The next-generation glucagon analog dasiglucagon consistently achieves rapid recovery from hypoglycemia across subgroups

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ABSTRACT

Background: The efficacy of dasiglucagon 0.6 mg, a glucagon analog stable in aqueous formulation approved for treatment of severe hypoglycemia (SH), has been established vs. placebo in previously reported randomized, double-blind, placebo-controlled trials in adults with type 1 diabetes mellitus (T1DM).
Objective: An integrated analysis was conducted to investigate efficacy in demographic and other subgroups.
Methods: To allow as many individuals as possible in the evaluation, the analysis comprised data from four trials in adults, including two pivotal trials, an additional phase 3 trial, and a phase 2 trial. The trials were conducted under similar conditions with respect to design characteristics, such as target population, background therapy, and treatment duration. All trials assessed efficacy following insulin-induced hypoglycemia and showed consistent results across trials. The primary endpoint was time to plasma glucose (PG) recovery, defined as first PG increase ≥20 mg/dL after treatment initiation without need for rescue intravenous glucose. A total of 220 participants were exposed to dasiglucagon 0.6 mg across trials.
Results: The results showed that the efficacy of dasiglucagon was highly consistent across subgroups, including sex, age, ethnicity, region, body mass index, duration of diabetes, injection site, and baseline PG. The median time to recovery from insulin-induced hypoglycemia was 10 minutes in most groups.
Conclusions: Dasiglucagon provided rapid and effective reversal of hypoglycemia in adults with T1DM. The ready-to-use, aqueous formulation of dasiglucagon is therefore an effective, consistent and reliable rescue agent for SH.

OBJECTIVES

- Dasiglucagon, a glucagon analoge stable in aqueous formulation, is effective in restoring blood glucose levels, and is approved by FDA for use in severe hypoglycemia (SH) in people with diabetes 6 years and older[1]
- An integrated efficacy analysis comprising data from one phase 2 trial and three phase 3 trials was conducted
- The purpose of this analysis was to investigate the efficacy of dasiglucagon among demographic and other subgroups

CONCLUSIONS

- **The efficacy of dasiglucagon was highly consistent across subgroups**
- **For most demographic and other subgroups analyzed, median time to plasma glucose (PG) recovery from insulin-induced hypoglycemia was 10 minutes**
- **Dasiglucagon is an effective, consistent, and reliable rescue agent for SH**

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INTRODUCTION

- Glucagon is recommended for all individuals at increased risk of level 2 hypoglycemia, but is often underutilized for the treatment of SH in patients with diabetes[2-4]
- Underutilization may be partly attributable to multi-step reconstitution required for glucagon emergency kits that can present a barrier to timely and effective administration of SH rescue therapy[4]
- Dasiglucagon is a novel, ready-to-use glucagon analog that has undergone a comprehensive clinical development program, and is effective in restoring PG levels in adults with type 1 diabetes mellitus (T1DM)[1,5]

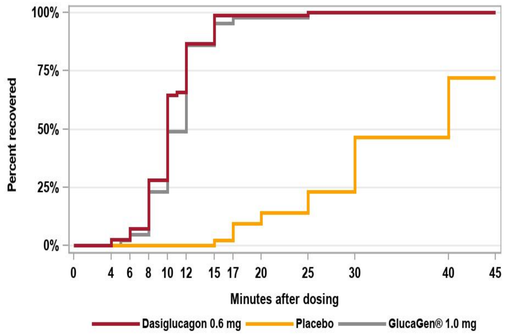
METHOD

- The integrated analysis comprised four trials in adult patients with T1DM. All trials were conducted under similar conditions with respect to design, study population, background therapy, and trial duration
- Trials included efficacy assessments following insulin-induced hypoglycemia
- Primary endpoint was time to PG recovery, defined as first PG increase ≥20 mg/dL after treatment initiation without need for rescue IV glucose

RESULTS

Time to PG recovery across trials

- Dasiglucagon was shown to be highly statistically superior to placebo in a phase 3 trial including 82 dasiglucagon treated subjects (Figure 1) and in a phase 3 trial including 34 subjects treated with dasiglucagon
- Consistent time to recovery was observed across these two trials as well as two other trials, that did not include a placebo comparator
- A total of 220 subjects were treated with dasiglucagon across the four trials. Investigation of differences between subgroups in this larger pool was justified by similarity in design and population as well as availability of an objective endpoint based on central laboratory PG results showing consistent results across trials



Time to PG recovery (minutes)	Dasiglucagon 0.6 mg 82 subj	Placebo 43 subj	GlucaGen® 1.0 mg 43 subj
Median (95% CI)	10 (10, 10)	40 (30, 40)	12 (10, 12)
Log-rank test, dasiglucagon vs placebo	p < 0.001		

Figure 1: One minus Kaplan-Meier plot of time to PG recovery in a pivotal phase 3 trial

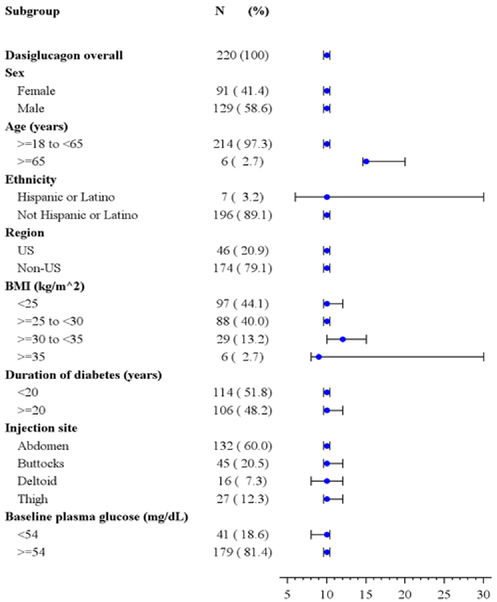
RESULTS (cont.)

Baseline demographics

- The majority of participants in this integrated analysis were male (58.6%), aged 18-65 years (97.3%) and not Hispanic or Latino (89.1%)
- Exposure was approximately evenly distributed between diabetes duration subgroups (<20 and ≥20 years)

Time to PG recovery in subgroups

- Consistent efficacy was observed across subgroups included in this analysis
- A median time to PG recovery of 10 minutes was observed in the majority of subgroups (Figure 2)



Note: There were too few subjects aged 65 years and older to determine whether these respond differently from younger adult subjects. Limited data were also available in Hispanic and Latino subjects and those with BMI ≥ 35

Figure 2: Forest plot of median time to PG recovery for dasiglucagon in adults with T1DM

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