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APRICOT - Anakinra for pustular psoriasis

Submission date	Recruitment status	[X] Prospectively registered
01/08/2016	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[X] Statistical analysis plan
01/08/2016	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
05/08/2020	Skin and Connective Tissue Diseases	[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Psoriasis is a skin condition that cases red, flaky, crusty patches of skin covered with silvery scales. Pustular psoriasis is a term used to describe a particular form of psoriasis that is characterised by sore, red skin covered in pustules. Sometimes it can be generalised, meaning that it covers most or all of the skin surface, which can be life threatening. Most forms of pustular psoriasis just affect the hands and feet when it is called palmo-plantar pustulosis (PPP). Although this condition affects the hands and feet exclusively, it makes the skin sore and painful and so walking and manual work are difficult. Treatment options are limited and unsatisfactory even the recent, 'biologic' treatments (a new type of medication which selectively targets the biological processes involved in the process of inflammation) that have been developed for the common form of psoriasis (plaque psoriasis) are usually ineffective. Very recently, studies have shown that the biological processes underlying PPP are very different from plaque psoriasis. This may explain the lack of response of PPP to standard treatments. These studies indicate that a group of proteins involved in inflammation called the interleukin (IL)-1 family are central to the disease process. These laboratory studies are supported clinically by anecdotal reports in the medical literature of a drug called anakinra, an IL1 inhibitor developed for other diseases such as arthritis, being effective for the treatment of PPP. The aim of this study is to investigate the effectiveness of anakinra in the treatment of PPP.

Who can participate?
Adults who have had PPP for more than six months which is not responding to treatment.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group are treated with daily injections of anakinra for eight weeks. Those in the second group are treated with daily injections of a placebo (dummy drug) for eight weeks. At the first study visit, participants are given the injection and taught how to do it, so they can inject themselves for the eight week study period. Participants in both groups are examined at the start of the study and then after two, four, six and eight weeks to assess whether their condition has improved. Participants also complete a number of questionnaires to measure their quality of life.

What are the possible benefits and risks of participating?
Participants who receive anakinra may benefit from an improvement to their symptoms. For participants on both treatment arms there is a risk of disease flare (i.e skin disease becoming

worse) and a risk of developing a temporary reaction on the skin at the site of the injection. Like many other treatments for psoriasis, anakinra is a biologic (suppresses the immune system) and therefore participants may also have an increased risk of developing an infection.

Where is the study run from?
St John's Institute of Dermatology, Guy's Hospital (UK)

When is the study starting and how long is it expected to run for?
November 2011 to August 2020

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

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2015-003600-23

Protocol serial number
31343

Study information

Scientific Title

Treatment of Pustular Psoriasis with the IL-1 receptor antagonist anakinra: a randomised, placebo controlled trial and associated mechanistic studies

Acronym
APRICOT

Study objectives
The aim of this study is to determine the efficacy of anakinra in treatment of adults with palmo-plantar pustulosis (PPP) compared to placebo.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London - Dulwich Research Ethics Committee, 01/04/2016, ref: 16/LO/0436

Study design
Randomised; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Palmo-plantar pustulosis

Interventions
Participants will be randomised at baseline to either active or placebo treatment arms, 1:1. Both treatments are in prefilled syringes and given by daily subcutaneous injection for eight weeks (treatment period).

Active group: Participants receive anakinra (Kineret®) 100mg/0.67ml
Placebo group: Participants receive a matched 0.67ml vehicle solution

Participants will attend clinic visits at the following time points: screening, baseline (treatment initiation - up to 3 months after screening), week 1, week 2, week 4, week 6, week 8, and follow up at week 12 and at 90 days post last treatment dose. Baseline to week 8 is the “treatment period” and at each visit clinical assessments of disease severity will be made to collect data for the outcome measures. Any adverse events and changes to other medication will also be recorded. The two follow up visits are for safety, and at both visits the participant will be asked about their health over the intervening weeks and any adverse events noted.

Intervention Type
Other

Phase
Phase IV

Primary outcome(s)

Disease severity as measured by fresh pustule count (i.e. number of macroscopically visible, sterile, white/yellow pustules present on the palms and soles) and/or palmoplantar pustulosis psoriasis area severity index (PP-PASI) score at baseline, 2, 4, 6 and 8 weeks.

Key secondary outcome(s))

Investigator assessed:
1. Disease severity as measured by total pustule count on palms and soles (i.e. number of macroscopically visible, sterile, brown/white/yellow pustules present) at baseline, 2, 4, 6 and 8 weeks
2. Global disease severity as measured using the Investigator's Global Assessment (PPP-IGA) (i.e. clinical opinion of disease severity as defined by the validated scale; clear, nearly clear, mild, moderate, severe, very severe, by the investigating physician) at baseline, 2, 4 and 8 weeks
3. Time to response of PPP (defined as a 75% reduction in fresh pustule count) and relapse rate (defined as a return to baseline fresh pustule count) as measured by clinical examination and fresh pustule count at baseline, 2, 4, 6 and 8 weeks
4. Achievement of 'clear' on PPP-IGA by 8 weeks as measured by the investigating physician at 8 weeks
5. Development of a disease flare (i.e. >50% deterioration in PP-PASI compared to baseline) as measured by clinical examination and PP-PASI score at baseline, 2, 4, 6 and 8 weeks
6. Pustular psoriasis at non acral sites as measured by change in percentage area of involvement at baseline and 8 weeks
7. Plaque type psoriasis (if present) measured using Psoriasis Area and Severity Index (PASI) at baseline and 8 weeks
8. Serious infection rate, defined by any infection leading to death, hospital admission or requiring IV antibiotics, as measured by adverse event reports at week 1, 2, 4, 6, 8, and 12 weeks.
9. Neutropenia (i.e. neutrophil count of 1.0x10-9/l on at least one occasion) as measured by blood tests at baseline, 1, 2, 4, 6, and 8 weeks.

Patient reported outcomes:
1. Patient reported disease severity as measured using the Patient's Global Assessment (measured on the scale: clear, nearly clear, mild, moderate, severe, very severe) at baseline, 2, 4, 6 and 8 weeks
2. Patient reported opinion of palmo-plantar specific quality of life as measured using the Palmoplantar Quality of Life Instrument (validated questionnaire) score at baseline and 8 weeks
3. Patient reported opinion of general quality of life as measured using the Dermatology Life Quality Index (validated questionnaire) at baseline and 8 weeks
4. Patient reported opinion of general health as measured using the EQ5D-3L (a European, validated questionnaire) score at baseline and 8 weeks
5. Treatment acceptability as evaluated using a brief questionnaire with a response scale of 1-5 at study end
6. Adherence to treatment measured by responses to daily text message over 8 weeks of treatment

Exploratory:
1. Expression levels of IL-1 related gene transcripts in blood, skin and keratinocytes derived from hair plucks as measured by RNA levels detected in collected samples by study end
2. Identification of disease-associated mutations as measured by whole-exome/whole-genome sequencing or by targeted screening of candidate genes in collected samples by study end
3. Identification of patient immune phenotypes as measured by functional assays on collected samples by study end

4. Curation of complete clinical, DNA, RNA, serum datasets (with optional tissue samples [skin and hair pluck]) on recruited study participants as measured by number of samples collected and subsequent storage of samples per participant by study end

Completion date
31/08/2020

Eligibility

Key inclusion criteria
1. Adults (18 years and over) with diagnosis of Palmo-Plantar Pustulosis (PPP) made by a trained dermatologist with disease of sufficient impact and severity to require systemic therapy
2. Disease duration of >6 months, not responding to an adequate trial of topical therapy including very potent corticosteroids
3. Evidence of active pustulation on palms and /or soles to ensure sufficient baseline disease activity to detect efficacy
4. At least moderate disease on the PPP Investigator's Global Assessment (PPP-IGA)
5. Women of child bearing potential who are on adequate contraception, who are not pregnant or breast feeding
6. Who have given written, informed consent to participate

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
64

Key exclusion criteria
1. Previous treatment with anakinra or other IL-1 antagonists
2. A history of recurrent bacterial, fungal or viral infections
3. Evidence of active infection or latent TB or who are HIV, Hepatitis B or C sero-positive
4. A history of malignancy of any organ system (other than treated, localised non melanoma skin cancer), treated or untreated, within the past 5 years
5. Use of therapies with potential or known efficacy in psoriasis during or within the following specified timeframe before treatment initiation (week 0, visit 2):
5.1. very potent topical corticosteroids within 2 weeks
5.2. topical treatment that is likely to impact signs and symptoms of psoriasis (e.g. corticosteroids, vitamin D analogues, calcineurin inhibitors, retinoids, keratolytics, tar, urea

within 2 weeks
5.3. methotrexate, ciclosporin, acitretin, alitretinoin within 4 weeks
5.4. phototherapy or PUVA within 3 months
5.5. etanercept or adalimumab within 4 weeks
5.6. infliximab or ustekinumab or secukinumab within 3 months
5.7. other TNF antagonists within 3 months
5.8. other immunosuppressive or immunomodulatory therapy within 30 days or 5 half lives prior to treatment initiation, whichever is longer
5.9. any other investigational drugs within 30 days (or 3 months for investigational monoclonal antibodies) or 5 half-lives prior to treatment initiation, whichever is longer
6. With moderate renal impairment [CrCl <50ml/min]
7. With neutropenia (<1.5x109/L)
8. With known moderate hepatic disease and/or raised hepatic transaminases (ALT/AST) > 2 x ULN at baseline. Patients who fail this screening criterion may still be considered following review by a hepatologist and confirmed expert opinion that study entry is clinically appropriate.
9. Live vaccinations within 3 months prior to the start of study medication, during the trial, and up to 3 months following the last dose
10. Women who are pregnant, breast feeding or of child bearing age not on adequate contraception or men planning conception
11. Poorly controlled diabetes mellitus, cardiovascular disease , asthma, concomitant therapy that may interact with anakinra (for example phenytoin or warfarin) or any condition where, in the opinion of the investigator, anakinra would present risk to the patient
12. Latex allergy (inner needle cover of pre-filled syringe contains natural rubber)
13. Unable to given written, informed consent.
14. Unable to comply with the study visit schedule

Date of first enrolment
01/09/2016

Date of final enrolment
30/11/2019

Locations

Countries of recruitment
United Kingdom

England

Wales

Study participating centre
Guy's Hospital
Great Maze Pond
London
United Kingdom
SE1 9RT

Study participating centre
Salford Royal Infirmary
Stott Lane
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United Kingdom
M6 8HD

Study participating centre
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Newcastle upon Tyne
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NE1 4LP

Study participating centre
University Hospital of Wales
Heath Park
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CF14 4XW

Sponsor information

Organisation
Guy's And St Thomas' NHS Foundation Trust

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

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	29/08/2018	05/08/2020	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Statistical Analysis Plan	statistical analysis plan	10/02/2020	12/02/2020	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes