SUMMARY OF CHANGES

NCI Protocol #: 10017
Local Protocol #: I 285416

NCI Version Date:
Protocol Date: 7/22/19

Protocol Title: A Randomized Phase 2 Trial of Atezolizumab (MPDL3280A), SGI-110 and CDX-1401 Vaccine in Recurrent Ovarian Cancer.

Summary of Change for Consent Revisions- Phase I and II

#	Page #	Revision
1.		Date updated for consent revision: **July 22 , 2019**
2.		**Phase I complete, no changes in the Phase I consent form**
3.	**1**	Title for Phase II consent revised to remove vaccine arm. **(Official study title unchanged.)**
4.	**1**	**Why is this study being done?** Group 3 removed.
5.	**1 to 3**	**What are the study groups?** Group 3 removed, schema and table updated accordingly.
6.	**6**	**What possible risks can I expect from taking part in this study?** Possible side effects of CDX-1401 and Poly-ICLC removed.
7.	**9**	**What are the costs of taking part in this study?** CDX-1401 and Poly-ICLC removed.
8.	**General**	Minor typos corrected.

Consent Form

Study Title for Study Participants: Phase II*:* Comparing Atezolizumab to Atezolizumab given with SGI-110 for relapsed ovarian cancer (*Phase 2*)

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol #10017, A randomized phase 2 trial of Atezolizumab (MPDL3280A), SGI-110, and CDX-1401 Vaccine in Recurrent Ovarian Cancer.

What is the usual approach to my cancer?

You are being asked to participate in this study because you have ovarian, fallopian tube or primary peritoneal cancer. You have already been treated with chemotherapy and your disease is now growing or has recurred. People who are not in a study are usually treated with other combinations of chemotherapy or supportive/palliative therapy.

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

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

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available
- or you may choose not to be treated for cancer but you may want to receive comfort care to relieve symptoms

Why is this study being done?

The purpose is to compare the safety and efficacy (anti- tumor effect) of the following 2 study drug groups:

Group 1) Atezolizumab alone
Group 2) Atezolizumab + SGI-110

Atezolizumab is a monoclonal antibody against PDL1 (a protein that allows tumor cells to escape the killing effect of T cells). SGI-110 is a drug that enhances the expression of the genes encoding tumor antigens on the surface of tumor cells and also enhances the activity of tumor-killing T cells against those tumor cells. There will be about 66 people participating in this phase of the study. (33 in each group)

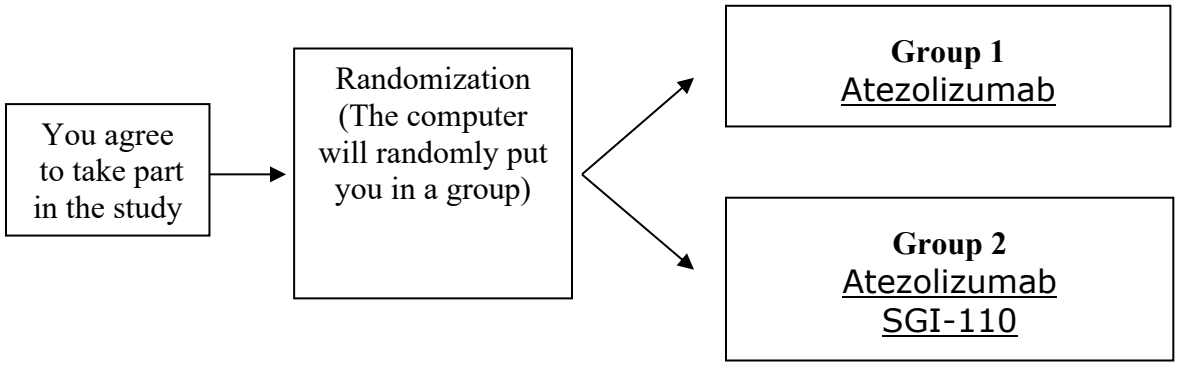
Atezolizumab and SGI-110 are both not FDA approved for treating your type of cancer.

What are the study groups?

This study has three study groups.
Group 1 will receive the study drug *Atezolizumab,*
Group 2 will receive *Atezolizumab* with *SGI-110*,

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

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



The following chart shows the schedule of the study drugs you may receive:

	Study Drug	How it is given	Day(s) in each Cycle	Cycle	Total Cycles
Group 1	Atezolizumab	By vein (IV infusion) over 60 minutes (or 30 minutes if first infusion is tolerated).	Days 1 and 15	28 days	up to 24 cycles 24 months
Group 2	Atezolizumab	By vein (IV infusion) over 60 minutes (or 30 minutes if first infusion is tolerated).	Days 8 and 22	28 days	up to 24 cycles 24 months
	SGI-110	Injection under skin	Days 1 - 5	28 days	Up to 6 cycles 6 months

How long will I be in this study?

You will receive the study drugs on the schedule explained above for up to 24 months. After you finish with the study drugs, your doctor will continue to watch you for side effects and follow your condition for 1 year."

What extra tests and procedures will I have if I take part in this study?

Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer (CT/MRI scans, blood test for count levels and metabolic profile) . However, there are some extra tests that you will need to have if you take part in this study.

Before you begin the study:

You will need to have the following extra tests to find out if you can be in the study:

- Electrocardiogram (EKG)
- Blood Draw for thyroid levels (the same sample drawn for standard blood test mentioned above will be used for this test)
- A urine pregnancy test if you are capable of getting pregnant.
- CT-guided biopsy (baseline)
- Blood work for research purposes (baseline) - about 4 tablespoons
- Stool collection within 7 days of starting study drug
- Questionnaire at the time of stool collection

If the exams, tests, and procedures show that you can take part in the study, and you choose to take part, then you will need the following extra tests. They are not part of the usual approach for your type of cancer.

During the study:
Your privacy is very important and the researchers will make every effort to protect it. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your sample and health information. The results will be available to the study participant or study doctor.

- Stool collection on cycle 4 Day 1 (or sooner if you stop study drug due to cancer growth (if applicable: or experience excessive side effects) before that point.
- Questionnaire at the time of each stool collection
- Blood work for research (about 4 tablespoons) every 2 weeks for first cycle of study drug, every 4 weeks for remaining cycles, at the end of study drug, and post study drug (30 days, 6 months and 12 months after last study drug).
- CT-guided biopsy of the tumor 4 weeks after start of study drugs

About mandatory samples for research:

You will be asked to provide an optional tumor biopsy at progression if it can be done safely. The research biopsy is done in a similar way to biopsies done for diagnosis. The tissue obtained during the biopsy will be tested for the presence of a) a protein called NY-ESO-1 and for a protein called PD-L1. This sample is required in order for you to take part in this study because the research on the sample is an important part of the study.

Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, pain at the biopsy site, which can be treated with regular pain medications, and bruising. Rarely, an infection can occur.

Any of the specimen left over from mandatory biopsies will be stored for biobanking. This is discussed in the Additional Studies Section of this consent form.

Your privacy is very important and the researchers will make every effort to protect it. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your sample and health information. The results will be available to the study participant or study doctor.

About the required Microbiome stool sample and questionnaires for research:

You will be given written instructions on what you should do to collect the Microbiome stool sample. We ask you to kindly follow all the instructions for collection, as we will not be able to use specimens that are not properly collected. Stool will be collected at the following time points:

-at baseline

-within 7 days of starting study drug

-once post study drug on cycle 4 Day 1 (or sooner if you stop study drug due to cancer growth before Cycle 4 Day 1).

You will be asked to fill out questionnaires at the time of stool collection as it will help us interpret data gathered from your normal gut bacterial make up. This will take about 5-10 minutes to complete and will include basic questions on nutrition and lifestyle habits. The questionnaires will be completed at the following time points:
- Stool Sample Collection Questionnaire: At baseline within 7 days of starting treatment.
- Microbiome Collection Questionnaire: At baseline within 7 days of starting study drug and once post study drug on cycle 4 day 1 (or sooner if you stop study drug due to cancer growth before cycle 4 day 1).

Procedure Risks:

Risk of Blood Draw:
Local pain or swelling; in rare cases, vein damage or irritation/phlebitis, excessive bleeding or bruising, feeling faint, infections.

Risks Associated with Tumor Biopsies:

In a needle biopsy, you will feel a small sharp pinch at the site of the biopsy. Risks associated with the biopsy include bleeding and infection in less than 1% of patients.

Risk of CT scan:
The CT scans are considered standard of care and would be done even if you were not participating in this study. This radiation may involve a low risk of a later cancer, however, we believe that this risk is not clinically relevant. If you have any questions regarding the use of radiation or the risks involved, please consult the physician conducting this study

Risk of MRI:
An MRI uses magnetic energy and radio waves rather than x-ray radiation. A few patients may experience anxiety due to claustrophobia, or an inability to be in a confined space without being given a sedative (a drug used to calm them). In addition, you will hear loud, knocking noises. Occasionally, subjects will report a mild headache from the "knocking" sound. There are no other reported side effects. If you have any metal implants within the body (cardiac pacemaker, orthopedic pins, plates, or screws) you will not be able to undergo an MRI since metal implants interfere with the MRI system's magnetic field.

Recently, it has been reported that a rare but serious adverse reaction called nephrogenic systemic fibrosis (NSF) may occur after exposure to the gadolinium-based contrast agent gadodiamide (OmniscanR, GE Health

Diagnostic, Amersham, United Kingdom). Nephrogenic systemic fibrosis is a condition wherein patients develop large areas of hardened skin with lesions called plaques and papules with or without skin discoloration. In some cases, NSF could lead to physical disability and may involve not only the skin, but also the liver, lungs, muscles and heart. The typical patient in whom this has occurred is middle aged and has end-stage kidney disease."

Reproductive risks:
You should not get pregnant or breastfeed a baby while in this study. The drugs used in this study could be very damaging to an unborn baby. Women of child-bearing potential must agree to use adequate contraception prior to study entry, for the duration of study participation, and for 5 months after the last dose of study agent.

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

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

Yoy may also 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 drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will testyour 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, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be mild. Some 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 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.
- 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 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.

Patients in Phase II (group 2) of the study:

Possible side effects of **SGI-110**

COMMON, SOME MAY BE SERIOUS
In 100 people receiving SGI-110, more than 20 and up to 100 may have:

- Anemia which may require blood transfusion
- Decrease in white blood cell count
- Nausea
- Tiredness
- Swelling, redness and pain at the site of the medication injection*
- Bruising, bleeding

**If pain occurs at injection site, ice packs will be applied to the injection site both before and after injection for 5 – 10 minutes each. Patients may be given pretreatment of topical or systemic analgesics can be considered*.

OCCASIONAL, SOME MAY BE SERIOUS
In 100 people receiving SGI-110, from 4 to 20 may have:

- Infection, especially when white blood cell count is low
- Constipation, diarrhea, vomiting
- Sores in the mouth which may cause difficulty swallowing
- Fever
- Pain
- Loss of appetite
- Dizziness, headache
- Difficulty sleeping
- Cough, shortness of breath
- Nose bleed
- Rash

PLEASE NOTE:
Since SGI-110 may make you more susceptible to infection, especially when your white blood cell count is low, you will be prescribed an injection called granulocyte colony-stimulating factor (G-CSF). G-CSF works by stimulating the bone marrow to produce more white blood cells in the body, and therefore may potentially help to prevent infection. At the time you start this medication, your doctor will provide you with specific information about G-CSF including dose, frequency and side effects.

Patients in all study groups:

Possible side effects of **Atezolizumab**

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 swelling 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
- Swelling of the brain (meningitis/encephalitis), which may cause: headache, confusion, sleepiness, seizures, and stiff neck
- 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 swellingLung problems (pneumonitis and pleural effusion). Symptoms may include: new or worsening cough, chest pain, shortness of breath.
- Skin: blisters on the skin

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

This study has only a small chance of helping you because we do not know if any of the drug or combination used in this study are effective. This study may help researchers learn things that may help other people in the future.

Can I stop taking part in this study?

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

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

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules

- If the study is stopped by the sponsor, IRB or FDA.

What are my rights in this study?

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

For questions about your rights while in this study, call the _____ *(insert name of center)* Institutional Review Board at _____ *(insert telephone number). (Note to Local Investigator: Contact information for patient representatives or other individuals at a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can also be listed here.)*

What are the costs of taking part in this study?

The following study drugs will be supplied at no charge while you take part in this study:

- Atezolizumab
- SGI-110

The cost of getting the study drugs ready and giving it to you is not paid by the study sponsor so you or your insurance company may have to pay for this. It is possible that the study drug may not continue to be supplied while you are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options.

You and/or your health plan/insurance company will need to pay for all of the other costs of caring for or treating your cancer while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for.

Examinations, scans, laboratory tests and other medical procedures and treatment that are required only for the clinical research study and are not needed for the usual care of a patient with your disease are known as "research related" services. Research related services will not be charged to you or your insurance.

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

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

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

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

Who will see my medical information?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that

is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

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

- The study sponsor and any drug company supporting the study
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration and the National Cancer Institute in the U.S., and similar ones if other countries are involved in the study.

Where can I get more information?

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

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

Who can answer my questions about this study?

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

ADDITIONAL STUDIES SECTION:

This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The researchers leading this optional study hope the results will help other people with cancer in the future. The results will be added to your medical records and you or your study doctor *will* know the results.

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

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

Optional biopsy – extra biopsy at progression

If you choose to take part in this study, you will have an optional extra CT-guided biopsy at disease progression. Researchers would use this tumor tissue sample at disease progression to compare with the sample taken earlier while tumor was responding to the study drug in order to learn more about how the study drug works on cancer.

[Type text]

If you agree to have this extra biopsy, it would involve the same procedure as the biopsy taken at baseline before starting the study drug and the one at 4 weeks after the start of the study drug. The risks would be the same as well.

Please circle your answer: I choose to take part in the extra biopsy at progression:

YES NO

WHAT IS INVOLVED?

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

1) At disease progression, a sample of tissue will be collected from the optional extra biopsy. The procedure will be the same as the prior mandatory CT guided biopsies in this study at baseline and at 4 weeks after the start of study drug.
2) Your sample and some related health information will be sent to a researcher for use in the study described above. Remaining samples may be stored in the Biobank, along with samples from other people who take part. The samples will be kept until they are used up.
3) Qualified researchers can submit a request to use the materials stored in the Biobanks. A science committee at the clinical trials organization will review each request. There will also be an ethics review to ensure that the request is necessary and proper. Researchers will not be given your name or any other information that could directly identify you.
4) 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.

WHAT ARE THE POSSIBLE RISKS?

In a needle biopsy, you will feel a small sharp pinch at the site of the biopsy. Risks associated with the biopsy include bleeding and infection in less than 1% of patients.

HOW WILL INFORMATION ABOUT ME BE KEPT PRIVATE?

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

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

WHAT ARE THE POSSIBLE BENEFITS?

You will not benefit from taking part.

Your samples may be helpful to research. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

WHAT IF I CHANGE MY MIND?

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

WHAT IF I HAVE MORE QUESTIONS?

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

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

SAMPLES FOR THE LABORATORY STUDIES:

I agree to have my specimen (blood, biopsy) collected and I agree that my specimen sample(s) and related information may be used for the laboratory study(ies) described above.

YES NO

I agree that my study doctor, or their representative, may contact me or my physician to see if I wish to learn about results from this(ese) study(ies).

YES NO

SAMPLES FOR FUTURE RESEARCH STUDIES:

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

YES NO

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

YES NO

My Signature Agreeing to Take Part in the Main Study

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

Participant's signature_____

Date of signature_____

(The following signature and date lines for the person(s) conducting the discussion may be included at the discretion of the study sponsor.)

Signature of person(s) conducting the informed consent discussion_____

Date of signature_____