Comparison of insulin degludec and glargine U100 in patients with type 1 diabetes prone to severe nocturnal hypoglycaemia

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Missed Bolus			
CGM Parameter	FiAsp (n=9)	Aspart (n=9)	P value
CGM% time 3.9-10 mmol/L, median (IQR)	95.8 (60.4, 100.0)	81.2 (37.5, 93.7)	0.23
CGM% time 3.9-7.8 mmol/L, median (IQR)	54.2 (16.7, 62.5)	33.3 (10.4, 54.2)	0.26
CGM% time >10 mmol/L, median (IQR)	4.2 (0.0, 39.6)	18.7 (0.0, 62.5)	0.34
CGM% time >13.9 mmol/L, median (IQR)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.93
CGM% time >16.7 mmol/L, median (IQR)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	n/a
CGM% time <3.9 mmol/L, median (IQR)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.16
CGM% time <3.0 mmol/L, median (IQR)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	n/a
Mean glucose mmol/L, median (IQR)	7.9 (7.3, 9.1)	7.9 (7.4, 10.6)	0.26
Coefficient of variation, median (IQR)	19.7 (14.2, 23.3)	20.2(16.1, 22.4)	0.86
Late Bolus			
CGM Parameter	FiAsp (n=8)	Aspart (n=8)	P value
CGM% time 3.9-10 mmol/L, median (IQR)	85.4 (78.1, 93.7)	90.62 (80.2, 96.9)	0.40
CGM% time 3.9-7.8 mmol/L, median (IQR)	69.8 (58.3, 84.3)	58.3 (44.8, 77.1)	0.12
CGM% time >10 mmol/L, median (IQR)	0.0 (0.0, 6.2)	1.0 (0.0, 9.4)	0.62
CGM% time >13.9 mmol/L, median (IQR)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	n/a
CGM% time >16.7 mmol/L, median (IQR)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	n/a
CGM% time <3.9 mmol/L, median (IQR)	6.2 (0.0, 21.9)	0.0 (0.0, 7.3)	0.36
CGM% time <3.0 mmol/L, median (IQR)	0.0 (0.0, 1.0)	0.0 (0.0, 0.0)	0.16
Mean glucose mmol/L, median (IQR)	6.1 (5.2, 6.5)	7.0 (5.8, 7.9)	0.12

each). Participants ate a matched standardised 40g carbohydrate evening meal on two occasions (one without a bolus and one with a late bolus administered 20-min post-meal commencement) each during the FiAsp and insulin aspart stages of the study. CGM data 0–4 hours post-meal was analysed by signed rank test.

Results: To date, nine and eight participants respectively have completed the missed and late meal bolus challenges. While not statistically significant, there was a higher time in target range with FiAsp with missed bolus and a higher time in hypoglycaemia range with late bolus (Table). There were no major hypoglycaemia or hyperglycaemic excursions.

Conclusions: Trends observed with a missed meal bolus suggest that FiAsp may offer advantages over insulin aspart with regard to full CL function though late meal-time bolus delivery remains a risk for hypoglycaemia.

279 / Abstract ID 358

POSTPRANDIAL GLYCEMIC CONTROL WITH FAST-ACTING INSULIN ASPART IN PATIENTS WITH TYPE 1 DIABETES USING SENSOR-AUGMENTED PUMP THERAPY

NEW INSULIN ANALOGUES

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Background and Aims: Fast-acting insulin aspart (fAsp) is a faster-acting insulin with a more rapid rate of absorption and greater early-glucose-lowering effect than conventional insulin (iAsp). The aim of this study was to assess the postprandial glycemic control in patients with sensor-augmented pump therapy after one month of treatment with fAsp.

Methods: Five patients (2males) treated with sensor-augmented pump therapy (at least 6 months prior to the initiation of fAsp) whose age were 41 ± 11 years and basal HbA1c 7,1 ± 0,4%, were included. Episodes of postprandial hyperglycemia (>140 mg/dL) were analysed before and after one-month treatment with fAsp. Other variables analysed were the area under the curve (AUC) >140 mg/dL, AUC <70 mg/dL, mean glucose and standard deviation (mg/dL), total insulin dose (IU/day) and basal/bolus distribution (%).

	iAsp	fAsp
Mean glucose (mg/dL)	151.8±22.3	151.6±11.1
Standard deviation (mg/dL)	53.6±9.0	49.4±7.2
Total insulin dose (IU/day)	41.8±19.2	41.7±16.4
Basal insulin (%)	44.8±9.0	44.8±6.3
Bolus insulin (%)	55.2±9.0	55.2±6.3
AUC >140 mg/dL	28.6±15.5	25.9±7.9
AUC <70 mg/dL	0.3±0.2	0.3±0.3

Results: Postprandial hyperglycemia episodes (>140 mg/dL) were reduced by 9.1% after one month of treatment with fAsp. The continuous glucose monitoring results are shown in the following table:

Conclusions: After one-month follow-up with fAsp, hyperglycemia events decreased without increasing the time in hypoglycemia and without changes in the basal/bolus distribution, in patients with sensor-augmented pump therapy.

280 / Abstract ID 793

COMPARISON OF INSULIN DEGLUDEC AND GLARGINE U100 IN PATIENTS WITH TYPE 1 DIABETES PRONE TO SEVERE NOCTURNAL HYPOGLYCAEMIA

NEW INSULIN ANALOGUES

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Background and Aims: Hypoglycaemia, especially nocturnal, remains the main limiting factor of achieving good glycaemic control in type 1 diabetes. This study aimed to investigate whether insulin degludec in comparison with insulin glargine U100 is superior in limiting the occurence of nocturnal hypoglycaemia in patients prone to nocturnal severe hypoglycaemia.

Methods: Danish investigator-initiated, prospective, randomised, open, blinded endpoint (PROBE), multicentre, crossover study. Adult patients with type 1 diabetes and at least one episode of nocturnal severe hypoglycaemia during the preceding two years were included. A 1-year plus 1-year treatment period was specified, consisting of two 3-month run-in period, each followed by a 9-month maintenance period. The primary endpoint was number of nocturnal symptomatic hypoglycaemic episodes during the maintenance period, analysed by intention-to-treat.

Results: A total of 149 patients were randomised to insulin degludec or insulin glargine U100. When defining night-time from 00:00 to 05:59 treatment with insulin degludec resulted in a 28% (95%CI:5-45; p = 0.02) and 37% (95%CI:16–53; p = 0.002) relative risk reduction (RRR) of nocturnal symptomatic hypoglycaemia ≤3.9 mmol/L and ≤3.0 mmol/L, respectively, compared to insulin glargine U100. Similar results with insulin degludec was demonstrated when defining night-time from 23:00 to 06:59 with a 27% (95%CI: 8–43; p = 0.01) and 34% (95%CI:18–48; p < 0.001) RRR of nocturnal symptomatic hypoglycaemia ≤3.9 mmol/L and ≤3.0 mmol/L, respectively. No significant differences in glycaemic control between treatments.

Conclusions: Type 1 diabetes patients prone to nocturnal severe hypoglycaemia had lower rates of nocturnal hypoglycaemia with insulin degludec as compared to with insulin glargine U100. The difference was relatively greater with increased severity of nocturnal hypoglycaemia.

281 / Abstract ID 54

COMPARISON OF EFFECTS WHEN SWITCHING LONG-ACTING INSULIN: RANDOMISED CROSSOVER STUDY

NEW INSULIN ANALOGUES

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Background and Aims: We investigated glycaemic variability from one day before to 6 days after switching in patients treated with long-acting insulin.

Methods: This study was conducted during hospitalization. 20 type 2 diabetic patients on basal insulin therapy were randomly allocated to two groups. In Group1, fasting blood glucose level was stabilized (not exceeding 180 mg/dL) using insulin glargine 300 U/mL (Glargine300); Glargine300 was continued for 6 days with the same dose; a continuous glucose monitoring device (FreeStyle Libre Pro) was worn on the fifth day of Glargine300 administration of the same dose (=attaching day:Day1); next, Glargine300 was switched to insulin degludec (Degludec) on Day3 with the same dose, and then Degludec was continued for 6 days with the same dose; Degludec was then switched to Glargine300 on Day9 with the same dose, and then Glargine300 was continued for 6 days with the same dose. Long-acting insulin was injected at 08:00. Test meals were given. In Group2, patients were administered in the order of Degludec, Glargine300, and Degludec, following the same regimen as Group1. Evaluation duration was from 24-h before to 144-h after switching.

	Degludec to Glargine300	Glargine300 to Degludec	p
MODD1 (over 7 days), mg/dL	17.4 (14.6-24.4)	17.5 (15.8-22.5)	0.71
MODD (day before switching [day0] vs day1), mg/dL	20.5 (15.8-24.6)	19.9 (13.8-23.8)	0.88
MODD (day2 vs day3), mg/dL	18.3 (17.4-25.2)	16.7 (15.6-21.3)	0.03
MODD (day5 vs day6), mg/dL	14.5 (12.2-20.8)	17.4 (12.8-19.0)	0.39
Continuous overlapping net glycaemic action (CONGA) 24 (day0 vs day1), mg/dL	13.8 (11.8-18.6)	14.3 (11.8-19.6)	0.74
CONGA24 (day2 vs day3), mg/dL	16.1 (12.1-19.0)	15.2 (12.9-16.0)	0.63
CONGA24 (day5 vs day6), mg/dL	11.4 (10.0-17.2)	13.1 (11.5-17.4)	0.37
Mean absolute glucose (over 7 days), mg/dL/hr	27.5 (22.0-34.1)	28.7 (24.1-33.0)	0.74
Glycemic variability percentage (over 7 days), %	16.5 (10.3-23.2)	17.2 (12.7-22.8)	0.68
Mean glucose level (over 7 days), mg/dL	135.1 (116.5-166.2)	135.4 (118.3-151.6)	0.39
Standard deviation (over 7 days), mg/dL	39.5 (32.0-49.4)	42.4 (34.3-49.3)	0.37

Results: Mean of daily difference (MODD) between day2 and day3 (switch day: day1) was significantly lower in patients who switched from Glargine300 to Degludec (pGtoD) than in patients who switched from Degludec to Glargine300 (pDtoG). The others endpoints weren't significantly different between pGtoD and pDtoG (table).

Conclusions: Day-to-day glycaemic variability between day2 and day3 was lower in pGtoD than in pDtoG.

282 / Abstract ID 494

A PROBABILISTIC FRAMEWORK TO DESIGN REALISTIC MEAL SCENARIOS IN IN SILICO TYPE 1 DIABETES (T1D) FREE-LIVING TRIALS

ARTIFICIAL PANCREAS

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Background and Aims: Clinical trials in free-living conditions is key in the development of an Artificial Pancreas (AP) for T1D subjects. Since the scenario plays a key role in the *synthesis and validation* of AP *control* algorithms, a probabilistic approach is proposed to automatically design meal scenarios. In particular, we exploit our real-life data to design realistic *in silico* scenarios.

Methods: The amount and time-of-day of ingested carbohydrates in a 1-month in 13 patients for a total of 1500 meals. have been considered. The joint distribution of these variables has been estimated via a copula function, in order to model their dependence. The use of a copula allows to generate Monte Carlo scenarios by drawing random samples, which represent a pair of amount and time-of-day.

Results: A Gaussian copula resulted suitable for the description of the dependence in the meal dataset with a p-value of 0.005 according to the χ^2 test based on Rosenblatt's transformation.