A Randomized, Placebo-controlled Phase 2b Study to Evaluate the Safety and Efficacy of MEDI6012 in Acute ST Elevation Myocardial Infarction

Published: 27-03-2018
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To evaluate the effect of MEDI6012 on infarct size compared with placebo.

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

Summary

ID

NL-OMON48930

Source
ToetsingOnline

Brief title
MEDI6012

Condition

- Myocardial disorders

Synonym
ST-Elevated Myocardial Infarction

Research involving
Human

Sponsors and support

Primary sponsor: MedImmune, LLC
Source(s) of monetary or material Support: MedImmune;LLC

Intervention

Keyword: Acute ST-elevated Myocardial Infarct, MEDI6012

Outcome measures

Primary outcome

Infarct size as a percentage of LV mass measured on delayed-enhanced (CV magnetic resonance [CMR]) imaging 10-12 weeks post-MI compared to placebo.

Secondary outcome

* EF measured by cine magnetic resonance imaging (MRI) at 10-12 weeks post-MI compared to placebo.

* Change in NCPV in the coronary arteries from index computed tomography angiography (CTA) to 10-12 weeks post-MI compared with placebo.

* Myocardial mass and LV volumes at end-systole and end-diastole.

* Incidence of treatment-emergent adverse events (TEAEs) and treatment-emergent serious adverse events (SAEs).

* Lecithin-cholesterol acyltransferase (LCAT) mass and anti-drug antibodies (ADAs).

Study description

Background summary

Acute STEMI is a major contributor to the development of heart failure (HF) and death in
patients with CHD. The risk of HF and death is related to the size of the MI and the impact it
has on heart function. Furthermore, the extent of coronary plaque burden is directly related to
the risk of death and MI. The only therapy shown to reduce infarct size in humans with acute

STEMI is primary percutaneous coronary intervention (PCI). In addition, statins and
proprotein convertase subtilisin kexin 9 inhibitors have demonstrated a reduction in the
progression of coronary atheroma and reductions in major adverse CV events. MEDI6012,
with its ability to increase functional HDL-C and apoA1, has the potential to be the first
therapeutic that can mitigate ischemia-reperfusion injury associated with primary PCI, confer
cardioprotection by decreasing infarct size and improving LV function, and induce regression
of coronary atheroma.

Study objective

To evaluate the effect of MEDI6012 on infarct size compared with placebo.

Study design

This is a Phase 2b randomized, blinded (subject/MedImmune blinded, investigator unblinded), placebocontrolled study to evaluate the efficacy, safety, PK/pharmacodynamic, and immunogenicity of repeat doses of MEDI6012 in adult subjects presenting with acute STEMI. At least 414 subjects are planned to be randomized across approximately 40 study sites in approximately 10 countries, to evaluate a 2-dose regimen and a 6-dose regimen of MEDI6012. The study will enrol subjects presenting with acute STEMI within 6 hours of symptom onset who are planned for primary percutaneous coronary intervention (pPCI). Following initial screening, subjects will be randomized in a 1:1 ratio to a 2-dose or 6-dose regimen and then randomized within that dose regimen to a 2:1 ratio to receive MEDI6012 or placebo. For both the 2-dose and the 6-dose regimens, the first two doses of investigational product will be administered in the inpatient setting on study Days 1 and 3. Subjects randomized to the 2-dose regimen will receive standard of care treatment post pPCI. Subjects randomized to the 6-dose regimen will receive standard of care treatment post pPCI and additional administration of investigational product on Days 10, 17, 24, and 31. For all subjects, an end of study CMR will be performed at 10-12 weeks (70-84 days following Dose 1). Subjects randomized to the 6-dose regimen will also undergo an index (Days 3-5) and an end of study CTA (70-84 days following Dose 1). If a subject*s Day 70-84 immunogenicity sample is confirmed as ADA positive and there is a > 30% decrease in HDL-C or a neutralizing antibody (nAb) is present, the subject will return for additional assessments

Intervention

Cohort A: 2-Dose Regimen

300 mg of MEDI6012 or placebo on Day 1 (loading dose) prior to pPCI followed by a second inpatient dose
of 150 mg or placebo on Day 3 by intravenous (IV) push.

Cohort B: 6-Dose Regimen
300 mg of MEDI6012 or placebo on Day 1 (loading dose) prior to pPCI followed by a second inpatient dose
of 150 mg or placebo on Day 3 and outpatient maintenance doses of 100 mg or placebo on Days 10, 17, 24,
and 31 by IV push.

Study burden and risks

Risks: possible side effects of the study drug and the study procedures.

Burden: Blood draws, physical examination, vital signs measurement, study visits

Contacts

Public
MedImmune, LLC

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Scientific
MedImmune, LLC

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Men and women without child-bearing potential aged 30-80 years of age who are capable and willing to provide informed consent.
2. Acute STEMI diagnosed by ST elevation (* 0.1 mV) in 2 contiguous leads
3. Planned for primary PCI
4. Ischemic symptoms for * 6 hours
5. Capable of completing study visit

Exclusion criteria

1. Pre-randomization cardiogenic shock or cardiopulmonary resuscitation
2. Fibrinolytic administration for index event
3. Known prior MI or prior coronary artery bypass grafting
4. Known pre-existing cardiomyopathy
5. History of anaphylaxis
6. Suspected non-thrombotic etiology (ie, vasospasm, dissection, Takotsubo cardiomyopathy)
7. Other condition or severe illness that the investigator feels would limit the prognosis of the patient (eg, malignancy with life-expectancy < 3 months) or would make the patient otherwise unsuitable for enrollment (eg, pose a hazard or undue burden to the patient [known chronic renal or hepatic impairment, recent (< 30 days), cerebrovascular accident or transient ischemic attack] unable to complete study visits)
8. Known contraindication to MR imaging (eg, metallic implant, claustrophobia, implantable cardioverter-defibrillator (ICD), pacemaker, known CrCl < 30 mL/min (Cockcroft Gault equation)
9. Pregnant women and/or breastfeeding women.
10. Current or previous participation within the last 30 days in a study using an investigational therapy or device.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	01-10-2018
Enrollment:	57
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	MEDI6012
Generic name:	NTB

Ethics review

Approved WMO Date:	27-03-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-08-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-09-2018
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-10-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-10-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-01-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-01-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-07-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-07-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-09-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-11-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-02-2020
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-06-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2017-004521-32-NL
CCMO	NL65065.091.18

Study results

Date completed:	18-01-2021
Results posted:	23-12-2021
Actual enrolment:	108

First publication
14-05-2021