

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

Sponsor: Cerexa, Inc.
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Alameda, California 94502
USA

Study Title: A Phase 3, Multi-Center, Randomized, Double-Blind, Comparative Study to Evaluate the Safety and Efficacy of Ceftaroline versus Ceftriaxone, with Adjunctive Clarithromycin, in the Treatment of Adult Subjects with Community-Acquired Pneumonia

Protocol Number: [P903-08]

Amendment Number: 2

Investigator:

Address:

Telephone Number:

You are being asked to take part in a clinical research study. However, before you agree to participate, you must understand the statements in this informed consent document. After that, please ask all the questions you want, especially to help you understand completely what will happen if you choose to participate in this study. You will be told of any important new information about the antibiotics used in this study which may effect your decision to participate.

Your doctor has diagnosed you with Community Acquired Pneumonia (CAP). This type of pneumonia happens when your lungs are infected with germs (bacteria). You may have some or all of the following symptoms: cough (with or without phlegm), abnormal breath sounds, difficulty catching your breath, low blood oxygen level (may or may not cause you to feel tired), fever, or abnormal cell counts in your blood. The standard treatment for CAP is antibiotic drugs. ***Therefore, you should immediately inform the study doctor or staff if you have a history of allergies or other problems when taking any antibiotics or other medications.***

[PK regions only] In addition to the main clinical trial, approximately 120 to 140 people in selected study centers will take part in pharmacokinetics (PK) study for ceftaroline. Pharmacokinetics can be defined as measuring how much of study drug is absorbed and how much reaches the bloodstream, how it is broken down and removed from the body. This is important information in determining how the drug can be used safely with as few side effects as possible. Procedures for the PK study are done on Day 3 during drug treatment and consist of 4 blood draws.

Your doctor has decided that you must receive antibiotics by vein to treat your CAP. The antibiotics used to treat CAP in this study must be given into your vein for at least five (5) days and no more than seven (7) days total. You will also receive an antibiotic pill taken by mouth

twice on the first day of treatment. These treatments will be provided in the hospital or an acute care facility.

PURPOSE

The purpose of this clinical research study is to learn if an investigational antibiotic known as ceftaroline can safely and effectively treat the type of CAP you have compared to another standard antibiotic. An “investigational” drug is one that has not been approved for sale by the local health authorities and is being tested to see if it safely and effectively treats a disease or infection.

DESIGN

This is a randomized, double-blind study. Randomization is a method based on chance by which you will receive either the investigational antibiotic or the standard antibiotic. In this study, there is an equal chance that you will receive the investigational antibiotic or the standard antibiotic. In a double-blinded study, neither you nor your study doctor or study staff know which antibiotic you are receiving. Not knowing your antibiotic will help your doctor treat you and other people in the study in the same way.

Approximately 610 people with CAP like yours will take part in this study at about 80 medical centers around the world. People who may take part are those who initially need to be in the hospital or acute care facility to receive antibiotic treatment by vein for their CAP. People who take part also must not have certain diseases, physical problems, or medical history that would prevent them from safely receiving the antibiotics used in this study. The study doctor and staff will ask you about your health and will do tests to decide whether you can take part in this study.

STUDY MEDICATIONS

If you are accepted into the study, you will receive medication or placebo in your vein (i.v.) every 12 hours. This will be given into your vein over 1 hour. Clarithromycin will be given to all patients on the first day of treatment (one pill at the start of the study and a second pill approximately 12 hours later). This medication is taken by mouth.

For iv therapy, you will be provided with EITHER:

- the investigational antibiotic **ceftaroline every 12 hours OR**
- the standard antibiotics **ceftriaxone every 24 hours plus a saline solution (placebo) and placebo alone every 24 hours.**

Ceftriaxone and clarithromycin are standard antibiotics which are known to treat most CAP like yours. You are just as likely to receive ceftaroline as you are to receive ceftriaxone plus placebo. The placebo is a liquid that cannot cure your CAP and usually has no side effects. The addition of placebo is to ensure that neither you nor your study doctor knows which treatment group you are in. You will not receive only the placebo as a treatment for your CAP.

DURATION

How long you are treated with the study antibiotics depends on how you feel during treatment and how well the treatment works on your CAP. The study doctor will decide how long you should be treated. You will be treated with antibiotics for up to 7 days.

Your overall study participation will last about 26 to 42 days. You will be asked to return to the clinic a minimum of 2 times during this time period for study procedures.

STUDY PROCEDURES

After you or your legally authorized representative have understood 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 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 routine complete physical examination including taking your temperature, blood pressure, heart rate, breathing rate, and weight.
- Obtain a chest X-ray or chest computed tomography (CT) to confirm your CAP (if one has not already been taken recently). This is a painless way to take a picture of your chest to see whether you have fluid in your lungs.
- Perform a 12-lead electrocardiogram (also known as ECG), which is a painless test to check 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 will be collected for a pregnancy test. If you are pregnant or nursing, you may **not** participate in this study. If you think you are pregnant, you must inform the study staff immediately.
- Collect a urine sample for routine laboratory tests.
- Collect blood samples (approximately 4 tablespoons) 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 2 separate veins.
- If possible, collect phlegm (sputum) by asking you to produce a deep cough into a container or a pleural fluid sample which is obtained by collecting a small sample of fluid from around your lung. The type of fluid you provide will determine the type of CAP you have.

If all the testing indicates that you can take part in the study, the study antibiotics will be given by vein (i.v.) shortly thereafter. During the time you take the study antibiotics, your progress will be evaluated by tests like those used whenever a person needs antibiotics by vein.

Routine procedures while on study:

- Ask you about any new symptoms (how you feel).
- Perform a routine brief physical examination including taking your temperature, blood pressure, heart rate, and breathing rate.
- Collect urine samples for routine testing.
- Collect blood samples (approximately 2 tablespoons) for routine testing. Blood samples (approximately 2 tablespoons) may also be collected to check for the presence of bacteria in your blood, if needed. Blood may be drawn from 2 separate veins for this test.
- Collect sputum or pleural fluid samples

Non-Routine procedures while on study:

- Perform several 12-lead electrocardiograms.
- Obtain one or two additional Chest X-Rays or Chest CTs.

[PK regions only] For study subjects that take part in the PK study, additional blood samples (approximately 4 tablespoons total) will be collected at each time point on Study Day 3.

- One sample immediately before the start of intravenous (IV) study drug or standard therapy infusion
- One sample immediately following the end of intravenous (IV) study drug or standard therapy infusion
- One sample between 1 and 3 hours after the end of intravenous (IV) study drug or standard therapy infusion
- Last sample between 4 and 8 hours after the end of intravenous (IV) study drug or standard therapy infusion

For most people, it is expected that the antibiotics will be given by vein for 5 to 7 days. If the study doctor determines that the study antibiotics are not helping cure the infection, you will need additional drugs not allowed in this study. If this happens, the study antibiotics will be stopped.

Approximately 8 to 15 days after your last dose of the study antibiotics, you will be asked to return to see the study doctor for routine tests, an ECG, and a chest X-ray or chest CT.

Approximately 21 to 35 days after your last dose of the study antibiotics you will be asked to return for a last set of tests, including blood work, a chest X-ray or chest CT, and a review of the medications you are taking. You may also be asked to provide a sputum or pleural fluid sample if your CAP has gotten worse since you finished taking your antibiotics.

RISKS AND DISCOMFORTS

Collection of Blood:

When blood samples are taken, you may have mild pain and/or bruising around the vein where the needle is inserted. 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.

Antibiotics:

Most antibiotics, of any kind, may cause the following side effects: pain and swelling of the vein where the antibiotic is given, allergic reactions that can cause a sudden drop in blood pressure or difficulty breathing, skin rashes and sloughing of the skin, kidney damage possibly leading to kidney failure, low blood cell counts (which can be associated with infection, bleeding or fatigue), liver problems, seizures (fits), pseudomembranous colitis (a disease of the large intestine characterized by watery, sometimes bloody, diarrhea), and vaginal and mouth yeast infections (thrush). Some of these side effects can be severe, and on rare occasions they may cause death. Not all potential side effects are listed as some may be unknown at this time.

Ceftaroline (the drug being tested in this study):

Ceftaroline belongs to a group of antibiotics called cephalosporins. Like other cephalosporins,

ceftaroline may cause certain side effects and discomforts. The most common known side effects and discomforts associated with ceftaroline are headache, microscopic crystals in urine, feeling sick to your stomach, creatine phosphokinase (an enzyme) increase in blood, difficulty sleeping, constipation, and abnormal liver tests. Since ceftaroline has been given to only a limited number of healthy people and people with skin infections, other side effects may be discovered, some of which could be severe.

Ceftriaxone:

In clinical studies, the most common side effects seen in at least 1% of all patients associated with ceftriaxone include changes in blood cell counts, diarrhea, skin rash, and elevations of liver enzymes in your blood. Other common side effects are described under the general antibiotics risks and discomforts section of this document.

Clarithromycin:

The most common side effects associated with clarithromycin are related to the gastrointestinal system. Side effects include diarrhea/loose stools, nausea, vomiting, heartburn, abdominal pain, abnormal taste, rash, and headache. Rare but serious allergic reactions and skin conditions have also been reported. Other common side effects are described under the general antibiotics risks and discomforts section of this document.

PREGNANCY

Ceftaroline might hurt an unborn child or a nursing infant (effects on infants and pregnant women are unknown at this time). 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 with 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 the study antibiotics are given. If you become pregnant while receiving treatment, you must inform your study doctor.

UNKNOWN AND UNFORESEEABLE RISKS/NEW FINDINGS

In addition to the risks and discomforts listed above, there may be some unknown or uncommon risks from the use of these study antibiotics. It may not be possible to predict some of these risks. You will be told by your doctor of any new information, findings or changes to the research that might change your wish to stay in this study. You will also receive this information in writing.

BENEFITS

You may benefit if the study antibiotics are able to cure your CAP. It is also possible that you may not personally benefit from being a part of this study. However, this study will provide additional information about the treatment of CAP to physicians. Therefore, future patients may benefit from the increased knowledge of physicians who treat them.

ALTERNATIVES

You do not need to take part in this research study to get treatment for your CAP. If you decide not to take part in this study, you will receive standard antibiotic(s) to treat infections like yours. Ask the study doctor to tell you about these alternative treatments, including how they work.

COSTS

You will not have to pay for any of the study antibiotics, medical examinations, tests, hospitalization, or laboratory tests that are used only for purposes of this study. You may be required to pay for costs associated with what your physician would normally do to treat your CAP.

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 money or financial payment of any type will be provided by 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. This study has been reviewed and approved by the applicable IRB/IEC.

VOLUNTARY PARTICIPATION

Taking part in this study is entirely voluntary (your choice). Your refusal to participate or your decision to discontinue your participation at any time will involve no penalty or loss of benefits to which you are otherwise entitled. If you stop taking part in the study, you may receive a standard treatment, and no prejudice or bias will be shown toward you for routine medical care. 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 (agreement) if it is decided that you need additional treatment, 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.

SPONSORSHIP/FUNDING

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

CONFIDENTIALITY AND AUTHORIZATION TO ACCESS AND USE MEDICAL INFORMATION

In order for your participation in this study to be useful for the development of medical treatments, the data collected need to be analyzed and provided to the Sponsors of the study, Independent Ethics Committee, and to health authorities. You should understand you will not be able to participate in this study and the data derived from your participation can't be used if you do not provide consent.

If you withdraw consent to study participation, you should understand that your consent to data processing is still valid unless specifically withdrawn. If you have an ongoing medical condition at the time of your decision to withdraw, information about you may continue to be collected until your condition stabilizes or improves. With the exception of ongoing medical conditions, 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.

Your full identity will not appear on any of the study documents collected and retained by the Sponsor for their analyses. Only your initials and a unique subject number for the study will link the data to you. These data will contain your date of birth, gender and race, as well as the medical and scientific data required by the study. These medical and scientific data may contain (but is not limited to):

- Information obtained from procedures to determine whether you can take part, including a routine medical history, physical examination, ECG, blood and urine tests, and urine 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.

However, the Sponsor, their representatives, auditors, the Independent Ethics Committee and national/international Regulatory Authorities will have access to your personal medical files at the study site, which contain your full name, for verification of clinical trial procedures and/or data. All personnel involved have the obligation of confidentiality.

Sometimes additional analyses can be conducted combining anonymous information from this study with others.

The data collected may be sent to other countries in the world for the purposes of analysis, for submission to their Health Authorities and possibly for publication. The data protection laws in these countries vary, however all the parties involved in this process have a duty to protect your identity and use the data for legitimate healthcare purposes only. If your data are sent to third parties all appropriate measures will be taken to protect your data.

Records identifying you will be kept confidential and, to the extent permitted by the applicable laws and/or regulations will not be made publicly available.

In the event of publication of the data it will be presented in a way that cannot allow for your personal identification.

The data recorded at the time of this study may be held on computer or as paper records by the Sponsor or on their behalf. You should note that under Data Protection legislation, you have a right of access to, and, if needed, correction of these data. You can request this through your study Doctor <NAME OF INVESTIGATOR>.

As this is a double-blind study, the exact treatment option you receive can, for scientific reasons, not be revealed until after all patients have completed the study and it has been analyzed.

You will be informed in the case of retention of samples for future analyses. You will also be informed of any plans for new analyses (not foreseen when you gave your consent) on these retained samples and you have a right to refuse.

SUBJECT'S STATEMENT OF CONSENT AND AUTHORIZATION

I have read and understand the statements in 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. I understand and consent to my primary care physician being informed of my participation in this research study.

[PK regions only] Check one of the boxes listed below for Day 3 pharmacokinetics study:☐ I will not participate in the PK study☐ I will participate in the PK study_____
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
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_____
Relationship of Legal Representative_____
Signature of Witness (if applicable)_____
Date_____
Printed name of Witness (if applicable)_____
Relationship of Witness