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).

Lumateperone in Pooled Late-Phase Schizophrenia Trials: Number Needed to Treat, Number Needed to Harm, and Likelihood to Be Helped or Harmed

Leslie Citrome, MD, MPH[1], Suresh Durgam, MD[2], John B Edwards, MD[2] and Robert E Davis, PhD[2]

[1]New York Medical College, Valhalla, New York, USA and [2]Intra-Cellular Therapies, Inc., New York, New York, USA

Abstract

Background. Lumateperone is an FDA-approved antipsychotic to treat schizophrenia and depressive episodes associated with bipolar I or bipolar II disorder as monotherapy and as adjunctive therapy with lithium or valproate. This post hoc analysis investigated the efficacy and tolerability of lumateperone in patients with schizophrenia via number needed to treat (NNT), number needed to harm (NNH), and likelihood to be helped or harmed (LHH).
Methods. Data were pooled from three late-phase 4–6 week placebo-controlled studies of lumateperone 42 mg/day in adults with schizophrenia and an acute exacerbation of psychosis (Study 005 [NCT01499563], Study 301 [NCT02282761], Study 302 [NCT02469155]). NNT and NNH were calculated vs placebo for several different Positive and Negative Syndrome Scale [PANSS] Total score response cutoffs (percent reduction from baseline) and for adverse events (AEs), respectively.
Results. In the two informative studies (placebo, n=221; lumateperone, n=224), the NNT vs placebo for lumateperone was statistically significant for PANSS Total score reductions from baseline to 4 weeks/endpoint of ≥20% (NNT=9, 95% confidence interval [CI] 5–36) and ≥30% (NNT=8; 95%CI 5–21). In all studies pooled (placebo, n=412; lumateperone, n=406), study discontinuations due to AEs were uncommon and the NNH (389) was not statistically significant from placebo. The only AE with NNH vs placebo <10 was somnolence/sedation (NNH=8; 95%CI 6–12). With lumateperone treatment, weight gain ≥7% from baseline was similar to placebo (NNH=112) and fewer patients experienced akathisia than placebo. Lumateperone LHH ratios were >>1 for all AEs (range 13.6–48.6) except somnolence/sedation (LHH~1).
Conclusion. Lumateperone's benefit-risk profile was favorable in late-phase schizophrenia trials.
Funding. Intra-Cellular Therapies, Inc.

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

Leslie Citrome, MD, MPH[1], Mariacristina Castelli, PhD[2], Sandeep Byreddy, MS[2], Masami Hasebe, MPharm[3], Takaaki Terahara, PhD[3], Justin Faden, DO[4] and Marina Komaroff, DrPH[2]

[1]Department of Psychiatry and Behavioral Sciences, New York Medical College, Valhalla, NY, USA, [2]Product Development, Noven Pharmaceuticals, Inc., Jersey City, NJ, USA, [3]Hisamitsu Pharmaceutical Co., Inc., Chiyoda-ku, Tokyo, Japan and [4]Department of Psychiatry, Lewis Katz School of Medicine at Temple University, Philadelphia, PA, USA

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.

https://doi.org/10.1017/S1092852923001773 Published online by Cambridge University Press

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/S1092852923001773 Published online by Cambridge University Press