A trial comparing efficacy, safety and tolerance between Levetiracetam and Valproic acid in children with epilepsy.

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

Samenvatting

ID

NL-OMON24550

Bron
Nationaal Trial Register

Verkorte titel
LEVVPA

Aandoening

epilepsy

Ondersteuning

Primaire sponsor: Prof.dr. O.F. Brouwer
Overige ondersteuning: ZonMW

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Retention rate after 52 weeks of treatment comparing LEV versus VPA. Retention rate is the percentage of children still on study medication at the end of the study (52 weeks).

Toelichting onderzoek

Achtergrond van het onderzoek

This double-blind, multi-centre study investigates the efficacy, safety and tolerability of levetiracetam (LEV) monotherapy 15-60mg/kg/day versus VPA monotherapy 10-40mg/kg/day as a first-line treatment in children aged 2 to 16 years with newly diagnosed epilepsy in the Netherlands. At least four large academic centres (Groningen, Utrecht, Rotterdam, Maastricht) with paediatric neurology departments and close cooperation with 5-10 paediatric centres per academic centre, and five paediatric neurologists from general hospitals will participate.
200 Children with a confident diagnosis of epilepsy before enrolment and no previous treatment for their seizures with valproate or levetiracetam at any time or with other AEDs in the year before intake will, if initiation of AEDs is indicated according to the treating physician, be randomized double-blindly to be treated with levetiracetam or valproic acid. Subjects will be treated for a maximum of 52 weeks with trial medication.
The study includes 6 visits (including a preselection visit), and 3 telephone contacts. During the phone calls and visits, changes in study- and/or concomitant medication and seizure activity between visits will be recorded. All seizures have to be recorded in a diary, and a standardized adverse event questionnaire will be filled-in during the visits.
At the start and end of the study, the parents/caregivers and, if applicable, the child and his/her teacher have to complete questionnaires about cognitive functioning and behaviour. Patients aged 6 years or older who are enrolled in one of the Groningen hospitals will receive an extensive neuropsychological assessment at the same time points.
The primary efficacy variable is retention rate after 52 weeks of treatment comparing LEV versus VPA. Secondary outcomes are influence of treatment on cognitive development and behaviour, terminal remission, time to withdrawal from study treatment, percentage of patients being seizure-free on AED treatment after 26 weeks and 52 weeks, percentage of patients with seizure reduction of more than 50% after 52 weeks, and incidence of side-effects. The outcomes will be determined for the group as a whole and for the epilepsy syndromes that occur most frequently in our cohort.

Addendum 6-aug-2014: Trial ended 1-aug-2014 due to limited patient inclusion.

Doel van het onderzoek

Very few antiepileptic drugs (AEDs) are licensed for initial use as monotherapy in children with newly diagnosed epilepsy. Valproic acid (VPA) is the most frequently prescribed AED in children with epilepsy. It is effective in a broad spectrum of different seizure types, but it is related to a number of (serious) side effects. An efficacious and broad spectrum AED with an improved safety profile that can be used as monotherapy in children is therefore needed. The

objectives of this multi-centre, double-blind, randomized, 2-parallelgroups study are to investigate the efficacy, safety and tolerability of levetiracetam (LEV) monotherapy 15-60mg/kg/day versus valproic acid (VPA) monotherapy 10-40mg/kg/day in 200 children aged 2 (previously 4) to 16 years with newly diagnosed epilepsy. We investigate whether LEV is just as effective as or even more effective than VPA with less side-effects. If LEV proves to be as effective as VPA with less side-effects, it might even take over its position as the first choice antiepileptic drug in children with epilepsy.

Onderzoeksopzet

1. Retention: 52 weeks.

2. Changes in cognitive development and quality of life: 52 weeks.

3. Terminal remission: 52 weeks.

4. Percentage of patients being seizure-free: 26 and 52 weeks.

5. Percentage of patients with >50% seizure reduction: 52 weeks.

6. Incidence of side-effects and interactions: 52 weeks.

Onderzoeksproduct en/of interventie

One group will receive levetiracetam (LEV) monotherapy 15-60mg/kg/day, the other group valproic acid (VPA) monotherapy 10-40mg/kg/day. Treatment will start with a low dose and can be increased every 2 weeks until the optimal dose is reached, i.e. with reduction of seizures or becoming seizure-free with no or few side-effects. The daily dose will be divided in two equal dosages to be given in the morning and evening. Subjects will be treated for a maximum of 52 weeks with trial medication.

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Children of either sex from age 2 until (and including) age 15 years with weight between 13 and 60 kilograms;
2. New but confident diagnosis of epilepsy made during the last year;
3. According to the treating physician initiation of antiepileptic medication is indicated.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. BMI >25;

2. Treatable underlying cause of epilepsy (e.g. GLUT1-deficiency syndrome);

3. Serious pre-existing behavioural disturbances (according to clinician’s judgment) or serious psychiatric disorders requiring hospitalization or medication;

4. Uncountable seizures (clusters) or history of convulsive status epilepticus or mitochondrial disease (based on clinical characteristics or laboratory tests);

5. Earlier treatment with any other AED for seizures, other than emergency treatment in the year before inclusion;

6. Earlier treatment with LEV or VPA for any indication;

7. Participation in another clinical trial with an investigational drug or device within 12 weeks of inclusion, or at any time during this study;

8. Known presence or history of allergy to the components of LEV or other pyrrolidine

derivates or VPA;

9. Any known disorder or condition that may interfere with the absorption, distribution, metabolisation or excretion of drugs (e.g. end stage renal disease, patients on dialysis, patients with hepatic disease, etc.);

10. Pregnancy or at risk of becoming pregnant (in case of active sexual life adequate contraception is obligatory);

11. Presence of progressive cerebral disease, any other progressively degenerative neurological disease or cerebral tumours with signs of progression.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Actieve controle groep

Deelname

Nederland

Status:	Werving tijdelijk gestopt
(Verwachte) startdatum:	01-02-2013
Aantal proefpersonen:	200
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:	07-01-2013
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	NL3618
NTR-old	NTR3784
Ander register	ZonMW : 113202003
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
Weijenberg A, Callenbach PMC, Brouwer OF for the LEV-VPA study group. Investigator-initiated randomized controlled trials in children with epilepsy: Mission impossible? Epilepsia Open 2016;2:32-8