Efficacy and Safety of Insulin Glargine 300 U/mL (Gla-300) Versus Insulin Icodec in People with Type 2 Diabetes (PWT2D): A Systematic Literature Review and Network Meta-Analysis

Robert Ritzel[1], Fernando Gomez-Peralta[2], Raffaele Napoli[3], Alexandria Ratzki-Leewing[4,5], Maria Aileen N. Mabunay[6], Matyas Szigeti[7], Shreosi Sanyal[8], Agustina Alvarez[9], Victoria Wan[10], Francesco Giorgino[11]

[1]München Klinik Schwabing, Munich, Germany; [2]General Hospital of Segovia, Segovia, Spain; [3]Federico II University School of Medicine, Napoli, Italy; [4]University of Maryland School of Medicine, Baltimore, U.S.; [5]University of Maryland Institute for Health Computing, North Bethesda, U.S.; [6]Sanofi, Global Medical, Singapore; [7]Sanofi, Global Medical, Budapest, Hungary; [8]Sanofi, Global Medical, Hyderabad, India; [9]Sanofi, Global Medical, Spain; [10]Evidinno Outcomes Research Inc., Vancouver, Canada; [11]University of Bari Aldo Moro, Bari, Italy.

POSTER #2852-LB
ADA
2026
June 5 – 8
NEW ORLEANS, USA

POSTER HIGHLIGHT: Gla-300 demonstrated lower non-severe hypoglycemia with comparable glycemic control versus Icodec.

BACKGROUND

- Basal insulin is initiated when individualized HbA1c targets are not achieved with oral and injectable non-insulin agents (NIAs).[1]
- Gla-300 is a once-daily basal insulin with comparable efficacy and lower hypoglycemia risk vs Glargine 100 U/mL, along with flexible titration.[2]
- Insulin Icodec (Icodec) is a once-weekly basal insulin offering dosing convenience.[3]

OBJECTIVE

- To compare the efficacy and safety (primary outcome: level 1 hypoglycemia) of Gla-300 and Icodec in insulin-naïve PWT2D uncontrolled on NIAs via a systematic literature review (SLR) and a network meta-analysis (NMA).

METHODS

Systematic Literature Review:

- An SLR was conducted following Cochrane guidelines, by searching MEDLINE®, Embase®, and CENTRAL from inception to July 3, 2025.
- Full-text eligibility was assessed by two reviewers using predefined PICO criteria: adult PWT2D, Gla-300 or Icodec, relevant glucose-lowering therapies, and glycemic and hypoglycemia outcomes in RCTs.

Network Meta-Analysis:

- Following the National Institute for Health and Care Excellence guidelines,[4] a Bayesian fixed-effect NMA evaluated outcomes at ~6 months:
  - Safety: 24-hour hypoglycemia (levels 1, 2, combined 2/3, and 3; cumulative incidence and event rate – definitions in **Table 1**), adverse events (AEs), serious AEs (SAEs), and discontinuation due to an AE.
  - Efficacy (glycemic control outcomes): HbA1c change, HbA1c <7% attainment (± level 2/3 hypoglycemia), fasting plasma glucose (FPG) change, body weight change, and final insulin dose (U/day; U/kg).
- A frequentist, fixed-effect NMA was conducted as a sensitivity analysis.

Table 1: Hypoglycemia Definitions

	Plasma Glucose Level
Level 1	< 70 mg/dL (< 3.9 mmol/L) and ≥ 54 mg/dL (≥ 3.0 mmol/L)
Level 2	< 54 mg/dL (< 3.0 mmol/L)
Level 3	Severe physical or mental impairment requiring external assistance for recovery
Combined Level 2/3	< 54 mg/dL (< 3.0 mmol/L) or Level 3 hypoglycemia

RESULTS

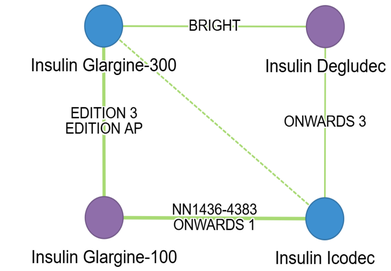
- The SLR identified 13 RCTs; five trials were included in the NMA (n = 3,246; Gla-300 n = 2,411; Icodec n = 835) (**Figure 1**)
- Baseline characteristics were broadly comparable (**Table 2**).
- Safety outcomes (**Figure 2**):
  - Gla-300 reduced risk and rate of level 1 hypoglycemia (primary outcome).
  - Gla-300 reduced risk and rates of level 2 and combined level 2/3 hypoglycemia.
  - No significant difference in level 3 hypoglycemia.
  - AE rates did not show differences between treatments.
- Efficacy outcomes (**Figure 3**):
  - HbA1c reduction and body weight change were similar between treatments.
  - Icodec achieved greater FPG reduction and higher HbA1c target attainment; however, *not* without level 2/3 hypoglycemia.
  - Insulin dose was higher with Gla-300 in U/day, but no difference in U/kg.
- Sensitivity analyses yielded consistent findings with the main analysis.

Table 2: Baseline Characteristics

	EDITION 3 (2015)[5]	EDITION AP (2020)[6]	NN1436-4383 (2020)[7]	ONWARDS 3 (2023)[8]	BRIGHT (2018)[9]
Sample size	878	604	247	588	929
Region	Global	Asia-Pacific	Europe and NA	Global	Europe and NA
Study follow-up, weeks	24	26	31	31	24
Target FPG, mmol/L	4.4–5.6	4.4–5.6	3.9–6.0	4.4–7.2	4.4–5.6
Age, years	57.7	58.3	59.6	58.5	60.6
Sex (male), %	57.7	56.3	56.3	62.8	54.5
Mean BMI, kg/m²	33.0	25.2	31.2	29.6	31.5
Mean HbA1c, %	8.5	8.6	8.0	8.5	8.6
Mean FPG, mg/dL	NR	177.4	181.0	181.5	186.5
Mean diabetes duration, years	9.9	10.6	9.7	10.6	10.6

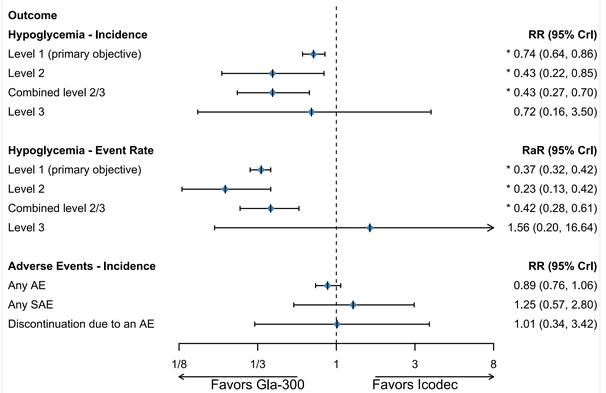
BMI, Body Mass Index, FPG, Fasting Plasma Glucose; NA, North America; NR, Not Reported

Figure 1: Network Diagram



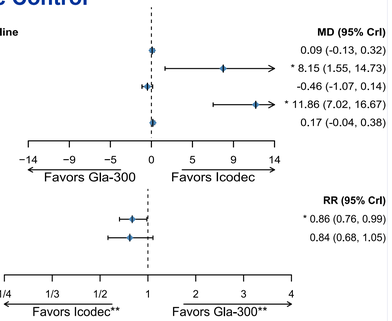
Blue circles represent interventions of interest; Purple circles represent comparators; Solid lines represent direct treatment comparison; Dotted line represents indirect treatment comparison

Figure 2: Forest Plot of Insulin Glargine-300 vs Insulin Icodec for 24-hour Hypoglycemia and AEs



*95% credible intervals exclude the null value (1 for risk and rate ratios; 0 for mean differences).
AE, Adverse Event; CrI, Credible Interval; RaR, Rate Ratio; RR, Risk Ratio; SAE, Serious Adverse Event

Figure 3: Forest Plot of Insulin Glargine-300 vs Insulin Icodec for Glycemic Control



*95% credible intervals exclude the null (1 for risk and rate ratios; 0 for mean differences).
**For these outcomes, higher values indicate greater HbA1c <7% attainment and favor Gla-300.
CrI, Credible Interval; FPG, Fasting Plasma Glucose; MD, Mean Difference; RR, Risk Ratio; U, Units

DISCUSSION

- At ~6 months, Gla-300 compared with Icodec reduced level 1, 2 and 2/3 hypoglycemia risk and rates with similar HbA1c reduction and effects on weight.
- FPG reduction with Icodec was greater (by 8.15 mg/dL); however, the absolute between-treatment difference represents 4.5% of the ~180 mg/dL mean baseline FPG. Thus, the clinical significance requires further evaluation.
- Icodec attained greater HbA1c <7% target when hypoglycemia was not considered
- AE-related outcomes were comparable between treatments.
- Overall, the findings suggest a favorable efficacy-safety profile for Gla-300 in PWT2D when compared with Icodec.
- Findings are based on indirect comparisons; additionally, fixed-effect models may not fully capture between-study heterogeneity despite broadly comparable baseline characteristics.

CONCLUSION

- In insulin-naïve PWT2D suboptimally managed on NIAs, Gla-300 use was associated with lower level 1, level 2, and combined level 2/3 hypoglycemia at ~6 months compared with Icodec.
- Glycemic measures and overall safety were broadly comparable.

REFERENCES

1. Becker RHA, *et al. Diabetes Care* 2015; 38: 637–643.
2. Davies MJ, *et al. Diabetologia* 2018; 61: 2461–2498.
3. Bajaj HS, *et al. Annals of Internal Medicine* 2023; 176: 1476–1485.
4. Dias S, *et al. NICE DSU TSD 2* 2014.
5. Bolli GB, *et al. Diabetes Metab* 2017; 43: 351–358.
6. Ji L, *et al. Diabetes Obes Metab* 2020; 22: 612–621.
7. Rosenstock J, *et al. N Engl J Med* 2020; 383: 2107–2116.
8. Lingvay I, *et al. JAMA* 2023; 330: 228–237.
9. Rosenstock J, *et al. Diabetes Care* 2018; 41: 2147–2154.

FUNDING

The study was sponsored by Sanofi. Medical writing support provided by Heather Berringer and Mir-Masoud Pourrahmat of Evidinno Outcomes Research Inc., Vancouver, Canada, funded by Sanofi.

DISCLOSURES

Robert Ritzel has acted as a consultant for Novo Nordisk and Sanofi; and has participated in speaker bureaus for Boehringer Ingelheim, Lilly, Pfizer, Novo Nordisk, and Sanofi. F. Gomez-Peralta has taken part in advisory panels for Dexcom, Insulcloud S.L., Abbott Diabetes, Novartis, Astra Zeneca, Sanofi and Novo Nordisk; has participated as principal investigator in Clinical Trials funded by Sanofi, Novo Nordisk, Boehringer Ingelheim Pharmaceuticals, and Lilly; and has acted as a speaker for Abbott Diabetes, Novartis, Sanofi, Novo Nordisk, Boehringer Ingelheim Pharmaceuticals, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Co., and Lilly. Raffaele Napoli, in this past 3 years, has received research support from AstraZeneca, Eli Lilly, NovoNordisk, and Sanofi; participated on advisory boards for Boehringer Ingelheim, Eli Lilly, and Sanofi; and he has also received presentation honoraria from AstraZeneca, Boehringer Ingelheim, Eli Lilly, Guidotti, MSD, NovoNordisk, and Sanofi. Alexandria Ratzki-Leewing, in this past 36 months, has received research support from Sanofi; participated on advisory boards for Sanofi; and served as a consultant for Sanofi, Vertex, Dexcom, and Abbott; she has also received presentation honoraria from Sanofi, Dexcom, and Abbott. Maria Aileen N. Mabunay, Matyas Szigeti, Shreosi Sanyal, and Agustina Alvarez are employees of Sanofi and may hold shares and/or stock options in the company. Victoria Wan was an employee of Evidinno Outcomes Research Inc at the time of the study conduct. Francesco Giorgino has participated on advisory boards for AstraZeneca, Biomea, Boehringer-Ingelheim, Eli Lilly, Kayothera, Lifescan, Merck Sharp & Dohme, Medtronic, NovoNordisk, Roche Diabetes Care, and Sanofi; has served on boards for the European Association for the Study of Diabetes (EASD)/European Foundation for the Study of Diabetes (EFSD) and the European Diabetes Forum (EUDF); has acted as a consultant for Eli Lilly, NovoNordisk, and Kayothera; has received presentation honoraria from AstraZeneca, Boehringer-Ingelheim, Eli Lilly, Lifescan, Merck Sharp & Dohme, Medtronic, NovoNordisk, Roche Diabetes Care, and Sanofi; has received research support from Eli Lilly and Roche Diabetes Care; and has received medical writing or statistical analysis support from Eli Lilly, NovoNordisk, Roche Diabetes Care, and Sanofi.