H8A-MC-LZAZ Informed consent form (Main study and Open-label extension Period)

NCT02008357

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Informed Consent to Act as a Research Subject in:

The A4 Study

This consent form describes a research study and your role as a research subject. This document is intended to inform you about the possible risks and benefits of the research study, other options that may be available to you and your rights as a research subject. Please read this consent form carefully and do not hesitate to ask the study doctor or study team any questions you may have about the study or the information provided below.

Your participation in this study is entirely voluntary. Please take as much time as you need to discuss the study with your doctors, family and friends. The decision to participate or not is yours. If you choose to participate, you have the right to withdraw from the study at any time without a penalty or loss of benefits to which you are otherwise entitled. You will be told about any new important information that might change your decision to be in this study.

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

Investigator(s)
Sample A Doctor, M.D.
Sample B Doctor, Ph.D.

Location
SITE ADDRESS

Site TEL

Protocol Title
Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease

Protocol Alias:
H8A-MC-LZAZ/ADC-040-A4

This study is being conducted by the Alzheimer's Therapeutic Research Institute (ATRI) in conjunction with Eli Lilly & Company, through a grant from the National Institute on Aging (NIA).

Why is this study being done?

Alzheimer's disease (AD) is a brain disease that results in loss of memory function.

Studies have shown that changes occur in the brain many years before a person shows the symptoms of AD dementia. We know that a protein called "amyloid" or "beta-amyloid" forms plaques in the brains of people with AD.

Scientists believe that the buildup of amyloid in the brain may play a key role in the eventual development of AD-related memory loss. Research studies suggest that people with elevated levels of brain amyloid are at increased risk for memory decline, but this does not mean that every person with amyloid build up will develop AD dementia.

Scientists believe that AD-related damage to the brain begins many years before the symptoms of memory loss emerge. It is hoped that starting treatment very early will help slow the progression of memory loss.

You are being asked to be in a research study of an investigational drug known as LY2062430 (also called "solanezumab").

The Anti-Amyloid Treatment in Asymptomatic Alzheimer's study (the "A4 study") is a clinical trial for older individuals who may be at risk for Alzheimer's disease memory loss.

The A4 study is testing an anti-amyloid investigational drug in older individuals who have evidence of elevated amyloid build-up in their brains, but who do not show symptoms of AD in order to slow possible AD-related damage in the brain and to delay progression of AD-related memory loss.

The purpose of this study is to test whether an investigational drug called solanezumab can slow the progression of memory problems associated with brain amyloid.

The A4 study will also test 1) whether the anti-amyloid treatment can slow evidence of AD-related brain injury on imaging tests to look at brain structure and function and 2) the effect of solanezumab on cerebrospinal fluid (CSF) biomarkers and blood biomarkers.

Three large studies in patients with Alzheimer's disease who had AD symptoms did not show a significant benefit of solanezumab, but it appeared there may be a small effect. It is possible the dose of solanezumab given in those studies (400 mg every 4 weeks) was not large enough. Also, drugs like solanezumab that target amyloid in the brain may work better at earlier stages of Alzheimer's disease, like preclinical AD. Therefore, the dose of solanezumab in the A4 study is being increased compared to these other studies from 400 mg every 4 weeks to 1600 mg every 4 weeks.

Solanezumab is an investigational drug which means that it has not been approved for routine clinical use or for the use described in this study by the U.S. Food and Drug Administration (FDA).

How many people will take part in this study?

Approximately 1150 individuals in the US, Canada, Japan and Australia with normal memory and thinking abilities who have evidence of elevated amyloid in their brain will be taking part in this study.

Can I participate in this study?

The study staff will discuss what is required for you to be part of this study.

You cannot be in the study if:

- You or your Study Partner are an employee of the Alzheimer's Disease Cooperative Study (ADCS), ATRI, or Eli Lilly and Company
- You are an employee of the investigative site or you are an immediate family member of an employee of the investigative site.

  Immediate family member is defined as a spouse, parent, child, or sibling, whether biological or legally adopted.
- You are a woman and you possibly could become pregnant during this study.

To participate in this study, you must have an individual (spouse, friend, or relative), called a "Study Partner", who is willing to:

- Accompany you to the first study visit and 5 additional visits for about 4.5 years.
- Answer questions about your memory and daily functioning
- The study partner must have contact with you in person, by phone or by computer approximately every week.
- The study partner may participate with you in the A4 study by phone if they are not able to come in to the clinic visit with you once a year.

What will happen if I take part in this research study?

Once enrolled, participants will receive infusions every 4 weeks and have routine clinic visits for testing and safety purposes. Your participation in this study is expected to last up to about 4.5 years.

During this study, Dr. [INSERT PI NAME] and [his/her] staff will be monitoring your condition.

There are two activity phases in this trial:



Screening Phase

The first phase of the study is called a screening phase. During this time, the study team will determine whether you qualify to be in the study.

The screening period includes up to 5 visits to the clinic. Each visit will take several hours to complete.

At the beginning of your first clinic visit, study staff will explain all of the study procedures and answer any questions that you and your study partner may have.

If you choose to take part in this study, study staff will ask you and your study partner to sign this consent form before any study procedures are done.

After you consent to participate you should report all adverse events that you experience (changes in health, any side effects/ reactions to medications, injuries or illnesses) to the study staff so that the events can be recorded in your study records.

If you choose to take part in this study, we will ask you not to donate bodily fluids (for example, blood) while you are participating in the study and also for 12 weeks after receiving the last dose of study medication.

If the results of any other screening tests are outside the acceptable range or if anything unusual is found, you will not be eligible to enroll in this study. In the event that this happens, study staff will talk with you in more detail about the tests and your options.

Identifying Your Amyloid Status

An important part of the Screening Phase is to identify your amyloid status through an amyloid Positron Emission Tomography (PET) scan. The scan allows doctors to detect amyloid plaques in the brain of a living person.

In the A4 Trial, participants will learn from their PET scan whether their amyloid level is “elevated” or “not elevated”.

What does "elevated" brain amyloid mean?

- An “elevated” amyloid result means that amyloid plaques are present in your brain.
- An “elevated” amyloid result means you may be eligible to join the A4 Trial.
- An “elevated” amyloid result does not mean you will develop Alzheimer’s disease dementia.

What does “not elevated” brain amyloid mean?

- A “not elevated” amyloid result means that it is unlikely you have high levels of amyloid plaques in your brain at this time.
- A “not elevated” amyloid result does not mean that you will never develop Alzheimer’s disease dementia.
- A person who has a “not elevated” amyloid level at the time of this PET scan could develop an “elevated” level of amyloid or Alzheimer’s disease dementia in the future.
- A “not elevated” amyloid result means that you are not eligible to participate in the A4 trial.

An experienced clinician will discuss your amyloid scan results with you. You may bring a relative, friend or study partner with you to learn about your amyloid status if you wish. You will be asked to fill out questionnaires about your feelings when learning your amyloid status. You will have a follow-up

phone call a few days after learning about your amyloid status to check on you and to answer any further questions that you may have.

Treatment Phase

If the screening phase shows that you qualify to participate in this study, you will be randomly assigned (or "randomized") into one of the study groups described below and you will start the Treatment Phase.

During the Treatment Phase, you will have an intravenous (IV) infusion of study drug or placebo every 4 weeks. "Intravenous" means that the study drug or placebo will be given through a vein in your arm.

You will also have at least 21 visits to the clinic and the visits will last up to 4-5 hours. The purpose of these visits is to evaluate how you are doing on study drug and to collect information about your memory and ability to perform certain tasks.

This is a randomized, double-blind, placebo-controlled study. This means it will be determined by chance (like the flip of a coin) which of the 2 study groups you may be assigned to:

- **Group 1**: Solanezumab, IV infusions every 4 weeks with active study drug
- **Group 2**: Placebo, IV infusions every 4 weeks with a liquid that looks like the study drug, but has no active drug

You will have a 50/50 chance of receiving study drug. Neither you nor the study personnel will know if you are taking study drug or placebo

Escalation of Study Drug Dose:

When the study started, participants were scheduled to receive IV infusions of 400 mg of solanezumab or placebo every 4 weeks. The study has been changed to raise the dose of solanezumab or placebo (called an escalation phase) as follows:

- 400 mg solanezumab or placebo via IV infusion every 4 weeks (at least 2 administrations). If you have already received at least 2 administrations of 400 mg, you can receive 800 mg at your next infusion.
- 800 mg solanezumab or placebo via IV infusion every 4 weeks (at least 2 administrations)
- 1600 mg solanezumab or placebo via IV infusion every 4 weeks (all remaining administrations in the study)

You will remain on the 1600 mg dose for the remainder of the study unless the study doctor decides to lower the dose of medication or skip some doses during your participation.

There may be reasons that prevent you from following this dose escalation schedule. For example, there may be safety reasons or you may decide that you are not ready to increase the study drug dose at this time. Your study doctor will discuss these options with you and make any adjustments to this dose escalation schedule if needed.

The infusions will take approximately 30 to 60 minutes depending on the dose level. The infusions with

the higher dose take longer than the infusions with the lower dose.

Escalation of Study Drug Dose: Additional Safety Procedures

At a minimum, first 200 participants who receive the increased study drug dose will have additional safety procedures at 6 additional time points including an MRI, ECGs, and blood draws. Additionally, there will be close monitoring for 1 hour after the first infusion of 800 mg and 1600 mg to make sure that there are no reactions or bad effects.

If you qualify to undergo these additional safety procedures, study staff will work with you to schedule these additional procedures so that they occur on days normally scheduled for a clinic visit or for an infusion visit. The safety procedures must be completed before your infusion occurs.

You will have the MRI at least 7 days before you are scheduled to increase the study drug dose from 800 mg to 1600 mg. If you are already scheduled to have an MRI as a part of the study, you may not have to undergo this additional MRI. The results of the MRI will determine if it is safe for you to continue to the higher dose or not. If it is determined that it is not safe (for example, if you have a significant increase in water content or small bleeds in the brain tissues), you may remain on the 800 mg dose until your study doctor decides it is safe to increase to the next dose. The study team will talk with you about this if this occurs.

The specific safety procedures and the associated risks are explained in the procedure table and risks section later in this consent from.

The study team will let you know if you will undergo these additional safety procedures, or if the first 200 participants (at a minimum) have already completed these additional safety procedures.

Description of Visit Activities

The following activities will be done at one or more visits over the course of this trial:

- You will be given memory and thinking skills tests and you and your study partner will be asked questions about your daily functioning.

  A voice recording of your responses to some memory tests may be made if the laws and guidelines at your study site allow this. These recordings are not being done to check your answers to questions, but rather if the site staff asked you the questions correctly. These recordings will be used to conduct quality reviews and will be destroyed at the end of the study. Subjects will not receive any results or feedback from these tests.
- Your height, weight and vital signs (blood pressure, heart rate, breathing rate and temperature) will be recorded
- A brief physical and neurological exam will be performed
- An electrocardiogram (ECG) will be performed. An ECG is a tracing test that measures electrical signals from your heart
- Your general medical history will be reviewed

- A list of medications you are currently taking will be collected. During the study, your reactions to the study drug will be carefully monitored. The study doctor must be informed of any medications, vitamins and herbal substances that you take or any medication that you may plan to start taking during the study.
- Blood will be drawn from a vein in your arm and you will be asked for a urine sample. These samples are for routine laboratory tests, genetic testing, biomarker and other research tests, sample storage and to measure the levels of solanezumab in your body.

  The routine laboratory tests ensure that there are no medical conditions that might interfere with your participation in the study or that could be responsible for any changes in your well-being throughout the study period.
- You will be asked about any adverse events (changes in health, any side effects/ reactions to medications, injuries or illnesses) that you may have experienced since your last visit.
- You will be asked to complete a Research Satisfaction Survey. The survey asks about what you like and dislike about this study.
- A magnetic resonance imaging (MRI) scan will be done. An MRI uses a large magnet and computer equipment to produce electronic pictures of your brain.

  You will lie on your back and enter the MR machine for the scan, during which time you will hear loud knocking noises.

  Each MRI scan will take approximately 45 minutes to complete.
- You will have positron emission tomography (PET) scans as part of the study.

  The PET scan in this study uses very small amounts of a radioactive imaging agent, called florbetapir (F 18), to make a picture showing how much amyloid is in your brain.

  You will be positioned on the scanner bed while the scanner takes pictures for 30 minutes. During this time you must hold your head as still as possible.
- A catheter (hollow plastic tube) will be placed in a vein in your arm and you will undergo an infusion.
- If you consent, a lumbar puncture (LP), also known as a “spinal tap” will be performed. **You do not have to participate in the optional lumbar puncture to be in the A4 trial**.

  A lumbar puncture is a procedure that involves inserting a needle in the lower back in order to collect a small amount of the spinal fluid that surrounds the brain and spinal cord.

  You will be asked to fast overnight (a minimum of 8 hours) prior to coming to the clinic for the LP. This means no food or drinks such as coffee, tea, milk and juice (water is permitted).

  During the procedure you will lie on your side curled up into a ball or you will sit on the edge of a chair or bed and lean forward, whichever is easier for you.

  The lower part of your back will be cleaned with antiseptic. A local anesthetic will be injected into the skin of your lower back at the area of the lumbar puncture.

When the area is numb, a very thin needle will be inserted into the spinal canal in the lower back, well below the level where the spinal cord ends. About 18 milliliters (less than 1½ tablespoons) of spinal fluid will be removed for analysis and storage. Your body replaces this spinal fluid within 1-2 hours.

After the lumbar puncture is completed, you will remain in the clinic for about 30 minutes. You will be given something to eat and drink before you leave.

You should avoid any strenuous physical activity for the next 24 hours. This includes lifting, bending, doing housework and gardening, or doing exercise such as jogging or bicycle riding.

Study staff will call you the day following your lumbar puncture to discuss how you are feeling.

Summary of Visit Activities

The following charts summarize the activities that will occur over the course of this study. Study staff will work with you to determine if any changes need to be made to this schedule of events.

Screening Phase					
Visit Number	1	2	3	4	5
Estimated Amount of Time Between Study Visits	<---------- 90 days or less ---------->				
Approximate Length of Visit (hours)	4-5	3-4	1-2	1-2	1-2
Sign Informed Consent	✓				
Medical History	✓				
Medication History	✓				✓
Adverse Event Collection	✓	✓		✓	✓
Assessment of Well Being	✓				
Answer Questionnaires	✓		✓		
Memory & Thinking Skills Tests	✓		✓		
Physical/Neurological Exams	✓				
Vital Signs	✓				
Electrocardiogram (ECG)	✓				
MRI Scan				✓	
PET Scan		✓			
Blood draw	✓		✓*		
Approximate Blood Draw Amount (mL)	**50.5**		**67.5***		
Urine collected	✓				
Fasting Lumbar Puncture (optional)					✓

**Fasting required for the optional blood draw for future research at Visit 3.*

During the Treatment Phase of the study, you will have an intravenous (IV) infusion of study drug or placebo every 4 weeks. These infusions visits will take approximately 30-60 minutes to complete. In addition to the infusion visits, the following activities will occur at your clinic visits during the Treatment Phase. The clinic visits will occur approximately every 12 weeks:

Treatment Phase																				
Visit Number	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63	66
Approximate Visit Length (hours)	3-4	4	3	2-3	3	2	2	4	2	3	2	2-3	2	2-3	4	2-3	2	2-3	2	2-3	8
Study Drug Infusion	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Medication History	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Adverse Event Collection	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Answer Questionnaires	✓	✓		✓	✓			✓		✓		✓			✓			✓			✓
Assessment of Well Being	✓	✓		✓		✓		✓		✓		✓		✓				✓			✓
Memory & Thinking Skills Tests	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Physical & Neurological Exam	✓							✓							✓						✓
Vital Signs	✓	✓	✓	✓	✓			✓		✓		✓		✓		✓		✓		✓	✓
ECG	✓	✓	✓		✓					✓					✓						✓
MRI Scan		✓						✓							✓						✓
PET Scan																					✓
Blood collected	✓	✓	✓		✓					✓					✓						✓
Approximate blood draw amount (mL)	55	45	45		45					55					55						55
Urine collected					✓					✓					✓						✓
Fasting LP(optional)																					✓

Dose Escalation: Additional Safety Procedures – First 200 Participants							
Dose (mg)	800	800	N/A	1600	1600	1600	1600
Week relative to the first dose of 800 mg:	0	4	<8*	8	12	16	20
Approximate Additional Length of Visit (hours)	1-2	<1	1-2	1-2	<1	<1	<1
Vital Signs	✓	✓		✓	✓	✓	✓
Electrocardiogram (ECG)		✓			✓		
MRI*			✓				
Blood Draw	✓	✓		✓	✓		✓
Urine collected		✓			✓		
Approximate Blood Draw Amount (mL)*	20.5	25		20.5	25		20.5
Study Drug Infusion (800 mg)	✓	✓					
Study Drug Infusion (1600 mg)				✓	✓	✓	✓
1-Hour Post-Infusion Monitoring	✓			✓			

** The MRI will be scheduled at least 7 days before your first dose of 1600 mg. If a study MRI is scheduled within ±2 months of the dose escalation MRI, you will receive the MRI based on the dose escalation schedule instead of the main study schedule so you will not have to receive 2 MRIs very close together. The results of the MRI will determine if it is safe to increase to the next dose or not. If the results of the MRI determine that it is not safe, you may remain on the 800 mg dose until your study doctor decides it is safe to increase to the next dose.*

*** If the blood draw is scheduled to occur at the same time as a blood draw for the main study, you will not undergo this additional blood draw amount.*

What will happen when I finish or stop participating in the study?

In the event that you stop taking the study drug earlier than scheduled, or you stop participating in the study completely for any reason (for example, the study team feels it is in your best interest, you decide not to continue or the study is stopped), study personnel will contact you and you will be asked to return to the research center to undergo a final evaluation. It is important for your health and safety to have these final procedures completed.

Your participation also may be stopped by the study doctor or sponsor without your consent. If this happens, it might be due to a bad reaction you have to solanezumab or new information about solanezumab safety or effectiveness.

This evaluation will include all of the procedures normally performed during visit number 66.

If you complete this study, you may be asked to participate in another long-term solanezumab study. In this other long-term study, all subjects will receive solanezumab. You may be contacted to discuss if you would like to participate in this long-term study.

Genetic Testing

Previous studies have shown that a gene called apolipoprotein E (APOE) may be linked to buildup of amyloid and development of Alzheimer's disease. We will test some of your blood to see what form of

the APOE gene you have. **This genetic testing is not an optional portion of the trial, as the APOE information will be used in the randomization process.**

The results of these tests will be maintained in scientific databases for research. The results will not be released to you or your family.

No information regarding your genetic or biomarker research will be entered into your regular medical record. If you are concerned about a potential genetic disorder, you should discuss this with your primary care doctor. You and your doctor may choose to test specifically for it, but this would require additional blood samples and would not be part of this research project.

Data from your tests will not be revealed to sites that are participating in the clinical study, family members, insurance companies, employers, or other individuals or organizations.

Although researchers will have access to coded individual data, any information gained from this research will be reported in publications in de-identified, summary form. Data will be stored in a locked file, and in a computer with restricted access.

Any information in the computer that could be used to potentially identify you will be stored in a separate file and encrypted. Only the researchers and their research assistants will have access to the original research data.

Will this research data be shared?

Data from this research will be shared with other researchers. Data sharing is important for further translation of research results into knowledge, products, and procedures to improve human health. All links with your identity will be removed from the data before they are shared.

What side effects or risks can I expect from being in the study?

Solanezumab treatment may involve risks that are not known at this time due to the investigational nature of this study. Some of these unknown risks may be life-threatening or result in death. However, you will be told of any new risks or significant findings that develop during the course of this study.

Participation in this study may involve some added risks or discomforts, which are outlined below. Please talk to the study staff if you have any questions or concerns about the procedures required for this study.

Randomization Risks

You will be assigned to a study group at random (by chance). Your assignment is based on chance rather than a medical decision made by the researchers. The study group you are assigned to might not be the group you would prefer to be in. Your assigned study group might also prove to be less effective or have more side effects than the other study groups, or other treatments available for your condition.

Study Drug (Solanezumab)

Information from Studies in People with mild to moderate Alzheimer's disease dementia

Three large solanezumab studies were completed in over 3435 people with mild AD. The people in these studies were given either solanezumab 400 mg or a substance that looked like solanezumab but had no medicine in it (placebo) every 4 weeks for 1½ years. In 2 studies, 22 patients were given solanezumab 400 mg every week, which is about the same as 1600 mg every 4 weeks, for 2 to 3 months. The safety at this higher dose was consistent with the safety at 400 mg every 4 weeks.

Some people with AD are being given solanezumab 400 mg every 4 weeks in a long study. Some of the people have been treated with solanezumab for 2 to 6 years. No new risks or discomforts with solanezumab have been identified in this study.

Information Based on How Solanezumab Works

When someone is immunized, special proteins called antibodies become active in the body. Antibodies help in a body's defense against germs or disease. "Active immunization" (vaccine) causes the body to make its own antibodies to fight against the infection or disease. "Passive immunization" (antibody) is when antibodies are given directly, so the body does not need to make its own antibodies. Solanezumab is a passive immunization approach for the possible treatment of AD.

Allergic Reactions

Some patients have had allergic reactions in solanezumab studies within 1 day after getting an infusion (2.6% of patients given solanezumab and 2.0% of patients given placebo). Most of these reactions were mild and did not require any treatment. If you have a serious allergic reaction, symptoms may include low blood pressure (which may cause fainting), and difficulty breathing. Milder reactions may include: rash, itching, fever, chills, nausea, vomiting, or a headache.

Itchy Rash: A small number of patients given solanezumab (0.4%) and placebo (0.1%) had complaints of rash along with itchiness. These rashes happened at any time during treatment and were mostly mild and did not require any extra treatment.

Increased Water Content of the Brain Tissue

An increase in the water content of the brain tissue has been seen in some people taking experimental medicines that lower Aβ, a brain protein thought to cause AD.

Symptoms that can happen if someone has an increase in water content in the brain include: headache, worsened confusion, change in level of consciousness, seizures, unsteadiness, and vomiting. It is also possible that there will not be any symptoms with this kind of increase in water content in the brain.

One or more scans of your brain will be done as part of this study to show if you have increased water content in your brain. Also, if you develop a combination of these symptoms at the same time, you will be asked to get an extra scan of your brain.

Based on brain scans during completed studies of solanezumab, small areas of increased water content of the brain tissue have been seen in 0.6% of people given solanezumab and 0.3% of people given placebo. Some of the time, the areas of increased water have gone away within a few weeks. In other cases, the increased water content went away more slowly, stayed the same, or increased.

Several of these people have continued or restarted study drug, and the increased water content of the brain tissue went away with continued infusions, or did not happen again. One patient had increased water content during placebo treatment, and developed it again during treatment with solanezumab. Only one of these people with increased water content in their brain had symptoms. This person had a burning or prickling sensation and weakness on one side of their body that lasted 10 minutes and did not come back.

Increase in Small Bleeds in the Brain Tissue

An increase in small bleeds in the brain has been seen in some people taking other potential new medicines that lower Aβ, the same protein that solanezumab lowers. An increase in the size or number of small bleeds in the brain tissue has been seen in about 6% of people given solanezumab and about 5% of people given placebo. There was no difference in the seriousness of small bleeds in solanezumab treated patients compared with placebo treated patients. The long term effects of these small bleeds are uncertain. These small bleeds were mostly found during regularly scheduled brain scans.

Injection Reactions

When a drug is given, either as a shot under the skin, or into the vein (intravenous, IV), certain effects may happen. Some people given solanezumab IV may have mild problems at the IV site, including: pain, swelling, redness, bruising, itching, infection, and minor bleeding. Some people may feel tiredness, dizziness, nausea, sweating, and/or faint after getting an IV. These injection reactions have happened in 2.1% of patients given solanezumab and 2% of patients given placebo.

Thoughts of Suicide or Suicide Attempts

Patients with mild AD dementia in a solanezumab study were periodically asked if they thought about committing suicide or tried to commit suicide. More patients who were given solanezumab said they thought about committing suicide (6.6%) than patients who were given placebo (4.6%). More patients who were given solanezumab tried to commit suicide (0.4%) than patients who were given placebo (0.1%). If you have thoughts of ending your life or harming yourself, you should tell someone immediately. You will also be asked periodically if you have tried to commit suicide or have had thoughts about committing suicide while you are taking part in studies of solanezumab.

Heart Problems

Heart problems have been seen in some people in previous solanezumab studies. More recent studies have shown that this is no longer a risk. Your heart will be checked regularly while you are taking part in studies of solanezumab.

Pregnancy

If you are a woman and you could become pregnant during this study, there may also be unknown risks to your embryo, fetus, or nursing infant.

Placebo

If you receive placebo as your study drug, you may experience memory problems consistent with aging and elevated amyloid.

ECGs

Electrocardiograms (ECGs) (electrical tracings of the heartbeat or heart rhythm) will be done during this study in which you will have pads placed on different parts of your body. There is no pain or discomfort during an ECG; however, removing the pads may cause some irritation to your skin.

Blood Tests

In total, about 473 mLs of blood (about 33 tablespoons) may be taken over the course of the 4.5 year study. If you are in the group of at least 200 people with the additional safety tests, then up to 111.5 mLs (about 7.5 tablespoons) more of blood will be taken. Your body will make up for this loss.

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.

Urinalysis

A urinalysis (UA) is a test of the urine. The test checks for infections. It can also check for diseases of both the bladder and the kidneys. You will be asked to urinate or “pee” into a small cup. The test involves only normal urination. There is usually no discomfort.

Intravenous (IV) Infusions

You will have up to 60 intravenous (IV) infusions during this trial. A needle will be placed inside a vein in your arm, causing a small hole or ‘puncture’. The study drug will be given through this needle.

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. Phlebitis is irritation of a vein. 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.

Magnetic Resonance Imaging (MRI) Risks

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 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.

Lumbar Puncture Risks

There are 2 optional lumbar punctures in this study - one at the beginning of the trial and one at the end of the trial. If you participate in both lumbar punctures, a total of up to 36 mls (less than 3 tablespoons) of cerebrospinal spinal fluid (CSF) may be taken during this entire study and your body will make up for this loss

For most people, a lumbar puncture does not cause any serious problems. The most common complaint is a bad headache. About half the people having a lumbar puncture complain about a headache. If the headache does not go away after 1 or 2 days, it may be due to a leak of the spinal fluid. A leak can be treated with a blood "patch". A blood "patch" is made with a small amount of your blood. Your blood is injected into the area where the leak is.

Some people also complain about back pain or stiffness, pain at the place where the needle was placed, and neck or shoulder pain. These complaints are not as common as a headache and can be treated.

Rare or very uncommon complaints include low blood pressure and dizziness, bleeding into the spinal canal, or an infection of the spinal fluid (known as meningitis). These rare complaints could be serious. They could require you to be put in the hospital.

You cannot participate in the optional LP if you are taking anticoagulants such as warfarin, Coumadin or dabigatran.

Positron Emission Tomography (PET) Scan Risks

Being in the PET scanner may cause you to experience discomfort or musculoskeletal pain (such as back or neck pain). Some people do not like the small space (claustrophobia) and might feel confined or bothered by being in the PET scan machine for a long period of time.

Florbetapir F 18 Imaging PET Scan Risks

Florbetapir F 18 Injection is approved by the United States Food and Drug Administration (FDA) and the European Medicines Agency (EMA) to estimate amyloid neuritic plaque density in adult patients with cognitive impairment who are being evaluated for Alzheimer's disease and other causes of cognitive decline. Use of Florbetapir F 18 outside the United States and European Economic Community is experimental.

Florbetapir (F 18) is an imaging agent that includes a small amount of radioactivity (radiation) necessary to create the PET scan images. Exposure to radiation is associated with an increased risk of developing cancer.

Before the PET scan, a small dose of the imaging drug will be injected. If the PET scanner at your site is able to perform a computed tomography (CT) scan, you will receive a CT scan right before the PET scan begins. Your doctor will let you know at the time of consent whether you will also receive the CT scan. The CT scan uses x-rays to take a picture of your head (including skull and brain) and provides information that helps to analyze the PET scan.

The total amount of radiation from the florbetapir (F 18) PET scan and the "low dose" CT scan performed as a part of the PET scan is about the same a patient receives from a routine abdominal/pelvis CT scan and is about 2 to 4 times as much as the average person receives per year from natural radiation (examples include soil, water and sun) and man-made radiation (examples include televisions, smoke detectors, and x-rays.

Toxicology: Florbetapir (F 18)

Florbetapir, the non-radioactive version of florbetapir (F 18), has been tested in laboratory and short-term animal studies to assess the risk of cancer.

In laboratory tests with bacteria cells, florbetapir showed positive results for genotoxicity (damage to genes). However, further studies conducted in living animals with florbetapir at doses up to 83 times the maximum human dose of florbetapir (F 18) 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 risks of the drug may still be unknown.

Side effects in humans: Florbetapir (F 18)

In clinical studies, the most common side effect of florbetapir F 18 injection was headache, which was reported in 2.1% of subjects. Uncommon side effects were: injection site reaction (0.2%) and flushing (0.1%). Rare side effects were: infusion site rash (<0.1%), dysgeusia (bad taste in the mouth) (<0.1%), pruritus (itching) (<0.1%), and urticaria (hives) (<0.1%).

Risks of Disclosure of Amyloid Status

It is possible that learning your amyloid status may cause some individuals to become anxious or upset. An experienced clinician will discuss the amyloid scan results with you and will be available to answer any questions you may have after the session.

Risks of Loss of Confidentiality

Study personnel will not release your study information to your doctor without your permission, and will code your study information to protect your confidentiality.

However, it is possible that information about your participation in this study could enter your medical record, particularly if you experience an adverse event requiring treatment.

It is possible that information about your amyloid status or participation in this study could influence your ability to obtain life insurance, health insurance, or long-term care insurance or affect your future employability.

To help us protect your privacy, the study staff has obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of Federally-funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

The Certificate of Confidentiality will not be used to prevent disclosure to state or local authorities of [INSERT STATE].

Risks of Cognitive Testing & Questionnaires

Cognitive testing may cause some individuals to become upset, frustrated, bored, or tired. You have the right to decline to answer any questions that you feel uncomfortable in answering.

General Information Regarding Sample Collection

Various blood, urine, and cerebrospinal fluid samples will be collected from you during this trial. The specific procedures for collecting these samples and the risks associated with collection are explained in the procedure table and risks section in this document. Your samples will be identified by your subject number, and not by your name.

The analysis of your samples may contribute to the creation of new laboratory tests, new drugs, 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 drug.

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 Drug 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. The 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 and/or RNA. DNA and RNA are genetic material that is found in all the cells of your body. DNA and RNA contain 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 drugs. For this reason, looking at DNA and RNA can sometimes help explain why people with a disease respond differently to the same drug. For example, some people taking this study drug may respond well. Others may have little or no response, or have side effects.

Researchers may study your DNA and RNA to learn how the study drug works for you. Information about your DNA and RNA may be used to create or improve tests to measure these genetic factors.

The DNA and RNA 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 and cerebrospinal fluid will be collected to identify or better understand biomarkers.

Researchers may use biomarkers to learn more about Alzheimer's disease or how patients respond to study drug or other medicines that you are taking during this study. Your samples may also be used to create or improve tests to help identify patients in the future who may respond to this study drug.

The samples may be stored for up to **15** years after this study is finished.

Samples for Antibody Research

Blood samples will be collected to determine if your body produces antibodies against the study drug. Antibodies may affect how a drug works in your body if you take it in the future. The samples may be stored for up to **15** years after this study is finished.

MRI and PET Imaging Storage & Future Use

Your MRI and PET images will be uploaded to secure databases being used for this research study and will be analyzed by researchers at other institutions. Study investigators will maintain your imaging data and be responsible for deciding how it will be used for future research. Study investigators may make some of these data available to investigators at other scientific institutions for research purposes.

Your name and all links with your identity will be removed from the data before they are shared. Your imaging data will be labeled with a coded research identifier to protect your identity.

Optional Sample Storage & Future Use

You have the opportunity to provide additional blood samples for research into proteins, RNA and DNA testing. These samples may help answer questions about this study, disease, and biomarkers in general. Since this study is supported by the United States National Institutes of Health (NIH), samples from the study may also be used by researchers to answer other important research questions. Blood samples will be stored and used for these purposes until they are used up. These additional blood samples will be collected at Visit 1 and Visit 3. You will be asked to fast overnight (a minimum of 8 hours) prior to coming to the clinic for the blood draw at Visit 3. This means no food or drinks such as coffee, tea, milk and juice (water is OK).

Providing these additional blood samples is optional. If you choose not to provide these samples, you can still participate in the study.

Are there benefits to taking part in this study?

There is no guarantee that you will personally benefit by participating in this research study.

Study staff will advise you to consult with your physician if any of your tests suggest that you have a medical problem.

What other choices do I have if I do not take part in this study?

You do not have to take part in this study.

There are currently no FDA approved medications for treating amyloid. There are medications available for treating symptoms of Alzheimer's disease, but these are approved only for patients who have been diagnosed with AD dementia.

Starting a new medication at any point during the course of the study should be discussed with your study doctor.

Will my medical information be kept private/confidential?

Research records will be kept as confidential as possible within the limitations of state and federal law.

The study staff and sponsors (NIA, ATRI, Eli Lilly and Company) will handle your personal health information in a confidential manner.

Your personal health information is information about you that could be used to find out who you are. For this research study, this includes information in your existing medical records needed for this study and new information created or collected during the study.

Your health information will be used and disclosed in accordance with the following U.S. Data Privacy Statement.

U.S. Data Privacy Statement

A federal government rule has been issued to protect the privacy rights of subjects/patients. This rule was issued under a law called the Health Insurance Portability and Accountability Act of 1996 (HIPAA). This rule is designed to protect the confidentiality of your personal health information. Your personal health information is information about you that could be used to find out who you are. For this research study, this includes information in your existing medical records needed for this study and new information created or collected during the study.

This Data Privacy Statement explains how your personal health information will be used and whom it will be given to ("disclosed") for this research study. It also describes your privacy rights, including your right to see your personal health information.

By signing the consent document for this study, you will give permission ("authorization") for the uses and disclosures of your personal health information that are described in this Data Privacy Statement. If you do not want to allow these uses, you should not participate in this study.

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

- **The study doctor and staff will use your medical records and information created or collected during the study to conduct the study.**
- **The study doctor and staff will send your study-related health information ("study data") to the sponsor of the study and its representatives ("sponsor"). Because the sponsor conducts business related to clinical research in many countries around the world, this may involve sending your study data outside of the United States. Other countries may have privacy laws that do not provide the same protections as the laws in this country. However, the sponsor will respect the terms of this Data Privacy Statement in all countries.**

- **The study data sent by the study doctor to the sponsor does not include your name, address, social security number, or other information that *directly* identifies you. Instead, the study doctor assigns a code number to the study data and may use your initials. Some study data sent to the sponsor may contain information that could be used (perhaps in combination with other information) to identify you (e.g., date of birth). If you have questions about the specific health information that will be sent to the sponsor, you should ask the study doctor.**
- **The sponsor will use the study data for research purposes to support the scientific objectives of the study described in the consent document, to assess the safety or efficacy of any drug or treatment included in the study, to better understand the disease(s) included in the study, or to improve the design of future studies.**
- **Your study data, either alone or combined with data from other studies, may be shared with regulatory authorities in the United States and other countries, doctors at other institutions participating in the study, and the ethical review board overseeing this study.**
- **Study data that does not directly 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, the ethical review board overseeing this study, and regulatory authorities in the United States and other countries. The purpose of these reviews is to assure the quality of the study conduct and the study data, or for other uses authorized by law.**
- **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 partners need the information as a part of this work with the sponsor, and only if the business partners signs a contract that requires it to protect your study data in the same way as the sponsor.**
- **The sponsor will not disclose personal health information to insurance companies unless required to do so by law, or unless you provide separate written consent to do so.**
- **Your medical records and study data may be held and processed on computers.**

Your personal health information may no longer be protected under the HIPAA privacy rule once it is disclosed by your study doctor to these other parties.

You have the right to see and copy your personal health information related to the research study for as long as this information is held by the study doctor or research institution. However, to ensure the scientific integrity of the study, you will not be able to review some of the study information until after the study has been completed.

You may cancel your authorization at any time by providing written notice to the study doctor. If you cancel your authorization, the study doctor and staff will no longer use or disclose your personal

health information in connection with this study, unless the study doctor or staff needs to use or disclose some of your personal health information to preserve the scientific integrity of the study. The sponsor will still use study data that was collected before you cancelled your authorization. If you cancel your authorization, you will no longer be able to participate in the study. However, if you decide to cancel your authorization and withdraw from the study, you will not be penalized or lose any benefits to which you are otherwise entitled.

Your authorization for the uses and disclosures described in this Data Privacy Statement does not have an expiration date.

A new Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally prohibits health insurers or health plan administrators from requesting or requiring genetic information of an individual or an individual's family members, or using such information for decisions regarding coverage, rates, or preexisting conditions.

GINA also prohibits employers from using genetic information for hiring, firing, or promotion decisions, and for any decisions regarding terms of employment.

Furthermore, the researchers have adopted strict privacy and confidentiality procedures for maintaining your genetic information as described in this consent form.

You should be aware, though, that if your genetic information were accidentally released to the wrong source, federal law does not protect against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance or by adoption agencies.

What are the costs of taking part in this research study?

Procedures related to the study and study drug will be provided at no cost to you. There will be no costs to you for participation in this study.

Will I be paid for taking part in this research study?

You [will/will not] be paid for your participation in this study. You will be compensated for your time in coming to study visits and your travel expenses will be reimbursed.

What happens if I am injured as a result of taking part in this research study?

All forms of medical findings and treatments – whether routine or experimental – involve some risk of injury. In spite of all safety measures, you might develop medical problems from participating in this study.

You must report any suspected illness or injury to the study doctor immediately. If such problems take place, the **[SITE INVESTIGATOR'S INSTITUTION]** will provide emergency medical treatment and will assist you in getting proper follow-up medical treatment.

If you follow the directions of the study doctor and staff and you are physically injured, because of a properly given drug or procedures necessary for this study, Eli Lilly and Company will pay the medical expenses for the treatment of that injury.

The National Institute on Aging (NIA) and the Alzheimer's Therapeutic Research Institute (ATRI) at the University of Southern California (USC) do not provide compensation for research-related injury.

IN ADDITION TO THIS STATEMENT, ADD YOUR INSTITUTION'S SUBJECT INJURY CLAUSE HERE (you will / will not pay for subject injury, etc).

Who is paying for this research?

This study is being conducted by the Alzheimer's Therapeutic Research Institute (ATRI) in conjunction with Eli Lilly & Company, through a grant from the National Institute on Aging (NIA). The study doctor and/or [name of Institution or site] is being paid for their work on this study.

If I have questions or concerns about this research, whom can I contact?

If you have any questions regarding this research or if you believe that you may have experienced a research related injury or a reaction to the study medication, you should contact Dr. [Insert Site PI Name] (study doctor) at (XXX)XXX-XXXX.

If you have any questions about your rights as a research subject, you may call the [SITE IRB's NAME] office at (XXX)XXX-XXXX for more information about this or to report research-related problems. The Institutional Review Board (IRB) is a group that serves to protect the rights of participants in research trials.

What happens if I want to drop out of the study?

Your participation in this research study is entirely voluntary. You have the right to refuse to participate, refuse to answer specific questions in an interview or on a questionnaire or may refuse to participate or discontinue participation in this project at any time without jeopardy to the medical care you receive at this institution.

Because study results might be affected, participation in any other clinical studies will not be permitted until your participation in this study has ended.

You have the right to not sign this form that allows us to use and share your health information for research; however, if you don't sign it, you cannot take part in this research study.

You have the right to withdraw your permission to use or disclose personal information about your health. If you choose to withdraw your permission, you must notify Dr. [Insert Site PI Name] in writing. Dr. [Insert Site PI Name]'s mailing address is:

[Insert Site Address]

If you cancel your authorization, the study doctor and staff will no longer use or disclose your personal health information in connection with this study, unless the study doctor or staff needs to use or disclose some of your personal health information to preserve the scientific integrity of the study.

If you cancel your authorization, you will no longer be able to participate in the study.

STATEMENT OF CONSENT

By signing this page, you are confirming the following:

- You have read all of the information in this Consent Form, and you have had time to think about it.
- All of your questions have been answered to your satisfaction.
- You voluntarily agree to be part of this research study, to follow the study procedures, and to provide necessary information to the study doctor, nurses, or other staff members, as requested.
- You may freely choose to stop being a part of this study at any time.
- **You allow the study doctor and the sponsor to use and disclose your personal health information as described in this document.**

You will receive a copy of this signed Consent Form to keep.

Unless you authorize the use and disclosure of your personal health information, you cannot participate in this research study. If you refuse to give your authorization, your medical care will not be affected.

Circle and initial your selections below:

You voluntarily agree to participate.	**Yes**	**No**	INTIALS
You understand that by enrolling in the A4 Study you will **undergo an amyloid imaging scan and will learn the result of this scan.**	**Yes**	**No**	INTIALS
You understand that some of the testing sessions may be recorded.	**Yes**	**No**	INTIALS
You understand that your **MRI and PET scan data may be shared** with other researchers.	**Yes**	**No**	INTIALS

Dose Escalation:

You agree to increase your dose from 400 mg every 4 weeks to 1600 mg every 4 weeks.	**Yes**	**Not at this time**	INTIALS

Circle and initial your selection below:

Optional Lumbar Puncture:

You agree to undergo the **optional Lumbar Puncture (LP) procedures**.	**Yes**	**No**	INTIALS

Optional Biobanking:

You agree to the additional blood collection and that your **blood samples** may be stored and used for future research.	**Yes**	**No**	INTIALS

You agree to the additional blood collection and that your **DNA samples** may be stored and used for future research.	**Yes**	**No**	INTIALS

Subject's Name (print)	**Signature**	**Date**
Person Obtaining Consent (print)	**Signature**	**Date**
Witness (print)	**Signature**	**Date**

STUDY PARTNER INFORMATION & CONSENT

As the subject's study partner, you have important tasks that need to be carried out in order for the study to be conducted in the safest and best manner possible. These responsibilities include:

1) You must have direct contact with the subject at least one day per week. This can be in person, by phone or by computer.
2) You must be able to accompany the subject to a few clinic visits, or be available via phone to answer questions from study staff.
3) You are an important source of information about the subject. You must agree to be asked questions about the subject's health, memory, thinking, functioning and emotional well-being.

If for some reason you become unable to carry out your responsibilities, please tell the study team immediately. You may be asked, if possible, to select a substitute who can take over your duties.

You have read all the preceding information which describes both the subject's participation in the study and your involvement as the subject's study partner. The study has been explained to you in detail. All your questions have been answered to your satisfaction.

You voluntarily agree to participate as a Study Partner.

☐ YES ☐ NO _____ Study Partner's Initials

Study Partner's Name (print)	**Signature**	**Date**
Person Obtaining Consent (print)	**Signature**	**Date**

Research Subject Addendum Information and Consent Form

The A4 Study
Open Label Period

Introduction

This consent form describes a research study and your role as a research subject. This document is intended to inform you about the possible risks and benefits of the research study, other options that may be available to you and your rights as a research subject.

As a participant in the A4 study, you are being invited to participate in an optional Open Label Period at the end of your participation in the main (placebo-controlled blinded phase) A4 study.

If you choose not to participate, this will have no effect on your participation in the main A4 study. You can decline participation in this Open Label Period and remain active in the main A4 study, completing your last visit at Visit 66 (Week 240).

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

This study is being conducted by the Alzheimer's Therapeutic Research Institute in conjunction with Eli Lilly & Company, through a grant from the National Institute on Aging (NIA).

This consent form addendum will give you information about the Open Label Period to help you decide whether you want to participate. Please read this form and ask any questions you have before agreeing to participate.

Please refer to the informed consent document you signed for the main A4 study for information regarding benefits, treatment, compensation, confidentiality, and contacts.

What is an Open Label Period?

In the main A4 study, participants were randomly selected to receive either intravenous (IV) infusions of solanezumab (active study drug) or placebo (looks like the study drug but has no active medication). Everyone had a 50/50 chance of receiving study drug or placebo. Neither you nor the study personnel were told if you were taking study drug or placebo. In the main consent form, this was referred to as

the Treatment Period.

In an Open Label Period, all participants receive active study drug. No participants will receive placebo.

Why is this Open Label Period being done?

The purposes of the Open Label Period are to:

- Continue to collect information on the long-term safety and efficacy of solanezumab in slowing the progression of memory problems associated with brain amyloid
- Give all participants the opportunity to receive active study drug

How many people will take part in the Open Label Period?

All participants who complete the placebo-controlled blinded Treatment Period (about 900), will have the option to continue their participation in the Open Label Period.

Can I participate in the Open Label Period?

You may participate in the Open Label Period of the study if:

- You completed the placebo-controlled blinded Treatment Period in the main A4 study (Visit 66).

What will happen if I take part in the Open Label Period?

If you agree to participate:

- On or before your main A4 Visit 66, you will be asked to sign this informed consent form.
- Your doctor will make sure you are able to continue into this Open Label Period.
- Visit 66 will become your first visit in the Open Label Period.
- You will continue to have up to 51 IV infusions every 4 weeks.
    - All participants will receive solanezumab through an IV infusion mixed in sterile saline (salt water) using an IV catheter placed in your arm by the study doctor or nurse, who will administer the study drug into your blood. The infusions will take approximately 30 to 60 minutes to complete.
- You will participate in up to 18 additional visits to the clinic, which will last approximately 2-4 hours. The purpose of these visits is to evaluate how you are doing on the study drug and to collect information about your memory and ability to perform certain tasks.

How will I transition into the Open Label Period?

In the Open Label Period, all participants will receive 400 milligrams (mg), 800 mg, or 1600 mg of solanezumab.

If you agreed to dose escalate up to 1600 mg of study drug (solanezumab or placebo) in the Treatment Period, you will remain on the same dose for the Open Label Period. If you were receiving placebo, your study drug dose will be gradually increased until you reach 1600 mg of solanezumab in the Open Label Period. This is called a "dose escalation." Your dose will be increased according to the following dose escalation schedule:

- At least 2 infusions of 400 mg solanezumab IV infusions every 4 weeks, followed by
- At least 2 infusions of 800 mg solanezumab IV infusions every 4 weeks, followed by
- 1600 mg solanezumab IV infusions every 4 weeks until the end of the study

There may be reasons that prevent you from following this dose escalation schedule; for example, the study doctor may decide to lower the dose of medication or skip some doses for safety reasons. Your study doctor will discuss these options with you and make adjustments to this dose escalation schedule if needed.

If you did not dose escalate, or you did dose escalate and your doctor decided to lower the dose, and you received either 400 mg or 800 mg of study drug (solanezumab or placebo) at your last infusion visit in the main A4 study, then you will remain on that dose while you are participating in the Open Label Period. This means that:

- If your last dose was 400 mg (solanezumab or placebo), you will either stay on active study drug at 400 mg solanezumab or you will begin to receive 400 mg of active study drug in the Open Label Period. You will remain on this dose until the end of the study.
- If your last dose was 800 mg (solanezumab or placebo), you will either stay on active study drug at 800 mg solanezumab or you will begin to receive solanezumab starting at 400 mg for 2 infusions, and will then increase your dose to 800 mg of solanezumab in the Open Label Period. This is described in the dose escalation schedule above. You will remain on 800 mg of solanezumab until the end of the study.

If you are on a lower dose of study drug (either 400 mg or 800 mg), you may have the option to increase your dose up to 1600 mg later. This may happen, for example, because the study doctor feels it is safe for you to increase your dose, or because you decide you are ready to increase your dose. If the decision is made to escalate your dose during the Open Label Period, you will follow the dose escalation schedule described above. Your study doctor will talk with you about this before your dose is increased.

As a reminder, neither you nor the study team will know if you received active study drug or placebo during the Treatment Period, at the time you transition to the Open Label Period, or at any time during

your participation in the Open Label Period. The infusions are given in such a way that it is not possible to tell who is transitioning from placebo to active study drug.

Summary of Visit Activities

The following chart summarizes the activities that will occur during the Open Label Period. Please refer to the main A4 study informed consent for a complete description of study visit activities. All Visit 66 activities described the main consent form (as a part of the Treatment Period) will occur prior to your first infusion in the Open Label Period. Study staff will work with you to determine if any changes need to be made to this schedule of events.

Open Label Period Visits																			
Visit Number	66*	69	72	75	78	81	84	87	90	93	96	99	102	105	108	111	114	117	ET
Approximate Visit Length (hours)	3-4	2	3	2	3	2	2	2	3	2	2	2	3	2	2	2	3	2	3-4
Informed Consent**	✓																		
Study Drug Infusion	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		
Answer Questionnaires					✓				✓				✓				✓		✓
Assessment of Well Being		✓		✓		✓		✓		✓		✓		✓		✓		✓	✓
Memory & Thinking Skills Tests***		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
MRI Scan			✓																

* You have up to 12 weeks from the end of the Treatment Period (Visit 66) to enroll in the Open Label Period and receive the first open label infusion.
** Informed consent for Open Label Period must be signed before the Visit 66 infusion occurs.
***A voice recording of your responses to some memory tests will be made if the laws and guidelines at your study site allow this. These recordings are not being done to check your answers to questions, but rather if the site staff asked you the questions correctly. As in the main study, these recordings will be used to conduct quality reviews and will be destroyed at the end of the study. You will not receive any results or feedback from these tests.
Abbreviations: ET = early termination; MRI = magnetic resonance image

How long will I be in the Open Label Period?

You will be in the Open Label Period for up to 204 weeks. You will have visits up to Visit 117 or once all participants have completed the Treatment Period of the study and the results are known, whichever comes first. At that time, everyone will stop study drug at the same time. Because everyone is stopping the study at the same time but not entering at the same time, the amount of time you spend in the study will depend on when you started.

What will happen if I want to end my participation early?

In the event that you stop taking the study drug earlier than scheduled, or you stop participating in the study completely for any reason, study personnel will contact you and you will be asked to return to the research center to undergo a final evaluation called an "Early Termination" visit or "ET" visit. It is important for your health and safety to have these final procedures completed. The ET visit activities are listed in the schedule of events table above and will include all of the procedures conducted during the Open Label Period except an infusion and a magnetic resonance image (MRI).

Your participation also may be stopped by the study doctor or sponsor without your consent. If this happens, it might be due to a bad reaction you have to solanezumab or new information about solanezumab safety or effectiveness. If you are stopped from participation in the Open Label Period, the study doctor or one of the staff members will talk with you about any medical issues regarding the stopping of your participation.

What are the risks of participating in the Open Label Period?

There are known side effects and/or discomforts associated with this study. You might experience all, some, or none of the side effects listed below. Let the study doctor and staff know if you experience any side effects. You will be told of any new risks or significant findings that develop during the course of this study.

The solanezumab (study drug) and study procedure risks are unchanged from what was listed in the main consent, but for your convenience are repeated below.

Electrocardiograms, blood tests, and urinalysis will not be routinely collected during the Open Label Period. However, they may be collected if the doctor thinks it's necessary for safety reasons. The risks for these tests are described in the main consent.

Solanezumab (study drug) Risks

Information from Studies in People with mild Alzheimer's disease (AD) dementia

Solanezumab treatment may involve risks that are not known at this time due to the investigational nature of this study. Some of these unknown risks may be life-threatening or result in death. However, you will be told of any new risks or significant findings that develop during the course of this study.

Three large solanezumab studies were completed in over 3435 people with mild AD. The people in these studies were given either solanezumab 400 mg or a substance that looked like solanezumab but had no medicine in it (placebo) every 4 weeks for 1½ years. In 2 studies, 22 patients were given solanezumab 400 mg every week, which is about the same as 1600 mg every 4 weeks, for 2 to 3 months. The safety at this higher dose was consistent with the safety at 400 mg every 4 weeks.

Some people with AD were given solanezumab 400 mg every 4 weeks in a long study. Some of the people have been treated with solanezumab for 2 to 6 years. No new risks or discomforts with solanezumab have been identified in this study to date.

Information Based on How Solanezumab Works

When someone is immunized, special proteins called antibodies become active in the body. Antibodies help in a body's defense against germs or disease. "Active immunization" (vaccine) causes the body to make its own antibodies to fight against the infection or disease. "Passive immunization" (antibody) is when antibodies are given directly, so the body does not need to make its own antibodies. Solanezumab is a passive immunization approach for the possible treatment of AD.

Allergic Reactions

Some patients have had allergic reactions in solanezumab studies within 1 day after getting an infusion (2.6% of patients given solanezumab and 2.0% of patients given placebo). Most of these reactions were mild and did not require any treatment. If you have a serious allergic reaction, symptoms may include low blood pressure (which may cause fainting), and difficulty breathing. Milder reactions may include: rash, itching, fever, chills, nausea, vomiting, or a headache.

Itchy Rash

A small number of patients given solanezumab (0.4%) and placebo (0.1%) had complaints of rash along with itchiness. These rashes happened at any time during treatment and were mostly mild and did not require any extra treatment.

Increased Water Content of the Brain Tissue

An increase in the water content of the brain tissue has been seen in some people taking experimental medicines that lower Aβ, a brain protein thought to cause AD. Symptoms that can happen if someone has an increase in water content in the brain include: headache, worsened confusion, change in level of consciousness, seizures, unsteadiness, and vomiting. It is also possible that there will not be any symptoms with this kind of increase in water content in the brain. One or more scans of your brain will be done as part of this study to show if you have increased water content in your brain. Also, if you develop a combination of these symptoms at the same time, you will be asked to get an extra scan of your brain.

Based on brain scans during completed studies of solanezumab, small areas of increased water content of the brain tissue have been seen in 0.6% of people given solanezumab and 0.3% of people given placebo. Some of the time, the areas of increased water have gone away within a few weeks. In other

cases, the increased water content went away more slowly, stayed the same, or increased. Several of these people have continued or restarted study drug, and the increased water content of the brain tissue went away with continued infusions, or did not happen again. One patient had increased water content during placebo treatment, and developed it again during treatment with solanezumab. Only one of these people with increased water content in their brain had symptoms. This person had a burning or prickling sensation and weakness on one side of their body that lasted 10 minutes and did not come back.

Increase in Small Bleeds in the Brain Tissue

An increase in small bleeds in the brain has been seen in some people taking other potential new medicines that lower Aβ, the same protein that solanezumab lowers. An increase in the size or number of small bleeds in the brain tissue has been seen in about 6% of people given solanezumab and about 5% of people given placebo. There was no difference in the seriousness of small bleeds in solanezumab-treated patients compared with placebo-treated patients. The long-term effects of these small bleeds are uncertain. These small bleeds were mostly found during regularly scheduled brain scans.

Injection Reactions

When a drug is given, either as a shot under the skin, or into the vein (IV), certain effects may happen. Some people given solanezumab IV may have mild problems at the IV site, including: pain, swelling, redness, bruising, itching, infection, and minor bleeding. Some people may feel tiredness, dizziness, nausea, sweating, and/or faint after getting an IV. These injection reactions have happened in 2.1% of patients given solanezumab and 2% of patients given placebo.

Thoughts of Suicide or Suicide Attempts

Patients with mild AD dementia in a solanezumab study were periodically asked if they thought about committing suicide or tried to commit suicide. More patients who were given solanezumab said they thought about committing suicide (6.6%) than patients who were given placebo (4.6%). More patients who were given solanezumab tried to commit suicide (0.4%) than patients who were given placebo (0.1%). If you have thoughts of ending your life or harming yourself, you should tell someone immediately. You will also be asked periodically if you have tried to commit suicide or have had thoughts about committing suicide while you are taking part in studies of solanezumab.

Heart Problems

Heart problems have been seen in some people in previous solanezumab studies. More recent studies have shown that this is no longer a risk.

Pregnancy

If you are a woman and you could become pregnant during this study, there may also be unknown risks to your embryo, fetus, or nursing infant.

Intravenous Infusions

You will have up to 51 IV infusions during this Open Label Period. A needle will be placed inside a vein in your arm, causing a small hole or "puncture." The study drug will be given through this needle.

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. Phlebitis is irritation of a vein. 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.

Magnetic Resonance Imaging Risks

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 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.

Risks of Loss of Confidentiality

Study personnel will not release your study information to your doctor without your permission, and will code your study information to protect your confidentiality.

However, it is possible that information about your participation in this study could enter your medical record, particularly if you experience an adverse event requiring treatment.

It is possible that information about your amyloid status or participation in this study could influence your ability to obtain life insurance, health insurance, or long-term care insurance or affect your future employability.

To help protect your confidentiality, this research is covered by a Certificate of Confidentiality (CoC) from the National Institutes of Health. With this Certificate, the researchers may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use.

Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the US federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the NIA, which is funding this project, or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration.

You should understand that a CoC does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The CoC will not be used to prevent disclosure as required by federal, state, or local law of [*list what will be reported, such as child abuse and neglect, or harm to self or others*].

Risks of Cognitive Testing & Questionnaires

Cognitive testing may cause some individuals to become upset, frustrated, bored, or tired. You have the right to decline to answer any questions that you feel uncomfortable in answering.

Are there benefits to taking part in this study?

There is no guarantee that you will personally benefit by participating in this research study.

Study staff will advise you to consult with your physician if any of your tests suggest that you have a medical problem.

What other choices do I have if I do not take part in the Open Label Period?

You do not have to take part in this Open Label Period. If you choose not to participate, you will receive your last infusion at Week 236 of the Treatment Period of the main A4 study.

Will this research data be shared?

Data from this research will be shared with other researchers. Data sharing is important for further translation of research results into knowledge, products, and procedures to improve human health. All links with your identity will be removed from the data before they are shared.

What are the costs of taking part in this research study?

Procedures related to the study and study drug will be provided at no cost to you. There will be no costs to you for participation in this study.

Will I be paid for taking part in this research study?

You [will/will not] be paid for your participation in this study. You will be compensated for your time in coming to study visits and your travel expenses will be reimbursed.

Is my participation voluntary?

Yes! Taking part in the Open Label Period is completely voluntary. You may choose not to take part in the Open Label Period, or you may choose to leave the study at any time and for any reason. You may refuse to participate in the Open Label Period without a penalty or loss of benefits to which you are otherwise entitled.

What about privacy?

Your personal health information will be handled by the study doctor and staff in a confidential manner. Your health information will be used and disclosed in accordance with the Data Privacy Statement provided with the main consent form for the A4 study.

What if I am injured while participating in the study?

The information about research-related injury described in the main consent form for the A4 study applies to the Open Label Period as well.

Who is paying for this research?

This study is being conducted by the Alzheimer's Therapeutic Research Institute (ATRI) in conjunction with Eli Lilly & Company, through a grant from the National Institute on Aging (NIA). The study doctor and/or [name of Institution or site] is being paid for their work on this study.

If I have questions or concerns about this research, whom can I contact?

If you have any questions regarding this research or if you believe that you may have experienced a research-related injury or a reaction to the study medication, you should contact Dr. [Insert Site PI Name] (study doctor) at (XXX)XXX-XXXX.

If you have any questions about your rights as a research subject, you may call the [SITE IRB's NAME] office at (XXX)XXX-XXXX for more information about this or to report research-related problems. The

Institutional Review Board is a group that serves to protect the rights of participants in research trials.

Can I withdraw from the study?

Yes! If you choose to participate in the Open Label Period, you can change your mind at any time. You have the right to refuse to participate, to refuse to answer specific questions in an interview or on a questionnaire, or to discontinue participation in this study at any time without jeopardy to the medical care you receive at this institution.

Because study results might be affected, participation in any other clinical studies will not be permitted until your participation in this study has ended.

As described in the main consent form that you signed, you have the right to withdraw your permission to use or disclose personal information about your health. If you choose to withdraw your permission, you must notify Dr. [Insert Site PI Name] in writing, using the address in the main consent form. If you cancel your permission, the study doctor and staff will no longer use or disclose your personal health information in connection with this study, unless the study doctor or staff needs to use or disclose some of your personal health information to preserve the scientific integrity of the study.

If you cancel your permission, you will no longer be able to participate in the study.

STATEMENT OF CONSENT

By signing and dating this consent form, you are agreeing to continue to participate in the A4 study Open Label Period.

- You have read all of the information in this Consent, and you have had time to think about it.
- All of your questions have been answered to your satisfaction.
- You voluntarily agree to continue to be part of this research study, to follow the study procedures, and to provide necessary information to the doctor, nurses, or other staff members, as requested. You may freely choose to stop being a part of this study at any time.
- You have received a copy of this Consent to keep for yourself.

Circle and initial your selections below:

Do you agree to participate in the Open Label Period?	**Yes**	**No**	INITIALS

Participant's Name (print)	**Signature**	**Date**
Study Partner's Name (print)	**Signature**	**Date**
Legally Authorized Representative (print), if applicable	**Signature**	**Date**
Person Obtaining Consent (print)	**Signature**	**Date**
Witness (print), if applicable	**Signature**	**Date**