TISSUE PRE-SCREENING INFORMED CONSENT FORM

TITLE:	**A PHASE II, SINGLE-ARM STUDY OF ATEZOLIZUMAB IN PATIENTS WITH LOCALLY ADVANCED, UNRESECTABLE STAGE III NON-SMALL CELL LUNG CANCER WHO HAVE NOT PROGRESSED AFTER PLATINUM-BASED CONCURRENT CHEMORADIATION**
PROTOCOL NUMBER:	MO43156
SPONSOR:	F. Hoffmann-La Roche Ltd
STUDY DOCTOR:	Assist. Prof. Martina Vrankar, MD, PhD Phone number: _____
NAME OF INSTITUTION:	Institute of Oncology Ljubljana
INSTITUTION ADDRESS:	Zaloška cesta 2, 1000 Ljubljana, Slovenia
NAME OF ETHICS COMMITTEE:	Republic of Slovenia National Medical Ethics Committee
ETHICS COMMITTEE APPROVAL DATE:	{Date}

SECTION 1: STUDY OVERVIEW

1.1 INTRODUCTION

- In this informed consent form (Tissue Pre-Screening Informed Consent Form), you are being informed about tests that you may allow to be performed on a sample of your cancer tissue. If you agree to participate and you sign the consent, your tissue will be tested to determine certain characteristics about your cancer. Having your tissue tested is a requirement to enroll in clinical study MO43156.
- F. Hoffmann-La Roche Ltd (hereafter referred to as Roche) is the sponsor of this study and is paying the Institute of Oncology Ljubljana to cover the costs of this study, including pre-screening testing of your tumor tissue.
- This consent form tells you what will happen if you agree to have your tumor tissue tested. It also tells you about the possible benefits and risks of the pre-screening testing.
- Taking part in this pre-screening testing is your choice. Please read the information carefully and feel free to ask questions. It may be helpful for you to discuss this information with your family and friends.
- Talk to your doctor about all of your choices and the benefits and risks of each choice.

- If you decide to take part in the pre-screening testing of your tissue sample, you will be asked to sign this consent form. You will be given a copy of your signed consent form. If you choose not to take part, you will not lose the regular care you receive from your doctors.

1.2 WHY IS THIS PRE-SCREENING TESTING BEING DONE?

The purpose of this consent form is to notify you about tests that will be performed on your tumor tissue prior to your entry into Study MO43156.

You were selected as a possible participant in MO43156 because you have unresectable Stage III non-small cell lung cancer (NSCLC) and will have received at least two cycles of platinum-based chemotherapy administered concurrently with radiotherapy (cCRT) prior to study entry. Testing of tumor tissue collected prior to your first dose of cCRT is a requirement for study entry in order to confirm important characteristics of your cancer. Therefore, before enrolling in Study MO43156, you are being asked to sign this consent form to indicate that you understand and will allow this tumor tissue testing.

Overall, the purpose of Study MO43156 is to evaluate the effects, good or bad, of atezolizumab in patients with locally advanced, unresectable Stage III NSCLC who have received at least two cycles of cCRT and have not had disease progression during or after cCRT. Atezolizumab is a monoclonal antibody that blocks the programmed death−ligand 1 (PD-L1) pathway. The PD-L1 pathway is involved in regulating the body's natural immune response, but tumors can take advantage of this regulation to partially resist or evade the immune system. By blocking the PD-L1 pathway, atezolizumab may help your immune system stop or reverse the growth of tumors.

Atezolizumab has been approved by the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), and other health authorities worldwide for the treatment of metastatic NSCLC that has not yet been treated (referred to as first-line treatment) in patients whose tumors have high PD-L1 expression. Atezolizumab has also been approved for the treatment of metastatic NSCLC that has progressed during or following chemotherapy (referred to as second-line treatment). In addition, atezolizumab administered in combination with chemotherapy has been approved for the first-line treatment of metastatic NSCLC.

Evidence indicates that cCRT may change the PD-L1 biomarker. Therefore, to fully understand the scientific and medical significance of the results from Study MO43156, it is essential to assess PD-L1 in your tumor tissue by the central laboratory and before you have received cCRT. This explains why pre-screening tumor tissue testing is a requirement for study entry.

The testing will include an analysis to determine whether the PD-L1 biomarker is present or not in your tumor and to measure the amount of the PD-L1 biomarker. This analysis will be performed using a laboratory test that is experimental, which means health authorities have not approved the use of this test on NSCLC patients for treatment with the experimental drugs used in this study. The PD-L1 test result is required in order to evaluate your participation in the study.

For the pre-screening testing, you may provide tumor tissue from previous surgeries or biopsies or undergo a new biopsy to provide a fresh tumor specimen, provided it is performed prior to your first dose of cCRT. You may also agree to provide one or both types of tumor tissue for the purpose of pre-screening testing for Study MO43156.

In addition, certain types of NSCLC can have a mutation in the epidermal growth factor receptor (*EGFR)* or anaplastic lymphoma kinase (*ALK)* gene and should therefore be treated with drugs that target these mutations. If you have a certain type of lung cancer (non-squamous NSCLC) and your tumor *EGFR* or *ALK* status is not known by your doctor, your tumor tissue will also need to be tested for these mutations. Your doctor may request that the testing be performed at the same time your tissue is submitted for PD-L1 biomarker testing. If you have one of these mutations, you will not be eligible to participate in the study.

There are also other requirements that you need to fulfill before you can participate in Study MO43156, and testing for the PD-L1 biomarker does not guarantee you will meet all these other requirements. If you decide to participate in the pre-screening tumor tissue testing, there is still a possibility that you may not be eligible to participate in Study MO43156 because you may not fulfill these other requirements. You may ask your study doctor for more explanation about this.

About 120 people with unresectable Stage III NSCLC who have received at least two cycles of cCRT and whose disease has not worsened will take part in this study at approximately 30 study centers worldwide.

1.3 WHAT WILL HAPPEN IF I PARTICIPATE?

If you choose to participate in PD-L1 testing by signing this consent form, your study doctor will do one or both of the following as described below:

- Archival tumor tissue testing
- Biopsy of fresh tumor tissue

ARCHIVAL TUMOR TISSUE

Your study doctor will request that a small section of your tumor tissue sample be sent from the pathology laboratory, where your tissue sample is currently located, to a central laboratory where the testing will be performed. No additional procedures are required.

If you submit tissue collected prior to the first dose of cCRT, it will be tested by a central laboratory for PD-L1, making you potentially eligible to participate in Study MO43156. If you enroll in the study, any remaining tissue will be stored and will be returned to your study doctor upon request or 18 months after the data collection process has been completed for all other people who participate in this study (whichever is sooner). If you do not enroll in the study, any remaining tissue from an archival block will be returned to your study doctor.

FRESH TUMOR TISSUE

Your study doctor will ask you if a small sample of your tumor tissue may be obtained for biopsy. This may require undergoing a bronchoscopy (insertion of a tube into your airway) to obtain tumor tissue. Alternatively, a small section of your tumor may be removed by cutting it out surgically with a special round-shaped knife (called a "punch biopsy" procedure) or with use of a large needle (called a "core biopsy" procedure). This may be performed using a type of radiation called computed tomography (CT) to visualize your tumor. Your study doctor will explain the details of the procedure to you, depending on how the biopsy will be performed. If the tumor tissue obtained during the biopsy is of insufficient quality, other attempts can be made after more discussion and reconfirmation of your consent.

If you have a biopsy performed as part of study screening procedures for testing of *EGFR* and *ALK* mutations, any remaining tissue will not be returned after the testing is completed.

1.4 ARE THERE ANY BENEFITS?

Taking part in this pre-screening study will not make your health better. The testing of your tumor sample will not affect your medical care. However, your participation in this pre-screening study fulfills the PD-L1 testing on tissue (collected prior to the first dose of cCRT) requirement for your participation in Study MO43156.

1.5 ARE THERE ANY RISKS?

The risks associated with archival tissue testing and biopsy of fresh tumor tissue are described below.

RISKS ASSOCIATED WITH ARCHIVAL TISSUE

A sample of your original tumor tissue has already been collected; therefore, there are no additional risks involved in this testing.

RISKS ASSOCIATED WITH BIOPSY

If you choose to allow collection of your fresh tumor tissue, your doctor will explain the risks of the biopsy procedure to you for you to decide if you want to participate.

Biopsies can cause pain, redness, swelling, excessive bleeding, bruising, or draining at the needle site. Abnormal wound healing, fever, infection, and allergic reaction to the medication used to numb the skin over the biopsy site can also occur. In patients who undergo a biopsy during a procedure called a bronchoscopy, during which the physician examines the windpipe that connects to your lungs, the risks also include lung collapse (this is rare). Your study doctor will explain the details and risks of the procedure, which may vary depending on how the biopsy will be obtained.

RISKS ASSOCIATED WITH CT IMAGING

CT imaging to visualize your tumor during a biopsy is a type of radiation. Although there are no proven harmful effects from the radiation, no one can say for certain that there are no long-term harmful effects of radiation exposure. The radiation exposure in this study will be less than or equal to the exposure that is allowed for medical radiation workers.

1.6 WILL I BE PAID TO PARTICIPATE IN PRE-SCREENING TESTING?

You will not be paid for your participation in this testing.

Information from this study, including information from research on your samples, may lead to discoveries, inventions, or development of commercial products. You and your family will not receive any benefits or payment if this happens.

1.7 WILL IT COST ME ANYTHING TO BE TESTED?

There are no costs to take part in this testing. The Sponsor of Study MO43156, Roche, will cover the cost for the testing. All procedures that are required only for testing in this study and that are not part of your regular medical care will be provided to you at no charge.

1.8 WHAT HAPPENS IF I AM INJURED?

If you get injured because you took part in this study, contact your study doctor as soon as possible at telephone number listed in Section 2.4. Your study doctor will explain your options and tell you where to get treatment.

Roche will pay for reasonable costs of immediate care for any physical injury that results from the pre-screening testing but only if all of the following are true:

- Roche and the study doctor agree that your injury resulted from the pre-screening test and not from a preexisting medical condition
- The costs are not paid for by your medical insurance
- Your injury was not because you or the study team did not follow instructions

You will not receive any other kind of payment.

To request payment for treatment costs, contact your study doctor, who will make sure Roche takes appropriate action. Roche maintains a contract with Insurance Company Allianz Global Corporate & Specialty SE to ensure Roche can pay for treatment costs.

If you get injured from the pre-screening testing performed for enrollment in this study, you will not lose any of your legal rights to seek payment by signing this form.

1.9 CAN I STOP BEING IN THE STUDY?

Yes. You can decide to stop at any time. If you change your mind, tell your study doctor that you no longer want your tumor sample to be tested for the PD-L1 biomarker. You do not need to give a reason for changing your mind.

If you change your mind and your tumor sample has already been tested, the remaining tumor material will be sent back, but the collected information related to your PD-L1 biomarker test, your demographic information, and your lung cancer medical history will still remain part of the overall research data and will be used for analysis and submission to regulatory authorities such as the U.S. FDA.

When your participation ends, no new information will be collected about you. Any laboratory samples collected prior to stopping will not undergo further testing. However, Roche will still be able to use information that was collected prior to stopping, including information from samples that were tested prior to stopping.

SECTION 2: STUDY DETAILS

2.1 USE AND HANDLING OF LABORATORY SAMPLES

Tumor tissue samples collected at pre-screening will be used to test for the PD-L1 protein and submittal of tissue samples is an eligibility requirement for the study. If you have a certain type of lung cancer (non-squamous NSCLC) and your tumor *EGFR* or *ALK* status is not known by your doctor, your tumor tissue will also be tested for these mutations at the same time your tissue is submitted for PD-L1 testing, if requested by your doctor.

Tumor tissue samples collected at pre-screening will be used for future research related to NSCLC or other types of cancer, common pathways (links) among diseases, the use of experimental drugs in disease therapy, and/or the development of tests or tools that help with detecting or understanding NSCLC and/or PD-L1, even if you are not eligible for or decide not to take part in this study.

Sample Storage

Samples will be securely stored for a defined period (as described below) and will then be destroyed, with one exception: Tumor tissue from archival blocks from a previous

biopsy will be returned to your doctor upon request or after all study information has been collected.

Samples for biomarker testing and tumor tissue samples will be stored for 15 years after the final study results have been reported.

2.2 PROTECTION, USE, AND SHARING OF INFORMATION

During this study, health and personal information ("information") about you will be collected. This section describes the protection, use, and sharing of your information, which consists of the following:

- Information in your medical record, which is held by the Institute of Oncology Ljubljana ("study site")
- Information (including imaging data) that is collected or produced during this study ("study data"), which is held by the study site, Roche, Roche affiliates, and Roche's representatives (people and companies who work for Roche)

  "Study data" includes screening information from all patients, even patients who are not eligible for or decide not to take part in the study.

Your privacy is very important, and Roche uses many safeguards to protect your privacy, in accordance with applicable data privacy laws and laws related to the conduct of clinical trials.

Your study data and samples will be labeled with a patient identification (ID) number that is unique to you and not related to or derived from information that identifies you (such as your name, your picture, or any other personally identifying information). Roche, Roche affiliates, and Roche's representatives will only have access to study data and samples labeled with a patient ID number, except when accessing your medical record under certain circumstances, as described below:

Your information (including your medical record, which contains personal information that can identify you) may need to be reviewed to make sure the study is being done properly or to check the quality of the information. This information will be kept private. The following people and groups of people may review this information:

- Study monitors of Roche and/or IQVIA, a company hired by Roche to perform certain study activities
- The Institutional Review Board or Ethics Committee (people responsible for protecting the rights and safety of people who take part in research studies)
- Regulatory authorities (government agencies involved in keeping research safe for people)

Roche, Roche affiliates, and Roche's collaborators and licensees (people and companies who partner with Roche) may use study data labeled with your patient ID

number. Your study data may also be shared with researchers or government agencies, but only after personal information that can identify you has been removed. Your study data may be combined with or linked to other data and used for research purposes, to advance science and public health, or for analysis, development, testing, and commercialization of products that treat or diagnose disease, or improve patient care. These data will not include information that identifies you.

Your information will not be given to your insurance company or employer, unless required by law. If the results from this study are published in a medical journal or presented at a scientific meeting, you will not be identified.

Information from this study will be retained by the study site for 15 years after the end of the study or for the length of time required by applicable laws, whichever is longer. In addition, Roche will retain the study data for 25 years after the final study results have been reported or for the length of time required by applicable laws, whichever is longer.

If you sign this consent form, you give permission to the study site to use and/or share your information, which includes study data and information in your medical record. Your study data may be used or shared for the purposes of this study and for research related to lung cancer or other types of cancer, common pathways (links) among diseases, the use of experimental drugs in disease therapy, and/or the development of tests or tools that help with detecting or understanding NSCLC. You do not have to sign this consent form, but if you do not, you cannot take part in this study.

Your study data may be used by and/or shared with Roche, Roche affiliates, Roche's collaborators and licensees, the Institutional Review Board or Ethics Committee, and regulatory authorities. Your study data and samples may be analyzed in any country worldwide. Such countries may have less data protection safeguards and rights than the country where your study site is located.

Transfer of your study data to Roche affiliates and Roche's collaborators and licensees who are located outside of the European Economic Area is protected adequately under separate agreements such as "Standard Data Protection Clauses."

You have the right to see and get a copy of your study data. However, by signing this consent form, you agree that you generally will not be able to review or receive some of your records related to the study until after the entire study has been completed. This is to protect the scientific integrity of the study. If you believe any of the personal data (that is, information that identifies you or could reasonably be used to identify you) in these records to be inaccurate or incomplete, you have the right to request that the data be corrected. You can request the deletion of any personal data that are no longer needed. You can also request the restriction of the use of any personal data. Because Roche only maintains study data labeled with your patient ID number, Roche may not be able to

fully respond to your request. Roche will try to be as responsive as possible to your requests, taking into consideration the impact on the scientific integrity of the study. To request a copy of your study data, request that your personal data be corrected or deleted, or request the restriction of the use of your personal data, contact your study doctor (see Section 2.4), who will forward your request to Roche.

You may change your mind and take back your consent at any time without penalty or loss of any benefits to which you are otherwise entitled. If you take back your consent, you will not be able to continue to take part in the study and no new information will be collected about you. However, to comply with regulatory requirements to protect the scientific integrity of the study, Roche will still be able to use and share any study data about you that have already been collected during this study. To take back your consent, you may contact your study doctor (see Section 2.4).

If you have any questions, concerns, or complaints as to how Roche is using your information, you can contact Roche's local Data Protection Officer. The study doctor can provide you with contact information for Roche's Data Protection Officer. For more information about your privacy rights or if you are not able to resolve a problem directly with Roche and wish to make a complaint, you may contact the Information Commissioner of the Republic of Slovenia (at email address gp.ip@ip-rs.si or telephone number 01 230 97 30), which is responsible for making sure that privacy law is followed in Slovenia.

2.3 STUDY RESULTS

Results from exploratory biomarker tests will not be shared with you or your doctor, unless required by law. Information from these tests will not be part of your medical record.

A clinical study report containing the results of this trial will be made available to anyone who requests a copy, provided the requirements of Roche's global policy on data sharing have been met. Before this report is provided, additional steps will be taken to protect your information from being linked to you.

A description of this clinical trial will be available at http://www.ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

2.4 CONTACT INFORMATION

If you have any questions, contact your study team, listed below:

	Study Doctor	Study Coordinator
Name:		
Address:		
Telephone number:		
Email address:		

If at any time during this pre-screening you feel that your study doctor has not provided you with satisfactory answers to your questions, you may also contact the following institutions, which will address your questions within their area of competence:

- Agency for Medicinal Products and Medical Devices of the Republic of Slovenia, Slovenčeva ulica 22, 1000 Ljubljana, info@jazmp.si
- Republic of Slovenia National Medical Ethics Committee, Ministry of Health, Štefanova 5, 1000 Ljubljana, kme.mz@gov.si
- Patient's rights representative, https://www.gov.si/teme/pacientove-pravice/
- Human Rights Ombudsman of the Republic of Slovenia, Dunajska cesta 56, 1000 Ljubljana, www.varuh-rs.si
- Information Commissioner of the Republic of Slovenia, Dunajska cesta 22, 1000 Ljubljana, www.ip-rs.si

Signature

I confirm that I have read this consent form or it has been read to me. I understand the information presented and have had my questions answered. I understand that I will be given a copy of all 12 pages of this form after it has been signed and dated. I voluntarily agree to take part in this PD-L1 pre-screening testing as described above and authorize the Institute of Oncology Ljubljana to use and share my information as described in this form.

Patient name (print)	
If applicable – Name of patient's legally authorized representative (print)	Relationship to patient
Patient signature or signature of patient's legally authorized representative	Date

I, the undersigned, have fully explained this informed consent to the patient named above and/or the patient's legally authorized representative.

Name of person conducting informed consent discussion (print)	
Signature of person conducting informed consent discussion	Date
Witness name [a] (print)	
Witness signature [a]	Date

Witness name [a] (print)

Witness signature [a]

Date

[a] If the investigator or Institutional Review Board or Ethics Committee deems a witness signature is necessary (as per ICH Guidelines, Good Clinical Practice [E6], 4.8.9, or local regulations).