Tolebrutinib Two-Year Safety and Efficacy in Relapsing Multiple Sclerosis Patients

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INTRODUCTION: Phase 2b trial (NCT03889639) findings in patients with relapsing multiple sclerosis showed brain-penetrant Bruton's tyrosine kinase inhibitor tolebrutinib was well tolerated over 12 weeks and elicited dose-dependent reductions in new gadolinium-enhancing T1 and new/enlarging T2 lesions.

AIMS: To characterise tolebrutinib's safety and efficacy at Week 96 (2 years) in the phase 2b trial's long-term safety (LTS) extension (NCT03996291).

METHODS: In LTS Part A, patients continued their core study tolebrutinib dose (5, 15, 30, or 60 mg/day) double-blind until phase 3 study dose selection (60 mg/day). In Part B, patients receive open-label tolebrutinib 60 mg/day. Safety was assessed via adverse event (AE) reporting. Efficacy outcomes included annualised relapse rate (ARR) and change from baseline Expanded Disability Status Scale (EDSS) score.

RESULTS: 124 of 125 patients completed Part A and transitioned to Part B; 114 (90.5%) remained on study by 7 March 2022. One patient receiving tolebrutinib 5 mg/day discontinued Part A because of progressive disease; 10 discontinued Part B because of AEs (n=3), perceived lack of efficacy (n=4), emigration (n=2), and patient decision (n=1). At Week 96, no new safety signals have been observed. The most common treatment-emergent AEs (TEAEs) were COVID-19 (20.8% [26/125]), headache (13.6% [17/125]), nasopharyngitis and upper respiratory tract infection (both 11.2% [14/125]), bacterial cystitis (7.2% [9/125]), and pharyngitis and arthralgia (both 5.6% [7/125]). No tolebrutinib dose effects for TEAEs or serious AEs were observed in Part A and no safety signals emerged for patients switching to tolebrutinib 60 mg/day in Part B. Of those who received tolebrutinib 60 mg/day for a minimum of 8 weeks, ARR was 0.17 (95%CI: 0.12, 0.25) and 80.6% remained relapse-free. Mean EDSS remained stable to Week 96.

CONCLUSIONS: Through LTS Week 96, tolebrutinib 60 mg/day continues to show favourable safety, and is associated with a low ARR and stable disability status.

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