Concomitant iGlarLixi and sodium-glucose co-transporter-2 inhibitor therapy in adults with type 2 diabetes: LixiLan-G trial and real-world evidence results

Authors: Cristian Guja¹, Francesco Giorgino², Lawrence Blonde³, Amar Ali⁴, Martin Prázný⁵, Juris J. Meier⁶, Elisabeth Souhami⁷, Robert Lubwama⁸, Chen Ji⁹, Julio Rosenstock¹⁰

Affiliations: ¹Department of Diabetes, Nutrition and Metabolic Diseases, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; ²Department of Emergency and Organ Transplantation, Section of Internal Medicine, Endocrinology, Andrology and Metabolic Diseases, University of Bari Aldo Moro, Bari, Italy; ³Frank Riddick Diabetes Institute, Department of Endocrinology, Ochsner Medical Center, New Orleans, LA, USA; ⁴Oakenhurst Medical Practice, Blackburn, UK; ⁵³rd Department of Internal Medicine, ¹st Faculty of Medicine, Charles University in Prague, Prague, Czech Republic; ⁶Diabetes Division, St Josef Hospital, Ruhr-University Bochum, Bochum, Germany; ⁷Sanofi, Paris, France; ⁸Sanofi, Bridgewater, NJ, USA; ⁹Sanofi, Beijing, China; ¹⁰Dallas Diabetes Research Center at Medical City, Dallas, TX, USA

Corresponding author:

Name: Cristian Guja

Address: Department of Diabetes, Nutrition and Metabolic Diseases, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Tel: +40212108499

Fax: +40212102295

Email: cristian.guja@b.astral.ro
Supplementary Table 1: Baseline demographics and disease characteristics by study

| Baseline characteristic          | LixiLan-G subgroup analysis | RWE study |
|----------------------------------|----------------------------|-----------|
|                                  | iGlarLixi; SGLT2i users    | iGlarLixi; SGLT2i non-users | iGlarLixi; SGLT2i users | iGlarLixi; SGLT2i non-users |
|                                  | (n=26)                     | (n=231)   | (n=320)   | (n=1054)   |
| Age, years                       | 59.7 (8.9)                 | 59.2 (9.7) | 55.1 (9.5) | 58.7 (11.0) |
| Sex (female), n (%)              | 15 (57.7)                  | 116 (50.2) | 163 (50.9) | 568 (53.9)  |
| BMI, kg/m²                       | 30.5 (4.0)                 | 33.1 (4.4) | -          | -           |
| BMI categories, kg/m², n (%)     |                            |           |            |             |
| <30                              | 12 (46.2)                  | 59 (25.5)  | 71 (22.2)  | 211 (20.0)  |
| ≥30                              | 14 (53.8)                  | 172 (74.5) | 247 (77.2) | 829 (78.7)  |
| Duration of type 2 diabetes, years | 12.3 (6.9)                | 11.1 (7.5) | -          | -           |
| HbA₁c, %                         | 7.8 (0.5)                  | 7.9 (0.6)  | 9.2 (1.6)  | 9.5 (1.7)   |

Data are mean ± SD unless otherwise stated. *All participants in LixiLan-G were also receiving metformin; baseline characteristics captured in the randomised population.

BMI, body mass index; iGlarLixi, a fixed-ratio combination of insulin glargine 100 U/mL and the glucagon-like peptide-1 receptor agonist, lixisenatide; RWE, real-world evidence; SD, standard deviation; SGLT2i, sodium-glucose co-transporter-2 inhibitor.
Supplementary Table 2. Safety outcomes in the LixiLan-G subgroup analysis

|                                             | LixiLan-G subgroup analysis<sup>a</sup> |           |           |
|---------------------------------------------|----------------------------------------|-----------|-----------|
|                                             | iGlarLixi; SGLT2i users                | iGlarLixi; SGLT2i non-users |
|                                             | (n=25)                                 | (n=230)   |
| Participants with ≥1 TEAE, n (%)           | 14 (56.0)                              | 149 (64.8)|
| Participants with ≥1 serious TEAE, n (%)   | 2 (8.0)                                | 8 (3.5)   |
| Participants with ≥1 TEAE leading to permanent treatment discontinuation, n (%) | 0                                       | 9 (3.9)   |
| Participants with ≥1 TEAE leading to death, n (%) | 0                                       | 0         |
| Participants with gastrointestinal TEAEs, n (%) |                                         |           |
| Nausea                                      | 1 (4.0)                                | 54 (23.5)|
| Diarrhoea                                   | 0                                      | 22 (9.6) |
| Vomiting                                    | 1 (4.0)                                | 14 (6.1) |
|                                             |                                        | 7 (3.0)   |

<sup>a</sup>All participants in LixiLan-G were also receiving metformin; G safety data captured in the safety population, which included all randomised participants who received ≥1 dose of iGlarLixi, reported using MedDRA Version 21.0; TEAEs defined as adverse events that developed or worsened (according to the Investigator's opinion) or became serious during the period from first dose of study treatments, up to 3 days after the last administration.

iGlarLixi, a fixed-ratio combination of insulin glargine 100 U/mL and the glucagon-like peptide-1 receptor agonist, lixisenatide; MedDRA, Medical Dictionary for Regulatory Activities; SGLT2i, sodium-glucose co-transporter-2 inhibitor; TEAE, treatment-emergent adverse event.
## Supplementary Table 3. Safety outcomes in the RWE study

| RWE study                              | Participants with diabetic ketoacidosis at Month 6, n (%) | Participants with acute kidney injury at Month 6, n (%) | Participants with urinary tract infections at Month 6, n (%) |
|----------------------------------------|----------------------------------------------------------|--------------------------------------------------------|-----------------------------------------------------------|
| iGlarLixi; SGLT2i users (n=320)         | 1 (0.3)                                                  | 0                                                      | 1 (0.3)                                                   |
| iGlarLixi; SGLT2i non-users (n=1054)    | 2 (0.2)                                                  | 0                                                      | 6 (0.6)                                                   |

iGlarLixi, a fixed-ratio combination of insulin glargine 100 U/mL and the glucagon-like peptide-1 receptor agonist, lixisenatide; RWE, real-world evidence; SGLT2i, sodium-glucose co-transporter-2 inhibitor.
Supplementary Table 4. Healthcare resource utilisation in participants in the RWE (descriptive analyses)

| RWE study                        | Hospitalisation, n (%) | ED visits, n (%) |
|----------------------------------|------------------------|-----------------|
|                                  | Baseline   | Month 6     | Baseline | Month 6 |
| iGlarLixi; SGLT2i users (n=320)  |            |             |          |          |
|                                  | 36 (11.3)   | 38 (11.9)   | 34 (10.6)| 38 (11.9)|
| iGlarLixi; SGLT2i non-users      |            |             |          |          |
| (n=1054)                         | 149 (14.1)  | 170 (16.1)  | 137 (13.0)| 148 (14.0)|

GLP-1 RA use was discontinued at iGlarLixi initiation.
ED, emergency department; GLP-1 RA, glucagon-like peptide 1 receptor agonist; iGlarLixi, a fixed-ratio combination of insulin glargine 100 U/mL and the glucagon-like peptide-1 receptor agonist, lixisenatide; RWE, real-world evidence; SGLT2i, sodium-glucose co-transporter-2 inhibitor.