

RESCUE ESES: a Randomized European trial of Steroids versus Clobazam Usage for Encephalopathy with Electrical Status Epilepticus in Sleep

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| Submission date 15/04/2013 | Recruitment status No longer recruiting | <input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol |
| Registration date 24/05/2013 | Overall study status Completed | <input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results |
| Last Edited 18/12/2023 | Condition category Nervous System Diseases | <input type="checkbox"/> Individual participant data |

Plain English summary of protocol

Background and study aims

Encephalopathy with Electrical Status Epilepticus in Sleep (ESES) syndrome is a rare epilepsy syndrome of childhood that is characterized by disturbed electrical brain activity (epilepsy) in sleep and problems with cognition (attention, memory, language, etc.) or behavior. ESES resolves spontaneously in puberty, but cognitive problems often remain. Adequate treatment is mandatory to prevent or reverse these cognitive deficits. However, it is unknown which treatment is the best. Treatment with "standard" anti-epileptic drugs is not very effective. Some studies suggest that clobazam and steroid treatment may be the best option. The only way to prove which treatment is best is to let a lottery decide which treatment a child gets (randomization) and then compare the effects of both treatments. The aim of this study is to establish which treatment is best for children with ESES syndrome, by treating 130 children with ESES syndrome with steroids (inflammation inhibitors) or clobazam and evaluating change in cognitive functioning after 6 and 18 months.

Who can participate?

Children aged 2 up to 12 years with a recent diagnosis of ESES syndrome (within the past six months) can participate in our study.

What does the study involve?

Children will be randomly allocated to either receive corticosteroids or clobazam for six months.

What are the possible benefits and risks of participating?

We hope to prove which of the two treatments is best for children with ESES syndrome. Because these two treatments are also given outside of this study, there are no specific benefits or risks associated with participating. Side-effects of corticosteroids can be e.g. fluid retention and increased infection risk, while e.g. drowsiness and coordination problems can occur while using clobazam. In most cases these side-effects can easily be resolved by changing the dosage.

Where is the study run from?

The study is run from the Brain Center Rudolf Magnus, department of Pediatric Neurology, University Medical Center Utrecht in the Netherlands. Participating centers are located in other European Union countries and include Italy (Pavia), France (Paris, Lyon, Strasbourg), United Kingdom (London, Edinburgh, Glasgow), Belgium (Brussels, Leuven), Germany (Kehl, Freiburg, Kiel, Vogtareuth), Denmark (Dianalund), Finland (Helsinki), Romania (Bucharest), Bulgaria (Sofia) and Spain (Madrid).

When is the study starting and how long is it expected to run for?

February 2014 to July 2023

Who is funding the study?

The study is funded by the National Epilepsy Fund of the Netherlands (NEF) and the Wilhelmina research fund.

Who is the main contact?

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Contact information

Type(s)

Scientific

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Additional identifiers

EudraCT/CTIS number

2013-000531-27

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

43510

Study information

Scientific Title

Corticosteroids or clobazam for ESES syndrome: a European, multicenter, randomized, controlled clinical trial

Acronym

RESCUE ESES

Study objectives

1. As compared with treatment with clobazam, treatment with steroids leads to a 25% increase in favourable outcome in children with Encephalopathy with Electrical Status Epilepticus in Sleep (ESES) syndrome
2. In children with atypical ESES syndrome, treatment with corticosteroids or clobazam also leads to cognitive improvement, with a superiority of steroids over clobazam
3. Pro-inflammatory cytokines are increased in patients with ESES syndrome and are potential biomarkers for disease activity and therapeutic outcome
4. Pulsed steroid therapy has the comparable efficacy and less side effects compared to continuous corticosteroid therapy in children with ESES syndrome

On 28/02/2014 the anticipated start date was changed from 01/01/2014 to 01/02/2014.

Ethics approval required

Old ethics approval format

Ethics approval(s)

1. Medical Ethics Committee Utrecht, the Netherlands, December 2013, ref: 13-275/G-M
2. In the other participating countries approval pending

Study design

Multi-center randomized controlled clinical trial with blinded outcome assessment

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied

Encephalopathy with electrical status epilepticus in sleep (ESES syndrome)

Interventions

Corticosteroids (either methylprednisolone pulse therapy or continuous oral prednisolone, depending on local preference) or clobazam.

Intervention Type

Other

Phase

Not Applicable

Primary outcome measure

1. Intelligence quotient, or developmental quotient
2. Cognitive sumscore

Improvement is defined as significant when improved by at least 75% of the standard deviation.

Secondary outcome measures

Secondary outcomes will be evaluated after 6 and 18 months:

1. Individual absolute test results, and IQ scores
2. Spike wave index during Non-rapid eye movement (non-REM) sleep. Improvement is defined as a decrease to less than 25%
3. Seizure frequency. Improvement is defined as a reduction of 50% or more as compared with baseline
4. Safety and tolerability, as assessed by the occurrence of serious adverse events
5. Differences in pro-inflammatory cytokine levels in patients with ESES who respond to either treatment strategies compared to non responders

Added 28/02/2014:

6. Assessment of global daily functioning assessed with a visual analogue scale (VAS, -5 to 5)

Overall study start date

01/02/2014

Completion date

31/07/2023

Eligibility

Key inclusion criteria

1. Age 2 to 12 years
2. A diagnosis within six months prior to study inclusion (preferentially as soon as possible) of either typical or atypical ESES syndrome (as defined in study protocol)
3. No previous treatment with anti-epileptic drugs in the context of ESES
4. No previous treatment with either clobazam or corticosteroids
5. No current treatment with carbamazepine, oxcarbazepine, vigabatrin, tiagabine, gabapentin and pregabalin and no treatment with any of these drugs in the previous three months
6. Written informed consent by parents / legal representatives

Participant type(s)

Patient

Age group

Child

Lower age limit

2 Years

Upper age limit

12 Years

Sex

Both

Target number of participants

130

Total final enrolment

45

Key exclusion criteria

1. Patients with a spike wave index during wakefulness of > 50%
2. Any condition that, in the investigators judgement, contraindicates the use of clobazam or corticosteroids

Date of first enrolment

21/07/2014

Date of final enrolment

01/01/2023

Locations**Countries of recruitment**

Belgium

Bulgaria

Denmark

Finland

France

Germany

Italy

Netherlands

Romania

Spain

United Kingdom

Study participating centre

University Medical Center Utrecht / Wilhelmina Children's Hospital

Utrecht

Netherlands

3584 AE Utrecht

Sponsor information

Organisation

University Medical Center Utrecht (Netherlands)

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Sponsor type

Hospital/treatment centre

Website

<http://www.umcutrecht.nl/>

ROR

<https://ror.org/0575yy874>

Funder(s)

Funder type

Charity

Funder Name

Dutch National Epilepsy Fund (NEF) (Netherlands)

Funder Name

Wilhelmina Children's Hospital, Research Fund (WKZ fund) (Netherlands)

Funder Name

Added 28/02/2014:

Funder Name

European Clinical Research Infrastructures Network (ECRIN)

Results and Publications

Publication and dissemination plan

After the end of the trial we will analyse the data and plan a publication in a high impact peer reviewed journal, expected in 2021.

Intention to publish date

31/07/2024

Individual participant data (IPD) sharing plan

The datasets generated (research online) and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|----------------------------------|----------|--------------|------------|----------------|-----------------|
| Protocol article | protocol | 23/11/2020 | 25/11/2020 | Yes | No |
| Results article | | 08/12/2023 | 18/12/2023 | Yes | No |