INDIANA UNIVERSITY INFORMED CONSENT STATEMENT FOR RESEARCH

A Randomized, Double Blind, Placebo-Controlled Single Center Phase 2 Pilot Study to Assess the Safety and Efficacy of Off-label Subcutaneous Administration of Erenumab-aooe in Patients with Temporomandibular Disorder

Investigator Initiated Trials (IITs) Program CAMG334AUS01T

ABOUT THIS RESEARCH

You are being asked to participate in a research study. Scientists do research to answer important questions which might help change or improve the way we do things in the future.

This consent form will give you information about the study to help you decide whether you want to participate. Please read this form, and ask any questions you have, before agreeing to be in the study.

TAKING PART IN THIS STUDY IS VOLUNTARY

You may choose not to take part in the study or may choose to leave the study at any time. Deciding not to participate, or deciding to leave the study later, will not result in any penalty or loss of benefits to which you are entitled, and will not affect your relationship with Indiana University.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to determine how safe and effective the brand-name prescription medication Aimovig® (Erenumab-aooe) is in reducing Temporomandibular Disorder (TMD) pain when compared to a placebo (Erenumab-aooe -P). A placebo is a pill that contains no active medicine and is often referred to as "dummy treatment". Aimovig® is currently approved by the Food and Drug Administration (FDA) for the prevention of migraine headaches. In this study, Aimovig® will be used for the treatment of TMD, and will be referred to as the investigational product because it is not approved by the FDA for this use.

You were selected as a possible participant because you indicated you have been diagnosed as having Temporomandibular Disorder (TMD).

This study is being conducted by Dr. Domenick Zero of the Oral Health Research Institute at the Indiana University School of Dentistry. The study is sponsored by the Trustees of Indiana University. It is funded by Amgen through the Investigator Sponsored Studies (ISS) Program.

HOW MANY PEOPLE WILL TAKE PART?

If you agree to participate, you will be one of 30 participants taking part in this research.

WHAT WILL HAPPEN DURING THE STUDY?

If you agree to be in the study, you will need to attend 8 visits over a 24-week period (6 months). Listed below is summary of what will occur at each visit.

Visit 1 – Screening (about 60 minutes)

You will be asked to read this consent and an Authorization for Release of Health Information for Research form. The information in these forms will be explained to you, and you will have the chance to ask questions. If you decide to participate, you will sign and date this form and the research assistant will also sign and date the form and give you a copy for your records.

A study dentist qualified to diagnose TMD will ask you questions about your medical history, medications and TMD history, and conduct a TMD examination to determine if you are eligible to participate. The TMD examination will involve assessing tenderness of your facial muscles and how well your jaw functions. There is a chance you may not qualify to participate in the study. If you are eligible to participate and have a smartphone, you will be asked to download an app called the "MyCap" app and will be trained on completing the PEG (Pain, Enjoyment, General Activity) Scale and the Pain Medication Assessment questionnaire using your smartphone. If you do not have a smartphone, or do not want to download an app on your smartphone, you will complete the assessments onsite using an app at your next visit (Baseline) and all future visits. At the completion of the visit you will be scheduled to return to the study site for your Baseline visit.

Visit 2 – Baseline (about 60 minutes)

You will be asked questions to determine if you qualify to continue in the study and we will update any changes in your medical history or medications since your last visit. The TMD examination will also be repeated. You will also be asked to complete the Brief Pain Inventory (BPI) and PEG (Pain, Enjoyment, General Activity) Scale assessments using the app on your smartphone or the app provided on a study device (tablet or laptop) onsite. You will also be asked to complete a Pain Medication Assessment, Jaw Function Limitation Scale (JFLS), Patient Health Questionnaire (PHQ-4) and Somatic Symptom Scale (SSS-8) assessments onsite.

You will be assigned by chance (like tossing a coin) to receive one of two products. One product is considered investigational (Erenumab-aooe) and the other product is a placebo (Erenumab-aooe -P). The assigned product will be given as two subcutaneous (under the skin) injections in the upper arm, thigh, or abdomen. The injections will be administered by the study dentist, but you will be given the option to choose the injection site location(s). Following the injections, you will be asked to report any side effects or symptoms you may be experiencing. You will receive two injections every 4 weeks for a total of 10 injections.

If you have a smartphone, you will be asked to complete the Brief Pain Inventory (BPI) and PEG (Pain, Enjoyment, General Activity) Scale assessments daily using the app on your smartphone until you return for your next visit in 4 weeks. The instructions for using the app at home will be reviewed with you and a practice text will be sent to make sure communication is working. During the study you will also receive text push-notifications daily reminding you to complete the BPI and PEG using the app.

If you do not have a smartphone, you will complete the Brief Pain Inventory (BPI) and PEG (Pain, Enjoyment, General Activity) Scale assessments at your next visit in 4 weeks using the app onsite. If you have a smartphone, and do not want to download the app on your smartphone, you can complete the assessments using the app onsite.

At the completion of the visit you will be scheduled to return to the study site for your next visit.

Visits 3-6 – Weeks 4, 8, 12 and 16 (about 60 minutes)

You will be asked questions to determine if you qualify to continue in the study and we will update any changes in your medical history or medications since your last visit. You will also be asked to complete the Brief Pain Inventory (BPI) and PEG (Pain, Enjoyment, General Activity) Scale assessments using the app on your smartphone or the app provided on a study device (tablet or laptop) onsite. You will also be asked to complete a Pain Medication Assessment, Jaw Function Limitation Scale (JFLS), Patient Health Questionnaire (PHQ-4), Somatic Symptom Scale (SSS-8) and Patient Global Impression of Change (PGIC) assessments onsite.

You will receive your assigned product (either the investigational Erenumab-aooe or placebo) via two injections in the upper arm, thigh, or abdomen. Following the injections, you will be asked to report any side effects or symptoms you may be experiencing.

If you have a smartphone, you will be asked to complete the Brief Pain Inventory (BPI) and PEG (Pain, Enjoyment, General Activity) Scale assessments daily using the app on your smartphone until you return for your next visit in 4 weeks. During this time, you will receive text push-notifications daily reminding you to complete the BPI and PEG using the app.

If you do not have a smartphone, you will complete the Brief Pain Inventory (BPI) and PEG (Pain, Enjoyment, General Activity) Scale assessments at your next visit in 4 weeks using the app provided on a study device (table or laptop) onsite.

At the completion of the visit you will be scheduled to return to the study site for your next visit.

Visits 7-8 – Weeks 20 and 24 (about 60 minutes)

The procedures described under visits 3-6 will be repeated every 4 weeks for 2 additional visits, except you will not receive any product.

Following the completion of Visit 8, your participation in this study will end.

However, you may be asked to attend an unscheduled follow up visit if you feel you had a problem or reaction after receiving the study product.

We do not plan to share the results of any of the research activities with you.

WHAT ARE THE RISKS OF TAKING PART IN THE STUDY?

Erenumab may cause all, some, or none of the side effects listed below. These side effects can be mild but could also be serious, life-threatening, or even result in death. You may have an allergic reaction to erenumab. In general, symptoms of an allergic reaction may include headache, rash, itching, flushing, swelling, shortness of breath, nausea and sometimes vomiting. Severe allergic reactions can cause dizziness, severe skin reactions, difficulty breathing or swallowing, a decrease in blood pressure, and could be life threatening.

As of 16 Nov 2022 approximately 7114 participants have received erenumab in Amgen sponsored clinical studies and approximately 2522 participants have received Novartis sponsored clinical studies. Since it was first approved for sale on 17 May 2018, approximately 880,000 people have been prescribed erenumab (Aimovig®) for treatment as of 16 Nov 2022.

Side effects that other people have had that are thought to have been caused by erenumab are:

Common side effects (which may affect between 1 and 10 people in every 100):

- Injection site reactions: which may include tenderness, pain, redness, itching, bruising, swelling, firmness or hypersensitivity
- Constipation
- Muscle spasms/cramps
- Itching (pruritus)

Since erenumab was approved on 17 May 2018, the following events have been reported in patients exposed to erenumab in the postmarketing setting:

- Severe allergic reactions such as rash, swelling, and difficulty breathing, or swallowing
- Serious constipation has been reported in patients prescribed erenumab. In some cases, hospitalization or surgery was required
- Mouth/lip sores (e.g., stomatitis, mouth ulcerations, and oral mucosal blistering)
- Skin and subcutaneous tissue disorders
  - Alopecia (loss of hair)
  - Rash (e.g., papular rash [small raised red rash], exfoliative rash [redness and/or peeling of skin], erythematous rash [red rash], urticaria [hives], and blisters).

Tell the study doctor or the study staff about any drugs you are taking, have recently taken or are planning to take, including herbal remedies, supplements and drugs you take without a prescription.

The side effects of using erenumab in combination with other drugs are unknown at this time. Please discuss any concerns you may have with the study doctor.

If you agree to take part in this study, you will be required to receive two injections using prefilled syringe with either erenumab or placebo into the tissue below your skin.

After receiving injections, you may experience all, some or none of the following:

- Pain or discomfort at the injection site during or after the injection
- Bleeding, bruising, redness, warmth, itching, swelling, or firmness of the skin near the injection site
- Infection at the injection site

When using the Prefilled Syringe you may experience the following:

- An allergic reaction to the dry natural rubber in a specific part of the syringe. The syringe plunger contains dry natural rubber, which is derived from latex. Tell your study doctor or the study staff if you are allergic to latex.

There could be some soreness from the TMD examination checking your facial muscles for tenderness and how much you can open your mouth. Cross contamination (germ spreading) is also a risk but will be reduced using experienced personnel applying strict infection control procedures (germ fighting) as outlined by the Infection Control Committee of the IU School of Dentistry.

A risk of completing the surveys/assessments is being uncomfortable answering the questions. While completing the survey, you can tell the researcher that you feel uncomfortable or that you do not want to answer a particular question.

Accidental loss of confidentiality of records is possible. To reduce this risk, all study records and data will be stored in locked cabinets and encrypted, password protected computer files that only study personnel can access. Except for the forms you sign (like this consent), a study number will be the only thing that identifies your records.

It is not known if erenumab is harmful to an unborn or breastfed baby. If you become pregnant during this study, potential risks could include the loss of the pregnancy (a miscarriage) or birth defects. Pregnant women, breastfeeding women and women planning to become pregnant should not participate in this study.

It is not known if erenumab is transferred into breast milk. If you are breastfeeding and wish to be in this study, you will be required to stop nursing during treatment and for an additional period of 16 weeks after stopping the study drug.

Please notify the study doctor if you become pregnant, or breastfeed, or father a child while you are taking erenumab because further information may be asked of you (the study doctor will discuss the details with you). Please refer to Section 3j regarding the Contraception Language.

Also, if you become pregnant while taking erenumab you or your family members should tell the study team immediately if you have any unusual health problems, injuries, or side effects, even if you do not think these problems are caused by the study or erenumab or the pre-filled syringe.

There also may be other side effects that we cannot predict.

BIRTH CONTROL INFORMATION

Female Participants

Pregnant or breastfeeding women, and women planning to become pregnant, should not participate in this study**.**

If you are unable to become pregnant for one of the following reasons, the use of birth control methods is not required during this study:

- Your healthcare provider has confirmed that you are postmenopausal
- You have had your uterus, or both ovaries, or both fallopian tubes removed

If you could become pregnant, you:

- Must agree to use a highly effective method of birth control during treatment and for an additional 16 weeks after the last dose of study drug.
- Must discuss your pregnancy prevention method with the study doctor to ensure it is acceptable. You should be aware that true sexual abstinence is the only 100% effective method of birth control.

Highly effective methods of birth control for female participants include:

- Hormonal methods (progestogen-only or combined estrogen and progestogen) to stop the release of the egg from the ovary: [pills, shots/injections, implants (placed under the skin by a healthcare provider), vaginal rings, or skin patches]
- Intrauterine device (IUD)
- Intrauterine hormonal-releasing system (IUS)
- Surgery to tie both fallopian tubes (bilateral tubal ligation/occlusion)
- Your male partner has had a vasectomy (male sterilization) and testing shows there is no sperm in the semen
- Sexual abstinence (not having sex)

Male Participants

Male participants are not required to use birth control during treatment with erenumab.

However, you should let your female partner know you are in this study.

WHAT ARE THE POTENTIAL BENEFITS OF TAKING PART IN THE STUDY?

We don't expect you to receive any benefit from taking part in this study, but we hope to learn things which will help scientists in the future. If you are assigned to receive the investigational product (Erenumab-aooe) there is a chance you may experience an improvement with your pain level associated with Temporomandibular Disorder (TMD). If you receive the placebo there is no expected benefit because it does not contain the active drug. No other benefits should be expected from being in this study.

WHAT ARE THE OTHER TREATMENT OPTIONS?

There may be other options for treatment of your Temporomandibular Disorder (TMD). You may speak with the study dentist about other treatment options.

HOW WILL MY INFORMATION BE PROTECTED?

Efforts will be made to keep your personal information confidential. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. No information which could identify you will be shared in publications about this study and databases in which results may be stored.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the study investigator and his/her research associates, the Indiana University Institutional Review Board or its designees, Amgen and its designee, and any state or federal agencies who may need to access your medical and/or research records (as allowed by law), including the U.S. Food and Drug Administration (FDA).

A description of this clinical trial will be available on **ClinicalTrials.gov**, as required by U.S. 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.

WILL MY INFORMATION BE USED FOR RESEARCH IN THE FUTURE?

Information collected from you for this study may be used for future research studies or shared with other researchers for future research. If this happens, information which could identify you will be removed before any information is shared. Since identifying information will be removed, we will not ask for your additional consent.

WILL I BE PAID FOR PARTICIPATION?

You will receive $25 cash for attending visit 1, regardless of whether you qualify to participate. If you qualify to participate in the study, you will receive $50 via a check for completing each of the 7 remaining visits for a total study payment of $375.

If you are asked to attend an extra visit, (for example, you feel you had a problem or reaction after receiving the study product), you will receive $25 cash for attending the extra visit.

You will only receive payment for visits completed and will receive that payment at the end of each visit. No other partial payments will be given.

WILL IT COST ME ANYTHING TO PARTICIPATE?

There is no cost to you for taking part in this study. The study will cover the cost of all procedures and the investigational product.

WHO WILL PAY FOR MY TREATMENT IF I AM INJURED?

In the event of physical injury resulting from your participation in this study, necessary medical treatment will be provided to you and billed as part of your medical expenses. Costs not covered by your health care insurer will be your responsibility. Also, it is your responsibility to determine the extent of your health care coverage. There is no program in place for other monetary compensation for such injuries. However, you are not giving up any legal rights or benefits to which you are otherwise entitled.

WHO SHOULD I CALL WITH QUESTIONS OR PROBLEMS?

For questions about the study or a research-related injury, contact the researcher, Dr. Domenick Zero or his staff, at (317) 274-8822.

In the event of an emergency, you may contact Dr. Zero or his staff by calling the after-hours emergency answering service at (317) 278-9095. A staff member will put you in touch with one of our researchers.

For questions about your rights as a research participant, to discuss problems, complaints, or concerns about a research study, or to obtain information or to offer input, please contact the IU Human Subjects Office at 800-696-2949 or at irb@iu.edu.

CAN I WITHDRAW FROM THE STUDY?

If you decide to participate in this study, you can change your mind and decide to leave the study at any time in the future. The study team will help you withdraw from the study safely. If you decide to withdraw, please call the study team or submit a written notification to Dr. Domenick Zero at 415

Lansing Street, Indianapolis, IN 46202. Your participation may be terminated by the investigator without regard to your consent in the following circumstances:

- if you do not follow the instructions of the study dentist or the study procedures
- if it is discovered that you do not meet the study requirements
- if the study is cancelled
- if it appears to be medically harmful to you

If you leave or are taken out of the study for any reason, you may be asked to return to the research site for a final visit. This is to make sure that you are in good health.

You will be told about new information that may affect your health, welfare, or willingness to stay in the study.

PARTICIPANT'S CONSENT

In consideration of all of the above, I give my consent to participate in this research study. I will be given a copy of this informed consent document to keep for my records. I agree to take part in this study.

Participant's Printed Name

Participant's Signature **Date and Time**

Printed Name of Person Obtaining Consent

Signature of Person Obtaining Consent **Date and Time**