

# A study of effectiveness and safety of delayed release prednisolone in patients with newly diagnosed Giant Cell Arthritis

<b>Submission date</b> 05/10/2011	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 13/10/2011	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 13/03/2018	<b>Condition category</b> Circulatory System	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims?

Giant Cell Arteritis (GCA) is a condition in which there is inflammation of the large arteries, predominately those in the head and neck. Symptoms can vary depending on which arteries are affected, but can include headache, scalp tenderness, jaw pain and visual problems including blindness.

Steroids are the standard treatment and usually results in rapid resolution of symptoms and signs, and can prevent visual loss. Most patients are required to remain on steroids for 12-36 months. Around 50% of people get a flare-up of their condition and up to 86% get side effects from steroids such as weight gain, fractures, bruising, diabetes, raised blood pressure and cataracts.

The main purpose of this study is to decide whether delayed release prednisolone taken by mouth, in doses similar to the commonly used oral immediate release prednisolone, can maintain control of symptoms in new cases of giant cell arteritis.

Other aims of this study will be to investigate how long lasting is the response and whether the new form of steroid is safe and well tolerated as compared to the standard form of oral immediate release prednisolone. If we show that delayed release prednisolone is safe and work well, results from this study will be used to design larger studies in giant cell arteritis.

Assessments used in this study will also help design assessments for larger studies in giant cell arteritis.

Delayed release prednisolone has been chosen for the study as it has been shown in other research studies and in the laboratory to work well in the control of various other serious inflammatory diseases such as rheumatoid arthritis.

### Who can participate?

To take part in the study you need to be:

1. Aged 50 or over
2. Newly diagnosed with giant cell arteritis and started on steroids no more than 4 weeks ago

### What does the study involve?

If you join the study you will be asked to come to your local research centre for a general

examination and assessment of your condition to decide if you qualify for the study. We will take your blood pressure, heart rate and weight. Samples of your blood and urine will be taken for laboratory testing. After being enrolled in the study, with your permission we will organise for you to have an ultrasound scan of your temporal and axillary arteries and also for a temporal artery biopsy (as is standard practice in the management of your condition). This is a small operation done under local anaesthetic to take a sample of the artery commonly inflamed in giant cell arteritis.

You will initially be treated with standard prednisolone for 4 weeks after diagnosis of giant cell arteritis. After this you will be randomly allocated to one of two groups to get either delayed release prednisolone or standard prednisolone, with an equal or 1 in 2 chance. This study is not blinded therefore you and the study doctors will know which treatment you have been allocated to. Both steroids are tablets taken by mouth. Standard prednisolone is taken in the morning and delayed release prednisolone is taken at night (approximately at 22h00).

You will be seen in the clinic 8 times over about 6 months and we will contact you by telephone between visits (total 5 times in 6 months). Each visit will take about 1-2 hours and telephone consultation about 30 minutes. You will be asked to fill out questionnaires about how you are feeling and what impact your disease has on your daily activity. You will undergo routine monitoring tests at each visit including taking your blood pressure, heart rate and weight. Samples of your blood and urine will be taken for laboratory testing.

What are the possible benefits and risks of participating?

During the study your condition will be closely monitored with regular clinic visits including blood tests and also telephone consultations in between visits. If you are in the delayed release prednisolone group it is possible that you may experience better control of your giant cell arteritis, require less amount of steroid and therefore fewer side effects. However we cannot be certain of this until we have completed this and further studies.

Risks are possible side effects of the steroids and those of taking blood samples. Steroids are the standard treatment of GCA and if you were not in this trial you would be treated with steroids anyway. The main side effects of steroids may include weight gain, bruising, raised blood pressure and increased risk of diabetes, fractures and cataracts.

The tests done at each visit are standard medical tests. The most unpleasant is often having blood samples taken. The risks of taking blood may include bruising and discomfort at the site of the blood test. They should not make you feel tired or cause anaemia as the amounts of blood taken are quite small.

Where is the study run from?

The study is being organised by Southend University Hospital.

There are two hospitals participating: Southend University Hospital and Basildon Hospital

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

Patients will be enrolled in the study between approximately December 2011 and June 2012.

The study will end 6 months after the last patient is enrolled, likely December 2012.

Who is funding the study?

This trial is funded by the pharmaceutical company Napp Pharmaceuticals Limited.

Who is the main contact?

Dr M Williams (Academic Research Fellow)

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## Contact information

**Type(s)**

Scientific

**Contact name**

Dr Mark Williams

**Contact details**

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**Additional identifiers**

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

001

**Study information****Scientific Title**

A study of efficacy and safety of delayed release prednisolone in newly diagnosed cases of Giant Cell Arthritis

**Study objectives**

1. Determine whether delayed release prednisolone, in doses equivalent to standard of care immediate release prednisolone, can effectively maintain disease control in new cases of giant cell arteritis.
2. To investigate the duration of the observed clinical response and safety and tolerance of said treatment. Data from this study will support further phase 3 study of efficacy and corticosteroid adverse event sparing effect of MR prednisolone in GCA. The validation of outcome assessments used in this study, will guide protocol development for future international multi-centre clinical trials in GCA.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Not provided at time of registration

**Study design**

Interventional feasibility study over 26 weeks using a randomised, open protocol with blinded evaluator in 2 centres using 30 subjects comparing delayed release prednisolone to standard prednisolone

**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**

Giant cell arteritis (GCA)

**Interventions**

New cases of GCA will be treated with high dose standard prednisolone (40-60 mg) daily for 4 weeks. Thereafter they will be randomised to 2 open arms with 15 cases in each arm to continue tapering steroid treatment with either standard (IR) or modified release (MR) prednisolone. A taper schedule will be followed and will only be instituted if the disease activity is controlled at each visit on symptoms review and laboratory assessment.

**Intervention Type**

Other

**Phase**

Not Applicable

**Primary outcome measure**

Proportion of patients achieving persistent disease control (without features of active disease and remaining flare free at 26 weeks) in each arm.

Disease Control:

Primary response criteria for assessing remission in patients will be as follows:

1. Patients maintaining a global improvement >70% (compared to pre-steroid state)
2. Absence of signs and symptoms of new, recurrent, worsening features of GCA
3. CRP < 10mg/L or ESR < 30mm/h

Complete control: patients fulfilling all three criteria items

Partial control: Fulfilling 2 out of 3

**Secondary outcome measures**

1. Relapse free subjects in each arm at 26 weeks
2. Time to the first flare
3. Time to second flare
4. Cumulative steroid dosage

5. Patient global VAS of disease activity
6. Reduction of ESR
7. Reduction of CRP
8. Improvement in HAQ and Euro QOL 5D
9. Visual Function Questionnaire (VFQ-25) in patients with vision loss.
10. Improvement in sleep and fatigue scores
11. Proportion with steroid related toxicity in each arm with particular reference to weight gain, fluid retention, bruising, glucose tolerance, hypertension, dyspepsia

**Overall study start date**

01/12/2011

**Completion date**

01/12/2012

## **Eligibility**

**Key inclusion criteria**

1. Age  $\geq 50$  years
2. New diagnosis of Giant Cell Arteritis (GCA) within last 4 weeks
3. Erythrocyte sedimentation rate (ESR)  $>30$  mm/h or CRP  $> 10$  mg/L
4. Unequivocal clinical and laboratory picture of GCA either fulfilling American College of Rheumatology criteria (see below) or typical features, as assessed by a clinician, including one or several of the following:
  - 4.1. New onset localised pain in the head after 50 years of age
  - 4.2. Jaw or tongue claudication
  - 4.3. Visual symptoms (amaurosis fugax, blurring and diplopia)
  - 4.4. Systemic symptoms not attributable to other causes
  - 4.5. Limb claudication
  - 4.6. Polymyalgia
  - 4.7. Abnormal temporal artery (tender, thickened, beading, decreased pulsation)
  - 4.8. Scalp tenderness
  - 4.9. Decreased visual acuity/visual field defect
  - 4.10. Anterior ischemic optic neuropathy or central retinal artery occlusion
  - 4.11. Upper cranial nerve palsies
5. Symptoms and signs of GCA with typical ischaemic complications (e.g. Anterior ischaemic optic neuropathy - AION)

The American College of Rheumatology classification criteria for GCA (3 out of 5 items fulfilled)

1. Age  $\geq 50$  years at disease onset
2. New onset of or new type of localized pain in the
3. Temporal artery abnormality - tenderness to palpation or decreased pulsation, unrelated to arteriosclerosis of cervical arteries.
4. Elevated erythrocyte sedimentation rate (ESR  $\geq 50$  mm/h by the Westergren method)
5. Abnormal artery biopsy showing vasculitis characterized by a predominance of mononuclear cell infiltration or granulomatous inflammation, usually with multinucleated giant cells

**Participant type(s)**

Patient

**Age group**

Adult

**Sex**

Both

**Target number of participants**

30

**Key exclusion criteria**

1. GCA on steroid therapy longer than 4 weeks
2. Previous exposure to DMARD/biologic therapy
3. Serious or chronic infection in the last 3 months
4. Diagnostic doubt
5. Failure to respond to high dose steroids within 5 days
6. Known other vasculitis
7. Patients with evolving ischemic symptoms requiring IV methylprednisolone
8. Malignancy
9. Patients lacking capacity to consent

**Date of first enrolment**

01/12/2011

**Date of final enrolment**

01/12/2012

## **Locations**

**Countries of recruitment**

England

United Kingdom

**Study participating centre**

**Southend University Hospital**

Westcliff-on-Sea

United Kingdom

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## **Sponsor information**

**Organisation**

Southend Univeristy Hospital (UK)

**Sponsor details**

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**Sponsor type**

Hospital/treatment centre

**Website**

<http://www.southend.nhs.uk/>

**ROR**

<https://ror.org/00p2x3741>

## Funder(s)

**Funder type**

Industry

**Funder Name**

Napp Pharmaceuticals Limited (UK)

## 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="#">Results article</a>	results	01/01/2018		Yes	No