A randomized, double-blind, placebo-controlled, parallel-group, multicenter study to evaluate cardiovascular outcomes during treatment with lixisenatide in type 2 diabetic patients after an Acute Coronary Syndrome event

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON39895

Source
ToetsingOnline

Brief title
ELIXA

Condition

- Coronary artery disorders
- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Diabetes Mellitus type 2

Research involving
Human

Sponsors and support

Primary sponsor: Sanofi-aventis
Source(s) of monetary or material Support: door verrichter

Intervention

Keyword: Acute Coronary Syndrome, AVE0010/lixisenatide, Cardiovascular outcomes, Diabetes type 2

Outcome measures

Primary outcome

To evaluate cardiovascular outcomes with lixisenatide compared to placebo (time

to first occurence: cardiovascular death, non-fatal myocardial infarction,

non-fatal stroke, hospitalization for unstable angina) in type 2 diabetic

patients who experienced an acute coronary syndrome event.

Secondary outcome

To assess the effect of lixisenatide compared to placebo on:

Composite cardiovascular endpoints

* Time to the first occurrence of any of the following clinical events,

positively adjudicated by the CAC:

• Cardiovascular death.

• Non-fatal MI.

• Non-fatal stroke.

• Hospitalization for unstable angina.

• Hospitalization for heart failure.

* Time to the first occurrence of any of the following clinical events,

positively adjudicated by the CAC:

• Cardiovascular death.

• Non-fatal MI.

• Non-fatal stroke.

• Hospitalization for unstable angina.

• Hospitalization for heart failure.

• Coronary revascularization procedure

• Urinary albumin/creatinine ratio: Percent change in the urinary

albumin/creatinine ratio from baseline to Week 108 (i.e., approximately 2

years).

To assess the safety and tolerability of lixisenatide.

Study description

Background summary

In the past two decades the prevalence of type 2 diabetes has increased to epidemic proportions worldwide; the number of subjects with type 2 diabetes is set to rise from the current estimate of 150 million to 220 million in 2010 and 300 million in 2025. Patients with diabetes have an increased risk of microvascular and macrovascular complications leading to decreased life expectancy. This is mainly due to cardiovascular deaths with a risk of coronary heart disease increased by two to fourfold in this population.

Results from large controlled trials as well as smaller studies and numerous epidemiologic studies have demonstrated that intensive glycemic control decreases the risk of microvascular complications. On the basis of these findings the American Diabetes Association (ADA) and International Diabetes Federation recommend a tight glycemic control with an HbA1c target < 7 % and < 6,5 % respectively.

Although an intensive glycemic management has also shown to have beneficial

effect of cardiovascular disease complications in type 1 diabetes, there is still controversy whether this demonstration can also apply in patients with type 2 diabetes. Recent individual studies conducted in type 2 diabetes have failed to demonstrate a beneficial effect on intensive diabetes therapy on cardiovascular disease. However, meta-analyses recently performed showed a reduction in coronary events; effect on cardiovascular death or all-cause mortality was less evident.

Lixisentatide belongs to the class of Glucagon-like peptide 1 (GLP-1) receptor agonist and is being developed for the treatment of patients with type 2 diabetes.

New types of antidiabetic, such as GLP-1 receptor antagonists may achieve physiological blood glucose-insulin response with a low risk of hypoglycemia and may offer a valuable new therapeutic approach. These drugs reduce the blood glucose by glucose dependent stimulation of insulin release and inhibition of glucagons secretions, which decreases the prandial blood glucose excursions and hepatic glucose production; they also delay gastric emptying and reduce appetite which is associated with weight loss.

Study objective

The primary objective of this phase III study is to demonstrate that lixisenatide can reduce cardiovascular morbidity and mortality (composite endpoint of cardiovascular (CV) death, non-fatal myocardial infarction (MI), non-fatal stroke, hospitalization for unstable angina) compared to placebo in type 2 diabetic patients who recently experienced a spontaneous, biomarker-positive acute coronary syndrome (ACS) event.

Study design

This will be a multicenter, multinational, double-blind, 1:1 randomized, placebo-controlled, 2-arm parallel-group phase III study. The study will be double-blind with regard to the active and placebo treatments. The study drug volume (i.e. dose of active drug or matching placebo) will not be blinded.

The study will comprise 3 periods:

-A placebo run-in period of 7 days (+3 days) that will start by a screening visit;
-A double-blind study treatment period that will include an initial 2-week titration period. The estimated maximum duration of this double-blind study treatment period will be approximately 250 weeks (i.e. approximately 58

months); assuming 37-month recruitment period, and a minimum of 10 months of further follow-up for the last randomized patient.
-A post-treatment safety follow-up period of 3 days (+ 1 day), only for patients still on study treatment at the time of the common study end date.

Intervention

Screening phase: 7 days placebo-run in
Double-blind treatment phase: maximum of 58 months treatment with lixisenatide or placebo and minimum of 10 months treatment with lixisenatide or placebo.

Study burden and risks

Risks are related to the bloodsampling and possible adverse events from the studymedication. The burden for the patient is the number of visits to the research center and phone calls because of this study. Also the patient will be asked to complete a diary and to perform self-measurements of plasma glucose.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

*Men and women who experienced a spontaneous ACS event (i.e., ST-segment elevation myocardial infarction [STEMI] or non-ST-segment elevation myocardial infarction [NSTEMI] or unstable angina [USA]) with the following requirements:
- a documented elevation above the normal reference range of a cardiac biomarker (Troponin or
CK-MB),
- The presentation of the event must be consistent with an acute coronary syndrome which leads to admission to an acute care facility (eg, ER, CCU, Cath Lab, hospital
- the screening visit must occur only after the patient is discharged from the acute care facility, and must take place within 180 days following the date of admission for the qualifying ACS event.
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*Patients with history of type 2 diabetes (for patients newly diagnosed, diagnosis will be based on the WHO criteria: i.e., fasting venous plasma glucose concentration >= 7.0 mmol/L [126 mg/dL] or 2-hour post glucose load venous plasma glucose >= 11.1 mmol/L [200 mg/dL], confirmed on 2 ccasions) prior to the screening visit.

Exclusion criteria

. Type 1 diabetes mellitus or history of ketoacidosis within 6 months prior to screening.;. HbA1c <5.5 % or >11% measured at screening Visit (1 retest within a week of receipt of the result is permitted with the result of the last sample being decisive).;. Required to use incretin-based agents (eg, GLP-1 agonists or DPP-4 inhibitors) other than the study drug during the doubleblind treatment period.;. Patients who have undergone CABG surgery following the qualifying ACS event.;. Patients who have undergone PCI within 15 days prior to screening.;. Patients with planned revascularization procedure (PCI or CABG) within 90 days after screening visit.;. History of unexplained pancreatitis, chronic pancreatitis, pancreatectomy, stomach/gastric surgery, inflammatory bowel disease, personal or family history of medullary thyroid cancer (MTC), or genetic conditions that predisposes to MTC (eg, multiple endocrine neoplasia syndromes).;. Any clinically significant abnormality identified at the time of screening that in the judgment of the Investigator or any sub-Investigator would preclude safe completion of the study or constrain endpoints assessment such as major systemic diseases.

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):	10-01-2011
Enrollment:	60
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	not applicable
Generic name:	lixisenatide

Ethics review

Approved WMO Date:	22-06-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-09-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United

	(Nieuwegein)
Approved WMO Date:	11-11-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-01-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-01-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-01-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-06-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-07-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	30-08-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-09-2011

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-10-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-10-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-06-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-06-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-07-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-08-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-12-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	19-12-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-03-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-03-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-03-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-04-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-11-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-12-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-03-2014
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-03-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-04-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-04-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-09-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2009-012852-26-NL
ClinicalTrials.gov	NCT01147250
CCMO	NL32257.060.10