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 Guja[1], Francesco Giorgino[2], Lawrence Blonde[3], Amar Ali[4], Martin Prázný[5], Juris J. Meier[6], Elisabeth Souhami[7], Robert Lubwama[8], Chen Ji[9], Julio Rosenstock[10]

Affiliations:
[1]Department of Diabetes, Nutrition and Metabolic Diseases, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; [2]Department of Emergency and Organ Transplantation, Section of Internal Medicine, Endocrinology, Andrology and Metabolic Diseases, University of Bari Aldo Moro, Bari, Italy; [3]Frank Riddick Diabetes Institute, Department of Endocrinology, Ochsner Medical Center, New Orleans, LA, USA; [4]Oakenhurst Medical Practice, Blackburn, UK; [5]3rd Department of Internal Medicine, 1st Faculty of Medicine, Charles University in Prague, Prague, Czech Republic; [6]Diabetes Division, St Josef Hospital, Ruhr-University Bochum, Bochum, Germany; [7]Sanofi, Paris, France; [8]Sanofi, Bridgewater, NJ, USA; [9]Sanofi, Beijing, China; [10]Dallas Diabetes Research Center at Medical City, Dallas, TX, USA

Introduction

iGlarLixi is a once-daily fixed-ratio combination of insulin glargine 100 U/mL (iGlar) and the glucagon-like peptide 1 receptor agonist (GLP-1 RA) lixisenatide (Lixi) that robustly improves glycaemic control in adults with T2D irrespective of previous treatment (oral antihyperglycaemic drugs [OADs], basal insulin or GLP-1 RAs)

Objective

To assess the effects of **concomitant iGlarLixi and SGLT2i** therapy in a post hoc exploratory analysis of the LixiLan-G randomised controlled trial (RCT) and a retrospective, observational (real-world evidence [RWE]) cohort study

Study design

LixiLan-G trial

26 week

26-week, randomised, open-label, parallel-group trial comparing efficacy and safety of switching to **iGlarLixi** vs continuing previous **GLP-1 RA** regimen (NCT02787551)

Adults with T2D

HbA_{1c} ≥7 % and ≤9 % (≥53 and ≤75 mmol/mol)

Inadequately controlled by the maximum tolerated dose of daily or weekly GLP-1 RA and OADs (metformin ± pioglitazone ± SGLT2i)

Post hoc analysis (iGlarLixi arm only)

Main efficacy endpoint
HbA_{1c} change from baseline to Week 26

- **iGlarLixi without SGLT2i** N=231
- **iGlarLixi + SGLT2i** N=26

RWE study

RWE study of electronic medical records data from the US Optum-Humedica database (2017–2018)

Adults with T2D

HbA_{1c} ≥7 % (≥53 mmol/mol) within 90 days prior to and 14 days after the date of the first iGlarLixi prescription

75–180 days

≥1 HbA_{1c} result 75–180 days after iGlarLixi initiation

RWE analysis

Main efficacy endpoint
HbA_{1c} change from baseline to Month 6

- **iGlarLixi without SGLT2i** N=1054
- **iGlarLixi + SGLT2i** N=320

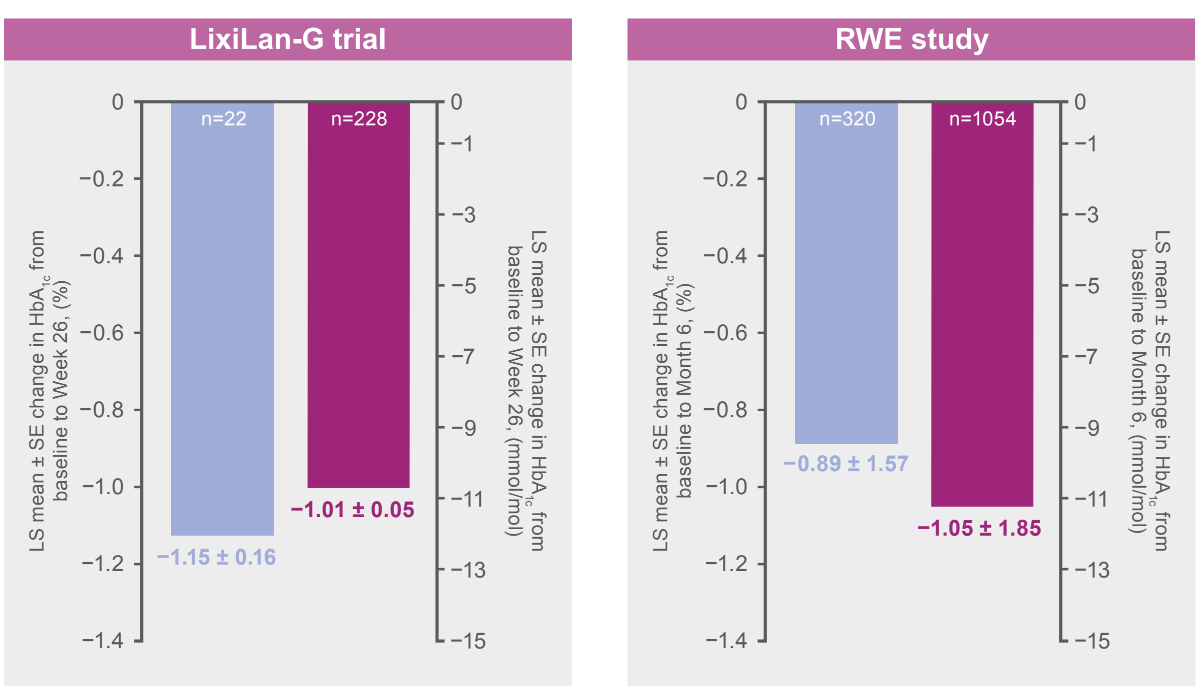
Key results

Baseline characteristics

In both studies, there were no major differences in baseline characteristics for those who initiated **iGlarLixi** while already using SGLT2i and those initiating **iGlarLixi** without concomitant SGLT2i therapy

Efficacy

HbA_{1c} changes were similar between SGLT2i users and non-users



Other efficacy endpoints were generally similar between SGLT2i users and non-users in the LixiLan-G trial post hoc analysis

LixiLan-G trial

LS mean (SE) change from baseline to Week 26	iGlarLixi + SGLT2i	iGlarLixi without SGLT2i
FPG, mmol/L	−2.83 (0.39)	−2.22 (0.13)
2-hour PPG, mmol/L	−5.04 (0.67)	−3.83 (0.22)
Body weight, kg	2.41 (0.6)	1.9 (0.2)

At Week 26, there was no difference in mean daily **iGlarLixi** dose between SGLT2i users and non-users in the LixiLan-G trial post hoc analysis

Safety

Prevalence and rates of hypoglycaemia were similar between SGLT2i users and non-users

LixiLan-G trial

	Documented symptomatic hypoglycaemia (≤3.9 mmol/L [≤70 mg/dL])		Severe hypoglycaemia*	
	iGlarLixi + SGLT2i	iGlarLixi without SGLT2i	iGlarLixi + SGLT2i	iGlarLixi without SGLT2i
% of participants (26-week period)	24.0%	28.3%	0%	0.4%
Events PPY (26-week period)	0.72	1.62	0	<0.01

*Event requiring assistance of another person to actively administer carbohydrate, glucagon or other resuscitative actions

RWE study

	Any hypoglycaemia		Hypoglycaemia events associated with an inpatient or ED visit	
	iGlarLixi + SGLT2i	iGlarLixi without SGLT2i	iGlarLixi + SGLT2i	iGlarLixi without SGLT2i
% of participants (6-month period)	7.5%	6.7%	1.3%	1.9%
Events PPY (6-month period)	0.26	0.24	0.05	0.05

Other safety endpoints were similar between SGLT2i users and non-users from baseline to Week 26/Month 6

		iGlarLixi + SGLT2i	iGlarLixi without SGLT2i
LixiLan-G trial	Participants with ≥1 TEAE, n (%)	14 (56.0)	149 (64.8)
LixiLan-G trial	Participants with TEAEs leading to permanent treatment discontinuation, n (%)	0 (0)	9 (3.9)
RWE study	Diabetic ketoacidosis, n (%)	1 (0.3)	2 (0.2)
RWE study	Acute kidney injury, n (%)	0 (0)	0 (0)
RWE study	Urinary tract infections, n (%)	1 (0.3)	6 (0.6)

Conclusions

Results from an RCT and a real-world clinical setting showed that **iGlarLixi** provided similar robust glycaemic control and comparably low risk of hypoglycaemia in people with T2D regardless of concomitant use of SGLT2i

This evidence supports the combined use of **iGlarLixi** and SGLT2i in the treatment of people with T2D

Abbreviations
ED, emergency department; FPG, fasting plasma glucose; GLP-1 RA, glucagon-like peptide 1 receptor agonist; HbA_{1c}, glycated haemoglobin; iGlar, insulin glargine 100 U/mL; Lixi, lixisenatide; LS, least squares; OAD, oral antihyperglycaemic drug; PPG, post-prandial plasma glucose; PPY, per participant-year; RCT, randomised controlled trial; RWE, real-world evidence; SD, standard deviation; SE, standard error; SGLT2i, sodium-glucose co-transporter-2 inhibitor; T2D, type 2 diabetes; TEAE, treatment-emergent adverse event.

Adis OPEN ACCESS PEER-REVIEWED INFOGRAPHIC