Alternative Definitions of Moderate Flares that Simulate Clinical Practice in Systemic Lupus Erythematosus: Post Hoc Exploration of Moderate Flares in Patients Treated with Dapirolizumab Pegol in a 48-Week Phase 3 Trial

1542

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

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

To receive a copy of this poster, scan the QR code
Link expiration: January 27, 2026

Objective

- **To report the impact of dapirolizumab pegol (DZP) on moderate flare outcomes in patients with systemic lupus erythematosus (SLE) in the phase 3 PHOENYCS GO trial, and explore alternative definitions of moderate flares to more accurately estimate flare frequency.**

Background

- Flares in SLE, referring to relapses in disease, can be identified by worsening or new onset manifestations.[1]
  - Severe British Isles Lupus Assessment Group (BILAG)-2004 flares are defined as worsening or new onset severe symptoms in any organ system, and moderate BILAG-2004 flares are defined as worsening or new onset moderate symptoms across at least two organ systems.[1]
- The accurate reporting of moderate flares in SLE clinical trials continues to be a challenge, and their frequency may be underestimated due to their evaluation over a single time interval.
  - Moderate flare definitions that require ≥2 new BILAG-2004 Grade Bs within a single time interval may fail to capture flares which evolve sequentially across distinct time intervals. Therefore, definitions which integrate symptoms reported across multiple time intervals may more accurately reflect observations in clinical practice.
- DZP is a novel CD40L inhibitor with broad modulatory effects on SLE immunopathology;[2,3] 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 BILAG-based Composite Lupus Assessment (BICLA) response versus placebo (PBO)+SOC at Week 48 (**Figure 1**), alongside improvements in other clinical measures.[4]
  - Through Week 48, a lower proportion of patients receiving DZP+SOC versus PBO+SOC experienced severe BILAG-2004 flares (11.6% versus 23.4%; nominal p=0.0257).[4]

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). Patients were randomized 2:1 to intravenous DZP 24 mg/kg+SOC or PBO+SOC every 4 weeks.
- Cumulative occurrence of moderate BILAG-2004 flares through Week 48 are reported, using pre-specified and alternative post hoc definitions (**Figure 2**).
  - Alternative definitions were applied to assess moderate BILAG-2004 flares across consecutive study visits.
- Time to moderate/severe BILAG-2004 flares is also reported, using the pre-specified and alternative post hoc definitions of moderate flares.
  - Severe flares were defined using the pre-specified definition as ≥1 BILAG-2004 Grade A due to a new/worse individual item(s) at a single visit.

Results

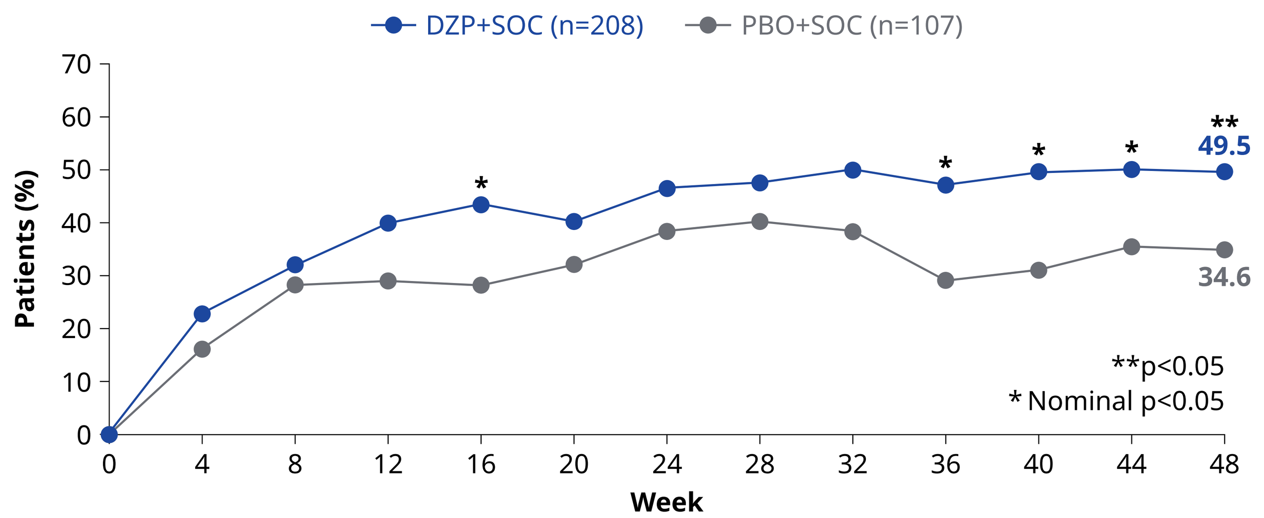
- Overall, 85.4% (182/213) of patients randomized to DZP+SOC and 79.6% (86/108) randomized to PBO+SOC completed PHOENYCS GO on treatment through Week 48.
- Baseline characteristics were typical for a moderate-to-severe SLE population (full analysis set; DZP+SOC: n=208; PBO+SOC: n=107; **Table 1**).
- Applying alternative definitions to capture moderate BILAG-2004 flares led to greater identification of moderate flares in patients receiving PBO+SOC, while identification in patients receiving DZP+SOC remained similar (**Figure 3 and 4**).
  - By all definitions, fewer patients receiving DZP+SOC had moderate BILAG-2004 flares through Week 48 versus patients receiving PBO+SOC.
- A similar trend was observed for moderate/severe BILAG-2004 flares through Week 48, and time to moderate/severe BILAG-2004 flares was longer for patients receiving DZP+SOC versus PBO+SOC by all definitions (**Table 2**).

Conclusions

Applying alternative definitions of moderate BILAG-2004 flares, which considered symptoms reported across multiple time intervals, led to greater identification of moderate flares in patients receiving PBO+SOC. The identification of moderate flares remained similar in patients receiving DZP+SOC with the alternative definitions, and was lower compared with patients receiving PBO+SOC.

These results suggest a need to re-evaluate how flares are identified in SLE clinical trials. The alternative definitions of moderate BILAG-2004 flares, which considered the worsening or new onset of SLE manifestations across multiple intervals, may better reflect clinical reality than the pre-specified definition.

Figure 1 Primary endpoint: BICLA response at Week 48[4]



Full analysis set; NRI. Data previously presented.[4]

Figure 2 Pre-specified and alternative definitions of moderate BILAG-2004 flares

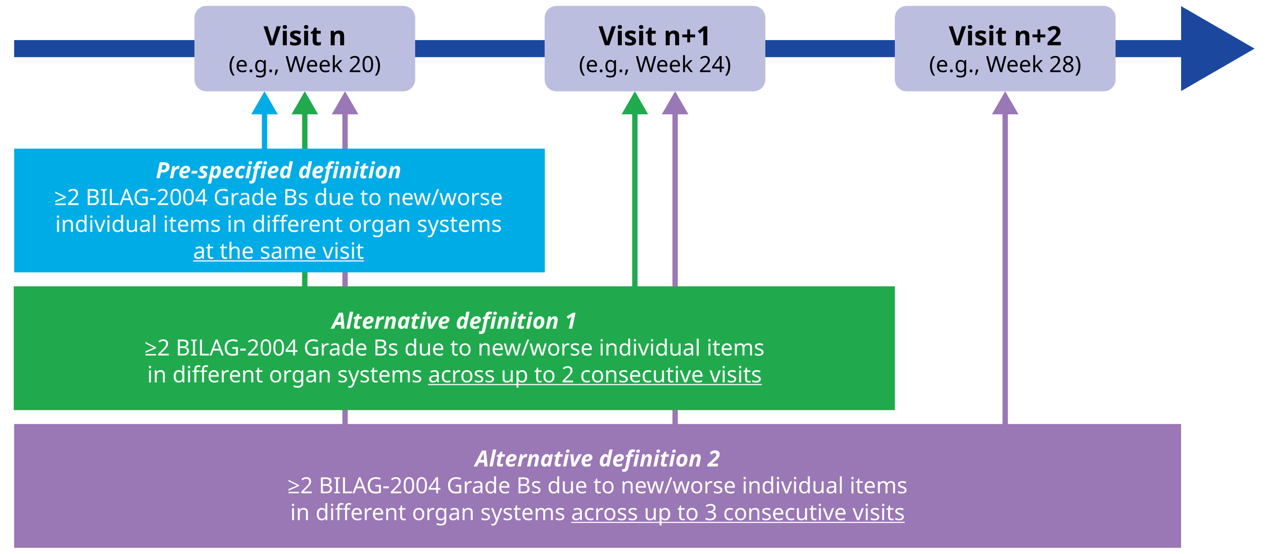
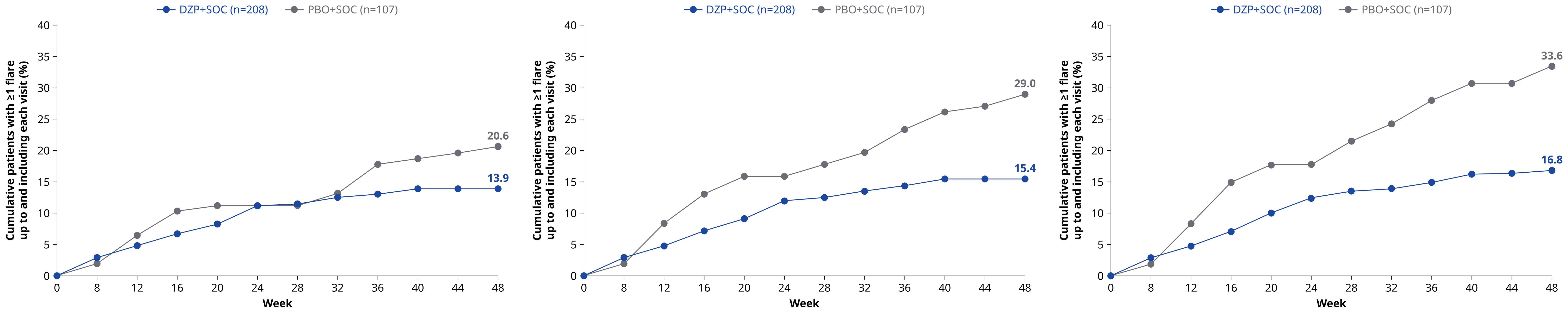


Figure 3 Cumulative patients with moderate BILAG-2004 flares across definitions

A) Pre-specified definition: ≥2 BILAG-2004 Grade Bs due to new/worse individual items in different organ systems at the same visit

B) Alternative definition 1: ≥2 BILAG-2004 Grade Bs due to new/worse individual items in different organ systems across up to 2 consecutive visits

C) Alternative definition 2: ≥2 BILAG-2004 Grade Bs due to new/worse individual items in different organ systems across up to 3 consecutive visits



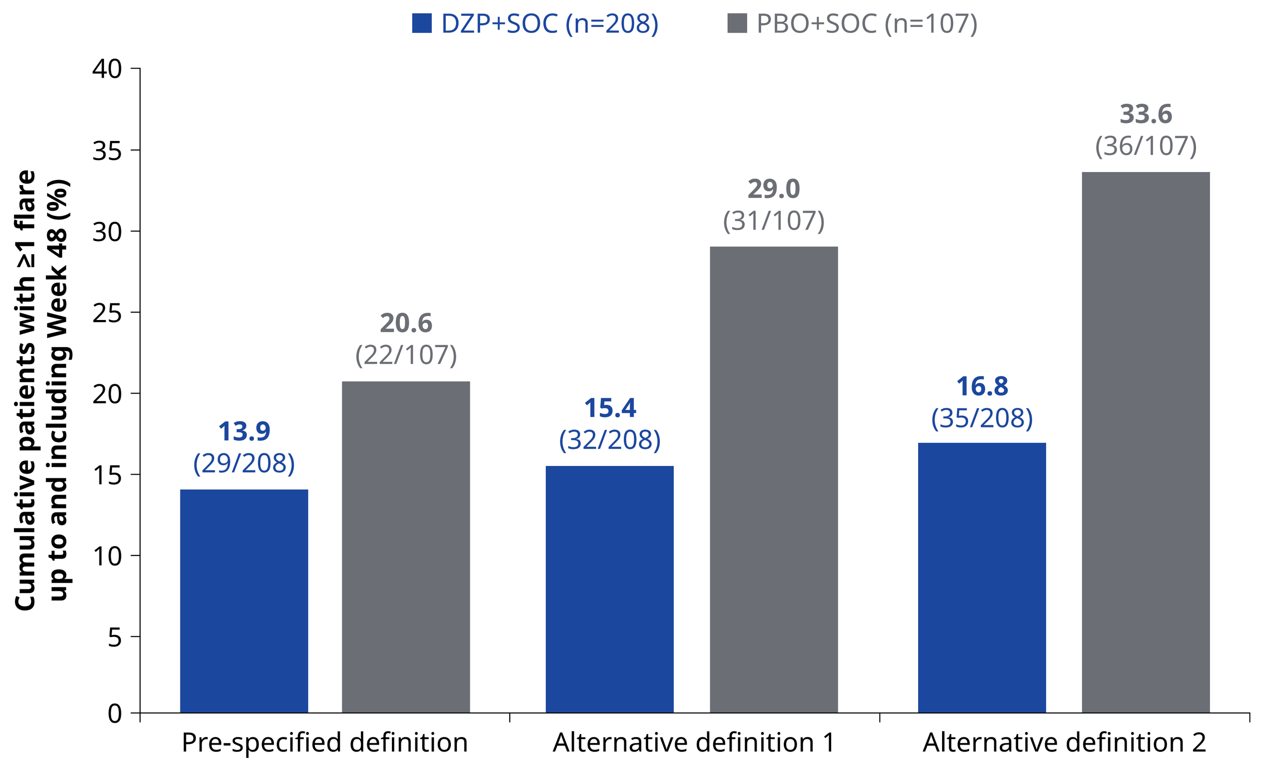
Full analysis set; OC. Pre-specified high levels of escape treatment were counted as flares; lower levels of escape treatment were not counted as flares and observed data after escape treatment was used to determine flare status.

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)
Concomitant SLE medications, n (%)	208 (100.0)	107 (100.0)
Antimalarials	166 (79.8)	91 (85.0)
Systemic glucocorticoids	171 (82.2)	87 (81.3)
Immunosuppressants	129 (62.0)	70 (65.4)
Glucocorticoid dose >7.5 mg/day, n (%)	105 (50.5)	51 (47.7)
Glucocorticoid dose, mg/day, mean (SD)	7.9 (5.9)	9.6 (8.1)
SLEDAI-2K, mean (SD)	10.7 (3.5)	11.2 (3.4)
SLEDAI-2K ≥10, n (%)	140 (67.3)	79 (73.8)
BILAG-2004 total score, mean (SD)	18.4 (4.0)	18.7 (4.4)

Full analysis set.

Figure 4 Cumulative patients with moderate BILAG-2004 flares across definitions up to Week 48



Full analysis set; OC. Pre-specified high levels of escape treatment were counted as flares; lower levels of escape treatment were not counted as flares and observed data after escape treatment was used to determine flare status.

Table 2 Time to moderate/severe BILAG-2004 flares across definitions through Week 48

	Pre-specified definition		Alternative definition 1		Alternative definition 2	
	DZP+SOC n=208	PBO+SOC n=107	DZP+SOC n=208	PBO+SOC n=107	DZP+SOC n=208	PBO+SOC n=107
Patients with moderate/ severe flares, n (%)	38 (18.3)	31 (29.0)	42 (20.2)	38 (35.5)	43 (20.7)	42 (39.3)
Time to moderate/ severe flare, weeks, 25th percentile	Not reached[a]	36.1[b]	Not reached[a]	29.1[b]	Not reached[a]	28.1[b]
p-value[c]	0.0228		0.0027		0.0004	

Full analysis set. **[a]** <25% of patients had a flare through Week 48. **[b]** 25% of patients had experienced a flare by the time point specified. **[c]** Differences in survival distributions between DZP+SOC and PBO+SOC were analyzed using the stratified log-rank statistic, adjusted for stratification factors. Patients who did not experience an event by Week 48 or the early termination visit were censored at the last assessment date, or Day 336, whichever came first.

BICLA: BILAG-based Composite Lupus Assessment; **BILAG:** British Isles Lupus Assessment Group; **DZP:** dapirolizumab pegol; **Fab':** antigen binding fragment; **NRI:** non-responder imputation; **OC:** observed case; **PBO:** placebo; **PEG:** polyethylene glycol; **SD:** standard deviation; **SLE:** systemic lupus erythematosus; **SLEDAI-2K:** SLE Disease Activity Index 2000; **SOC:** standard of care.

References: [1]Adamichou C. Mediterr. J Rheumatol 2017;28:4–12; [2]Powlesland AS. Ann Rheum Dis 2024;83 (suppl 1):261; [3]Cutcutache I. Arthritis Rheumatol 2023;75 (suppl 9); [4]Clowse M. Arthritis Rheumatol 2024;76 (suppl 9). **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **RAF**, **GB**, **LMC**, **EFM**, **MM**, **MP**, **VT**, **AN**, **EV**, **CS**; Drafting of the publication, or reviewing it critically for important intellectual content: **RAF**, **GB**, **LMC**, **EFM**, **MM**, **MP**, **VT**, **AN**, **EV**, **CS**; Final approval of the publication: **RAF**, **GB**, **LMC**, **EFM**, **MM**, **MP**, **VT**, **AN**, **EV**, **CS**. **Author Disclosures: RAF:** Consultant for Biogen; received grant/research support from Biogen and UCB. **GB:** Consultant for Argenx and Novartis; speaker's bureau for AbbVie, AstraZeneca, Eli Lilly, GSK, Novartis, and Otsuka; received grant/research support from AstraZeneca and MSD. **LMC:** Consultant for UCB; paid instructor for Alumis Inc.. **EFM:** Consultant for AbbVie, AstraZeneca, Biogen, BMS, Cabaletta, Cullinan, Dragonfly, Eli Lilly, EMD Serono, GSK, Janssen, Novartis, Quell, Remegen, and UCB; speaker's bureau for AstraZeneca, BMS, and Novartis; received grant/research support from AbbVie, Amgen, AstraZeneca, Biogen, BMS, Eli Lilly, EMD Serono, Genentech, GSK, Janssen, Novartis, Takeda, and UCB. **MM:** Consultant for AbbVie, AstraZeneca, Biogen, BMS, GSK, Idorsia, Milteny, Novartis, Otsuka, and UCB; speaker's bureau for AstraZeneca, Eli Lilly, GSK, Otsuka, and UCB; received grant/research support from GSK. **MP:** Consultant for AstraZeneca, BMS, and UCB. **VT**, **CS:** Employees and shareholders of UCB. **AN:** Employee and shareholder of Biogen. **EV:** Consultant for AbbVie, Alpine, AstraZeneca, Aurinia, BMS, Eli Lilly, Merck, Novartis, Otsuka, Pfizer, Roche, and UCB; paid instructor for Novartis; speaker's bureau for AstraZeneca, Novartis, and Otsuka; received grant/research support from AstraZeneca and Sandoz. **Acknowledgements:** We would like to thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. The authors acknowledge Heather Edens, PhD, UCB, Atlanta, GA, USA, and Valerie Zediak, PhD, Biogen, Pittsburgh, PA, USA, for publication coordination, Teri Jimenez and Raphaëlle Beau Lejdstrom for their contributions to the data analysis, Rebecca Light, BSc, and Beverley Wilson, PhD, Costello Medical, UK, for medical writing and editorial assistance, and the Costello Medical Creative team for design support. Funded by UCB and Biogen. All costs associated with development of this poster were funded by UCB and Biogen.

PHOENYCS GO

Presented at ACR 2025 | October 24–29 | Chicago, IL, USA