



APRICOT

Anakinra for Pustular psoriasis: Response In a ControlleD Trial

OPEN LABEL EXTENSION PARTICIPANT INFORMATION LEAFLET

- You are being invited to take part in the Open Label Extension (OLE) part of a trial that investigates the effects of a medication called anakinra in palmo-plantar pustulosis (PPP).
- As part of the OLE you will receive daily injections of anakinra (the active drug).
- If you take part, you may need to stop some of the treatments you are currently taking for your pustular psoriasis. If you are on injection treatments this 'washout' period may be as long as 3 months.
- Everyone participating will make a real difference to our knowledge of pustular psoriasis and potential treatments.
- If you are interested to learn more about the OLE, please read the rest of this information leaflet where we explain what it will involve and how we will use the data you provide.
- The contact details for the central APRICOT study team are provided on the last page of this leaflet

If you have any questions about the study please contact:

Principal Investigator: Dr Andrew Pink

Research Nurse: Louise Griffiths

Please take sufficient time to read this information sheet carefully and talk to others, including your doctor and family, about the study if you wish.

Part 1: The Trial and Open Label Extension - what it involves

What is the purpose and design of the study?

The short name of the trial is APRICOT (Anakinra for Pustular psoriasis: Response In a Controlled Trial).

The purpose of this study is to determine whether 8 weeks of anakinra injections are an effective treatment for PPP.

We have chosen anakinra because it has been shown to have beneficial effects in early studies of patients with pustular psoriasis, it has a good safety profile, and it is already licensed for use in other inflammatory conditions (for example rheumatoid arthritis).

The first stage of the study is designed as a randomised, double blind, placebo-controlled clinical trial. The details of this can be found in the APRICOT Participant Information Leaflet (Version 6, dated 18-DEC-2018).

What is the, "Open Label Extension," to the APRICOT Study?

In this part of the study, everyone knowingly receives the active drug (anakinra). This gives all participants the opportunity to try the active drug (anakinra). The visit schedule details are described below and vary depending on whether you have already completed participation in the randomised trial or are still in the study/due to take part in the study.

Why have I been invited?

You have been invited to take part in the OLE because you are considering taking part in, or are currently taking part in, or, have completed the randomised clinical trial stage of the APRICOT Study. Only people who have taken part in, and completed, the randomised clinical trial stage can take part in the OLE.

Do I have to take part?

No. It is up to you to decide whether or not to take part. Please read this information sheet carefully and ask the study team any questions you might have to help inform your decision. Your decision will not affect the standard of care nor the treatment that you receive in any way.

You are under no obligation to take part, however you will only be offered to take part in the OLE once.

What will happen to me if I take part? What will I have to do?

If you decide to take part, you will be asked to sign a consent form. You will then need to attend the study schedule visits as detailed below.

I am starting the Open Label Extension directly after completing my 12 week trial visit. What do I need to do?

If you are starting the OLE directly following on from your 12 week follow up visit (as part of the randomised clinical trial stage), you will be invited to an OLE baseline visit to commence your anakinra treatment immediately (see below). This OLE baseline visit can be on the same day as your 12 week follow up visit for the APRICOT trial.

I am starting the Open Label Extension at some time after completing the 12 week trial visit. What do I need to do?

You will need to come in for an OLE screening visit before you start the anakinra treatment. At this screening visit we will ask you what medication you are currently taking for your pustular psoriasis (if any), to determine how long you will need to washout before beginning anakinra treatment, and we will take some blood and urine samples to check that it is safe for you to start a course of anakinra treatment. You will then be invited to the OLE baseline visit.

Open Label Extension Baseline Assessment (one visit*)

At this appointment we will repeat blood tests to make sure nothing has changed and will assess your skin to accurately record your baseline skin scores.

At the OLE baseline visit, you will start treatment and receive your first anakinra injection. If required, the clinical research team will show you how to administer the medication and will provide whatever support you need to gain confidence in injecting the medication yourself so that you are happy to continue at home for the 8 week treatment period. Please don't worry about this. Many people take daily injections (e.g. diabetics needing daily insulin) and you will soon get used to it. The trial team will provide you with enough injections for 8 weeks and will set you up for the daily text message reminder service and/or give you a diary card.

You will also be re-issued a patient information card in case of an emergency. Please carry this with you at all times.

Treatment Period over 8 weeks (3 visits)

You will self-administer (at home) daily anakinra injections under the skin for 8 weeks. Your research nurse will provide you with all the necessary supplies, support and instructions, including a sharps bin which can be returned to your GP or local pharmacy (depending on local guidance) or to the study team when full. Every day you will be asked to fill out your diary card as a record of your injections. **If you miss an injection do not take a double dose, but let your research nurse or doctor know as soon as possible.** Please return all empty packaging and unused syringes at every clinic visit.

You will be seen in the outpatient clinic a further 3 times following the baseline OLE visit after your first dose in the clinic; at week 1, 4, and 8. We estimate that these visits will take approximately 1 hour each, and will consist of an assessment of your symptoms, and providing urine and blood samples for routine monitoring of the effects of the study medication.

Whilst taking the trial medication you may continue taking other medication as directed by your doctor or GP for other conditions. However, you must not take the following:

- Medications which may help your PPP: Systemic retinoids, ciclosporin, other immunosuppressants, methotrexate, biologic psoriasis treatments (e.g: adalimumab or ustekinumab)
- Oral or injectable forms of glucocorticoids (steroids)

The trial team will ask for details of all medication at each visit. It is important you let your study team know if you feel unwell, need to visit a Doctor, need new or have any changes to your existing medication, or are worried about any aspect of your involvement at any time. Don't wait for your next visit. Use the contact details in this leaflet and that the team provide to you to get in touch immediately.

If you do decide to take part in the OLE, the final follow up visit will be 90 days post your last dose of anakinra.

Table Summarising study assessments and timing for the Open Label Extension

Tests	OLE Study Visit (Screening to 8 weeks)	Purpose
Medical History	Screening	To find out about past and present disease and medications
Routine Blood tests and Urine sample	Screening, Baseline (and up to 4 weeks beforehand if applicable), Week 1, 4 & 8	Screening bloods will be used to exclude the presence of infections (Tuberculosis, HIV, Hepatitis B and C), as part of routine care. Routine safety monitoring will also include urine analysis, full blood count and liver function tests, as well as markers for disease monitoring. This is the same sort of monitoring that is undertaken for patients with PPP.
Physical Examination	Screening, Baseline & Week 8	Clinical assessment to ensure safety
Assessment of hands and feet	Screening, Baseline & Week 8	To identify any changes in PPP symptoms (e.g. fresh pustule count) during the open label extension
Monitor study medication	Week 1, 4, 8	You will be asked to return any unused syringes and empty packaging at every clinic visit, and will be asked how you are managing with your injections. In addition, automated daily text messages will be sent to remind you to take your medication, or you will complete a diary card.

Monitor other medication and side effects	Baseline, Week 1, 4 & 8	Check for any side effects and collect information about other medications you may be taking. If something happens between study visits that means you see a doctor or need any new medication please call your study team immediately.
---	-------------------------	---

Which moisturisers can I use during the Open Label Extension? Can I use anything else?

You can use any moisturiser and other topical treatments during the OLE.

If your PPP flares during this stage of the study your study doctor may prescribe additional treatment with a topical corticosteroid eg: betnovate, mometasone furoate (Elocon™) which you should use as instructed.

What are the alternative treatments?

You do not have to take part in this OLE. Your study doctor can tell you about other treatment choices for your PPP. These alternatives may include treatments which are applied on top of the skin like ointments and creams with or without corticosteroids, Vitamin A preparations, photo therapies (UVB, PUVA), or systemic treatments (taken orally) such as retinoids or ciclosporin.

You may choose to:

- Continue to get regular care from your doctor
- Take part in another study
- Get no treatment at this time.

Talk with your study doctor about your choices.

Expenses and payments

You will be reimbursed for reasonable travel expenses during the course of the study.

What are the possible benefits of taking part?

There is the possibility that patients taking part in APRICOT OLE will see benefits to their health including seeing a reduction in PPP symptoms. Although we cannot predict this, you will be monitored very closely by the clinical research team and will have access to a dedicated research nurse. Close monitoring and contact will allow the team to answer any questions or concerns you have relating to your care and well-being throughout the study.

Very little research has been done into this condition, so while your participation in this OLE may not benefit you directly, it will provide invaluable new information about the effectiveness of anakinra in patients with PPP and might lead to significant improvements in treatment options for the future.

What are the possible disadvantages and risks of taking part?

To take part in the OLE you will need to attend up to 6 study visits and learn how to self-administer the anakinra injections which may be time consuming. Your study team will endeavour to make your visits as streamlined as possible but we recommend you allow up to 2hrs per study visit and set aside a regular time each day for the injection.

Anakinra is licensed as a daily injection so its disadvantages and risks are well documented. The main ones to consider, alongside general trial related risks, are below:

(i) Risks related to stopping your normal treatments for PPP

If you are starting the OLE after you have completed the entire APRICOT trial (including follow-up visits), and have started to take another treatment for your PPP, you may need to stop your normal treatments prior to the OLE and will be limited to taking anakinra as your only systemic (ie by mouth or injection) treatment for psoriasis for the duration of the OLE.

Moisturisers and topicals are allowed in the OLE. You will be closely monitored all the time so that in the event of new symptoms and signs of PPP, assessment and treatment can be given promptly by specialists experienced in caring for patients with the condition.

(ii) Risks related to the trial treatments

The anakinra injections may not help or may even worsen your symptoms of PPP. You may experience injection site reactions such as stinging and itching; these are usually minor and very rarely lead to withdrawal of treatment.

(iii) Possible side effects

Very common side effects (affecting more than 10% of patients) are injection site reactions and headaches. Injection site reactions usually appear a few days or weeks after the injection as a rash or red inflamed area around the site of injection but can also be more immediate with a stinging or burning sensation at the time of injecting. The research nurses will explain what to expect and will tell you what to do to minimise discomfort and treat any reactions that you might experience – for example using a cold pack and antihistamine creams.

Common side effects (affecting 1 - 10% of patients) include upper respiratory tract (throat or chest) infections, and a decrease in neutrophil & platelet counts.

Uncommon side effects (affecting 0.1 – 1% of patients) of anakinra therapy are allergic reactions, changes in liver function, and rash.

Your treatment will be monitored closely through regular clinical assessments and blood testing so that any infections or side effects can be detected and treated promptly, and/or the trial treatment discontinued. Please don't hesitate to talk to your study team if you are worried about any of the above at any point during the trial.

(iv) Risks to the unborn child.

Anakinra may present unknown risks to an unborn child; therefore women who are pregnant or breast-feeding will be excluded from this study.

Women taking part in the OLE will be advised to carefully follow adequate contraception guidelines during the treatment period **and for up to 14 weeks after the last dose of study drug**. If you could become pregnant, you will be asked to have a pregnancy test before taking part, during and at the end of the APRICOT OLE. You should be using reliable forms of contraception during the study, e.g. oral contraceptive and condom, intra-uterine device (IUD) and condom, diaphragm with spermicide and condom. If you do become pregnant during the course of the OLE, we would ask that you tell your research doctor immediately so they can decide on appropriate action. We would discuss referral for specialist counselling on the possible risks to your unborn baby and arrangements will be offered to monitor the health of both yourself and your unborn baby.

It is unknown if anakinra will effect sperm or semen and therefore it is advised that men taking part in the OLE do not father a child during the trial period without discussing the risks with your doctor. Male subjects will need to use adequate contraception during the period of treatment dosing **and for up to 14 weeks after the last dose of study drug**. If your partner might become pregnant you must use reliable forms of contraception e.g. oral contraceptive and condom, intra-uterine device (IUD) and condom, diaphragm with spermicide and condom. If your partner becomes pregnant while you are taking anakinra, or within 6 months of stopping treatment, you should inform your study doctor immediately. As the risk to your partner and baby is unknown, it is desirable for your partner to agree to medical supervision during her pregnancy and for the baby after it is born.

(v) Breast feeding

Participants must not breast feed during the period of study medication and **up to 14 weeks after the last dose of study drug**.

(vi) Risks related to having blood taken

Blood tests may be uncomfortable and cause some bruising or light headedness. On very rare occasions, infection can arise as a result of having blood taken. To reduce the discomfort all samples, both for clinical monitoring and the genetic/immune function tests, will be taken at the same time by a clinical professional trained and experienced in taking blood from patients.

(vii) Live vaccines

Participants should not have live vaccines during the period of treatment dosing and for up to 3 months after the last dose of anakinra.

What will happen if I don't want to carry on with the Open Label Extension?

You can withdraw from the OLE at any time and stop taking anakinra without having to give a reason. This will not affect your medical care in any way. Your

Dermatologist will explain your current condition and advise you on all the available next options.

All samples and clinical information that we have obtained up until the point of withdrawal will continue to be used. Even if you are no longer taking the trial medication we would also very much like to continue to collect clinical data and safety samples from you for some or all of the remaining scheduled OLE visits, if you give permission. For safety reasons you will be asked to attend at week 8 and a follow up visit 90 days after your last dose even if you decide to withdraw.

If you would like to withdraw from the OLE your trial doctor will make arrangements for your care to be continued in the routine clinical setting.

What happens at the end of the Open Label Extension?

At the end of the OLE, you will be followed up again 90 days after your last dose of anakinra, and your study doctor will assess your symptoms, discuss the treatment options and prescribe any appropriate further treatment.

Part 2: Further information

What if new information becomes available?

If new information about anakinra becomes available during the OLE, your study doctor will tell you about it and discuss with you what to do next. If you decide to withdraw, you and your study team will decide upon your future care. If you decide to continue in the study you will be asked to sign an updated consent form.

To protect patient safety, an independent committee of experts will review the results of the APRICOT study and OLE at regular intervals during the APRICOT trial, as well as information from other relevant trials. This means that if information emerges during the trial period suggesting that, for example, subjects receiving anakinra have unfavourable outcomes, then the trial and the OLE may be stopped early or adapted. Your local study team will keep you informed.

Will my taking part in this Open Label Extension be kept confidential?

Yes. All the information about your participation in APRICOT will be kept confidential. When you consent to take part in the trial you will be assigned an anonymised patient identification number (PIN). Your data and samples will be identified with this PIN number and only the Chief Investigator and approved delegated members of the study team will know which anonymised number relates

to you. . All those involved in the study will have a strict duty of confidentiality to you as a research participant and towards your data.

By consenting to take part you are agreeing that, in the event of an inspection or audit by the sponsor or Regulatory Authorities, authorised people may have access to your medical records to check the trial is being conducted properly.

Involvement of the General Practitioner/ Family doctor (GP)

With your consent, we will notify your GP about your involvement in the OLE. Your study doctor will also keep them informed about any changes in your condition during the course of the study, in line with current medical practice. If you have private medical insurance, you should inform your insurer that you are considering taking part in this study.

What will happen to my data?

APRICOT data will be stored on an online system maintained by the King's Clinical Trial Unit and hosted on a dedicated secure server within King's College London. Only authorised trial personnel will have password restricted access to the system. All data will be handled, computerised and stored in accordance with the Data Protection Act 1998.

What will happen to any samples I give?

As part of the process of monitoring the safety of the treatment you receive, you will also be asked to give clinical blood samples at every study visit. These samples will not be stored, but will be processed and analysed by the hospital's clinical laboratory (as per routine blood tests). The results will be stored on the hospital computer system and recorded in the study documents, and will be reviewed by the doctor who is looking after you.

Will any genetic tests be done?

No genetic samples are collected during the APRICOT OLE.

What will happen to the results of the APRICOT study?

The results of the APRICOT study, including the OLE, will be collected by the Chief Investigator and the APRICOT study team. Their intention is to present the findings at dermatology meetings and publish the results in medical journals to circulate as widely as possible information about the best ways to treat individuals with PPP. This will take at least 4 years from the beginning of the study. When the results are published we will be happy to inform you on the specific treatment arm that you received and the overall results of the trial. No individual patient will be identified in any report or publication arising from this study.

Who is organising and funding the research?

This research is funded by a grant awarded to the Chief Investigator, Professor Catherine Smith, by the National Institute for Health Research as part of its Efficacy and Mechanism Evaluation Programme. The study is being sponsored by the Guy's and St Thomas' NHS Foundation Trust. The APRICOT study was conceived by the APRICOT trial steering committee and is not a drug company sponsored clinical trial. The pharmaceutical company who make anakinra (SOBI) have agreed to provide the drug free of charge.

Who has reviewed the trial?

All research in the NHS is reviewed in detail by an independent group of people called a Research Ethics Committee, with the specific objective to protect your safety, rights, wellbeing and dignity. The APRICOT study has been reviewed and given a favourable opinion by the London Dulwich Research Ethics Committee.

Advice has been sought from patients that have worked with the dermatology team at Guy's and St Thomas' NHS Foundation Trust, and a patient representative has also been invited to join the Trial Steering Committee.

The Research and Development Department of Guy's and St Thomas' NHS Foundation Trust have also examined all study documents independently to confirm that the study is feasible and that it will be conducted by clinical teams who have the expertise and appropriate facilities to carry out such as study. They have also received independent reviews by statisticians experienced in clinical trial design and experts in rheumatoid arthritis.

What if there is a problem?

(i) Questions and Concerns

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. Alternatively, you can contact the Chief Investigator, Professor Catherine Smith. Contact details are provided on the final page of this information leaflet.

(ii) Complaints

If you have a complaint, you should talk to the research team who will do their best to answer your questions. If you remain unhappy, you can make a formal complaint through the NHS complaints procedure. Details can be obtained through the Patient Advisory Liaison Service (PALS) on 020 7188 8801. Address: PALS, Ground Floor, Tower Wing, Great Maze Pond, London, SE1 9RT. This study is insured by Guy's & St Thomas' NHS Foundation Trust under the Clinical Negligence Scheme for trials.

(iii) Harm

All research staff will be fully trained and certified before taking part in any related activities, and every care will be taken during the OLE. In the unlikely event that you are harmed during the research and this is due to negligence then you may have grounds for legal action for compensation against that NHS Trust but you may have to pay your legal costs. The normal NHS complaints mechanisms are available to you.

Further information and contact details

If you have any questions about the APRICOT study at any time, please feel free to contact your consultant dermatologist, local APRICOT study team, or the Chief Investigator and central trial office via the contact details below.

CONTACT DETAILS	
<p>Principal Investigator: Dr Andrew Pink</p> <p>Research Nurse Louise Griffiths</p> <p>Skin Therapy Research Unit, 1st Floor - Counting House, Guy's Hospital, Guy's and St Thomas' NHS Foundation Trust, Great Maze Pond, London. SE1 9RT.</p> <p>Telephone Number: 0207 188 6273 Research Mobile: 07717 697 435 Email: APRICOT@gstt.nhs.uk</p>	<p>Chief Investigator: Professor Catherine Smith Professor of Dermatology & Therapeutics Consultant Dermatologist St John's Institute of Dermatology Guy's Hospital, London</p> <p>Tel: 0207 188 7188</p>
<p>APRICOT Study Team Skin Therapy Research Unit 9th Floor, Tower Wing, Guys Hospital, London, SE1 9RT www.apricot-trial.com</p> <p>Trial Manager: Prakash Patel - APRICOT@gstt.nhs.uk APRICOT Research Nurse: dermatologytrials@gstt.nhs.uk Tel: 07717 697435 (during working hours)</p> <p style="text-align: center;">In emergencies please contact your trial doctor or local emergency services</p>	

