Safety profile characterization of evobrutinib in over 1000 patients from phase II clinical trials in multiple sclerosis, rheumatoid arthritis and systemic lupus erythematosus

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Abstract

Introduction: Evobrutinib, a highly selective oral Bruton's tyrosine kinase inhibitor (BTKi), targets B cells, macrophages and microglia involved in autoimmunity.

Objective: To analyze the safety profile, including class-related treatment-emergent adverse events (TEAEs), of evobrutinib using pooled data from phase II trials in MS, rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE).

Methods: Data from three phase II, randomized, double-blind, placebo-controlled trials of evobrutinib were analyzed (MS: n=213, 48 weeks, NCT02975349; RA: n=390, 12 weeks, NCT03233230; SLE: n=480, 52 weeks, NCT02975336).

Results: Data from 1083 patients were pooled (evobrutinib: n=861; placebo: n=271; 49 MS patients received both placebo [Week 0–24] and evobrutinib [Week 25–48]). The proportion of patients with TEAEs and the exposure-adjusted incidence rate (EAIR) was similar for evobrutinib and placebo (66.2% [247.6 events/100 pt-years] vs 62.4% [261.4 events/100 pt-years]). The EAIR of TEAEs (events/100 pt-years) for evobrutinib vs placebo were similar by indication: MS: 119.7 vs 148.3; RA: 331.8 vs 306.8; SLE: 342.9 vs 302.1. The proportion of Grade ≥3 or Grade ≥4 TEAEs with evobrutinib vs placebo was 11.8% vs 11.8% and 0.8% vs 0.7%, respectively. TEAEs reported in ≥5% of evobrutinib-treated patients were urinary tract infections (9.5% vs 8.5% placebo), nasopharyngitis (7.3% vs 5.5% placebo) and diarrhea (6.2% vs 4.8% placebo). The EAIR of transient elevated ALT and AST (events/100 pt-years) with evobrutinib vs placebo was 4.84 vs 2.76 and 3.48 vs 0.69, respectively. The EAIR of serious infections was 2.72 and 2.07 events/100 pt-years for evobrutinib and placebo, with no imbalance between evobrutinib doses. There were no serious infections with the highest evobrutinib dose in MS and RA; the EAIR in SLE was similar to placebo (50mg BID: 2.06 vs 2.00 events/100 pt-years).

Conclusions: These results represent the first BTKi integrated safety analysis including MS patients. Evobrutinib treatment was generally well tolerated across indications.

Disclosures:

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