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Long-term Safety and Efficacy of Ozanimod in RMS: Interim Analysis of DAYBREAK

Short title: Ozanimod: Long-term Safety & Efficacy in RMS

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Introduction:

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Ozanimod is approved in multiple countries for the treatment of adults with relapsing forms of multiple sclerosis (RMS). We report safety and efficacy of ozanimod from an ongoing open-label extension trial.

Methods:

Patients with RMS who completed phase 1–3 ozanimod trials were eligible to enrol in DAYBREAK (NCT02576717), where they received ozanimod 0.92 mg/d. The primary objective was to evaluate safety in the overall population; treatment-emergent adverse events (TEAE) were monitored. Efficacy was evaluated with annualised relapse rate (ARR), calculated via negative binomial regression. Number of new/enlarging T2 and gadolinium-enhancing (GdE) MRI brain lesions were reported only for patients who entered DAYBREAK from an active-controlled phase 3 trial.

Results:

In total, 2639 patients completed the parent trials; this interim analysis (data cutoff February 2021) included 2494 patients with mean (range) ozanimod exposure of 46.8 (0.03–62.7) months (9725.6 patient-years) in DAYBREAK. Adjusted ARR was 0.103 (95% CI, 0.086–0.123). At 48 months, 71% of patients were relapse free. Rates of 3- and 6-month confirmed disability progression were low (13.9% and 11.4%, respectively). Adjusted mean number of new/enlarging T2 lesions/scan at 48 months was similar, regardless of parent-trial treatment group (range, 0.85–1.03), as were adjusted mean number of GdE lesions at month 48 (range, 0.06–0.12). In DAYBREAK, 2143 patients (85.9%) had any TEAE, 298 (11.9%) had a serious TEAE, and 75 (3.0%) discontinued due to a TEAE. The most common TEAEs were nasopharyngitis (19.6%), headache (15.8%), and upper respiratory tract infection (11.1%). There were no serious opportunistic infections at the time of this data cut; however, a case of progressive multifocal leukoencephalopathy was reported in March 2021.

Conclusions:

In DAYBREAK, ozanimod treatment demonstrated sustained efficacy with low ARR, new/enlarging T2 and GdE lesion counts, and disability progression over 4 years. Long-term ozanimod was generally safe and well tolerated.

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