

**SUBJECT INFORMATION AND CONSENT FORM AND
AUTHORIZATION TO USE AND DISCLOSE PERSONAL HEALTH
INFORMATION FOR RESEARCH**

Name of Research Study: A Phase 2 Multi-Center, Randomized, Double-Blind, Non-Controlled Study Comparing the Safety, Tolerance, and Efficacy of 2 Doses of TR-701 in Patients with Complicated Skin and Skin Structure Infections

Protocol Number: TR701-104

Sponsor: Trius Therapeutics, Inc

Principal Investigator Name:

Research Site Address(es):

Daytime Telephone Number(s):

24-hour contact number(s)_____

Introduction

You are being asked to take part in a clinical research study. Before you agree to participate, you must understand the following explanation of the proposed study and the statements in this informed consent document. Your decision is completely voluntary and will not affect your medical care if you choose not to participate. It is important for you to ask all the questions you want and become informed regarding the research risks, benefits and alternatives, to help you understand what will or may happen if you choose to participate in this study. No guarantees or assurances can be made as to the results of the study.

If you are not completely truthful with your study doctor regarding your health history, you may harm yourself by participating in this study.

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You will be told of any important new information about the study drug used in this study which may affect your decision to participate.

This study is being conducted for Trius Therapeutics, Inc., a company engaged in the research and development of pharmaceutical products. Your doctor is being paid by Trius Therapeutics, Inc. to conduct this study.

Background

You are being asked to take part in this study because your doctor has diagnosed you with a skin infection. Skin infections happen when your skin is infected with germs called 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 other problems when taking any antibiotics or other medications.**

Your doctor has decided that you should receive antibiotics to treat your skin infection. The study drug used to treat your skin infection in this study will be taken by mouth for 5 days to 7 days.

Everyone who decides to participate in this study will take part in a pharmacokinetics (PK) study for an experimental antibiotic called TR-701. A PK study measures how much of the study drug is absorbed into your body and how much reaches your bloodstream, as well as how the drug is broken down and removed from your body. This information is important because it helps us determine 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 study drug treatment which consists of 2 blood draws and on Day 5 during study drug treatment which consists of 5 blood draws.

PURPOSE

The purpose of this clinical research study is to learn if an experimental antibiotic known as TR-701 can safely and effectively treat the type of skin infection you have. An “experimental” drug is one that has not been approved for sale by the U.S. Food and Drug Administration (FDA) and is being tested to see if it safely and effectively treats a disease or infection. We also refer to this experimental antibiotic in this document as the “study drug.”

DESIGN

This is a randomized study. Randomization is a method based on chance by which you will receive one of two doses of the experimental antibiotic. In this study, there is a 50% chance that you will receive either dose of the experimental antibiotic. Neither you nor the study doctor will know which dose you will receive. In case of an emergency, this information will be available to the study doctor.

Approximately 120 people with skin infections like yours will take part in this study at about 10 medical centers in the United States. People who take part must not have certain diseases, physical problems, or medical history that would prevent them from safely receiving the study drug. The study doctor and staff will ask you about your health and will conduct tests to decide whether you are eligible to take part in this study.

STUDY MEDICATIONS

If you qualify to participate in the study, you will receive the experimental antibiotic TR-701 at one of 2 doses. You will not receive only a placebo for your skin infections. There are 2 groups in this study and you will be provided with EITHER:

- **the experimental antibiotic TR-701 300 mg (which is one 200 mg capsule plus one matching 100 mg capsule)**
- **the experimental antibiotic TR-701 400 mg (which is two 200 mg capsules)**

If you are accepted into the study and decide to participate, you will receive the study drug by mouth once every day for 5 – 7 days. You will receive either TR-701 at a dose of 300 mg by mouth OR TR-701 at a dose of 400 mg by mouth.

DURATION

How long you are treated with the study drug depends on how well the treatment works on your skin infection. The study doctor will decide how long you should be treated. You will be treated with the study drug for a minimum of 5 days to a maximum of 7 days. Your overall study participation will last about 28 to 35 days. You will be asked to return to the clinic a minimum of 6 times during this time period for study procedures.

STUDY PROCEDURES

After you (or your legally authorized representative) have read this informed consent, you will be asked to sign and date this form if you are willing to participate in the study. The study staff will then do the following to decide if you are eligible 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 height and weight.
- Perform a 12-lead electrocardiogram (also known as ECG), which is a painless test to check the electrical activity of the heart.
- Collect a urine sample and a blood sample for a pregnancy test if you are a woman who is able to have children. 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 (about 1 and ½ tablespoons) to determine if you are eligible to take part in the study
- Collect blood sample (about 1 tablespoon) to check for the presence of bacteria in your blood. Blood will be drawn from 2 separate veins.

- Perform a complete examination of your skin infection, which will include taking a sample of tissue or fluid from the infection itself to check for bacteria.
- Perform routine care of your skin infection to help heal the infection.
- If you agree to have a test for HIV, Hepatitis B, and Hepatitis C, an additional blood sample (about 1 teaspoon) will be drawn. You will be informed if any of these tests are positive and you will be provided counseling on what follow-up steps you can take. These results may need to be reported to local and/or state health authorities which will also be discussed with you.

If all the testing indicates that you are eligible take part in the study, we will give you the study drug to take by mouth. During the time you take the study drug, your progress will be evaluated by tests like those used whenever a person needs antibiotics. Some additional procedures will be done because this is a research study.

If you are accepted into the study and choose to participate, the following routine tests and procedures will be performed:

- 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.
- Perform a complete examination of your skin infection, which will include taking a sample of tissue or fluid from the infection itself to check for bacteria.
- Perform routine care of your skin infection to help healing of the infection.
- Collect blood samples (about 1 tablespoon) for routine testing.
- Collect urine samples for routine testing.
- Other blood samples (about 1 tablespoon) 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.

We may also ask you to participate in the following non-routine procedures as part of the study:

- If you have a skin infection that is close to a bone, your doctor may perform an X-ray, MRI (magnetic resonance imaging) or CT scan (computed tomography). Each of these tests are painless and allow us to see whether the bones were affected. If you have a bone infection, you will not be able to participate in this study.
- If you are a woman who is able to have children, we will collect an additional urine sample for a pregnancy test on the last day the study drug is administered.
- One follow-up 12-Lead ECG will be done on your last day of therapy.

On the third (3rd) day that you take the study drug, additional blood samples (2 blood samples of 1 and ½ teaspoon each) will be collected as follows:

- One sample immediately before you take the study drug.
- One sample approximately 1 hour after you take the study drug.

On the fifth (5th) day that you take the study drug, we will collect additional blood samples (5 blood samples of about 1 and ½ teaspoon each) as follows:

- One sample immediately before you take the study drug.
- One sample approximately 1 hour after you take the study drug.
- One sample approximately 2 hours after you take the study drug.
- One sample approximately 4 hours after you take the study drug.
- The last sample approximately 8 hours after you take the study drug.

For most people, we expect that the study drug will be given for 5 to 7 days. If the study doctor determines that the study drug is not helping cure the infection, you will need additional drugs not allowed in this study. If this happens, the study drug will be stopped.

Follow-Up Phase

Approximately 7 to 14 days after your last dose of the study drug, you will be asked to return to see the study doctor for routine tests and check on how your infection is doing.

- 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.

- Perform a complete examination of your skin infection, which will include taking a sample of tissue or fluid from the infection itself to check for bacteria.
- Perform routine care of your skin infection to help healing of the infection.
- Collect blood samples (about 1 tablespoon) for routine testing.
- Collect urine samples for routine testing.
- Other blood samples (about 1 tablespoon) 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.

Approximately 21 to 28 days after your last dose of the study drug your study doctor will verify that your infection has not come back. This visit may be conducted over the telephone if your study doctor does not feel they need to see you in person to evaluate your infection.

Unscheduled Visit

If you experience any unusual medical problems during the study, you should contact your study doctor immediately. Your study doctor may ask you to visit the study center in between your regularly scheduled study visits. During these visits, your study doctor will advise you if any procedures are necessary or advisable.

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 infrequent side effects: 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.

TR-701 (the experimental antibiotic being tested in this study)

TR-701 belongs to a group of antibiotics called oxazolidadone. Like other oxazolidadones, TR-701 may cause certain side effects and discomforts. The most common known side effects and discomforts associated with TR-701 are nausea (14.8%), headache (9.3%), abdominal pain (7.4%), dizziness (7.4%) and diarrhea (7.4%). Since TR-701 has been given to only a limited number of healthy people other side effects may be discovered, some of which could be severe.

REPRODUCTION RISKS

The effects of TR-701 on a pregnant woman, an embryo, fetus (unborn baby), or nursing infant are unknown and may be harmful. TR-701 has not been studied in women who are pregnant or nursing. Therefore, women who are pregnant, nursing, or able to have children but not using at least two highly effective types 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. Antibiotics such as TR-701 may make oral contraceptives ineffective. All women who can have children must receive a negative result on a pregnancy test before the study drug is given.

If you become pregnant or suspect you are pregnant while participating in the study, you must inform your study doctor immediately. If a pregnancy is confirmed, the study drug will be stopped, your participation in this study will be ended, and your pregnancy will be followed to outcome.

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 the study drug. Since the study drug is investigational, there may be other risks related to the study drug, when taken alone or in combination with other medications, which are

unknown. It may not be possible to predict some of these risks. Your study doctor will inform you of any relevant 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. If this happens, you should discuss with your study doctor whether or not you want to continue in this study. If you decide to continue in the study you may be asked to read and sign an updated consent form. If new information becomes available and your study doctor thinks that it is in your best interest to withdraw from the study, he or she will explain the reasons to you. You may contact the study doctor at any time after your participation ends to find out if any new information about this study has become available

As with any drug, side effects can occur, so please report any unusual symptoms to your study doctor immediately.

If any of your current medications are stopped in order for you to participate in this study, there is a risk that you may lose the benefits of those medications or that you may have reactions from stopping these medications. You should discuss these risks with your study doctor and/or the doctor who prescribed these medications before agreeing to participate in this study.

The study drug is for **your use only**. You are cautioned to keep the study drug out of the reach of children or other people who cannot read or understand written directions. The use of the study drug by anyone who has not been authorized to use it could be dangerous.

BENEFITS

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

ALTERNATIVE TREATMENTS

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 may ask your doctor for standard antibiotic(s) to treat infections like yours. There is no penalty or loss of benefit of other treatments if you do not participate. Ask the study doctor to tell you about these alternative treatments, including how they work.

COSTS

There will be no charge to you for your participation in this study. You will not have to pay for any of the study drug, 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 skin infection

COMPENSATION:

For your participation, you will be paid \$_____ for each completed visit for a possible total of up to \$_____. If you withdraw from the study early, you will be paid for each of the visits you have completed. You will not receive any other compensation for your participation in this study, and you will not have any right in any inventions, new techniques or technology that may result from this study.

CONFIDENTIALITY AND RELEASE OF MEDICAL RECORDS

We will protect information about you and your taking part in this research study to the best of our ability. If information about this study is published, your name will not be given. However, the U.S. Food and Drug Administration (FDA), The [REDACTED] Independent Institutional Review Board (IRB), and Trius Therapeutics or their designee may sometimes look at the medical records and study information of those who take part in this study. A court of law could order medical records shown to other people, but that is unlikely. Therefore, absolute confidentiality cannot be guaranteed.

COMPENSATION FOR RESEARCH RELATED 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. There is no policy in place to provide additional compensation beyond the cost of treatment and no financial payment of any type will be provided by the company responsible for this study.

You must follow the directions of the study doctor to be eligible for this coverage.

LEGAL RIGHTS

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.

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, such as if the study is canceled.

If your study participation is ended early for any reason, it is recommended that you finish the end of study examinations and laboratory tests.

WITHDRAWAL

Your doctor, the sponsor company, or the FDA has the right to stop your participation in the study at any time, with or without your consent, for any of the following reasons: if you have an adverse effect from the study drug the doctor feels requires you to stop taking the study drug, if you need a treatment not allowed in this study, if you do not keep appointments, if you do not take the study drug as instructed, if you become pregnant, or if the study is canceled by the FDA or the sponsor company. The sponsor may decide to stop the study and your access to the study drug under certain circumstances even if the study drug appears to be safe and effective.

WHOM TO CONTACT FOR QUESTIONS

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 questions about your rights as a research subject, you may contact the [REDACTED] IRB at [REDACTED] (toll free). An Independent Review Board is a group of scientific and non-scientific individuals who perform the initial and ongoing ethical review of the research study with the study subject's safety and welfare in mind. If you have study-related comments, complaints or concerns, you should first contact the study investigator. Please call the IRB if you want to talk to someone other than the study investigator or have difficulty reaching the study investigator. For further information regarding the clinical trials process and your role as a research subject, you may visit the [REDACTED] IRB website at [REDACTED]

SPONSORSHIP/FUNDING

The study doctor (and clinic or hospital) receives support payments from Trius Therapeutics Inc., which is the company responsible for this study. S/he/they do not have any other financial interests in this study.

CONFIDENTIALITY AND AUTHORIZATION TO ACCESS AND USE MEDICAL INFORMATION

The United States government has issued a new privacy rule to protect the privacy rights of patients. This rule was issued under a law called the Health Insurance Portability and Accountability Act of 1996 (HIPAA). The Privacy Rule is designed to protect the confidentiality of your personal health information. The document you are reading, called an "Authorization," describes your rights and explains how your health information will be used and disclosed (shared).

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 (for example, mentioned by name) 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
- 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 (legally 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 participate 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):

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- Information obtained from procedures to determine whether you are eligible to 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.

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:

- Trius Therapeutics, Inc. or other agents designated by Trius Therapeutics, Inc., to collect or review study data.
- [REDACTED] IRB
- Government regulatory agencies including the FDA and other governmental agencies in other countries.

Once your information is disclosed to the study sponsors, the IRB, or government agencies as described above, it is possible that your medical information will be re-disclosed and will no longer be protected by U.S. federal privacy regulations. Other laws may provide further protection. Because of the need to disclose information to these parties, absolute confidentiality cannot be guaranteed.

You have the right to see and get a copy of your records related to the study for as long as the study doctor has this information. However, by signing this Authorization you agree that you might not be able to review or receive some of your records related to the study until after the study has been completed.

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.

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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 no new information will be collected for study purposes unless the information concerns an adverse event (bad effect) related to the study. If an adverse event occurs, your entire medical record may be reviewed. All information that has already been collected for study purposes, and any new information about an adverse event related to the study, will be sent to the study sponsor.

With the exception of adverse events, 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.

If you withdraw from the study but do not withdraw your Authorization, new personal health information may be collected until this study ends.

This Authorization does not have an expiration date. If you do not withdraw this Authorization in writing, it will remain in effect indefinitely. Your study doctor will keep this Authorization for at least 6 years.

If you do not sign this Authorization, you cannot participate in this research study or receive study-related treatment. If you withdraw this Authorization in the future, you will no longer be able to participate in this study. Your decision to withdraw your Authorization or not to participate will not involve any penalty or loss of access to treatment or other benefits to which you are entitled.

Signature of Subject

Date

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EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

Any person who is requested to consent to participate as a subject in a research study involving a medical experiment, or who is requested to consent on behalf of another, has the right to:

1. Be informed of the nature and purpose of the experiment.
2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be used.
3. Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.
4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.
5. Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.
6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.
7. Be given an opportunity to ask any questions concerning the experiment or the procedures involved.
8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time, and the subject may discontinue participation in the medical experiment without prejudice.
9. Be given a copy of a signed and dated written consent form when one is required.
10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

Signature of Subject

Date

SUBJECT'S STATEMENT OF CONSENT AND AUTHORIZATION

I have read and understand the statements in this informed consent and authorization to use and disclose personal health information related to my participation in this research study. I have discussed all aspects of the study with my study doctor or study staff, have been able to ask any and all questions, and I am satisfied with the answers provided. I understand that I may withdraw from the study at any time or refuse procedures without affecting my ongoing medical care. I agree to the use and disclosure of my information in connection with the study as described in this informed consent and authorization to use and disclose personal health information. I understand that I (or my legally acceptable representative) will receive a signed copy of this consent and authorization form. I consent to participate in this research 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 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