Informed consent form • notice page

Dear madam

We will invite you to participate in a clinical trial study of "the application of MRD combined with personalized immune regulation diagnosis and treatment technology in the adjuvant treatment of postoperative recurrence prevention of epithelial ovarian cancer".

Before you decide whether to participate in this study, please read the following content as carefully as possible. It can help you understand the content of this study, why to conduct this study, and the benefits, risks and discomfort this study may bring to you. A total of 20 patients are planned to be recruited in this study, of which 5 patients are planned to be recruited by the center. The research plan has been reviewed by the medical ethics committee of the Second Affiliated Hospital of Wenzhou Medical University and the Yuying children's Hospital of Wenzhou Medical University. It complies with the relevant laws and regulations of China and the declaration of Helsinki and other ethical principles to protect the rights and interests of subjects.

Research Introduction

一、Research background

Epithelial ovarian cancer (EOC) is the most common type of ovarian cancer. It is the main cause of ovarian cancer, which is the female reproductive system malignant tumor with the highest mortality rate, and seriously threatens women's health and life. Although in recent years, EOC has formed a new model of "surgery + platinum containing chemotherapy + targeted drug maintenance therapy + immunotherapy", 70% will recur within 3 years, and there is still a long way to go before the 2030 healthy China target of a 5-year survival rate of no less than 46.6%. Neoantigen basedImmune regulation diagnosis and treatment technology, such as peptide, nucleic acid and dendritic cell immunomodulatory diagnosis and treatment technology are being evaluated in clinical trials for patients with different types of tumors. In 2017, 2018 and 2023, nature successively published five research achievements on personalized neoantigen immunomodulation technology for postoperative recurrence prevention, including melanoma, glioma and pancreatic cancer, which achieved milestone breakthroughs. However, how to screen the high-risk group of EOC recurrence early and intervene has become a new exploration. From several levels of early detection of tumors, the

main reasons for recurrence and metastasis are the presence of minimal residual disease (MRD), circulating tumor DNA（Circluting-Tumor DNA,CtDNA）The positive detection of MRD is positively correlated with tumor recurrence and prognosis. It was successively incorporated into the international guidelines for colon cancer and the consensus of Chinese experts on lung cancer and breast cancer in 2021. In aCtDNA Monitoring is used in early recurrence detection research of EOC,CtDNAIt was 10 months earlier than the radiological findings and 9.1 months earlier than CA-125 (a specific marker of ovarian cancer). Based on this series of high-level evidence-based medical evidence, we urgently need to establish a new monitoring system and recurrence prevention adjuvant treatment system after EOC.

二、research objective

This study used patients' individualized tumor neoantigens to prepare peptide drugs targeting neoantigens. The main purpose was to evaluate and explore the safety and tolerability of tumor neoantigen immunomodulatory diagnosis and treatment technology for MRD positive patients with epithelial ovarian cancer to prevent recurrence. The secondary objective was to observe and evaluate the anti-tumor activity of tumor neoantigen polypeptides for preventing recurrence in patients with MRD positive epithelial ovarian cancer after surgery. The purpose of exploratory research is to observe and compare the changes of immune related indicators of patients before and after treatment.

三、What will I need to do if I take part in the research?

The first 8 weeks of this study are the preparation time of neoantigen screening, ifYou meetThe inclusion criteria and consent to participate. Taking the medication time as the first day, you will cooperate with the doctor / nurse to complete the following operations:

1. you will cooperate with the doctor to complete hematological and imaging examinations (1 day before medication);

2. you will cooperate with the doctor to complete the peptide immunomodulation diagnosis and treatment technology injection (on the 1st, 4th, 8th, 15th, 22nd, 54th and 84th days after the start of medication);

3. on the 15th, 22nd, 30th, 54th, 84th, 90th and 120th days of clinical research, you will need to

visit the hospital and cooperate with the researcher to complete hematological and imaging examinations.

四、What are the inclusion and exclusion conditions?

- **Inclusion criteria**

1. voluntarily join this study and sign the informed consent;

2.18-70 years old;

3. be able to comply with the research protocol in the judgment of the researcher;

4. patients with stage II, III and IV EOC who can undergo satisfactory surgical resection and provide sufficient tumor materials;

5. sufficient tumor material must be provided in formalin fixed paraffin embedded (FFPE) blocks or sectioned tissues (only approved by the sponsor), preferably from resection. Specimens should be submitted together with the relevant pathology report. Multiple samples can be provided according to the situation, but priority should be given to the tissue with the highest tumor content and the lowest necrosis area;

6. patients should meet the following biochemical indicators: total bilirubin ≤ 2 × upper limit of normal (ULN); Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤ 2 × upper limit of normal (ULN); Creatinine clearance ≥ 60 ml/min;

7. patients should meet the following hematological indicators: neutrophil count ≥ 1.5 × 109 /l; Hemoglobin ≥ 10.0 g/dl; Platelet count ≥ 100 × 109 /l;

8. expected survival ≥ 3 months;

9. Eastern Cooperative Oncology Group (ECoG) performance status is 0 or 1;

10. postoperativeCtDNAMRD was positive, routine blood indicators were negative, and imaging was negative.

- **Exclusion criteria**

1. the patient has human immunodeficiency virus (HIV) infection, hepatitis B virus (HBV) infection, hepatitis C virus (HCV) infection, uncontrollable coronary artery disease or asthma, uncontrollable cerebrovascular disease or other diseases that the investigator believes are not eligible;

2. those with a history of bone marrow or organ transplantation;

3. coagulation dysfunction;

4. those with gastrointestinal bleeding or gastrointestinal bleeding tendency;

5. subjects with immunodeficiency or autoimmune diseases;

6. Patients who have received other immunotherapies within 1 month (such as immune checkpoint inhibitor therapy, therapeutic antibody therapy, immune cell therapy and immune system regulator therapy);

7. those who may be allergic to immunotherapy;

8. patients whose informed consent or research implementation is affected by drug abuse, clinical or psychological or social factors;

9. pregnant and lactating women;

10. patients who are participating or have participated in other clinical trials within 1 month;

11. any uncertain factors affecting the safety or compliance of patients.

五、If you participate in this study, what benefits will you get?

1) Testing your specimen will help diagnose the diseasemakeDiagnosis, provide necessary suggestions for your treatment, or provide useful information for disease research.
2) For some (but not all) patients who are suitable for this study, tumor neoantigen peptide therapy may or may not reduce your tumor burden.
3) The knowledge gained in this study may also help other cancer subjects in the future.

六、What are the risks for me to participate in the research?

A total of 20 patients are planned to be recruited in this study, of which 5 patients are planned to be recruited in this center. We will keep all your information confidential. Your sample collection will strictly follow the aseptic requirements. There may be some very small risks in the sample collection, including transient pain, local cyanosis, mild dizziness for a few people, or extremely rare needle infection.

You have been clearly informed of the potential clinical risks of enrolling in this clinical trial. Each patient will be different according to their own condition.The principal investigator of this clinical trial, has been associated withYou knowInform and discuss the specific operation contents of relevant clinical trials. If the patient has questions, the patient can discuss with the main investigator of this clinical trial at any time. Some uncommon risks may not be

listed here:

1. There are potential risks to any treatment.

2. Any drug used may produce side effects, including mild nausea, rash and other symptoms to severe anaphylactic shock, and even life-threatening.

3. Tumor neoantigens are closely related to tumor specific mutations. If your tumor gene sequencing analysis fails to find the appropriate neoantigens, you will not be able to complete the next step of treatment and will be excluded from this study.

4. Possible risks of tumor neoantigen peptide therapy and doctors' Countermeasures:

Tumor neoantigen peptide therapy may cause one or more side effects, as shown in the list below. This information comes from the data of tumor subjects in other clinical trials of tumor neoantigen peptide therapy. IfYou happenPlease inform your doctor or nurse immediately of any side effects.

The side effects of local injection of tumor neoantigen peptide therapy include:

1) Local reaction at injection site
2) Flu like symptoms
3) weak
4) rash
5) pruritus
6) fever
7) headache

The main adverse reactions were grade 1 adverse reactions, grade 2-5 adverse reactions were rare, and the incidence of adverse events was mild and controllable.

Your responsible doctor and nurse will work closelyWatch youSymptoms and signs, and routine examination, including physical examination, blood examination, imaging examination, etc. And treat the side effects symptomatically.

5. If you suffer from hypertension, heart disease, diabetes, liver and kidney dysfunction, venous thrombosis and other diseases, or have a history of smoking, these risks may increase, or there may be related intraoperative or postoperative exacerbations or cardiovascular and cerebrovascular accidents, or even death.

6. The treatment of tumor is a complex and difficult process, and no treatment method can guarantee the complete control of tumor growth. Tumor neoantigen peptide therapy does not ensure that you will have obvious benefits in the treatment process, and the tumor may still continue to progress and deteriorate during the treatment process.

Safety assurance of clinical trials is an important part of clinical trials. We have the following risk response plans to ensure that clinical trials can be carried out smoothly and avoid irreversible serious consequences.

1. emergency prediction and disposal: safety risk prevention and control, close monitoring and data reporting, emergency disposal and related declaration and notification procedures.

2. situation handling process: if you have any discomfort during the study, or new changes in your condition, or any unexpected situation, whether related to the study or not, you should notify your doctor in time, and he / she willmakeJudge and give appropriate medical treatment. During the study period, you need to go to the hospital for follow-up and do the corresponding examinations on time, which takes up your time and may cause trouble or inconvenience to you.

3. plan drilling and revision: regularly organize drills every half a year, train and train participants, find out deficiencies and problems, and timely improve and revise the emergency plan.

七、Will participating in this study increase my medical expenses?

All patients with ovarian cancer need tumor tissue gene sequencing before immunotherapy. This research group will be responsible for the specimen transportation, tumor tissue gene mutation sequencing, gene expression sequencing, and tumor neoantigen polypeptide preparation involved in this study; Part of the costs incurred by the relevant immune tests during the treatment and the standardized clinical diagnosis and treatment received during the treatment (such as hospitalization, blood test and imaging diagnosis, etc.) areYou are normalYou should pay for the clinic at your own expense according to the hospital charging standard andHealth insurance relatedPolicy. Therefore, this study will not add additional financial burden to you.

八、What will be the compensation for participating in this study?

You will not receive any financial compensation for participating in this study.

九、Damages

If you are injured due to your participation in this study: in case of any damage related to this clinical study, you can receive free treatment and / or corresponding compensation according to China GCP (quality management code for clinical trials of drugs) and general principles of civil law.

十、Is personal information confidential?

If you decide to participate in this study, your personal information and related materials during the trial and your participation in the trial are confidential. All test results (including personal data, test documents, etc.) appearing in the original medical records will be completely confidential within the scope of the law, and only your initials and numbers assigned when you participate in the test will appear. If necessary, only your initials and numbers will appear in relevant research summaries, articles, and public publications.

When necessary, the drug regulatory department, the ethics committee or the project funding department can consult the data of the subjects participating in the study according to the regulations. However, without permission, they will not use the information of the subjects participating in the study for other purposes or disclose it to other groups.

十一、How can I get more information?

You can ask any question about this experimental study at any time. You can consult Dr. Zhang Xinxin at 15067810815. (mobile number)

If there is any important new information during the trial that may affect your willingness to continue participating in the study, your doctor will notify you in time.

十二、Do I have to take part in this research or can I quit halfway?

It is entirely up to you to participate in this study. You may refuse to participate in this study. You have the right to withdraw from the study at any time during the study. IfYou refuseIf you participate in or withdraw, your benefits will not be affected, nor will you be discriminated against or retaliated for it. If you choose to participate in this study, we hope you can insist on completing the whole trial process.

Your doctor or researcher may suspend your participation in this trial at any time for the best interests of you.

十三、Is there any other treatment currently available?

At present, the preferred chemotherapy after EOC is: Paclitaxel / carboplatin, 3 weeks treatment; Paclitaxel/carboplatin/ShellfishValgus chinensisFor anti maintenance, please consult the investigator or your doctor for your specific treatment. This study is a supplement and improvement to the normal diagnosis and treatment procedures, and participation in this study does not affectYou are normalDiagnosis and treatment process.

十四、What should we do now?

Whether to participate in this pilot study is up to you. You can discuss with your family or friends before making a decision.

Before you make the decision to participate in the trial, please ask your doctor for relevant questions as far as possible until you fully understand the trial.

十五、Ethics committee

If you have any dissatisfaction in the study, please contact the medical ethics committee of the Yuying children's Hospital Affiliated to Wenzhou Medical University, the Second Affiliated Hospital of Wenzhou Medical University.

Ethics Committee Office: Longwan District Ethics Committee Office of Yuying children's Hospital Affiliated to Wenzhou Medical University, the Second Affiliated Hospital of Wenzhou Medical University.

Contact: Teacher Chen Tel.: 0577-85676879

Thank you for reading the above materials. If you decide to participate in this experimental study, please tell your doctor, and he / she will arrange all matters related to the experiment for you.

Please keep this information.

Informed consent form • consent signature page

Declaration of consent

1. I have read this informed consent form, and the relevant person in charge of the project has explained the purpose, content, risks and benefits of this test to me in detail.

2. I have discussed and asked relevant questions about this study, and the answers to these questions are satisfactory to me.

3. I have enough timemakeDecision.

4. I voluntarily agree to participate in the clinical research described in this article.

5. if I withdraw due to the reason of this product, I will inform the doctor of the change of my condition in time,

6. if I need to take any other treatment due to the change of my condition, I will consult the doctor in advance or tell the doctor truthfully afterwards.

7. I agree with the representatives of the drug regulatory department, the ethics committee or the project funding department to consult my research materials.

8. I will obtain a signed and dated copy of the informed consent form.

Finally, I decided to agree to participate in this pilot study and promised to follow the doctor's advice.

Signature of the subject: Date:

Contact number of the subject:

Signature of legal representative: Date:

Relationship with the subject: legal representative Tel.:

No

I confirm that I have explained the details of this study to the subject, including his rights and possible benefits and risks, and gave him a copy of the signed informed consent.

Signature of doctor: Date:

Contact information of study doctor:

(this page is a necessary part of the subject's informed consent. Each "subject's informed consent" must be signed and dated by the subject or legal representative and the research doctor before it is valid.)