Clinical trial results:
A Study to Assess the Pharmacokinetics, Glucodynamics, Safety, and Tolerability of LY900027 in Patients with Type 1 Diabetes Mellitus on Continuous Subcutaneous Insulin Infusion Therapy

Summary

EudraCT number	2019-002318-37
Trial protocol	DE
Global end of trial date	14 July 2020

Results information

Result version number	v1 (current)
This version publication date	18 July 2021
First version publication date	18 July 2021

Trial information

Trial identification

Sponsor protocol code	J2H-MC-IUAA

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04161976
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 17489

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

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	14 July 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to learn more about a new formulation of insulin lispro when given by an insulin pump to participants with type 1 diabetes mellitus. The study will investigate how the body processes the drug and how the drug affects the body. Information about side effects will be collected. The study will last from six to 12 weeks for each participant.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 December 2019
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	Germany: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	20
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Not Applicable.

Period 1

Period 1 title	Period 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Sequence 1 (LY900027 - Insulin Lispro)

Arm description:

Participants received LY900027 and Insulin lispro in one of two dosing periods as per below dosing schedule:
Period 1: 100 units/milliliter (U/mL) LY900027 administered to participants with type 1 diabetes mellitus (T1DM) using continuous subcutaneous insulin infusion (CSII) for 10 days; Period 2: 100 U/mL Insulin lispro (Humalog) administered to participants with T1DM using CSII for 10 days.

Arm type	Experimental
Investigational medicinal product name	LY900027
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

100 /mL LY900027 administered to participants with T1DM using CSII for 10 days.

Investigational medicinal product name	Insulin Lispro
Investigational medicinal product code	LY275585
Other name	Humalog
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

100 U/mL insulin lispro (Humalog) administered to participants with T1DM using CSII for 10 days.

Arm title	Sequence 2 (Insulin Lispro - LY900027)

Arm description:

Participants received insulin lispro and LY900027 in one of two dosing periods as per below dosing schedule:
Period 1: 100 U/mL Insulin lispro (Humalog) administered to participants with T1DM using CSII; Period 2: 100 U/mL LY900027 administered to participants with T1DM using CSII.

Arm type	Experimental
Investigational medicinal product name	Insulin Lispro
Investigational medicinal product code	LY275585
Other name	Humalog
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details: 100 U/mL insulin lispro (Humalog) administered to participants with T1DM using CSII for 10 days.	
Investigational medicinal product name	LY900027
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

100 /mL LY900027 administered to participants with T1DM using CSII for 10 days.

Number of subjects in period 1	Sequence 1 (LY900027 - Insulin Lispro)	Sequence 2 (Insulin Lispro - LY900027)
Started	10	10
Received at Least One Dose of Study Drug	10	10
Completed	10	9
Not completed	0	1
Consent withdrawn by subject	-	1

Period 2

Period 2 title	Washout of 7-21 days
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Sequence 1 (LY900027 - Insulin Lispro)

Arm description:

Participants received LY900027 and Insulin lispro in one of two dosing periods as per below dosing schedule:
Period 1: 100 units/milliliter (U/mL) LY900027 administered to participants with type 1 diabetes mellitus (T1DM) using continuous subcutaneous insulin infusion (CSII) for 10 days; Period 2: 100 U/mL Insulin lispro (Humalog) administered to participants with T1DM using CSII for 10 days.

Arm type	Experimental
Investigational medicinal product name	LY900027
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

100 U/mL LY900027 administered to participants with T1DM using CSII for 10 days.

Investigational medicinal product name	Insulin Lispro
Investigational medicinal product code	LY275585
Other name	Humalog
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

100 U/mL insulin lispro (Humalog) administered to participants with T1DM using CSII for 10 days.

Arm title	Sequence 2 (Insulin Lispro - LY900027)

Arm description:

Participants received insulin lispro and LY900027 in one of two dosing periods as per below dosing schedule:
Period 1: 100 U/mL Insulin lispro (Humalog) administered to participants with T1DM using CSII; Period 2: 100 U/mL LY900027 administered to participants with T1DM using CSII.

Arm type	Experimental
Investigational medicinal product name	Insulin Lispro
Investigational medicinal product code	LY275585
Other name	Humalog
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

100 U/mL insulin lispro (Humalog) administered to participants with T1DM using CSII for 10 days.

Investigational medicinal product name	LY900027
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

100 U/mL LY900027 administered to participants with T1DM using CSII for 10 days.

Number of subjects in period 2	Sequence 1 (LY900027 - Insulin Lispro)	Sequence 2 (Insulin Lispro - LY900027)
Started	10	9
Completed	10	9

Period 3

Period 3 title	Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes

Arm title	Sequence 1 (LY900027 - Insulin Lispro)

Arm description:

Participants received LY900027 and Insulin lispro in one of two dosing periods as per below dosing schedule:
Period 1: 100 units/milliliter (U/mL) LY900027 administered to participants with type 1 diabetes mellitus (T1DM) using continuous subcutaneous insulin infusion (CSII) for 10 days; Period 2: 100 U/mL Insulin lispro (Humalog) administered to participants with T1DM using CSII for 10 days.

Arm type	Experimental
Investigational medicinal product name	LY900027
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

100 U/mL LY900027 administered to participants with T1DM using CSII for 10 days.

Investigational medicinal product name	Insulin Lispro
Investigational medicinal product code	LY275585
Other name	Humalog
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

100 U/mL LY900027 administered to participants with T1DM using CSII for 10 days.

Arm title	Sequence 2 (Insulin Lispro - LY900027)

Arm description:

Participants received insulin lispro and LY900027 in one of two dosing periods as per below dosing schedule:
Period 1: 100 U/mL Insulin lispro (Humalog) administered to participants with T1DM using CSII; Period 2: 100 U/mL LY900027 administered to participants with T1DM using CSII.

Arm type	Experimental
Investigational medicinal product name	Insulin Lispro
Investigational medicinal product code	LY275585
Other name	Humalog
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

100 U/mL insulin lispro (Humalog) administered to participants with T1DM using CSII for 10 days.

Investigational medicinal product name	LY900027
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

100 U/mL LY900027 administered to participants with T1DM using CSII for 10 days.

Number of subjects in period 3	Sequence 1 (LY900027 - Insulin Lispro)	Sequence 2 (Insulin Lispro - LY900027)
Started	10	9
Completed	10	8
Not completed	0	1
Consent withdrawn by subject	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Period 1
Reporting group description:	
100 U/mL LY900027 administered to participants with T1DM using CSII for 10 days and 100 U/mL Insulin lispro (Humalog) administered to participants with T1DM using CSII for 10 days as per the dosing sequence in each period.	

Reporting group values	Period 1	Total	
Number of subjects	20	20	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 43.0 ± 12.50	 -	
Gender categorical Units: Subjects			
Female	2	2	
Male	18	18	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	20	20	
More than one race	0	0	
Unknown or Not Reported	0	0	
Region of Enrollment Units: Subjects			
Germany	20	20	

End points

End points reporting groups

Reporting group title	Sequence 1 (LY900027 - Insulin Lispro)

Reporting group description:

Participants received LY900027 and Insulin lispro in one of two dosing periods as per below dosing schedule:
Period 1: 100 units/milliliter (U/mL) LY900027 administered to participants with type 1 diabetes mellitus (T1DM) using continuous subcutaneous insulin infusion (CSII) for 10 days; Period 2: 100 U/mL Insulin lispro (Humalog) administered to participants with T1DM using CSII for 10 days.

Reporting group title	Sequence 2 (Insulin Lispro - LY900027)

Reporting group description:

Participants received insulin lispro and LY900027 in one of two dosing periods as per below dosing schedule:
Period 1: 100 U/mL Insulin lispro (Humalog) administered to participants with T1DM using CSII; Period 2: 100 U/mL LY900027 administered to participants with T1DM using CSII.

Reporting group title	Sequence 1 (LY900027 - Insulin Lispro)

Reporting group description:

Participants received LY900027 and Insulin lispro in one of two dosing periods as per below dosing schedule:
Period 1: 100 units/milliliter (U/mL) LY900027 administered to participants with type 1 diabetes mellitus (T1DM) using continuous subcutaneous insulin infusion (CSII) for 10 days; Period 2: 100 U/mL Insulin lispro (Humalog) administered to participants with T1DM using CSII for 10 days.

Reporting group title	Sequence 2 (Insulin Lispro - LY900027)

Reporting group description:

Participants received insulin lispro and LY900027 in one of two dosing periods as per below dosing schedule:
Period 1: 100 U/mL Insulin lispro (Humalog) administered to participants with T1DM using CSII; Period 2: 100 U/mL LY900027 administered to participants with T1DM using CSII.

Reporting group title	Sequence 1 (LY900027 - Insulin Lispro)

Reporting group description:

Participants received LY900027 and Insulin lispro in one of two dosing periods as per below dosing schedule:
Period 1: 100 units/milliliter (U/mL) LY900027 administered to participants with type 1 diabetes mellitus (T1DM) using continuous subcutaneous insulin infusion (CSII) for 10 days; Period 2: 100 U/mL Insulin lispro (Humalog) administered to participants with T1DM using CSII for 10 days.

Reporting group title	Sequence 2 (Insulin Lispro - LY900027)

Reporting group description:

Participants received insulin lispro and LY900027 in one of two dosing periods as per below dosing schedule:
Period 1: 100 U/mL Insulin lispro (Humalog) administered to participants with T1DM using CSII; Period 2: 100 U/mL LY900027 administered to participants with T1DM using CSII.

Subject analysis set title	LY900027
Subject analysis set type	Per protocol

Subject analysis set description:

100 U/mL LY900027 administered to participants with T1DM using CSII for 10 days in treatment period 1 or treatment period 2.

Subject analysis set title	Insulin Lispro (Humalog)
Subject analysis set type	Per protocol

Subject analysis set description:

100 U/mL insulin lispro (Humalog) administered to participants with T1DM using CSII for 10 days in treatment period 1 or treatment period 2.

Primary: Pharmacokinetics (PK): Pharmacokinetics (PK): Area Under the Insulin Lispro Curve (AUC) 0 to 5 hours after Bolus Administration Prior to a Mixed Meal Tolerance Text (MMTT)

End point title	Pharmacokinetics (PK): Pharmacokinetics (PK): Area Under the Insulin Lispro Curve (AUC) 0 to 5 hours after Bolus Administration Prior to a Mixed Meal Tolerance Text (MMTT)[1]

End point description:

Area under the concentration curve from time Zero to 5 hours post dose [AUC(0-5h)] after bolus administration prior to a mixed meal tolerance text was evaluated. Analysis population included all randomized participants who received at least one dose of study drug with evaluable PK data

End point type	Primary

End point timeframe:

Day 1; day 3; day 5; day 7 and day 10 postdose in each dosing period

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: No inferential statistical analysis planned for this end point between two treatment groups.

End point values	LY900027	Insulin Lispro (Humalog)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	18[2]	18[3]		
Units: picogram*hour per milliliter (pg*h/mL)				
geometric mean (geometric coefficient of variation)				
Day 1	4470 (± 34.2)	4270 (± 32.6)		
Day 3	4510 (± 33.9)	4270 (± 34.1)		
Day 5	4240 (± 37.8)	4180 (± 33.2)		
Day 7	4090 (± 37.7)	4130 (± 27.2)		
Day 10	3640 (± 35.1)	3620 (± 45.0)		

Notes:

[2] - Day 1: n = 17, Day 3: n = 18, Day 5: n = 17, Day 7: n = 17, Day 10: n =17

[3] - Day 1: n = 18, Day 3: n = 16, Day 5: n = 15, Day 7: n = 15, Day 10: n =15.

Statistical analyses

No statistical analyses for this end point

Primary: PK: Maximum Observed Insulin Lispro Concentration (Cmax)

End point title	PK: Maximum Observed Insulin Lispro Concentration (Cmax)[4]

End point description:

Cmax of insulin lispro was evaluated. Analysis population included all randomized participants who received at least one dose of study drug with evaluable PK data.

End point type	Primary

End point timeframe:

Day 1; day 3; day 5; day 7 and day 10 postdose in each dosing period

Notes:

[4] - 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: No inferential statistical analysis planned for this end point between two treatment groups.

End point values	LY900027	Insulin Lispro (Humalog)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	18[5]	18[6]		
Units: picogram per milliliter (pg/mL)				
geometric mean (geometric coefficient of variation)				
Day 1	1630.107 (± 29.9)	1531.681 (± 40.2)		
Day 3	1777.294 (± 35.5)	1811.699 (± 40.1)		
Day 5	1943.419 (± 45.0)	2070.839 (± 46.4)		
Day 7	2089.719 (± 53.6)	2523.452 (± 43.1)		
Day 10	2057.372 (± 53.6)	2702.065 (± 48.3)		

Notes:

[5] - Day 1: n = 17, Day 3: n = 18, Day 5: n = 17, Day 7: n = 17, Day 10: n =17

[6] - Day 1: n = 18, Day 3: n = 16, Day 5: n = 15, Day 7: n = 15, Day 10: n =15

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics (PD): Incremental Area Under the Plasma Glucose Curve Above Baseline Between 0-5 hours After Bolus Infusion

End point title	Pharmacodynamics (PD): Incremental Area Under the Plasma Glucose Curve Above Baseline Between 0-5 hours After Bolus Infusion

End point description:

PD: Incremental area under the plasma glucose curve above baseline between 0-5 hours after bolus infusion was evaluated. Analysis population included all randomized participants who received at least one dose of study drug with evaluable PD data.

End point type	Secondary

End point timeframe:

Day 1; day 3; day 5; day 7 and day 10 postdose in each dosing period

End point values	LY900027	Insulin Lispro (Humalog)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	18	18		
Units: milligram*hour per deciliter(mg*hr/dL)				
arithmetic mean (standard deviation)				
Day 1	683.076 (± 233.4230)	695.868 (± 187.8017)		
Day 3	649.082 (± 186.3946)	643.283 (± 197.5600)		
Day 5	741.215 (± 185.9439)	721.094 (± 192.6689)		
Day 7	871.364 (± 212.5231)	868.358 (± 204.0137)		
Day 10	972.250 (± 213.6539)	1043.319 (± 184.4819)		

Statistical analyses

No statistical analyses for this end point

Secondary: PD: Total Daily Insulin Dose

End point title	PD: Total Daily Insulin Dose

End point description:

Total daily insulin dose analysed using a linear mixed model. Analysis population included all randomized participants who received at least one dose of study drug with evaluable PD data.

End point type	Secondary

End point timeframe:

Day 1; day 3; day 5; day 7 and day 10 postdose in each dosing period

End point values	LY900027	Insulin Lispro (Humalog)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	18	18		
Units: units of insulin				
arithmetic mean (standard deviation)				
Day 1	52.885 (± 15.7492)	49.911 (± 12.9665)		
Day 3	53.779 (± 15.1662)	52.878 (± 16.5585)		
Day 5	51.852 (± 12.6773)	54.393 (± 17.0805)		
Day 7	55.464 (± 13.8645)	58.134 (± 19.7199)		
Day 10	22.827 (± 5.1951)	24.549 (± 7.3692)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration Until Catheter Failure

End point title	Duration Until Catheter Failure

End point description:

No participants had a catheter failure after Day 3, so time to catheter failure after Day 3 was not assessed.

End point type	Secondary

End point timeframe:

Day -1 through Day 10 in each dosing period

End point values	LY900027	Insulin Lispro (Humalog)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[7]	0[8]		
Units: days				
arithmetic mean (standard deviation)	()	()		

Notes:

[7] - Time to catheter failure after Day 3 was not assessed.

[8] - Time to catheter failure after Day 3 was not assessed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up To 120 days	
Adverse event reporting additional description:	
All randomized participants who received at least one dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	Insulin Lispro (Humalog)
Reporting group description:	
100 U/mL insulin lispro (Humalog) administered to participants with T1DM using CSII for 10 days in treatment period 1 or treatment period 2.	
Reporting group title	LY900027
Reporting group description:	
100 U/mL LY900027 administered to participants with T1DM using CSII for 10 days in treatment period 1 or treatment period 2.	

Serious adverse events	Insulin Lispro (Humalog)	LY900027	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Insulin Lispro (Humalog)	LY900027	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 20 (80.00%)	13 / 19 (68.42%)	
Injury, poisoning and procedural complications			
phlebitis			
alternative dictionary used: MedDRA 21.0			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	
occurrences (all)	1	2	
Vascular disorders			

thrombophlebitis alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all)	 0 / 20 (0.00%) 0	 1 / 19 (5.26%) 1	
Nervous system disorders headache alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1	 2 / 19 (10.53%) 2	
General disorders and administration site conditions injection site reaction alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all) pyrexia alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all)	 15 / 20 (75.00%) 18 0 / 20 (0.00%) 0	 12 / 19 (63.16%) 12 1 / 19 (5.26%) 1	
Gastrointestinal disorders noninfective gingivitis alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all) pulpitis dental alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all)	 0 / 20 (0.00%) 0 0 / 20 (0.00%) 0	 1 / 19 (5.26%) 1 1 / 19 (5.26%) 1	
Metabolism and nutrition disorders decreased appetite alternative dictionary used: MedDRA 21.0 subjects affected / exposed occurrences (all)	 0 / 20 (0.00%) 0	 1 / 19 (5.26%) 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? Yes

Date	Interruption	Restart date
23 March 2020	New enrollment was paused during the initial global pause of Lilly studies due to COVID.	18 May 2020

Notes:

Limitations and caveats

None reported