# PARTICIPANT INFORMATION SHEET

## Impact of Semaglutide in Amyloid Positivity (ISAP) study

**Chief Investigator**: Doctor Ivan Koychev

**Sponsor**: University of Oxford

We would like to invite you to take part in a clinical trial. Before you decide, it is important for you to understand why the research is being done and what it will involve for you. Please take time to read the following information carefully and discuss it with friends, family or your GP if you wish. If there is anything that you do not understand, or if you would like more information, please ask us.

### Key Points

- We are testing how the diabetes drug semaglutide interacts with proteins in the brain linked to Alzheimer's disease (AD).
- We will include around 90 people in two groups. One group will be given semaglutide and the other placebo or "dummy pills" to take for one year.
- We will assess thinking ability and measure the amount of AD proteins and brain inflammation, using brain scans, at the start and end of the study.
- Treatment with any medication can cause side effects; the most common side effects from semaglutide are feeling sick and diarrhoea.

### How to contact us

If you have any questions about this study, please talk to your study doctor or nurse:
Dr Ivan Koychev (Chief Investigator)
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## 1 Why are we doing this study?

Finding a treatment that delays or even prevents Alzheimer's disease (the main cause of dementia) is one of the key challenges in medicine today. Studies that tested medications targeting directly the two proteins thought to cause Alzheimer's have so far been disappointing.

However, a diabetes drug (semaglutide) may offer a new way to delay or prevent nerve cell damage. Studies in animals have shown that drugs of semaglutide's class (glucagon-like peptide-1 receptor agonists or GLP-1 RAs) protect nerve cells from toxic agents, reduce the Alzheimer's disease protein build-up and improve the animal's memory. Studies of these diabetes drugs have also found a 50% reduction in dementia diagnoses in people taking them.

In this study, we will investigate how a tablet form of semaglutide may affect the processes thought to lead to Alzheimer's disease (AD). We will recruit individuals thought to be at risk for AD (because of high amyloid protein build-up), but with no diagnosis of dementia. Amyloid build-up in the brain is what is known as a 'risk factor' for AD. This means that studies have linked it shown people with high amyloid levels to have 2-3 times higher risk of AD. However, not everyone who has high amyloid levels goes on to develop Alzheimer's dementia.

Participants will be given either semaglutide or a dummy pill (placebo) to take for a year. Placebo does not have an active drug; it is often referred to as a 'dummy pill'. We will assess the effects of semaglutide on AD protein build-up and levels of inflammation in the brain, using a positron emission tomography (PET) head scan at the beginning and end of the study. We will measure levels of AD protein in the blood at each study visit. We will also assess memory and thinking ability using paper and computer-based tests at the beginning, middle and end of the study.

## 2 Why am I being invited to take part?

You are invited because you have agreed to be contacted about research for AD through a research register or your health provider. We are also inviting you because a combination of factors (your age, memory and thinking ability, genetic information and/or medical history) indicate you may be at higher risk of developing AD in the future.

If you are part of a research register, we would like to share your baseline results from this study with the researchers who referred you to us. It is your decision whether or not to allow this access and saying no will not prevent you from taking part in this study.

We plan to include 88 participants in the study from five centres within England.

## 3 Do I have to take part?

No. It is up to you to decide whether or not to take part. Even after you have signed the consent form, you are free to withdraw from the study at any time without giving a reason. Deciding not to participate or withdrawing later will not affect your clinical care in any way. If you decide to take part, you will be asked to sign a consent form. You will be given a copy of this information sheet and the signed consent form to keep.

## 4 What will I need to do if I decide to take part?

We will contact you by telephone to see if you are suitable to take part. If you do not feel comfortable sharing the relevant information by phone we could skip this step and book to see you directly for Visit 1 (see below).

### Visit 1 (Screening)

If you are suitable and agree to take part, you will be invited to a study visit (Visit 1) at your local study centre. The goal of this visit will be to determine if you fit the criteria for the study, including if the medication would be safe for you. At this study visit, you will have a further discussion about the study with one of our doctors and will sign a consent form if you are happy to proceed.

At this screening visit, we will then confirm that you are able to take part by performing the following checks:

- collect information about your medical history and current medication,
- examine you physically, measure height, weight and waist circumference and check vital signs (blood pressure and heart rate),
- do an electric trace of your heart (an ECG),
- take blood samples to check that it is safe for you to take part in the study
- take blood samples for research into potential blood biomarkers for AD,
- send a small part of the blood for genetic testing at Imperial College London to check if you have a rare gene variant that would make one of the head scans difficult to interpret,
- speak to someone that knows you well (your partner, a family member or a friend) to check how well you are doing day-to-day. We can do this at the visit if the person is with you or we can speak to them on the telephone.
- complete a questionnaire to check it is safe for your to have an MRI scan
- ask you to complete some questionnaires to check on your mood and anxiety level.
- If you have diabetes and have not had your eyes examined in the last 1 year, we will arrange for a specialist to perform an examination.

The whole visit will last around 6 hours with breaks and refreshments provided as needed.

If it has been more than 8 weeks since your screening visit (Visit 1), some checks may be repeated to check you are still able to take part.

If there is any reason why this study is unsuitable for you, your participation will end at this visit but we will compensate you for your time. The blood samples we obtain

during this visit will be stored and used for brain health research, regardless of whether you go on to participate in the research.

## Screening Scans

In addition to making sure the study is safe for you (Visit 1), we also need to check if you have elevated levels of amyloid in the brain. To do this, you will be asked to attend a visit at Imperial College London for a head scan. The scan will determine the levels the amyloid protein in the brain. If you have had one of these head scans in the last 2 years, you may not need to repeat this. At the visit, you will be asked to lie on a padded table that glides you into a scanner. You will have a plastic tube inserted into your arm that will allow us to inject a small amount of a substance that shows us the amount of protein in your brain. The scan will take around 30 minutes to complete and the whole visit is expected to take approximately 2 hours. Sometimes the scan result is difficult to interpret, so we may ask you to have an MRI to confirm the levels of amyloid in the brain. We will reimburse you for any costs in getting to the facility and our team can help you with arranging the travel.

If your result shows elevated levels of protein in your brain, you will be able to continue with the study. It is important to note that having increased amyloid levels is one of many risk factors for developing Alzheimer's disease. This means that while there is a link between having high levels and dementia across many people, the significance for the individual is uncertain as not everyone with high levels of amyloid will develop dementia. If you are interested in finding out more, you will be able to discuss the significance of having high amyloid levels with the study team before agreeing to take part. If you are included in the study, we will check on your anxiety, mood and distress levels during its course. If the scan shows you do not have elevated protein levels, your participation in the study will end at this visit but you will be compensated for your time. Even if you cannot take part in the study, we will store the blood samples you had already given us for brain health research unless you specifically ask for it to be destroyed.

## Visit 2 (Before Treatment)

If you satisfy criteria for the study (based on Visit 1 assessment and amyloid head scan), you will be included in the study. You will attend a further study visit (Visit 2) at your local study centre where we will take blood for research and do memory and thinking tests with you on paper, as well as on a tablet computer. Two of the tablet tests require you to say out loud the numbers; if you agree, we would like to keep a recording of your voice to check if certain speech characteristics can help us detect dementia.

You will be given tablets, which will be either the study drug semaglutide, or a dummy tablet. They will look the same and neither you nor the study team will be able to tell which one you are on, but your study doctor can find out if they need to for your safety or to decide your future treatment. The whole visit will last around 4 hours.

We will also post you a device to wear on your wrist for a week after your study visit (Visit 2) at your local study centre. We will provide a pre-paid envelope to return this device after you have worn it for 7 days. This device records movements and can tell us about your levels of activity and sleep quality,

which have both been linked to developing dementia.

In addition, we will also ask you to complete memory and thinking tasks on your home PC or tablet computer. These will take 30 minutes to complete on average and will be done on three consecutive days.

Pre-treatment Scans

You will be asked to visit the Imperial College London scanning facility for three further head scans : one PET scan to determine the levels of another protein associated with AD (called tau), another PET scan to determine the levels of inflammation in your brain and then a MRI scan to check the structure of the brain. If you have already had an MRI as part of your screening visit, you will not need to have another one at this visit. One of the PET scans will be around 1 hour scanning time and the other scan around 30 minutes. Similar to the amyloid scans, you will have to wait a period of time of up to 90 minutes, depending on the tracer. The MRI scan will take 30 minutes. Your total time in the scanner across the three scans will be 2-3 hours.

Once these scans are completed, you will be asked to start taking the study drug once per day with half a glass of water, starting on the morning after your second scan. We will ask that you:

- Do not split, crush or chew the tablet before swallowing.
- Take the tablet in the morning before you eat or drink anything.
- Not to eat, drink or take any other medicines or supplements for at least 30 minutes after taking the tablet.

If you forget to take the tablet in the morning, you can take it up to the time of your evening meal, after this time you should miss that tablet and restart taking the tablet as normal from the next morning.

If you have diabetes, the study doctor will speak to your diabetes team to see if a decrease in the dose of some of your usual diabetes medications should be made to minimise the likelihood of you having low blood sugars (hypoglycaemia). If that is not possible we will not be able to include you in the study.

## Visits Three to Seven (Follow-up after treatment)

Once you have started taking the drug, we will ask you to come to your local study centre on five further occasions (visits 3, 4, 5, 6 and 7, respectively weeks 4, 8, 26, 39 and 52 after starting to take the drug). The visits will take from 3 hours (visits 3, 4, 5 and 6) to 6 hours (visit 7).

At these visits, you will have the following tests and checks:

- Standard health checks including any side effects or problems with taking the medication (visits 3, 4, 5, 6 and 7) as well as a physical exam on visit 7.
- Blood sample taken for research (visits 3, 4, 5, 6 and 7) and for safety checks (visits 4, 5 and 7)
- A repeat of the three head scans from visit 2 at visit 7
- an electric trace of your heart (ECG) at visit 7
- Eye check by a specialist (if you are diabetic) at visit 7
- Memory and thinking tests (pen and paper as well as tablet computer) (2, 4 and 7)

- Mood and anxiety questionnaires (visits 2, 4 and 7)
- Quality of life questionnaires (visits 2 and 7)

Two of the memory tests on the tablet computer will record the sound of your answers so that we can study if there are speech changes that can inform us about dementia risk.

In addition, we will also ask you to complete memory and thinking tasks on your home PC or tablet computer on two further occasions (at the middle and end of the study). These will take 30 minutes to complete on average and will be done on three consecutive days. We will also post you a device to wear on your wrist for a second occasion (at the end of the study) in the week before you come in for your final visit. We will provide a pre-paid envelope to return this device in the same way we did at the start of the study.

Finally, we will telephone you five to six weeks after the last visit to check if you have had any problems since stopping the study drug.

### Unscheduled Visits

If you have any problems whilst taking the study drug, you may be asked to have an additional visit to your local study site. At this visit the amount of study drug you are taking might be changed.

## 5 What is semaglutide?

There are 2 study medicines:

- Semaglutide (the medicine being tested)
- Placebo (a "dummy" medicine)

You will only take 1 of these medicines.

Semaglutide is a medicine doctors can already prescribe in the UK. It is approved for the treatment of type 2 diabetes. In this study, the study doctors will investigate if semaglutide has a positive effect on to the speed at which people build up a protein (tau) thought to play a role in AD.

<u>About semaglutide</u>
Semaglutide is similar to a hormone (Glucagon Like Peptide-1) in the body. Semaglutide has been shown to reduce inflammation in the body, which may help in AD and may improve memory. Semaglutide works like your body's own hormone. It helps to reduce blood sugar levels and it may reduce your appetite. However, semaglutide is not expected to lower your blood sugar level if you do not have diabetes. If you are given the drug, you will start on the lowest dose (3 mg per day) and will gradually increase in two steps to the effective dose (7 and then 14 mg per day). The study team will check on you and there will be option for them to reduce the dose if you are experiencing side effects.

<u>About placebo</u>
Placebo does not have an active drug; it is often referred to as a 'dummy pill'.

<u>Which study medicine will you get?</u>
The study medicine you get is decided by chance - like flipping a coin. This is called randomisation.

- The study medicine for each person is allocated by a computer.
- The chance of you getting semaglutide or the "dummy" medicine is the same.
- A "dummy" medicine (placebo) looks like the study medicine but it is not a medication.

Once you have the medicine, we would like you to keep it in a dry place at room temperature. Please make sure you:

- Do not store above 30°C (86°F)
- Do not freeze or refrigerate
- Store in the original package

## 6 What are the possible disadvantages or risks of taking part?

There are side effects we know about from other studies with oral semaglutide as well as from its use in clinical practice. **See section 24 and 25 for common and uncommon & rare side effects.**

<u>Very common side effects (may affect more than 1 in 10 people):</u>

- Feeling sick (nausea)
- Diarrhoea (loose, watery and more frequent stools)

These side effects are usually mild to moderate and do not last longer than a few days or weeks. They also happen more often at the start of treatment.

If you have sickness (vomiting) or diarrhoea which is bad or does not go away this may lead to insufficient water in the body ('dehydration'). Severe dehydration may lead to kidney problems. Make sure you drink enough fluids and talk to a doctor or the study staff.

If you have diabetes:

- Low blood sugar ('Hypo')

  Early signs may include:
  - feeling hungry, very tired, shaky, worried or irritable
  - rapid or irregular heartbeats
  - pale skin and sweating
  - finding it hard to think and focus

  Signs during the night may also include:
  - damp sheets or bedclothes from sweating
  - nightmares
  - feeling tired or irritable or confused when waking up

  Signs of severe low blood glucose may include:
  - feeling confused
  - strange behaviour such as slurred speech or being clumsy
  - problems with your sight
  - fits (seizures) or passing out

  Low blood glucose is more likely to happen if you:
  - use the study medicine with other anti-diabetic medicines or insulin
  - exercise more than usual
  - eat too little or miss a meal
  - drink alcohol

If you have any signs of low blood glucose, eat or drink something sweet (juice, soft drinks with real sugar, sweets, glucose tablets).
If this does not work, talk to a doctor or the study staff straight away.

**Please tell the study doctor or staff about all problems, illnesses, or injuries that happen to you during the study, even if you think**

**they are not related to you taking part in this study. If you see a health professional during the study for any reason, it is important that you tell them of your participation in this trial by showing them your trial identification card. Please carry this card with you at all times during your study participation.**

Possible side effects from study procedures:

Blood sampling
During this study, small amounts (6-7 tea spoons at a time) of your blood will be taken. This allows the study doctor to see how you are doing and if the study medicine works. You may feel a little discomfort, bruising, bleeding or swelling where the needle goes in. There is also a very small risk of infection where the needle goes in.

Electrocardiogram (ECG)
When making a recording of the electrical activity of your heart by an ECG, your skin may react to the sticky electrode patches. Any skin irritation usually disappears when the patches are removed.

Eye examination (only if you have diabetes)
As part of the eye exam, you will get eye drops to dilate your pupils, which will make your eyes more sensitive to light, and may cause temporary blurred vision. It can take hours before the effects of the eye drops are gone. Occasionally, the eye drops may cause local irritation, an allergic reaction or higher eye pressure. If any of these happen, medication will be given to treat the side effect.

Magnetic resonance imaging (MRI) scan of your brain
MRI is safe and non-invasive and does not involve any ionising radiation (x-rays). However, because they use a large magnet to work, MRI scans are not suitable for everybody. Because of this, you will be asked pre-screening safety questions to help determine if you are able to take part. For example, if you suffer from claustrophobia or have certain types of metal in your body (e.g., heart pacemaker, hip replacement, clips from an operation or iron eye splints), you could not be scanned.

As some of the scans are noisy, we would give you earplugs, head padding or headphones to make this quieter for you. In preparation for your scan we may ask you to change into pocketless and metal free "pyjama-style" top and trousers. You may keep your underwear and socks on, but we would ask you to remove any underwired bras and so recommend wearing a sports type bra if you have one. Metal jewellery, including piercings, must also be removed and eye shadow and mascara must also be avoided, since some types contain materials that can interact with the magnetic field. Lockers are provided to secure your personal belongings and clothing.

Positron emission tomography (PET) scan of your head (special imaging test)
Allergy to the substance radio-labelled drug (tracer) is possible and can cause difficulty with breathing or swallowing, fever, nausea, unusual tiredness, weakness hives, itching skin, rash, reddening of the skin, swelling of the eyes, face, or inside the nose. To check the level of the tracer in your blood, we will need to place a plastic tube in one of your hands. The placement of the tube may cause mild discomfort initially.

If you take part in this study, you will have Positron Emission Tomography scans. All of these will be extra to those that you would have if you did not take part. These procedures use ionising radiation to form images of your body. Ionising radiation may cause cancer many years or decades after the exposure. We are all at risk of developing cancer during our lifetime. 50% of the population is likely to develop one of the many forms of cancer at some stage during our lifetime. Taking part in this study may increase the chances of this happening to you by about 0.14% (1 in 704).

If you agree to take part the images and reports taken will be stored on the NHS Picture Archiving Communications System (PACS). The results of the PET and MRI scans you go through as part of the study will be uploaded to your NHS records at Imperial College London and Imperial College Healthcare NHS trust (NHS Cerner and Integrated Primary and Acute Care Systems (PACS)). Some NHS Trusts also require sites to link the blood test results done at the local site with your NHS records.

## 7 What should I consider?

Driving and using machines

If you have signs of low blood sugar, such as feeling tired or confused, do not drive or use tools or machines. Following the use of eye drops for the eye examination, you may experience temporary blurred vision for some hours. You should not drive as long as your vision is affected. Talk to a doctor or study staff if you are in doubt.

Pregnancy

There are limited data on semaglutide use in pregnancy and therefore women of childbearing potential are excluded from the study. The study staff will confirm during screening that potential female participants are not of childbearing potential.

In the unlikely event that you think you may have become pregnant during the study, tell the study doctor or staff straight away. If it is confirmed that you are pregnant, your study doctor will tell you how to stop taking the study medicine safely. With your permission, the study team will continue to collect information on you and your pregnancy to check for anything unusual.

## 8 What are the possible benefits of taking part?

While there are no immediate benefits for those people participating in the project, it is hoped that this research will lead to potential new treatment for AD for which there is currently no effective treatment.

## 9 Will I receive any payments or travel costs for taking part?

You will receive £500 at the end of the trial in recognition of the inconvenience you have experienced and for giving your time freely to participate in this study. If you are unable to complete the study for any reason, you will receive a payment of £100. If you are excluded following the screening visits you will receive £75. You will also be reimbursed reasonable travel expenses to attend the study appointments on production of receipts. Reimbursement will be coordinated and paid by the University of Oxford. Your bank details will be retained for 7 years within the University finance system, in accordance with University of Oxford Policy.

## 10 Will my General Practitioner (GP) be informed of my participation?

Yes, we will send your GP a letter to let them know you are taking part in the study.

## 11 What if you find something unexpected?

It is important to note that we do not carry out scans for diagnostic purposes, and therefore these scans are not a substitute for a doctor's appointment. Occasionally a possible abnormality may be detected. In this case, we would have the scan checked by a doctor. If the doctor felt that the abnormality was medically important, we would also contact your GP so that they can arrange ongoing clinical care for you, but we would only do this after discussing the finding with you.

We will also contact your GP to inform them of any other abnormal results from the study that may be relevant to your clinical care (*e.g.,* high blood pressure or increased cholesterol).

We will not give you the results of the genetic variant test, as this is not relevant to your clinical care. The results of the genetic variant test will be added to your NHS records at Imperial College London and Imperial College Healthcare NHS trust (NHS Cerner) so you can be correctly identified before your scans.

## 12 What if new information becomes available?

Sometimes during a study, new information becomes available about the treatment that is being studied. If this happens, your trial doctor will tell you about it and discuss with you whether you want to continue in the study. This may mean you will be asked to sign an updated consent form.

## 13 What if I don't want to carry on with the study?

You can stop taking part in all of this study, or in any part of it, at any time and without giving a reason. Leaving the study will not affect your current or future medical care. It is important that you talk to your study doctor or nurse first so that they can advise you about any concerns you may have.

If you choose to stop taking the study medication, you will be asked to continue to attend study visits and have study assessments performed. If you stop attending study visits, we will contact your GP to obtain health information relevant to your study participation (unless you have told us that you no longer wish to be part of the study).

If you choose to withdraw from the study completely, unless you state otherwise, any data or blood samples which have been collected during the study will be used as detailed in this participant information sheet. You are free to request that any stored blood samples are destroyed if you wish.

## 14 Will my taking part in the study be kept confidential?

The information that directly identifies you, such as your name, NHS number and address, will remain at the local study centre and with the University of Oxford's Department of Psychiatry ISAP study team, Imperial College London study team, and Imperial College Healthcare NHS Trust staff processing your blood results and scans, and can be accessed by the study doctor and

other people at your local study centre who are assisting with the trial or your care or are checking that is run properly.

This information may also be checked at the local study centres by the

- University of Oxford (the sponsor), or their representatives (including monitors hired by the sponsor), and/or
- Novo Nordisk (the funder), and/or
- Regulatory agencies.

These persons check that the study is carried out correctly and are bound by a duty of confidentiality.

## 15 What will happen to the information collected about me during the study?

The University of Oxford (the sponsor) is the data controller and is responsible for looking after your information and using it properly. Data protection regulations require that we state the legal basis for processing information about you. In the case of research, this is 'a task in the public interest'.

We will be using information obtained from you (interviews, tests, scans and blood results) and your existing medical or research study records, in order to undertake this study and will use the minimum personally identifiable information possible. The data collected will be used and stored in accordance with the General Data Protection Regulation (UK GDPR).

Your personally identifiable information and health information collected in this clinical trial will be labelled with a unique code number.

- The code number will be used in place of your name.
- Only your local study centre, University of Oxford's Department of Psychiatry ISAP study team and Imperial College London and Imperial College Healthcare NHS Trust staff (scanning and genetic testing facilities) will have the link between your personal information and the coded data. This link will only be provided to sponsor employees involved in the trial who have a need to access this. All other data will be coded before being sent securely to the sponsor.
- Coded data may also include data/information such as images (e.g., MRI/PET scans) or ECGs (electro-cardiograms), biological material and genetic information.
- We will use Royal Mail to send you and receive the wrist-worn actigraphs. Royal Mail will have no access to the data recorded on the devices.

The sponsor will take measures to protect the confidentiality and security of your coded data and your privacy in accordance with current law.

The coded study data will be stored indefinitely after publication or public release of the results of this study. However, the link between the research data and you personally will be broken after 25 years – at that point you will not be able to ask us to destroy the research data. We would like your permission to use this data in future studies and to share this with other researchers (*e.g.,* in online databases). These data will not allow the identification of individual participants. Coded research data

may be securely transferred to, and stored at, a destination outside the UK and the European Economic Area for analysis. The sponsor will ensure that its affiliated companies or its third-party data processors who analyse the data on behalf of the sponsor have a similar level of data protection. However, in countries where the data protection rules are not as strict as the rules in the UK, the same level of privacy cannot be guaranteed.
Specifically, the online cognitive testing platform (Cognitron) based at Imperial College London will analyse your test results and will retain your data for the study duration. The voice recordings will be retained for the study duration by the cognitive testing company (Cambridge Cognition) at a database facility in the United States and then stored at Oxford University for a further period of 25 years after the end of the study. Also, the imaging data you provide will be analysed by our academic partners at Imperial College London using specialist software (AnalyzeDirect), which will retain the data for the study duration (the imaging data will be transferred to the University of Oxford at the study end for 25 year storage). The imaging data will be held separately from your personal data except for the clinical imaging reports, which will be associated with your NHS records (NHS Cerner system and PACS). Both have had their data security procedures approved by Oxford University.

The local study team and University of Oxford's Department of Psychiatry ISAP study team will use your name, home address, and contact details, to contact you about the research study, and to oversee the quality of the study. Hard copies of this information will be stored securely, and electronic information will be stored on encrypted, and password protected computers. They will keep identifiable information about you from this study, including your consent form, which will be held securely for up to 25 years after the study has finished.

The Imperial College London / Imperial College Healthcare NHS Trust team will use your name, date of birth, NHS number, home address and contact details to correctly identify the samples we send them and to ensure the study scans are done to the right person. They will keep your contact details for the duration of the study in case they need to contact you regarding your scanning visits. Hard copies of this information will be stored securely, and electronic information will be stored on encrypted, and password protected computers. The Imperial College London team will delete your personal identifiable data at the end of the study. Your medical records will be retained in line with the local NHS policies.

Data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those rights may be limited in order for the research to be reliable and accurate.

Further information about your rights with respect to your personal data is available at: https://compliance.web.ox.ac.uk/individual-rights

You can find out more about how we use your information by contacting Dr. Ivan Koychev at ivan.koychev@psych.ox.ac.uk or telephone number 01865 613124.

## 16 What will happen to any samples I give?

All samples collected to assess your suitability for the study (including the genetic sample sent to Imperial) and monitor your safety during your participation in the study will be destroyed after the local labs have finished analysing the samples. Any information regarding your local laboratory samples uploaded to your NHS local medical records will be retained in line with the local NHS policies

Some of the blood samples you give us will be stored and used for research purposes. To help keep your information confidential, your research sample will be assigned a study code instead of being labelled with your name. However, your DNA is unique to you so it can never be completely anonymous. Your consent form will be held at your study site until the samples have been depleted or destroyed and will be retained for up to 5 years after study completion.

Your coded samples will be used mainly by local researchers, but ethically approved research projects may take place in hospitals, universities, non-profit institutions, or commercial laboratories worldwide. Samples may be transferred to, and stored or analysed at, a destination outside the UK and the European Economic Area. No identifying information will be shared with collaborators.

We will store your samples and analyse them even if we find that after the Screening Visit (Visit 1) we are not able to include you in the main study.

## 17 What will happen at the end of the study?

At the end of the study your participation will come to an end and the trial treatment will also stop.

## 18 What will happen to the results of the study?

A description of this clinical trial will be available on the International Standard Randomised Controlled Trial Number website: https://www.isrctn.com/. This website will include a summary of the results, but will not include information that can identify you. You can search this website at any time.

The findings from the research will be written up for conference presentations and academic publications, so that other doctors can see them. You can ask they study doctor for a copy of any publication. Your identity and any personal details will be kept confidential. No named information about you will be published in any report of this study.

## 19 How have patients and the public been involved in this study?

Service users and caregivers helped develop the research topic and what research questions should be asked. One of them is a member of the Trial Steering Committee who will continue to be involved in the study and has reviewed the Participant Information Sheet.

You can find out more about taking part in research here: www.crn.nihr.ac.uk/can-help/patients-carers-public/how-to-take-part-in-a-study/.

## 20 Who has reviewed this study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect participants' interests. This study has been reviewed and given a favourable opinion by West Midlands – Edgbaston Research Ethics Committee.

It has been authorised by the Medicines and Healthcare products Regulatory Agency (MHRA), as well as by the Health Research Authority (HRA).

## 21 Who is organising and funding the study?

The study is sponsored and organised by the University of Oxford and is paid for by Novo Nordisk, a company that makes medicines. Novo Nordisk will pay for the cost of the study medicine, the tests and checks, the time spent by the study doctor and staff and use of the clinics.

## 22 What if there is a problem?

The University of Oxford, as Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study.

If you wish to complain about any aspect of the way in which you have been approached or treated, or how your information is handled during the course of this study, you should contact Dr Ivan Koychev at ivan.koychev@psych.ox.ac.uk or tel no. 01865 613124 or you may contact the University of Oxford Research Governance, Ethics and Assurance Team (RGEA) office on 01865 616480, or the Head of RGEA, email rgea.sponsor@admin.ox.ac.uk.

The Patient Advisory Liaison Service (PALS) is a confidential NHS service that can provide you with support for any complaints or queries you may have regarding the care you receive as an NHS patient. PALS is unable to provide information about this research study. If you wish to contact the PALS team, please contact Tel: 01865 613124 and email PALS@oxfordhealth.nhs.uk.

## 23 Taking part in future research

If you agree to your details being held to be contacted regarding future research, your contact details will be held separately from this study on a password protected computer at the local centre where you are taking part in this study. They will retain a copy of your consent form until your details are removed from their database but will keep the consent form and your details separate. Any future contact will be made by the local research team in the first instance. Agreeing to be contacted does not oblige you to take part in future research, and you can ask to be removed from this register at any time if you

wish by contacting the study staff using the details below.

## 24 Appendix 1 - Common side effects

Common side effects (may affect up to 1 in 10 people):

If you have diabetes:

- Worsening of an eye problem caused by diabetes (diabetic retinopathy). Contact your study doctor if you experience eye problems.

Other common side effects include:

- Being sick (vomiting)
- Pain in your stomach area
- Feeling bloated
- Constipation
- Upset stomach or indigestion
  - Pain or discomfort in your stomach – you may also feel sick (nausea) or be sick (vomiting), have heartburn or feel bloated
- Inflamed stomach
  - Signs may include: Gnawing or burning ache or pain ('indigestion') in your stomach that may become either worse or better with eating. Feeling sick (nausea) and being sick (vomiting)
- Heartburn
  - Heartburn is a burning pain in the chest – usually after eating and often at night. The pain may be worse when lying down or bending over
- Passing wind (or gas)
- Feeling very tired
- Low appetite
- Increased pancreatic enzymes (shown in blood tests)
- Gallstones
  - Gallstones may not cause any signs. If they do, they may include: pain in your upper right stomach area, yellowing of your skin or whites of your eyes ('jaundice') or pale stools.
  - If you have any signs of gallstones, talk to a doctor or the study staff as soon as possible.

## 25 Appendix 2 - Uncommon & Rare side effects

Uncommon side effects (may affect up to 1 in 100 people):

- Fast heartbeat (pulse)
- Burping
- Weight decreased

Rare side effects (may affect up to 1 in 1,000 people):

- Serious allergic reactions
  - Signs of serious allergic reactions may include: Swelling of your throat tongue and/or face, trouble breathing, wheezing, fast heart-beat, pale and cold skin, feeling dizzy or weak.

Allergic reactions may become severe and could lead to shock (very low blood pressure) and/or death if not treated (this is called 'anaphylaxis').

If you have any signs of a serious allergic reaction stop taking the study medicine and get emergency help straight away.

- Inflamed pancreas
  - Signs may include severe and long-lasting pain in your stomach (the pain may move to your back), feeling sick (nausea) or being sick (vomiting).

This is a serious problem that can lead to death. If you have any signs of an inflamed

pancreas, talk to a doctor or the study staff straight away.

Other side effects (we do not know how often these may happen):

- Tumours in the thyroid gland
    - A type of tumour (including medullar thyroid cancer) that has been seen in studies with animals. It is not known if this can also happen in humans.