

CONSENT FORM

PART I NOTICE TO PATIENTS

Dear patients and families,

We are going to carry out a “Optimizing the treatment for uncomplicated acute appendicitis: a multicentre, randomized double-blinded placebo-controlled study (OPTIMA trial)”. And you may meet the inclusion requirements of this study, therefore, we would like to invite you to participate in this study. We will introduce the purpose, process, benefits and risks of this study to you. Please read it carefully before deciding whether to participate in this study. You are able to ask questions and communicate when your doctor explains and discusses this informed consent. You can make your decision after full discussion with your family, friends and doctor.

If you are currently participating in another clinical study, please inform your doctor.

WHY IS THIS STUDY BEING DONE?

Acute appendicitis (AA) is one of the most common indications for emergency surgery in the world. In 2019, there were an estimated 17.7 million cases (incidence 228/100,000). Appendectomy was first proposed by Mc Burney in 1894. For more than a century since then, appendectomy has been the golden standard treatment for appendicitis and has been widely applied in clinical practice. Although appendectomy is generally well tolerated, it is a major surgical intervention and can lead to some postoperative complications, such as bleeding, incision infection, adhesion of intestinal obstruction, fecal fistula, appendiceal stump inflammation. Therefore, how to treat acute appendicitis more effectively and safely has aroused the attention of clinicians.

Currently, laparoscopic surgery is widely used in the treatment of acute appendicitis. However, in recent years, more and more international clinical trials have confirmed that non-surgical treatment (conservative treatment) or conservative treatment followed by surgery have better therapeutic effects and lower incidence of complications. Conservative treatment also costs less, but there is a risk of recurrence. According to literature reports, the recurrence rate in Europe and America is 25%-35%. However, the choice of conservative treatment for appendicitis is varied and lack of medication standards. In addition, recent high-quality studies have reported that placebo treatment is as effective as antibiotic treatment for uncomplicated appendicitis in an Asian population.

Therefore, it is urgent for domestic clinicians to promote the standardized treatment of this most common disease in general surgery combined with national conditions and disease characteristics, so as to ensure the maximum efficacy and reduce the consumption of human, material and financial resources of patients.

WHAT ARE THE OBJECTIVES OF THE STUDY?

To explore the difference in efficacy, complication rate and medical cost between ceftazidime combined with placebo and ceftazidime combined with ornidazole in the treatment of acute uncomplicated appendicitis.

WHAT KIND OF PARTICIPANTS ARE NEEDED FOR THE STUDY?

2,400 acute appendicitis patients will be enrolled nationwide in accordance with government regulations and relevant institutional policies and procedures. The enrolled patients are eligible for the diagnosis of acute appendicitis, aged between 18 and 65 years old, and have no allergic reaction to the treatment drugs involved, no history of acute or chronic appendicitis, no liver or kidney dysfunction, sepsis and other symptoms. Female patients who are pregnant, in lactation or planning pregnancy will be excluded.

STUDY PROCEDURE AND FOLLOW-UP SCHEDULE?

The study will be conducted by 80 centers nationwide, with 2,400 cases planned to be collected, led by the General Hospital of Eastern Theater Command. During the period of your participation in this clinical study, your doctor will collect your health information periodically to evaluate the effect of this treatment from the date of formal enrollment to 1 year after the end of your treatment.

We will assign you to ceftazidime combined with ornidazole or ceftazidime combined with placebo for no more than 7 days after you agree to enroll. The doctor will evaluate treatment effect at any time, take the effectiveness and safety of treatment as the first consideration, and perform surgical treatment for you if the conservative treatment effect is not ideal.

During the study period, you should not take any medications other than those prescribed or permitted by your study physician. For your safety and to ensure the effectiveness of the study, you should not participate in any other clinical studies involving drugs and medical devices during this period. Use effective contraceptive methods throughout the study period up to 2 weeks after treatment.

We will follow you up 1 day before treatment and 1 day, 3 days, 5 days, 7 days, 1 week, 2 weeks, 1 month, 3 months, half a year and 1 year after treatment according to your treatment status. The follow-up will cover your daily health status, discomfort and treatment-related complications. All measures based on your situation are required

instead of additional examinations. If there is no need for further hospitalization, the follow-up after your treatment can be conducted by phone, outpatient service or WeChat, etc. Please confirm that you can cooperate with the doctor for follow-up within the specified follow-up time.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

Regardless of which group you are in, all ceftazidime and ornidazole used for your participation in this study will be provided free of charge, including ceftazidime and ornidazole used if conservative treatment fails and surgical treatment is required. However, the expenses related to other diseases shall be borne by you. Your doctor will closely observe you after your treatment and follow you up for at least 1 year, which will help to detect and treat any health problems during your follow-up. In the research process, professional doctors will do disease diagnosis, disease tracking observation, treatment guidance and disease consultation for you. The tests required to confirm your diagnosis, determine the extent of your disease, and assess the effect of your treatment are normal medical examinations, and this study will not add to your burden in this regard.

All drugs involved in this study have been approved in China for the treatment of patients with conditions similar to or even worse than yours. The information obtained from this study will help us develop a more reasonable, comprehensive and reliable diagnosis and treatment path and treatment norms for this disease, and promote it in patients with similar conditions to yours.

If the adverse reactions occurred during the study period due to the use of the study drugs need to be treated, the relevant expenses shall be covered by the company that provides drugs. If the adverse reactions are caused by medical negligence, the relevant expenses shall be borne by the relevant hospitals.

WHAT ARE THE RISKS OF THE STUDY?

Recurrence

Antimicrobial drugs can save you from surgical injury, but there is a certain risk of recurrence. According to the team's preliminary research results, the recurrence rate is 19% in Chinese population and 25%-35% in European and American population. But studies have shown that surgery after recurrence does not have a higher complication rate than surgery directly.

Transferring to surgery

Conservative treatment of acute appendicitis may still require surgical treatment. However, according to existing reports, reoperation after the failure of conservative treatment does not increase the incidence of surgical complications.

Adverse drug reaction

All drugs involved in this study have been extensively validated for safety and efficacy and have been approved for marketing by CFDA in China. But no drug is completely safe. During the treatment, you may not have any adverse reactions, or some drug-related adverse reactions may occur, but the adverse reactions mentioned in the study can be basically recovered after withdrawal.

According to the description in the drug instructions, the adverse reactions of the various drugs to be used in this study are as follows:

Ornidazole is generally well tolerated and the following reactions may occur during administration: 1. Digestive system: including mild stomach discomfort, nausea, bad breath, etc. 2. Nervous system: including dizziness and drowsiness, vertigo, etc.; 3. Irritation: rash, itchy, etc. 4. Others: leukopenia and so on

The adverse reactions of ceftazidime are rare and mild. A few patients may have skin rash, itching, drug fever; Nausea, diarrhea, abdominal pain; Mild phlebitis at the injection site; Occasionally transient elevation of serum aminotransferase, blood urea nitrogen and blood creatinine can occur. Leukopenia, thrombocytopenia and eosinophilia.

Your doctor and nurse will monitor your reaction at all times. If you experience any discomfort during the trial, you should inform your doctor at any time. Your doctor will give you other medications to relieve the discomfort. If you or your doctor determines that you cannot tolerate it, the study drug will be completely discontinued and you may be withdrawn from the study.

In addition to the risks of drugs, there are some related risks such as:

Imaging examination

You will be exposed to a minuscule amount of radiation during the CT examination, but these are necessary for routine diagnosis and evaluation.

Draw blood for examinations

The risks of taking blood from your arm include temporary discomfort and/or bruising. Infection, excessive bleeding, clotting, or fainting may occur, but they are highly unlikely.

Operation

Any operation may have surgical complications, and appendectomy in this project may cause bleeding, incision infection, adhesive intestinal obstruction, fecal fistula, appendicitis, etc.

WHAT ARE YOUR RIGHTS AS A PARTICIPANT?

You can choose not to participate in this study, which will have no adverse impact on your access to conventional treatment.

After you agree to participate in the study, you can change your mind at any time and tell the investigator to withdraw from the study in time. Your withdrawal will not affect your access to regular medical services. After the study is completed or discontinued, you will no longer be provided with the drugs in the study program free of charge.

COMPENSATION?

Please inform your responsible investigator of any study related injury to your health during your participation in this study and provide your contact number _____. We will take the necessary medical measures. According to China's relevant laws and regulations, in case of irreversible injury related to the study, the person in charge of this study will deal with and treat it in time and provide corresponding economic compensation.

If you have questions related to the rights and interests of patients, you may contact the clinical trial ethics committee of your hospital at: _____.

WHAT ABOUT CONFIDENTIALITY?

Your participation and personal data in the study are confidential. All study members and sponsors are required to keep your identity confidential. No personal information about you will be disclosed when the results of this study are published.

PART II STATEMENT OF CONSENT AND AUTHORIZATION

Patient informed consent Statement:

I have been informed of the research background, purpose, procedure, risks, benefits and rights of “Optimizing the treatment for uncomplicated acute appendicitis: a multicentre, randomized double-blinded placebo-controlled study (OPTIMA trial)”. I have ample time and opportunity to ask questions and I am satisfied with the answers. I am also told who to contact when I have questions or want further information. I have read this informed consent and agree to participate in this study. I know that during the study I can withdraw from the study at any point without any reason. I am told that I will get a copy of the informed consent, which contains my signature and that of the researcher.

Patient Signature:

Date:

Signature of Legal Representative [if applicable]:

Date:

Relationship with Patient:

When the patient or his/her legal representative is unable to read or write, at least one impartial witness must be present to confirm that the information in the informed consent has been correctly interpreted and that the patient and/or the subject's legal representative have understood the information. The patient voluntarily agreed to participate in the study.

Fair Witness Signature:

Date:

Statement from the researchers

I have informed the patient (and his/her legal representative) of the background, objectives, procedures, risks, and benefits of the “Optimizing the treatment for uncomplicated acute appendicitis: a multicentre, randomized double-blinded placebo-controlled study (OPTIMA trial)”, and have given him/her sufficient time to read the informed consent, discuss with others, and answer his/her questions about the study; I have informed the patient of the contact information in case of problems; I have advised the patient (or legal representative) that he/she may withdraw from the study at any time during the study period without any reason.

Signature of Researchers:

Date: