

Brain Volume Changes During 3 to 5 Years of Ozanimod in Relapsing MS

Short title: Effect of Ozanimod on Brain Volume in RMS

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Introduction:

Ozanimod reduced whole brain volume (WBV), cortical grey matter volume (CGMV), and thalamic volume (TV) loss vs interferon beta-1a (IFN) in phase 3 SUNBEAM (NCT02294058) and RADIANCE (NCT02047734) trials. We evaluated brain volume loss among SUNBEAM/RADIANCE participants who entered an ongoing extension trial (DAYBREAK, NCT02576717).

Methods:

The 2 randomised, double-blind trials compared oral ozanimod 0.92 and 0.46 mg/day with intramuscular IFN 30 µg/week in adults with relapsing multiple sclerosis (RMS). Completers were eligible to receive open-label ozanimod 0.92 mg/day in DAYBREAK. MRI was performed at months 6 (SUNBEAM), 12 (SUNBEAM/RADIANCE), and 24 (RADIANCE), then every 12 months (DAYBREAK). Baseline WBV and CGMV were measured using SienaX, and TV using ThalamicVolume software; percentage change in WBV, CGMV, and TV was

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quantified using Jacobian integration. Data are reported through DAYBREAK month 36 (December 2020 data cutoff).

Results:

DAYBREAK includes 2257 SUNBEAM/RADIANCE participants. Loss of WBV, CGMV, and TV was less in ozanimod-treated participants than IFN-treated participants and remained less after switching from IFN to ozanimod, especially for WBV and TV. CGMV was lost to a much greater extent while on IFN, and recovered substantially, but not completely, upon switching to ozanimod.

Conclusion:

Switching from IFN to ozanimod reduced the rate of WBV, CGMV, and TV loss. Global and regional brain volume loss after 4–5 years of follow-up remained greater in participants who started on IFN than in continuous ozanimod users. These results support early treatment with ozanimod to reduce brain volume loss in patients with RMS.

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