Glucocorticoid-sparing maintenance of disease control in patients with systemic lupus erythematosus: 48-week results from a phase 3 trial of dapirolizumab pegol

Eric F. Morand,[1] George Bertsias,[2,3] Lucy M. Carter,[4] Richard A. Furie,[5] Marta Mosca,[6] Marilyn Pike,[7] Edward Vital,[4,8] Vanessa Taieb,[9] Annette Nelde,[10] Christian Stach[11]

[1]Monash University, Centre for Inflammatory Diseases, Melbourne, Australia; [2]University Hospital of Heraklion and University of Crete Medical School, Rheumatology and Clinical Immunology, Heraklion, Greece; [3]Institute of Molecular Biology and Biotechnology, Foundation for Research and Technology-Hellas (FORTH), Infections and Immunity, Heraklion, Greece; [4]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, UK; [5]Northwell, Division of Rheumatology, Great Neck, USA; [6]University of Pisa, Rheumatology Unit, Department of Clinical and Experimental Medicine, Pisa, Italy; [7]MedPharm Consulting, Inc., Rheumatology, Bethesda, USA; [8]Leeds Teaching Hospitals NHS Trust, NIHR Leeds Biomedical Research Centre, Leeds, UK; [9]UCB, Colombes, France; [10]Biogen, Baar, Switzerland; [11]UCB, Monheim am Rhein, Germany

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Objective

- **To evaluate the maintenance of disease control in the context of glucocorticoid tapering in patients with systemic lupus erythematosus (SLE) treated with dapirolizumab pegol (DZP) in the phase 3 PHOENYCS GO trial.**

Introduction

- DZP is a novel CD40L inhibitor with broad modulatory effects on SLE immunopathology;[1,2] it consists of a polyethylene glycol (PEG)-conjugated antigen-binding fragment (Fab'), which lacks an Fc domain.
- Glucocorticoid exposure in SLE is associated with toxicity and organ damage accrual;[3,4] treatment guidelines encourage tapering and/or withdrawal.[4,5]
- 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 versus placebo (PBO)+SOC at Week 48 (49.5% versus 34.6%; p=0.0110), alongside improvements in other clinical measures.[6] The PHOENYCS GO Primary manuscript is available now (see QR code in the bottom right corner). A confirmatory phase 3 trial (PHOENYCS FLY; NCT06617325) is ongoing (see QR code in the bottom left corner).

Methods

- PHOENYCS GO, a 48-week, randomised, double-blind, PBO-controlled trial, included patients aged ≥16 years with moderate-to-severe, active SLE (**Figure 1**).
- 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,[4] with tapering starting no later than Week 8.
- Stable reduction of glucocorticoid dose (achievement of ≤7.5 mg/day prednisone equivalent by Week 24 and maintenance of this through Week 48 in patients with baseline dose >7.5 mg/day) was analysed alone and alongside clinical outcomes.
- Moderate BILAG-2004 flares were defined using a post hoc definition of ≥2 BILAG-2004 Grade Bs in different organ systems across up to three consecutive visits (i.e. over three months).[7] Severe BILAG-2004 flares were defined using a pre-specified definition of ≥1 BILAG-2004 Grade A, confirmed by blinded adjudication.

Results

- At baseline, approximately half of the patients had glucocorticoid dose >7.5 mg/day prednisone equivalent; baseline characteristics by glucocorticoid dose are presented in **Table 1**.
- Overall, and in patients with a baseline dose >7.5 mg/day prednisone equivalent,[6] a higher proportion of patients receiving DZP+SOC versus PBO+SOC achieved ≤7.5 mg/day prednisone equivalent by Week 48 (**Figure 2A**).
- In patients with baseline dose >7.5 mg/day prednisone equivalent, a higher proportion receiving DZP+SOC versus PBO+SOC reduced to ≤7.5 mg/day by Week 24 and maintained this through Week 48 (**Figure 2B**), and also:
  - Achieved BICLA response at Week 48 (**Figure 2C**);
  - Achieved SRI-4 response at Week 48 (**Figure 2D**);
  - Remained moderate/severe BILAG-2004 flare-free through Week 48 (**Figure 2E**);
  - Achieved BICLA response at Week 48 AND remained moderate/severe BILAG-2004 flare-free through Week 48 (**Figure 2F**).

Conclusions

In patients with SLE receiving moderate-to-high dose glucocorticoids at baseline, treatment with DZP+SOC versus PBO+SOC was associated with greater proportions simultaneously achieving low glucocorticoid dose while maintaining disease control.

These data suggest a durable glucocorticoid-sparing effect of DZP alongside achievement of response endpoints and reduction of flares, which could enable patients to reach recommended treatment targets.

Figure 1 PHOENYCS GO study design

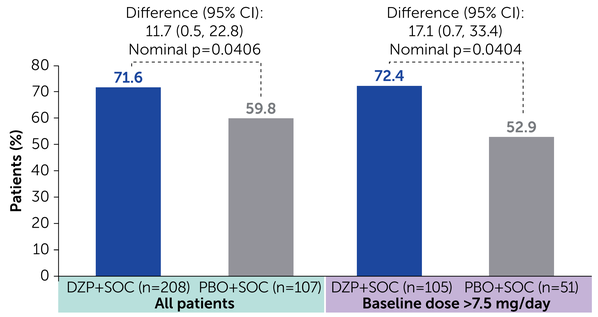
Table 1 Baseline demographics and disease characteristics by baseline glucocorticoid dose

	≤7.5 mg/day		>7.5 mg/day	
	DZP+SOC (n=103)	PBO+SOC (n=56)	DZP+SOC (n=105)	PBO+SOC (n=51)
Age, years, mean (SD)	45.7 (13.7)	44.5 (11.8)	41.4 (10.3)	38.3 (12.3)
Female, n (%)	92 (89.3)	53 (94.6)	101 (96.2)	47 (92.2)
Time since diagnosis, years, mean (SD)	10.7 (8.5)	11.2 (9.1)	9.5 (7.3)	8.2 (7.5)
SLEDAI-2K total score, mean (SD)	10.1 (3.0)	10.2 (2.9)	11.3 (3.7)	12.4 (3.6)
SLEDAI-2K ≥10, n (%)	60 (58.3)	34 (60.7)	80 (76.2)	45 (88.2)
BILAG-2004 total score, mean (SD)	17.8 (3.4)	17.6 (3.3)	19.0 (4.5)	19.8 (5.1)
Concomitant systemic glucocorticoids, n (%)	66 (64.1)	36 (64.3)	105 (100.0)	51 (100.0)
Glucocorticoid dose,[a] mg/day, mean (SD)	3.5 (2.8)	3.7 (3.0)	12.3 (4.8)	16.0 (6.8)
Glucocorticoid dose,[a] mg/day, median (min, max)	5.0 (0.0, 7.5)	5.0 (0.0, 7.5)	10.0 (8.0, 40.0)	15.0 (10.0, 40.0)
Concomitant immunosuppressants, n (%)	61 (59.2)	32 (57.1)	68 (64.8)	38 (74.5)

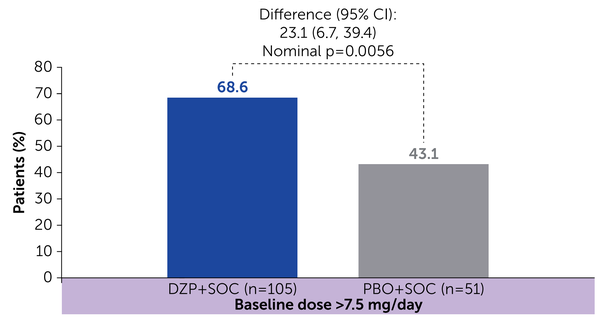
Full analysis set. [a] Prednisone equivalent dose.

Figure 2 Proportion of patients who achieved glucocorticoid dose ≤7.5 mg/day prednisone equivalent by Week 48 (A), and by Week 24 with maintenance through Week 48 alongside other clinical outcomes (B–F)

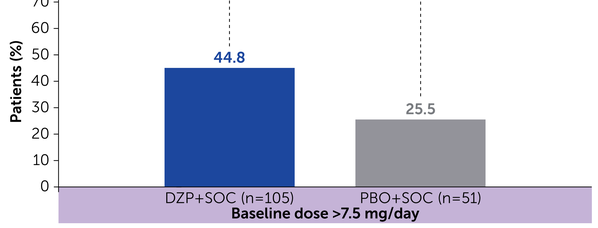
A) Glucocorticoid dose ≤7.5 mg/day by Week 48



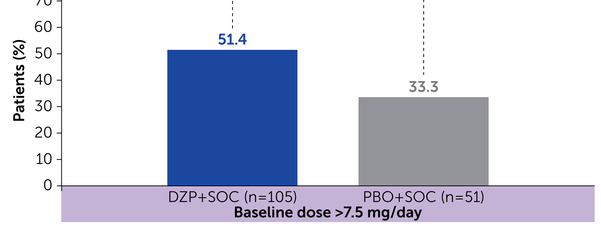
B) Stable reduction of glucocorticoids (dose tapered to ≤7.5 mg/day at Week 24 and maintained through Week 48)



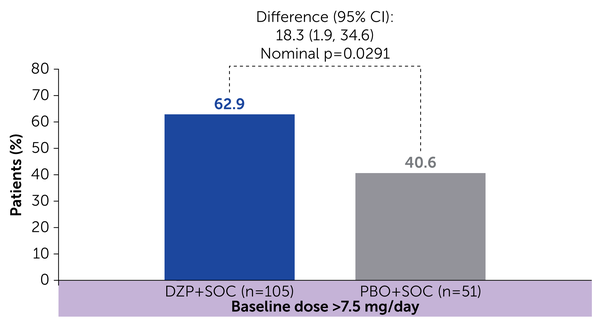
C) Stable reduction of glucocorticoids plus achievement of **BICLA response** at Week 48



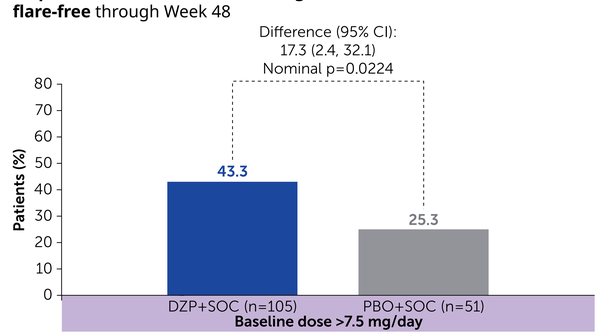
D) Stable reduction of glucocorticoids plus achievement of **SRI-4 response** at Week 48



E) Stable reduction of glucocorticoids plus **remaining moderate/severe BILAG-2004 flare-free** through Week 48



F) Stable reduction of glucocorticoids plus achievement of **BICLA response** at Week 48 and **remaining moderate/severe BILAG-2004 flare-free** through Week 48



Full analysis set; NRI. All p-values are nominal and were not controlled for multiplicity. Difference (95% CI) in proportions responding between DZP+SOC and PBO+SOC and p-values were estimated and tested using the CMH risk difference estimate controlling for the randomisation stratification factors. For the analyses including BICLA and SRI-4, a composite strategy was used for escape treatment intervention, premature withdrawal from the study or permanent discontinuation of study medication, where patients were counted as non-responders. After intercurrent event handling, remaining missing data were handled using NRI. For the moderate/severe BILAG-2004 flare analyses, pre-specified escalations of SLE escape treatment, expected to be associated with moderate/severe flares, were counted as flares; low levels of SLE escape treatment, not expected to be associated with moderate/severe flares, were not counted as flares, and observed data after escape treatment were used to determine flare status. Missing data were handled using MI-MAR. For the BICLA component of the moderate/severe BILAG-2004 flare analyses, a composite strategy was used for escape treatment intervention, premature withdrawal from the study or permanent discontinuation of study medication, where patients were counted as non-responders. After intercurrent event handling, remaining missing data were handled using NRI.

BICLA: BILAG-based Composite Lupus Assessment; **BILAG:** British Isles Lupus Assessment Group; **CI:** confidence interval; **CMH:** Cochran Mantel Haenszel; **DZP:** dapirolizumab pegol; **Fab':** antigen-binding fragment; **iv:** intravenous; **MI-MAR:** multiple imputation-missing at random; **NRI:** non-responder imputation; **OLE:** open label extension; **PBO:** placebo; **PEG:** polyethylene glycol; **Q4W:** every 4 weeks; **SD:** standard deviation; **SFU:** safety follow-up; **SLE:** systemic lupus erythematosus; **SLEDAI-2K:** SLE Disease Activity Index-2K; **SOC:** standard of care; **SRI-4:** SLE Responder Index-4

For more information on PHOENYCS FLY, scan the QR code

References: [1]Cutcutache I. Arthritis Rheumatol 2023;75 (suppl 9); [2]Powlesland AS. Ann Rheum Dis 2024;83 (suppl 1):261; [3]Ugarte-Gil MF. Lupus Sci Med 2021;8:e000590; [4]Fanouriakis A. Ann Rheum Dis 2019;78:736–45; [5]Sammaritano LR. Arthritis Care Res 2025;0:1–25; [6]Clowse M. Arthritis Rheumatol 2024;76 (suppl 9); [7]Furie R. Arthritis Rheumatol 2025;77 (suppl 9).
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