Does ticagrelor modulate the inflammatory respons to human endotoxemia?

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To study whether ticagrelor, added to acetylsalicylic acid, modulates the inflammatory response to the administration of lipopolysaccharide (LPS) in humans in vivo.

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

Summary

ID

NL-OMON42008

Source
ToetsingOnline

Brief title
TICA-LPS trial

Condition

- Other condition
- Coronary artery disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Inflammation and atherosclerosis

Health condition

inflammatie/immuunsysteem

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Astra Zeneca,AstraZeneca

Intervention

Keyword: Human endotoxemia model, Inflammation, Lipopolysaccharide (LPS), Ticagrelor

Outcome measures

Primary outcome

Area under the curve of various pro-inflammatory cytokines

Secondary outcome

platelet-monocyte complex formation and markers of platelet function; plasma

concentration of adenosine

Study description

Background summary

In patients suffering a myocardial infarction, the administration of P2Y12 receptor antagonists clearly improve prognosis. It appeared that both the irreversible inhibitor prasugrel and the reversible inhibitors ticagrelor improved cardiovascular mortality compared to clopidogrel. One of the hypothesis that might explain the superiority of these compounds compared to clopidogrel, is that they might affect the inflammatory response which occurs in the setting of an acute myocardial infarction.

Study objective

To study whether ticagrelor, added to acetylsalicylic acid, modulates the inflammatory response to the administration of lipopolysaccharide (LPS) in humans in vivo.

Study design

Prospective randomized controlled-trial, according to a PROBE design (prospective randomized open blinded-endpoint study).

Intervention

Participants will be randomized to receive either:

- acetylsalicylic acid (80 mg once daily, after a loading dose of 160 mg) + placebo (once daily)
- acetylsalicylic acid (80 mg once daily, after a loading dose of 160 mg)+ ticagrelor (90 mg twice daily for 7 days, after a loading dose of 180 mg)
- acetylsalicylic acid (80 mg once daily, after a loading dose of 160 mg)+ clopidogrel (75 mg once daily for 7 days, after a loading dose of 300 mg)
- placebo (twice daily

Study burden and risks

A physical examination, electrocardiography and blood sampling will be performed in all participants. All subjects will be treated with ticagrelor (90 mg twice a day) or clopidogrel on top of acetylsalicylic acid or placebo. Potential side effects of ticagrelor and the other P2Y12 inhibiotors/acetylsalicyclic acid include bleeding (epistaxis, skin haematomas, gingival bleeding, gastro-intestinal bleeding, bleeding on puncture side). Ticagrelor might also induce dyspnea. These risks however are limited due to the short treatment period of 7 days and selection of healthy volunteers. There is no direct benefit for the participants from this study.

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

- Age >= 18 and <= 35 years
- Male
- Healthy

Exclusion criteria

- History, signs or symptoms of cardiovascular disease
- History of chronic obstructive pulmonary disease (COPD) or asthma
- History of hemorrhagic diathesis, or any other disorder associated with increased risk of bleeding
- Previous spontaneous vagal collapse
- Use of any medication
- Smoking
- Cardiac conduction abnormalities on the ECG consisting of a 2nd degree atrioventricular block, third degree atrioventricular block or a complex bundle branch block
- Hypertension (defined as RR systolic > 160 mmHg or RR diastolic > 90 mmHg)
- Hypotension (defined as RR systolic < 100 or RR diastolic < 50)
- Renal impairment (defined as MDRD < 60 ml/min)
- Liver enzyme abnormalities ((defined as ALAT and/or ASAT > twice upper limit of normality)
- Thrombocytopenia (<150*109/ml) or anemia (haemoglobin < 8.0 mmol/L)
- Any obvious disease associated with immune deficiency
- Febrile illness in the week before the LPS challenge.
- Hypersensitivity to ticagrelor or any excipients
- Active pathological bleeding
- History of intracranial haemorrhage
- history of dyspepsia
- quantitative bleeding assessment tool (BAT) score > 3
- Participation in another drug trial or donation of blood 3 months prior to the planned LPS challenge

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-10-2015
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	acetylsalicylic acid
Generic name:	acetylsalicylic acid
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Brilique
Generic name:	ticagrelor
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Plavix
Generic name:	clopidogrel
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	29-01-2015
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-06-2015
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-10-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-10-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-11-2015
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	EUCTR2014-005537-30-NL
CCMO	NL51923.091.14

Study results

Date completed:	02-12-2015
Actual enrolment:	40