Improvement of Fatigue, Musculoskeletal Pain, and Morning Stiffness in Patients with Systemic Lupus Erythematosus Treated with Dapirolizumab Pegol: 48-Week Results from a Phase 3 Trial

Ioannis Parodis,[1,2] Caroline Gordon,[3] Joan T. Merrill,[4] Matthias Schneider,[5] Zahi Touma,[6] Teri Jimenez,[7] Thomas Morel,[8] Mina Nejati,[9] Christian Stach,[10] Christine de la Loge,[11] Laurent Arnaud[12]

[1]Division of Rheumatology, Department of Medicine Solna, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden; [2]Department of Rheumatology, Faculty of Medicine and Health, Örebro University, Örebro, Sweden; [3]Department of Inflammation and Ageing, College of Medicine and Health, University of Birmingham, Birmingham, UK; [4]Oklahoma Medical Research Foundation, Oklahoma City, Oklahoma, USA; [5]Clinic of Rheumatology and Hiller Research Unit, Heinrich-Heine-University, Düsseldorf, Germany; [6]University of Toronto Lupus Clinic, Division of Rheumatology, Schroeder Arthritis Institute, Krembil Research Institute, University Health Network, Toronto, Ontario, Canada; [7]UCB, Raleigh, North Carolina, USA; [8]UCB, Basel, Switzerland; [9]Biogen, Cambridge, Massachusetts, USA; [10]UCB, Monheim am Rhein, Germany; [11]UCB, Brussels, Belgium; [12]Department of Rheumatology, National Reference Center for Autoimmune Diseases (RESO), University Hospitals Strasbourg, Strasbourg, France

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Objective

- **To report the impact of dapirolizumab pegol (DZP) on patient-reported fatigue, musculoskeletal pain, and morning stiffness in patients with systemic lupus erythematosus (SLE) in the phase 3 PHOENYCS GO trial.**

Background

- Fatigue, musculoskeletal pain, and joint stiffness are common manifestations of SLE, presenting considerable treatment challenges, particularly in addressing chronic fatigue.[1–3]
- DZP is a novel CD40L inhibitor with broad modulatory effects on SLE immunopathology;[4,5] it consists of a polyethylene glycol (PEG)-conjugated antigen-binding fragment (Fab'), which lacks an Fc domain.
- In the phase 3 PHOENYCS GO trial (NCT04294667), the primary endpoint was met; DZP plus standard of care (DZP+SOC) resulted in a significantly higher rate of BICLA response compared with placebo (PBO)+SOC at Week 48 (49.5% versus 34.6%; p=0.0110), alongside improvements in other clinical measures.[6]

Methods

- PHOENYCS GO, a 48-week, randomized, double-blind, PBO-controlled trial, included patients aged ≥16 years with moderate-to-severe, active SLE characterized by persistently active or frequently flaring/relapsing-remitting disease activity despite stable SOC medication (antimalarials, glucocorticoids, and/or immunosuppressants; **Figure 1**).
- Fatigue was assessed using Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue and FATIGUE-PRO (which consists of three domains: Physical Fatigue, Mental and Cognitive Fatigue, and Susceptibility to Fatigue).[7–11]
  - An improvement of ≥4 points was considered to represent a minimal clinically important difference (MCID) for FACIT-Fatigue and was used to define response.[12] An MCID has not been established yet for FATIGUE-PRO.
- Musculoskeletal pain and morning stiffness were evaluated using the visual analogue scales (VAS) from the Lupus Arthritis and Musculoskeletal Disease Activity (LAMDA) instrument.

Results

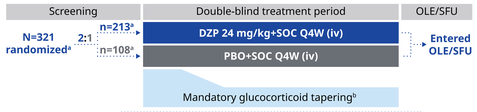
- The study was completed on treatment through Week 48 by 85.4% (182/213) of patients randomized to DZP+SOC and 79.6% (86/108) randomized to PBO+SOC.
- Baseline fatigue, musculoskeletal pain, and morning stiffness scores were comparable between the groups (full analysis set; DZP+SOC: n=208; PBO+SOC: n=107; **Table 1**).
- Patients receiving DZP+SOC demonstrated consistently larger improvements in FACIT-Fatigue at all assessed timepoints (nominal p<0.05; **Figure 2A**). By Week 48, a greater proportion of patients receiving DZP+SOC (50.5%) achieved an improvement of ≥4 points (MCID) compared with those receiving PBO+SOC (35.5%); achievement over time is shown in **Figure 2B**.
- Patients receiving DZP+SOC demonstrated greater improvements from baseline to Week 48 in all three FATIGUE-PRO scores compared with those receiving PBO+SOC, with greater improvements versus PBO+SOC seen as early as Week 4 for Physical fatigue and Week 8 for Susceptibility to fatigue (nominal p<0.05; **Figure 3**).
- Improvements in musculoskeletal pain and morning stiffness were also larger for those receiving DZP+SOC versus PBO+SOC at Weeks 24, 36 and 48 (nominal p<0.05; **Figure 4**).

Conclusions

Improvements in fatigue, musculoskeletal pain, and morning stiffness were greater in patients treated with DZP+SOC versus PBO+SOC.

Alongside the previously reported improvements in clinical measures of SLE disease activity,[6] the current data suggest that DZP improves core patient-reported symptoms in SLE.

Figure 1 PHOENYCS GO study design



[a] Randomized set; **[b]** Investigators were required to initiate glucocorticoid tapering for patients with a dose >7.5 mg/day prednisone equivalent at baseline with the goal of reaching ≤7.5 mg/day, in line with EULAR 2019 treatment guidelines,[13] with tapering starting no later than Week 8. Guidance was provided on tapering, but the exact tapering regimen was at the discretion of the investigator and adapted to the individual patient's disease state. Tapering between Week 44 and 48 was avoided.

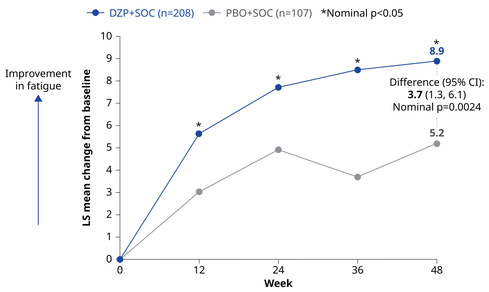
Table 1 Baseline demographics and disease characteristics

	DZP+SOC n=208	PBO+SOC n=107
Age, years, mean (SD)	43.5 (12.3)	41.5 (12.4)
Female, n (%)	193 (92.8)	100 (93.5)
Time since first diagnosis of SLE, years, mean (SD)	10.1 (7.9)	9.8 (8.5)
SLEDAI-2K, mean (SD)	10.7 (3.5)	11.2 (3.4)
SLEDAI-2K ≥10, n (%)	140 (67.3)	79 (73.8)
Concomitant systemic glucocorticoids, n (%)	171 (82.2)	87 (81.3)
Glucocorticoid dose, mg/day, mean (SD)	7.9 (5.9)	9.6 (8.1)
Glucocorticoid dose >7.5 mg/day, n (%)	105 (50.5)	51 (47.7)
FACIT-Fatigue, mean (SD)	28.5 (11.2)	27.7 (10.5)
FATIGUE-PRO, mean (SD)		
Physical Fatigue	49.2 (22.7)	51.4 (23.0)
Mental and Cognitive Fatigue	35.2 (23.8)	38.2 (24.1)
Susceptibility to Fatigue	49.3 (24.1)	49.7 (23.4)
LAMDA, mean (SD)		
Musculoskeletal pain	56.0 (23.1)	54.1 (25.5)
Morning stiffness	54.9 (26.2)	52.7 (26.1)

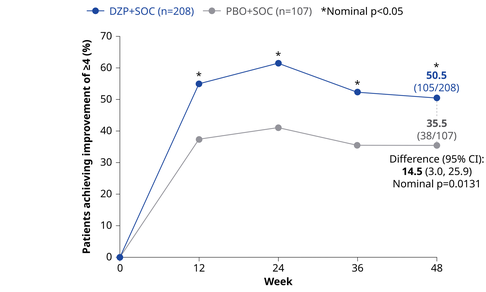
Full analysis set.

Figure 2 Improvements in FACIT-Fatigue

A) LS mean change from baseline in FACIT-Fatigue

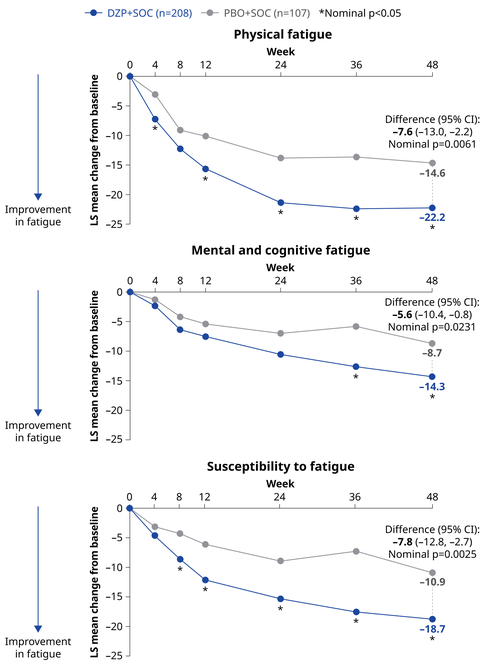


B) Proportion of patients with improvement from baseline in FACIT-Fatigue ≥MCID



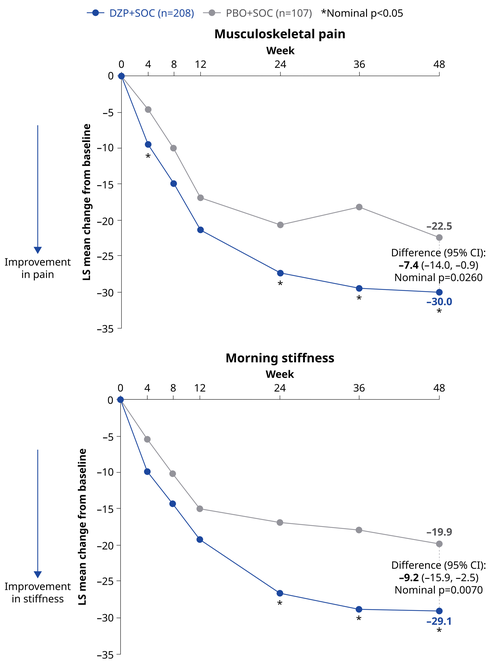
Full analysis set. FACIT-Fatigue score range: 0–52, lower scores indicate greater fatigue and an increase in score over time reflects improvement. All p-values are nominal and were not controlled for multiplicity. A hypothetical strategy (A) or composite strategy (B) was used for escape treatment intervention, premature withdrawal from the study or permanent discontinuation of study medication (while remaining in the study), where data were set to missing (A) or patients were assigned as non-responders (B). (A) MMRM. After intercurrent event handling, MMRM with fixed effects for treatment, stratification factors, baseline value, visit, treatment by study week interaction and baseline value by study week interaction was conducted on the remaining data. The LS mean, difference between DZP+SOC and PBO+SOC, 95% CIs, and p-values were computed from the MMRM. (B) NRI. After intercurrent event handling, remaining missing data were handled using NRI. Difference in proportion responding between DZP+SOC and PBO+SOC, 95% CIs, and p-values were estimated and tested using the CMH risk difference estimate controlling for the randomization stratification factors.

Figure 3 LS mean change from baseline in FATIGUE-PRO



Full analysis set; MMRM. FATIGUE-PRO score range: 0–100 calculated for each of the three domains, higher scores indicate greater fatigue and a decrease in score over time reflects improvement. All p-values are nominal and were not controlled for multiplicity. A hypothetical strategy was used for escape treatment intervention, premature withdrawal from the study or permanent discontinuation of study medication (while remaining in the study), where data were set to missing. After intercurrent event handling, MMRM with fixed effects for treatment, stratification factors, baseline value, visit, treatment by study week interaction and baseline value by study week interaction was conducted on the remaining data. The LS mean, difference between DZP+SOC and PBO+SOC, 95% CIs, and p-values were computed from the MMRM.

Figure 4 LS mean change from baseline in LAMDA musculoskeletal pain and morning stiffness



Full analysis set; MMRM. LAMDA is a composite musculoskeletal disease activity measure; VAS range: 0–100, higher scores indicate more musculoskeletal pain or morning stiffness and a decrease in score over time reflects improvement. All p-values are nominal and were not controlled for multiplicity. A hypothetical strategy was used for escape treatment intervention, premature withdrawal from the study or permanent discontinuation of study medication (while remaining in the study), where data were set to missing. After intercurrent event handling, MMRM with fixed effects for treatment, stratification factors, baseline value, visit, treatment by study week interaction and baseline value by study week interaction was conducted on the remaining data. The LS mean, difference between DZP+SOC and PBO+SOC, 95% CIs, and p-values were computed using a MMRM.

BICLA: BILAG-based Combined Lupus Assessment; **BILAG:** British Isles Lupus Assessment Group; **CI:** confidence interval; **CMH:** Cochran-Mantel Haenszel; **DZP:** dapirolizumab pegol; **EULAR:** European Alliance of Associations for Rheumatology; **Fab':** antigen-binding fragment; **FACIT:** Functional Assessment of Chronic Illness Therapy; **iv:** intravenous; **LAMDA:** Lupus Arthritis and Musculoskeletal Disease Activity; **LS:** least squares; **MCID:** minimal clinically important difference; **MMRM:** mixed model for repeated measurements; **NRI:** non-responder imputation; **OLE:** open-label extension; **PBO:** placebo; **PEG:** polyethylene glycol; **PRO:** patient-reported outcome; **Q4W:** every 4 weeks; **SD:** standard deviation; **SFU:** safety follow-up; **SLE:** systemic lupus erythematosus; **SLEDAI-2K:** Systemic Lupus Erythematosus Disease Activity Index-2K; **SOC:** standard of care.

References: [1]Tench CM. Rheumatology 2000;39:1249–54; [2]Ahn GE. Int J Clin Rheum 2012;7:217–27; [3]Sukhoranna M, Ital J Ped 2024;50:149; [4]Cutcutache I, Arthritis Rheumatol 2023;75 (suppl 9); [5]Powlesland AS. Ann Rheum Dis 2024;83 (suppl 1):261; [6]Clowse M, Arthritis Rheumatol 2024;76 (suppl 9); [7]Cella D. Semin Hematol 1997;34:13–9; [8]Hellen SB. J Pain Symptom Manage 1997;13:63–74; [9]Piper BF. J Natl Compr Canc Netw 2010;8:958–66; [10]Cella D. J Patient Rep Outcomes 2024;8:92; [11]Morel T. Rheumatology 2022;61:3329–40; [12]Lai J. J Rheumatol 2011;38:672–9; [13]Fanouriakis A. Ann Rheum Dis 2019;78:736–45.
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PHOENYCS GO

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