CHILDREN'S ONCOLOGY GROUP
25TH ANNIVERSARY 2000 – 2025

NCI Pediatric Early Phase Clinical Trials Network

A program funded by the National Cancer Institute of the National Institutes of Health

[redacted]

October 31, 2025

[redacted]

[redacted],

Enclosed please find Amendment #7 to protocol PEPN2121, *A Phase 1/2 Study of Tiragolumab (NSC# 827799, IND# [redacted]) and Atezolizumab (NSC# 783608, IND# [redacted]) in Patients with Relapsed or Refractory SMARCB1 or SMARCA4 Deficient Tumors*.

The primary purpose of Amendment #7 is to specify the correlative samples are no longer being collected due to study closure. Additionally, updated descriptions have been added for the banked correlative samples that are now being shipped to NCI for analysis.

Administrative changes have been made; specific changes are detailed in the Summary of Changes table below. Minor administrative updates (such as the correction of typographical errors, spelling, or updates to the numbers of referenced sections) are tracked in the protocol but not specified.

Please let me know if you have any questions or need additional information.

Sincerely,

[redacted]

[redacted]

II. Changes Made to the Informed Consent Document by the Principal Investigator:

#	Section	Page(s)	Comment
1.	Throughout	Throughout	• The page numbers were updated throughout. • The version date was updated throughout.
2.	Additional Required Research Study Tests	9	The section was revised as follows: • ~~Immunohistochemistry~~ was revised to **Correlative Analysis**. • The following statement was added: **As of 8/15/2025, these samples are no longer being collected**
3.	Additional Optional Research Study Tests	11	The following statement was added for each sample: **As of 8/15/2025, these samples are no longer being collected**

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This model informed consent form has been reviewed by the DCT/NCI and is the official consent document for this study. Institutions must use the 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 local IRB insists on making deletions or more substantive modifications to any of the sections in bold type, they must be justified in writing by the investigator at the time of the institutional audit.

SAMPLE RESEARCH INFORMED CONSENT/PARENTAL PERMISSION FORM

A Phase 1/2 Study of Tiragolumab (NSC# 827799, IND# [redacted]) and Atezolizumab (NSC# 783608, IND# [redacted]) in Patients with Relapsed or Refractory SMARCB1 or SMARCA4 Deficient Tumors

A study to see if Tiragolumab and Atezolizumab helps patients with SMARCB1 or SMARCA4 Deficient cancers

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.

Overview

You are being asked to take part in this research study because:

For Patients on Part A:
You are 12 months or older and less than 18 years of age and have been diagnosed with a SMARCB1 or SMARCA4 deficient cancer that has either come back ("relapsed") or does not respond to therapy ("is refractory") or have been newly diagnosed with a SMARCB1 or SMARCA4 deficient cancer that has no known standard treatment.

For Patients on Part B:
You are 12 months of age or older and have been diagnosed with a SMARCB1 or SMARCA4 deficient cancer that has either come back ("relapsed") or does not respond to therapy ("is refractory") or have been newly diagnosed with a SMARCB1 or SMARCA4 deficient cancer that has no known standard treatment. Patients less than 18 years may only enroll in Part B once Part A of the study has been completed.

Taking part in this study is voluntary. You may choose not to be in this study. If you decide not to be in this study, you will not be penalized and you will not lose any benefits to which you are entitled. You will still receive medical care.

The overall goal of this study is to:

- **To learn more about the safety of tiragolumab in children;**
- **Find out how well the combination of tiragolumab and atezolizumab works when given to children and adults with SMARCB1 and SMARCA4 deficient tumors;**
- **To learn what kind of side effects may be caused by tiragolumab alone in patients younger than 18 years of age and tiragolumab and atezolizumab in all patients;**
- **To learn more about the pharmacology (how your body handles the drug) of tiragolumab and atezolizumab.**

In Part A of the study, you will receive a dose of tiragolumab that is similar to the recommended dose in adults with cancer. To achieve a dose that is similar to adults, the dose of tiragolumab will be based on your body weight. The dose will be different if you are less than or equal to 15 kg (about 33 pounds), more than 15 kg (about 33 pounds) and less than or equal to 40 kg (about 88 pounds) or more than 40 kg (greater than 88 pounds). You will be monitored closely for side effects that are severe or not acceptable. During cycle 1 you will receive tiragolumab alone. If you do not have serious side effects, you may be able to receive tiragolumab in combination with atezolizumab as described below.

In Part B of the study, if you are 18 years old or older, you will receive atezolizumab at the same dose as what is recommended for adults and the dose for tiragolumab will be the same as what has been used in previous studies of this medicine. If you are <18 years of age, the dose for atezolizumab will be the same as what has been used in previous studies of this medicine for children. And the dose of tiragolumab will be based on your body weight as described above. Part B will open at the same time as Part A, but only patients who are 18 years or older will be initially enrolled on Part B. Patients younger than 18 years old will be included in Part B only after tiragolumab has been determined to be safe in the Part A portion.

All people who receive cancer treatment are at risk of having side effects. In addition to killing tumor cells, cancer treatment can damage normal tissue and produce side effects.

This study uses the investigational drugs tiragolumab and atezolizumab. Common side effects of these drugs are tiredness, infections, diarrhea, reaction during drug infusion or allergic reactions, and flu-like symptoms. Tiragolumab or atezolizumab may also cause your immune system to attack normal organs and cause side effects in many parts of the body including your thyroid gland, heart, liver, kidney, skin, intestine, and lungs The full list of risks for tiragolumab and atezolizumab are available in the section What side effects or risks can I expect from being in the study?

You can ask your study doctor questions about side effects at any time.

We hope that this study will help you personally, but we do not know if it will. The potential benefits to you associated with participation in this study are described in the section Are there benefits to taking part in the study?

You have a choice between another treatment for your cancer and this clinical trial.

The rest of this form provides detailed information about the study and what to expect should you decide to participate.

Why am I being invited to take part in this study?

You are being asked to take part in this research study because you are in one of the groups of patients described below:

For Patients on Part A:
You are at least 12 months of age and less than 18 years of age and have been diagnosed with a SMARCB1 or SMARCA4 deficient cancer that has relapsed or is refractory, or newly diagnosed with a SMARCB1 or SMARCA4 deficient cancer that has no known standard treatment.

For Patients on Part B:
You are 12 months of age or older have been diagnosed with a SMARCB1 or SMARCA4 deficient cancer that has relapsed or is refractory, or newly diagnosed with a SMARCB1 or SMARCA4 deficient cancer that has no known standard treatment. Patients less than 18 years may only enroll in Part B once Part A of the study has been completed.

This study is called a clinical trial. A clinical trial is a research study involving treatment of a disease in human patients. This study has public funding from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH) in the United States Department of Health and Human Services.

This study is being carried out by the Children's Oncology Group (COG) Pediatric Early Phase Clinical Trial Network (PEP-CTN). COG is an international research group that consists of more than 200 hospitals that treat children with cancer. The PEP-CTN is the group within COG that consists of 21 hospitals and participation in this study will be limited to these hospitals.

It is common to enroll children and adults with cancer in a clinical trial that seeks to improve cancer treatment over time. Clinical trials include only people who choose to take part. You have a choice between another treatment for relapsed or refractory SMARCB1 or SMARCA4 deficient cancer or a newly diagnosed SMARCB1 or SMARCA4 deficient cancer and this clinical trial.

Please take your time to make your decision. You may want to discuss it with your family and friends. We encourage parents to include their child in the discussion and decision to the extent that the child is able to understand and take part.

What is the current standard of treatment for this disease?

Standard treatment is the treatment that most cancer doctors would recommend you receive even if you decide not to participate in a clinical trial.

We are asking if you want to participate in this study because there is not a standard treatment for your cancer at this point.

Why is this study being done?

This study looks at how well tiragolumab and atezolizumab works when given to children and adults with SMARCB1 and SMARCA4 deficient cancers. This means that tumor cells are missing the SMARCB1 and SMARCA4 genes, which is seen with some aggressive cancers that are typically hard to treat. Tiragolumab and atezolizumab are experimental because they have not been proven to work in situations like yours. We want to see if using tiragolumab and atezolizumab together might help your immune system fight your cancer.

We are using tiragolumab and atezolizumab because it seems to work against cancer in test tubes and animals. Tiragolumab and atezolizumab has been used in adults and atezolizumab has also been used in children but there is a lot that we do not know about it yet. Atezolizumab is approved by the Food and Drug Administration (FDA) for the treatment of adults with certain types of cancer. Atezolizumab is approved for use in children with unresectable or metastatic alveolar soft part sarcoma. Tiragolumab has not been approved by the FDA; tiragolumab is not approved for use in children.

The overall goals of this study are to

- **To learn more about the safety of tiragolumab in children;**
- **Find out how well the combination of tiragolumab and atezolizumab works when given to children and adults with SMARCB1 and SMARCA4 deficient tumors;**
- **To learn what kind of side effects are caused by tiragolumab alone in patients less than 18 years of age and the tiragolumab and atezolizumab in all patients;**
- **To learn more about the pharmacology (how your body handles the drug) of tiragolumab and atezolizumab.**

What will happen on this study that is research?

The treatment involves cancer fighting medicines called tiragolumab and atezolizumab. The treatment on this study can continue for a maximum period of time of up to 5 years, as long as your cancer does not grow and you do not have any bad side effects from tiragolumab and atezolizumab.

The treatments on this study are different from standard therapy. These parts are experimental and involve being treated with tiragolumab and atezolizumab.

Blood will be drawn to perform tests to see how your body handles the drug and to monitor for side effects. Imaging studies will be done to monitor the tumor. While enrolled in this study, even when you will not be receiving tiragolumab and atezolizumab, you will still be involved and will continue to be monitored.

Treatment with tiragolumab and atezolizumab is experimental and is described below.

Summary of Study Treatments

If the exams, tests, and procedures show that you can be in the study, and you choose to take part, you will either be enrolled in Part A or Part B of the study.

Part A: Tiragolumab

Part A is open to patients who are at least 12 months of age and younger than 18 years old. Patients enrolled in Part A will receive only tiragolumab for their first cycle (21 days) of treatment. If the dose of tiragolumab is assessed to be safe after your first cycle of treatment, you may be able to receive tiragolumab and atezolizumab in subsequent cycles.

The dose for the children enrolled on the study will be based on the dose and side effects seen in adults and will be based on your weight. Between 2 and 6 children will receive tiragolumab at this dose.

Part B: Tiragolumab and Atezolizumab

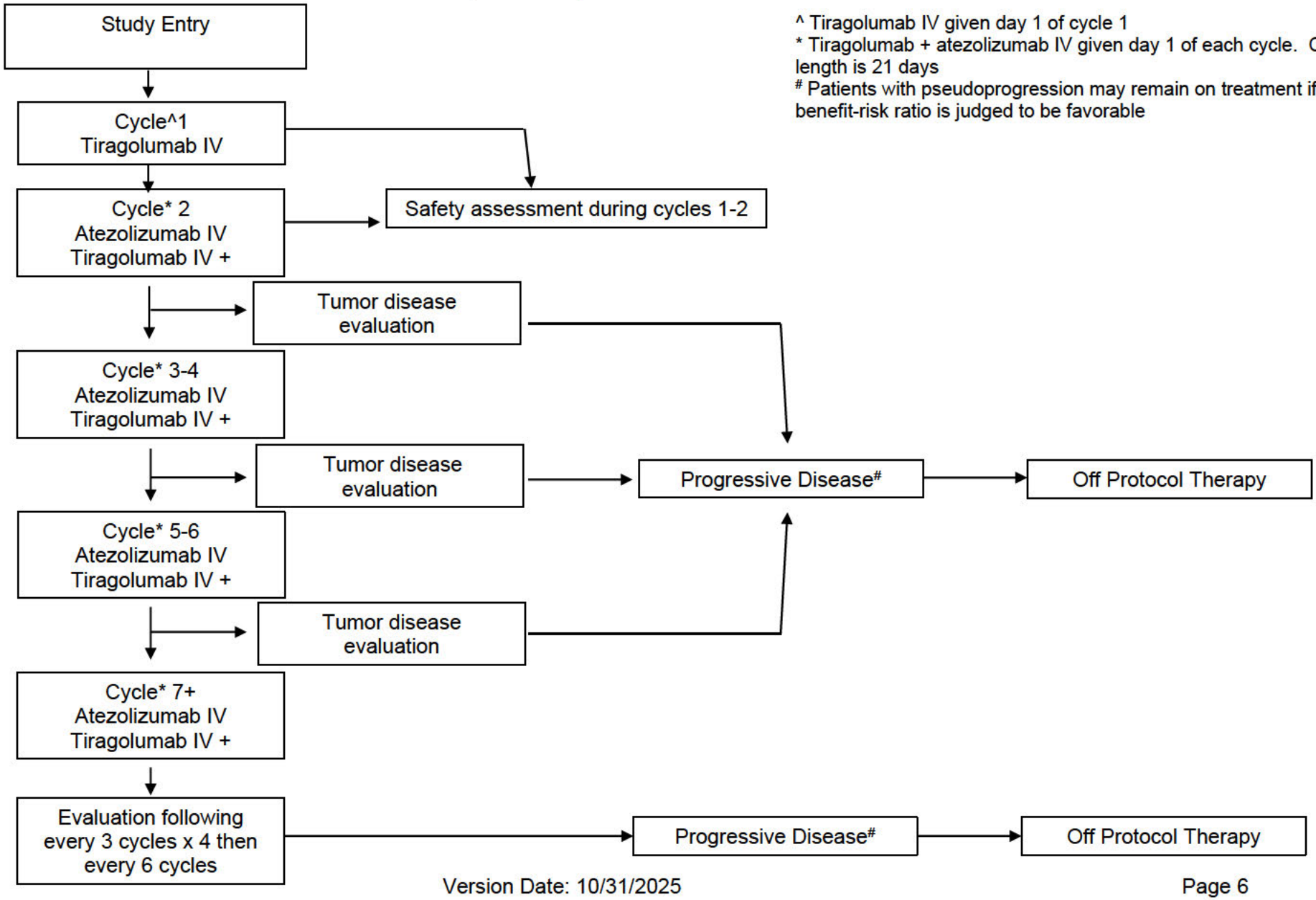
Patients enrolled in Part B will be treated with tiragolumab and atezolizumab once on the first day of each cycle of therapy. Tiragolumab and atezolizumab will be given to you by vein on Day 1 of each 21-day cycle. You may continue to receive tiragolumab and atezolizumab for a maximum period of time of up to 5 years, as long as you do not develop serious side effects or your tumor worsens. A cycle lasts 21 days (3 weeks). Part B is initially open to patients who are 18 years old or older. Patients less than 18 years may only enroll in Part B once Part A of the study has been completed.

The dose of atezolizumab will be based on your age and weight. If you are 18 years old or older, you will be given the same dose of atezolizumab recommended for adults. If you are less than 18 years old, you will be given atezolizumab based on your body weight and your dose will not exceed the dose recommended for adults.

Diagram of Treatment

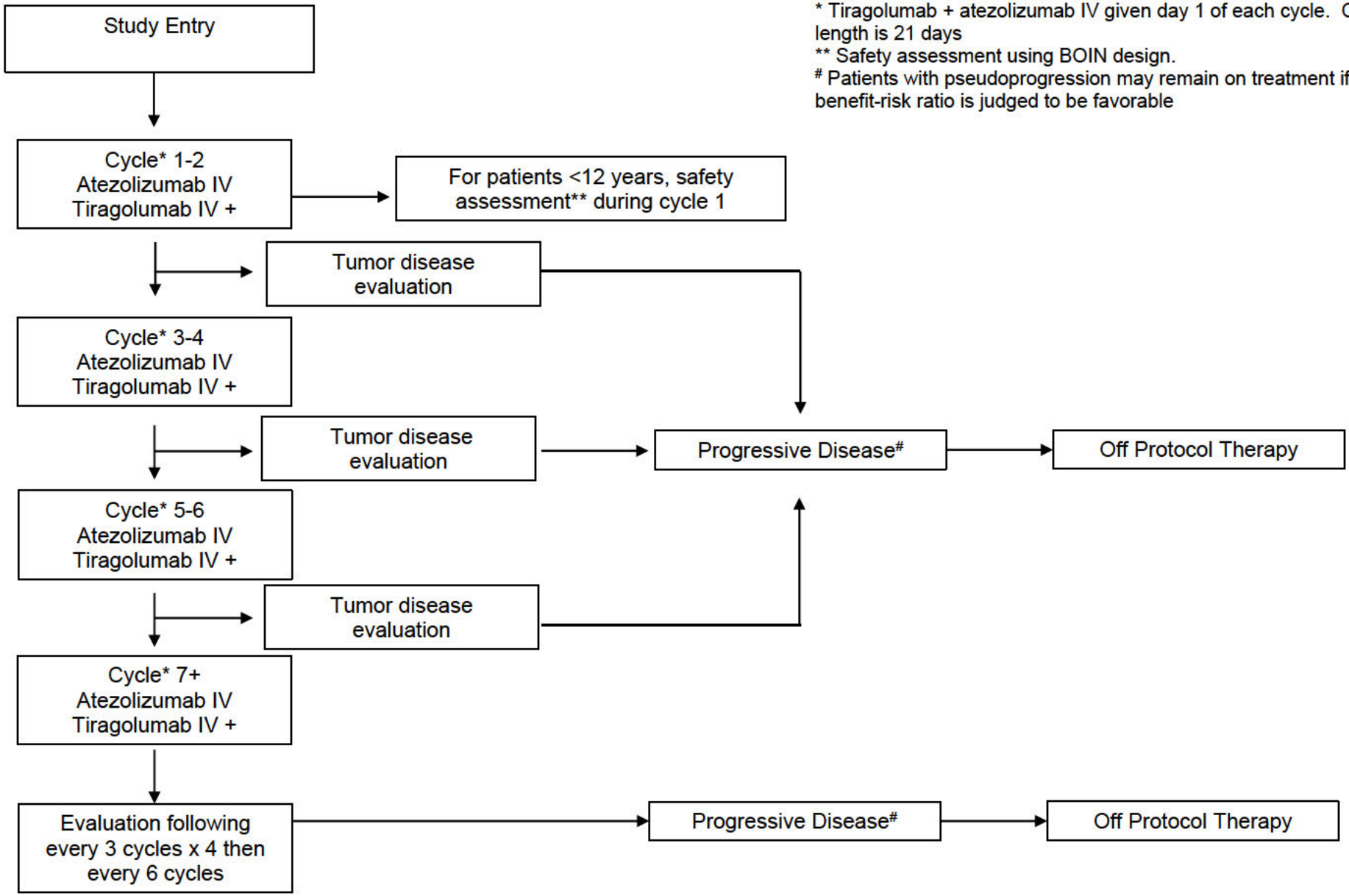
The chart on the following pages shows the treatments (Part A and Part B) on this study.

EXPERIMENTAL DESIGN SCHEMA (PART A)



^ Tiragolumab IV given day 1 of cycle 1
* Tiragolumab + atezolizumab IV given day 1 of each cycle. Cycle length is 21 days
# Patients with pseudoprogression may remain on treatment if benefit-risk ratio is judged to be favorable

EXPERIMENTAL DESIGN SCHEMA (PART B)



* Tiragolumab + atezolizumab IV given day 1 of each cycle. Cycle length is 21 days
** Safety assessment using BOIN design.
# Patients with pseudoprogression may remain on treatment if benefit-risk ratio is judged to be favorable

Experimental Parts of Treatment

For Patients on Part A

The treatment described below is the full study treatment for a single cycle of treatment. Each cycle lasts for 21 days.

Methods for Giving Drugs

- **IV** - Drug is given using a needle or tubing inserted into a vein. Drug will be given slowly over minutes or hours ("infusion").

Drug	How the drug will be given	Days
Tiragolumab	IV given over 90 (± 10) minutes during cycle 1; IV given over 60 (± 10) minutes for cycle 2 if well tolerated in cycle 1; 30 (± 10) minutes for all other subsequent cycles, if well tolerated in cycle 2.	Day 1 of each cycle
Atezolizumab*	IV given over 60 (± 10) minutes prior to tiragolumab in cycle 2; 30 (± 10) minutes for all other subsequent cycles if well tolerated in cycle 2.	Day 1 of cycle 2 and beyond

* Patents in Part A get tiragolumab alone in cycle 1 and get both medications only in cycle 2 and later cycles.

For Patients on Part B

The treatment described below is the full study treatment for a single cycle of tiragolumab and atezolizumab. Each cycle lasts for 21 days.

Methods for Giving Drugs

- **IV** - Drug is given using a needle or tubing inserted into a vein. Drugs will be given slowly over minutes or hours ("infusion").

Treatment with experimental agents tiragolumab and atezolizumab

Drug	How the drug will be given	Days
Atezolizumab	IV given over 60 (± 10) minutes prior to tiragolumab; 30 (± 10) minutes for all other subsequent cycles if well tolerated in cycle 1.	Day 1 of each cycle
Tiragolumab	IV given over 90 (± 10) minutes during cycle 1; 60 (± 10) minutes for cycle 2 if well tolerated in cycle 1;	Day 1 of each cycle

	30 (± 10) minutes for all other subsequent cycles, if well tolerated in cycle 2.	

Additional Required Research Study Tests

The following tests will be done because you are part of this study. If you were not in the study you would probably not have these tests.

Archival Tumor Tissue for Correlative Analysis (*As of 8/15/2025, these samples are no longer being collected*):
We would like to collect tumor tissue to do some extra tests for immunohistochemistry. These tests will help us learn more about your type of tumor, particularly how they express the proteins that can be targeted by tiragolumab and atezolizumab. This may help patients who receive this drug in the future. The information learned would not change the way you are treated, and the results of these tests will not be given to you.

Immunohistochemistry studies can help us learn how tiragolumab and atezolizumab treat your cancer.

Pharmacokinetic (PK) and Anti-Drug Antibody (ADA) Studies (*As of 8/15/2025, these samples are no longer being collected*):
We would also like to do some extra tests called pharmacokinetic studies (PK) and anti-drug antibody (ADA) tests. These tests will help us learn more about tiragolumab and atezolizumab and may help patients who receive this drug in the future. The information learned would not change the way you are treated, and the results of these tests will not be given to you.

PK studies help us determine how much tiragolumab and atezolizumab is in your blood.

For Patients on Part A
A total of up to 23 blood samples will be collected, split between samples for each drug (about 3.5 mL or roughly 1 teaspoon for each sample) for the PK and ADA tests throughout the entire study. These blood samples will be obtained through an extra needle stick that you would not normally receive if you were not participating in this study.

ADA tests will help us determine how your immune system is reacting to tiragolumab. A total of up to 15 ADA samples will be collected from all participants throughout the entire duration of Part A. These samples are collected at the same time the PK samples are being collected and will not require an additional poke with an IV to obtain.

A maximum volume of up to 84 mL (or about 17 teaspoons) will be drawn for PK and ADA tests in Part A. This amount of blood is safe to draw even from small children. PK and ADA samples will be taken in the following order for both atezolizumab and tiragolumab:

- Cycle 1, Day 1: Prior to infusion (same day as treatment administration)
- Cycle 1, Day 1: 30 minutes after end of tiragolumab infusion*
- Cycle 1, Day 15: Anytime during the visit*
- Cycle 2, Day 1: Prior to infusion (same day as treatment administration)
- Cycle 2, Day 1: 30 minutes after end of atezolizumab infusion*
- Cycle 2, Day 1: 30 minutes after end of tiragolumab infusion*

- Cycle 2, Day 15: Anytime during the visit*
- Cycle 3, Day 1: Prior to infusion (same day as treatment administration)
- Cycle 4, Day 1: Prior to infusion (same day as treatment administration)
- Cycle 4, Day 1: 30 minutes after end of atezolizumab infusion*
- Cycle 4, Day 1: 30 minutes after end of tiragolumab infusion*
- Cycle 8, Day 1: Prior to infusion (same day as treatment administration)
- Cycle 12, Day 1: Prior to infusion (same day as treatment administration)
- Cycle 16, Day 1: Prior to infusion (same day as treatment administration)
- End of therapy visit: Any time during visit

*These timepoints will only have PK samples taken and not ADA.

For Patients on Part B

A total of up to 22 blood samples will be collected, split between 11 samples for each drug (about 3.5 mL or roughly 1 teaspoon for each sample) for the PK and ADA tests throughout the entire study. These blood samples will be obtained through an extra needle stick that you would not normally receive if you were not participating in this study.

ADA tests will help us determine how your immune system is reacting to tiragolumab and atezolizumab. A total of up to 16 ADA samples will be collected from all participants throughout the entire duration of the study; 8 samples collected for atezolizumab and 8 samples collected for tiragolumab. These samples are collected at the same time the PK samples are being collected and will not require an additional poke with an IV to obtain.

A maximum volume of up to 77 mL (or about 16 teaspoons) will be drawn for PK and ADA tests in this study, split between 38.5 mL for atezolizumab (or about 8 teaspoons) and 38.5 mL for tiragolumab. This amount of blood is safe to draw even from small children. PK and ADA samples will be taken in the following order for both atezolizumab and tiragolumab:

- Cycle 1, Day 1: Prior to infusion (same day as treatment administration)
- Cycle 1, Day 1: 30 minutes after end of atezolizumab infusion*
- Cycle 1, Day: 1 30 minutes after end of tiragolumab infusion*
- Cycle 1, Day 15: Anytime during the visit*
- Cycle 2, Day 1: Prior to infusion (same day as treatment administration)
- Cycle 3, Day 1: Prior to infusion (same day as treatment administration)
- Cycle 4, Day 1: Prior to infusion (same day as treatment administration)
- Cycle 4, Day 1: 30 minutes after end of atezolizumab infusion*
- Cycle 4, Day 1: 30 minutes after end of tiragolumab infusion*
- Cycle 8, Day 1: Prior to infusion (same day as treatment administration)
- Cycle 12, Day 1: Prior to infusion (same day as treatment administration)
- Cycle 16, Day 1: Prior to infusion (same day as treatment administration)
- End of therapy visit: Any time during visit

*These timepoints will only have PK samples taken and not ADA.

Central Review:

Some of the copies of the scans used to diagnose the cancer will be sent to a central review center to help confirm findings. The results of these reviews will not be returned to you.

Additional Optional Research Study Tests

Whole Blood for Biobanking (*As of 8/15/2025, these samples are no longer being collected*)

We would like to take blood samples at several different times while you are on this study for future research. This is called “specimen banking” or “biobanking”. A biobank is a lab where specimens (such as tumor, blood, or bone marrow) are kept for use in future research studies. This blood will be collected from you based on your weight as described below:

- Patients who weigh less than 14 kg (or less than 31 pounds) will not have blood drawn, as they are not allowed to participate in optional blood specimen banking.
- Patients who weigh 14 to <19 kg (or between 31-42 pounds) will have 5 mL of blood (or 1 teaspoon) drawn at each timepoint.
- Patients who weigh 19 to <25 kg (or between 42-55 pounds) will have up to 15 mL of blood (or 3 teaspoons) drawn at each timepoint.
- Patients who weigh greater than or equal to 25 kg (or 55 pounds) will have up to 20 mL of blood (or 4 teaspoons) drawn at each timepoint.

If you weigh greater than or equal to 14 kg, or 31 pounds, blood will be drawn for specimen banking at the following timepoints:

- After enrollment, prior to the start of therapy
- Cycle 1, Day 8
- Cycle 2, Day 21
- Cycle 4, Day 21
- Cycle 6, Day 21
- Cycle 9, Day 21
- Cycle 12, Day 21
- Cycle 15, Day 21
- Then every 3 cycles for a maximum of 5-years total of participation in this study, or until the disease worsens.
- End of therapy visit

You do not have to provide these samples if you do not want to. You can still be in the study if you do not want to provide these samples. At the end of this consent form, there is a place to record your decision about taking part in banking.

Archival Tumor Tissue for Biobanking (*As of 8/15/2025, these samples are no longer being collected*)

We would also like to take some of your tumor tissue for future research. If any tissue is left over from your previous biopsy, we would like to keep it for future research.

You do not have to provide these samples if you do not want to. You can still be in the study if you do not want to provide these samples. At the end of this consent form, there is a place to record your decision about taking part in specimen banking.

What side effects or risks can I expect from being in the study?

Treatment Risks

All people who receive cancer treatment are at risk of having side effects. In addition to killing tumor cells, cancer treatment can damage normal tissue and produce side effects.

Risks of Study

If you choose to take part in this study, there is a risk that atezolizumab (MPDL3280A) and tiragolumab may not be as good as the usual approach for your cancer or condition at shrinking or stabilizing your cancer.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

The atezolizumab (MPDL3280A) and tiragolumab 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 test 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 things to know 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, and some may never go away.
- Some side effects may make it hard for you to have children.
- Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your 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 doctors know about. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Possible side effects of atezolizumab (MPDL3280A)

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

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 inflammation and heart failure. Symptoms and signs of heart problems may include: shortness of breath, swelling of the ankle 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 (myositis, rhabdomyolysis), 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
- Swelling or tenderness of blood vessels

Possible side effects of tiragolumab (RO7092284)

COMMON, SOME MAY BE SERIOUS

In 100 people receiving tiragolumab (RO7092284), more than 20 and up to 100 may have:

- Tiredness
- Rash

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving tiragolumab (RO7092284), from 4 to 20 may have:

- Anemia which may require blood transfusion
- Pain
- Constipation, diarrhea, nausea, vomiting
- Reaction during or following a drug infusion which may cause chills, low blood pressure
- Bruising, bleeding
- Infection, especially when white blood cell count is low
- Weight loss, loss of appetite
- Numbness, tingling or pain of the arms and legs
- Hair loss, itching

Tiragolumab (RO7092284) 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 • 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

RARE, AND SERIOUS In 100 people receiving tiragolumab (RO7092284), 3 or fewer may have:
• Prior viral infection that returns • Damage to the organs (lungs, heart) which may cause shortness of breath • Cough • Blisters on the skin Tiragolumab (RO7092284) 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 inflammation and heart failure. Symptoms and signs of heart problem may include: Shortness of breath, swelling of the ankle and body. • A condition with high blood sugar which leads to tiredness, frequent urination or excessive thirst • Swelling and redness of the eye • Pain in belly • Life threatening disorder where the immune system attacks the cells/organs of the body which may cause fever, rash, yellow eyes and skin, shortness of breath, headache, weakness, swollen lymph nodes • Damage to muscle which may cause muscle pain, dark red urine • Abnormal movement of the facial muscles • Inflammation of the brain (meningitis/encephalitis), which may cause: headache, confusion, sleepiness, seizures, and stiff neck • 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. • Swelling or tenderness of blood vessels

In addition to the risks described above, there may be unknown risks, or risks that we did not anticipate, associated with being in this study.

Reproductive risks

Women should not become pregnant and men should not father a baby while on this study because the drug(s) in this study can be bad for an unborn baby. If you or your partner can get pregnant, it is important for you to use birth control or not have sex while on this study for at least 90 days after final dose of tiragolumab and 150 days after final dose of atezolizumab, whichever is later. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some birth control methods might not be approved for use in this study. If you are a woman and become pregnant or suspect you are pregnant while participating in this study, please inform your treating physician immediately. Women should not breastfeed a baby while on this study and at least 90 days after final dose of tiragolumab and 150 days after final dose of atezolizumab, whichever is later.

Are there benefits to taking part in the study?

We hope that this study will help you personally, but we do not know if it will.

With any cancer treatment, sometimes treatment does not make the cancer go away. Or, sometimes treatment makes the cancer go away for a while but the cancer comes back later.

Information learned from this study may benefit other patients in the future.

The potential benefit of the treatment with tiragolumab and atezolizumab is that it may cause your cancer to stop growing or to shrink for a period of time. It may lessen the symptoms, such as pain, that are caused by the cancer. However, we do not know if you will benefit from taking part in this study. Information learned from this study may help future patients with cancer.

What other options are there?

Instead of being in this study, you have these options:

- **Getting treatment for your cancer without being in a study**
- **Taking part in another study.**
- **Getting comfort care, also called palliative care.** This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly. Instead it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Please talk to your doctor about these and other options.

How many people will take part in the study?

The maximum number of participants enrolled on this study is expected to be 78. This is divided among Parts A and B of the study.

Part A:
There will be a minimum of 2 participants, up to a maximum of 6.

Part B:
There will be a minimum of 36 participants, up to a maximum of 84 participants.

How long is the study?

Although it is difficult to predict who may benefit, it is possible that people in this clinical trial may receive treatment on this study for up to 5 years, so long as they are deriving benefit and their disease does not get worse.

We would like to continue to find out about your health for about 5 years after you enter this study. By keeping in touch with you for a while after you complete treatment, we can better understand the long-term effects of the study treatments.

You can stop taking part in the study at any time. However, if you decide to stop participating in the study, we encourage you to talk to the study doctor and your regular doctor first. They will help you stop safely.
Your doctor or the study doctor may decide to take you off this study:

- if he/she believes that it is in your best interest
- If the tumor gets worse
- if your disease comes back during treatment
- if you experience side effects from the treatment that are considered too severe
- if new information becomes available that shows that another treatment would be better for you
- pregnancy

What about privacy?

We will do our best to make sure that the personal information in your medical record will be kept private. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. The Children's Oncology Group has 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 Children's Oncology Group will do their best to make sure that any information that goes out to others will not identify who you are. Information about this Certificate of Confidentiality is included in Attachment 2.

Organizations that may look at and/or copy your research or medical records for research, quality assurance and data analysis include groups such as:

- **Children's Oncology Group and research partners**
- **Representatives of the National Cancer Institute (NCI), Food and Drug Administration (FDA), and other U.S. and international governmental regulatory agencies involved in overseeing research.**
- **The Institutional Review Board of this hospital**
- **Pediatric Central Institutional Review Board (CIRB) of the National Cancer Institute**
- **The study sponsor and any drug company supporting the study or their designated reviewers.**
- **Site of Data Coordinating Center for COG**

What are the costs?

Taking part in this study may lead to added costs to you or your insurance company. There are no plans for the study to pay for medical treatment. Please ask about any expected added costs or insurance problems. Staff will be able to assist you with this.

In the case of injury or illness resulting from this study, emergency medical treatment is available but will be provided at the usual charge. No funds have been set aside to compensate you in the event of injury. However, by signing this form, you are not giving up any legal rights to seek to obtain compensation for injury.

You or your insurance company will be charged for continuing medical care and/or hospitalization.

The NCI will supply tiragolumab and atezolizumab at no charge while you take part in this study. The NCI does not cover the cost of getting tiragolumab and atezolizumab ready and giving it to you, so you or your insurance company may have to pay for this.

Even though it probably won't happen, it is possible that the manufacturer may not continue to provide tiragolumab and atezolizumab to the NCI for some reason. If this does happen, other possible options are:

- You might be able to get tiragolumab and atezolizumab from the manufacturer or your pharmacy but you or your insurance company may have to pay for it.
- If there is no tiragolumab and atezolizumab available at all, no one will be able to get more and the study would close.

If a problem with getting tiragolumab and atezolizumab occurs, your study doctor will talk to you about these options.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://www.cancer.gov/clinicaltrials/learningabout.

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 are my rights as a participant?

Taking part in this study is voluntary. You may choose not to be in this study. If you decide not to be in this study, you will not be penalized and you will not lose any benefits to which you are entitled. You will still receive medical care.

You can decide to stop being in the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are entitled. Your doctor will still take care of you.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study. A committee outside of COG closely monitors study reports and notifies COG if changes must be made to the study. Members of COG meet twice a year to discuss results of treatment and to plan new treatments.

During your follow-up visits after treatment, you may ask to be given a summary of the study results, which will only be available after the study is fully completed. *A summary of the study results will also be posted on the Children's Oncology Group website (http://www.childrensoncologygroup.org/)*. To receive the results, you may either (1) go to the

COG website to check if results are available or (2) register your information with the COG on its web site and have an email sent to you when the results are available. Your pediatric oncology team from your hospital can give you additional instructions on how to do this. Please note, that the summary of results may not be available until several years after treatment for all people on the study is completed, and not only when you complete treatment.

Whom do I call if I have questions or problems?

For questions about the study or if you have a research related problem or if you think you have been injured in this study, you may contact Dr. *XXXX* or your doctor at *XXXX*.
If you have any questions about your rights as a research participant or any problems that you feel you cannot discuss with the investigators, you may call *XXXX* Institutional Review Board (IRB) Administrator at *XXXX*.

If you have any questions or concerns that you feel you would like to discuss with someone who is not on the research team, you may also call the Patient Advocate at *XXXX*.

Where can I get more information?

The COG Family Handbook for Children with Cancer has information about specific cancers, tests, treatment side effects and their management, adjusting to cancer, and resources. Your doctor can get you this Handbook, or you can get it at https://www.childrensoncologygroup.org/index.php/cog-family-handbook.

Visit the NCI's Web site at http://www.cancer.gov.

If you are in the United States, you may call the NCI's *Cancer Information Service* at: 1-800-4-CANCER (1-800-422-6237).

Information about long term follow-up after cancer treatment can be found at: http://www.survivorshipguidelines.org/.

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 will get a copy of this form. You may also ask for a copy of the protocol (full study plan).

Specimens for Optional Biobanking

If you agree to Biobanking, your sample will be stored in the *Biopathology Center at Nationwide Children's Hospital,* in a locked location. The Biopathology Center is supported by the NCI. The samples will be kept until they are used up, unless you request that they be destroyed. Some information from your medical record will also be kept in secure databases at the Biobank and updated from time to time. The information and samples will be kept under a code, not your name.

This is a publicly funded study. Samples from publicly funded studies are required to be shared as broadly as possible. Qualified researchers can submit a request to use the materials stored in the Biobank. The research may be about your type of cancer, about other cancers, or even about conditions unrelated to cancer. A science committee at the Children's Oncology Group, and/or the National Cancer Institute, will review each request. The goal of this is to make more research possible that may improve people's health. Researchers will not be given your name or any other information that could directly identify you. Your sample will not be sold to third parties. 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, unless something is discovered that could directly affect your health. If that happens your study doctor will be notified and will decide whether and how to contact you.

Right now, 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 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.

Unknown future research studies may include sequencing of all or part of your DNA. This is called genomic sequencing. Sequencing allows researchers to identify your genetic code. Changes in your genetic code may just be in your tumor tissue. These are called somatic changes. Changes may also be in your normal tissue and passed down through your family. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. These are called germline changes. If only tumor tissue is sequenced, we will not know if a genetic change in your tumor is also in your normal tissue. This is why sometimes both normal tissue and tumor tissue are sequenced. This helps researchers understand if a genetic change happened only in your cancer tissue, or in your normal tissue as well.

Some of your genetic and health information may be placed in central databases that may be made available to qualified researchers, along with information from many other people. Information that could directly identify you will not be included.

Even without your name or other identifiers, your genetic information is unique to you. If you agree to Biobanking, there is a risk of a data security breach and that someone could trace the genetic information in a central database back to you. Although this has never happened in real life and we have many safeguards in place to prevent it from happening, the risk may change in the future as people come up with new ways of tracing information. There are laws against the misuse of genetic information, but they may not give full protection. In some cases, misuse of the information could be used to make it harder for you to get or keep a job or insurance.

There can also be risks in learning about your own genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. Sometimes this is upsetting to families or they wish they didn't know the information. We encourage you to discuss this study with your relatives before you decide whether to participate in the Biobanking part.

If you want to learn more about tissue research with banked specimens, the NCI website has an information sheet called “Providing Your Tissue For Research: What You Need To Know.” This sheet can be found at: https://www.cancer.gov/publications/patient-education/providing-tissue.

Please read the information below and think about your choices. After making your decisions, check “Yes” or “No”, then add your initials and the date after your answer. If you have any questions, please talk to your doctor or nurse, or call our research review board at the IRB’s phone number included in this consent.

1) Check YES if you agree to have your blood samples kept (banked) for use in research to learn about, prevent, or treat cancer or other health problems (for example: diabetes, Alzheimer's disease, or heart disease). Check NO if you do not want samples banked.

Yes _____ No _____ _____ / _____
Initials Date

2) Check YES if you agree to have your tissue samples kept (banked) for use in research to learn about, prevent, or treat cancer or other health problems (for example: diabetes, Alzheimer's disease, or heart disease). Check NO if you do not want samples banked.

Yes _____ No _____ _____ / _____
Initials Date

Signature

I have been given a copy of all _____ pages of this form. The form includes 2 attachments.

I have reviewed the information and have had my questions answered.
I agree to take part in this study.

Participant_____Date _____

Parent/Guardian_____Date _____

Parent/Guardian_____Date _____

Physician/PNP obtaining consent_____Date _____

Attachment 1

Study Treatment and Procedures

Methods for Giving Drugs

- **IV** - Drug is given using a needle or tubing inserted into a vein. Drugs will be given slowly over minutes or hours ("infusion").

Central Line

Your doctor may recommend that you get a special kind of IV called a "central line." This is a kind of IV placed into a big vein in your body, usually in the chest, that can stay in for a long time. The risks connected with central lines will be explained to you and all of your questions will be answered. If you are to have a central line inserted, you will be given a separate informed consent document to read and sign for this procedure. A description of the types of central lines is in the COG Family Handbook for Children with Cancer.

Treatment Tables

The treatment described below is the full study treatment for patients on this study. Each cycle lasts for 21 days.

Treatment with experimental agents tiragolumab and atezolizumab

Drug	How the drug will be given	Days
Atezolizumab*	IV given over 60 (± 10) minutes prior to tiragolumab in during cycle 1; 30 (± 10) minutes for all other subsequent cycles if well tolerated in cycle 1;	Day 1 of each cycle
Tiragolumab	IV given over 90 (± 10) minutes on 1st cycle; 60 (± 10) minutes for cycle 2 if well tolerated during cycle 1; 30 (± 10) minutes for all other subsequent cycles, if well tolerated in cycle 2.	Day 1 of each cycle

*Patents in Part A only get tiragolumab in cycle 1 and get both medication only in cycle 2 and later cycles

Standard Tests and Procedures

The following tests and procedures are part of regular cancer care and may be done even if you do not join the study.

- Frequent labs to monitor your blood counts and blood chemistries.
- Urine tests to measure how your kidneys are functioning.
- Pregnancy test for females of childbearing age before treatment begins.
- X-rays and scans to monitor your response to treatment.
- Tests to monitor your heart and lung function.

Attachment 2

Certificate of Confidentiality

The Children's Oncology Group is covered by a Certificate of Confidentiality from the federal government, which will help us protect the privacy of our research subjects. The Certificate protects against the involuntary release of information about subjects collected during the course of our covered studies. The researchers involved in the studies cannot be forced to disclose the identity or any information collected in the study in any legal proceedings at the federal, state, or local level, regardless of whether they are criminal, administrative, or legislative proceedings. However, the subject or the researcher may choose to voluntarily disclose the protected information under certain circumstances. For example, if the subject or his/her guardian requests the release of information in writing, the Certificate does not protect against that voluntary disclosure. Furthermore, federal agencies may review our records under limited circumstances, such as a DHHS request for information for an audit or program evaluation or an FDA request under the Food, Drug and Cosmetics Act.

The Certificate of Confidentiality will not protect against the required reporting by hospital staff of information on suspected child abuse, reportable communicable diseases, and/or possible threat of harm to self or others.