Insulin analogue glargine 300 U/mL and 100 U/mL: the same active principle with a higher concentration involves a reduced subcutaneous depot and a different insulin dissolution rate, determining an improved clinical-pharmacological drug profile.

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Background: Unmet medical needs lead to discover different drug formulations in order to improve clinical outcomes. Some chemical-physical changes of the same molecule can determine different PK/PD profiles. The new insulin glargine 300U/mL (Gla-300) forms a more compact subcutaneous depot with a reduced surface area compared to Gla-100 that determines a lower re-dissolution rate.

Aims: To compare the two formulations of insulin glargine concerning their PK/PD profiles and clinical outcomes .

Methods: We report the most updated literature evidences from clinical studies and meta-analysis, focusing on PK/PD and clinical profiles of Gla-300 vs Gla-100 in Type2 Diabetes Mellitus (T2DM). Results: Two studies, focused on Gla-300 vs Gla-100 PK/PD profiles, demonstrate a more prolonged glycaemic control and a more even activity with a lower within-/between-day intra-subject variability in exposure vs Gla-100 , . Consistent data emerge from a recent study comparing the two glycaemic profiles through Continuous Glucose Monitoring in Type1 DM . A patient-level meta-analysis of 1-year data of the EDITION 1, 2 and 3 studies in T2DM, comparing efficacy and safety of Gla-300 vs Gla-100, demonstrated that glycaemic control (Primary Endpoint) was sustained in both groups, with a more sustained A1c reduction for Gla-300 at 12 months: least squares [LS] mean change from baseline to month 12 was −0.91 [SE 0.03] % (−9.84 [0.33] mmol/mol) with Gla-300 and −0.80 [0.03] % (−8.74[0.33] mmol/mol) with Gla-100; the LS mean difference for the change in A1c between the groups was statistically significant. Hypoglycaemic risk (Secondary Endpoint) showed that fewer participants experienced ≥1 confirmed (≤70 mg/dL [≤3.9mmol/L]) or severe hypoglycemic event during the night (00:00–05:59 h) (RR 0.85; 95% CI: 0.77, 0.92) and at any time of day (RR 0.94; 95% CI: 0.90, 0.98) with Gla-300 compared with Gla-100. The annualized rates of hypoglycemia (≤70mg/dL) during the night were lower with Gla-300 compared with Gla-100. The benefit of Gla-300 was seen during the night and beyond the pre-defined nocturnal period, for both the participants experiencing ≥1 confirmed (≤70mg/dL) or severe event and events/participant-year. These benefits are confirmed by a retrospective observational study in real-life regarding 881 patients with T2DM who switched to Gla-300 from other basal insulins: mean reduction in A1c levels from baseline to follow-up (0-6 months) was 0.64% (8.97% vs 8.33%; 95% CI: 0.45, 0.84; P<0.0001). The reduction in A1c levels was seen as early as the first 3 months following Gla-300 initiation. Switching to Gla-300 from other basal insulins was associated with a 0.9% reduction in the subjects with hypoglycemia from baseline to follow-up (0-3 months) (6.0% vs 5.1%).

Conclusions: Gla-300 vs Gla-100, due to a more compact subcutaneous depot, is associated with modifications of the kinetics, with a more stable and prolonged PK/PD profile and a sustained 24-hglycaemic control with a lower risk of hypoglycaemia. U300, a novel long-acting insulin formulation.Sutton et al.Expert Opin.Biol.Ther2014

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