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IgNiTE: Immunoglobulin in the treatment of encephalitis

Submission date	Recruitment status	[X] Prospectively registered
24/06/2015	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
24/06/2015	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
13/11/2023	Nervous System Diseases	

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

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT02308982

Clinical Trials Information System (CTIS)
2014-002997-35

Protocol serial number
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

Study type(s)
Treatment

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

Key secondary outcome(s))
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. Occurence 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

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 >38oC 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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
6 weeks

Upper age limit
16 years

Sex

All

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
United Kingdom

England

Study participating centre
University of Oxford
Department of Paediatrics
Headley Way
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Sponsor information

Organisation
University of Oxford

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

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?
Results article		09/11/2023	13/11/2023	Yes	No
Protocol article	protocol	03/11/2016		Yes	No
HRA research summary			28/06/2023	No	No