A 36 week, multicenter, randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy and safety of aliskiren on the prevention of left ventricular remodeling in high risk post-acute myocardial infarct patients when added to optimized standard therapy

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

Summary

ID

NL-OMON30339

Source
ToetsingOnline

Brief title
ASPIRE

Condition

- Myocardial disorders

Synonym
heart attack, myocardial infarct

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Acute Myocardial Infarction (AMI), Aliskiren, left ventricular remodeling

Outcome measures

Primary outcome

Echocardiography:

The primary efficacy endpoint will be change in left ventricular end systolic volume (LVESV) from baseline to end of study. Additional echocardiographic measures will serve as secondary endpoints, including left ventricular end-diastolic volume (LVEDV) and left ventricular ejection fraction (LVEF).

Secondary outcome

Cardiac MRI (in a subset of patients- not in the Netherlands):

*RV and LV volumes, LVEF, and myocardial infarct related scarring as determined by contrast enhanced MRI.

Composite clinical endpoints:

*a composite outcome of CV death, hospitalization for heart failure, or a reduction in left ventricular ejection fraction greater than 6 units (absolute percentage points)

*a composite outcome of CV death, hospitalization for heart failure, recurrent

myocardial infarction, stroke or resuscitated sudden death.

Study description

Background summary

This study is designed to provide surrogate marker data [change in left ventricular end systolic volume (LVESV) as determined by echocardiography] for the efficacy and safety of aliskiren compared to placebo when given in addition to optimized standard therapy in high-risk post-AMI patients. This trial will serve as a proof-of-concept study to plan and potentially conduct future clinical outcomes studies in this patient population.

Study objective

The primary objective of this trial is to demonstrate that aliskiren 300 mg, in addition to standard therapy, has superior efficacy compared to placebo in reducing the primary index of adverse cardiac remodeling (defined as the change in LVESV from baseline to end of study) in patients after high risk acute myocardial infarction.
The secondary objectives of this trial are to evaluate the effect of aliskiren compared to placebo on:
* a composite outcome of CV death, hospitalization for heart failure, or a reduction in ejection fraction greater than 6 units (absolute percentage points)
* a composite outcome of CV death, hospitalization for heart failure, recurrent myocardial infarction, stroke or resuscitated sudden death
* change in left ventricular ejection fraction (LVEF) between baseline and end of study
* change in left ventricular end-diastolic volume (LVEDV) between baseline and end of study
* RV and LV volumes, LVEF, and myocardial infarct related scarring as determined by contrast enhanced MRI (in a subset of patients)
* overall safety and tolerability in combination with standard therapy in patients post acute myocardial infarction.

Study design

This is a multicenter, multinational, randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy and safety of aliskiren on the prevention of left ventricular remodeling in high risk post-AMI patients when added to optimized standard therapy. Patients who have a documented AMI will be evaluated for left ventricular dysfunction. Patients

who meet echocardiographic criteria for reduced LVEF and who are on optimized background therapy will be randomized to aliskiren or placebo with stratification based on the patients* baseline (Visit 2) use of aldosterone receptor antagonist medications. The purpose of stratification is to ensure equal assignment of patients to each stratum [stratum 1 will represent patients on baseline (Visit 2) aldosterone receptor blockers while stratum 2 will represent patients not on baseline (Visit 2) aldosterone receptor blockers] in the 2 treatment groups. There are no constraints on the number of patients in each stratum. Study medication will be administered for 36 weeks, followed by assessments for adverse cardiac remodeling.

Intervention

There are two treatment groups:
1) Aliskiren 75 mg, force-titrated via 150 mg Aliskiren to 300 mg Aliskiren (in a period of 2 weeks)
2) Placebo

Study burden and risks

Risks are possible side effects of study medicine or another medicine, and those of taking blood. The most common side effects reported in research studies to date with aliskiren were:
* Headache
* Dizziness
* Fatigue
* Abdominal pain
* Nausea
* Diarrhea
Problems or side effects that are not now known could also occur.

10 study visits will be payed to the medical center. The tests done at each study visit are standard medical tests. The most unpleasant is often having blood samples taken, which will be done every visit. The risks of taking blood may include pain and/or bruising.

The blood pressure cuff may also cause discomfort or bruising to the upper arm. Bloodpressure will be taken every visit. Physical examinations (3 times), electrocardiograms (ECGs; 3 times) and echocardiograms (ECHO; 2 times) are routine procedures in clinical practice and present practically no risk to the patient.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

See protocol for complete criteria (page 17);*Male and female patients 18 years and older.
*Patients within 7-42 days of an acute myocardial infarction.
*Documented left ventricular systolic dysfunction associated with the qualifying acute myocardial infarction obtained as a clinical study at least 5 days after the qualifying MI but prior to Visit 1.
*Patients must be on stable doses of the following concomitant medications for at least 2 weeks prior to Visit 1 unless contraindicated due to intolerance:
* A Beta-blocker
* An Anti-platelet agent
* A Statin
* An evidence-based dose of an Angiotensin Converting Enzyme Inhibitor (ACEI) or Angiotensin Receptor Blocker (ARB) but not both.

Exclusion criteria

See protocol for complete criteria (page 18)
*Patients requiring both ACE and ARB combination therapy at Visit 1.
*Severe refractory hypertension defined as MSSBP *180 mmHg and/or MSDBP * 110 mmHg at randomization (visit 2).
*Secondary forms of cardiomyopathy such as restrictive cardiomyopathy or infective cardiomyopathy
*Stroke or transchemient ischemic event (TIA) within 6 months of Study visit 1.
*Serum potassium *5.1 mEq/L, or dehydration at study visit 1
*Estimated Glomerular filtration rate < 30ml/min/1.73m2 using the MDRD formula at visit 1
*Unstable angina requiring intervention between visit 1 and visit 2.
*Any coronary artery revascularization procedure within 7 days prior to visit 1.

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):	05-02-2007
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nog niet geregistreerd voor deze indicatie

Generic name:	aliskiren

Ethics review

Approved WMO Date:	10-10-2006
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-11-2006
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-05-2007
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-08-2007
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-11-2008
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-05-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-12-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2006-001704-37-NL
CCMO	NL14110.042.06