#0687: Effect of Siponimod on Grey Matter Atrophy in Patients with Secondary Progressive Multiple Sclerosis: Subgroup Analyses from the EXPAND Study

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Type

Abstract

Topic

MS and related disorders

Category

ePoster or Oral

Background and aims

Several studies suggest that grey matter (GM) atrophy is associated with long-term irreversible disability accumulation and cognitive decline. As reported previously, siponimod significantly reduced GM atrophy in patients with secondary progressive multiple sclerosis (SPMS). Here we investigated the effect of siponimod versus placebo in reducing cortical GM (cGM) and thalamic atrophy in subgroups of SPMS patients from the Phase 3 EXPAND study.

Methods

Percent volume change in cGM and the thalamus relative to baseline at Month (M)12 and M24 was assessed (EXPAND per protocol set, N=1560). The effect of siponimod versus placebo was determined using a mixed-model for repeated measures in patient subgroups defined by age and disease characteristics.

Results

In the placebo group, percentage volume change in cGM from baseline to M24 was similar across all subgroups (−1.17 to −0.94); whereas for thalamus it differed (−3.56 to −1.31) and was more pronounced in subgroups ‘with gadolinium-lesion activity’ (−3.56), ‘active disease’ (−2.15), ‘age <=45 years’ (−2.12), and ‘disease duration <=15 years’ (−2.09). Across the subgroups studied, siponimod reduced cGM atrophy versus placebo by 48% to 116% ($p<0.01$) and thalamic atrophy by 31% to 68% ($p<0.05$). Details on select subgroups in Table; further data on all subgroups will be presented.

	cGM			Thalamus		
Parameters	No. of patients[a] (siponimod/ placebo)	siponimod vs placebo (% relative reduction) M12	M24	No. of patients[a] (siponimod/ placebo)	siponimod vs placebo (% relative reduction) M12	M24
All patients	692/337	0.01 vs −0.60 (102%)***	−0.39 vs −1.04 (63%)***	696/342	−0.47 vs −0.94 (50%)***	−1.02 vs −1.77 (42%)***
Age <=45 y	246/120	0.10 vs −0.61 (116%)***	−0.30 vs −0.94 (68%)***	247/121	−0.38 vs −1.16 (67%)***	−0.82 vs −2.12 (61%)***
Age >45 y	466/217	−0.04 vs −0.60 (93%)***	−0.45 vs −1.08 (58%)***	449/221	−0.53 vs −0.82 (35%)*	−1.12 vs −1.63 (31%)*
EDSS score <6	319/165	0.02 vs −0.59 (103%)***	−0.37 vs −1.04 (64%)***	320/169	−0.40 vs −0.98 (59%)***	−0.98 vs −1.71 (43%)*
EDSS score >=6	373/172	0.00 vs −0.61 (100%)***	−0.42 vs −1.04 (60%)***	376/173	−0.54 vs −0.90 (40%)*	−1.00 vs −1.88 (47%)**
Active disease[b]	347/169	−0.02 vs −0.68 (97%)***	−0.50 vs −1.14 (56%)***	348/173	−0.74 vs −1.24 (40%)**	−1.41 vs −2.15 (34%)*
Non-active disease	344/167	0.04 vs −0.53 (108%)***	−0.27 vs −0.94 (71%)***	347/168	−0.20 vs −0.63 (68%)*	−0.56 vs −1.34 (58%)**
No prior DMT	152/74	−0.08 vs −0.71 (89%)***	−0.61 vs −1.36 (55%)***	154/77	−0.79 vs −1.47 (46%)*	−1.57 vs −2.64 (41%)*
Prior DMT	540/263	0.04 vs −0.57 (100%)***	−0.33 vs −0.94 (65%)***	542/265	−0.38 vs −0.78 (51%)**	−0.85 vs −1.53 (44%)**

***p<0.0001; **p<0.001, *p<0.05

[a]Per-protocol set, patients with major protocol deviations and data after the treatment switch were excluded from the analysis

[b]Active disease defined as the presence of relapses in the 2 years before screening and/or >= T1 Gd+ lesion at baseline

cGM, cortical grey matter; DMT, disease modifying therapy; EDSS, expanded disability status scale; Gd+, gadolinium enhancing; M, month

Data for additional subgroups by disease duration, presence or absence of relapses and Gd+ lesions will be presented in the poster

Percentage brain volume change from baseline at Month 12 and 24, as assessed by mixed model for repeated measures

Conclusion

Siponimod consistently slowed cGM and thalamic atrophy across all SPMS patient subgroups, including those with less active disease and higher disability. These effects on GM atrophy are in line with the favorable impact of siponimod on long-term clinical outcomes.

Disclosure

This study was funded by Novartis Pharma AG, Basel, Switzerland. A detailed disclosure from each author will be included in the oral/poster presentation. Abstract also submitted to AAN 2020; acceptance pending.

Affirmations

Authors agreement: I confirm, that all authors mentioned in the author block of this abstract have been informed about, and agreed to this submission. (I confirm)

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