A Multi-Center, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study
Comparing SYR-322 Alone and Combination SYR-322 with Pioglitazone versus Placebo on Postprandial Lipids in Subjects with Type 2 Diabetes

Published: 28-05-2008
Last updated: 07-05-2024

The primary objective of this study is to evaluate the effects of SYR-322 and SYR-322coadministered with pioglitazone HC1 versus placebo on postprandial triglycerides in subjectswith type 2 diabetes.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON32102

Source
ToetsingOnline

Brief title
SYR-322_301

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Diabetes, Diabetes Mellitus Type 2

Research involving
Human

Sponsors and support

Primary sponsor: Takeda
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: Diabetes, Pioglitazone, Postprandial Lipids, SYR-322

Outcome measures

Primary outcome

The primary endpoint is the change from Baseline in postprandial incremental

area under the curve

for triglycerides at Week 16.

Secondary outcome

The secondary objectives of this study are to evaluate effect of SYR-322 and

SYR-322

coadministered with pioglitazone HC1 versus placebo on postprandial lipid

parameters,

postprandial lipoprotein parameters, postprandial GLP-1, postprandial glucagon,

postprandial

glucose, postprandial insulin, measurements of glycemic control (ie, HbA1C,

fasting plasma

glucose, C-peptide, insulin, proinsulin), inflammatory markers (ie, adiponectin

and CRP),

cardiovascular risk (ie, VCAM, ICAM, and e-Selectin), and endothelial function

(pulse wave

tonometry).

Safety variables will include incidence of treatment emergent adverse events (AEs), clinical laboratory evaluations, physical examination findings, vital signs, and 12-lead ECGs readings.

The effects of SYR-322 and SYR-322 coadministered with pioglitazone HC1 on the exploratory variables of; markers of oxidative stress, short term glycaemic control and HDL composition and function will be evaluated.

The secondary efficacy endpoints are as follows:

* Postprandial incremental AUC changes for triglycerides at Week 4.
* Postprandial incremental AUC changes for lipid parameters.
* Postprandial incremental AUC changes for lipoprotein parameters.
* Postprandial changes over time in GLP-1, glucose, insulin, and glucagon.
* Fasting plasma glucose.
* C-peptide.
* High-sensitive CRP.
* Adiponectin.
* HbA1C.
* Insulin.
* Proinsulin.
* VCAM.

* ICAM.

* e-Selectin.

* Endothelial function (pulse wave tonometry).

To address the secondary objective of evaluating safety, the following

variables will be used:

* Physical examination findings.

* Clinical laboratory evaluations.

* Vital sign measurements.

* 12-lead electrocardiogram (ECG) findings.

* Incidence of adverse events.

Other exploratory efficacy variables:

The following markers of oxidative stress, short term glycaemic control and HDL

composition and function will be analyzed at baseline and week 16:

* MDA (Malondialdehyde)

* PGF (Prostaglandin F2* / F2-isoprostanes)

* oxLDL (Oxidized low-density lipoprotein)

* 1,5 A.G (1,5Anhydroglucitol)

* HDL composition and function (HDL AOX, HDL tot chol, HDL free chol, HDL Tg,

HDL

PL)

Study description

Background summary

As the rate of newly diagnosed cases of type 2 diabetes continues to grow, so does the need for products that will provide better glycemic control and improved safety and tolerability. SYR-322 and pioglitazone HCl have complementary actions; SYR-322 inhibits the degradation of GLP-1 by inhibiting the enzyme DPP-IV, thus augmenting glucose-dependent insulin secretion while pioglitazone HCl is peripheral and hepatic insulin sensitizer. Given the complementary mechanisms of action of SYR-322 (stimulates insulin secretion) and pioglitazone (enhances insulin sensitivity), the addition of combination therapy in type 2 diabetes patients may potentially allow patients to reach and maintain their HbA1c goal more effectively. In addition to the improvement of glycemic control, SYR-322 alone and the combination of SYR-322 and pioglitazone HCl may provide a further reduction in lipid parameters including a further reduction in postprandial triglycerides.
The purpose of this study is to assess the effects of SYR-322 and SYR-322 coadministered with pioglitazone HCl versus placebo on postprandial lipid and lipoprotein metabolism in subjects with type 2 diabetes.

Study objective

The primary objective of this study is to evaluate the effects of SYR-322 and SYR-322 coadministered with pioglitazone HC1 versus placebo on postprandial triglycerides in subjects with type 2 diabetes.

Study design

This is a multi-center, randomized, double-blind, placebo-controlled, parallel-group study. This study is being conducted in approximately 75 subjects with type 2 diabetes.
The study includes a Screening period and a 16-week treatment period followed by a 2-week follow-up period. The duration of the study will be approximately 18 weeks, not including the Screening period. The subjects will be randomly assigned to 1 of 3 treatment groups in a 1:1:1 ratio as follows: 25 mg SYR-322 with 30 mg pioglitazone HCl

(N=25), 25 mg SYR-322 with 30 mg pioglitazone HCl placebo (N=25), 25 mg SYR-322 placebo with 30 mg
pioglitazone HCl placebo (N=25).

Intervention

At Baseline, subjects will be randomized to 1 of the following 3 treatment groups:
* SYR-322 25 mg placebo + pioglitazone HC1 30 mg placebo (N=25).
* SYR-322 25mg + pioglitazone HC1 30 mg placebo (N=25).
* SYR-322 25mg + pioglitazone HCl 30mg (N=25).

Study burden and risks

-Complications related to blood sample collection, i.e. bruces.
-Side effects: SYR-322 has been found to be well tolerated. The majority of side effects have been mild in intensity.

-Pioglitazone, like other thiazolidinediones, can cause fluid retention, which in a small number of cases may lead to or exacerbate heart failure. Although heart failure is one of the exclusion criteria, participants will be observed for edema and signs and symptoms of heart failure. Pioglitazone should be discontinued if any deterioration in cardiac status occurs. Participants will be instructed to report any episode of unusual rapid increase in weight, occurrence of edema, shortness of breath or other symptoms compatible with heart failure during the study to the
investigator.
-Bloodsampling: A total volume of 960 mL blood will be collected: A venous cannula will be placed from which blood will be taken during the mealtests: approximately 300 mL during one day. To determine safety parameters 30 mL blood will be taken twice through vena punction.
-Volunteers will have to travel 6 times to the study site.

Contacts

Public
Takeda

Takeda Global Research & Development Center (Europe) Ltd Arundel Great Court, 2 Arundel Street
WC 2R 3DA, London
Great Britain
Scientific
Takeda

Takeda Global Research & Development Center (Europe) Ltd Arundel Great Court, 2 Arundel Street
WC 2R 3DA, London
Great Britain

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. The subject is male or female, with a historical diagnosis of type 2 diabetes, and must be aged
18 to 70 years, inclusive.
2. A female subject of childbearing potential who is sexually active agrees to use adequate contraception from screening throughout the duration of the study. Women NOT of child bearing potential are defined as those who have been surgically sterilized (hysterectomy, oophorectomy, tubal ligation) or who are post-menopausal (defined as at least 2 years since last regular menses). Acceptable methods of contraception are defined in Section 9.1.11 Contraception and Pregnancy Avoidance Procedure.
3. The subject is capable of understanding and complying with the protocol requirements.
4. The subject has either failed treatment with diet and exercise for 3 months prior to Screening or
has been receiving a stable dose of metformin, sulfonylurea, nataglinide, or repaglinide for more than 3 months prior to Screening.
5. The subject has inadequate glycemic control as defined by HbA1C concentration between 6.5 and 9.0%, inclusive.
6. The subject has a fasting plasma glucose <13.3 mmol/L.
7. The subject has a fasting serum triglyceride level of 1.7 to 5.0 mmol/L, inclusive.
8. The subject has not been receiving any lipid-lowering therapy within 3 months prior to Screening or on a stable statin and/or ezetimibe therapy (same drug and dose) for at least 3 months.
9. The subject has a body mass index >23 kg/m2 and <45 kg/m2.
10. If the subject has regular use of other, nonexcluded medications, subject must be on a

stable
dose for at least 4 weeks prior to Screening. Use of PRN (as needed) prescription medications and over-the-counter medications is allowed at the discretion of the investigator.
11. The subject or subject*s legally authorized representative signs a written informed consent
prior to the initiation of any study procedures.
12. The subject is to be Apolipoprotein E 3/3 or Apolipoprotein E 3/4 phenotype positive prior to
baseline

Exclusion criteria

1. The subject has a history of type 1 diabetes.
2. The subject has a history of drug abuse (defined as illicit drug use) or a history of alcohol abuse
(defined as regular or daily consumption of more than 4 alcoholic drinks per day) within the past 2 years.
3. The subject has a diastolic blood pressure greater than 100 mm Hg or a systolic blood pressure
of greater than 160 mm Hg.
4. The subject has a previous history of cancer, other than basal cell carcinoma, that has not been
in remission for at least 5 years prior to the first dose of study medication. (This criterion does
not include those subjects with basal cell or Stage 1 squamous cell carcinoma of the skin.)
5. The subject has a hemoglobin <120 g/L for males and <100 g/L for females.
6. The subject has an alanine transaminase (ALT) level of greater than 2.5 times the upper limit of
normal, active liver disease, or jaundice.
7. The subject has a serum creatinine level >133 µmol/L.
8. The subject has a fasting total cholesterol >6.5 mmol/L.
9. The subject has New York Heart Association heart failure of any Class (I-IV) regardless of therapy.
10. The subject has a history of coronary angioplasty, coronary stent placement, coronary bypass
surgery, or myocardial infarction within 6 months prior to Screening.
11. The subject has a history of acute metabolic diabetic complications.
12. The subject has a history of any hemoglobinopathy that may affect determination of HbA1C.
13. The subject has a history of infection with human immunodeficiency virus.
14. The subject has a history of diabetic gastro paresis.
15. The subject has a history of gastric bypass surgery.
16. The subject is unwilling or unable to comply with the protocol or scheduled appointments.
17. The subject has a history of hypersensitivity or allergies to SYR-322, pioglitazone or any related compounds.

18. The subject is pregnant, intends to become pregnant during the course of the study, or is lactating.
19. The subject is currently participating in another investigational study or has participated in an
investigational study within the past 30 days.
20. The subject has any other serious disease or condition at Screening or at randomization that
might affect life expectancy or make it difficult to successfully manage and follow the subject according to the protocol.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-08-2008
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	-
Generic name:	Alogliptine
Product type:	Medicine
Brand name:	Actos
Generic name:	Pioglitazone

Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	28-05-2008
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-07-2008
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-06-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-12-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2007-000486-38-NL

Register	ID
CCMO	NL22649.029.08