



Clinical trial results:

Suliqua® (iGlarLixi) in Participants Uncontrolled on Basal Insulin to Evaluate the Change of Time in Target Range By Using Continuous Glucose Monitoring

Summary

EudraCT number	2019-004080-43
Trial protocol	HU CZ
Global end of trial date	04 April 2022

Results information

Result version number	v1 (current)
This version publication date	14 April 2023
First version publication date	14 April 2023

Trial information

Trial identification

Sponsor protocol code	LPS16664
-----------------------	----------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	U1111-1242-0304

Notes:

Sponsors

Sponsor organisation name	Sanofi-Aventis Private Co. Ltd.
Sponsor organisation address	Váci út 133. E building, 3rd floor, Budapest, Hungary, 1138
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	12 May 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	04 April 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the effect of Suliqua® once-daily on glycemic control as evaluated by Continuous Glucose Monitoring (CGM) in subjects with type-2 diabetes mellitus (T2DM) uncontrolled on their previous basal insulin.

Protection of trial subjects:

Subjects 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 subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject 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: -

Evidence for comparator: -

Actual start date of recruitment	08 January 2021
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: 29
Country: Number of subjects enrolled	Hungary: 22
Worldwide total number of subjects	51
EEA total number of subjects	51

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)	22
From 65 to 84 years	29
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study was conducted at 6 active sites in Hungary and the Czech Republic. A total of 70 subjects were screened from 08 January 2021 to 12 November 2021, out of which 19 subjects were screen failures mainly due to not meeting eligibility criteria.

Pre-assignment

Screening details:

A total of 51 subjects were enrolled and treated with study intervention.

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	Suliqua® (All subjects)
------------------	-------------------------

Arm description:

Subjects self-administered subcutaneous (SC) injection of Suliqua® once daily before a meal for 17 weeks in addition to the mandated background therapy with metformin with or without optional background therapy with sodium-glucose Cotransporter-2 (SGLT-2).

Arm type	Experimental
Investigational medicinal product name	Insulin glargine, lixisenatide
Investigational medicinal product code	
Other name	Suliqua® 100/50 or Suliqua® 100/33
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects self-administered SC injection of fixed ratio combination of insulin glargine/lixisenatide using a pre-filled disposable SoloStar® pen-injector (100 Units per millilitre [U/ml] insulin glargine with 50 micrograms per millilitre [mcg/ml] or 33 mcg/ml lixisenatide depending on the pen Suliqua® 100/50 or Suliqua® 100/33, respectively in the hour before the meal once daily for 17 weeks.

Number of subjects in period 1	Suliqua® (All subjects)
Started	51
Completed	51

Baseline characteristics

Reporting groups

Reporting group title	Suliqua® (All subjects)
-----------------------	-------------------------

Reporting group description:

Subjects self-administered subcutaneous (SC) injection of Suliqua® once daily before a meal for 17 weeks in addition to the mandated background therapy with metformin with or without optional background therapy with sodium-glucose Cotransporter-2 (SGLT-2).

Reporting group values	Suliqua® (All subjects)	Total	
Number of subjects	51	51	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	65.0 ± 8.36	-	
Gender categorical Units: Subjects			
Female	17	17	
Male	34	34	

End points

End points reporting groups

Reporting group title	Suliqua® (All subjects)
Reporting group description: Subjects self-administered subcutaneous (SC) injection of Suliqua® once daily before a meal for 17 weeks in addition to the mandated background therapy with metformin with or without optional background therapy with sodium-glucose Cotransporter-2 (SGLT-2).	

Primary: Mean Change From Baseline in Percentage of Time of Glucose Concentration Within the Target Range of Greater Than or Equal to (\geq) 70 to Less Than or Equal to (\leq) 180 Milligrams per Decilitre (mg/dL) at Week 18

End point title	Mean Change From Baseline in Percentage of Time of Glucose Concentration Within the Target Range of Greater Than or Equal to (\geq) 70 to Less Than or Equal to (\leq) 180 Milligrams per Decilitre (mg/dL) at Week 18 ^[1]
-----------------	---

End point description:

The Continuous Glucose Monitoring (CGM) system combined frequent interstitial glucose measurements (every 5 minutes) with ability to analyse glucose levels in real time. Analysis was performed on per-protocol analysis set (PPAS) which included all subjects who had received at least one dose of Suliqua®, and had at least one post Baseline assessment of any efficacy variable; had at least 12 weeks of exposure with Suliqua® with no major violation of study entry criteria (inclusion/exclusion) and no major violation of trial procedures and had a valid Baseline and follow-up CGM for assessment for the primary endpoint.

End point type	Primary
----------------	---------

End point timeframe:

Baseline, Week 18

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: Statistical analysis data chart is added as attachment.

End point values	Suliqua® (All subjects)			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: percentage of time				
arithmetic mean (standard deviation)	-6.53 (\pm 20.011)			

Attachments (see zip file)	Statistical Analysis for Primary endpoint/Statistical Analysis for
-----------------------------------	--

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percentage of Time of Glucose Concentration Within the Target Range of ≥ 70 to ≤ 180 mg/dL at Week 18

End point title	Mean Percentage of Time of Glucose Concentration Within the Target Range of ≥ 70 to ≤ 180 mg/dL at Week 18
-----------------	--

End point description:

CGM system combined frequent interstitial glucose measurements (every 5 minutes) with ability to analyse glucose levels in real time. Analysis was performed on PPAS.

End point type Secondary

End point timeframe:

Week 18

End point values	Suliqua® (All subjects)			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: percentage of time				
arithmetic mean (confidence interval 95%)	78.32 (74.01 to 82.64)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Percentage of Time in Hyperglycemia Range With Glucose Concentrations Greater than (>) 10 millimoles per Litre (mmol/L) and >13.9 mmol/L at Week 18

End point title	Mean Change From Baseline in Percentage of Time in Hyperglycemia Range With Glucose Concentrations Greater than (>) 10 millimoles per Litre (mmol/L) and >13.9 mmol/L at Week 18
-----------------	--

End point description:

The CGM system combined frequent interstitial glucose measurements (every 5 minutes) with ability to analyse glucose levels in real time. Analysis was performed on PPAS.

End point type Secondary

End point timeframe:

Baseline, Week 18

End point values	Suliqua® (All subjects)			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: percentage of time				
arithmetic mean (standard deviation)	-9.56 (± 11.727)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Glucose Standard Deviation at Week 18

End point title	Mean Change From Baseline in Glucose Standard Deviation at Week 18
End point description: Analysis was performed on PPAS.	
End point type	Secondary
End point timeframe: Baseline, Week 18	

End point values	Suliqua® (All subjects)			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[2]			
Units: mg/dL				
arithmetic mean (standard deviation)	()			

Notes:

[2] - Not enough data was available to allow calculation for this endpoint, hence no analysis performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Glucose Coefficient of Variation (CV%) at Week 18

End point title	Mean Change From Baseline in Glucose Coefficient of Variation (CV%) at Week 18
End point description: CV% was a measure of spread of variability relative to mean of population. Analysis was performed on PPAS.	
End point type	Secondary
End point timeframe: Baseline, Week 18	

End point values	Suliqua® (All subjects)			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: percentage of CV				
arithmetic mean (standard deviation)	1.12 (± 6.27)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Mean Amplitude of Glucose Excursions (MAGE) at Week 18

End point title	Mean Change From Baseline in Mean Amplitude of Glucose Excursions (MAGE) at Week 18
-----------------	---

End point description:

Analysis was performed on PPAS.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline, Week 18

End point values	Suliqua® (All subjects)			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[3]			
Units: mg/dL				
arithmetic mean (standard deviation)	()			

Notes:

[3] - Not enough data was available to allow calculation for this endpoint, hence no analysis performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Glycated Hemoglobin A1c (HbA1c) at Week 18

End point title	Mean Change From Baseline in Glycated Hemoglobin A1c (HbA1c) at Week 18
-----------------	---

End point description:

Analysis was performed on full analysis set (FAS) which included all subjects who received at least one dose of Suliqua® and had at least one post baseline assessment of any efficacy variables, irrespective of compliance with the study protocol and procedures.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline, Week 18

End point values	Suliqua® (All subjects)			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: percentage of HbA1c				
arithmetic mean (standard deviation)	1.17 (± 0.854)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With HbA1c Response Rate <7.5%, <7.0% and <=6.5% at Week 18

End point title	Percentage of Subjects With HbA1c Response Rate <7.5%, <7.0% and <=6.5% at Week 18
-----------------	--

End point description:

Percentage of subjects with HbA1c response rate of less than (<) 7.5%, <7.0% and <=6.5% at Week 18 are reported in this endpoint. Analysis was performed on FAS. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 18

End point values	Suliqua® (All subjects)			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: percentage of subjects				
number (confidence interval 95%)				
HbA1c < 7.5% (n=37)	72.5 (58.3 to 84.1)			
HbA1c < 7.0% (n=25)	49.0 (34.8 to 63.4)			
HbA1c <= 6.5% (n=15)	29.4 (17.5 to 43.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Fasting Plasma Glucose (FPG) at Week 18

End point title	Mean Change From Baseline in Fasting Plasma Glucose (FPG) at Week 18
-----------------	--

End point description:

Mean change from Baseline in FPG at Week 18 was reported in this endpoint. Change was calculated by subtracting Week 18 values from the Baseline values. Analysis was performed on FAS population.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline, Week 18

End point values	Suliqua® (All subjects)			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: mmol/L				
arithmetic mean (standard deviation)	0.864 (± 1.750)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Suliqua® Dose at Week 18

End point title	Mean Change From Baseline in Suliqua® Dose at Week 18
End point description: Change from Baseline in Suliqua® dose at week 18 was reported in this endpoint. Analysis was performed on FAS population.	
End point type	Secondary
End point timeframe: Baseline, Week 18	

End point values	Suliqua® (All subjects)			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: units per micrograms (U/mcg)				
arithmetic mean (standard deviation)	-19.0 (± 9.04)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Body Weight at Week 18

End point title	Change From Baseline in Body Weight at Week 18
End point description: Change from Baseline in body weight at Week 18 was reported in this endpoint. Analysis was performed on FAS population.	
End point type	Secondary
End point timeframe: Baseline, Week 18	

End point values	Suliqua® (All subjects)			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: kilograms (kg)				
arithmetic mean (standard deviation)	-0.72 (± 4.11)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Diabetes Treatment Satisfaction Questionnaire (DTSQ) at Week 18

End point title	Change From Baseline in Diabetes Treatment Satisfaction Questionnaire (DTSQ) at Week 18
-----------------	---

End point description:

The DTSQ contains 8 items assessing overall treatment satisfaction, treatment convenience and flexibility, satisfaction with understanding of diabetes, willingness to continue present treatment and to recommend it to others, and frequency of unacceptably high and unacceptably low blood glucose levels. It uses a 7-point scale where 0=very dissatisfied to 6= very satisfied for a total possible score of 0 (very dissatisfied) to 36 (very satisfied), where higher scores indicate higher satisfaction from treatment. Analysis was performed on PPAS

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline, Week 18

End point values	Suliqua® (All subjects)			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: score on a scale				
arithmetic mean (standard deviation)	-3.97 (± 6.186)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Percentage of Time in Hypoglycemia Ranges With Glucose Concentrations ≤3.9 mmol/L and <3.0 mmol/L at Week 18

End point title	Mean Change From Baseline in Percentage of Time in Hypoglycemia Ranges With Glucose Concentrations ≤3.9 mmol/L and <3.0 mmol/L at Week 18
-----------------	---

End point description:

CGM system combined frequent interstitial glucose measurements (every 5 minutes) with ability to analyse glucose levels in real time. Analysis was performed on Safety population which included all subjects with at least one dose of Suliqua®, regardless of the amount of treatment administered.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline, Week 18

End point values	Suliqua® (All subjects)			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: percentage of time				
arithmetic mean (standard deviation)	6.61 (± 11.187)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With at Least One Hypoglycemic Event

End point title	Number of Subjects With at Least One Hypoglycemic Event
-----------------	---

End point description:

Severe hypoglycemia was an event in which the subject required the assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions, because the subject was not capable of helping self. Documented symptomatic hypoglycemia was an event during which typical symptoms of hypoglycemia was accompanied by a measured plasma glucose concentration of ≤ 3.9 mmol/L (≤ 70 mg/dL) or < 3.0 mmol/L (< 54 mg/dL). Analysis was performed on Safety population.

End point type	Secondary
----------------	-----------

End point timeframe:

From first IMP administration up to 3 days post last IMP administration (i.e., up to Week 18)

End point values	Suliqua® (All subjects)			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: subjects				
Any hypoglycemia	21			
Severe hypoglycemia	0			
Documented symptomatic hypoglycemia	16			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Hypoglycemia Events Per Subject-Year

End point title	Number of Hypoglycemia Events Per Subject-Year
-----------------	--

End point description:

Number of hypoglycemia events (any, severe and documented) per subject-year of exposure were reported. Severe hypoglycemia was an event in which the subject required the assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions, because the subject was not capable of helping self. Documented symptomatic hypoglycemia was an event during which typical symptoms of hypoglycemia was accompanied by a measured plasma glucose concentration of <3.9 mmol/L (<70 mg/dL) or < 3.0 mmol/L (< 54mg/dL). Analysis was performed on Safety population.

End point type	Secondary
----------------	-----------

End point timeframe:

From first IMP administration up to 3 days post last IMP administration (i.e., up to Week 18)

End point values	Suliqua® (All subjects)			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: events per subject-year				
number (not applicable)				
Any hypoglycemia	2.814			
Severe hypoglycemia	0.000			
Documented symptomatic hypoglycemia	2.031			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first IMP administration up to 3 days post last IMP administration (i.e., up to Week 18)

Adverse event reporting additional description:

Reported AEs were TEAEs that developed/worsened or became serious during on-treatment period (time from first IMP administration up to 3 days post last IMP administration). Analysis was performed on safety population.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	24.1
--------------------	------

Reporting groups

Reporting group title	Suliqua® (All subjects)
-----------------------	-------------------------

Reporting group description:

Subjects self-administered SC injection of Suliqua® once daily before a meal for 17 weeks in addition to the mandated background therapy with metformin with or without optional background therapy with SGLT-2.

Serious adverse events	Suliqua® (All subjects)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 51 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Suliqua® (All subjects)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 51 (29.41%)		
Investigations			
Ultrasound Examination			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Ear Injury			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences (all)	1		

Fall subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 2		
Falling Down subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1		
Shoulder Injury subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1		
Toe Injury subjects affected / exposed occurrences (all)	2 / 51 (3.92%) 2		
Vascular disorders Chronic Venous Insufficiency subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1		
Hypertension Worsened subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1		
Surgical and medical procedures Drug Therapy subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1		
Emergency Care subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1		
Suturing Of Wound subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1		
Tetanus Immunisation subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1		
General disorders and administration			

site conditions Fever subjects affected / exposed occurrences (all) Flu Like Symptoms subjects affected / exposed occurrences (all) Weakness subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1 1 / 51 (1.96%) 1 1 / 51 (1.96%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	3 / 51 (5.88%) 4 1 / 51 (1.96%) 1 1 / 51 (1.96%) 1		
Skin and subcutaneous tissue disorders Exanthema subjects affected / exposed occurrences (all) Psoriasis subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1 1 / 51 (1.96%) 1		
Musculoskeletal and connective tissue disorders Knee Swelling subjects affected / exposed occurrences (all) Muscle Pain subjects affected / exposed occurrences (all) Pain Knee	1 / 51 (1.96%) 1 1 / 51 (1.96%) 1		

subjects affected / exposed	1 / 51 (1.96%)		
occurrences (all)	1		
Painful Knee			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences (all)	1		
Rotator Cuff Syndrome			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences (all)	1		
Infections and infestations			
Covid-19			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences (all)	1		
Erysipelas			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences (all)	1		
Pelvic Abscess			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences (all)	1		
Viral Infection			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported