S11.2 EFFICACY AND SAFETY OF DEUCRAVACITINIB, A SELECTIVE TYK2 INHIBITOR, IN PATIENTS WITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM A PHASE 2, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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Purpose Tyrosine kinase 2 (TYK2) mediates signaling of Type I interferons, IL-23, and IL-12, key cytokines involved in lupus pathogenesis. Deucravacitinib (DEUC) is an oral, selective, allosteric TYK2 inhibitor with a unique mechanism of action, distinct from Janus kinase (JAK) 1/2/3 inhibitors, and has demonstrated a favorable safety and efficacy profile in patients with moderate to severe plaque psoriasis and in psoriatic arthritis. This study assessed efficacy and safety of DEUC in patients with active systemic lupus erythematosus (SLE).

Methods This was a 48-week (wk), randomized, double-blind, placebo (PBO)-controlled, phase 2 trial (NCT03252587). Eligible patients met the Systemic Lupus International Collaborating Clinics (SLICC) criteria, were seropositive (ANA/anti-dsDNA/anti-Sm), and had a Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score ≥6 and ≥1 British Isles Lupus Assessment Group (BILAG) index A or ≥2 BILAG B manifestations from the musculoskeletal or mucocutaneous domain. Patients on standard background medications were randomized 1:1:1:1 to PBO or DEUC (3 mg BID, 6 mg BID, 12 mg QD). Oral corticosteroid tapering to 7.5 mg/day was required from wks 8–20, and further tapering was optional from wks 32–40. The primary endpoint was the proportion of patients achieving SRI(4) at wk 32. Key secondary endpoints at wk 48 included SRI(4), BICLA, LLDAS, CLASI-50, and change from baseline in active (tender and swollen) joint count.

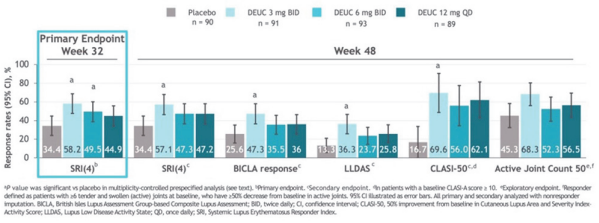
Results A total of 363 patients were randomized, with baseline demographic and disease characteristics being similar across treatment groups. Of randomized patients, 275 (76%) completed 48 wks of treatment. The primary endpoint at wk 32 was met, with significantly greater proportions of patients in the DEUC 3 mg BID and 6 mg BID groups vs PBO achieving SRI(4) responses (PBO: 34.4%; DEUC 3 mg BID: 58.2%, P=0.0006; DEUC 6 mg BID: 49.5%, P=0.021; DEUC 12 mg QD: 44.9%, P=0.078). SRI(4) response was sustained across all DEUC groups up to 48 wks (Figure). At wk 48, the DEUC 3 mg BID group demonstrated statistical significance in BICLA, LLDAS, CLASI-50, and active joint count, and the two other DEUC groups demonstrated clinically meaningful differences vs PBO (Figure 1). Rates of adverse events (AEs), serious AEs, and AEs of interest were similar between DEUC and PBO groups (Table 1). Most common AEs (≥10%) with DEUC were upper respiratory tract infection, nasopharyngitis, headache, and urinary tract infection. No deaths, major adverse cardiac events, thrombotic events, systemic opportunistic infections, or active tuberculosis occurred. Malignancies were rare with similar rates across all groups (Table 1). No meaningful laboratory abnormalities in mean levels of hematology and chemistry laboratory parameters were observed.

Conclusion In patients with active SLE, DEUC showed statistically significant and sustained clinical efficacy in SRI(4), improvement across multiple composite and organ-specific measures up to 48 wks, and was well tolerated. DEUC shows promise as a novel therapy for SLE and warrants further investigation in phase 3 trials.

Abstract S11.2 Table 1 Summery of adverse events through week 48

AE, n[a] (%)	Placebo n = 90	DEUC 3 mg BID n = 91	DEUC 6 mg BID n = 93	DEUC 12 mg QD n = 89
AE	79 (87.8)	85 (93.4)	81 (87.1)	75 (84.3)
SAE	11 (12.2)	7 (7.7)	8 (8.6)	7 (7.9)
AEs leading to treatment discontinuation	3 (3.3)	8 (8.8)	6 (6.5)	11 (12.4)
Skin-related AEs[b]	12 (13.3)	15 (16.5)	32 (34.4)	30 (33.7)
Overall infections/infestations	48 (53.3)	60 (65.9)	60 (64.5)	45 (50.6)
Serious infections/infestations	1 (1.1)	1 (1.1)	2 (2.2)	1 (1.1)
Infections of interest				
Tuberculosis	0	0	0	0
Herpes zoster[c]	4 (4.4)	3 (3.3)	3 (3.2)	2 (2.2)
Influenza	1 (1.1)	3 (3.3)	1 (1.1)	3 (3.4)
COVID-19	3 (3.3)	3 (3.3)	5 (5.4)	3 (3.4)
Malignancy events	1 (1.1)[d]	1 (1.1)[e]	0	1 (1.1)[f]
MACE	0	0	0	0
Thrombotic events	0	0	0	0

[a]n is the number of patients who experienced an event. [b]The most commonly occurring skin-related AEs (≤8.6% in any arm) included acne, rash, dermatitis acneiform, pruritus, skin lesion, and urticaria. [c]Includes herpes zoster, herpes ophthalmic, and genital herpes zoster. [d]Basal cell carcinoma. [e]Breast carcinoma. [f]Vaginal squamous cell carcinoma.
All patients who received ≥1 dose of any study treatment assessed. AE, adverse event; BID, twice daily; COVID-19, coronavirus disease 2019; DEUC, deucravacitinib; MACE, major adverse cardiac events; QD, once daily; SAE, serious adverse event.



Abstract S11.2 Figure 1 Summary of key efficacy results

S11.3 LOW-DOSE INTERLEUKIN-2 THERAPY IN ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS (LUPIL-2): A MULTICENTER, DOUBLE-BLIND, RANDOMIZED AND PLACEBO-CONTROLLED PHASE 2 TRIAL

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Purpose A regulatory T cell (Treg) insufficiency due to shortage of interleukin-2 (IL-2) is central to the pathophysiology of systemic lupus erythematosus (SLE). We performed a multicenter, double-blind, randomized, placebo-controlled phase-2 proof-of-concept trial to evaluate the efficacy of low-dose IL-2 therapy in patients with SLE having moderate-to-severe disease activity while receiving standard treatment.

Methods We randomly assigned 100 patients in a 1:1 ratio to receive either 1.5 million IU/day of subcutaneous IL-2 (ILT-101) or placebo for 5 days followed by weekly injections for 12 weeks. Clinical efficacy was assessed at week-12 in a predefined hierarchical analysis of (1) the SLE responder index-4