

Informed Consent Authorization to Participate in a Clinical Investigation (April 5, 2007)

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**INFORMED CONSENT AUTHORIZATION TO PARTICIPATE
IN A CLINICAL INVESTIGATION**

Title: (Protocol: TAR-ORI-VT001) A Phase 1 Injection Site Vein Toleration Study in Healthy Subjects Administered Intermittent Intravenous Doses of Oritavancin

Principal Investigator: David Carter, M.D.

Site of Investigation: 313 East Anderson Lane, Suites 200 & 300
Austin, Texas 78752

24 hour Telephone #: 512-491-0700

Sponsor: Targanta Therapeutics Corporation

Participant's Name: _____

You are invited to participate in a drug research study. However, before you give your consent to be a volunteer, we want you to read the following and ask as many questions as necessary to be sure that you understand what your participation will involve.

This form provides you with information on the risks and benefits of the study and seeks your authorization for the use and disclosure of your health information that will be obtained from you if you take part in this study. The study doctor or his or her designee will answer any questions you may have about this consent form and about the study. Please read this consent form carefully and do not hesitate to ask any questions you may have about the information provided below or about any words that you may not understand. If you are considering participating in this study and meet all eligibility requirements, it is important that every effort be made to remain in the study for its full duration. However, your participation in this study is voluntary, and you reserve the right to end your participation at any time.

NATURE AND PURPOSE OF THE STUDY

Oritavancin is an investigational drug for the treatment of bacterial infections. An "investigational" drug is one that has not been approved by the United States FDA (Food and Drug Administration) for use in the United States, but may be tested in research studies such as this one. Oritavancin is administered by intravenous (IV) infusion.

The purpose of this research study is to evaluate the injection site toleration of oritavancin after two single doses of oritavancin (200 mg and 800 mg or 800 mg and 200 mg) are given 14 days apart to healthy male subjects.

Information about any side effects that may occur will also be collected. This study is for research purposes only and is not intended to treat any medical condition. The study doctor is being paid by the sponsor to conduct this research study.

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SUBJECT SELECTION

- You have been offered an opportunity to participate in this research study because you are a healthy male 18 years of age and older,
- Must not be a user of tobacco-containing products,
- Met screening criteria for inclusion and exclusion in the study and all study-related test results are satisfactory.

It is important that you answer all of the screening questions completely. You must disclose all past and present diseases, allergies, and all medications that you are taking, including prescription and non-prescription drugs including herbal remedies.

Approximately 15 subjects will be enrolled in this single site research study.

STUDY DURATION

The duration of your participation in this study will be 23 days. This does not include the screening visit. The screening visit will be required within 10 days before the start of the study to determine if you qualify and are willing to participate in this research study. The study requires that you complete (two) 2 day/ 1 night clinic confinements each followed by an outpatient visit and 1 telephone follow-up visit 7 days after clinic discharge on Day 16. In the event of an adverse event requiring follow-up, you may be required to complete an additional outpatient visit.

Study Design

You will receive both treatments in a random (by chance) order. The treatments will be administered 14 days apart (i.e., you will receive one treatment on Day 1 and the other treatment on Day 15). Each treatment consists of two infusions of 60 minutes each. The treatments are as follows:

200 mg Oritavancin administered as a first infusion of 500 ml of 5% Dextrose (no active study medication) and a second infusion of 200 mg oritavancin in 500 ml of 5% Dextrose.

800 mg Oritavancin administered as a first infusion of 400 mg oritavancin in 500 ml of 5% Dextrose and a second infusion of 400 mg oritavancin in 500 ml of 5% Dextrose.

In the event that there is an unacceptable incidence of injection site vein swelling, the volume of all infusion solutions will be increased to 1000 ml.

At any time during the study drug administration you experience pain, swelling, or redness you must inform the study doctor immediately.

Neither you nor the study staff will know which treatment you are receiving. However, this information can be obtained if it becomes medically necessary. At the end of the study, you will have received 2 separate doses of the study medication, one on Day 1 and the other on Day 15. You will not have a choice as to which of the treatments you receive on Day 1 or Day 15.

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Screening

You will come to the clinic for a screening visit to determine if you are eligible and willing to participate in this study. You will be asked to sign this Informed Consent Form. During this screening visit, a medical history will be recorded including your use of medications, tobacco, alcohol and caffeine and personal information such as age, sex, and ethnicity. A physical examination including measurement of your height and weight, vital signs (temperature, pulse, blood pressure, respiration), ECG (electrocardiogram - heart rhythm tracing) and review of inclusion and exclusion criteria will be performed. Blood and urine samples will be taken for clinical laboratory testing including a screening for HIV, hepatitis and drugs of abuse will be completed. An alcohol breathalyzer test will be performed.

State law requires that positive test results for hepatitis or HIV be reported to a local health agency. This is the legal obligation of medical personnel in this state. A separate consent form for the HIV testing is required.

You will be permitted to participate in the study at the discretion of the study doctor if the results of the study screening laboratory tests and other assessments are satisfactory. You will be advised of the study restrictions and when to report to the clinic to begin the study. You will be considered an alternate for this study until such time that you have received study medication.

STUDY PROCEDURES

Periodically during the study your vital signs (blood pressure, pulse rate, temperature and respiratory rate) will be measured, you will be asked how you are feeling, and if you have taken any medications.

CLINIC CONFINEMENTS

You will come to the clinic on the evening of Day 0 and Day 14 to begin your clinic confinement.

Days 0 and 14:

On Day 0, you will be assigned to a study group. On Days 0 and 14, prior to the infusions, the following procedures will be performed:

- Review and update your medical and medication history.
- Review of the inclusion/exclusion criteria for the study.
- You will have a physical exam including an examination of the injection site.
- Your vital signs will be measured.
- Blood and urine samples for clinical laboratory tests.
- Drug screen for drugs of abuse and alcohol breathalyzer test.
- You will be asked to report any adverse events on Day 14 that you have experienced since the first infusion on Day 1.
- You will remain in the clinic overnight.

Days 1 and 15 (Dosing Procedures)

- An IV catheter (small tube) will be inserted into a vein in your arm with an infusion of 5% Dextrose until the study drug infusion is started. If possible, your opposite arm will be used for the next dosing day.

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- You will receive the study medication as two consecutive 60 minute infusions. The IV catheter will be flushed and removed after the second infusion.
- Your vital signs will be measured after the last infusion on each dosing day.
- You will be asked how you are feeling during and after the infusion of study medication.
- You will be permitted to leave the study clinic at the discretion of the study doctor with instructions to return the next day (Day 2 or Day 16).

OUTPATIENT VISITS

Day 2 and Day 16:

The following procedures will be performed:

- Your vital signs will be measured.
- You will have a physical exam, including an examination of the injection site.
- You will be asked how you are feeling.
- You will be permitted to leave the clinic at the discretion of the study doctor.
- You will be instructed to call the study clinic should you experience any adverse event.

Follow up Telephone Visit Day 23

You will receive a phone call from a study staff member. At this time:

- Your medical history will be reviewed.
- You will be asked how you are feeling and if you have taken any medication.

Should you experience an adverse event, you may be asked to return to the study clinic and have these additional procedures performed:

- Physical examination,
- Measurement of your height, weight and vital signs,
- Blood and urine samples for clinical laboratory tests.

Following completion of the above procedures and review of the medical and safety evaluations, you will be discharged from the study. The study doctor may require that you have a longer stay at the clinic or additional laboratory testing based on assessments and results of lab testing.

Early Withdrawal

If you do not complete this study for any reason, you will be asked to undergo the same procedures as described in the Follow up Visit.

Blood Sampling

Blood samples will be taken approximately 3 times throughout the course of the study. Approximately 60 mL of blood (approximately ¼ cup) will be drawn throughout the study. Additional blood samples may be required if any of your lab values are abnormal. It is possible that more than one attempt to obtain a blood sample may be necessary.

For comparison, a standard blood donation at a blood collection center, once in any 56-day period, is about 2 cups of blood.

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Meals

Standard meals will be provided throughout the clinic confinements except where fasting is required.

Restrictions/Requirements

- You must not consume any alcohol-containing beverages from 72 hours prior to baseline procedures on Days 0 and 14.
- You must be a non-user of tobacco products in order to participate in this study.

PHYSICIAN AVAILABILITY

A physician will be present at the time of drug administration and on-call at all other times. In the event of any type of medical emergency, the study physician will be on call and available, throughout the study.

RISKS, INCONVENIENCES AND DISCOMFORT

All drugs have side effects, and there are risks associated with participation in any drug study. Because this drug is still being developed, there may be other risks or side effects that are not known at this time. You will be told of any important new information regarding this drug during the course of the study, and you may choose to discontinue your participation at any time.

Risks from Oritavancin

As of March, 2007, 1566 subjects have taken oritavancin. Out of these 1566 subjects, 231 were healthy adults. Adverse events (side effects) observed in completed and ongoing studies for which information is available are as follows:

The most common side effects related to oritavancin include rash, diarrhea and pain and irritation at the site of the study drug infusion (phlebitis). Phlebitis (inflammation of the vein that could result in permanent damage to the vein) has been observed in previous studies in which oritavancin was given to healthy adult volunteers two or more days in a row. In some of the volunteers, the phlebitis was considered painful and it did not go away for several weeks. In other volunteers, the phlebitis took longer to go away.

Side effects may occur when the drug is being given to you (infusion reactions) including rash/redness, flushing, nausea, vomiting, diarrhea, shortness of breath and low blood pressure.

Other side effects associated with oritavancin include a decrease in the number of red blood cells (anemia), fast breathing rate, temporary (reversible) changes in liver enzyme tests without symptoms, abnormal kidney function, abdominal pain, water retention (edema), shaking chills (rigors), chest tightness, fever, itching, difficulty sleeping and mouth infection (thrush).

Oritavancin may interfere with some blood clotting tests, but no bleeding problems have been noted. Based on in vitro data (data obtained from studies done in a test tube), oritavancin may interact with ion channels in the heart that could affect the normal beating

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of the heart. Electrocardiograms (which measure the electrical activity of the heart) have been done on human subjects as well as animals that have been exposed to oritavancin. At this time, there is no evidence that oritavancin causes abnormalities of the heart rhythm.

Because oritavancin is similar to the antibiotics vancomycin or teicoplanin (Targocid®), people who are known to be allergic to either of these two antibiotics should not receive oritavancin.

Rare or unknown side effects could possibly occur, including life-threatening reactions. You will be watched for the development of any side effects throughout the study and the study staff will provide you with appropriate treatment, where possible, to resolve the side effect.

Risks from Intravenous (IV) Placebo

A placebo is a substance that resembles the drug being studied but contains no active medicine. Placebos are used primarily in research studies to compare the effects of the medications being studied. In this study, the placebo is sugar water (5% dextrose in sterile water), which is commonly infused into people requiring IV infusions or fluids. Complications from receiving a placebo infusion include more frequent urination or swelling of the extremities (edema). This effect is temporary and usually resolves once the infusion is discontinued. These effects are uncommon in healthy people.

Risks from Intravenous (IV) Lines

Qualified medical professionals will place IV lines in your arm. Intravenous lines are usually safe and well tolerated and complications are rare, but can include phlebitis and infection. If the line is not positioned properly, it may not be possible to draw blood or give medications through the line. If this is the case, the positioning can be changed. The line may come out accidentally or blood may leak from around the line. Rarely, a clot can develop in the line itself. If this happens, the staff may remove the old IV line and start a new IV line.

Other Possible Side Effects and Risks

The time you spend in the research unit may make you bored or uncomfortable.

You will be undergoing tests and procedures as part of this study, some of which may be associated with potential side effects or risks. For example, blood being taken from a vein for tests may cause some discomfort and may occasionally cause some bleeding or bruising, infection, fainting, pain at the needle site, dizziness or the development of a collection of blood under the skin (hematoma). The study staff will offer you treatment for any side effects.

If you have any injury, side effect, or any other unusual health experience during this study, make sure that you tell the nurses, study coordinator or your physician immediately.

There may be unknown risks of possible harmful interaction with other medications. Therefore, it is very important that you tell the study staff if you take any medications (including over-the-counter medications, herbal treatments, dietary and herbal supplements, and vitamins) other than the study drug during course of the study.

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UNKNOWN/UNFORESEEABLE RISKS

In addition to the risks listed above, there may be some unknown or infrequent and unforeseeable risks associated with the use of this medication, including allergic reaction or interaction with another medication. You will be informed in a timely manner, both verbally and in writing of any new information, findings or changes to the way the research will be performed that might influence your willingness to continue your participation in this study.

Pregnancy and Contraception

The risks of the study medication are unknown and may be hazardous to the unborn. The risks of fathering a child while taking the study medications are unknown.

BENEFITS

It is understood that participation in this study is purely for research purposes, and that no therapeutic benefit may be derived.

PAYMENT

The total payment for the completion of the study is \$1,650.00. You will not be paid for the screening visit. If you choose to withdraw from the study prior to completion, you will be paid for the portion of the study that you have completed based on the following schedule:

Schedule of Study Compensation

Screening Visit	No Compensation
Check-in Visits Day 0, Day 14 (2 x \$250.00)	\$500.00
Dose Visits Day 1, Day 15 (2 x \$250.00)	\$500.00
Outpatient Visits Days 2 and 16 (2 x \$250.00)	\$500.00
Follow-up Phone Visit (\$150.00)	\$150.00

In agreeing to participate in this study, you will be acting as an independent contractor, not as an employee of Covance Clinical Research Unit. Because payments made to you for participating in this study will be reported to the IRS as income as required by law, you are required to provide your social security number. No deductions for any state or federal withholding or any other similar taxes will be made. It is the responsibility of the participant to report this compensation on state and federal tax returns and for the payment of any taxes that are due on this compensation.

All subjects will be paid within fourteen days of the completion of their participation in the study. If you are selected as an alternate you will be paid \$150.00 after coming to the clinic prior to dosing, if you are not selected to participate in the study.

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COST

There will be no cost to you for your participation in this study.

TREATMENT ALTERNATIVE

Since this study is not intended to provide any therapeutic or other health-related benefit, your alternative is to not participate in this study.

RIGHT TO WITHDRAW OR REMOVAL FROM STUDY

Your participation in the study is voluntary. You understand that you are free to withdraw from this study at any time, and you agree to inform the physician immediately if you intend to withdraw. It is understood that your decision not to participate in this study or to withdraw from this study will not influence the availability of your future medical care and will involve no penalty or loss of benefits to which you are otherwise entitled. You may withdraw from this study at any time.

You agree that the physician in charge of the study or the Sponsor can remove you from this study without your consent for any reason, including, but not limited to:

- a. His/her judgment that any condition or circumstance may jeopardize your welfare or the integrity of the study.
- b. Your failure to follow the instructions of the investigator(s).
- c. If the study is stopped by the sponsor and/or doctors participating in the study prior to completion.

If you are asked to leave the study, you will not lose any benefits to which you are otherwise entitled. If you are asked to leave the study, the doctor may examine you and do some final tests.

OFFER TO ANSWER ANY QUESTIONS ABOUT THIS STUDY


If you have any questions or problems during this study, or if you think that you may have experienced a research-related injury, you should contact Dr. Carter at Covance Clinical Research Unit, at 512-349-0459.

If you have any questions regarding your rights as a research volunteer, please contact Kim Lerner, Chairman of the Independent Investigational Review Board, Inc. at toll free (877) 888-irb (4472) during regular working hours. The Independent Investigational Review Board is a committee established for the purpose of protecting the rights of volunteers in a research study.

USE AND DISCLOSURE OF MEDICAL INFORMATION

As part of this study, David Carter, MD, the Study Doctor, and his team at the research facility will keep records of your participation in the study. These study records will include personal information that you provide including your age, sex, etc., the results of procedures and tests you undergo during the study or had before the study, information about your response to treatments you receive while participating in the study, and other medical information relating to your participation in the study. Under federal law your study

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records cannot be used or disclosed by the research clinic for research purposes unless you sign this authorization. You may not participate in the study unless you sign this authorization. If you sign this informed consent form, you will be agreeing to the disclosures described below:

- a. Some or all of the test results and other information will be reported to Targanta Therapeutics Corporation, the sponsor of this study. The Sponsor and its consultants will analyze and evaluate these results and information and may report them to the U.S. Food and Drug Administration (the FDA) or other regulatory agencies in the United States and/or foreign countries. Your study records will be assigned a code number by the study team and you will ordinarily not be identified by name in the study records that are sent to the Sponsor and its consultants. However, The Sponsor and its consultants will have the right to see your complete study records, including your name, and might choose to do so.
- b. In addition, personnel from the Sponsor and its consultants will be visiting the research facility to monitor the conduct of the study, and they will be reviewing your study records and your medical records for this purpose.
- c. Your study records and medical records may also be reviewed by the Independent Investigational Review Board, Inc., which is an ethics committee that reviews the conduct of human research studies.
- d. Covance Clinical Research-Austin, an agent for the Study Doctor will also have access to your medical records for this purpose.

The research facility and the Independent Investigational Review Board, Inc., will review and use your study records only for purposes of this study. They will keep your identity confidential and, except for the disclosures described above, will not disclose your study records to other parties unless disclosure is required by law. Once the research facility discloses information in your study records or medical records to the Sponsor or its consultants, the information will no longer be protected by federal law. Because of the need to release information to these parties, absolute confidentiality can not be guaranteed. However, the Sponsor and its consultants will only use your information for purposes of the study and will not disclose your study records to parties other than the FDA and similar government agencies, unless disclosure is required by law. If reports or articles are written about the study, you will not be identified by name in them. Your study records may be retained at the research facility indefinitely following the completion of the study. You will not have the right to review your records while the research is in progress. However, you will be able to review your records after the research has been completed and request to make any correction to your personal health information if necessary.

This authorization has no expiration date. However, you have the right to revoke this authorization at any time. You can do this by giving written notice to the study doctor, informing them that you are revoking your authorization to use and disclose medical information. The study doctor's contact information is listed on page 1.

If you revoke this authorization to use and disclose your medical information, you will not be permitted to continue your participation in the study after the revocation. If you drop out of the study, you do not have to revoke your authorization to use and disclose your

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medical information. However, if you drop out of the study and do decide to revoke your authorization to use and disclose your medical information, the information that has already been collected in your study record may continue to be used and disclosed as described above, however, no new information will be obtained or added.

IN CASE OF INJURY

If during the course of this study any injury occurs to you as a direct result of the administration of the study medication or properly performed procedures, the study sponsor agrees to pay all medical expenses necessary to treat such injury (1) to the extent you are not otherwise reimbursed by medical insurance, and (2) provided you have followed the directions of the investigators.

Financial compensation for such things as lost wages, disability or discomfort due to injury is not available.

You **DO NOT** waive your legal rights by signing this form.

CLOSING STATEMENT

You have read and understood the information which has been stated above and have received satisfactory answers to all of the questions which you have asked and you willingly sign this consent form. You will receive a copy of the signed informed consent. You hereby consent to be a participant in this study.

SIGNATURES



I have read in a language that I understand well, the above information. The content and meaning of this information has been explained to me. I hereby voluntarily consent and offer to take part in this study and authorize the use and disclosure of my medical information.

_____ Date/Time	_____ Print Subject Name	_____ Subject Signature
_____ Date/Time	_____ Name of Person conducting the Informed Consent discussion	_____ Signature of Person conducting the Informed Consent discussion
_____ Date	_____ Print Investigator Name	_____ Investigator Signature

Copy of consent form given to subject on (date) _____ by (initials) _____

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