Clinical trial results:
A 24-Week, Single-Arm, Phase 4 Clinical Study to Evaluate the Efficacy and Safety of Switching to iGlarLixi in People with Type 2 Diabetes Mellitus Uncontrolled on Once or Twice Daily Premixed Insulin Regimen

Summary

EudraCT number	2021-003711-25
Trial protocol	CZ PL
Global end of trial date	21 July 2023

Results information

Result version number	v1 (current)
This version publication date	14 July 2024
First version publication date	14 July 2024

Trial information

Trial identification

Sponsor protocol code	LPS17008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	U1111-1261-7471

Notes:

Sponsors

Sponsor organisation name	Sanofi Aventis Recherche & Développement
Sponsor organisation address	1 Avenue Pierre Brossolette, Chilly-Mazarin, France, 91380
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 August 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 July 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe glycemic control, as measured by glycated hemoglobin (HbA1c), in people with type 2 diabetes mellitus (T2DM) switching from premixed insulins to iGlarLixi using an algorithm based on doses of both insulin components (basal plus mealtime).

Protection of trial subjects:

Participants were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the participant and considering the local culture. During the course of the trial, participants were provided with individual participant cards indicating the nature of the trial the participant is participating, contact details and any information needed in the event of a medical emergency.
Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy:

Participants were allowed to continue using metformin and/or sodium glucose co-transporter-2 (SGLT2) inhibitor throughout the study period.

Evidence for comparator: -

Actual start date of recruitment	07 April 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czechia: 1
Country: Number of subjects enrolled	Korea, Republic of: 64
Country: Number of subjects enrolled	Poland: 84
Country: Number of subjects enrolled	Türkiye: 13
Worldwide total number of subjects	162
EEA total number of subjects	85

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	65
From 65 to 84 years	96
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 25 centers in Czech Republic, Turkey, Korea, and Poland. A total of 255 participants were screened between 07 April 2022 and 31 January 2023, of which 93 were screen failures. Screen failures were mainly due to not meeting the inclusion criteria.

Pre-assignment

Screening details:

A total of 162 participants were enrolled in the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	iGlarLixi

Arm description:

Participants received iGlarLixi (Suliqua 100/50 or Suliqua 100/33) subcutaneous injection once daily (QD) for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	iGlarLixi
Investigational medicinal product code	
Other name	Suliqua
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

iGlarLixi (Suliqua 100/50 or Suliqua 100/33) was self-administered QD in the morning within 60 minutes before breakfast.

Number of subjects in period 1	iGlarLixi
Started	162
Completed	153
Not completed	9
Consent withdrawn by subject	4
Study terminated by Sponsor	1
Participant enrolled in error	1
Protocol-specified withdrawal criterion met	1
Adverse event, non-fatal	2

Baseline characteristics

Reporting groups	
Reporting group title	iGlarLixi
Reporting group description:	
Participants received iGlarLixi (Suliqua 100/50 or Suliqua 100/33) subcutaneous injection once daily (QD) for 24 weeks.	

Reporting group values	iGlarLixi	Total	
Number of subjects	162	162	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	65.1		
standard deviation	± 8.69	-	
Gender categorical			
Units: Subjects			
Female	73	73	
Male	89	89	

End points

End points reporting groups

Reporting group title	iGlarLixi

Reporting group description:

Participants received iGlarLixi (Suliqua 100/50 or Suliqua 100/33) subcutaneous injection once daily (QD) for 24 weeks.

Primary: Change in Glycated Hemoglobin From Baseline to Week 24

End point title	Change in Glycated Hemoglobin From Baseline to Week 24[1]

End point description:

Blood samples were collected to measure HbA1c at different time points during the study. Evaluable set included all enrolled participants who received at least 1 dose of iGlarLixi and had evaluable data for the primary endpoint (that is, HbA1c) at baseline and >=1 time point postbaseline.

End point type	Primary

End point timeframe:

Baseline (Day 0) and Week 24

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	iGlarLixi			
Subject group type	Reporting group			
Number of subjects analysed	145			
Units: percentage of HbA1c				
least squares mean (standard error)	-1.20 (± 0.074)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved an HbA1c Target of <7% From Baseline to Week 24

End point title	Percentage of Participants Who Achieved an HbA1c Target of <7% From Baseline to Week 24

End point description:

Blood samples were collected to measure HbA1c at different time points during the study. Percentage of participants who achieved a HbA1c target of <7% were determined. Evaluable set included all enrolled participants who received at least 1 dose of iGlarLixi and had evaluable data for the primary endpoint (that is, HbA1c) at baseline and >=1 time point postbaseline.

End point type	Secondary

End point timeframe:

Week 24

End point values	iGlarLixi			
Subject group type	Reporting group			
Number of subjects analysed	157			
Units: percentage of participants				
number (not applicable)	37.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Total Daily Insulin Dose From Baseline to Week 24

End point title	Change in Total Daily Insulin Dose From Baseline to Week 24

End point description:

Total daily insulin dose was calculated by the total daily insulin dose divided by the body weight on the same scheduled visit. Evaluable set included all enrolled participants who received at least 1 dose of iGlarLixi and had evaluable data for the primary endpoint (that is, HbA1c) at baseline and >=1 time point postbaseline. Total daily insulin dose at baseline was the starting dose of iGlarLixi.

End point type	Secondary

End point timeframe:

Baseline (Day 0) and Week 24

End point values	iGlarLixi			
Subject group type	Reporting group			
Number of subjects analysed	154			
Units: units				
arithmetic mean (standard deviation)	14.6 (± 11.67)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Fasting Plasma Glucose (FPG) From Baseline to Week 24

End point title	Change in Fasting Plasma Glucose (FPG) From Baseline to Week 24

End point description:

Blood samples were collected to measure FPG levels at different time points during the study. Evaluable set included all enrolled participants who received at least 1 dose of iGlarLixi and had evaluable data for the primary endpoint (that is, HbA1c) at baseline and >=1 time point postbaseline.

End point type	Secondary

End point timeframe:

Baseline (Day 0) and Week 24

End point values	iGlarLixi			
Subject group type	Reporting group			
Number of subjects analysed	144			
Units: milligram per deciliter (mg/dL)				
least squares mean (standard error)	-45.9 (± 2.99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Postprandial Glucose (PPG) at 2 Hours After Breakfast From Baseline to Week 24

End point title	Change in Postprandial Glucose (PPG) at 2 Hours After Breakfast From Baseline to Week 24

End point description:

Participants were supplied with a glucometer and an electronic diary to measure PPG levels at 2 hours after breakfast derived from 7-point self-measured plasma glucose (SMPG) profile during the study. The 7-point SMPG profile was measured at the following 7 points: preprandial (fasting) and 2 hours postprandial for breakfast, lunch, and dinner and at bedtime. Evaluable set included all enrolled participants who received at least 1 dose of iGlarLixi and had evaluable data for the primary endpoint (that is, HbA1c) at baseline and >=1 time point postbaseline.

End point type	Secondary

End point timeframe:

Baseline (Day 0) and Week 24

End point values	iGlarLixi			
Subject group type	Reporting group			
Number of subjects analysed	117			
Units: mg/dL				
least squares mean (standard error)	-68.2 (± 3.19)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Average Daily Blood Glucose From Baseline to Week 24

End point title	Change in Average Daily Blood Glucose From Baseline to Week 24

End point description:

Participants were supplied with a glucometer and an electronic diary to measure average daily blood glucose derived from 7-point SMPG profile during the study. The average daily blood glucose value was calculated as the mean of the plasma glucose values over the 7 time points. The 7-point SMPG profile was measured at the following 7 points: preprandial (fasting) and 2 hours postprandial for breakfast, lunch, and dinner and at bedtime. Evaluable set included all enrolled participants who received at least 1 dose of iGlarLixi and had evaluable data for the primary endpoint (that is, HbA1c) at baseline and >=1 time point postbaseline.

End point type	Secondary

End point timeframe:

Baseline (Day 0) and Week 24

End point values	iGlarLixi			
Subject group type	Reporting group			
Number of subjects analysed	117			
Units: mg/dL				
least squares mean (standard error)	-42.41 (± 2.614)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Body Weight From Baseline to Week 24

End point title	Change in Body Weight From Baseline to Week 24

End point description:

Participants body weight was measured at different time points during the study. Evaluable set included all enrolled participants who received at least 1 dose of iGlarLixi and had evaluable data for the primary endpoint (that is, HbA1c) at baseline and >=1 time point postbaseline.

End point type	Secondary

End point timeframe:

Baseline (Day 0) and Week 24

End point values	iGlarLixi			
Subject group type	Reporting group			
Number of subjects analysed	148			
Units: kilogram				
least squares mean (standard error)	-1.04 (± 0.264)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved an HbA1c Target of <7% Without Clinically Relevant Hypoglycemia From Baseline to Week 24

End point title	Percentage of Participants Who Achieved an HbA1c Target of <7% Without Clinically Relevant Hypoglycemia From Baseline to Week 24

End point description:

Blood samples were collected to measure HbA1c at different time points during the study. Percentage of participants who achieved a HbA1c target of <7% without clinically relevant hypoglycemia, defined as

severe hypoglycemia [American Diabetes Association (ADA) Level 3] or any hypoglycemia (ADA Level 2) event were determined. ADA Level 2 was defined as a measurable glucose concentration of <54 mg/dL [3.0 millimoles (mmol)/L] that needs immediate action. ADA Level 3 was defined as a severe event characterized by altered mental and/or physical functioning that requires assistance from another person for recovery. Evaluable set included all enrolled participants who received at least 1 dose of iGlarLixi and had evaluable data for the primary endpoint (that is, HbA1c) at baseline and >=1 time point postbaseline.

End point type	Secondary

End point timeframe:

Week 24

End point values	iGlarLixi			
Subject group type	Reporting group			
Number of subjects analysed	157			
Units: percentage of participants				
number (not applicable)	29.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved an HbA1c Target of <7% Without Clinically Relevant Hypoglycemia and Without Body Weight Increase From Baseline to Week 24

End point title	Percentage of Participants Who Achieved an HbA1c Target of <7% Without Clinically Relevant Hypoglycemia and Without Body Weight Increase From Baseline to Week 24

End point description:

Blood samples were collected to measure HbA1c at different time points during the study. Percentage of participants who achieved a HbA1c target of <7% without clinically relevant hypoglycemia, defined as severe hypoglycemia (ADA Level 3) or any hypoglycemia (ADA Level 2) event, and without body weight change >0. ADA Level 2 was defined as a measurable glucose concentration of <54 mg/dL (3.0 mmol/L) that needs immediate action. ADA Level 3 was defined as a severe event characterized by altered mental and/or physical functioning that requires assistance from another person for recovery. Evaluable set included all enrolled participants who received at least 1 dose of iGlarLixi and had evaluable data for the primary endpoint (that is, HbA1c) at baseline and >=1 time point postbaseline.

End point type	Secondary

End point timeframe:

Week 24

End point values	iGlarLixi			
Subject group type	Reporting group			
Number of subjects analysed	157			
Units: percentage of participants				
number (not applicable)	22.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With At Least One Hypoglycemia Event

End point title	Percentage of Participants With At Least One Hypoglycemia Event

End point description:

Participants were instructed to document any hypoglycemia events (including any reasons possibly contributing to hypoglycemia, for example, physical exercise, skipped meal) in their electronic Diary. Hypoglycemia was reported in the specific hypoglycemia event information form in the electronic case report form with onset date and time, symptoms and/or signs, the SMPG value, if available, and the treatment.
ADA Level 1 was defined as a measurable glucose concentration of <70 mg/dL (3.9 mmol/L) but >=54 mg/dL (3.0 mmol/L) that can alert a person to take action.

ADA Level 2 was defined as a measurable glucose concentration of <54 mg/dL (3.0 mmol/L) that needs immediate action.

ADA Level 3 was defined as a severe event characterized by altered mental and/or physical functioning that requires assistance from another person for recovery.

Safety set included all participants who took at least 1 dose of iGlarLixi.

End point type	Secondary

End point timeframe:

From the first dose of study treatment (Day 0) up to 24 weeks

End point values	iGlarLixi			
Subject group type	Reporting group			
Number of subjects analysed	162			
Units: percentage of participants				
number (not applicable)	65.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Hypoglycemia Events Per Participant-Year

End point title	Number of Hypoglycemia Events Per Participant-Year

End point description:

Participants were instructed to document any hypoglycemia events (including any reasons possibly contributing to hypoglycemia, for example, physical exercise, skipped meal) in their electronic Diary. Hypoglycemia was reported in the specific hypoglycemia event information form in the electronic case report form with onset date and time, symptoms and/or signs, the SMPG value, if available, and the treatment. Event rate of hypoglycemia per person year = total number of hypoglycemia events from all

participants/total participant-years of exposure from all participants Total person years: sum of (last dose date – first dose date + 2)/365.25 over all participants in the safety set. Safety set included all participants who took at least 1 dose of iGlarLixi.

End point type	Secondary

End point timeframe:

From the first dose of study treatment (Day 0) up to 24 weeks

End point values	iGlarLixi			
Subject group type	Reporting group			
Number of subjects analysed	162			
Units: Events per participant-year				
number (not applicable)	8.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Treatment-Emergent Serious Adverse Events (SAEs) and Treatment-Emergent Adverse Events of Special Interest (AESI)

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Treatment-Emergent Serious Adverse Events (SAEs) and Treatment-Emergent Adverse Events of Special Interest (AESI)

End point description:

An AE is any untoward medical occurrence in a participant or clinical study participant, whether or not considered related to the study drug. An SAE is defined as any AE that, at any dose, meets one of the following criteria: results in death or is life-threatening or requires inpatient hospitalization or prolongation of existing hospitalization or results in persistent or significant disability/incapacity or congenital anomaly/birth defect. An AESI is an AE (serious or nonserious) of scientific and medical concern specific to the sponsor's product or program, for which ongoing monitoring and immediate notification by the investigator to the sponsor is required. TEAEs are defined as AEs that developed, worsened, or became serious during the treatment-emergent period, defined as the time from the first administration of the study drug (Day 0) to the last administration of the study drug + 3 days. Safety set included all participants who took at least 1 dose of iGlarLixi.

End point type	Secondary

End point timeframe:

TEAEs data was collected from the first administration of the study drug (Day 0) up to 3 days after last administration of the study drug (maximum exposure duration: up to 24 weeks).

End point values	iGlarLixi			
Subject group type	Reporting group			
Number of subjects analysed	162			
Units: participants				
Any TEAE	60			
Any treatment-emergent SAE	4			
Any treatment-emergent AESI	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

TEAEs data was collected from the first administration of the study drug (Day 0) up to 3 days after last administration of the study drug (maximum exposure duration: up to 24 weeks).

Adverse event reporting additional description:

Analysis was performed on the safety set.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	iGlarLixi

Reporting group description:

Participants received iGlarLixi (Suliqua 100/50 or Suliqua 100/33) subcutaneous injection QD for 24 weeks.

Serious adverse events	iGlarLixi		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 162 (2.47%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Facial bones fracture			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Ischaemic stroke			
subjects affected / exposed	1 / 162 (0.62%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	iGlarLixi		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 162 (5.56%)		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	9 / 162 (5.56%)		
occurrences (all)	13		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 November 2021	• For participant recruitment, the HbA1c range in people with T2DM whose diabetes was uncontrolled on premixed insulins was clarified to read as >=7.5% and <=10.0% (previously 7.5% to 10.0%). • An additional premixed combination insulin (that is, human insulin isophane suspension [75%] and human insulin injection [recombinant DNA origin, 25%]) was included in the list of allowed premixed combination insulins (that is, insulin aspart [30%] + insulin aspart protamine [70%]; insulin lispro [25%] + insulin lispro protamine [75%]; human insulin isophane suspension [70%] and human insulin injection [recombinant DNA origin, 30%]) of <50 units/day. • The hypertriglyceridemia limit was increased to >500 mg/dL (previously >400 mg/dL) in the exclusion criteria to align with the Common Terminology Criteria for Adverse Events version 5.0. • The section on concomitant therapy was updated to clarify that the systemic glucocorticoid therapy (excluding topical, intraarticular, or ophthalmic application, nasal spray or inhaled forms) was also not permitted during the screening or the treatment period. • The section on clinical laboratory tests was updated to include amylase, lipase, and triglycerides, as they represented the eligibility criteria and the potential discontinuation criteria.
02 August 2022	• A clarification was made in study design and accordingly updates were made in inclusion criteria to reflect that participants were allowed to continue to use their protocol-allowed background oral antidiabetic drugs (OADs), except daily dipeptidyl peptidase 4 inhibitor (DPP-4i) and sulfonylurea (SU). • The study design section, including the schedule of events and schematic of study design, was updated to clarify that dose adjustment was a continuous process; therefore, phone contact should occur continuously at least twice weekly. • Inclusion criteria was updated to clarify reduced FPG cut off value that is, >=130 mg/dL (previously >=140 mg/dL) to ease recruitment in Korea and other countries. • Exclusion criteria was updated to align with inclusion criteria that allowed metformin alone or metformin plus 1 or 2 OADs. Exclusion criteria was updated to clarify that participants who had previously received combination of insulin degludec and insulin aspart were to be excluded from the study. • Sections on temporary discontinuation, handling of withdrawal and rescue therapy was updated for further clarifications. • The text in the treatment administration section was updated to clarify that for previous full premixed insulin dose <12 units/day, corresponding iGlarLixi starting dose was <10 units, which was technically not possible to dispense with SoloStar [10/40] pen. Therefore, the starting dose of iGlarLixi was set at 10 units. • Text in the section on concomitant therapy was updated to further clarify the list of medications not permitted during the screening period or the treatment period of the study. • Schedule of events was updated to include 2 new footnotes related to discontinuation of DPP-4i and SU before switching to iGlarLixi and for the clarification that for baseline HbA1c value a screening HbA1c value would be used and when to plan HbA1c test in case rescue therapy was required.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported