

**Safety and Efficacy of Dalbavancin vs. Vancomycin
in Catheter-related Bloodstream Infections**

Informed Consent Form For:

Phase II, Randomized, Open-Label, Multi-Center Study to Evaluate the
Safety and Efficacy of Dalbavancin Versus Vancomycin in the Treatment of
Catheter-Related Bloodstream Infections with Suspected or Confirmed
Gram-Positive Bacterial Pathogens

Protocol: VER001-4

Sponsor: Versicor, Inc.
34790 Ardentech Court
Fremont, CA 94555

Investigator: Name
Affiliation
Street Address
City, State
Telephone Number (24 hours)
Beeper number

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Invitation to Participate: You are being asked to participate in a clinical research study being conducted by Dr. _____ and his/her designated study staff to test the safety and effectiveness of the experimental antibiotic dalbavancin on catheter-related bloodstream infections. This research is funded by Versicor, Inc. (the sponsor company). In order for you to decide whether or not you agree to be part of this research study, you should understand enough about its risks and benefits to make an informed judgment. This process is known as informed consent.

This informed consent form gives you detailed information about the research study, which the investigator or a member of his/her study staff will discuss with you. This discussion should go over all parts of this research study: its purposes, the procedures that will be performed, any risks of the procedures, possible benefits, and possible alternative treatments. Once you understand the study and all your questions have been answered, if you still wish to participate, you, along with the investigator or a member of his/her study staff and a witness, will be asked to sign this informed consent and you will receive a copy of it to keep as a record.

You understand that although the study will be under the direct supervision of this investigator, other professionals (doctors, nurses, etc.) who work with the investigator may be designated to assist or act for him/her.

Purpose: The number of bacterial infections that are resistant to currently available antibiotics is increasing. These types of infections can be especially dangerous to individuals who have weakened immune systems and/or who are hospitalized. Versicor, Inc. is developing a new antibiotic, known as dalbavancin, which may be effective against a variety of bacterial infections that are difficult to treat. The purpose of this study is to evaluate the potential effectiveness, safety, and tolerance of dalbavancin with that of vancomycin, which is approved by the US Food and Drug Administration (FDA) for use in the treatment of adults with catheter-related bloodstream infections.

Duration: Your participation in this study will last for a maximum of 52 days.

Selection of Subjects: This research study will be conducted at 30 to 40 sites within North America and Europe and will involve approximately one hundred and eighty (180) subjects, who are at least 18 years old. Approximately eight (8) subjects will participate from _____ (institution name).

You are eligible to participate in this research study because you have been diagnosed with a catheter-related bloodstream infection.

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The investigator and/or study staff will evaluate your medical condition and history to determine whether you are eligible to participate in this study. In addition, you may **NOT** participate in this study if any of the following apply to you:

1. Participation in any investigational drug or device study within the previous 30 days;
2. Known allergy to any glycopeptide antibiotic (for example, vancomycin);
3. Current substance abuse (including drugs of any kind and alcohol);
4. If you are a female: Pregnant or nursing, or unwilling to practice an effective method of birth control during the study and for at least 6 weeks after your last dose of study drug;
5. No means of contacting or visiting the investigator and/or study staff as required by the study or in the event of an emergency.

Procedures: Both you and the investigator will know what treatment you are receiving. Subjects participating in this study will be assigned by chance (like picking a name from a hat) to receive one of the following treatments:

- standard intravenous (IV, in your vein) antibiotic treatment given two to six times a day;
- a single IV 1000 mg dose of dalbavancin, followed by a 500 mg dose of IV dalbavancin, given once a week;
- a single IV 650 mg dose of dalbavancin, followed by a 65 mg dose of IV dalbavancin, given once a day.

You have a 2 in 3 (approximately 67%) chance of receiving the investigational study drug, dalbavancin.

If you are randomized to the standard IV antibiotic treatment, you will receive vancomycin 1000 mg every 12 hours until a determination of your type of infection is known. Thereafter, the investigator may continue to treat you with vancomycin, or you may be treated with nafcillin or oxacillin depending on the type of your infection. Nafcillin and oxacillin are standard antibiotic treatments and will be given IV at a dose of 2000 mg every 4 or 6 hours.

In addition and regardless of the study arm you are randomized to, if the investigator knows or thinks that you have a mixed infection (both gram-positive and gram-negative bacteria), you will also receive IV aztreonam or ceftazidime treatment.

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Before entering this study or undergoing any tests for the study, you will be asked to sign this informed consent form, indicating your willingness to participate in this study.

In order to be eligible to participate in this study, you must meet certain criteria that will be evaluated and determined by the investigator and/or study staff. You must agree to attend all scheduled visits and follow instructions given to you by the study staff. If you agree to participate in this study, the following events will occur:

Baseline/Screening: Before receiving study drug, you will be asked about your medical/surgical history and any medications you have taken in the past 4 weeks and/or are currently taking. You will also be given a physical examination including vital signs (heart rate, temperature, and blood pressure). Urine will be collected and blood (about 1 tablespoon) will be drawn for laboratory tests. The blood and urine will be used to evaluate blood counts and chemistries, and to determine the type of your infection. If you are a female of childbearing potential, some of the blood or urine sample will be for pregnancy testing.

The catheter exit site will be examined and blood samples may be taken from the catheter if it has not been removed.

If you are to receive dalbavancin, one additional teaspoon of blood will be collected to make sure there is no dalbavancin in your blood before you start the study.

In addition, you will have an electrocardiogram (ECG, electrical tracing of heart activity) and you may also have an echocardiogram (an ultrasound recording of the position and motion of the heart walls) to rule out endocarditis (inflammation of the lining of the heart). Note that the echocardiogram will only be performed if you are diagnosed with a specific type of bacterial infection. So this test may not be done until after the investigator knows the results of your blood test.

The state of your body organ functions will be determined, using SOFA (Sequential Organ Failure Assessment) scoring. SOFA scoring involves assessments of your blood pressure, your respiratory (breathing) function, counts of your blood platelets (blood cells that help your blood clot), and the function of your liver, kidneys, and central nervous system.

If you are a subject in the Intensive Care Unit (ICU), the investigator and/or study staff will also evaluate the status of your health using a scoring system called APACHE (Acute Physiology and Chronic Health Evaluation). This type of evaluation includes assessing your overall health status, vital signs (temperature, blood pressure, heart rate), respiratory (breathing) function, and the numbers and types of cells in your blood as well as the minerals and elements present in your blood.

On treatment: If the procedures and test results indicate that you are eligible for this study, you will be assigned to one of the three study groups, as described below:

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- A single 1000 mg IV infusion of dalbavancin followed by a 500 mg IV infusion of dalbavancin given once-a-week for up to 3 additional weeks;
- A single 650 mg IV infusion of dalbavancin followed by a 65 mg IV infusion of dalbavancin daily for up to 27 additional days;
- Standard IV antibiotic treatment for up to 28 days.

Study drug will be administered according to the specified groups above. You will receive each dose of dalbavancin IV over approximately 30 minutes or each dose of vancomycin IV over 1 hour. If either nafcillin or oxacillin is chosen as the standard antibiotic treatment they will be administered IV over 1 hour at a dose of 2000 mg every 4 or 6 hours.

On Day 1 and for the duration of the study, you will be monitored closely for possible side effects. At each visit, you will be asked about any symptoms or illnesses that you may have experienced. In addition, you will be asked to inform the investigator and/or study staff of any medications or therapies you are taking while you are participating in this study.

On Day 1, you will have your vital signs taken (heart rate, temperature, and blood pressure) before your first dose of study drug and at 1, 2, 4, and 12 hours after you have received your first dose of study drug. From the second day on, you will have vital signs assessed daily. You will have an ECG within 2 hours of the completion of your first study drug dose. On Days 2, 4, and 8, urine will be collected and blood (about 1 tablespoon) will be drawn for laboratory tests. The blood and urine will be used to evaluate blood counts, chemistries and your infection.

If you are taking dalbavancin, you will have three (3) additional blood draws (approximately 1 teaspoon at each of the three time points) taken on ONE of the following days: Day 3, 4, 5, 6, 7, or 8 (immediately before dosing, within 15 minutes after dosing and 3 to 7 hours after your dosing) to determine the amount of study drug in your blood. If you are taking the standard IV antibiotic treatment, you will have additional two blood draws (approximately 1 tablespoon) on either Day 3, 4, or 5 to determine the amount of vancomycin in your blood. If you are receiving nafcillin or oxacillin you will not need to have these additional blood draws.

The catheter exit site will be examined daily until you have no more signs or symptoms of infection, and samples may be taken from the catheter, if the catheter is still in place. The state of your body organ functions will be determined.

End of treatment: You will be given a physical exam including vital signs (heart rate, temperature, and blood pressure). Urine will be collected and blood (about 1 tablespoon) will be drawn for laboratory tests. The blood and urine will be used to evaluate blood counts, chemistries and your infection. If you are taking dalbavancin,

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you will have an additional blood draw (approximately 1 teaspoon) to determine the amount of drug in your blood. The catheter exit site will be examined, and samples may be taken from the catheter, if the catheter is still in place. You will be asked about any symptoms or illnesses that you may have experienced. In addition, you will be asked to inform the investigator and/or study staff of any medications or therapies you are taking.

Follow-up: Depending on the study arm you are randomized to this will be between 18 to 31 days after your last dose of study drug. You will be given a physical exam including vital signs (heart rate, temperature, and blood pressure). Urine will be collected and blood (about 1 tablespoon) will be drawn for laboratory tests. The blood and urine will be used to evaluate blood counts, chemistries and your infection. If you are taking dalbavancin, you will have an additional blood draw (approximately 1 teaspoon) to determine the amount of drug in your blood. The catheter exit site will be examined, and samples may be taken from the catheter, if the catheter is still in place. You will be asked about any symptoms or illnesses that you may have experienced. In addition, you will be asked to inform the investigator and/or study staff of any medications or therapies you are taking.

You have the right to either refuse to participate and/or stop your participation in this study at any time and for any reason without penalty or loss of benefits to which you would otherwise be entitled.

Benefits: If the drug works, you may receive some benefit. If it does not work, you personally will not receive any clinical benefit from your participation in this study. No direct benefit can be guaranteed to you by participating in this clinical study. While you may not receive direct benefits, your participation in this study may benefit future patients with catheter-related bloodstream infections.

Risks: Dalbavancin has been well tolerated in healthy subjects administered up to 1120 mg dalbavancin as a single IV dose. Possible side effects are similar to those associated with taking marketed antibiotics that are in the same class of drugs as dalbavancin. Possible side effects may include diarrhea, abdominal pain, heartburn, liver damage, and kidney damage. In exceptional cases, hearing impairment was observed with other drugs in this class.

Thirty nine (39) healthy volunteers have received dalbavancin in a study conducted at the University of Medicine and Dentistry of New Jersey. There were no signs of any of the above-mentioned side effects. In several of the volunteers, a slight increase in body temperature of about 1-2 degrees Fahrenheit was observed.

Risks associated with drawing blood from your arm include pain, bruising, swelling, lightheadedness, and on rare occasion, infection and nerve damage (some numbness

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and tingling.

The ECG procedure may cause minimal discomforts during the attachment and removal of the ECG leads to and from the skin of your chest area.

The echocardiogram procedure to rule out endocarditis (inflammation of the lining of the heart) uses ultrasound. To perform this procedure, a conducting gel is applied to the chest area. In rare cases, you may have an allergic reaction to this gel.

If you become pregnant during the course of this study, you should notify the investigator as soon as possible, since the risks to pregnant women, the embryo, the fetus and nursing children are unknown.

There also may be risks and discomforts that are not yet known.

New Findings: You will be told in a timely manner of any significant new information regarding the safety and/or effectiveness of dalbavancin that may affect your willingness to stay in this study.

Costs: You will not incur any charges for study drug or study related procedures.

Compensation: You will not receive any payment for participation in this study.

Alternatives: Standard antibiotic therapy is available if you choose not to participate in this study. Your medical doctor would determine alternative therapy. Consult your medical doctor for more information regarding alternative treatments.

Confidentiality: You should understand that all information collected in this study will be kept strictly confidential, except as required by law. In addition, representatives of the Institutional Review Board (IRB) who oversee the conduct of the study for the protection of the subject's rights and welfare, the sponsoring company (Versicor, Inc.) and/or their representatives, the US Food and Drug Administration (FDA) and other appropriate governmental agencies may review the data collected from this study. Your medical records and information will be kept confidential within the limits of the law. If any publication results from this research your identity will not be revealed.

Withdrawal: Your participation in this study is completely voluntary and you may either refuse to participate or withdraw at any time without penalty, without affecting your present or future care by the hospital, or without loss of benefits to which you would otherwise be entitled. Also understand that should the investigator and/or study staff, the sponsor (Versicor, Inc.), the Institutional Review Board (IRB), or the US Food and Drug Administration (FDA) find it necessary and/or in your best interests, they may withdraw you from this study or stop the entire study without your consent.

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In the event that you stop participating in the study for any reason, you will be asked to return to the research center to undergo the final evaluations. It is important for your health and safety to have these final procedures completed.

Injury: If you participate in this study you will be exposed to certain risks of physical injury, in addition to those connected with standard forms of therapy (see "Risks" section). In addition, it is possible that in the course of this study, new side effects of dalbavancin that result in physical injury may be discovered. Medical therapy will be arranged by _____ (institution name) if you have been injured as a direct result of participation in this research study.

Versicor, Inc. (sponsor) will pay for medical care to treat any physical injury incurred as a direct result of the study drug or study procedures. You agree to cooperate in obtaining any proceeds from insurance or other third party coverage that may be available to you for such medical care. No financial payments or other forms of compensation (such as lost wages or discomfort) or medical treatment beyond that which is offered above will be available; however, your legal rights are not waived by signing this form.

Subject Rights and Research–Related Injury: If you need further information regarding your rights as a research subject, you may contact _____ at (xxx) xxx-xxxx. This individual is an impartial person who is not involved in the conduct of the study. If you believe you have been injured due to study procedures or if you have any questions about the research, or your rights as a research subject, contact Dr. _____ by calling (xxx) xxx-xxxx. You should take this opportunity to ask questions and have them answered to your satisfaction.

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SIGNATURE OF SUBJECT or LEGALLY ACCEPTABLE REPRESENTATIVE

You, ([] subject, [] legal guardian, [] surrogate or [] caregiver) understand this informed consent form after having read it and having it explained to you in your primary language (or interpreted accordingly). You freely agree to participate (or agree to the subject's participation, if you are a legally acceptable representative) in this research study. Upon signing below, you will receive a copy of the consent form.

Printed Name of Subject

Date & Time

Signature of Subject

Printed Name of Legally Acceptable Representative, *if applicable*

Date & Time, *if applicable*

Signature of Legally Acceptable Representative, *if applicable*

Relationship to Subject, *if applicable*

***SIGNATURE OF READER/TRANSLATOR IF
THE SUBJECT / LEGALLY ACCEPTABLE REPRESENTATIVE
DOES NOT READ ENGLISH WELL***

The person, who has signed above, _____, does not read English well. You, the reader / translator, read English well and are fluent in (name of the language) _____, a language the subject or legally acceptable representative understands well. You have translated for the subject or legally acceptable representative the entire content of this informed consent form. To the best of your knowledge, the subject or legally acceptable representative understands the contents of this informed consent form and has had an opportunity to ask questions regarding the informed consent form and the study, and that these questions have been answered to the complete satisfaction of the subject or legally acceptable representative.

Printed Name of Reader / Translator, *if applicable*

Date & Time, *if applicable*

Signature of Reader / Translator, *if applicable*

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SIGNATURE OF WITNESS

You, the witness, confirms, to the best of your knowledge, that the subject or legally acceptable representative understands the contents of this informed consent form and has had an opportunity to ask questions regarding the informed consent form and the study, and that these questions have been answered to the complete satisfaction of the subject or legally acceptable representative.

Printed Name of Witness

Date & Time

Signature of Witness

***SIGNATURE OF PERSON CONDUCTING THE INFORMED CONSENT
(Investigator or Designated Study Staff Representative)***

To the best of my knowledge the subject, (or legally acceptable representative) _____, has assimilated the entire content of the above consent form, and understands the study and its risks well. The subject's questions and/or those of his/her legally acceptable representative have been accurately answered to his/her/their complete satisfaction.

Printed Name of Person Conducting Informed Consent

Date & Time

Signature of Person Conducting Informed Consent