A Single-Blind, Two-Period Study to Assess the Safety and Pharmacodynamics of an Orally Delivered GLP-1 Analog (Exenatide) in Healthy Subjects

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INTRODUCTION

Glucagon-like peptide 1 (GLP-1), secreted within minutes of food ingestion, is associated with a gamut of physiological processes, including induction of insulin release, support of normoglycemia, β-cell function preservation, improved lipid profiles, increased insulin sensitivity, inhibition of glucagon secretion and delayed gastric emptying. Thus, GLP-1 harbors significant therapeutic potential for regulating Type 2 diabetes, where GLP-1 secretion is reduced. However, clinical use of the native GLP-1 is limited due to its rapid enzymatic inactivation resulting in a t1/2 of 2-3 minutes. To overcome this obstacle, both natural and synthetic, long-acting degradation-resistant peptides, GLP-1 mimetic agents have been designed and introduced to the clinic. To date, GLP-1 analogs are only available as injectable dosage forms and its oral delivery is expected to provide physiological portal/peripheral concentration ratios while fostering patient compliance and adherence.

OBJECTIVES

To evaluate the safety and tolerance of ORMD-0901

To test the insulinogenic response of subjects orally treated with ORMD-0901 versus placebo before a glucose challenge.

DESIGN

First-in-human, single-blind, two-period study focusing on the induced insulinogenic responses to orally administered exenatide. Six fasting, healthy, male volunteers (ages: 18-19; BMI: 18.4-20.1) were administered a placebo or exenatide-based capsule (150 μg), on visits 1 and 2, respectively. The oral formulation of exenatide was well tolerated by all six subjects (visit 2) and no serious adverse events occurred. Nausea is the most frequently reported adverse reaction to subcutaneous exenatide treatments and typically occur in a dose-dependent fashion. Other common side effects include vomiting, diarrhea and dyspepsia. Thus, the safety data collected from this preliminary study suggest improved exenatide tolerance when delivered via Oramed’s oral formulation technology.

SAFETY RESULTS/DISCUSSION

The oral formulation of exenatide was well tolerated by all six subjects (visit 2) and no serious adverse events occurred. Nausea is the most frequently reported adverse reaction to subcutaneous exenatide treatments and typically occur in a dose-dependent fashion. Other common side effects include vomiting, diarrhea and dyspepsia. Thus, the safety data collected from this preliminary study suggest improved exenatide tolerance when delivered via Oramed’s oral formulation technology.

REFERENCES


CONCLUSIONS

This first-in-human study has demonstrated that Oramed’s proprietary technology provides for retained biological functionality or orally delivered exenatide. In addition, the drug preparation was safe and failed to induce any adverse events. These encouraging results provide a strong impetus for us to continue the development of this promising drug.

Development of oral delivery platforms for exenatide and other incretins and incretin mimetics may convey physiological portal/peripheral concentration ratios while fostering patient compliance and adherence.

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