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Safety and Efficacy of Ozanimod Over 1 Year in Patients with Early Relapsing Multiple Sclerosis: an Interim Analysis of the ENLIGHTEN Study

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Introduction:

ENLIGHTEN is an ongoing 3-year study of ozanimod in patients with early relapsing MS (RMS).

Objectives/Aims:

This ad hoc interim analysis describes the efficacy and safety profile of ozanimod over 1 y.

Methods:

ENLIGHTEN (NCT04140305) is a phase 3, multicenter, single-arm, open-label study of ozanimod 0.92 mg in adults with early RMS (≤1 disease-modifying therapy [DMT]; Expanded Disability Status Scale [EDSS] score ≤3.5; ≤5 y since RMS diagnosis; ≤10 gadolinium-enhancing [GdE] lesions). The primary endpoint of proportion with an increase in Symbol Digit Modalities Test (SDMT) score of ≥4 points (pt) or 10% from baseline and secondary endpoints of new/enlarging T2 lesion count on MRI and proportion of patients GdE lesion-free were assessed at 1 y. Treatment-emergent adverse events (TEAEs) were assessed from study start (16/1/2020) through data cutoff (14/2/2023), and exposure-adjusted incidence rates (EAIR) were calculated.

Results:

Mean (standard deviation [SD]) ozanimod exposure among 185 enroled patients was 13.7 (8.6) mos (210.9 person-years [PY] total exposure); 1 patient had completed and 155 (83.8%) were on treatment at data cutoff. Baseline characteristics (N=185) included mean (SD) age 39.5 (10.7) y; 78.4% female; 85.9% White; 10.8% Black; 72.4% DMT naïve; mean 4.1 (5.5) y since MS symptom onset; mean 0.8 (0.8) relapses in prior 12 mos; and median EDSS score 2.0 (range 0–4). At baseline, mean (SD) SDMT score was 53.9 (11.4); after 1 y of ozanimod, 55/116 (47.4%) had ≥4-pt or 10% improvement, 30 (25.9%) remained stable, and 31 (26.7%) had a ≥4-pt or 10% worsening. Mean (SD) T2 lesion count at baseline (n=184) was 22.4 (16.9); mean (SD) new/enlarging T2 lesion count at 1 y (n=101) was 0.4 (0.8). Also, 91/100 (91.0%) patients with MRI data were GdE lesion-free at 1 y vs 123/185 (66.5%) at baseline. TEAEs occurred in 122 (65.9%) patients (EAIR 161.8/100 PY); TEAEs present in ≥5% were (%; EAIR/100 PY): COVID-19 (17.3%; 16.3), headache (10.3%; 9.3), fatigue (9.2%; 8.5), urinary tract infection (6.5%; 5.7), sinusitis (5.9%; 5.2), nasopharyngitis (5.4%; 4.8), muscle weakness (5.4%; 4.7), and hypertension (5.4%; 4.7).

Conclusion:

Nearly half of this population with early RMS had ≥4-pt or 10% improvement in SDMT score after 1 y of ozanimod, and MRI lesion counts were reduced. COVID-19 was the most frequent TEAE during ENLIGHTEN, which began just before the start of the COVID-19 pandemic. Other common TEAEs were largely consistent with those reported in the overall ozanimod clinical development program.

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