Oral Insulin: Type I Diabetes (T1DM) Patient Response Upon Preprandial Administration

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INTRODUCTION

Oral insulin (ORMD-0801) formulated with Oramed Pharmaceutical’s proprietary technology has been previously shown to be absorbed and to impart clinically relevant pharmacodynamic effects in both healthy and Type 2 diabetic volunteers. This Phase IIa study describes a first exposure of Type I diabetic (T1DM) patients to Oramed’s oral insulin, evaluation of the pharmacokinetics (PK) and pharmacodynamics (PD) of the drug and assessment of the influence of time to food ingestion on ORMD-0801 absorption.

OBJECTIVES

• To evaluate the safety of ORMD-0801 when administered preprandially to T1DM patients.
• To evaluate the PK and PD of ORMD-0801 in T1DM patients.

METHODS

Single-blind, open-label, single-center; 8 T1DM, male subjects (ages 24-41, diabetics for 2-28 years, HgA1C 6.63-8.63%), regularly treated with no-peak insulin. Two capsules of ORMD-0801 (8 mg insulin each) were orally administered to fasting subjects. A standard 400 kcal meal was served at 10, 45 or 90 min thereafter. Blood samples were routinely collected over the 6-hr post-ORMD-0801 administration to monitor insulin levels. In parallel, at each sampling time, mean glucose levels were calculated from the readings of two different glucometers. A minimum 72-hr washout period was required between treatment sessions.

RESULTS: INSULIN

Significant increases in insulin levels were detected in 61% of the treatment sessions (Tmax 40-180 min), irrespective of timing of meals. In these cases, Cmax values were a mean 45.0 ± 23.5% (range 22-91%) above baseline. An additional 26% reached insulin Cmax at 6-13% above baseline values. Fluctuations in insulin levels were undetectable in only 3/23 sessions. In all cases, insulin levels returned to baseline within 45-300 minutes of peak recordings, demonstrating full clearance from the bloodstream. In addition, the potency of insulin absorption did not demonstrate dependence on caloric intake initiated at different intervals after drug administration.

Correlations between insulin and postprandial glucose profiles were weighed by co-plotting the two monitored parameters for each treatment session (Figure 1). In most cases, classic ORMD-0801 uptake and peaking mirrored tight control of postprandial glucose levels. Even slight increases in plasma insulin concentrations proved sufficient in regulating glucose levels (Figure 1, meal: t=10 min).

RESULTS: GLUCOSE

Plasma glucose levels rose after meal ingestion but were effectively kept in check in all sessions, regardless of the time lapse between ORMD-0801 administration and mealtime. Cmax was reached at an approximate 100-min lag from start of meal (Table 1, range: 60-150 min), which in 17/23 cases returned to basal levels before the end of the monitoring session. Failure to resume normal glucose levels after caloric intake was often paralleled with undetectable insulin absorption or low or fluctuating absorption patterns.

RESULTS: SAFETY

No serious adverse events were recorded throughout the study. In 1/24 sessions, the subject used injectable insulin due to high glucose levels. The data of this session was not included in the analysis.

CONCLUSIONS

ORMD-0801 is safe for use in T1DM patients.
ORMD-0801 is cleared within 300 min.
ORMD-0801 is biologically active upon oral, preprandial administration.
ORMD-0801 prevents the expected rise of glucose levels in fasting T1DM individuals upon insulin withdrawal.

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