The effect of ticagrelor on the adenosine system

Published: 13-02-2013
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To investigate whether ticagrelor increases adenosine receptor stimulation in humans in vivo by ENT inhibition.

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

Summary

ID

NL-OMON38826

Source
ToetsingOnline

Brief title
Ticagrelor adenosine

Condition

- Coronary artery disorders

Synonym
forearm blood flow

Research involving
Human

Sponsors and support

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

Intervention

Keyword: adenosine, forearm blood flow, ticagrelor

Outcome measures

Primary outcome

Forearm blood flow response to the intrabrachial administration of adenosine

and to 2 and 5 minutes of forearm ischemia (i.e. post-occlusive reactive

hyperemia).

Secondary outcome

Forearm blood flow response to the intrabrachial administration of

dipyridamole.

Transport characteristics of the ENT transporter, determined ex vivo on

isolated erythrocytes.

Study description

Background summary

Preclinical studies have shown that the P2Y12 receptor antagonist ticagrelor can increase the extracellular concentration of the endogenous nucleoside adenosine by inhibiting the cellular uptake of adenosine via the equilibrative nucleoside transporter (ENT). This mechanism can contribute to the beneficial effects and to the side effects (dyspnea) of ticagrelor in patients with an acute myocardial infarction.

Study objective

To investigate whether ticagrelor increases adenosine receptor stimulation in humans in vivo by ENT inhibition.

Study design

Single centre, double-blinded, randomized placebo-controlled cross-over trial.
- Medical screening: history taking, physical examination, electrocardiogram, venous puncture of three 3 ml-vacutainers for the determination of creatinin, ALAT, thrombocytes, cholesterol and glucose.
- Experiment:

* Insertion of venous cannula into the antecubital vein of the dominant arm for blood drawing (20 ml before administration of the study drug for ex vivo ENT transport measurements, and measurement of the circulating caffeine and ticagrelor concentration; 20 ml immediately before the administration of adenosine for measurement of ticagrelor and ENT transport characteristics, and 10 ml before the administration of dipyridamole, the administration of acetylcholine, and before forearm ischemia for determination of the ticagrelor concentration.)
* Insertion of 27 Gauge needle into the brachial artery of the nondominant arm for drug administration of adenosine, dipyridamole, and acetylcholine (please see previous paragraph for dosages).
* Venous occlusion plethysmography of the forearm to determine the forearm blood flow responses to the administration of these drugs, and to 2 and 5 minutes of forearm ischemia.

Intervention

The single dose administration of ticagrelor (180 mg) or placebo

Study burden and risks

Given the administration of a single dose of ticagrelor to healthy male subjects without bleeding problems and with normal circulating thrombocytes, and given the very small 27 gauge needle used for intrabrachial administration of adenosine, dipyridamole, and acetylcholine, we think that the potential risks for the volunteers are low. Also, the methods used (venous blood drawing, venous occlusion plethysmography, and insertion of a cannula into the brachial artery) are well-established and have been performed very often by our research group, without any serious events.

Contacts

Public
Universitair Medisch Centrum Sint Radboud

Geert Grooteplein 21
Nijmegen 6525 EZ
NL
Scientific
Universitair Medisch Centrum Sint Radboud

Geert Grooteplein 21
Nijmegen 6525 EZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
- Male sex
- Age 18-40 years
- Healthy
- Written informed consent

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Smoking;
- Hypertension (Blood pressure >140 mmHg and/or >90 mmHg - SBP/DBP-)
- Diabetes Mellitus (fasting glucose > 7.0 mmol/L or random > 11.0 mmol/L);
- History of any cardiovascular disease
- History of chronic obstructive pulmonary disease (COPD) or asthma
- Bleeding tendency
- Concomitant use of medication
- Renal dysfunction (MDRD < 60 ml/min)
- Liver enzyme abnormalities (ALAT > twice upper limit of normality
- Thrombocytopenia (<150*109/ml)
- Second/third degree AV-block on electrocardiography

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-04-2013
Enrollment:	14
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Brilique
Generic name:	Ticagrelor
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	13-02-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO Date:	03-04-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date:	28-11-2013
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	EUCTR2012-004560-21-NL
CCMO	NL43379.091.13