



## **PARTICIPANT INFORMATION SHEET AND CONSENT FORM**

### **(Healthy Volunteers)**

You are being invited to participate in a research study. Your participation in this study is entirely voluntary. Before you take part in this research study, the study will be explained to you, and you must be given the chance to ask any questions that you may have. Your questions will be answered clearly and to your satisfaction. Please read carefully the information provided here. If you agree to participate, please sign the consent form. You will be given a copy of this document.

### **STUDY INFORMATION**

**Protocol Title:**

Phase 1/2 Trial integrating allogeneic NK cells in high-risk advanced Stage III–IV nasopharyngeal cancer patients

**NCT Number:** NCT07247201

This research study is recruiting at the following SingHealth institution(s). Please note that the word “SingHealth” refers to the institution where you are recruited into the study.

☐ Singapore General Hospital

Principal Investigator:

A/Prof Lim Chwee Ming

Otorhinolaryngology- Surgery of head and neck

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### **PURPOSE OF THE RESEARCH STUDY**

The purpose of this research study is to determine how effective Natural Killer (NK) cell therapy (Study Drug) combined with Chemotherapy and Radiotherapy can help in reducing Nasopharyngeal cancer (NPC) recurrence and determine the highest amount of allogeneic NK cells that is safe and tolerable. The allogenic means that the NK cells is extracted from another healthy person. Allogenic NK cell therapy has shown to be well-tolerated among cancer patients previously. However, this method has not been investigated in NPC before. This is a first-in-man study in Singapore using allogeneic cells in NPC treatment. This means that this is the first-time allogenic NK cell therapy is tested in NPC patients in Singapore.

This study targets to recruit 40 to 70 healthy volunteers aged between 21 to 50 with body mass index of 19.0 - 30.0 kg/m<sup>2</sup> to provide the source of allogenic NK cells that is required for this study.

You were selected as a healthy donor for this study. Your blood that is donated will be used as the starting material for the NK cells manufacturing which will be used for this clinical trial.

This informed consent form is for the healthy volunteers participating in the clinical trial.

**How your blood will be used:**

Your donated blood will be processed in a specialised laboratory to extract and grow NK cells. These NK cells must meet strict quality standards (at least 90% purity) before they can be used in the clinical trial. The NK cells will be given to NPC patients at different dose levels (ranging from  $0.5 \times 10^7$  to  $1.8 \times 10^7$  cells per kilogram of patient body weight) to find the safest and most effective amount.

**STUDY PROCEDURES & YOUR RESPONSIBILITIES IN THIS STUDY**

The study involves the following:

**Biological Material:**

**A) Screening phase (7-10 days)**

We will take blood from your arm using a syringe and needle for the screening test. We would take about 20 ml of blood and the blood sample will be screened for Human immunodeficiency virus type 1 and type 2 (HIV-1/2), Human T-lymphotropic virus type I/II (HTLV-I/II), Syphilis, Cytomegalovirus (CMV), Hepatitis B virus (HBV), Hepatitis C (HCV), Hepatitis E virus (HEV), and Vesicular stomatitis virus (VSV). These are basically to test for any possible infectious agents present in your blood prior to blood donation.

Once your blood tests have returned, and if you have been tested negative for all the possible infectious agents mentioned above, you would be deemed suitable for this blood donation. The screening results are valid for 7 days, so we will arrange your blood donation visit within this timeframe.

Also, a baseline blood count will be done to ensure that your haemoglobin is more than the required amount of 12.5 g/dl (for females) and 13 g/dl (for males).

Please note that you would be requested to complete a questionnaire which would approximately take about 10 minutes to complete. Your consent would be obtained before proceeding for screening test.

**B) Blood donation phase (“biological” materials)**

Once you are certified to be fit for blood donation, you will be asked to donate about 300 – 400 ml of blood. The blood donation process will last approximately 15-30 minutes.

After the blood donation is completed, you would be observed for 10-15 minutes to ensure that you are feeling well before you are allowed to leave. The whole process should take no more than 1 hour.

For the blood donation, the blood will be collected using a needle and blood bag.

*Your participation in the study will last up to 10 days. You will need to visit the doctor for 2 times in the course of the study.*

**Questionnaire:**

You will be asked to complete a “Healthy Donor Screening” questionnaire which would take about 10 minutes. The questionnaire will cover about your general health, past and current medical conditions, medications you are taking, history of any chronic medical conditions, travel history, lifestyle factors (such as smoking and alcohol use) and any recent exposure to infectious diseases. The purpose of this questionnaire is to ensure that you are medically suitable to donate blood.

Your information will be kept confidential and only the study team will have access to your questionnaire responses.

**WHAT IS NOT STANDARD CARE OR IS EXPERIMENTAL IN THIS STUDY**

The study is being conducted because administration of NK cells is not yet proven to be a standard treatment in patients with nasopharyngeal cancer. We hope that your participation will help us to determine whether this treatment is equal or superior to existing treatments.

In this study, the collection of blood will be used as the starting material for NK cell manufacturing.

**POSSIBLE RISKS, DISCOMFORTS OR INCONVENIENCES**

**Collection of blood:**

Taking blood may cause momentary discomfort, pain, bleeding, bruising or swelling at the site of the needle stick. Rarely, taking blood may cause fainting or infection.

**Blood donation:**

Blood donation may cause some discomfort, bruising or swelling at the side of the collection. Local anesthesia is usually administered at the site of the collection, and there will be minimal pain experienced.

**Questionnaires:**

Some of the questions might make you feel uncomfortable or upset. You may refuse to answer any of the questions and/or take a break at any time during the process.

**Personal privacy and confidentiality:**

This study uses information that may affect your privacy. To protect your confidentiality, only a unique code will be used to identify data and biological material that we collected from you.

As there will be a link between the code and your identifiable information, there is still a possibility of data breach. A data breach is when someone sees or uses data without permission. If there is a data breach, someone could see or use the data we have about you. Even without your name, there is a chance someone could figure out who you are. They could misuse your data. We believe the chance of this is very small, but it is not zero.

## **POTENTIAL BENEFITS**

There is no assurance you will benefit from this study. However, your participation may add to the medical knowledge about the use of this NK cells infusion as treatment for Nasopharyngeal cancer.

## **IMPORTANT INFORMATION FOR FEMALE PARTICIPANTS**

Pregnant and breast-feeding women may not take part in this study. If you become pregnant at any time during the screening or donation period, you must stop participating in the blood donation program and call your doctor or the Principal Investigator immediately.

## **ALTERNATIVE IF YOU DO NOT PARTICIPATE IN THE STUDY**

There is no alternative to the study procedures. You can choose not to take part in this study.

## **COSTS & PAYMENTS IF PARTICIPATING IN THIS STUDY**

There will be no reimbursement to you for the study procedure as this blood donation is purely on volunteer bases. However, the cost for the blood donation and the screening procedures will be borne by the study.

## **INCIDENTAL FINDINGS**

Incidental findings are not expected to arise from participation in this study, you will only undergo standard pre-donation screening tests to determine eligibility for blood donation. No investigation or research specific procedures will be performed.

As part of the eligibility screening, tests for infectious diseases will be done. If any abnormal or positive results are found, you will be informed. Your study doctor or another qualified healthcare professional will explain the finding and discuss what steps you should take next. You may choose to do further tests or seek medical advice to confirm the result. Please note that any costs for follow-up care, diagnosis, or treatment will not be covered by the study.

## **WHAT HAPPENS TO THE SAMPLES COLLECTED FOR THE RESEARCH**

The biological materials (blood) collected for this research study will be deemed to be donated to SingHealth as a gift. By agreeing to this, you give up your rights to the biological materials. If the use of your biological materials and/or your data results in intellectual property rights and commercial benefits, you will not receive any financial benefits or proprietary interest.

The biological materials collected will be destroyed upon completion of the study, unless you give permission for any leftover samples to be kept for future use in other research studies. For this purpose, your consent for future research will be sought from you.

## **PARTICIPANT'S RIGHTS**

Your participation in this study is entirely voluntary. You have a right to ask questions, which the study team will do their best to answer clearly and to your satisfaction.

In the event of any new information becoming available that may be relevant to your willingness to continue in this study, you (or your legal representative, if relevant) will be informed in a timely manner by the Principal Investigator or his/her representative and will be contacted for further consent if required.

## **WITHDRAWAL FROM STUDY**

You are free to withdraw your consent and discontinue your participation in the study at any time, without your medical care being affected. If you decide to stop taking part in this study, you should tell the Principal Investigator.

Any remaining biological materials that have been collected for the study will be destroyed following the withdrawal of your consent if they are individually-identifiable and (i) have not been used for research; OR (ii) have been used for research but it is practicable to discontinue further use of the samples for the research unless you give consent at the time of withdrawal for your archival tissue samples to be used for correlative analyses with those who have completed the trial.

However, any research information or data obtained before your withdrawal of consent will be retained and may continue to be used. This is to allow a complete and comprehensive evaluation of the research study.

Your study doctor, the Principal Investigator of this study may stop your participation in the study at any time for one or more of the following reasons:

- Failure to follow the instructions of the Principal Investigator and/or study staff.
- The Principal Investigator decides that continuing your participation could be harmful to your health or safety
- Development of a significant health disorder
- Pregnancy

## **RESEARCH RELATED INJURY AND COMPENSATION**

If you follow the directions of the Principal Investigator of this research study and you are injured due to the study procedure given under the plan for the research study, our institution will provide you with the appropriate medical treatment.

Payment for management of the normally expected consequences of your treatment (i.e. consequences of your treatment which are not caused by your participation in the research study) will not be provided.

You still have all your legal rights. Nothing said here about treatment or compensation in any way alters your right to recover damages where you can prove negligence.

## **CONFIDENTIALITY OF STUDY AND MEDICAL RECORDS**

Your participation in this study will involve the collection of Personal Data. "Personal Data" means data about you which makes you identifiable (i) from such data or (ii) from that data and other information which an organisation has or likely to have access. Examples of personal data include name, national registration identity card (NRIC), nationality, passport information, date of birth, and telephone number.

Personal Data collected for this study will be kept confidential and stored in Singapore. Your study records and medical records (if applicable), to the extent required by the applicable laws and regulations, will not be made publicly available. To protect your identity, your Personal Data will be labelled with a unique code. The code will be used in place of your name and other information that directly and easily identifies you. The study team will keep a separate file that links your code to your Personal Data. This will be kept in a safe place with restricted access. In the event of any data sharing with third parties (e.g. funding agencies, research collaborators) whether locally or overseas and publication regarding this study, your identity will remain confidential.

**Data deposition into scientific database:**

We will deposit data collected in this study, including the data we collect about you to public and/or controlled-accessed scientific databases. It will not include your name or other data that directly identifies you. This will enable other researchers, whether locally or overseas, to use the data to investigate other important research questions.

However, the monitor(s), the auditor(s), the Institutional Review Board, and the regulatory authority(ies) will be granted direct access to your original medical records (if applicable) and study records to verify study procedures and data, without making any of your information public.

By signing the Consent Form, you consent to (i) the collection, access to, use and storage of your Personal Data by SingHealth, and (ii) the disclosure of such Personal Data to our authorised service providers and relevant third parties as mentioned above. To the fullest extent permitted by applicable law, under no circumstances will SingHealth and/or its affiliates be liable for any direct, indirect, incidental, special or consequential loss or damages arising out of any data breach event.

All data collected in this study are the property of SingHealth. The data will be used for the purpose of this research study only, unless you give permission for your data to be made available for future use in other research studies. For this purpose, consent for future research will be sought from you.

By participating in this research study, you are confirming that you have read, understood and consent to the SingHealth Data Protection Policy, the full version of which is available at [www.singhealth.com.sg/pdpa](http://www.singhealth.com.sg/pdpa).

**WHO HAS REVIEWED THE STUDY**

This study has been reviewed by the SingHealth Centralised Institutional Review Board for ethics approval.

If you have questions about your rights as a participant, you can call the SingHealth Centralised Institutional Review Board at 8126 3660 during office hours (8:30 am to 5:30pm).

**WHO TO CONTACT IF YOU HAVE QUESTIONS REGARDING THE STUDY**

If you have questions about this research study or in the case of any injuries during the course of this study, you may contact your study doctor, the Principal Investigator listed under STUDY INFORMATION section, at the beginning of this document.

If you have any feedback about this research study, you may contact the Principal Investigator or the SingHealth Centralised Institutional Review Board.

## CONSENT FORM FOR RESEARCH STUDY

### Study Title:

Phase 1/2 Trial integrating allogeneic NK cells in high-risk advanced Stage III–IV nasopharyngeal cancer patients

### Declaration by Research Participant

- I agree to participate in the research study as described and, on the terms, set out in the Participant Information Sheet. The nature, risks and benefits of the study have been explained clearly to me, and I fully understand them.
- I understand the purpose and procedures of this study. I have been given the Participant Information Sheet and the opportunity to discuss and ask questions about this study and am satisfied with the information provided to me.
- I understand that the de-identified data collected about me in this study may be deposited in open-access or access-controlled scientific database for potential use by other researchers, whether locally or overseas, to answer other important research questions, to advance medical research.
- I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reasons.
- By participating in this research study, I confirm that I have read, understood and consent to the SingHealth Data Protection Policy.

\_\_\_\_\_  
Name of participant

\_\_\_\_\_  
Signature/Thumbprint (Right / Left)

\_\_\_\_\_  
Date of signing

### To be completed by translator, if required

The study has been explained to the participant/ legal representative in

\_\_\_\_\_ by \_\_\_\_\_  
 Language Name of translator

**To be completed by witness, where applicable**

I, the undersigned, certify that:

- I am 21 years of age or older.
- To the best of my knowledge, the participant or the participant's legal representative signing this informed consent form had the study fully explained to him/her in a language understood by him/ her and clearly understands the nature, risks and benefits of the participant's participation in the study.
- I have taken reasonable steps to ascertain the identity of the participant or the participant's legal representative giving the consent.
- I have taken reasonable steps to ascertain that the consent has been given voluntarily without any coercion or intimidation.

Witnessed by: \_\_\_\_\_  
 Name of witness Date of signing

\_\_\_\_\_  
 Signature of witness

1. An impartial witness (who is 21 years of age or older, has mental capacity, who is independent of the research study, and cannot be unfairly influenced by people involved with the research study) should be present during the entire informed consent discussion if a participant or the participant's legal representative is unable to read, and/or sign and date on the consent form (i.e. using the participant's or legal representative's thumbprint). After the written consent form and any written information to be provided to participant is read and explained to the participant or the participant's legal representative, and after the participant or the participant's legal representative has orally consented to the participant's participation in the study and, if capable of doing so, has signed and personally dated the consent form, the witness should sign and personally date the consent form. This is applicable for Clinical Trials regulated by HSA and Human Biomedical Research under the HBRA.

2. For HBRA studies, the witness may be a member of the team carrying out the research only if a participant or the participant's legal representative is able to read, sign and date on the consent form.

**Investigator's Statement**

I, the undersigned, certify to the best of my knowledge that the participant/ participant's legal representative signing this consent form had the study fully explained to him/her and clearly understands the nature, risks and benefits of the participant's participation in the study.

\_\_\_\_\_  
 Name of Investigator/ Signature Date  
 Person obtaining consent



## INFORMATION & CONSENT FORM FOR FUTURE RESEARCH

This is an optional component that is separate from the research study. You may still participate in the research study if you say “No” to this. Please ask questions if you do not understand why we are asking for your permission.

In this Consent Form for Future Research, we seek your permission to keep all information collected about you (Personal Data and research data) and leftover biological materials (blood related product such as peripheral blood mononuclear cells (PBMCs) or expanded Natural Killer cells) for Future Research. Except if you withdraw your consent or there are limits imposed by law, there is no limit on the length of time we will store the data and biological materials. Researchers will use the data and biological materials for research long into the future.

This is what will be done with the data and leftover biological materials:

- We may use the data and biological materials to answer additional research questions in other research studies, which are outside the scope of the research study (“Future Research”).
- We may also share the data and biological materials with other researchers within and/or outside of Singapore, for use in Future Research. The biological materials will not be used in research involving human-animal combinations, which is restricted by Singapore law.
- We may deposit the data into research data repository for long-term use by the wider research community, for use in Future Research. Researchers share information with each other by depositing data into research databases. These databases store information from many other research studies. Researchers can then study the combined information to learn even more about human health and diseases, to advance medical research.
  - We may deposit the data into one or more open-access (public scientific database) and/or controlled-access research databases. Anyone on the Internet can access publicly accessible database. Only researchers (including private companies involved in publicly funded research) who apply and are granted approval can access controlled-access databases.
  - Where required, researchers may request that the research data be combined or linked with data from other sources, including but not limited to healthcare billing information, government administrative and/or research data such as health, and health-related data, social data, education data, birth and death data, economic and housing data, data from disease registries and databases, whether by itself or with the assistance of a data intermediary. This will enrich their data analysis and provide valuable information for policy and research into health and wellbeing of the population (public interest). The data intermediary will use strict privacy preserving policies, protocols and procedures to ensure security of the data and confidentiality of the individuals the records relate to.
- You should not expect to get personal test results from Future Research. However, it may be possible that incidental findings will be detected in the course of conducting Future Research. If this happens, we may contact you to find out if you would like to learn more. Only medically actionable incidental findings (where medical treatment is available) will be disclosed. You will be asked to indicate whether you wish to be re-identified and notified in the event of an important incidental finding that is related to you.
- We may also use the data and biological materials for purposes other than research such as teaching, or training future researchers, development of health policy, quality control, validation testing.

This is what will be done to protect confidentiality of the data and biological materials:

- Any information that could identify you will be removed (de-identified) before this de-identified data and biological materials are used and/or shared with other researchers and/or deposited into research data repository.
- The open-access and controlled-access research data repositories have robust procedures in place to protect confidentiality of the stored data. Although these repositories do not have your identifying information, it may be possible to identify you based on information in the databases when combined with information from other public sources (including information you tell people or post about yourself). We believe the chance of this happening is currently very low.
- If you decide at a later time that you do not want the data and biological materials to be used for Future Research, you can contact the Principal Investigator or study team at any time. All the stored data and biological materials that have not been used or shared with other researchers will be removed from the storage facility and/or destroyed, unless this information is already deposited into the research data repository or included in analyses or used in publications.

The leftover biological materials will be deemed to be donated to SingHealth as a gift. By agreeing to this, you give up your rights to the leftover biological materials. The use of your data and leftover biological materials in Future Research may result in intellectual property rights and commercial profits. If this should occur, you will not be compensated and will not receive any financial benefits or proprietary interest.

If you have questions or wish to provide feedback on the purposes for which the leftover biological materials will be used, you may contact the Principal Investigator.

## CONSENT FORM FOR FUTURE RESEARCH

This component is optional. You do not have to agree to it in order to participate in the research study.

Please indicate your choice using the relevant checkbox.

- ☐ I do not agree to have my data and leftover biological materials stored for future use in other research studies.
- ☐ I agree to have my data and leftover biological materials stored for future use in other research studies, as described above. I understand that I will not be contacted again personally, for approvals to use and share my data biological materials for such Future Research. Research arising in the future, will be subject to review by the relevant institutional review board, where applicable.

I understand the purpose and nature of this optional component (storage of data and leftover biological materials for future use). I have been given the Information & Consent Form for Future Research and the opportunity to discuss and ask questions about this optional component and am satisfied with the information provided to me.

I confirm that I have read, understood and consent to the SingHealth Data Protection Policy.

\_\_\_\_\_  
Name of participant

\_\_\_\_\_  
Signature/Thumbprint (Right / Left)

\_\_\_\_\_  
Date of signing

**To be completed by translator, if required**

The optional component (storage of data and leftover biological materials for future use) has been explained to the participant/ participant's legal representative in

\_\_\_\_\_ by \_\_\_\_\_.  
Language Name of translator

**To be completed by witness, where applicable**

I, the undersigned, certify that:

- I am 21 years of age or older.
- To the best of my knowledge, the participant or the participant's legal representative signing this Information & Consent Form for Future Research had the optional component fully explained to him/her in a language understood by him/ her and clearly understands the purpose and the nature of this optional component.
- I have taken reasonable steps to ascertain the identity of the participant or the participant's legal representative signing this Information & Consent Form for Future Research.
- I have taken reasonable steps to ascertain that the participant or the participant's legal representative has not been coerced into giving consent.

Witnessed by: \_\_\_\_\_  
Name of witness Date of signing

\_\_\_\_\_  
Signature of witness

1. An impartial witness (who is 21 years of age or older, has mental capacity, who is independent of the research study, and cannot be unfairly influenced by people involved with the research study) should be present during the entire informed consent discussion if a participant or the participant's legal representative is unable to read, and/or sign and date on the consent form (i.e. using the participant's or legal representative's thumbprint). After the written consent form and any written information to be provided to participant, is read and explained to the participant or the participant's legal representative, and after the participant or the participant's legal representative has orally consented to the participant's participation in the study and, if capable of doing so, has signed and personally dated the consent form, the witness should sign and personally date the consent form. This is applicable for Clinical Trials regulated by HSA and Human Biomedical Research under the HBRA.

2. For HBRA studies, the witness may be a member of the team carrying out the research only if a participant or the participant's legal representative is able to read, sign and date on the consent form.

**Investigator's Statement**

I, the undersigned, certify to the best of my knowledge that the participant/ participant's legal representative signing this Information & Consent Form for Future Research had the optional component (storage of data and leftover biological materials for future use) fully explained to him/her and clearly understands the purpose and the nature of this optional component.

Name of Investigator/ Person obtaining consent	Signature	Date