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Study of treatments for pyoderma gangrenosum

Submission date	Recruitment status	[X] Prospectively registered
02/04/2009	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
26/05/2009	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
06/02/2017	Skin and Connective Tissue Diseases	

Plain English summary of protocol

Background and study aims
Pyoderma gangrenosum is a rare skin disease. It causes painful, rapidly spreading ulcers on the skin, and can take many months to heal. Although there are different medications available to treat pyoderma gangrenosum, there is no information on which of these is best to use. The two most commonly prescribed tablet (oral) medications for pyoderma gangrenosum are ciclosporin and prednisolone. This study compares these treatments head-to-head to find out whether one works better than the other, and the likely side effects of treatment.

Who can participate?
Patients aged 18 or over who have been diagnosed with pyoderma gangrenosum and have a measurable ulceration (e.g. not pustular pyoderma gangrenosum).

What does the study involve?
Participants are randomly allocated to receive either oral prednisolone or oral ciclosporin. Scheduled clinic visits take place at week 0, week 2, week 6 and after 6 months of treatment (or sooner if the ulcer has healed). Ulcer healing is assessed using digital images of the ulcer by a clinician unaware of the treatment allocation.

What are the possible benefits and risks of participating?
Both ciclosporin and prednisolone cause side effects in some people. It is not known whether one medication will be better (more effective) than the other, as that is what our study is looking at.

Where is the study run from?
The trial is being managed through the Nottingham Clinical Trials Unit at the University of Nottingham (UK).

When is the study starting and how long is it expected to run for?
Recruitment is taking place over a four-year period, starting April 2009, in approximately 50 hospitals across the UK.

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
Prof. Hywel Williams
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2008-008291-14

Protocol serial number
UKDCTN0901

Study information

Scientific Title
Randomised controlled trial of treatments for pyoderma gangrensoum

Acronym
STOP GAP

Study objectives
Pyoderma gangrenosum (PG) is a mutilating, very painful skin disease that often affects people with an underlying internal disease (such as inflammatory bowel disease, monoclonal gammopathy and rheumatoid arthritis). It starts as a reddish purple bump in the skin that

develops into a large, deep, spreading ulcer in a matter of days. People with PG are often misdiagnosed, and spend a long time in hospital waiting for the affected areas to heal (ulcers can last for a variable time on average healing after 3 - 4 months). Patients are not able to work, require daily dressings, have a high need for health care resources, and have very poor quality of life. Patients often have repeat episodes of PG and may have multiple lesions. Treatment of PG usually involves immunosuppression or immunomodulation.

The purpose of this trial is to evaluate the efficacy and safety of the two most commonly used systemic treatments for pyoderma gangrenosum (PG). The study aims to test the hypothesis that systemic ciclosporin (4 mg/kg/day) is more effective than systemic prednisolone (0.75 mg/kg /day) for oral therapy of PG. The hypothesis is that ciclosporin gains control of PG more rapidly, and reduces the time to healing for patients with PG compared to treatment with oral prednisolone.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Northern and Yorkshire Research Ethics Committee, 15/02/2009, ref: 09/H0903/5

Study design
Multicentre parallel-group single-blind randomised controlled trial with a parallel observational study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Pyoderma gangrenosum (PG)

Interventions
Patients entered into the RCT will be randomised to prednisolone (0.75 mg/kg/day) or ciclosporin (4 mg/kg/day), up to a ceiling dose of 75 mg/day prednisolone and 400 mg/day ciclosporin. Patients entered into the observational study will be prescribed topical therapy.

Participants will be treated for up to 6 months during the trial and followed up until the end of the trial.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Ciclosporin, prednisolone

Primary outcome(s)

Velocity of healing at 6 weeks. This will be captured for a single target lesion per patient and measured using digital photography and vascular endothelial volume (VEV) computerised planimetry. If multiple lesions are present, the target lesion should be the lesion that is most able to be photographed on a single plane (i.e., not around the curvature of a limb) for study will be the largest of those present. Digital images will be taken at baseline, 6 weeks and when the ulcer has healed (maximum of 6 months). In addition, maximum longitudinal length and maximum perpendicular width will be measured in order to provide some measure of improvement in case of difficulties with the digital images. This will be converted to approximate area by the formula: length x width x 0.785, which approximates to an ellipse for the purpose of randomisation and analysis.

Key secondary outcome(s))
1. Time to healing - assessed by participants (estimated to the nearest week) based on the time at which sterile dressings are no longer required for the wound. Healing will be confirmed using digital photography at the first opportunity. Information will be provided to participants with instructions on how to report healing of the ulcer. Lesions that remain unhealed after 6 months will be considered to be treatment failures. Time to healing is a more clinically relevant outcome than velocity of healing. It also gives some indication of duration of treatment, which therefore gives an indication of cumulative drug toxicity.
2. Global assessment of improvement (PG specific) - as assessed by the clinician and the patient at 2 weeks, 6 weeks and at 6 months (or healed). This will also be assessed on the digital images by an independent assessor.
3. Inflammation assessment scale - combination scale including erythema, border elevation and exudate based on a scale reported by Foss et al. Assessed at baseline, 2 weeks, 6 weeks and when the ulcer has healed (maximum 6 months). Assessed by the clinician, patient and assessed on digital images.
4. Self-reported pain - assessed daily in diaries for the first 6 weeks
5. Impact on health-related quality of life - assessed at baseline, 6 weeks and 6 months (or healed), using a dermatology specific tool 'Dermatology Life Quality Index', and a general utility measure, the 'EQ-5D'
6. Time to recurrence in each treatment group at the end of the trial. A recurrence is defined as being a repeat episode of PG (at any site) that appears after the lesion has been confirmed as being healed by a physician (or nurse). Self-reported healing that has not been confirmed by a medical professional, and which subsequently recurs, will not be classed as a recurrence and handled as a continuation of the initial episode.
7. Number of treatment failures - treatment failures are defined as being participants who withdraw (or are withdrawn) from their randomised treatment because of treatment intolerance or worsening of the PG, or those who continue to have any unhealed ulcers after 6 months of follow-up
8. Adverse reactions to study medications - adverse events that are classed as possibly, probably or definitely relating to the study medication
9. Cost-effectiveness of the compared treatments

Completion date
31/08/2013

Eligibility

Key inclusion criteria
1. PG as diagnosed by the recruiting dermatologist. An ulcerative lesion may have mixed aetiology, but provided the investigator has confidence that a clinical diagnosis of PG is

appropriate then they are eligible. Other contributing factors and atypical features will be captured in the case report form.
2. Must have a measurable ulceration (e.g., not pustular pyoderma gangrenosum)
3. Age over 18 years, either sex
4. Able to provide written, informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Patients cannot participate in either arms of the trial if they have any of the following:
1. Granulomatous PG - this condition is very rare and may respond differently to treatment
2. Concomitant ciclosporin, prednisolone or intravenous immunoglobulin (IVIG) therapy in the previous month
3. Already participating in another clinical trial

Exclusions for the randomised controlled trial only are as follows:
4. Pregnant, lactating or at risk of pregnancy
5. Hypersensitivity to prednisolone or ciclosporin
6. Biopsy not consistent with PG
7. Clinically significant renal impairment that would result in the investigator not normally treating with either study drug
8. Any pre-treatment investigations, the results of which would prompt the investigator not to use either study drug
9. A diagnosis of malignancy or pre-malignant disease where treatments might interfere with ongoing therapy or might cause harm (e.g., history of lymphoma, cervical epithelial neoplasia [CIN], systemic cytotoxic therapy)
10. The patient has a concurrent medical condition that means the investigator would not normally treat the patient with either of the study drugs (for example: a degree of hypertension that would not lead to using either of the study drugs, advanced heart failure, poorly-controlled diabetes, history of peptic ulcer, malignancy in previous years)
11. Administration of a live vaccine (bacillus calmette-guerin [BCG], measles, mumps, rubella, yellow fever, oral polio, oral typhoid) within the last 2 weeks

Date of first enrolment
08/06/2009

Date of final enrolment
31/08/2013

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Nottingham
Nottingham
United Kingdom
NG7 2NR

Study participating centre
Approximately 50 hospitals across the UK
United Kingdom
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Sponsor information

Organisation
Nottingham University Hospitals NHS Trust (UK)

ROR
https://ror.org/05y3qh794

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research (NIHR) (UK) - Programme Grant for Applied Research (PGfAR) (ref: RP-PG-0407-10177): awarded to the Centre of Evidence Based Dermatology at the University of Nottingham

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	12/06/2015		Yes	No
Results article	results	02/02/2017		Yes	No
Protocol article	protocol	28/04/2012		Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes