

Cirted

Combined Immunosuppression and Radiotherapy in Thyroid Eye Disease Trial

Patient Information Sheet

Study Title:

Combined Immunosuppression and Radiotherapy in Thyroid Eye Disease (CIRTED)

Invitation to take part in this research project:

You have been sent this information because you have been referred to either Moorfields Eye Hospital or Bristol Eye Hospital for the specialist care of your Thyroid Eye Disease, and we are conducting a research study into the best treatment for this condition. If we confirm at your first outpatient visit that you have active Thyroid Eye Disease and are eligible to participate in this research you will be invited to take part.

Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with your friends, relatives and your GP if you wish. Ask us if there is anything that is not clear or if you would like more information (telephone numbers are listed at the end of this sheet). Take time to decide whether or not you would wish to take part.

Thank you for reading this Information Sheet.

What is the purpose of the study?

To establish whether:

- a. Radiotherapy or
- b. Azathioprine (a tablet which suppresses the immune system) are effective treatments for Thyroid Eye Disease.

Eye specialists do not know which treatments work best in patients with severe Thyroid Eye Disease. Some doctors recommend radiotherapy (while others do not) and some doctors recommend taking tablets which suppress the immune system such as azathioprine (while others do not). Both treatments are used widely, but the decision to prescribe radiotherapy or azathioprine largely depends on the beliefs of the eye specialist caring for the patient. Whether a patient receives either, both or none of these treatments really depends on which hospital they attend, and at present there is no high-quality medical evidence to say whether it is right or wrong for patients to be given these treatments.

The main goal of this study is to provide information about whether these treatments are useful for patients with active Thyroid Eye Disease. It should establish the evidence we need to give proper advice to patients about the benefits and risks of these treatments

Patients attending the Thyroid Eye Disease Clinics at Moorfields Eye Hospital, London and Bristol Eye Hospital are being invited to take part. Between both Centres we hope to involve 160 patients.

Why have I been sent this information sheet?

You are being sent information about this study because you have been referred to either Bristol Eye Hospital or Moorfields Eye Hospital for the specialist care of your Thyroid Eye Disease. You will only be formally chosen to take part in the study if we find that your Thyroid Eye Disease is active enough to potentially benefit from Radiotherapy or Azathioprine treatment when you are examined at your first outpatient visit.

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What is Radiotherapy, why is it used in Thyroid Eye Disease and is it safe?

Thyroid Eye Disease is caused by inflammation in the eye socket (orbit). Radiation is thought to destroy this inflammation and reduce the damage it causes. Modern radiotherapy techniques apply frequent, low-doses of radiation to a strictly defined area behind the eyeball, and it is generally considered to be a very safe form of treatment.

What is Azathioprine, why is it used in Thyroid Eye Disease and what are its side-effects?

You may already have received steroid tablets to treat your Thyroid Eye Disease. Steroids suppress the immune system and reduce inflammation. However, steroids have many side-effects and they cannot be continued long-term. This means that although patients often have a good initial response to steroids their Thyroid Eye Disease may get worse again when treatment stops.

Azathioprine is an alternative to steroids which can be used for longer periods of time. Used together with steroids it may control the orbital inflammation better than when steroids are used alone, and it has the potential to stop the disease becoming active again when steroid treatment stops. Azathioprine has been used by doctors for several decades and its safety profile is well known because it is used in many other inflammatory conditions. Most patients can take azathioprine without any problems but, like all immunosuppressant drugs, it has several potential side-effects.

A blood test is now available to calculate a person's risk of developing the main rare, but serious, side-effect (called bone marrow suppression) from taking Azathioprine. This will be taken at your first visit to the Eye Hospital. If you are found to be at-risk you will not be asked to take part in this study.

More minor side-effects, such as tiredness and nausea are not uncommon, but usually subside after a few weeks. Azathioprine can also cause changes in liver function which need to be monitored with blood tests. If you suffer any significant side-effects you will be asked to stop the treatment.

Do I have to take part in this study?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this Information Sheet to keep and you will be asked to sign a consent form.

If you decide to take part you are still free to withdraw at any time and without giving a reason. If you withdraw, this will not affect the standard of care that you receive.

What will happen before my first Eye Hospital appointment?

If you return the slip at the bottom of the letter which accompanies this patient information sheet a member of staff at the Eye Hospital will phone you to check a few details about your Thyroid Eye Disease and Past Medical History. We will also contact your General Practitioner and / or Thyroid Gland Specialist (Endocrinologist) so that we can find out the results of your most recent Thyroid Gland Function tests before you attend your first Eye Hospital visit. This preparation for your visit will be very helpful to us even if you do not decide to take part in this research.

What will happen at my first Eye Hospital appointment?

You will be reviewed by a team of doctors, nurses and eye movement experts (orthoptists) who will ask questions about your Thyroid Eye Disease and Past Medical History, take measurements of your eyes and (if appropriate) perform a general physical examination. You will also be asked for a urine sample. These are all standard assessments which will be done whether or not you participate in the trial.

If your Thyroid Eye Disease is found to be severe enough and there is no special reason why you should not take part in this

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research, you will be invited to enrol in the study. We will then do some blood tests to make sure it is safe for you to take Azathioprine. In addition you may have photographs taken of your face and eyes.

You will have as much time as you need to choose which treatments you wish to have and whether you want to enrol in this study. You will not be required to decide this at your first visit.

If you enrol in the study we will ask you to complete a questionnaire to measure how you feel about your Thyroid Eye Disease, appearance, vision and 'quality of life' as well as the personal financial costs you incur because of your Thyroid Eye Disease (for example, travel costs to attend medical appointments and income lost through time off work or spent on cosmetics and sunglasses).

If you enrol in the study you will be given a course of oral steroid tablets (prednisolone). This treatment is well known to be effective for Thyroid Eye Disease and would be recommended regardless of whether or not you decide to take part.

What will happen to me if I take part?

You will be reviewed at the Eye Hospital 2 weeks after starting steroid tablets. If your TED has not improved despite this treatment there is unlikely to be any benefit in treating you with Radiotherapy and Azathioprine and you will not continue to take part in the study.

If, as expected, your TED improves with steroid treatment, you will continue in the trial. This means that (in addition to steroids) you will be given either:

1. Azathioprine

OR

2. Azathioprine placebo (see 10b below)

PLUS either:

1. Radiotherapy

OR

2. Sham-radiotherapy (see 10b below)

We do not know whether treatment with Radiotherapy and / or Azathioprine is beneficial for active Thyroid Eye Disease, and the aim of this study is to compare patients receiving these different treatments.

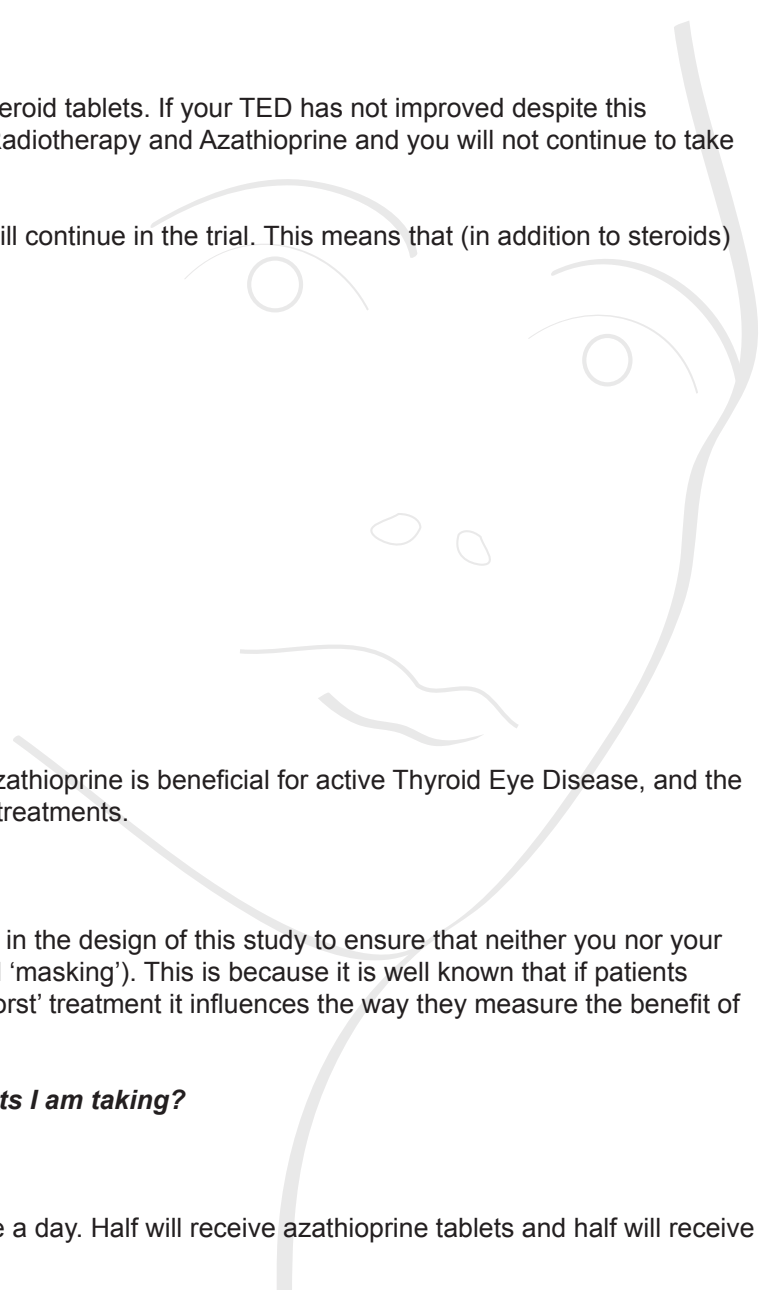
a. *Will I know what treatments I am taking?*

No, not until the end of the study. Great lengths have been taken in the design of this study to ensure that neither you nor your doctor will know what treatments you receive (a procedure called 'masking'). This is because it is well known that if patients receive what they and / or their doctor believes is the 'best' or 'worst' treatment it influences the way they measure the benefit of the treatment.

b. *How will I be prevented from knowing what treatments I am taking?*

Azathioprine

All patients enrolled in the study will be given tablets to take once a day. Half will receive azathioprine tablets and half will receive



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a dummy azathioprine tablet (called a placebo), which looks like the real thing but is not (it contains no active ingredient).

The number of tablets you are asked to take will initially be determined by your body weight and the 'dose' may change later in the study (regardless of whether you are taking azathioprine or placebo).

Radiotherapy

All patients enrolled in the study will be referred for radiotherapy, but half the patients will receive 'sham' treatment. This means that they will attend for their radiotherapy appointments but that the radiotherapy machine will not be turned on. All the treatment preparation will be the same, and the machine will still make the sound it does during normal treatment, but it will not emit any radiation.

c. *In an emergency, can I find out what treatments I am taking?*

Yes. The doctors running the study carry a pager which you can contact 24 hrs a day for this purpose. However, if you find out which treatments you have been given you will no longer be able to take part in the study.

d. *How will the decision about which treatments I receive be made?*

Neither you nor the study staff will have any influence over which treatments you receive. This will be selected by a computer on the basis of chance, that is randomly, like flipping a coin.

You have an equal chance of being allocated to any of the treatments. So, if you take part in this study there is a:

1 in 2 chance (50%) of receiving azathioprine tablets and a 1 in 2 chance (50%) of receiving placebo tablets

PLUS a

1 in 2 chance (50%) of receiving radiotherapy and a 1 in 2 chance (50%) of receiving sham-radiotherapy

Because 2 treatments are being tested in this study this means that there is a:

- 1 in 4 chance (25%) of you receiving azathioprine tablets and radiotherapy
- 1 in 4 chance (25%) of you receiving azathioprine tablets and sham-radiotherapy
- 1 in 4 chance (25%) of you receiving placebo tablets and radiotherapy
- 1 in 4 chance (25%) of you receiving placebo tablets and sham-radiotherapy

No patients will be left 'untreated' and all study participants will receive a standard 6 month course of oral steroids (prednisolone)

e. *How long will I be in the study?*

1 year

f. *How often will I need to be reviewed and will this involve more visits to the Eye Hospital than if I did not take part?*

Timing of follow-up visits:

You will be seen 2 weeks after enrolling in the study and starting high-dose steroids to check how well you are responding to (and tolerating) this treatment. A further review will be arranged 4 weeks later. Subsequent visits will be booked every 12 weeks. This is standard practice at the Eye Hospitals, whether or not you participate in this study.

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Timing of Azathioprine Treatment and Follow-up:

Two weeks after enrolling in the study you will start azathioprine or placebo tablets. These will continue for the remaining 11 ½ months of the study.

Regular blood tests are required to monitor for azathioprine side-effects. These will be taken every week for 4 weeks after starting the treatment, and then every 2 months. They can be done at your General Practitioner's surgery or the Eye Hospital, whichever is more convenient. These blood tests are required for patients taking Azathioprine whether or not they take part in the study. The members of the research team who review your blood test results (who you will never meet) will know whether you are taking azathioprine or placebo. If the results are abnormal, they will arrange a repeat blood test and /or for your drug dose to be adjusted (or stopped) accordingly.

Timing of Radiotherapy and Follow-up:

Radiotherapy will typically begin about 6 weeks after you enrol in the study (depending on the availability of the radiotherapy appointments). It lasts for 2 - 3 weeks and involves 12 visits for treatment.

This is exactly the same radiotherapy treatment regime that London patients will receive whether or not they participate in the trial. However, some of the appointments for patients who participate in the trial in London will be outside usual working hours. We expect that this will be more convenient for some individuals. If you are entitled to patient transport this will still be provided out-of-hours.

Bristol patients receiving radiotherapy for Thyroid Eye Disease, but who do not take part in this study, will have the same total radiation dose given over 10 sessions rather than 12. This means that if you take part in the study in Bristol you will have 2 extra visits for radiotherapy than you would have if you did not take part. We will pay the travel costs for these extra visits.

g. Will I still need the blood tests to monitor for azathioprine side-effects if I am taking the placebo?

Yes. This is the only way to make sure that you and your doctor do not know what treatment you have been given. Not all these blood tests will be unnecessary and you would need to have some tests done to check your Thyroid Gland Function and response to steroids anyway.

A small number of patients taking azathioprine (less than 5%) will need to be recalled for repeat blood tests and have their drug dose changed. In order to make sure that this does not reveal which treatment group they are in we will also ask some patients taking placebo tablets to have repeat blood tests and to change the number of tablets they take each day. If you are in the placebo group of treatment, the chance that you will be recalled for these unnecessary tests is also less than 5%.

All blood tests can be done at your General Practitioner's surgery or the Eye Hospital, whichever is most convenient.

h. What will happen at each of the follow-up visits?

You will be seen by the same Eye Specialist and Orthoptist at each visit.

They will conduct a detailed examination of your eyes and ask questions about your Thyroid Eye Disease, general health, and medications. In addition your urine will be checked and you may need further blood tests as well as repeat photographs of your face and eyes.

The questionnaire you will have completed at your first visit (regarding your appearance, visual function and 'quality of life') will only be repeated on 2 further occasions - 6 weeks after you receive radiotherapy and at the end of the trial (1 year after you enrol). It is not required at every follow-up visit.

i. Are there any other assessments I may be asked to have if I take part in the study?

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Sixteen patients (10% of the total number participating in the trial) will be interviewed by a member of the research staff to explore the issues covered by the quality of life questionnaires in more detail. The aim of these interviews is to gain a better understanding of how Thyroid Eye Disease and its treatment affects your life, and to determine whether the questionnaires we use are able to measure this appropriately.

These interviews are entirely optional and you will be asked at the start of the study whether or not you would be happy to take part - there is absolutely no obligation for you to do so. The researchers will decide which patients are selected for interview from those who volunteer.

If you take part in the interviews you will be interviewed on 3 separate occasions; at the first follow-up visit, 6 weeks after radiotherapy and at the end of the trial. These times coincide with planned hospital appointments and will not involve extra visits. The interview will take the form of an informal conversation-style talk lasting about 30 minutes. With your permission the conversation will be tape-recorded. This is to save time during the interview session, since taking notes is very time-consuming, and it also results in less confusion about what you said during the conversation. Before the interview takes place you will be given an opportunity to ask any questions. It should be noted that you can withdraw at any time - including during the interview itself.

The conversation will be transcribed resulting in a script of the conversation. The scripts from all the interviews will be analysed for important issues and a report will be generated.

What you say in the interview will be confidential. The tape of the conversation will be kept in a secure place until it has been transcribed, resulting in a script. Care will be taken to ensure that any information which might identify you is removed. Only the researcher will have access to the tape and script. Once the script has been generated the tape will be erased. The script will carry no identifying marks, so no one will be able to tell that it was your interview. When not in use by the researcher, all the scripts will be kept in a locked filing cabinet. The scripts will be destroyed at the end of the study.

j. If I take part in the study will I be asked to give any blood samples, or have any other tests?

Yes. These tests fall into 3 categories.

- **Necessary** blood tests that are required as part of your usual care, and would be taken whether or not you participate in the study. For example, thyroid gland function tests and tests to make sure that you are tolerating the medications we prescribe for you.
- **Optional** blood tests which would not be taken if you were not taking part in the study. These can be done at the same time that you are having the 'necessary' blood tests. You can choose which (if any) of these blood tests you are happy to give.
- **Optional** tear tests which would not be taken if you were not participating in the study.
- **Optional** Magnetic Resonance Imaging (MRI) scans of your eyes (applies only to London patients):

Details of the OPTIONAL blood and tear tests are given below:

OPTIONAL BLOOD TESTS BEFORE AND AFTER STARTING STEROID TREATMENT:

We are developing a new laboratory test to predict and monitor an individual's response to steroids and other immunosuppressive drugs. This has the potential to enable drug treatments to be tested and tailored to an individual before they start therapy, which would be of great benefit to patients with TED and other inflammatory conditions.

In order to see whether our new test works we need a special blood sample (up to 50mls, which is roughly equivalent to a small cup-full) before you begin taking high-dose steroids at the start of the study, and again 2 weeks later. This is larger than a normal blood test but it is not harmful.

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OTHER OPTIONAL BLOOD TESTS:

There are two more blood tests that we would like to take at each visit as part of the research study. If you agree to this an additional 20 mls (just over a table-spoon full) of blood will be taken.

These tests will help us to find out more about the causes of TED. We will also use them to try out new ways of monitoring and improving Azathioprine treatment.

None of the blood tests described (above) will be kept for use in future research. However, with your permission, we would keep 20mls (just over a tablespoon full) of the blood you give over the whole course of the study in storage as a resource for use in future experiments. At present, we do not know exactly what tests will be done on these samples, but they may include investigations into the role the immune system or genes in the development of TED.

Stored samples will be made anonymous, which means that they cannot be traced back to you and you will never be able to find out the results of tests done on them. A Research Ethics Committee would also need to specifically review and approve their use once the details of the planned experiments were known.

TEAR TESTS:

We are also developing a new test which uses tears to try and calculate the severity of an individual's TED. If it works, this would potentially be very useful in deciding which patients should receive immunosuppressive treatment.

If you agree, we will take a small tear sample at each visit for use in this research. The tears are taken either with a piece of filter paper (or sponge) which rests on the edge of your eyelid (this takes about 5 minutes), or by placing a small 'capillary' tube on the outer corner of your eye.

This is a very simple test and you should not come to any harm from it. Most people don't mind having the tear sample taken, but if you are irritated by the filter paper or tube resting on your eyelid a drop of local anaesthetic can be put in the eye to make it comfortable.

Some of the tear samples will also be stored, with your permission, for use in future research. Like the stored blood samples, these will be made anonymous and their use would be subject to the approval of a Research Ethics Committee.

Details of the OPTIONAL Magnetic Resonance Imaging (MRI) scans of your eyes are given below (applies only to London patients):

We currently measure patients' eye position, appearance and range of movement in order to determine the severity of their Thyroid Eye Disease. Recently, however, researchers have tried to improve on this by using Magnetic Resonance Imaging (MRI) scans to directly measure the 'amount' of inflammation behind the eye ball, and the initial results have been promising. We are therefore hopeful that MRI will enable us to better identify patients who will benefit from treatment and also better assess their response to treatment. In addition, newly available MRI techniques may be able to improve our understanding of the physical processes underlying Thyroid Eye Disease.

To establish whether these advances can truly be achieved with MRI we will ask 50 of the expected 120 CIRTED recruits in London to participate in an additional MRI study. This is entirely optional and you will be asked at the start of the study whether or not you would be happy to take part - there is absolutely no obligation for you to do so. The researchers will decide which patients are selected for interview from those who volunteer.

If you agree to take part you will have 3 scans – one when you enter the trial, another 3 months later, and a final scan when you leave the trial. The scans will take place at the National Hospital for Neurology and Neurosurgery, and each scan will take about 25 minutes to complete. Your travel expenses for these visits will be reimbursed.

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Magnetic Resonance Imaging (MRI) is a scanning procedure that uses a combination of a strong magnet, radiowaves and a computer to produce very detailed pictures of your body. Applied to the eye, it can show the size of the muscles around the eye, and the contents of the eye socket behind the eye, and reveal whether these are inflamed and swollen. It does not use X-rays and does not involve any radiation, although you will hear a loud knocking noise when the pictures are being taken.

You will be asked to lie on a couch inside a short tunnel for the duration of the scan, and we would therefore discourage people who feel uncomfortable in enclosed spaces from taking part. You will be able to communicate with the scanner staff via an intercom throughout the examination. If you want the scan to stop at any stage, or you wish to withdraw your consent to take part in the study you are free to do so without this affecting in any way the quality of care you receive.

All patients participating in the study will be given the standard National Hospital for Neurology and Neurosurgery information about MRI scans, which explains what to expect and any precautions which need to be taken in more detail. In particular, if you have had an operation which involved the use of metallic implants (such as a joint replacement, some types of head or spine surgery, insertion of pacemaker or artificial heart valve) you will need to notify the trial doctors because the scanner uses a strong magnet and it may not be safe for you to have the scan.

At the end of the trial we will compare the results of the MRI scans with our clinical assessment of your Thyroid Eye Disease, and establish which better predicts your response to the treatment you have received. In addition, we will study changes in the scan appearances over the 12 month period you participate in the trial to see if this reveals any new information about the way Thyroid Eye Disease progresses over time.

k. *What if my Thyroid Eye Disease gets worse despite taking part in this research, or if I receive Azathioprine and do not tolerate it?*

- If your Thyroid Eye Disease gets worse at one of your follow-up visits you will be recalled 2 weeks later to double check the measurements. If these have not improved at the second visit you will be withdrawn from the trial.
- If you are concerned that your Thyroid Eye Disease is getting worse you can contact your research doctor at any time and they can arrange to review you before your planned appointment. If they confirm that your condition is deteriorating (as above) you will be withdrawn from the trial.
- If you are taking azathioprine and the results of your blood tests are consistently abnormal (despite a change in your azathioprine dose) you will be withdrawn from the trial.

11. *What happens to my treatment when I leave the trial?*

When you finish (or are withdrawn from) the trial you will be told what treatments you have taken. If it turns out that you did not receive either radiotherapy or azathioprine (or both) and you would like to try these treatments, they will be made available to you (if appropriate).

12. *What other treatments are available?*

There are alternative immunosuppressant agents to azathioprine, but there is no evidence to suggest that they would be a better treatment for your Thyroid Eye Disease. If you wish to discuss the other options please raise this when you attend the Eye Hospital.

Various other drugs such as Octreotide and new Monoclonal Antibody therapies have been used to treat Thyroid Eye Disease, but they have not been proven to be effective.

You do not have to receive any treatments for your Thyroid Eye Disease. It often improves of its own accord, but it is very uncommon for patients with severe disease to return to normal without treatment and it can sometimes get worse. If you choose not to have radiotherapy, steroids or other drug treatments there are a number of corrective surgical procedures available to reposition and realign the eyes and eyelids once the active orbital inflammation has settled (typically 1 – 3 years after the start of the disease).

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13. If I did not take part in this research what treatment would I receive?

The standard treatments for patients with severe Thyroid Eye Disease currently used in the two Study Centres are:

a. Moorfields Eye Hospital

Steroids: High-dose oral steroids at the start of treatment (as in this study), but this would continue for less than 6 months
Radiotherapy: Almost all patients eligible for this study would be referred for radiotherapy.
Long-term immunosuppressant drugs like Azathioprine: Would only be used in selected patients.

b. Bristol Eye Hospital

Steroids: Lower dose oral steroids at the start of treatment than are used in this study, but the overall duration of steroid therapy would continue for longer than this study (ie > 6 months)

Radiotherapy: Almost all patients eligible for this study would be referred for radiotherapy.
Long-term immunosuppressant drugs like Azathioprine: Would be used to treat almost all patients.

The differences between the two Centres shows that the treatment patients with severe Thyroid Eye Disease currently receive depends on the Hospital they are referred to, and highlights the need for this study.

14. If both Moorfields and Bristol Eye Hospitals currently use Radiotherapy for all patients, why is this treatment being with-held from half the people taking part in this trial?

Radiotherapy has been used for many years as a treatment of Thyroid Eye Disease. However, several recent research studies have questioned its benefit. Unfortunately, these studies were of varying quality and they have produced conflicting results. Few of them have looked at the long-term results of treatment (1 year or more) or at levels of patient satisfaction with treatment. Despite this, some Eye Specialists have stopped using radiotherapy and we are no longer sure whether it is necessary (especially if other treatments like azathioprine are used).

15. It is a lot to ask me to attend 12 radiotherapy visits if I have the sham-treatment.

This is true. However, if we were not conducting this study you are very likely to have been referred for this treatment anyway, so participating should not take any more of your time.

16. If Azathioprine has so many potential side-effects, is taking it worth the risk?

This is a matter of judgement, and you should not take part in the trial if you feel the potential benefit of reducing the severity of your Thyroid Eye Disease is outweighed by the risks.

Roughly 5 – 10% of patients who start azathioprine suffer side-effects (such as nausea) which make them wish to discontinue therapy (in which case you would leave the study). Significant and harmful side-effects are rare, especially as you will have had a blood test to make sure that you are not at particular risk of this.

In theory, azathioprine has the potential to gain (and maintain) better control of your Thyroid Eye Disease than the use of steroids alone. It has been used successfully in other inflammatory conditions and one previous study has suggested that it is a good treatment for TED. However, azathioprine has never been tested in a proper clinical trial such as this, which is the only way to really establish whether or not it is of benefit to TED patients.

17. Are there any other risks or disadvantages associated with taking part in this research?

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Azathioprine

The use of any immunosuppressant drug may increase your risk of infection, so if you feel unwell please inform your research doctor. We have no reason to believe that azathioprine poses any greater risk to you than alternative immunosuppressant drugs.

Although Azathioprine is not known to cause birth deformities we recommend that women who could become pregnant should use an effective contraceptive during the course of this study. Any woman who finds that she has become pregnant while taking part in the study should immediately tell her research doctor. Men taking part in this study should also take contraceptive precautions.

Radiotherapy

Any radiation exposure has some potential risks and radiotherapy could potentially cause damage to the lens and retina of the eye. However, this would be extremely rare using modern radiotherapy techniques which take special precautions to avoid this. If you have a condition which makes you particularly susceptible to retinal damage (such as diabetes) you will not be able to take part in this study.

There is also a theoretical risk that radiation can cause cancers, but the dose you will be exposed to is very low. Radiotherapy has been used to treat Thyroid Eye Disease for many years and nobody is known to have developed a cancer as a result (anywhere in the world).

Occasionally, radiotherapy can cause a brief flare-up of your orbital inflammation, but this is very unlikely as you will also be taking steroids.

Steroids

Steroids are recommended for the treatment of active Thyroid Eye Disease, (regardless of whether you participate in this trial). However, they have several potential side-effects. In particular they can cause weight gain, mood changes, irritate the stomach and weaken your bones (which might put you at increased risk of fractures later in life). You will be put on medication to try and prevent some of these side-effects.

18. What are the possible benefits of taking part?

If the treatment you receive is found to be better than the current standard treatment used at your Eye Hospital you will benefit from participating in this study. Otherwise, taking part may not be of direct benefit to you. It should, however, help us to provide better care for TED patients in the future.

19. What if new information becomes available?

Sometimes during the course of a research project, new information becomes available about the treatments that are being studied. If this happens, your research doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw, your research doctor will make arrangements for your care to continue. If you decide to continue in the study you will be asked to sign an updated consent form.

Also, on receiving new information your research doctor might consider it to be in your best interests to withdraw you from the study. They will explain the reasons and arrange for your care to continue.

20. What if something goes wrong?

Compensation for any injury caused by taking part in the study will be provided by the University of Bristol who have arranged insurance to cover such an eventuality.

Broadly speaking, our insurers, without legal commitment, will compensate you without you having to prove that anyone is at fault.

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Your right at law to claim compensation or injury where you can prove negligence is not affected by this insurance policy.

Regardless of this, if you have concerns about any aspect of the way you have been approached or treated during the course of this study you may wish to contact the following:

Bristol

The Patient Advice and Liaison Service (PALS) on 0117 928 3571, minicom number 0117 934 9261, or write to PALS, Bristol Royal Infirmary, Main BRI Front Entrance, Queens Building, Bristol, BS2 8HW.

If you wish to make a formal complaint please write to Mr Ron Kerr, Chief Executive UBHT Headquarters, Marlborough Street, Bristol, BS1 3NU or telephone Patient Complaints Manager on 0117 928 3604

London

The Moorfields Patient Advice and Liaison Service (PALS) on 0207 566 2324 / 2325 or write to PALS office, Moorfields Eye Hospital NHS Trust, 162 City Road, London, EC1V 2PD.

21. Will my taking part in this study be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential. However, employees from the study's regulatory authorities may look at your medical records to check that the research is being carried out correctly. Any information about you which leaves the hospital will be anonymised so that you cannot be recognised from it.

Your GP will be told that you are taking part in the study, as will any other doctors who are involved in your care, such as your endocrinologist.

22. What will happen to the results of the research study?

The results of the study may be presented at relevant medical and scientific meetings and published in an appropriate medical or scientific journal. At your request, your hospital doctor will inform you of where the study results have been published or provide you with a copy of the publication.

23. Who is organising and funding the research?

This research has been organised by a group of collaborating doctors (Ophthalmologists and Endocrinologists) from Bristol and Moorfields Eye Hospitals.

It has been funded by the following Charitable bodies:

- The National Eye Research Centre
- Moorfields Eye Hospital Special Trustees
- The Medical Research Committee of the Charitable Trusts for the United Bristol Hospitals

24. Who has reviewed the study?

The Study has been reviewed by a Central and South Bristol Research Ethics Committee, the National Eye Research Centre and Moorfields Eye Hospital Special Trustees.
