Clinical Trials: An overview

This information is produced by the Psoriasis and Psoriatic Arthritis Alliance

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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.

To learn more about psoriasis and psoriatic arthritis, see our leaflets ***What is Psoriasis?*** and ***What is Psoriatic Arthritis?***

Introduction to treatments

There are many available treatments for psoriasis and psoriatic arthritis, including topical applications to the skin, systemic therapies taken as tablets and liquids, injections, physical therapy, surgery, light treatment, mechanical pain relief, talking therapies, self-help and complementary supplements that might include dietary interventions. For more information, see our leaflets ***Treatments for Psoriasis: an overview*** and ***Treatments for Psoriatic Arthritis: an overview***.

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 develop, 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 which is 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 to evaluate medical, surgical or behavioural intervention.

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.

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 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 the following.

- **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 and nurses**
  From the relevant specialty, such as dermatology for psoriasis or rheumatology for psoriatic arthritis.

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 and address of anybody else 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 process 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
- protocol is suitable for the needs of the trial
- probable benefits of a new treatment outweigh the risks of side effects
- information given to participants is sufficient
- way in which people will be recruited is correct
- 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 or other intervention 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.

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. Although, this is not the end of the process, in the interest of safety, continuous monitoring of the drug takes place. This will include doctors and patients reporting any adverse events.

Terminology

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. Below are some of the terms used when discussing clinical research trials.

Randomised and blinded trials
When someone takes part in a research trial which involves testing one treatment against another or against a placebo, the treatment will usually be

based on randomisation, which means that the treatment for each patient is chosen at random (the researcher may give the volunteer a number rather than the 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 a 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 the possibility that new treatments may not necessarily be effective for the disease at all.

What questions should volunteers ask?

Most practical questions will be answered in the patient information leaflet, a mandatory leaflet which is given to any potential research volunteer. Below are some of the questions often asked.

- **What is the aim of the research?**
  Clinical research should be carried out with the aim of achieving specific 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 their condition 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 the trial is seeking to answer 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.
- **Will travelling expenses be reimbursed?**
  This is something that needs to be considered given that it may require attendance on a regular basis.
- **Can trial participants withdraw at any time?**
  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.

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

What will a trial participant be asked to do?

This will depend on the clinical trial and can be complicated. Generally, for both psoriasis and psoriatic arthritis, there may be a number of clinical assessments to undertake. These will possibly be overseen by a nurse, and may include blood pressure, psoriasis scores, measurements of pain and swelling in joints etc. Sometimes blood, or skin samples in the form of a skin biopsy, might be taken to assess and measure other benefits or risks that you may not be able to notice.

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 conditions from a patient's perspective, so more detailed information can benefit the trial.

Questionnaires are designed to see how the condition affects you and whether the intervention or treatment has improved or helped you to feel better.

You may be asked to use a new treatment, an existing treatment or in some cases a dummy treatment (placebo) if the trial is comparing the effectiveness of new compounds such as a tablet, cream or injection.

At all times you will be asked to report the benefits and any adverse events (side effects) that you have experienced. These will all be included in the data collection to provide an accurate assessment of the benefits and risks, which usually can only be obtained from real people who act as volunteers within a clinical 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. More widely, clinical trials are advertised via newspapers, TV, radio, online and social media. 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, and even other healthcare providers, including your general practitioner or a specialist, BEFORE you take part.

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, consultant rheumatologist and NIHR clinical scientist, University of Oxford and Nuffield Orthopaedic Hospital, in February 2016 and January 2019, with minor editorial revisions by PAPAA in January 2020.

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.

Quality and accuracy

The standard by which we produce information is based on the Information Standard scheme that was developed by the Department of Health and administered by NHS England. The scheme ended on 31 July 2019.

As a former member organisation of the scheme, we have committed to continue to uphold the principals of the scheme and will produce material that is clear, accurate, evidence-based, up-to-date and easy to use, which allows people, patients and communities to become better informed and more involved in their health and care.

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