Individualized therapy in patients with primary membranous nephropathy

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

Samenvatting

ID

NL-OMON28712

Bron
NTR

Verkorte titel
Antibody guided therapy in MN

Aandoening

primary membranous nephropathy

Ondersteuning

Primaire sponsor: Radboud UMC Nijmegen
Overige ondersteuning: Radboud UMC Nijmegen

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

- Cumulative incidence of remissions (complete- and partial remission), for a duration of at least 6 months.

Complete remission (CR) is defined as a protein-creatinine ratio ≤0.2 g/10 mmol creatinine with stable kidney function, and partial remission (PR) is defined as protein-creatinine ratio <3.0 g/10 mmol creatinine with a reduction of >50 % from baseline and stable kidney function. Achieving remission includes both partial and complete remission)

Toelichting onderzoek

Achtergrond van het onderzoek

In 70 % of patients anti-PLA2R antibodies (aPLA2R) can be identified. Although spontaneous remissions do occur, up to 50 % of patients may need immunosuppressive therapy. The KDIGO guideline recommend initial therapy with a 6-month course of alternating monthly cycles of an alkylating agent and steroids. In the literature different treatment protocols with variable duration of drug therapy are used, however in all studies treatment was not personalized. In previous studies it was shown that disappearance of aPLA2R preceded clinical remission by 2-3 months. We observed that in the majority of patients treated with cyclophosphamide (CP) and mycofenolic acid (MMF) aPLA2R disappeared after 2 months. Since august 2013 we use aPLA2R response to determine treatment duration in the individual patient. We use an antibody guided therapy protocol in patients treated with CP, MMF and tacrolimus. We expect that we will shorten the duration of therapy in many patients.

Doel van het onderzoek

In 70 % of patients anti-PLA2R antibodies (aPLA2R) can be identified. Although spontaneous remissions do occur, up to 50 % of patients may need immunosuppressive therapy. The KDIGO guideline recommend initial therapy with a 6-month course of alternating monthly cycles of an alkylating agent and steroids. In the literature different treatment protocols with variable duration of drug therapy are used, however in all studies treatment was not personalized. In previous studies it was shown that disappearance of aPLA2R preceded clinical remission by 2-3 months. We observed that in the majority of patients treated with cyclophosphamide (CP) and mycofenolic acid (MMF) aPLA2R disappeared after 2 months. We use an antibody guided therapy protocol in patients treated with CP, MMF and tacrolimus. We expect that this will shorten the duration of therapy in many patients.

Onderzoeksopzet

24 months

Onderzoeksproduct en/of interventie

Since august 2013 we use aPLA2R response to determine treatment duration in the individual patient. In the case of treatment with CP and MMF (both in combination with steroids), aPLA2R are measured after resp. 8, 16 and 24 weeks with a commercial IFT. If antibodies are negative the CP/MMF is stopped and the steroids are tapered. If the aPLA2R antibodies are

still positive after 24 weeks of treatment and no complete remission is achieved further treatment with another agent is recommended. A maximum treatment duration of 6 months after the achievement of a partial remission is prescribed.

In case of tacrolimus (also in combination with prednisone); aPLA2R are measured after 24 weeks. If antibodies are negative the tacrolimus and the steroids are tapered. If the aPLA2R are still positive after 24 weeks of treatment further treatment is recommended and aPLA2R are measured again after 48 weeks. If, after 48 weeks of treatment continuation of treatment is recommended and aPLA2R are measured again after 48 weeks. If, after 48 weeks of treatment aPLA2R are still positive and no complete remission is achieved, further treatment with Rituximab (1000 mg) is recommended and the tacrolimus and the steroids are tapered.

For the cyclophamide group a comparison with a historical control group (treated with cyclophosphamide and steroids for 6-12 months) will be made.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- patients with primary membranous nephropathy

- 18 years or older

- anti-PLA2R antibodies positive

- high risk of disease progression. High risk is defined as patients with a persisting nephritic syndrome (>6 months) despite conservative treatment, an urinary βeta-2-microglobulin (β2m) excretion of >1000 ng/min or deteriorating kidney function, or severe symptoms related to the nephrotic syndrome.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- anti-PLA2R antibodies negative

- participation in another clinical trial

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Niet-gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland
Status: Werving gestart

(Verwachte) startdatum:	30-08-2013
Aantal proefpersonen:	100
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	31-08-2016
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	NL5890
NTR-old	NTR6078
Ander register	commissie CMO Arnhem-Nijmegen. : 2014-1418

Resultaten