ALTASCIENCES

CASE STUDY

A Multi-Centre, Randomized, Controlled, Single-Blind, 2-Way Crossover Study to Compare 2 Glucagon Formulations for Induced Hypoglycemia Rescue in Adults with Type 1 Diabetes Mellitus (T1DM)

STUDY OVERVIEW

This study was a non-inferiority, multi-centered, randomized, controlled, single-blind, two-way crossover, in-patient study in subjects with T1DM. The primary objective was to demonstrate the efficacy of a glucagon injectable device when compared to an existing treatment in treating insulin-induced hypoglycemia. Up to 85 male and female subjects diagnosed with T1DM were randomized to the investigational product or comparator in a crossover fashion over 2 periods.

The Altasciences site in Montreal participated in this multi-center trial and was able to recruit and randomize 8 patients in a two-week period despite the restrictive inclusion and exclusion criteria and the need to qualify by demonstrating a capacity to maintain stable glucose levels.

STUDY DETAILS

- **Class of Drug:** Anti-hypoglycemic agent
- **Indication:** Type 1 diabetes mellitus
- **Population Type:** Patients
- **# of Participants:** 85 across multiple sites
- **Time to recruit panel at Altasciences:** 2 weeks for 8 patients (FSFV-LSFV)
- **Study Design:** Multi-center, randomized, single blind, 2-way crossover.
- **Key Inclusion Criteria:**
  - Males and females 18 to 75 years old diagnosed with type 1 diabetes mellitus for at least 24 months
  - Current usage of daily insulin treatment that included having an assigned “correction factor” for managing hyperglycemia
  - Random serum C-peptide concentration < 0.5 ng/mL
- **Key Exclusion Criteria:**
  - Pregnant or breastfeeding.
  - HbA1c greater than 9.0% at screening
  - BMI greater than 40 kg/m2
  - Renal or hepatic insufficiency
  - Hematocrit of less than or equal to 30%
  - BP readings at screening where SBP is less than 90 or greater than 150 mm Hg, and DBP is less than 50 or greater than 100 mm Hg
  - Clinically significant ECG abnormalities
  - Use of more than 2.0 U/kg total insulin dose per day
  - Congestive heart failure
  - Active malignancy within 5 years from screening
  - Current seizure disorder (other than with suspect or documented hypoglycemia)
  - Current bleeding disorder, treatment with warfarin, or platelet count below 50 x 10e9/L
- **Services Provided:** Recruitment and clinical conduct

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STUDY PURPOSE

To demonstrate the non-inferiority of the investigational product versus the comparator with respect to efficacy as measured by a return to plasma glucose greater than 70.0 mg/dL in T1DM subjects in a state of insulin-induced hypoglycemia.

METHODS

Subjects were admitted the evening prior to check-in for continuous glucose monitoring and to begin fasting. Eligible subjects were evaluated for their capacity to maintain plasma glucose levels within a pre-specified range for at least 30 minutes when given a stable infusion of insulin. These subjects then continued to the insulin-induced hypoglycemia phase of the study that was performed through a monitored, standardized induction protocol. Once a stable state of hypoglycemia was reached, subjects were administered a subcutaneous injection of either the investigational product or comparator product. Glucose monitoring continued for 3 hours post-dose and subjects were discharged once medically stable and glucose levels returned to normal. After a pre-defined washout period, subjects returned to the clinic and the study procedures were repeated as each subject crossed over to the other treatment. Subjects were evaluated for hypoglycemia symptoms, injection site discomfort and reactions, and other measures of safety and tolerability.

The key assessments used in this study were:

- Continuous glucose monitoring (via Dexcom G4)
- Euglycemic steady state maintenance
- Insulin-induced hypoglycemia via insulin infusion, and bedside glucose readings via Yellow Strings Instrument's (YSI) glucose analyzer
- Safety and tolerability assessments related to injection site reactions and hypoglycemia

CHALLENGES AND SOLUTIONS

Time constraints to complete study enrollment were tight. To overcome the challenge, our Montreal site proactively used our internal database of over 750 type 1 diabetic patients weeks in advance to quickly enroll and dose 8 patients in 2 weeks (from IRB approval). Recruitment was executed mainly through targeted patient reach-outs, with little study-specific advertising. The flexibility of our recruitment strategies and robustness of our diabetic patient database proved to be key factors in meeting enrollment milestones.

Altasciences was the only clinical facility able to complete validation and use the state-of-the-art YSI 2900 Biochemistry analyzer for confirmatory bedside glucose measurements during the insulin-induced hypoglycemia procedure. This device accommodates 96-well formats and can support high throughput measurements of a range of chemistries, including glucose, lactate, glutamate, and ethanol.

ABOUT ALTASCIENCES

Altasciences is a forward-thinking, mid-size contract research organization offering pharmaceutical and biotechnology companies a proven, flexible approach to preclinical and clinical pharmacology studies, including formulation, manufacturing, and analytical services. For over 25 years, Altasciences has been partnering with sponsors to help support educated, faster, and more complete early drug development decisions. Altasciences' integrated, full-service solutions include preclinical safety testing, clinical pharmacology and proof of concept, bioanalysis, program management, medical writing, biostatistics, and data management, all customizable to specific sponsor requirements. Altasciences helps sponsors get better drugs to the people who need them, faster.