ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

PROTOCOL UPDATE TO ALLIANCE A021502

RANDOMIZED TRIAL OF STANDARD CHEMOTHERAPY ALONE OR COMBINED WITH ATEZOLIZUMAB AS ADJUVANT THERAPY FOR PATIENTS WITH STAGE III COLON CANCER AND DEFICIENT DNA MISMATCH REPAIR

[X] **Update:**	[ ] **Status Change:**
[ ] Eligibility changes	[ ] Activation
[X] Therapy / Dose Modifications / Study Calendar changes	[ ] Closure
[ ] Informed Consent changes	[ ] Suspension / temporary closure
[ ] Scientific / Statistical Considerations changes	[ ] Reactivation
[X] Data Submission / Forms changes	
[X] Editorial / Administrative changes	
[X] Other: CTSU template language	

No recommended IRB level of review is provided by the Alliance as the CIRB is the IRB of record for this trial. The site has 30 days after the posting of this amendment to implement it at their site. Please refer to the CIRB amendment application and guidelines for further instructions.

UPDATES TO THE PROTOCOL:

Cover Page (p.1)

- Language has been added to the cover page regarding the status as an FDA registration trial.
- The spelling of Dr. Matin's name has been corrected.
- Kabir Mody has been removed as study Co-Chair
- Lisa Kottschade has replaced Alexandra Connelly as the nursing contact.

Study Resources (p. 2)

- The Alliance Biorepository information has been updated.

CTSU Address and contact information (p. 3)

- CTSU Template language has been updated.

Section 5.0 (Study Calendar)

- Survival follow-up information has been removed from footnote *** and replaced with 'See Section 12.0.'

- In footnote #9, a second sentence has been added as follows: 'After the end of FOLFOX treatment, the timing of CEA testing should correspond with timing of radiographic imaging studies, where possible, but more frequent testing is at provider discretion.'
- A new section 5.1 **Vital Status (Survival)** has been added.

Section 6.1 (Data Collection and Submission)

- CTSU Template language has been updated.
- In section 6.1.1, the following information has been added to the list of baseline reports: 'Germline mutation testing report when requested by Alliance Statistics and Data Management Center to resolve discordant data entries.'

Section 11.1 (Schedule of Evaluations)

- A third sentence has been added to the second bullet point: 'After the end of FOLFOX treatment, the timing of CEA should correspond with the timing of radiographic imaging, where possible, but more frequent testing is at provider discretion.

Section 12.0 (End of Treatment)

- Sections 12.4 (Survival Follow-Up) and 12.5 (Lost to Follow-up) have been added.

Appendix V (AIO Sites and Investigators) has been added back into the protocol. It was removed by mistake in a previous update. The remaining appendices have been renumbered.

'Gender' has been replaced with 'Sex' throughout the protocol document (schema, eligibility and Correlative Science Companion Studies sections) as directed by NCI.

UPDATES TO THE MODEL CONSENT:

No changes to the model consent form

A replacement protocol and consent document have been issued.

ATTACH TO THE FRONT OF EVERY COPY OF THIS PROTOCOL

Consent Form

Study Title for Study Participants: Testing the addition of the antibody atezolizumab to usual chemotherapy after surgery in patients with colon cancer

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: A021502 Randomized Trial of Standard Chemotherapy Alone or Combined with Atezolizumab as Adjuvant Therapy for Patients with Stage III Colon Cancer and Deficient DNA Mismatch Repair (NCT02912559)

This study is being conducted by the Alliance for Clinical Trials in Oncology, a national clinical research group supported by the National Cancer Institute. The Alliance is made up of cancer doctors, health professionals, and laboratory researchers, whose goal is to develop better treatments for cancer, to prevent cancer, to reduce side effects from cancer, and to improve the quality of life of cancer patients.

If you are a parent or legal guardian of a child who may take part in this study, permission from you is required. The assent (agreement) of your child may also be required. When we say "you" in this consent form, we mean you or your child; "we" means the doctors and other staff.

What is the usual approach to my colon cancer?

You are being asked to take part in this study because you have colon cancer that was surgically removed but has spread to lymph nodes and is known as stage III colon cancer. If your colon cancer is found to have 'deficient DNA mismatch repair,' which occurs in approximately 10-12% of stage III colon cancers, then you may be eligible to participate in this study.

The mismatch repair (MMR) system corrects errors made during the copying of DNA and serves as a proofreading function. If corrections are not made, as occurs with deficient MMR (dMMR), then microsatellite instability (MSI) develops whereby repeats in nucleotides (the subunits of DNA) within the DNA sequence change the length of the DNA strand, resulting in errors when it's copied and therefore multiple mutations in these cancers.

People who are not in a study are usually treated with chemotherapy drugs. One of the common combinations of chemotherapy drugs used to treat your type of cancer is a three-drug regimen that includes 5-fluorouracil (also called 5-FU), leucovorin and oxaliplatin, and it is also called "FOLFOX". At the present time, the Food and Drug Administration (FDA) has approved each of these drugs as treatment for colon cancer. FOLFOX is a standard treatment used to prevent colon cancer from coming back (recurrence).

This study evaluates whether the addition of immune therapy to usual FOLFOX chemotherapy can improve your outcome compared to FOLFOX alone. The immune therapy drug, atezolizumab, may allow your body's immune system to do a better job of attacking the cancer cells in your body. One of the purposes of this study is to determine if giving atezolizumab and the chemotherapy FOLFOX decreases the risk of colon cancer recurrence to a greater degree than does FOLFOX chemotherapy alone.

What are my other choices if I do not take part in this study?

If you decide not to take part in this study, you have other choices. For example:

- You may choose to have the usual approach of chemotherapy treatment outside of a study
- You may choose to take part in a different study, if one is available
- Or you may choose not to be treated for cancer but you may want to receive comfort care to relieve any symptoms.

Why is this study being done?

The purpose of this study is to compare any good and bad effects of using the drug atezolizumab along with the usual chemotherapy compared to the usual chemotherapy alone. The addition of atezolizumab to the usual chemotherapy could prevent or reduce the chances of your cancer from returning, but it could also cause side effects. This study will allow the researchers to know whether this different approach is better, the same, or worse than the usual approach. To be better, the study drug would need to demonstrate increased chances of survival without the tumor returning by 10% or more compared to the usual approach. This drug, atezolizumab, is being tested in several types of cancer and has been granted FDA approval for its use in the treatment of bladder cancer. Atezolizumab is investigational for this study.

There will be about 700 people taking part in this study.

What are the study groups?

This study has two study groups.

- **Group 1** will get the usual chemotherapy treatment of FOLFOX plus the drug atezolizumab for 6 months, then patients will take atezolizumab alone for an additional 6 months.
- **Group 2** will get the usual chemotherapy which is FOLFOX for 6 months.

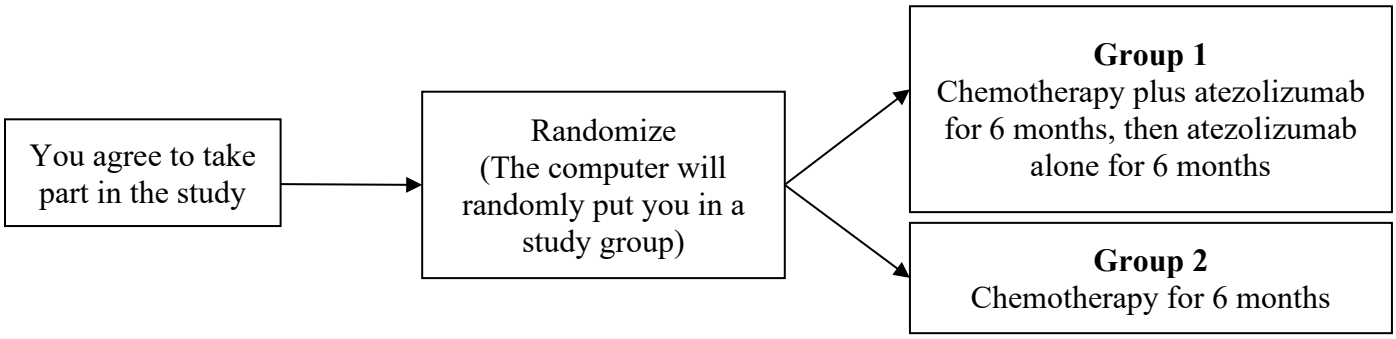
<u>How Treatments are Administered and How Often Treatments are Administered:</u>

- Oxaliplatin will be given as an IV infusion over a 2 hour window on the first day of every cycle*.
- Leucovorin will be given as an IV infusion over a 2 hour window on the first day of every cycle*.
- Fluorouracil will be given as an IV bolus on the first day of the cycle and as an IV infusion over a 46 hour window on the first through third days of every cycle*.
- Atezolizumab (Group 1 only) will be given as an IV infusion over a 1 hour window for the first infusion, and then over a 30 minute window for all subsequent infusions on the first day of every cycle*.

*One cycle is defined as 14 days.

A computer will by chance assign you to treatment groups in the study. This is called randomization. This is done by chance because no one knows if one study group is better or worse than others.

Another way to find out about your treatment during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



How long will I be in this study?

If you are in Group 1, you will receive chemotherapy and atezolizumab for 6 months, then you will take atezolizumab alone for an additional 6 months (25 cycles in total). If you are in Group 2, you will receive chemotherapy for 6 months (12 cycles in total). You will be able to start one cycle of chemotherapy before you are randomized if you choose while waiting for the test results described in the next section. If you choose this option and are then put in Group 1, you will receive chemotherapy and atezolizumab for 6 months, then you will take atezolizumab alone for an additional 6 months (24 cycles in total). For both groups, after treatment is complete, your doctor will continue to watch you for side effects and will follow your condition for up to 8 years since you started the study. If you do not complete treatment, your doctor will still watch you for side effects and follow your condition for up to 8 years since you started the study. The follow-up of your condition will occur at minimum every 6 months.

If your cancer returns you will not be required to complete the recurring blood test or scans, but your doctor will continue to watch you for side effects and follow your condition for up to 8 years since you started the study.

What exams, tests, and procedures are involved in this study?

Before you begin the study, your doctor will review the results of your exams, tests and procedures to make sure it is safe for you to participate. If you join the study, there will be exams, tests and/or procedures that will be done to monitor your safety and health care closely. Most of these are included in the usual care you would receive even if you were not in a study.

If your tissue is tested and found to have ‘deficient DNA mismatch repair,’ then you will be able to enroll on the study and start treatment. You will be able to start one cycle of FOLFOX if you choose, prior to getting your test results. A sample of your colon cancer tissue that was collected during your previous surgery is required to be sent to a central laboratory agreed upon by the Alliance and the drug company supporting the study for future central testing to confirm the deficient DNA mismatch repair testing result. There will be no additional procedures you need to complete for this required tissue collection and future analysis.

At the end of the study, the researchers will ask the National Cancer Institute (NCI) for permission to look at tumor DNA changes in your tissue sample that was sent to the Alliance Biobank. There will be no additional procedure you need to complete for this analysis.

At a future date, the study doctor may wish to collect the radiographic images taken while you were involved in the study.

Listed below are those exams, tests, and procedures that may not be needed with the usual approach, but are needed or are needed more frequently if you are in the study. The purpose of these procedures is to ensure your safety. We will use them to carefully monitor the effects of the study treatment, including preventing and managing side effects. In addition to your doctor's follow-up of your condition, you will be asked to complete the following:

- Two Quality of Life Assessments before you begin study treatment, and then one Quality of Life Assessment on the first day of each treatment cycle and at the end of treatment (for patients age 18 and up only)
- A thyroid test before you begin study treatment
- A colonoscopy after registration, but within 6 weeks of completing chemotherapy if you did not receive a colonoscopy before surgery

What possible risks can I expect from taking part in this study?

If you choose to take part in this study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual
- You may be asked sensitive or private questions which you normally do not discuss
- The study drugs/study approach may not be better, and could possibly be worse, than the usual approach for your cancer.
- There is a risk someone could get access to the personal information in your medical records or other information researchers have kept about you. Someone might be able to trace this information back to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information. In some cases, this information could be used to make it harder for you to get or keep a job. There are laws against misuse of genetic information, but they may not give full protection. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.
- There can also be a risk in finding out new genetic information about you. New health information about inherited traits that might affect you or your blood relatives could be found during a study.

The drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drugs.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.

The tables below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Study Group 1 and Group 2 - Possible side effects of FOLFOX, which is the usual approach for this type of cancer:

Possible Side Effects of FOLFOX (Leucovorin, 5-Fluorouracil, Oxaliplatin) Version Date: 11/14/2016

COMMON, SOME MAY BE SERIOUS In 100 people receiving FOLFOX (Leucovorin, 5-Fluorouracil, Oxaliplatin), more than 20 and up to 100 may have:
• Hair loss • Redness, pain or peeling of palms and soles • Rash, increased risk of sunburn, itching • Diarrhea, nausea, vomiting, constipation, loss of appetite • Difficulty swallowing • Sores in mouth • Heartburn • Infection, especially when white blood cell count is low • Anemia which may require a blood transfusion • Bruising, bleeding • Headache • Tiredness • Numbness, tingling or pain, "pins and needles" of the hands, feet, arms and legs • Tingling or a loss of feeling in your hands, feet, nose, or tightness in throat or jaw, or difficulty swallowing or breathing which may be made worse by exposure to cold • Cough • Fever, pain

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving FOLFOX (Leucovorin, 5-Fluorouracil, Oxaliplatin), from 4 to 20 may have:
• Chest pain • Abnormal heartbeat which may cause fainting • Swelling and redness at the site of the medication injection • Hives • Skin changes • Weight gain, weight loss, belly pain • Internal bleeding which may cause black tarry stool, blood in vomit or urine, or coughing up blood • Changes in taste • Blood clot which may cause swelling, pain, shortness of breath • Bleeding from multiple sites including vaginal bleeding, bleeding of the testis, or bleeding of the brain • Liver damage which may cause yellowing of eyes and skin • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Change in voice

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving FOLFOX (Leucovorin, 5-Fluorouracil, Oxaliplatin), from 4 to 20 may have:
• Confusion, dizziness • Muscle weakness • Inability to move shoulder or turn head • Blurred vision, watering eyes • Discomfort from light • Abnormal body movement including the eye and eyelid • Difficulty walking, using your hands, opening mouth, talking, with balance and hearing, smelling, eating, sleeping, emptying the bladder • Hearing loss • Swelling of the body which may cause shortness of breath • Kidney damage which may require dialysis • Scarring of the lungs • Blockage of the airway which may cause shortness of breath, cough, wheezing • Dehydration

RARE, AND SERIOUS In 100 people receiving FOLFOX (Leucovorin, 5-Fluorouracil, Oxaliplatin), 3 or fewer may have:
• Damage to the heart which may cause shortness of breath • A new cancer resulting from treatment of a prior cancer • Redness, pain or peeling of palms and soles

Study Group 1 Only - Possible Side Effects of Atezolizumab **Version Date: September 14, 2023**

COMMON, SOME MAY BE SERIOUS In 100 people receiving atezolizumab (MPDL3280A), more than 20 and up to 100 may have:
• Tiredness • Infection

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving atezolizumab (MPDL3280A), from 4 to 20 may have:
• Anemia which may require blood transfusion • Diarrhea, nausea, vomiting • Difficulty swallowing • Fever • Flu-like symptoms including body aches • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Reaction during or following a drug infusion which may cause fever, chills, rash • Loss of appetite • Pain in back • Cough, shortness of breath, stuffy nose • Itching, acne, rash

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving atezolizumab (MPDL3280A), from 4 to 20 may have:

Atezolizumab (MPDL3280A) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior decreased sex drive; weight loss or weight gain; excessive thirst or urine; dizziness or fainting.
- Pain in belly
- Pain or swelling of the joints
- Rash that develops on skin, nails, scalp and inside of mouth or vagina that may be painful

RARE, AND SERIOUS

In 100 people receiving atezolizumab (MPDL3280A), 3 or fewer may have:

- Bruising, bleeding

Atezolizumab (MPDL3280A) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Heart problems including swelling and heart failure. Symptoms and signs of heart problems may include: shortness of breath, swelling of the ankles and body.
- A condition with high blood sugar which leads to tiredness, frequent urination or excessive thirst.
- Swelling and redness of the eye
- Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness.
- Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe nausea or vomiting; drowsiness; pain in the right upper belly.
- Damage to organs in the body when the body produces too many white cells
- Swelling of the brain (meningitis/encephalitis), which may cause: headache, confusion, sleepiness, seizures, and stiff neck.
- Abnormal movement of the facial muscles
- Swelling of the spinal cord
- Problem of the muscle, including swelling, which can cause muscle pain and severe muscle weakness sometimes with dark urine.
- Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs.

RARE, AND SERIOUS In 100 people receiving atezolizumab (MPDL3280A), 3 or fewer may have:
• Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling. • Lung problems (pneumonitis and pleural effusion). Symptoms may include: new or worsening cough, chest pain, shortness of breath. • Skin: blisters on the skin, including inside the mouth (can be severe), rash with blisters, skin rash developing 1-8 weeks after a drug is given, which may be accompanied by fever, lymph node swelling and organ failure.

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Reproductive Risks: You should not get pregnant, breastfeed, or father a baby while in this study. The drugs used in this study could be very damaging to an unborn baby. Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study. You should utilize contraceptive measures to avoid pregnancy while undergoing atezolizumab or chemotherapy treatment and for at least 150 days (5 months) after the last dose of atezolizumab or chemotherapy.

What possible benefits can I expect from taking part in this study?

It is not possible to know at this time if the study drug is better than the usual approach, so this study may or may not help you. This study will help researchers learn things that will help people in the future.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB, or FDA.

What are my rights in this study?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, call the _____ *(insert name of center)* Institutional Review Board at _____ *(insert telephone number). (Note to Local*

Investigator: Contact information for patient representatives or other individuals at a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can also be listed here.)

What are the costs of taking part in this study?

There are no costs to you or your insurance for those exams, tests, and procedures done for research purposes only. These include the central testing on your tumor DNA. The costs will not be billed to you or your insurance company.

Your Potential Costs:
Administration of the study drug, non-study drugs and all premedications, fluids and procedures are going to be billed to your insurance and are your responsibility. Some exams, tests and procedures may be needed to manage side effects and to monitor your safety while you are on the study. You and your health plan/insurance company will be responsible for the costs of these exams, tests and procedures and will not be paid for by the study. You are responsible for all co-pays and deductibles according to your benefit plan with your insurance.

It is important for you to speak to your insurance company/health plan to ensure that you understand your coverage and whether you might need a pre-authorization to participate in a study. While most plans cover clinical trials, it is your responsibility to check with them. If you participate in a Medicare Advantage Plan, your health care bills while you are in this study will be sent to the regular Medicare for processing. This may result in a higher co-pay, which should be directed to your Medicare Advantage plan for payment after Medicare reimburses for your care. Ask your doctor, nurse, case manager, or financial counselor/advisor if you are unsure what will be billed to your insurance/health plan. If you have additional questions about what your plan covers, you may also ask to speak to a hospital/clinic financial counselor/advisor or case manager.

Costs Paid by the Study:
For patients in both Group 1 and Group 2, the thyroid test performed before you begin study treatment will be at no charge to you or your insurance company.

The atezolizumab will be supplied to patients in Group 1 at no charge to your or your insurance company while you take part in this study. Rarely, unexpected problems in drug supply could occur, but if that event occurs, your doctor will talk with you about your options.

You will not be paid for taking part in this study. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

What happens if I am injured or hurt because I took part in this study?

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. The study sponsors will not offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

Who will see my medical information?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The Alliance and their agents
- The BTRC & Research Support Services Core at Duke University
- The drug company supporting the study, Genentech, and their agents, or any drug company supporting the study
- Other organizations from the National Clinical Trials Network that take part in this study
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study
- The Food and Drug Administration and the National Cancer Institute in the U.S.

Where can I get more information?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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

Who can answer my questions about this study?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

ADDITIONAL STUDIES SECTION

This section is about optional studies you can choose to take part in.

This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The researchers leading these optional studies hope the results will help other people with cancer in the future.

The results will not be added to your medical records and you or your study doctor will not know the results.

You will not be billed for these optional studies. You can still take part in the main study even if you say "no" to any or all of these studies. If you sign up for but cannot complete any of the studies for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for each of the following studies.

Optional Quality of Life Study (for patients age 18 and up only)

If you choose to take part in this quality of life study, you will be asked to fill out forms with questions about your physical and emotional well-being, as well as about any side effects you may experience. These forms are in addition to the Quality of Life Assessments you are asked to fill out as part of the main study.

We want to know your view of how your life has been affected by cancer and its treatment. This "Self-Reporting of Symptoms" part of this study looks at how you are feeling physically and emotionally during your cancer treatment. It also looks at how you are able to carry out your day-to-day activities.
This information will help doctors better understand how patients feel during treatments and what effects the medicines are having. In the future, this information may help patients and doctors as they decide which medicines to use to treat cancer.
You will be asked to fill out two forms at the following time points:

- If you are in Group 1: before you start treatment, before Cycle 4 of treatment, before Cycle 7 of treatment, before Cycle 13 treatment, after you finish atezolizumab treatment, and 3 years after the date you enrolled in the study
- If you are in Group 2: before you start treatment, before Cycle 4, before Cycle 7, after you finish FOLFOX treatment, 12 months after the date you enrolled in the study, and 3 years after the date you enrolled in the study

The forms will take about 30 minutes to complete at each of these time points. The forms will ask about things like fatigue, diarrhea, and depression. You may feel uncomfortable answering some of the questions, and you can skip any you do not want to answer.

Please circle your answer: I choose to take part in the Quality of Life study and will fill out these forms:

1) YES NO

Optional Biobanking for Possible Future Studies

Researchers are trying to learn more about cancer, diabetes, and other health problems. Much of this research is done using samples from your tissue, blood, or other specimens. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you.

If you choose to take part, the researchers ask your permission to store and use your samples and related health information (for example, your response to cancer treatment, results of study tests and medicines you are given) for future medical research. The research that may be done is unknown at this time. Storing samples for future studies is called "biobanking". The Biobank is being run by the Alliance and supported by the National Cancer Institute.

If you choose to take part in this study, your study doctor will submit some of the tissue that was already collected from your surgery or biopsy. This tissue collection would be in addition to the tissue you are required to submit as part of the main study.

In the event that your cancer returns, the researchers would like to collect some of the tissue that would be collected from any future surgeries or biopsies for the possible research mentioned above.

In addition, the researchers would like to collect additional samples of your blood. The researchers would like to investigate whether substances in your blood (sometimes called biomarkers) are related to the way that your body responds or doesn't respond to the therapy you receive in this trial. While you are on the study, approximately 4 tablespoons of additional blood for this research would be collected at the following time points:

- At the beginning of the study
- Approximately 1 month after the start of therapy (only ~2 tablespoons)
- Approximately 4.5 months after the start of therapy
- 6 months after the end of therapy
- In the event your cancer returns (only ~2 tablespoons)

The researchers would also like to collect a sample of your stool. The researchers would like to investigate whether organisms in your stool called 'gut microbiota' are related to the way that your body respond to or doesn't respond to the study treatment. You would provide a stool sample at the following time points:

- At the beginning of the study
- Approximately 6 months after you start the study
- 6 months after the end of therapy

WHAT IS INVOLVED?

If you agree to take part, here is what will happen next:

1) Before you start study treatment about 4 tablespoons of blood will be collected from a vein in your arm. Some of this blood will be sent directly to Duke University along with your initials and the collection date and time. A sample from the tissue that was collected at the time of your previous or future biopsy or surgery will be sent to the Biobank. A sample of your stool will be collected.
2) Your sample and some related health information will be sent to a researcher for use in the studies described above. Remaining samples may be stored in the Biobank, along with samples from other people who take part. The samples will be kept until they are used up.
3) Your blood and stool will also be collected during and after study treatment at the time points listed above and will be sent to a researcher for use in the studies described above. Remaining samples may be stored in the Biobank, along with samples from other people who choose to take part. The samples will be kept until they are used up.
4) Qualified researchers can submit a request to use the materials stored in the Biobanks. A science committee at the clinical trials organization, and/or the National Cancer Institute, will review each request. There will also be an ethics review to ensure that the request is necessary and proper. Researchers will not be given your name or any other information that could directly identify you.
5) Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples.

6) Some of your genetic and health information may be placed in central databases that may be public, along with information from many other people. Information that could directly identify you will not be included.

WHAT ARE THE POSSIBLE RISKS?

1) The most common risks related to drawing blood from your arm are brief pain and possibly a bruise.
2) There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
3) There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.
4) In some cases, this information could be used to make it harder for you to get or keep a job or insurance. There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

HOW WILL INFORMATION ABOUT ME BE KEPT PRIVATE?

Your privacy is very important to the researchers and they will make every effort to protect it. Here are just a few of the steps they will take:

1) When your sample(s) is sent to the researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.
2) The list that links the unique code to your name will be kept separate from your sample and health information. Any Biobank and Alliance staff with access to the list must sign an agreement to keep your identity confidential.
3) Researchers to whom the Alliance sends your sample and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.
4) Information that identifies you will not be given to anyone, unless required by law.
5) If research results are published, your name and other personal information will not be used.

WHAT ARE THE POSSIBLE BENEFITS?

You will not benefit from taking part.

Your samples may be helpful to research whether you do or do not have cancer. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

ARE THERE ANY COSTS OR PAYMENTS?

There are no costs to you or your insurance for these optional studies. You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

WHAT IF I CHANGE MY MIND?

If you decide you no longer want your samples to be used, you can call the study doctor, _____, *(insert name of study doctor for main trial)* at _____ *(insert telephone number of study doctor for main trial)* who will let the researchers know. Then, any sample that remains in the bank will no longer be used and related health information will no longer be collected. Samples or related information that have already been given to or used by researchers will not be returned.

WHAT IF I HAVE MORE QUESTIONS?

If you have questions about the use of your samples for research, contact the study doctor, _____, *(insert name of study doctor for main trial)*, at _____ *(insert telephone number of study doctor for main trial)*.

Please circle your answer to show whether or not you would like to take part in each option:

SAMPLES FOR FUTURE RESEARCH STUDIES

I agree to have my blood collected, and I agree that my blood samples and related information may be kept in a Biobank for use in future health research.

2) YES NO

I agree to have my tissue collected, and I agree that my tissue samples and related information may be kept in a Biobank for use in future health research.

3) YES NO

I agree to have my stool collected, and I agree that my stool samples and related information may be kept in a Biobank for use in future health research.

4) YES NO

I agree that my study doctor, or their representative, may contact me or my physician to see if I wish to participate in other research in the future.

5) YES NO

This is the end of the section about optional studies.

My Signature Agreeing to Take Part in the Main Study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the main study and any additional studies where I circled 'yes'.

Participant's signature_____

Date of signature_____

Parent/Guardian signature (if applicable) _____

Date of signature_____

Parent/Guardian signature (if applicable) _____

Date of signature_____

Signature of person(s) conducting the informed consent discussion_____

Date of signature_____

INFORMATION SHEET REGARDING RESEARCH STUDY
(for teens from 12 through 17 years of age)

A study to compare treatments with or without atezolizumab for stage 3 colon cancer

1. We have been talking with you about your stage 3 colon cancer. Colon cancer is a type of cancer that grows in the abdomen. Tests have also shown that your colon cancer has a "DNA mismatch repair deficiency." This means that one of the ways cells fix damage to their DNA (genes) is not working the way it should in your colon cancer. After doing tests, we have found that you have this type of cancer.

2. We are asking you to take part in a research study because you have stage 3 colon cancer, and the cancer's DNA mismatch repair system is not working the way it should. A research study is when doctors work together to try out new ways to help people who are sick. In this study, we are trying to learn more about how to treat this type of cancer you have. We will do this by adding another drug to one of the standard treatments for this type of cancer.

   A standard treatment for stage 3 colon cancer is a combination of 3 chemotherapy (anti-cancer) drugs called "FOLFOX" therapy. This study will compare FOLFOX therapy to FOLFOX plus another cancer-fighting drug called atezolizumab. We do not know whether adding atezolizumab to your treatment will make it more effective or cause more side effects. That is why we are doing this study.

3. Children and teens who are part of this study will be randomly assigned to either Group 1 - FOLFOX chemotherapy plus atezolizumab or Group 2 - FOLFOX chemotherapy. This is called randomization. This is a lot like flipping a coin. A computer decides which treatment plan you will get and not your doctor.

   - Group 1 will receive FOLFOX plus atezolizumab for 6 months, and then only atezolizumab for 6 more months.
   - Group 2 will receive FOLFOX for 6 months.

4. Sometimes good things can happen to people when they are in a research study. These good things are called "benefits." We hope that a benefit to you of being part of this study is to prevent or reduce the chances of your cancer coming back but we don't know for sure if there is any benefit of being part of this study.

5. Sometimes bad things can happen to people when they are in a research study. These bad things are called "risks." The risks to you from this study are that the study treatments may cause bad side effects. There is also the risk that the treatments may not work and that your cancer may come back. Other things may happen to you that we don't yet know about.

6. Your parents can choose for you to be part of this study or not. Your parents can also decide for you to stop being in this study at any time once you start. The doctors and nurses will take care of you just like they did before. If you have any questions or don't like what is happening, please tell your parent, the doctor, or nurse. There may be other treatments for your cancer that your doctor can tell you about.

7. We are asking your permission to collect additional blood, tissue, and stool samples. We want to see if there are ways to tell how the cancer will respond to treatment. The blood samples will usually be taken when other

standard blood tests are being performed to avoid extra procedures when possible. The tissue samples will be taken from tissue already collected from your surgery or biopsy, so there would be no extra procedures. You can still be treated on this study even if you don't allow us to collect the extra samples for research.

8. After the treatment is completed, you will have checkups with your doctor for up to 8 years.

9. You have had the study explained to you. You have been given a chance to ask questions.

10. Your doctors will speak privately with you before you are asked to decide if you want to take part on the study.

11. If you are a female patient who is menstruating, you will take pregnancy tests and be asked about birth control.