Participant Information Sheet

1. Protocol title:

Adjunct omeprazole or resveratrol in non-transfusion dependent thalassemia patients with secondary hemochromatosis: a randomized, double-blind, placebo-controlled trial

2. Investigators:

Investigator	Responsibility
1. Thanapong Chopetgool, M.D.	Conceptualization, Researcher, Data and Laboratory analysis, Report writing, Discussion
2. Adisak Tantiworawit, M.D., Associate Professor	Conceptualization, Researcher, Data analysis, Sponsoring, Report writing, Discussion
3. Sirichai Srichairatanakool, M.D.	Conceptualization, Researcher, Data analysis, Sponsoring, Report writing, Discussion
4. Pimpisid Koonyosying, Ph.D. Assistant Professor	Conceptualization, Researcher, Data and Laboratory analysis, Sponsering, Report writing, Discussion
5. Somdet Srichairatanakool, Ph.D. Professor	Conceptualization, Researcher, Data and Laboratory analysis, Sponsoring Drug and Laboratory Equipment, Report writing, Discussion

3. Ethics

This study has been approved by the Human Experimentation Committee Research Institute for Health Sciences and authorized by Associate Professor Nimit Morakote, Ph.D., a Chairman of the Committee, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand, Certificate Number: 476/2024 (476/2567 for Thai version), Date: 17th December 2024. Adherence to ethical guidelines was of prime importance throughout the study process. All patients were fully informed about the particulars of the study and willingly provided their signatures on the consent forms before any study procedures were performed. This study followed the guidelines of the Helsinki Declaration 2008, revised in 2013: Ethical Principles for Medical Research Involving Human Subjects. Subjects' rights have been protected by an appropriate Institutional Review Board and written informed consent was granted from subjects.

4. Objectives

Primary objective

To evaluate the efficacy of adjunct omeprazole or resveratrol in combination with iron chelators in reducing serum ferritin compared to placebo in non-transfusion dependent thalassemia patients

Secondary objectives

1. To evaluate the efficacy of adjunct omeprazole or resveratrol in combination with iron chelators in reducing labile plasma iron, non-transferrin bound iron and serum iron compared to placebo

2. To study the association between adjunct omeprazole or resveratrol in combination with iron chelators and the levels of erythroferrone (ERFE) and hepcidin (Hcd)

3. To study the association between resveratrol and changes in hemoglobin F levels

4. To assess the adverse effects of adjunct omeprazole or resveratrol with iron chelators

5. You have been invited/selected to participate in the research study because:

- You are 20-65 years old.
- You are diagnosed with non-transfusion-dependent thalassemia (NTDT) patients.
- You have iron overload with serum ferritin 300-1000 ng/mL or >1000 ng/mL with maximum iron chelator
- Your concurrent iron chelators are expected to have no dose changing during 3 months before enrollment and no tendency to adjust the dose of iron chelators between study
- You are not pregnant, breastfeeding, chronically ill, or have normal liver and kidney function.
- You are not currently receiving omeprazole or resveratrol.

6. Participants:

A total 60 patients visit the Outpatient Department numbers 9 or 23 at the Division of Hematology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand between 10th February 2025 and 30th April 2026.

7. Tasks for the participants:

- Participants will be randomly assigned to receive one of the three study drugs including omeprazole, resveratrol or placebo by which you and your doctor would not know what drug you are receiving.
- Taking study drugs twice daily before meals in the morning and evening for 6 months with your current iron chelators and supplements.
- Follow up on schedule 3 times at the 1st visit and the next 3 and 6 months which you will be asked for physical and blood examination.
- 30 ml of blood will be taken in each visit [total 90 ml]

8. Benefits for participants and the overall study:

You may not receive direct benefit from this study because the study drugs may not further decrease serum ferritin. However, the information from this study will be helpful for the treatment of thalassemia patients with iron overload in the future.

9. Risks associated with participating in the research project:

- Risk from blood drawing that may be pain, bruising, or a less common side-effect which is vasovagal syncope.
- Risk from study drugs: omeprazole may cause you to feel nausea, vomiting, diarrhea, abdominal pain, bloating, constipation, back pain or fewer side effects which are chest pain, myocardial infarction, intraabdominal infection, lower respiratory tract infection, pancreatitis, osteoporosis or other unexpected side effects.
- Risk from resveratrol is nausea, vomiting, diarrhea or fewer common side-effect is pancreatitis or other unexpected side effects.

10. In case participants experience any signs or symptoms suspected of study drugs, the participants may contact Dr. Thanapong Chopetgool, MD. at the Division of Hematology,

Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand 053-935482-3 or 1669 in an emergency.

11. Participants will receive assistance and care for any side effects resulting from the research according to medical standards by contacting Dr. Thanapong Chopetgool at the Division of Hematology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand 053-935482-3.

12. Participants' personal information will be kept confidential in a secure document cabinet, and only researchers can access it. Researchers will disclose information for academic purposes without identifying individuals. The personal data of research participants will be kept confidential and not disclosed to the public individually but will be reported collectively.

13. Participants have the right to withdraw from the research project at any time. Their decision will not affect future treatment, care, or any loss of benefits. If participants decide not to continue or withdraw from the study at any time, the information they have disclosed will remain confidential.

Note: If there are any parts of this document that you do not understand, please ask the project leader or representative for clarification until you fully understand. You can take this document home to read and understand or discuss it with your family, friends, or dentist to help make decisions about participating in this research project