obese populations. Both drug combinations displayed these benefits after approximately 7 weeks. OLZ/MET's weight mitigation was largely commensurate with increases in both dosage and duration of treatment. OLZ/SAM's most efficacious dosage was not readily apparent. The maximum reduction in weight gain was achieved when MET was titrated to a daily dose of 2000 mg, although significant prevention of weight gain has been reported with lower doses as well. The mean weight change for OLZ/MET over 24 weeks was +5.5 lbs on 2000 mg per day. The mean weight change for OLZ/SAM over 24 weeks was +7.0 lbs., however, the average dose of OLZ/SAM was not reported. These results were seen in both adult and non-adult populations. OLZ/MET is considerably more affordable in comparison to OLZ/SAM. Other notable differences included dosage flexibility and scheduling, contraindications in select populations, and common side effects, among others.

Conclusions. Weight gain is a serious side effect of many antipsychotics and can greatly impair a patient's quality of health and life. Drug combinations such as OLZ/SAM and OLZ/MET are crucial to help minimize the morbidity caused by medication-induced obesity. Both combinations showed effectiveness in reducing rates of weight gain but these effects were delayed until approximately 7 weeks. OLZ/MET's effectiveness was positively correlated with increased dosages and duration, unlike OLZ/SAM in which no such relation could be convincingly established. OLZ/SAM's relatively high cost is likely prohibitive for many persons, especially considering mental illness' often devastating socioeconomic impact.

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Impact of Cariprazine on Anhedonia Symptoms in Patients with Bipolar I Depression: Pooled Analysis of 3 Pivotal Clinical Trials

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Purpose. Anhedonia characterizes major depressive episodes in bipolar depression and is associated with more severe illness/poor prognosis. These post hoc analyses assess effect of cariprazine 1.5 and 3 mg/d on anhedonia symptoms in patients with bipolar I depression.

Methods. Data were pooled from 3 randomized, double-blind, placebo-controlled bipolar I depression trials in cariprazine. Cariprazine 1.5 and 3 mg/d versus placebo were evaluated in patient subgroups stratified by median baseline MADRS anhedonia score (higher anhedonia=score ≥19; lower anhedonia=score <19). Outcomes included mean change from baseline to week 6 in MADRS total and anhedonia factor score (sum of apparent sadness, reported sadness, concentration, lassitude, and inability to feel items). The proportion of patients with week 6 anhedonia factor response (≥50% improvement from baseline) was also determined. Changes from baseline were analyzed using a mixed-effect model for repeated measures.

Results. There were 760 patients in the higher anhedonia subgroup (placebo=249, cariprazine: 1.5 mg/d=261; 3 mg/d=250) and 623 patients in the lower anhedonia subgroup (placebo=211, cariprazine: 1.5 mg/d=200; 3 mg/d=212). Mean baseline MADRS total score was higher in the higher anhedonia subgroup (total=33.6) than in the lower anhedonia subgroup (total=27.6). Change from baseline to week 6 in MADRS total score was greater for both cariprazine doses versus placebo in the higher anhedonia subgroup (least squares mean difference [LSMD] and 95% confidence interval [CI]: 1.5 mg/d=-3.01 [-4.84, -1.19], *P*=.0012; 3 mg/d: -3.26 [-5.12, -1.40], *P*=.0006); in the lower anhedonia subgroup, cariprazine 1.5 mg/d was statistically significant versus placebo (-2.61 [-4.28, -0.93], *P*=.0024). In the higher anhedonia subgroup at week 6, change from baseline in anhedonia factor score was significant versus placebo for both cariprazine doses (1.5 mg/d=-1.97 [-3.13, -0.81], *P*=.0009; 3 mg/d=-2.07 [-3.26, -0.89], *P*=.0006); in the lower subgroup, the difference was significant versus placebo for cariprazine 1.5 mg/d (-1.70 [-2.77, -0.62], *P*=.0021). After adjusting for changes in other depressive symptoms, LSMDs versus placebo in the anhedonia factor score remained significant for cariprazine 1.5 mg/d (-1.21 [-2.05, -0.36], *P*=.0052) and 3 mg/d (-1.00 [-1.86, -0.14], *P*=.0233) in the higher anhedonia subgroup, and for 1.5 mg/d (-1.06 [-1.92, -0.19], *P*=.0164) in the lower subgroup. In the higher anhedonia subgroup, rates of anhedonia factor response were greater versus placebo (31.7%) for cariprazine 1.5 mg/d (44.8%, *P*=.0028) and 3 mg/d (45.6%, *P*=.0019); in the lower subgroup, response rates were 39.3% for placebo, 48.0% for 1.5 mg/d, and 46.7% for 3 mg/d. Adverse events in ≥5% cariprazine and twice placebo were nausea, akathisia, restlessness, and EPS.

Importance. Those with bipolar depression and anhedonia cariprazine demonstrated a potent antidepressant and antianhedonic effect in higher/lower anhedonia subgroups.

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Impact of Predominant Polarity on Cariprazine Efficacy in Patients with Bipolar I Disorder: A Pooled Analysis

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