Sequential Transplantation of Umbilical Cord Blood Stem Cells and Islet Cells in Children and Adolescents with Monogenic Immunodeficiency Type 1 Diabetes Mellitus

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Informed consent form

Dear parents of _____:

Your child was diagnosed as monogenic immunodeficiency type 1 diabetes mellitus in our hospital. This disease is a rare disease due to congenital deficiency of the immune system, resulting in abnormal immune function, and type 1 diabetes mellitus occurs in the course of the disease. At present, there is no specific treatment for this disease at home and abroad. The main treatment methods are insulin injection for diabetes, anti-infection, immune regulation and other comprehensive treatment measures. These treatment measures are non-radical measures, which can alleviate the disease in a certain period of time, but with time prolonging, the disease will gradually damage the health of children and even lead to death.

Umbilical cord blood stem cell transplantation (UCBST) and islet cell transplantation (IST) are mature clinical treatment technologies at home and abroad, but the combination of the two technologies is a new technology for the treatment of monogenic immunodeficiency type 1 diabetes mellitus in children.

Before you decide whether to take part in the treatment, please read the following as carefully as possible. It can help you understand the treatment and why to take the treatment, and the benefits, risks and discomforts that may be brought to you by taking

part in the treatment. If you want, you can also discuss it with your relatives and friends, or ask your doctor for explanation and help you make a decision.

1. Background, purpose and significance of new technology

Type 1 diabetes mellitus is a major disease endangering human health. Chronic complications of diabetes restrict the long-term survival of diabetic patients. Studies show that 20%-40% of diabetic patients will suffer from diabetic nephropathy. In 5-10 years of illness, about 58%-80% of diabetic patients will develop diabetic ophthalmopathy. After 20 years of illness, 99% of diabetic patients will have diabetic ophthalmopathy. Even among children and adolescents with a course of only 4.9 years, the incidence of diabetic ophthalmopathy in different degrees is as high as 36%. The etiology of type 1 diabetes mellitus is complex, but some rare single gene defects lead to the occurrence of type 1 diabetes mellitus. Because of the deficiency of immune function, patients are prone to repeated infection and even sepsis, which can lead to the damage of multiple organs such as colitis, kidney, liver and endocrine glands, such as adrenal gland, and even lead to early death. Due to the coexist of immune deficiency and diabetes, it is more harmful.

Umbilical cord blood stem cell transplantation is a radical treatment for immunodeficiency at home and abroad. Its principle is to replace the hematopoietic system of children with umbilical cord blood stem cells matched with your child by transplantation, so as to correct the defective immune function. Islet cell transplantation is a technique that isolates islet cells from the normal pancreas of donors and injects

them into children through the portal vein to secrete insulin to treat diabetes. For children with monogenic immunodeficiency type 1 diabetes mellitus, umbilical cord blood stem cell transplantation is used to restore the defective immune function, and then islet cell transplantation is used to correct diabetes mellitus. The application of these two techniques may maximize the recovery of children's health and prolong their lives as far as possible.

2. Interventions and advantages

The interventions will be divided into two stages. The first stage is the transplantation of umbilical cord blood stem cells: (1) the diagnosis of monogenic immunodeficiency T1DM confirmed by islet function, autoantibody and gene analysis; (2) high resolution typing of histocompatibility antigens in children; (3) matching of stem cells in the national umbilical cord blood bank; (4) admitting children to the transplantation cabin to obtain matching umbilical cord blood stem cells after immune clearance; (5) after successful transplantation, they were removed from the transplantation cabin and entered the follow-up stage of outpatient clinic.

The second stage is islet cell transplantation. After successful umbilical cord blood transplantation and stable immune function, the children begin islet cell transplantation: (1) obtaining the pancreas of donors; (2) extracting pancreatic cells; (3) purifying islet cells to obtain high purity and high activity islet cells; (4) using immunosuppressive agent Basiliximab (Simulect) 6 hours before operation and injecting purified islet through portal vein puncture; (5) Tacrolimus combined with mycophenolate mofetil

(Mycophenolate) will be used after operation, and blood concentrations will be measured. The amount of immunosuppressive drugs will be gradually reduced. Finally, gradually reduce insulin according to blood glucose. We will follow up the glucose metabolism, immunity and growth of patients for in long term

In this new technology, cord blood hematopoietic stem cells have no harm to donors. The incidence of graft-versus-host disease (GVHD) after transplantation is low and mild, and the effect of graft-versus-leukemia (GVL) is not decreasing. Islet cell transplantation is performed by percutaneous hepatic puncture and direct injection of purified islet cells into the portal vein. It can be accomplished in a few hours and the dosage of immunosuppressive agents is low compared with traditional combined pancreas-kidney transplantation.

3. The current diagnosis of the child and the possible benefits this new technology may bring to the child

Your child is eligible for the diagnosis of monogenic immunodeficiency type 1 diabetes. With this new technology, the disease manifestation can be reversed by complete immune reconstruction after successful transplantation of umbilical cord blood stem cells. Early stem cell transplantation can avoid further development of organ toxicity related to disease, and avoid the irreversible predicament after the disease enters the advanced stage. If islet cell transplantation is successful, insulin can be greatly reduced until insulin is discontinued. Therefore, it may improve or restore the state of hyperglycemia, reduce chronic complications caused by diabetes and hyperglycemia,

and achieve the goal of prolonging life and even healthy life.

4. Possible adverse reactions, risks and risk prevention measures

All transplantation treatments are at high risk. Whether the transplantation is successful or not, the new technique may have the following side effects:

1. Related to pretreatment chemotherapy or radiotherapy: nausea, vomiting, diarrhea, hematuria, alopecia, oral ulcer, bone marrow suppression, liver and kidney damage, infection, bleeding, skin damage, etc.

2. Graft-versus-host reaction (GVHD).

3. Opportunistic infection of immunodeficiency.

4. Infertility.

5. The possibility of tumorigenesis.

6. Allergic reactions caused by anesthetics, contrast agents and therapeutic drugs.

7. Islet injection leads to vascular embolism and abnormal liver function.

8. If puncture is difficult, open portal vein injection may be used instead.

9. Immunosuppressive agents cause kidney and other toxic and side effects.

10. Portal vein puncture may lead to intrahepatic and extrahepatic vascular hemorrhage.

11. Opportunistic infections (viral fungi, etc.) occur after transplantation.

12. The migration process may fail and will have to be replanted, resulting in additional costs to be borne.

13. Cardiovascular events, graft exfoliation, coagulation dysfunction, pulmonary embolism and other cardiovascular events.

14. There are other unpredictable risks, adverse reactions and consequences that may endanger the lives of children.

In the course of treatment, the doctor will observe your child's condition at any time. If there is any discomfort in the process of diagnosis and treatment, please contact the doctor who is in charge. The doctor will treat any discomfort and adverse reactions in time. Throughout the treatment process, risk prevention measures will be strictly implemented, including eliminating contraindications, strictly following the treatment process and norms, and closely monitoring the vital signs and indicators of the subjects.

5. Alternatives

If you decide not to take part in this new technology treatment program, we will continue to provide your child with insulin injection of traditional treatment, and in the case of infection, organ damage to the corresponding treatment.

6. Relevant expenses

The cost of participating in this treatment is entirely at the patient's own expense, and can’t be reimbursed through the Children's Fund. the patient will consult with the insurance company on his own whether other commercial insurance can be reimbursed or not. Because of the particularity of stem cell transplantation and islet cell transplantation, the transplanted cells can’t be recycled. The waste caused by discontinuation of treatment due to patient's reasons can’t be compensated and the cost can’t be refunded.

7. Is personal information confidential?

Your child's medical records (including medical records, physical and chemical examination reports, etc.) will be kept intact in the hospital. Doctors, professional academic committees, ethics committees and health supervision and management departments will be allowed to access your medical records. The public report on the results of this new technology will not disclose your child's personal identity. We will make every effort to protect the privacy of your child's personal medical data within the limits permitted by law.

8. How to get more information?

You can ask any questions about this treatment at any time. Your doctor will leave you a call so that you can answer your questions.

9. Voluntary participation in treatment and withdrawal from treatment

Whether you take part in treatment depends entirely on your willingness. You may refuse to participate in the treatment or withdraw from the treatment at any time during the treatment. Your doctor or therapist may suspend your participation at any time for your best interests. If you do not participate in this treatment, you may withdraw halfway. If you choose to take part in this treatment, we hope you can persist in completing the whole treatment process.

10. What should do now?

Whether to participate in this treatment, you can discuss with your family, children, relatives before making a decision. Before you make a decision to participate in the treatment, please ask your doctor as many questions as possible until you fully understand the treatment.

To ensure your accurate understanding of the above, read the informed consent carefully and make a decision.