

# Treatment of autoimmune encephalitis in adults with intravenous immunoglobulin

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<b>Registration date</b> 18/03/2021	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 25/11/2025	<b>Condition category</b> Nervous System Diseases	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Autoimmune encephalitis is inflammation and swelling of the brain caused by the body's own immune defence system. It affects about 1 in 100,000 people per year in the UK. The symptoms can include abnormal behaviour, memory problems and seizures. Some patients recover completely, but in others it can cause death or severe disability.

Autoimmune encephalitis is treated with steroids, which reduce inflammation and swelling. If patients are not improving, intravenous immunoglobulin (IVIG) is often also given, usually after a couple of weeks. IVIG is a protein product extracted from the blood of healthy donors. It is given through a drip into a vein each day for 5 days and is used for other diseases that affect the nervous system.

Some doctors think that if IVIG is used from the start of treatment, patients may recover more quickly and have fewer side effects from the illness. While IVIG may help patients it can have side effects, including blood clots or allergic reactions, is expensive and may not help recovery. Currently it is used in about 50% of patients with autoimmune encephalitis. This study is looking at whether or not early treatment with IVIG improves recovery. The aims of the trial are to:

1. To work out whether, in adults with autoimmune encephalitis, early treatment with IVIG leads to a different time to recovery and improves the outcome.
2. To carry out scientific studies to better understand the disease processes in autoimmune encephalitis and see how IVIG affects them.

### Who can participate?

Patients aged 16 age or older admitted to hospital with suspected autoimmune encephalitis

### What does the study involve?

All patients in the study will receive steroid treatment. This is the standard treatment for autoimmune encephalitis. In addition, participants may be given a short course of IVIG or a product which looks identical (a placebo), but which does not contain the active protein. All participants will undergo regular clinical assessments at the hospital and be asked to complete a series of questionnaires to assess their recovery, and general health and wellbeing.

### What are the possible benefits and risks of participating?

There are no guarantees that participating in the study will have any benefits. It is possible

patients will benefit from the IVIG treatment and additional monitoring and assessments. The disadvantage in taking part in this study may be the risk of having the side-effects of IVIG (this will not be the case in the group that does not take IVIG). There is also the discomfort of receiving the IVIG through a drip and having a lumbar puncture. There are also risks associated with receiving steroids while pregnant or breastfeeding.

Where is the study run from?

The University of Liverpool and the Centre for Trials Research, Cardiff University (UK)

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

April 2020 to April 2026

Who is funding the study?

National Institute for Health Research Efficacy and Mechanism Evaluation Programme (UK)

Who is the main contact?

Paula Foscarini-Craggs  
EncephIG@Cardiff.ac.uk

## Contact information

### Type(s)

Public

### Contact name

Dr Paula Foscarini-Craggs

### Contact details

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## Additional identifiers

### Clinical Trials Information System (CTIS)

2020-004428-40

### Protocol serial number

CPMS 47478, UoL001570

## Study information

### Scientific Title

Intravenous immunoglobulin in autoimmune encephalitis in adults – a randomised double-blind placebo-controlled trial

**Acronym**

Enceph-IG

**Study objectives**

To determine if early treatment with intravenous immunoglobulin (IVIG) changes the time to recovery as measured on the Glasgow Outcome Scale-Extended.

**Ethics approval required**

Ethics approval required

**Ethics approval(s)**

approved 25/03/2021, Wales REC 3 (15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 (0)29 2078 5741; Wales.REC3@wales.nhs.uk), ref: 21/WA/0050

**Study design**

Multicentre double-blind two-arm placebo-controlled randomized superiority trial, incorporating an internal pilot study

**Primary study design**

Interventional

**Study type(s)**

Treatment

**Health condition(s) or problem(s) studied**

Autoimmune encephalitis

**Interventions**

Patients will be randomized 1:1 to IVIG or placebo using random permuted blocks stratified by site, and time from symptom onset. Patients will receive 2 g/kg IVIG or placebo over 5 days. All patients will also receive methylprednisolone 1 g daily intravenously for 5 days, followed by 1 mg/kg bodyweight (maximum dose 60 mg) oral prednisolone daily for 2 weeks. This is followed by a reduction of 10 mg per week until the patient is taking 10 mg daily, and then a further reduction of 1 mg per week until it is stopped.

**Intervention Type**

Drug

**Phase**

Phase III

**Drug/device/biological/vaccine name(s)**

IVIG, methylprednisolone, prednisolone

**Primary outcome(s)**

Recovery measured using the Glasgow Outcome Scale-Extended (GOSE) every 2 weeks for the first 3 months and then monthly until 12 months post-randomization

**Key secondary outcome(s)**

1. Recovery measured using the Glasgow Outcome Scale-Extended (GOSE) at 3 months (all patients), then at 12 months and annually for the duration of the trial for patients who reach those timepoints
2. Neuropsychological outcomes measured using a standard battery of tests (Addenbrooke's Cognitive Examination III, Weschsler Memory Scale version IV, Wechsler Adult Intelligence (WAIS) test version IV, Confrontational Naming Task, Trail Making Test Parts A and B, Test of Premorbid Functioning, Beck Depression Inventory, Beck Anxiety Inventory, and Perceived Deficits Questionnaire) as well as the Modified Rankin Scale, and The Liverpool Outcome Score. This will be administered at 12 months post-randomization.
3. Health utility and self-rated health measured using EuroQoL five dimension Scale (EQ5D5L) and European Brain Injury Questionnaire (EBIQ) at 3 months, then at 12 months and annually for patients who reach those timepoints
4. Clinical outcomes including adverse events, time to hospital discharge, use of additional immunotherapy rescue treatments, relapse, HDU/ITU admission, seizures, use of ventilator support, and mortality, measured using medical notes and assessment at clinical follow-up appointments at 2 weeks, 3 months and 12 months

## **Completion date**

30/04/2025

## **Eligibility**

### **Key inclusion criteria**

Current inclusion criteria as of 05/03/2024:

1. Adults ( $\geq 16$  years) with altered consciousness level AND/OR behavioural change AND/OR working memory deficit AND/OR psychiatric symptoms
2. Persisting for  $>24$  hours and  $<12$  months but no more than 3 months since diagnosis
3. In whom clinician thinks autoimmune encephalitis is the most likely diagnosis
4. CSF polymerase chain reaction (PCR) negative for HSV 1 and 2, and varicella zoster virus
5. CSF microscopy and culture-negative at 48 hours for organisms

PLUS two or more of:

1. Seizures (not explained by previously known seizure disorder) OR new movement disorder
2. Cerebrospinal fluid (CSF) white blood cell count  $6-1000/\text{mm}^3$
3. Electroencephalogram consistent with encephalitis
4. Brain magnetic resonance imaging (MRI) or computer tomography (CT) changes consistent with encephalitis (including normal scan)

Previous inclusion criteria:

1. Adults ( $\geq 16$  years) with altered consciousness level AND/OR behavioural change AND/OR working memory deficit AND/OR psychiatric symptoms
2. Persisting for  $>24$  hours and  $<3$  months
3. In whom clinician thinks autoimmune encephalitis is the most likely diagnosis
4. CSF polymerase chain reaction (PCR) negative for HSV 1 and 2, and varicella zoster virus
5. CSF microscopy and culture-negative at 48 hours for organisms

PLUS two or more of:

1. Seizures (not explained by previously known seizure disorder) OR new movement disorder
2. Cerebrospinal fluid (CSF) white blood cell count  $6-1000/\text{mm}^3$
3. Electroencephalogram consistent with encephalitis

4. Brain magnetic resonance imaging (MRI) or computer tomography (CT) changes consistent with encephalitis

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Mixed

**Lower age limit**

16 years

**Upper age limit**

100 years

**Sex**

All

**Total final enrolment**

21

**Key exclusion criteria**

1. No other likely diagnosis
2. Current or recent (within last 6 months) treatment with IVIG
3. Contraindication to IVIG
4. Intolerance of corticosteroids
5. Recent history of gastric ulcers
6. CSF analysis not performed
7. CSF polymerase chain reaction (PCR) positive for any viruses
8. Brain imaging not performed
9. Alternative diagnosis on brain imaging (CT or MRI)
10. Known HIV infection
11. On steroids or other disease-modifying anti-inflammatory therapies
12. Not able to live independently prior to onset of condition

**Date of first enrolment**

11/11/2021

**Date of final enrolment**

31/10/2024

**Locations**

**Countries of recruitment**

United Kingdom

England

Scotland

**Study participating centre**

**Walton Centre**

Lower Ln  
Liverpool  
England  
L9 7LJ

**Study participating centre**

**University College London**

235 Euston Rd  
Bloomsbury  
London  
England  
NW1 2BU

**Study participating centre**

**The Royal Liverpool University Hospital**

Prescot St  
Liverpool  
England  
L7 8XP

**Study participating centre**

**Royal Hallamshire Hospital**

Sheffield Teaching Hospitals NHS Foundation Trust  
Glossop Road  
Sheffield  
England  
S10 2JF

**Study participating centre**

**John Radcliffe Hospital**

Headley Way  
Oxford  
England  
OX3 9DU

**Study participating centre**  
**University Hospital Coventry**  
Clifford Bridge Road  
Coventry  
England  
CV2 2DX

**Study participating centre**  
**Royal Cornwall Hospital**  
Royal Cornwall Hospitals NHS Trust  
Treliske  
Truro  
England  
TR1 3LJ

**Study participating centre**  
**Royal Devon and Exeter Hospital**  
Royal Devon and Exeter NHS Hospital Foundation Trust  
Barrack Road  
Exeter  
England  
EX2 5DW

**Study participating centre**  
**Royal Stoke University Hospital**  
Newcastle Road  
Stoke-on-Trent  
England  
ST4 6QG

**Study participating centre**  
**Addenbrooke's Hospital**  
Cambridge University Hospitals NHS Foundation Trust  
Hills Road  
Cambridge  
England  
CB2 0QQ

**Study participating centre**  
**Ashford and St Peter's Hospital NHS Foundation Trust**  
London Road

Ashford  
England  
TW15 3AA

**Study participating centre**  
**Aberdeen Royal Infirmary**  
NHS Grampian  
Aberdeen  
Scotland  
AB25 2ZN

**Study participating centre**  
**Royal Preston Hospital**  
Sharoe Green Lane North  
Fulwood  
Preston  
England  
PR2 9HT

**Study participating centre**  
**Leicester Royal Infirmary**  
University Hospitals of Leicester NHS Trust  
Infirmary Square  
Leicester  
England  
LE1 5WW

**Study participating centre**  
**Salford Royal Hospital**  
Stott Lane  
Salford  
England  
M6 8HD

## **Sponsor information**

**Organisation**  
University of Liverpool

ROR

<https://ror.org/04xs57h96>

## Funder(s)

### Funder type

Government

### Funder Name

Efficacy and Mechanism Evaluation Programme

### Alternative Name(s)

NIHR Efficacy and Mechanism Evaluation Programme, Efficacy and Mechanism Evaluation (EME), EME

### Funding Body Type

Government organisation

### Funding Body Subtype

National government

### Location

United Kingdom

## Results and Publications

### Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from the research team by email to the trial email address, [EncephIG@cardiff.ac.uk](mailto:EncephIG@cardiff.ac.uk), and follow the standard CTR data sharing assessment process.

### IPD sharing plan summary

Available on request

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Protocol file</a>	version 5.1	04/05/2022	23/02/2023	No	No
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes