Safety profile of baricitinib in patients with systemic lupus erythematosus: An integrated analysis

Supplemental Information

Table S1. Risk factors for serious infection in the placebo-controlled analysis set.

Risk factor	**Hazard Ratio (95% CI)**
Treatment group	
Bari 2 mg vs. placebo	1.64 (0.808, 3.322)
Bari 4 mg vs. placebo	2.10 (1.058, 4.162)
Age	
≥65 years vs. <65 years	3.77 (1.717, 8.298)
History of Diabetes Mellitus	
Yes vs. no	2.61 (1.199, 5.686)
Corticosteroid at baseline	
≥10 mg/day vs. < 10 mg/day	2.52 (1.487, 4.286)
COVID infection during study	
Yes vs. no	5.36 (2.938, 9.790)

Bari, baricitinib; CI, confidence interval; vs, versus

Demographic and clinical risk factors for serious infections were assessed using a multivariable-adjusted Cox model in the placebo-controlled data set. Backward elimination and stepwise selection were used to select the final model, using a $p<0.05$ to add or retain variables.

S1. Additional laboratory results

Haematology

When assessed through up to 52 weeks, small declines from baseline in mean haemoglobin levels were observed for both the placebo and baricitinib groups (at Week 52: placebo −0.09 mmol/L, baricitinib 2 mg −0.13 mmol/L, baricitinib 4 mg −0.18 mmol/L).

Baricitinib treatment was associated with an initial decrease in mean neutrophil count that returned to baseline by Week 12 and remained stable through Week 52. Neutropenia grade ≥1 (neutrophils <2 billion /L) was common in all treatment groups (placebo: 19.6%, baricitinib 2 mg: 22.9%, baricitinib 4 mg: 30.4%). Among all patients with grade ≥1 neutropenia in the placebo-controlled data set, serious infections were reported in 0.9% with placebo, 4.6% with baricitinib 2 mg, and 3.5% with baricitinib 4 mg.

Mean lymphocyte counts increased during the first 8 weeks of baricitinib treatment (baricitinib 2 mg: $+0.23\times10^9$/L, baricitinib 4 mg: $+0.29\times10^9$/L above baseline), then decreased to baseline levels by Week 12, and then remained stable through Week 52. Among patients with lymphopenia, the frequency of infections was similar across treatment arms, but serious infections were more common in baricitinib groups during the placebo-controlled period.

With baricitinib treatment, mean platelet counts increased up to Week 8 and remained stable through Week 52. Thrombocytosis (platelets >600 billion/L) was more common with baricitinib 4 mg (2.4%) versus baricitinib 2 mg (0.6%) or placebo (0.3%) in the placebo-controlled period and was also more common with baricitinib 4 mg (2.5%) versus 2 mg (0.5%) in the extended period. Platelet increases were not associated with MACEs or DVT/PE events.

Creatine phosphokinase

During the placebo-controlled period, increases in creatine phosphokinase (CPK) up to 2.5 times the upper limit of normal (ULN) were observed in 30.6% and 24.4% of baricitinib-4-mg and 2-mg-treated patients, respectively, compared to 12.9% of placebo-treated patients. Dose-related differences in CPK increases were also observed in the extended data set.

Cholesterol

In the placebo-controlled data set, higher proportions of patients had increases (≥130 mg/dL) in low-density lipoprotein (LDL) in the baricitinib groups versus placebo. In the extended period, the proportions of patients with LDL increases ≥130 mg/dL were similar between baricitinib doses. In the placebo-controlled period, higher proportions of patients treated with baricitinib 4 mg had increases in triglycerides ≥500 mg/dL compared to patients treated with baricitinib 2 mg or placebo, though patient numbers were low. None of the patients with a positively adjudicated MACE in All-Bari-SLE were observed with triglycerides ≥500 mg/dL around the time of the MACE.

Liver enzymes

Increases in alanine transaminase (ALT) and aspartate transaminase (AST) to ≥3 times ULN were more common in the baricitinib groups than placebo. No patients were identified as potential Hy's Law or cholestatic liver injury cases.