Study into treatment of children with difficult to treat epilepsy due to Tuberous sclerosis complex with Rapamycin.

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Treating children with TSC and intractable epilepsy with rapamycin in addition to their standard drug regimen will decrease the frequency of their epileptic seizures.

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

Samenvatting

ID

NL-OMON28870

Bron
Nationaal Trial Register

Verkorte titel
RATE

Aandoening

TSC
Tuberous sclerosis complex
Tubereuze sclerose complex
Rapamycin
Rapamycine
Epilepsy
Epilepsie
mTOR
mTORC1

Ondersteuning

Primaire sponsor: Erasmus University Medical Center
Overige ondersteuning: Nationaal Epilepsie Fonds (NEF)

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The primary outcome is change in frequency of epileptic seizures. This will be assessed by comparing the seizure frequency at baseline to the seizure frequency after 6 months of rapamycin added to the standard care. Seizure frequency is recorded by the parents, using an epilepsy diary.

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale:

Tuberous sclerosis complex (TSC) is a genetic disease that leads to epilepsy in up to 90% of patients and mental retardation in over 50% of patients. It has been shown that the development of intractable epilepsy leads to irreversible loss of cognitive development in children with TSC. The underlying deficit of TSC, loss of inhibition of the mTOR protein, can be rescued by rapamycin. There is evidence in human and animal studies that rapamycin can treat epilepsy in patients with TSC.

Objective:

To evaluate the efficacy and tolerability of rapamycin in children with intractable epilepsy. Study design: A randomized controlled open label cross-over study.

Study population:

Children older than 3 months up to 12 years old with intractable epilepsy (defined as 1 or more seizures/week despite two or more adequate trials of anti-epileptic drug regimens, including vigabatrin).

Intervention:

Children will be randomized to treatment with oral rapamycin or standard care with cross-over of treatment after 6 months.

Main study parameters/endpoints:

Primary endpoint: change in seizure frequency in the last month of the study as compared to the month before start with rapamycin. Secondary endpoints: EEG changes, psychomotor development.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

Due to the disease targeted nature of the intervention this study can only be done in this group. Children with intractable epilepsy in this age group are usually admitted to an academic hospital for treatment, or are in frequent contact with their treating pediatric neurologist. The visits for the study will hardly increase the regular burden of visits.

At the visits blood levels will be taken, side effects and growth will be monitored. Routine EEGs will be timed to coincide with entry and endpoint of the study; one or two extra EEGs will be made. Potential benefits are improved seizure control, improved psychomotor development and reduced need for other anti-epileptic drugs. Potential dose-dependent side effects are gastro-intestinal (oral sores and diarrhoea) and immunosuppression.

01-09-2014: On September 1st, the investigators have decided to stop the recruitment of the trial, with permission of the data safety monitoring board. Twenty-three participants have been included in the trial. The planned inclusion of 30 patients was therefore not reached.

The trial was stopped before patient recruitment was complete for various reasons, including slow inclusion, mainly due to a competing clinical trial in the same patient group. The decision to stop the inclusion was made without any knowledge of the results of the trial. The premature ending of the trial resulted in a decrease of power of 90% to 80%, which we except.

Doel van het onderzoek

Treating children with TSC and intractable epilepsy with rapamycin in addition to their standard drug regimen will decrease the frequency of their epileptic seizures.

Onderzoeksopzet

Baseline, during treatment, before or after treatment (cross over).

Onderzoeksproduct en/of interventie

Treatment: Rapamycin added to the standard care for 6 months.
Control group: Cross-over study. Every patient in the trial will receive rapamycin added to standard care for 6 months. Depending on randomization, patients will receive only standard care during 6 months before or after the rapamycin treatment period.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Children with definite TSC;

2. Older than 3 months, up to 12 yrs old;

3. With catastrophic epilepsy (West syndrome or intractable epilepsy defined as 1 or more seizures/week despite two adequate trials of anti-epileptic drug regimens).

Belangrijkste redenen om niet deel te kunnen nemen

(Exclusiecriteria)

1. Renal dysfunction;

2. Surgery during 6wk before inclusion;

3. Current infection.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	07-09-2011
Aantal proefpersonen:	23
Type:	Werkelijke startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	02-12-2011
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	NL3030
NTR-old	NTR3178
Ander register	METC Erasmus MC : MEC-2010-362
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A