Centre Number: _____ **Patient Study Identification Number:** _____

PARTICIPANT INFORMATION SHEET – REFINE-Lung Translational Sub-Study: predicting immunotherapy outcomes

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Full title: A randomised open-label phase III trial of REduced Frequency pembrolizumab ImmuNothErapy for first-line treatment of patients with advanced non-small cell lung cancer (NSCLC) utilising a novel multi-arm frequency-response optimisation design

REFINE-Lung = **R**educed **F**requency pembrolizumab **I**mmu**N**oth**E**rapy: can the frequency of pembrolizumab treatment for non-small cell lung cancer be reduced without reducing its effectiveness?

Introduction

We would like to invite you to take part in our research study. Before you decide if you want to take part, we would like you to understand why the research is being done and what it would involve for you. **Someone from our team will go through the information sheet with you and answer any questions you have**. Please read the information carefully and talk to others, including your GP, about the study if you wish.

Please ask us if there is anything that is not clear, or if you would like more information. Take as much time as you need to decide whether or not you wish to take part. Once you have decided if you want to take part, you will be asked to sign the informed consent form. You will get a copy of this form.

Thank you for taking the time to read this information sheet.

1. What is the purpose of the study?

Pembrolizumab is often used to treat people diagnosed with advanced non-small cell lung cancer (NSCLC). Pembrolizumab helps to fight cancer by activating the immune system, the body's natural defence against disease.

Whilst an effective treatment for many people, pembrolizumab does not work in all cases and we do not understand why. This sub-study aims to better understand why some but not all patients benefit. This understanding will help us develop better therapies and ways of finding people who are unlikely to benefit so they can be offered more effective treatments.

We will do this by collecting blood samples when you attend for routine tests and obtain any previously stored cancer samples, for instance from when you had a biopsy or surgery in the past. We will also collect CT scans that are done routinely and information on your response to immunotherapy during the course of your treatment.

The REFINE-Lung trial gives us a unique opportunity to study why some people benefit and others do not from immune therapy. Pembrolizumab is usually given every 3 or 6 weeks for up to 2 years. Our research suggests that standard treatment is too frequent. We think that after 6 months, how often pembrolizumab is given can be reduced without reducing how well the treatment works. For instance, we may be able to give pembrolizumab every 9 or 12 weeks instead of 3 or 6 weeks. Safely

reducing treatment frequency is the main aim of the REFINE-Lung study and will have many potential benefits, including fewer visits to hospital, fewer side-effects and improvements in quality of life.

2. Why have I been invited to take part?

You have been invited to take part in this sub-study because you have advanced NSCLC and you are about to receive pembrolizumab every 3 or 6 weeks. We would like to collect data and samples during this period to better understand NSCLC. This sub-study is part of the main REFINE-Lung study and your oncologist thinks you may be suitable to take part in that after 6 months of treatment. For further information on this your doctor can give you the information sheet.

3. Do I have to take part?

No. It is up to you to decide whether or not to join the study. If you prefer not to take part, you do not have to give a reason. If you do decide to take part after reading this information leaflet, you will be asked to sign a consent form and you will be given a copy to take away with you. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive.

Your cancer specialist or the study sponsor (Imperial College London) may decide at any time, and for any reason, to stop the study, even though you may want to continue. Full details are included in section 9 to 11.

4. What will happen to me if I take part?

The study is split into 3 steps. Each step is explained in this section.

Step 1: Consent

If you are interested in joining the sub-study, you will be asked to sign and date the study consent form and your details will be registered with the trials office responsible for coordinating the study.

Step 2: Data and sample collection

As part of your first 6 months of pembrolizumab, your clinical team will ask you to attend hospital for treatment every 3 or 6 weeks. You will be reviewed by your oncologist and have blood taken before each treatment to check on your progress and whether it is safe to continue. You will have CT scans every 2 or 3 months to check how the treatment is working, with the exact timings decided by your oncologist. We will collect data from these scans as well as data from your routine bloods and pembrolizumab treatment.

In this study, before you start treatment and at 6 and 12 weeks after starting, we may collect approximately 5 teaspoons (up to 25ml) of blood for research purposes. The sample will be taken when you attend for routine bloods so you will not have an extra blood tests, the research team will let you know if these will be collected. Taking this blood sample will not affect your treatment plan in any way. We may also collect one further sample if your tumour grows.

In addition, we will collect any cancer samples taken from your previous biopsy or surgery that is stored in your local hospital.

Step 3: After 6 months of treatment

Once you have been on treatment for 6 months, if your oncologist decides it is ok to continue on the treatment, they will approach you to take part in the main REFINE-Lung study looking at reducing the frequency of pembrolizumab. You will have to sign another consent form to take part in this. If you do take part and agree, we will continue collecting blood samples and CT scans until your treatment is finished.

5. What do I have to do?

If you take part in this study, you should not need to attend hospital more often than if you did not take part. Extra blood samples for research will be taken when you have routine blood tests, but we might ask for an extra blood test if the treatment stops working.

6. Will I be compensated for taking part in the study?

You will not be paid for taking part in the study. You should not have to attend hospital for any extra visits above those you would for any standard treatment, so you will not be reimbursed for your travel expenses.

7. What are the possible disadvantages and risks of taking part?

You will have regular blood samples taken whether you take part in this study or not. As with all blood tests, there is a possibility of slight redness, swelling and/or bruising developing at the site where the needle is placed into your arm. It is also possible that you may feel lightheaded or faint. Please tell the study doctor or study staff if you do not feel well after having your blood taken.

8. What are the possible benefits of taking part?

You will not benefit directly as a result of taking part in this sub-study.

The results of this sub-study will help understand the reasons why some people benefit from immunotherapy and why others do not and may lead to better management of people with advanced NSCLC in the future.

9. What will happen if I don't want to carry on with the study?

You must tell your study doctor immediately if you no longer wish to take part in the study. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will not collect any new information about you, but we will keep the information about you that we have already obtained including any research samples. To safeguard your rights, we will use the minimum personally-identifiable information possible.

10. What if something goes wrong?

Imperial College London holds insurance policies which apply to this study. If you experience harm or injury as a result of taking part in this study, you will be eligible to claim compensation without having to prove that Imperial College London is at fault. This does not affect your legal rights to seek compensation.

If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Imperial clinical trials team by phoning 020 7594 2180. The normal National Health Service mechanisms are also available to you. Details can be obtained from your study doctor or nurse. If you are still not satisfied with the response, you may contact the Imperial College, Research Governance and Integrity Team.

11. How will we use information about you?

Imperial College London is the sponsor for this study, based in the United Kingdom, and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. Imperial College will keep your personal data for:

- 10 years after the main study has finished in relation to data subject consent forms
- 10 years after the main study has completed in relation to primary research data.

We will need to use information from your medical records for this research project. This information will include your month and year of birth. People will use this information to do the research or to check your records to make sure that the research is being done properly. If you decide to take part in the study, you give individuals from the Imperial College study team and its representatives, the National Institute for Health Research (NIHR), contracted companies conducting review of radiological imaging, regulatory authorities, or the NHS Trust/Health Board where it is relevant to

your taking part in this research permission to use, analyse, and evaluate any information gathered about you in this study and share it with others as described in the subsection below.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a unique code number (study ID) instead.

Stored tissue and copies of CT scans for independent review will be labelled with your study ID, and the month and year of your birth, and not with any personal identifiers such as your name.

We will keep all information about you safe and secure.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

LEGAL BASIS

As a university we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study.

Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research

INTERNATIONAL TRANSFERS

There may be a requirement to transfer information to countries outside the United Kingdom (for example, to a research partner). Where this information contains your personal data, Imperial College London will ensure that it is transferred in accordance with data protection legislation. If the data is transferred outside of the United Kingdom, Imperial College London will enter into a data sharing agreement with the recipient organisation to safeguard how your personal data is processed. You will not be able to be identified when sharing this data but it may include demographic information such as the month and year of your birth as well as your study ID.

SHARING YOUR INFORMATION WITH OTHERS

For the purposes referred to in this privacy notice and relying on the bases for processing as set out above, we will share your personal data with certain third parties, including the Medical Research Council Clinical Trials Unit and University College London who will perform the analysis of the study data.

Other College employees, agents, contractors and service providers (for example, suppliers of printing and mailing services, email communication services or web services, or suppliers who help us carry out any of the activities described above). Our third party service providers are required to enter into data processing agreements with us. We only permit them to process your personal data for specified purposes and in accordance with our policies.

WHAT ARE YOUR CHOICES ABOUT HOW YOUR INFORMATION IS USED?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have. If you choose to stop taking part in the study, we would like to continue collecting information about your health from your hospital. If you do not want this to happen, tell us and we will stop.

We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

WHERE CAN YOU FIND OUT MORE ABOUT HOW YOUR INFORMATION IS USED

You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- by asking one of the research team
- by sending an email to REFINE-Lung@imperial.ac.uk or
- by ringing us on 020 7594 2180.

COMPLAINT
If you wish to raise a complaint on how we have handled your personal data, please contact Imperial College London's Data Protection Officer via email at dpo@imperial.ac.uk, via telephone on 020 7594 3502 and/or via post at Imperial College London, Data Protection Officer, Faculty Building Level 4, London SW7 2AZ.

If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO). The ICO does recommend that you seek to resolve matters with the data controller (us) first before involving the regulator.

12. Public Involvement

To help the research team in the running of this study, we have a panel made up of 5 members advising us: three people are lung cancer patients, another has breast and ovarian cancer and one person was a carer for a relative who had lung cancer.

When the public gets involved in research, they work alongside researchers to help shape what research gets done, how it's carried out, and how the results are shared and used in practice. Prior to beginning this research, we discussed the design with several potential patients at conferences. We asked questions about the procedures and tests that we want to carry out, to ensure these were acceptable for patients and collected at appropriate times throughout the study. Our panel has also reviewed all the documents that will be given to you. This was to ensure that the documents are easy to understand and contain the information patients would like to know before signing up. When the study is finished, we will ask our panel to help ensure we share the results using clear language and in patient friendly ways, such as letters, posters, podcasts and videos and that we make them available in places where patients will find them.

Our panel is not the same as taking part in research to test the new frequency of treatment. It's about being a member of the research team that works together to design and run the study.

13. What will happen to any samples that I give?

Your tissue samples will be looked at for quality control purposes in order to confirm the presence of NSCLC. They will also be kept for future analysis at the Experimental Cancer Medicine laboratory at Imperial College London and Imperial College Healthcare Tissue Bank.

If you consent, additional blood samples will be taken throughout your initial phase of treatment and kept for future analysis, along with your tissue, at the Experimental Cancer Medicine laboratory at Imperial College London.

If you withdraw your consent after your tissue or blood sample has been sent, the study doctor will ensure that your blood sample and any extracted genetic material are destroyed. Your tissue sample will be returned to your hospital. However, if genetic research has already been performed the study sponsor is not obliged to destroy results of this research. In this case only the blood sample and extracted genetic material will be destroyed and tissue returned.

14. What rights do I have to see the results of the genetic / biomarker research and personal data?

These parts of the study are for exploratory research purposes only. You will not be provided with your test results, nor will any results be made available to any insurance company, your employer, your family, your study doctor, your GP, or any other doctor who treats you now or in the future.

15. What rights do I have to the results of the genetic / biomarker research?

Any information derived directly or indirectly from this research, as well as any patents, diagnostic tests, drugs, or biological products developed directly or indirectly as a result of this research, are the sole property of the study sponsor (and its successors and licensees) and may be used for commercial purposes by the collaborators. You will have no right to this property or to any share of the profits that may be earned directly or indirectly as a result of this research. However, in signing the consent form and offering samples for research, you do not give up any rights that you would otherwise have as a participant in research.

16. What will happen to the results of the research study?

Your cancer specialists, the study team and the sponsor Imperial College London, plan to publish the results of this study in a scientific journal and/or present them at national and/or international meetings, so that the information will be widely available to all. Lay summaries will be published on websites as appropriate. You will not be personally identified in any publications or reports.

17. Who is organising the research?

Imperial College London is the legal sponsor of this study and is organising the study through the Imperial Clinical Trials Unit – Cancer (ICTU-Ca).

The sponsor of this study will pay your hospital for including you in this sub-study, but your doctor will not receive any personal financial payment if you take part.

18. Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given a favourable opinion by North West – Haydock Research Ethics Committee.

19. Further information and contact details

If you have any questions or concerns about this study, including study-related injury, you can talk to *<insert name of doctor and tel.no>* or the study staff *<insert name and tel. no.>.*

<insert out of hours emergency details and tel.no>

Cancer Research UK provides general information about cancer and its treatment on their website www.cancerhelp.org.uk and a confidential information service by specialist nurses on Tel: 0808 800 4040. Macmillan Cancer Support (www.macmillan.org.uk; Tel: 020 7840 7840 also provides support and counselling to help people living with cancer.

If you would like to speak to an independent advice service, then please contact your local NHS Patient Advice and Liaison Service (PALS): *<insert contact details and tel.no>*

Thank you for taking the time to read this information sheet.
If you decide you would like to take part, you will be given a copy of this information sheet to keep together with a copy of your signed consent form