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.

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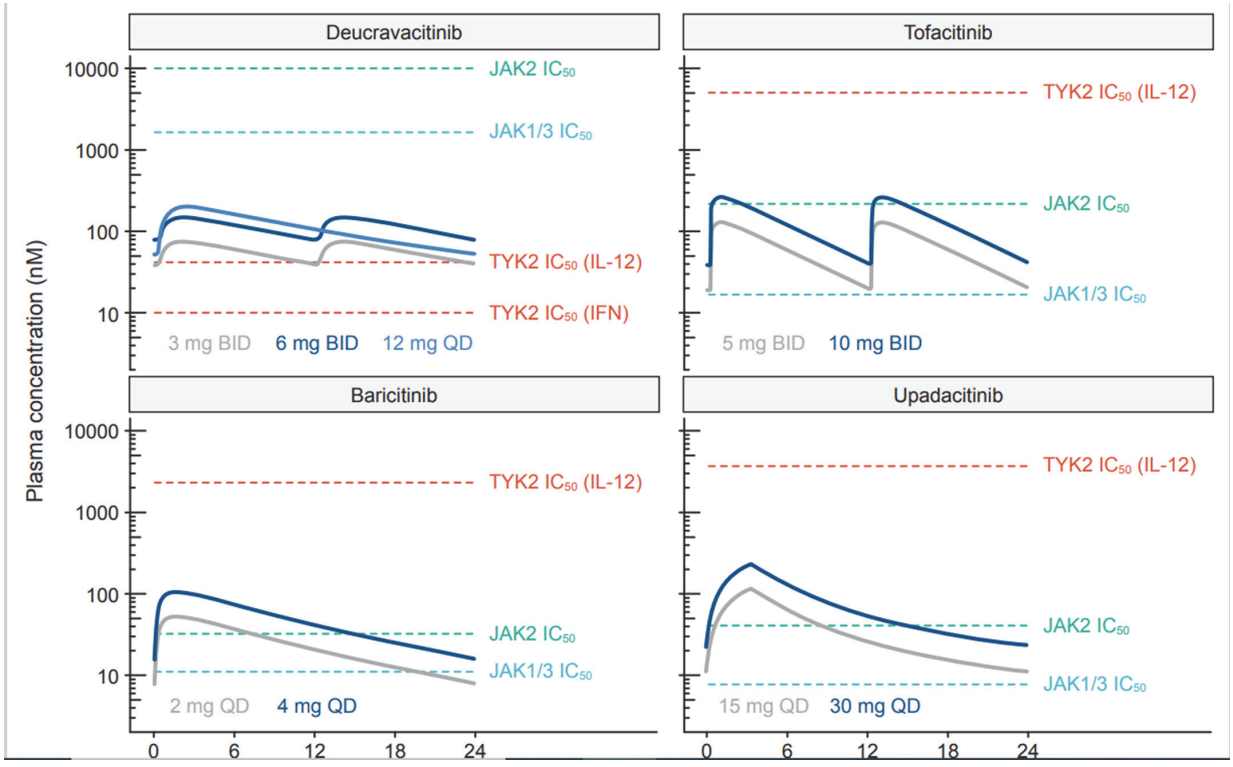

Abstract LP-182 Figure 1 Plasma concentration-time profile of deucravacitinib, baricitinib, tofacitinib, and upadacitinib along with their respective whole blood IC50 curves