anxiety disorder, clipped-intracranial aneurysm. She had been taking Duloxetine for major depressive disorder and fibromyalgia, and Carbamazepine was initiated to manage abnormal movements and her depressive symptoms. She reported improvement in the frequency and severity of abnormal movements after initiating Carbamazepine. Unfortunately, her depression worsened, and she was admitted to the inpatient unit for suicidal ideation and auditory and visual hallucinations commanding her to end her life. She was initiated on Aripiprazole. She was admitted for four days and was discharged after she demonstrated improvement in mood and severity of auditory hallucinations.
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Solriamfetol for Excessive Sleepiness in Narcolepsy and Obstructive Sleep Apnea: Effect Sizes and Numbers Needed to Treat or Harm

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Introduction. Solriamfetol (Sunosi®), a dopamine/norepinephrine reuptake inhibitor that has been shown to activate TAAR1, is approved (US and EU) to treat excessive daytime sleepiness (EDS) in adults with narcolepsy (75-150 mg/day) or obstructive sleep apnea (OSA) (37.5-150 mg/day).Effect size, number needed to treat (NNT) and number needed to harm (NNH) are statistical representations of efficacy and tolerability that clinicians may find helpful in guiding treatment decisions. This analysis characterized these statistical parameters from two registrational studies.

Methods. Post-hoc analysis of data from two phase 3 studies in adults with excessive daytime sleepiness associated with narcolepsy (TONES 2) or obstructive sleep apnea (TONES 3). Effect size compared to placebo, NNT, and NNH were calculated based on previously published endpoints, post-hoc analyses, and adverse events.

Results. On the maintenance of wakefulness test (MWT), effect size compared to placebo (*Cohen's d*) was 0.29, 0.82, and 1.13 for 75mg, 150mg, and 300mg doses of solriamfetol in TONES 2 and 0.46, 0.89,1.08, and 1.28 for 37.5mg, 75mg, 150mg, and 300mg, respectively. On the Epworth sleepiness scale (ESS), *d* was 0.47, 0.80, and 1.02 for 75mg, 150mg, and 300mg doses in TONES 2, and 0.42, 0.37, 0.99, and 1.04 for 37.5mg, 75mg, 150mg, and 300mg doses in TONES 3. NNT for patients achieving an ESS ≤10 was 7, 5, and 3 for 75mg, 150mg, and 300mg doses in TONES 2 and 8, 6, 4, and 3 for 37.5mg, 75mg, 150mg, and 300mg doses in TONES 3. On the patient global impression of change (PGIc), NNT was 4, 3, and 3 for 75mg,150mg, and 300mg doses in TONES 2 and 16, 5, 3, and 3 for 37.5, 75mg, 150mg, and 300mg in TONES 3. Similar NNT were found for the clinician global impression of change (CGIc) as for the PGIc. In both TONES 2 and TONES 3, NNH pooled across doses for adverse events occurring in at least 5% of patients and greater than placebo were all >10, with the exception for headache in TONES 2 (NNH=6).

Conclusion. This post-hoc analysis demonstrates favorable effect size, NNT and NNH values for solriamfetol in the treatment of EDS associated with narcolepsy and OSA.
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Comparison of the Literature Regarding Weight Gain Between Olanzapine/Metformin and Olanzapine/Samidorphan Combinations

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Introduction. Many potent antipsychotics, such as olanzapine (OLZ), can cause significant and rapid weight gain as a potential side effect. This can lead to medication non-adherence and recurrence of psychiatric outcomes, or developing cardiometabolic risk factors that increase the risk of heart disease. The olanzapine-samidorphan (OLZ/SAM) drug combination has demonstrated ability to mitigate the weight gain caused by OLZ. However, olanzapine-metformin (OLZ/MET) combinations have also been studied for weight gain problems before the introduction of OLZ/SAM. The authors will review the similarities and differences between OLZ/SAM and OLZ/MET combinations regarding weight gain.

Methods. In this literature review, we conducted a non-systematic search in PubMed and Google Scholar, utilizing specific key words, such as "Olanzapine", "Metformin", "Samidorphan", and "Weight Gain." Case reports/series and narrative reviews were excluded, and only English-language studies reporting weight change or rate of weight change outcomes were included. Data extraction and qualitative synthesis were performed for the selected studies.

Results. OLZ/SAM has shown the ability to effectively reduce weight gain in non-obese populations, however, OLZ/MET has shown the ability to decrease weight gain in both obese and non-

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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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