

**CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY  
AND  
AUTHORIZATION TO DISCLOSE HEALTH INFORMATION**

**Sponsor** Cerexa, Inc.

**Study Title:** A Phase 2, Multi-Center, Randomized, Observer-Blinded Study to Evaluate the Safety and Efficacy of PPI-0903 Versus Standard Therapy in Adult Subjects with Complicated Skin and Skin Structure Infections

**Protocol Number:** P903-03 Amendment 2

**Principal Investigator:**

**Address:**

**Telephone Number:**

You are being asked to participate in a clinical research study. However, before you give your agreement to take part, you must read the following information. After you have read the information, please ask any questions necessary for you to understand what will happen if you take part in this study. You will be informed as quickly as possible of any new information that is learned about the drugs used in this study which could change your mind about taking part in this study.

You have a skin infection. Skin infections are a condition in which your skin becomes infected with germs referred to as bacteria. Symptoms of a skin infection may include discharge ("pus") from the skin, warmth, pain, tenderness, redness, swelling, and/or fever. The standard treatment for many skin infections is antibiotic drugs. **Therefore, you should immediately inform the study doctor or staff if you have a history of allergies or problems when taking any antibiotics.** Your doctor has decided that you must be hospitalized for several days to receive antibiotics by vein to treat your infection. The antibiotics used to treat skin infections in this study must be given into your vein.

**PURPOSE**

The purpose of this clinical research study is to determine if an investigational antibiotic drug, referred to as "PPI-0903", is safe and effective in the treatment of skin infections, compared to standard antibiotics. An "investigational" drug is a drug that is being tested to demonstrate if it safely and effectively treats a disease or infection.

**DESIGN**

If you are accepted into the study, you will be assigned to receive either PPI-0903 or standard antibiotic therapy. Two-thirds (2/3) of the people in this study will receive PPI-0903 600 mg into their vein over 1 hour every 12 hours and one-third (1/3) of the people will receive standard therapy starting with an antibiotic called vancomycin given at a dose of 1000 mg, also into their vein over 1 hour every 12 hours. Determining which treatment you get will be done by random choice; you will be twice as likely to receive PPI-0903 as the standard therapy. Should you be selected to receive standard antibiotics, you might receive drugs called vancomycin, nafcillin, oxacillin, cloxacillin, flucloxacillin, or aztreonam. These medicines are all given into a vein; the

decision of exactly which drug you will receive if you receive standard therapy will depend on the bacteria identified from your infection. This decision will be made by your doctor. All the "standard" antibiotics are known to be effective in treating most skin infections.

Approximately 100 people with infections similar to yours will be enrolled in this study. Approximately 30 medical centers in the U.S., South America, South Africa and Russia will take part in this study. People who may take part in this study are those who require hospitalization and antibiotic treatment by vein for their skin infections and who do not have certain disease conditions, physical problems, or a medical history that would prevent them from safely receiving the drugs used in this study. The study doctor and staff will ask you about your health and will conduct tests to decide whether you can take part in the study.

### DURATION

The length of time you receive study medicine depends on how well you feel during treatment and how well the treatment works on your skin infection, which will be decided by the study doctor. The expected number of days you will receive study medicine is from 7 days up to a maximum of 21 days.

### STUDY PROCEDURES

After you have read this informed consent and agreed to take part in this research study, you will be asked to sign and date this form. The study staff will then do the following procedures to decide if you can take part in the study:

- Ask you about your medical history, current and prior medicines, and current symptoms.
- Perform a complete physical examination including taking your temperature, blood pressure, heart rate, breathing rate, height, and weight.
- Perform a complete examination of the infected area of your skin, which will include taking a sample of tissue or fluid from the infected site to check for bacteria at the infected site. This test may determine if any additional study medicine should be given to treat your infection.
- Perform an electrocardiogram ("ECG"), which evaluates the electrical activity of the heart. This recording of your heart activity will be repeated 3 times.
- If you are a woman who is able to have children, urine or blood will be collected for a pregnancy test. If you know or think you are pregnant, you must inform the study staff immediately.
- Collect a urine sample for routine tests.
- Collect blood samples (approximately 6 teaspoons) to determine if you can take part in the study and to check for the presence of bacteria in your blood. Blood will be drawn from two separate veins.
- Perform routine wound care to help healing of the infection.

If all the testing indicates that you can take part in the study, the study antibiotic will be given by vein shortly thereafter. While you take study drug, your progress will be evaluated by tests similar to those used whenever a person needs antibiotics by vein. Some additional tests will be conducted because this is a research study. The person evaluating your progress will not know which antibiotic you have received. You are asked not to reveal this information to them.

Routine tests while on therapy:

- Ask you about any new symptoms.
- Perform a brief physical examination including taking your temperature, blood pressure, heart rate, and respiratory rate.

- Perform an examination of the infected area of your skin, to include taking a sample of tissue or fluid from the infected site to check for the presence of germs. This test may determine if any additional study medicine should be given to treat your infection.
- Collect urine samples for routine testing.
- Collect blood samples (approximately 6 teaspoons) for routine testing and to check for the presence of bacteria in your blood. Blood will be drawn from two separate veins.
- Perform routine wound care to help healing.

#### Non-Routine procedures while on therapy

- Perform several 12-lead ECGs, which is an evaluation of the electrical activity of the heart.
- If you receive the investigational drug PPI-0903, 5 blood samples (approximately 1 teaspoon each) will be taken at 5 different times on the third day after the first or second dose of PPI-0903. These blood samples will be used to measure the levels of PPI-0903 in your body. These blood samples may be drawn by either a needle stick or by placement of a catheter in your arm.

For most people, treatment is expected to last 7 or 14 days. However, in unusual cases up to 21 days of treatment may be needed. If the study doctor determines that the study drugs are not helping cure the infection, you will need additional medicines not allowed in this study. In any of these situations, study therapy will be stopped. At the end of therapy, routine tests will be conducted to assess your progress. Approximately 8 to 14 days after your last dose of study medicine you will be asked to return to see the study doctor for routine tests. Approximately 21 to 28 days after your last dose of study drug you will be asked to return to for a last set of tests. If you are unable to return to see the study doctor, the study staff will contact you by phone.

#### RISKS AND DISCOMFORTS

Most antibiotics, of any kind, may cause the following side effects: pain and swelling of the vein where the antibiotic is given (phlebitis); allergic reactions that can cause a sudden drop in blood pressure, difficulty breathing and even death (anaphylaxis); skin rashes and sloughing of the skin; mouth ulcers; pseudomembranous colitis (a disease of the large intestine characterized by watery, sometimes bloody, diarrhea); and vaginal and mouth yeast infections (thrush).

#### PPI-0903:

PPI-0903 is a member of a group of antibiotics called cephalosporins. Like other cephalosporins, PPI-0903 may cause certain side effects and discomforts. The most common known side effects and discomforts are pain, redness, swelling or tenderness of the vein where the drug is given; change in urine color, urine odor and body odor; skin rash; and headache. Since PPI-0903 has been given to only a limited number of healthy people, other side effects may be discovered; some of these could be serious. In animal studies, doses approximately 4 times higher than the dose used in this study caused some rats to experience seizures (fits).

#### Vancomycin

The most common side effects include chills, fever, feeling sick to your stomach, ringing in the ears, hives, skin rash, and redness, and swelling or pain of the vein where the medicine is given. A flushing of the head and neck may occur if the vancomycin is given into the vein too quickly. Serious side effects that may happen with vancomycin include decreases in some blood counts, making you more prone to bleeding or infection. In addition, vancomycin may damage the kidney, possibly leading to kidney failure, and/or damage the nerves of the ear, which may lead to hearing loss or dizziness.

**Oxacillin, Cloxacillin, Flucloxacillin, and Nafcillin:**

These medicines are very similar and have similar side effects. Their most common side effects include feeling sick to your stomach, vomiting, diarrhea, abdominal (stomach) pain, headache, and skin rash. Serious side effects that may occur include severe allergy, kidney problems, seizures (fits), low blood counts, and liver problems such as inflammation of the liver (hepatitis) with yellowing of skin and eyes (jaundice), all of which can be severe and, in rare cases, fatal.

**Aztreonam:**

The most common side effects include pain and swelling at the vein where the antibiotic is given, diarrhea, feeling sick to your stomach, vomiting, and rash. Serious side effects that may occur with aztreonam include rare severe skin reactions.

During the collection of blood samples, you may experience mild pain and/or bruising around the vein where the needle is placed. Although rare, blood clots and infection of the vein may occur. Lightheadedness and/or fainting may also occur during or shortly after the blood is taken.

**Pregnancy**

PPI-0903 might hurt an unborn child or a nursing infant. Therefore, women who are pregnant, nursing, or able to have children but not using a highly effective type of birth control may NOT take part in this study. Examples of highly effective birth control are use of a condom +/- spermicide, combined oral contraceptive (birth control pills), implant, injectable, intrauterine device (IUD), not having any sex (abstinence), or a vasectomized partner). All women who can have children must have a test that shows they are not pregnant before study drug is given.

**Unknown and Unforeseeable Risks**

In addition to the risks listed above, there may be some unknown or uncommon and unpredictable risks from the use of these study medicines, including an allergic side effect or a side effect caused by use with another medicine. You will be informed orally and in writing by your doctor of any new information, findings or changes to the research that might change your desire to continue in this study.

**BENEFITS**

You may benefit if the study medicine is able to cure your skin infection. However, it is possible that you may not personally benefit from being a part of this study. However, by taking part in this study, you may possibly benefit future patients.

**ALTERNATIVES**

You do not need to take part in this research study to get treatment for your skin infection. If you decide not to take part in this study, you will receive standard medicine(s) to treat infections like yours. Ask the study doctor for more information about these alternative treatments, including risks and side effects.

**COSTS**

You will not have to pay for any of the study medicines, medical examinations, tests, hospitalization, or laboratory tests that are exclusively required by this study.

**COMPENSATION**

You will not be paid for taking part in this study.

**IN CASE OF INJURY**

If you are injured because of your taking part in this study, treatment for the injury will be made through

[name of physician]

and

[this institution].

The company responsible for this study will pay whatever costs of this treatment are not paid by your medical insurance. No other financial payment (money) will be provided from the company responsible for this study. You retain all legal rights while taking part in this study. You have the right to talk to a lawyer for advice and/or find other treatments if you are injured during the study.

**WHOM TO CONTACT**

If you have any questions or problems during this study, or if you think that you may have had a research-related injury, you should contact:

[investigator name]

[address].

[telephone number].

If you have any questions regarding your rights as a research volunteer, please contact during regular working hours:

[insert name],

Chairman of the Institutional Review Board/Independent Ethics Committee (IRB/IEC)

[insert telephone number(s)].

The Institutional Review Board/Independent Ethics Committee (IRB/IEC) is a committee established for the purpose of protecting the rights of volunteers in a research study.

**VOLUNTARY PARTICIPATION**

Taking part in this study is entirely at your choice (voluntary). You may decide not to take part and may stop taking part at any time during the study without penalty or loss of any benefits which you otherwise would receive. If you stop taking part in the study, you may receive a standard treatment, and no prejudice (bias) will be shown toward you for routine medical care or taking part in future research studies. In addition, the study doctor or the company paying for this study may decide that you should no longer take part in the study. This may be done without your consent if it is decided that you need additional medicine, do not follow the study plan, have a study-related injury, or for administrative reasons. If it is decided that you can no longer take part in the study, it is recommended that you finish the end of study examinations and laboratory tests for your own safety.

**SPONSORSHIP/FUNDING**

The study doctor receives payments from Cerexa, Inc., which is the company responsible for this study.

**CONFIDENTIALITY AND AUTHORIZATION TO ACCESS AND USE MEDICAL INFORMATION**

The information collected during this study will be kept confidential (private) to the extent permitted by the applicable laws and regulations. Only a study identification number and your initials will be used to identify you. You will not be personally identified in any reports or publications that may result from this research study. Because of the research goals of this study, however, your study records cannot be kept completely confidential. Medical records which identify you and the consent form signed by you will be looked at and/or copied for research or regulatory purposes by authorized representatives of the following:

- The study personnel
- The sponsor and its agents and [insert CRO name]
- The FDA (the U.S. drug agency) and other regulatory agencies may review your medical records in order to review the study findings
- The Institutional Review Board/Independent Ethics Committee (IRB/IEC))
- The hospital where you are being treated

The following sections provide a specific description of how your information will be used and disclosed (shared) if you take part in this research study. If you decide to take part in the study, you will be asked to authorize (agree to) those uses and disclosures by signing this form. If you choose not to authorize these uses and disclosures of your information, you will not be able to take part in the study.

The medical information that will be collected from you if you take part in the study includes (but is not limited to):

- Information obtained from procedures to determine whether you can take part in the trial, including a routine medical history, physical exam, x-rays, ECG, blood and urine tests, vital signs, and pregnancy test
- Information that is created, or collected from you, during the study, including all tests performed during the study.
- Information contained in your medical records related to your medical history and treatment.

The above information may identify you by name, address, telephone number, social security number, health plan number, study number, date of birth, dates relating to various medical procedures, or other identifying information, as appropriate for the area in which you live.

If you sign this form and take part in the study, the study staff will be authorized to use the information described above to carry out the research study. The study staff will also be authorized to disclose the information described above to the following parties involved in the research study:

- Cerexa, Inc., [insert CRO name] or other agents designated by Cerexa, Inc., to collect or review study data.
- The Institutional Review Board/Independent Ethics Committee (IRB/IEC)
- Government regulatory agencies including the FDA (the U.S. drug Agency) and other governmental agencies in other countries.

Once your information is disclosed to the study sponsors, the IRB/IEC, or government agencies as described above, it is possible that your medical information will be re-disclosed and will no longer be protected by US federal privacy regulations. Other laws may provide further

protection. Because of the need to disclose information to these parties, absolute confidentiality cannot be guaranteed.

While the study is in progress, you will not be able to look at your study records. You will be able to look at your records when the research study is completed. You have the right to see and copy the medical information collected from you during the study for as long as that information is kept by the study staff and other groups subject to federal privacy regulation.

Your agreement to share the information from the study does not end when the study ends.. In signing this form, you agree to the use and disclosure of your information for purposes of the study at any time in the future.

You may change your mind and decide to withdraw your approval to share this information at any time by sending a written request to:

[insert name of responsible study personnel]

[insert address].

If you withdraw your approval, you will no longer take part in the study, and the study staff will stop collecting medical information from you. In addition, the study staff will stop using your information and will stop disclosing your information to the groups described above, except to the extent the study staff has depended on information that has already been collected from you. For example, the study staff may need to use or disclose information obtained before you withdrew your approval in order to preserve the scientific truth of the study.

**SUBJECT'S STATEMENT OF CONSENT AND AUTHORIZATION**

I have read and understand this informed consent. I have been able to ask any and all questions, and I am satisfied with the answers provided. I agree of my free will to take part in the study, and I agree to the use and disclosure of my information in connection with the study. I understand that I (or my legally acceptable representative) will receive a signed copy of this consent and authorization form.

\_\_\_\_\_  
Signature of Subject\_\_\_\_\_  
Date (personally by Subject)\_\_\_\_\_  
Printed name of Subject\_\_\_\_\_  
Signature of Person conducting the  
Informed Consent Discussion\_\_\_\_\_  
Date (personally by Person conducting the  
the Informed Consent Discussion)\_\_\_\_\_  
Printed name of Person conducting Informed Consent Discussion

I certify that under local law I am the legally authorized representative of the participant named above and that I am authorized to sign this consent to his/her participation in the medical research study described above. I also am authorized to sign this authorization to release medical records and health information as described above.

\_\_\_\_\_  
Signature of Legal Representative\_\_\_\_\_  
Date\_\_\_\_\_  
Printed name of Legal Representative