Informed Consent

We invite you to participate in a randomized controlled study of the "Early Initiation of Tafolecimab for Patients With Acute Coronary Syndrome undergoing Percutaneous Coronary Intervention in Chinese Population" funded by Chinese Academy of Medical Sciences. This study has been approved by the Ethics Committee of Fuwai Hospital of Chinese Academy of Medical Sciences (Tel: 010-88396281, 010-88396282). Please read the instructions carefully to understand your rights and obligations in the study and to clarify the nature and risks of the study. Participation in this study is entirely voluntary and will not affect your treatment and other legal rights during your stay in the hospital. When the investigator explains and discusses the informed consent form with you, you can ask questions at any time and ask the investigator to explain to you what you do not understand. You will have plenty of time to discuss with your family, friends and doctor before making a decision.

If you are currently participating in other clinical studies, please inform the investigator.

The project leader of this study is researcher Zhou Zhou (Laboratory Diagnosis Center, Fuwai Hospital, Chinese Academy of Medical Sciences).

1. Why was this study conducted?

For patients with acute coronary syndrome, low-density lipoprotein cholesterol (LDL-C) target values are <1.8 mmol/L and ≥50% reduction from baseline. Studies have shown that Proprotein Convertase Subtilisin/Kexin Type 9 monoclonal antibodies (PCSK9mAb) can further reduce the occurrence of major cardiovascular adverse events (MACEs) on the basis of statin combined with (or without) cholesterol absorption inhibitors. The guidelines emphasize the timing and status of clinical use of PCSK9mAb, a novel lipid-lowering drug. However, the current guidelines recommend that 4-6 weeks after receiving the maximum tolerated dose of statin, if LDL-C is not up to standard, cholesterol absorption inhibitors should be combined, and observation should continue for 4-6 weeks. If LDL-C is still not up to standard, PCSK9mAb should be considered.

The aim of this study was to investigate whether early initiation of intensive lipid-lowering with PCSK9mAb during acute onset of acute coronary syndrome, i.e., achieving lower LDL-C levels as soon as possible, reduces the incidence of major adverse cardiovascular events in patients after

discontinuation compared with conventional lipid-lowering regimens.

2. Why are you invited to participate in this study?

When you have a clinical diagnosis of acute coronary syndrome, you may be invited to participate in the study. However, the study doctor will judge whether you are suitable to participate in this study according to your actual situation and the inclusion and exclusion criteria in the study protocol. Inclusion criteria for this study: Patients aged 18-75 years with non-ST elevation acute coronary syndrome (NSTE-ACS) undergoing PCI, baseline LDL-C<3.4 mmol/L. NSTE-ACS includes non-ST-elevation myocardial infarction and unstable angina.

Exclusion criteria: 1). Severe heart failure (Killip classification III or IV) or cardiogenic shock; 2). History of cerebrovascular disease;3). Uncontrolled or recurrent arrhythmic events; 4). Poorly controlled hypertension;5). Severe hepatic and renal insufficiency (ALT/AST> 3 times the upper limit of normal, eGFR<30 ml/kg/1.73m2, or ongoing dialysis) or creatine kinase elevation>5 times the upper limit of normal; 6). Malignant tumor;7). Intolerance to statins or cholesterol absorption inhibitors; 8). Intolerance to injections;9). Life expectancy <1 year;10). Poor compliance. Inclusion in the study required written informed consent after PCI and prior to receiving any study-related medication.

We invite you to participate in this study. Whether you are finally selected or not will be judged by the researchers according to your actual situation.

3. Process and method of this study

The study was a multicenter randomized controlled study, randomized into two groups: Group 1 (G1, experimental group): intensive lipid-lowering (statin + PCSK9mAb); Group 2 (G2, control group) Conventional lipid lowering (statin + cholesterol absorption inhibitor), PCSK9mAb in this study is defined as TafoleciMab 150mg q2w subcutaneously. The study period is 2 years, and 4 visit periods are set up. Follow-up is carried out in the form of return to hospital: Visit 0 (V0) is the day of enrollment, sign the informed consent form, complete the collection of all baseline data, and give the treatment regimen of the corresponding group. Visit 1 (V1) is the end of one month after enrollment, draw blood for relevant examinations, and follow up your tolerance to the treatment regimen. Visit 2 (V2) is at the end of the 6th month after enrollment, blood samples will be drawn for relevant examinations to follow up on your treatment effect and safety, and we will

record the occurrence of MACEs. Visit 3 (V3) is the end of the first year after enrollment, blood samples will be drawn for relevant examinations, and we will record the occurrence of major adverse cardiovascular and cerebrovascular events (MACCE). Visit 4 (V4) is at the end of the second year after enrollment, blood samples will be drawn for relevant examinations, and we will record the occurrence of MACCE.

4. Duration of the study and number of participants

This study plans to recruit 3684 study participants, eligible patients were enrolled, random 1:1 group. Proposed 17 sub-centres (Fuwai Hospital is the leading site, and the participating units are Peking University First Hospital, Anzhen Hospital Affiliated to Capital Medical University, Jishuitan Hospital, China-Japan Friendship Hospital, Tongren Hospital Affiliated to Capital Medical University, Beijing Luhe Hospital Affiliated to Capital Medical University, General Hospital of Tianjin Medical University, Hebei Province People's Hospital, Daqing City's Hospital of Heilongjiang Province, Affiliated Hospital of Xuzhou Medical University, Xuzhou City Hospital, Second Affiliated Hospital of Dalian Medical University, The first hospital of Beijing City Fangshan District, songyuan jilin oilfield hospital, jilin university sino-japanese union hospital, Tangshan City hospital).

The planned duration of this study is from December 2023 to December 2025, and you are expected to participate for 24 months (from the day you are enrolled).

5. What do you need to do to participate in this study?

- Provide accurate information about past medical history and current condition.
- Tell the researchers about any health problems you have experienced during the study.
- Visits on request.
- Do not participate in any other medical research.
- Follow the investigator's instructions.
- If there is anything unclear, you can always ask.

6. Risks and adverse events for participants in this study?

Your investigator will monitor the side effects of lipid-lowering drugs (PCSK9mAb, statins, cholesterol absorption inhibitors). Risks for study participants participating in this study include: If you are randomly assigned to the trial group, your LDL-C levels may drop to lower levels.

There is no agreement on how low LDL-C levels will have adverse effects on the body, but current guidelines and expert consensus indicate that very-low LDL-C levels have not been found to have serious adverse effects on the body. In terms of adverse reactions, regardless of whether you are assigned to the trial group or the control group, you will need to be treated with statins, which may increase transaminases, muscle-related symptoms, and risk of new diabetes. However, you will need to be treated with statins regardless of whether you participate in this study. It is important that you report any side effects or discomfort to the study staff immediately if you experience them during the trial. The investigator may prescribe other medications to control side effects. If you or your investigator believes that you cannot tolerate these side effects, the PCSK9mAb used in the study may be discontinued completely and you may withdraw from the study.

Risk of Blood Draw

The risks of drawing blood from the arm include temporary discomfort and/or bruising. Although unlikely, infection, excessive bleeding, clotting, or syncope may occur.

reproductive risk

For female study participants: You cannot participate in this study if you are breastfeeding, pregnant, or think you may be pregnant or about to become pregnant. If you are pregnant or breastfeeding, there may be risks to you and your baby that are not yet clear. Pregnancies in women of childbearing age will be checked during the study. For women taking the study drug, there is no information on whether the study drug is safe for nursing or unborn infants. In order to participate in this study, you must use contraception. If you are sexually active, you should use a method of contraception that is acceptable to you, the investigator, and the sponsor.

It is important that you tell the study staff immediately if you become pregnant or think you may become pregnant while participating in this study. If you become pregnant, you will be discontinued from the study and the investigator will discuss with you what you should do. The researchers will give you contact details for the project and you may be asked questions about pregnancy and babies even after the study ends.

For male study participants: Participation in this study may damage your sperm and harm the children you conceive during the study. This injury is currently unpredictable. Please inform your

partner of this risk to the unborn baby. She should understand that if she is pregnant, you need to tell your research staff immediately, and she should tell her doctor immediately.

other risks

There may also be risks, discomforts, drug interactions, or adverse reactions that are currently unforeseen.

If the research involves personal privacy issues, please describe the harm that may result, such as: If you accidentally disclose personal information, it may have an adverse impact on your work, study and life.

7. Is there a direct benefit to participating in this study?

You will not benefit directly from this study, but we hope that the information we get from your participation in this study will benefit future patients with the same condition as you.

8. Are there alternative treatment options if you do not participate in this study?

You can choose not to participate in this study, which will not have any adverse effect on your access to regular treatment. Current treatments for your health include: Statins and/or cholesterol absorption inhibitors and other PCSK9mAb for lipid lowering and anti-myocardial ischemia.

9. Costs and compensation for participation in the study

If you are randomly assigned to the PCSK9mAb group, PCSK9mAb drugs will be provided by the project group. Study participants will not be provided with study-related test costs and will be responsible for them. Study participants will participate in this medical study free of charge, but you will not be paid or compensated for this study. You can ask any questions about this study and this consent form at any time and get answers accordingly.

10. Treatment of Study-related Damage

Please inform the investigator (Dr. Wu Naqiong, contact number: 15699870239), we will take necessary medical measures in a timely manner and determine compensation or compensation liability in accordance with relevant laws and regulations of China.

11. Will my information be kept confidential?

If you decide to participate in this study, your participation and personal information in the study will be kept confidential. When your study data is used in this study, your personal information will be kept confidential and all your information will be stored properly and used only for this

study.

The information in the study database and samples is strictly desensitized to eliminate personal identifiers, and information that may identify you will not be disclosed to anyone other than the researchers unless your permission is obtained.

In order to ensure that the study is conducted in accordance with regulations, inspectors of the project team, ethics committee, drug regulatory authorities and health authorities may consult the original medical records of study participants to verify the process and data of clinical study without violating the confidentiality principle and relevant laws and regulations.

If the results of the study are published publicly, your personal information will not appear in any public medical records and publications, nor will we disclose this information to anyone or any organization.

12. What are the rights and interests of study participants during the study?

You may be informed of information about this study at any time during the study. Whether you participate in this study is entirely up to you. You are free to participate or refuse to participate in this study.

Whether or not you agree to participate in this study will not affect the clinical routine measures you should take during your visit to our hospital, nor will you receive special medical treatment. You can refuse to participate at any time or have the right to withdraw from the study at any time at any stage of the study without any reason, without discrimination or retaliation, and without affecting the corresponding medical treatment or rights.

If you want to withdraw from the study, please inform the investigator and complete the withdrawal procedures in writing as required; The researchers will no longer collect and use your study/trial data, but data that has been anonymized for population analysis or anonymized for publication prior to your withdrawal will not be deleted or withdrawn.

If you want to participate in this study, you need to read this informed consent form carefully and sign it after confirming that you fully understand the relevant issues. By signing this document, you will not lose any legal rights granted to you by law.

During the study, you have the right to obtain new information about this study, and you also have the right to obtain the informed consent form and re-sign the new version of the informed consent

form. Study participants and their guardians will be informed of new information that may affect your continued participation in the trial.

If you agree to sign this document, Fuwai Hospital of Chinese Academy of Medical Sciences will obtain your biological samples and study data free of charge, and the investigators of our hospital and the co-study institutions participating in this study may use your biological samples and study data for the purpose of this study.

13. Circumstances and reasons why study participants may be terminated

(1) After randomization, serious violations of inclusion criteria or exclusion criteria were found, affecting the efficacy evaluation;

(2) Serious complications, complications or special physiological changes occur, and it is not suitable to continue the trial;

(3) In case of allergic reaction or serious adverse event, the trial should be stopped according to the judgment of the doctor.

The project team and study sponsor may also terminate the study during the study period. In the event of premature termination of this study, we will notify you in a timely manner, and your research staff will advise you on the next treatment plan based on your health status. For study participants who drop out halfway, we have a final follow-up plan for safety reasons, and you have the right to refuse. If, after you opt out, we discover new information relevant to your health and rights, we may contact you again.

After you withdraw from the study, no new data will be collected about you in the future. The investigator will keep the relevant information before you withdraw from the study until it is finally destroyed, and will not continue to use or disclose it. However, in rare cases, this information needs to be used. For example, when the government supervision department carries out supervision, inspection and statistics, it will ask to see all the research information, including relevant information about your participation in the research at that time.

14. Would you like to participate in future research?

If you agree to participate in future research, you will need to check the consent to participate in future research on the signing page of this informed consent form. We want to keep the remaining samples that you test during the study. In addition, we would like to continue to follow you up for

a long time after the end of the study to understand your health status and medication information. Your de-identified residual biological samples, research data, clinical diagnosis and treatment data (including but not limited to medical records, imaging data, clinical test and monitoring data, including examination data from other hospitals, etc.) and follow-up data will continue to be used for subsequent approved genetic and non-genetic medical research on cardiovascular diseases, so as to explore the causes, mechanisms and influencing factors of disease occurrence and development, and develop and evaluate disease prevention and treatment measures. If you do not agree, after the completion of this study, the remaining samples of your study will be destroyed according to clinical routine, and the study data and clinical diagnosis and treatment data will be stored for a specified period of time according to national regulations and kept strictly confidential.

15. If there is a problem or difficulty, who should I contact?

We will keep you or your guardian informed of new information that may affect your continued participation in the study/clinical trial.

If you would like information about this study/clinical trial, please contact the project team at: 15699870239。

If you experience symptoms, injuries or other medical problems related to participation in this study/clinical trial, please contact the study doctor promptly: Wu Naqiong; Tel: 15699870239.

If you have any questions about your rights and interests, please contact the Ethics Committee of Fuwai Hospital at: 010-88396281。

Thank you for taking the time to read this consent form. If you and your family agree to participate in this study after due consideration, we hope that you and your family will complete this study as requested by the investigator. Please complete and sign the last page (signature page) of this document in duplicate with your investigator prior to participating in this study, one copy each for you and the hospital.

Signature Page

Study Participant Statement

- I have carefully read, understood and agreed to all terms and conditions of this informed consent form.
- I have been informed of the objectives, contents, procedures, possible risks, compensation and rights of this clinical trial; I had ample time and opportunity to ask questions and received answers to my satisfaction.
- I agree to participate in this study and authorize you to collect my biological samples and study data for this study.
- I promise that the information I provide is true; If false information is provided, I promise to be responsible for the consequences.
- I was also told who to contact when I had questions or wanted further information.
- I confirm that the contact information left in the signature office is my valid contact information. If I change my contact information, I shall inform your hospital in time. Otherwise, I am willing to bear the corresponding consequences of not being able to contact and receive notification.
- I know that I can withdraw from this study at any time without affecting my medical treatment and rights, and that the investigator may suspend/terminate my participation in this study at any time.
- I will receive an original copy of this informed consent form, signed by me and the investigator.
- **I agree to participate in this study.**

Consent to participate in future research ☐**Agree** ☐**Do not agree (please choose)**

To donate remaining test samples, clinical diagnosis, study data and long-term follow-up data for future research, authorize investigators and co-research units of relevant medical research projects to use and process my anonymous remaining samples and data in approved cardiovascular related genetic and non-genetic medical research.

Name of study participant: Signature:

Date:

(Signature of guardian if study participant is incapacitated or with limited capacity)

Name of guardian Signature:

Relationship to study participants: Date:

- I confirm that the information in the informed consent form was correctly interpreted and understood by the study participant and/or the study participant's legal representative. Study participants voluntarily agreed to participate in this study.

Investigator's statement

- I confirm that the details of this study have been explained to the study participants. Including their rights as well as benefits and risks, answered questions from study participants, and gave them a copy of the signed informed consent form. Study participants volunteered to participate in the study.

Investigator: Signature:

Date: