Improving treatment for people with kidney transplants

CAMPATH, Calcineurin inhibitor reduction and Chronic allograft nephropathy trial

SECOND RANDOMISATION INFORMATION SHEET

Thank you very much for your participation in the 3C Study so far. As you know, you were randomly allocated to receive either Campath- or basiliximab-based "induction" treatment at the time of your transplant operation. The health information we have collected about you so far will help answer one important question about kidney transplantation.

The 3C study is testing two ways to make kidney transplants a much more effective treatment in the long term.

One way of doing that may be for patients to switch from the standard tacrolimus-based maintenance treatment to a sirolimus-based treatment at about 6 months after transplantation. This may help to protect kidney function and prolong the lifespan of the transplant.

You will shortly be entering the period (between 5 and 7 months after transplantation) when you could help answer this question.

Whether or not you decide to take part in this part of the trial will not affect the standard of your care in any way. Even if you decide not to take part, we should be most grateful if you could still provide information about your health. The longer we are able to follow your health, the more we can be certain that the results of the study are valid.

WHY IS THE 3C STUDY TESTING SIROLIMUS?

Kidney transplantation is a very good treatment for people whose kidneys no longer function sufficiently to keep them alive. Unfortunately, kidney transplant function inevitably declines over time. On average, after about 8 - 10 years the transplant "fails" and the recipient either receives another transplant or returns to dialysis (see Figure 1).

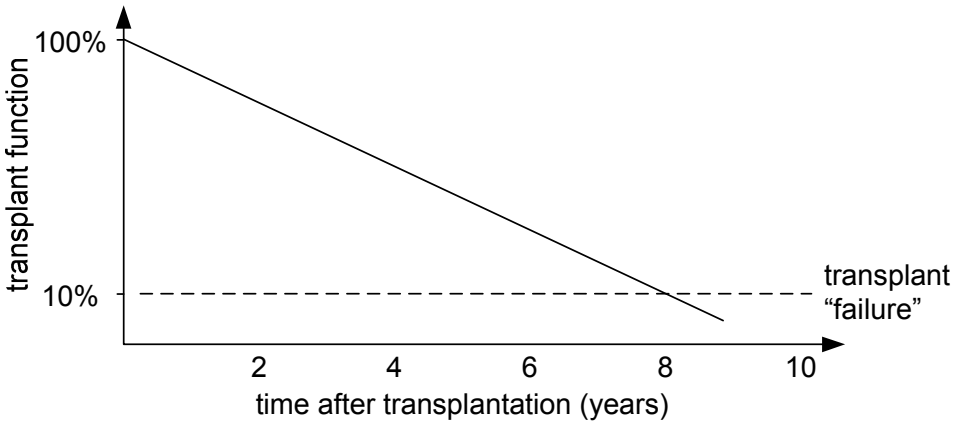

Figure 1: Transplant function progressively declines such that the transplant fails on average 8 - 10 years after transplantation.

A common cause of such "transplant failure" is a type of drug very commonly used to prevent your immune system from rejecting the kidney: tacrolimus is one of these. It is known as an immunosuppressant drug. Although these drugs are very good at preventing the patient from rejecting the transplant, over the long-term these drugs cause scarring in the new kidney. This gradually impairs the kidney's function and may make it fail.

Sirolimus is a different type of immunosuppressant. It is much less likely to damage the transplanted kidney in the long-term. Previous trials have shown that moving to sirolimus-based treatment within the first year after transplantation improves transplant function in the short-term. However, there is not enough reliable evidence on the long-term effects of such a change in treatment; it is intended the 3C study will provide this.

Heart disease is also a major cause of illness and death in kidney transplant patients. It is possible that some of the side-effects of tacrolimus (diabetes and high blood pressure) might contribute to this. Switching patients to sirolimus may help to prevent some of unwanted side effects from taking place.

WOULD I BE SUITABLE FOR THIS SECOND RANDOMISATION?

Most participants in the 3C Study are suitable for this second part of the trial. However, there are two reasons why you may not be suitable: Firstly, if you have had an episode of "acute rejection" within the last few weeks; Secondly, if there is a large amount of protein in your urine you may not suitable for this part of the study.

WHAT IS INVOLVED IN THIS SECOND PART OF THE STUDY?

If you are thinking about participating in this second part of the study, then it is important that you discuss this with your consultant. This needs to take place between 5 and 7 months after your transplant. If you decide to go ahead with the second part of the study, a decision will be made at random (like tossing a coin) whether you remain on tacrolimus-based treatment or switch to sirolimus-based treatment.

Tacrolimus-based treatment (standard treatment)
If you are allocated to remain on tacrolimus-based treatment then your treatment will not change. Your dose of tacrolimus might be reduced slightly as you will need slightly less tacrolimus from this time on. This may require a few extra blood tests to get the new dose of tacrolimus correct. The rest of your care (including your other treatment) continues as normal.

Sirolimus-based treatment (new treatment)
If you are allocated to switch to sirolimus-based treatment then you would take the last dose of your tacrolimus that evening and start on the sirolimus the next morning. You will need a few extra blood tests to ensure the dose of sirolimus correct. The rest of your care (including your other treatment) continues as normal.

WHAT IF I DECIDE NOT TAKE PART (OR I AM NOT ELIGIBLE)?

In this case you remain on tacrolimus-based treatment. The dose might be reduced slightly as you may need slightly less. If you decide not to take part this will not affect the care you receive in any way.

WHAT ARE THE POTENTIAL RISKS AND BENEFITS OF TAKING PART?

	Converting to sirolimus	Remaining on tacrolimus
Potential benefits	• Withdrawal of tacrolimus may reduce long-term damage to your new kidney and therefore preserve its function for longer • Withdrawal of tacrolimus may reduce risk of future cardiovascular disease	• Well established treatment which effectively prevents “rejection” of your new kidney
Potential risks	• Small increased risk of rejection at time of conversion (although this is usually mild and easily treated) • Side-effects of mouth ulcers, rashes, abdominal pain, proteinuria	• Potential long-term damage to your kidney • Side-effects of diabetes, high blood pressure, tremor, diarrhoea

WHAT ARE THE SIDE-EFFECTS OF THE TREATMENTS?

Tacrolimus
The common side-effects of tacrolimus include infections, high blood sugar (including diabetes), high blood pressure, tremor, headache, diarrhoea, insomnia, high potassium and impaired kidney function.

Sirolimus
The common side-effects of sirolimus include infections, elevated concentrations of fats in the blood, headache, rashes, high blood pressure, mouth ulcers, abdominal pain, diarrhoea, joint pain, swollen ankles and protein in the urine. Some of these (especially mouth ulcers, gastrointestinal upset and rashes) may occur shortly after you start taking these medications, but often settle if you can persist for a few weeks.

HOW ARE THESE SIDE-EFFECTS MANAGED?

Many of the side-effects of treatments with drugs like tacrolimus and sirolimus that suppress your immune system are related to the dose you take. If you develop side-effects your doctors will try and minimise the dose of treatment you receive, while ensuring that you take enough to avoid rejection. Side-effects such as high blood pressure, high blood sugar and elevated blood fats usually respond well to treatment if lifestyle advice (e.g. eating a healthy diet and taking exercise) is not sufficient.

Some side-effects have specific treatment. For example, if you develop protein in your urine while taking sirolimus this usually responds well to certain blood pressure treatments. Mouth ulcers can be treated with good mouth care, certain topical treatments and drinking pineapple juice.

If you develop any side-effects please either contact your transplant team or you can call a doctor at the 3C Coordinating Centre on (Freefone) 0800 585323 who can advise you further.

WHAT DO I DO NEXT?

If you would like to participate in this second part of the 3C study then please ensure that your consultant knows (they will also ask you about it). It may be necessary to provide a urine sample so that your doctor can check your levels of protein. It may be possible to reduce high levels of protein in your urine with blood pressure treatments, so that you become eligible for the second part of this study.

If you do not wish to participate then please inform your consultant when they contact you next. This will not affect the standard of care that you receive.