**BACKGROUND**

Uncontrolled hepatic gluconeogenesis is suggested to play a central role in unstable T1DM. Restoration of normal portal insulin/glucagon ratios may enable tighter regulation of gluconeogenesis and glucogenolysis. Orally administered insulin is speculated to induce similar effects, while offering the benefit of hepatic first-pass insulin metabolism, reduced systemic exposure and ease-of-use.

**OBJECTIVE**

To assess the safety and impact of an orally delivered insulin in combination with standard patient insulin therapy, on the stability of glycemic readings in uncontrolled T1DM patients.

**RESULTS**

No adverse events were reported throughout the 15-day study period. Oral insulin support yielded more frequent blood glucose recordings below 70 mg/dL, when compared to the pretreatment phase (Figure 1; 1.99±0.88% versus 0.45±0.2%, respectively; p=0.06). In parallel, the frequency of glucose readings >200 mg/dL was 24.4% lower upon addition of ORMD-0801 to the treatment regimen (Figure 2; p=0.026). ORMD-0801 treatment led to a 16.6% decrease in glucose area under the curve values, with the largest reductions (21.2%) measured between 5-7 PM (Figure 3).

**CONCLUSIONS**

Concomitant administration of orally and subcutaneously delivered insulins was safe and well tolerated by the participating uncontrolled T1DM patients. Moreover, the recorded glucose profiles suggest that ORMD-0801 can stabilize blood glucose concentrations, with a most prominent effect during evening hours. Future studies will be required to assess translation of this therapy into reduced levels of HbA1c, and of risks associated with uncontrolled T1DM.

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