The ASPECT-2 Trial: A Phase 3, Randomized, Double-Blind Trial of Apadenoson for the Detection of Myocardial Perfusion Defects Using Single-Photon Emission Computed Tomography (SPECT) Myocardial Perfusion Imaging (MPI)

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Primary:* To demonstrate non-inferiority between the level of agreement in diagnosis (i.e. patient classification of normal, mild/moderate or severe ischemic disease based on the number of reversible perfusion segments) between sequential adenosine...

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

Summary

ID

NL-OMON35903

Source
ToetsingOnline

Brief title
The Aspect2 Trial

Condition

- Coronary artery disorders

Synonym
Coronary heart disease

Research involving
Human

Sponsors and support

Primary sponsor: Forest Research Institute, a subsidiary of Forest Laboratories, Inc.
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: - apadenoson, - coronary artery disease, - Myocardial Perfusion Imaging (MPI), - Single-Photon Emission Computed Tomography (SPECT)

Outcome measures

Primary outcome

Primary efficacy endpoint:

-The level of agreement of diagnosis (i.e. patient classification of normal,

mild/moderate or severe ischemic disease based on the number of reversible

perfusion segments) between sequential adenosine SPECT-MPI versus the level of

agreement in diagnosis between an adenosine and an apadenoson SPECT-MPI.

Secondary outcome

Secondary efficacy variables:

- a.o. the 'summed stress score' (SSS), wall motion, extent of ischemia,

location of perfusion defects according to coronary artery territory and

calculation of sensitivity and specificity using angiography results compared

to diagnostic classification (ischemic versus non-ischemic based on the number

of reversible perfusion defects) resulting from SPECT-MPI.

Safety:

-comparison of the incidences and VAS Symptom-Intensity Measure for commonly

reported TEAEs as dyspnea, flushing, chest pain, headache, nausea, dizziness

and abdominal discomfort.

- incidence and severity of AEs, changes in clinical laboratory findings,

physical examinations, vital signs, ECGs, the number of discontinuations due to

AEs, incidence of second or third degree AV block, and subject-rated Overall

Bother Measure.

Study description

Background summary

Currently available pharmacological stress agent used in myocardial perfusion is considered to be nonselective and can cause several adverse events. Apadenoson is a new A2A agonist that exhibits greater binding selectivity for the A2A receptor over other adenosine receptors: the A1, A2B, and A3 receptor subtypes. Apadenoson has the potential to be as effective as adenosine for SPECT-MPI and to have a lower incidence of undesirable side effects.
The objective of the study is to demonstrate non-inferiority between the level of agreement in diagnosis (i.e. patient classification of normal, mild/moderate or severe ischemic disease based on the number of reversible perfusion segments) between sequential adenosine SPECT-MPI versus sequential SPECT-MPI with adenosine and apadenoson.

Study objective

Primary:
* To demonstrate non-inferiority between the level of agreement in diagnosis (i.e. patient classification of normal, mild/moderate or severe ischemic disease based on the number of reversible perfusion segments) between sequential adenosine SPECT-MPI versus sequential SPECT-MPI with adenosine and apadenoson.

Secondary Gatekeeper Objective:
* Compare the safety and tolerability of pharmacologic stress with apadenoson compared to adenosine based on incidence and severity of treatment-emergent dyspnea, flushing, chest pain, headache, nausea, dizziness and abdominal discomfort.

Other Secondary Objectives:

* Assess the safety and tolerability of apadenoson based on incidence and severity of treatment emergent AEs (TEAEs), changes in clinical laboratory findings, physical examinations, vital signs, ECGs, and the number of discontinuations due to AEs.
* Compare incidence of second or third degree AV block associated with apadenoson treatment to that seen following treatment with adenosine.
* Compare subject*s treatment experience with apadenoson to that of adenosine, based on the subject-rated Overall Bother Measure.
* Evaluate comparability of pharmacologic stress imaging with apadenoson versus adenosine based on additional endpoints of efficacy including summed stress score (SSS), wall motion, extent of ischemia, location of perfusion defects according to coronary artery territory and calculation of sensitivity and specificity using angiography results compared to diagnostic classification (ischemic versus non ischemic).
* Estimate PK parameters of apadenoson and ATL146a by sparse PK sampling (select sites only).

Study design

A Phase 3, Randomized, Double-Blind Trial

Intervention

Subjects will receive two pharmacologic stress SPECT-MPI sessions: Period 1, a clinically-indicated rest/stress gated SPECT-MPI with adenosine; followed by Period 2, in which subjects will be randomized to a second rest/stress gated SPECT-MPI with either adenosine or apadenoson (in a 1:1 assignment ratio). Subjects will receive a single, bolus IV injection of apadenoson (50 µg/mL sterile solution) in either a 2 mL (100 µg) or 3 mL (150 µg) final volume. Subjects weighing less than 100 kg will receive 100 µg apadenoson, and subjects weighing *100 kg will receive 150 µg apadenoson.

Study burden and risks

The most common side effects of Adenosine and Apadenoson include: chest pain and discomfort, uncomfortable breathing, dizziness, headache, flushing (blushing of the skin) and nausea. Adenosine and Apadenoson may cause a slight increase in your heart rate and a decrease in your blood pressure, which could cause dizziness or light-headedness.

Summary of procedures:
- 2x Clinical Labs and Serum Pregnancy test
- 2x Urine Pregnancy test
- 1x Height and Weight
- 2x Resting SPECT-MPI
- 2x Stress SPECT-MPI

- 2x Vital signs
- 2x ECG
- 1x Physical Examination
- 1x questionnaire

patients will be expected to:
* Not drink or eat caffeine-containing products (such as coffee, tea, sodas and chocolate) or methylxanthine-containing foods for at least 24 hours before SPECT-MPI tests
* Not receive a treatment of dipyridamole for at least 24 hours before SPECT-MPI tests
* Not take certain medications, such as theophylline and methylxanthine-containing medications for chronic obstructive pulmonary disease, for at least 72 hours (3 days) before SPECT-MPI tests.

Contacts

Public
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US
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

* Referred for a clinically indicated rest /pharmacologic stress SPECT-MPI study
* Subjects must have either high pretest probability of CAD based on age and gender and chest pain symptomatology assessed using the ACC/AHA guidelines for relative risk
OR
Have previously demonstrated known coronary artery disease based on medical history of prior myocardial infarction (MI), percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG) or diagnostic angiogram demonstrating 50% or greater stenosis in one or more vessel, as well as reporting chest pain indicative of angina or anginal equivalents within the month prior to Pre-Study Evaluation (based on ACC criteria, e.g. dyspnea or extreme fatigue).
* Can safely abstain from caffeine or methylxanthine containing foods for 24 hours, from dipyridamole for 24 hours, and from theophylline and methylxanthine containing medications for at least 72 hours (or 4 half-lives, whichever is longer)
* Cardiovascular medication routine must remain stable from the time of signed informed consent through the Period 2 SPECT-MPI

Exclusion criteria

* Treatment with dipyridamole within 24 hours, or theophylline, aminophylline, or pentoxifylline within 72 hours (or 4 half-lives, whichever is longer) prior to receiving apadenoson or adenosine
* Acute MI, new onset of ischemia or PCI within 30 days prior to SPECT-MPI at either Period 1 or Period 2; or CABG within 90 days prior to SPECT-MPI at either Period 1 or Period 2
* Active severe asthma or severe chronic obstructive pulmonary disease (COPD) which, in the Investigator*s opinion, places the subject at risk for severe bronchoconstriction
* History or evidence of clinically significant high grade AV block (including type 2 second or third degree block) or sinus node disease, such as sick sinus syndrome or symptomatic bradycardia, in the absence of a functioning permanently implanted pacemaker
* Evidence of hemodynamically significant valvular disease or outflow tract obstruction
* Uncontrolled severe hypertension or malignant ventricular arrhythmias
* Pretreatment hypotension (systolic BP < 90 mm Hg) or tachycardia (HR > 100 bpm)
* Known history of cerebral vascular accident or suspected transient ischemic attack within 30 days prior to signed informed consent

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:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-03-2012
Enrollment:	78
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	-
Generic name:	Apadenoson
Product type:	Medicine
Brand name:	Adenoscan®
Generic name:	-
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	07-07-2011
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	07-11-2011
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	19-12-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	21-12-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	02-01-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	10-02-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	17-02-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	12-03-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	03-07-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2011-001245-32-NL
ClinicalTrials.gov	NCT01313572
CCMO	NL37108.098.11