

IgNiTE: Immunoglobulin in the treatment of encephalitis

Submission date 24/06/2015	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 24/06/2015	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 13/11/2023	Condition category Nervous System Diseases	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

Encephalitis is a rare, serious condition that causes inflammation of the brain. The aim of this study is to find out whether early treatment with intravenous immunoglobulin (IVIG) benefits children with encephalitis. The children who are treated with IVIG will be compared to those who are not.

Who can participate?

Children aged from 6 weeks to 16 years and diagnosed with encephalitis, admitted to NHS hospitals in the United Kingdom.

What does the study involve?

Participants are randomly allocated to two groups to receive either IVIG or placebo (a 'treatment' that looks like IVIG but has no medical effect in encephalitis) in addition to standard treatment. All children are followed up for 12 months after treatment and we are collecting information on their health and wellbeing through the use of questionnaires, brain scan and neuropsychologist (an expert who studies how the brain works) assessment.

What are the possible benefits and risks of participating?

Not provided at time of registration

Where is the study run from?

University of Oxford, Department of Paediatrics (UK)

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

August 2015 to July 2020

Who is funding the study?

The CSL Behring Foundation and National Institute for Health Research (UK)

Who is the main contact?

Dr Mildred Iro

Contact information

Type(s)

Scientific

Contact name

Dr Mildred Iro

Contact details

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Additional identifiers

EudraCT/CTIS number

2014-002997-35

IRAS number

ClinicalTrials.gov number

NCT02308982

Secondary identifying numbers

18993

Study information

Scientific Title

A phase III multicentre randomised, double blind, placebo controlled trial to assess the role of intravenous immunoglobulin in the management of children with encephalitis (The IgNiTE study)

Acronym

IgNiTE

Study objectives

The aim of this study is to determine whether early treatment with intravenous immunoglobulin (IVIG) benefits children with encephalitis.

Ethics approval required

Old ethics approval format

Ethics approval(s)

14/SC/1416; First MREC approval date 29/12/2014

Study design

Randomized; Interventional; Design type: Treatment

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Other

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied

Encephalitis

Interventions

1. Intravenous immunoglobulin, Treatment group: 2 doses (1g/kg per dose) of intravenous immunoglobulin administered 24 hours apart, in addition to standard treatment
2. Matching placebo, Control group: 2 doses of placebo administered 24 hours apart, in addition to standard treatment. Volume equivalent to 1g/kg/dose of intravenous immunoglobulin

Intervention Type

Biological/Vaccine

Phase

Phase III

Drug/device/biological/vaccine name(s)

IVIG

Primary outcome measure

Proportion of participants in both study groups making good recovery (GOSE-Peds score of 2 or lower); Timepoint(s): 12 months post randomisation

Secondary outcome measures

1. Comparison of duration of invasive ventilation (if ventilated) between both study groups; Timepoint(s): During the acute admission period
2. Comparison of anti-epileptic treatment use in participants in both study groups; Timepoint(s): Up to 12 months post randomisation
3. Comparison of auto-antibody levels in blood and/or CSF in both study groups; Timepoint(s): Before receipt of study treatment and up to 6 months after treatment
4. Comparison of brain imaging findings of participants in both study groups; Timepoint(s): 6

months post randomisation

5. Comparison of cognitive function between participants in both study groups; Timepoint(s): At 12 months post randomisation

6. Comparison of duration of hospitalisation between both study groups; Timepoint(s): During acute admission

7. Comparison of length of stay on the intensive care unit between both study groups; Timepoint(s): During acute admission

8. Comparison of neurological outcomes using age appropriate questionnaires (e.g SDQ, ABAS-II, GMFCS); Timepoint(s): Up to 12 months post randomisation

9. Number of deaths in children enrolled to the study and comparison between both study groups; Timepoint(s): 12 months post randomisation

10. Occurrence of adverse events of special interest in both study groups; Timepoint(s): Within 5 days of study treatment

11. Occurrence of serious adverse events in study participants; Timepoint(s): 6 months post randomisation; Presence and levels of specific autoantibodies in blood and/or CSF; Timepoint(s): Before receipt of study treatment

12. Proportion of participants in both study groups diagnosed subsequently with epilepsy; Timepoint(s): Up to 12 months post randomisation

13. Proportion of participants in both study groups with GOSE-Peds score of 2 or lower; Timepoint(s): 6 months post randomisation

Overall study start date

03/08/2015

Completion date

31/07/2020

Eligibility

Key inclusion criteria

1. 6 weeks to 16 years of age (day before 17th birthday)

AND

2. Acute (within 24 hours) or subacute (between 24 hours and 4 weeks) onset of altered mental state (reduced or altered conscious level, irritability, altered personality or behaviour, lethargy) not attributable to a metabolic cause

AND

3. At least two of:

3.1. Fever $>38^{\circ}\text{C}$ within 72 hours before or after presentation to hospital

3.2. Brain imaging evidence consistent with encephalitis or immune-mediated encephalopathy that is either new from prior studies or appears acute in onset

3.3. CSF pleocytosis >4 white blood cells (WBCs)/microlitre

3.4. Generalised or partial seizures not fully attributable to a preexisting seizure disorder

3.5. New onset focal neurological signs (including movement disorders) for >6 hours

3.6. Abnormality on EEG that is consistent with encephalitis and not clearly attributable to another cause.

AND

4. Parent/guardian/legal representative/child (if 16 years at the time of enrolment and has capacity to give consent) able to give informed consent and assent (if <16 years and has capacity)

Participant type(s)

Patient

Age group

Adult

Lower age limit

6 Weeks

Upper age limit

16 Years

Sex

Both

Target number of participants

Planned Sample Size: 308; UK Sample Size: 308

Total final enrolment

18

Key exclusion criteria

1. High clinical suspicion of bacterial meningitis or TB meningitis (for example: presence of frankly purulent CSF; CSF WBCs >1000/microlitre; bacteria on Gram stain and/or culture)
2. Receipt of any IVIg product during the index admission where this was administered prior to obtaining written informed consent for the IgNiTE study
3. Traumatic brain injury
4. Known metabolic encephalopathy
5. Toxic encephalopathy (i.e. encephalopathy secondary to exposure to intoxicants, including alcohol, prescription or recreational drugs)
6. Hypertensive encephalopathy/posterior reversible encephalopathy syndrome
7. Preexisting demyelinating disorder; preexisting antibody mediated CNS disorder; preexisting CSF diversion
8. Ischaemic or haemorrhagic stroke
9. Children with a contraindication to IVIG or albumin (i.e. history of anaphylactic reaction to IVIG or albumin, known IgA deficiency and history of hypersensitisation)
10. Known hypercoagulable state
11. Significant renal impairment defined as GFR of 29mls/min/1.73m² and below (Chronic Kidney Disease Stage 4)
12. Known hyperprolinaemia
13. Known to be pregnant
14. Any other significant disease or disorder which, in the opinion of the Investigator, may either put the participants at risk because of participation in the trial, or may influence the result of the trial, or the participant's ability to participate in the trial
15. Participants who are being actively followed up in another research trial involving an investigational medicinal product
16. Administration of study drug not feasible within 120 hours from hospital presentation for the index admission for new patients admitted to a study hospital OR 72 hours from admission to the study hospital for patients transferred from other hospitals, as determined by the study team
17. Any other condition which, in the opinion of the investigator, may interfere with the ability to fulfil study requirements, especially relating to the primary objective of the study (this includes plans to be outside the UK for more than 12 months after enrolment)

Date of first enrolment

03/08/2015

Date of final enrolment

31/07/2020

Locations

Countries of recruitment

England

United Kingdom

Study participating centre

University of Oxford

Department of Paediatrics

Headley Way

Headington

Oxford

United Kingdom

OX3 9DU

Sponsor information

Organisation

University of Oxford

Sponsor details

Old Road

Headington

Oxford

England

United Kingdom

OX3 7LF

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no@email.provided

Sponsor type

Hospital/treatment centre

ROR

<https://ror.org/052gg0110>

Funder(s)

Funder type

Government

Funder Name

CSL Behring Foundation for Research and Advancement of Patient Health

Alternative Name(s)

Funding Body Type

Private sector organisation

Funding Body Subtype

Trusts, charities, foundations (both public and private)

Location

United States of America

Funder Name

National Institute for Health Research

Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Publication and dissemination plan

Planned publication in a high-impact peer reviewed journal around one year after the trial ends

Intention to publish date

01/01/2024

Individual participant data (IPD) sharing plan

All data requests should be submitted to the primary contact Prof. Andrew J Pollard (andrew.pollard@paediatrics.ox.ac.uk) for consideration. A fully anonymised dataset will be shared upon reasonable request. The anonymisation will take into account the small sample size to ensure that no individual participant could be identified from any of the data shared. Dates of availability: 2024. Consent was required from all participants, all consent for data was obtained.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	03/11/2016		Yes	No
HRA research summary			28/06/2023	No	No
Results article		09/11/2023	13/11/2023	Yes	No