Participant Information for Participation in Medical-Scientific Research

Title of the Study:
Predicting the Effectiveness and Possible Side Effects of Immunotherapy Using Bacterial Research in Lung Cancer Patients

Official Title: Response and Toxicity Prediction by Microbiome Analysis in Locally Advanced NSCLC Treated with IO (durvalumab MEDI4736) after Concurrent or Sequential Chemoradiotherapy.

Introduction
Dear Sir/Madam,

With this information letter, we would like to ask if you are willing to participate in a medical-scientific study. Participation is voluntary. You are receiving this letter because you are being treated with chemoradiotherapy for locally advanced non-small cell lung cancer, and your doctor has proposed follow-up treatment with immunotherapy (durvalumab).

This letter explains what the study involves, what it means for you, and what the benefits and risks are. It contains a lot of information. Would you like to read through it and decide whether you wish to participate? If you choose to participate, you can fill out the form included in Appendix C.

Ask Your Questions
You can make your decision based on the information in this letter. In addition, we recommend that you:

- Ask questions to the doctor or researcher providing you with this information.
- Discuss the study with your partner, family, or friends.
- Ask questions to the independent expert, Dr. J. Stolk, pulmonologist.
- Read the information on www.rijksoverheid.nl/mensenonderzoek.

1. General Information

The Leiden University Medical Center (LUMC) has set up this study together with researchers from the Antoni van Leeuwenhoek - Netherlands Cancer Institute (AvL-NKI, Amsterdam), Jessa Hospital, Hasselt (Belgium), AZ Turnhout, Turnhout (Belgium), AZ Delta, Roeselare (Belgium), and OLV Aalst, Aalst (Belgium). Hereafter, we refer to the LUMC as the 'sponsor'. Researchers, including doctors, research nurses, and specialist nurses, will conduct the study with a total of 126 patients in various hospitals in the Netherlands and Belgium. AstraZeneca supports this study.

The Medical Ethics Review Committee METC Leiden | The Hague | Delft has approved this study.

2. What is the purpose of the study?

Our body contains many microorganisms such as bacteria, viruses, and fungi, which together are called the microbiome. One important function of the microbiome is protecting against pathogens. This study examines how the microbiome affects the disease progression in patients like you. We aim to determine if a specific composition of bacteria can predict whether immunotherapy will be successful. We also investigate whether the microbiome can help predict who will develop side effects from immunotherapy.

3. What is the background of the study?

A healthy microbiome is crucial for several functions in our body, such as protection against pathogens. The microbiome also plays a key role in developing and maintaining our immune system. The immunotherapy you will receive utilizes your immune system to fight the cancer.

When immunotherapy is given after chemoradiotherapy for non-small cell lung cancer, it increases the chances of recovery. Previous studies have shown that cancer patients with a healthy microbiome have a better chance of success with immunotherapy. A disturbed microbiome may influence the occurrence of side effects related to immunotherapy treatment.

4. How does the study work?

How long does the study last?

If you participate, the study will last about 52 weeks, the same duration as your immunotherapy follow-up treatment.

Step 1: Are you eligible to participate?
We first want to determine if you are eligible to participate. Therefore, the researcher will check:

- Your medical history.
- Whether the chemoradiotherapy treatment has been completed and when you will begin the follow-up immunotherapy.

Step 2: The study
Your follow-up treatment with immunotherapy (the drug is called durvalumab) will be administered every 4 weeks via an IV (intravenous) infusion at the hospital. The follow-up treatment will last a maximum of 52 weeks. Specific tests for this study will be conducted during your regular hospital visits, so you do not need to make extra visits for the study.

Step 3: Examinations and measurements
For the study, we will conduct the following tests:

- **Blood tests:** Blood tests will only be conducted at the LUMC and AvL/NKI. At the start of the study and after 4 weeks, the researcher will take 2 tubes of

blood. A total of 40 ml of blood will be drawn. This amount poses no problems for adults. By comparison, someone who donates blood gives 500 ml per donation. Researchers will perform various tests on this blood to gain a better understanding of how the immune system works. You will not receive any results from this.
- **Stool sample:** At the start of the treatment, we will ask you to collect a stool sample.
- **Throat swab:** At the start of the treatment, we will take a throat swab. The procedure is brief. The researcher will use a cotton swab to rub the back of your throat to collect some mucus.
- **Lung function test:** You will be asked to undergo a lung function test during the study. These tests will be done three times, on the same day you are already at the hospital for your treatment. Therefore, you will not need to make extra trips to the hospital. The lung function tests will take place at the start of the study and after 24 and 52 weeks.

What is different from regular care?

You will not need to make extra visits to the hospital for this study. However, some additional tests will be conducted, as described in Step 3. Appendix B lists the tests done at each hospital visit.

3. What agreements are we making with you?

We want the study to proceed smoothly, so we agree on the following:

- You will not participate in another clinical trial involving treatment while taking part in this study.
- You will attend all scheduled appointments.
- You will contact the researcher in the following situations:
    - If you need to take antibiotics on a doctor's advice.
    - If you experience health issues before or during the study, we will assess together whether the study can continue.
    - If you decide to stop participating in the study.
    - If your phone number, address, or email changes.

4. What side effects, adverse effects, or discomfort might you experience?

Can I experience side effects from the tests conducted?

- Blood samples can cause pain at the injection site and may occasionally result in bruising. Some people feel faint after a blood test. We will ask you to give an extra blood sample at two points, which will coincide with the standard blood draws for your treatment, so no additional needle sticks will be needed.
- Taking a throat swab can trigger a gag reflex in some people. If you are sensitive to this, please let the researcher know beforehand.
- For the lung function test, you will need to breathe in and out deeply a few times using a device. No great breathing force is required, so don't worry if you feel you lack sufficient lung capacity. Some people may cough during or after the test.

Can I experience side effects from immunotherapy treatment? You will receive a standard follow-up treatment with immunotherapy called Durvalumab (brand name: Imfinzi°). Your doctor has already explained the benefits and risks of this treatment when discussing the follow-up therapy. If this was not explained or you cannot remember, please inform the researcher so that they can provide you with the correct information.

5. What are the benefits and disadvantages of participating in the study?

Participating in the study may have both benefits and drawbacks. Here is an overview to help you consider and discuss with others.

Benefits: You will not personally benefit from taking part in this study. However, by participating, you help researchers gain more insight into lung cancer treatment and contribute to the search for better therapies. Participation will not affect your illness or treatment.

Disadvantages:

- You may experience discomfort from the tests described in section 6.
- Participating in the study requires additional time.
- You must adhere to the study protocols.

If you do not wish to participate: You are free to decide whether or not to participate in the study. If you choose not to participate, you will still receive the follow-up immunotherapy treatment that you and your doctor agreed upon. You cannot take part in the study if you do not undergo the follow-up immunotherapy.

6. When does the study end?

The researcher will inform you if new information arises during the study that is important to you. The researcher will ask if you wish to continue.

The study ends for you in the following situations:

- All scheduled tests are completed.
- You decide to stop participating, which you can do at any time by informing the researcher. You do not need to provide a reason, and your immunotherapy treatment will continue, even if you withdraw from the study.
- The researcher believes it is in your best interest to stop. The researcher will still invite you for a follow-up visit.
- One of the following authorities decides to stop the study:
    - The government, or
    - The medical ethics committee overseeing the study.

What happens if you stop the study? The researchers will use the data and biological samples (such as blood, stool, and throat swabs) collected up until the time of withdrawal. If you wish, the biological samples can be destroyed. Please inform the researcher if this is your preference.

The entire study ends when all participants have completed it.

7. What happens after the study?

Will you receive the study results? About two years after your participation, the researcher will inform you of the study's main findings. If you do not want to know, please tell the researcher, and they will not share the results with you.

8. What happens to your data and biological samples?

If you participate in the study, you consent to the collection, use, and storage of your data and biological samples.

Which data will be stored? The following data will be stored:

- Your name
- Your gender
- Your date of birth
- Health-related information
- Information about your illness
- (Medical) data collected during the study

Which biological samples will be stored? Blood samples, stool samples, and throat swabs will be stored.

Why do we collect, use, and store your data and biological samples? We collect, use, and store your data and biological samples to answer the research questions and to publish the results.

How is your privacy protected? To protect your privacy, your data and biological samples will be assigned a code. Only this code will be used to label your data and samples. The key to the code will be stored securely at the hospital. When processing your data and biological samples, only the code will be used. The data sent to the study sponsor (LUMC) will be coded and will not include your name or any information that could identify you. No data will be shared with AstraZeneca, the company that financially supports this study. In reports and publications, no one will be able to trace the information back to you.

Who can access your data? Some individuals may view your uncoded data and personal information. These include:

- A monitor working for the sponsor.
- National and international supervisory authorities, such as the Health and Youth Care Inspectorate.

These individuals are obligated to keep your data confidential. We ask for your permission to allow this access.

How long will your data and biological samples be stored? Your data will be stored in the hospital for 15 years. Your biological samples will also be stored in the

hospital for 15 years, allowing additional tests to be conducted if needed for this study. Once no longer needed, your samples will be destroyed.

Can your data and biological samples be used for other research? After this study, your data and remaining biological samples may be valuable for other lung cancer research. Your data and samples will be stored in the hospital for 15 years for potential future research. You can indicate on the consent form whether you approve this. If you do not consent, you can still participate in the current study and receive the same care.

Can you withdraw your consent for the use of your data? You can withdraw your consent for the use of your data at any time, both for this study and other research. However, if data or biological samples have already been collected, they can still be used. Biological samples will be destroyed upon withdrawal of consent, but any test results already obtained can still be used.

Want to learn more about your privacy rights?

- For more information about your privacy rights, visit www.autoriteitpersoonsgegevens.nl.
- If you have questions or complaints about how your data is handled, contact the party responsible for data processing, which is the LUMC. See Appendix A for contact details and the website.
- If you have privacy complaints, discuss them first with the research team. You can also consult the privacy statement of your institution.

9. Will you receive compensation for participating in the study?

The research tests and extra procedures will not cost you anything. However, you will not receive any compensation for your participation.

10. Are you insured during the study?

You are not covered by additional insurance for this study because participation involves no extra risks. Therefore, the sponsor is not required to arrange extra insurance for this study.

11. Will your general practitioner be informed?

Since this study does not affect your treatment or increase the risk of side effects, your general practitioner will not be informed.

12. Do you have questions?

If you have questions about the study, contact the researcher. If you want advice from someone not involved in the study, you can consult Dr. J. Stolk, a pulmonologist knowledgeable about the study but not participating in it.

Do you have a complaint? If you have a complaint, discuss it with the researcher or your treating physician. If you prefer not to do so, contact the hospital's complaints officer. Appendix A provides information on how to contact them.

13. How do you give consent to participate?

Take your time to consider the study. Afterward, inform the researcher whether you understand the information and whether you wish to participate. If you decide to participate, you will fill out the consent form attached to this information letter. Both you and the researcher will keep a signed copy of this consent form.

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

16. Attachments to this information
    A. Contact Details
    B. Research Procedure Schedule
    C. Consent Form(s)

Attachment A: Contact Information for SITE

If after reading the information, before or during the research:

- You need further information
- You have additional questions
- Problems arise during the research

You can always contact the research team during office hours:

Research Center (to be filled in by each site)
Phone Number:
Email:

Principal Investigator
Name:
Position:
Phone Number:

Independent Doctor
Name:
Position:
Phone Number:

Complaints

For more information about your rights

Attachment B: Research Procedure Schedule

Research Period	Screening	During Immunotherapy Treatment (weeks)
	Before starting immunotherapy	4
Research Procedures		
Signing consent form	x	
Discussing research criteria with staff to determine eligibility for the study	x	
Demographic information, medical history including smoking history	x	
Questions about antibiotic use	x	x
Assessment of disease progression	x	x
Stool sample collection	x	
Throat swab collection	x	
Blood test#	x	x
Lung function test	x	

#The blood test is only conducted at LUMC and AvL/NKI.

Attachment C: Participant Consent Form

Related to
Predicting the effectiveness and potential side effects of immunotherapy based on bacterial analysis in lung cancer patients

PREDICTION trial

- I have read the information leaflet. I was also able to ask questions. My questions were answered satisfactorily. I had enough time to decide whether I want to participate.
- I understand that participation is voluntary. I also know that I can decide at any time to withdraw from the study. I do not need to give a reason for withdrawing.
- I give permission to the researcher to inform my general practitioner that I am participating in this study.
- I give the researchers permission to collect and use my data and biological material. The researchers do this to answer the research question of this study.
- I give permission for storing a (copy) of my signed consent form at LUMC.

- I understand that for the purpose of monitoring the study, certain people may review all of my data. These people are listed in this information leaflet. I give these people permission to review my data for monitoring purposes.

- Please check yes or no in the table below:

I give permission to store my data for use in other research, as stated in the information leaflet. Yes ☐ No ☐
I give permission to store my (remaining) biological material for use in other research, as stated in the information leaflet. The biological material will be stored for 15 years. Yes ☐ No ☐
I give permission to be contacted after this study to ask if I would like to participate in follow-up research. Yes ☐ No ☐

- I agree to participate in this study.

My name (participant): ……..

Signature: …… Date: __ / __ / __

I declare that I have fully informed this participant about the mentioned study.

If any information arises during the study that may affect the participant's consent, I will inform the participant in a timely manner.

Name of researcher (or representative):…….

Signature:…… Date: __ / __ / __

The participant receives a complete information leaflet along with a signed version of the consent form.

16.