Title

Two Expanded Disability Status Scale Subscales Evaluated in Patients With Relapsing-Remitting or Secondary Progressive Multiple Sclerosis

Authors

Gary Cutter[1], Xiangyi Meng[2], Jamie L Weiss[2], Ralph HB Benedict[3], Stanley L Cohan[4], Bruce AC Cree[5], Wendy Su[2], Florian P Thomas[6,7]

Affiliations

[1]UAB School of Public Health, Birmingham, AL, USA; [2]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [3]University at Buffalo, State University of New York, Buffalo, NY, USA; [4]Providence Multiple Sclerosis Center, Providence Brain Institute, Portland, OR, USA; [5]UCSF Weill Institute for Neurosciences, Department of Neurology, University of California San Francisco, San Francisco, CA, USA; [6]Multiple Sclerosis Center, Department of Neurology and Neuroscience Institute, Hackensack University Medical Center, Hackensack, NJ, USA; [7]Hackensack Meridian School of Medicine, Nutley, NJ, USA

Abstract

BACKGROUND: In phase 3 trials using the Expanded Disability Status Scale (EDSS), fingolimod and siponimod reduced disability worsening in patients with relapsing-remitting multiple sclerosis (RRMS) and secondary progressive MS (SPMS), respectively. However, EDSS components may differentially contribute to worsening, and contribution of each component may depend on disease stage. Also, EDSS assessments can be burdensome for patients and clinicians. Using factor analysis, different EDSS functions can be allocated to two novel subscales, including parameters most relevant to disease worsening.

OBJECTIVES: Evaluate the effects of fingolimod and siponimod using EDSS subscales derived by factor analysis of phase 3 trial data.

METHODS: PROC FACTOR procedure was used to determine best fit of baseline EDSS data to the following subscales: Motor Integration (MI: ambulation, cerebellar and pyramidal functions) and Collateral (C: bowel and bladder, brainstem, cerebral, sensory and visual functions). Treatment effect sizes (ES) on disability (mean change from baseline vs placebo) were determined overall and by each subscale up to 24 months (M) in RRMS patients from

FREEDOMS and up to 27M in SPMS patients from EXPAND. Statistical significance was assessed using rank analysis of covariance (FREEDOMS) and a covariance mixed-effect, repeat-measurement model (EXPAND). Subgroup analyses of patients in EXPAND with/without lesion activity or relapses prior to screening were also performed and will be presented. Analyses were for hypothesis generation without multiple comparison adjustment.

RESULTS: Treatment ES in FREEDOMS (N=843: fingolimod, n=425; placebo, n=418) at 24 months were −0.14, p=0.002 (EDSS); −0.18, p=0.002 (MI); −0.07, p=0.081 (C). Significant effects ($p<0.05$) were seen on MI from M6; effects on C were mostly nonsignificant. In EXPAND (N=1645: siponimod, n=1099; placebo, n=546), overall treatment effects were detected over 27M for EDSS (p=0.020), MI (p=0.014) and C (p=0.021). Significant ES were seen on MI (all $p<0.01$) at M9 (−0.28), 15 (−0.34) and 18 (−0.34), and on C at M18 (−0.24, $p<0.05$) and 27 (−0.54, $p<0.001$).

CONCLUSIONS: The benefits of fingolimod in patients with RRMS mainly impacted the MI subscale. For patients with SPMS, the benefits of siponimod were seen on both MI and C. In SPMS, effects on MI appeared earlier than on C, however the largest ES was seen later on C. Defining EDSS subscales with factor analyses may help improve their clinical usefulness.

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Disclosures

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