ClinicalTrials.gov PRS
Protocol Registration and Results System

ID: 10937 Comparison of Two Basal Insulin Therapies for Patients With Type 1 Diabetes NCT00487240

Protocol Registration and Results Preview

Comparison of Two Basal Insulin Therapies for Patients With Type 1 Diabetes (IOOZ)

This study has been completed.

Sponsor:
Eli Lilly and Company

Information provided by:
Eli Lilly and Company

ClinicalTrials.gov Identifier:
NCT00487240

First received: June 14, 2007
Last updated: October 20, 2010
Last verified: October 2010

Purpose

The purpose of this study is to examine the efficacy and safety of insulin lispro protamine suspension (ILPS) as compared to insulin detemir as basal insulin combined with mealtime insulin therapy in patients with type 1 diabetes. A gatekeeper strategy will be employed for sequentially testing the secondary objectives.

Condition	Intervention	Phase
Diabetes Mellitus, Type 1	Drug: Insulin Lispro Protamine Suspension Drug: Insulin Levemir	Phase 3

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Open Label, Randomized, Safety/Efficacy Study

Official Title: Comparison of Two Basal Insulin Analogs (Insulin Lispro Protamine Suspension and Insulin Detemir) in Basal-Bolus Therapy for Patients With Type 1 Diabetes

Further study details as provided by Eli Lilly and Company:

Primary Outcome Measure:

- Change in Hemoglobin A1c (HbA1c) From Baseline to Endpoint [Time Frame: baseline and 32 weeks] [Designated as safety issue: No]

Secondary Outcome Measures:

- Actual and Change From Baseline Hemoglobin A1c (HbA1c) Values [Time Frame: Baseline, 8,16, 24, 32 Weeks] [Designated as safety issue: No]
  The summary statistics represents the mean of all subjects. Change from baseline is calculated for each individual subject for the specific visit and then the "mean change from baseline" is calculated by averaging out for all subjects. [Sum over all (i) {A1c at Week 8 for Subject(i) minus A1c Baseline for Subject (i)}/Total Subjects]. Therefore, for example, the Change from Baseline is not equal to the difference of Mean A1c for Week 8 minus Mean A1c for baseline.

- Percentage of Patients With Hemoglobin A1c (HbA1c) Less Than or Equal to 7.0% and HbA1c Less Than or Equal to 6.5% [Time Frame: 32 Weeks] [Designated as safety issue: No]

- 7-Point Self-Monitored Blood Glucose (SMBG) at Endpoint [Time Frame: 32 Weeks] [Designated as safety issue: No]
  Actual daily mean blood glucose levels at endpoint. The SMBG excursion is the difference between the postprandial and preprandial blood glucose concentration taken at the morning, midday and evening meals.

- Glycemic Variability at Endpoint [Time Frame: 32 Weeks] [Designated as safety issue: No]
  Glycemic variability was measured by standard deviation (SD) value of fasting blood glucose as measured by intra-patient glycemic variability (determined by the 7-point self-monitored blood glucose [SMBG] profiles at endpoint); mean value (M-value), which was the mean of the intra-days self-monitored blood glucose values, and by the mean of daily difference (MODD), which was the mean of the between-days self-monitored blood glucose values.

- Number of Self-Reported Hypoglycemic Episodes (Including Nocturnal, Non-Nocturnal, and Severe Hypoglycemia) Overall and at Endpoint [Time Frame: Baseline to 32 Weeks] [Designated as safety issue: Yes]
  Nocturnal: Defined as any hypoglycemic event that occurs between bedtime and waking. Non-Nocturnal: Defined as any hypoglycemic event that occurs between waking and bedtime. Severe: An episode with symptoms consistent with neuroglycopenia in which the patient requires the assistance of another person; associated with either a blood glucose level of <2.8 mmol/L (<50 mg/dL) or prompt recovery after oral carbohydrate, glucagon, or intravenous glucose.

- 1-Year Adjusted Rates of Self-Reported Hypoglycemic Episodes (Including Nocturnal, Non-Nocturnal, and Severe) Overall and at Endpoint [Time Frame: baseline to 32 weeks] [Designated as safety issue: Yes]
  Nocturnal: Defined as any hypoglycemic event that occurs between bedtime and waking. Non-Nocturnal: Defined as any hypoglycemic event that occurs between waking and bedtime. Severe: An episode with symptoms consistent with neuroglycopenia in which the patient requires the assistance of another person; associated with either a blood glucose level of <2.8 mmol/L (<50 mg/dL) or prompt recovery after oral carbohydrate, glucagon, or intravenous glucose.

- 30-Day Adjusted Rates of Self-Reported Hypoglycemic Episodes (Including Nocturnal, Non-Nocturnal, and Severe) Overall and at Endpoint [Time Frame: baseline to 32 weeks] [Designated as safety issue: No]

- Change From Baseline in Absolute Body Weight at 32 Week Endpoint [Time Frame: Baseline, 32 Weeks] [Designated as safety issue: No]

- Insulin Dose Per Body Weight (Total and By Component [Basal and Bolus]) [Time Frame: 32 Weeks] [Designated as safety issue: No]
  Total daily insulin dose adjusted for body weight (U/kg/day) was assessed.

- Insulin Dose (Total and By Component [Basal and Bolus]) [Time Frame: 32 weeks] [Designated as safety issue: No]
  Total daily insulin dose (U/day) was assessed.

Enrollment: 387
Study Start Date: June 2007
Study Completion Date: August 2008
Primary Completion Date: August 2008

Arms	Assigned Interventions
Experimental: Insulin Lispro Protamine Suspension Insulin Lispro Protamine Suspension twice daily	Drug: Insulin Lispro Protamine Suspension Patient specific dose, twice daily (BID), within 15 minutes before meals, subcutaneous (SC) injection x 32 weeks. Other Names: • ILPS • NPL • Humalog • LY275585
Active Comparator: Detemir Insulin Levemir (detemir) subcutaneous (SC) twice daily.	Drug: Insulin Levemir Patient specific dose insulin Levemir (detemir) twice daily (BID) subcutaneous (SC) injection x 32 weeks

Phase 3b, randomized, multicenter, multinational, open-label, two-arm, active control, parallel study to determine safety, efficacy, and noninferiority of basal analog insulin lispro protamine suspension (ILPS, also referred to as NPL [neutral protamine Hagedorn]), injected two times a day, compared with basal analog insulin detemir, injected two times a day, as measured by change in hemoglobin A1c (HbA1c) from baseline (Visit 2) to 32 weeks in adult patients with type 1 diabetes when used in combination with bolus insulin lispro, injected three times a day.

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Inclusion Criteria:

- Clinical diagnosis of type 1 diabetes for one year or more
- Age 18 years or older
- Body mass index (BMI) less than or equal to 35 kilograms per square meter (kg/m2)
- Have a hemoglobin A1c (HbA1c) 1.2 to 2.0 times the upper limit of the normal (ULN) reference range within 30 days prior to Visit 1 or collected and analyzed at a local laboratory at Visit 1
- As determined by the investigator, are capable and willing to do the following:
  - perform self monitoring of blood glucose (SMBG),
  - complete patient diaries as required for this protocol,
  - use the insulin injection device(s) according to the instructions provided,
  - are receptive to diabetes education,
  - comply with the required study visits.

Exclusion Criteria:

- Have taken any oral antihyperglycemic medications (OAMs) within 3 months prior to Visit 1.
- Have had more than one episode of severe hypoglycemia, as defined in the Abbreviations and Definitions section of the protocol, within 6 months prior to entry into the study
- Are pregnant or intend to become pregnant during the course of the study or are sexually active women of childbearing potential not actively practicing birth control by a method determined by the investigator to be medically acceptable or women who are breastfeeding
- Are receiving chronic (lasting longer than 14 consecutive days) systemic glucocorticoid therapy (excluding topical, intra-articular, intraocular, and inhaled preparations) or have received such therapy within the 4 weeks immediately preceding Visit 1.
- Have received treatment within the last 30 days with a drug that has not received regulatory approval for any indication at the time of study entry.

Contacts and Locations

Locations

United States, Idaho

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Idaho Falls, Idaho, United States, 83404

United States, Illinois

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Springfield, Illinois, United States, 62704

United States, Kansas

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Topeka, Kansas, United States, 66606

United States, Texas

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

San Antonio, Texas, United States, 78229

Argentina

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Buenos Aires, Argentina, C1213AAH

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

La Plata, Argentina, B1902AWL

Australia, New South Wales

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Wollongong, New South Wales, Australia

Australia, Victoria

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Box Hill, Victoria, Australia, 3128

Brazil

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Fortaleza, Brazil, 60120-020

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

São Paulo, Brazil, 04020041

Greece

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Athens, Greece, 11527

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Thessaloniki, Greece, 56429

Hungary

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Budapest, Hungary, 1088

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Mosonmagyarovar, Hungary, 9200

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Pecs, Hungary, 7623

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Szentes, Hungary, 6600

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Zalaegerszeg, Hungary, 8900

Mexico

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Guadalajara, Mexico, 44600

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Pachuca, Mexico, 42090

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Puebla, Mexico, 72160

Romania

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Baia Mare, Romania, 430071

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Brasov, Romania, 500326

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Bucharest, Romania, 70266

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Iasi, Romania, 6600

Russian Federation

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Arkhangelsk, Russian Federation, 163045

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Moscow, Russian Federation, 115478

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Rostov-On-Don, Russian Federation, 344022

For additional information regarding investigative sites for this trial, contact 1-877-CTLILLY (1-877-285-4559, 1-317-615-4559) Mon - Fri from 9 AM to 5 PM Eastern Time (UTC/GMT - 5 hours, EST), or speak with your personal physician.

Saint Petersburg, Russian Federation, 193257

Investigators

Study Director:	Call 1-877-CTLILLY (1-877-285-4559) or 1-317-615-4559 Mon - Fri 9 AM - 5 PM Eastern time (UTC/GMT - 5 hours, EST)	Eli Lilly

More Information

Lilly Clinical Trial Registry

Results Publications:

Chacra AR, Kipnes M, Ilag LL, Sarwat S, Giaconia J, Chan J; COMPLETE T1D investigators. Comparison of insulin lispro protamine suspension and insulin detemir in basal-bolus therapy in patients with Type 1 diabetes. Diabet Med. 2010 May;27(5):563-9. doi: 10.1111/j.1464-5491.2010.02986.x.

Responsible Party: Eli Lilly (Chief Medical Office)
Study ID Numbers: 10937
F3Z-MC-IOOZ [Eli Lilly and Company]
Health Authority: United States: Food and Drug Administration

Study Results

Participant Flow

Recruitment Details	
Pre-Assignment Details	First 4 weeks (Titration Period): acclimate patients to insulin regimen and optimize insulin dose. Final 28 weeks (Maintenance Period): Minimum of 6 months' stable insulin dosage. 456 patients were screened; 69 did not

	meet entry criteria and 387 were randomized; 6 patients were excluded from the 387 randomized to create the Full Analysis Set.

Arm/Group Title	Insulin Lispro Protamine Suspension	Detemir	Total (Not public)
▼ Arm/Group Description	Patient specific dose insulin lispro protamine suspension, twice daily (BID), within 15 minutes before meals, subcutaneous (SC) injection x 32 weeks	Patient specific dose insulin Levemir (detemir) twice daily (BID) subcutaneous (SC) injection x 32 weeks	
Period Title: **Overall Study**			
Started	195	192	387
Full Analysis Set (ITT Population)	192	189	381
Completed	164	166	330
Not Completed	31	26	57
Reason Not Completed			
Withdrawal by Subject	12	6	18
Lost to Follow-up	7	6	13
Adverse Event	0	4	4
Protocol Violation	5	5	10
Entry Criteria Not Met	3	4	7
Sponsor Decision	2	1	3
Physician Decision	2	0	2
(Not Public)	Not Completed = 31 Total from all reasons = 31	Not Completed = 26 Total from all reasons = 26	

Baseline Characteristics

Arm/Group Title	Insulin Lispro Protamine Suspension	Detemir	Total
▼ Arm/Group Description	Patient specific dose insulin lispro protamine suspension, twice daily (BID), within 15 minutes before meals, subcutaneous (SC) injection x 32 weeks	Patient specific dose insulin Levemir (detemir) twice daily (BID) subcutaneous (SC) injection x 32 weeks	
Overall Number of Baseline Participants	192	189	**381**
▼ Baseline Analysis Population Description [Not specified]			
Age, Continuous Mean (Standard Deviation) Units: years	36.10 (13.33)	36.19 (13.09)	36.14 (13.20)
Gender, Male/Female			

Measure Type: Number Units: participants			
Female	96	91	187
Male	96	98	194
Region of Enrollment Measure Type: Number Units: participants			
United States	34	35	69
Hungary	16	17	33
Mexico	14	12	26
Greece	16	16	32
Argentina	16	16	32
Brazil	20	19	39
Romania	22	21	43
Australia	17	17	34
Russian Federation	37	36	73
Race/Ethnicity Measure Type: Number Units: participants			
African	2	1	3
Caucasian	165	160	325
East Asian	0	0	0
Hispanic	25	28	53
Native American	0	0	0
West Asian	0	0	0
Aboriginal and/or Torres Strait Islander	0	0	0
Body Mass Index (BMI) [1] Mean (Standard Deviation) Units: kilograms per square meter (kg/m^2)	25.15 (4.17)	25.46 (4.17)	25.30 (4.17)
	[1] Body mass index is an estimate of body fat based on body weight divided by square height.		
Duration of Diabetes Mean (Standard Deviation) Units: years	14.58 (10.69)	13.83 (9.80)	14.20 (10.26)
Hemoglobin A1c (HbA1c) Mean (Standard Deviation) Units: percent of HbA1c	8.87 (1.29)	8.64 (1.27)	8.75 (1.28)

Outcome Measures

1. Primary Outcome

Title:	Change in Hemoglobin A1c (HbA1c) From Baseline to Endpoint
▼ Description:	[Not specified]
Time Frame:	baseline and 32 weeks

Safety Issue?	No

▼ Outcome Measure Data ✔

▼ Analysis Population Description

Number of randomized patients with baseline and at least one post-baseline value. Intent to treat population. Last observation carried forward.

Arm/Group Title	Insulin Lispro Protamine Suspension	Detemir
▼ Arm/Group Description:	Patient specific dose insulin lispro protamine suspension, twice daily (BID), within 15 minutes before meals, subcutaneous (SC) injection x 32 weeks	Patient specific dose insulin Levemir (detemir) twice daily (BID) subcutaneous (SC) injection x 32 weeks
Number of Participants Analyzed	187	185
Least Squares Mean (Standard Error) Units: percent of HbA1c		
Baseline	8.88 (0.10)	8.68 (0.10)
Change from Baseline	-0.69 (0.07)	-0.59 (0.07)

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	Hypothesis: basal analog insulin lispro protamine suspension (ILPS), is inferior to basal analog insulin detemir, as measured by change in HbA1c from baseline to endpoint.
	Non-Inferiority or Equivalence Analysis?	Yes
	Comments	Noninferiority limit of 0.4% using the upper limit of a two-sided test at a significance level of 0.05 with 90% power assuming a 1.1 Standard Deviations (SD)
Statistical Test of Hypothesis	P-Value	0.332
	Comments	[Not specified]
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment + Baseline + Country.

Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	-0.10
	Confidence Interval	(2-Sided) 95% -0.29 to 0.10
	Estimation Comments	Least Squares Mean Difference = Insulin Lispro Protamine Suspension minus Detemir.

2. Secondary Outcome

Title:	Actual and Change From Baseline Hemoglobin A1c (HbA1c) Values
▼ Description:	The summary statistics represents the mean of all subjects. Change from baseline is calculated for each individual subject for the specific visit and then the "mean change from baseline" is calculated by averaging out for all subjects. [Sum over all (i) {A1c at Week 8 for Subject(i) minus A1c Baseline for Subject (i)}/Total Subjects]. Therefore, for example, the Change from Baseline is not equal to the difference of Mean A1c for Week 8 minus Mean A1c for baseline.
Time Frame:	Baseline, 8,16, 24, 32 Weeks
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Number of randomized patients with baseline and at least one post-baseline value. Intent to treat population.

Arm/Group Title	Insulin Lispro Protamine Suspension	Detemir
▼ Arm/Group Description:	Patient specific dose insulin lispro protamine suspension, twice daily (BID), within 15 minutes before meals, subcutaneous (SC) injection x 32 weeks	Patient specific dose insulin Levemir (detemir) twice daily (BID) subcutaneous (SC) injection x 32 weeks
Number of Participants Analyzed	187	185
Least Squares Mean (Standard Error) Units: percent of HbA1c		
Baseline	8.88 (0.10)	8.68 (0.10)
8 Week HbA1c (n=184, n=179)	8.08 (0.07)	8.11 (0.07)
8 Week Change from Baseline	-0.68 (0.07)	-0.64 (0.07)
16 Week HbA1c (n=174, n=173)	7.94 (0.07)	8.08 (0.08)
16 Week Change from Baseline	-0.81 (0.07)	-0.67 (0.08)
24 Week HbA1c (n=171, n=174)	8.07 (0.08)	8.11 (0.08)

24 Week Change from Baseline	-0.69 (0.08)	-0.65 (0.08)
32 Week HbA1c (n=165, n=165)	8.09 (0.08)	8.14 (0.08)
32 Week Change from Baseline	-0.68 (0.08)	-0.62 (0.08)

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.718
	Comments	P-value for 8 Week Change from Baseline.
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country.
Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	-0.03
	Confidence Interval	(2-Sided) 95% -0.22 to 0.15
	Estimation Comments	Least Squares Mean Difference=Insulin Lispro Protamine Suspension minus Detemir.

▼ Statistical Analysis 2 ✔

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.187
	Comments	P-value for 16 Week Change from Baseline.
	Method	ANCOVA

	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country
Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	-0.14
	Confidence Interval	(2-Sided) 95% -0.34 to 0.07
	Estimation Comments	Least Squares Mean Difference = Insulin Lispro Protamine Suspension minus Detemir.

▼ Statistical Analysis 3 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.704
	Comments	P-value for 24 Week Change from Baseline.
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country
Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	-0.04
	Confidence Interval	(2-Sided) 95% -0.25 to 0.17
	Estimation Comments	Least Squares Mean Difference = Insulin Lispro Protamine Suspension minus Detemir.

▼ Statistical Analysis 4 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.599
	Comments	P-value for 32 Week Change from Baseline.
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country
Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	-0.06
	Confidence Interval	(2-Sided) 95% -0.27 to 0.15
	Estimation Comments	Least Squares Mean Difference = Insulin Lispro Protamine Suspension minus Detemir.

3. Secondary Outcome

Title:	Percentage of Patients With Hemoglobin A1c (HbA1c) Less Than or Equal to 7.0% and HbA1c Less Than or Equal to 6.5%
▼ Description:	[Not specified]
Time Frame:	32 Weeks
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Number of randomized patients with baseline and at least one post-baseline value. Intent to treat population. Last observation carried forward.

Arm/Group Title	Insulin Lispro Protamine Suspension	Detemir
▼ Arm/Group Description:	Patient specific dose insulin lispro protamine suspension, twice daily (BID), within 15 minutes before meals, subcutaneous (SC) injection x 32 weeks	Patient specific dose insulin Levemir (detemir) twice daily (BID) subcutaneous (SC) injection x 32 weeks
Number of Participants Analyzed	187	185
Measure Type: Number Units: percentage of participants		
With HbA1c ≤7.0%	18.5	18.7
With HbA1c >7.0%	81.5	81.3
With HbA1c <7.0%	15.2	15.4
With HbA1c ≥7.0%	84.8	84.6
With HbA1c ≤6.5%	8.7	9.9
With HbA1c >6.5%	91.3	90.1

With HbA1c <6.5%	7.1	8.2
With HbA1c ≥6.5%	92.9	91.8

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	1.000
	Comments	P-value for With HbA1c ≤7.0%.
	Method	Fisher Exact
	Comments	[Not specified]

▼ Statistical Analysis 2 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	1.000
	Comments	P-value for With HbA1c <7.0%
	Method	Fisher Exact
	Comments	[Not specified]

▼ Statistical Analysis 3 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.722
	Comments	P-value for With HbA1c ≤6.5%

	Method	Fisher Exact
	Comments	[Not specified]

▼ Statistical Analysis 4 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.699
	Comments	P-value for With HbA1c <6.5%
	Method	Fisher Exact
	Comments	[Not specified]

4. Secondary Outcome

Title:	7-Point Self-Monitored Blood Glucose (SMBG) at Endpoint
▼ Description:	Actual daily mean blood glucose levels at endpoint. The SMBG excursion is the difference between the postprandial and preprandial blood glucose concentration taken at the morning, midday and evening meals.
Time Frame:	32 Weeks
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

Number of randomized patients with baseline and at least one post-baseline value. Intent to treat population. Last observation carried forward.

Arm/Group Title	Insulin Lispro Protamine Suspension	Detemir
▼ Arm/Group Description:	Patient specific dose insulin lispro protamine suspension, twice daily (BID), within 15 minutes before meals, subcutaneous (SC) injection x 32 weeks	Patient specific dose insulin Levemir (detemir) twice daily (BID) subcutaneous (SC) injection x 32 weeks
Number of Participants Analyzed	192	189
Mean (Standard Deviation) Units: millimoles per Liter (mmol/L)		
Daily Mean 7-Point SMBG (N=164,N=172)	8.67 (1.97)	8.48 (1.80)
	8.77 (2.37)	8.56 (2.10)

Daily Mean Pre-Meal (N=174,N=181)		
Daily Mean Postprandial Meal (N=168,N=176)	8.70 (2.08)	8.58 (2.09)
Daily Mean Morning+Evening Pre-Meal (N=174,N=181)	9.00 (2.55)	8.75 (2.48)
Actual Morning Pre-Meal (N=175,N=182)	9.09 (3.18)	8.62 (3.00)
Actual Morning Postprandial Meal (N=171,N=178)	8.68 (2.89)	8.56 (2.73)
Actual Midday Pre-Meal (N=175,N=181)	8.29 (2.92)	8.19 (2.39)
Actual Midday Postprandial Meal (N=170,N=177)	8.54 (2.49)	8.61 (2.44)
Actual Evening Pre-Meal (N=174,N=181)	8.92 (2.72)	8.87 (2.90)
Actual Evening Postprandial Meal (N=172,N=181)	9.05 (2.97)	8.60 (2.71)
Actual 0300 Hours (N=167,N=173)	8.49 (2.85)	8.29 (2.57)
Actual Morning SMBG Excursion (N=171,N=178)	-0.34 (2.94)	-0.12 (2.83)
Actual Midday SMBG Excursion (N=170,N=176)	0.38 (2.52)	0.46 (2.59)
Actual Evening SMBG Excursion (N=172,N=181)	0.12 (2.72)	-0.24 (3.05)
Actual Daily Mean SMBG Excursion (N=168,N=176)	0.06 (1.68)	0.01 (1.71)

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.259
	Comments	P-value for Daily Mean 7-Point SMBG.
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country

▼ Statistical Analysis 2 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.468
	Comments	P-value for Daily Mean Pre-Meal
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country

▼ Statistical Analysis 3 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.395
	Comments	P-value for Daily Mean Postprandial Meal
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country

▼ Statistical Analysis 4 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.414
	Comments	P-value for Daily Mean Morning and Evening Pre-Meal
	Method	ANCOVA

	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country

▼ Statistical Analysis 5 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.275
	Comments	P-value for Actual Morning Pre-Meal
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country

▼ Statistical Analysis 6 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.611
	Comments	P-value for Actual Morning Postprandial Meal
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country

▼ Statistical Analysis 7 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
	P-Value	0.763

Statistical Test of Hypothesis	Comments	P-value for Actual Midday Pre-Meal
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country

▼ Statistical Analysis 8 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.977
	Comments	P-value for Actual Midday Postprandial Meal
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country

▼ Statistical Analysis 9 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.586
	Comments	P-value for Actual Evening Pre-Meal
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country

▼ Statistical Analysis 10 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.093
	Comments	P-value for Actual Evening Postprandial Meal
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country

▼ Statistical Analysis 11 ✔

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.516
	Comments	P-value for Actual 0300 Hours
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country

▼ Statistical Analysis 12 ✔

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.576
	Comments	P-value for Actual Morning SMBG Excursion
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country

▼ Statistical Analysis 13 ✔

	Comments	Insulin Lispro Protamine Suspension, Detemir

Statistical Analysis Overview	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.876
	Comments	P-value for Midday SMBG Excursion
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country

▼ Statistical Analysis 14 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.261
	Comments	P-value for Evening SMBG Excursion
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country

▼ Statistical Analysis 15 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.567
	Comments	P-value for Daily Mean SMBG Excursion
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country

5. Secondary Outcome

Title:	Glycemic Variability at Endpoint
▼ Description:	Glycemic variability was measured by standard deviation (SD) value of fasting blood glucose as measured by intra-patient glycemic variability (determined by the 7-point self-monitored blood glucose [SMBG] profiles at endpoint); mean value (M-value), which was the mean of the intra-days self-monitored blood glucose values, and by the mean of daily difference (MODD), which was the mean of the between-days self-monitored blood glucose values.
Time Frame:	32 Weeks
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

Number of randomized patients with baseline and at least one post-baseline value. Intent to treat population. Last observation carried forward.

Arm/Group Title	Insulin Lispro Protamine Suspension	Detemir
▼ Arm/Group Description:	Patient specific dose insulin lispro protamine suspension, twice daily (BID), within 15 minutes before meals, subcutaneous (SC) injection x 32 weeks	Patient specific dose insulin Levemir (detemir) twice daily (BID) subcutaneous (SC) injection x 32 weeks
Number of Participants Analyzed	187	185
Mean (Standard Deviation) Units: millimoles per Liter (mmol/L)		
Standard Deviation (SD) Value (N=172, N=180)	2.64 (2.09)	2.30 (1.84)
Mean Value (M-Value) (N=175, N=182)	36.39 (31.82)	32.19 (25.79)
Mean Daily Difference (MODD) Value (N=172, N=180)	3.04 (1.90)	2.78 (1.79)

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	If the primary analysis achieves statistical significance at a 0.05 level (that is, the null hypothesis for the primary analysis [primary outcome measure] is rejected), then the first secondary hypothesis (glycemic variability) is tested at an error rate of 0.05.
		Yes

	Non-Inferiority or Equivalence Analysis?	
	Comments	A noninferiority margin of 0.8 mmol/L was chosen to prove noninferiority of ILPS to detemir.
Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	0.36
	Confidence Interval	(2-Sided) 95% -0.03 to 0.75
	Estimation Comments	Least Squares Mean difference = Insulin Lispro Protamine Suspension - Detemir

▼ Statistical Analysis 2 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.132
	Comments	P-value for M-Value
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country

▼ Statistical Analysis 3 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.179
	Comments	P-value for MODD
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country

6. Secondary Outcome

Title:	Number of Self-Reported Hypoglycemic Episodes (Including Nocturnal, Non-Nocturnal, and Severe Hypoglycemia) Overall and at Endpoint
Description:	Nocturnal: Defined as any hypoglycemic event that occurs between bedtime and waking. Non-Nocturnal: Defined as any hypoglycemic event that occurs between waking and bedtime. Severe: An episode with symptoms consistent with neuroglycopenia in which the patient requires the assistance of another person; associated with either a blood glucose level of <2.8 mmol/L (<50 mg/dL) or prompt recovery after oral carbohydrate, glucagon, or intravenous glucose.
Time Frame:	Baseline to 32 Weeks
Safety Issue?	Yes

Outcome Measure Data

Analysis Population Description

Number of randomized patients with baseline and at least one post-baseline value. Intent to treat population. Last observation carried forward.

Arm/Group Title	Insulin Lispro Protamine Suspension	Detemir
Arm/Group Description:	Patient specific dose insulin lispro protamine suspension, twice daily (BID), within 15 minutes before meals, subcutaneous (SC) injection x 32 weeks	Patient specific dose insulin Levemir (detemir) twice daily (BID) subcutaneous (SC) injection x 32 weeks
Number of Participants Analyzed	192	189
Measure Type: Number Units: episodes of hypoglycemia		
Endpoint Hypoglycemic Episodes	134	135
Overall Hypoglycemic Episodes	173	173
Endpoint Nocturnal Hypoglycemic Episodes	69	55
Overall Nocturnal Episodes (N=191,N=186)	125	111
Endpoint Non-Nocturnal Hypoglycemic Episodes	127	129
Overall Non-Nocturnal Hypoglycemic Episodes	172	172
Endpoint Severe Hypoglycemic Episodes	11	3
Overall Severe Hypoglycemic Episodes (N=171,N=170)	24	13

Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.737
	Comments	P-value for Endpoint Hypoglycemic Episodes
	Method	Fisher Exact
	Comments	[Not specified]

▼ Statistical Analysis 2 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.724
	Comments	P-value for Overall Hypoglycemic Episodes
	Method	Fisher Exact
	Comments	[Not specified]

▼ Statistical Analysis 3 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.157
	Comments	P-value for Endpoint Nocturnal Hypoglycemic Episodes
	Method	Fisher Exact
	Comments	[Not specified]

▼ Statistical Analysis 4 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.287
	Comments	P-value for Overall Nocturnal Episodes
	Method	Fisher Exact
	Comments	[Not specified]

▼ Statistical Analysis 5 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.664
	Comments	P-value for Endpoint Non-Nocturnal Hypoglycemic Episodes
	Method	Fisher Exact
	Comments	[Not specified]

▼ Statistical Analysis 6 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.730
	Comments	

		P-value for Overall Non-Nocturnal Hypoglycemic Episodes
	Method	Fisher Exact
	Comments	[Not specified]

▼ Statistical Analysis 7 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.053
	Comments	P-value for Endpoint Severe Hypoglycemic Episodes
	Method	Fisher Exact
	Comments	[Not specified]

▼ Statistical Analysis 8 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.081
	Comments	P-value for Overall Severe Hypoglycemic Episodes
	Method	Fisher Exact
	Comments	[Not specified]

7. Secondary Outcome

Title:	1-Year Adjusted Rates of Self-Reported Hypoglycemic Episodes (Including Nocturnal, Non-Nocturnal, and Severe) Overall and at Endpoint
▼ Description:	Nocturnal: Defined as any hypoglycemic event that occurs between bedtime and waking. Non-Nocturnal: Defined as any hypoglycemic event that occurs between waking and bedtime. Severe: An episode with symptoms consistent with neuroglycopenia in which the patient requires the assistance of another person; associated with either a blood glucose level

	of <2.8 mmol/L (<50 mg/dL) or prompt recovery after oral carbohydrate, glucagon, or intravenous glucose.
Time Frame:	baseline to 32 weeks
Safety Issue?	Yes

▼ Outcome Measure Data ✓

▼ Analysis Population Description

Number of randomized patients with baseline and at least one post-baseline value. Intent to treat population. Last observation carried forward.

Arm/Group Title	Insulin Lispro Protamine Suspension	Detemir
▼ Arm/Group Description:	Patient specific dose insulin lispro protamine suspension, twice daily (BID), within 15 minutes before meals, subcutaneous (SC) injection x 32 weeks	Patient specific dose insulin Levemir (detemir) twice daily (BID) subcutaneous (SC) injection x 32 weeks
Number of Participants Analyzed	192	189
Mean (Standard Deviation) Units: hypoglycemic events per 1 year		
Endpoint Hypoglycemic Rate	66.41 (90.91)	52.60 (70.62)
Overall Hypoglycemic Rate	76.45 (85.07)	61.21 (64.25)
Endpoint Nocturnal Hypoglcemic Rate	8.90 (18.65)	5.60 (13.20)
Overall Nocturnal Hypoglycemic Rate	9.65 (15.01)	6.01 (10.31)
Endpoint Non-Nocturnal Hypoglycemic Rate	57.08 (83.17)	46.88 (65.28)
Overall Non-Nocturnal Hypoglycemic Rate	66.58 (78.63)	54.83 (58.94)
Endpoint Severe Hypoglycemic Rate	0.63 (3.08)	0.10 (0.79)
Overall Severe Hypoglycemic Rate	0.42 (1.43)	0.25 (1.26)

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.280
	Comments	P-value for Endpoint Hypoglycemic Rate
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country. Hypoglycemic Rate (Adjusted for 1 year) was used in the analysis.

▼ Statistical Analysis 2 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.193
	Comments	P-value for Overall Hypoglycemic Rate
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country. Hypoglycemic Rate (Adjusted for 1 year) was used in the analysis.

▼ Statistical Analysis 3 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.042
	Comments	P-value for Endpoint Nocturnal Hypoglycemic Rate
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country. Hypoglycemic Rate (Adjusted for 1 year) was used in the analysis.

▼ Statistical Analysis 4 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.001
	Comments	P-value for Overall Nocturnal Hypoglycemic Rate
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country. Hypoglycemic Rate (Adjusted for 1 year) was used in the analysis.

▼ Statistical Analysis 5 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.579
	Comments	P-value for Endpoint Non-Nocturnal Hypoglycemic Rate
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country. Hypoglycemic Rate (Adjusted for 1 year) was used in the analysis.

▼ Statistical Analysis 6 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
	P-Value	0.531

Statistical Test of Hypothesis	Comments	P-value for Overall Non-Nocturnal Hypoglycemic Rate
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country. Hypoglycemic Rate (Adjusted for 1 year) was used in the analysis.

▼ Statistical Analysis 7 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.017
	Comments	P-value for Endpoint Severe Hypoglycemic Rate
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country. Hypoglycemic Rate (Adjusted for 1 year) was used in the analysis.

▼ Statistical Analysis 8 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.038
	Comments	P-value for Overall Severe Hypoglycemic Rate
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country. Hypoglycemic Rate (Adjusted for 1 year) was used in the analysis.

8. Secondary Outcome

Title:	30-Day Adjusted Rates of Self-Reported Hypoglycemic Episodes (Including Nocturnal, Non-Nocturnal, and Severe) Overall and at Endpoint
▼ Description:	[Not specified]
Time Frame:	baseline to 32 weeks
Safety Issue?	No

▼ Outcome Measure Data ✔

▼ Analysis Population Description

Number of randomized patients with baseline and at least one post-baseline value. Intent to treat population. Last observation carried forward.

Arm/Group Title	Insulin Lispro Protamine Suspension	Detemir
▼ Arm/Group Description:	Patient specific dose insulin lispro protamine suspension, twice daily (BID), within 15 minutes before meals, subcutaneous (SC) injection x 32 weeks	Patient specific dose insulin Levemir (detemir) twice daily (BID) subcutaneous (SC) injection x 32 weeks
Number of Participants Analyzed	192	189
Mean (Standard Deviation) Units: hypoglycemic events per 30 days		
Endpoint Hypogylcemic Rate	5.45 (7.47)	4.32 (5.80)
Overall Hypoglycemic Rate	6.28 (6.99)	5.03 (5.28)
Endpoint Nocturnal Hypoglycemic Rate	0.73 (1.53)	0.46 (1.08)
Overall Nocturnal Hypoglycemic Rate	0.79 (1.23)	0.49 (0.85)
Endpoint Non-Nocturnal Hypoglycemic Rate	4.69 (6.83)	3.85 (5.36)
Overall Non-Nocturnal Hypoglycemic Rate	5.47 (6.46)	4.50 (4.84)
Endpoint Severe Hypoglycemic Rate	0.05 (0.25)	0.01 (0.06)
Overall Severe Hypoglycemic Rate	0.03 (0.12)	0.02 (0.10)

9. Secondary Outcome

Title:	Change From Baseline in Absolute Body Weight at 32 Week Endpoint
▼ Description:	[Not specified]
Time Frame:	Baseline, 32 Weeks
Safety Issue?	No

▼ Outcome Measure Data ✔

▼ Analysis Population Description

Number of randomized patients with baseline and at least one post-baseline value. Intent to treat population.

Arm/Group Title	Insulin Lispro Protamine Suspension	Detemir
▼ Arm/Group Description:	Patient specific dose insulin lispro protamine suspension, twice daily (BID), within 15 minutes before meals, subcutaneous (SC) injection x 32 weeks	Patient specific dose insulin Levemir (detemir) twice daily (BID) subcutaneous (SC) injection x 32 weeks
Number of Participants Analyzed	192	189
Mean (Standard Deviation) Units: kilograms		
Baseline	72.76 (15.53)	72.69 (14.59)
Change from Baseline	1.54 (3.18)	0.58 (3.19)

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	If the first secondary null hypothesis (glycemic variability) is rejected, then the second secondary hypothesis (weight change) is tested at an error rate of 0.05.
	Non-Inferiority or Equivalence Analysis?	Yes
	Comments	A noninferiority margin of 1.5 kg was chosen to prove noninferiority of ILPS to detemir.
Statistical Test of Hypothesis	P-Value	0.003
	Comments	P-value for Change from Baseline.
	Method	ANCOVA
	Comments	ANCOVA Model: Variable=Treatment+Baseline+Country.
Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	0.97
	Confidence Interval	(2-Sided) 95% 0.34 to 1.60
	Estimation Comments	Least Squares Mean Difference = Insulin Lispro Protamine Suspension minus Detemir.

10. Secondary Outcome

Title:	Insulin Dose Per Body Weight (Total and By Component [Basal and Bolus])
Description:	Total daily insulin dose adjusted for body weight (U/kg/day) was assessed.
Time Frame:	32 Weeks
Safety Issue?	No

Outcome Measure Data

Analysis Population Description

Number of randomized patients with baseline and at least one post-baseline value. Intent to treat population. Last observation carried forward.

Arm/Group Title	Insulin Lispro Protamine Suspension	Detemir
Arm/Group Description:	Patient specific dose insulin lispro protamine suspension, twice daily (BID), within 15 minutes before meals, subcutaneous (SC) injection x 32 weeks	Patient specific dose insulin Levemir (detemir) twice daily (BID) subcutaneous (SC) injection x 32 weeks
Number of Participants Analyzed	192	189
Mean (Standard Deviation) Units: units of insulin per kilogram per day		
Total Insulin (N=192, N=188)	0.91 (0.30)	0.99 (0.41)
Total Bolus Insulin (N=191, N=187)	0.39 (0.17)	0.45 (0.22)
Total Basal Insulin (N=192, N=188)	0.53 (0.20)	0.55 (0.26)

Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.023
	Comments	P-value for Total Insulin
	Method	ANOVA
	Comments	ANOVA Model: Variable=Treatment+Country

▼ Statistical Analysis 2 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.004
	Comments	P-value for Total Bolus Insulin
	Method	ANOVA
	Comments	ANOVA Model: Variable=Treatment+Country

▼ Statistical Analysis 3 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.282
	Comments	P-value for Total Basal Insulin
	Method	ANOVA
	Comments	ANOVA Model: Variable=Treatment+Country

11. Secondary Outcome

Title:	Insulin Dose (Total and By Component [Basal and Bolus])
▼ Description:	Total daily insulin dose (U/day) was assessed. NOTE : Outcome Measure Description is shorter than the Outcome Measure Title.
Time Frame:	32 weeks
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

Number of randomized patients with baseline and at least one post-baseline value. Intent to treat population. Last observation carried forward.

Arm/Group Title	Insulin Lispro Protamine Suspension	Detemir
▼ Arm/Group Description:	Patient specific dose insulin lispro protamine suspension, twice daily (BID), within 15 minutes before meals, subcutaneous (SC) injection x 32 weeks	Patient specific dose insulin Levemir (detemir) twice daily (BID) subcutaneous (SC) injection x 32 weeks
Number of Participants Analyzed	192	189
Mean (Standard Deviation) Units: units of insulin per day (U/day)		
Total Insulin (N=192, N=188)	67.78 (27.42)	73.84 (38.38)
Total Bolus Insulin (N=191, N=187)	28.94 (14.69)	33.32 (20.41)
Total Basal Insulin (N=192, N=188)	38.99 (17.37)	40.70 (22.29)

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.82
	Comments	P-value for Total Insulin
	Method	ANOVA
	Comments	ANOVA Model: Variable=Treatment+Country

▼ Statistical Analysis 2 ✔

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.19
	Comments	P-value for Total Bolus Insulin

	Method	ANOVA
	Comments	ANOVA Model: Variable=Treatment+Country

▼ Statistical Analysis 3 ✓

Statistical Analysis Overview	Comparison Groups	Insulin Lispro Protamine Suspension, Detemir
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.416
	Comments	P-value for Total Basal Insulin
	Method	ANOVA
	Comments	ANOVA Model: Variable=Treatment+Country

Adverse Events

Time Frame		
Additional Description		
Source Vocabulary Name	[Not specified]	
Assessment Type	[Not specified]	
Arm/Group Title	Insulin Lispro Protamine Suspension	Detemir
▼ Arm/Group Description	Patient specific dose insulin lispro protamine suspension, twice daily (BID), within 15 minutes before meals, subcutaneous (SC) injection x 32 weeks	Patient specific dose insulin Levemir (detemir) twice daily (BID) subcutaneous (SC) injection x 32 weeks

▼ Serious Adverse Events

	Insulin Lispro Protamine Suspension		Detemir	
	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events
Total	10/---		3/---	
Endocrine disorders				
Autoimmune thyroiditis †A	1/192 (0.52%)	1	0/189 (0%)	0
Hyperthyroidism †A	1/192 (0.52%)	1	0/189 (0%)	0
Gastrointestinal disorders				

Abdominal pain †A	1/192 (0.52%)	1	0/189 (0%)	0
Mouth cyst †A	1/192 (0.52%)	1	0/189 (0%)	0
General disorders				
Chest pain †A	1/192 (0.52%)	1	0/189 (0%)	0
Infections and infestations				
Cellulitis †A	1/192 (0.52%)	1	0/189 (0%)	0
Osteomyelitis †A	0/192 (0%)	0	1/189 (0.53%)	1
Respiratory tract infection †A	1/192 (0.52%)	1	0/189 (0%)	0
Metabolism and nutrition disorders				
Diabetic foot †A	0/192 (0%)	0	1/189 (0.53%)	1
Diabetic ketoacidosis †A	1/192 (0.52%)	2	0/189 (0%)	0
Hypoglycaemia †A	1/192 (0.52%)	1	1/189 (0.53%)	1
Musculoskeletal and connective tissue disorders				
Back pain †A	1/192 (0.52%)	1	0/189 (0%)	0
Nervous system disorders				
Diabetic neuropathy †A	0/192 (0%)	0	1/189 (0.53%)	1
Hypoglycaemic coma †A	1/192 (0.52%)	1	0/189 (0%)	0
Respiratory, thoracic and mediastinal disorders				
Pleural effusion †A	1/192 (0.52%)	1	0/189 (0%)	0

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 11.0

▼ Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	2%			
	Insulin Lispro Protamine Suspension		**Detemir**	
	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events
Total	93/---		86/---	
Gastrointestinal disorders				
Abdominal pain upper †A	3/192 (1.56%)	4	7/189 (3.7%)	8
Nausea †A	6/192 (3.12%)	7	5/189 (2.65%)	8
Toothache †A	1/192 (0.52%)	2	5/189 (2.65%)	5
Vomiting †A	5/192 (2.6%)	6	2/189 (1.06%)	2
General disorders				
Fatigue †A	2/192 (1.04%)	2	4/189 (2.12%)	7
Pyrexia †A	4/192 (2.08%)	5	0/189 (0%)	0
Infections and infestations				
Gastroenteritis †A	5/192 (2.6%)	5	3/189 (1.59%)	4
Influenza †A	15/192 (7.81%)	16	16/189 (8.47%)	18
Nasopharyngitis †A	27/192 (14.06%)	30	18/189 (9.52%)	24
Pharyngitis †A	6/192 (3.12%)	6	4/189 (2.12%)	4
Sinusitis †A	7/192 (3.65%)	7	7/189 (3.7%)	7
	0/192 (0%)	0	6/189 (3.17%)	6

Upper respiratory tract infection †A				
Urinary tract infection †A	3/192 (1.56%)	3	4/189 (2.12%)	4
Musculoskeletal and connective tissue disorders				
Arthralgia †A	0/192 (0%)	0	5/189 (2.65%)	5
Back pain †A	2/192 (1.04%)	3	4/189 (2.12%)	5
Nervous system disorders				
Headache †A	18/192 (9.38%)	32	14/189 (7.41%)	35
Migraine †A	5/192 (2.6%)	5	1/189 (0.53%)	2
Reproductive system and breast disorders				
Dysmenorrhoea †A	4/192 (2.08%)	16	3/189 (1.59%)	8
Respiratory, thoracic and mediastinal disorders				
Cough †A	6/192 (3.12%)	8	10/189 (5.29%)	12
Pharyngolaryngeal pain †A	5/192 (2.6%)	5	5/189 (2.65%)	18

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 11.0

Limitations and Caveats

[Not Specified]

More Information

Certain Agreements

Principal Investigators are NOT employed by the organization sponsoring the study.

The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is more than 60 days but less than or equal to 180 days from the time submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot extend the embargo.

Results Point of Contact

Name/Official Title: Chief Medical Officer
Organization: Eli Lilly and Company
Phone: 800-545-5979
Email: ---