

Unique Protocol ID: 11654

Secondary ID: H9X-MC-GBCT

Brief Title: PK, PD and Safety of LY2189265 in Elderly Patients With Type 2 Diabetes Mellitus

Official Title: A Study to Evaluate the Pharmacokinetics, Pharmacodynamics, Safety, and Tolerability of LY2189265 in Elderly Patients With Type 2 Diabetes Mellitus

Study Type: Interventional

Sponsor: Eli Lilly and Company

Collaborators: Covance

Brief Summary: The purpose of this study is to assess the safety and tolerability of different doses of LY2189265 in the older population.

Detailed Description: The risk of developing type 2 diabetes mellitus increases with age therefore it is likely that a significant number of patients prescribed LY2189265 will be elderly. It is possible that BMI and co-morbidity differences from the younger T2DM population may impact exposure levels.

This trial will assess the safety and tolerability of LY2189265 in this population and PK from the different doses (0.5, 0.75 and 1.5 mg) will provide information on the optimum dose for this group of patients.

Overall Status: Completed

Study Start Date: February 2010

Study Completion Date: August 2010

Study Design:

Primary Purpose: Treatment

Study Phase: Phase 1

Interventional Model: Parallel Assignment

Number of Arms: 4

Masking: Double Blind (Subject, Caregiver, Investigator)

Allocation: Randomized

Control: Placebo Control

Endpoint Classification: Safety Study

Enrollment: 40 Actual

Primary Outcome Measure:

Measure: Clinically Significant Effects

Timeframe: baseline to 9 weeks

Secondary Outcome Measure:

Measure: pharmacokinetics of LY2189265, Area Under the Curve (AUC)

Timeframe: 7 weeks

Measure: pharmacodynamics of insulin, area under the curve (AUC)

Timeframe: baseline to week 6

Measure: pharmacodynamics of glucose, area under the curve (AUC)

Timeframe: baseline to week 6

Measure: pharmacodynamics of C-peptide, area under the curve (AUC)

Timeframe: baseline to week 6

Measure: pharmacokinetics of LY2189265, Maximum Concentration (Cmax)

Timeframe: 7 weeks

Measure: Pharmacodynamics - body weight

Timeframe: baseline to 9 weeks

Condition(s): Diabetes Mellitus, Type 2

Keywords:

diabetes

T2DM

Elderly

safety

tolerability

PK

PD

Arms	Assigned Interventions
Placebo Comparator: Placebo	Drug: Placebo Subcutaneous injection once per week for 6 weeks
Experimental: 0.5 mg LY2189265	Drug: LY2189265 Subcutaneous injection once per week for 6 weeks
Experimental: 0.75 mg LY2189265	Drug: LY2189265 Subcutaneous injection once per week for 6 weeks
Experimental: 1.5 mg LY2189265	Drug: LY2189265 Subcutaneous injection once per week for 6 weeks

Eligibility Criteria:

Inclusion Criteria:

- Are males or females, diagnosed with T2DM for greater than or equal to 3 months prior to screening.
- Male patients:
 - Agree to use a reliable method of birth control during the study and for 3 months following the last dose of study drug.
- Female patients:
 - Must be of non-child-bearing potential due to surgical sterilization (hysterectomy, bilateral oophorectomy or tubal ligation) or menopause.
- Women with an intact uterus are deemed postmenopausal if they:
 - have had cessation of menses for at least 1 year or,
 - have had >12 months of spontaneous amenorrhea, with follicle stimulating hormone (FSH) >40 IU/mL, and estrogen <30 pg/mL;
 - have not taken hormone replacement therapy (HRT) or oral contraceptives within 1 year of study start and are otherwise healthy.
- Women who have had cessation of menses for at least 2 years are permitted to take HRT.
- Are between the BMI of 18.5 and 35.0 kg/m², inclusive.
- Have T2DM controlled with diet or exercise alone or are stable on a single oral antidiabetic medication (metformin, sulfonylureas, acarbose [or other disaccharidase inhibitors], thiazolidinediones or meglitinides) for at least 3 weeks (3 months for thiazolidinediones) prior to screening. However, patients receiving sulfonylureas, acarbose (or other disaccharidase inhibitors), or meglitinides may participate only if this treatment is stopped and metformin substituted. If substituted with metformin, patients will receive metformin for at least 3 weeks and should be taking a stable dose for at least 7 days prior to receiving study medication.
- Have a HbA1c value at screening (or within 4 weeks prior to screening) of 6.5% to 9.5%. If HbA1c is between 6.1% and 6.5%, patients may participate in the study providing they are receiving permissible oral antidiabetic medication, or have had their treatment substituted with metformin prior to receiving study medication (see inclusion criteria 4).

- Have a fasting blood glucose value at screening >126 mg/dL (7.0 mmol/L) for patients on a controlled diet, and >108 mg/dL (6.0 mmol/L) for patients on oral antidiabetic medication (applies to second screening assessment for patients who have changed to metformin), with an upper limit of 180 mg/dL (approximately 9.9 mmol/L) in each case. If fasting blood glucose is outside this range, repeat measurements are allowed but 2 consecutive measurements must be within range for the patient to be eligible.
- Have clinical laboratory test results within normal reference range for the population or investigator site, or results with acceptable deviations that are judged to be not clinically significant by the investigator. Abnormalities of serum glucose, serum lipids, urinary glucose, and urinary protein consistent with T2DM are acceptable.
- Have a normal blood pressure (after approximately 5 minutes supine and approximately 3 minutes standing) as determined by the investigator.
- Have venous access sufficient to allow blood sampling as per the protocol.
- Are reliable and willing to make themselves available for the duration of the study and are willing to follow study procedures.

Exclusion Criteria:

- Are currently enrolled in, or discontinued within the last 30 days from, a clinical trial involving an investigational drug or device, or are concurrently enrolled in any other type of medical research judged not to be scientifically or medically compatible with this study.
- Have known allergies to GLP-1 related compounds including LY2189265.
- Are persons who have previously completed or withdrawn from this study or any other study investigating LY2189265 or have received glucagon-like peptides or incretin mimetics in the past 3 months.
- Have taken insulin, chlorpropamide or alpha-glucosidase inhibitors within 30 days prior to screening.
- Have an abnormality in the 12-lead ECG that, in the opinion of the investigator, increases the risks associated with participating in the study.
- Have poorly controlled hypertension (systolic blood pressure >160 mmHg and/or diastolic blood pressure >100 mmHg) and/or evidence of labile blood pressure including symptomatic postural hypertension.
- Have a history or presence of respiratory, hepatic, renal, endocrine, hematological, or neurological disorders capable of significantly altering the absorption, metabolism, or elimination of drugs; of constituting a risk when taking the study medication; or of interfering with the interpretation of data.
- Have a history or presence of cardiovascular disorder (including myocardial infarction, cerebrovascular accident, venous thromboembolism, arrhythmia [judged by the investigator to be clinically significant], or angina), have symptoms or signs of congestive heart failure, or are expected to require coronary artery bypass surgery or angioplasty.
- Have a history or presence of gastrointestinal disorder (including pancreatitis [history of chronic pancreatitis or idiopathic acute pancreatitis], or gall bladder disease), or gastrointestinal disease that impacts gastric emptying (e.g. gastric bypass surgery, pyloric stenosis) or could be aggravated by GLP analogs (e.g. esophageal reflux). Subjects having had cholecystectomy (removal of gall bladder) in the past with no further sequelae, may be included in the study at the discretion of the screening physician.
- Show evidence of significant active neuropsychiatric disease.
- Regularly use known drugs of abuse and/or show positive findings on urinary drug screening.
- Show evidence of human immunodeficiency virus (HIV) and/or positive human HIV antibodies.
- Show evidence of hepatitis C and/or positive hepatitis C antibody.
- Show evidence of hepatitis B and/or positive hepatitis B surface antigen.

- Intend to start new concomitant medication during the study, including over-the-counter and herbal medication, regularly use drugs that directly reduce gastrointestinal motility and/or regularly use systemic corticosteroids by oral, intravenous, or intramuscular route, or potent, inhaled, or intranasal steroids known to have a high rate of systemic absorption.
- Are taking prescription medications (for example, antihypertensive agents, aspirin, lipid lowering agents, thyroxine, and/or HRT) for the treatment of concurrent medical conditions and have not been stable on these medications at least for the last 3 months (1 month for thyroxine replacement therapy).
- Have donated blood of more than 500 mL within the last month.
- Have an average weekly alcohol intake that exceeds site guidelines or have a significant history of alcoholism or drug/chemical abuse as determined by the investigator, or are unwilling to stop alcohol consumption from at least 24 hours prior to each dose and while resident in the research unit.
- Smoke more than 10 cigarettes or equivalent in nicotine use or nicotine substitutes per day

Minimum Age: 65 years

Maximum Age: N/A

Gender: Both

Contact for Public Queries: Call 1-877-CTLILLY (1-877-285-4559) or 1-317-615-4559 Mon – Fri 9AM – 5PM Eastern time (UTC/GMT – 5 hours, EST)

Contact for Scientific Queries: Call 1-877-CTLILLY (1-877-285-4559) or 1-317-615-4559 Mon – Fri 9AM – 5PM Eastern time (UTC/GMT – 5 hours, EST)

Locations:

Lilly Clinical Trial Site
Neuss, Germany
Completed

Lilly Clinical Trial Site
Munich, Germany
Completed

Lilly Clinical Trial Site
Berlin, Germany
Completed