

## PATIENT INFORMATION SHEET AND CONSENT FORM FOR PARTICIPATION IN A CLINICAL STUDY

**STUDY NAME:** A Multicenter, Double-Blind, Randomized Study to Evaluate the Efficacy and Safety of Single-Dose IV Oritavancin versus IV Vancomycin for the Treatment of Patients with Acute Bacterial Skin and Skin Structure Infection (ABSSSI) (SOLO I)

**PROTOCOL NUMBER:** TMC-ORI-10-01

**INVESTIGATOR:** [Investigator to add]

### Dear Patient,

You are being invited to take part in a research study. Taking part in this study is completely voluntary. Before you decide if you would like to take part or not it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to your doctor, the staff and others about the study if you wish.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

The study will be run by Dr. [Investigator] at [Name of Hospital]. Once the study has been explained to you, you will be asked to read and sign this form if you wish to participate. You may refuse to participate without penalty or loss of benefits or treatment to which you are otherwise entitled.

### INFORMATION ON RESEARCH

#### Background

Oritavancin is an investigational drug for the treatment of bacterial infections (an infection caused by germs) such as acute bacterial skin and skin structure infection (ABSSSI). An “investigational” drug is one that has not been approved by the United States FDA (Food and Drug Administration) for use in the United States, but may be tested in research studies such as this one. Oritavancin is administered by intravenous (IV) infusion (a needle into the vein of your arm). An intravenous line is a small tube that is attached to a catheter and inserted into a vein usually in your hand or arm.

#### Why have I been chosen?

You are being asked to be in this study because you have an acute bacterial skin and skin structure infection (ABSSSI).

### **Do I have to take part?**

No. It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw from the study at any time and without giving a reason. The decision to withdraw at any time, or not to take part, will not affect the standard of care you receive or have any influence on your further treatment. Please be aware that if you choose to withdraw after your data has been collected, the data will still be used in the trial evaluation. If you choose not to participate, your study doctor will inform you about your future treatment.

### **Why is this study being done?**

The purpose of this study is to look at the effects and safety of oritavancin or an alternative medicine (vancomycin) to treat your ABSSSI. The results of the study will let us compare the two study drugs (oritavancin or vancomycin) and understand how they work against different skin infections. Vancomycin is an FDA approved medication for the treatment of ABSSSI.

### **Description of Study**

If you agree to participate, health information, such as the length of your hospital stay, the procedures you have while in the hospital and information about your skin infection will be collected throughout the study. Information on the safety and any side effects of the study drug as well as any other medication you are given will be recorded throughout the study. At all times your individual identity will be protected in the gathering of this information.

This study will be divided into 3 parts: Part 1 is the screening period where your doctor will determine if you are eligible to participate in the study; Part 2 is the treatment period where you will receive one of the two study drugs and Part 3 is the follow-up period during which time you will be monitored after receiving study drug.

### **Part 1 – Screening Period (up to 24 hours):**

The screening period will last no longer than 24 hours. During this period your doctor will perform the following tests to find out if you are eligible to be in this study:

- Medical history including all questions regarding medicines that you are taking, even herbal treatments or over-the-counter products and if you are taking part in any other studies
- Physical exam including measurement of your height and weight
- Measurement of your vital signs (blood pressure, heart rate, and respiratory rate) and several measurements of your temperature
- A pregnancy test, if you are a woman who is able to have children. You should tell your doctor if you are pregnant, or if you think that you may be pregnant. Blood (less than one teaspoon) and urine samples will be required for this test. Test results must be negative in order for you to participate in the study

- An electrical tracing of the heartbeat (electrocardiogram; ECG). For the ECG, electrodes (small discs) will be taped to your chest and a recording of your heart will be made
- An exam of your skin infection. The doctor will ask you about the history of your infection, any symptoms you have experienced including the level of pain you feel. Your infection site will be measured using a ruler and by tracing the shape onto a piece of plastic. A picture will also be taken. A sample of fluid or other material from your skin infection may be taken to find out what type of bacteria has caused this infection
- You will have five blood samples taken (about 10 teaspoons total). Three blood samples (two samples will require about 1 to 2 teaspoons and the third sample approximately half a teaspoon) will be used for routine laboratory testing; to measure the amount of C-Reactive Protein (a way to monitor how your body is reacting to your infection) and to check your Hepatitis B and C status. The other two blood samples (about 4 teaspoons each) will be taken with a needle in two different veins to see if your infection has spread to your blood.
- A urine sample will be collected for routine laboratory testing

**Part 2 - Treatment Period (7 to 10 days):**

If you qualify for this study and agree to take part in it, you will be placed into one of two treatment groups: oritavancin or vancomycin. There is an equal chance (like flipping a coin) of being placed in either of these two groups. You, your doctor, and your nurses will not know whether you are being given oritavancin or vancomycin. The pharmacist (or the person who is preparing or managing the dose of your study drug) who works with your doctor and nurses is the only one who will know which study drug you are receiving.

On Day 1 you will be given study drug (oritavancin or vancomycin) by IV infusion (through a needle into the vein of your arm). The amount of drug needed to treat skin infections is different between the two study drugs: a full dose of oritavancin requires only 1 infusion, while a full dose of vancomycin may require several infusions. Therefore, if you are in the oritavancin group you will also be given a placebo (a placebo is a substance, such as a mixture of sugar and water that looks like the study drug but contains no active medicine). If you are in the vancomycin group all infusions you receive will contain a dose of vancomycin. This is done so that you, your doctor, and your nurses will not know which study drug you are being given.

The treatment period will last from 7 to 10 days depending on how long your doctor feels you need study drug for your skin infection. Throughout this period you will receive between 1 to 3 infusions each day. The number of infusions you are given will depend upon what your doctor thinks is necessary to treat your infection.

The first infusion of study drug will last about 3 hours and each additional infusion will last at least 1 hour. Your subsequent infusions may occur in the hospital or clinic or at home in the presence of a trained member of the study team. If you are sent home from

the hospital before the end of the treatment period, your doctor may require you to come to the hospital or clinic each day to receive your study drug infusions.

In addition to the infusions, the following measurements and procedures will be done during the treatment period to monitor your health and track the progress of your infection:

Measurement of your temperature several times each day

- If you are at home during the 48-72 hour time period after your first infusion of study drug, it is essential that you record your temperature 4 times a day during waking hours (for example, at breakfast, lunch, dinner and before bed). A thermometer will be given to you for taking oral temperature readings.
- Examination and measurement of your skin infection each day using a ruler; you will be asked about any symptoms you are experiencing
- ECGs will be done on Day 1 only
- Additional tests and/or samples may be required if your doctor thinks they are necessary
- ***For PK Sites only: 4 blood samples (about 1 teaspoon each) to measure the level of study drug in your body. The study doctor can tell you if you are at a PK site.***

In addition to the tests and procedures described above, you will have the following tests done between 48 to 72 hours after you start study drug:

- Measurement of your vital signs (blood pressure, heart rate, and respiratory rate)
- Three blood samples (about 1 to 2 teaspoons each) will be taken. Two samples will be used for routine laboratory testing and to measure your amount of C-Reactive Protein. The other blood sample will be used to measure the level of study drug in your body (more samples may be required if your doctor feels it is necessary). An additional sample (less than half a teaspoon) may be taken if your blood sugar levels were high at screening to check for diabetes mellitus.
- You will be asked about the level of pain you feel as a result of your skin infection
- A picture of your skin infection will be taken
- Your infection site will be measured by tracing the shape onto a piece of plastic

**Part 3 – Follow-up Period (about 50 to 53 days from the time you stop study drug):**

During this period, up to 4 additional visits to your doctor may be required. Depending on how long your treatment lasts, some of the visits listed below may be combined:

- End of treatment visit - within 24 hours of your last infusion of study drug
- Study Day 10 will occur 10 days after your first infusion of study drug
- Post-treatment evaluation visit - about 7-14 days after your last infusion of study drug

During each visit in this period, you will have the following tests and procedures:

- Measurement of your vital signs (blood pressure, heart rate, and respiratory rate)
- Measurement of your temperature several times
- Examination and measurement of your skin infection using a ruler; you will be asked about any symptoms you are experiencing and will have a picture of your infection taken
- Your infection site will also be measured by tracing the shape onto a piece of plastic
- Two blood samples (about 1 to 2 teaspoons each) will be collected for routine laboratory testing and to measure the amount of C-reactive protein
- You will be asked about the level of pain you feel as a result of your skin infection
- Additional tests and/or samples may be required if your doctor thinks they are necessary

***For PK Sites Only:*** One additional visit will be required 24 days after your first infusion of study drug

- 1 additional blood sample (about 1 teaspoon) taken about 24 days after your first infusion of study drug. This sample will be used to measure the level of study drug in your body

Follow-up period telephone call

During the follow-up period you will also receive a follow-up phone call about 60 days after you first started study drug to check your condition. You will be asked if you experienced any illnesses or symptoms in the time since you left the hospital. Your doctor may ask for you come in for a visit if he/she feels it is necessary.

### **Length of Participation**

Your participation in this study starts with signing this consent and is expected to last about 60 days. Approximately 960 patients will be participating in this study, which will be conducted in about 100 study sites around the world.

### **Withdrawal from Study**

You can end your participation in this study at any time. Your doctor may also decide to end the study early.

Your doctor will stop your treatment:

- if new information about the treatment suggests that it will not work;
- if new information about the treatment suggests that it will be unsafe for you.
- If you feel unwell on the treatment

If you or your doctor decides to stop the study you may be asked to have additional laboratory tests and examinations that your doctor thinks are necessary.

## **RISKS/BENEFITS**

### **Risks associated with participation in this research study**

Oritavancin has been administered to about 1977 people in other studies. All drugs have side effects, and there are risks associated with participation in any drug study. Because oritavancin is still being developed, there may be other risks or side effects that are not known at this time. You will be told of any important new information regarding this drug during the course of the study, and you may choose to discontinue your participation at any time.

### ***Risks from oritavancin***

The most common side effects (experienced by more than 1 in 100 patients but less than in 1 in 10 patients) possibly related to oritavancin include:

- Insomnia – difficulty falling or staying asleep
- Headache or dizziness
- Phlebitis - Pain and irritation around the vein, particularly at the site of infusion. In some cases, the phlebitis was considered painful and did not go away for several weeks. In other cases, the phlebitis took longer to go away.
- Nausea
- Itching

Side effects that are uncommon (experienced by fewer than 1 out of every 100 patients, but more than 1 out of every 1000 patients) included constipation, diarrhea, vomiting, rash, temporary changes in laboratory tests that look at the health of your liver and your kidney, increased sweating/night sweats, chills, tiredness or excessive sleep, increase or decrease in cells that help fight infections, fever, anxiety, high and/or low blood pressure, abdominal pain, abnormal taste, heart beating too fast, too slow, or irregularly, flushing, dry mouth, redness of skin, tingling, fainting, red spots or bumps on the skin, hives (itchy rash), sudden kidney failure, stomach pain, muscle spasms (shaking), pain in extremities such as your hands and feet, cardiac arrest (heart stopping), infections of the bone or blood (sepsis/septic shock), and allergic reactions.

Side effects that are rare (experienced by fewer than 1 out of every 1000 patients) include a decrease in the number of cells that help your blood clot, passing gas, sour stomach, skin infections (not related to your original infection) including abscess (a sore with pus) and cellulitis (swelling and soreness of your tissues), Candida pneumonia, Candida sepsis (widespread infections not related to your original infection), low blood volume, and changed mental status. It is unclear if these side effects which occurred less than 1% of the time were related to study drug.

Unknown side effects, including life-threatening reactions, could occur. The doctor and nurses will watch for the development of any side effects throughout the study and will provide appropriate treatment to resolve any side effects observed.

### ***Risks from placebo***

Risks of receiving a placebo infusion may include more frequent urination, edema (swelling of the hands and feet), and phlebitis (pain and irritation around the vein). These effects are temporary and usually resolve soon after the infusion is discontinued. Complications in persons with heart or kidney disease receiving a placebo infusion may additionally include fluid overload, generalized swelling, excess fluid in the lungs, or electrolyte imbalances (abnormal levels of the salts in the blood and body).

### ***Risks from vancomycin***

The most common side effects possibly related to vancomycin include:

- Severe allergic reaction
- Low blood pressure
- Wheezing
- Shortness of breath
- Hives
- Itching
- Flushing of the upper body
- Pain or muscle spasms of the neck and back (usually resolves within 20 minutes)
- Changes in the lab tests that look at the health of the kidney
- Decrease in urination/kidney function or kidney failure
- Hearing loss
- Dizziness
- Ringing in the ear
- Change in the number of cells that fight infection
- Fever
- Nausea
- Rash, including flaky skin or blistering skin
- Stevens-Johnson syndrome (a potentially fatal skin disease)
- Inflammation of veins

Uncommon/rare and unknown side effects, including life-threatening reactions, could occur. The doctor and nurses will watch for the development of any side effects throughout the study and will provide appropriate treatment to resolve any side effects observed.

### ***Risks associated with both Study Drugs***

Some side effects may occur for either study drug. These include Pseudomembranous colitis, an infection of the large intestine caused by a germ called *Clostridium difficile*. Symptoms of colitis may include stomach pain, loss of appetite, tiredness, bloody diarrhea, cramping, need to go to the bathroom and feeling full. In some cases, a “super infection” can occur, when the use of a drug kills the bacteria (germs) that cause your infection, allowing overgrowth of other bacteria that are usually in normal amounts in your body.

***Risks associated with the IV line***

An intravenous line is a small tube that is attached to a catheter and inserted into a vein usually in your hand or arm. IV lines are usually safe and well tolerated and complications (problems) are rare, but can include infusion site reaction, phlebitis and infection. The IV may come out accidentally or blood may leak around the line. If the IV is not in the vein, medication or fluid can be infused into your tissues, and can be associated with swelling, discomfort and irritation of the tissues. Rarely, a clot can develop in the IV line itself. If this happens, the staff may remove the old IV line and start a new IV line.

Side effects may occur when study drug is being given to you (infusion reactions) including rash, flushing/reddening of the face and/or upper body, hives, itching, swelling, pain or spasms (shaking) of the chest or back muscles, wheezing, shortness of breath and low blood pressure. To reduce the chance that you will experience these side effects, study drug will be given over a period of at least one hour.

***Other Possible Side Effects and Risks***

You will be undergoing tests and procedures as part of this study, some of which may be associated with potential side effects or risks. For example, blood being taken from a vein for tests may cause some discomfort or pain at the needle site and may occasionally cause some bleeding, bruising, a hematoma (development of a collection of blood under the skin), infection, dizziness, or fainting.

There may be unknown risks of possible harmful interaction with other medications. Therefore, it is very important that you tell the study staff if you will be taking any medications (including over-the-counter medications, herbal treatments, dietary and herbal supplements, and vitamins) other than the study drug during course of the study.

If you have any injury, side effect, or any other unusual health experience during this study, makes sure that you tell the nurses, study coordinator or your physician immediately.

***Reproductive Risks***

The effects of oritavancin on the unborn child are unknown. It is not known if oritavancin could affect male sperm. There is no information on the long-term effects of oritavancin on fertility. Do not participate in this study if you are pregnant or if you think you might be pregnant. Be sure to tell your doctor if you think you may be pregnant, or if you are unsure. During the course of this study both the male and female partner is advised to at least two forms of contraception (for example: oral contraceptives and condoms; or ovulation method and abstinence where active contraception is not acceptable).

***New Findings***

If any important new information is found during this study that may affect you wanting to continue to be part of this study, you will be told about it right away.

*Benefits associated with participation in this research study*

Your skin infection may improve because of your participation in this study. However, although oritavancin is being tested as a treatment for a condition that you have, there is no guarantee that you will receive any medical benefit.

The information from this research study may lead to a better treatment in the future for people with skin infections. You may receive information about your health from the examinations and laboratory tests to be done in this study.

**ALTERNATIVE TREATMENTS**

You do not need to be in this study to receive treatment for your condition. Other treatments and therapies for your condition that are available include linezolid, daptomycin, cefazolin, Bactrim/Septra, ceftriaxone, Augmentin, ampicillin with or without gentamicin, or other antibiotics. Ask the study doctor to discuss these alternatives with you.

**COSTS**

The regular cost of treatment for your condition and your procedures will be billed to you or your insurance carrier. The study drug, oritavancin or vancomycin will be provided to you at no charge by the sponsor. The sponsor will also pay for any procedures that are done specifically for the study, which would not be a part of normal care.

**PATIENT COMPENSATION/REIMBURSEMENT**

You will not receive payment for participation in this research study.

*[OR: You may receive compensation for your time and/or travel at the end of your participation in the study in the total amount of \$XX should you complete the whole study.]*

**MEDICAL TREATMENT**

If you are injured as a result of participating in this study, the Sponsor of the study, The Medicines Company, will provide medical treatment to the extent that the injuries resulted from: (a) oritavancin, the drug being studied in the study, so long as it was administered according to the study procedures, or (b) procedures your doctors performed as part of the study, so long as they were performed according to the study procedures.

**CONFIDENTIALITY****Purpose for collecting Protected Health Information**

If you join in this study, you are giving permission for your health information to be collected. Research staff will use this information to find out the benefits or risks of oritavancin. Some of this information called Protected Health Information is protected by law. By signing this consent form, you give permission for your Protected Health Information to be collected and used inside and outside the United States for research.

You will not be identified (by name, street address, social security number, etc.) in any information used outside of the medical center. If the study results are published, no information will be included that can identify you. The information that will be collected could be a part of your medical record filed at [Hospital Name]. You may ask for your medical records at any time. Your agreement to allow the research staff to use your information begins when you sign this document and does not have an expiration date [change if you know the site has a different expiration timeframe].

The following health information will be collected from you for this study:

- Your initials, age, gender, race
- The dates that you were admitted and discharged from the hospital, relating to this study
- Any past illnesses or risk factors that may have helped lead to your skin infection
- Your medication, schedule for taking medication, and any changes
- Your present health and medical condition
- Information about your skin infection (for example, procedures, measurements, photographs, notes on related symptoms)
- Any changes in your health and medical condition for a period of approximately 60 days after your first infusion in study drug

#### **Access to your Protected Health Information**

The research staff at the medical center will use your Protected Health Information to treat you correctly, manage the medical center, and perform research. To make sure that your information is kept confidential, you will be assigned a code number. All information needed for the study will be recorded and tracked using that code.

You should know that by signing this form, you are giving permission for employees or other people connected with the groups listed below to see your medical records. This makes it possible for your safety to be assured, for the research procedures and result of the study to be verified as reliable, and for information to be sent to health care insurers. To the extent that the law allows, your original medical records or copies may be given to the following groups:

- The Medicines Company (the company that sponsors this study) or individuals associated with The Medicines Company
- Members, consultants and staff of the Institutional Review Board at your medical center
- Billing or quality assurance staff at your medical center
- The Joint Commission of Accreditation of Health Care Organizations
- The Food and Drug Administration or other authorities

Your Protected Health Information will be kept as confidential as possible, but the medical center cannot promise complete privacy. Laws stop the medical center from using your Protected Health Information in any way other than described in this form.

Once your information leaves the medical center, we will not be able to control how it is used because laws no longer protect the information. If your research records are kept with your medical records, only the information that is needed for the research will be sent to the groups listed above. This information will show why you have been asked to participate in this research study.

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by US Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the study results. You can search this Web site at any time.

**Withdrawing consent to your protected information**

You can withdraw your permission for us to use your Protected Health Information at any time. You can do this by contacting your doctor. This will also end your participation in the study. Any information collected before you stop participating in the study can be used for the purposes of the study as described above.

**VOLUNTARY PARTICIPATION**

It is your choice whether or not to participate in this research study. You do not need to sign this form. If you decide not to sign this form, you cannot be in the research study. You are free to stop taking part in the study at any time and for any reason. If you withdraw, there will be no penalty. This decision will not affect your access to health care.

**QUESTIONS ABOUT RESEARCH**

If you have any questions about the research or develop a research-related injury, you should contact **Dr. Name** at **phone #**. During non-business hours you should contact **Dr. Name** at **phone #**.

If you have questions about your rights as a participant in this research, you should contact **Name** at the **Organization/IRB** at **phone #**. This office is responsible for reviewing research and protecting your rights. You will receive a copy of this form.

**Statement of Consent:**

I understand that this study involves research. I have read this information sheet. My questions have been answered. I will be given a copy of this document. I know that taking part in this study is voluntary. I may withdraw from this study without losing any benefits I would otherwise receive. The study and its risks and benefits, alternative treatments, procedures and purpose have been explained to me. By signing this form, I have not lost any legal rights. I allow access of my medical records to government agencies and The Medicines Company or their designees for this purpose. My identity will be kept confidential if the data collected from this study is used for publication or educational purposes.

I will be told about new findings the investigators learn during the study that may affect my willingness to stay in the study. If I want to have this information sent to my personal doctor, I should tell the [Dr. Investigator].

I agree to take part in this study.

\_\_\_\_\_  
Printed Name of Patient

\_\_\_\_\_  
Signature of patient

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature of patient's legal guardian (if applicable)

\_\_\_\_\_  
Date/Time

I explained the study to the patient and witnessed their consent to the study:

\_\_\_\_\_  
Investigator/Designee Name

\_\_\_\_\_  
Investigator/Designee Signature

\_\_\_\_\_  
Date/Time