Vasospastic angina treatment by Endothelin Receptor Antagonism; a proof of concept study

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON28727

Source
NTR

Brief title
VERA

Health condition

vasospastic angina

Sponsors and support

Primary sponsor: AMC
Source(s) of monetary or material Support: Actelion Pharmaceuticals Nederland

Intervention

Outcome measures

Primary outcome

The burden of anginal complaints, calculated as:
1. the duration (in minutes) * severity (on a VAS scale 1-10) during the study period up to 2 weeks after discontinuation of the study medication;

2. the frequency of angina attacks * severity (on a VAS scale 1-10) during the study period up to 2 weeks after discontinuation of the study medication;

Secondary outcome

Efficacy endpoint:
• Incidence and severity of angina complaints as obtained by the Seattle Angina Questionnaire during the study period up to 2 weeks after discontinuation of the study medication.
Safety endpoints:
• Detrimental changes in physical, laboratory or ECG parameters during the study period up to 2 weeks after discontinuation of the study medication.
• The occurrence of adverse events (i.e. hospitalization for anginal symptoms and/or myocardial infarction) during the study period up to 2 weeks after discontinuation of the study medication.
All possible side effects will be recorded during the study period up to 2 weeks after discontinuation of the study medication.

Study description

Background summary

This pilot proof-of-concept, multicenter, randomized, cross-over, double-blind placebo-controlled trial is aimed to determine whether VSA treatment with the novel ERA macitentan reduces the frequency and severity of anginal complaints among patients with clinically defined VSA and to determine side effects related to treatment with macitentan in patients with VSA.

Study objective

Patients diagnosed with vasospastic angina (VSA) are at increased risk for cardiovascular events. VSA is characterized by endothelial dysfunction and abnormal vasodilatory reserve. Endothelin (ET)-1 is a potent vasoconstrictor peptide produced by vascular endothelium which plays an important role in cardiovascular regulation. ET-1 levels have been shown to be elevated among patients with vasospastic angina and levels are associated with impaired coronary vasodilatory response. Treatment of VSA is conceptually even more interesting with selective ETA-receptor blockers that leave the ETB-receptor and its downstream denominator nitric oxide relatively unopposed. In vitro, the novel endothelin receptor blocker (ERA) macitentan is 100x more selective for ETA-receptor than ETB-receptor.

Study design

baseline (Visit1), 4 weeks (Visit 2), 8 weeks (Visit 3), 10 weeks (visit 4), 14 weeks (Visit 5), end 16 weeks (Visit 6)

Intervention

Macitentan

Contacts

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Eligibility criteria

Inclusion criteria

• Male and female patients ≥ 18 and <75 years old;
• Patients with a high frequency (>3 times per week) and duration of anginal complaints, presumed to be caused by VSA;
• Absence of significant obstructive coronary artery disease (defined as stenosis > 50% in an epicardial coronary artery) documented by invasive coronary angiography;
• Supporting evidence of myocardial ischemia or spasm, defined as either:
o documented dynamic ECG abnormalities during an episode of angina, or
o (b) documented troponin rise during an episode of angina, or
o (c) documented coronary spasm during invasive coronary angiography with or without acetylcholine provocation testing;
• Anginal complaints for at least 3 months despite optimal anti-anginal treatment, which is at the discretion of the treating cardiologist.

Exclusion criteria

• Patients who are pregnant or nursing and those who plan pregnancy in the period up to 1 months after the study;
• Women of childbearing potential not using contraception;
• Patients with a limited life expectancy less than one year;

• Patients unable to provide written informed consent, or are otherwise not suitable for inclusion according to the investigator.

• Contraindication for macitentan
• Patients with active liver disease or severe liver dysfunction with ASAT and/or ALAT >3x upper limit of normal (ULM);
• Patients with known renal impairment (GFR<60 ml/min);
• Patients with anemia;
• Use of potent CYP3A4 inducers (rifampicin, St. John's wort, carbamazepine, phenytoin) due to reduced efficacy of macitentan.
• Use of potent CYP3A4 inhibitors (itraconazole, ketoconazole, voriconazole, clarithromycin, ritonavir, saquinavir).

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-10-2019
Enrollment:	30
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	20-02-2019

Application type: First submission

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
NTR-new	NL7546
Other	METC AMC : 2018_213

Study results