Title

Siponimod First-Dose Effects in Patients With SPMS Receiving Concomitant Selective Serotonin Reuptake Inhibitor Therapy

Authors

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Abstract

BACKGROUND: Selective serotonin reuptake inhibitors (SSRIs), citalopram and escitalopram, are associated with prolonged QTc and torsades de pointes; transient heart rate decrease at initiation is a known effect of S1P modulators. Siponimod is a sphingosine 1-phosphate (S1P) receptor type 1,5 modulator, and is metabolized mainly by CYP2C9, followed by CYP3A4. It is approved in the USA for relapsing forms of multiple sclerosis (MS), including CIS, RRMS and active SPMS. First-dose observation with siponimod is only required in certain cardiac conditions but it is important to understand the cardiac effects in patients receiving concomitant SSRIs.

OBJECTIVES: Evaluate first-dose effects of siponimod in patients receiving concomitant SSRIs during the EXPAND trial.

METHODS: Analyses included data for the overall siponimod group (with or without SSRI), and subgroups of concomitant siponimod and any SSRI at first dose (Day 1), and concomitant siponimod and citalopram or escitalopram on Day 1.

RESULTS: In all, 1105 patients were randomized to siponimod; 167 received an SSRI on Day 1 and 85 received citalopram or escitalopram. For those with extended monitoring, in

the overall siponimod group, and the any SSRI and citalopram/escitalopram subgroups, most were discharged at 6 h post first dose (91.1%, 91.4% and 89.6%, respectively). Day 1 after first dose, 4 patients (0.4%) in the overall siponimod group had serious AEs (SAEs), 2 (0.2%) had bradycardia and 1 (0.1%) had second-degree atrioventricular (AV) block; no SAEs occurred in the any SSRI or citalopram/escitalopram subgroups. Few patients in the overall siponimod group had cardiac AEs on Day 1: 29 patients (2.6%) had bradycardia, 4 (0.4%) had first-degree AV block, 3 (0.3%) had second-degree AV block and 3 (0.3%) had prolonged QT interval. Incidence of cardiac AEs was low in the any SSRI subgroup: 3 patients (1.8%) had bradycardia and 3 (1.8%) had prolonged QT interval; in the citalopram/escitalopram subgroup, 2 patients (2.4%) had bradycardia and 1 (1.2%) had prolonged QT interval. In the overall siponimod group, 3 patients (0.3%) discontinued drug due to first- or second-degree AV block, or bradycardia. No patient receiving SSRIs had a cardiac AE causing treatment discontinuation.

CONCLUSIONS: Concomitant SSRI use did not appear to affect cardiac outcomes or heart rate changes associated with siponimod treatment initiation.

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Suggested submission category

Categories: Disease modifying therapy

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