SWOG CANCER RESEARCH NETWORK

Version Date: January 9, 2024

TO: ALL NATIONAL CLINICAL TRIALS NETWORK (NCTN) MEMBERS; CTSU

FROM: SWOG Network Operations Center (protocols@swog.org)

RE: **S1806**, "Phase III Randomized Trial of Concurrent Chemoradiotherapy with or without
Atezolizumab in Localized Muscle Invasive Bladder Cancer." Primary Study Chairs: Parminder Singh, M.D. and Jason Efstathiou, M.D., D.Phil.

REVISION #9

Study Chair: Parminder Singh, M.D.
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Action Codes
(√) Expedited review allowed

Key Updates
(√) Specimen Submission changes
(√) Editorial / Administrative changes

The protocol and/or informed consent form changes have been approved by the CIRB and must be activated within 30 days for distribution of this notice through the CTSU Bi-Monthly Broadcast email.

REVISION #9

This revision includes additional details for the shipment of specimens from the SWOG Biospecimen Bank for the purposes of PD-L1 IHC analysis. Language has also been added that references an updated funding sheet for venipuncture coverage.

Protocol Changes

1. The **version date** has been updated.

2. Throughout the protocol, formatting, typographical errors, pagination, and cross-references have been corrected as needed.

3. **Table of Contents**: This has been updated.

4. **Section 9.1 and 9.2:** Calendar footnote X has been added to refer to the Funding Sheet for funds associated with Weeks 54 and 104 blood collection timepoints.

5. **Section 14.4k:** A reference to the Funding Sheet for funds associated with Weeks 54 and 104 blood collection timepoints has been added.

6. **Section 15.1a.1b, FFPE Tissue Specimen Collection and Submission Instructions:** Cold pack exception has been added to slide submission.
7. **Section 15.1a.2a:** The word "top" has been added to Lavender EDTA tubes.

8. **Section 15.1a.2b:** A reference to the Funding Sheet for funds associated with Weeks 54 and 104 blood collection timepoints has been added.

9. **Section 15.1a.2c:** Shipping instructions have been added for Whole Blood Collection.

10. **Section 15.1a.2d:** The last two paragraphs regarding shipment have been removed, as it has been addressed in the section above.

11. **Section 15.1d:** Required documents for shipping have been added.

12. **Section 15.1e:** Clarifications have been made to the specimen shipping instructions.

13. **Section 18.1:** The references in this section have been updated.

14. **Section 18.1b, PD-L1 IHC:** Additional details regarding PD-L1 IHC analysis has been added.

15. **Section 18.2:** Information about kits has been removed, as it is included in Section 15.1. Additional instructions for the SWOG Biospecimen Bank regarding the PD-L1 IHC have been added.

Model Consent Form Changes

1. The **version date** has been updated.

The updated protocol and model informed consent form can be accessed from the CTSU website (www.ctsu.org). Please discard any previous versions of the documents and replace with the updated versions. Please contact guquestion@crab.org or 206/652-2267 with any questions.
This study has been reviewed and approved by the NCI's Central Institutional Review Board (CIRB).

This memorandum serves to notify the NCI and SWOG Statistics and Data Management Center.

cc: PROTOCOL & INFORMATION OFFICE

Felix Feng, M.D.
Monika Joshi, M.D.
Bishoy Morris Faltas, M.D.
Brian A. Costello, M.D, M.S.
Joanne C. Hunter – IROC
Srikala Sridhar, M.D. M.Sc., FRCPC
Michelle Brockman – Genentech

Informed Consent Model for S1806

*NOTES FOR LOCAL INSTITUTION INFORMED CONSENT AUTHORS:

This model informed consent form has been reviewed by the DCTD/NCI and is the official consent document for this study. Local IRB changes to this document are allowed. (Institutions should attempt to use sections of this document that are in bold type in their entirety.) Editorial changes to these sections may be made as long as they do not change information or intent. If the institutional IRB insists on making additions, deletions, or more substantive modifications to the risks or alternatives sections, they may be justified in writing by the investigator and approved by the IRB. Under these circumstances, the revised language, justification and a copy of the IRB minutes must be forwarded to the SWOG Operations Office for approval before a patient may be registered to this study.

Please particularly note that the questions related to banking of specimens for future study are in bolded type and may not be changed in any way without prior approval from the SWOG Operations Office.

Readability Statistics:	
Flesch Reading Ease	62.8 (targeted above 55)
Flesch-Kincaid Grade Level	8.3 (targeted below 8.5)

- Instructions and examples for informed consent authors are in *[italics]*.
- A blank line, _____, indicates that the local investigator should provide the appropriate information before the document is reviewed with the prospective research participant.
- The term "study doctor" has been used throughout the model because the local investigator for a cancer treatment trial is a physician. If this model is used for a trial in which the local investigator is not a physician, another appropriate term should be used instead of "study doctor".
- The dates of protocol updates in the header and in the text of the consent is for reference to this model only and should not be included in the informed consent form given to the prospective research participant.
- The local informed consent must state which parties may inspect the research records. This includes the NCI, the drug manufacturer for investigational studies, any companies or grantors that are providing study support (these will be listed in the protocol's model informed consent form) and SWOG.

"SWOG" must be listed as one of the parties that may inspect the research records in all protocol consent forms for which patient registration is being credited to SWOG. This includes consent forms for studies where all patients are registered directly through the SWOG Data Operations Office, all intergroup studies for which the registration is being credited to SWOG (whether the registration is through the SWOG Data Operations Office or directly through the other group), as well as consent forms for studies where patients are registered via CTSU and the registration is credited to SWOG.

- When changes to the protocol require revision of the informed consent document, the IRB should have a system that identifies the revised consent document, in order to preclude continued use of the older version and to identify file copies. An appropriate method to identify the current version of the consent is for the IRB to stamp the final copy of the consent document with the approval date. The stamped consent document is then photocopied for use. Other systems of identifying the current version of the consent such as adding a version or approval date are allowed as long as it is possible to determine during an audit that the patient signed the most current version of the consent form.

*NOTES FOR LOCAL INVESTIGATORS:

- The goal of the informed consent process is to provide people with sufficient information for making informed choices about participating in research. The consent form provides a summary of the study, the individual's rights as a study participant, and documents their willingness to participate. The consent form is, however, only one piece of an ongoing exchange of information between the investigator and study participant. For more information about informed consent, review the "Recommendations for the Development of Informed Consent Documents for Cancer Clinical Trials" prepared by the Comprehensive Working Group on Informed Consent in Cancer Clinical Trials for the National Cancer Institute. The Web site address for this document is http://cancer.gov/clinicaltrials/understanding/simplification-of-informed-consent-docs/
- Suggestion for Local Investigators: An NCI pamphlet explaining clinical trials is available for your patients. The pamphlet is titled: "Taking Part in Cancer Treatment Research Studies". This pamphlet may be ordered on the NCI Web site at *https://cissecure.nci.nih.gov/ncipubs* or call 1-800-4- CANCER (1-800-422-6237) to request a free copy.
- Optional feature for Local Investigators: Reference and attach drug sheets, pharmaceutical information for the public, or other material on risks. Check with your local IRB regarding review of additional materials.

*These notes for authors and investigators are instructional and should not be included in the informed consent form given to the prospective research participant.

Research Study Informed Consent Document

Study Title for Participants: S1806, Testing combined chemotherapy and radiation therapy with and without the use of Atezolizumab Immunotherapy in Muscle Invasive Bladder Cancer.

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:

S1806, Phase III Randomized Trial of Concurrent Chemoradiotherapy with or without Atezolizumab in Localized Muscle Invasive Bladder Cancer (Study SWOG/NRG 1806) (NCT#03775265)

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

You are being asked to take part in this study because you have bladder cancer that has not spread beyond the bladder.

Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

Why is this study being done?

The purpose of this study is to compare the effects, good and/or bad, of chemotherapy and radiation therapy with or without the use of atezolizumab, which is used to treat bladder cancer. The combination of chemotherapy, radiation therapy and the immunotherapy atezolizumab is considered experimental.

What is the usual approach to my muscle invasive bladder cancer?

The usual approach for patients who are not in a study is to proceed with radical cystectomy with or without Food and Drug Administration (FDA) approved chemotherapy or receive chemoradiation without immunotherapy.

The usual approach for patients who are not in a study is to monitor the effect of treatment by taking pictures of their tumor(s) with a CT or MRI machine over time. This means that you will get more than one CT or MRI scan with a machine that uses radiation or magnets.

What are my choices if I decide not to take part in this study?

- You may choose to have the usual approach described above.
- You may choose to take part in a different research study, if one is available.
- You may choose not to be treated for cancer.
- You may choose to only get comfort care to help relieve your symptoms and not get treated for your cancer.

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will receive combined chemotherapy and radiation therapy which is called "chemoradiotherapy" either with or without the study drug. The chemoradiotherapy you will receive is standard of care and what your doctor thinks is best. You will receive chemoradiotherapy for up to 7 weeks. If you are assigned to the group receiving study drug, you will take the drug for up to 6 months in addition the chemoradiotherapy.

About 18-weeks after you start the study treatment, you will have a surgery as part of your regular cancer care. A sample of your tissue will be sent to a central laboratory for review.

Your doctor will continue to follow your condition for up to 5 years after you register to the study, even though you have finished treatment in the first year. Your doctor will watch you for side effects and to see how your cancer affects you. You will have clinic visits at 3 months from the time you stop taking treatment for the first two years and then twice a year for the third year and once a year thereafter until 5 years after you register to the study.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the "What risks can I expect from taking part in this study?" section.

If you choose to take part in this study, there is a risk that the study approach (treating patients with chemoradiotherapy and atezolizumab) may not be as good as the usual approach (treating patients with chemoradiotherapy only).

There is also a risk that you could have side effects from the study drugs. These side effects may be worse and may be different than you would get with the usual approach for your cancer. There may be some risks that the study doctors do not yet know about.

Benefits

There is evidence that the study approach is effective in reducing the amount of cancer in your body. It is not possible to know now if the study drug with chemoradiotherapy will affect how long you live compared to the usual approach. This study will help the study doctors learn things that will help people in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your 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.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- The study is stopped by the National Cancer Institute (NCI), Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor (SWOG). The study sponsor is the organization who oversees the study.

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

What is the purpose of this study?

The purpose of this study is to compare the effects, good and/or bad, of chemotherapy and radiation therapy with or without the use of the immunotherapy drug atezolizumab, which is used to treat bladder cancer. The addition of atezolizumab to the usual treatment could help patients live longer. But it could also cause side effects which are described in the risks section below.

This study will help find out if this different approach is better, the same, or worse than the usual approach. To decide if it is better, the study doctors will be looking to see if the study approach increases the life of patients compared to the usual approach.

There will be about 475 people taking part in this study.

What are the study groups?

This study has 2 study groups. You will be told which group you are in.

- **Group 1**

  If you are in this group, you will get radiation therapy and one of the usual chemotherapy regimens used to treat this type of cancer.

  You will receive radiation treatment Monday through Friday for up to seven weeks.

  Your doctor will choose which chemotherapy regimen you will take. He/she will choose one of the following three options:

  1. Cisplatin. This would be given by IV (into your vein) once a week for six weeks.
  2. Gemcitabine. This would be given by IV twice a week for six weeks.
  3. 5-Fluoruracil (5-FU) and mitomycin-C. 5-FU would be given by IV on the same days as your first five radiation treatments and your 16th through 20th radiation treatments. Mitomycin-C would be given by IV on the same day as your first radiation treatment.

  There will be about 237 people in this group.

- **Group 2**

  If you are in this group, you will get radiation therapy, chemotherapy and the study drug atezolizumab.

  You will receive the study drug atezolizumab by IV (into your vein) every three weeks for up to six months (nine total doses).

  You will receive radiation treatment Monday through Friday for up to seven weeks.

  Your doctor will choose which of the usual chemotherapy regimens used to treat this type of cancer you will take. He/she will choose one of the following three options:

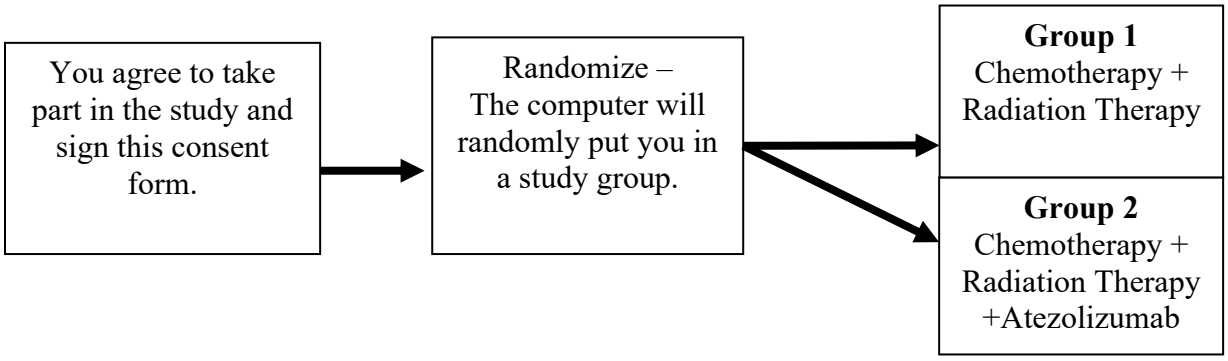
  1. Cisplatin. This would be given by IV (into your vein) once a week for six weeks.
  2. Gemcitabine. This would be given by IV twice a week for six weeks.
  3. 5-Fluoruracil (5-FU) and mitomycin-C. 5-FU would be given by IV on the same days as your first five radiation treatments and your 16th through 20th radiation treatments. Mitomycin-C would be given by IV on the same day as your first radiation treatment.

  There will be about 237 people in this group.

For both study groups: About 18 weeks after you start the study treatment, you will have a surgery as part of your regular cancer care. A sample of your tissue from the surgery will be sent to a central laboratory for review. This is done to help the study doctors make sure that all the surgery results are being read and reported in the same way for all study participants.

We will use a computer to assign you to one of the two study groups. This process is called "randomization." It means that your doctor will not choose and you cannot choose which study group you are in. You will be put into a group by chance. You have an equal chance of being in Group 1 or Group 2.

Another way to find out what will happen to you during this study is to read the chart below. Start reading from the left and read to the right, following the lines and arrows.



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. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Some exams, tests, and procedures are a necessary part of the research study but would not be included in the usual care. Listed below is a procedure that will be done for research purposes only.

Quality of Life

Patients in both study groups who can read and write in English or Spanish, must take part in the quality of life study. This part of the study looks to compare whether urinary, sexual, bowel function and other aspects of quality of life are different using chemotherapy and radiation therapy versus chemotherapy and radiation therapy with atezolizumab.

You will complete four forms with questions about your symptom status, physical and emotional well-being. Researchers will use this information to learn more about how cancer and cancer treatment affects people. You will be asked to fill out the forms at the following times:

- before you begin treatment
- about 3 months after starting treatment
- about 5 months after starting treatment
- about 12 months after starting treatment
- about 24 months after starting treatment
- about 36 months after starting treatment

You will complete the forms by paper and pencil. It should take you about 20 minutes or less to fill out the forms at each time point.

What 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 atezolizumab (MPDL3280A) 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 drug(s)/study approach.

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 mild. Other side effects may be serious and may even result in death.

You can ask your study doctor questions about side effects at any time. 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. The side effects with chemotherapy and radiation are expected to be present with or without atezolizumab (immunotherapy).

Risk Profile for Atezolizumab (MPDL3280A) (CAEPR Version 2.4, September 14, 2023)

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

OCCASIONAL, SOME MAY BE SERIOUS

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

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 people 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
- 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.

Possible Side Effects of Gemcitabine (Table Version Date: January 19, 2016)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Gemcitabine, more than 20 people and up to 100 may have:
• **Flu-like symptoms of muscle pain, fever, headache, chills and fatigue** • **Nausea, vomiting** • **Rash** • **Hair loss** • **Infection, especially when white blood cell count is low** • **Bruising, bleeding** • **Anemia which may require a blood transfusion** • **Muscle weakness** • **Blood in urine** • **Feeling of "pins and needles" in arms and legs** • **Numbness and tingling of the arms and legs** • **Tiredness** • **Difficulty sleeping** • **Swelling of arms, legs**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Gemcitabine, from 4 to 20 people may have:
• **Swelling and redness of the area of radiation** • **Blisters on the skin** • **Diarrhea, constipation** • **Sores in mouth which may cause difficulty swallowing** • **Liver damage which may cause yellowing of eyes and skin, swelling** • **Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat** • **Scarring of the lungs** • **Shortness of breath** • **Fluid in the organs which may cause low blood pressure, shortness of breath, swelling of ankles** • **Brain damage, Reversible Posterior Leukoencephalopathy Syndrome, which may cause headache, seizure, blindness**

RARE, AND SERIOUS In 100 people receiving Gemcitabine, 3 or fewer people may have:
• **Severe blood Infection** • **Anemia, kidney problems which may require dialysis** • **Blood clot** • **Blockage of the airway which may cause cough**

Possible Side Effects of Cisplatin (Table Version Date: April 20, 2015)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Cisplatin, more than 20 people and up to 100 may have:
• **Nausea, vomiting** • **Infection, especially when white blood cell count is low** • **Anemia which may cause tiredness, or may require blood transfusions** • **Bruising, bleeding** • **Kidney damage which may cause swelling, may require dialysis** • **Hearing loss including ringing in ears**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Cisplatin, from 4 to 20 people may have:
• **Hair loss** • **Change in taste** • **Diarrhea** • **Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat** • **Confusion** • **Difficulty with balance** • **Numbness and tingling of the arms and legs** • **Blurred vision or changes in ability to see colors (especially blue or yellow)**

RARE, AND SERIOUS In 100 people receiving Cisplatin, 3 or fewer people may have:
• **Cancer of bone marrow caused by chemotherapy later in life** • **Seizure**

Possible Side Effects of 5- Fluorouracil (Table Version Date: November 9. 2016)

COMMON, SOME MAY BE SERIOUS In 100 people receiving 5-Fluorouracil, 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, loss of appetite** • **Difficulty swallowing** • **Sores in mouth** • **Heartburn** • **Headache**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving 5-Fluorouracil, from 4 to 20 may have:
• **Chest pain** • **Blood clot** • **Belly pain** • **Internal bleeding which may cause black tarry stools** • **Infection, especially when white blood cell count is low** • **Anemia which may require blood transfusions** • **Bruising, bleeding** • **Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat** • **Confusion** • **Abnormal eye movement, blurred vision, watering eyes** • **Discomfort from light** • **Difficulty with balancing** • **Skin changes** • **Tiredness**

RARE, AND SERIOUS In 100 people receiving 5-Fluorouracil, 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**

Possible Side Effects of Mitomycin-C (Table Version Date: January 4, 2016)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Mitomycin, more than 20 and up to 100 may have:
• **Infection, particularly when white blood cell counts are low** • **Anemia which might require blood transfusion** • **Bruising, bleeding** • **Tiredness** • **Swelling of the body** • **Difficult, painful or frequent urination (when the drug is administered into the bladder)** • **Blood clot**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Mitomycin, from 4 to 20 may have:
• **Loss of appetite** • **Nausea, vomiting** • **Sores in the mouth** • **Rash** • **Hair loss** • **Loss of fertility** • **Swelling and redness at the site of the medication injection** • **Fever** • **Anemia, kidney problems which may cause tiredness, bruising, swelling, or may require dialysis**

RARE, AND SERIOUS In 100 people receiving Mitomycin, 3 or fewer may have:
• **Shortness of breath, cough, scarring of the lungs** • **Kidney failure that could require treatment with dialysis**

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 atezolizumab 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. You must use birth control for 5 months after your last treatment with atezolizumab. If you or your partner becomes pregnant, contact the study doctor immediately**.**

Possible Side Effects of Radiation Therapy

Early reactions:

COMMON, SOME MAY BE SERIOUS: In 100 people receiving radiation, more than 20 and up to a 100 may have:
• **Inflammation of bowel causing cramping and diarrhea** • **Inflammation of rectum and anus causing pain, spasm, discharge** • **Bladder inflammation causing burning, frequency, spasm, pain** • **Skin changes: redness, irritation, coloration, thickening, hair loss, scaliness, blistering** • **In women there could be disturbance in menstrual cycle, vaginal discharge, pain, irritation, bleeding and painful intercourse.**

OCCASIONAL, SOME MAY BE SERIOUS: In 100 people receiving radiation, from 4 to 20 may have:
• **Inflammation of rectum and anus causing bleeding** • **Bladder inflammation causing bleeding**

RARE AND SERIOUS: In 100 people receiving radiation, 3 or fewer may have:
• **Skin changes: ulceration** • **Inflammation of bowel causing bleeding** • **Depression of blood count leading to increased risk of infection and/or bleeding**

Late reactions:

COMMON, SOME MAY BE SERIOUS: In 100 people receiving radiation, more than 20 and up to a 100 may have:
• **Loss of bladder capacity** • **Frequency of urination** • **Bladder spasms or pain** • **Changes in skin texture and/or coloration, permanent hair loss, scarring of skin.** • **Testicular damage causing reduced sperm counts, infertility, sterility, or risk of birth defects.** • **Impotence (loss of erection) or sexual dysfunction** • **Ovarian damage causing infertility, sterility, or premature menopause.** • **Vaginal damage leading to dryness, shrinkage, pain, bleeding, or sexual dysfunction.**

OCCASIONAL, SOME MAY BE SERIOUS: In 100 people receiving radiation, from 4 to 20 may have:
• **Blood in urine** • **Recurrent urinary tract infections** • **Chronic diarrhea or poor absorption of food elements**

RARE AND SERIOUS: In 100 people receiving radiation, 3 or fewer may have:
• **Bowel damage causing narrowing or adhesions of the bowel with obstruction, ulceration, bleeding and may require surgical correction or colostomy.** • **Bladder damage which may require urinary diversion and/or removal of bladder.** • **Bone damage leading to fractures.** • **Swelling of the genitalia or legs.** • **Nerve damage causing pain, loss of strength or feeling in legs, and/or loss of control of bladder or rectum.** • **Fistula between the bowel and other organs.** • **Second malignancies are also possible in adults.**

Additional risks should be discussed with your treating Radiation Oncologist.

You should talk to your study doctor about any side effects that you have while taking part in the study.

What are my responsibilities in this study?

If you choose to take part in this study you will need to:

- Keep your study appointments.
- Tell your doctor about:
    - all medications and supplements you are taking
    - any side effects
    - any doctors' visits or hospital stays outside of this study
    - if you have been or are currently in another research study.

For patients: Do not get pregnant or breastfeed while taking part in this study. Do not father a baby while taking part in this study. Tell your study doctor right away if you think that you or your partner has become pregnant during the study or within 5 months after your last dose of study drug.

What are the costs of taking part in this study?

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your bladder cancer. This includes:

- the costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety and prevent and treat side effects.
- the costs of getting chemotherapy and radiation therapy.
- the costs of getting the study drugs ready and giving them to you.
- your insurance co-pays and deductibles.

You or your insurance provider will not have to pay for atezolizumab while you take part in this study.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

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

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- The study sponsor and any company supporting the study now or in the future.
- The Institutional Review Board (IRB), which 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 (FDA) and the groups it works with to review research
- The National Cancer Institute (NCI) and the groups it works with to review research.
- The NCI's National Clinical Trials Network and the groups with which it works with to conduct research.

Your study records also will be stored for future use. However, your name and other personal information will not be used. Some types of future research may include looking at your records and those of other patients to see who had side effects across many studies or comparing new study data with older study data. However, we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

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.

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 treating doctor)* at _____(*insert number of treating doctor*).

For questions about your rights while in this study, call the _____ (i*nsert name of organization or center*) Institutional Review Board at _____ (*insert telephone number*).

Optional studies that 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. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading these optional studies hope the results will help other people with your type of 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.

Taking part in these optional studies is your choice. You can still take part in the main study even if you say "no" to these optional studies. There is no penalty for saying "no." You and your insurance company will not be billed for these optional studies. If you sign up for, but cannot complete these studies for any reason, you can still take part in the main study.

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

Optional sample collections for storage for possible future studies

Researchers are trying to learn more about cancer and other health problems using blood, urine and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person's response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

Unknown future studies

If you choose to take part in this optional study, blood, urine, and a sample of tissue from your biopsies will be collected and stored.

Storing samples for future studies is called "biobanking." The biobank is being run by SWOG and is supported by the NCI. Also, any health-related information, such as your response to cancer treatment, results of study tests, and medicines you took, will be stored for future use.

We don't know what research may be done in the future using your samples. This means that:

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.

Future research studies may include sequencing of all or part of your DNA called genomic sequencing. All your genetic information makes up your genome. Genomic sequencing is a test that records all or part of the pieces of DNA that are in your genes, piece by piece. This is usually done to look for changes in your genome that may cause health problems.

- You will not get reports or other information about any research that is done using your samples.

What is involved in this optional sample collection?

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

1. About 1 Tablespoon of blood will be collected from a vein in your arm before you begin the study, at about 18weeks, 1 year, and 2 years after you start the study, and at the time the cancer gets worse. Patients will also have less than a teaspoon of blood collected before you start treatment on Week 1, Day 1, and Week 4, Day 1. Your doctor will tell you if you will have these samples collected. These samples are drawn at the same time as other blood draws. Also, about 2 tablespoons of urine will be collected before you begin the study, at about 18 weeks, 1 year, and 2 years after you start the study, and at the time the cancer gets worse. A sample of tissue will be collected from a biopsy you had before you began the study and from a biopsy about 18 weeks after you start the study. (The 18-week biopsy is part of the usual care you would receive even if you were not on a study.)
2. Your samples will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
3. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
4. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

- Generally, hospitals will keep some of your tissue. This tissue may be used to help treat your cancer in the future. There is a small risk that when this tissue sample is submitted to the biobank for this optional sample collection, your tissue could be used up.
- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find 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 and get or keep health insurance. There are laws against the misuse of genetic information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: https://www.genome.gov/10002328/

How will information about me be kept private?

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

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information.
2. Researchers who study your sample and information will not know who you are. They also must agree that they will not try to find out who you are.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

What are the benefits to taking part in this optional sample collection?

You will not benefit from taking part.

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 to this optional sample collection?

There are no costs to you or your insurance. You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What if I change my mind about this optional sample collection?

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 biobank know. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

What if I have questions about this optional sample collection?

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 below to show if you would or would not like to take part in each optional study:

Samples for unknown future studies:

My samples and related information may be kept in a Biobank for use in future health research.

YES NO

Contact for Future Research

Occasionally, researchers working with SWOG may have another research idea that relates to people who were on a SWOG study. In some cases, to carry out the new research, we would need to contact participants in a particular study. You can agree or not agree to future contact.

I agree to allow my study doctor, or someone approved by my study doctor, to contact me regarding future research involving my participation in this study.

Yes No

This is the end of the section about optional studies.

My signature agreeing to take part in the 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 and dated copy of this form. I agree to take part in the main study. I also agree to take part in any additional studies where I circled "yes".

Participant's signature_____

Date of signature _____

Signature of person(s) conducting the informed consent discussion

_____

Date of signature_____