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Re:Cognition Health Brain and Mind Experts

Patient Information Sheet and Consent Form

Short Study Title: TRAILBLAZER-ALZ 6

Protocol Number: I5T-MC-AACQ

EU Trial Number: 2022-502268-18-00

Study Sponsor: Eli Lilly and Company Limited

Investigator: Dr Stephen Pearson

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INTRODUCTION

We would like to invite you to take part in a research study of donanemab in adults with early symptomatic Alzheimer's Disease (AD) Joining the study is entirely up to you. Before you decide, it is important for you to understand why the research is being done and what it would involve for you. We will give you information about the study and one of our team will go through an information sheet with you to help you decide whether or not you would like to take part and to answer any questions which you may have.

- Part 1 tells you the purpose of this study and what will happen to you if you take part.
- Part 2 gives you more detailed information about the conduct of the study.

Individuals with Alzheimer's disease (AD) have elevated levels of a toxic protein called abeta amyloid protein in their brain, which is the recognised "hallmark" for AD. Elevated abeta amyloid protein damages the brain cells, to cause the typical symptoms of AD, and continues to accumulate resulting in the progression of AD and its symptoms. During the screening period, you will have a PET scan of your brain to determine whether you have elevated abeta protein in your brain, and only if it is elevated above a certain threshold, you are eligible to participate in this study.

Please take time to read the following information carefully and discuss it with relatives, friends and your GP if you wish. Do ask us if anything is unclear.

PART 1

WHAT IS THE PURPOSE OF THE STUDY?

The main reason for you to take part in this study is not to treat you for your condition but to help in answering the following research question(s):

- How different donanemab doses compare in their safety (any side effects you might experience) in treating people with AD.
- How different donanemab doses compare in their effectiveness (decreasing the amount of amyloid biomarker in your brain) in treating people with AD.

Our study is taking place internationally and there will be about 800 other patients all around the world who will be taking part including approximately 85 in the UK. It will take up to 91 weeks to complete the whole study.

- The maximum total duration of study participation for each participant, including screening and the posttreatment follow-up period is up to 91 weeks:
- Screening period: up to 7 weeks
- Treatment period: 76 weeks
- Follow-up period: up to 8 weeks

Study visits may last 3-7 hours (longer visits include MRI and/or PET imaging).

WHY HAVE YOU BEEN INVITED TO TAKE PART?

We are inviting you to take part in this study because you have Alzheimer`s disease, The study doctor or their study team will discuss with you the requirements for participation in this study. There may be reasons why it would not be good for you to take part in the study. We will ask you about your health, your family history, and any other medicines you are taking so that we can decide whether you can take part or not. It is important that you are completely truthful with the study doctor and their staff about your past medical history as well as any symptoms experienced during the study.

To participate in this study, you must have a reliable study partner with whom you live or have regular contact, and who can come with you to study visits or can be called during study visits.

You cannot participate in the study if:

- You have a significant disease other than Alzheimer's disease that may affect cognition or your ability to complete the study.
- You have had cancer in the past 5 years (with the exception of certain cancers that the study doctor will discuss with you).
- You are not able to have magnetic resonance imaging (MRI) or positron emission tomography (PET) scans.
- You are taking or have taken certain medications or therapies that your study doctor will discuss with you.

- You have unstable health problems that could interfere with the study or make it unsafe for you to be in the study.
- You have multiple or severe drug allergies that the study doctor will discuss with you.

Your doctor will ask questions about your mental state. Based on your answers, your study doctor will decide if you are actively suicidal or at significant risk for suicide. Your doctor may recommend additional follow up or discontinuation of study medicine based on this assessment.

There may be unknown risks to your embryo, foetus, or nursing infant. That is why you will not be allowed to take part in this study if you are pregnant, plan to become pregnant or you plan to father a child during the study. If you are male, you should not donate semen/sperm.

Please see the section “Reproductive Risks” for further details.

DO YOU HAVE TO TAKE PART?

No, you do not have to take part in this study. Participation in this study is entirely voluntary and it is up to you to decide if you want to take part or not. We will go through this information sheet and describe the study. We will also give you this sheet and allow you time to think about the study. If you are still interested, we will ask you to sign a consent form to show you have agreed to take part. We will give you a copy of this information sheet and your signed consent form to keep. You are free to stop taking part in the study at any time without giving a reason. This will not affect the standard of your patient care.

Sometimes new information is discovered during the course of the research study, which may affect your willingness to continue participation in this study. If this is the case, you will be informed about the new information, and you may be asked to sign a new consent form. If you decide, in the light of the new information, to stop your participation in the study, your study doctor will discuss how your medical care will continue.

We or the company paying for the study (Eli Lilly) may need to decide, at any time and for any reason, to stop the study or stop your participation in the study, even though you may want to continue. This may happen if you have a bad reaction to the study medicine or because of new information about the safety or effectiveness of study medication donanemab. We will explain the reasons why you have to stop and discuss with you how your medical care will continue.

WHAT WILL YOU HAVE TO DO?

If you take part in the study you must agree to:

- attend your hospital /clinic appointments – please notify your study doctor as soon as possible if you cannot attend your hospital/clinic appointment;
- take any given medication regularly as instructed by your study doctor or study team
- provide blood and urine samples;
- have genetic tests on your blood samples;

- complete questionnaires during hospital visits;
- carry with you a small card (about the size of a credit card) which says which study you are taking part in and has a telephone number where you, or any doctor who has to treat you, can contact someone 24 hours a day for advice about the study and/or your treatment;

You must tell your study doctor, or nurse, immediately if you have:

- any accident or injury; or
- any symptoms or illnesses that are new or different in any way; or
- any medical treatment, including surgery, that you have from your GP or another doctor who is not your study doctor; or
- become pregnant or father a child.

Whilst you are taking the study medicine and for 6 months after the last dose you must not donate blood or blood products.

Exceptional Circumstances

In case of exceptional circumstances, you could be asked by your study doctor to perform study visits and procedures differently from the normal study process, including but not limited to:

- dispensation of additional study drug during an extended treatment period
- alternative delivery of study drug (such as delivery at home, provided through your designee, or at another study site)
- provision of personal or medical information required before implementation of these activities
- remote consenting process in case of Informed Consent Form updates
- longer than normal intervals between study visits

If you have concerns, please discuss those with the study team.

EXPENSES AND PAYMENTS

Study medication and study procedures will be provided at no cost to you.

Reasonable travel and additional overnight stay expenses (wherever applicable) related to your and your caregiver's participation in this study will be reimbursed. We will also provide reimbursement for you and your caregivers refreshments for all hospital visits that are over 3 hours long. If you withdraw from the study early, you and your caregiver will be reimbursed for these expenses for the portion of the study that you completed.

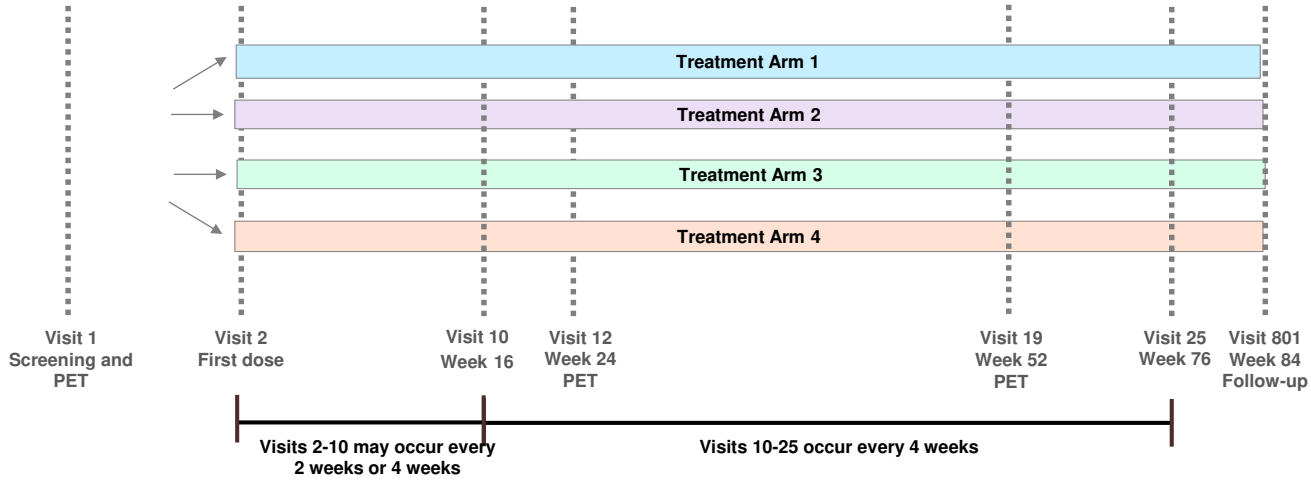
WHAT WILL HAPPEN TO YOU IF YOU TAKE PART?

If you take part in this study, you will be agreeing to undergo more study visits and procedures than you would otherwise have to experience as standard care for your condition. It is not possible to tell you exactly how many additional procedures or visits to the hospital/clinic you might have . However, we can tell you that you will definitely experience several more blood and urine samples taken than normal. You will also need to complete questionnaires, undergo electrocardiograms (ECGs), MRI scans, PET scans, Florbetapir or Florbetaben PET Scans and Cognitive Testing

Below you will see an overview of the different parts of our study and what happens during each part. However, please also see Attachment 3 at the end of this document since this will give you information about all the different study procedures that will happen to you. For example: how often you will have to come to see us; how long each visit may take; how much blood will be taken; and when tests and procedures will be performed.

Our study is divided into 3 separate periods:

1. Screening period – lasting up to 7 weeks
2. Treatment period – lasting up to 76 weeks
3. Post-treatment follow-up period - lasting up to 8 weeks



1. Screening period

The study will be explained to you (and your legally authorized representative, if applicable) and your study partner. You will sign an informed consent and have certain laboratory tests, MRI, PET, and assessment on your cognition to determine your eligibility to participate in this study.

2. Study treatment period

<u>Randomized treatment allocation and placebo</u>

- Sometimes we don't know the best way to treat a certain illness or condition. To find out, we need to compare different treatments. To do that we put patients into different groups and give each group a different treatment. The results are then compared to see if one is better.
- We use a computer programme to put patients at random into treatment groups. Neither you nor your study doctor can choose the group that you will be placed in. Random allocation helps to ensure that similar groups of patients will be compared. If one group does better than the other, we will know that it is likely because the treatment has different effects, and not because of differences between patients in the group.

You will receive study drug (donanemab) for up to 76 weeks in the treatment period

- donanemab given as an intravenous (IV) infusion

- placebo (only at certain visits during the first 14 weeks of the study) given as an intravenous (IV) infusion

All participants will receive donanemab at different dose levels and frequency. Neither you nor the study doctor will know at what dose level or frequency you are taking donanemab.

At certain visits in the first 14 weeks of the study, you might receive placebo instead of donanemab to preserve the blind for the different dosing regimens. A placebo is an infusion that looks like the study drug (donanemab) but has no medicine.

You will receive donanemab or placebo through an infusion into your vein about every 2-4 weeks. Each infusion will last over a minimum of 30 minutes.

As you are receiving donanemab, the amount of the amyloid biomarker in your brain will be measured at certain visits using a PET scan. If amyloid biomarker level in your brain drops below a certain level, you will stop receiving study drug for the remainder of the study.

3. Follow-up period
This will start when you stop receiving the study treatment and are no longer taking donanemab or Placebo. It will last 8 weeks, and it is likely that you will have one visit to the hospital clinic.

COLLECTION OF BLOOD AND URINE SAMPLES
Various blood and urine samples will be collected from you during this trial.

The specific procedures for collecting these samples and the risks associated with collection are explained below and in the risk section in this document. Your samples will be identified by your patient number only, and not by your name or NHS number. Your patient number is a unique code assigned to you in the beginning of the trial. Your patient number is pseudonymised – this means that your patient number cannot be linked to you directly without additional information.

It is possible that you have already done testing that would be helpful for this research. This may have included biomarker and/or genetic testing that was done as part of your care prior to this study. If this information is available, we may request that it be provided to the sponsor to use for the research described in this consent.

The analysis of your samples may contribute to the creation of new laboratory tests, new medicines, or other items that may be commercially valuable to the sponsor. The sponsor has no plans to provide you, either now or in the future, any compensation, royalty, or any other financial benefit that might result from any product, procedure, or other item that may be developed from studying your samples or any information or data that is derived from such research.

• Samples for Study Qualification and Health Monitoring

Blood and urine samples will be collected to determine if you meet the requirements to participate in this study.

Additional blood and urine samples will be collected throughout the study to monitor your health and your response to study medication.

All samples collected for Study Qualification and Health Monitoring will be destroyed within 60 days of confirmation of the test results, unless laws, regulations, or international laboratory certification standards require a longer retention period. This confirmation will either occur immediately after initial testing or may require that samples be held to be retested at a defined later point in time.

• Samples for Measuring Study Medication Levels

Blood samples will be collected to measure the amount of study drug that is in your body and how your body breaks it down. These samples will be stored for a maximum of 1 year after this study is finished.

• Samples for Genetic Research

Blood will be collected to study your DNA. DNA is genetic material that is found in all the cells of your body. DNA contains instructions that your body reads to understand how it should be built and work. Some of these instructions tell your body how to react to medicines. For this reason, looking at DNA can sometimes help explain why people with a disease respond differently to the same medicine. For example, some people taking this study medicine may respond well. Others may have little or no response or have side effects.

Researchers may study your DNA to learn how donanemab works for you. Information about your DNA may be used to create or improve tests to measure these genetic factors. Researchers may also study your DNA to understand the disease for which this study medication or class of medications is being developed. The results from genetic testing will not be shared with you.

The DNA sample may be stored for up to 15 years after this study is finished.

• Samples for Biomarker Research

Sometimes scientists measure substances in the body to diagnose, evaluate, or monitor a person’s medical condition or disease. For example, cholesterol levels in the blood can be used to monitor a person’s risk for heart disease. In this example, cholesterol is a biomarker.

Blood will be collected to identify or better understand biomarkers.

Researchers may use biomarkers to learn more about Alzheimer`s disease or how study participants respond to study medication or other medicines that you are taking during this study. Your sample(s) may also be used to create or improve tests to help identify study participants in the future who may respond to this study medication.

The sample(s) may be stored for up to 15 years after this study is finished.

• Samples for Antibody Research

Blood sample(s) will be collected to determine if your body produces antibodies against the study medication donanemab. Antibodies may affect how study medication works in your body if you take it in the future.

The sample(s) may be stored for up to 15 years after this study is finished. The samples are pseudonymized.

During the study, your blood samples will be stored at Q2 Solutions Europe, Rosebank, West Lothian, United Kingdom of Great Britain and Northern Ireland, EH54 7EG.

For long-term storage, after the study has ended your blood biomarker, genetic and antibody samples will be sent to Azenta Life Sciences Im Leuschnerpark 1b, 64347 Griesheim Germany.

Please note your samples may be moved at the request or notification of the Sponsor to another appropriate facility.

WHAT HAPPENS WHEN THE RESEARCH STUDY STOPS?

The study doctor or one of the doctor's staff members team may try to reach you after you have stopped study treatment. They will want to talk to you to see how you are doing. They may also want to ask about any other treatment you received since leaving this study. Your study doctor can discuss the treatment and therapy options that are available to you on the NHS at that point in time.

If you are not able to attend a planned study visit or maintain telephone contact, the team may try to contact you to check on your health status and to see if you have experienced a serious health event. They may try to locate you and search for your information by contacting your family doctor or GP, and hospitals or clinics that treat you. The study team will try to contact you unless you withdraw consent of getting contacted further. Attempts to determine your health status may also be done by searching public records such as national registries or databases and voter records, if not prohibited by your local laws and regulations.

If you move or lose contact with the study doctor, they may give your name and last known contact information to a patient locator service to try to find your current information, if not prohibited by your local laws and regulations. The patient locator service will not contact you directly and any new information they find will be shared with the study team.

WHAT ARE THE ALTERNATIVES FOR TREATMENT?

You do not have to take part in this study in order to receive treatment for your Alzheimer`s disease. There are other treatments and therapies for your condition and your study doctor can discuss these treatments with you if you wish.

Your other choices may include:

- Getting treatment or care for your AD without being in a study
- Getting no treatment

The study doctor can discuss these treatments and therapies with you.

WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART?

Although donanemab is being tested as a treatment for Alzheimer`s disease, we cannot promise that the study will help you. The information we get from this study, however, may help us improve the treatment of people with Alzheimer`s disease in the future.

You may receive information about your health from any physical examinations and laboratory tests to be done in the study.

WHAT ARE THE POSSIBLE SIDE EFFECTS OF THE STUDY MEDICATION AND POSSIBLE DISADVANTAGES AND RISKS OF TAKING PART?

There may be risks to you if you take part in this study.

Safety information from 1402 participants with Alzheimer's disease who received donanemab in 3 completed and 3 ongoing studies for a maximum duration of 18 months, as of 16 June 2022 has been reviewed.

Treatments and procedures in this study may have unwanted or harmful effects (side effects).

In studies of donanemab, participants had these important side effects:

Side effects in the brain: swelling or areas of bleeding in the brain or lining the brain.

- Swelling or small areas of bleeding in the brain or lining the brain are side effects very commonly seen in people taking donanemab.
- Most people who have swelling or bleeding in the brain do not have any symptoms. Swelling or small areas of bleeding are usually found during the routine brain scans that are part of the study. These scans are called MRIs (magnetic resonance imaging).
- If tests find that you have swelling or bleeding in the brain, your study doctor may ask you to have extra MRIs. This is to see if the side effect stays the same, gets worse, or gets better.
- Some people do have symptoms when they have swelling or bleeding in areas of the brain. These symptoms can include, but are not limited to:
- headache
- worsened confusion
- speech difficulties
- problems with your sense of balance
- disorientation (for example, difficulty understanding what is happening or where you are)
- feeling tired
- visual disturbances
- shaking and uncontrolled muscle movements
- muscle weakness
- seizures, and
- vomiting.
    - Call your study doctor right away if you experience any new or worsening symptoms.
    - Symptoms may be treated with medicine, a hospital stay, or physical therapy, which could be short-term or long-term.
    - Swelling or bleeding in the brain can be life threatening or result in permanent disability or death, but this is not common.

- The risks of swelling or bleeding in the brain are different for people with particular genes. Most people with Alzheimer's disease have a particular form of the Apolipoprotein E or APOE gene. This form is known as APOE e4. The risk of swelling or small areas of bleeding in the brain or lining the brain is higher for people who have the APOE e4 gene. In Table 1, you can see how often these side effects in the brain happened in an earlier study in all people who got donanemab and in people with the APOE e4 gene who got donanemab.

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Table 1. Side Effects in the Brain in Participants with and without APOE e4 Gene

Side effect	**Percentage Of All Participants in The Study Who Had Side Effects**	**Percentage of all Participants in the Study with the APOE e4 Gene who had Side Effects**
Swelling in the brain	26%	33%
Small areas of bleeding in the brain or lining the brain	28%	33%

Allergic reactions, including reaction to the drug being given into the vein (known as "infusion reaction")

- Allergic reactions are side effects commonly seen in people taking donanemab.
- These allergic reactions may occur at the time the medication is given or afterward.
- Some reactions include reddening of skin, chills, headache, chest tightness, shortness of breath, muscle aches, and changes in blood pressure.
- Other reactions are feeling sick to the stomach, rashes, fever, throat irritation, hives or wheals, itching, and vomiting.
- More serious allergic reactions can include low blood pressure, wheezing, or difficulty breathing. These can be life threatening.
- During visits with infusions, the study staff will check you for signs of allergic reactions. At other times, if you feel the above reactions, report to the study staff.

In Table 2, you can see how often these important side effects, and other side effects happened in studies of donanemab. The side effects listed below occurred in at least 1 in 100 people who received the study drug.

Table 2. Very Common and Common Side Effects Seen in People Taking Donanemab

Very Common (10 or more out of 100 study participants)	Common (1 or more out of 100 study participants)
Swelling in the brain	Reaction to drug being given into the vein (infusion reaction)
Small areas of bleeding in the brain or lining the brain)	Feeling sick to the stomach
	Vomiting

Other common (1 or more out of 100 study participants) side effects reported in participants included (not all side effects listed below may be caused by donanemab)

- Headache
- COVID-19 infection
- Falling down
- Common cold
- Dizziness
- Urinary tract infection (for example, kidneys, ureters, urinary bladder, and urethra)
- Fatigue
- High blood pressure
- Pain in joints
- Diarrhea
- Pneumonia (Infection in the lungs)
- Fainting/passing out
- Feeling nervous, restless, or tense
- Sinusitis (infection in the hole areas around the bones in your face)
- Back pain
- A common type of skin cancer (scientific term for this condition is basal cell carcinoma) that is usually treatable
- Pain in arms or legs
- Cut or tear in the skin

Other safety information - Antibodies to the study treatment

- The main purpose of antibodies is to get rid of infections. Your immune system makes antibodies to viruses and other unknown substances that get inside your body. Antibodies make the unknown substance inactive or less powerful. Antibodies can also cause allergic reactions.

- Immune systems often react to drugs like donanemab in the same way they react to other unknown substances. If you receive donanemab, your immune system will likely make antibodies to it at some time during the study. This may affect how well the treatment works or increase the likelihood of an allergic reaction.

Nonclinical Safety Data

Donanemab has been studied in animals. There is no relevant additional information from these studies about side effects of this drug in humans.

Reproductive Risks

Women not of childbearing potential and males may participate in this study.

If you are a female and could possibly become pregnant, you cannot be in this study.

No male birth control is needed unless it is a study requirement by the local government.

There is currently no information on the effects of florbetapir 18F or florbetaben 18F to a developing fetus. However, it is known that higher levels of radiation can cause damage to a developing fetus. Therefore, if you are pregnant, planning to become pregnant, or are breastfeeding a child, you cannot participate in this study.

There may be unknown risks to an embryo, foetus, or nursing infant. That is why you will not be allowed to take part in this study if you are pregnant, plan to become pregnant or you plan to father a child during the study.

If you become pregnant during the study or think you/your partner are pregnant it is important that you tell your study doctor right away. If you are pregnant, the study medication will be stopped, and you might be discontinued from the study. The study doctor will discuss with you how your care will continue. Lilly (the Sponsor) will contact your study doctor to obtain additional pregnancy information (eg. due date, length of time medication was taken prior / during pregnancy, any reported problems etc.). If your study doctor is unable to provide pregnancy information and if you do not want to disclose all / any part of the pregnancy information, Lilly will document this and will not pursue follow up.

Other Risks and Discomforts

All participants will receive standard treatment for Alzheimer`s disease during this study, your study doctor will explain the risks that may be associated with the use of this treatment. Your study doctor can also provide you with the Patient Information Leaflet (PIL) for Alzheimer`s disease medication.

At any time during this study, you may have a return, or worsening, of your symptoms and/or you may be advised to take supportive medication to treat symptoms that may arise during the study. The study doctor will discuss any risks with you.
During the study, you will continue to take your current medication unless it is not allowed in the study, which the study doctor will discuss with you. There may be unknown risks of possible harmful interaction with other medication you may be taking. You must inform your study doctor about any other medication you are taking.

Tell your study doctor about any new medications or procedures that you have received while you are participating in this study. Ask them about any risks that may be associated with your current medication(s). Your study doctor may suggest continuing the medication at the same dose or change the dose.

You also may be advised to take medication to treat symptoms that may arise during the study. The study doctor will discuss any risks with you. Whilst you are taking the study medicine you must not give blood.

If you have private medical insurance or travel/holiday insurance, you should check with your insurance company that taking part in a clinical trial will not affect your policy.

Risks and Discomforts of Study Procedures

1. **Blood Tests**

For most people, needle punctures for blood draws do not cause any bad problems. However, sometimes they may cause bleeding, bruising, discomfort, infections and/or pain where you had the blood drawn. You may also feel dizzy. Your blood will be taken around 10 times during the entire study and a maximum of 3 to 5 tablespoons will be collected per draw.

2. **Cognition Testing and Questionnaires**

Some people may find that doing the questionnaires is upsetting or embarrassing. Cognitive testing may cause some individuals to become upset, frustrated, bored, or tired. You will complete two sets of questionnaires Mini Mental State Examination (MMSE) will be completed by you once during the screening visit and Columbia Suicide Severity Rating Scale (CSSRS) which will completed by you at approximately every visit. MMSE takes about 7-8 minutes to complete and CSSRS takes around 5 minutes to complete.

3. **Electrocardiograms (ECGs)**

There is no pain or discomfort during an ECG; however, removing the pads may cause some irritation to your skin.

4. **Intravenous (IV) infusion**

For most people, needle sticks for IV injections do not cause any serious problems. Sometimes they may cause bleeding or bruising. They may also cause infections and/or pain at the needle site. Putting the IV in your arm is done with sterile equipment, but germs on the skin may enter through the skin around the IV, causing swelling, redness, and fever. You may feel swelling, pain, and redness around the vein. A blood clot or an air bubble can be delivered into the circulation through an IV and end up blocking a vessel; this is called embolism. There is a low risk of this. Extravasation is accidentally putting the drugs into the surrounding tissue instead of the vein. Fluid may leak or flow outside the vein if the vein becomes damaged.

5. **Magnetic Resonance Imaging (MRI) Scan**

MRI scans do not usually have bad effects unless you have metal in your body. Do not take part in this test if you have any pieces of metal in your body because of earlier injury or surgery. Some older tattoo ink may contain metal, so you should also tell the study doctor or MRI staff if you have any tattoos.

People who do not like to be in small spaces (claustrophobia) might feel confined by an MRI. You may be bothered by the noise the scanner makes. You will be given ear plugs or headphones to reduce the noise of the scanner. MRI scan last for about 45 minutes.

6. **Positron Emission Tomography (PET) Scan**

PET-CT scans use a carefully controlled amount of radioactivity (known as a tracer, which is injected intravenously) and X-rays from a low-dose CT scan to create detailed images of the brain. The images of the tracer are combined with the CT scan to give very detailed pictures of your brain. Information on the radiation risks is given below. The scan itself causes no pain. There is a very small chance that you may be allergic to the radioactive tracer you are given by vein. You may have some pain when the fluid is placed in your vein. You may experience anxiety if you are afraid of close spaces. If you tell your doctor ahead of time, they may prescribe a medicine that will relax you during this test. The scan requires no recovery time and the radioactivity from the tracer will leave your body very quickly. You will be advised if you need to avoid contact with other persons immediately after the scan, although is not usually necessary. PET scan usually takes around 20 minutes to complete.

7. Risks of Radiation Exposure

Florbetapir 18F, florbetaben 18F are imaging agents. Each one includes a small amount of radioactivity (radiation) that is necessary to create PET scan images or pictures.

Florbetapir 18F and florbetaben 18F is/are approved by the United States Food and Drug Administration and the European Medicines Agency to see how much amyloid (an abnormal protein) has accumulated in the brains of adult patients who are being checked for AD and other possible causes of problems with thinking and remembering.

The total amount of radiation from each PET-CT scan is about the same as we receive from around three years of natural background radiation. If you take part in this study, you will have four PET-CT scans of your brain. All of these will be extra to those that you would have if you did not take part in the trial. PET-CT scans use ionising radiation to form images of your brain and provide your doctor with other essential information about your response to the study drug. 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 will increase the chances of this happening to you to a maximum of about 50.1%, an increase of 0.1% or less.

8. Risks of Florbetapir 18F Injection

Avid Radiopharmaceuticals, a wholly owned subsidiary of Eli Lilly and Company that develops florbetapir, regularly reviews all important safety information for investigational products. Review of the most recent data (through 06 April 2021) included approximately 38,745 subjects who have been administered florbetapir 18F injection in clinical studies and approximately 49,519 patients who have received florbetapir 18F injection where the product is marketed for clinical use. Information about the side effects of florbetapir 18F injection is based on a combined database of 2105 subjects (through 06 January 2017) who received florbetapir 18F injection in clinical studies.

9. Risks and Discomforts Associated with Florbetapir 18F Injection

In clinical studies, the most common side effect of florbetapir 18F injection was headache, which was reported in 2.1% of subjects. Uncommon side effects (reported by 1 or more of 1,000 subjects) were: injection site reaction and flushing. Rare side effects (reported by 1 or more of 10,000 subjects) were: infusion site rash, dysgeusia (altered or impaired sense of taste), pruritus (itching), and urticaria (hives).

Toxicology: Florbetapir 18F

Florbetapir, the non-radioactive version of florbetapir 18F, has been tested in laboratory and animal studies to measure the risk of developing cancer. In laboratory tests,

florbetapir showed the potential to cause damage to genes. However, further studies conducted in living animals with florbetapir at doses up to 83 times the maximum human dose of florbetapir 18F did not produce any evidence for damage to genes. Damage to genes can lead to the development of cancer.

Other safety studies in animals did not identify any drug-associated risks; however, some potential risks of the drug may still be unknown.

Risks of Florbetaben 18F Injection

The overall safety of florbetaben is based on approximately 1080 people who have received injections.

Risks and Discomforts Associated with Florbetaben 18F Injection

Side effects that were reported as common (reported by 1 or more of 10 subjects) include injection site pain and redness of the skin at the injection site.

Toxicology: Florbetaben 18F

Long-term studies and cancer studies have not been conducted. No studies on reproduction have been performed. Damage to genes can lead to the development of cancer. Studies conducted in animals with Florbetaben 18F at doses greater than 20 times the maximum human dose did not produce any adverse effects.

Other Important Information:

You will not be able to donate blood from the time the study starts until 6 months after you have stopped taking the study medicine.

Avoid excessive alcohol use during the study. Excessive alcohol consumption is defined for men as consuming an average of more than 3 drinks per day or more than 21 drinks per week. For women, excessive use of alcohol is defined as consuming an average of more than 2 drinks per day or more than 14 drinks per week.

You should not start any new medicine while you are in the study without first consulting the study doctor.

WHAT IF THERE IS A PROBLEM?

In addition to the risks already described, the study medications and the study procedures may have other unknown risks. If you have any injury, side effect or other unusual health experience during the study, make sure that you let us know immediately by calling the following number 07388992013. You can call at any time, day or night, to report such health experiences.

WILL YOUR TAKING PART IN THIS STUDY BE KEPT CONFIDENTIAL?

Yes. All information about you will be kept confidential. Eli Lilly and Company Limited is the sponsor for this study based in the United Kingdom. We will be using information from you and/or your medical records in accordance with the Data Privacy statement included with this document. In order to undertake this study Eli Lilly will act as Data controller. This means that we are responsible for looking after your study information and using it properly. Eli Lilly and Company Limited will keep your study information for 15 years or for as long as it is required for legitimate business purposes.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. Some of your information may not be available to you until the study has been completed. To safeguard your rights, any data that is sent away from your study site will be identified by a code and not by your name / NHS number. The minimum amount of data necessary will be collected for the purpose of the study. If you withdraw from the study, the sponsor will keep the coded information about you that we have already obtained and use it for the purposes outlined in this consent form. This is necessary to ensure the scientific integrity of the study and to follow legal and other requirements on how information is used in research studies. If you allow it, we may also continue to collect information about you from your study doctor. If you do not want any further information about you collected and provided to the sponsor for the purpose of this study, you may let your study doctor know that you withdraw your permission. Your study doctor will then need to inform the sponsor in writing of your decision and will update your medical records accordingly. In addition, you would no longer be able to participate in the study.
You can find out more about how we use your information by contacting your study doctor. Your study doctor will act as liaison with Eli Lilly for any questions you may have. You can also find out more about how we use your information by contacting us directly at Privacy@lilly.com.

Re:Cognition Health will collect information from you and/or your medical records for this research study in accordance with our instructions.

Re:Cognition Health will keep your name, NHS number and contact details confidential and will not pass this information to Eli Lilly and Company Limited. Re:Cognition Health will use this information as needed, to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Certain individuals from Eli Lilly and Company Limited and regulatory organisations may look at your medical and research records to check the accuracy of the research study. Eli Lilly and Company Limited will only receive coded information without any identifying information. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

Re:Cognition Health will keep identifiable information about you from this study for 15 years after the study has finished.

There are also types of information that your doctor must share with others. If something happens to a person in the study that could harm them or someone else, your doctor will share this information with only the people that need to know. Examples of this are bad treatment or something that is against the law.
Your personal health information will be stored in limited-access databases. Your health information will be used and disclosed in accordance with the Data Privacy Statement included with this document. Steps are taken to reduce the risk of your personal health information being misused or accessed by unauthorized people. However, these risks cannot be eliminated.

Your study data will be saved for as long as it is needed for legitimate business purposes according to the sponsor’s records retention policies and applicable laws and regulations.

If you have concerns about how your information has been handled, please contact the Information Commissioners Office (ICO).

If you have concerns about how your information has been handled, information and advice from the Information Commissioners Office (ICO) can be accessed at https://ico.org.uk . If you have had a problem accessing your personal information related to your involvement in this clinical trial, or if you're unhappy about how yours or other people's information has been handles, you can contact the Information Commissioners Office (ICO) online at https://ico.org.uk/make-a-complaint/, via live chat on the website, or by calling the ICO helpline on 0303 123 1113.

INVOLVEMENT OF THE GENERAL PRACTITIONER / FAMILY DOCTOR

With your permission, your GP will be informed that you are taking part in a study so that your study doctor and your GP can provide proper medical care. We may also contact your GP to obtain your relevant medical history.

This completes Part 1 of the Information Sheet.

If the information in Part 1 has interested you and you are considering taking part, please continue to read the additional information in Part 2 before making any decision.

Patient Information Sheet and Consent Form

Part 2

WHAT IF NEW INFORMATION BECOMES AVAILABLE?

Sometimes we get new information about the treatment/medication that is being studied. If this happens, we will tell you about it and discuss whether you want to continue in the study. If you decide to carry on in the study, we will ask you to sign an updated consent form.

If you decide not to continue, we will make arrangements for your care to continue. If the study is stopped for any other reason, we will tell you and arrange your continuing care.

WHAT WILL HAPPEN IF YOU DON'T WANT TO CARRY ON WITH THE STUDY?

You are free to decide, for any reason, to stop taking part in the study at any time without your medical care being affected. We will discuss with you how your care will continue. You will no longer receive treatment with the study drug. Your study doctor will discuss the treatment and therapy options that are available to you on the NHS at that point in time.

We will talk to you about any medical problems that may happen if you stop taking part in the study.

For information regarding your data collected up until the point at which you decide to stop, please refer to Attachment 1, Data Privacy Statement.

WHAT IF YOU HAVE A CONCERN ABOUT THIS STUDY?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed.

The sponsor, Eli Lilly and Company Limited, agrees to abide by the Association of the British Pharmaceutical Industry (ABPI) The sponsor will pay compensation where the injury probably resulted from: a drug being tested or administered as part of the trial protocol; or any test or procedure you receive as part of the trial. The sponsor will not compensate you if an injury results from a procedure carried out which is not in accordance with the protocol for the study. Your legal right to claim compensation for injury, where you can prove negligence, is not affected. Your study doctor can give you a copy of the ABPI. The ABPI Code of Practice can be accessed at https://www.abpi.org.uk/reputation/abpi-2021-code-of-practice/. The web interactive ABPI Code of Practice can be found at https://www.pmcpa.org.uk/the-code/2021-interactive-abpi-code-of-practice/.

If you have a concern about any aspect of this study, you should ask to speak to one of the study team who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the hospital or GP surgery.
Re:Cognition Health Compliance team,compliance@re-cognitionhealth.com, Tel: 020 45311926 / 020 3355 3536

WHO IS ORGANISING AND PAYING FOR THE RESEARCH?

The sponsor, Eli Lilly and Company Limited, is paying the Dr Pearson and/or Re:Cognition Health for their work in this study.

WHO HAS REVIEWED THE STUDY?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee (REC) to protect your safety, rights, well-being and dignity. The study has been reviewed and given favourable opinion by North West - Liverpool Central Research Ethics Committee REC.

HOW CAN YOU GET MORE INFORMATION?

If you have any questions about this study or your rights please contact Dr Pearson or one of the study team on 01752875604.

If you would like to find out more information about clinical trials, please ask your study doctor/study nurse or visit the following website: https://bepartofresearch.nihr.ac.uk/

The information in this informed consent document is intended to help you determine whether participating in this study is right for you. You may wish to discuss this information with others for the purposes of helping you decide whether to participate in the study or as needed for medical treatment. You are asked to treat this information as confidential and to inform any others with whom you share this information that it is confidential. During the course of this study, you and/or a family member or caregiver of yours may learn, or have access to, proprietary information of the Sponsor, including drug product information. Proprietary information should be maintained as confidential. Please ask your study doctor for more specifics if you have a question about the nature of any particular information.

Thank you for reading this information sheet and for taking part in this study (if you decide to do so. To take part in this study, you must personally sign and date the consent form. We will give you a copy of this information sheet and your signed consent form to keep. The original signed informed consent form will be put in your medical records.

Attachment 1- Data Privacy Statement

By signing the consent document for this study, you are giving permission for your personal health information and study data to be used and shared as described in this Data Privacy Statement. Your personal health information includes information from your existing medical records needed for this study and new information created or collected during the study.

If you agree to participate in the research study, your personal health information will be used and shared in the following ways:

• The study doctor and staff will send your study-related health information ("study data") to the sponsor of the study, its associated companies and its representatives ("the sponsor"). The sponsor conducts business related to clinical research in many countries around the world so this may involve sending your study data outside of the UK and Europe. Other countries may have privacy laws that do not provide the same protection as the laws in this country and the EU. However, the sponsor will respect the terms of this Data Privacy Statement in all countries.

• The sponsor will use the study data for research purposes to support the scientific objectives of the study described in the Patient Information Sheet and Consent Form. They will also use your data to assess the safety or efficacy of any medication or treatment included in the study and to better understand the disease(s) included in the study. Your data may also help the sponsor to improve the design of future studies.

• Your 'pseudonymised' (non-identifiable) study data, either alone or combined with data from other studies, may be shared with regulatory authorities in this country and other countries including the United States.

• Study data that does not identify you may be published in medical journals or shared with others as part of scientific discussions.

• Your original medical records, which may contain information that directly identifies you, may be reviewed by the sponsor and regulatory authorities in this country and/or other countries including the United States.

The sponsor works with business partners in drug development. The sponsor may share your study data with these business partners, but only if the business partner signs a contract that requires it to protect your study data to the same level and in the same way that the sponsor has agreed to protect your data.

You may request to see and copy your personal health information related to the research study for as long as the study doctor or research institution holds this information. However, some of your study related health information may not be available to you until after the study has been completed. This is to ensure the study retains its scientific credibility.

Your study data will be kept for as long as it is needed for legitimate business purposes according to the sponsor's records retention policies and applicable laws and regulations.

: Unit 2, 5 Research Way
: Plymouth Science Park
: Plymouth
: PL6 8BT
: www.re-cognitionhealth.com
: Telephone: 01752 875604

Attachment 2 – Consent Form

Re:Cognition Health Brain and Mind Experts

Study Title: Exploration of Different Donanemab Dosing Regimens

Study Code: I5T-MC-AACQ **Centre Number:** 74594

Name of Researcher: Dr Stephen Pearson **Patient Identification Number for this trial:**

To take part in this study, and to authorise use and disclosure of your personal health information, you must initial the boxes against each statement below, and sign and date this page.

	Patient initials
• I confirm I have read and understood all of the information in this Patient Information Sheet and Consent Form for the above study. I have had time to think about it, ask questions and have these answered to my satisfaction.	
• 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.	
• I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from the sponsor company, from 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.	
• I allow the study doctor and the sponsor to use and disclose my personal health information as described in the Data Privacy Statement (Attachment 1 to this document).	
• I voluntarily agree to take part in this research study, to follow the study procedures, and to provide necessary information to the doctor, nurses, or other staff members, as requested.	
• I agree to my DNA, Biomarker and Antibody samples being stored for 15 years after this study is complete and that they may be used in future ethically approved research by the Sponsor (Lilly) to create or improve tests to identify patients who may respond to Alzheimer`s disease treatments in the future;	
• I agree that my GP will be contacted about my participation in this study and will be asked about my relevant medical history.	
• I have received a copy of this Patient Information Sheet and Consent Form to keep for myself.	

PATIENT		
PRINT NAME HERE	SIGN NAME HERE	PERSONALLY ADD TODAY'S DATE TIME HERE

Signature for Patient/Parent/Impartial Witness

Instructions**:** Signature boxes may be amended as need for the study, e.g. for parents providing consent for minors or for impartial witnesses. Consent may be changed to assent in cases of minors' signatures.

INVESTIGATOR		
PRINT NAME HERE	SIGN NAME HERE	PERSONALLY ADD TODAY'S DATE TIMEHERE

Study Schedule for I5T-MC-AACQ
Period I - Screening

I5T-MC-AACQ	Period I Screening	Notes
Visit Number	**Visit 1**	
Days Relative to Start of Study	-49 to -1	
You and your partner will sign informed consent forms as directed	X	
You will discuss your medical history and habits	X	Alcohol, caffeine, tobacco use.
You will discuss how you are feeling and any medicine you are taking	X	
Your height and weight will be measured	X	
Your blood pressure and pulse will be measured	X	Your body temperature will be measured along with blood pressure.
You will have a physical and neurological examination	X	
You will have an ECG	X	May be done a greater number of times if required as per the study doctor.
Your doctor will ask questions to assess your cognition	X	
You will have blood drawn (Approximate amount in mL)	40	
You will give a urine sample	X	
Screening PET scans and MRI		
You will have a PET and a MRI scan	X	You will have 4 amyloid PET scans during the study.

Period II - Treatment Visits 2-15

I5T-MC-AACQ	Period II Treatment														Notes
Visit Number	2	3[a]	4	5[a]	6	7[a]	8	9[a]	10	11	12	13	14	15	
Week Relative to Start of Study	0	2	4	6	8	10	12	14	16	20	24	28	32	36	[a] Depends on your dosing regimen
You will discuss how you are feeling and any medicines you are taking	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Your weight will be measured	X						X				X			X	
Your blood pressure, pulse and temperature will be measured	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
You will have a physical and neurological examination	X						X				X			X	
Your doctor will ask questions about your mental state	X		X		X		X		X	X	X	X	X	X	
You will have blood drawn (Approximate volume in mL)	66		65		62		69				69			53	
You will have an MRI			X				X				X				You may have unscheduled MRIs at the discretion of the study doctor
You will have a PET scan											X				
Dosing															
You will be given the study medicine	X	X	X	X	X	X	X	X	X	X	X	X	X	X	You will stay for at least 30 minutes after each infusion.

Period II - Treatment Visits 16-25, the Early Discontinuation Visit, and Period III Posttreatment Follow-Up Visit 801

I5T-MC-AACQ	Period II Treatment											Period III	Notes
Visit Number	16	17	18	19	20	21	22	23	24	25	ED	801	
Week Relative to Start of Study	40	44	48	52	56	60	64	68	72	76		84	
You will discuss how you are feeling and any medicine you are taking	X	X	X	X	X	X	X	X	X	X	X	X	
Your weight will be measured				X			X			X	X		
Your blood pressure, pulse and temperature will be measured	X	X	X	X	X	X	X	X	X	X	X	X	
You will have a physical and neurological examination				X			X			X	X		
Your doctor will ask questions about your mental state	X	X	X	X	X	X	X	X	X	X	X	X	
You will have blood drawn (Approximate amount in mL)				69			53			66	66	13	
You will have an MRI				X							X		You may have unscheduled MRIs at the discretion of the study doctor
You will have a PET scan				X						X	X		In the event a repeat scan is required, for example, the scan is not analyzable, you may have 1 additional scan in 1 year.
You will be given the study medication	X	X	X	X	X	X	X	X	X				You will stay for at least 30 minutes after each infusion.

Abbreviations: ED = early discontinuation; IV = intravenous; MRI = magnetic resonance imaging; PET = positron emission tomography.