when the lower dose range of CAR is used, a more favorable NNH regarding discontinuation because of an AE.
Importance. The benefit-risk profile of CAR is favorable for adjunctive treatment of MDD.
Funding. AbbVie

Effect of Adjunctive Cariprazine on Symptoms of Anhedonia in Patients with Major Depressive Disorder

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Purpose. Anhedonia, a multidimensional domain including the reduced ability to experience pleasure, is a core diagnostic symptom of major depressive disorder (MDD) and a common residual symptom. In patients with MDD, anhedonia has been associated with poor treatment outcomes, suicide and reduced functioning and quality of life. This post-hoc analysis of data from a phase 3 trial (NCT03738215) evaluated the efficacy of adjunctive cariprazine (CAR) treatment on anhedonia symptoms in patients with MDD.
Methods. Patients with MDD and inadequate response to ongoing antidepressant therapy (ADT) were randomized to CAR 1.5 mg/d + ADT, CAR 3 mg/d + ADT, or placebo + ADT for 6 weeks of double-blind treatment. Post hoc analyses evaluated the change from baseline to Week 6 in Montgomery–Åsberg Depression Rating Scale (MADRS) total score, MADRS anhedonia subscale score (items: 1 [apparent sadness], 2 [reported sadness], 6 [concentration difficulties], 7 [lassitude], and 8 [inability to feel]), and MADRS anhedonia item 8 in the overall modified intent-to-treat (mITT) population and in subgroups of patients with baseline MADRS anhedonia item 8 score of ≥4 or baseline anhedonia subscale score of ≥18. Least square (LS) mean change from baseline to Week 6 was analyzed using a mixed-effects model for repeated measures.
Results. There were 751 patients in the mITT population (CAR + ADT: 1.5 mg/d=250, 3 mg/d=252; placebo + ADT=249). At baseline, 508 (67.6%) patients had MADRS anhedonia item 8 scores ≥4, and 584 (77.8%) had MADRS anhedonia subscale scores ≥18. In the overall mITT population, LS mean change from baseline to Week 6 in anhedonia subscale score was significantly greater for CAR 1.5 mg/d + ADT (-8.4) and CAR 3 mg/d + ADT (-7.9) than for placebo + ADT (-6.8; both $P<.05$). The LS mean change from baseline in MADRS individual item 8 was also significantly greater for CAR 1.5 mg/d + ADT (-1.7) vs placebo + ADT (-1.3; $P=.0085$). In both subgroups of patients with baseline anhedonia, CAR 1.5 mg/d + ADT was associated with significantly greater reduction in MADRS total score, MADRS anhedonia subscale score, and MADRS item 8 score compared with placebo + ADT (all $P<.05$). In the CAR 3 mg/d + ADT group, significantly greater reductions vs placebo + ADT were observed for MADRS total score and MADRS anhedonia subscale score in the subgroup of patients with baseline anhedonia subscale scores ≥18 (both $P<.05$).
Importance. Adjunctive treatment with CAR was associated with a reduction in symptoms of anhedonia relative to adjunctive placebo in patients with MDD and inadequate response to ADT alone. In subgroups of patients with moderate-to-severe anhedonia at baseline, CAR + ADT demonstrated greater improvements than placebo + ADT in overall depressive symptoms and symptoms of anhedonia. These results suggest that adjunctive CAR treatment may be effective for improving symptoms of anhedonia in patients with MDD who have symptoms of anhedonia.
Funding. AbbVie

Incidence and Characteristics of Akathisia with Adjunctive Cariprazine Treatment in Patients with Major Depressive Disorder

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Purpose. Akathisia is a common adverse effect associated with use of dopamine receptor blocking agents.[1,2] Symptoms of akathisia, in severe cases, may lead to discontinuation of treatment. Cariprazine is a dopamine D_3-preferring D_3/D_2 receptor partial agonist and serotonin 5-HT_{1A} receptor partial agonist approved to treat schizophrenia and acute manic, mixed, and depressive episodes of bipolar 1 disorder. Cariprazine is well tolerated in patients across its indications, but is associated with a higher incidence of akathisia compared with placebo.[3,4] This pooled post hoc analysis of data from phase 3 clinical trials of adjunctive cariprazine aimed to characterize the incidence, severity, and management of akathisia and other extrapyramidal symptoms (EPS) in adult patients with MDD.
Methods. Patients with MDD and inadequate response to ongoing antidepressant therapy (ADT) were randomized to cariprazine 1.5 mg/d + ADT, cariprazine 3 mg/d + ADT, or placebo + ADT for 6 weeks of double-blind treatment. Post hoc analysis evaluated incidence, severity, and time to resolution of akathisia, restlessness, and other EPS; use of rescue medications; and the rate of discontinuation due to these treatment-emergent adverse events (TEAEs).
Results. A total of 1508 patients (cariprazine + ADT: 1.5 mg/d, n=502, 3 mg/d, n=503; placebo + ADT, n=503) were included in these 2 studies. The incidence of akathisia was greater with cariprazine 3 mg/d + ADT (9.7%) than with cariprazine 1.5 mg/d + ADT (6.4%) and placebo + ADT (2.0%). Most patients treated with

https://doi.org/10.1017/S1092852924001597 Published online by Cambridge University Press