

GAR-936 Study 3074A1-202-US
Prototype version 26 October 2000

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INFORMED CONSENT TO PARTICIPATE IN A MEDICAL RESEARCH STUDY

Title of Protocol: A Multicenter Open-Label Study of the Safety and Efficacy of GAR-936 to Treat Complicated Intra-Abdominal Infections in Hospitalized Patients (Incorporating Amendment 1 to Protocol)

PROTOCOL NO.: 3074A1-202-US

SPONSOR: Wyeth-Ayerst Research

INVESTIGATOR: _____

DESCRIPTION/PURPOSE OF THE STUDY

You are invited to participate in a research study of an experimental antibiotic, GAR-936, to treat your abdominal infection. GAR-936 is given through a vein in the arm.

In order to decide whether you wish to participate in this research study, you should understand enough about its risks and benefits to be able to make an informed decision. This process is known as informed consent.

This consent form provides detailed information about the research study. Your doctor will also discuss the study with you. Once you understand the study, you will be asked to sign this consent form if you wish to participate. You will be given a signed copy of the form to keep as a record.

The study doctor has determined that you have an infection in your abdomen. The standard treatments for your infection include: 1) the administration of infection-fighting drugs called antibiotics; 2) surgery of the abdomen to drain pus or correct any underlying problems that may have caused the infection; and/or 3) x-ray-guided drainage of pus.

The purpose of this study is to evaluate the effectiveness and safety of GAR-936 for the treatment of your abdominal infection. The way the body uses GAR-936 and the susceptibility of the germs causing your infection will also be studied.

Approximately 120 patients will participate in this study at approximately 15 centers in the United States. All patients will receive the same dose of GAR-936.

DURATION

You will participate in the study for approximately 4 to 6 weeks. This period includes a 1-day screening period, up to 2 weeks of treatment with GAR-936, an early follow-up visit about 9 days after the antibiotic is discontinued, and a final visit about 5 weeks after your first dose of the antibiotic.

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The exact duration of treatment will depend on the seriousness of your infection as determined by the study doctor. You will be treated with GAR-936 for at least 5 days, but no more than 14 days. If the tests to determine the type of infection show that GAR-936 won't fight the germs, the study doctor may stop GAR-936 and switch you to another antibiotic.

PROCEDURES

Before you can enter the study, you will have the following tests or procedures to determine whether or not you may participate:

1. A review of your medical history and a physical examination.
2. Measurements of blood pressure, heart rate, and temperature.
3. Blood samples will be taken for routine blood tests and to check if there are any germs in your blood. The total amount of each blood sample will be about 10 mL (two tablespoons).
4. A urine sample will be obtained.
5. Cultures of the infected fluid in your abdomen will be sent to the laboratory during your surgery or your abdominal infection will be drained, guided by x-rays.
6. If you are a woman of childbearing potential, a blood or urine sample will be taken to determine whether you are pregnant. If the pregnancy test is positive, you cannot participate in the study.
7. A 12-lead electrocardiogram (ECG) will be performed.

If you are found to be eligible based on these tests, the following will occur:

1. You will receive an infusion of GAR-936 through a vein twice a day over a period of approximately 60 minutes.
2. The treatment period will last at least 5 days but not more than 14 days.
3. During the treatment period, your temperature and blood pressure will be taken and your abdominal infection will be assessed on a daily basis.
4. Blood and urine samples will be taken on Days 3, 5 and the last day you receive the study drug.
5. Two additional ECGs will be performed on or after Day 3, one before you receive your morning dose, and another 1 hour following your dose.
6. Approximately 4 ounces of blood will be withdrawn for study purposes during the 4-6 week study period.
7. You will be asked to return to your doctor's office for two additional visits after GAR-936 has been stopped. These visits will take place at approximately nine days and at five weeks after the first infusion. It is **essential** that these follow-up visits be completed. The blood and urine tests will be repeated at the final follow-up visit.

RISKS ASSOCIATED WITH THE STUDY

You should not participate in this study if you have any of the following conditions:

- a history of allergies to tetracycline, or a tetracycline-like drug
- pregnancy

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- serious kidney, heart, lung, or liver disease
- a history of bleeding disorders

You should discuss all of your past and present diseases and allergies with your doctor. If you have any questions regarding diseases and/or allergies that you may have had in the past, ask your doctor.

The most common side effects of GAR-936 are nausea, vomiting, and headaches. Other symptoms include fatigue, stomach pain, indigestion, diarrhea, loss of appetite, numbness and rash in the arm used for infusing GAR-936, paleness, and increased blood cells that could indicate an allergy.

GAR-936 is a tetracycline antibiotic. Some other side effects caused by drugs of this class include: inflammation of the pancreas; bacterial and yeast overgrowth in the bowel causing fever, chills, diarrhea, and anogenital inflammation; liver inflammation and/or failure; kidney failure; severe allergies; severe skin rashes; a clinically significant decrease in red blood cells, white blood cells and platelets; and allergies triggered by exposure to light. Some of these side effects associated with tetracyclines can be life-threatening.

The antibiotic used in this study may also involve unknown risks.

The risks of drawing blood and giving GAR-936 through a vein include pain and bruising at the puncture site. Fainting may occur. Infection at the site where blood is drawn and/or at the site where your intravenous needle was inserted could occur. When you have imaging x-rays you will be exposed to radiation.

You will be informed of any significant new information that could affect your willingness to continue to participate in the study.

WOMEN OF CHILDBEARING POTENTIAL ONLY

GAR-936 may involve currently unforeseeable risks to pregnant women, the embryo, the fetus, or to children of nursing women. For this reason, all women of childbearing potential are required to undergo pregnancy testing before entering the study and, if they are sexually active, to use a medically acceptable contraceptive throughout the study.

A woman of childbearing potential is defined as one who is biologically capable of becoming pregnant. This includes a woman who is using contraceptives or whose sexual partner is either sterile or using contraceptives.

If you miss a period or think you might be pregnant during the study, you must notify the study doctor immediately so that you can be withdrawn from the study. If you become pregnant at any time during the study or within 5 weeks after your first dose of GAR-936 (completion or dropout) and your pregnancy is carried to term, the study doctor will follow the course of your pregnancy and delivery as well as the condition of your infant at birth.

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BENEFITS ASSOCIATED WITH THE STUDY

You and society may benefit from any experimental research. Such benefits include the possibility that your condition may improve and that this study may help develop a new therapy for others with similar conditions.

PAYMENT

You will not be paid for your participation.

ALTERNATIVE THERAPY

Other treatments that use different types and combinations of antibiotics are available to treat your condition. Examples are ciprofloxacin, piperacillin and imipenem/Cilastatin. Their effectiveness varies according to their suitability for an individual patient. You do not have to participate in this study to be treated for your abdominal infection.

CONFIDENTIALITY

Representatives of Wyeth-Ayerst Research, the US Food and Drug Administration (FDA), other regulatory agencies, and the Institutional Review Board (IRB) will be allowed to review your medical records. Your identity will remain confidential unless disclosure is required by law.

RIGHT TO ASK QUESTIONS AND TO WITHDRAW FROM THE STUDY

- If you have any questions concerning this study, call _____ at () ____ - ____.
- If you think you have experienced a research-related injury and if you have any questions concerning the availability of medical care call _____ at () ____ - ____.
- If you have any questions about your rights as a research subject, call _____ of the Institutional Review Board at () ____ - ____.

RESEARCH-RELATED INJURY

If you become injured during this study, and your injury is a direct result of the effects of GAR-936, reasonable medical treatment will be provided. The cost of this treatment will be paid by the sponsor, Wyeth-Ayerst Research, to the extent it is not covered by health insurance.

COSTS

You will not incur any additional costs as a participant in this study. You may be reimbursed (up to \$____.00) for your travel to and from the doctor's office.

VOLUNTARY PARTICIPATION AND CONDITIONS OF WITHDRAWAL

Your participation in this study is voluntary. You may refuse to participate or you may withdraw at any time without penalty or loss of benefits to which you are otherwise entitled. Your doctor may withdraw you from the study at any time he or she feels it is in your best interest, without first obtaining your consent.

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If you withdraw from the study for any reason, you may be asked questions about your experience with GAR-936. You also may be asked to undergo whatever laboratory tests and physical examinations the doctor considers necessary.

CONSENT

I, _____, have read and understood the preceding information. I will receive a signed copy of this consent form.

Signature of Patient (Parent/Guardian/Representative)

Date of Signature

Signature of Person Administering Consent

Date of Signature

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