

Clinical trials for brain tumours

The purpose of clinical trials for brain tumour patients is to gain a better understanding of these tumours and improve diagnosis and treatment.

Some trials also seek to control symptoms more effectively and improve quality of life for those living with a tumour.

By their definition, clinical trials are experimental, and while the hope is that they will be beneficial, there's no guarantee.

As well as clinical trials for adults there are also dedicated trials for children and young people.

In this fact sheet:

- What is a clinical trial?
- What are the different phases of a clinical trial?
- What are the benefits and risks of taking part in a clinical trial?
- How do I find clinical trials?
- Answers to some commonly asked questions you may have about clinical trials.

What is a clinical trial?

A clinical trial is an experiment that involves patients in a new way of managing a condition. This might include:

- investigating a new treatment
- giving an existing treatment in a new way
- a new approach to diagnosing an illness
- assessing an outcome after treatment.

The term treatment includes drugs, cells and other biological products; treatment procedures; and treatment devices.

A clinical trial aims to find out:

- if the treatment works
- what the best dose/length of treatment is
- how different people and tumours react to the treatment
- if it's safe
- if it can be used with other treatments safely and effectively
- if it's better than the treatments we are using now.

Trials are vital to establish whether a new approach is better than the old one - if it isn't, there's little point in persisting with it.

Before treatments can be tested on people, pre-clinical studies on the treatment have to be carried out in the laboratory. These are to test for safety and whether the treatment is likely to be effective.

If the treatment shows promise and is safe, it will then be tested on people in clinical trials.

What are the different phases of a clinical trial?

A clinical trial has up to 5 phases, each of which can take some time. Developing a new way of treating a condition can therefore be a lengthy process.

It can take 10 to 15 years or more for a treatment to go from initial design to becoming a standard treatment in the clinic.

(This is sometimes referred to as the journey from bench to bedside.)

Many treatments don't make it at all.

Phase 0

Not all treatments will go through a phase 0 trial.

A phase 0 clinical trial usually uses small, non-therapeutic doses of a drug to see what it does in people.

Non-therapeutic means the dose is too small to treat your tumour, but it also means you're less likely to have side-effects.

Their aim is to speed up the development of promising drugs by testing them in humans rather than animals. This can give the scientists the information more quickly and may mean the results are more reliable.

Phase 1

A phase 1 clinical trial is usually the earliest trial of a treatment in people. It aims to find out:

- if the treatment is safe for people to use
- the right dose to use, how often to give it and for how long (this is called the dose regime or dosage regimen.)
- what the side-effects are.

Often a very low dosage is given to the first few patients. If there are no side-effects amongst this group, the next group of patients is given a slightly higher dose, and so on until side-effects are experienced that suggest it would be unsafe to increase the dosage any further.

This is known as the maximum tolerated dose or MTD. It's the last dose where there were little or no side-effects and it helps determine the dose for the next studies.

Sometimes a researcher may stop the trial before an MTD is reached, or sometimes a drug is considered to be safe enough to progress with the study at, or near, the maximum treatment dose.

As well as safety, researchers will also look at how the body copes with the treatment and if it might be useful. If the treatment is safe, it will be progressed to phase 2.

Phase 1 trials tend to:

- **be carried out in specialised clinical research units, rather than local hospitals**
- **recruit only a few patients**
- **last several months.**

Patients will receive optimum care and attention while in the unit.

Phase 2

Not all treatments tested in phase 1 make it to phase 2.

A phase 2 clinical trial aims to find out:

- more about the safety
- more about the side-effects
- initial evidence about whether the new treatment does what is hoped (this is called its efficacy).

The new treatment is often compared to an existing treatment or to a dummy drug (placebo).

It may be what is called a randomised trial. This means that people are put into the different treatment groups at random.

Researchers will ask questions such as:

- Is it any good?
- Does it shrink the tumour?
(known as the response to the treatment)
- Does it keep the tumour away for longer?
(This is known as progression-free survival or PFS.)
- Does it make the patient feel better?
- Is the treatment safe and well-tolerated?

Phase 2 trials tend to:

- use a larger group of patients (up to about 100)
- last for a couple of years.

If the technique looks promising, then it will proceed to phase 3.

Most drugs that fail during clinical trials do so at phase 2 because they turn out to be ineffective, have safety problems or have intolerable side-effects.

Phase 3

A phase 3 aims to find out:

- whether the new treatment works better than the best existing 'standard' treatment.

This is done by comparing two groups of patients with similar characteristics. Some of the patients receive the standard treatment and some receive the new treatment. The outcome of the two groups is compared to see whether the new treatment is better.

These trials are often 'randomised, blind trials', which are the most successful way of ensuring that the results of the trial are not biased and a true comparison has been made. The researchers can therefore be more confident in the validity (certainty) of the results of the trial.

Some phase 3 trials also look at whether the new treatment produces fewer side-effects.

Phase 3 trials tend to:

- involve thousands of patients
- take place in many different hospitals across different countries
- last for several years.

Randomisation

Which treatment a patient receives (standard or new) is allocated by chance (at random) – like tossing a coin. Neither the researcher nor the patient can influence this decision.

Blinding

Single blind - the trial researcher knows which treatment the patient is receiving, but the patient doesn't.

Double blind - neither the patient nor the researcher knows which treatment the patient is receiving.

Placebo

A dummy drug which is given in blind tests, so that the patient doesn't know if they're getting the new treatment.

Phase 4

Phase 4 trials are conducted when a drug has been shown to work and has been licensed to treat an illness. This phase aims to find out what happens when the drug is given to thousands of people in the general community. The aim is to assess any long-term risks and benefits of the drug, and any rare side-effects.

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

- The clinical trial is running because it's believed that the new treatment may be better than the standard treatment. This means you may be receiving a better treatment - but there's no guarantee.
- It gives you access to a treatment that you would not normally be offered - and, if the trial treatment is an improvement, you may be one of the first patients to benefit from it.
- Some patients report that they are pleased to be helping advance science, even if they don't benefit directly. Without trialling a new treatment, no further progress could ever be made.
- While you're taking part in a trial, you're often even more carefully monitored. This means that any changes to your health – even if they're not related to the new drug - might be picked up and dealt with quickly.

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

- The clinical trial is going ahead because the researchers have a good reason to believe it may be better than the standard treatment. However, clinical trials are experimental by nature and there's a chance that the new

treatment will be no better than, or even not as good as, the standard treatment.

- In a randomised, blind trial, you may not be receiving the new treatment.
- Unexpected side-effects are a possibility, although the researchers will monitor you closely while you're in the trial and make every effort to keep these to a minimum.
- As trial participation may require additional visits to hospital, you should also consider the possible extra costs in time and money. This is particularly the case if you take part in a trial in another area of the country or abroad.
- Before participating you should consider if taking part in the trial will affect any insurance you have, and seek advice if necessary.

How do I know if a clinical trial is safe to enter?

The UK has some of the most rigorous patient protection practices in the world, including (but not limited to):

- **Medicines and Healthcare Products Regulatory Agency (MHRA)**
A body that ensures the trial products meet international standards of good practice.
- **Research Ethics Committee**
A board that makes sure patients' well-being and rights are maintained. They also make sure that information given to patients tells them everything they need to know and is easy to understand.
- **Clinical trial committees**
All trials are scrutinised at national or local level (often both) to ensure their design and implementation are appropriate and scientifically sound.

How do I find clinical trials?

Please speak to your health team about trials that may be suitable for you.

In addition, The Brain Tumour Charity's Information and Support Team can search online clinical databases for clinical trials for your specific tumour type. Please contact 0808 800 0004 or ***support@thebraintumourcharity.org***

If you are looking for clinical trials for children, please get in touch with our dedicated Children and Families Team who are here to help – ***childrenandfamilies@thebraintumourcharity.org***

It's important to be aware that every trial has a set of entry criteria that you must fit to be able to enter.

The following websites also list current clinical trials:

- **Cancer Research UK**
cancerresearchuk.org/about-cancer/find-a-clinical-trial
- **Clinical Trials.gov**
Provided by the US National Library of Medicine, it's a database of privately and publicly funded studies around the world.
clinicaltrials.gov
- **UK Clinical Trials Gateway**
Provided by the NHS National Institute for Health Research.
ukctg.nihr.ac.uk
- **SHARE**
SHARE is an NHS Research Scotland initiative created to establish a register of people interested in participating in health research. People on the register agree to allow SHARE to use the coded data in their various NHS computer records to check whether they might be suitable for health research studies.
registerforshare.org

How am I selected for a clinical trial?

Some entry criteria will be specified before you enter. Others won't, but will require trial-specific tests, which can only be carried out once you've agreed in principle to enter the trial.

What happens if I agree in principle to enter a trial, but then don't meet all of the criteria?

You won't be allowed to enter a clinical trial unless you meet all of the criteria. If you can't enter the trial, your doctor will talk through any alternative treatments available to you or suitable clinical trials.

What happens if I agree to enter a trial, but then change my mind?

You're free to leave a trial at any time without having to explain why.

How can I get on to a trial if my hospital doesn't offer it?

This may not be easy. Individuals in clinical trials often require close surveillance, which means having easy access to the trial site. It can mean travelling and staying near the site.

Sometimes a trial is geared to taking patients from other regions. The best thing is to discuss your wishes with your health team to see if particular arrangements can be made.

How long do I stay on the trial?

The trial will go on until one of the following happens:

- The trial comes to an end - as defined in its protocol.

This is a document detailing the design and implementation of the trial, e.g. in phase 1, when the maximum tolerated dose is reached.
- If the treatment is clearly failing or there are safety concerns, the trial will be stopped.
- If your doctors believe it's in your best interest to take you off the trial, they'll do so, as they have a duty of care to you.
- You decide to withdraw. It's your right to leave the trial at any time you wish, without having to give a reason.

Will I be paid to take part?

No, it would be unusual for patients to be paid for taking part in an oncology trial. You can ask your local doctor or nurse if there are any local arrangements they can offer, e.g. access to hospital transport or free/reduced parking.

Potential new ways of running research

Adaptive clinical trials

Traditional clinical trials test only one drug or different aspect of treatment at a time and take several years to produce results - positive or negative.

This lack of flexibility in clinical trials has been one reason for the historically slow progress towards more effective treatments for high grade brain tumours.

These tumours progress very quickly and there is simply not enough time for a patient to take part in different trials, each of which tests a single potential treatment.

In an adaptive clinical trial, researchers can make changes to improve the existing trial, if early results suggest it isn't working or that something else might work better.

These changes are planned and made in such a way that the trial, and the evidence it provides, remain reliable.

Examples of some of the changes they can make include:

- adding in new drugs, combinations of therapies or different drug doses in response to a patient's improved or deteriorating condition
- changing the inclusion/exclusion criteria, i.e. who can and cannot take part in the trial
- changing the number of patients required.

The Brain Tumour Charity supports the development and funding of more adaptive clinical trials for patients with high grade brain tumours.

Find out more on our website:

thebraintumourcharity.org/media-centre/news/latest-news/what-adaptive-clinical-trial/

Research Involvement Network (RIN)

If you would like to be involved in shaping future research to make sure it meets the needs of those affected by brain tumours, you may like to become part of our Research Involvement Network.

You don't need a scientific or research background, just experience.

For more information, visit thebraintumourcharity.org/our-research/get-involved-in-research/research-involvement-network or contact us via rin@thebraintumourcharity.org

BRIAN

BRIAN (the **B**rain tumou**R** Information and **A**nalysis **N**etwork) is a new way for those affected by a brain tumour to learn from each other's experiences and about different parts of the journey. It will also help doctors and scientists access speed up research.

BRIAN is a databank – which isn't as scary as it sounds. It's somewhere where we'll securely and anonymously store data about people's treatment,

tumour types, experiences, side-effects, decisions and more, and then gain insights into all different types of brain tumour and help us reach a cure quicker.

Up till now, there's never been an easy way of learning on a large scale how and what other people living with a brain tumour have been through. BRIAN will change that.

The only way BRIAN will work properly is if people living with a brain tumour share information about what they've been through and are currently experiencing.

For more information, visit thebraintumourcharity.org/understanding-brain-tumours/getting-a-diagnosis/brian

What if I have further questions or need other support?

You can contact our Information and Support Team in the following ways:

- Call 0808 800 0004 (free from landlines and most mobiles including 3, O2, EE, Virgin and Vodafone)
- Email: support@thebraintumourcharity.org
- Live Chat: Get in touch with us online via thebraintumourcharity.org/live-chat
- Join one or more of our closed Facebook groups: bit.ly/FBSupportGroups
- Website: thebraintumourcharity.org/getsupport

Disclaimer

This resource contains information and general advice. It should not be used as a substitute for personalised advice from a qualified specialist professional. We strive to make sure that the content is accurate and up-to-date, but information can change over time.

Patients must seek advice from their medical teams before beginning or refraining from taking any medication or treatment.

The Brain Tumour Charity does not accept any liability to any person arising from the use of this resource.

About this information resource

The Brain Tumour Charity is proud to have been certified as a provider of high quality health and social care information by The Information Standard – an NHS standard that allows the public to identify reliable and trustworthy sources of information.

Written and edited by our Information and Support Team, the accuracy of medical information in this resource has been verified by leading health professionals specialising in neuro-oncology.

Our information resources have been produced with the assistance of patient and carer representatives and up-to-date, reliable sources of evidence.

We hope that this information will complement the medical advice you have already been given. Please do continue to talk to your medical team if you are worried about any medical issues.

If you would like a list of references for any of our information resources, or would like more information about how we produce them, please contact us.

We welcome your comments on this information resource, so we can improve. Please give us your feedback via our Information and Support Team on **0808 800 0004** or support@thebraintumourcharity.org

About us

The Brain Tumour Charity is at the forefront of the fight to defeat brain tumours and is the only national charity making a difference every day to the lives of people with a brain tumour and their families. We fund pioneering research worldwide, raise awareness of the symptoms and effects of brain tumours and provide support for everyone affected to improve quality of life.

We wouldn't be able to make the progress we have without the incredible input we receive from you, our community.

Whether it's reviewing our information resources, campaigning for change, reviewing research proposals or attending cheque presentations, everything you do helps to make the difference.

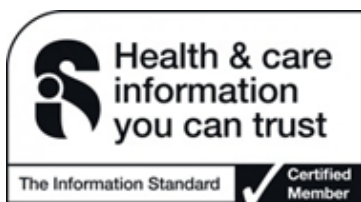
To find out more about the different ways you can get involved, please visit thebraintumourcharity.org/volunteering

We rely 100% on charitable donations to fund our vital work. If you would like to make a donation, or want to find out about other ways to support us including leaving a gift in your will or fundraising through an event, please get

in touch: Visit thebraintumourcharity.org/get-involved, call us on 01252 749043 or email fundraising@thebraintumourcharity.org

Clinical trials

Your notes



Hartshead House
61-65 Victoria Road
Farnborough
Hampshire
GU14 7PA
01252 749990
enquiries@thebraintumourcharity.org
www.thebraintumourcharity.org

© The Brain Tumour Charity 2018. Registered Charity Number 1150054 (England and Wales) and SC045081 (Scotland).

Version 8.0 (clear print). First produced in standard print format June 2018.
Review date, May 2021.