University of California, Los Angeles

CONSENT TO PARTICIPATE IN RESEARCH

A phase II trial on rizatriptan for Vestibular Migraine

Robert W. Baloh, M.D. from the *Department of Neurology* at the University of California, Los Angeles (UCLA) are conducting a research study.

You were selected as a possible participant in this study because you have a condition called Vestibular Migraine. You are older than 18 years and younger than 65 years of age. You have experienced at least 5 lifetime episodes of vertigo lasting more than 2 hours and less than 72 hours. You have had at least 2 moderate to severe episodes of vertigo in the past 6 months. Your participation is completely voluntary; you do not have to participate if you don't want to. If you decide to participate you can leave the study at any time. UCLA Medical Center and Mayo Clinic are conducting this study with the sponsor, National Institute on Deafness and other Communication Disorders (NIDCD). Please read the form carefully and ask the person obtaining consent any questions that you may have before deciding whether or not to participate.

This form has important information, and telephone numbers, so you should keep this copy to refer to as the study proceeds. This consent will be printed; a copy will given to you during the consent process to keep. The Vertigo Symptom Diary & Package Insert for rizatriptan will also be provided to you.

Vestibular Migraine, affects about 1% of the general population and about 10% of patients seen in dizziness clinics; yet, relatively little is known about the cause, and there is no proven treatment. The aim of this study is to see if rizatriptan is effective treatment for vertigo associated with migraine and secondarily to evaluate its tolerability and its impact on treatment satisfaction and health-related quality of life in patients with Vestibular Migraine.

Why is this study being done?

The primary Specific Aim is to conduct the first successful controlled study of a treatment for Vestibular Migraine. We hypothesize that rizatriptan will be superior to a look alike inactive capsule for:

1a. Reducing the severity and duration of vertigo attacks in patients with Vestibular Migraine,
1b. Reducing the severity of symptoms commonly associated with vertigo attacks in patients with Vestibular Migraine (e.g., nausea, vomiting, motion sensitivity, gait disturbance, headache, light and sound senstitvity), and
1c. Improving treatment satisfaction and health-related quality of life in patients with Vestibular Migraine, and that
1d. Rizatriptan will be well tolerated by patients with Vestibular Migraine.

The investigators plan to publish and share what they find out during this research study. However, when the results are published, no information that could identify you will be shared; your identity will be protected.

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

If you volunteer to participate in this study, the researcher will ask you to do the following:

A total of about 200 patients with Vestibular Migraine will be evaluated at the following 2 sites: University of California, Los Angeles, CA, and the Mayo Clinic, MN. If you have had at least two episodes of vertigo during screening, and if you agree to participate in this study, you will come to the Clinical Research Center for an out-patient visit consisting of the following activities:

Visit 1:
Prior to study entry, you will be evaluated clinically, including medical history, examination, and laboratory testing. These steps will be part of routine clinical care, not study procedures. Investigators will then abstract baseline data from your medical records including demographics, medical history, list of allergies and current medications, family history, and results of neurological and ear examinations and testing. You will be asked to provide detailed descriptions of all symptoms experienced during vertigo attacks. If this information indicates that you meet the criteria for entering our study, you will be instructed on how to proceed, including use of the Vertigo Symptom Diary. You will also be asked to complete the symptom self-report measures.

Observation Phase:
You will complete up to 1 year of observation to document the frequency and severity of your vertigo attacks, associated symptoms, and other medical conditions. You will record data about all vertigo attacks that you experience during this period in your Vertigo Symptom Diary. Study personnel will review this information with you by telephone on a monthly basis and will inquire about any changes in your health and medications that you are taking. You will be permitted to treat your symptoms according to usual clinical care. You will record all treatments in your Vertigo Symptom Diary and then relate this information to study personnel during the monthly telephone calls. Extra visits to the study clinics will be arranged as needed to re-evaluate your health and treat problematic symptoms.

Visit 2:
When you have had two qualifying attacks or at the end of 1 year, if you have not had two attacks you will return to study sites for re-evaluation. You will complete self-report measures. If you continue to meet inclusion/exclusion criteria, you will be instructed in the use of study medication, how to report treatment response and how to report any problems with the medication. You will receive written information on how to take the medication and possible side effects of rizatriptan.

Treatment Phase:
If you qualify for the study, you will enter the Treatment Phase, during which you will treat three vertigo attacks with study medication. Some will receive active medication

and some will receive placebo, a capsule that looks like the investigational drug but contains no active ingredients. Two out of three will receive active medication and one out of three will receive placebo. Neither you nor the researchers will know who receives the active and inactive capsules until after the study is completed. You will be instructed to ingest one study capsule as soon as possible after onset of Grade 3/2 vertigo. You will record treatment response in your Vertigo Symptom Diary by rating the severity of vertigo and associated symptoms at the time you take study medication and at 0.5, 1, 1.5, 2, 4, 24, and 48 hours post-dose. You will complete questionnaires regarding possible side effects, treatment satisfaction and overall benefit of the medication. You will then contact study personnel by phone to review the attack and treatment response.

You will treat only one attack with study medication in a 48-hour period. You must have a vertigo-free period of at least 48 hours before treating a subsequent vertigo attack with study medication. You may use other medications to treat symptoms that persist for more than one hour after taking the study medication. These will be reported to study personnel together with other attack data. You will remain in the Treatment Phase until you have treated three separate vertigo attacks, experience any serious or intolerable adverse effects, withdraw for other reasons, or reach the end of the study. Study personnel will conduct telephone assessments on a monthly basis as they did during the Observation Phase. Extra visits to study clinics will be arranged as needed to re-evaluate your health and treat problematic symptoms.

Visit 3:
You will return to the study center as soon as possible after treating your third attack with study medication, preferably within two weeks of your last treated attack. You will complete rating scales listed in Table 1 and review your Vertigo Symptom Diary with study personnel. Arrangements will be made for follow-up clinical care, and you will be discharged from the study. A summary of visits and what will occur at each visit is listed on the following Schedule of Activities.

Table 1. Procedures conducted during the study.

Procedures	1st visit	1 year visit	Final visit
Informed consent	X		
History and exam	X		
Describe vertigo episodes	X	X	X
Instruct on completing paper diary	X		
Dizziness questionnaire	X		
Anxiety questionnaire	X	X	X
Depression questionnaire	X	X	X
Randomize for treatment		X	
Review paper diary		X	X
Quality of Life scale		X	X
Treatment satisfaction questionnaire			X
Review side effects			X
Common toxicity questionnaire			X

How long will I be in the research study?

You will participate in the observation period for up to 1 year or until you experience 2 qualifying attacks and then for as long as it takes to treat three vertigo attacks (no longer than 3 ½ years).

Are there any potential risks or discomforts that I can expect from this study?

Rizatriptan and similar drugs called triptans are well tolerated with minimal side effects, the most common being mild difficulty sleeping. Patients with ischemic or other heart disease, high blood pressure that is not controlled with medication, and basilar migraine (a rare variant in which headache is accompanied by paralysis or visual loss) are typically excluded from treatment with triptans because of concerns about worsening the underlying conditions. In a single report of three women with vestibular migraine treated with triptans, the vertigo attacks resolved but headaches developed. This has not been reported in any other patients with vestibular migraine who have been treated with triptans. Breeches in confidentiality are possible but as described below the investigators will do everything possible to prevent such breeches.

There are no anticipated risks or discomforts associated with the examination.

Are there any potential benefits if I participate?

Taking part in this study may or may not reduce or relieve your vertigo. The knowledge gained from this study may help in the future treatment of Vestibular Migraine and contribute to medical knowledge in general.

What other choices do I have if I choose not to participate?

You do not have to participate in this study. Choosing not to participate will not affect your current or future medical care.

Will I be paid for participating?

- The initial and 2 follow-up visits, history and physical examination, and medications during participation in this study will be provided at no cost to you.
- To compensate for your time, you will receive a payment of $50 for each of the three study visits.

Will information about me and my participation be kept confidential?

The researchers will do their best to make sure that your private information is kept confidential. Information about you will be handled as confidentially as possible, but participating in research may involve a loss of privacy and the potential for a breach in confidentiality. Study data will be physically and electronically secured. As with any use of electronic means to store data, there is a risk of breach of data security. The investigators may share data on NIH sponsored data bases but any data shared with other researchers, will not include your name or other personal identifying informat

What are my rights if I take part in this study?

- You can choose whether or not you want to be in this study, and you may withdraw your consent and discontinue participation at any time.
- Whatever decision you make, there will be no penalty to you, and no loss of benefits to which you were otherwise entitled.
- You may refuse to answer any questions that you do not want to answer and still remain in the study.

Who can I contact if I have questions about this study?

- **The research team:**
  If you have any questions, comments or concerns about the research, you can talk to the one of the researchers. Please contact: Roxana

- **Robert W. Baloh, MD**: (310) 825-5910, email: rwbaloh@ucla.edu
- **Joanna Jen, MD, PhD:** (310) 825-5910, e-mail: jjen@ucla.edu.
- **Roxana Gonzalez, Study Coordinator :** (310) 206-8511,
  e-mail: GRGonzalez@mednet.ucla.edu

- **UCLA Office of the Human Research Protection Program (OHRPP):**
  If you have questions about your rights while taking part in this study, or you have concerns or suggestions and you want to talk to someone other than the researchers about the study, please call the OHRPP at (310) 825-7122 or write to:

  UCLA Office of the Human Research Protection Program
  11000 Kinross Avenue, Suite 211, Box 951694
  Los Angeles, CA 90095-1694

You will be given a copy of this information to keep for your records.

SIGNATURE OF STUDY PARTICIPANT

_____
Name of Participant

_____ _____
Signature of Participant Date

SIGNATURE OF PERSON OBTAINING CONSENT

_____ _____
Name of Person Obtaining Consent Contact Number

_____ _____
Signature of Person Obtaining Consent Date