

**Clinical trial results:****An Open-label, Randomized, Multicenter, Phase III Study to Compare the Immunogenicity, Efficacy, and Safety of Gan & Lee Pharmaceuticals Insulin Glargine Injection to Lantus® (Insulin Glargine Injection) in Adult Subjects with Type 1 Diabetes Mellitus****Summary**

EudraCT number	2017-001450-34
Trial protocol	HU CZ ES
Global end of trial date	19 August 2019

Results information

Result version number	v2 (current)
This version publication date	17 June 2022
First version publication date	14 July 2021
Version creation reason	<ul style="list-style-type: none">• New data added to full data set The study result analysis and the study report were delayed because of both technical challenges with data collection which needed verification at the study sites, and Covid-19 over the past year. The results are now available and are ready to be uploaded.
Summary attachment (see zip file)	Response to EudraCT May 2021 (Response to EudraCT May 2021.pdf)

Trial information**Trial identification**

Sponsor protocol code	GL-GLAT1-3001
-----------------------	---------------

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Gan & Lee Pharmaceuticals, USA
Sponsor organisation address	520 US Highway 22 Ste 302, Bridgewater, United States, 08807
Public contact	Mike Hu, CEO, Gan & Lee Pharmaceuticals, USA, 1 8882885395, mike.hu@ganlee.us
Scientific contact	Mike Hu, CEO, Gan & Lee Pharmaceuticals, USA, 1 8882885395, mike.hu@ganlee.us

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	11 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 August 2019
Global end of trial reached?	Yes
Global end of trial date	19 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate equivalence of Gan & Lee Pharmaceuticals insulin glargine and Lantus® in terms of immunogenicity and efficacy

Protection of trial subjects:

In this study, safety was assessed by evaluating the following:

- AEs, AEs of hypoglycemia, serious AEs (SAEs), fatal SAEs, AEs leading to discontinuation of the study treatment and/or withdrawal from the study, IP-related AEs, and injection site reactions
- Treatment-emergent AEs (TEAEs)
- Clinical laboratory parameters
- Vital signs (blood pressure, pulse, and body weight)
- 12-lead electrocardiogram (ECG)

AEs were collected at every in-person visit and telephone visit.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 October 2017
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	Poland: 74
Country: Number of subjects enrolled	Spain: 54
Country: Number of subjects enrolled	Czechia: 49
Country: Number of subjects enrolled	Germany: 57
Country: Number of subjects enrolled	Hungary: 41
Country: Number of subjects enrolled	United States: 301
Worldwide total number of subjects	576
EEA total number of subjects	275

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)	508
From 65 to 84 years	68
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A Total of 576 subjects (80.2%) met the entry criteria and were randomly assigned to treatment. Of these 576 subjects, a total of 513 subjects (89.1%) completed the study (89.9% in the GL Glargine Injection treatment group and 88.2% in the EU Lantus treatment group).

Pre-assignment

Screening details:

A total of 718 subjects with T1DM were screened for enrollment into this study.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not Blinded

Arms

Are arms mutually exclusive?	Yes
------------------------------	-----

Arm title	Gan & Lee Insulin Glargine Injection
------------------	--------------------------------------

Arm description:

Gan & Lee Insulin Glargine Injection for subcutaneous injection, 100 U/mL, in the integrated, disposable 3.0-mL pre-filled Gan & Lee injector pen

Arm type	Experimental
Investigational medicinal product name	Gan & Lee Insulin Glargine Injection
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Injection

Dosage and administration details:

Gan & Lee Insulin Glargine Injection will be contained in Gan & Lee injector pens (3.0-mL pre-filled glass cartridge) for multiple dose administration. Gan & Lee Insulin Glargine should be administered once daily at any time but at the same time each day.

Arm title	Lantus®
------------------	---------

Arm description:

Lantus® (insulin glargine injection) solution for subcutaneous injection, 100 U/mL, in the SoloStar® 3-mL pre-filled insulin pen

Arm type	Active comparator
Investigational medicinal product name	Lantus®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled injector
Routes of administration	Injection

Dosage and administration details:

Lantus® should be administered once daily at any time but at the same time each day.

Number of subjects in period 1	Gan & Lee Insulin Glargine Injection	Lantus®
Started	287	289
Completed	287	289

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial
Reporting group description: -	

Reporting group values	Overall Trial	Total	
Number of subjects	576	576	
Age categorical			
Male or nonpregnant, nonlactating female subjects between the ages of 18 and 75 years, inclusive.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	508	508	
From 65-84 years	68	68	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	215	215	
Male	361	361	

Subject analysis sets

Subject analysis set title	GL Glargine Injection
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects in this set received GL Glargine Injection, 100 U/mL, in the integrated, disposable 3.0-mL prefilled Gan & Lee UnoPen injection pen

Subject analysis set title	Lantus
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Lantus® Injection for subcutaneous injection.

Reporting group values	GL Glargine Injection	Lantus	
Number of subjects	287	289	
Age categorical			
Male or nonpregnant, nonlactating female subjects between the ages of 18 and 75 years, inclusive.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	

Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	256	252	
From 65-84 years	31	37	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	101	112	
Male	184	177	

End points

End points reporting groups

Reporting group title	Gan & Lee Insulin Glargine Injection
Reporting group description: Gan & Lee Insulin Glargine Injection for subcutaneous injection, 100 U/mL, in the integrated, disposable 3.0-mL pre-filled Gan & Lee injector pen	
Reporting group title	Lantus®
Reporting group description: Lantus® (insulin glargine injection) solution for subcutaneous injection, 100 U/mL, in the SoloStar® 3-mL pre-filled insulin pen	
Subject analysis set title	GL Glargine Injection
Subject analysis set type	Per protocol
Subject analysis set description: Subjects in this set received GL Glargine Injection, 100 U/mL, in the integrated, disposable 3.0-mL prefilled Gan & Lee UnoPen injection pen	
Subject analysis set title	Lantus
Subject analysis set type	Sub-group analysis
Subject analysis set description: Lantus® Injection for subcutaneous injection.	

Primary: Immunogenicity

End point title	Immunogenicity
End point description:	
End point type	Primary
End point timeframe: The percentage of subjects in each treatment group who develop treatment induced AIA, defined as treatment-emergent AIA development or important (at least 4-fold) increase in titers and up to visit Week 26	

End point values	Gan & Lee Insulin Glargine Injection	Lantus®	GL Glargine Injection	Lantus
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	287	289	287	289
Units: percentage protection				
number (confidence interval 90%)	287 (258 to 287)	289 (260 to 289)	287 (258 to 287)	289 (260 to 289)

Statistical analyses

Statistical analysis title	Statistical Analysis
Statistical analysis description: The primary endpoint was met. The percentages of subjects positive for treatment-induced AIA (composite of newly developed or important increase in AIA) up to Week 26 were similar between the GL Glargine Injection (25.8%) and EU Lantus (25.3%) treatment groups, with a	

90% CI (-5.4, 6.5) of the difference in proportions (0.6 percentage points) that fell completely between the similarity margins (-11.3, 11.3) for equivalence.

Comparison groups	GL Glargine Injection v Lantus
Number of subjects included in analysis	576
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.4
Method	Regression Logic
Parameter estimate	Risk difference (RD)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events will be recorded beginning at the screening visit. Nonserious adverse events will be recorded from the time informed consent is signed through the subject's last study visit.

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

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups

Reporting group title	GL Glargine Injection
-----------------------	-----------------------

Reporting group description:

Subjects who met the eligibility criteria to receive GL Glargine Injection or EU Lantus treatment for 26 weeks.

Reporting group title	Lantus
-----------------------	--------

Reporting group description:

Subjects who met the eligibility criteria and received Lantus treatment for 26 weeks.

Serious adverse events	GL Glargine Injection	Lantus	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 287 (3.48%)	14 / 289 (4.84%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	1	
Cardiac disorders			
Carotid artery occlusion			
subjects affected / exposed	1 / 287 (0.35%)	0 / 289 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	0 / 287 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Benign neoplasm of spinal cord			
subjects affected / exposed	1 / 287 (0.35%)	0 / 289 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			

subjects affected / exposed	0 / 287 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	0 / 287 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Peripheral ischaemia			
subjects affected / exposed	0 / 287 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Appendicitis			
subjects affected / exposed	0 / 287 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 287 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 287 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	1 / 287 (0.35%)	0 / 289 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prurigo			

subjects affected / exposed	0 / 287 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 287 (0.00%)	2 / 289 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 287 (0.00%)	2 / 289 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	0 / 287 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Cellulitis			
subjects affected / exposed	1 / 287 (0.35%)	0 / 289 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	1 / 287 (0.35%)	0 / 289 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 287 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 287 (0.35%)	0 / 289 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 287 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 287 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 287 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Localised infection			
subjects affected / exposed	0 / 287 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 287 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	1 / 287 (0.35%)	0 / 289 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	0 / 287 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Septic shock			
subjects affected / exposed	0 / 287 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	3 / 287 (1.05%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycinaemia			
subjects affected / exposed	1 / 287 (0.35%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	0 / 287 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	0 / 287 (0.00%)	1 / 289 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	GL Glargine Injection	Lantus	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	172 / 287 (59.93%)	165 / 289 (57.09%)	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 287 (1.05%)	0 / 289 (0.00%)	
occurrences (all)	3	0	

Dizziness subjects affected / exposed occurrences (all)	1 / 287 (0.35%) 1	0 / 289 (0.00%) 0	
Herpes zoster subjects affected / exposed occurrences (all)	1 / 287 (0.35%) 1	0 / 289 (0.00%) 0	
Blood and lymphatic system disorders Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	1 / 287 (0.35%) 1	0 / 289 (0.00%) 0	
Endocrine disorders Diabetes mellitus subjects affected / exposed occurrences (all)	1 / 287 (0.35%) 1	0 / 289 (0.00%) 0	
Musculoskeletal and connective tissue disorders Contusion alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) Facial edema alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) Foot fracture alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	0 / 287 (0.00%) 0 1 / 287 (0.35%) 1 1 / 287 (0.35%) 1	1 / 289 (0.35%) 1 0 / 289 (0.00%) 0 0 / 289 (0.00%) 0	
Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all) Weight increased subjects affected / exposed occurrences (all) Hyperglycaemia	158 / 287 (55.05%) 158 3 / 287 (1.05%) 0	161 / 289 (55.71%) 161 1 / 289 (0.35%) 0	

subjects affected / exposed	2 / 287 (0.70%)	1 / 289 (0.35%)	
occurrences (all)	2	1	
Blood glucose increased			
subjects affected / exposed	0 / 287 (0.00%)	1 / 289 (0.35%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 April 2018	Amendment 1.0
01 November 2018	Amendment 2

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported