REduceren van STEroiden bij kinderen met een Recidief Nefrotisch syndroom – de RESTERN studie

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The main hypothesis is that relapses of the nephrotic syndrome in children can be treated adequately by a reduced duration of alternate day prednisone (2 weeks instead of the currently used 4-6 weeks) after a similar induction of remission.

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

Samenvatting

ID

NL-OMON20897

Bron
NTR

Verkorte titel
RESTERN

Aandoening

Nephrotic syndrome Nefrotisch syndroom

Ondersteuning

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Overige ondersteuning: Dutch Kidney Foundation

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Time to first relapse after study randomization (censored at 12 and 24 months)

Toelichting onderzoek

Achtergrond van het onderzoek

Most children with steroid sensitive nephrotic syndrome experience several relapses, which are treated with steroids. For most children, long-term prognosis is for complete resolution of their disease over time and maintenance of normal kidney function. It is therefore vital to focus on minimizing adverse events of the disease and its therapy. Unfortunately, no randomized controlled trials are available to determine the optimal steroid treatment of an infrequent relapse of the nephrotic syndrome.

Recent studies show that treatment schedules of the first episode can safely be reduced (Hahn et al., 2015; Hoyer, 2015), which may reduce steroid toxicity. The hypothesis of the REducing STEroids in Relapsing Nephrotic syndrome (RESTERN) study is that a 2-4-week reduction of alternate day steroids after inducing remission is effective and safe, reduces steroid exposure by 35% on average, and is therefore preferable.

Using a nation-wide placebo-controlled randomized controlled trial, this hypothesis will be tested. A similar daily dose of prednisone is used until the induction of remission. Randomization in blocks (immunosuppressive maintenance therapy vs. no maintenance therapy) will be performed for either 4-6 weeks of alternate day prednisone (standard therapy) or 2 weeks alternate day prednisone followed by 2-4 weeks of alternate day placebo. For a non-inferiority trial with 80% power, 72 patients per group are needed, for which an estimated inclusion rate of 53% is needed.

The RESTERN project aims to improve clinical care for children with nephrotic syndrome by showing that at least equal clinical benefits can be obtained by reduced corticosteroid exposure, which minimizes toxicity.

Doel van het onderzoek

The main hypothesis is that relapses of the nephrotic syndrome in children can be treated adequately by a reduced duration of alternate day prednisone (2 weeks instead of the currently used 4-6 weeks) after a similar induction of remission.

Onderzoeksopzet

12 months

24 months

Onderzoeksproduct en/of interventie

Treatment schedule

• Prednisone 60mg/m2 (max 60mg) daily in 1 dose until complete remission for 3 days (according to the KDIGO guideline)

• Randomization:

o Standard treatment: 4-6 weeks prednisone 40mg/m2 (max 40mg) every other day, then stop (no tapering)

o Study treatment: 2 weeks prednisone 40mg/m2 (max 40mg) every other day, then 2-4 weeks placebo every other day, then stop (no tapering)

Treatment of subsequent relapses according to Dutch standards (prednisone 60mg/m2 (max 60mg) daily in 1 dose until complete remission for 3 days, continued with prednisone 40mg/m2 (max 40mg) every other day during 6 weeks)

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

• Age over 1 and less than 18 years

• Steroid sensitive nephrotic syndrome. This will include the following groups:

o Subjects without maintenance immunosuppressive therapy;

o Subjects with maintenance immunosuppressive therapy:

• Long-term immunosuppressive therapies, including levamisole, ciclosporine, tacrolimus, MMF, mycophenolate sodium, prednisolone;

• Subjects with prednisolone maintenance therapy may be included when administered every other day at a maximum of 4mg/m2 (10% of the study dose)
• Subjects experience a relapse nephrotic syndrome, defined as Albustix positive proteinuria (3+ or greater) for three consecutive days or the presence of generalised oedema plus 3+ proteinuria;

• Informed consent;

• The last prednisolone use (at a dose over 10 mg/m2 on alternate days) for the treatment of a previous episode was at least 4 weeks ago.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

• Steroid resistant nephrotic syndrome;

• Documented or suspected significant non-compliance.

• Daily prednisolone maintenance therapy at any dose

• Alternate day prednisolone maintenance therapy at a dose over 4 mg/m2

• Pregnancy

• Stimulant drug use

• Comorbidity;

o Kidney transplant recipient

o Any disease that requires the variation in oral prednisolone to be at the discretion of the treating physician(s);

• Concomitant use of drugs that induce CYP 3A4: carbamazepine, phenobarbital, phenytoin and/or rifampicin;

• Concomitant use of drugs that inhibit CYP 3A4: ketaconazole, itraconazole, ritonavir, indinavir, macrolide antibiotics (erythromycin), diltiazem, verapamil.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-12-2016
Aantal proefpersonen:	144
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:	16-01-2016
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 47536
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL5549
NTR-old	NTR5670
Ander register	Dutch Kidney Foundation : 15OKG16
CCMO	NL58185.091.16
OMON	NL-OMON47536

Resultaten

Samenvatting resultaten
Schijvens AM, Dorresteijn EM, Roeleveld N, Ter Heine R, van Wijk JAE, Bouts AHM, Keijzer-Veen MG, van de Kar N, van den Heuvel L, Schreuder MF. REducing STEroids in Relapsing Nephrotic syndrome: the RESTERN study- protocol of a national, double-blind, randomised, placebo-controlled, non-inferiority intervention study. BMJ Open. 2017