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Haploidentical stem cell transplantation for paediatric patients with thalassemia major

Submission date
04/08/2020

Recruitment status
No longer recruiting

Registration date
10/08/2020

Overall study status
Completed

Last Edited
08/02/2021

Condition category
Haematological Disorders

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims:
Thalassemia major (or beta-thalassemia) is a genetic disorder in which there are abnormal beta haemoglobin chains in red blood cells. Patients with thalassemia major require lifelong blood transfusions for survival, but these may bring complications including iron overload, failure to thrive, or transfusion-transmitted infections. Hematopoietic stem cells are the stem cells that give rise to other blood cells. Haematopoietic stem cell transplantation (HSCT) is currently the only cure for thalassemia major. Although alternative donors have greatly improved the choice of donors for thalassemia major patients, long-term safety and effectiveness varies between different protocols. The aim of this study is to investigate the outcomes of thalassemia major patients who received HSCT using a newly developed protocol with alternative donors.

Who can participate?
Patients aged 2 to 18 who have been diagnosed with thalassemia major and have indications for haematopoietic stem cell transplantation

What does the study involve?
All participants receive HSCT using a newly developed protocol with alternative donors. The duration of the treatment will be about 1 year but can be longer depending on the condition of the patient. The follow-up time will be at least 2 years after the transplant but the researchers expect to follow the patients as long as possible.

What are the possible benefits and risks of participating?
The recruited patients will be given the information at the time of recruitment.

Where is the study run from?
Shenzhen Children's Hospital (China)

When is the study starting and how long is it expected to run for?
August 2020 to August 2023

Who is funding the study?
1. Shenzhen Key Medical Discipline Construction Fund (China)

2. Shenzhen Fund for Guangdong Provincial High-level Clinical Key Specialties (China)
3. Sanming Project of Medicine in Shenzhen (China)

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Additional identifiers

Protocol serial number
SZCHXYK2020001

Study information

Scientific Title
Combined haematopoietic stem cell transplantation with haploidentical graft and cord blood for paediatric patients with thalassemia major: a single centre, prospective study (SZTM2020)

Acronym
SZTM2020

Study objectives
This study is to study the outcomes of patients with thalassemia major who received haematopoietic stem cell transplantation using a protocol developed for haploidentical donors. The primary hypothesis is that this protocol will promote stable engraftment of hematopoietic cells, support normal erythropoiesis, prevent severe graft versus host diseases, life-threatening infections, and other severe transplant-related complications, and result in an event-free survival of > 90% of children with thalassemia major.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 28/01/2021, Shenzhen Children's Hospital Ethics Committee (Shenzhen Children's Hospital, 7019 Yitian Road, Futian, Shenzhen, China; +86 (0)755 8300 8379; seyllwyh@163.com), ref: 202000302

Primary study design
Interventional

Study design
Non-randomised single-centre study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Thalassemia major

Interventions
Conditioning chemotherapy:
1. Cyclophosphamide (CY, 50 mg/kg/day x 2 days, day -8 to -7)
2. Busulfan (BU, 2.8-4.4 mg/kg/day x 3 days, day -6 to -4)
*The dose of BU is determined based on risk assessments of thalassemia patients and adjusted according to pharmacokinetic evaluation after the seventh dose of BU.
3. Fludarabine (FLU, 40 mg/m²/day x 5 days, day -6 to -2)
4. Anti-thymoglobulin (ATG, 1 mg/kg/day x 3 days, day -3 to -1)
5. Thiotepa (TT, 5 mg/kg/dose x 2 doses at 12 h interval, day -3)

Cell transfusions:
D0: Bone marrow (BM) and/or peripheral blood stem cell (PBSC)
D1: Umbilical cord blood (UCB) and/or peripheral blood stem cell (PBSC)
*Cell dose: A total of up to 20 x 10^8/kg mononuclear cells (MNCs) for patients with negative results for donor-specific antigen (DSA) before transplant. A total of up to 25 x 10^8/kg MNCs for patients with positive DSA results before transplant.

Prophylaxis for graft versus host diseases:
1. Cyclophosphamide (CY, 50 mg/kg/day x 2 days, day +3 to +4)
2. Tacrolimus (FK506, 0.04 mg/kg/d, from day +5)

* The dose of FK506 is adjusted according to blood concentration.
3. Mycophenolate mofetil (MMF, 10 mg/kg/day, from day +5)

The duration from conditioning chemotherapy to the end of GVHD prophylaxis will take approximately 1 year but can be longer depending on the condition of the patient. The follow-up time for patients recruited for this trial will be at least 2 years post-transplant but the researchers expect to follow the patients as long as possible.

Intervention Type
Mixed

Primary outcome(s)
1. Overall survival (OS) using Kaplan-Meier estimator at 2 years
2. Thalassemia-free survival (TFS) using R at 2 years

Key secondary outcome(s)
1. Engraftment: myeloid engraftment (absolute neutrophils count ≥ 0.5×10^9/L for 3 consecutive days) at day +30
2. Transplant-related mortality: using Kaplan-Meier estimator at 2 years
3. Cumulative incidence of acute graft versus host disease (GVHD): acute GVHD by day +180. The classification of aGVHD is determined using either Glucksberg scoring system or IBMTR scoring system
4. Cumulative incidence of chronic GVHD by 2 years. The classification of cGVHD is determined according to the overall severity chronic GVHD grading system
5. Cumulative incidence of sinusoidal obstruction syndrome (SOS, also known as hepatic veno-occlusive disease, VOD): cumulative incidence of SOS/VOD at day +180
6. Cumulative incidence of infectious complications: cumulative incidence of bacterial, fungal, and viral infections by 2 years

Completion date
31/08/2023

Eligibility

Key inclusion criteria
1. Age 2 to 18 years
2. Diagnosed with thalassemia major
3. Indication of haematopoietic stem cell transplantation
4. A cardiac ejection fraction of >50%; normal pulmonary function tests and pulmonary examination results; and normal kidney function

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
2 Years

Upper age limit
18 Years

Sex
All

Key exclusion criteria
1. Uncontrolled bacterial, viral, or fungal infections before transplant
2. Severe liver and heart overload: liver MR T2* value > 1.4 ms or heart MR T2* value > 10 ms
3. Any other restriction for transplant

Date of first enrolment
01/11/2020

Date of final enrolment
28/02/2023

Locations

Countries of recruitment
China

Study participating centre
Shenzhen Children's Hospital
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Sponsor information

Organisation
Shenzhen Children's Hospital

ROR
https://ror.org/0409k5a27

Funder(s)

Funder type
Research organisation

Funder Name
Shenzhen Key Medical Discipline Construction Fund (SZXK034)

Funder Name
Sanming Project of Medicine in Shenzhen (SZSM201512033)

Funder Name
Shenzhen Fund for Guangdong Provincial High-level Clinical Key Specialties (SZGSP012)

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other