Tolebrutinib Two-Year MRI Outcomes in Patients with Relapsing Multiple Sclerosis

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INTRODUCTION: In the phase 2b trial (NCT03889639), brain-penetrant inhibitor of Bruton's tyrosine kinase tolebrutinib was well tolerated by patients with relapsing multiple sclerosis over 12 weeks with dose-dependent reduction in new gadolinium (Gd)-enhancing T1 and new/enlarging T2 lesions.

AIMS: Report MRI outcomes at Week (W) 96 (Year 2) in the ongoing phase 2b long-term safety (LTS) extension (NCT03996291).

METHODS: In LTS Part A, patients continued receiving their double-blind period dose (5, 15, 30, or 60 mg/day) until the phase 3 dose was selected. In open-label Part B, all patients receive tolebrutinib 60 mg/day. MRI outcomes include numbers of new Gd-enhancing and new/enlarging T2 lesions, T2 lesion volume change from baseline, slowly evolving lesions (SEL), and paramagnetic rim lesions (PRL).
RESULTS: 124 of 125 patients completed LTS Part A and transitioned to Part B; 114 (90.5%) remain on study as of 18 February 2022 (W96 cut-off). Numbers of new Gd-enhancing lesions remained low in the 60/60-mg arm through W96 and were reduced in other arms at W48 through W96 (W96 mean±SD: 0.85±2.5, 0.41±0.91, 0.90±2.16, 0.31±0.66 in 5/60-, 15/60-, 30/60-, 60/60-mg arms, respectively). New/enlarging T2 lesion counts remained low for 60/60 mg. T2 lesion volume change remained low for 60/60 mg (W96 vs baseline [mean±SD]: +0.38±2.11 cm^3). Median (IQR) W96 SEL volume was 247.5 (84–420), 258 (66–906), 570 (133.5–1011), and 244.5 (87–939) mm^3 for 5/60-, 15/60-, 30/60-, and 60/60-mg, respectively. PRL count remained unchanged in 18 patients; 2 patients had 1 PRL at baseline but none at W96, and 3 patients had 1–3 additional PRL at W96 vs baseline (none in the 60/60 mg arm).

CONCLUSIONS: New Gd-enhancing lesion counts remained low for tolebrutinib 60/60 mg and were reduced in the lower dose arms by LTS W48 through W96, when all patients had switched to 60 mg.

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