

# Intravenous immunoglobulin (IVIg) treatment of transverse myelitis in adults and children

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<b>Registration date</b> 09/01/2015	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 12/12/2019	<b>Condition category</b> Nervous System Diseases	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Transverse myelitis (TM) is a rare immune-mediated disease of the spinal cord which can affect both adults and children. It causes inflammation and swelling of the spinal cord and damage to the myelin sheath surrounding the nerve cells in the spine. This stops the messages, or nerve impulses, travelling down the spinal cord from being transmitted properly. The inflammation occurs most commonly in the middle (thoracic region) of the back. Symptoms include numbness, tingling, a burning sensation and an increased sensitivity to touch, cold and heat. It also results in weakness of the arms and legs which can range from one limb feeling slightly heavy to complete paralysis. In the worse cases, sufferers can become paraplegic (paralysed from the waist down) or even tetraplegic (paralysed from the neck down); it is potentially a devastating and sometimes life-threatening condition. Patients can recover fully from TM but a large number are left significantly disabled. Neuromyelitis-optica (NMO) is an uncommon relapsing condition (a condition that keeps reappearing) where TM can be the first symptom, with damage also to the optic nerve; over time this can lead to a reduction or loss of vision. There are a number of treatments available for these conditions and evidence suggests that the sooner patients are treated, the less damage is done to the nerves and the better the long-term prognosis. The standard therapy offered is intravenous steroids over 3-5 days. However, treatment with intravenous immunoglobulins (IVIg) have also proven to be very successful as has the rather costly plasma exchange (PLEX). Ways to reduce disability in these patients are urgently required, but there is not, as present, any reliable clinical trial data that would help to determine the best form of treatment. This study looks at whether early treatment with IVIg in addition to the standard steroid therapy is of extra benefit to children and adults with TM when compared to the current standard therapy alone.

### Who can participate?

Patients who are at least 1 year old and have been diagnosed with TM or NMO.

### What does the study involve?

Participants are randomly allocated into one of two groups. Those in group 1 (control group) are given the standard therapy, intravenous methylprednisolone (IV-MP), for up to 5 days. Those in group 2 (intervention group) are given the standard therapy and IVIg for up to 5 days. The patients are then followed up 6 months later to see whether there has been an improvement to

the extent and severity of damage to their spinal cord. The degree of patient disability, the extent in which this disability affects patient's lives and economic implications on the health service are also measured.

What are the possible benefits and risks of participating?

Interventions that can reduce the disability in TM patients are urgently required. The current management recommendation is largely based on expert opinion as there is no clinical trial data available to help determine the best treatment. This trial seeks to test if IVIg would be beneficial in the management of TM. As both treatments are already used in current clinical practice, participants face almost no additional risk beyond what they would experience in having the treatment.

Where is the study run from?

King's College London (UK)

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

December 2014 to November 2017

Who is funding the study?

National Institute for Health Research (UK)

Who is the main contact?

Dr Onyinye Diribe

## Contact information

**Type(s)**

Scientific

**Contact name**

Dr Onyinye Diribe

**Contact details**

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## Additional identifiers

**EudraCT/CTIS number**

2014-002335-34

**IRAS number**

**ClinicalTrials.gov number**

NCT02398994

## Secondary identifying numbers

17935

# Study information

## Scientific Title

A multicentre randomised controlled TRial of Intravenous immunoglobulin (IVIg) versus standard therapy for the treatment of transverse myelitis in adults and children

## Acronym

STRIVE

## Study objectives

Transverse myelitis (TM) is a rare immune-mediated disorder of the spinal cord affecting children and adults, characterised by a rapid onset of paraplegia or tetraplegia, loss of sensation and sphincter disturbance; in severe cases, it is potentially a devastating and sometimes life threatening condition. There are various treatments for these conditions and evidence suggests that the sooner they are administered, the less damage that is done to the nerves and the better the long term prognosis. At present the standard therapy that is offered is intravenous steroids for 3-5 days, although treatment with intravenous immunoglobulins (IVIg) has also proven to be very successful, as has plasma exchange (PLEX), although the latter is very costly. Strategies to reduce disability in these patients are urgently required, yet there are no robust controlled trials to inform on optimal treatment. This will be a multicentre, randomised controlled trial involving children and adults, to evaluate if the early addition of IVIg treatment to standard therapy with intravenous steroids is of extra benefit in TM, when compared to the current standard therapy alone.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

NRES Committee South Central - Berkshire B, 30/10/2014, ref: 14/SC/1329

## Study design

Randomised; Interventional

## 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 to request a patient information sheet

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

Topic: Children, Neurological disorders; Subtopic: All Diagnoses, Neurological (all Subtopics);  
Disease: Nervous system disorders, All Diseases

### **Interventions**

Admin of immunoglobulin, Eligible participants will be randomised to treatment or control group.

1. Participants randomised to the control arm of this study will be prescribed intravenous methylprednisolone in line with the local clinical practice (variations of practice will be recorded)
2. Paediatric patients (treatment arm) will receive 30mg/kg or 500 mg/m<sup>2</sup> capped to a maximum dose of 1g/day for 5 days
3. Adult patients (treatment arm) will be given 1gram/day for 5 days

### **Intervention Type**

Drug

### **Phase**

Not Applicable

### **Primary outcome measure**

Improvement of 2 points or greater on the ASIA Impairment scale (classified A-E); Timepoint(s): 6 months

### **Secondary outcome measures**

1. Change in ASIA motor scale (0-100) and ASIA sensory scale (0-112) at 3, 6, and 12 months post randomisation
2. Change in Kurtzke expanded disability status scale (EDSS) measured by Neurostatus scoring at 3, 6, and 12 months
3. EQ-5D-Y for patients aged 8-12 years (at presentation) at 3,6 and 12 months post randomisation
4. EQ-5D-5L for patients aged  $\geq 13$  years (at presentation) at 3, 6 and 12 months post randomisation
5. Individuals  $\geq 13$  years at presentation: International SCI Quality of Life Basic Data Set at 3, 6 and 12 months post randomisation
6. Client Service Receipt Inventory (CSRI) at 3, 6 and 12 months post randomisation

### **Overall study start date**

15/12/2014

### **Completion date**

11/05/2016

## **Eligibility**

### **Key inclusion criteria**

Patients will be eligible for inclusion on the trial if on presentation they:

1. Are aged 1 year or over

2. Have been diagnosed with:

2.1. EITHER acute first onset transverse myelitis

(The TM CONSORTIUM WORKING GROUP 2002 criteria for probable TM will be used. Hence, following clinical and radiological exclusion of a compressive myelopathy, patient will be diagnosed to have TM if they meet all the following criteria:

2.1.1. Sensory, motor, or autonomic dysfunction attributable to the spinal cord

2.1.2. Bilateral signs and/or symptoms (not necessarily symmetric)

2.1.3. Sensory level (except in young children <5 years where this is difficult to evaluate)

2.1.4. Lack of MRI brain criteria consistent with MS (McDonald 2010 space criteria)

2.1.5. Progression to nadir between 4 h and 21 days)

2.2. OR Have been diagnosed with first presentation of neuromyelitis optica.

(Patients with definite modified NMO will meet the following criteria (Wingerchuck et al, 2006).

Absolute criteria, both:

2.2.1. Optic neuritis

2.2.2. Acute myelitis

2.3. Plus two out of three supportive criteria:

2.3.1. Brain MRI not meeting criteria for MS at disease onset

2.3.2. Spinal cord MRI with contiguous T2weighted signal abnormality extending over three or more vertebral segments, indicating a relatively large lesion in the spinal cord

2.3.3. AQP 4 seropositive status)

3. Have an ASIA Impairment score of A, B or C

4. Have commenced steroid treatment but will be randomised no later than day 5 of steroids, and if definitely known, randomisation will not exceed 21 days from the onset of symptoms

5. Give assent (8-16 years)/consent to participate in the trial

## **Participant type(s)**

Patient

## **Age group**

All

## **Sex**

Both

## **Target number of participants**

Planned Sample Size: 170; UK Sample Size: 170; Description: This constitutes 2 groups 85 on the control arm and 85 on the treatment arm; these numbers include a compensation for an estimated 10% attrition.

## **Key exclusion criteria**

Patients would be excluded if they show evidence of:

1. Contraindication to IVIg as stated in the product SmPC, or receiving IVIg for other reasons

2. Previously known systemic autoimmune disease (eg systemic lupus erythematosus) or any evidence of systemic inflammation during current presentation.

3. Direct infectious aetiology (eg varicella zoster)

4. Previous episode of CNS inflammatory demyelination

5. Acute disseminated encephalomyelitis (ADEM)

6. Other causes of myelopathy not thought to be due to myelitis (eg nutritional, ischaemic, tumour etc.)

7. Other disease which would interfere with assessment of outcome measures
8. Pregnancy
9. Circumstances which would prevent follow-up for 12 months

**Date of first enrolment**

04/03/2015

**Date of final enrolment**

11/03/2016

## **Locations**

**Countries of recruitment**

England

United Kingdom

**Study participating centre**

**King's College London**

Institute of Psychiatry

London

United Kingdom

SE5 8AF

## **Sponsor information**

**Organisation**

Guy's and St Thomas' NHS Foundation Trust

**Sponsor details**

Research & Development Dept 2nd Floor Conybeare House

Great Maze Pond

London

England

United Kingdom

SE1 9RT

**Sponsor type**

Hospital/treatment centre

**ROR**

<https://ror.org/00j161312>

# Funder(s)

## Funder type

Government

## 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

Not provided at time of registration

## Intention to publish date

## Individual participant data (IPD) sharing plan

## IPD sharing plan summary

Not provided at time of registration

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol article</a>	protocol	25/05/2015		Yes	No
<a href="#">Results article</a>	results	01/05/2017		Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No