Title: A Single-Arm, Open-Label, Single-Center Phase I-II Study of the Safety and Feasibility of Sulforaphane in Promoting Early Hematopoietic Recovery After Umbilical Cord Blood Transplantation

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Informed Consent Form for the Clinical Study: A Single-Arm, Open-Label, Single-Center Study on the Safety and Feasibility of Sulforaphane in Promoting Early Hematopoietic Recovery After Umbilical Cord Blood Transplantation

Dear Potential Participant,

As you are currently preparing to undergo an unrelated donor umbilical cord blood transplantation (UCBT) at our hospital, we invite you to participate in a clinical research study titled "A Single-Arm, Open-Label, Single-Center Study on the Safety and Feasibility of Sulforaphane (SFN) in Promoting Early Hematopoietic Recovery After Umbilical Cord Blood Transplantation." This study will be conducted in the Cord Blood Transplantation and Cord Blood Cell Therapy Unit of the Center for Regenerative Medicine at the Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College. This study has been reviewed and approved by the Ethics Committee of the Institute of Hematology & Blood Diseases Hospital and has been filed with the relevant national regulatory authorities.

This informed consent form will help you decide whether to participate in this study. It provides information about the study's background and purpose, the procedures involved, potential risks and benefits, as well as explanations regarding alternative treatment options, how your personal information will be used, and your right to withdraw from the study at any time.

Before you decide whether to participate, please read this document carefully and ensure you fully understand its contents. If you have any questions, please feel free to ask the study doctor or research staff at any time to ensure you receive satisfactory answers.

If you agree to participate, you will receive a copy of this informed consent form signed by both you and the study doctor.

Part 1: Participant Information

I. Study Purpose and Background

- **Study Purpose**

(1) To determine the safety and feasibility of using SFN during the peri-infusion period of UCBT in adults.

(2) To determine the impact of using SFN during the peri-infusion period of UCBT on hematopoietic recovery, particularly neutrophil engraftment.

(3) To establish a high-quality clinical cohort of adult patients transplanted with long-term cryopreserved umbilical cord blood.

- **Investigational Product Introduction:** Sulforaphane (SFN) is a potent bioactive compound derived from cruciferous vegetables, known for its significant antioxidant, anti-inflammatory, and potential anti-cancer properties. It has demonstrated utility in the prevention and management of various diseases, including anti-diabetic, antioxidant, anti-inflammatory, and anti-cancer effects. SFN can be administered via diet or dietary supplements. Commercially available SFN-containing supplements have been utilized in several internationally registered clinical trials, which have reported its beneficial effects. SFN has been proven effective in mitigating the decline in in vivo hematopoietic reconstitution capacity associated with long-term cryopreservation of umbilical cord blood. These important findings are based on observed functional improvements of umbilical cord blood in immunodeficient animal models. This study aims to evaluate SFN intervention during the peri-infusion period in adult patients undergoing Umbilical Cord Blood Transplantation (UCBT), with the goal of promoting early hematopoietic recovery in UCBT patients receiving long-term

cryopreserved umbilical cord blood.

II. Study Design and Population

- **Study Design**

This is a single-arm, open-label, single-center study. Phase I will enroll 4 patients. Upon meeting the safety evaluation criteria in Phase I, Phase II will enroll 32 patients for observation.

- **Inclusion Criteria**

You may be eligible to participate if you meet all the following criteria:

(1) Diagnosis of a high-risk hematologic malignancy: including Acute Myeloid Leukemia (AML), Acute Lymphoblastic Leukemia (ALL), or high-risk Myelodysplastic Syndromes (MDS).

(2) Age and Sex: ≥18 years old, no gender restriction.

(3) Karnofsky Performance Status (KPS) score ≥70%, Eastern Cooperative Oncology Group (ECOG) performance status of ≤2, and Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI) score ≤2.

(4) Selection of Unrelated Donor Umbilical Cord Blood (UCB): The UCB unit must meet the following criteria: donor-recipient high-resolution HLA match ≥4/6 or 7/10, and a post-thaw CD34+ cell dose ≥0.83×10^5/kg (recipient body weight). Furthermore, only UCB units cryopreserved for ≥10 years meeting these criteria are available for you from Chinese public cord blood stem cell banks.

- **Exclusion Criteria**

You will not be able to participate if you meet any of the following criteria:

(1) Positive test results for: Human Immunodeficiency Virus (HIV-1/2), detectable Human Cytomegalovirus DNA (HCMV-DNA), detectable Epstein-Barr Virus DNA (EBV-DNA), Hepatitis B (positive for Hepatitis B surface antigen [HBsAg] or detectable Hepatitis B virus DNA [HBV-DNA]), positive Hepatitis C antibody (HCV-Ab), or positive Treponema pallidum

antibody (TP-Ab).

(2) Active bacterial, viral, fungal, or parasitic infection judged by the investigator to be clinically significant at screening.

(3) Availability of an HLA-identical willing donor and eligibility for allogeneic hematopoietic stem cell transplantation from that donor.

(4) Prior receipt of gene therapy or allogeneic hematopoietic stem cell transplantation.

(5) First-degree relative(s) with a known or suspected hereditary cancer syndrome (including, but not limited to, hereditary breast and ovarian cancer syndrome, Lynch syndrome, familial adenomatous polyposis, etc.).

(6) Diagnosis of a major psychiatric disorder or condition that would severely impair the ability to participate in the clinical study; or history of substance abuse related to psychotropic drugs and inability to abstain.

(7) History of significant organ dysfunction, including:

- Hepatic: AST or ALT > 3 × Upper Limit of Normal (ULN); total serum bilirubin > 2.5 × ULN; or, if consistent with Gilbert's syndrome, total bilirubin > 3 × ULN with direct bilirubin > 2.5 × ULN; history of bridging hepatic fibrosis, cirrhosis, or active hepatitis.
- Cardiac: Left ventricular ejection fraction (LVEF) <45% at screening; New York Heart Association (NYHA) Class III or IV congestive heart failure; severe arrhythmia requiring treatment; uncontrolled hypertension; history of hypertensive emergency, hypertensive encephalopathy, or unstable angina; myocardial infarction, coronary artery bypass grafting, peripheral artery bypass graft/implantation, or stent placement within 12 months prior to enrollment; clinically significant valvular heart disease; estimated glomerular filtration rate (eGFR) <60 mL/min/1.73m².
- Pulmonary: FEV1/FVC ratio <60% and/or diffusing capacity <60% of predicted value; evidence of clinically significant pulmonary hypertension requiring medical intervention.

(8) Uncorrectable coagulation dysfunction or history of a severe hemorrhagic disorder.

(9) Any other condition considered by the physician to render you unsuitable for hematopoietic stem cell transplantation.

(10) Known allergy or hypersensitivity to the investigational product (Sulforaphane) or any of its components.

(11) Participation in another interventional clinical study within 3 months prior to screening or current participation.

(12) Administration of live attenuated vaccines within 6 weeks prior to screening.

(13) Pregnant or lactating women.

(14) Poor compliance with the study protocol expected, as judged by the investigator.

(15) Any other condition considered by the investigator to make you unsuitable for participation.

(16) Unwillingness to provide valid pre-existing diagnostic evidence or undergo bone marrow examination before treatment, and/or unwillingness to undergo bone marrow and blood examinations after treatment.

(17) Diagnosis of acute promyelocytic leukemia (APL).

(18) Clinically significant gastrointestinal abnormalities that may affect drug intake, transport, or absorption (e.g., inability to swallow, chronic diarrhea, intestinal obstruction), or total gastrectomy.

(19) A definite tendency for gastrointestinal bleeding, judged by the investigator to pose a risk for major gastrointestinal hemorrhage.

(20) History of solid organ transplantation.

III. Study Procedures

- **Study Interventions**
- **Conditioning Regimen:** A dose-stratified conditioning regimen will be used, with intensity adjusted based on your age and comorbidities:

(1) For patients aged ≤50 years and ECOG ≤1: A myeloablative regimen will be used (either Flu/Bu/Cy or Flu/Bu/Mel):

1) Flu/Bu/Cy: Fludarabine (Flu) 30 mg/m²/day for 4 days; Busulfan (Bu) 0.8 mg/kg every 6 hours for 4 days; Cyclophosphamide (Cy) 60 mg/kg/day for 2 days.

2) Flu/Bu/Mel: Fludarabine and Busulfan as above; Melphalan (Mel) 80-100 mg/m² on one day.

(2) For patients aged >50 years or ECOG ≥2: A myeloablative regimen (Flu/Ara-C/Bu/Mel) will be used:

1) Flu 30mg/m² daily for 4 days; Granulocyte Colony-Stimulating Factor (G-CSF) 5μg/kg daily for 3 days; Cytarabine (Ara-c) 1.5-2.0g/m² daily for 3 days; Bu 0.8mg/kg every 6 hours for 3 days; Mel 80-100 mg/m² on one day.

For patients with a history of meningeal leukemia, high-risk factors for meningeal leukemia, or extramedullary disease: Add Semustine (250 mg/m²) or Thiotepa (8-10 mg/kg daily for 1 day).

For patients with active disease (not in remission) at transplantation: Add Decitabine (20 mg/m²/day for 3 days) or Thiotepa (8-10 mg/kg daily for 1 day)**.**

- **UCB Infusion:** You will receive a single unit of umbilical cord blood that meets the following criteria: high-resolution HLA match ≥4/6 or 7/10, CD34+ cell dose ≥0.83 × 10^5/kg (recipient body weight), and cryopreserved for ≥10 years.
- **SFN Intervention:** SFN will be administered orally from day -1 (one day before transplantation) until day +7 (seven days after transplantation). The dose is two tablets, three times daily, to be taken with meals or after meals (recommended to be taken with a fat-containing meal).
- **GVHD Prophylaxis:** Cyclosporine A (CsA) combined with short-course Mycophenolate Mofetil (MMF) will be used.

(1) CsA: Starting on day -1 at 2.5 mg/kg/day via continuous 24-hour intravenous infusion, targeting a blood concentration of 200-300 ng/mL.

After neutrophil engraftment, this will be switched to oral administration at twice the intravenous dose. Tapering of CsA will begin at 2 months post-transplant based on disease relapse risk, GVHD, and infection status, with planned discontinuation at 5-6 months post-transplant.

(2) MMF: 30 mg/kg/day (in two divided doses), starting on day +1. Tapering will begin after neutrophil engraftment, with gradual discontinuation by 3-4 months post-transplant.

IV. Your Responsibilities

Your participation in this study requires you to:

(1) Follow the instructions of the study doctor, adhere to the scheduled follow-up visits, and cooperate with the collection of biological samples (e.g., blood draws).

(2) Take the Sulforaphane tablets as instructed during your participation in the study. Supportive care, such as acceptable anti-nausea medication, will be available if you experience nausea or vomiting. If vomiting occurs shortly after taking the dose and intact tablets are visible, the dose should be re-taken based on the number of tablets identified. However, you are expected not to miss doses intentionally.

(3) Promptly notify your doctor of any health problems or side effects you experience. If any other treatments are required due to changes in your condition, you should seek your doctor's opinion beforehand or report them truthfully afterwards.

V. Potential Risks and Discomforts

During the study, the research team will monitor for any adverse reactions to Sulforaphane. It is crucial that you immediately report any discomfort you experience to the research staff. The researchers may use other medications or treatments to manage side effects of the investigational product. If you or the researcher believe you cannot tolerate these side effects, the dose of the

investigational product may be reduced, temporarily stopped, or permanently discontinued, and you may be withdrawn from the study.

Please note that many of the treatment risks described above may also exist during standard medical care, even if you do not participate in this clinical research. If you withdraw from the study, you can discuss other treatment options, such as continued chemotherapy, with your study doctor.

VI. Withdrawal from the Study

The study doctor may withdraw you from the study or discontinue the study treatment for any important reason and will discuss other treatment options with you. Such reasons include:

(1) You experience a life-threatening adverse reaction.

(2) You develop an intolerance to SFN (Sulforaphane) that cannot be managed by supportive measures.

(3) You experience any clinical adverse event, laboratory abnormality, or other medical condition which, in the judgment of the study doctor, makes continued administration of SFN (Sulforaphane) no longer in your best interest.

(4) You also have the right to withdraw your consent and leave the study at any time, discontinuing the study drug and procedures. Regardless of the reason for withdrawal, the researchers will retain the research medical records and any biological samples collected up to the point of withdrawal.

VII. Study Termination

The study might be paused or terminated early under the following circumstances:

(1) Serious safety concerns are identified during the study.

(2) The treatment effect of SFN (Sulforaphane) is found to be poor or ineffective, lacking clinical value.

(3) Major flaws are found in the clinical study protocol or serious deviations occur during its implementation.
(4) The regulatory authority or the Ethics Committee orders the termination of the study for any reason.

VIII. Potential Benefits of Participation

Participation in this clinical study may potentially have a beneficial effect on your disease treatment, but it might also not lead to any improvement. We hope to gain more information through this research to benefit future patients with similar conditions. We sincerely thank you for your active contribution.

IX. Alternative Treatment Options

If you choose not to participate in this study, other treatment options, such as chemotherapy, are available to you.

X. Study-Related Costs

Participation in this study: The oral Sulforaphane supplement will be provided free of charge. However, due to limited research funding, the costs associated with standard post-transplant engraftment monitoring and other routine examinations required by the study will be your responsibility.
You will not receive financial compensation for participating in this study. The study doctor will not provide financial compensation for medical treatment costs resulting from treatment failure or disease progression during the study.

XI. Insurance and Compensation

Please promptly inform your study doctor of any discomfort or accidental injury that occurs during the study, regardless of whether it is related to the investigational product. He/She will make a judgment and provide appropriate medical treatment.
If you experience harm related to the study, such as an adverse reaction or

serious adverse reaction, you will receive active treatment at the hospital. For study-related injuries occurring during the trial, reasonable medical expenses and compensation will be provided in accordance with the relevant laws and regulations of the People's Republic of China.

XII. Confidentiality of Your Information

During the study, the researchers will collect your personal information, including but not limited to your name, date of birth, gender, ethnicity, and physical or mental health status. This information will be stored securely at the hospital and kept strictly confidential. To the extent permitted by law, researchers, Ethics Committee members, or regulatory authority representatives may review your relevant research records, such as your study medical chart.

Your personal identity will not be disclosed under any circumstances. We will make every effort to protect your privacy within the limits of the law. If the study results are published, your identity will remain confidential.

If you withdraw from the study midway, no further follow-up data will be collected from you, unless you provide consent for information regarding your health, disease status, and treatments received to be collected via alternative means.

XIII. Your Rights

Your participation in this clinical trial is entirely voluntary. You may refuse to participate. Your decision to participate should not be influenced by any individual or organization. You have the right to withdraw from the study at any stage without facing discrimination or reprisal, and this will not affect your future medical care or rights. If you decide to stop participating, we ask that you inform your study doctor promptly. The study doctor can then provide advice and guidance regarding your health. Furthermore, if you do not comply with the study requirements during the clinical trial, or if your study doctor

believes it is no longer in your best interest to continue, the study doctor has the right to decide whether you should continue participating in the study to protect your welfare.

New important information may become available during the course of the research that could affect your willingness to continue participating. If this occurs, you will be informed in a timely manner.

If the study is terminated early, you will also be notified promptly, and your study doctor will provide recommendations regarding your subsequent treatment plan based on your health status.

XIV. Obtaining More Information

You may inquire about information related to this study at any time. If you have questions related to the research, please contact your study doctor promptly.

Study Doctor: Telephone:

If you have questions regarding your rights as a participant, wish to report difficulties, dissatisfaction, or concerns encountered during your participation, or would like to provide suggestions or comments related to the study, you may contact the hospital's Ethics Committee by phone.

Ethics Committee Contact Person: Telephone:

Part 2: Informed Consent Form

Consent Signature Page

Investigator's Statement

I, _____, as the Investigator, have thoroughly explained the nature and purpose of this study to the subject, including the study procedures, potential benefits and risks, principles of participation, and confidentiality of data. I have informed the subject that they may withdraw from the study at any time without prejudice to future treatment and have provided them with a copy of the signed informed consent form.

Signature of Investigator: _____ Date:_____

Subject's Statement

I have read the above information regarding this study and have had the opportunity to discuss it with the Investigator and ask questions. All questions I have asked have been answered to my satisfaction.

I understand the potential risks and benefits associated with participating in this study and voluntarily agree to participate. I confirm that I have had sufficient time to consider this decision and understand that:

- I may ask the Investigator for more information at any time.
- I may withdraw from this study at any time without discrimination or retaliation, and my medical treatment and rights will not be affected.
- If my condition changes and requires any other treatment, I will consult the doctor in advance or inform the doctor truthly afterward.
- I agree to allow the investigators, the Ethics Committee, or regulatory authorities to review my research data.
- I will receive a copy of this signed and dated informed consent form.

Finally, I have decided to consent to participate in this study.

Signature of Subject: _____ Date: _____

Contact Information of Subject: _____

For subjects unable to provide informed consent due to lack of capacity, etc., the legal guardian should sign.

Signature of Legal Guardian: _____ Date: _____

Relationship to Subject: _____

Contact Information of Legal Guardian: _____