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Biochaperone® Glucagon, A Stable Ready-to-use Liquid Glucagon Formulation Enabled by Biochaperone Technology, is Well Tolerated and Quickly Restores Euglycaemia after Insulin-induced Hypoglycaemia

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Introduction & Background

- Human glucagon is approved as an emergency rescue treatment for people with diabetes experiencing severe hypoglycaemia.
- Usability of commercially available emergency kits is limited due to the complexity of the reconstitution and administration process, especially in stressful circumstances.
- BioChaperone® Glucagon (BCG) is a stable, ready-to-inject, aqueous formulation of human glucagon for hypoglycaemia rescue therapy enabled by the BioChaperone® technology.

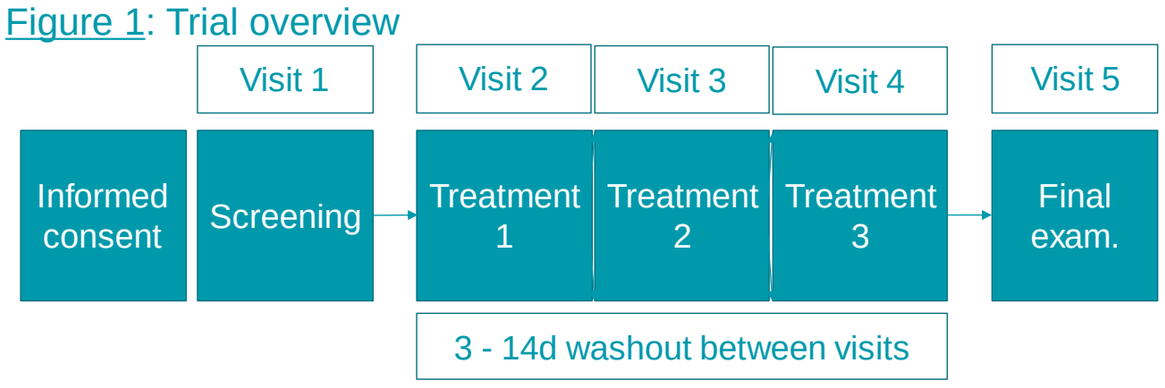
Aims of the study

- To assess safety and tolerability of two compositions of BCG (BCG1 and BCG2) and GlucaGen® HypoKit® (all dosed at 1 mg).
- To compare pharmacodynamic (PD) and pharmacokinetic (PK) properties of BCG1, BCG2 and GlucaGen® HypoKit®.

Methods

- Phase 1, randomised, double-blind, three-period cross over trial.
- Male or female participants with type 1 diabetes (T1DM) were allowed to participate in the trial after having given written informed consent.
- Subjects were fasted and hypoglycaemia was induced with individualized i.v. insulin infusion to reach plasma glucose (PG) levels <60 mg/dL.
- At t=0, single subcutaneous 1 mg dose of BCG1, BCG2 and Glucagen® HypoKit® on 3 separate dosing visits were administered.
- An individualised constant insulin infusion rate (up to 4x subject's average basal rate; same for all dosing visits) was maintained from -30 to +240 min relative to dosing.
- If PG value ≤ 55 mg/dL within 8-30 min after dosing, an i.v. dose of glucose was administered.

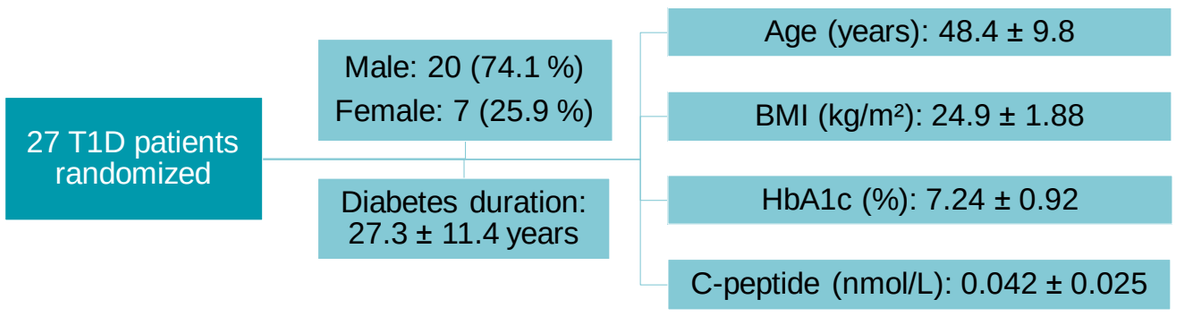
Figure 1: Trial overview



Demographic data

- 27 subjects with type 1 diabetes (Figure 2)
- 3 withdrawals (1 SAE, 2 personal reasons)

Figure 2: Characteristics of the study population (mean±SD)



Adverse Events

- GI side effects are the most frequent AEs, and the vast majority of AEs are commonly observed in hypoglycaemia.
- All subjects recovered from AEs.

Table 1: Adverse events

Period	BCG1	BCG2	GlucaGen
Inpatient	**15 AEs in 11 subjects** 10 nausea 2 vomiting 2 headache 1 vertigo	**13 AEs in 8 subjects** 8 nausea 1 vomiting 1 headache 2 inj site react. 1 hyperhydrosis	**6 AEs in 5 subjects** 5 nausea 1 vomiting
Outpatient	5 AE in 4 subjects (2 SAE: Gastroenteritis and troponin T increase / both unrelated to treatment)		

Hypoglycaemic episodes during dosing visits

- Majority of hypoglycaemic episodes were asymptomatic and occurred more than 2 hours after dosing.
- All subjects recovered from hypoglycaemia.

Table 2: Hypoglycaemic episodes during dosing visits

Treatment	N	Mean time (h) ± SD
BCG1	9	2.3 ± 1.71
BCG2	10	2.5 ± 1.42
Glucagen	13	3.0 ± 0.50

Glucose response

- BCG1, BCG2 and Glucagen® induce rapid and marked increases in blood glucose levels.
- Blood glucose rise with BCG1 and BCG2 is slightly delayed compared to Glucagen®.

Figure 3: Mean (±SE) plasma glucose profiles

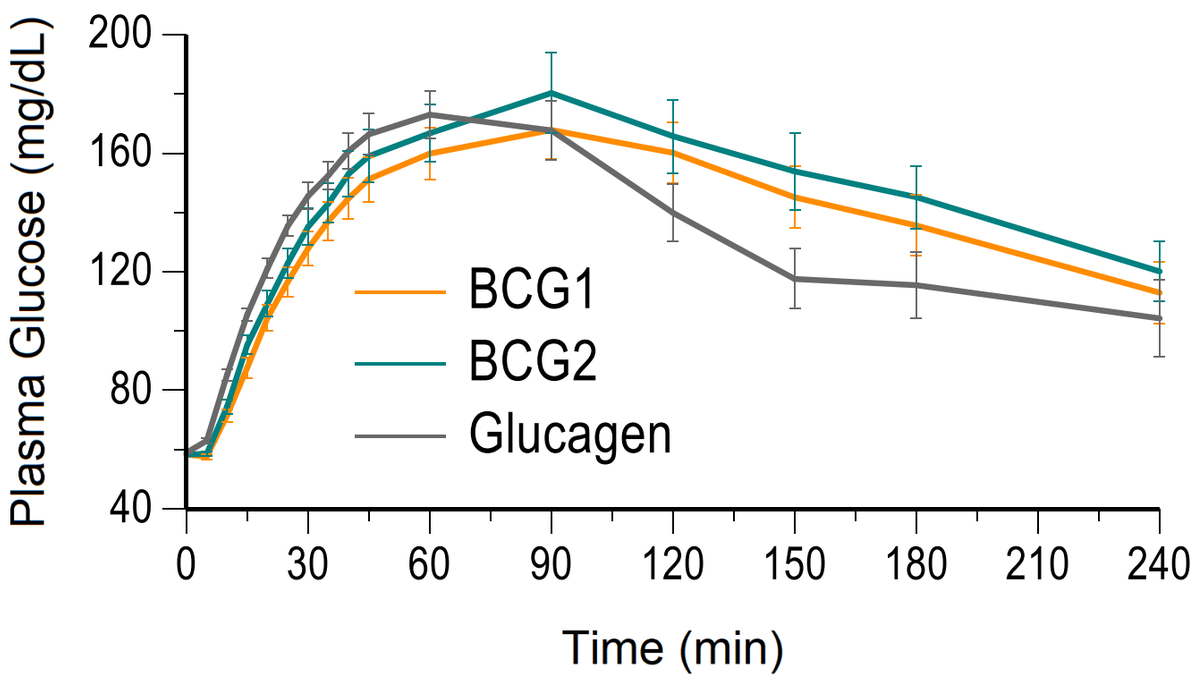


Table 3: Pharmacodynamic parameters (plasma glucose)

Mean [sd]	BCG1	BCG2	GlucaGen
$t_{PG \geq 70\ mg/dL}$ (min)	11.5 [5.0]	10.0 [3.5]	7.3 [1.8]
ΔPG_{15min} (mg/dL)	29 [17]	36 [16]	47 [11]
ΔPG_{30min} (mg/dL)	69 [29]	77 [29]	87 [22]
N $PG_{\geq 70\ mg/dL}$ (% N total)	26/26 (100%)	24/25 (96%)	24/24 (100%)

Conclusions

- **BCG1, BCG2 and Glucagen® 1 mg were safe**
- **BCG1, BCG2 and Glucagen® 1 mg induce rapid and marked increases in blood glucose levels after subcutaneous administration.**

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