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Comparison of insulin glargine 300U/mL, insulin degludec and insulin glargine 100U/mL, in basal insulin therapy using continuous glucose monitor: a randomised triple crossover study

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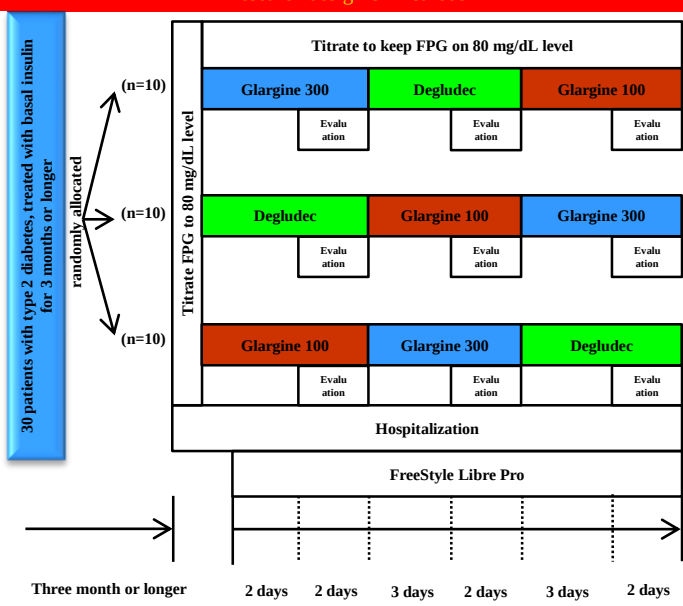
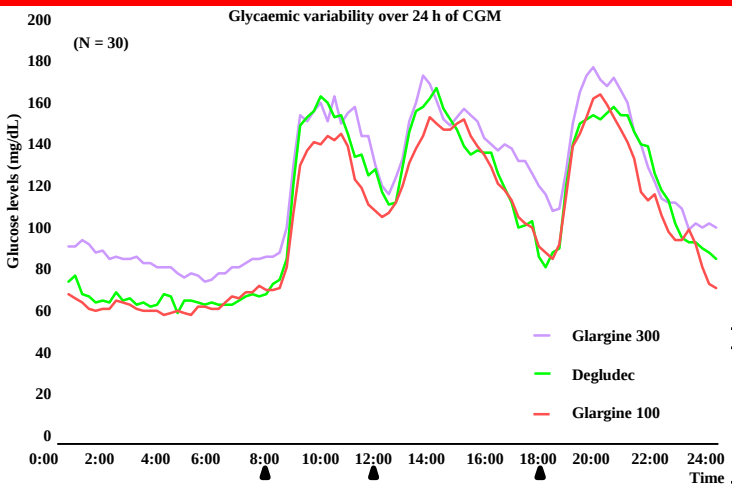
Background

- The role of long-acting insulin seems to support stable basal insulin secretion, not to cause hypoglycaemia.
- FreeStyle Libre Pro is a continuous glucose monitor (CGM) which monitors glucose levels in interstitial fluid continuously per 15 minutes for 14 consecutive days and does not require the drawing of blood.
- The FreeStyle Libre Pro's mean absolute relative difference (MARD) compared to self-monitoring of blood glucose (SMBG) was reported to be almost the same as Medtronic iPro 2's that (11.1% vs. 11.0%), although FreeStyle Libre Pro does not need calibration
- There has been no study yet that has investigated the differences in the risk of hypoglycaemia, between insulin glargine 300U/mL (Glargine300), insulin degludec (Degludec), and insulin glargine100 U/mL (Glargine100), when used at the same time.

Research design & Methods



Result



Patient characteristics

Characteristic	Total	Characteristic	Total
N (Male / Female)	30 (11 / 19)	FPG, mg/dL	113.0 (80.0-158.3)
Age, years	76.5 (73.0-82.0)	CPI	0.6 (0.4-1.0)
Duration of diabetes, years	13.0 (5.0-20.0)	U-CPR, μg/day	21.9 (11.6-37.8)
BMI, kg/m^2	22.1 (17.9-25.3)	Biguanide agent, n (%)	15 (50.0)
HbA1c (NGSP), %	8.1 (7.1-9.4)	Thiazolidine, n (%)	5 (16.7)
GA, %	23.7 (20.9-29.0)	α- glucosidase inhibitor, n (%)	3 (10.0)
CPR, ng/mL	0.8 (0.4-1.5)	DPP4 inhibitor, n (%)	23 (76.7)

Parameters of glycaemic variability in patients treated with Glargine300, Degludec or Glargine100

	a: Glargine 300	b: Degludec	c: Glargine 100	p	p (a vs. b)	p (b vs. c)	p (a vs. c)
0:00 to 6:00 area over the glucose curve (AOC) (<70 mg/dL), mg･min/dL	**0 (0-146.3)**	**1710.0 (495.0-5079.4)**	**3836.3 (2115.0-5810.6)**	**<0.0001**	**0.002**	**0.006**	**<0.0001**
8:00 to 24:00 AOC (<70 mg/dL), mg･min/dL	**0 (0-0)**	**146.3 (0-635.6)**	**1091.3 (140.6-2002.5)**	**<0.0001**	**0.04**	**0.0007**	**<0.0001**
24 h AOC (<70 mg/dL), mg･min/dL	**0 (0-180.0)**	**3453.8 (905.6-7621.9)**	**6120.0 (3538.1-10558.1)**	**<0.0001**	**0.0002**	**0.04**	**<0.0001**
24 h M-value (target glucose level = 100 mg/dl)	5.6 (3.4-9.1)	9.7 (7.3-17.4)	13.5 (9.1-20.0)	<0.0001	0.0002	0.01	<0.0001
0:00 to 6:00 M-value (target glucose level = 90 mg/dl)	**0.5 (0.3-0.9)**	**4.7 (2.0-10.5)**	**10.0 (4.7-23.4)**	**<0.0001**	**0.0002**	**0.004**	**<0.0001**
Mean amplitude of glycemic excursion (MAGE), mg/dL	52.5 (41.8-65.0)	62.2 (51.6-72.6)	67.2 (54.8-77.3)	<0.0001	0.004	0.004	<0.0001
Mean of daily difference (MODD), mg/dL	**19.5 (15.7-24.8)**	**23.2 (20.6-29.0)**	**29.2 (23.3-40.7)**	**<0.0001**	**0.0006**	**0.002**	**<0.0001**
Average daily risk range (ADRR)	9.5 (6.3-17.3)	22.1 (15.3-34.3)	36.4 (26.3-36.4)	<0.0001	0.001	0.005	<0.0001
24 h mean glucose level, mg/dL	113.2 (108.5-127.3)	113.3 (102.2-131.7)	109.6 (100.3-123.3)	0.65	0.66	0.81	0.97
0:00 to 6:00 mean glucose level, mg/dL	81.8 (74.2-87.8)	74.0 (67.2-85.6)	72.7 (63.5-83.9)	0.08	0.2	0.97	0.12
24 h standard deviation (SD), mg/dL	38.0 (30.5-47.4)	45.5 (35.9-52.4)	49.7 (37.6-58.8)	<0.0001	0.004	0.004	<0.0001
0:00 to 6:00 SD, mg/dL	**6.3 (4.6-9.3)**	**9.1 (7.7-12.0)**	**13.4 (10.6-16.8)**	**<0.0001**	**0.0009**	**0.0009**	**<0.0001**
24 h AUC (≥0 mg/dL), mg･min/dL	162986.3 (156288.7-183318.7)	163087.5 (147202.5-189607.5)	157758.8 (144493.1-177601.9)	0.65	0.66	0.81	0.97
Basal insulin dose, U/day	16.5 (11.8-28.0)	16.0 (13.3-28.3)	17.5 (13.3-32.3)	0.18	0.53	0.78	0.19

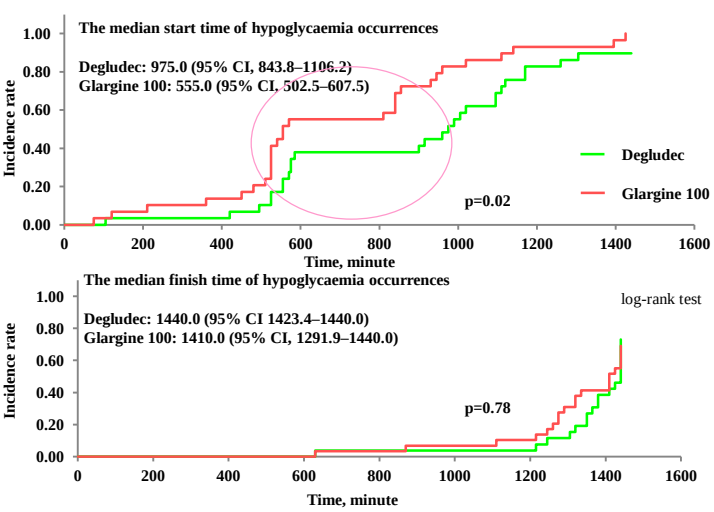
Data are shown as median (interquartile range), p: Friedman's test, Primary endpoint parameters are represented in bold font.

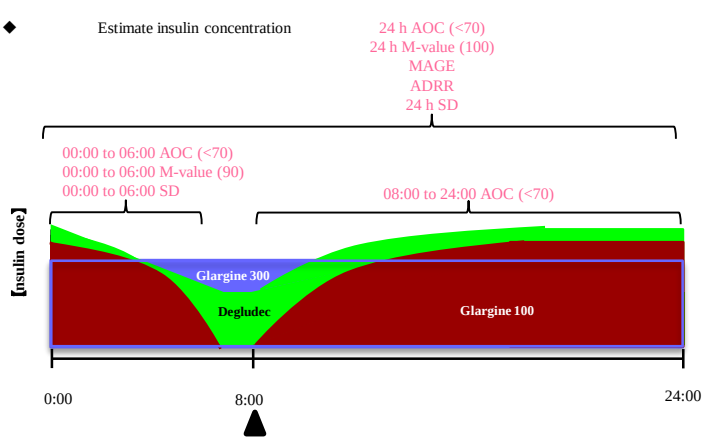
MARD compared to SMBG and comparison of FreeStyle Libre Pro values and SMBG values

	MARD, %	Before breakfast, mg/dL		p	Before lunch, mg/dL		p	Before dinner, mg/dL		p	Bedtime, mg/dL		p
		FreeStyle Libre Pro value	SMBG value		FreeStyle Libre Pro value	SMBG value		FreeStyle Libre Pro value	SMBG value		FreeStyle Libre Pro value	SMBG value	
Glargine 300	8.7	85.5 (82.0-89.8)	85.5 (82.3-88.8)	0.54	121.5 (100.3-149.8)	118.0 (101.3-155.0)	0.98	101.0 (94.3-131.0)	103.0 (89.5-132.5)	0.51	150.5 (115.0-189.5)	142.5 (119.0-176.8)	0.33
Degludec	8.9	79.0 (71.0-89.8)	85.0 (82.0-88.0)	0.11	118.5 (104.3-147.8)	120.5 (101.3-149.3)	0.2	88.0 (71.0-117.0)	95.0 (87.3-110.8)	0.12	140.0 (101.0-168.3)	132.0 (98.0-162.8)	0.28
Glargine 100	9.0	81.0 (72.3-87.5)	85.0 (82.0-87.0)	0.1	99.0 (88.3-127.5)	100.0 (88.0-135.3)	0.82	90.0 (67.3-112.8)	89.0 (81.3-109.3)	0.11	141.0 (97.8-152.8)	131.5 (98.8-152.8)	0.76

Data are shown as median (interquartile range), p: Wilcoxon signed-rank test

➢ **FreeStyle Libre Pro values were significantly correlate to SMBG values on before breakfast, before lunch, before dinner and bedtime in patients on Glargine300, Degludec, and Glargine100.**
(r=0.36~0.94, p=0.048~<0.0001)





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Conclusion

- Glargine300 may be the best long-acting insulin to reduce hypoglycaemia.