

Clinical Trials: An Overview



papaa

A positive approach

to psoriasis and

psoriatic arthritis



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What are the aims of this leaflet?

This information is intended to help you understand how treatments for psoriasis or psoriatic arthritis are developed, what a clinical trial involves and what to consider if you are volunteering.

- About psoriasis and psoriatic arthritis
- What happens in psoriasis?
- What happens in psoriatic arthritis?
- Introduction to treatments
- What is a clinical trial?
- How is a clinical trial planned?
- Types of clinical trials
- Who is in charge of a clinical trial?
- Why are people asked to take part in a clinical trial?
- Who can participate in a clinical trial?
- What questions should volunteers ask?
- What might a volunteer be asked to do during a clinical trial?
- What are the risks and benefits of taking part in a clinical trial?
- Further sources of information about clinical trials.

About psoriasis and psoriatic arthritis

Psoriasis (sor-i'ah-sis) is a long-term (chronic) scaling disease of the skin that affects about 2% of the UK population. It usually appears as red, raised, scaly patches known as plaques. Any part of the skin surface may be involved but the plaques most commonly appear on the elbows, knees and scalp.

About 10% to 20% of people with psoriasis may develop an associated psoriatic arthritis, which causes pain, inflammation and swelling in the joints and tendons, accompanied by stiffness, particularly in the mornings.

What happens in psoriasis?

Normally a skin cell matures in 21-28 days and during this time it travels to the surface, where it is lost in a constant invisible shedding of dead cells. In patches of psoriasis the

turnover of skin cells is much faster, around four to seven days, and this means that even live cells can reach the surface and accumulate with dead cells. The extent of psoriasis and how it affects an individual varies from person to person. Some may be mildly affected with a tiny patch hidden away on an elbow which does not bother them, while others may have large visible areas of skin involved which significantly affect daily life and relationships. The process is the same wherever it occurs on the body. Psoriasis is not contagious. For more detailed information, see our leaflet ***What is Psoriasis?***

What happens in psoriatic arthritis?

In psoriatic arthritis and some inflammatory diseases, the immune system does not work properly, instead causing damage by working against the body's own tissues. In psoriatic arthritis, inflammation is characterised by redness, warmth, swelling and pain. Inflammation is a process by which the body's inner defence mechanisms - the white blood cells and other substances - protect the body against infection and foreign invaders such as bacteria and viruses.

The most commonly affected sites in psoriatic arthritis are the hands, feet, lower back, neck and knees, with movement in these areas becoming severely limited. For more detailed information, see our leaflet ***What is Psoriatic Arthritis?***

Introduction to treatments

There are many available treatments for psoriasis and psoriatic arthritis, including skin cream treatments (topical therapies), UV light treatment (phototherapy) and tablets and injections.

Where do treatments come from?

Some treatments for psoriasis and psoriatic arthritis have been around for decades, such as tar treatments and UV light treatment for psoriasis and anti-inflammatory drugs for psoriatic arthritis. However, as scientists have gained a better understanding of the immune system and how psoriasis and psoriatic arthritis develops, new treatments have become available.

It can take many years after discovery/invention for a treatment to become available for doctors to prescribe. A pharmaceutical company will spend millions of pounds over the course of a drug development process in the hope that the future treatment becomes successful and profitable. Many potential therapies are never developed as a medicine. Overall, approximately 1 in 10,000 potential medicines makes it all the way through the process to reach patients.

The process of drug development is focused on delivering safe and effective treatments. The process is long, since treatments are initially developed in the laboratory, with extensive scientific testing of short- and long-term effectiveness, possible side effects, any implications of taking the new drug in combination with existing medicines, optimal dosage and suitable ways to administer the treatment.

A potential new medicine in development is named an Investigational Medicinal Product (IMP) to separate it from an authorised medicine. Once an IMP has passed laboratory investigations, the pharmaceutical company in control of the IMP will apply for permission to conduct a clinical trial of its use in humans.

What is a clinical trial?

Most research in the National Health Service (NHS) involves people, often patients, and is usually referred to as clinical research or medical research.

Clinical trials may compare a new medical approach to one that is already available or to a placebo (a substance that has no therapeutic effect) or to no intervention at all. Some clinical trials compare interventions that are already available to each other.

A clinical trial may be researching a particular IMP, and may therefore be called a Clinical Trial of an Investigational Medicinal Product (CTIMP). However, the clinical trial may also be looking at medical devices, procedures, or changes to participants' behaviour, such as their diet.

When a new product or approach is being studied, it is not usually known whether it will be helpful, harmful, or no different from available alternatives (including no intervention). The investigators try to work out the safety and efficacy (effectiveness) of the intervention by measuring certain outcomes. For example, they can measure how

psoriasis or psoriatic arthritis improves by using a scoring system.

Clinical trials used in drug development are sometimes described by phase. This highly controlled process is regulated by the Medicines and Healthcare products Regulatory Authority (MHRA), which is the government agency responsible for making sure medicines and medical devices work and are acceptably safe.



How is a clinical trial planned?

A CTIMP of a potential new medicine for psoriasis or psoriatic arthritis may involve a large number of people or groups, including:

■ **pharmaceutical company**

The company which owns and has developed the IMP in the laboratory will organise the clinical trials necessary to develop the IMP for humans

■ **a contract research organisation**

Clinical trials are sometimes conducted by a contract research organisation, which is an independent company with specific scientific expertise

■ **specialist doctors**

From the relevant specialty, such as dermatology for psoriasis or rheumatology for psoriatic arthritis.

Specialists in the relevant medical speciality will be consulted and/or directly involved in the application for and running of a clinical trial.

These people or groups will decide the best way to investigate the IMP. The first stage involves writing a very detailed document containing all relevant information about the IMP and a plan that describes how the clinical trial will be conducted, where and by whom. This is called the clinical trial protocol. Once a clinical trial protocol is in place, a request for clinical trial approval is made.

What's included in a clinical trial protocol?

- The name and description of the new treatment
- A summary of findings of other studies already carried out
- When and how the patient uses or takes the treatment
- A description of the population to be studied
- A detailed description of trial design, including the measures taken to avoid bias
- The expected duration of participation
- A description of the stopping rules (when a trial or treatment stops or a participant needs to withdraw).

Evaluations

- Methods, timing and specification of the efficacy and safety parameters
- Procedure for generating reports and reporting any side effects and intercurrent illnesses (an illness happening at the same time and which may affect the illness being tested)
- Description of the statistical procedures for analysing the data obtained during the trial.

General information

- Name and address of the pharmaceutical company carrying out the trial
- Name and address of the investigator carrying out the trial
- Name, address and telephone number of everybody involved in the conception, design and carrying out of the clinical trial.

Regulatory section

- Financing and insurance of the study
- Data handling and record-keeping procedures
- Description of the ethical considerations relating to the trial
- Description of quality control and quality assurance to be adopted during the trial.

The process for approval is complex in order to ensure the research is justified and acceptably safe. A key part of the approval is ethical approval. This is where the clinical trial protocol is submitted to an ethics committee – an

independent group of people, appointed by the local health authority, which includes doctors, nurses, medical staff, lawyers and members of the public. They will decide whether the research is justified, including checks that:

- the researchers are qualified to carry out the trial
- the protocol is suitable for the needs of the trial
- the probable benefits of a new treatment outweigh the risks of side effects
- there is enough information given to participants
- the way in which people will be recruited is correct
- the local health facilities can support the trial.

Once the ethics committee has approved the protocol, other formal approvals must follow and once these are all complete, the clinical trial may begin.

Types of clinical trials

Clinical trials may be divided into types, or phases. Each new IMP must proceed through the phases in turn. Unless they pass each phase, they cannot proceed to the next.

Phase one:

Phase one clinical trials are the first time that a potential new medicine is given to a human being. This is done using a small number of healthy volunteers. The main aim of a phase one trial is to check that there are no serious side effects, known as adverse events, with the planned dose of the potential medicine. Phase one studies go ahead with extreme caution to prevent multiple side effects; each volunteer is closely monitored by doctors and research staff. The trial starts by giving healthy volunteers very small doses of the potential new medicine, then increasing the dose to check what doses are acceptably safe.

Phase two:

Phase two studies involve giving the IMP to a slightly larger group, this time consisting of patients rather than healthy volunteers. For example, a phase two clinical trial of a potential new treatment for psoriasis would go ahead with the help of specialist dermatology centres and overseen by a senior dermatologist. Here, a key aim is to find out whether the medicine dose which was found to be acceptably safe in the first phase actually works for the disease it is intended to treat. Safety is vital and any side effects are analysed. In phase two testing, the patients

selected for testing usually share very similar characteristics, such as their age range. One reason for this approach is that if any problem occurs, the researchers can prove that it was due to the medicine rather than because of any other medical conditions the volunteers suffer from.

Phase three:

A phase three study tests the medicine on a larger group of patients. In phase three trials, patients treated with the new product may have other medical problems, rather than sharing similar characteristics as in a phase two trial. This is to ensure that all types of patients can be successfully and safely treated with the new medicine. Often trial populations are not truly representative of the general psoriasis or psoriatic arthritis population.

At the end of phase three the information needed for the product information leaflet (PIL) and drug label will be completed.

There is a lot of medical jargon involved in explaining types of clinical trials. It is essential that anyone involved in any type of research completely understands the procedure, has all the facts and gives consent to take part. Any researcher must be responsible for minimising jargon used and explaining any unclear terms.

Phase four:

Once a drug has completed phase three trials, the pharmaceutical company will apply for a medical licence for the drug to become available for doctors to prescribe. Once this happens, phase four trials continue to monitor use of the drug and its results, such as any adverse events reported by doctors and patients, in the interest of safety.

Some terms used when discussing clinical research trials include:

Randomised and blinded trials

When someone takes part in a research trial which involves testing either one treatment against another or against a placebo, the treatment will be chosen at random (such as the researcher giving the volunteer a number rather than a name of treatment); participants cannot choose their treatment.

The researcher in charge of the trial may or may not be aware of which treatment each participant receives. If they are not aware, the trial is known as blind. The medicine that all the patients are given will look the same, whether it is

the new treatment, an existing treatment, or placebo.

A double-blinded clinical trial is where neither the volunteer nor the person in charge of the clinical trial knows which treatment is being used.

This process of randomisation and blinding is designed to make sure that any positive effect of a new medicine is because the treatment is effective, and not because researchers chose patients who were more likely to respond positively. While there may be no doubt that the clinical trial is being carried out properly, these processes are used as proof to all medical professionals that the research has been conducted to the highest standards.

Placebo-controlled

A placebo is an inactive dummy treatment that may be given instead of the drug being tested. A placebo is used to prevent volunteers, and often researchers, knowing whether they are taking the potential treatment or not. Consciously or otherwise, knowing they're taking the drug can affect the results of a trial. A placebo-controlled trial is a clinical trial where a placebo is used to test results against those of the potential treatment.

Who is in charge of the clinical trial?

The person in charge of a clinical trial is called the chief investigator (CI). The CI may oversee trials taking place in many centres across the UK. The person in charge of one hospital's volunteers is called the principal investigator (PI). The person who asks people to take part in a clinical trial (typically a doctor, nurse or researcher) should have all the information a volunteer may need to know about the study. Any information about a trial which is distributed should contain the CI's name and the name and contact details of someone who can be contacted with questions in the event of an emergency.

Why are people asked to take part in clinical trials?

Clinical research is vital to improve the lives of people with diseases by enabling improvements in healthcare. No new medicines would become available unless volunteers took part in clinical trials, because products must be considered safe and effective before being made more widely available.

Who can participate in clinical trials?

Each trial will have a defined set of criteria to work out who can volunteer for which trial. Each volunteer is asked a set of questions to decide whether he or she would qualify for the clinical trial. For example, if a patient has psoriasis without psoriatic arthritis, it would not be useful to hear all the details of a clinical trial for a treatment requiring volunteers to have both.

Where a clinical trial requires a change in treatments, a participant must consider how their psoriasis or psoriatic arthritis may respond to time with no treatment or to changes in treatment, and that new treatments may not necessarily be effective for the disease at all.

What questions should volunteers ask?

■ What is the aim of the research?

Clinical research should be done with a specific aim of improvements and these should be clearly explained by the researcher asking you to take part.

■ Who qualifies?

Many research projects have specific lists of the types of patients, such as their age when psoriasis first developed, which treatments they currently use, etc.

■ What is the point of the trial and how will it help people?

Participants should feel satisfied that the trial is worthwhile and that it is asking a useful question.

■ How long will the clinical trial last?

This varies greatly but must be practical for the volunteer. Considerations to take into account include the venue, frequency of visits and any impact on work or family life. If attendance involves travelling, travel expenses can be reimbursed.

■ Can trial participants withdraw at any time?

Yes. All ethics committees require this for all trials. Patients have the right to withdraw at any time; they do not have to give a reason if they prefer not to.

Most practical questions will be answered in the patient information leaflet, a mandatory leaflet which is given to any potential research volunteer. Volunteers should be asked if they have any questions before volunteering or taking part.

Remember, all participation in research is entirely voluntary and volunteers should never feel obliged to take part in any way. Any volunteer who later changes their mind must always be allowed to make this choice.

Receiving care should in no way depend on volunteering for research.

Questions that should have been answered by the researcher include:

- what are the possible side effects of the treatment?
- who can be contacted if there is a problem?
- will someone be available to contact 24 hours a day?

What might a volunteer be asked to do during a clinical trial?

This will depend on the clinical trial and can be complicated. Some common measurements that may take place include:

- measurements of psoriasis: the most common form completed is the Psoriasis Area Severity Index (PASI). PASI is a measure of how severe psoriasis is, based on looking at redness, scaling and thickness of plaques across areas of the body
- measurements of psoriatic arthritis: this may include “counting” the number of tender and/or swollen joints, assessing pain at different sites, the amount of swelling of fingers and toes, and movement of the spine



- questionnaires about their disease: often researchers use questionnaires to assess symptoms of psoriasis or psoriatic arthritis, quality of life and impact of the disease on your daily life
- blood or skin samples in the form of a skin biopsy.

Researchers may measure psoriasis in other ways. The researcher may ask for opinions or measure it by looking at the area themselves.

- **Erythema (redness):** the investigator will assess the extent of redness on the treated areas
- **Dryness:** this is defined as tight sensations on the treated area due to the unusual dryness of the skin. The dermatologist will feel the treated area and ask if the participant has experienced sensations of this sort during the treatment period
- **Desquamation:** the abnormal shedding or peeling of the skin. The dermatologist will assess this by looking closely at the treated area
- **Infiltration:** this is a simple evaluation to assess the hardness or firmness of the tissue around the lesion.

When measuring activity of psoriatic arthritis, researchers commonly assess tenderness and swelling in the joints, tenderness at tendon insertions and measurements of flexibility in the spine.

In patient-completed questionnaires, patients are often asked about their symptoms of psoriasis and psoriatic arthritis and how these conditions impact on their life. For psoriasis, questions ask about symptoms such as burning or itching related to psoriasis. For psoriatic arthritis, questions ask about symptoms such as pain and stiffness.

Psoriasis and psoriatic arthritis are known to affect quality of life, to varying degrees depending on the individual. Many studies use questionnaires to assess this. It may seem that some of the questions asked during a trial are rather unnecessary and may be more detailed or personal than you expect. Participants don't have to answer if they don't want to, but researchers are trying to assess the full impact of the disease from the patient's perspective, so more detailed information can benefit the trial.

What are the risks and benefits of taking part in a clinical trial?

Participants will be monitored carefully during and after any trial. They will have regular evaluations and will sometimes

be asked questions about how they are feeling in general. This process might mean going to the hospital more regularly than usual.

Taking part in a clinical trial does not guarantee better treatment, nor will it automatically guarantee receiving the treatment being tested. However, because participants are so closely monitored, any changes, for better or for worse, will be quickly picked up and acted upon.

Being part of a research trial helps to improve scientific understanding of psoriasis and psoriatic arthritis and the best means of treatment. However, this does not mean that anyone should feel obliged to take part and it is always possible to withdraw from a trial at any time.

What should researchers tell participants?

Researchers, or anybody else who suggests taking part in a trial, should explain everything about the study and answer any questions.

- They cannot give out a copy of the protocol since this is a scientific document containing confidential information
- They should give volunteers a leaflet or fact sheet about the trial, which can be taken away and read at leisure
- Volunteers will be asked to give written consent. Withdrawing or refusing consent will not affect overall care and doctors will not hold it against them.

A new treatment may have side effects that cannot be predicted. This is why it's so important to have the name and number of a contact for the clinical trial to contact in the event of an emergency.

How can I find out more about clinical trials in psoriasis or psoriatic arthritis?

You can ask your general practitioner, nurse, dermatologist or rheumatologist. Often clinical trials are advertised in local and national media, including newspapers or on the radio. Sometimes hospitals will advertise on the outpatient notice board and on their websites.

You may also find the following website useful: www.nhs.uk/Conditions/Clinical-trials

Are there guidelines about research?

Yes, there are guidelines for researchers about the sort of information that volunteers need in order to decide whether to take part in a clinical trial. However, there is a lot of debate about how much information volunteers actually require, since this varies from person to person. The important thing is that participants are satisfied that they have enough information to make an informed decision. So, you should feel free to ask any questions and be given enough time to consider your options before making a decision. Remember, if you are considering taking part in a trial you are always free to discuss this decision with friends and relatives or other healthcare providers, including your general practitioner or a specialist.

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Further references used in the production of PAPAA information can be found at: www.papaa.org/resources/references.

About this information

This material was produced by PAPAA. Please be aware that research and development of treatments is ongoing. For the latest information or any amendments to this material please contact us or visit our website www.papaa.org. The site contains information on treatments and includes patient experiences and case histories.

This material was reviewed and fully revised in 2012 by Dr Amy Foulkes, MRC clinical research fellow based at the University of Manchester and by Dr Laura Coates, rheumatologist and NIHR clinical lecturer, University of Leeds, Chapel Allerton Hospital, February 2016.

A lay and peer review panel has provided key feedback on this leaflet. The panel includes people with or affected by psoriasis and/or psoriatic arthritis.

Published: March 2016

Review date: October 2018

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The charity for people with psoriasis and psoriatic arthritis

**PAPAA, the single identity of the
Psoriatic Arthropathy Alliance and the
Psoriasis Support Trust.**

**The organisation is independently funded and is a
principal source of information and educational
material for people with psoriasis and psoriatic
arthritis in the UK.**

**PAPAA supports both patients and professionals by
providing material that can be trusted (evidence-
based), which has been approved and contains no
bias or agendas.**

**PAPAA provides positive advice that enables people
to be involved, as they move through
their healthcare journey, in an informed way
which is appropriate for their needs and any
changing circumstances.**

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Registered Charity No. 1118192

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