Figure 2. Panel A) Clusters analysis, correlated with clinical status of the patients by correspondence analysis ($p < 0.0001$). Panel B) Network analyses of the interferon regulated genes networks among groups.

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EFFICACY OF ANIFROLUMAB IN ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS: PATIENT SUBGROUP ANALYSIS OF BICLA RESPONSE IN 2 PHASE 3 TRIALS

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Background: Treatment of patients with systemic lupus erythematosus (SLE) with the type I interferon (IFN) receptor inhibitor anifrolumab resulted in higher British Isles Lupus Assessment Group (BILAG)-based Composite Lupus Assessment (BICLA) response rates vs placebo at Week 52 in the phase 3 randomized trials, TULIP-2 (primary endpoint; 16.3% difference)¹ and TULIP-1 (secondary endpoint; 16.4% difference).² BICLA is a validated composite global disease measure that registers both partial and complete improvement within organ systems.

Objectives: TULIP-2 and TULIP-1 data were analyzed to evaluate BICLA responses to anifrolumab vs placebo at Week 52 in protocol-defined subgroups of patients with active SLE.

Methods: TULIP-2 and TULIP-1 were randomized, double-blind, placebo-controlled trials that evaluated efficacy and safety of intravenous anifrolumab vs placebo administered every 4 weeks, with the primary endpoints assessed at Week 52, in patients with moderate to severe SLE despite standard-of-care treatment.^{1,2} BICLA responses are defined by all of the following: reduction of baseline BILAG-2004 A and B domain scores to B/C/D and C/D, respectively, and no worsening in any organ system; no worsening of the SLE Disease Activity Index 2000 (SLEDAI-2K) score; no worsening of ≥ 0.3 points in the Physician's Global Assessment (range 0–3); no trial treatment discontinuation; and no use of medications restricted by the protocol.³ BICLA responses were compared between anifrolumab 300 mg and placebo groups, and robustness of BICLA responses was assessed across protocol-defined subgroups. TULIP-1 data were analyzed incorporating the amended restricted medication rules, as described.²

Results: In TULIP-2 and TULIP-1, 180 patients in each trial received anifrolumab 300 mg (182 and 184 patients received placebo, respectively). Baseline demographics, disease characteristics, and standard-of-care medications were balanced between anifrolumab and placebo groups

within both TULIP trials. Patients in TULIP-2 and TULIP-1 had comparable BICLA responses (**Figure**). Across multiple subgroups, higher percentages of patients achieved BICLA responses at Week 52 in the anifrolumab vs placebo arms (**Figure**). There was concordance of BICLA responses favoring anifrolumab across the protocol-defined subgroups of baseline disease severity (SLEDAI-2K < 10 points [difference 15.3%, TULIP-2; 16.9%, TULIP-1] vs ≥ 10 points [difference 16.7%, TULIP-2; 17.1%, TULIP-1]) and baseline oral corticosteroid use (prednisone or equivalent < 10 mg/d [difference 20.1%, TULIP-2; 16.2%, TULIP-1] vs ≥ 10 mg/d [difference 12.0%, TULIP-2; 17.7%, TULIP-1]). Numerically different BICLA effect sizes between the anifrolumab vs placebo arms were observed in both studies in relation to baseline IFN gene signature status (high [difference 17.3%, TULIP-2; 19.1%, TULIP-1] vs low [difference 11.2%, TULIP-2; 7.5%, TULIP-1]). Other subgroups including age, sex, age at onset, race, and anti-drug antibody status showed similar uniformity of response.

Conclusion: The uniformity of robust BICLA response rates across prespecified subgroups in both phase 3 trials shows consistent clinical benefit of anifrolumab irrespective of patient baseline characteristics. However, given the small patient numbers in some subgroups, these results should be interpreted with caution.

References:

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Figure. BICLA Response Rates by Subgroup Comparing Anifrolumab 300 mg With Placebo in the TULIP-2 and TULIP-1 Trials at Week 52

ADA, anti-drug antibody; BICLA, BILAG-based Composite Lupus Assessment; BILAG, British Isles Lupus Assessment Group; BMI, body mass index; CI, confidence interval; IFNGS, interferon gene signature; N, number of patients in treatment group; n, number of patients with response; OCS, oral corticosteroid; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000.

Note: TULIP-1 data were analyzed using the amended restricted medication rules.²

*Includes native Hawaiian or other Pacific Islander and American Indian or Alaska natives.

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