

Comparing two treatments for Graves' disease.

Short title: Rituximab in Graves' Disease 2 (RiGD2)

PATIENT INFORMATION SHEET 12-15 YEARS

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A BIT ABOUT THE TRIAL

We are comparing two different treatments for Graves' disease (GD) in young people to find out which one is better. Usually, patients with GD take anti-thyroid drugs (ATD) for around 2 years. But unfortunately, this does not completely treat most patients, and their disease comes back once they stop taking the ATD.

We want to test whether taking an extra drug called rituximab (RTX), alongside your normal ATD treatment helps treat GD more efficiently. This trial is called a 'randomised controlled trial' because patients who take part are randomly put into one of the two treatment groups. Half of the patients in the trial will be given rituximab, at the beginning of the trial while the other half will be given saline, or salty water. This salt water is called a placebo, and it doesn't have any medicine in it. Salt water is already in our bodies, so it will not change anything or help with the GD.

We are doing this to see if the medicine, RTX, actually helps participants get better from GD, or if it makes no difference. By comparing the participants who get RTX with the participants who get salt water, we can see if the medicine really works. Everyone will also take ATD for at least 2 years. Because it is random, it means neither you nor your doctor will be able to decide which trial treatment you receive. You will not know, until the end of the trial, which treatment you were given.

WHY ARE WE DOING THIS TRIAL?

We would like to know if giving a patient RTX, as well as taking their usual ATD, helps to keep a patient's thyroid gland working normally again even after they stop taking the ATD. We think

that rituximab might help treat your GD, but we do not know this for sure, which is why we need to do this trial.

HOW HAVE PATIENTS AND THE PUBLIC BEEN INVOLVED IN THIS TRIAL?

The RiGD2 Steering Group based in Newcastle upon Tyne have reviewed this Patient Information Sheet and the consent form. This group contains patients with GD of different ages and locations around the UK. The head of the British Thyroid Foundation has also reviewed this Patient Information Sheet and consent form.

DO I HAVE TO TAKE PART?

No, you do not have to take part. If you decide not to take part, you will still have the normal treatment for GD by your medical team.

WHAT DO I HAVE TO DO?

If you choose to take part, you will come to hospital to have the treatment. A small needle attached to a tube will be put into a vein in your arm. This is known as a cannula. The nurse or doctor will put some special cream on your arm before putting in the needle so that you cannot feel it going in. The RTX or salty water will be given through the tube directly into your vein. This is called an 'intravenous infusion' and will take around 3 hours in total. An intravenous infusion is when a medicine or fluid is given slowly through a vein. There is the possibility this infusion might take longer than three hours but it depends on the person.

If you are female, your doctor will ask you to take a pregnancy test before you have the treatment. For this test we will either use some of the blood sample you have given us to test for a pregnancy or you will be given a small pot to take into the toilet to wee into, which the doctor or nurse will test. It is very important to know if you could be pregnant because we do not know if RTX can harm an unborn baby. If you do not agree to take a pregnancy test then you will not be allowed to take part in the trial. If the test shows that you are pregnant, we can speak with you in private about the result and what this means for you and your care.

At this first visit and over the course of the 3 years you are in the trial you will come into hospital to give some blood (between 2-3 teaspoons) so we can check how you are doing and whether your ATD dose needs changing. You would need to have these blood tests taken anyway, even if you were not part of the trial. You will also be asked to fill in some questionnaires about how you are feeling; they take around 15 minutes.

The next section of this Patient Information Sheet has a diagram of the trial visits that you would be asked to attend if you take part.

TRIAL VISITS

Screening and consent

This is when we chat to you more about the trial and check you are happy to join.

Visit 1

At this visit we will check how you are doing and feeling. We will take some blood. This is when you would be given a pregnancy test (for females). We will ask you to fill out some questionnaires.
This is also when you will be randomised and be given either RTX or the salty water.

Randomised to either:

1 dose of RTX plus the normal
ATD for at least 2 years

1 dose of salty water plus the
normal ATD for at least 2 years

Visit 2 to Visit 14 (take place in years 1 & 2)

At these visits we will check how you are doing and feeling. We will take bloods. At some of these visits we will ask you to fill out some questionnaires. We will also check how often you have been taking your ATD or other medicines. If you are female we will ask you to take a pregnancy test at 1 year.

Visit 14 (end of year 2)

This is the visit where the doctor will tell you to stop taking your ATD (if they think it is safe for you to do so).

Visits 15-18 (year 3)

At these visits we will check how you are doing and feeling. We will take bloods. At the final visit we will ask you to fill out some questionnaires. We will also find out how you are doing with any medication you may be taking.

Return to normal NHS care

After your final visit you will finish being in the trial and will continue to be seen for normal clinical appointments with your usual doctors and nurses.

WHAT ARE THE DIFFERENT TREATMENTS?

Anti-thyroid drugs (ATD)

Patients with GD are treated using ATD for around 2 years. Everyone taking part will be given their usual ATD tablets to take daily by mouth (orally).

Rituximab

The body protects itself from illness and infection by making special types of cells called 'B cells'. In GD, the body mistakenly makes B cells that attack the thyroid gland and force it to make too much thyroid hormone. RTX helps kill these B cells. The good B-cells come back but we think that the bad ones will not come back, helping treat Graves'.

Placebo

Saline (salty water) is often used as a placebo in trials. It is often used in hospital if people cannot drink enough or need extra fluid. The amount of salt in the water is the same amount of salt found in tears, blood, and other body fluids in humans. We are using it because the RTX is dissolved in saline anyway, so you will not be able to tell which one you are receiving.

WHAT IS IT LIKE TO HAVE RITUXIMAB?

RTX has been used for a long time in many different conditions in children, so we know it is very safe. Some people may feel hot, cold or shivery, feel sick, or itch while the rituximab going in through the drip. We will give you some other medication first to stop this happening. If it does happen then the nurse or doctor will stop the treatment for a few minutes, until you feel better, and then will restart it, but more slowly. The nurse or doctor will watch you carefully for any signs that you are feeling poorly.

WHAT IS IT LIKE TO HAVE SALINE (PLACEBO)?

Normal saline (salty water) is regularly used in hospital, so we know it is very safe. It is very rare to get any side-effects from this.

WHAT ARE YOU TRYING TO FIND OUT?

We are trying to find out whether using RTX and ATD together is better than just ATD at treating GD.

WHAT ARE THE GOOD THINGS ABOUT TAKING PART?

We do not know if taking part in the trial will help you right now because you may not get the RTX and even if you did, we do not know if it works better than just giving ATD. But once we have finished the trial it will tell us which treatment is better. This will help patients like you in the future.

WHAT ARE THE BAD THINGS ABOUT TAKING PART?

There is a very small chance that you might develop an infection after the rituximab infusion. If this happens you may have to be reviewed by a doctor and take extra medicine.

The trial will last for 3 years. If you decide to take part in the trial, you will have to come into hospital 19 times during the 3-years of the trial. This is only about 2 extra visits to your hormone doctor compared to if you were not taking part in the trial. However, your doctor may want to see you more or less than this. You will need to think carefully about whether you feel you can do this number of visits.

WILL INFORMATION ABOUT ME BE SAFE?

All your information will be kept safe. We will only show it to people who are part of the trial and have a right or a need to know.

WHO ELSE WILL KNOW I AM TAKING PART?

With your permission we will tell your GP that you are taking part in the trial. This will help keep you safe while you take part in the trial.

WHAT WILL HAPPEN AT THE END OF THE TRIAL?

After the trial, you will continue to see the doctors and nurses at your hospital as normal. We will write about what we find out in scientific reports. We will also talk about what we find at

scientific meetings with other doctors and scientists. No one will know that you took part in the trial. The hospital where you take part in the trial will send you and/or your parent a short report on what the trial found.

WHO CAN I TALK TO IF I HAVE MORE QUESTIONS?

If you have questions about the trial or would like to discuss anything further, please ask your parent or carer to contact your local research team at [email] or [phone number].

Thank you for reading this information sheet.