Mavoglurant in adult patients with Fragile X Syndrome: Results of a randomized, double-blind study

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Background

Mavoglurant (AFQ056), a selective metabotropic glutamate receptor 5 antagonist, has been evaluated for the treatment of behavioral symptoms of fragile X syndrome (FXS). Here, the efficacy and safety of mavoglurant in adult patients (18-45 years) with FXS are reported.

Methods

This was a phase II, multicenter, randomized, double-blind (DB), placebo-controlled, parallel-group study (NCT01253629). After a 4-week, single-blind placebo run-in period, patients were randomized to mavoglurant (25, 50, or 100 mg BID) or placebo (1:1:1:1). In the DB phase, patients were initiated on 25 mg BID and were up-titrated to the target dose. The key endpoints were change from baseline to Week 12 in the Aberrant Behavior Checklist—Community edition using the FXS specific algorithm (ABC-C_{FX}) total score in patients with completely methylated (CM) (primary endpoint) and partially methylated (PM) Fragile X Mental Retardation 1 (FMR1) gene, individual subscales of the ABC-C_{FX}, and rating of change on Clinical Global Impression—Improvement (CGI-I). Safety assessments included adverse events (AEs), serious AEs, ECGs and laboratory evaluations.

Results

Of 175 randomized patients, 162 completed the study. Eleven of the 13 non-completers discontinued due to AEs. In the CM stratum, reduction in the mean ABC-C_{FX} total score was highest with mavoglurant 25 mg BID (-14.3), but there was no statistical significance for any of the mavoglurant groups (50 mg BID: 1.8; 100 mg BID: -1.8) vs placebo (-11.4). In the PM stratum, reduction was highest in the placebo group (-8.9), and there was no significant difference compared with the mavoglurant groups (25 mg BID: -1.9; 50 mg BID: -5.1; 100 mg BID: -4.6). Changes in ABC-C_{FX} subscale and CGI-I scores for the mavoglurant groups did not demonstrate benefits compared with placebo. The majority of AEs were mild with no clinically relevant changes in ECGs and laboratory test results.

Conclusion

Treatment with mavoglurant over 12 weeks did not demonstrate benefits compared with placebo for multiple behavioral symptoms on various efficacy scales. There is no evidence for an impact of methylation of FMR1 gene on response to mavoglurant on any of the efficacy measures assessed. Overall, mavoglurant was well tolerated.

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