Informed Consent Form

Cognitive Decline and Alzheimer's Disease in the Dallas Lifespan Brain Study

NCT04080544

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The University of Texas Southwestern Medical Center

CONSENT TO PARTICIPATE IN RESEARCH

Title of Research:	18F-AV-1451-A14 – Clinical Evaluation of 18F-AV-1451 Cause or effect? Untangling the relationship of amyloid and tau deposits to cognitive decline and Alzheimer's disease in the Dallas Lifespan Brain Study
Funding Agency/Sponsor:	National Institute on Aging UT Dallas and UT Southwestern
Principal Investigator:	Denise. C. Park, Ph.D., Director of Research, UT Dallas Center for Vital Longevity
Co-Investigator:	Carol Tamminga, M.D., Chair of UTSW Psychiatry
Faculty Sponsor:	Neil Rofsky, M.D., Chair of UTSW Radiology

You may call Dr. Denise Park and research personnel during regular office hours at 972-883-3700. Kelli Key and Dr. Neil Rofsky can be reached at 214-645-1568.
At other times, you may call Dr. Denise Park at 214-470-8673.

Instructions:
Please read this consent form carefully and take your time making a decision about whether to participate. As the research assistant discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. The purpose of the study, risks, inconveniences, discomforts, and other important information about the study are listed below. If you decide to participate, you will be given a copy of this form to keep.

Why is this study being done?
There is a sticky, plaque-like protein that forms outside brain cells as we age, called beta-amyloid. In addition there is a tangle-like protein that forms inside the brain cells as we age called tau. It is known that both amyloid and tau proteins accumulate in the brains of people with Alzheimer's disease. However, both amyloid plaques and tau tangles can be detected in the brains of healthy people without the dementia associated with Alzheimer's disease. This study is being done to understand the role of amyloid and tau in normal aging and the risk for developing Alzheimer's disease in the future. The drug used in this study has recently been approved by the FDA for medical use. This study is being conducted as part of a clinical trial to test further the safety of 18F-AV-1451 and the optimal conditions for measurement of tau accumulation by the UTDallas/UT Southwestern.

Why is this considered research?
This is a research study because it is currently unknown how deposition of amyloid plaques and tau tangles in the brain interact and affect the brain and cognition. This study is designed to investigate that knowledge gap.

The following definitions may help you understand this study:

- Standard medical care means the regular care you would receive from your personal doctor if you choose not to participate in this research.
- Researchers means the study doctor and research personnel at the University of Texas at Dallas and at University of Texas Southwestern Medical Center and its affiliated hospitals.

Why am I being asked to take part in this research study?
You are being asked to take part in this study because you previously participated in the Dallas Lifespan Brain Study (IRB STU-072010-112).

Do I have to take part in this research study?
No. You have the right to choose whether you want to take part in this research study. If you decide to participate and later change your mind, you are free to stop participation at any time.

If you decide not to take part in this research study it will not change your legal rights or the quality of health care that you receive at this center.

How many people will take part in this study?
Up to 125 people will take part in this phase of the study, which is part of the Dallas Lifespan Brain Study at UT Southwestern.

What is involved in the study?
If you volunteer to take part in this research study, you will be asked to sign this consent form and will have the tests and procedures described below. These procedures are being done solely for the purposes of this study. These visits may be combined or certain procedures may be done on different days depending on your schedule.
If you are here as a wait-listed alternate, you should complete this consent form by assuming you will have the procedure today. If the scheduled participant is not available, we want you to be ready to take his or her place today. If you do not participate today, you will complete a new consent form the day you are scheduled.

Screening Procedures :
Prior to today's visit, a study member contacted you by phone to determine your eligibility for the study. To help decide if you qualified to be in this study, the researchers asked you questions about your health, including medications you take, family history of neurological disease, and any surgical procedures you have had, and you may have completed the Mini-Mental State Examination (MMSE). The consent you provided over the phone allowed the research team to collect this information prior to completing the

current written consent form, but does not constitute enrollment in the full study. You may still choose to not participate in the study now or at any time hence.

Additionally, a physician has reviewed your medical forms and determined that you are eligibility for this PET/CT imaging procedure.

Day of PET Scan Procedures:
This study will take place in the clinic at Clements Advanced Imaging Research Center. This visit may take up to 180 minutes.
You may have to fill out certain forms or have the following tests or procedures completed:

- Sign this consent form
- Demographic information (age, sex, ethnic origin, level of education)
- Medical history and current medications
- Vital signs (blood pressure and pulse)
- Urine pregnancy test (if you are a woman of childbearing potential)
- A brief quiz to make sure you are ready for the scan

If these exams or tests have been done recently, they may not need to be repeated. These tests include:

- Demographic information
- MMSE

During this study visit, you will be asked to sign the consent and HIPAA forms, and complete the MMSE. In addition, your height and your weight will be taken. Vital signs (heart rate, blood pressure, and breathing rate) will be taken before the 18F-AV-1451 injection and at the completion of the PET/CT scan. You may also be asked to complete a brief cognitive task during this visit.

If you are present as a wait-listed alternate, you will be asked to wait a maximum of three hours from your scheduled arrival time. You will be dismissed as soon as we verify that the scheduled participants are available.

If you are a woman who may be able to become pregnant, prior to injection, a urine sample will be collected for a pregnancy test. The result of the pregnancy test must show that you are not pregnant for you to continue participation in the study.

After completing the initial procedures and providing a negative pregnancy test (if applicable), a needle will be inserted into a vein in your arm and a small amount of the imaging agent, 18F-AV-1451, will be injected.

Approximately 80 minutes after the injection of 18F-AV-1451, you will be placed in the PET/CT scanner for a 20 minute PET/CT scan. During the PET/CT scan procedure, you will lie quietly on a small table while the camera around you takes pictures of your brain. A member of our staff will be nearby during the procedure. After completing the scan a

doctor will see you to assess your vital signs before you leave the clinic. In total, the imaging portion takes about 2 hours but the complete visit could take up to 3 hours.

Follow-up Phone Call:
You will receive a follow-up phone call between 2 or 3 business days following the 18F-AV-1451 PET/CT scan to confirm your well-being and to collect information about any changes to your health.

The brain imaging data in this study is designed for research, not for medical purposes. Because the scans done in this study are not for medical purposes, neither the scan nor any research results will be given to you or to your doctors.

Follow-up Research Procedure*:*
In approximately 3 or 4 years, a member of the Park Aging Mind Lab may contact you and schedule follow-up research sessions.

Are samples being collected?
Only women of child bearing potential will have samples collected during this study. Urine samples will be collected for a pregnancy test. Females of child bearing potential must have a negative pregnancy test to participate in the study. All samples collected for the pregnancy test will be destroyed immediately after the confirmation of the test results unless laws, regulations, or international laboratory certification standards require a longer retention period.

How long can I expect to be in this study?
The study will consist of a maximum of 1 in-person visit and 1 or more study check-up phone calls over the course of up to 2 months. You can choose to stop participating for any reason at any time. However, if you decide to stop participating in the study, we encourage you to tell the researchers.

What are the risks of the study?
Because of your participation in this study, you are at risk for the following side effects. You should discuss any questions or concerns with the researchers and with your regular health care provider.

PET/CT (Positron Emission Tomography) Scan and 18F-AV-1451 Administration:
You will receive one 18F-AV-1451 PET/CT brain scan. PET/CT scans use radiation, or nuclear medicine imaging, to produce 3-dimensional images. During the PET/CT scan, you will need to lie quietly and stay still while the camera around you takes pictures of your brain.

Being in the PET/CT 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/CT scan machine for a long period of time.

The following side effects have been reported in clinical studies of the PET radiotracer (18F-AV-1451): diarrhea, headache, muscle spasms, and altered taste. All reported events were mild to moderate in intensity and all subjects recovered from these events. In 2020, 18F-AV-1451 was FDA approved for safe clinical use.

Intravenous Catheter:
A needle will be used to inject 18F-AV-1451 into your vein. Insertion of the needle may cause pain or a stinging bruising, bleeding, a blood clot, and leakage of study drug or infection at the site of insertion.

Psychological Stress:
Some of the questions we will ask you as part of this study may make you feel uncomfortable. You may refuse to answer any of the questions, take a break or stop your participation in this study at any time.

Loss of Confidentiality:
Any time information is collected there is a potential risk for loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

Risks to Sperm, Embryo, Fetus or Breast-fed Infant:
There is currently no information on the effects of 18F-AV-1451 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 breast-feeding a child, you cannot participate in this study.

In order to reduce the risk of pregnancy, you must not have sexual intercourse or you must use an effective method of birth control for 90 days after the administration of 18F-AV-1451. If you are already using a method of birth control, the study doctor or study staff will discuss with you whether your current method of birth control is acceptable for use during this study.

If, during this study, you become pregnant or are male with a female partner who becomes pregnant within 90 days after injection of 18F-AV-1451, you should notify the study doctor as soon as possible.

Males: Being in this research may damage your sperm, which could cause harm to a child that you may father while on this study. If you take part in this study and are sexually active, you must agree to use a medically-acceptable form of birth control. Medically-acceptable forms of birth control include:

(1) surgical sterilization (vasectomy), or
(2) a condom used with a spermicide (a substance that kills sperm).

Females: If you are part of this study while pregnant or breast-feeding an infant, it is

possible that you may expose the unborn child or infant to risks. For that reason, pregnant and breast-feeding females cannot participate in the study. If you can become pregnant, a urine pregnancy test will be done, and it must be negative before you participate in this study. If you take part in this study and you are sexually active, you and any person that you have sex with must use medically-acceptable birth control (contraceptives) during the study. Medically-acceptable birth control (contraceptives) includes:

(1) surgical sterilization (such as hysterectomy or "tubes tied"),
(2) approved hormonal contraceptives (such as birth control pills, patch or ring; Depo-Provera, Implanon),
(3) barrier methods (such as condom or diaphragm) used with a spermicide (a substance that kills sperm), or
(4) an intrauterine device (IUD).

If you do become pregnant during this study, you must tell the researchers immediately.

Risks of Radiation – Diagnostic Test:
Being part of this study will expose you to radiation that you may not receive as part of your standard care. The radiation you receive for your everyday care outweighs risks the radiation poses because it allows your doctor to provide appropriate medical care. The extra radiation you receive from this study may not help you in this way. However, everyone is exposed daily to a background of radiation from the earth, outer space, the food we eat, and the air we breathe. Some people may be exposed to larger amounts of radiation (up to about 15 times more than this natural and background each year) because of their jobs working with radiation. Regulations limit the amount of radiation these workers can receive each year to make sure their risks are low. The added radiation dose you will receive from this study is less than the yearly regulatory limit set to protect radiation workers in the U.S.

Other Risks:
There may possibly be other side effects that are unknown at this time. If you are concerned about other, unknown side effects, please discuss this with the researchers.

How will risks be minimized or prevented?
Potential risks and discomforts will be prevented and/or minimized to the greatest extent. Trained personnel will be present for the duration of the visit and a physician will be present after the scan. Vital signs (blood pressure and heart rate) will be measured before and after the scan. You will not be discharged without the physician's approval. A follow-up phone call to check on you will occur approximately 2 days after imaging.

What will my responsibilities be during the study?
While you are part of this study, the researchers will follow you closely to determine whether there are problems that need medical care. It is your responsibility to do the following:

- Ask questions about anything you do not understand.
- Keep your appointments.
- Follow the researchers' instructions.
- Let the researchers know if your telephone number or address changes.
- Tell the researchers before you take any new medication, even if it is prescribed by another doctor for a different medical problem or something purchased over the counter.
- Tell your regular doctor about your participation in this study.
- Report to the researchers any injury or illness while you are in the study, even if you do not think it is related to the study imaging agent.
- If you are here as a wait-listed alternate participant, you will have the above-listed responsibilities only if you are tested today as an alternate to a scheduled participant. The research staff will inform you if you are needed as soon as they verify the status of the scheduled participants. The maximum you will be asked to wait is three hours from your scheduled arrival time. During the wait period, you may read or use electronic devices. Please inform us if you leave the room for any reason.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?
Yes. You will be told if any new information becomes available during the study that could cause you to change your mind about continuing to participate or that is important to your health or safety.

What should I do if I think I am having problems?
If you have unusual symptoms, pain, or any other problems while you are in the study, you should report them to the researchers right away. Telephone numbers where they can be reached are listed on the first page of this consent form.

If you have a sudden, serious problem, like difficulty breathing or severe pain, go to the nearest hospital emergency room, or call 911 (or the correct emergency telephone number in your area). Tell emergency personnel about any medications you are taking.

What are the possible benefits of this study?
You may or may not receive any benefit from being in this study. If you take part in this study, it may help us to understand the development of Alzheimer's disease and other tauopathies.

What do we hope to learn from this study?
Although researchers will see your brain scan results, they will not be able to make any conclusions from the scan. Until a large number of healthy volunteers have received brain scans using 18F-AV-1451, no one will be able to determine whether these scans have value in predicting or diagnosing Alzheimer's Disease. Therefore, the results of your brain scan will not be shared with you or with any doctor who might be treating you.

What options are available if I decide not to take part in this research study?
This is not a treatment study. You do not have to participate in this research.

Will I be paid if I take part in this research study?
Yes. In addition to the $25 received after completing the screening procedures, you will be paid $200 for the PET/CT scanning procedures.

You will be issued a UT Dallas GalaxyPay card, which can be used as a credit or debit card. You will also receive instructions on how to use the card.

For this visit, we will reimburse you $200 which includes $170 for the visit and $30 travel costs. If roundtrip travel exceeds 50 miles, you will receive $0.58.5 a mile for each additional mile. If you prefer not to drive, you may arrange transportation with an outside source (e.g., Uber, Lyft, Cab service) and you will get reimbursed if you provide your receipts. If you prefer, we can arrange travel with a university-approved service and charge it directly to our accounts—If you require air travel to reach Dallas, and overnight accommodations, the study will cover the cost of the hotel and flight. In addition the study will cover the cost of a rental car and a travel stipend in concordance with federal regulations to cover other costs/needs during your stay.

If you are a wait-list alternate today, you will receive $100 for serving as an alternate. If you participate in a scan today by replacing a scheduled participant, you will receive the $200 described above for participation in the scan.

You will not otherwise be paid for transportation to and from the research center, lost time away from work and other activities, lost wages, or child care expenses.

Will my insurance provider or I be charged for the costs of any part of this research study?
No. Neither you, nor your insurance provider, will be charged for anything done only for this research study (i.e., the Screening Procedures, Experimental Procedures, or Monitoring/Follow-up Procedures described above).

What will happen if I am harmed as a result of taking part in this study?
It is important that you report any illness or injury to the research team listed at the top of this form immediately. In the event of a side effect occurring during the day of the study procedure which requires immediate medical treatment, you will be referred for such treatment to a UT Southwestern facility.

Compensation for an injury resulting from your participation in this research is not available from the University of Texas Southwestern Medical Center or The University of Texas at Dallas.

You retain your legal rights during your participation in this research.

Can I stop taking part in this research study?
Yes. If you decide to participate and later change your mind, you are free to stop taking part in the research study at any time.

If you decide to stop taking part in this research study, it will not affect your relationship with the UT Southwestern staff or doctors. Whether you participate or not will have no effect on your legal rights or the quality of your health care.

If you are a medical student, fellow, faculty, or staff at the Medical Center, your status will not be affected in any way.

If I agree to take part in this research study, can I be removed from the study without my consent?
Yes. The researchers may decide to take you off this study if:

- The researchers believe that participation in the research is no longer safe for you.
- Information is revealed that indicates that you fall outside of the inclusion/exclusion criteria for the study.
- The sponsor or the FDA stops the research for the safety of the participants.
- The sponsor cancels the research.
- You are unable to keep appointments or to follow the researcher's instructions.

Will my information be kept confidential?
Information, about you, that is collected for this research study will remain confidential unless you give your permission to share it with others, or if we are required by law to release it. You should know that certain organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- Avid Radiopharmaceuticals, Inc. (a wholly owned subsidiary or Eli Lilly and Company) and its representatives (Avid was the original developer of 18F-AV-1451-A14 ligand);
- The National Institutes of Health and the National Institute of Aging;
- Representatives of government agencies, like the U.S. Food and Drug Administration (FDA), involved in keeping research safe for people;
- The UT Southwestern Institutional Review Board; and
- The UT Dallas Institutional Review Board.

Information from this research study has been or will be entered into a clinical trial databank that is maintained by the National Institutes of Health/National Library of Medicine.

The sponsor may also use the PET/CT scan images obtained during the study to develop and evaluate various training and image analysis methods, and to train

personnel and third parties who may participate in other studies. In such cases your identity will be kept confidential.

In addition to this consent form, you will be asked to sign an "Authorization for Use and Disclosure of Protected Health Information." This authorization will give more details about how your information will be used for this research study, and who may see and/or get copies of your information.

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.

Are there procedures I should follow after stopping participation in this research?
Yes. If you, the researchers, or the sponsor stops your participation in the research, you may be asked to do the following:

- Let the researchers know immediately that you wish to withdraw from the research.
- Return to the research center for tests that may be needed for your safety.
- Discuss your future medical care, if any, with the researchers and/or your personal doctor.

Is there anything else I should know before I decide?
You should feel free to ask any questions you may have about this.

Whom do I call if I have questions or problems?
For questions about the study, contact Dr. Park at 972-883-3700 during regular business hours and Dr. Denise Park at 214-470-8673 after hours and on weekends and holidays.

For questions about your rights as a research participant, contact the UT Southwestern Institutional Review Board (IRB) Office at 214-648-3060.

SIGNATURES:

YOU WILL BE GIVEN A COPY OF THIS CONSENT FORM TO KEEP.

Your signature below certifies the following:

- You have read (or been read) the information provided above.
- You have received answers to all of your questions and have been told who to call if you have any more questions.
- You have freely decided to participate in this research.
- You understand that you are not giving up any of your legal rights.

_____

Name of Participant (Printed)

_____ _____ _____ AM / PM

Signature of Participant Date Time

_____

Name of Person Obtaining Consent (Printed)

_____ _____ _____ AM / PM

Signature of Person Obtaining Consent Date Time