Efficacy of Anifrolumab in Active Systemic Lupus Erythematosus: Patient Subgroup Analysis of BICLA Response in 2 Phase 3 Trials


1Monash University, Melbourne, Australia; 2Zucker School of Medicine at Hofstra/Northwell, Great Neck, United States of America; 3University of Occupational and Environmental Health, Japan, Kitakyushu, Japan; 4BioPharmaceuticals Medical, AstraZeneca, Gothenburg, Sweden; 5BioPharmaceuticals Medical, AstraZeneca, Gaithersburg, United States of America; 6Biopharmaceuticals Medical, AstraZeneca, Tokyo, Japan; 7Monash University, Melbourne, Australia

Background: Treatment of patients with systemic lupus erythematosus (SLE) with the type I interferon (IFN) receptor inhibitor anifrolumab resulted in higher efficacy of anifrolumab 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).2,3 BICLA is a validated composite global disease measure that registers both partial and complete improvement within organ systems.

Objective: 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.1,2,3 BICLA responses are defined by all of the following: reduction of baseline BILAG-2004 A and B domain scores to B/C 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.2,3 BICLA responses were assessed across protocol-defined subgroups. TULIP-1 data were analyzed incorporating the amended restricted medication rules, as described.3

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). The 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]) 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: