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 COMMITTEEE:	Republic of Slovenia National Medical Ethics Committee
ETHICS COMMITTEE APPROVAL DATE:	{Date}

SECTION 1: STUDY OVERVIEW

1.1 INTRODUCTION

- You are being asked to take part in this research study (also known as a clinical trial) because you have non-small cell lung cancer (NSCLC) that is locally advanced (Stage III) and unresectable (cannot be removed by surgery) and you have received at least two cycles of chemoradiotherapy (chemotherapy plus radiotherapy) without your disease worsening. This study is testing a drug called atezolizumab.
- 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.
- This consent form tells you what will happen if you take part. It also tells you about the possible benefits and risks of being in the study.
- Taking part in this study 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.

- Instead of participating in this study, you may choose to
  - Get treatment for your cancer without being in this study
  - Join a different study
  - Get no treatment
  - Get comfort care (also called "palliative care")
- Talk to your doctor about all of your choices, and the risks and benefits of each choice. If you choose not to take part, you will not lose the regular care you receive from your doctors.
- If you decide to take part, you will be asked to sign this consent form. You will be given a copy of your signed consent form.

1.2 WHAT IS THE PURPOSE OF THIS STUDY?

The purpose of this study is to examine the effects, good or bad, of atezolizumab in patients with Stage III unresectable NSCLC who have received at least two cycles of chemoradiotherapy and have not experienced a subsequent worsening of disease.

Atezolizumab is an 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 (also referred to as first-line treatment), as well as for metastatic NSCLC that has progressed during or following chemotherapy (also 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.

Atezolizumab has not been approved by health authorities in patients who have your specific type of NSCLC and your specific treatment history, that is, Stage III unresectable NSCLC that has been treated with chemoradiotherapy and has not progressed further. Therefore, in this clinical trial, atezolizumab is considered to be an experimental drug.

About 120 people will take part in this study. All 120 patients will receive atezolizumab therapy.

Certain types of NSCLC can have a mutation in the epidermal growth factor receptor (*EGFR*) or anaplastic lymphoma kinase (*ALK)* gene. 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 be tested for these mutations. If you have one of these mutations, you will not be eligible to participate in the study.

1.3 WHAT WILL HAPPEN IF I PARTICIPATE?

This study has three parts:

1. Screening (to see if you are eligible for the study)
2. Treatment
3. Post treatment assessments, some of which require a visit and some of which can be done by phone, to check on you after treatment is finished

Your participation in the post treatment part of the study is critical to understand the effects of atezolizumab.

You will receive atezolizumab by intravenous infusion (into the vein) once every 4 weeks. In total, you may receive up to 13 atezolizumab infusions over approximately 1 year. You may receive less than 13 atezolizumab infusions if your disease worsens before completing the 1-year treatment period or if your doctor determines there is no benefit to you of continuing therapy with atezolizumab or you experience side effects that prevent continued treatment or you withdraw your consent from treatment.

Each atezolizumab infusion will occur at a clinic visit lasting from 1 to 3 hours. In addition, you will be contacted by phone approximately 2 weeks after each atezolizumab infusion.

After you have completed or stopped treatment, your study doctor will ask you to visit the hospital or clinic for a follow-up examination (also known as the treatment discontinuation/completion visit) within 30 days after your final dose of study treatment.

You will then be asked to return for regular post-treatment follow-up assessments, possibly including scans, to see if your disease comes back or becomes worse.

During the post-treatment period, information about how you are doing (well-being checks), your disease, and any additional treatments you receive will also be collected. This may be by telephone (to you or your family or caregiver), through your medical records and/or a clinic visit. The purpose of collecting this information is to determine the effect of the study treatment on your health. If you decide that you no longer want to be contacted or allow access to your medical records for follow-up information, tell your study doctor. If the study personnel are unable to reach you during the treatment or follow-up phases of the study, the study personnel may use a public information source (e.g., public county records) to obtain information about your health status.

The state of your disease and your response to atezolizumab therapy will be assessed throughout this study by computed tomography (CT) scans, positron emission tomography (PET)/CT scans, and/or magnetic resonance imaging (MRI) scans. You may also (possibly) undergo bone scans. For more information on the scanning procedures used in this study and their associated risks, refer to Section 2.2 of this consent form.

The scans are scheduled to occur during screening, every 8 weeks (± 1 week) for 48 weeks following your first atezolizumab administration, and every 12 weeks (± 1 week) thereafter. The scans will occur on this schedule, even if your atezolizumab therapy has been delayed or discontinued permanently, until confirmed radiographic disease progression, withdrawal of consent, or study termination by the Sponsor, whichever occurs first.

With drugs like chemotherapy, an increase in the size or number of tumors (tumor burden) detected by scans or a physical examination can be a sign that your disease has worsened and that chemotherapy should be discontinued. However, with treatments such as atezolizumab that stimulate your immune system to attack your tumors (immunotherapy), an early increase in tumor burden may be a sign of your body's immune cells invading your tumors instead of a sign that your disease has worsened. Because of this possibility, you will have the option of continuing to receive study treatment even after a scan shows what may appear to be an increase in tumor burden, if your study doctor determines there is no increased risk for you if you continue to receive study treatment and you meet certain conditions. For example, you should not have unmistakable signs and symptoms of disease progression or tumor growth in critical parts of your body.

The option to continue treatment in spite of an apparent increase in tumor size should be carefully discussed with your study doctor. Your study doctor will explain the possible benefits and risks of continuing treatment in spite of an apparent increase in tumor burden, including the risk of delaying treatment options such as chemotherapy, immunotherapy other than that used in this trial, or combinations of chemotherapy and immunotherapy, and participation in alternative clinical trials.

If, after discussion with your study doctor, you decide to continue treatment in spite of apparent disease progression, you will be asked to sign a form to indicate that you have reviewed and understood the risks of doing so. Your doctor will monitor you closely. A follow-up scan will help to determine whether the increase in tumor burden was caused by immune cells invading your tumors or if it was due to a worsening of your disease. Your study doctor may want to perform a biopsy of your tumor (if the doctor decides it is safe) and additional tests to help determine the cause for the increase in tumor burden. If disease worsening occurs, you will discontinue study treatment.

Your total length of time in the study, including screening, up to 1 year of study treatment, and the post-treatment period, may be up to approximately 8 years total.

The study procedures are described in detail in Section 2.2. Some procedures will be the same as your regular care for cancer, and some procedures will be just for this study.

1.4 ARE THERE ANY BENEFITS?

Your health may or may not improve in this study, but the information that is learned may help other people who have a similar medical condition in the future.

1.5 ARE THERE ANY RISKS?

You may have side effects from the drugs or procedures used in this study, as described in Sections 2.1 and 2.2. Side effects can be mild to severe and even life threatening, and they can vary from person to person. Talk to your study doctor right away if you have any of the following during the study:

- Symptoms that are new or have worsened
- Changes in your prescribed or over-the-counter medications (including herbal therapies)
- Visits to the doctor or hospital, including urgent care or emergency room visits

There may be a risk in exposing an unborn child to study drug, and all risks are not known at this time. Women and men must take precautions to avoid exposing an unborn child to study drug, as described in Section 1.6. If you are pregnant, become pregnant, or are currently breastfeeding, you cannot take part in this study.

1.6 ARE THERE ANY SPECIAL REQUIREMENTS?

While participating in this study, there are certain requirements, as listed below:

- You should not join another research study.
- For women: If you can become pregnant, you must use a reliable birth control method during the study and for 5 months after your final dose of atezolizumab. Talk with your study doctor about what method may be best for you. Tell your study doctor right away if you get pregnant during this period. If you get pregnant, the study doctor will want to follow up with you on the outcome of the pregnancy and collect information on the baby.
- You should not use certain medications during this study. Your study doctor will talk to you about these medications.

1.7 WILL I BE PAID TO PARTICIPATE?

You will not be paid for taking part in this study.

You will be reimbursed for your reasonable costs (for example, transportation, parking) to travel from your home to the study site.

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.

1.8 WILL IT COST ME ANYTHING?

While participating in this study, you will not have to pay for drugs or procedures that are required only for this study and are not part of your regular medical care. You or your health plan will have to pay for medicines and clinic, hospital, and doctors' services that are part of your regular medical care.

1.9 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 2.8. 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 study drug but only if all of the following are true:

- Roche and the study doctor agree that your injury resulted from the study drug 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 in this study, you will not lose any of your legal rights to seek payment by signing this form.

1.10 CAN I STOP BEING IN THE STUDY?

You can leave this study at any time. Tell your study doctor if you are thinking about stopping, and your study doctor will tell you how to stop safely. If you leave this study, you will not lose access to any of your regular care.

If there are important new findings or changes in this study that may affect your health or willingness to continue, your study doctor will let you or your legally authorized representative know as soon as possible.

You may be required to stop participating in the study, even if you wish to continue. Below are some of the reasons why you may be asked to stop:

- Your safety would be at risk if you continued
- You were unable to or did not follow study instructions or procedures
- You need medical care that is not allowed by this study
- This study has been stopped by Roche or a health authority

When your participation ends, no new information will be collected about you with one exception: information may be obtained from records available to the public to help track the course of your disease. 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 STUDY TREATMENT RISKS

Atezolizumab is designed to increase the number of immune system cells in your body that can fight cancer. These cells may cause inflammation within the tumor, as well as in normal tissue. Therefore, by taking atezolizumab, you may develop a condition where there is inflammation against a part of your own body (an autoimmune condition).

Risks Associated with Atezolizumab

The side effects associated with atezolizumab are listed below. There may be side effects that are not known at this time.

Side Effects Known to Be Associated with Atezolizumab		
Very common (occurs in more than 10% of patients)	• Cough • Decreased appetite • Diarrhea • Fatigue • Fever • Headache • Itching of the skin (pruritus) • Joint pain (arthralgia)	• Lack of energy (asthenia) • Muscle and bone pain (myalgia, musculoskeletal pain and bone pain) • Nausea • Rash • Shortness of breath (dyspnea) • Urinary tract infection • Vomiting
Common (occurs in 1%–10% of patients)	• Allergic reaction or intolerance to medication (hypersensitivity) • Chills • Decreased level of potassium in blood (hypokalemia)	• Increase in liver enzymes, which may indicate inflammation of the liver • Inflammation of the intestines (colitis) • Inflammation of the liver (hepatitis)

	• Decreased level of sodium in blood (hyponatremia) • Decreased oxygen supply in body resulting in shortness of breath (hypoxia) • Difficulty swallowing (dysphagia) • Dry skin • Flu-like symptoms • Increased blood level of creatinine, a substance normally eliminated by the kidneys into the urine • Increased blood sugar level (hyperglycemia)	• Inflammation of the lungs (pneumonitis) • Infusion-related reaction • Low blood pressure (hypotension) • Low platelet count in the blood, which may make you more likely to bruise or bleed (thrombocytopenia) • Nasal congestion • Pain at the back of the throat (oropharyngeal pain) • Stomach area pain (abdominal pain) • Underactive thyroid gland (hypothyroidism)
Less common but important (occurs in less than 1% of patients)	• Decreased production of hormones by the adrenal glands (adrenal insufficiency) • Diabetes • Inflammation of the brain and membrane surrounding the brain and spinal cord (meningoencephalitis) • Inflammation of the heart muscle (myocarditis) • Inflammation of the kidneys (nephritis) • Inflammation of the pancreas (pancreatitis), including increase in pancreatic enzymes (such as amylase and lipase)	• Inflammation of the pituitary gland (hypophysitis) • Inflammation or damage of the muscles (myositis) • Nerve damage resulting in muscle weakness (myasthenic syndrome/myasthenia gravis) • Nerve damage that may cause muscle weakness and/or paralysis (Guillain-Barré syndrome) • Overactive thyroid gland (hyperthyroidism) • Severe high levels of sugar and acids in the blood or urine (diabetic ketoacidosis) • Severe skin or mucosal reactions (severe cutaneous adverse reactions)

Among the side effects known to be associated with atezolizumab, Roche and your study doctors would like you to pay more attention to the following:

- Inflammation of the intestines (colitis); symptoms may include diarrhea, blood in stool, and pain in stomach area
- Inflammation of the thyroid glands (hypothyroidism, hyperthyroidism); symptoms may include headaches, fatigue, weight loss, weight gain, change in mood, hair loss, and constipation
- Inflammation of the adrenal glands (adrenal insufficiency); symptoms may include dizziness, irritability, fainting, low blood pressure, skin darkening, and craving of salty foods

- Inflammation of the pituitary gland (hypophysitis); symptoms may include fatigue and headaches that will not go away, increased thirst, increased urination, and changes in vision

  Side effects that may occur at the same time include hypothyroidism and adrenal insufficiency (see above for details).
- Inflammation of the liver (hepatitis); symptoms may include yellowing of skin, pain in stomach area, nausea, vomiting, itching, fatigue, bleeding or bruising under the skin, and dark urine
- Inflammation of the brain and membrane surrounding the brain and spinal cord (meningoencephalitis); symptoms may include neck stiffness, headache, fever, chills, vomiting, seizure, irritability, and eye sensitivity to light
- Nerve damage resulting in muscle weakness (myasthenic syndrome/myasthenia gravis); symptoms may include weakness in the arm and leg muscles, double vision, and difficulties with speech and chewing
- Nerve damage that may cause muscle weakness and/or paralysis (Guillain-Barré syndrome); symptoms may include tingling in fingers and toes, fatigue, and difficulty walking
- Inflammation of the lungs (pneumonitis); symptoms may include new or worsening cough, shortness of breath, and chest pain
- Inflammation of the heart muscle (myocarditis); symptoms may include shortness of breath, decreased exercise tolerance, fatigue, chest pain, swelling of the ankles or legs, irregular heartbeat, and fainting
- Reactions associated with infusion (events occurring during or within 1 day of infusion); symptoms may include fever, chills, shortness of breath, and sudden reddening of the face, neck, or chest
- Inflammation of the pancreas (pancreatitis); symptoms may include abdominal pain, nausea, vomiting, and fever
- Condition of high levels of sugar in the blood (diabetes mellitus); symptoms may include increased thirst, increased hunger, frequent urination, irritability, and fatigue
- Inflammation of the kidneys (nephritis); symptoms may include changes in urine output and color, pain in pelvis, and swelling of the body and may lead to failure of the kidneys
- Inflammation or damage of the muscles (myositis, myopathies including rhabdomyolysis); symptoms may include muscle pain and weakness, urine with a dark brown or reddish color, nausea, and vomiting
- Severe skin or mucosal reactions (severe cutaneous adverse reactions); symptoms may include itching, skin blistering, peeling or sores, and/or ulcers in mouth or in lining of nose, throat, or genital area

Allergic Reactions

Allergic reactions may occur with atezolizumab and typically occur while it is being given into your vein or shortly after it has been given. Symptoms could include nausea, vomiting, skin reactions (hives or rash), difficulty breathing, or low blood pressure. These reactions could be mild or severe and might lead to death or permanent disability. If you experience any of these symptoms, your study doctor will interrupt, or even stop, the delivery of atezolizumab into your vein. Your study doctor may also give you some drugs to treat these symptoms.

Side Effects Potentially Associated with Atezolizumab

The following are side effects that may be associated with atezolizumab:

- Development of special antibodies to atezolizumab (proteins made in the body that respond to a substance that is foreign to the body) by your immune system

  If you develop these special antibodies, it may affect your body's ability to respond to atezolizumab in the future. Blood samples will be drawn to monitor for the development of these antibodies during study treatment and at your treatment discontinuation visit.
- Potential to cause harm to a developing fetus
- Inflammation of the eye (uveitis); symptoms may include eye pain and redness, vision problems, and blurry vision
- Inflammation of the blood vessels that can lead to damage of different organs (vasculitis); symptoms may include fever, fatigue, weight loss, weakness, general aches and pains, rash, headache, lightheadedness, shortness of breath, and numbness
- Breakdown of red blood cells (autoimmune hemolytic anemia); symptoms may include fatigue, fever, lightheadedness, paleness of the skin, yellowing of the skin and/or eyes, weakness, and inability to do physical activity

Immune Reaction

In rare situations, an immune reaction can occur with administration of atezolizumab. This reaction can cause side effects related to severe inflammation and/or severe infection. Several organs in your body (for example, liver, kidney, lungs, and bone marrow) may become involved, causing a serious condition, which could lead to hospitalization, life-threatening circumstances, or even death. Symptoms may include very low blood pressure that does not respond to standard treatment, very high fever, cough, severe shortness of breath requiring oxygen therapy and/or intubation, severe dizziness, confusion, weakness, decreased urination with failure of the kidneys, abnormal liver function, very low blood cell counts, and/or bleeding within the organs.

If you experience any of these symptoms, you should notify your doctor immediately, as you may need immediate treatment and hospitalization. Your study doctor may give you drugs to treat these symptoms.

2.2 STUDY PROCEDURES AND POTENTIAL RISKS

Procedures with associated risks are listed below. The study doctor will provide more detailed information about the risks and their frequency.

Procedures with Associated Risks		
Procedure	Approximate Timing	Potential Risks
Tumor tissue sample (biopsy)	• Screening Note: A biopsy will not be needed at screening if a previously collected sample is available and meets study requirements.	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 have biopsy tissue collected while undergoing a bronchoscopy (a procedure that examines the windpipe that connects to your lungs), risks may also include lung collapse (this is rare). Your doctor will explain the details and risks of your biopsy procedure, which may vary depending on how the biopsy will be obtained.
Test for PD-L1 in tumor tissue to find out how variations in this biomarker affect your disease or your response to study drug	• Screening	The biopsy tissue sample (see above) will be used for PD-L1 testing. Therefore, there are no additional risks associated with PD-L1 testing beyond those described above for biopsies.
Blood sample (about 5 tablespoons at each visit)	• Screening • Day 1 of every 28-day cycle while on study treatment • At the end of treatment	Drawing blood can cause pain, bruising, or infection where the needle is inserted. Some people experience dizziness, fainting, or upset stomach when their blood is drawn.

Procedures with Associated Risks		
Procedure	Approximate Timing	Potential Risks
Tumor assessments: scans of your internal organs and bones, such as the following: • Computed tomography (CT) scan: X-ray test that gives off radiation at a dose similar to natural radiation people are exposed to over 3–6 years • Positron emission tomography (PET)/CT scan: imaging test that requires a radioactive tracer to be swallowed, injected, or inhaled and gives off radiation at a dose similar to natural radiation people are exposed to over 4–5 years • Magnetic resonance imaging (MRI) scan: imaging test that uses magnets and radio signals but does not give off radiation • Bone scan: imaging test that gives off radiation at a dose similar to natural radiation people are exposed to over 2 years To increase visibility, a contrast agent may be swallowed, injected, or inserted into the rectum (enema). You cannot have an MRI if you have any metal or electronic devices in your body or if your kidneys are not working properly. Study staff will ask questions and (if needed) run tests to make sure the scans are safe for you.	• Screening • Approximately every 8 weeks for the first 48 weeks and then approximately every 12 weeks afterward until your disease worsens after which, you will have scans according to the standard of care in your area. • Your doctor may want to perform scans more often You may have undergone some of these scans as part of your regular care.	• You may have an allergic reaction to a tracer or contrast agent. • Oral and rectal contrast agents may cause nausea, constipation, diarrhea, and abdominal bloating. • Injected contrast agents may cause nausea, headache, hives, temporary low blood pressure, chest pain, back pain, fever, weakness, and seizures. There may be pain, bruising, or infection at the injection site. • CT, PET, and MRI scanners may cause some anxiety and claustrophobia (fear of being in small places). You may be given a mild sedative or anti-anxiety drug to help manage your symptoms. • Although there are no known long-term harmful effects from the radiation of a single scan, the risk of harmful effects from multiple scans over a period of time is not known. Talk to your doctor if you are concerned about your radiation exposure prior to or during this study. • Recent reports indicate that deposits of gadolinium-based contrast agents may remain in the brain long after MRI scan completion in some patients undergoing four or more scans. It is not known if these deposits are harmful or may lead to harmful health effects.

Non-invasive procedures with minimal risks are listed below.

Non-Invasive Procedures with Minimal Risks	
Procedure	Approximate Timing
Review of medical history, including medications	• Screening
Recording of demographic information, such as age, sex, race/ethnicity	• Screening
Vital signs: temperature, pulse rate, blood pressure, breathing rate	• Every visit
Complete or limited physical examination (may include height or weight)	• Every visit
Assessment of performance status (daily functioning)	• Screening • Day 1 of every cycle • At the end of treatment
Review changes in your health or medications	• Every visit
Electrocardiogram (ECG): measures electrical activity of your heart	• Screening • At the end of treatment • As needed at other visits
Urine sample	• Screening
Urine sample for pregnancy test (for women of childbearing potential only)	• Day 1 of each 28-day cycle • At the end of treatment • 5 months after the final dose of atezolizumab
Follow-up after you discontinue treatment: telephone call or clinic visit to check your health and find out if you are taking any anti-cancer drugs	• Every 3 months for as long as you agree to it

2.3 ACCESS TO STUDY DRUG AFTER COMPLETING THE STUDY

Currently, Roche does not have any plans to provide the Roche study drug (atezolizumab) or any other study treatments to you after you complete the study.

2.4 USE AND HANDLING OF LABORATORY SAMPLES

Sample Use

Blood, urine, and tumor tissue samples will be collected for reasons such as the following:

• Check your health through standard laboratory tests • Find out if you are pregnant • Check how quickly your blood clots • Check for an infection with hepatitis B or C • Check for a prior or current infection with HIV • Check your thyroid function • Measure blood sugar level • Find out how study drug is processed by your body • Measure antibodies produced by your immune system • Find out if your body is making antibodies to study drug	• Perform additional analyses related to processing of study drug or development of antibodies to study drug (if needed) • Test for PD-L1 protein in your tumor tissue sample This screening test is experimental, which means health authorities have not approved the use of this test on NSCLC patients for treatment with the experimental drugs in this study • Additional tests for other related biomarkers may be performed to find out how these markers affect your disease and/or your response to study drugs • Find out how variations in other biomarkers (such as cancer-specific proteins or genes) affect your disease or your response to study drugs

Blood and tumor tissue samples collected at 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, unless you specifically ask for your samples to be returned or destroyed.

Genome Testing

Biomarker testing may involve analysis of your genome (DNA), an "instruction book" for the cells in your body. Your blood and tissue samples may be tested for genome variations. Some of the genome variations may be inherited. Testing may include analysis of all of your DNA (whole genome sequencing) or analysis of all of your DNA that codes for proteins (whole exome sequencing). Analyses of samples from a large number of people may help researchers learn more about atezolizumab and similar drugs, lung cancer and other diseases, possible links among diseases, genome variations and how they might affect a disease or a person's response to treatment, and new avenues for drug development and personalized therapies.

Sample Storage

Samples will be securely stored for a defined period (as described below) and will then be destroyed, with one exception: if your tumor tissue does have the PD-L1 biomarker present, any remaining archival tumor 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 6 weeks after you are determined to not be eligible for the study.

Samples will be stored for up to 5 years after the final study results have been reported, with the following exceptions:

- Samples for whole genome sequencing or whole exome sequencing will be stored for up to 15 years after the final study results have been reported.
- Samples for other biomarker testing, including fresh biopsy samples, will be stored for 15 years after the final study results have been reported.

2.5 PROTECTION, USE, AND SHARING OF INFORMATION

Protection, use, and sharing of information is described in Appendix 1. By signing this consent form, you acknowledge having taken note of Appendix 1.

2.6 HANDLING OF GENETIC INFORMATION

Testing of your samples may provide information related to your genome ("genetic information"), including information about inherited characteristics. Your samples and genetic information will not be labeled with your name, your picture, or any other personally identifying information. Roche uses many safeguards to protect your privacy.

2.7 STUDY RESULTS

Results from exploratory biomarker tests, including tests for genome variations, 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. Before this report is provided, additional steps will be taken to protect your information from being linked to you.

2.8 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 study 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

You will receive a card with the name and phone number of the study doctor. Please keep this card with you at all times, for as long as you remain in the study.

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 24 pages of this form after it has been signed and dated. I voluntarily agree to take part in this research study 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).

Signature Acknowledging Treatment Continuation after Apparent Disease Worsening

I understand that because of the nature of this experimental treatment, there is a possibility of continuing study treatment after apparent disease worsening, which may not be considered standard care for the treatment of cancer. My study doctor has explained the possible benefits and risks of continuing study treatment, including the risk of delaying initiation of alternative treatments or participation in alternative clinical trials. I understand that there has been an apparent worsening of my disease, and I voluntarily agree to continue study treatment. I understand that all sections of the main consent form (previously signed by me) are still in effect.

Participant name (print)

If applicable – Name of participant's legally authorized representative (print) | Relationship to participant

Participant signature or signature of participant's legally authorized representative | Date

I, the undersigned, have fully explained this informed consent to the participant named above and/or the participant'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).

Appendix 1
Data Privacy Information Sheet: Protection, Use, and Sharing of Your Personal Data

Data Privacy Information

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. During the study, personal data about you, including your health data, will be collected ("personal data"). This Data Privacy Information Sheet outlines the categories of personal data Roche may collect within the scope of the study you are participating in, how and for which purpose Roche may collect, use, or share these personal data, the recipients of your personal data, and your rights regarding the use of your personal data.

Categories of Personal Data

During the study, personal data about you will be collected. These personal data consist of the following categories:

- Personal data in your medical record, which is held by the Institute of Oncology Ljubljana ("study site")
- Personal data (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.

Labeling Your Personal Data

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). The labeling is a coding method performed by the study site. Only the study site owns the key that allows for you to be identified by your patient ID number.

Recipients of Your Personal Data

Recipients of your personal data are described below:

- Recipients of personal data in your medical records

  Your personal data in your medical records (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 such personal data. This information will be kept private. The following people and groups of people may review your personal data in your medical records:

- Authorized individuals (such as study monitors and auditors) representing Roche and Roche's collaborators and licensees (people and companies who partner with Roche)
- 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)

- Recipients of study data
  - Roche, Roche affiliates, and Roche's collaborators and licensees, including those in countries outside the European Economic Area with privacy standards different from those in your country, may receive your study data for the purposes described in the sections below.

    Compliance with European Union (EU) data privacy regulations is ensured through contracts containing the EU Standard Contractual Clauses according to EU Commission decisions of 27 December 2004 (2004/915/EC) and 5 February 2010 (C(2010) 593) and through additional measures as appropriate.
  - Your study data may also be shared with independent researchers or government agencies, but only after an additional assessment and confirmation that any personal data that can identify you has been removed.

Your personal data will not be provided to third parties like 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.

HIV and hepatitis are reportable diseases where you live. If you test positive for these diseases, the law requires your study doctor to report your name to the appropriate authority. Please ask your study doctor for details if you have concerns about this report.

Purposes and Legal Basis for Processing Data for the Study

Your study data may be used for the primary purpose of the study and for secondary purposes, as described below.

Primary Purpose

Roche processes your study data to conduct the study, to perform certain activities that are required by law to ensure the transparency of the study data and the safety of Roche's products, and for scientific research purposes. This includes scientific research to better understand the 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 non-small cell lung cancer. The purposes and legal

bases for processing personal data for the primary purpose are described in a separate table below (see Table 1).

Secondary Purposes

Your study data may be used for secondary purposes in the interest of advancing science and public health, including the development of innovative treatments for patients with unmet medical needs. Use of study data for secondary purposes will comply with Roche policies on data use and the sharing of clinical study information aimed at advancing science, research, and medical innovation. Your study data may be combined with other people's data and/or linked to other data collected from you and may also be shared with recipients as described above. Your study data may be used to help better understand why people get diseases and how to best prevent, diagnose, and treat diseases, and to develop and provide access to new medicines, medical devices, and healthcare solutions, thus advancing patient care. The purposes and legal bases for processing personal data for secondary purposes are described in a separate table below (see Table 1).

Your study data may be used for a secondary purpose that is compatible with the primary purpose of the study, as described above. If this is not the case, your data must be either anonymized in accordance with applicable law or labeled with a patient ID and processed as necessary for scientific research purposes and in Roche's legitimate interest to conduct research to advance science, per GDPR Article 6(1)(f) combined with Article 9(2)(j).

Storage Period

Personal data maintained by the study site will be retained for 15 years after the end of the study or for the length of time required by applicable laws, whichever is longer. Study data maintained by Roche will be retained for 25 years after the final study results have been reported or for the length of time required by applicable laws, whichever is longer.

Identity and Contact Details of Data Controller

The data controller is F. Hoffmann-La Roche Ltd ("Roche"), the global sponsor of the study, located at Grenzacherstrasse 124, CH-4070 Basel, Switzerland (email: global.privacy@roche.com).

The EU representative for F. Hoffmann-La Roche Ltd is Roche Privacy GmbH, Emil-Barell-Str. 1, D-79639 Grenzach-Wyhlen.

Please direct any questions and requests related to this Data Privacy Information Sheet to Roche via your study doctor or the study site (see Section 2.8 of the Informed Consent Form).

Data Sources

For the purposes of the study, Roche collects personal data from you and the study site.

Information about Your Rights

You have certain rights available to you regarding the processing of your personal data. You have the right to access and get a copy of your personal data. If you have found that your personal data are inaccurate or incomplete, you have the right to request that these data be corrected. You can request the deletion of personal data that are no longer needed. You can also request the restriction of the use of any personal data to the extent that the processing of personal data is based on legitimate interest.

In order to make any of the above requests, contact your study doctor or study site (see Section 2.8 of the Informed Consent Form) or Roche (see contact information above). There may be certain limitations to Roche's ability to respond to these requests. Roche will try to be as responsive as possible to your requests, taking into consideration the impact on the scientific integrity of the study. For example, in general, you may not be able to review or receive some of your records related to the study until after the entire study has been completed in order to protect the scientific integrity of the study. Roche only maintains study data labeled with your patient ID number, which may limit Roche´s ability to fully respond to your request.

If you withdraw your consent to participate in the study, 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 the study.

If you have any questions, concerns, or complaints as to how Roche is using your personal data, you should contact Roche via your study doctor or the study site. In the event you have the impression that Roche's study data processing is not compliant with GDPR or you are unable to resolve a privacy complaint with Roche, you are entitled to lodge a complaint with the Information Commissioner of the Republic of Slovenia (at email address gp.ip@ip-rs.si or telephone number 01 230 97 30), the supervisory authority responsible for making sure that privacy law is followed in Slovenia.

Table 1 Purposes and Legal Basis for Processing Your Personal Data Contained in the Study Data

Purpose	Legal Basis	Citation in GDPR
Your study data will be used and shared for the purposes of the study and for research related to the disease or condition being analyzed in the study.	This processing is necessary for scientific research purposes and in the legitimate interest of Roche to conduct studies.	Article 6(1)(f) and Article 9(2)(j)
Your study data may be used to screen you to identify whether you are a suitable candidate for this study.	This processing is necessary for scientific research purposes and in the legitimate interest of Roche to conduct studies.	Article 6(1)(f) and Article 9(2)(j)
Your personal data in your medical record and study data will be used and shared to monitor the study and to make sure that it is being conducted in accordance with applicable laws.	This processing is necessary to comply with legal obligations set forth in laws, such as the Clinical Trials Regulation and Clinical Trials Directive, to ensure the safety and reliability of products in the interest of public health.	Article 6(1)(c) and Article 9(2)(i)
Your study data will be used and shared for the purposes of safety reporting.	This processing is necessary to comply with legal obligations set forth in laws, such as the Clinical Trials Regulation and Clinical Trials Directive, to ensure the safety and reliability of products in the interest of public health.	Article 6(1)(c) and Article 9(2)(i)
Your study data will be used and shared to enable study data to be archived and stored in accordance with applicable legal requirements.	This processing is necessary to comply with legal obligations set forth in laws, such as the Clinical Trials Regulation and Clinical Trials Directive, to ensure the safety and reliability of products in the interest of public health.	Article 6(1)(c) and Article 9(2)(i)
Your study data may be disclosed to national authorities in the event of an inspection.	This processing is necessary to comply with legal obligations set forth in laws, such as the Clinical Trials Regulation and Clinical Trials Directive, to ensure the safety and reliability of products in the interest of public health.	Article 6(1)(c) and Article 9(2)(i)
Your study data may be used for secondary research purposes to advance science and public health.	This processing is necessary for scientific research purposes and in the legitimate interest of Roche to conduct studies.	Article 6(1)(f) and Article 9(2)(j)