Association of fasting C-peptide levels with glycaemic efficacy and risk of hypoglycaemia in people with type 2 diabetes commencing insulin glargine 100 U/ml

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Background and aims: To investigate the prognostic value of fasting C-peptide levels for efficacy and safety outcomes when starting insulin glargine 100 U/ml (Gla-100) at bedtime in combination with oral agents.
Materials and methods: Standardized patient-level data were pooled from 16 randomized controlled trials (≥ 24 weeks duration). Outcomes were assessed descriptively up to week 24 stratified according to fasting C-peptide (≤ 0.40, > 0.40-1.20, > 1.20-2.00, >2.00 nmol/l) at start of Gla-100 (baseline).
Results: Overall, 2,165 participants (54% male) were included. Mean ± SD age by baseline C-peptide level (≤ 0.40, > 0.40-1.20, > 1.20-2.00, >2.00 nmol/l) were 58 ± 11, 58 ± 10, 59 ± 9, and 59 ± 10 years. Increasing baseline fasting C-peptide levels were associated with a shorter duration of diabetes (10.4 ± 7.0 vs 10.0 ± 6.6 vs 8.5 ± 5.6 vs 7.6 ± 5.5 years), higher BMI (25.7 ± 3.6 vs 29.5 ± 4.8 vs 31.9 ± 5.2 vs 32.2 ± 5.3 kg/m^2), lower baseline fasting plasma glucose (11.5 ± 3.3 vs 10.9 ± 3.0 vs 10.8 ± 2.8 vs 10.3 ± 2.7 mmol/l), and slightly lower baseline HbA_{1c} (9.0 ± 1.1 vs 8.8 ± 1.0 vs 8.7 ± 1.0 vs 8.8 ± 1.0 %). Week 24 outcomes for HbA_{1c}, Gla-100 dose and hypoglycaemia are shown in the Table. From a slightly higher HbA_{1c} level, with smallest titrated and final Gla-100 doses, those in the lowest C-peptide group had a lesser HbA_{1c} reduction (-1.34 vs -1.40 to 1.54%), thus being less likely to achieve the target HbA_{1c} of <7.0% (26%, 43%, 42%, and 44% in the lowest to highest C-peptide groups, respectively). Lower FPG levels were achieved in the lower C-peptide groups (6.3 ± 2.2 vs 6.5 ± 2.1 vs 6.7 ± 2.1 vs 7.0 ± 2.2 mmol/l). Final Gla-100 insulin dose was least in the lowest C-peptide group (0.34 U/kg), 0.42 U/kg in the >0.40−1.20 C-peptide group, and highest in the upper two C-peptide groups at 0.51, 0.50 U/kg, respectively. For all definitions and time periods of hypoglycaemia, incidence and event rates were higher with lower C-peptide levels (**Table**). The percentage of participants achieving HbA_{1c} <7.0% without hypoglycaemia (confirmed plasma glucose < 3.9 mmol/l) was 9%, 18%, 20%, and 25% in the lowest to highest C-peptide groups, respectively. Body weight change was greater with lower C-peptide levels (3.3 ± 3.7 vs 2.3 ± 3.5 vs 2.0 ± 4.0 vs 1.7 ± 3.2 kg).
Conclusion: This pooled analysis in people with T2D suggests that fasting C-peptide levels may help predict hypoglycaemia, insulin dose, and blood glucose control achieved when commencing Gla-100 therapy.

Table: Clinical outcomes in people with T2D starting Gla-100 stratified by baseline fasting C-peptide levels

		Baseline fasting C-peptide groups (nmol/l)			
		≤0.40 n=100	>0.40–1.20 n=1267	>1.20–2.00 n=621	>2.00 n=177
C-peptide	baseline (nmol/l)	0.30 (0.08)	0.84 (0.21)	1.51 (0.22)	2.62 (0.73)
Gla-100 dose	at start (U/kg)	0.21 (0.10)	0.17 (0.08)	0.16 (0.08)	0.15 (0.10)
	week 24 (U/kg)	0.34 (0.20)	0.42 (0.22)	0.51 (0.29)	0.50 (0.27)
Hypoglycaemia[a]	overall (% people)	66	51	43	34
	overall (events/person-yr)	12.8 (2.2)	6.6 (0.4)	4.0 (0.3)	2.5 (0.4)
	nocturnal (% people)	35	22	16	11
	nocturnal (events/person-yr)	3.3 (0.8)	1.4 (0.1)	0.8 (0.1)	0.6 (0.2)
Severe hypoglycaemia[b]	(% people)	5.0	2.4	2.1	0
	(events/person-yr)	0.18 (0.09)	0.11 (0.03)	0.10 (0.05)	0

Mean (SD) or percent.; Group numbers may vary if missing values; [a], confirmed plasma glucose < 3.9 mmol/l; [b], ADA definition; yr, year

Supported by: Sanofi
Disclosure: **D.R. Owens:** Employment/Consultancy; Boehringer Ingelheim, Roche Diagnostics, Eli Lilly, Sanofi and Takeda. Lecture/other fees; Boehringer Ingelheim, Roche Diagnostics, Eli Lilly, Sanofi and Takeda.