Skeletal muscle glucose uptake in patients with chronic myeloid leukemia on tyrosine kinase inhibitor therapy

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Skeletal muscle glucose uptake will be impaired in CML patients receiving nilotinib treatment when compared to imatinib users and non-CML controls.

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON29160

Bron
Nationaal Trial Register

Verkorte titel
GLUPTAKE

Aandoening

CML

Ondersteuning

Primaire sponsor: Radboudumc, Nijmegen
Overige ondersteuning: Radboudumc, Nijmegen

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Differences in area under the curve (AUC) of glucose disappearance upon a single glucose

bolus after an exercise bout.

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale: Disturbances in glucose metabolism upon treatment with the tyrosine kinase inhibitor (TKI) nilotinib frequently occur in patients with chronic myeloid leukemia (CML), causing diabetes mellitus and metabolic syndrome. It is suggested that insulin resistance plays a role in the pathophysiology of nilotinib-induced hyperglycaemia, however the underlying mechanism remains unclear. Since skeletal muscle insulin resistance is considered to be the initiating defect in the development of diabetes type II, even before β-cell failure and overt hyperglycemia develops, it is of highly clinical interest to study the effects of TKIs on skeletal muscle. This study aims to confirm these in vitro findings in skeletal muscle of CML patients and to assess its clinical relevance. In order to be able to study glucose uptake in skeletal muscle tissue in vivo, it is necessary to stimulate the glucose uptake by either an exercise or insulin stimulus. Interestingly, the mechanism by which exercise and insulin stimulate glucose uptake is different. Therefore, we designed a study to examine skeletal muscle glucose uptake under both exercise and hyperinsulinemic conditions to further explore glucose dysregulation in TKI users.

Objective: To compare skeletal muscle glucose uptake after 1) an exercise stimulus and 2) under hyperinsulinemic conditions between CML patients on nilotinib, CML patients on imatinib and non-CML controls.

Study design: Cross-sectional study

Study population: We will enrol 15 CML patients on nilotinib treatment, 15 CML patients on imatinib treatment and 15 non-CML controls (aged ≥ 18 years). All participants will perform an exercise protocol after which a single glucose bolus will be given to study skeletal muscle glucose uptake. In a subgroup of 15 participants (6 male CML patients on nilotinib treatment, 6 male CML patients on imatinib treatment, and 3 male non-CML controls) an additional [18F]FDG PET-CT scan during a clamp procedure will be performed to study glucose uptake dynamics under hyperinsulinemic conditions.

Main study parameters/endpoints: Differences in area under the glucose disappearance curve upon a single glucose bolus after an exercise bout. Standard uptake value (SUV) of [18F]FDG as determined on PET/CT images.

Doel van het onderzoek

Skeletal muscle glucose uptake will be impaired in CML patients receiving nilotinib treatment when compared to imatinib users and non-CML controls.

Onderzoeksopzet

Cross-sectional: 1 time point

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Age: ≥18 years

Fasting glucose level: ≤ 6,0 mmol/l
Specifically for CML patients:
- Nilotinib treatment for at least 6 months prior to study inclusion OR
- Imatinib treatment for at least 6 months prior to study inclusion

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

Contra-indication to exercise testing according to the ACC/AHA guidelines

Incapable to provide informed consent

Specifically for subgroup op participants undergoing [18F]FDG PET/CT scanning:
- Renal dysfunction with MDRD <60
- Known prior allergic reaction to [18F]FDG

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Parallel
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	25-11-2019
Aantal proefpersonen:	45
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:	21-11-2019
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	NL8176
Ander register	CMO regio Arnhem-Nijmegen : 2019-5612

Resultaten