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The Bullous Pemphigoid Steroids and Tetracyclines Study

Submission date	Recruitment status
11/11/2008	No longer recruiting
Registration date	**Overall study status**
12/11/2008	Completed
Last Edited	**Condition category**
18/04/2017	Skin and Connective Tissue Diseases

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims

Bullous pemphigoid (BP) is a skin condition affecting mainly the elderly, which causes tense, itchy blisters and painful skin erosions that can affect the whole body. Between 20% and 40% of patients die within 1 year of diagnosis. It is an auto-immune disease, which means that the immune system makes antibodies against parts of the skin in error. In BP, these antibodies are directed at the basement membrane zone - the area between the top layer of skin (the epidermis) and the next layer (the dermis). BP is usually treated with long-term prednisolone tablets (a corticosteroid), which can cause many unwanted side effects such as high blood pressure, osteoporosis (brittle bones), infections and diabetes. It is thought that these side effects are at least in part responsible for the deaths of some BP patients. A safer alternative treatment is sought for this condition. Tetracyclines might be effective in treating BP, but a larger study is needed to confirm if this is the case. Tetracyclines are readily available, cheap and are likely to have a better safety profile than prednisolone, but may be slightly less effective. This study will determine whether doxycycline (a member of the tetracycline family) would be a good alternative to prednisolone for treating BP - i.e. whether the benefits of less severe side effects outweigh any reduction in effectiveness.

Who can participate?

Patients aged 18 or over with bullous pemphigoid

What does the study involve?

Participants are randomly allocated to be treated with either prednisolone or doxycycline. After 4 weeks the investigator counts the number of blisters that remain to see if the treatment has worked. The medication dose is then reduced every few weeks until the blisters have virtually all cleared. To assess which drug is safer, all adverse events, including deaths, are recorded for up to a year after starting the study.

What are the possible benefits and risks of participating?

Not provided at time of registration

Where is the study run from?

The study will be carried out in hospitals by dermatologists in the UK, the Netherlands and

Germany. It will be run through the UK Dermatology Clinical Trials Network with the support of the University of Nottingham Clinical Trials Support Unit.

When is the study starting and how long is it expected to run for?
October 2008 to September 2013

Who is funding the study?
NIHR Health Technology Assessment Programme - HTA (UK)

Who is the main contact?
Prof Hywel Williams

Contact information

Type(s)
Scientific

Contact name
Prof Hywel Williams

Contact details
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Additional identifiers

Protocol serial number
HTA 06/403/51; 8024

Study information

Scientific Title
A randomised controlled trial to compare the safety and effectiveness of doxycycline (200 mg /day) with prednisolone (0.5 mg/kg/day) for initial treatment of bullous pemphigoid

Acronym
BLISTER

Study objectives
1. Doxycycline is not inferior in effectiveness to prednisolone in treating bullous pemphigoid given an accepted non-inferiority margin
2. Doxycycline is less likely to result in severe adverse reactions than prednisolone

Ethics approval required
Old ethics approval format

Ethics approval(s)
Central Manchester Research Ethics Committee, 12/11/2008, ref: 08/H1008/174

Study design
Prospective two-arm single-blind parallel-group multi-centre randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Bullous pemphigoid

Interventions
Prednisolone (0.5 mg/kg/day; oral) vs doxycycline (200 mg/day; oral)

The initial clinician-blinded phase will last for 6 weeks when participants will receive one of either prednisolone or doxycycline. After this 6 weeks the clinician will be able to adjust the dose of the medication and will prescribe for as long as is clinically necessary. However, the patient will be followed up for 1 year from randomisation.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Prednisolone, doxycycline

Primary outcome(s)
Current primary outcome measure(s) as of 05/04/2012:
Absolute differences in the two treatment arms in the:
1. Proportion of participants classed as treatment success (3 or less significant blisters present on examination) at 6 weeks
2. Number of reported grade 3, 4 and 5 (mortality) adverse events for one year

Previous primary outcome measure(s):
Differences in the two treatment arms in the:
1. Proportion of participants classed as treatment success (3 or less significant blisters present on examination) at 6 weeks
2. Number of reported grade 3, 4 and 5 (mortality) adverse events for one year

Key secondary outcome(s))
Differences in the two treatment arms in the:
1. Proportion of participants classed as treatment success (3 or less significant blisters present on examination) at 6 weeks and are alive at one year
2. Proportion of participants classed as treatment success (3 or less significant blisters present on examination) after 3 and 12 months of treatment

3. Proportion of participants who have a further episode of bullous pemphigoid during their participation in the study after previously being classed as a treatment success
4. Number of reported grade 1 and 2 adverse events for one year following the start of study treatment
5. Cost-effectiveness

Completion date
30/09/2013

Eligibility

Key inclusion criteria
1. Both males and females, aged at least 18 years old
2. Able to provide written informed consent
3. Clinical features consistent with bullous pemphigoid
4. Either a direct or indirect (serum) immuno-fluorescence (linear IgG/C3 at epidermal basement membrane zone) positive for bullous pemphigoid
5. At least three significant blisters spread over two or more body sites that have appeared in the week prior to study enrolment
6. Free of blisters and any treatment for previous episodes of bullous pemphigoid for at least one year

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Received any of the study medications or other recognised systemic medications for the treatment of this episode of bullous pemphigoid prior to study entry. Prior topical treatment for this episode is permitted.
2. Recent administration of a live virus vaccine
3. Mainly or entirely mucosal pemphigoid
4. Known allergy to tetracyclines
5. Presence of any condition which precludes the use of either of the study drugs
6. Women of childbearing potential who are not taking adequate contraception or who are pregnant, plan to become pregnant during the study duration or lactating
7. Has active cancer (apart from basal cell carcinoma and Bowen's disease)

8. Has any other condition which would, in the Investigator's opinion, deem the patient unsuitable for participation in the study
9. Taking part in any other intervention study

Date of first enrolment
30/03/2009

Date of final enrolment
30/09/2013

Locations

Countries of recruitment
United Kingdom

England

Germany

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

Sponsor information

Organisation
University of Nottingham (UK)

ROR
https://ror.org/01ee9ar58

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)

NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/03/2017		Yes	No
Results article	results	22/04/2017		Yes	No
Protocol article	protocol	01/07/2015		Yes	No
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes