SUPPLEMENTARY DATA

Supplementary Table S1. Demographic and baseline characteristics (safety analysis set)

Parameter	Group 1	Group 2	Group 3	Group 4	Total
	N = 8	**N = 17**	**N = 17**	**N = 16**	**N = 58**
Sex (m)	**62.5 %**	**41.2%**	**52.9%**	**62.5%**	**53.4%**
Sex (f)	37.5%	58.8%	47.1%	37.5%	46.6%
Age [years]	41.6 (8.31)	35.4 (8.66)	34.0 (9.17)	37.5 (8.15)	36.4 (8.76)
Weight [kg]	76.56 (5.494)	76.81 (6.368)	78.67 (7.897)	73.94 (8.777)	76.53 (7.493)
BMI [kg/m^2]	24.39 (0.960)	24.65 (1.945)	26.21 (2.776)	24.74 (2.962)	25.09 (2.486)
HbA1c [%]	7.41 (0.210)	6.88 (0.494)	7.24 (0.585)	7.19 (0.571)	7.14 (0.539)
HbA1c [mmol/mol]	57.5	51.7	55.6	55.1	54.5
Diabetes duration [years]	19.9 (11.49)	18.4 (10.28)	19.2 (10.43)	18.6 (5.29)	18.9 (9.17)

For sex, relative (%) numbers of male (m) and female (f) patients are shown. For all other parameters, arithmetic means with standard deviations (SD) are shown. All Patients were white. BMI, body mass index; HbA_{1c}, glycosylated hemoglobin; N, number of subjects.

SUPPLEMENTARY DATA

Supplementary Table S2. Dose Proportionality

Parameter	Treatment/ Comparison	Slope	95% Confidence Interval
$AUC_{0\text{-}30min}$	Overall	0.885	(0.7403; 1.0292)
$AUC_{0\text{-}360min}$	Overall	1.029	(0.9667; 1.0904)
$AUC_{0\text{-}inf}$	Overall	1.030	(0.9683; 1.0916)
C_{max}	Overall	0.888	(0.7791; 0.9972)

SUPPLEMENTARY DATA

Supplementary Table S3. *Treatment-Emergent Adverse Events (TEAEs)*

	Dasiglucagon				GlucaGen	
Dose	**0.1 mg**	**0.3 mg**	**0.6 mg**	**1.0 mg**	**0.5 mg**	**1.0 mg**
N	6	16	17	16	17	34
Number of total TEAE	6	26	27	23	21	40
Most frequent-Treatment-Emergent Adverse Events						
Nausea	1	9	9	7	9	18
Vomiting	0	6	6	2	4	4
Headache*	3	8	6	5	1	7
Injection Site Reactions	1	2	1	3	1	4
Others	1	3	6	6	6	7
Treatment-Emergent Hypoglycemic Events (post-dose)						
	Dasiglucagon				**GlucaGen**	
Dose	**0.1 mg**	**0.3 mg**	**0.6 mg**	**1.0 mg**	**0.5 mg**	**1.0 mg**
N	6	16	17	16	17	34
Post-dose dasiglucagon injection	2[#]	0	1[†]	2[†]		
Post-dose GlucaGen® injection					3[**]	6[**]

No severe adverse events occurred. *22 headache events occurred in 19 patients after dosing with dasiglucagon. 3 of these events were considered to be not or unlikely related to study drug due to start time beyond observation period (6 h). [#]Two hypoglycemic events occurred in the one patient 0.1 and 1.5 h post-dose. The early event after 0.1 h was due to a protracted decline of blood glucose after dosing, as consequence of the insulin-induced hypoglycemic procedure. [†]Three other patients experienced hypoglycemia more than 100 h after dosing with dasiglucagon. [**]After GlucaGen, 2 hypoglycemic events occurred immediately post-dose (0.08 and 0.1 h) and seven events occurred after about 4-6 h. The early event after 0.08 h was due to a protracted decline of blood glucose after dosing, as consequence of the insulin-induced hypoglycemic procedure.

SUPPLEMENTARY DATA

Supplementary Figure S1. Chemical structure of dasiglucagon Abbreviated Chemical Name:

H-His-Ser-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-Lys-Tyr-Leu-Asp-Aib-Ala-Arg-Ala-Glu-Glu-Phe-Val-Lys-Trp-Leu-Glu-Ser-Thr-OH, hydrochloride salt

Supplementary Figure S2. Trial Design