Background: DISCOVER-2 was a Phase 3 trial of the first-in-class anti-IL-23-specific mAb guselkumab (GUS) in patients (pts) with psoriatic arthritis (PsA). PsA impacts patients' productivity at work and in daily activity.1

Objectives: To evaluate the effect of GUS on work productivity and daily activity in DISCOVER-2 through 1 year using the Work Productivity and Activity Impairment Questionnaire: PsA (WPAI- PsA).

Methods: Bio-naïve adults with active PsA despite nonbiologic DMARDs &/or NSAIDs received subcutaneous GUS 100 mg every 4 weeks (Q4W); GUS 100 mg W0, W4, then Q8W; or placebo (PBO). At W24, PBO pts crossed over to GUS 100 mg Q4W. WPAI-PsA assesses PsA-related work time missed (absenteeism), impairment while working (presenteeism), impaired overall work productivity (absenteeism + presenteeism), and daily activity during the previous week. A shift analysis evaluated proportions of pts employed vs unemployed (regardless of desire to work) over time. Among pts working at baseline, least-squares (LS) mean changes from baseline in WPAI-PsA domains were determined using a mixed-effects model for repeated measures analysis, whereby mean changes in WPAI-PsA domains were calculated for each multiple imputation (MI) dataset using an analysis of covariance (ANCOVA); the reported LSmean is the average of all MI datasets. Also, among pts employed at baseline, indirect savings from improved overall work productivity were estimated using 2020 EU mean yearly wage estimate (all occupations).2

Results: In pts working at baseline, significant improvement in work productivity and non-work activity vs PBO was observed at W24. Productivity gains seen with GUS at W24 continued to improve through 1 year (Table 1). Shift analysis showed relatively stable employment in pts employed at baseline (62% of shift analysis cohort) through 1 year of GUS (>91% continued to work when assessed at W16, W24, and W52 [data not shown]). For those unemployed at baseline (38% of cohort), the proportion of pts working increased by ~10% following 1 year of GUS (Figure 1). Potential yearly indirect savings from improved overall work productivity were: *€7409* GUS Q4W and *€7039* GUS Q8W vs *€4075* PBO at W24 and were *€8520* GUS Q4W, *€9632* GUS Q8W, and *€6668* PBO→GUS Q4W at W52.

Conclusion: Improvement in work productivity and non-work activity was greater with GUS vs PBO among pts with active PsA through W52. Improvements demonstrated may result in reduction in PsA costs associated with work productivity.

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Table 1. Model-based estimates of LSmean change[a] (95% CI) from baseline in WPAI-PsA domains among pts working at baseline and with an observed change through W24 (N=474) and W52 (N=475)

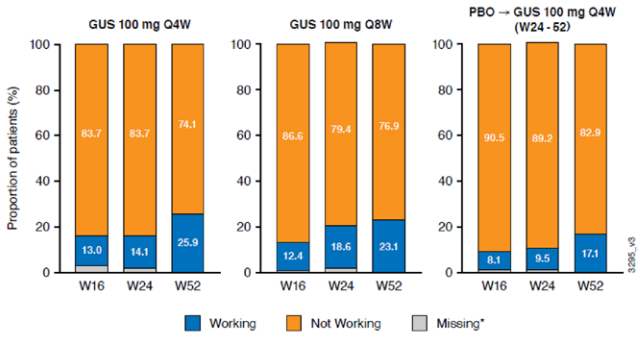
Change from baseline	GUS 100mg Q4W		GUS 100mg Q8W		PBO (W0-24)	PBO → GUS 100 mg Q4W (W24-52)
Visit	**W24**	**W52**	**W24**	**W52**	**W24**	**W52**
Absenteeism, N	145	145	147	147	162	163
LSmean	-3.4 (-6.5,-0.3)	-4.1 (-6.8,-1.5)	-3.0 (-6.0,0.1)	-4.0 (-6.6,-1.3)	-3.0 (-6.0, 0.04)	-3.0 (-5.5,-0.4)
Diff vs. PBO	-0.4 (-4.6,3.8)		-0.01 (-4.2, 4.2)			
Presenteeism, N	145	145	147	147	162	163
LSmean	-20.1 (-23.7,-16.6)	-22.4 (-26.3,-18.6)	-19.6 (-23.2,-16.1)	-25.7 (-29.5,-21.8)	-10.5 (-13.9,-7.0)	-18.5 (-22.2,-14.7)
Diff vs PBO	-9.7* (-14.4,-5.0)		-9.2* (-13.9,-4.5)			
Work productivity, N	145	145	147	147	162	163
LSmean	-20.1 (-24.1,-16.1)	-22.6 (-26.8,-18.3)	-19.2 (-23.1,-15.2)	-25.9 (-30.0,-21.7)	-10.6 (-14.4,-6.8)	-17.6 (-21.7,-13.6)
Diff vs PBO	-9.5* (-14.8,-4.2)		-8.6* (-13.9,-3.3)			
Non-work Activity, N	242	242	246	246	245	245
LSmean	-20.5 (-23.3,-17.7)	-25.7 (-28.6,-22.7)	-21.2 (-23.9,-18.4)	-25.4 (-28.4,-22.5)	-9.9 (-12.6,-7.1)	-22.3 (-25.3,-19.4)
Diff vs PBO	-10.6* (-14.4,-6.8)		-11.3* (-15.1,-7.5)			

CI=Confidence interval

a. LSmean for each MI dataset is calculated based on an ANCOVA model for the change from baseline at W24/W52. The combined LSmean, which is the average of the LSmean, taken over all the MI datasets, is presented.

*p<0.05

Figure. Shift Analysis of Working Status: Not Employed at Baseline



GUS 100 mg Q4W (N = 92), GUS 100 mg Q8W (N = 97), PBO → GUS 100 mg Q4W (W24-52) (N = 74)
* GUS 100 mg Q4W: W16, 3.3%; W24, 2.2%. GUS 100 mg Q8W: W16, 1.0%; W24, 2.1%. PBO → GUS 100 mg Q4W (W24-52): W16, 1.4%; W24, 1.4%.

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POS1027

EFFICACY AND SAFETY OF GUSELKUMAB, A MONOCLONAL ANTIBODY SPECIFIC TO THE P19-SUBUNIT OF INTERLEUKIN-23, THROUGH 2 YEARS: RESULTS FROM A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY CONDUCTED IN BIOLOGIC-NAÏVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

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Background: Guselkumab (GUS), a selective IL-23 inhibitor dosed every 4 or 8 weeks (Q4W or Q8W), demonstrated efficacy for joint and skin symptoms, inhibition of structural damage progression (Q4W), and safety vs. placebo (PBO) through Week 24 (W24) of the Ph3, double-blind, PBO-controlled trial in biologic-naïve pts with PsA (DISCOVER-2).[1] Favorable benefit-risk was also seen through 1 year.[2]

Objectives: To assess GUS efficacy and safety through 2 years.

Methods: Biologic-naïve adults with active PsA (≥5 swollen joint count [SJC] + ≥5 tender joint count [TJC]; CRP ≥0.6 mg/dL) were randomized (1:1:1) to GUS 100 mg Q4W; GUS 100 mg at W0, W4, Q8W; or PBO with crossover to GUS 100 mg Q4W (PBO→Q4W) at W24. Clinical efficacy (ACR/PASI/IGA/HAQ-DI) was assessed in the modified intention to treat (mITT) population through W100 with missing data imputation (nonresponse for categorical endpoints; no change/multiple imputation for continuous endpoints). Observed PsA-modified van der Heijde Sharp (vdH-S) scores derived from blinded radiographic images collected at W0, W24, W52, W100 (or at discontinuation [d/c]) and adverse events (AEs) through W112 were collected.

Results: 712/739 (96%) randomized pts continued study agent at W24; 687/739 (93%) continued at W52; 652/739 (88%) completed W100. ACR20 response rates in the mITT population continued to increase after W24, and at W100 were 76% for Q4W and 74% for Q8W (Figure 1). Similar response patterns were seen for ACR50/70, HAQ-DI and PASI90/100 (Table 1), and IGA0/1 and PASI75 response rates were consistent through W100 in pts randomized to Q4W and Q8W; W100 data for PBO→Q4W pts were consistent with pts treated with Q4W and Q8W (Table 1). GUS improvements in SF-36 PCS/MCS at W52 also persisted through W100 (data not shown). Low rates of radiographic progression (as measured by PsA-modified vdH-S scores) were observed during W52-100 for Q4W (n=227; 0.75) and Q8W (n=232; 0.46). In the PBO→Q4W group (n=228), radiographic progression was 1.12 during W0-24 (while on PBO), 0.51 during W24-100 (while on Q4W), and 0.13 during W52-100. Through W112, the incidences of AEs, serious AEs (SAEs), AEs leading to d/c, infections, serious infections, and injection site reactions were generally consistent with the PBO-controlled period and through 1 year. Of the pts in the Q4W (n=245), Q8W (n=248), and PBO→Q4W (n=238) groups, 9%, 9% and 7% had ≥1 SAE; 2%, 3% and 3% had ≥1 serious infection; 2 Q8W pts (fungal esophagitis, disseminated herpes zoster) and 1 PBO→Q4W pt (listeria meningitis) had opportunistic infections; 1 PBO→Q4W pt died (road traffic accident); 1 PBO-randomized pt had IBD; no pt had anaphylactic or serum sickness reaction, or active TB.

Conclusion: In biologic-naïve PsA pts, GUS improvements in joint and skin symptoms, physical function, and low rates of radiographic progression persisted through 2 years. GUS safety in PsA through 2 years was comparable with safety at 6 months and 1 year, similar between Q4W and Q8W, and consistent with GUS safety in psoriasis.

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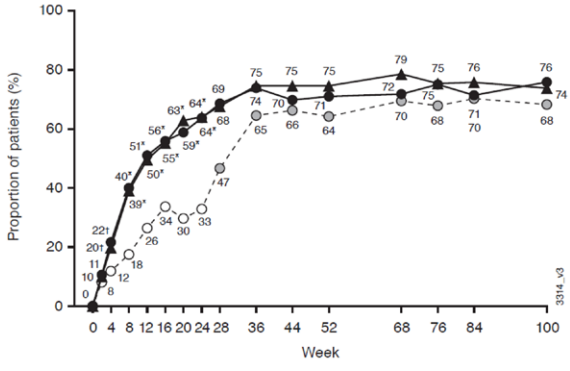
Table 1. Efficacy Through W100 (NRI)

Data are %	GUS Q4W			GUS Q8W			PBO→GUS Q4W		
	W24	W52	W100	W24	W52	W100	W24	W52	W100
Analysis set, n		245			248			246	
ACR 50	**33**	**46**	**56**	**32**	**48**	**55**	**14**	**41**	**48**
ACR 70	**13**	**26**	**35**	**19**	**28**	**36**	**4**	**18**	**30**
BL HAQ-DI ≥0.35, n		228			228			236	
Improvement ≥0.35[a]	**56**	**59**	**63**	**50**	**58**	**64**	**31**	**48**	**56**
BL ≥3% BSA psoriasis + IGA ≥2, n		184			176			183	
IGA0/1	**69**	**63**	**62**	**71**	**58**	**55**	**19**	**63**	**67**
PASI75	**78**	**87**	**83**	**79**	**86**	**82**	**23**	**83**	**80**
PASI90	**61**	**77**	**74**	**69**	**74**	**70**	**10**	**72**	**77**
PASI100	**45**	**58**	**59**	**45**	**53**	**53**	**3**	**52**	**61**

BL, Baseline; BSA, Body surface area; HAQ-DI, Health assessment questionnaire disability index; IGA, Investigator global assessment; NRI, nonresponder imputation; PASI, Psoriasis area and severity index. [a]≥0.35 improvement among pts with HAQ-DI ≥0.35 at BL.

Figure. ACR 20 Response Through W100 (NRI)
(Note: Patients randomized to PBO crossed over to GUS 100 mg Q4W at W24)



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POS1028

PATIENT CHARACTERISTICS & CLINICAL FEATURES ASSOCIATE WITH HEALTH-RELATED QUALITY OF LIFE IN BIO-NAÏVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS THROUGH WEEK 24 OF THE DISCOVER-2 STUDY

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease characterized by peripheral arthritis, axial inflammation, dactylitis, enthesitis, & skin/nail psoriasis. Patients (pts) with PsA often experience reduced health-related quality of life (HRQoL) due to these features.

Objectives: Using EuroQoL-5 dimension-5 level (EQ-5D-5L) questionnaire index & visual analog scale (EQ-VAS) scores, we assessed HRQoL in pts with PsA & its association with pt characteristics & clinical features of PsA, including fatigue.

Methods: The Phase 3 DISCOVER-2 trial evaluated guselkumab (GUS), a human monoclonal antibody targeting the IL-23p19-subunit, in bio-naïve adults with active PsA (swollen joint count [SJC] ≥5, tender joint count [TJC] ≥5, C-reactive protein [CRP] ≥0.6 mg/dL) despite standard therapies.[1] Pts were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at Week 0 (W0), W4, then Q8W; or placebo (PBO). EQ-5D-5L index assesses mobility, self-care, usual activities, pain/discomfort, & anxiety/depression. EQ-VAS assesses pt health state. Spearman correlation testing was used to evaluate relationships between baseline (BL) pt characteristics & PsA clinical features & BL EQ-5D-5L index & EQ-VAS scores (Figure 1). Employing absolute observed scores at both W0 & W24, univariate linear regression was used to assess the association between EQ-5D-5L index & EQ-VAS scores & pt characteristics/PsA clinical features. Variables with $p<0.20$ in the univariate analysis were included in a multivariate analysis employing mixed-effect model for repeated measures (MMRM), controlling for all other variables; resulting p values <0.05 were considered statistically significant. Least-squares (LS) mean changes in EQ-5D-5L index & EQ-VAS were assessed at W24 using MMRM.

Results: Among 738 pts, BL EQ-5D-5L index & EQ-VAS scores were moderately to strongly correlated (ie, ≥0.4) with BL pt-reported pain (0-10 VAS), physical function (Health Assessment Questionnaire-Disability Index [HAQ-DI]),