CD19 CAR-T Expressing IL7 and CCL19 Combined With PD1 mAb for Relapsed or Refractory Diffuse Large B Cell Lymphoma

Informed Consent Form

Dear patient,

We invite you to participate in a " CD19 CAR-T Expressing IL7 and CCL19 Combined With PD1 mAb for Relapsed or Refractory Diffuse Large B Cell Lymphoma". Before you decide whether to participate in this study, please read the following content carefully. It can help you understand the study and why to carry out this study, the procedures and duration of the study, and the benefits, risks and inconvenience that may be brought to you after you participate in the study.

The following is the introduction of this study:

1, Research background and purpose

CAR-T cells modified by chimeric antigen receptor is a new therapy for refractory and relapsed leukemia, lymphoma and multiple myeloma. A large number of basic research and clinical trials have proved that car-t cell therapy has a huge application prospect in the field of blood tumor, and has become the most hot spot of tumor immunotherapy in recent years. It is reported that the complete remission rate of CD19-CAR-T in the treatment of refractory/relapsed B-cell acute lymphoblastic leukemia is 71-100%, and the complete remission rate in the treatment of B-cell lymphoma is about 50%. Therefore, FDA and EU have approved two products of CD19-CAR-T cells to be marketed for the treatment of refractory/relapsed B-cell acute lymphoblastic leukemia and B-cell lymphoma.

In recent years, studies have shown that targeting tumor microenvironment

is an important new method to overcome the drug resistance and poor efficacy of CAR-T cells. IL-7 and CCL19 can increase the number of CAR-T cells entering the tumor and promote the survival of T cells in the tumor. Preclinical research can significantly enhance the antitumor effect of car-t. Our team has developed a new type of CD19-CAR-T cell (CD19-7×19 CAR-T for short) expressing IL-7 and CCL19. Preclinical and preliminary clinical studies have shown that it can effectively treat refractory and relapsed B-cell lymphoma, but further clinical studies are needed to confirm it. CD19-7×19 car-t combined with PD1 mAb may further improve the therapeutic effect of CAR-T cells. The purpose of this study was to observe the safety and efficacy of the new CD19-7×19 CAR-T cell therapy combined with PD1 mAb in the treatment of refractory / relapsed B-cell lymphoma. You may obtain complete or partial remission of the disease from the treatment in this study, so as to prolong your life; however, it may not be effective and beneficial. This study is a clinical study initiated by researchers and has been reviewed and approved by the ethics committee of the Second Affiliated Hospital of Zhejiang University Medical College.

2, Specific procedures and processes

The main process of this study is as follows: (1) before entering CAR-T cell therapy, the researcher (Doctor) will evaluate whether you meet the entry conditions of this study according to your condition and relevant

examination results; (2) if you meet the entry conditions, your T cell will be collected 8-12 days before cell therapy; (3) before cell transfusion, you will receive a course of chemotherapy with the purpose of reducing swelling After the preparation, identification and quality control of CD19-7×19 car-t cells (about 10-14 days), you will be hospitalized in hematology ward to receive cell reinfusion; (5) after cell reinfusion, you will continue to be hospitalized for about 2 weeks to observe the side effects; (6) CD19-7×19 On the 31st day after car-t cell transfusion, PD1 mAb should be infused; (7) you need to go to the hospital regularly to review the examination related to lymphoma and car-t cell therapy after discharge; (8) you also need to receive regular telephone follow-up from the doctor. About 24 patients are expected to participate in this study. The start and end time of the study is from the time you sign the informed consent, and the follow-up time is 2 years.

3, What do you need to do if you participate in the research

During the study period, you need to receive pre CAR-T clinical evaluation, including blood routine, biochemical examination, physical fitness examination, imaging examination, etc.; after entering the group, you need to cooperate to complete leukocyte monoculture; before reinfusion, you need to go back to the hospital for a course of chemotherapy and cell reinfusion; after reinfusion, you need to continue to be hospitalized for observation or corresponding treatment; after discharge, you need to

cooperate with our follow-up, and regularly go back to the hospital for reexamination and phase examination Check and evaluate the therapeutic effect.

4, Possible benefits from participating in this study

If you agree to participate in this study, you may have direct medical benefits, including complete or good partial remission of lymphoma. But it may not benefit. We hope that the information from the study you participated in will be instructive to the patients with the same condition in the future.

5, Possible adverse reactions, risks and risk prevention measures

The possible side effects of CD19-7×19 CAR-T cell therapy are as follows:

(1) Common (incidence more than 10%): fever; leukopenia; Thrombocytopenia; nausea, poor appetite; diarrhea; tachycardia.

(2) Common (incidence > 1% - < 10%): infection; hypotension; transaminase rise; hydrothorax.

(3) Uncommon (incidence > 0.1% - < 1%): poor coagulation; renal insufficiency; brain edema.

(4) Rare (incidence < 0.1%): very few patients may be life-threatening due to severe cytokine storms and other side effects, leading to death.

(5) Unknown risks: there may be some unpredictable risks and adverse reactions.

Possible side effects of PD1 mAb treatment:

Hypothyroidism, hyperthyroidism, pneumonia, enteritis, severe skin reactions and hepatotoxicity.

You may not have any adverse reactions, or some of them may be mild, moderate or severe. If the above adverse events occur, your research doctor will give you active symptomatic treatment.

The risk of chemotherapy

Fludarabine and cyclophosphamide should be used as pretreatment before CAR-T cell treatment.

Side effects of fludarabine: the most common side effects include myelosuppression (leukopenia, thrombocytopenia, and anemia), fever, chills, and infections including pneumonia. Other frequently reported adverse reactions are edema, discomfort, fatigue, weakness, peripheral neuropathy, visual impairment, anorexia, nausea, vomiting, diarrhea, gastritis, and skin erythema.

Side effects of cyclophosphamide: myelosuppression (minimum 1-2 weeks, generally 7-10 days, 3-5 weeks recovery), alopecia, gastrointestinal reaction, stomatitis, cystitis, pneumonia, excessive antidiuretic hormone secretion were reported in some cases. The general dose has little effect on platelets, and rarely causes anemia. In addition, cyclophosphamide can kill sperm, but it is reversible.

Risk of bleeding

The risk of drawing blood from an arm vein includes brief discomfort and / or cyanosis. Infection, bleeding, clotting, or syncope may occur, although the possibility is small.

(Note: the content is only for the possible risks related to the measures or interventions in this study, please distinguish it from the content of routine clinical treatment)

6, Description of expenses

Participation in this study, CAR-T cell preparation and related tests are free of charge, and the cost is borne by the researchers. In addition, the medical expenses incurred shall be paid by you or your medical insurance.

7, Compensation for participating in the study, including compensation for damages

Compensation: there is no economic subsidy for participating in this test.

Compensation: during the period of participating in the clinical study, if there is damage related to the study, you will receive free treatment; the hospital has purchased insurance for the research project initiated by the researcher after passing the ethical review, if there is damage related to the study, you will be compensated according to the relevant laws and regulations.

8, Alternatives

In addition to participating in this study, you have the following options:

Routine treatment plan

Clinical trials of other new drugs

Please discuss these and other possible options with your doctor.

9, Confidentiality of your personal information

Your medical records (including research medical records, physical and chemical examination reports, etc.) will be kept in the hospital as required. In addition to the researchers, ethics committee, supervision, audit, drug administration and other relevant personnel will be allowed to access your medical records, other personnel not related to the study have no right to access your medical records without permission. A public report of the results of this study will not disclose your personal identity. We will make every effort to protect the privacy of your personal medical data to the extent permitted.

10, Termination of study

Whether or not to participate in this study depends entirely on your willingness. You may refuse to participate in the study, or withdraw from the study at any time during the study without any reason, which will not affect your relationship with the doctor, and will not affect the loss of your medical or other benefits. In addition, your participation in this study may be terminated for the following reasons:

1. You did not comply with the study doctor's orders.

2. You have a serious situation that may require treatment.

3. The study doctor believes that termination of the study is best for your health and well-being.

11, Ethics committee

This study has been reported to the human body research ethics committee of the Second Affiliated Hospital of Zhejiang University Medical College, and has been approved by the committee after comprehensive review and risk assessment including the subjects. In the process of research, please contact the human body research ethics committee of the Second Affiliated Hospital of Zhejiang University Medical College, Tel: 0571-87783759 during the day; evening (total class): 13757118366; email address: hrec2013@126.com

---

I confirm that I have read and understood the informed consent of this study, voluntarily accepted the treatment methods in this study, and agreed to use my medical data for the publication of this study.

Subject signature:

Contact:

Date:

Signature of agent:

contact information with subject date(if required)

Witness (if required):

Contact:

Date:

I confirm that I have explained the details of this study to patients, including their rights, potential benefits and risks, and have given them a copy of the signed informed consent.

Signature of researcher:

Contact: (mobile)

Date: