Official Title Blinatumomab as a bridge to allo-HSCT in HR BCP-ALL patients

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Informed Consent Form for Subjects
(Informed Consent Form)

Prospective Multicenter Clinical Study of Blinatumomab as a Bridge to Allo-HSCT in High Risk B-cell precursor ALL

Dear Ms./Mr.

You are being invited to participate in a clinical study. The following items describe the background of the study, the purpose of the study, the methods of the study, the benefits and possible discomfort and inconvenience of the study, and your rights and interests, and should be read carefully before you participate in the clinical study. This informed consent form provides you with information to help you decide whether to participate in this clinical study. If you have any questions, please ask the physician in charge of the study to ensure that you fully understand the content. Your participation in this study is voluntary. If you agree to participate in this clinical study, please sign the signature page of the informed consent form.

I. Background of the study

With the use of intensive chemotherapy regimens, complete remission rates are 70 to 90%,but and 30 to 50% of them still have MRD positive.The five-year haematological recurrence rate is 56% to 100% in MRD-positive patients, compared with 18% to 33% in MRD-negative patients. Pre-transplant MRD levels affect overall survival (OS) and relapse-free survival (RFS). Patients with lower MRD have longer survival and lower recurrence rates. Therefore, complete molecular remission before allogeneic hematopoietic stem cell transplantation is extremely important to improve the prognosis of acute lymphoblastic leukemia.

In recent years,immunotherapy developed rapidly and effectively.The B-lineage surface antigen CD19 is expressed on more than 90% of B-cell precursor ALL blasts. Blinatumomab is a bispecific T-cell engager antibody construct,which binds to CD3-positive cytotoxic T cells and to CD19-positive B cells. Patient's endogenous T cells recognize and eliminate CD19-positive ALL blasts immediately.In BLAST study,blinatumomab induced MRD negativity in most patients and resulted in high rates of RFS and OS. In our center,three high risk BCP-ALL recevied Blinatumomab and allo-HSCT.High response rate,no severe CRS/ICANS,no serious infection,and three patients sustained remission.

II. Study name and purpose

This is a prospective clinical trial study to investigate the efficacy and safety of blinatumomab as a bridge to HR BCP-ALL,and explore the prognosis .

III. Study methods and content

The study is a multicenter, open, randomized, controlled, prospective study with an expected study duration of 2 years. 80 high risk subjects are planned to be included in the experimental and control groups in a 1:1 ratio. Patients were randomly assigned to each experimental group and numbered according to the envelope method.

Experimental group: 40 patients received Blinatumomab for 2 weeks (9 μg per day during day 1 to 3 and 28 μg per day for day 4 to 14).BUCY allogeneic hematopoietic stem cell transplantation were

strarted on day 15.
Control group: 40 patients are treated with BUCY allo-HSCT.

IV. Study procedure and time frame
The efficacy was assessed within 2 years after treatment, and the assessment indexes included bone marrow, MRD, and immune function.

V. Possible benefits of participating in the study
With this study, immune function before and after Blinatumomab is free, and this study may be beneficial to improve the prognosis of HR BCP-ALL, potentially providing benefits for other patients in the future.

VI. Possible risks and discomforts of participating in the study
CRS/ICANS may occur during Blinatumomab.Steroid and IL-6 receptor can be used to alleviate CRS/ICANS.During allo-HSCT,we will be faced with infection,bleeding,GVHD and transplant-related toxicity.If a very small number of patients do not recover completely from discontinuation of the drug, we can provide therapeutic support.

VII. Treatment and financial compensation for subjects with study-related injuries
In case of study-related injuries, the study sponsor will bear the relevant medical treatment costs and corresponding financial compensation according to the relevant laws and regulations of China.

VIII. Conventional treatment plan outside the study
None.

IX.Subjects rights
Subjects rights to participate in the study include voluntary participation and withdrawal at any time, informed participation, consent or non-consent, confidentiality, compensation, free treatment and compensation in case of damage, no discrimination or retaliation at any time after withdrawal, and medical treatment and rights will not be affected as a result.

X. Confidentiality of clinical research data
The information and data recorded by the subjects participating in the study will be kept strictly confidential and will not be disclosed, and if the study results are published, the subjects identity information will also be kept confidential.

XI. Collection and management of biological samples involving human subjects
3ml of peripheral blood and 3ml bone marrow will be collected from the subjects each time according to the follow-up plan, separated from the routine examination, without additional collection times, mainly for immune cell biology analysis and translational medicine research, and the specimens will not be used for product development, sharing and secondary use, etc., and privacy protection, destruction and disposal will be strictly observed.

XII. Contact information

Contact person and contact information of the investigator (contact person: KangHuizhu, contact information: 0512-67781521), contact person and contact information of the ethics committee (contact person: Wu Shangejie, contact information: 0512-67972743), contact person and contact information in case of problems.

XIII. Declaration and signature

Subject declares that I have read this informed consent form carefully and that I have had the opportunity to ask questions and that all questions have been answered. I understand that participation in this study is voluntary and that I may choose not to participate in this study or withdraw from the study at any time with notice to the investigator without discrimination or reprisal, and that any of my medical treatment and rights will not be affected as a result.

If I require other treatment, or if I fail to comply with the study plan, or for any other valid reason, the study physician may terminate my continued participation in this clinical research study.

I voluntarily agree to participate in this clinical study, and I will receive a signed copy of the "Informed Consent" form.

Subjects name (in block letters);
Subjects signature:
Date: Month and year:
Mobile phone number:
Name of legal representative (in block letters):
Signature of legal representative:
Date: Month and year.
Mobile phone number:
Relationship to subject:
Subjects reason for not being able to sign informed consent:

The investigator declares that I have accurately informed the subject of the contents of the informed consent form and have answered the subjects questions, and that the subject is voluntarily participating in this clinical study.

Investigators name (in block letters):
Investigators signature:
Date: Month and year:
Mobile phone number: