A double-blind, randomised, placebo-controlled trial of prolonged antibiotic treatment after intravenous ceftriaxone in patients with (possible) persistent Lyme disease.

Gepubliceerd: 02-08-2010 Laatst bijgewerkt: 10-01-2025

Prolonged antibiotic treatment of patients diagnosed with presumed PLD (as endorsed by the international ILADS guidelines) leads to better patient outcome than short-term treatment as endorsed by the Dutch CBO guidelines.

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

Samenvatting

ID

NL-OMON20560

Bron
NTR

Verkorte titel
PLEASE

Aandoening

Borrelia, Lyme

Ondersteuning

Primaire sponsor: University Medical Center St Radboud
Overige ondersteuning: ZonMw: The Netherlands Organisation for Health Research and Development

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Because different operationalizations of the term ‘Global score 36-item Short-form General Health Survey (SF 36)’ exist, the primary outcome measure is specified here as the ‘physical component summary score’ (PCS) of the RAND-36 Health Status Inventory (RAND SF-36, Hays 1998), which is similar to the Medical Outcomes Study (MOS) 36-item Short-Form General Health Survey (SF-36). The PCS is also known as the physical health composite score (PHC). This specification has been communicated to the local Ethics Committee on March 1, 2011, and was approved on April 6, 2011.

Toelichting onderzoek

Achtergrond van het onderzoek

This study is a double blind, randomised, placebo-controlled trial of prolonged antibiotic treatment after intravenous ceftriaxone. All patients will initially receive open-label i.v. ceftriaxone in a home-care setting for two weeks, which is the standard of care for presumed or proven neuroborreliosis according to both guidelines. Then patients will be randomised to one of 3 treatment arms. Subsequently, blinded oral follow-on treatment will be given in 3 randomisation arms:

1. Oral doxycycline for 12 weeks;

2. Oral clarithromycin plus hydroxychloroquine for 12 weeks, or;

3. Oral placebo for 12 weeks.

The primary goal of the study is to establish whether prolonged antibiotic treatment of patients diagnosed with presumed PLD (as endorsed by the international ILADS guidelines) leads to better patient outcome than short-term treatment as endorsed by the Dutch CBO guidelines. Secondary objectives will be studied in an explorative way. The secondary goals include the effect of randomised treatment modalities on pain, functional impairment, psychological functioning, social behaviour, cognitive functioning, and safety. Moreover, cost-effectiveness will be determined by assessment of costs from societal perspective and quality-adjusted life years.

Screening will be done according standard clinical and laboratory protocols. After obtaining informed consent, baseline assessments include clinical, laboratory, microbiological and (neuro)psychological evaluation and objective assessment of physical activity, using an accelerometer.

Study visits will be performed at baseline, week 2, 8 and 14 for safety evaluation. Efficacy evaluation will be performed at week 14 (end of treatment period, EOT), and at week 26 (12 weeks after EOT) and week 40 (end of study, EOS, 26 weeks after EOT), consisting of clinical and psychological assessment and accelerometer registration.

Doel van het onderzoek

Prolonged antibiotic treatment of patients diagnosed with presumed PLD (as endorsed by the international ILADS guidelines) leads to better patient outcome than short-term treatment as endorsed by the Dutch CBO guidelines.

Onderzoeksopzet

Weeks 0, 14, 26 and 40.

Onderzoeksproduct en/of interventie

Arm 1: After open-label i.v. ceftriaxone 2000 mg qd via a peripheral i.v. catheter: oral Doxycycline 100 mg combined with a placebo b.i.d. for 12 weeks.

Arm 2: After open-label i.v. ceftriaxone 2000 mg qd via a peripheral i.v. catheter: clarithromycin 500 mg combined with hydroxychloroquine 200 mg b.i.d. for 12 weeks.

Arm 3: After open-label i.v. ceftriaxone 2000 mg qd via a peripheral i.v. catheter: 12 weeks' course of double placebo b.i.d.

Contactpersonen

Publiek

Postbus 9101, Postnummer 463
A. Berende
UMC St Radboud, Algemene Interne Geneeskunde
Nijmegen 6500 HB

The Netherlands
+31 (0)24 3618819

Wetenschappelijk

Postbus 9101, Postnummer 463
A. Berende
UMC St Radboud, Algemene Interne Geneeskunde
Nijmegen 6500 HB
The Netherlands
+31 (0)24 3618819

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Males or non-pregnant, non-lactating females who are 18 years or older;

2. Women of child-bearing potential must agree to use contraception methods other than oral contraceptives during the study therapy period, since failure of oral contraceptives due to long-term antibiotic use has been described and doxycycline might be teratogenic;

3. Patients with presumed or proven PLD. In this study, clinical suspicion of PLD is defined as complaints of musculoskeletal pain, arthritis or arthralgia, neuralgia or sensory disturbances (such as paraesthesias or dysesthesias), neuropsychological or cognitive disorders, and persistent fatigue, that are:

temporally related to an episode of erythema migrans or otherwise proven symptomatic Lyme disease (defined as within 4 months after erythema migrans as assessed by a physician, or positive biopsy, PCR, culture, intrathecal B. burgdorferi antibodies), OR

accompanied by a positive B. burgdorferi IgG or IgM immunoblot (as defined by strict criteria in line with the European Union Concerted Action on Lyme Borreliosis (EUCALB)), regardless of prior ELISA IgG/IgM screening results;

4. Subjects must sign a written informed consent form.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Subjects with a known history of allergy or intolerance to tetracyclines, macrolides,

hydroxychloroquine or ceftriaxone;

2. Subjects who have had more than 5 days of antimicrobial therapy with activity against B. burgdorferi within the previous 4 weeks;

3. Subjects with a presumed diagnosis of neuroborreliosis (CSF pleiocytosis or intrathecal antibody production) for which intravenous antimicrobial therapy is required;

4. Subjects with a known diagnosis of HIV-seropositivity or other immune disorders. (No HIV serologic testing is required for the study);

5. Subjects with positive syphilis serology or signs of other spirochetal diseases;

6. Subjects with moderate or severe liver disease defined as alkaline phosphatase, ALAT, or ASAT greater than 3 times upper limit of normal;

7. Subjects who are receiving and cannot discontinue cisapride, astemizole, terfenadine, barbiturates, phenytoin, or carbamazepine (The concentrations of these drugs may increase during clarithromycin therapy and/or lead to reduced availability of doxycycline);

8. Subjects who are currently enrolled on other investigational drug trials or receiving investigational agents;

9. Subjects who have been previously randomized into this study;

10. Severe physical or psychiatric co-morbidity that interferes with participation in the study protocol, including previous medical diagnosis of rheumatic conditions, chronic fatigue syndrome or chronic pain conditions as well as insufficient command of the Dutch language;

11. Co-morbidity that could (partially) account for the symptoms of the subject (e.g. vitamin B12 deficiency, anemia, hypothyroidism).

Onderzoeksopzet

Opzet

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

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	03-09-2010
Aantal proefpersonen:	270
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:	02-08-2010
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	NL2362
NTR-old	NTR2469
CCMO	NL27344.091.09

Resultaten

Samenvatting resultaten
N/A