TrimetaziDine as a Performance-enhancING drug in Heart Failure with Preserved Ejection Fraction

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We hypothesize that trimetazidine improves left ventricular diastolic dysfunction in HFpEF, by improving mitochondrial function and increasing myocardial energy content

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

Samenvatting

ID

NL-OMON25612

Bron
Nationaal Trial Register

Verkorte titel
DoPING-HFpEF

Aandoening

Heart failure with preserved ejection fraction

Ondersteuning

Primaire sponsor: Amsterdam UMC, location VUmc
Overige ondersteuning: funding by the Amsterdam Cardiovascular Sciences

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Exercise pulmonary capillary wedge pressure (PCWP) measured by right heart catheterisation

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale: currently, no treatment exists for heart failure with preserved ejection fraction (HFpEF) (except diuretics and exercise). Heart failure with preserved ejection fraction is associated with lowered cardiac energy levels, furthermore left ventricular relaxation is a highly energy-consuming process (comparable to stretching of a spring). We hypothesize that trimetazidine (a fatty acid oxidation inhibitor) improves left ventricular diastolic dysfunction in HFpEF, by improving mitochondrial function and increasing myocardial energy content.
Main objective: assess whether: trimetazidine treatment 1) improves LV diastology; 2) improves LV myocardial energy content in HFpEF.
Study design: double-blind placebo-controlled cross-over intervention study.
Study population: patients with stable HFpEF: 1) signs and/or symptoms of heart failure; 2) LVEF >50%; 3) evidence of left ventricular diastolic dysfunction; with the exclusion of other significant co-morbidity (especially other severe cardiac conditions, severe kidney failure, parkinsonism) and able to comply the complete protocol (RHC, MRI/MRS).
Intervention: Trimetazidine tablet 20mg TID (BID if eGFR 30-60 ml/min) or placebo for 2 times 3 months with a 2-week washout period.
Main study parameters/endpoints: Primary endpoint: exercise pulmonary capillary wedge pressure (PCWP) measured by right heart catheterization (RHC);
Key secondary endpoint: myocardial PCr/ATP-ratio measured by 31-phosphorus-magnetic resonance spectroscopy;
Safety endpoint: (S)AE; Metabolic: trimetazidine plasma levels, mitochondrial function, insulin resistance (HOMA); Exploratory: NT-proBNP, 6-Minute-Walk-Distance (6-MWD), quality-of-life (KCCQ, EQ-5D).

Doel van het onderzoek

We hypothesize that trimetazidine improves left ventricular diastolic dysfunction in HFpEF, by improving mitochondrial function and increasing myocardial energy content

Onderzoeksopzet

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Onderzoeksproduct en/of interventie

Trimetazidine tablet 20mg TID (BID if eGFR 30-60 ml/min) or placebo for 2 times 3 months with a 2-week washout period.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Diagnosis of Heart failure with preserved ejection fraction (HFpEF):
a) signs/and or symptoms of heart failure, NYHA II or higher (and ambulant).
b) LVEF >50%
c) evidence of LV diastolic dysfunction; with the exclusion of other significant co-morbidity (especially other severe cardiac conditions, severe kidney failure, parkinsonism) and able to comply the complete protocol (RHC, MRI/MRS).
d. no other significant cardiac (e.g. significant valvular disease) or extra-cardiac condtion (e.g. severe COPD) that explains symptoms.
2. Clinically stable (no change in diuretics >1 month), co-morbidities managed.
3. Informed consent.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Current acute decompensated heart failure, requiring augmented therapy with intravenous diuretics, vasodilator and/or inotropic drugs;
2. Acute coronary syndrome, TIA/CVA, major surgery within the 3 months prior;
3. Suspected septal scar (e.g. due to myocardial infarction) which prohibits the measurement of PCr/ATP with magnetic resonance spectroscopy (MRS))
4. Unable to undergo the complete study protocol (right heart catheterization, MRI/MRS, 6-

MWD)
5. Contra-indication for trimetazidine (severe kidney failure with an eGFR <30ml/min, parkinsonism or patients requiring medication that cause parkinsonism)
6. Doubt about compliance
7. Pre-menopausal women who are nursing, pregnant, or of child-bearing potential and not practicing an acceptable method of birth control
8. Chronic absorption problems
9. Estimated life-expectancy < 1 year.

Onderzoeksopzet

Opzet

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

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	04-03-2019
Aantal proefpersonen:	25
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

Ethische beoordeling

Positief advies

Datum:	26-06-2019
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	NL7830
Ander register	METC VUMC / CCMO : METC2018.370

Resultaten