Alzheimer's Disease Cooperative Study
UC San Diego

Prazosin for Disruptive Agitation in Alzheimer's Disease (AD) (PEACE-AD)
Short Title: Prazosin for Agitation in AD
Protocol Number: ADC-042-PRAZ

NCT03710642

Main Informed Consent Form (ICF)

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Informed Consent to Participate in a Research Study:

Study Title: Prazosin for Disruptive Agitation in Alzheimer's Disease-(AD) – PEACE-AD

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Study Site: <<INSTITUTION NAME>>
Principal Investigator: <<INVESTIGATOR NAME>>
Contact info: <<INVESTIGATOR PHYSICAL ADDRESS, PHONE, FAX, EMAIL>>
Central IRB Application Identifier: <<IRB Number>>

This consent form describes a research study and your role as a research participant. 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 participant. 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 to participate is yours to make. If you choose to participate, you have the right to withdraw from the study at any time.

If the person being asked to be in this research study is not able to give consent to be in the study, the person's legally authorized representative (LAR) is being asked to give permission for this person to be in the study as his/her decision maker. In this consent form, referring to "you" may also refer to the loved one of the LAR.

If you decide to participate in this study, you will need a Study Partner or legal representative. The Study Partner/legal representative will be able to remove you from this study if you become unable to say that you wish to remain in the study. Your study partner/legal representative will be asked to read and sign this Informed Consent.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov. This web site will not include information that can identify you. The web site will only include a summary of the results when they become available. You may access this web site at any time.

PEACE-AD is being conducted by the Alzheimer's Disease Cooperative Study (ADCS), through a grant from the National Institute on Aging (NIA).

Why is this study being done?

You are being invited to take part in a research study because you have Alzheimer's disease (AD) and have also been having symptoms of disruptive agitation, such as irritability, anger outbursts, and pacing. The purpose of this study is to see if a drug called prazosin can help make these agitation symptoms better.

Prazosin is a drug that is approved to treat people with high blood pressure. It has not been approved by the Food and Drug Administration (FDA) to treat agitation in people with AD and related disorders which is the purpose of this research study. Some people in this study will take placebo, which are capsules that look like the study drug but do not contain any active drug in them.

How many people will take part in this study?

This study is being done at multiple sites across the U.S. If you are eligible and agree to participate, you will be one of approximately 186 adults with AD and disruptive agitation who will be taking part in this study. Participants may either be residing in a Long-Term Care (LTC) facility/nursing home or living at home with a full-time caregiver. If you are living at home, your full-time caregiver will be assigned as your Study Partner.

What will happen if I take part in this study?

Neither you nor the study personnel will know whether you are receiving the active study drug or placebo. This study will last up to 16 weeks. All of the procedures during this study are research procedures. This study is not meant to replace visits with your regular doctor. You will continue to be seen by your regular doctor for ongoing medical care. Depending on the safety recommendations and where you are living, the study staff will be able to perform your first visit either at the Long Term Care facility, the clinic, through a home visit, or by using remote technology (using telephone or video). If you are living in a Long Term Care facility, the study staff may come to you in your care facility/nursing home for your first screening visit, or may visit you using remote technology (telephone and video). If you are living at home, you and your Study Partner may be asked to come into the study clinic for your first screening visit, or a study team member will come to you for a home visit, or you may be visited using remote technology (telephone and video). All remaining study visits may be conducted either in person or by remote visit (telephone or video).

Please tell your study doctor or study staff if you would like to stop being in the study at any time. During this study, the local study team will be monitoring your condition.

Description of study visits

The first part of the study is called the Screening period. This period will last up to 28 days. If you qualify and agree to participate in the study, there will be a study drug dose adjustment period during the first 29 days of the study drug regimen. From the time study drug is started, your participation will last up to 12 weeks. During this time, the study doctor will determine the best dose of drug for you to take and you will remain on this dose and be monitored throughout the study until the end, up to week 12.

You or your legally authorized representative (LAR) must sign this consent form before beginning the screening process.

Screening (Visit 1)

During your **Screening** appointment, we will determine your eligibility to enroll in PEACE-AD, and if this study is right for you. The screening period may take up to 28 days, and may occur over two visits. The study staff will explain these procedures and answer any questions you and your LAR may have.

During this screening visit, the following things will happen:

- We will ask you about your general medical and psychiatric history. We may request additional records if we have questions about your medical history. We will ask you to sign a release of information form to get these medical records, if needed.
- We will ask you questions about your behavior and mood. We will ask you if you are feeling irritable or angry, restless, depressed or sad, if you have had problems sleeping, or any strange or unusual experiences. Some questions may make you feel uncomfortable, and you are free not to answer those questions. We will also ask your nurse and LAR or your Study Partner if you are living at home some of the same questions about your behavior and mood.
- We will review and update (if needed) your risk of having a fall. We will discuss with you any added risks of having a fall while on this trial and a care plan to prevent falls from occurring.
- We will review and record your current medications.
- When possible, you will have a brief physical and neurological exam. If your screening is done as a remote visit, a combination of telephone and video conference will be used. The study doctor will ask you to move your arms and legs and walk if it is safe to walk. If conducting screening as a remote visit, a combination of telephone and video conference can be used; at a minimum, the observational elements of the Physical and Neurological Exam including visual assessment of participant gait should be done via video conference.
- We will measure your blood pressure and heart rate while you are lying down and again when you are standing up (or sitting up if you cannot stand up). Your blood pressure may be taken several times over a 7 to 14 day period to see if you may continue in the study.

- If your blood pressure is too low, and you are given medicines to keep it low, the study doctor will contact your regular doctor (primary care physician) to talk about adjusting your blood pressure medicines. The study doctor and your regular doctor will work together to decide if it is safe for you to continue in the study. You may have an electrocardiogram (ECG—tracing that measures the electrical signals of your heart) if you have not one within 12 months of this visit.
- If you have not had routine laboratory tests (complete blood count and blood chemistries) done within 12 months of this visit, we may collect about between 10 to 20 ml (a little more than 1 tablespoon) of blood from your arm. This is to make sure you have no medical conditions that prevent your participation in this study.
- We may collect a urine sample from you if the study doctor determines that it needs to be collected.

Baseline (Visit 2)

Baseline procedures will be completed within 28 days of your screening visit, and before you can be assigned to one of the 2 study groups. Baseline procedures include:

- We will measure your blood pressure and heart rate while you are lying down and again when you are standing up (or sitting up if you cannot stand up).
- We will ask you if you have had any illnesses or changes in your health since your last visit.
- We will update the list of any medications that you are currently taking.
- We will ask some questions about your behavior and your daily functioning. We will ask you if you are depressed or sad, if you have had problems sleeping or feelings of worthlessness. We will also ask you questions such as if you get angry a lot, have trouble sitting still, or have changes in your appetite. Some questions may make you feel uncomfortable, and you are free not to answer those questions.
- We will also ask your nurse, other care facility/nursing home staff, and LAR some of the same questions about your behavior like the ones we asked you. If you are living at home with full-time caregiving, we will ask your Study Partner some of the same questions about your behavior like the ones we asked you. We will also ask questions about your daily functioning and your ability to do things such as dressing yourself.

At the end of this visit, you will be randomly assigned (like flipping a coin) to one of two groups. Group 1 will take prazosin capsules, and Group 2 will take capsules that do not contain any active medication (placebo). Since two-thirds of the subjects will receive the active drug, there is a greater chance that you will receive prazosin rather than the placebo. Neither you nor the study staff will know which group you are in, although that information will be available if there is an emergency.

Dose adjustment (Days 1-29)

The dose adjustment period will happen after all the baseline procedures are done. During the dose adjustment period, we will determine what the best dose of study drug is for you. The nursing home staff or your Study Partner will be asked to help you in taking your study drug. Your starting dose will be 1 mg of prazosin (or placebo) per day (one capsule of study drug to be taken at bedtime). After the first day of taking the study drug, we will ask you if you are having any side effects. If you are not having any side effects, you will keep taking this dose for 2 more days. On day 4 and for the rest of the 12-week study, you will take the study drug twice a day, at approximately at 10:00AM and at bedtime.

We will ask if you have been having any side effects and will ask some questions about your symptoms of agitation. If your agitation has not markedly improved and if you are *not having any side effects*, we will increase your dose of prazosin (or placebo). We will continue increasing your dose until your agitation gets better, or until the maximum dose of 10 mg per day of prazosin (or placebo) is reached.

The care facility/nursing home staff or your Study Partner at home will measure your blood pressure and heart rate while you are lying down and again while you are standing up (or sitting if you cannot stand) every day while your dose is being adjusted and through the following week. Care facility/nursing home staff or your Study Partner may measure your blood pressure more than once a day if needed to more closely monitor any changes observed in blood pressure measurements during the dose adjustment period.

If you have intolerable side effects during the dose adjustment period, the dose will be reduced to the last tolerated dose, until the side effect resolves. When the side effect resolves, the study doctor may recommend you take a higher dose of the study drug again during this adjustment period. For safety purposes, the dose may be decreased any time throughout the study.

Study Weeks 5, 6, 8, 10, 12

At each of these visits, we will ask you whether you have been having any side effects, if there has been any change in your medications (including over-the-counter medications and supplements), and whether you have been sick or had any other adverse events since your last visit. We will measure your vital signs (blood pressure and heart rate while lying down and standing up) every day until Day 35, and then every 3 days for the rest of the study.

At Weeks 8 and 12, we will also ask questions about your mood, behavior, and ability to do daily tasks. You will be asked the same questions we asked you at your baseline visit. You are free not to answer any questions you do not wish to answer.

After your Week 12 visit, you will be done with the study. We will discuss with you, your family, and the care facility staff or Study Partner whether you would like to continue taking active drug. If you would like to continue taking prazosin, we will work with your regular doctor to set up a dosing schedule.

You will be asked to report any side effects or adverse events that happen to you during the study and for 30 days after you leave the study.

Early Discontinuation

Participation in this research study is entirely voluntary. You can stop participating at any time without losing or changing your current medical care. If you choose to stop being in the study for any reason, you will be asked to have a final study visit. This visit will include all of the procedures normally performed at Week 12. It is important for your health and safety to have these final procedures completed.

Your participation in the study may be stopped by the study doctor or sponsor if you experience a medical condition that makes it unsafe for you to continue your participation in the study. You may also be removed from the study if the study is cancelled or for other reasons we do not know at this time.

Potential Study Risks

Participation in this study may involve some added risks or discomforts, which are described below:

Risks of the Study Drug

The most common side effects of prazosin (seen in up to 10% of people) include:

- Dizziness
- Drowsiness
- Lightheadedness
- Headache
- Nausea
- Lack of energy
- Weakness
- Palpitations (abnormal heartbeat)

Other side effects (less than 4% of people) include:

- Vomiting
- Diarrhea
- Constipation
- Drop in blood pressure when standing
- Indigestion
- Fainting
- Vertigo
- Shortness of breath
- Depression
- Nervousness
- Rash
- Increased urinary frequency
- Blurred vision
- Reddened eyes
- Dry mouth
- Nasal congestion
- Nosebleeds
- Edema (swelling)

Dizziness or lightheadedness may occur after the first dose of the study drug. Your first dose of study drug will be taken right before you go to bed for the night. Dizziness, lightheadedness, or fainting may occur, especially when getting up from a lying or sitting position. Getting up slowly may help lessen the problem. Your nurse or your Study Partner will check up on you after you take your first dose to make sure you are tolerating the study drug. Also, use extra care if standing for long periods. Check with one of the study

doctors if you have any questions.

Other side effects (less than 1% of people) include:

- Abdominal discomfort or pain
- Heart beating faster than usual
- Tingling sensation (pins and needles)
- Hallucinations
- Severe itching in the skin
- Unable to control going to the bathroom
- Not able to achieve erection (men)
- Pain in the penis when there is an erection

If your doctor thinks you need additional medication for your agitation, he will order for you to take a medication called lorazepam, which risks include:

- Increased drowsiness
- Physical and mental fatigue
- Increased anxiety
- Confusion and disorientation
- Memory loss
- Learning difficulties
- Slow, shallow breathing
- Pale or bluish skin

Procedure Risks

All of the study procedures will cause some inconvenience to you. Having your blood drawn may cause temporary discomfort or in some cases, a bruise may form where the needle enters the vein. Rarely, an infection may develop. The total amount of blood drawn during this study is between 10 and 20 mls (a little more than 1 tablespoon).

During the interviews, you may feel uncomfortable talking about your behavior and mood. We will make these interviews as stress-free as possible.

Although there is no pain or discomfort during the electrocardiogram (ECG), which is a test that records the electrical activity of your heart, removing the pads that are placed in your skin may cause some irritation.

Some people taking prazosin, or other drugs related to prazosin, had a side effect when they had cataract surgery. This effect is called Intraoperative Floppy Iris Syndrome (IFIS). If you are planning any eye surgery or ever need cataract surgery in the future, your eye surgeon needs to know if you ever took prazosin in order to reduce the risk of IFIS. If you ever need cataract surgery, be sure to tell your eye surgeon that you may have taken prazosin in a research study.

Women who are pregnant, breastfeeding, or of childbearing potential may not participate in this study.

It is very important during the study that you tell us before you start taking any new medications (prescriptions, herbal, or over-the-counter medications or supplements) or change the dose of medications you already take. It is also very important that you tell us of any changes in your health.
For your safety, the study doctor may need to do extra visits. This would mean you may have extra blood samples taken, physical exams, or your vital signs taken more often.

In addition to the side effects already described, the study drug and the study procedures may have other unknown risks. As with any new medicine, there is a risk of rare or previously unknown side effects. You must tell your study doctor if you experience any side effects.

There is also a potential risk for loss of confidentiality.

What are the benefits of taking part in this study?

Your participation in this study may help the investigators learn more about the safety and benefits of prazosin in disruptive agitation for Alzheimer's disease to help other people who have a similar medical problem in the future.

Participation in this study may help to improve your condition, but it is also possible that your condition may not improve or worsen. There is no guarantee that you will personally benefit by participating in this research study.

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

Currently there are no FDA-approved treatments for disruptive agitation in Alzheimer's disease. There are five FDA-approved treatments for people with Alzheimer's disease. These are donepezil (Aricept®), rivastigmine (Exelon®), galantamine (Razadyne®), tacrine (Cognex®), and memantine (Namenda®). If you are currently taking any of these medications, you will be able to continue to take them while you are participating in this study. The research staff can inform you about any other investigational drugs that are being studied for treatment of Alzheimer's disease and related disorders.

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 will handle your personal health information in a confidential manner.

Federal Privacy Regulations require that you authorize the release of any health information that may reveal your identity. This includes information in your existing medical records needed for this study and new information created or collected during the study.

The persons and entities that you are authorizing to access your personal health information may include:

- The study team members
- The institution where this research is conducted
- The institution's Institutional Review Board (IRB)
- Johns Hopkins Single Institutional Review Board (sIRB)
- The Alzheimer's Disease Cooperative Study (ADCS)
- The National Institute on Aging (NIA), the study sponsor

In order to analyze the data collected during this research study, all of the health information generated about you during this study may be inspected by the Department of Health and Human Services (DHHS) agencies or ethics committees like the Institutional Review Board (IRB).

Because of the need to release information to these parties, absolute confidentiality cannot be guaranteed. Once your personal health information is released it may be re-disclosed, at which point your health information will no longer be protected by federal privacy regulations.

The purpose of this access is to review the study and make sure that it meets all legal, compliance, and administrative requirements. If a review of this study takes place, your records may be examined. The reviewers will protect your privacy.

Your data for this study will be kept indefinitely. All the information collected for the study will be labeled with a study code number and will not have any identifying information on it. The link between your name and study code number will be stored separately from the data in a password-protected computer file and will also be kept indefinitely. The study data will be kept in locked offices that only the study staff will have keys to. Only the study investigators listed on this consent form and their staff will have access to identifying data.

All of the information you provide will be confidential. However, if we learn that you intend to harm yourself or others, we must report that to appropriate authorities.

At any point during the study if we find any medical conditions of concern, we will discuss this information with you and refer you to your personal doctor for follow-up.

There may be publications about this study in the future. If so, your identity will be held confidential. No personal information will be given in a publication without your approval in writing.

Your study information will be used only for research purposes and will not be sold.

What Are The Costs Of Taking Part In This Research Study?

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 not be paid for your participation in this study. At the completion of your week 12 visit, you will receive a hand-crafted quilt, donated by the Quilt Guild for study participants, as a gift, not as compensation for your participation.

Should you not have your own access to remote video visit technology, an electronic tablet can be provided to your Study Partner to help with video tele-conferencing. The electronic tablet will allow your Study Partner easy to use access to video conferencing for remote visits that occur during the study. Your Study Partner will receive training on how to use the electronic tablet. The device (approximately $200.00 value) will be provided at no cost to you. The electronic tablet will not be returned at the end of the study. Any internet-link between the study team and you will be removed from the electronic tablet. You will be responsible for internet connectivity, device maintenance or technical upkeep.

No research data will be collected or stored on this electronic tablet.

Study Partner Stipend

A stipend of $50.00 for each visit completed up to a total of 10 completed visits (up to $500) will be paid to your Study Partner for time and effort needed for learning to use the electronic tablet, the Omron blood pressure machine, taking and documenting participant blood pressure, administering study drug and participating in remote study visits.

What Happens If I Experience An Injury Or Illness As A Result Of Participating In This 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. Neither financial compensation nor reimbursement for such things as pre-existing conditions, illness or disease unrelated to study participation, lost wages, property damage, disability, or discomfort is available.

The National Institute on Aging and the Alzheimer's Disease Cooperative Study do not provide compensation for research-related injury. [SITES TO ADD INSTITUTION'S SUBJECT INJURY CLAUSE HERE (you will / will not pay for subject injury, etc)]

By signing this consent form you do not give up any of your legal rights.

What if there is a Certificate of Confidentiality for this study?

Your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means.

It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

Who Do I Contact If I Have Questions Or Concerns About This Research?

If you have any questions regarding this research or if you believe that you may have experienced a research related injury, you should contact Dr. **[Insert Site PI Name]** (study doctor) at [**TELEPHONE**] to report this or other research-related problems. The Johns Hopkins Medicine IRB will serve as the central IRB for this study. The IRB reviews human research studies. It protects the rights and welfare of the people taking part in those studies. You may contact the IRB if you have questions about your rights as a participant or if you think you have not been treated fairly. The IRB office number is 410-955-3008. You may also call this number for other questions, concerns or complaints about the research.

STATEMENT OF CONSENT

You have read (or have had read to you) the description of PEACE-AD study. You have been informed of the risks and benefits involved, and all of your questions have been answered to your satisfaction. By signing this form, you voluntarily consent to participate in the research study and you authorize the use of your data for the research described above.

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

You will receive a copy of this consent form.

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

Legally Authorized Representative Consent

I, as the legally authorized representative of the participant, give consent for his/her participation in this study.

You have read all the preceding information that describes the participant's involvement in PEACE-AD. The study has been explained to you in detail, and all of your questions have been answered to your satisfaction.

Legally Authorized Representative Name (print)	**Signature**	**Date**
Person Obtaining Consent (print)	**Signature**	**Date**

California Site Only: Insert the Experimental Bill of Rights