Informed Consent Form

Introduction

We sincerely invite you to participate in this phase I clinical study called ″ Camrelizumab combined with Apatinib to induce pathological efficacy of locally advanced oral squamous cell carcinoma.″ This study was conducted by Zhong Laiping (doctor) and planned to enroll 20 subjects. This study has been reviewed and approved by the Ethics Committee of the Ninth People ' s Hospital affiliated to Shanghai Jiao tong University School of Medicine.

Before you decide to participate, it is necessary to understand the purpose and content of the study. Please read this introduction carefully and discuss it with your doctor, family and friends. If there is anything unclear, or you want to know more, please ask the doctor or directly contact the person listed after the introduction.

Purposes

Neoadjuvant therapy is currently considered to be an effective adjuvant therapy. It can shrink the tumor body or reduce its growth rate for advanced tumors, which can greatly improve the probability of complete resection of the original lesion during surgery and the effect of postoperative radiotherapy. The research drugs used in this study are the targeted drugs Apatinib and Camrelizumab, which are anti-tumor targeted drugs and immune drugs, respectively. Both anti-tumor drugs are Anti-tumor drugs developed and approved by Hengrui Medicine. Humanized PD-1 antibody binds to human PD-1 receptor and blocks its pathway to restore the body's anti-tumor immunity. At present, tumor immunotherapy has a long duration of remission to the tumor and a low incidence of adverse reactions, but there are also Some patients are unable to relieve the therapy, leading to abandonment due to disease progression. On the other hand, although anti-tumor targeted therapy can achieve remission early in the treatment, the duration of remission is short and it is prone to drug resistance. Combining the characteristics of the above two therapies, anti-tumor immunotherapy combined with targeted therapy has very good application prospects, which can not only improve the remission rate, but also obtain continuous clinical treatment benefits. Therefore, immunotherapy combined with targeted therapy is inevitably one of the future trends of anti-tumor therapy. How to carry out combined medication is a problem that needs to be further solved.

Oral squamous cell carcinoma is the most common malignant tumor of the oral and maxillofacial region, with a poor prognosis. Improving the survival rate of patients after treatment is the common goal of clinicians and patients. At present, the treatment of patients with locally advanced oral squamous cell carcinoma mainly includes

surgery, radiotherapy and chemotherapy. Preoperative induction therapy is still being studied at home and abroad in terms of whether it can improve patient survival. In this study, strict clinical research design standards were used to induce treatment of patients with locally advanced oral squamous cell carcinoma by Camrelizumab combined with Apatinib, combined with pathological efficacy and drug safety results The feasibility has important clinical significance for improving the overall survival rate of patients with locally advanced oral squamous cell carcinoma.

Selection criteria

Inclusion criteria:
1 Age: 18 to 75 years old
2 Gender: male and female
3 ECOG PS score: 0-2 points;
4 Histopathological diagnosis of oral squamous cell carcinoma (including tongue, gums, cheeks, mouth floor, hard palate, posterior molar region)
5 The primary tumor is clinical stage III / IVA (T1-2, N1-2, M0 or T3-4, cN0-2, M0, AJCC 2018)
6 blood routine: white blood cells> 3,000 / mm3, hemoglobin> 8g / L, platelets> 80,000 / mm3
7 Liver function: ALAT / ASAT <2.5 times the upper limit of normal, bilirubin <1.5 times the upper limit of normal
8 Renal function: serum creatinine <1.5 times the upper limit of normal
9 Sign the informed consent
Exclusion criteria:
1 There are still any toxic reactions of CTCAE level 2 or above caused by previous anti-cancer treatment;
2 Obvious cardiovascular abnormalities (such as myocardial infarction, superior vena cava syndrome, heart disease of grade 2 or higher diagnosed according to the classification criteria of the New York Heart Association (NYHA) 3 months before enrollment);
3 Active severe clinical infection (> NCI-CTCAE5.0 version 2 infection);
4 Uncontrollable hypertension (systolic blood pressure> 150 mmHg and / or diastolic blood pressure> 90 mmHg) or cardiovascular disease with clinical significance (such as activity)-such as cerebrovascular accident (≤ 6 months before randomization), myocardial infarction (≤6 months before randomization), unstable angina, New York Cardiology Society (NYHA Appendix 5) congestive heart failure grade II or above, or severe arrhythmia that cannot be controlled with drugs or has potential impact on experimental treatment;

5 Women during pregnancy or lactation;
6 Those who have participated in other clinical studies and received any other research medication within 30 days before entering the group;
7 Other circumstances that the investigator considers unsuitable to participate in the study.

Research procedure:
If you agree to participate and meet the eligibility criteria, you will be included in the study. This clinical study uses a prospective single-arm single-center phase I clinical study. Your doctor will perform preoperative induction therapy, surgery and postoperative radiotherapy, and various methods of comprehensive sequential treatment in accordance with current domestic and foreign treatment standards.
The research process includes three stages: screening stage, treatment stage and follow-up stage.
• Screening stage: if you are willing to participate, the doctor will collect your clinical data (which may include the results of previous medical examinations) and improve the relevant examinations to determine whether you are suitable for entering the study after obtaining your written signed consent .
• Treatment stage: If you meet the enrollment criteria for this clinical study, the doctor will use three cycles of Camrelizumab combined with induction therapy of Apatinib, surgical treatment, and postoperative radiotherapy and chemotherapy to complete your treatment.
• Follow-up phase: The doctor ’ s follow-up observation of your study will continue until 24 months after treatment, and the follow-up observation time may be extended if necessary. During this time, you may also need to undergo some safety medical observations or examinations.
Possible benefits and risks
In order to compensate for the inconvenience that you may bring to participate in this study, this study will provide you with the full cost of the drug Camrelizumab during the induction treatment of this study. Patients can receive priority access to the green channel rights of expert teams for diagnosis, consultation, surgery, follow-up and various related auxiliary examinations.
If you combine the treatment and examination required for other diseases at the same time, and the cost of switching to other treatments due to ineffective treatment, it will not be free.
All treatments have certain risks.
Targeted therapies and immunotherapeutics have certain toxic / side

effects. The main adverse reactions of Camrelizumab are: weakness, fatigue, nausea, decreased appetite, rash, etc. Most immune-related adverse reactions can be controlled or even reversed by delayed administration in combination with corticosteroids. The main adverse reactions of Apatinib are: (1) Hand and foot syndrome, which is characterized by numbness, dullness, abnormal sensation, tingling, no pain or pain, swelling of the skin, or erythema, scaling, chapped, and hard Blisters and severe pain. (2) Hypertension should be entered into the group in strict accordance with the blood pressure requirements in the entry criteria before the subjects are enrolled. Hypertensive subjects can adjust the dosage of antihypertensive drugs or add new antihypertensive drugs before taking the test drugs Achieve blood pressure control (3) Proteinuria Closely monitor proteinuria for all patients throughout the treatment period, and strengthen monitoring for patients with a history of hypertension; for subjects who have 2 consecutive urine protein ≥2 +, 24-hour urine protein Determination. (4) Gastrointestinal bleeding Including upper gastrointestinal bleeding and lower gastrointestinal bleeding, hemostasis, blood transfusion, and supportive treatment should be given; for those who cannot control the bleeding, surgical assistance should be sought immediately. (5) Thrombosis Any arterial thrombosis (such as cerebral ischemia, stroke, angina, myocardial infarction, etc.) should be stopped immediately with Apatinib.

Any treatment may cause unpredicted adverse reactions. We will regularly observe blood routine, blood biochemistry, electrolytes, coagulation mechanism, maxillofacial and chest CT to observe possible side effects / adverse reactions caused by this study, and professional doctors will take relevant measures to prevent and treat them. If any discomfort and adverse reactions occur, please contact the research doctor in time, and the research doctor will give active diagnosis and treatment.

The researcher will inform you or your legal representative in time if they receive information that may affect the subject ’s continued participation in the trial. For reasons of your health or safety, the doctor has the right to terminate your continued participation in this study at any time, including but not limited to the following reasons: 1. It is found that you do not meet the enrollment requirements; 2. You did not follow the requirements of the research plan Treatment and follow-up; 3. The doctor thinks it is better to choose other treatment methods; 4. During the study, other safety factors were found and it was determined that you are not suitable for continuing to participate in the study; 5. The study was terminated early.

In addition, any treatment may be ineffective, and the disease may continue to develop due to ineffective treatment or other diseases.

Alternative treatment options
If you choose not to participate in or withdraw from this study, you still have the right to accept other surgical or non-surgical treatment options under the professional advice of the attending physician.
Whether you will ultimately participate in this study will not affect your doctor's medical objective evaluation and decision-making judgment of your condition and related treatment options.

Rights and obligations
Participation in the study is completely voluntary, you can withdraw from this study at any time without conditions, but it will never affect your relationship with medical staff and future diagnosis and treatment. All your information will be kept strictly confidential, and only relevant personnel can view your medical records, so that they can check the accuracy of the information collected and ensure that the research is carried out normally. Any electronically transmitted information will be renamed to ensure the confidentiality of the information. All information in the computer will be protected with a password. When the results of the study are reported at medical conferences and published in scientific journals, no personally identifiable information will be disclosed. If you decide to participate, we will ask you to sign an informed consent. You keep a copy.
During the research process, you are obliged to provide the research doctor with true information about your medical history and current physical condition; tell the research doctor about any discomforts that occurred during the study; you must not take restricted medicines, food, etc .; tell the research doctor Whether you have participated in other studies recently or are currently participating in other studies; at the same time, please follow the requirements of the study to complete the follow-up and carefully cooperate with the research doctor during the follow-up to complete the entire study process.
After reading the introduction and discussing with your doctor, if you have other questions or concerns, please contact the following persons:
Researcher: Zhong Laiping
Address: No.639, Manufacturing Bureau Road, Huangpu District, Shanghai
Department of Oral and Maxillofacial Head and Neck Oncology, Ninth People's Hospital, Shanghai Jiao tong University School of Medicine
Anyone who has questions or complaints about this study can contact the Medical Ethics Committee directly: 021-63057795.

Signature page of the subject ’ s informed consent

I have fully understood the nature, purpose, method, duration, possible risks and benefits of this clinical study. My consultation with the research doctor has been answered satisfactorily. After full

consideration, I voluntarily participated in this study and was willing to cooperate closely with the research doctor to complete the entire treatment observation process prescribed by the research plan.
1. I can consult the doctor for more relevant information at any time;
2. I can withdraw from this study at any time without discrimination or retaliation, and medical treatment and rights will not be affected;
3. I agree that relevant regulatory authorities, ethics committees, and researcher representatives should consult my research materials when needed;
4. I have obtained a copy of my informed consent signed by the research doctor and dated by me;
5. I decided to participate in this study and am willing to strictly follow the requirements of the study plan and cooperate with the doctor to complete the whole process of the study.

Subject: _____
Legal representative: _____
Subject (signature): _____
Legal representative (signature): _____
Telephone number: _____
Relationship with subjects: _____
Date:_____
signature: _____
contact number: _____
Date: _____

Research doctor (block letters): _____
Research doctor (signature): _____
contact number: _____
Date of signing: _____