same population to test its efficacy in not just Pacific Islanders, but all youth.
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REFERENCES:

1. Birmaher, B.; *et al.* "Practice Parameter for the Assessment and Treatment of Children and Adolescents With Depressive Disorders".
2. Richardson, L; D DiGiuseppe; M. Garrison. "Depression in Medicaid-Covered Youth". *Arch Pediatr Adolesc*. 2003; **157**: 984-989.
3. Rossom, R; S Shortreed; K Coleman; *et. al.* "Antidepressant Adherence across Diverse Populations and Healthcare Settings". *Depress Anxiety*. 2016; **33**: 765–774.

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Insulin Sensitivity and Glucose Metabolism of Olanzapine and Combination Olanzapine and Samidorphan: A Phase 1 Exploratory Study in Healthy Volunteers

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ABSTRACT: Background: A combination of olanzapine and samidorphan (OLZ/SAM) is in development for schizophrenia to provide the efficacy of olanzapine while mitigating olanzapine-associated weight gain. The objective of this phase 1 exploratory study was to assess metabolic treatment effects of OLZ/SAM.

METHODS: Healthy, non-obese adults (18–40 years) were randomized 2:2:1 to once-daily OLZ/SAM, olanzapine, or placebo for 21 days. Assessments included oral glucose tolerance test (OGTT), hyperinsulinemic-euglycemic clamp, weight gain, and adverse event (AE) monitoring. Treatment effects were estimated with analysis of covariance.

RESULTS: Sixty subjects were randomized (OLZ/SAM, n=24; olanzapine, n=24; placebo, n=12); 19 (79.2%), 22 (91.7%), and 11 (91.7%), respectively, completed the study. In the OGTT, olanzapine led to significant hyperinsulinemia (P<0.0001) and significantly reduced insulin sensitivity (2-hour Matsuda index) at day 19 vs baseline (P=0.0012), changes not observed with OLZ/SAM. No significant between-group differences were observed for change from baseline in clamp-derived insulin sensitivity index at day 21. Least squares mean weight change from baseline was similar with OLZ/SAM (3.16 kg) and olanzapine (2.87 kg); both were significantly higher than placebo (0.57 kg; both P<0.01). Caloric intake significantly decreased from baseline to day 22 with OLZ/SAM (P=0.015) but not with olanzapine or placebo. Forty-nine subjects (81.7%) experienced ≥1 AE (OLZ/SAM, 87.5%; olanzapine, 79.2%; placebo, 75.0%).

CONCLUSIONS: In this exploratory study, hyperinsulinemia and decreased insulin sensitivity were observed in the OGTT with olanzapine but not with OLZ/SAM or placebo. Clamp-derived insulin sensitivity index and weight changes were similar with OLZ/SAM and olanzapine in healthy subjects during the 3-week study.
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The Safety and Tolerability of Lumateperone 42 mg for the Treatment of Schizophrenia: A Pooled Analysis of 3 Randomized Placebo-Controlled Trials

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ABSTRACT: Introduction: Lumateperone (ITI-007) is in late-phase clinical development for schizophrenia. Lumateperone has a unique mechanism of action that modulates serotonin, dopamine, and glutamate neurotransmission.

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