Official title A Multicenter Clinical Study of a TPO Receptor Agonist (Eltrombopag) in the Acceleration of Engraftment Post Hematopoietic Stem Cell Transplantation of Bone Marrow Failure Diseases

NCT number N/A

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Informed Consent Form

Dear Madam/Sir,

You will be invited to participate in a clinical study. The following describes the research background, purpose, research methods, the procedure, benefits and possible side effects. Please be sure to read carefully the benefits, possible discomfort, and your rights during the study before participating in the clinical study. This informed consent provides you with information to help you decide whether to participate in this clinical study. If you have any questions, please do not hesitate to ask the physicians 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 on the signature page of the informed consent.

1. Background

Bone marrow failure syndrome (BMFS) is a kind of hematopoietic dysfunction disease caused by congenital or acquired hemopoietic stem cell (HSC) function deficiency. Its main manifestation is continuous and progressive bone marrow failure. The blood cells of one or more lineages are reduced and it is more likely to progress towards hematological malignancies. BMFS includes secondary bone marrow failure caused by infection, tumor, drugs, as well as aplastic anemia (AA), myelodysplastic syndromes (MDS), paroxysmal nocturnal haemoglobinuria (PNH), Fanconi anaemia (FA) and other primary bone marrow failure. For secondary BMFS, the treatment is mostly targeted at the causes of the disease, while the treatment of the primary BMFS depends on immune regulation and allogeneic hematopoietic stem cell transplantation. However, a single traditional treatment is difficult to satisfy the efficiency. Eltrombopag is a kind of novel TPO receptor agonist (TPO-RA). Due to its small molecule non-peptide substance and different binding site from traditional TPO, eltrombopag has a higher binding rate with C-MPL and is not easy to generate endogenous antibodies, which has a more promising application prospect.

2. Research aims

The main objective of this study is to evaluate the efficacy and safety of eltrombopag in acceleration of engraftment post HSCT of BMFS patients. Eltrombopag can improve the condition of poor hematopoietic reconstruction and increase the overall survival. In this study, we aim to improve the prognosis of BMFS patients who undergo HSCT.

3. Research methods

You will be randomly assigned to either the eltrombopag group or the control group. In the eltrombopag group, eltrombopag will be administered orally 50mg once daily for the first week, starting on day 4 after HSCT. If well tolerated, the dose will be increased to 75mg/d (maximum 100mg/d) in the second week, otherwise, the dose will be gradually reduced until tolerated. After day 31 post HSCT (4 weeks of treatment), the use of eltrombopag was discontinued regardless of the presence or absence of treatment response. The control group received recombinant human thrombopoietin (rhTPO)

300U/d subcutaneously for 14 days from day 4 to day 17 post HSCT.

4. Procedure and possible duration

Once enrolled in the study, you will undergo three stages: screening period, experimental period and follow-up period. The screening period will be completed within 3 days right after transplantation, mainly including evaluation of liver and kidney function and physical strength. If the requirements are met, the experimental period will be started with a maximum of 4 weeks. Of course, if platelet reconstruction occurs during the process, we will stop the drug in time to prevent the occurrence of possible thrombosis events. After 4 weeks, your condition will be evaluated by the investigator, followed by a 2-year follow-up period, during which you will have regular complete blood cell test, organ function, virus antibody monitoring and other related tests to ensure that the investigator can know your disease status.

5. Benefits

Once you are enrolled in the clinical trial, the investigator will provide eltrombopag for free (25mg/ tablet) during the enrollment period (4 weeks). For patients undergoing HSCT, eltrombopag offers a novel therapeutic option with the potential to promote platelet graft inactivation in patients with BMFS.

6. Possible discomfort

Referring to the adverse reactions in the current clinical trials of eltrombopag, the main adverse events are thrombotic events, mild liver dysfunction and cataract, but the reported incidence is less than 5%.

7. Treatment related to side effects of eltrombopag

During the clinical trial, if there is a thrombosis event, eltrombopag will be stopped immediately and low molecular weight heparin will be given subcutaneously. Blood coagulation routine examination, regular evaluation of B-ultrasound of thrombosis changes will be implemented. Filters will be placed to prevent further damage if necessary. If liver dysfunction occurs, eltrombopag will be reduced, and treatment will be carried out to lower the enzyme of liver. If you have drug intolerance, the dosage should be reduced. If you develop cataracts, you will stop the drug and receive eye evaluation and suggestions from specialists. If you suffer from any injury related to the study, the researcher will bear the relevant medical expenses and corresponding economic compensation according to the relevant laws and regulations of China.

8. Rights of participants

You have the following rights to participate in the clinical trial, including voluntary participation and withdrawal at any time, confidentiality of your data, free medical treatment and compensation in case of injury related to eltrombopag.

9. Confidentiality of clinical research data

The investigator is responsible for handling your study data in accordance with

applicable data protection regulations. The information is available during departmental inspection. The results may all be published in medical journals/conferences, but your identity will not be made public. Your authorization to use your health information remains valid until the study is completed. However, you can withdraw the informed consent at any time through the study of the doctor in charge.

10. Sample collection and management

We need to collect your samples of body fluid, peripheral blood and bone marrow for blood and urine routine test, peripheral blood smear, organ function, HBV, HCV, and HIV infection, curative effect evaluation of TB infection, blood and urine pregnancy test. The specimen will be destroyed by us when the clinical trial is over. It is guaranteed that the samples won't be used for anywhere else.

Statement

I have read this INFORMED CONSENT carefully. I own the opportunity to ask questions and all questions have been answered. I understand it’s voluntary to participate in this study. I can choose not to participate in this study. I can withdraw from the study after informing the researcher at any time without being subjected to discrimination. I voluntarily agree to participate in the clinical study and I will receive a signed copy of the informed consent.

My name _____

Phone number _____

Date _____