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

Submission date	Recruitment status	[X] Prospectively registered
05/10/2011	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
13/10/2011	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
13/03/2018	Circulatory System	

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

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Additional identifiers

Protocol serial number
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

Study type(s)

Treatment

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(s)
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

Key secondary outcome(s))
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

Completion date
01/12/2012

Eligibility

Key inclusion criteria

1. Age ≥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 ≥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 ≥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

Healthy volunteers allowed
No

Age group
Adult

Sex
All

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
United Kingdom

England

Study participating centre
Southend University Hospital
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Sponsor information

Organisation
Southend Univeristy Hospital (UK)

ROR
https://ror.org/00p2x3741

Funder(s)

Funder type
Industry

Funder Name
Napp Pharmaceuticals Limited (UK)

Results and Publications

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?
Results article	results	01/01/2018		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes