Early MRI parameters associated with long-term outcomes in ozanimod MS studies

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Short Title: Early MRI parameters & long-term RMS outcomes

Introduction: Relationships between early magnetic resonance imaging (MRI) parameters and long-term clinical outcomes of relapsing multiple sclerosis (RMS) are not fully understood.

Objectives: To explore relationships between early MRI parameters and long-term clinical outcomes in patients with RMS treated with ozanimod in phase 3 trials.

Methods: This post hoc analysis pooled data from patients receiving ozanimod 0.92 mg/d in SUNBEAM (NCT02294058) and RADIANCE (NCT02047734) who entered the DAYBREAK (NCT02576717) open-label extension (OLE), wherein all patients received ozanimod 0.92 mg/d. Early MRI parameters included observed (baseline [BL]) and % change in month 12 (M12) whole brain volume (WBV), thalamic volume (TV), cortical grey matter volume; BL and M12 gadolinium-enhancing (GdE) lesion count and T1 and T2 lesion volumes; and M12 new/enlarging T2 lesions. Clinical outcomes included

relapses during OLE, as well as cognitive processing speed (Symbol Digit Modalities Test [SDMT]) and disability (Expanded Disability Status Scale [EDSS]) at OLE month 48 (M48). Spearman correlation coefficients were calculated for MRI parameters vs clinical outcomes.

Results: Of the BL MRI parameters, SDMT scores at OLE M48 correlated most strongly ($\rho>0.46–<0.49$) with T1 lesion volume (inverse correlation) and TV; EDSS at OLE M48 correlated less strongly with these MRI parameters ($\rho>0.38–<0.42$). For EDSS scores at OLE M48, the strongest correlations ($\rho>0.41–<0.42$) were with BL TV and WBV (inverse correlations). SDMT and EDSS correlated poorly with BL GdE lesion count ($\rho<0.11$). Of the M12 MRI parameters, SDMT and EDSS scores correlated most strongly with T1 and T2 lesion volumes (SDMT, $\rho>0.44–<0.50$, inverse correlations; EDSS scores, $\rho>0.34–<0.39$). Relapses during the OLE correlated poorly with BL and M12 MRI parameters ($\rho<0.19$).

Conclusions: Lesion volumes and TV had stronger correlations with SDMT than with EDSS long term, suggesting these MRI measures may be better long-term predictors of cognition than physical disability.

Previously presented: ECTRIMS-2022, Oct 26-28, Amsterdam, Netherlands

Funding: SUNBEAM, RADIANCE, and DAYBREAK were supported by Celgene International II.

Disclosures

DLA: reports consulting fees from Biogen, Celgene, Frequency Therapeutics, Genentech, Merck, Novartis, Race to Erase MS, Roche, and Sanofi-Aventis, Shionogi, Xfacto Communications, grants from Immunotec and Novartis, and an equity interest in NeuroRx.

LF: consultancy fees from Genentech, Novartis, Celgene/Bristol Myers Squibb, EMD Serono, and TG Therapeutics; program sponsorship from EMD Serono; and grant support from NIH/NINDS, PCORI, Genentech, and EMD Serono.

HPH: personal fees for consulting, serving on steering committees, and speaking from Bayer Healthcare, Biogen, Celgene, GeNeuro, Genzyme, MedImmune, Merck, Novartis, Octapharma, Roche, Sanofi, and Teva.

XM: speaking honoraria and travel expenses for participation in scientific meetings, has been a steering committee member of clinical trials or participated in advisory boards of clinical trials in the past 3 years with Actelion, Alexion, Bayer, Biogen, Bristol Myers Squibb/Celgene, EMD Serono, EXCEMED, Genzyme, Hoffmann-La Roche, Immunic,

Janssen Pharmaceuticals, MedDay, Merck, Mylan, MSIF, NervGen, NMSS, Novartis, Roche, Sanofi-Genzyme, Teva Pharmaceuticals, and TG Therapeutics

JAC: personal compensation for consulting for Biogen, Bristol Myers Squibb, Convelo, Genentech, Janssen, NervGen, Novartis, and PSI; speaking for H3 Communications; and serving as an editor of *Multiple Sclerosis Journal*

ABO: participated as a speaker in meetings sponsored by and received consulting fees and/or grant support from Atara Biotherapeutics, Biogen, BMS-Celgene, EMD Serono, Sanofi Genzyme, Novartis, and Roche-Genentech.

LS: consulting for AbbVie, Atreca, Celgene, Novartis, Teva, Tolerion, and EMD Serono, and research support from Atara, Biogen, and Celgene.

JDL: personal compensation for consulting from Celgene, Biogen IDEC, Consortium of MS Centers, and Novartis; speaker for Sanofi Genzyme, Canadian MS Society, and EXCEMED; grant funding from Biogen IDEC, EMD Serono, Canadian MS Society, National MS Society, and Consortium of MS Centers.

CC, **JVR, DS, and CP**: employees and shareholders of Bristol Myers Squibb.

BACC: personal compensation for consulting for Alexion, Atara, Autobahn, Avotres, Biogen, EMD Serono, Gossamer Bio, Horizon, Neuron23, Novartis, Sanofi, TG Therapeutics and Therini, and received research support from Genentech.