Anifrolumab, a type I interferon receptor antibody, has shown efficacy in patients with systemic lupus erythematosus (SLE), ≥30% of whom develop lupus nephritis (LN). Objectives: To evaluate the efficacy and safety of anifrolumab vs placebo alongside standard therapy in patients with active proliferative LN.

Methods: TULIP-LN (NCT02547922) was a phase 2 double-blind trial in adult patients with active, biopsy-proven LN and 24-hour (h) urine protein-creatinine ratio (UPCR) >1 mg/mg. Patients were randomized (1:1:1) to anifrolumab basic regimen (BR, 300 mg, based on SLE dosing [2],) anifrolumab intensified regimen (IR, 900 mg for 3 doses, 300 mg thereafer), or placebo, intravenously every 4 weeks alongside standard therapy of oral glucocorticoids (GCs; mandatory taper ≤7.5 mg/day by Week [W]12, ≤7.5 mg/day by W24) and mycophenolate mofetil (target 2 g/day by W8). The primary endpoint was the relative difference in change from baseline to W52 in 24-h UPCR, measured with a geometric mean ratio (GMR) of the change in the combined anifrolumab vs placebo groups (GMR <1 favors anifrolumab). The key secondary endpoint was complete renal response (CRR) at W52 (24-h UPCR ≤0.7 mg/mg, estimated glomerular filtration rate ≥60 ml/min/1.73 m² or no decrease ≥20%, no treatment discontinuation, and no restricted medication use). Sustained GC taper (≥7.5 mg/day, W24–52) was an exploratory endpoint. CRR(0.5) (CRR with UPCR ≤0.5 mg/mg) and time to CRR(0.5) sustained to W52 were analyzed post hoc. Responder rates were calculated with a stratified Cochran–Mantel–Haenszel approach.

Results: Patients received anifrolumab BR (n=45) or IR (n=51) or placebo (n=49); demographics and baseline disease characteristics were generally balanced across groups. No difference in change from baseline to W52 in 24-h UPCR was observed for combined anifrolumab vs placebo groups (Table 1). Anifrolumab clearance was higher in patients with LN vs SLE; proteinuria in LN elicited suboptimal anifrolumab serum concentrations (early trough from BR 50%–60% lower than in SLE trials [1,2], so anifrolumab IR results are presented. CRR rate at W52 was numerically higher with the IR vs placebo (45.5% vs 31.1%) (Table 1). Time to sustained CRR(0.5) (Figure 1, rate of CRR(0.5) at W52, and rate of sustained GC taper ≤7.5 mg/day (Table 1) were improved with the IR vs placebo. Most adverse events were nonserious, mild, or moderate and did not lead to discontinuation; rates were similar in the combined anifrolumab vs placebo groups (89.8% vs 93.8%). In the combined anifrolumab vs placebo groups, there was a higher incidence of herpes zoster (HZ, 16.7% vs 8.2%); most HZ cases were of mild to moderate intensity, cutaneous, and resolved with treatment.

Conclusion: Although the primary endpoint was not met, the anifrolumab IR was associated with numeric improvements across clinical endpoints vs placebo; thus, intensified dosing may be required to reach clinical efficacy in LN vs SLE without active renal disease. Anifrolumab had a similar safety profile in patients with LN and SLE; despite higher frequency of HZ vs placebo, anifrolumab was well tolerated.

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