

Safety and Efficacy of Dalbavancin vs. Cefazolin in Uncomplicated Skin and Soft Tissue Infections

Informed Consent Form For:

Phase III, Randomized, Double-Blind, Multi-Center Study to Evaluate the Safety and Efficacy of Dalbavancin Versus Cefazolin in the Treatment of Uncomplicated Skin and Soft Tissue Infections with Suspected or Confirmed Gram-Positive Bacterial Pathogens

Protocol: VER001-8

Sponsor: Versicor, Inc.
455 South Gulph Road
Suite 310
King of Prussia, PA 19406

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 uncomplicated skin and soft tissue 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. When bacteria become resistant to an antibiotic, it means that there is a good chance that the antibiotic will not help your body get rid of the infection the bacteria are causing. These types of infections can be especially dangerous to individuals who have weakened immune systems (the system in your body that helps you fight off infection) and/or individuals 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 cefazolin and cephalexin, two antibiotics which are approved by the US Food and Drug Administration (FDA) for use in the treatment of adults with skin and soft tissue infections.

Duration: Your participation in this study will last for a maximum of 30 days.

Selection of Subjects: This research study will be conducted at approximately 80 sites primarily within North America and will involve approximately five hundred and fifty five (555) subjects, who are at least 18 years old.

You are being asked to participate in this research study because you have been diagnosed with a skin and soft tissue infection.

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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.

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. You participated in an investigational drug or device study within the previous 30 days;
2. You previously participated in this study or another dalbavancin study
3. You are currently a substance abuser (including drugs of any kind and alcohol);
4. If you are a female: you are 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. You have 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: Neither you nor 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 three times a day for up to 7 or 14 days

OR

- a single IV 1000 mg dose of dalbavancin on Day 1, followed by placebo (an inactive solution, like sugar water) given IV three times a day through Day 7, possibly followed by a single IV 500 mg dose of dalbavancin on Day 8, followed by placebo given three times a day through Day 14

You have a 2 in 3 (66%) chance of receiving the investigational study drug, dalbavancin.

If you are assigned to the standard IV antibiotic treatment, you will receive cefazolin 500 mg every 8 hours (three times a day) for 7 OR 14 days.

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Since dalbavancin and cefazolin may have a slightly different color, a cover will be placed over your IV bag so that you, the investigator, and his/her study staff can not see what you are receiving.

Once you have received at least 24 hours of IV treatment, and either you have not had a fever for the previous 24 hours or your infection shows signs of improvement, the investigator may decide to switch you to oral (a pill taken by mouth) antibiotic treatment.

If you had previously been receiving the standard antibiotic treatment (cefazolin) you will receive a pill called cephalexin 500 mg every 6 hours (4 times a day). If you had previously been receiving dalbavancin, you will receive a placebo pill (like a sugar pill) identical in appearance to cephalexin, which you will take every 6 hours.

In addition, and regardless of the study arm you are assigned to, if the investigator knows or thinks that you have a mixed infection (an infection caused by a few different types of bacteria), you may also receive one of the following additional antibiotics: aztreonam (IV) or fluconazole (IV or oral).

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 in the last 2 months and any medications you have taken in the past 3 weeks and/or are currently taking. You will also be given a physical examination including vital signs (heart rate, temperature, and blood pressure) and an electrocardiogram (ECG, electrical tracing of your heart activity). Urine will be collected and blood (about 1 - 2 tablespoons) will be drawn for laboratory tests. The blood and urine will be used to monitor your safety as well as the status of your infection. Some of the blood may be sent to the laboratory for culture, if the investigator thinks you have an infection in your blood. If you are a female of childbearing potential, a portion of the blood and/or urine sample will be used for pregnancy testing.

Your skin and soft tissue infection site (wound site) will be examined by the investigator and photographs of your wound will be taken. The photographs will be used to document how the healing of your wound is progressing. Additionally, samples from your wound will be taken and sent to the laboratory for culture. This will be done by rubbing a swab over the infected area or using a needle or sharp instrument to remove some of the infected fluid (also called pus) or tissue. The test results from the culture will allow the investigator to see which types of bacteria are causing your infection and to make sure the antibiotics that you are receiving as treatment are appropriate.

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

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- A single 1000 mg IV infusion of dalbavancin on Day 1 followed by placebo infusions every 8 hours until Day 7, possibly followed by a second IV infusion of dalbavancin (500 mg) on Day 8, followed by placebo infusions every 8 hours until Day 14;
- Standard antibiotic therapy - cefazolin 500 mg IV infusion every 8 hours for 7 OR 14 days.

Both dalbavancin and cefazolin will be infused over 30 minutes.

Once the investigator receives the test results from the culture of your wound infection he/she will review the results to ensure that your participation in the study is still appropriate. Your participation will no longer be appropriate if the test results show that the bacteria causing your infection are resistant to an antibiotic called methicillin, since this means that the bacteria are most likely also resistant to cefazolin (one of the study medications). If this is the case, you will be discontinued from study medication, and the investigator will choose a more appropriate antibiotic. You will still be asked to return to the research center to undergo a set of final evaluations. It is important for your health and safety to have these final procedures completed.

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, the investigator and/or study staff will monitor 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 and after your first dose of study medication. Your vital signs will also be taken on Day 4. From the second day on (while you are in the hospital), you will have your temperature assessed daily. You will have an ECG within 2 hours of the completion of your first dose of study medication. Blood (about 1 tablespoon) may be drawn and sent to the laboratory for culture during the study if the investigator suspects that you have an infection in your blood.

Your wound site will be examined and photographs of the wound will be taken on Day 4. Additionally, samples may be taken of your wound on this day and sent to the laboratory for culture. If your wound has begun to heal (the skin is beginning to close) and there is no material to sample, this test will not be done. Additional samples will be obtained for culture and photographs taken if at any time the investigator feels that your antibiotic treatment is not working, and you need to be switched to a different antibiotic.

After you have received at least 24 hours of IV treatment, the investigator may decide to switch you to an oral (taken by mouth) antibiotic. In order for you to be switched, you must not have had a fever within the previous 24 hours or your wound must show signs of improvement (healing). If you were previously receiving standard antibiotic treatment (cefazolin) you will begin receiving cephalexin 500 mg every 6 hours by mouth. If you were previously receiving dalbavancin/placebo, you will begin receiving a placebo pill,

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identical in appearance to cephalexin. If you are switched to oral therapy, your vital signs will be taken and your wound will be examined on the day the switch is made.

If the investigator feels that you are well enough, it is possible that you could be discharged from the hospital while on study medication. If you are still receiving IV treatment, arrangements will be made to provide your infusions at an infusion facility, hospital, office, or at your home with the help of a home health care agency. If you are discharged from the hospital on oral medication, you will be sent home with your pills. It is important that you store the medication in a safe location, and that you take the medication as instructed. If you are sent home prior to Study Day 4, you will need to return for an assessment of your wound on Study Day 4. You will also need to return for an assessment on Study Day 8. If at any time you feel that you have experienced a side effect from the study medication, or that your wound is getting worse, you should contact the investigator or his/her study staff immediately.

On Day 8, you will be evaluated by the investigator and a decision will be made on the total duration of your treatment. The decision will be based upon the progress of the healing of your wound. During this evaluation one of three determinations will be made:

- Your wound has healed and no further antibiotic treatment is needed
- Your wound is healing, however you will need an additional week of antibiotic treatment
- Your wound is not healing and you need to be switched to an alternative antibiotic

If it is determined on Day 8 that your wound has healed and no further antibiotic treatment is needed, or your wound is not healing, and you need to be switched to an alternative antibiotic, the end of treatment procedures, as described below will be performed.

If it is determined on Day 8 that your wound is healing, but that you require an additional week of antibiotic treatment, you will receive an additional IV infusion of study medication. If you had previously been receiving dalbavancin/placebo, you will receive a 500 mg infusion of dalbavancin, followed by either IV placebo every 8 hours or oral placebo every 6 hours. If you had previously been receiving standard antibiotic therapy (cefazolin or cephalexin), you will receive an IV placebo infusion, followed by either IV cefazolin every 8 hours or oral cephalexin every 6 hours. You will continue to receive study medication until Day 14.

If it is determined that you require an additional week of antibiotic treatment, during the Day 8 visit you will also have your wound photographed, your vital signs taken and blood (about 1 – 2 tablespoons) will be drawn for laboratory tests. If the results of your previous urine test were abnormal, urine will also be collected. The blood and urine will be used to monitor your safety as well as the status of your infection.

The total number of days you will receive antibiotic treatment (IV plus oral) will be 7 OR 14

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days, and will be determined by the investigator, based upon the progress of the healing of your wound.

End of treatment: After you have completed your study medication you will have an End of treatment assessment. This assessment will occur within 2 days after you have completed your study medication. If you have been discharged from the hospital, you will need to return to the hospital, clinic or investigator's office for this assessment. If you have any unused study medication, it is important that you bring this with you.

During this assessment, you will have your vital signs taken (heart rate, temperature, and blood pressure) and blood (about 1 – 2 tablespoons) will be drawn for laboratory tests. If the results of your previous urine test were abnormal, urine will also be collected. The blood and urine will be used to monitor your safety as well as the status of your infection. Your wound will be examined, and samples will be taken, if possible for culture. If the skin around your wound has healed, no samples will be taken. Additionally, your wound will be photographed to document any healing that has occurred. 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: You will have a follow up assessment 12 – 16 days after you have completed your study medication. If you have been discharged from the hospital, you will need to return to the hospital, clinic or investigator's office for this assessment. During this assessment, you will have your vital signs taken (heart rate, temperature, and blood pressure) and blood (about 1 – 2 tablespoons) will be drawn for laboratory tests. If the results of your previous urine test were abnormal, urine will also be collected. The blood and urine will be used to monitor your safety as well as the status of your infection. Your wound will be examined, and samples will be taken, if possible for culture. If the skin around your wound has healed, no samples will be taken. Additionally, your wound will be photographed to document any healing that has occurred. 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: No direct benefit can be guaranteed to you by participating in this clinical study. 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. While you may not receive direct benefits, your participation in this study may benefit future patients with skin and soft tissue infections.

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Risks: Dalbavancin has been given to 56 healthy patients in single doses of up to 1120 mg (a dosage higher than the one planned for this study) and multiple doses of up to 1600 mg over 7 days. In addition, 41 patients with skin and soft tissue infections received single and multiple doses of dalbavancin. So far dalbavancin has been well tolerated. The side effects that have been reported have been mild to moderate in severity and are similar to those associated with FDA approved antibiotics that are in the same category of drugs as dalbavancin. These include redness at the IV site, fatigue, fever, headache, dizziness, abdominal pain, diarrhea, sour/upset stomach, nausea, nasal congestion, and itching/rash. There have also been some abnormal laboratory findings, including increased number of eosinophils in the blood, increased levels of glucose in the blood, protein in the urine and blood in the urine. In exceptional cases, hearing impairment has been observed with other drugs in this class. Tests have been done to see if dalbavancin causes hearing impairment. To date there has been no evidence of hearing impairment due to dalbavancin.

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

Risks to pregnant women, the embryo, the fetus and nursing children are unknown. Therefore, if you are a female who is capable of becoming pregnant (have not had a hysterectomy and/or are not at least one year post menopause) you must use a reliable method of preventing pregnancy from the time of the first dose of study medication through 6 weeks after the last dose of study medication. Adequate birth control methods include: intrauterine device (IUD), hormonal contraceptives plus barrier contraceptive, hormone delivery system plus barrier contraceptive or condom in combination with contraceptive cream, jelly or foam. Hormonal contraceptives alone are not sufficient. If you become pregnant during the course of the study, you should notify the investigator as soon as possible.

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. The investigator and his/her study staff do receive compensation from the sponsor (Versicor, Inc.) for your participation in the study as well as for the time and materials they use to track your progress in the study.

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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 and Health Insurance Portability and Accountability Act

Compliance: You should understand that all information collected in this study will be kept strictly confidential, except as required by law. All personal health information collected in this research study (the "study information"), including, but not limited to medical/surgical history, past and current medications, vital signs, physical examination and laboratory results, other assessments and photographs and samples of your wound may be disclosed by the investigator or other research study staff to the study sponsor, Versicor and its employees, agents and/or contractors. Versicor, in turn, will collate and interpret the study information and report it to the U.S. Food and Drug Administration ("FDA") and/or other appropriate governmental agencies, who will use this information for the purposes of determining whether or not to grant regulatory approval for the drug dalbavancin. The investigator or other research study staff may also disclose study information to the Institutional Review Board ("IRB") that oversees the conduct of the research study for the purpose of protecting the rights and welfare of subjects enrolled in the research 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.

Your signature on this informed consent form also serves as the authorization for the disclosure of the study information as outlined above. This authorization will expire at the end of the research study. You have the right to revoke this authorization at any time, provided that the revocation is in writing. However, if you exercise your right to revoke this authorization, you will be discontinued from participation in the research study.

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.

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).

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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