Participant Information Sheet

Type 1 Diabetes TrialNet Protocol TN-18

CTLA4-Ig (Abatacept) for Prevention of Abnormal Glucose Tolerance and Diabetes in Relatives At-Risk for Type 1 Diabetes Mellitus

SCREENING

Principal Investigator:	Dr Isy Douek
Address:	Taunton and Somerset NHS Foundation Trust Musgrove Park Hospital Taunton Somerset TA1 5DA
Telephone:	01823 342083

You (you means you or your child) are being asked to be screened for this study. You have been participating in the TrialNet Natural History Study (Pathway to Prevention) and have had blood tests that show you have markers associated with risk of type 1 diabetes. You are now being invited to be screened to see whether you could take part in another TrialNet research study which is a diabetes prevention study.

This information sheet describes the tests and procedures you will have if you choose to be screened for participation in the TrialNet Abatacept Prevention of Type 1 Diabetes Study. If the results of the screening tests show that you are eligible, you will be asked if you would like to join the study. You will be given a participant handbook and information sheet that explain the prevention study in more

detail. You will also be asked to sign a separate consent form. Signing the screening consent form does not mean you have to be in the study, it only means that you agree to have the tests done to see if you can be in the study.

What is the purpose of the study?

We know that development of type 1 diabetes occurs over time as the immune system destroys insulin producing cells. As this takes place, blood glucose values increase gradually until they are high enough to diagnose diabetes. Before this, blood glucose values may be higher than normal but not high enough to diagnosis. We call these “abnormal glucose levels”.

The purpose of the study is to see if giving a medication called abatacept can help delay or prevent the development of abnormal glucose levels and diabetes in people who have markers associated with risk of type 1 diabetes.

What is the drug that is being tested?

The medication is an intravenous infusion containing abatacept. Abatacept is approved as a treatment for rheumatoid arthritis and juvenile idiopathic arthritis. In a previous TrialNet study abatacept was shown to have some effect on preserving insulin secretion after diagnosis. There is also a placebo (dummy drug) group in the study. This group will be given infusions which contains no active ingredient. This is a ‘blinded’ randomised trial so that neither you nor the researchers will know which infusions you are receiving until the study has been completed.

What will happen during the study?

The study will have two phases, a treatment phase for the first year and then a monitoring phase. During the treatment phase, you will receive the study medication 14 times over a year. During the monitoring phase you will have visits every six months. The exact duration of the study is not known. We anticipate that your

participation will be no longer than 5-6 years. If you do develop diabetes, you will no longer be in this study. However, we will let you know if there are other TrialNet studies are available to you. There will be about 206 research volunteers enrolled in the study.

What will happen during screening?
If you agree to be screened for this study, you will need to have the screening tests as described below:

- **History and physical examination**
  We will ask you questions about your health and perform a routine physical examination. This is to be sure that you do not have any health problems that would prevent you from being in the study.

- **Blood tests**
  A total of 3-4 tablespoons of blood will be taken from your vein to gather some information about your immune system and overall health. This includes testing your blood for a number of infections including HIV (the virus that causes AIDS) and hepatitis. Having an infection would prevent you from being on the treatment. If you test positive for an infection we may be required to report this information to the public health authorities. We will also arrange for someone to discuss the test results with you.

- **Tuberculosis Skin Test (Purified Protein Derivative (PPD))**
  The PPD tests for a reaction to substances placed with a needle just under your skin. This test helps to tell us if you have had tuberculosis. You will need to have a qualified person look at the site where you received your injection in 48-72 hours to see if you have developed a reaction.

- **Urine Pregnancy Test** (if you are female)

What are the risks?

Blood tests:

There are some risks to having your blood taken. These risks are discomfort and/or a bruise at the needle puncture site. Once in a while, some people may faint. It is rare, but some people may get an infection, form a small blood clot, have swelling of the vein and surrounding tissue, or bleeding at the needle puncture site.

Tuberculosis Skin Test (PPD):

If you have a reaction to the material placed under your skin, you may develop a rash on your skin where the test was done. The rash may be itchy and/or sore, but it will usually disappear within a few days.

Are there any benefits?

If you agree to have this screening done, you will find out if you meet the requirements to enter the study. If you qualify, you may or may not directly benefit from being in the study. It is hoped that the abatacept will stop the destruction of your insulin producing cells, but there is no guarantee that this will happen.

What will happen to my blood samples?

If you agree, we would also like to store samples of your blood. Your blood samples will be used to help us learn more about how the immune system might cause type 1 diabetes and about new ways of identifying people at risk for type 1 diabetes. They also could help us learn more about type 1 diabetes, its complications (such as eye, nerve and kidney problems) and other conditions for which patients with type 1 diabetes may be at increased risk. While TrialNet is ongoing, these samples will be used only by TrialNet-approved researchers. As such, we will be collecting blood samples, including genetic samples, for these studies at most of your visits. You will not routinely be provided with test results from these studies. There is more information about this in Part 2 of the form.

Are there any alternative treatments?

Before you decide to take part in this study, we will talk with you about the other options available to you. You may choose not to participate in this study. At present, there is no approved medical treatment that will preserve beta cells and the ability to make insulin for people with type 1 diabetes. There may be other research studies that you can choose to be in.

Will I receive anything for taking part?

You will receive a small amount to cover your expenses for each visit that you complete. By signing this screening consent form, you understand and agree that, if this research project results in the development of any product that can be sold, you will not receive a share of any money that is made.

Do I have to take part in the study?

No. It is up to you to decide whether or not to take part. Participation in this study is voluntary. If you are eligible but choose not to be in this study, you can remain in the Natural History Study (Pathway to Prevention) to be monitored.

You can withdraw your consent at any time. If you chose to stop being in the study, tell a study staff member. Your current or future care will not be any different if you decide not to be in this study or to stop being in this study at any time. Your doctor may choose to take you out of the study at any time, even without your consent. You will be told of any new findings that may affect your being in this study.

What happens when the research stops?

The treatment will not be available after the research finishes. If you develop diabetes during the course of the study or after the study has ended you may be eligible to take part in other TrialNet studies.

What if there is a problem?

Any complaint about the way you have been dealt with during the

study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

What will happen to my data?
All the information about your participation in this study will be kept confidential. The details are included in Part 2.

Where can I get more information?
You will get a copy of this information sheet. Please ask questions about this study or screening at any time. You are welcome to talk about this study or screening with your family, doctor, or anyone else. The staff of the research study will be happy to discuss any questions with you. You may direct any questions to the TrialNet team on 01823 342083.

This completes Part 1 of the information sheet. If the information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision.

Part 2

What will happen to my data?

Your consent gives the TrialNet researchers permission to collect study information (data) related to this study and to use it for research purposes. This information may be shared with other TrialNet centres as needed to help with the study. Your consent also includes permission for the sponsor of this study (NIDDK) and the UK and US regulatory agencies (the Medicines and Healthcare products Regulatory Agency (MHRA) and the Food and Drug Administration (FDA)) to review your records.

Information from your research records will be sent to our central coordinating centre at The University of South Florida, USA for statistical analysis. No personal information that directly identifies you will be included with these data. Personal information is information such as your name that directly identifies you. Instead you will be assigned a unique study code. This personal information will be kept in a database at the UK TrialNet Coordinating Centre at the University of Bristol. The key to the code, linking your personal information to you, will be kept in a locked file here at the University of Bristol. Only Prof. Polly Bingley and her research staff will have access to the key to the code.

When TrialNet is completed, your data (but not your personal identifying information) will be moved to another location that will be under the supervision of the NIDDK. Once this happens, it will no longer be possible to link your code to your name or other personal identifying information.

An agreement between the Department of Health and the UK Insurance industry is in place until 2017 (Concordat and Moratorium on Genetics and Insurance). This is intended to protect the confidentiality of information that we obtain about you during the research. By having this agreement, we cannot be forced to give

information about you to insurance companies. You do not have to disclose results of clinical research to insurance companies. They may impose underwriting terms if there is a family history of illness and you must disclose this family history if asked.

TrialNet researchers are not prevented from disclosing information about matters such as child abuse, certain infectious diseases, or threatened violence to yourself or others.

TrialNet researchers will consider your records private. Rarely, representatives of the MHRA, U.S. Department of Health and Human Services (DHHS) or TrialNet may review or ask for a copy of your study records. If this happens, we will provide your records. Also, employees of the University of Bristol, the NHS Trust R&D group or its agents could be allowed to see your study records to make sure that the study is being done properly.

Please understand that we will maintain the confidentiality of your research record. Our procedures for handling, processing, storage and destruction of data are compliant with the Data Protection Act 1998

The results of this study may be published for scientific purposes. By signing this form, you are agreeing to this. Your records and results will not be identified as belonging to you in any publication.

Who else will be informed that I am taking part in the study?
With your permission we will contact your GP to inform him or her that you are taking part in a research study. He or she will be sent some information about the study. We will not routinely send results of the study investigations. We may need to contact your GP if we find you have developed diabetes during the course of the study. We may also need to talk to other healthcare professionals about your care during the study. With your permission we will inform the diabetes consultant who cares for the person in your family with

diabetes.

What will happen to my stored blood samples?
Your blood samples will be stored without your name or any other identifying information on them. You will not routinely be provided with test results from stored samples. Your blood samples could be stored for a number of years, but we can't say for how long. Even if you do not want to have your samples stored, you can still participate in the rest of the study.

As long as TrialNet continues, your stored blood samples could be used by TrialNet researchers and researchers from outside of TrialNet. However, if researchers from outside of TrialNet want to use your samples, they must first get permission from TrialNet researchers and the sponsor of this study, the National Institute of Diabetes & Digestive & Kidney Diseases (NIDDK).

When TrialNet is over, your blood samples will continue to be stored under the supervision of the NIDDK. Researchers would not be able to use your blood samples without the permission of the NIDDK.

Your blood sample will be treated as a gift to the custodian of the NIDDK sample repository. They will assume responsibility for your sample's use, storage and disposal.

What if something goes wrong?
If you need to get medical care right away, you should go to your GP or to the nearest Accident and Emergency. Be sure to explain that you are in a research study. If you do not need emergency care, the TrialNet researchers will help you get the care you need.

In the event that something does go wrong and you are harmed during the research study the University of Bristol has arranged insurance to provide compensation for an injury caused due, on the balance of probabilities, to taking part in this research study.

The University will pay compensation where the injury probably resulted from the drug (abatacept) or any test or procedure you receive as part of the research study.
The University would not be bound to pay compensation where the injury results from some cause outside the scope of the research study.
This does not affect your legal rights. Please ask if you would like to receive more information about this.

How is the study funded?
This study is funded by the United States National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), with additional funding from the US National Institute of Allergy and Infectious Diseases (NIAID), the US National Institute of Child Health and Human Development (NICHD), and the National Center for Research Resources (NCRR). Other support is from the Juvenile Diabetes Research Foundation and the American Diabetes Association. Bristol Myers Squibb will donate the abatacept being used in the study and may pay for some of the study's costs.

Who has reviewed the study?
This study was given a favourable ethical opinion for conduct in the NHS by the South West – Central Bristol Research Ethics Committee

Additional Information:

A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time

Thank you for taking time to read this information.

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SCREENING CONSENT FORM

Name of Researcher: Dr Isy Douek, Taunton and Somerset NHS Foundation Trust, Musgrove Park Hospital, Taunton, Somerset, TA1 5DA

Please read the Information sheet before you complete this form.

1. I have read and understood the information sheet (dated 30th March 2015, Version 02) about the study or it was read to me. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐

3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from the TrialNet Study Group, the University of Bristol, the regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐

4. I agree to my GP being informed of my participation in the study. ☐

5. I agree to my contact details being sent to the TrialNet coordinating team at the University of Bristol for administrative purposes. These will not be passed on to any third party outside of the TrialNet study team and will be treated in confidence. ☐

6. I agree to take part in the above study. ☐

The following sections are choices you can make. Ticking the "no" box does not mean you cannot take part in the study:

Information about other research

I consent to the research team contacting me about other research for which I may be eligible.

YES ☐ ***NO*** ☐ ***INITIALS*** ☐

Storage of Samples in NIDDK Repository

When TrialNet is over, we intend to put any remaining samples into the National Institute of Diabetes & Digestive & Kidney Diseases (NIDDK) repository for future studies related to type 1 diabetes and its complications. They will be stored there indefinitely without your name or any other identifying information on them. As such, once in the repository you will not be able to have them removed. Researchers must first get permission from the National Institute of Diabetes & Digestive & Kidney Diseases (NIDDK) to use samples from the repository.

The following checkbox gives you the choice of allowing us to put any remaining blood samples in the NIDDK repository. Even if you decide not to have your remaining blood samples stored, you can

still participate in this study.

*I give permission for my blood samples to be stored for further testing as indicated in this form (mark **one** of the options below).*

- **Yes, store all samples including the genetic samples**

INITIALS ☐

- **Yes, store all samples, but not the genetic samples**

INITIALS ☐

- **No, I do not give permission to have any samples stored**

INITIALS ☐

SIGNATURES: By signing this consent form, you agree that you have read the information sheet and consent form and that the study has been explained to you. You also agree that your questions have been answered and that you agree to be in this study. You do not give up any of your legal rights by signing this informed consent form. You will receive a copy of this consent form and the information sheet.

CONSENT FOR SUBJECTS 18 YEARS OF AGE AND OLDER:			
Signature of Subject		**Date**	
Date of Birth			

Print Name of Subject			
Signature of Person Obtaining Consent		**Date**	
Print Name of Person Obtaining Consent			
Role of Person Obtaining Consent	**Research Nurse / Investigator / Co-Investigator**		
CONSENT FOR CHILDREN UNDER 18 YEARS OF AGE:			
Print Name of Subject			
Date of Birth			
Signature of Mother/Guardian			
Print Name of Mother/Guardian		**Date**	
OR			
Signature of Father/Guardian		**Date**	
Print Name of Father/Guardian			
Signature of Person Obtaining Consent		**Date**	
Print Name of Person Obtaining Consent			
Role of Person Obtaining Consent	**Research Nurse / Investigator / Co-Investigator**		