Guselkumab Q4W	Guselkumab Q8W	Placebo
Randomized and treated patients, N	373	375	372
Age (years)	46.5 (11.5)	46.2 (11.9)	47.2 (11.5)
Male, n (%)	208 (55.8)	197 (52.5)	178 (47.8)
BMI (kg/m^2)	29.4 (5.8)	29.1 (6.3)	29.2 (6.1)
PsA duration (years)	5.9 (6.1)	5.6 (5.7)	6.2 (6.4)
Swollen joint count (0-66)	11.4 (7.5)	11.4 (7.7)	11.5 (7.0)
Tender joint count (0-68)	20.8 (13.6)	19.9 (12.8)	21.0 (13.5)
Patients with enthesitis (LEI>0), n (%)[a]	243 (65.1)	230 (61.5)	255 (68.7)
LEI score (1-6)	3.0 (1.6)	2.7 (1.5)	2.8 (1.6)
Patients with dactylitis, n (%)[a]	159 (42.6)	160 (42.8)	154 (41.5)
Dactylitis score (1-60)[b]	8.8 (10.3)	8.1 (9.7)	7.7 (8.7)
Patient assessment of pain (VAS 0-10 cm)	6.1 (2.0)	6.2 (2.0)	6.1 (2.0)
Patient global assessment of disease activity (arthritis, VAS 0-10 cm)	6.3 (2.0)	6.5 (2.0)	6.4 (2.0)
Physician global assessment of disease activity (VAS 0-10 cm)	6.5 (1.6)	6.4 (1.6)	6.5 (1.6)
CRP (mg/dL)	1.6 (2.0)	1.9 (2.4)	1.9 (2.4)
PASI (0-72)[c]	10.4 (11.2)	9.2 (11.1)	8.8 (9.5)
HAQ-DI (0-3)	1.2 (0.6)	1.3 (0.6)	1.3 (0.6)
DAPSA score (remission ≤4; high disease activity >28)	46.2 (20.7)	45.9 (20.9)	46.9 (20.2)
cDAPSA score (remission ≤4; high disease activity >27)	44.6 (20.3)	44.1 (20.4)	45.0 (19.9)
PASDAS score[d] (low disease activity ≤3.2; high disease activity >5.4)	6.4 (1.1)	6.5 (1.1)	6.5 (1.0)
Patients receiving methotrexate, n (%)	218 (58.4)	209 (55.7)	227 (61.0)
Mean dose (mg/week)	15.6 (4.7)	15.8 (5.3)	15.4 (4.6)
Patients receiving oral corticosteroids, n (%)	62 (16.6)	68 (18.1)	69 (18.5)
Mean dose (mg/day)	6.9 (2.4)	6.6 (2.4)	7.4 (2.6)

Data are mean (SD) unless otherwise indicated.
[a]Guselkumab Q4W, n = 373; guselkumab Q8W, n = 374; placebo, n = 371.
[b]Each of 20 digits is scored from 0 (no dactylitis) to 3 (severe dactylitis), resulting in a total score range of 0-60; mean scores shown here are for patients with dactylitis (score ≥1) at baseline.
[c]Guselkumab Q4W, n = 373; guselkumab Q8W, n = 375; placebo, n = 371.
[d]Guselkumab Q4W, n = 369; guselkumab Q8W, n = 372; placebo, n = 367.
BMI: body mass index; cDAPSA: clinical DAPSA (excludes CRP); CRP: C-reactive protein; DAPSA: Disease Activity Index for Psoriatic Arthritis; HAQ-DI: Health Assessment Questionnaire-Disability Index; LEI: Leeds Enthesitis Index; PASDAS: Psoriatic Arthritis Disease Activity Score; PASI: Psoriasis Area and Severity Index; PsA: psoriatic arthritis; Q4W: every 4 weeks; Q8W: every 8 weeks; SD: standard deviation; VAS: visual analog scale.