Unique Considerations in the Treatment of Psychosis in DiGeorge Syndrome: A Case Report

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Abstract

Introduction. DiGeorge Syndrome is a microdeletion of chromosome 22q11.2 and is most commonly de novo. Manifestations of DiGeorge are wide-spread including cardiac malformations, palatal abnormalities, intellectual disability, hypocalcemia, dysmorphic facial features, and psychiatric disorders (psychotic disorders, Autism, ADHD, etc). This case report highlights difficulties with diagnosis and treatment of psychosis in DiGeorge. This 29 yo male with history of DiGeorge and associated cardiac anomalies presented to the outpatient clinic with prior diagnoses of schizoaffective disorder, bipolar disorder, DMDD, autism, and ADHD. Patient denied all symptoms, though mother noted hallucinations for 5–6 years. He was previously on aripiprazole and developed a resting tremor. With family history of Parkinson’s disease (PD), increased risk of PD in DiGeorge, and no improvement in tremor with dose reduction of aripiprazole or discontinuation of divalproex, neurology diagnosed PD, which was later negated when tremor resolved with complete discontinuation of aripiprazole. In our clinic we slowly increased divalproex and olanzapine, though parent concern of sedation limited higher doses. Patient had moderate improvement in symptoms per parents, but after several months on moderate-dose olanzapine, he developed a tremor. Sensitivity to extrapyramidal symptoms limits medication selection. Furthermore, QT prolongation in a population with cardiac abnormalities poses a unique risk. Given complexity and poor response, we researched pathogenesis and treatment of psychosis in DiGeorge.

Methods. We reviewed literature on PubMed with keywords including “DiGeorge,” “treatment,” “psychosis.” Specifically, we looked at articles addressing treatment response, efficacy, side effects, novel treatments, and the pathogenesis as it relates to treatment.

Results. Literature indicates that psychotic symptoms are more treatment resistant compared to psychotic disorders not associated with DiGeorge and there is little consensus on which antipsychotics are more effective. The 22q11.2 deletion contains the gene segment for catechol-O-methyltransferase (COMT) and the resulting COMT deficiency leads to excess catecholamines. The presence of the low activity COMT variant on the remaining allele is associated with possibly more severe psychiatric symptoms. Metyrosine may be a potential medication in the treatment of psychosis in DiGeorge by interfering with dopamine synthesis. Overall there is sparse research on treatment of psychosis in DiGeorge and a lack of firm recommendations.

Conclusion. This case study exemplifies the need for further research on DiGeorge Syndrome and treatment of psychosis. Treatment is complicated by cardiac abnormalities, comorbid neuropsychiatric conditions confounding diagnosis, and little research on treatments that target the unique pathogenesis. Research is inconsistent concerning recommendations and novel treatments are primarily anecdotal.

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Safety And Efficacy of Aripiprazole 2-Month Ready-to-Use 960 mg in Adult Patients With Schizophrenia

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Abstract

Background. Aripiprazole 2-month ready-to-use 960 mg (Ari 2MRTU 960) is a new long-acting injectable (LAI) antipsychotic formulation for gluteal administration every 2 months. This 32-week trial evaluated the safety, pharmacokinetics, and efficacy of multiple-dose administration of Ari 2MRTU 960 in clinically stable adults with schizophrenia or bipolar I disorder (BP-I), versus that of aripiprazole once-monthly 400 mg (AOM 400; an LAI indicated for the maintenance treatment of schizophrenia in adult patients stabilized with oral aripiprazole [indication varies by country]). Safety and efficacy outcomes in the subgroup of patients with schizophrenia are reported here.

Methods. Patients with schizophrenia were randomized to receive Ari 2MRTU 960 every 56±2 days or AOM 400 every 28±2 days. Safety and tolerability assessments included adverse event (AE) reporting, Visual Analogue Scale (VAS) scores (scale range: 0–100) for patient-reported injection site pain, and extrapyramidal symptom (EPS) monitoring. Efficacy was evaluated at Week 32 using mean (standard deviation [SD]) Clinical Global Impression – Improvement (CGI-I) score, and mean (SD) change from baseline in Clinical Global Impression – Severity (CGI-S) score, Subjective Well-being under Neuroleptic Treatment – Short Form (SWN-S) Total score, and Positive and Negative Syndrome Scale (PANSS) Total score.

Results. Study completion rate was 79.3% (73/92 patients) in the Ari 2MRTU 960 group and 67.7% (63/93 patients) in the AOM 400 group. Demographics and disease characteristics were well

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Balanced between groups at baseline (mean [SD] PANSS Total score: Ari 2MRTU 960, 62.0 [13.5]; AOM 400, 61.8 [13.5]; mean (SD) CGI-S score: Ari 2MRTU 960, 3.3 [0.9]; AOM 400, 3.1 [0.9]). Treatment-emergent AE (TEAE) incidence was 66.3% with Ari 2MRTU 960 and 63.4% with AOM 400. The most frequent TEAEs were increased weight (Ari 2MRTU 960, 21.7%; AOM 400, 18.3%) and injection site pain (Ari 2MRTU 960, 15.2%; AOM 400, 9.7%). Mean (SD) VAS score for pain after last injection was 1.5 (4.58) with Ari 2MRTU 960 and 1.3 (2.79) with AOM 400. Minimal change was seen in EPS in either group. At Week 32, mean (SD) CGI-I score was similar between groups (Ari 2MRTU 960, 3.5 [1.0]; AOM 400, 3.6 [0.9]). Minimal change from baseline was seen at Week 32 in CGI-S score and SWN-S Total score. There was no clinically meaningful difference between the groups for PANSS Total score (difference of least squares mean change from baseline [95% confidence interval]: -0.9 [-3.5, 1.8]; p=0.5154).

Conclusions. In patients with schizophrenia, administration of Ari 2MRTU 960, as compared with AOM 400, was generally well tolerated, and clinical stability was maintained during the study. Funding. Otsuka Pharmaceutical Development & Commercialization, Inc. (Princeton, NJ, USA) and H. Lundbeck A/S (Valby, Denmark).

Factor Analysis Investigating the Efficacy of HP-3070 Transdermal System in Positive and Negative Syndrome Scale Five Adults With Schizophrenia

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Abstract

Introduction. HP-3070, a once-daily asenapine transdermal system, is FDA-approved for adults with schizophrenia. In a pivotal phase 3 randomized controlled study, patients with schizophrenia who were treated once daily with HP-3070 demonstrated significant improvement in Positive and Negative Syndrome Scale (PANSS) total scores compared with placebo. The PANSS score’s five-factor structure can also assess treatment efficacy across different domains. This post-hoc analysis of the pivotal study evaluated the efficacy of HP-3070 by examining these domains.

Methods. In the pivotal phase 3 study, adults with acute exacerbations of schizophrenia were randomized to 6 weeks of treatment with HP-3070 3.8mg/24h, 7.6mg/24h, or placebo. Factor analysis of PANSS scores was performed using five domains (negative symptoms, positive symptoms, disorganized thought, uncontrolled hostility/excitement, anxiety/depression). Mixed-model repeated-measures (MMRM) analysis included change from baseline in PANSS factor score as the repeated dependent variable, with country, treatment, visit, treatment by visit interaction, and baseline PANSS score as covariates.