ClinicalTrials.gov PRS
Protocol Registration and Results System

ID: 10935 Comparison of Two Basal Insulins for Patients With Type 2 Diabetes (IOOY) NCT00494013

**Protocol Registration and Results Preview**

Close

# Comparison of Two Basal Insulins for Patients With Type 2 Diabetes (IOOY)

**This study has been completed.**

| | |
|---|---|
| Sponsor: | Eli Lilly and Company |
| Collaborators: | |
| Information provided by: | Eli Lilly and Company |
| ClinicalTrials.gov Identifier: | NCT00494013 |

## Purpose

The purpose of this study is to examine the effectiveness and safety of insulin lispro protamine suspension (ILPS) as compared to insulin detemir as basal insulin therapy in adults with type 2 diabetes. A gatekeeper strategy will be employed for sequentially testing the secondary objectives.

| Condition | Intervention | Phase |
|---|---|---|
| Diabetes Mellitus Type 2 | Drug: Insulin Lispro Protamine Suspension<br>Drug: Detemir | Phase 3 |

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

Official Title: Treat-to-Target Comparison of Two Basal Insulin Analogs (Insulin Lispro Protamine Suspension and Comparator) in Basal Therapy for Patients With Type 2 Diabetes Mellitus

**Further study details as provided by Eli Lilly and Company:**

Primary Outcome Measure:

- Change From Baseline to 24 Week Endpoint in Hemoglobin A1c (HbA1c) [Time Frame: Baseline, 24 Weeks] [Designated as safety issue: No]

Secondary Outcome Measures:

- Actual and Change From Baseline Hemoglobin A1c (HbA1c) Value at 12 Weeks and at 24 Weeks [Time Frame: Baseline, 12 Weeks, 24 Weeks] [Designated as safety issue: No]

- Percentage of Patients With HbA1c <7.0% and HbA1c < or = 6.5% at Endpoint [Time Frame: 24 Weeks] [Designated as safety issue: No]
  Percentage of patients achieving Hemaglobin A1c (HbA1c) targets of less than 7.0% and less than or equal to 6.5% at endpoint.

- Glycemic Variability [Time Frame: 24 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-monitoring blood glucose [SMBG] profiles at endpoint) for the actual morning pre-meal blood glucose value.

- 7-point Self-monitored Blood Glucose (SMBG) Profile at Endpoint [Time Frame: 24 Weeks] [Designated as safety issue: No]
  Actual daily mean blood glucose levels at endpoint.

- Number of Participants With Self-reported Hypoglycemic Episodes (Including All, Nocturnal, and Severe Hypoglycemia) Overall for All Study Periods [Time Frame: Baseline to 24 Weeks] [Designated as safety issue: Yes]
  Overall: any time after randomization. Hypoglycemic: any time patient experienced sign/symptom associated with hypoglycemia, or had old Roche blood glucose level <7 mg/dL. Nocturnal: any hypoglycemic event that occurred between bedtime and waking. Severe: event with symptoms consistent with neuroglycopenia in which patient requires assistance, and is associated with: a Roche blood glucose value <2.8 mmol/L or prompt recovery after oral carbohydrate, glucagon, or IV glucose. Results are for the combined titration and maintenance periods.

- 1-Year Adjusted Rates of Self-Reported Hypoglycemic Episodes (Including All, Nocturnal, and Severe) Overall [Time Frame: Baseline to 24 Weeks] [Designated as safety issue: Yes]
  Overall: any time after randomization. Hypoglycemic: any time patient experienced sign/symptom associated with hypoglycemia, or had old Roche blood glucose level <7 mg/dL. Nocturnal: any hypoglycemic event that occurred between bedtime and waking. Severe: event with symptoms consistent with neuroglycopenia in which patient requires assistance, and is associated with: a Roche blood glucose value <2.8 mmol/L or prompt recovery after oral carbohydrate, glucagon, or IV glucose. 1-year adjusted rate=(total number of episodes between 2 time intervals/number of days between intervals) X 365.25 days.

- 30-Day Adjusted Rates of Self-Reported Hypoglycemic Episodes (Including All, Nocturnal, and Severe) Overall [Time Frame: Baseline to 24 Weeks] [Designated as safety issue: Yes]
  Overall: any time after randomization. Hypoglycemic: any time patient experienced sign/symptom associated with hypoglycemia, or had old Roche blood glucose level <7 mg/dL. Nocturnal: any hypoglycemic event that occurred between bedtime and waking. Severe: event with symptoms consistent with neuroglycopenia in which patient requires assistance, and is associated with: a Roche blood glucose value <2.8 mmol/L or prompt recovery after oral carbohydrate, glucagon, or IV glucose. 30-day adjusted rate=(total number of episodes between 2 time intervals/number of days between intervals) X 30 days.

- Change in Absolute Body Weight (kg) From Baseline to 24 Week Endpoint [Time Frame: Baseline, 24 Weeks] [Designated as safety issue: Yes]

- Total Daily Insulin Dose (Units) at Endpoint [Time Frame: 24 Weeks] [Designated as safety issue: No]
  Insulin dose at endpoint was analyzed by 24-hour total daily insulin (units).

- Total Daily Insulin Dose Per Body Weight (Units/Kilograms) at Endpoint [Time Frame: 24 Weeks] [Designated as safety issue: No]
  Insulin dose at endpoint was analyzed by 24-hour total daily insulin per body weight (Units/kilograms).

- Number of Injections of Basal Insulin Analog at Endpoint [Time Frame: 24 Weeks] [Designated as safety issue: No]

Enrollment: 442
Study Start Date: August 2007
Study Completion Date: September 2008
Primary Completion Date: September 2008

| Arms | Assigned Interventions |
|---|---|
| Experimental: Insulin Lispro Protamine Suspension<br>Insulin Lispro Protamine Suspension: Patient specific dose administered subcutaneously once daily or twice daily x 24 weeks. | Drug: Insulin Lispro Protamine Suspension<br>Patient specific dose administered subcutaneously once daily or twice daily x 24 weeks.<br>Other Names:<br>• Neutral Protamine Lispro (NPL)<br>• Humalog<br>• ILPS |
| | |

| | |
|---|---|
| Active Comparator: Detemir<br>Detemir: Patient specific dose administered subcutaneously once or twice daily x 24 weeks. | Drug: Detemir<br>Patient specific dose administered subcutaneously once or twice daily x 24 weeks. |

**Eligibility**

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

1. Have type 2 diabetes mellitus for at least 1 year.
2. Are at least 18 years old.
3. Have been receiving oral antihyperglycemic medications (OAMs), without insulin, for at least 3 months immediately prior to the study and have been on stable doses of at least 2 of the following OAMs for the 6 weeks prior to Visit 1, at or above the doses defined in the following: Metformin--1500 milligrams per day (mg/day); Sulfonylureas--1/2 the maximum daily dose, according to the local package insert; Dipeptidyl peptidase-intravenous (DPP-IV) inhibitors-- 1/2 the maximum daily dose, according to the local package insert; Thiazolidinediones (TZDs)--30 mg/day pioglitazone or 4 mg/day rosiglitazone.
4. Have a hemoglobin A1c (HbA1c) greater than or equal to 7.5% and less than or equal to 10.0%, as measured by a central laboratory before Visit 2.
5. Body mass index (BMI) greater than or equal to 25 and less than or equal to 45 kilograms per square meter (kg/m2).

Exclusion Criteria

1. Have used insulin therapy (outside of pregnancy) any time in the past 2 years, except for short-term treatment of acute conditions, and up to a maximum of 4 weeks.
2. Have taken any glucose-lowering medications not included in Inclusion Criterion [3] (for example, acarbose, miglitol, pramlintide, exenatide, repaglinide, or nateglinide) in the past 3 months before Visit 1.
3. Have had more than 1 episode of severe hypoglycemia, within 6 months prior to entry into the study, or is currently diagnosed as having hypoglycemia unawareness.
4. Have a history of renal transplantation or are currently receiving renal dialysis or creatinine greater than or equal to 2.0 milligrams per deciliter (mg/dL) (177 micromoles per liter [micromol/L]).
5. Have obvious clinical signs or symptoms, or laboratory evidence, of liver disease (alanine transaminase [ALT], or aspartate transaminase [AST] greater than 2 times the upper limit of the reference range, as defined by the local laboratory) or have albumin value above or below the normal reference range, as defined by the local laboratory.

**Contacts and Locations**

**Locations**

**United States, Alabama**

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.

Hueytown, Alabama, United States, 35023

**United States, Arizona**

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.

Litchfield Park, Arizona, United States, 85340

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.

Phoenix, Arizona, United States, 85016

**United States, California**

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.

Buena Park, California, United States, 90620

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.

Fountain Valley, California, United States, 92708

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.

Los Angeles, California, United States, 90057

**United States, Florida**

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.

Jacksonville, Florida, United States, 32257

**United States, Georgia**

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.

Atlanta, Georgia, United States, 30312

**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.

Chicago, Illinois, United States, 60612

**United States, Indiana**

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.

Evansville, Indiana, United States, 47714

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.

Indianapolis, Indiana, United States, 46202

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.

Newburgh, Indiana, United States, 47630

**United States, Kentucky**

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.

Lexington, Kentucky, United States, 40503

**United States, Louisiana**

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.

Slidell, Louisiana, United States, 70458

**United States, Maryland**

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.

Prince Frederick, Maryland, United States, 20678

**United States, Michigan**

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.

Novi, Michigan, United States, 48374

**United States, Nevada**

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.

Las Vegas, Nevada, United States, 89101

**United States, New York**

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.

Syracuse, New York, United States, 13210

**United States, North Carolina**

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.

Goldsboro, North Carolina, United States, 27530

**United States, Ohio**

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.

Cincinnati, Ohio, United States, 45236

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.

London, Ohio, United States, 43140

**United States, Oregon**

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.

Bend, Oregon, United States, 97701

**United States, Pennsylvania**

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.

Lansdale, Pennsylvania, United States, 19446

**United States, South Carolina**

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.

Taylors, South Carolina, United States, 29687

**United States, Tennessee**

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.

Johnson City, Tennessee, United States, 37604

**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.

Grand Prairie, Texas, United States, 75052

**United States, Wisconsin**

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.

Menomonee Falls, Wisconsin, United States, 53051

**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, C1188AAF

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.

Ramos Mejia, Argentina, B1704ETD

**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, H-1139

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.

Eger, Hungary, 3300

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.

Mako, Hungary, 6900

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.

Szekesfehervar, Hungary, 8000

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.

Szekszard, Hungary, 7100

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.

Veszprem, Hungary, 8200

**India**

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.

Bangalore, India, 560052

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.

Chennai, India, 600086

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.

Cochin, India, 682026

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.

Mumbai, India, 400 067

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.

Pune, India, 411011

**Korea, Republic of**

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.

Goyang-Si, Korea, Republic of, 410-719

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.

Sungnam-Si, Korea, Republic of, 463-712

**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.

Chihuahua, Mexico, 31238

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, 44340

**Poland**

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.

Krakow, Poland, 30-349

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.

Poznan, Poland, 61-495

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.

Rzeszow, Poland, 35-068

**Spain**

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.

Lugo, Spain, 27004

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.

Palma De Mallorca, Spain, 07014

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.

Santa Cruz De Tenerife, Spain, 38320

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.

Valencia, Spain, 46015

**Taiwan**

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.

Chiayi City, Taiwan, 600

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.

Neihu Taipei, Taiwan, 114

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.

Tainan, Taiwan, 704

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.

Taipei, Taiwan, 100

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.

Yung-Kang, Tainan, Taiwan, 710

**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

Responsible Party: Eli Lilly (Chief Medical Officer)
Study ID Numbers: 10935
F3Z-MC-IOOY
Health Authority: United States: Food and Drug Administration

# Study Results

## Participant Flow

| | |
|---|---|
| Recruitment Details | |
| Pre-Assignment Details | 789 patients were screened; 347 patients failed screening or discontinued before randomization. Demographics and outcomes are reported on the "Full Analysis Set": all randomized patients who received at least one dose of study drug and had at least one post-baseline measurement for the dependent variable, according to Intent to Treat principles. |

| Arm/Group Title | Insulin Lispro Protamine Suspension | Detemir | Total (Not public) |
|---|---|---|---|
| Arm/Group Description | Insulin Lispro Protamine Suspension: Patient specific dose administered subcutaneously once daily or twice daily x 24 weeks. | Detemir: Patient specific dose administered subcutaneously once daily x 24 weeks. | |
| Period Title: **Overall Study** | | | |
| Started | 223 | 219 | 442 |
| Full Analysis Set (Intent to Treat) | 219 | 210 | 429 |
| Completed | 193 | 183 | 376 |
| Not Completed | 30 | 36 | 66 |
| Reason Not Completed | | | |
| Adverse Event | 0 | 1 | 1 |
| Entry Criteria Not Met | 1 | 4 | 5 |
| Lost to Follow-up | 5 | 6 | 11 |
| Physician Decision | 3 | 5 | 8 |
| Protocol Violation | 8 | 5 | 13 |
| Withdrawal by Subject | 13 | 14 | 27 |
| Sponsor Decision | 0 | 1 | 1 |
| (Not Public) | Not Completed = 30<br>Total from all reasons = 30 | Not Completed = 36<br>Total from all reasons = 36 | |

## Baseline Characteristics

| Arm/Group Title | Insulin Lispro Protamine Suspension | Detemir | Total |
|---|---|---|---|
| Arm/Group Description | Insulin Lispro Protamine Suspension: Patient specific dose administered subcutaneously once daily or twice daily x 24 weeks. | Detemir: Patient specific dose administered subcutaneously once daily x 24 weeks. | |
| **Overall Number of Baseline Participants** | 219 | 210 | **429** |
| Baseline Analysis Population Description [Not specified] | | | |
| Age, Continuous<br>Mean (Standard Deviation)<br>Units: years | 56.32 (9.91) | 55.73 (10.20) | 56.03 (10.04) |
| Gender, Male/Female<br>Measure Type: Number<br>Units: participants | | | |
| Female | 108 | 97 | 205 |
| Male | 111 | 113 | 224 |
| Region of Enrollment<br>Measure Type: Number<br>Units: participants | | | |
| Argentina | 10 | 11 | 21 |
| Hungary | 36 | 34 | 70 |
| India | 42 | 39 | 81 |
| Korea, Republic of | 10 | 11 | 21 |
| Mexico | 28 | 27 | 55 |
| Spain | 13 | 13 | 26 |
| Taiwan | 20 | 19 | 39 |
| United States | 60 | 56 | 116 |
| Race/Ethnicity<br>Measure Type: Number<br>Units: participants | | | |
| African | 8 | 8 | 16 |
| Caucasian | 88 | 82 | 170 |
| East Asian | 35 | 33 | 68 |

| | | | |
|---|---|---|---|
| Hispanic | 45 | 47 | 92 |
| West Asian | 43 | 40 | 83 |
| Sulfonylurea Group [1]<br>Measure Type: Number<br>Units: participants | | | |
| Yes | 170 | 158 | 328 |
| No | 49 | 51 | 100 |
| Unavailable | 0 | 1 | 1 |
| | [1] Patients with previous sulfonylurea use. | | |
| Body Mass Index (BMI) [1]<br>Mean (Standard Deviation)<br>Units: kilogram per square meter (kg/m^2) | 30.03 (5.01) | 30.10 (5.12) | 30.06 (5.06) |
| | [1] Body mass index is an estimate of body fat based on body weight divided by height squared. | | |
| Body Weight<br>Mean (Standard Deviation)<br>Units: kilograms (kg) | 81.10 (17.46) | 82.72 (19.32) | 81.89 (18.39) |
| Duration of Diabetes<br>Mean (Standard Deviation)<br>Units: years | 9.48 (6.09) | 8.94 (5.59) | 9.22 (5.85) |
| Height<br>Mean (Standard Deviation)<br>Units: centimeters (cm) | 163.94 (10.19) | 165.14 (10.94) | 164.53 (10.57) |

## Outcome Measures

1. Primary Outcome

| | |
|---|---|
| Title: | Change From Baseline to 24 Week Endpoint in Hemoglobin A1c (HbA1c) |
| ▼ Description: | [Not specified] |
| Time Frame: | Baseline, 24 Weeks |
| Safety Issue? | No |

▼ Outcome Measure Data ✓

▼ Analysis Population Description

Number of randomized patients who received at least one dose of study drug and at least one post-baseline measurement. Last observation carried forward.

| Arm/Group Title | Insulin Lispro Protamine Suspension | Detemir |
|---|---|---|
| ▼ Arm/Group Description: | Insulin Lispro Protamine Suspension: Patient specific dose administered subcutaneously once daily or twice daily x 24 weeks. | Detemir: Patient specific dose administered subcutaneously once daily x 24 weeks. |
| Number of Participants Analyzed | 219 | 210 |
| Least Squares Mean (Standard Error)<br>Units: percent of HbA1c | | |
| Baseline (n=209, n=202) | 8.79 (0.06) | 8.77 (0.06) |
| Change from Baseline (n=209, n=202) | -1.52 (0.08) | -1.31 (0.08) |

▼ Statistical Analysis 1 ✔

| Statistical Analysis Overview | Comparison Groups | Insulin Lispro Protamine Suspension, Detemir |
|---|---|---|
| | Comments | Hypothesis: Basal analog insulin lispro protamine suspension, injected once or twice daily is noninferior to basal analog insulin determir, injected once or twice daily, with regard to glycemic control as measured by change in HbA1c from baseline to endpoint (last observation carried forward). |
| | Non-Inferiority or Equivalence Analysis? | Yes |
| | Comments | The noninferiority margin was 0.4%. |
| | | |
| | P-Value | 0.026 |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | Comments | [Not specified] |
| | Method | ANCOVA |
| | Comments | ANCOVA Model: Variable=Treatment + Baseline + Country + Baseline Sulfonylurea Group. |
| | | |
| Method of Estimation | Estimation Parameter | Mean Difference (Net) |
| | Estimated Value | -0.21 |
| | Confidence Interval | (2-Sided) 95% -0.39 to -0.03 |
| | Estimation Comments | The two-sided 95% confidence interval is for the Least Squares Mean difference between the two treatments (Insulin Lispro Protamine Suspension minus Determir). |

2. Secondary Outcome

| | |
|---|---|
| Title: | Actual and Change From Baseline Hemoglobin A1c (HbA1c) Value at 12 Weeks and at 24 Weeks |
| ▼ Description: | [Not specified] |
| Time Frame: | Baseline, 12 Weeks, 24 Weeks |
| Safety Issue? | No |

▼ Outcome Measure Data ✓

▼ Analysis Population Description

Number of randomized patients who received at least one dose of study drug and at least one post-baseline measurement.

| Arm/Group Title | Insulin Lispro Protamine Suspension | Detemir |
|---|---|---|
| ▼ Arm/Group Description: | Insulin Lispro Protamine Suspension: Patient | Detemir: Patient specific dose administered |

| | | |
|---|---|---|
| | specific dose administered subcutaneously once daily or twice daily x 24 weeks. | subcutaneously once daily x 24 weeks. |
| Number of Participants Analyzed | 219 | 210 |
| Least Squares Mean (Standard Error)<br>Units: percent hemoglobin | | |
| Baseline | 8.79 (0.06) | 8.77 (0.06) |
| Week 12 HbA1c | 7.44 (0.08) | 7.55 (0.07) |
| Week 12 Change from Baseline | -1.33 (0.08) | -1.22 (0.07) |
| Week 24 HbA1c | 7.14 (0.09) | 7.34 (0.08) |
| Week 24 Change from Baseline | -1.63 (0.09) | -1.43 (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 | 0.213 |
| | Comments | P-value for 12 Week Change from Baseline. |
| | Method | ANCOVA |
| | Comments | ANCOVA Model: Variable = Treatment + Baseline + Country + Baseline Sulfonylurea Group. |
| | | |
| Method of Estimation | Estimation Parameter | Mean Difference (Net) |
| | Estimated Value | -0.11 |

| | | |
|---|---|---|
| | Confidence Interval | (2-Sided) 95%<br>-0.28 to 0.06 |
| | Estimation Comments | The two-sides 95% confidence interval is for the Least Squares Mean difference between the two treatments (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 | 0.213 |
| | Comments | P-value for 12 Week HbA1c. |
| | Method | ANCOVA |
| | Comments | ANCOVA Model: Variable = Treatment + Baseline + Country + Baseline Sulfonylurea Group. |
| | | |
| Method of Estimation | Estimation Parameter | Mean Difference (Net) |
| | Estimated Value | -0.11 |
| | Confidence Interval | (2-Sided) 95%<br>-0.28 to 0.06 |
| | Estimation Comments | The two-sided 95% confidence interval is for the Least Squares Mean |

| | | |
|---|---|---|
| | | difference between the two treatments (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 | 0.038 |
| | Comments | P-value for 24 Week Change from Baseline. |
| | Method | ANCOVA |
| | Comments | ANCOVA Model: Variable = Treatment + Baseline + Country + Baseline Sulfonylurea Group. |
| | | |
| Method of Estimation | Estimation Parameter | Mean Difference (Net) |
| | Estimated Value | -0.20 |
| | Confidence Interval | (2-Sided) 95% -0.38 to -0.01 |
| | Estimation Comments | The two-sides 95% confidence interval is for the Least Squares Mean difference between the two treatments (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 | 0.038 |
| | Comments | P-value for Week 24 HbA1c. |
| | Method | ANCOVA |
| | Comments | ANCOVA Model: Variable = Treatment + Baseline + Country + Baseline Sulfonylurea Group. |
| Method of Estimation | Estimation Parameter | Mean Difference (Net) |
| | Estimated Value | -0.20 |
| | Confidence Interval | (2-Sided) 95% -0.38 to -0.01 |
| | Estimation Comments | The two-sided 95% confidence interval is for the Least Squares Mean difference between the two treatments (Insulin Lispro Protamine Suspension minus Detemir). |

3. Secondary Outcome

| | |
|---|---|
| Title: | Percentage of Patients With HbA1c <7.0% and HbA1c < or = 6.5% at Endpoint |
| ▼ Description: | |

| | |
|---|---|
| | Percentage of patients achieving Hemaglobin A1c (HbA1c) targets of less than 7.0% and less than or equal to 6.5% at endpoint. |
| Time Frame: | 24 Weeks |
| Safety Issue? | No |

▼ Outcome Measure Data

▼ Analysis Population Description

Number of randomized patients who received at least one dose of study drug and at least one post-baseline measurement. Last observation carried forward.

| Arm/Group Title | Insulin Lispro Protamine Suspension | Detemir |
|---|---|---|
| ▼ Arm/Group Description: | Insulin Lispro Protamine Suspension: Patient specific dose administered subcutaneously once daily or twice daily x 24 weeks. | Detemir: Patient specific dose administered subcutaneously once daily x 24 weeks. |
| Number of Participants Analyzed | 219 | 210 |
| Measure Type: Number Units: percentage of participants | | |
| HbA1c <7.0% | 34.9 | 31.2 |
| HbA1c ≤6.5% | 22.5 | 16.3 |

▼ 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 | 0.463 |
| | Comments | P-value for 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 | 0.135 |
| | Comments | P-value for HbA1c ≤6.5%. |
| | Method | Fisher Exact |
| | Comments | [Not specified] |

4. Secondary Outcome

| | |
|---|---|
| Title: | Glycemic Variability |
| ▼ 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-monitoring blood glucose [SMBG] profiles at endpoint) for the actual morning pre-meal blood glucose value. |
| Time Frame: | 24 Weeks |
| Safety Issue? | No |

▼ Outcome Measure Data ✔

▼ Analysis Population Description

Number of randomized patients who received at least one dose of study drug and at least one post-baseline measurement. Last observation carried forward.

| Arm/Group Title | Insulin Lispro Protamine Suspension | Detemir |
|---|---|---|
| ▼ Arm/Group Description: | Insulin Lispro Protamine Suspension: Patient | Detemir: Patient specific dose administered |

| | | |
|---|---|---|
| | specific dose administered subcutaneously once daily or twice daily x 24 weeks. | subcutaneously once daily x 24 weeks. |
| Number of Participants Analyzed | 218 | 208 |
| Mean (Standard Deviation) Units: millimoles per Liter (mmol/L) | 1.14 (0.64) | 1.04 (0.69) |

▼ Statistical Analysis 1 ✔

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Insulin Lispro Protamine Suspension, Detemir |
| | Comments | The first gatekeeping hypothesis was that Insulin Lispro Protamine Suspension was noninferior to determir. |
| | Non-Inferiority or Equivalence Analysis? | Yes |
| | Comments | Noninferiority margin of 0.8 millimoles per Liter (mmol/L). |
| | | |
| Statistical Test of Hypothesis | P-Value | 0.107 |
| | Comments | [Not specified] |
| | Method | ANOVA |
| | Comments | ANOVA model: Variable=Treatment + Country + Baseline HbA1c + Baseline Sulfonylurea Group. |
| | | |
| Method of Estimation | Estimation Parameter | Mean Difference (Net) |
| | Estimated Value | 0.10 |

| | | |
|---|---|---|
| | Confidence Interval | (2-Sided) 95%<br>-0.02 to 0.23 |
| | Estimation Comments | The two-sided 95% confidence interval is for the Least Squares Mean difference between the two treatments (Insulin Lispro Protamine Suspension minus Determir). |

5. Secondary Outcome

| | |
|---|---|
| Title: | 7-point Self-monitored Blood Glucose (SMBG) Profile at Endpoint |
| ▼ Description: | Actual daily mean blood glucose levels at endpoint.<br>NOTE : Outcome Measure Description is shorter than the Outcome Measure Title. |
| Time Frame: | 24 Weeks |
| Safety Issue? | No |

▼ Outcome Measure Data

▼ Analysis Population Description

Number of randomized patients who received at least one dose of study drug and at least one post-baseline measurement. Last observation carried forward.

| Arm/Group Title | Insulin Lispro Protamine Suspension | Detemir |
|---|---|---|
| ▼ Arm/Group Description: | Insulin Lispro Protamine Suspension: Patient specific dose administered subcutaneously once daily or twice daily x 24 weeks. | Detemir: Patient specific dose administered subcutaneously once daily x 24 weeks. |
| Number of Participants Analyzed | 219 | 210 |
| Mean (Standard Deviation)<br>Units: millimoles per liter (mmol/L) | | |
| Average 7-Point SMBG | 8.25 (1.58) | 8.26 (1.73) |

| | | |
|---|---|---|
| Average Pre-Meal | 7.48 (1.69) | 7.43 (1.69) |
| Average Post-Meal | 9.37 (1.91) | 9.42 (2.21) |
| Average Morning+Evening Pre-Meal | 7.49 (1.68) | 7.40 (1.86) |

▼ 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 | 0.952 |
| | Comments | P-value for Average 7-Point SMBG. |
| | Method | ANOVA |
| | Comments | ANOVA Model: Variable = Treatment + Country + Baseline HbA1c + Baseline Sulfonylurea Group. |

▼ 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 | 0.856 |
| | Comments | P-value for Average Pre-Meal. |
| | Method | ANOVA |
| | | |

| | | |
|---|---|---|
| | Comments | ANOVA Model: Variable = Treatment + Country + Baseline HbA1c + Baseline Sulfonylurea Group. |

▼ 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 | 0.790 |
| | Comments | P-value for Average Post-Meal. |
| | Method | ANOVA |
| | Comments | ANOVA Model: Variable = Treatment + Country + Baseline HbA1c + Baseline Sulfonylurea Group. |

▼ 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 | 0.632 |
| | Comments | P-value for Average Morning+Evening Pre-Meal. |
| | | |

| | | |
|---|---|---|
| | Method | ANOVA |
| | Comments | ANOVA Model: Variable = Treatment + Country + Baseline HbA1c + Baseline Sulfonylurea Group. |

6. Secondary Outcome

| | |
|---|---|
| Title: | Number of Participants With Self-reported Hypoglycemic Episodes (Including All, Nocturnal, and Severe Hypoglycemia) Overall for All Study Periods |
| ▼ Description: | Overall: any time after randomization. Hypoglycemic: any time patient experienced sign/symptom associated with hypoglycemia, or had old Roche blood glucose level <7 mg/dL. Nocturnal: any hypoglycemic event that occurred between bedtime and waking. Severe: event with symptoms consistent with neuroglycopenia in which patient requires assistance, and is associated with: a Roche blood glucose value <2.8 mmol/L or prompt recovery after oral carbohydrate, glucagon, or IV glucose. Results are for the combined titration and maintenance periods. |
| Time Frame: | Baseline to 24 Weeks |
| Safety Issue? | Yes |

▼ Outcome Measure Data ✔

▼ Analysis Population Description

Number of randomized patients who received at least one dose of study drug and at least one post-baseline measurement.

| Arm/Group Title | Insulin Lispro Protamine Suspension | Detemir |
|---|---|---|
| ▼ Arm/Group Description: | Insulin Lispro Protamine Suspension: Patient specific dose administered subcutaneously once daily or twice daily x 24 weeks. | Detemir: Patient specific dose administered subcutaneously once daily x 24 weeks. |
| Number of Participants Analyzed | 219 | 210 |
| Measure Type: Number Units: participants | | |

| | | |
|---|---|---|
| All Hypoglycemic Episodes | 151 | 137 |
| Nocturnal Hypoglycemic Episodes | 99 | 68 |
| Severe Hypoglycemic Episodes (N=214, N=207) | 5 | 2 |

▼ 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 | 0.472 |
| | Comments | P-value for All Hypoglycemic Events. |
| | 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 | 0.005 |
| | Comments | P-value for Nocturnal Hypoglycemic Events. |
| | 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 | 0.450 |
| | Comments | P-value for Severe Hypoglycemic Events. |
| | Method | Fisher Exact |
| | Comments | [Not specified] |

7. Secondary Outcome

| | |
|---|---|
| Title: | 1-Year Adjusted Rates of Self-Reported Hypoglycemic Episodes (Including All, Nocturnal, and Severe) Overall |
| ▼ Description: | Overall: any time after randomization. Hypoglycemic: any time patient experienced sign/symptom associated with hypoglycemia, or had old Roche blood glucose level <7 mg/dL. Nocturnal: any hypoglycemic event that occurred between bedtime and waking. Severe: event with symptoms consistent with neuroglycopenia in which patient requires assistance, and is associated with: a Roche blood glucose value <2.8 mmol/L or prompt recovery after oral carbohydrate, glucagon, or IV glucose. 1-year adjusted rate=(total number of episodes between 2 time intervals/number of days between intervals) X 365.25 days. |
| Time Frame: | Baseline to 24 Weeks |
| Safety Issue? | Yes |

▼ Outcome Measure Data ✔

▼ Analysis Population Description

Number of randomized patients who received at least one dose of study drug and at least one post-baseline measurement.

| Arm/Group Title | Insulin Lispro Protamine Suspension | Detemir |
|---|---|---|
| ▼ Arm/Group Description: | Insulin Lispro Protamine Suspension: Patient specific dose administered subcutaneously once daily or twice daily x 24 weeks. | Detemir: Patient specific dose administered subcutaneously once daily x 24 weeks. |
| Number of Participants Analyzed | 219 | 210 |
| Mean (Standard Deviation) Units: hypoglycemic events per 1 year | | |
| Hypoglycemic Rate | 24.23 (32.99) | 16.23 (26.05) |
| Nocturnal Hypoglycemic Rate | 6.32 (12.11) | 3.75 (13.18) |
| Severe Hypoglycemic Rate | 0.05 (0.45) | 0.01 (0.15) |

▼ 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 | 0.001 |
| | Comments | P-value for Hypoglycemic Rate. |
| | Method | ANOVA |
| | Comments | Nonparametric ANOVA Model: Rank of Variable = Treatment + Country + Baseline HbA1c + Baseline Sulfonylurea Group. |

▼ 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 | 0.001 |
| | Comments | P-value for Nocturnal Hypoglycemic Rate. |
| | Method | ANOVA |
| | Comments | Nonparametric ANOVA Model: Rank of Variable = Treatment + Country + Baseline HbA1c + Baseline Sulfonylurea Group. |

▼ 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 | 0.226 |
| | Comments | P-value for Severe Hypoglycemic Rate. |
| | Method | ANOVA |
| | Comments | Nonparametric ANOVA Model: Rank of Variable = Treatment + Country + Baseline |

| | | |
|---|---|---|
| | | HbA1c + Baseline Sulfonylurea Group. |

8. Secondary Outcome

| | |
|---|---|
| Title: | 30-Day Adjusted Rates of Self-Reported Hypoglycemic Episodes (Including All, Nocturnal, and Severe) Overall |
| ▼ Description: | Overall: any time after randomization. Hypoglycemic: any time patient experienced sign/symptom associated with hypoglycemia, or had old Roche blood glucose level <7 mg/dL. Nocturnal: any hypoglycemic event that occurred between bedtime and waking. Severe: event with symptoms consistent with neuroglycopenia in which patient requires assistance, and is associated with: a Roche blood glucose value <2.8 mmol/L or prompt recovery after oral carbohydrate, glucagon, or IV glucose. 30-day adjusted rate=(total number of episodes between 2 time intervals/number of days between intervals) X 30 days. |
| Time Frame: | Baseline to 24 Weeks |
| Safety Issue? | Yes |

▼ Outcome Measure Data

▼ Analysis Population Description

Number of randomized patients who received at least one dose of study drug and at least one post-baseline measurement.

| Arm/Group Title | Insulin Lispro Protamine Suspension | Detemir |
|---|---|---|
| ▼ Arm/Group Description: | Insulin Lispro Protamine Suspension: Patient specific dose administered subcutaneously once daily or twice daily x 24 weeks. | Detemir: Patient specific dose administered subcutaneously once daily x 24 weeks. |
| Number of Participants Analyzed | 219 | 210 |
| Mean (Standard Deviation) Units: hypoglycemic events per 30 days | | |
| Hypoglycemic Rate | 1.99 (2.71) | 1.33 (2.14) |
| Nocturnal Hypoglycemic Rate | 0.52 (0.99) | 0.31 (1.08) |
| | 0.00 (0.04) | 0.00 (0.01) |

| | | |
|---|---|---|
| Severe Hypoglycemic Rate | | |

9. Secondary Outcome

| | |
|---|---|
| Title: | Change in Absolute Body Weight (kg) From Baseline to 24 Week Endpoint |
| ▼ Description: | [Not specified] |
| Time Frame: | Baseline, 24 Weeks |
| Safety Issue? | Yes |

▼ Outcome Measure Data ✓

▼ Analysis Population Description

Number of randomized patients who received at least one dose of study drug and at least one post-baseline measurement. Last observation carried forward.

| Arm/Group Title | Insulin Lispro Protamine Suspension | Detemir |
|---|---|---|
| ▼ Arm/Group Description: | Insulin Lispro Protamine Suspension: Patient specific dose administered subcutaneously once daily or twice daily x 24 weeks. | Detemir: Patient specific dose administered subcutaneously once daily x 24 weeks. |
| Number of Participants Analyzed | 219 | 209 |
| Mean (Standard Deviation) Units: kilograms (kg) | | |
| Baseline | 81.10 (17.46) | 82.56 (19.22) |
| Change from Baseline | 1.88 (3.16) | 0.36 (2.85) |

▼ Statistical Analysis 1 ✓

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Insulin Lispro Protamine Suspension, Detemir |
| | Comments | The second gatekeeping hypothesis was that Insulin Lispro Protamine |

| | | |
|---|---|---|
| | | Suspension was noninferior to detemir with regard to change in absolute body weight from baseline to endpoint (last observation carried forward). |
| | Non-Inferiority or Equivalence Analysis? | Yes |
| | Comments | Noninferiority margin of 1.5 kilograms (kg). |
| | | |
| Statistical Test of Hypothesis | P-Value | <0.001 |
| | Comments | P-value for Change from Baseline. |
| | Method | ANCOVA |
| | Comments | ANCOVA Model: Variable=Treatment + Baseline + Country + Baseline HbA1c + Baseline Sulfonylurea Group. |
| | | |
| Method of Estimation | Estimation Parameter | Mean Difference (Net) |
| | Estimated Value | 1.50 |
| | Confidence Interval | (2-Sided) 95% 0.93 to 2.06 |
| | Estimation Comments | The two-sided 95% confidence interval is for the Least Squares Mean difference between the two treatments (Insulin Lispro Protamine Suspension minus Determir). |

10. Secondary Outcome

| | |
|---|---|
| Title: | Total Daily Insulin Dose (Units) at Endpoint |
| ▼ Description: | Insulin dose at endpoint was analyzed by 24-hour total daily insulin (units). |
| Time Frame: | 24 Weeks |
| Safety Issue? | No |

▼ Outcome Measure Data ✓

▼ Analysis Population Description

Number of randomized patients who received at least one dose of study drug and at least one post-baseline measurement. Last observation carried forward.

| Arm/Group Title | Insulin Lispro Protamine Suspension | Detemir |
|---|---|---|
| ▼ Arm/Group Description: | Insulin Lispro Protamine Suspension: Patient specific dose administered subcutaneously once daily or twice daily x 24 weeks. | Detemir: Patient specific dose administered subcutaneously once daily x 24 weeks. |
| Number of Participants Analyzed | 219 | 210 |
| Mean (Standard Deviation) Units: Units of insulin | 31.78 (19.14) | 37.30 (29.45) |

▼ 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 | 0.074 |
| | Comments | [Not specified] |
| | Method | ANCOVA |
| | Comments | |

| | | |
|---|---|---|
| | | ANCOVA Model: Variable=Treatment + Country + Baseline HbA1c + Baseline Sulfonylurea Group + Change in HbA1c from Baseline. |

11. Secondary Outcome

| | |
|---|---|
| Title: | Total Daily Insulin Dose Per Body Weight (Units/Kilograms) at Endpoint |
| ▼ Description: | Insulin dose at endpoint was analyzed by 24-hour total daily insulin per body weight (Units/kilograms). |
| Time Frame: | 24 Weeks |
| Safety Issue? | No |

▼ Outcome Measure Data ✔

▼ Analysis Population Description

Number of randomized patients who received at least one dose of study drug and at least one post-baseline measurement. Last observation carried forward.

| Arm/Group Title | Insulin Lispro Protamine Suspension | Detemir |
|---|---|---|
| ▼ Arm/Group Description: | Insulin Lispro Protamine Suspension: Patient specific dose administered subcutaneously once daily or twice daily x 24 weeks. | Detemir: Patient specific dose administered subcutaneously once daily x 24 weeks. |
| Number of Participants Analyzed | 219 | 210 |
| Mean (Standard Deviation) Units: Units of Insulin/kilograms (U/kg) | 0.39 (0.23) | 0.46 (0.36) |

▼ 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 | 0.039 |
| | Comments | [Not specified] |
| | Method | ANCOVA |
| | Comments | ANCOVA Model: Variable=Treatment + Country + Baseline HbA1c + Baseline Sulfonylurea Group + Change in HbA1c from Baseline. |

12. Secondary Outcome

| | |
|---|---|
| Title: | Number of Injections of Basal Insulin Analog at Endpoint |
| ▼ Description: | [Not specified] |
| Time Frame: | 24 Weeks |
| Safety Issue? | No |

▼ Outcome Measure Data 

▼ Analysis Population Description

Number of randomized patients who received at least one dose of study drug and at least one post-baseline measurement. Last observation carried forward.

| Arm/Group Title | Insulin Lispro Protamine Suspension | Detemir |
|---|---|---|
| ▼ Arm/Group Description: | Insulin Lispro Protamine Suspension: Patient specific dose administered subcutaneously once daily or twice daily x 24 weeks. | Detemir: Patient specific dose administered subcutaneously once daily x 24 weeks. |
| | 219 | 210 |

| | | |
|---|---|---|
| Number of Participants Analyzed | | |
| Measure Type: Number Units: participants | | |
| Patients with 1 Injection | 89 | 108 |
| Patients with 2 Injections | 130 | 102 |

▼ 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 | 0.026 |
| | Comments | [Not specified] |
| | Method | Fisher Exact |
| | Comments | [Not specified] |

## 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 | Insulin Lispro Protamine Suspension: Patient specific dose administered subcutaneously once daily or twice daily x 24 weeks. | Detemir: Patient specific dose administered subcutaneously once daily x 24 weeks. |

## Serious Adverse Events

| | Insulin Lispro Protamine Suspension | | Detemir | |
|---|---|---|---|---|
| | Affected / at Risk (%) | # Events | Affected / at Risk (%) | # Events |
| Total | 7/219 (3.2%) | | 1/210 (0.48%) | |
| Infections and infestations | | | | |
| Bronchitis †A | 1/219 (0.46%) | 1 | 0/210 (0%) | 0 |
| Cellulitis †A | 0/219 (0%) | 0 | 1/210 (0.48%) | 1 |
| Injury, poisoning and procedural complications | | | | |
| Fall †A | 1/219 (0.46%) | 1 | 0/210 (0%) | 0 |
| Operative haemorrhage †A | 1/219 (0.46%) | 1 | 0/210 (0%) | 0 |
| Rib fracture †A | 1/219 (0.46%) | 1 | 0/210 (0%) | 0 |
| Metabolism and nutrition disorders | | | | |
| Hypoglycaemia †A | 2/219 (0.91%) | 4 | 0/210 (0%) | 0 |
| Musculoskeletal and connective tissue disorders | | | | |
| Musculoskeletal chest pain †A | 1/219 (0.46%) | 1 | 0/210 (0%) | 0 |
| Tenosynovitis †A | 1/219 (0.46%) | 1 | 0/210 (0%) | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | | |
| Lung neoplasm malignant †A | 1/219 (0.46%) | 1 | 0/210 (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 | 1% |

| | Insulin Lispro Protamine Suspension | | Detemir | |
|---|---|---|---|---|
| | Affected / at Risk (%) | # Events | Affected / at Risk (%) | # Events |
| Total | 78/219 (35.62%) | | 70/210 (33.33%) | |

| | | | | |
|---|---|---|---|---|
| Eye disorders | | | | |
| Diabetic retinopathy †A | 4/219 (1.83%) | 4 | 2/210 (0.95%) | 2 |
| Gastrointestinal disorders | | | | |
| Diarrhoea †A | 6/219 (2.74%) | 8 | 7/210 (3.33%) | 7 |
| Gastritis †A | 5/219 (2.28%) | 5 | 2/210 (0.95%) | 2 |
| Nausea †A | 2/219 (0.91%) | 4 | 4/210 (1.9%) | 5 |
| Vomiting †A | 4/219 (1.83%) | 4 | 2/210 (0.95%) | 2 |
| General disorders | | | | |
| Chest pain †A | 1/219 (0.46%) | 1 | 3/210 (1.43%) | 3 |
| Oedema peripheral †A | 3/219 (1.37%) | 3 | 1/210 (0.48%) | 2 |
| Pain †A | 0/219 (0%) | 0 | 3/210 (1.43%) | 3 |
| Pyrexia †A | 5/219 (2.28%) | 5 | 1/210 (0.48%) | 1 |
| Infections and infestations | | | | |
| Bronchitis †A | 2/219 (0.91%) | 3 | 3/210 (1.43%) | 3 |
| Gastroenteritis †A | 4/219 (1.83%) | 4 | 1/210 (0.48%) | 1 |
| Influenza †A | 4/219 (1.83%) | 4 | 3/210 (1.43%) | 5 |
| Nasopharyngitis †A | 12/219 (5.48%) | 14 | 10/210 (4.76%) | 10 |
| Sinusitis †A | 3/219 (1.37%) | 3 | 0/210 (0%) | 0 |
| Upper respiratory tract infection †A | 6/219 (2.74%) | 7 | 7/210 (3.33%) | 8 |
| Investigations | | | | |
| Weight increased †A | 5/219 (2.28%) | 5 | 0/210 (0%) | 0 |
| Musculoskeletal and connective tissue disorders | | | | |
| Arthralgia †A | 1/219 (0.46%) | 1 | 3/210 (1.43%) | 3 |
| Back pain †A | 3/219 (1.37%) | 3 | 3/210 (1.43%) | 3 |
| Muscle spasms †A | 3/219 (1.37%) | 3 | 3/210 (1.43%) | 3 |
| Nervous system disorders | | | | |
| Dizziness †A | 2/219 (0.91%) | 2 | 4/210 (1.9%) | 7 |
| Headache †A | 5/219 (2.28%) | 6 | 8/210 (3.81%) | 8 |
| Respiratory, thoracic and mediastinal disorders | | | | |
| Cough †A | 3/219 (1.37%) | 3 | 3/210 (1.43%) | 3 |
| Skin and subcutaneous tissue disorders | | | | |
| Pruritus †A | 1/219 (0.46%) | 1 | 4/210 (1.9%) | 4 |
| Vascular disorders | | | | |
| Hypertension †A | 4/219 (1.83%) | 4 | 3/210 (1.43%) | 3 |

† 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 | Chief Medical Officer |
| Title: | |
| Organization: | Eli Lilly and Company |
| Phone: | 800-545-5979 |
| Email: | --- |

Close