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

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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…

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON28727

Bron
NTR

Verkorte titel
VERA

Aandoening

vasospastic angina

Ondersteuning

Primaire sponsor: AMC
Overige ondersteuning: Actelion Pharmaceuticals Nederland

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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;

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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

Onderzoeksproduct en/of interventie

Macitentan

Contactpersonen

Publiek

Amsterdam UMC-AMC
Rutger Feenstra

0205666405

Wetenschappelijk

Amsterdam UMC-AMC
Rutger Feenstra

0205666405

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

• 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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

• 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).

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-10-2019
Aantal proefpersonen:	30
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	20-02-2019
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL7546
Ander register	METC AMC : 2018_213

Resultaten