Effect of Concurrent Use of Memantine on The Efficacy of Masupirdine (SUVN-502): A Post-hoc Analysis of a Phase-2 Randomized Placebo-Controlled Study

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Abstract

Background: Alzheimer’s disease (AD) is a neurodegenerative disorder manifested by progressive deterioration in cognition, memory and activities of daily living. The commonly used treatments in the management of cognitive and memory deficits associated with AD are either minimally effective, provide temporary relief or limited to use in a highly selected population. Selective blockade of serotonin-6 (5-HT6) receptors, which are exclusively localized in the central nervous system, is reported to play an important role in learning and memory. Masupirdine is a potent and selective 5-HT6 receptor antagonist with pro-cognitive properties in animal models of cognition.

Method: The efficacy and safety of masupirdine were evaluated in patients with moderate AD concurrently treated with donepezil and memantine. A total of 564 patients were randomized in a 1:1:1 ratio, using permuted blocked randomization. The study consisted of a 2 to 4-week screening period, a 26-week double blind treatment period, and a 4-week washout period. The primary efficacy outcome was the 11-item cognitive subscale of the Alzheimer’s Disease Assessment Scale (ADAS-Cog 11). In post-hoc analyses, patients were subdivided based on the use of memantine dosage form and memantine plasma concentrations to assess the impact of memantine on the efficacy of masupirdine.

Result: In this exploratory post-hoc analysis, less worsening of cognition (ADAS-Cog 11 scores) was observed with masupirdine treatment as compared to placebo in subjects whose trough memantine plasma concentrations were \( \leq 100 \text{ ng/mL} \).

Conclusion: These exploratory and thought provoking observations merit better understanding and further possible investigations of masupirdine effects and its role as a potential future drug in the AD pharmaceutical armamentarium.