Mavoglurant in adolescents with Fragile X Syndrome: Qualitative analysis of the Clinical Global Impression-Improvement (CGI-I) scale in a double-blind, placebo-controlled study

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Background

Mavoglurant (AFQ056), a selective metabotropic glutamate receptor subtype 5 antagonist, has been evaluated for the treatment of behavioral symptoms of patients with Fragile X Syndrome (FXS). Here, we present the qualitative analyses of the overall symptoms in adolescent patients with FXS from a phase II, randomized, double-blind (DB), placebo-controlled study (NCT01357239) using the narratives associated with the clinician-rated Clinical Global Impression-Improvement (CGI-I) scale.

Methods

Patients were randomized to receive either mavoglurant (25, 50, or 100 mg BID) or placebo over 12-weeks. Treatment response was assessed using the CGI-I scale for global improvement. Investigators who assigned patients a CGI-I score of 1 (very much improved), 2 (much improved), 6 (much worse), or 7 (very much worse) at any time during the study were provided with a standard narrative template for further information about the changes observed in these patients. These narratives were subsequently clustered into 6 overarching domains of function categories (Communication, Engagement, Behavior and Mood, Anxiety, Functional skills, Cognition and Academic performance), and then coded by an independent party (RTI International) under blinded conditions. After unblinding, an analysis of the repartition of patients who responded to

treatment (placebo or active at different doses) was performed for each of the six 6 function categories.

Results

134 patients reached 2 weeks or more of DB treatment on October 4, 2013. Thirty-four instances of a CGI-I score of 1 or 2 were reported in 29 patients. One patient had a CGI-I score of 6; none of the patients had a CGI-I score of 7. The most frequently reported domains of improvement were behavior and mood (82.8%), engagement (79.3%), and communication (75.9%). Individuals in the active treatment group did not perform better on any of the outcome domains compared with placebo. Worsening was reported in one patient on placebo.

Conclusion

Analysis of the CGI-I narratives did not indicate a higher level of treatment response in patients on mavoglurant compared with placebo. However, many of the comments made by investigators were based on parental report, and thus they do not represent a completely objective alternative assessment. The lack of efficacy observed in this study could be due to lack of efficacy of mavoglurant, however this analysis does not rule out the possibility that efficacy could have been evident with other measures.

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