

Unique Protocol ID: 12774
Secondary IDs: B5K-EW-IBHA

Brief Title: Comparison of HRI U-500 PK/PD With HRI U-100 in Healthy Obese Subjects

Official Title: Comparative Pharmacokinetics and Pharmacodynamics of Common Clinical Doses of Human Regular U-500 Insulin versus Human Regular U-100 Insulin in Healthy Obese Subjects

Study Type: Interventional

Sponsor: Eli Lilly and Company

Brief Summary: This study will compare how the body interacts with 2 different formulations of Human Regular Insulin; the standard U100 formulation and a 5 times stronger formulation, U500. Two different doses (50 Units and 100 Units) will be studied for each formulation.

Overall Status: Completed

Study Start Date: September 2009

Study Completion Date: December 2009 [Actual]

Primary Outcome Measure: Relative exposure (AUC_{0-t'}) for U-500 (500 U/mL) versus U-100 (100 U/mL) after subcutaneous injection of 50-U and 100-U doses

Time Frame: predose to 24 hours post dose

Secondary Outcome Measures: Relative exposure (AUC_{0-t'}) and the overall effect (G_{tot}) for U-500 (500 U/mL) versus U-100 (100 U/mL) after subcutaneous injection of 50-U and 100-U doses

Time Frame: predose to 24 hours post dose

Measure: to compare PK (C_{max} and t_{max}) and PD [Glucose Infusion Rate (GIR, the maximum GIR (R_{max}), time of maximum GIR (tR_{max}) and time of last GIR measurement (tR_{last})] parameters between formulations and dose levels

Time Frame: predose to 24 hours post dose

Conditions: Diabetes Mellitus

Arms: Experimental: U-500/U100

Each subject will receive 1 injection of each formulation/dose (4 doses in total) in a randomized fashion.

Drug: Human Regular U-500 Insulin

single 50 U, subcutaneous injection

Drug: Human Regular U-500 Insulin

single 100 U, subcutaneous injection

Drug: Human Regular U-100 Insulin

single 50 U, subcutaneous injection

Drug: Human Regular U-100 Insulin

single 100 U, subcutaneous injection

Interventions: Drug: Human Regular U-500 Insulin

Drug: Human Regular U-100 Insulin

Eligibility Criteria: Inclusion Criteria:

1. Are overtly healthy obese males or females, as determined by medical history and physical examination.
2. Are between the body mass index (BMI) of 30 and 40 kg/m², inclusive, at screening and have a body weight of ≤ 125 kg at screening.
3. 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.
4. Have venous access sufficient to allow blood sampling as per the protocol.
5. Are reliable and willing to make themselves available for the duration of the study and are willing to follow study procedures.
6. Have given written informed consent approved by Lilly and the ethical review board (ERB) governing the site.

Exclusion Criteria:

7. Are investigator site personnel directly affiliated with this study and their immediate families. Immediate family is defined as a spouse, parent, child, or sibling, whether biologically or legally adopted.
8. Are Lilly employees.
9. Women who are pregnant or intend to become pregnant during the course of the study.
10. Women who are breast-feeding.

11. Women of childbearing potential who are not willing to use a medically acceptable form of contraception during the study.
12. Are currently enrolled in, or discontinued within the last 30 days from, a clinical trial involving an investigational drug or device other than the study drug used in this study, or are concurrently enrolled in any other type of medical research judged not to be scientifically or medically compatible with this study.
13. Have known hypersensitivities or allergies to insulin, excipients contained in insulin products, or related compounds.
14. Are persons who have previously completed or withdrawn from this study.
15. Have an abnormality in the 12-lead ECG that, in the opinion of the investigator, increases the risks associated with participating in the study.
16. Have an abnormal supine blood pressure (mean systolic ≥ 140 mm Hg/mean diastolic ≥ 90 mm Hg) at screening or with deviations that are judged to be clinically significant by the investigator.
17. Have a significant history of or current cardiovascular, respiratory, hepatic, renal, gastrointestinal, 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.
18. Show evidence of significant active neuropsychiatric disease.
19. Regularly use known drugs of abuse.
20. Have a history of diabetes mellitus, gestational diabetes, impaired glucose tolerance, or impaired fasting glucose.
21. Have a fasting blood glucose ≥ 100 mg/dL at screening and prior to the oral glucose challenge test (OGCT).
22. Have a 2-hour post 75-g glucose challenge blood glucose ≥ 140 mg/dL at screening.
23. Positive human immunodeficiency virus (HIV) antibodies at screening.
24. Positive hepatitis C antibody at screening.
25. Positive hepatitis B surface antigen at screening.
26. Have acute infection with fever.
27. Initiation of new over-the-counter medication within 7 days prior to dosing, or prescription medications and herbal medication within 14 days prior to dosing, will not be permitted. Occasional intake of acetaminophen or vitamin/mineral supplements will be allowed. Ongoing medications may be permitted following prior agreement between the investigator and the Lilly clinical pharmacologist
28. Have used systemic glucocorticoids within 3 months prior to screening.
29. Have donated blood of more than 400 mL within the last 3 months.
30. Have an average weekly alcohol intake that exceeds 21 units per week (males) and 14 units per week (females), or are unwilling to stop alcohol consumption for 24 hours prior to each clamp visit and while resident in the CRU (1 unit = 12 oz or 360 mL of beer; 5 oz or 150 mL of wine; 1.5 oz or 45 mL of distilled spirits).
31. Are not willing to refrain from use of tobacco products while resident in the CRU.
32. Are determined by the investigator to be unsuitable for any other reason.

Gender: Both

Minimum Age: 21 years

Maximum Age: 65 years

Accepts Healthy Volunteers? Yes

Central Contact:

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