Reversal of Antipsychotic-Induced Weight Gain in Rats with Miricorilant, a Selective Glucocorticoid Receptor (GR) Modulator

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The following poster describes a use that has not been approved by the U.S. Food and Drug Administration.

ABSTRACT
Background: Antipsychotic-induced weight gain is a significant problem for patients with schizophrenia and can contribute significantly to the observed elevated morbidity and mortality [4]. Although second-generation antipsychotic medications have been associated with a lower incidence of metabolic adverse events compared to first-generation antipsychotics, the use of antipsychotics continues to contribute significantly to the observed elevated morbidity and mortality [4]. A clinical trial of olanzapine-induced weight gain in rats

Medications: Glucocorticoid receptor agonists and ligands

AIMS: Aims of this study were to evaluate the safety, efficacy, and pharmacokinetics of miricorilant in reversing antipsychotic-induced weight gain in rats. We now report the ability of miricorilant to reverse olanzapine-induced weight gain in rats. Miricorilant has successfully attenuated olanzapine-induced weight gain in healthy male subjects, and the present study aimed to extend these findings to rats. Therefore, the purpose of this study was to evaluate the safety, efficacy, and pharmacokinetics of miricorilant in reversing antipsychotic-induced weight gain in rats with schizophrenia.

METHODS: Male Sprague-Dawley rats were randomized to 4 different interventions and remained on study until day 57: (1) OLZ-only (Olanzapine, 1.2 mg/kg BID); (2) OLZ + 1 mg/kg BID miricorilant; (3) OLZ + 2 mg/kg BID miricorilant; (4) OLZ + 10 mg/kg/day miricorilant once daily. Subjects were assessed on a weekly basis for body weight, food consumption, mortality, and clinical observations. Conclusions: Miricorilant was effective in reversing the weight gain associated with olanzapine in Sprague-Dawley rats. This finding is consistent with our previous research in healthy male volunteers and extends our findings to rats with schizophrenia.

REFERENCES

ACKNOWLEDGMENTS
The Grantee (Corcept Therapeutics) is supported by Corcept Therapeutics.

DISCLOSURES
APL, JK, AAM, HR: Employees, Corcept Therapeutics.

Table 1. Key Inclusion and Exclusion Criteria for the GRATITUDE Study

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<th>Criteria</th>
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Protocol version.

Editorial support was provided by Tina K. Schlafly of Corcept Therapeutics. Funding for editorial, design, and production support was provided by Corcept Therapeutics.

Supported by funding from Concept Therapeutics

Prepared for the American Psychiatric Association Annual Meeting, April 25–29, 2020, Philadelphia, PA