Results. The analysis included 607 patients. Least-squares mean estimates (standard error) of the difference from placebo in change from baseline to Week 6 for each factor were as follows: negative symptoms, 3.8mg/24h, -0.9 (0.43), P=0.045, and 7.6mg/24h, -0.4 (0.43), P=0.41; positive symptoms, 3.8mg/24h, -2.3 (0.57), P<0.001, and 7.6mg/24h, -2.0 (0.57), P<0.001; disorganized thought, 3.8mg/24h, -1.5 (0.38), P<0.001, and 7.6mg/24h, -0.9 (0.38), P=0.03; uncontrolled hostility/excitement: 3.8mg/24h, -1.1 (0.30), P<0.001, and 7.6mg/24h -0.9 (0.30), P=0.002; anxiety/depression, 3.8mg/24h, -0.5 (0.31), P=0.14, and 7.6mg/24h, -0.6 (0.31), P=0.07.
Conclusions. HP-3070 demonstrated treatment effects on a PANSS five-factor model, with the results indicating impact on negative symptoms, positive symptoms, disorganized thought, uncontrolled hostility/excitement, and anxiety/depression. These findings suggest that HP-3070 may address a broad range of symptoms in schizophrenia.
Funding. Noven Pharmaceuticals, Inc., a wholly-owned subsidiary of Hisamitsu Pharmaceutical, Co.

Safety and Efficacy of Aripiprazole 2-Month Ready-to-Use 960 mg in Adult Patients With Bipolar I Disorder

Jessica Madera-McDonough[1], Pedro Such[2], Murat Yildirim[2] and Roger S. McIntyre[3]

[1]Otsuka Pharmaceutical Development & Commercialization, Inc., Princeton, NJ, USA, [2]H. Lundbeck A/S, Valby, Denmark and [3]University of Toronto, Toronto, Canada

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 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 and maintenance monotherapy treatment of BP-I [indication varies by country]). Safety and efficacy outcomes in the subpopulation of patients with BP-I are reported here.
Methods. Patients with BP-I 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 assessed at Week 32 by Clinical Global Impression – Improvement (CGI-I), Clinical Global Impression – Bipolar Version (CGI-BP), Subjective Well-being under Neuroleptic Treatment – Short Form (SWN-S), Montgomery–Åsberg Depression Rating Scale (MADRS), and Young Mania Rating Scale (YMRS).
Results. Study completion rate was 72.5% (29/40 patients) in the Ari 2MRTU 960 group and 70.7% (29/41 patients) in the AOM 400 group. Demographics and baseline disease characteristics were generally well balanced between treatment groups. Treatment-emergent AE (TEAE) incidence was 82.5% with Ari 2MRTU 960 and 87.8% with AOM 400. The most frequent TEAEs were increased weight (Ari 2MRTU 960, 25.0%; AOM 400, 26.8%) and injection site pain (Ari 2MRTU 960, 25.0%; AOM 400, 7.3%). Mean (standard deviation [SD]) VAS score for pain after last injection was 1.2 (2.07) with Ari 2MRTU 960 and 1.3 (2.19) with AOM 400. Minimal change was seen in EPS in either group. At Week 32, mean (SD) CGI-I score was 3.1 [1.2] with Ari 2MRTU 960 and 3.2 [1.5] with AOM 400, and there was minimal mean (SD) change from baseline in CGI-BP score (Ari 2MRTU 960, -0.2 [1.0]; AOM 400, -0.6 [1.2]). Mean (SD) change from baseline in SWN-S Total score was 10.3 (16.1) with Ari 2MRTU 960 and 3.4 (21.4) with AOM 400. There was no clinically meaningful difference between the groups in MADRS Total score or YMRS Total score (difference of least squares mean change from baseline [95% confidence interval]: MADRS Total score -2.1 [-6.3, 2.1], p=0.3185; YMRS Total score 0.1 [-1.8, 2.1], p=0.8995).
Conclusions. In patients with BP-I, Ari 2MRTU 960 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).

Adjunctive Cariprazine in Patients With Major Depressive Disorder: Post Hoc Analysis of Efficacy by Baseline Antidepressant Response

George I. Papakostas[1], Paul Yeung[2], Chen Chen[2], Simranpreet Waraich[2] and Majid Kerolous[2]

[1]Massachusetts General Hospital, Boston, MA, USA and [2]AbbVie, Madison, NJ, USA

Abstract

Introduction. Patients with major depressive disorder (MDD) often have inadequate response to antidepressant treatment (ADT) requiring augmentation with other treatments. Cariprazine is a D_3-preferring D_3/D_2 and serotonin $5\text{-}HT_{1A}$ receptor partial agonist approved to treat schizophrenia and manic, mixed, and depressive episodes of bipolar I disorder. The efficacy of cariprazine as an adjunctive treatment for patients with MDD and inadequate response to ADT alone has been evaluated in phase 2/3 randomized, double-blind, placebo-controlled trials. Post hoc analyses of one phase 3 trial (NCT03738215) evaluated cariprazine + ADT for improving depressive symptoms in subgroups of patients categorized by 1) the level of response to ongoing ADT at baseline and 2) the number of ADTs associated with inadequate response during the current episode.

https://doi.org/10.1017/S1092852923001797 Published online by Cambridge University Press

Methods. Patients were randomized to placebo + ADT (n=254), cariprazine 1.5 mg/d + ADT (n=252), or cariprazine 3 mg/d + ADT (n=253) for 6 weeks of double-blind treatment. Post hoc analyses evaluated change from baseline to week 6 in MADRS total score in subgroups of patients who had ≥25%–<50% or <25% response to ongoing ADT at baseline, and in subgroups of patients who had inadequate response to 1 or ≥2 ADTs in the current episode. Analyses used a mixed-effects model for repeated measures; least squares mean differences (LSMD) versus placebo with 95% confidence interval (95% CI) were calculated.
Results. At baseline, 65.1% (n=486) of patients had an ADT response level between 25%–<50% and 34.9% (n=261) of patients had an ADT response level <25%. Mean MADRS total score reductions were greater for cariprazine 1.5 mg/d + ADT versus placebo + ADT in both ADT response subgroups (25%–<50% ADT response: -14.8 vs -11.9, LSMD [95% CI]=-2.3 [-4.2, -0.3]; <25% response to ADT: (-14.7 vs -11.7, LSMD [95% CI]=-2.6 [-5.5, 0.3]). For cariprazine 3 mg/d + ADT, mean change in MADRS total score was numerically greater versus placebo in both response subgroups (25%–<50% response=-14.2, LSMD [95% CI]=-1.5 [-3.5, 0.4]; <25% response= -12.3, LSMD [95% CI]=-0.74 [-3.6, 2.1]). Approximately 86% (n=644) and 14% (n=105) of patients in this study had inadequate response to 1 ADT or ≥2 ADTs, respectively, during the current episode. The LSMD (95% CI) in MADRS total score change for cariprazine 1.5 mg/d + ADT versus placebo + ADT was -2.3 (-4.1, -0.6) in the subgroup of patients with 1 previous ADT and -3.2 [-7.1, 0.8]) in the subgroup of patients with ≥2 previous ADTs. For cariprazine 3 mg/d + ADT, the LSMD (95% CI) in MADRS total score change versus placebo was -0.7 (-2.5, 1.0) in the 1 previous ADT subgroup and -4.7 (-8.8, -0.6) in the ≥2 previous ADTs subgroup.
Conclusions. In these post hoc analyses, cariprazine + ADT was associated with greater reductions in MADRS total score versus placebo regardless of the level of response to ongoing ADT at baseline or number of prior ADT failures in the current episode.
Funding. AbbVie

Categorical Improvement in Depressive Symptom Severity: Results From a Randomized Controlled Trial of Cariprazine for Adjunctive Treatment of MDD

Prakash S. Masand[1], Chen Chen[2], Julie L. Adams[2], Ken Kramer[2] and Majid Kerolous[2]

[1]Duke-NUS (National University of Singapore), Singapore and [2]AbbVie, Madison, NJ, USA

Abstract

Background. Patients with major depressive disorder (MDD) often do not respond to antidepressant (ADT) monotherapy alone and may require adjunctive treatment to provide adequate symptom relief. Cariprazine (CAR) is a dopamine D_3-preferring D_3/D_2 and serotonin 5-HT_{1A} receptor partial agonist approved to treat adults with schizophrenia and manic, mixed, or depressive episodes of bipolar I disorder. Post hoc analysis of data from a randomized controlled trial evaluated clinically relevant improvements in depressive symptom severity with adjunctive cariprazine in patients with MDD and inadequate response to ADT monotherapy.
Methods. Post hoc analysis evaluated data from a randomized, double-blind, placebo-controlled MDD trial (NCT03738215) in patients treated with CAR (1.5 mg/d or 3 mg/d) + ADT or placebo + ADT; the primary outcome was change from baseline to week 6 in Montgomery-Åsberg Depression Rating Scale (MADRS) total score. Post hoc analysis evaluated category shifts from baseline to week 6 in MADRS severity (normal <6, mild 7–19, moderate 20–34, severe ≥35). MADRS severity shifts were reported as the percentage of patients with no change or worsened severity, 1 category improvement, ≥1 category improvement, and ≥2 category improvement. Examples of categorical shifts in depressive symptoms at week 6 include change from severe at baseline to moderate (1 category improvement) and change from severe at baseline to mild (2 category improvement).
Results. Of the 751 patients in the intent-to-treat (ITT) population (CAR: 1.5 mg/d=250, 3.0 mg/d=252; placebo=249), baseline MADRS severity was mild in 1.5%, moderate in 64%, and severe in 35%. Fewer CAR + ADT patients compared to placebo + ADT had no change or worsened MADRS severity at week 6 (CAR: 1.5 mg/d=32%, 3.0 mg/d=33%; placebo=42%). Approximately 68% of patients treated with CAR + ADT demonstrated a MADRS severity improvement of 1 category or greater by week 6 (CAR: 1.5 mg/d=68%, 3.0 mg/d=67%; placebo=58%). A greater percentage of patients in the CAR 1.5 mg/d group also had a 2 or greater category improvement versus CAR 3.0 mg/d or placebo 6 (CAR: 1.5 mg/d=28%, 3.0 mg/d=17%; placebo=19%).
Conclusions. In this post hoc analysis, CAR + ADT was associated with a greater proportion of patients with improvements in depressive symptom severity categories compared with placebo + ADT. These results may suggest that CAR + ADT is associated with clinically meaningful depressive symptom improvement in MDD patients.
Funding. AbbVie

Vilazodone-Induced Glycolimia

Maria de Guadalupe Jimenez Ayasta, MD and Alan Richard Hirsch, MD

Smell and Taste Treatment and Research Foundation, Chicago, Illinois

Abstract

Introduction. Glycolimia is observed in a plethora of medical conditions including burning mouth syndrome, opioid withdrawal, as well as from a variety of medications including vortioxetine, l-methylfolate, lisdexamfetamine, and gabapentin. While vilazodone, an antidepressant with agonist like effects on 5-HT1A receptors, has been found to induce hyperglycemia, it has not heretofore been reported to induce glycolimia. Such a case is described.
Method. Case study: A 60-year-old, left-handed (pathological) male presented with a past history of depression, minimally

https://doi.org/10.1017/S1092852923001797 Published online by Cambridge University Press