Characterization immuno-modulatory effects of Tecfidera: feasibility study.

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We hypothesize that we can get insight in the immunomodulatory effects of Tecfidera with heavy water as methodology.

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

Samenvatting

ID

NL-OMON27762

Bron
NTR

Verkorte titel
Not Applicable

Aandoening

Tecfidera induced lymphocytopenia

Ondersteuning

Primaire sponsor: Not Applicable
Overige ondersteuning: Not Applicable

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Primary objectives:
1. Quantification of CD4+, naive and memory CD8+ T-cell and CD19+ B-cell numbers in Tecfidera-treated MS patients and untreated healthy subjects over time;

2. Quantification of production and disappearance rates of CD4+, naive and memory CD8+ T-cells and CD19+ B-cells in Tecfidera-treated MS patients and untreated healthy subjects;
3. Assessment of markers for cell death and cellular stress, in relation to cell production and disappearance rates.

Toelichting onderzoek

Achtergrond van het onderzoek

Long-term treatment of MS patients with Tecfidera results in reduced lymphocyte counts. This does not appear to be disease-related since reductions in lymphocyte counts are also observed in fumarate-treated psoriasis patients. It is not known whether the Tecfidera-induced reductions in blood lymphocyte counts can be explained by a diminished production, by an enhanced cell death, or by homing of the immune cells to lymphoid tissues. To obtain mechanistic insight into the Tecfidera-induced reductions in lymphocyte counts, circulating lymphocytes can be labelled in vivo with deuterium. This procedure will allow quantification of the production rate and disappearance rate of the cell populations of interest. By combining these cell kinetic parameters with cellular markers for cellular stress (mitochondrial dysfunction) and cell death and, we aim to investigate whether reduced lymphocyte numbers in Tecfidera-treated RRMS patients are explained by a reduced production rate, or a shorter life span due to cell death. Two parallel cohorts (8 MS patients on Tecfidera and 8 healthy volunteers as control) will be included. This study does not involve the use of investigational medical products. MS patients enrolled in this study will be on Tecfidera treatment for at least 6 months. Tecfidera, which is a marketed drug, is the standard treatment of these patients, prescribed by their treating neurologist. For this reason, Tecfidera is not regarded as investigational product in this study. All subjects enrolled in this study will be administered deuterated water for 9 weeks. The administration of deuterated water is a methodological intervention, and as such deuterated water is not regarded as investigational medical product.
Recruitment will take place in the Netherlands

Doel van het onderzoek

We hypothesize that we can get insight in the immunomodulatory effects of Tecfidera with heavy water as methodology.

Onderzoeksopzet

Week 1, 2, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 14, 15, 17, 22, 31 optional week 41, 52

Onderzoeksproduct en/of interventie

None

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

MS patients

1. male and female subjects;

2. minimal age 18 years at the time of informed consent;

3. confirmed relapsing remitting multiple sclerosis (RRMS) patients, with:

i. a diagnosis of RRMS according to the revised McDonald criteria;

ii. a baseline score of 0 to 5.0 on the Expanded Disability Status Scale;

4. patients on Tecfidera treatment for at least 6 months;

5. ability to participate, and willingness to give written informed consent and to comply with the study restrictions and protocol requirements.

Healthy subjects
1. healthy male and female subjects;
2. minimal age of 18 years at the time of informed consent;
3. ability to participate, and willingness to give written informed consent and to comply with the study restrictions and protocol requirements.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

MS patients

1. positive test result for human immunodeficiency virus antibody (HIV-Ab), hepatitis C antibody (HCV-Ab), anti HB core and/or hepatitis B surface antigen (HbsAg) at screening;

2. evidence of any active or chronic disease or condition, other than MS (based on medical history, a physical examination, vital signs, 12 lead ECG, haematology, blood chemistry and urinalysis) that could, in the opinion of the investigator, interfere with the conduct of the study or the study objectives, or pose an unacceptable risk to the subject;

3. a treatment history that includes steroids within one month prior to screening, or any other therapy that in the judgment of the investigator potentially interferes with the study objectives (in case of an insufficient washout period);

4. body weight < 50 kg.

5. subject is pregnant or breast feeding;

6. current substance abuse, including alcohol and drugs;

7. positive alcohol test or test for drugs of abuse at screening, with the exception of a positive test due to medicinal cannabis use;

8. previous deuterium administration;

9. participation in an investigational drug or device study within 3 months prior to screening;

10. loss or donation of blood over 500 mL within three months (males) or four months (females) prior to screening;

11. unwillingness or inability to comply with the study protocol for any other reason.

Healthy subjects

1. positive test result for human immunodeficiency virus antibody (HIV-Ab), hepatitis C antibody (HCV-Ab), anti HB core and/or hepatitis B surface antigen (HbsAg) at screening;

2. evidence of any active or chronic disease or condition (based on medical history, a physical examination, vital signs, 12 lead ECG, haematology, blood chemistry and urinalysis) that could, in the opinion of the investigator, interfere with the conduct of the study or the study objectives, or pose an unacceptable risk to the subjects;

3. a treatment history that includes steroids within 1 months prior to screening, or any other therapy that in the judgment of the investigator potentially interferes with the study objectives (in case of an insufficient washout period);

4. body weight < 50 kg;

5. subject is pregnant or breast feeding;

6. current substance abuse, including alcohol and drugs;

7. positive alcohol test or test for drugs of abuse at screening;

8. previous deuterium administration;

9. participation in an investigational drug or device study within 3 months prior to screening;

10. loss or donation of blood over 500 mL within three months (males) or four months (females) prior to screening;

11. unwillingness or inability to comply with the study protocol for any other reason.

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Parallel

Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	22-08-2016
Aantal proefpersonen:	16
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	27-09-2016
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	NL5908
NTR-old	NTR6096
Ander register	: CHDR1519

Resultaten

Samenvatting resultaten
Not Applicable