doses. Consistent with its mechanism, RZ358 increased plasma glucose levels in an exposure-dependent fashion, and only when needed (disease-severity dependent). These properties make it uniquely suited as a potential treatment for heterogenous and variable hyperinsulinemic conditions such as PGBH.

Diabetes Mellitus and Glucose Metabolism

CLINICAL TRIALS IN DIABETES AND METABOLIC DISEASE

Accuracy and Reliability of Tempo Pen and Tempo Smart Button™

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Background: Understanding the extent and causes of suboptimal insulin dosing is key for the coordinated diabetes management. Integrating the benefits of monitoring, education, and clinical support can facilitate self-care among people with diabetes mellitus. **Methods:** This study presents the technical aspects and performance tests on Tempo Pen, a new connection-enabled insulin pen available for Humalog (insulin lispro), Basaglar/Abasaglar (insulin glargine), and Lyumjev (ultra-rapid lispro) U100 formulations. Tempo Pen, as part of the connected care system, work with the Tempo Smart Button™ (pending CE mark), which captures insulin dosing information and transmits it to mobile applications to display. The Tempo device (Tempo Pen + Tempo Smart Button™) can track the date, time of day, insulin dose, and type of insulin accurately. **Results:** The pen met the ISO 11608-1:2014 requirements for dose accuracy at all doses and conditions tested, and all results were within the ISO specification limits. Tempo Smart Button™ has been found to be compatible with Tempo Pen, and met the acceptance criteria and target k-values for glide force, dose accuracy, and attachment/detachment force testing. It demonstrated >95% dose recording accuracy with 95% confidence, and also met requirements for data transfer after every injection. Battery life of Tempo Smart Button™ was found to be at least one year. **Conclusions:** Tempo device is the first connected system with a smart disposable pen. It accurately captures real-time insulin dosing information which can help patients and healthcare professionals address suboptimal insulin management to reach the desired glycemic goal.

Diabetes Mellitus and Glucose Metabolism

CLINICAL TRIALS IN DIABETES AND METABOLIC DISEASE

Basal Insulin Fc (BIF), A Novel Insulin Suited For Once Weekly Dosing For The Treatment of Patients With Diabetes Mellitus

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An optimally designed once-weekly basal insulin with reduced day-to-day pharmacokinetic (PK)/pharmacodynamic (PD) fluctuations compared to daily basal insulins should have a low peak-to-trough ratio at steady state. An insulin with this flat profile could improve glycemic efficacy while reducing hypoglycemia. Basal insulin Fc (BIF; LY3209590) is an insulin IgG Fc-fusion protein developed for once weekly dosing. The results of the first in-human studies of BIF assessing the safety, tolerability, PK, and PD following single and once-weekly doses of BIF are presented below. The single ascending dose (SAD) study assessed 6 dose levels of BIF, administered to healthy subjects or patients with type 2 diabetes mellitus (T2DM). In the multiple ascending dose (MAD) study, patients with T2DM previously treated with basal insulin received a one-time loading dose at Week 1 followed by a once-weekly maintenance dose for 5 additional weeks. Four fixed-dose maintenance dose levels were evaluated. The loading dose was implemented to rapidly achieve steady-state BIF concentration at each dose level. Patients with T2DM in the control group received insulin glargine at the same dose as their previous daily insulin dose. Key objectives were safety and tolerability, PK endpoints with a focus on half-life and peak-to-trough ratio at steady state, and finally PD measures. The SAD study included 57 patients with T2DM and 16 healthy subjects. The mean age of patients with T2DM was 58.4 years and the mean BMI was 29.5±3.2 kg/m^2. The mean age of healthy subjects was 35.8±9.3 years and the mean BMI was 26.1±3.1 kg/m^2. In the SAD study, BIF demonstrated linear PK with dose-proportional concentration profiles in healthy subjects and patients with T2DM. The maximum BIF concentration was reached on Day 4. BIF had a mean half-life of approximately 17 days in patients with T2DM. Following a single dose of BIF, a decrease in FBG was observed on Day 1 and was sustained until at least 5 days post-dose. In the MAD study in 33 subjects with T2DM aged between 40 and 69 years, BIF demonstrated a nearly peak-less PK profile over a one-week dosing interval with a peak-to-trough ratio of ~1.1 at steady state. This flat profile is in contrast to insulin glargine. Following once-daily dosing, insulin glargine has a daily peak-to-trough ratio of ~2. Over the 6-week duration, the 7-point glucose profiles remained constant over time and were similar to insulin glargine profiles. BIF was well tolerated and had a safety profile similar to insulin glargine-treated subjects. In particular, hypoglycemia rates were also similar to insulin glargine and there was no occurrence of hypoglycemic events with cognitive dysfunction. These data support continued development of BIF as a once-weekly insulin treatment of diabetes mellitus.

Diabetes Mellitus and Glucose Metabolism

CLINICAL TRIALS IN DIABETES AND METABOLIC DISEASE