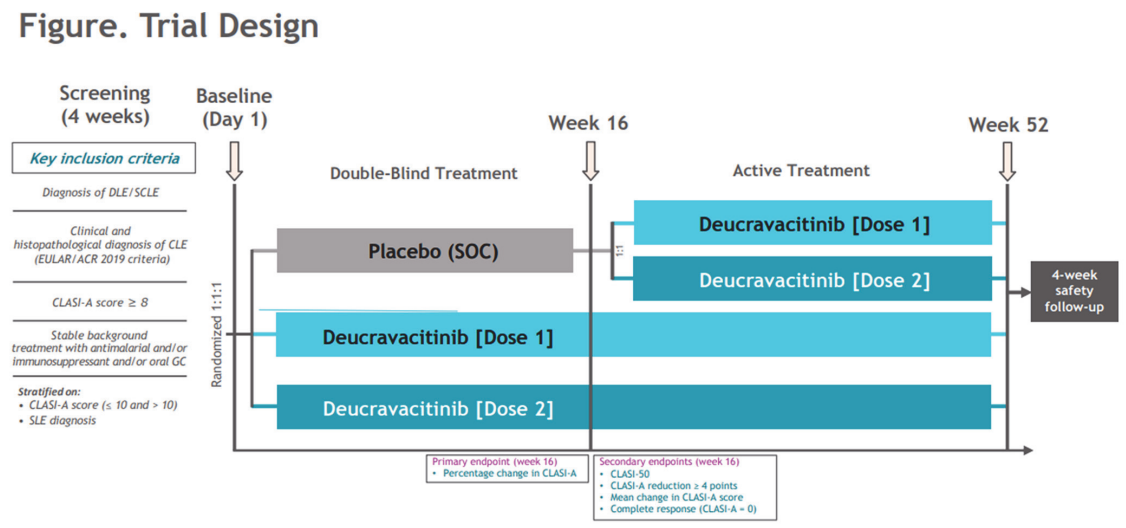

Abstract LP-180 Figure 1 Trial design

Abstract LP-180 Table 1 Primary and secondary endpoints assessed at week 16

Primary Endpoint
• Mean percentage change from baseline in CLASI-A score
Secondary Endpoints
• Percentage of patients who achieve a ≥ 50% reduction in CLASI-A score (CLASI-50) from baseline • Percentage of patients who achieve a ≥ 4-point improvement in CLASI-A from baseline • Mean change from baseline in CLASI-A score • Percentage of patients who achieve a complete response (defined as a CLASI-A score of 0)

CLASI-A, Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity.

or 2 until week 52. Patients originally randomized to deucravacitinib will continue treatment until week 52. The primary and secondary endpoints are depicted below (table 1). This trial will also assess the safety and tolerability of 2 doses of deucravacitinib, exploratory efficacy endpoints, patient-reported outcomes, and pharmacodynamics.

Results Planned enrollment is 75 total patients (25 per double-blind treatment group) in 8 countries in North and South America, Europe, and Asia-Pacific regions.

Conclusions This phase 2 trial will characterize the efficacy, safety, and tolerability of deucravacitinib in patients with active DLE/SCLE.

REFERENCES

1. Armstrong A, *et al. J Am Acad Dermatol* 2023;**88**(1):29–39.
2. Strober B, *et al. J Am Acad Dermatol* 2023;**88**(1):40–51.
3. Morand E, *et al. Arthritis Rheumatol* 2022 Nov 11 (Epub ahead of print).
4. Braunstein I, *et al. Br J Dermatol* 2012;**166**(5):971–975.
5. Burke JR, *et al. Sci Transl Med* 2019;**11**(502):eaaw1736.

LP-181 EFFECT AND SAFETY PROFILE OF BELIMUMAB AND TACROLIMUS COMBINATION THERAPY IN THIRTY-THREE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Belimumab in conjunction with mycophenolate mofetil has been proven to be effective for treating systemic lupus erythematosus (SLE) in several randomized controlled trials. Usefulness of calcineurin inhibitors has also been reported in controlling the activity of SLE. However, the safety and effectiveness of belimumab-calcineurin inhibitor combination therapy have not been addressed. Therefore, we conducted a single-center retrospective study to analyze the safety/efficacy profile of belimumab-tacrolimus (B-T) combination therapy in patients with SLE.

Methods Patients with SLE administered belimumab and tacrolimus during their treatment were included in the study, and samples collected were analyzed for the drug retention rate/SLE flare rate/infection incidence rate/glucocorticoid-sparing effect of the B-T combination therapy.

Results Thirty-three patients with SLE were treated with B-T combination therapy at our institution. Four patients discontinued the treatment because of insufficient response/adverse events. The drug retention rate was over 90% at week 52 and approximately 80% at day 1000. Only one patient developed serious infection.

The lupus low disease activity state (LLDAS) achievement ratio was 9.1% on the day of initiation and improved to 64.0% at 52 weeks after initiation.

SLE flares were observed in only three patients (9.1%) in the first 52 weeks after initiation, and in five patients (15.2%) throughout the study period. A glucocorticoid-reducing effect

was also observed in patients treated with B-T combination therapy.

Conclusions In most patients with SLE, B-T combination therapy was well tolerated, and showed a good efficacy profile and glucocorticoid-reducing effect. Thus, B-T combination therapy can be a feasible option for patients with refractory lupus.

LP-182 PHARMACOKINETICS, SELECTIVITY PROFILE, AND EXPOSURE-RESPONSE RELATIONSHIP FOR EFFICACY AND SAFETY IN A PHASE 2 STUDY OF DEUCRAVACITINIB, AN ORAL, SELECTIVE, ALLOSTERIC TYK2 INHIBITOR, IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Deucravacitinib is a first-in-class, oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor approved in multiple countries for the treatment of adults with plaque psoriasis.[1 2] Deucravacitinib binds the unique TYK2 regulatory domain, conferring greater functional selectivity vs JAK inhibitors, which bind the catalytic domain. Deucravacitinib showed superior efficacy vs placebo in a phase 2 trial in SLE (NCT03252587).[3] This analysis assessed the pharmacokinetics (PK), selectivity profile compared to JAK inhibitors, and exposure-response (E-R) relationship for efficacy and safety of deucravacitinib in SLE.

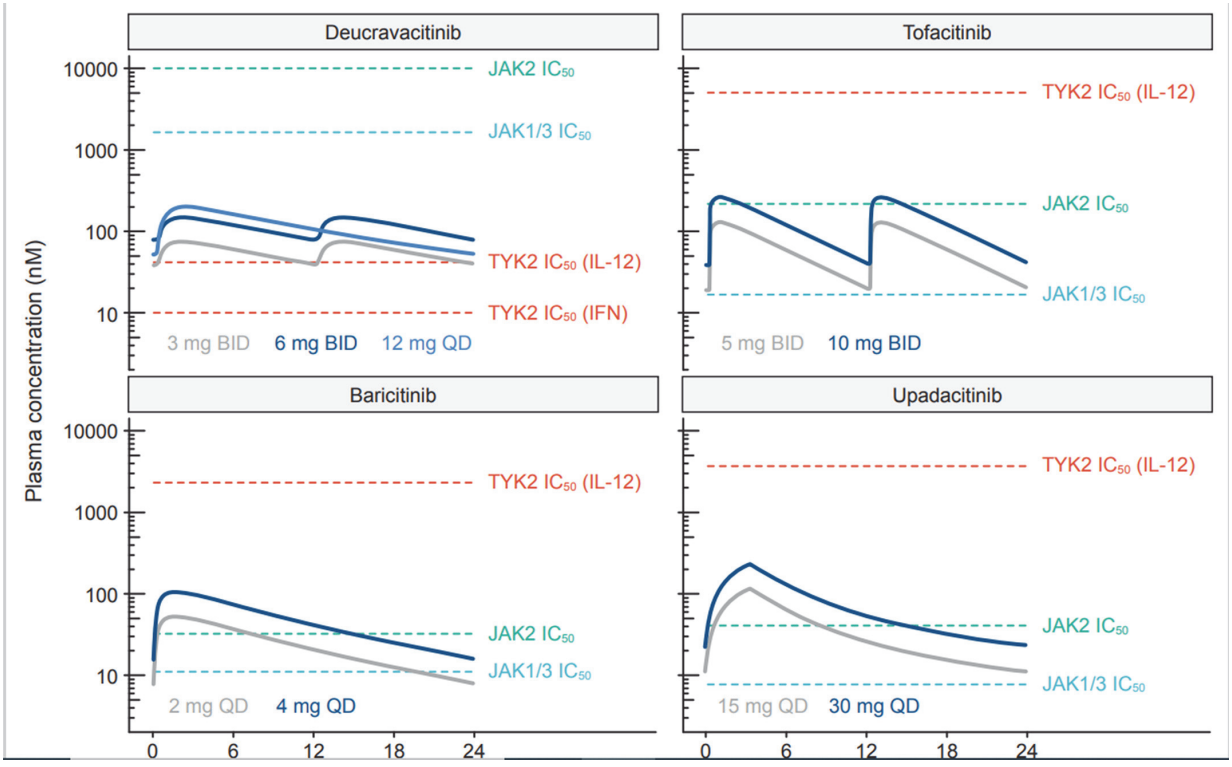
Methods In the phase 2 trial, patients with active SLE were randomized 1:1:1:1 to placebo or deucravacitinib (3 mg BID, 6 mg BID, 12 mg QD). PK analysis included pooled concentration data from 266 SLE patients and 328 phase 1 participants. IC_{50} was determined by in vitro whole blood assays and plotted against PK profiles. E-R analyses included data from 356 patients. Logistic regression analyses assessed the relationship between deucravacitinib exposure and probability of achieving efficacy endpoints and safety events at weeks 32 and 48.

Results Deucravacitinib PK in SLE patients was not meaningfully different from that in phase 1 participants. At 12 mg QD, deucravacitinib Cmax was 8-fold lower than JAK 1/3 IC_{50} and 47-fold lower than JAK 2/2 IC_{50} (figure 1). In the E-R analyses, the probability of achieving SRI(4) and BICLA at week 32 increased with increasing deucravacitinib CminSS, with 3 mg BID providing near-maximal response. The E-R relationship for infection and infestation was relatively flat, while skin and subcutaneous tissue disorders increased with increasing deucravacitinib CminSS. These E-R relationships were similar at week 48.

Conclusions Deucravacitinib PK in SLE patients is not meaningfully different from that in phase 1 participants. At clinically relevant exposures, deucravacitinib demonstrates highly selective inhibition of TYK2 vs JAK 1/2/3. The deucravacitinib E-R relationships are well characterized for various efficacy endpoints and safety events.

REFERENCES

1. Armstrong A, *et al. J Am Acad Dermatol* 2023;**88**(1):29–39.
2. Strober B, *et al. J Am Acad Dermatol* 2023;**88**(1):40–51.
3. Morand E, *et al. Arthritis Rheumatol* 2022 Nov 11 (Epub ahead of print).



Abstract LP-182 Figure 1 Plasma concentration-time profile of deucravacitinib, baricitinib, tofacitinib, and upadacitinib along with their respective whole blood IC50 curves