8. Samples and Tests

You will be asked for blood and urine samples at each visit (except research visit 5). If you are female and pre-menopausal, you will also be asked to take a pregnancy test. Participants at some sites will be invited to provide a self-collected genital swab, this will be optional. Blood tests that may be important for your clinical care (such as blood glucose, kidney function or cholesterol) will be analysed by your local NHS laboratory and copied to your GP. Research blood and urine samples will be anonymised (the samples will be stored using a code without your name or other personal details) and stored for further specialist tests. Genetic material (DNA) will be extracted and stored anonymously. We will test this to see if there are any genetic changes which may explain your response to treatment. Access to samples or information related to samples is restricted to members of the research team only. Once all sample analysis is complete, samples not transferred to a research bank will be disposed of in accordance with the Human Tissue Act (2004) Code of Practice 5 and the local NHS waste management procedures.

9. Optional Extras

You will also be given the option to donate the samples and data collected for this study to a research bank to be used in future research. This research bank is based in Exeter and is managed by a steering committee of members of the public who have also participated in research. The committee will ensure that samples and data are used anonymously on studies that they feel are ethically appropriate. These studies may be in the UK or abroad and may involve collaboration with companies, but samples and data will not be sold for profit, not shared with non-research organisations and not used in animal research or reproductive cloning. Your DNA may be used in future studies, but will not be actively screened for genes predictive of disease. You will also be given the opportunity to join a local research database to be contacted about future studies local to you.

10. What will I be asked to agree to?

Thank you for reading this information. If you are happy to participate, you will be asked to consent to the following statements at your screening visit in the presence of a member of the research team.

I confirm that:

- I have been given study information leaflet and supplementary information about the treatments used in this study. I have had the opportunity to ask questions and have had these answered satisfactorily.

I am happy to:

- attend 6 appointments, having fasted overnight for 4 of these.
- try 3 different regularly prescribed diabetes treatments for up to 16 weeks each.
- provide information about my diabetes for use in this project.
- allow the research team to contact my clinicians/GP about my diabetes treatment and study participation, and to provide them with clinical results relevant to my care.
- provide blood and urine samples for use by this study.

I understand that:

- my participation is voluntary and that I may withdraw at any time without my clinical care being affected.
- individuals from the study team, regulatory authorities or the NHS Trust will have access to relevant sections of my medical notes and data collected during the study for research, monitoring and audit purposes.

Optional consent statements

- I agree for DNA to be extracted from samples for the purpose of this project
- I am happy to provide self-collected genital swabs (Exeter site only). .
- I am happy to gift samples and data from the project to the Peninsula Research Bank in Exeter to be used for future research.
- I agree that information held by the NHS and in my medical records may be used to follow up on my future health status.
- I am happy to be contacted by my local research team about participating in other future studies.

Before you make a decision about participating in this study, you may want to discuss the project with your GP or family members.

Sponsored by the Royal Devon and Exeter NHS Foundation Trust

University of Exeter Medical School

GIG CYMRU NHS WALES
Bwrdd Iechyd Prifysgol Caerdydd a'r Fro
Cardiff and Vale University Health Board

TriMaster

A research study to help improve treatment of type 2 diabetes, by learning how individuals respond to different blood sugar-lowering drugs

Would you be willing to try three regularly prescribed diabetes medicines over a year, to see which one works best for you and to help us improve diabetes care for others?

- **Before you decide whether to take part, it is important to understand why the research is being done and what it will involve.**
- **Please take the time to read the following information carefully.**
- **You are free to decide if you want to take part in this research study.**
- **You can decide to stop taking part in the study at any time without giving a reason.**
- **Please ask us if anything is not clear or if you would like more information.**

Important things you need to know

•The study will involve taking three standard diabetes drugs alongside your current medication: sitagliptin, canagliflozin and pioglitazone. They will be prescribed randomly, one drug at a time, for 16 weeks. There will be an appointment before starting each drug.

• Participation in this study will involve six visits over a year (2 x 30 minute visits, 3 x 60 minute visits and 1 x 3 hour visit) The 30 and 60 minute visits may be able to be conducted at your home if you are unable to attend the hospital.

• We will ask you to provide blood samples to ensure you are safe and eligible to participate in the study.

• All the drugs will be made to look identical, so that you and the study team will not know which drug you are taking. A dedicated team will be available to help if you suffer any side-effects and your doctor needs to find out what you are taking.

Contents

How to contact us:

If you have any questions about this study, please contact us on:

Telephone: 02920 746718
Email: hemanth.bolusani@wales.nhs.uk

1. Why are we doing this research?

We are trying to understand why some diabetes medicines do not work for some people so that we can help to choose the most effective medicine in the future. In type 2 diabetes, it is common for additional treatments to be added over time to maintain, or lower, blood sugar levels. We know that the response to these medications can be variable and their effect may be different between individuals. However, very little is known about why this response is different or whether it would be possible to predict if a medicine is likely to work for someone. If we could predict which medicine is likely to work for a person, we could choose the most effective treatment, avoiding ineffective medicines and unnecessary side effects. This study is looking at three standard diabetes treatments which can be added when one or two existing medicines stop maintaining good blood sugar levels. We will compare how patients with different blood sugar levels, weight and kidney function respond, and which treatment each patient prefers.

2. Why have I been invited to participate?

We are inviting you because you are already taking one or two diabetes treatments, but your diabetes may be improved with an extra treatment. We are inviting you to try three common diabetes treatments to see which one improves your diabetes the best and which one suits you. We will first invite you to a screening appointment to see it is safe for you to participate. By participating you may help us to choose more effective treatment in the future and in some cases your study results may help you and your doctor decide on your future diabetes care.

3. Are there any risks in taking part?

The treatments being used in this study are drugs that are regularly prescribed for people with diabetes. In the screening visit we shall check that it is safe for you to take all of the different drugs being tested. We will also provide a specific guide which describes the drugs and what to do if you experience any side effects. A dedicated team will be on-call to talk to your doctors if they need to know what you are taking. The research team will carefully monitor you for any adverse effects and withdraw you from the study, or transfer you to the next treatment, if necessary. As with your standard diabetes care, the blood tests may be uncomfortable, but they will be carried out by experienced staff.

4. What happens if I don't get on with the drugs?

You will be on each treatment for 16 weeks. Just as with your normal diabetes care, if you have a bad reaction to one of the drugs, we can transfer you onto the next treatment at any point or can withdraw you from the study completely. Your doctors will be able to contact the research team if they need to know which drug you are currently taking.

5. Will my participation be kept confidential?

If you are enrolled in the study, you will be given a unique study ID number. A copy of your consent form will be sent securely to the coordinating team in Exeter. Your name and date of birth will be entered on the study database to allow limited members of the Exeter team to know this information if there is an urgent problem with your drug treatment**.** All information that is collected about you will be listed against your study ID number and held on a password-protected computer. All samples and research data will be stored securely using numerical barcodes and researchers involved in data analysis will only have access to anonymised data. Access to this data and samples will be available to the research team only. As this study involves taking a new treatment, we will ask for your consent to inform your GP and/or hospital diabetes team about your participation in this study and to share relevant findings with them. In addition, tests your doctor would often request (such as blood sugar (HbA1c) will be copied to your GP and/or hospital diabetes team to avoid unnecessary repeat blood tests. At the end of the study anonymised research data will be kept for a minimum of 5 years, or with your permission, will be transferred to a research bank (Section 9).

6. What will I need to do if I take part?

The study involves 6 appointments. Details of what will happen at each visit and how you will be asked to prepare are shown below. We will ask you to fast before each visit (not to eat or drink anything except water for 8 hours), except the screening visit and research visit 5. We will provide travel expenses and may be able to see you in your own home for some of the visits if you are unable to travel.

At the end of the study your doctor will decide your future treatment.

Screening Visit
30 minutes

- Discussion of eligibility and detailed study overview
- Written consent for screening
- Blood sample taken to confirm eligibility
- Questions about medical history, diabetes and current medication

Maximum 2 week interval

Baseline Research Visit 1

3 hours

- Re-consent for the full study
- Clinical data; height, weight, body fat and blood pressure
- Fasted urine and blood sample
- Participants at some sites will be asked to provide a self-collected genital swab to see how bacteria are affected by the study drugs and whether there is an increased risk of developing infections - this will be optional
- A meal test where you will be asked to drink a liquid meal drink, that is a bit like a milkshake, followed by a series of blood tests for 2 hours
- You will receive a prescription for 16 weeks of the first drug, along with information about all three drugs and the potential side-effects. Although you will not know which drug you have been given, we will explain how and when to take the daily tablet and give an opportunity to ask any questions
- Breakfast will be provided at the end of the visit

After 16-18 weeks of starting new drug

Research Visits 2, 3, 4

1 hour each

- Fasted blood and urine test
- If provided at visit one, an optional repeat swab
- Clinical data including weight and any changes to non-diabetic medication
- You will be asked about your experience of the drug in terms of side effects, your quality of life and willingness to remain on therapy
- Any leftover medication will be collected, and at Visits 2 and 3 the next prescription will be issued, again for 16 weeks
- At each visit, the information you received at the first visit will be reviewed and any questions answered

Maximum 4 week interval

Research Visit 5

30 minutes

- The research team will provide you with feedback of your blood results and weight change during the study, and will discuss the feed-back on side effects and your experience you gave throughout the study
- You will be asked for your final drug preference overall
- With your consent, this final preference will be passed on to your GP

This may include one, or none of the study drugs. The research team will not be involved in this decision.

7. Who is organising this study?

This project is being run by Cardiff & Vale University Health Board. It is centrally coordinated by the NIHR Exeter Clinical Research Facility with funding from the Medical Research Council. The project has been reviewed by the TriMaster Public Involvement Focus group at the Exeter CRF and by the National Research Ethics Committee South Central—Oxford A.