**ABSTRACT NUMBER: L16**

# Dapirolizumab Pegol Demonstrated Significant Improvement in Systemic Lupus Erythematosus Disease Activity: Efficacy and Safety Results of a Phase 3 Trial

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## SESSION INFORMATION

**Date:** Tuesday, November 19, 2024

**Session Type:** Late-Breaking Abstracts

**Title:** Late-Breaking Abstracts (L15–L20)

**Session Time:** 8:00AM-9:30AM

**Background/Purpose**: Dapirolizumab pegol (DZP) is a novel, polyethylene glycol (PEG)-conjugated antigen-binding (Fab') fragment, lacking an Fc domain, that inhibits CD40L signaling. By binding to CD40L, DZP has broad modulatory effects on systemic lupus erythematosus (SLE) immunopathology, including reducing B and T cell activation and downregulating interferon pathways.[1,2] The phase 3 PHOENYCS GO trial (NCT04294667) evaluated the efficacy and safety of DZP in patients (pts) with moderate-to-severe SLE.

**Methods**: PHOENYCS GO was a 48-week (wk), randomized, placebo (PBO)-controlled trial. After the treatment period pts could enter an open-label extension or complete a 6-wk safety follow-up. Pts aged ≥16 years with moderate-to-severe SLE characterized by persistently active or frequently flaring/relapsing-remitting disease activity despite stable standard of care (SOC) medication (antimalarials, corticosteroids, and/or immunosuppressants) were included. Pts were randomized 2:1 to intravenous DZP 24 mg/kg plus SOC medication (DZP+SOC) or PBO+SOC every 4 wks. The primary endpoint was British Isles Lupus Assessment Group (BILAG)-based Composite Lupus Assessment (BICLA) response at Wk 48. Secondary endpoints included SLE Responder Index (SRI)-4 response at

Wk 48 and prevention of severe BILAG flares through Wk 48.

**Results**: Overall, 90.1% of pts receiving DZP+SOC and 84.3% receiving PBO+SOC completed the study to Wk 48. Baseline characteristics were generally similar between treatment groups (**Table**).

The primary endpoint was met; 49.5% (103/208) vs 34.6% (37/107) of pts receiving DZP+SOC vs PBO+SOC had BICLA response at Wk 48 (p=0.0110; difference 14.6%; **Figure 1**). With respect to SRI-4, 60.1% (125/208) vs 41.1% (44/107) of pts receiving DZP+SOC vs PBO+SOC had response at Wk 48 (nominal p=0.0014; difference 18.8%; **Figure 1**). 11.6% vs 23.4% of pts receiving DZP+SOC vs PBO+SOC had severe BILAG flares through Wk 48 (nominal p=0.0257; difference 11.5%; **Figure 2**). Per protocol, pts with a corticosteroid dose >7.5 mg/day prednisone equivalent were required to start tapering no later than Wk 8 to reach ≤7.5 mg/day. In pts with corticosteroid dose >7.5 mg/day at baseline, 72.4% (76/105) vs 52.9% (27/51) of pts receiving DZP+SOC vs PBO+SOC reduced their dose to ≤7.5 mg/day at Wk 48 (nominal p=0.0404; difference 17.1%).

A higher proportion of pts receiving DZP had ≥1 treatment-emergent adverse event (TEAE; DZP+SOC: 82.6%; PBO+SOC: 75.0%); however, the proportion of pts with serious TEAEs was lower (DZP+SOC: 9.9%; PBO+SOC: 14.8%). Opportunistic infections were reported in 2.8% and 0.9% of pts receiving DZP+SOC and PBO+SOC, respectively. There was 1 thromboembolic TEAE (myocardial infarction) and 1 death (due to gangrene-related sepsis) in pts with predisposing medical history receiving DZP+SOC.

**Conclusion**: Treatment with DZP, a novel CD40L inhibitor, resulted in improvement in disease activity and corticosteroid tapering in pts with SLE; significantly more pts who received DZP+SOC achieved BICLA response vs PBO+SOC. DZP was generally well tolerated.

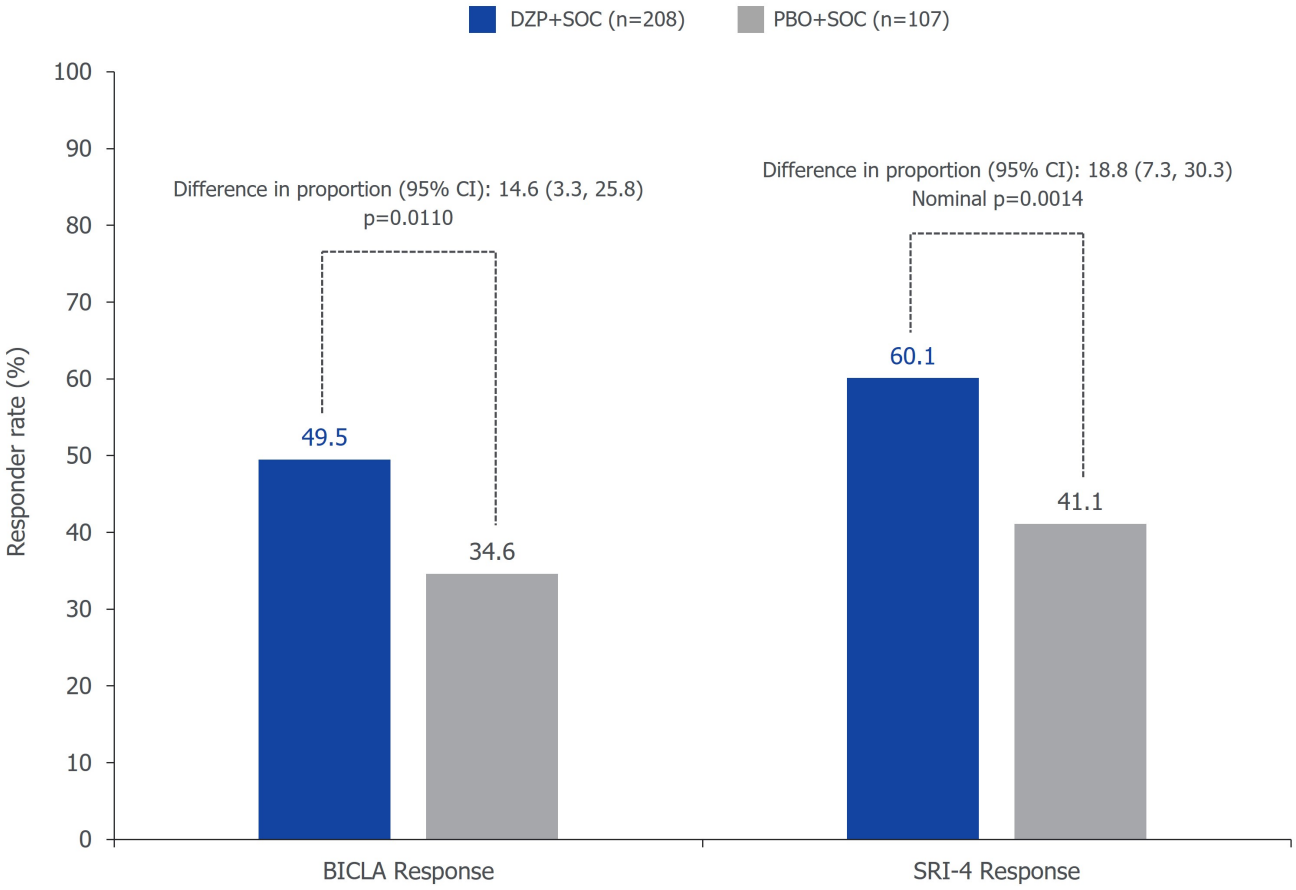
**References: 1.** Cutcutache I. Arthritis Rheumatol 2023;75 (suppl 9). **2.** Powlesland A. Annals Rheum Dis 2024;83 (suppl 1):261.

| | 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 diagnosis**, years, mean (SD) | 10.1 (7.9) | 9.8 (8.5) |
| **SLEDAI-2K total score**, mean (SD) | 10.7 (3.5) | 11.2 (3.4) |
| <10, n (%) | 63 (30.3) | 31 (29.0) |
| ≥10, n (%) | 145 (69.7) | 76 (71.0) |
| **anti-dsDNA (EliA) >10 IU**, n (%) | 91 (43.8) | 62 (57.9) |
| **C3 <LLN**, n (%) | 66 (31.7) | 43 (40.2) |
| **C4 <LLN**, n (%) | 112 (53.8) | 55 (51.4) |
| **Any aPLs**, n (%) | 129 (62.0) | 64 (59.8) |
| **LAC ratio >ULN**, n (%) | 16 (7.7) | 13 (12.1) |
| **Concomitant SLE medications at baseline**, n (%) | 208 (100.0) | 107 (100.0) |
| Antimalarials, n (%) | 166 (79.8) | 92 (86.0) |
| Systemic corticosteroids, n (%) | 171 (82.2) | 88 (82.2) |
| Immunosuppressants, n (%) | 128 (61.5) | 70 (65.4) |
| **Systemic corticosteroid dose >7.5 mg/day**, n (%) | 105 (50.5) | 51 (47.7) |

Full analysis set. aPLs include anti-phosphatidylserine and anti-prothrombin. Anti-dsDNA: anti-double stranded DNA;

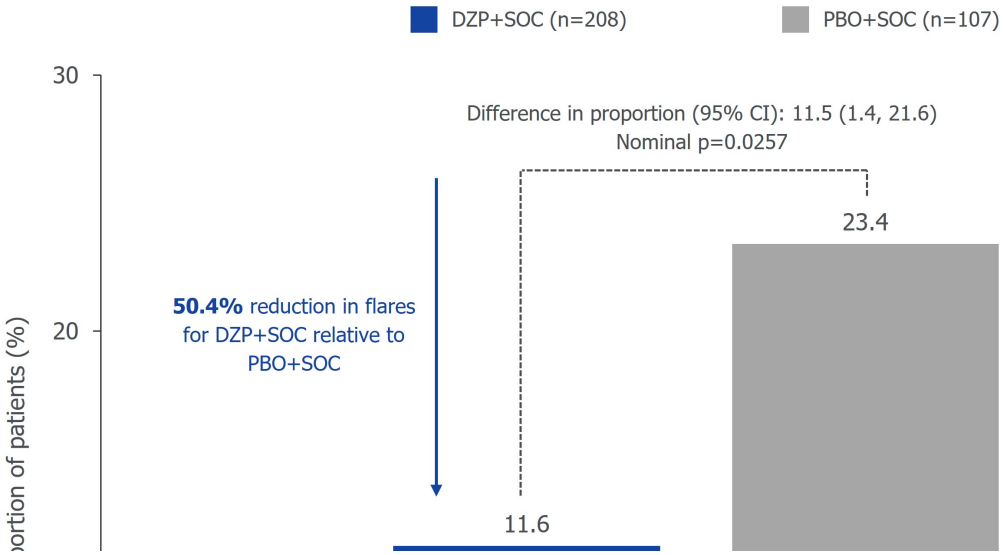
aPLs: antiphospholipid antibodies; C3: complement 3; C4: complement 4; DZP: dapirolizumab pegol; IU: international unit; LAC: lupus anticoagulant; LLN: lower limit of normal; PBO: placebo; SD: standard deviation; SLE: systemic lupus erythematosus; SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index-2K; SOC: standard of care; ULN: upper limit of normal.

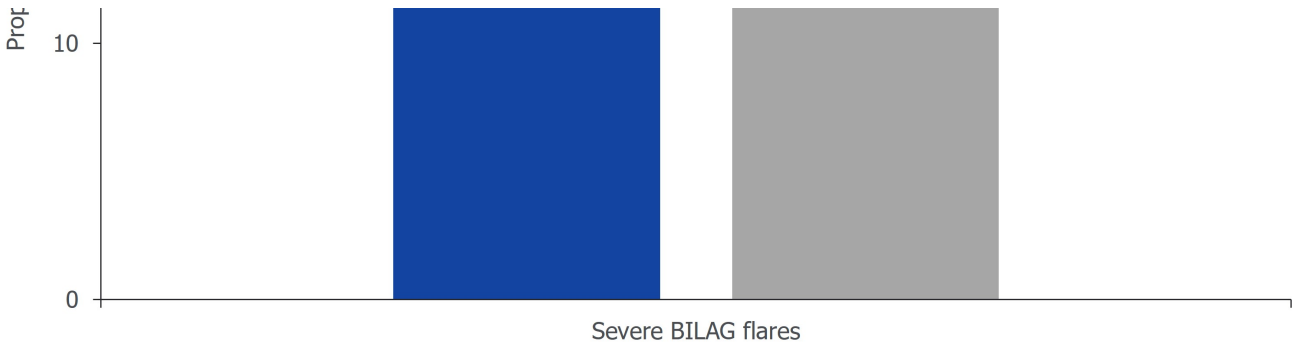
Table. Baseline demographics and disease characteristics




Full analysis set. Difference in proportion responding between DZP+SOC and PBO+SOC, 95% CI for difference in proportions, and p-value were estimated and tested using the Cochran-Mantel-Haenszel (CMH) risk difference estimate controlling for stratification factors. BICLA: British Isles Lupus Assessment Group-based Composite Lupus Assessment; CI: confidence interval; CHM: Cochran-Mantel-Haenszel; DZP: dapirolizumab pegol; NRI: non-responder imputation; PBO: placebo; SOC: standard of care; SRI-4: Systemic Lupus Erythematosus Responder Index-4.

Figure 1. Achievement of BICLA response and SRI-4 response at Week 48 (NRI)






Full analysis set. Difference in proportion responding between DZP+SOC and PBO+SOC, 95% CI for difference in proportions, and p-value were estimated and tested using the Cochran-Mantel-Haenszel (CMH) risk difference estimate controlling for stratification factors. BILAG: British Isles Lupus Assessment Group; CI: confidence interval; CHM: Cochran-Mantel-Haenszel; DZP: dapirolizumab pegol; MI-MAR: multiple imputation assuming missing at random; PBO: placebo; SOC: standard of care.

Figure 2. Proportion of patients with severe BILAG flares through Week 48 (MI-MAR)

**Disclosures: M. Clowse**: GSK, 2, 5, UCB, 2, 5; **D. Isenberg**: AstraZeneca, 2, Eli Lilly, 2, GSK, 2, Merck Serono, 2, Novartis, 2, Servier, 2, UCB, 2; **J. Merrill**: AbbVie, 2, 12, Paid instructor, Amgen, 2, AstraZeneca, 2, 5, Aurinia, 2, Biogen, 2, 12, Paid instructor, BMS, 2, 5, 6, 12, Paid instructor, Eli Lilly, 2, EMD Serono, 2, Genentech, 2, GSK, 2, 5, Kezar, 2, Merck, 2, Pfizer, 2, Provention, 2, Remegen, 2, 12, Paid instructor, Sanofi, 2, Takeda, 2, Tenet, 2, UCB, 2, Zenas, 2, 6, 12, Paid instructor; **T. Dörner**: AbbVie, 2, Eli Lilly, 2, Janssen, 2, Novartis, 6, Roche/GNE, 2, UCB, 2; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, Arthros-FocusMedEd, 6, AstraZeneca, 2, 5, 6, Atara Biosciences, 2, Aurinia, 2, 5, 6, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletta Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, DualityBio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent Biosolutions, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GSK, 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **E. Vital**: AbbVie, 2, Alpine, 2, AstraZeneca, 2, 5, 6, Aurinia, 2, BMS, 2, Eli Lilly, 2, Merck, 2, Novartis, 2, 6, 12, Paid instructor, Otsuka, 2, 6, Pfizer, 2, Roche, 2, Sandoz, 5, UCB, 2; **E. Morand**: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 2, 5, 6, 12, Paid instructor, Biogen, 2, 5, BMS, 2, 5, 6, Dragonfly, 2, Eli Lilly, 2, 5, EMD Serono, 2, 5, Genentech, 5, GSK, 2, 5, Janssen, 5, Novartis, 2, 5, Remegen, 2, Roche, 6, Takeda, 2, 5, UCB, 2, 5; **T. Jimenez**: UCB, 3, 12, Shareholder; **S. Brookes**: Biogen, 3, 12, Shareholder; **J. Gaiha-Rohrbach**: Biogen, 3, 12, Shareholder; **C. Martin**: UCB, 3, 12, Shareholder; **A. Nelde**: Biogen, 3, 12, Shareholder; **C. Stach**: UCB, 3, 12, Shareholder.

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