Document Coversheet

Study Title : A Phase II Study of Type-1 Polarized Dendritic Cell (aDC1) -based Treatment in Combination with Tumor-Selective Chemokine Modulation (CKM: Interferon alpha-2b, Rintatolimod and Celecoxib) in Melanoma Patients with Primary PD-1/PD-L1 Resistanc

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ROSWELL PARK CANCER INSTITUTE

Title: A Phase II Study of Type-1 Polarized Dendritic Cell (αDC1) -based Treatment in Combination with Tumor-Selective Chemokine Modulation (CKM: Interferon alpha-2b, Rintatolimod and Celecoxib) in Melanoma Patients with Primary PD-1/PD-L1 Resistance

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Consent Form Given to Patient Taking Part in an Investigational/Clinical Research Study

KEY INFORMATION ABOUT THIS RESEARCH STUDY

This is a clinical research study being done by the doctors at the Roswell Park Comprehensive Cancer Center. Clinical research studies include only those patients who choose to take part. Your participation is voluntary. Please take your time to make your decision. Discuss it with your family and with people who are important to you.

We are asking you to take part in this research study because you have advanced-stage melanoma that has become resistant to treatment with anti-PD-1/ PD-L1 drugs (i.e., they are no longer effective in treating your cancer).

Study Purpose:

The purpose of this trial is to see if the combination of the study cell-based treatment (αDC1 dendritic cells) and drugs, in patients with your type of cancer, can prevent the growth and/or progression of the cancer.

The study drugs are a combination of celecoxib (Celebrex®), Interferon-alpha-2b (IFN), and rintatolimod (Ampligen®): this is what is called the chemokine modulating regimen or CKM.

- Celecoxib is FDA approved for the treatment of colorectal polyps (fleshy growths on the lining of the colon or rectum), pain, and swelling. It has not been approved for commercial use in cancer treatment. Celecoxib is taken by mouth. You will take 200 mg -twice a day on days of the vaccine and the CKM cycle(s).
- There is no longer a U.S. FDA-approved source of interferon alfa-2b (IFN) being marketed. Therefore, a new source of IFN is being used for this study which is not approved by the U.S. FDA and is considered an investigational new drug. IFN can improve the body's natural response to infections and other diseases. It can also interfere with the division of cancels and slow tumor growth. IFN is administered intravenously (IV) through a small tube in your vein. It takes about 20 minutes to administer the full dose.
- Rintatolimod is not FDA approved but it has been tests for illnesses including chronic fatigue syndrome (CFS) and acquired immunodeficiency syndrome (AIDS). It is believed to stimulate the immune system. This is administered by IV. It takes about 2 hours to deliver the full dose.

The cell-based treatment contains white blood cells (dendritic cells or DCs) that stimulate your immune system. The cell-based treatment will be produced at Roswell Park using your own white blood cells. The cell-based treatment (including the procedures and facilities used in generating, preserving and preparing the cell-based treatment) is designated by the FDA as a "Biologically Based-Investigational New Drug" and as such is deemed safe to proceed for investigational use in a clinical trial. Therefore, the cell-based treatment is considered an experimental or investigational therapy. The investigators believe that combining the cell-based treatment with the CKM regimen will allow the vaccination-induced immune cells to be more effective in delaying or preventing tumor growth.

Study Costs: The following drugs that you will receive as part of this study will be provided to you at no cost by the study sponsor:

- The αDC1 cell-based treatment will be made and provided to you at no cost while you are on the study.
- The drugs that make up the chemokine modulating regimen [(celecoxib (Celebrex®), Interferon-alpha-2b (IFN), and rintatolimod (Ampligen®)] will also be provided at no cost while you are on the study.

Section 9 of this document provides additional information on how to find out what costs are part of standard of care or related to this research study.

Study Duration and Number of Participants: It is expected this study will take about 3 years or will continue until the needed number of participants are enrolled. We expect to enroll 24 patients from Roswell Park over this time period.

Your participation in this study will be for approximately 2 and one-half years from the start of treatment (this includes follow-up after completing the treatment regimen).

Exams, Tests and Procedures: This study involves exams, tests and procedures, some of which will be done as standard of care for your disease or condition, and some will be done for research-related purposes.

Listed below are **key research-related tests** and procedures that you will undergo during the study:

Pre Screening HLA Testing

Buccal Cell Collection/Blood draw: Buccal cell collection is a test that involves swabbing the surface of the buccal mucosa, or inside of the cheek. You may also elect to have a blood draw instead of the buccal swab.

Treatment, Testing and Procedure:

You will have extra clinic visits that include a physical exam, on Days 2 & 3 of each cycle

EKG: during screening

Tumor Biopsy: A tumor biopsy is required before starting the treatment regimen and at the end of the last cycle (Cycle 4) of treatment (Week 12 ± 1 week).

Leukapheresis: Leukapheresis will occur once all study inclusion and exclusion criteria have been met. The leukapheresis is required to obtain the cells necessary to produce the cell-based treatment that will be given with the cytokine modulation therapy. The length of the procedure can vary from 90 minutes to 240 minutes. If a sufficient number of cells have not been obtained for you to receive

the 3 scheduled study injections of the cell-based treatment, a 2nd leukapheresis will be performed within 14 days of the first one. If a sufficient number of cells were not obtained following the 2nd procedure, you will be withdrawn from the study.

Blood tests: Research-related blood draws will be done each cycle (on Day 1 and Day 3) prior to starting the study treatment for that cycle and following the last infusion on that day of treatment. A research-related blood draw will also be taken at the completion of all study treatment (± 3 days).

Section 3 of this document provides additional information on exams, tests and procedures involved with this study, including those being done as part of standard of care. Exams, tests and procedures being done as standard of care are required for your participation in the study according to the schedule outlined in Section 3.

Side Effects and Risks: While you take part in this study, you may be at risk for side effects. The side effects may be mild, moderate, or severe. Many side effects go away shortly after the treatment stops, but occasionally, side effects can be serious, long lasting, or may be permanent or life-threatening. The most common side effects of the study drug(s) are:

- *DC-based vaccination*: development of autoimmune diseases such as vitiligo (patches of your skin losing pigment and becoming discolored), development of allergic reaction to the cell-based treatment
- *Interferon Alpha-2b*: Pain, swelling and redness or skin damage at the injection site, hair loss, dizziness, changes in appetite, stomach or abdominal pain, diarrhea, nausea (feeling sick), viral infection, depression, mood swings, insomnia, anxiety, sore throat and painful swallowing, fatigue, chills and shivering, fever, flu-like reaction, feeling of general discomfort, headaches, weight loss, vomiting, irritability, weakness, changes in mood, cough (sometimes severe), shortness of breath, itching, dry skin, rash, sudden and severe muscle pain, joint pain, muscle and/or bone pain, changes in laboratory blood values including decreased white blood cell count.
- *Celecoxib*: dyspepsia (uncomfortable recurrent pain in your upper abdomen) , headaches, elevated liver function tests
- *Rintatolimod*: mild flu-like symptoms, transient headache, fever, myalgia (muscle pain), arthralgia (joint pain), injection site reaction, pruritus (skin itching), dilation of blood vessels, diarrhea, and fatigue/malaise

Section 6 of this document provides more detailed information on possible side effects and risks.

Potential Benefits: It is not known if this treatment will help you or not. If the treatment is successful, you might see a decrease in your symptoms and improvement in your quality of life. It is also possible the investigational treatments may prove to be less useful or even harmful to you. You understand there is no guarantee that being on the study will help you. Future patients may be helped from the results and information gained from this study.

Other Options: If you do not join this study, you should discuss what other options there are with your doctor. Other options may include:

1 Usual/standard treatment for your disease or condition may be appropriate. This may include treatment with other drugs, drug combinations, surgery, radiation therapy, or possibly other research programs here or at other centers which may be testing new drugs for your type of cancer.

2 No treatment, but medications and measures to keep you comfortable. This is sometimes called supportive care.

Feel free to talk with your health care team about your disease and your treatment choices.

The type of study, the risks, benefits, discomforts, and other important information about this study are discussed below.

DETAILED INFORMATION ABOUT THIS RESEARCH STUDY

It is important that you read and understand the following facts that apply to anyone that takes part in our studies:

a. This study is considered research. It is investigational.
b. Taking part in the study is voluntary.
c. You may withdraw from the study at any time without penalty, loss of any benefits or access to care at Roswell Park to which you are otherwise entitled.
d. If you should decide not to take part in this study, it will not affect your care at Roswell Park now or in the future.
e. You should feel free to get a second opinion. This will not affect your ability to receive care and treatment here if you get one.
f. Your disease may not be helped from taking part in this study, but we may get information that will help others.
g. If we become aware of important new findings that relate to your participation or continued participation in this study we will discuss them with you.
h. If you decide to stop being in the study, you should talk with your doctor first about this decision so you are informed about any effects that stopping study participation may have on your health.

1. What is the purpose of this study?

The purpose of this study is to find out what effects (good and bad) the αDC1/ TBVA cell-based treatment (i.e., the cell-based treatment that is manufactured from your own blood monocytes: a monocyte is a type of an immune white blood cell that helps destroy cancer cells) when given in combination with the Chemokine Modulation (CKM) Therapy has on you and your type of melanoma. The investigators also want to examine the effect/s that this combination therapy has on your immune system and how your cancer cells respond to the therapy.

2. What are the study groups?

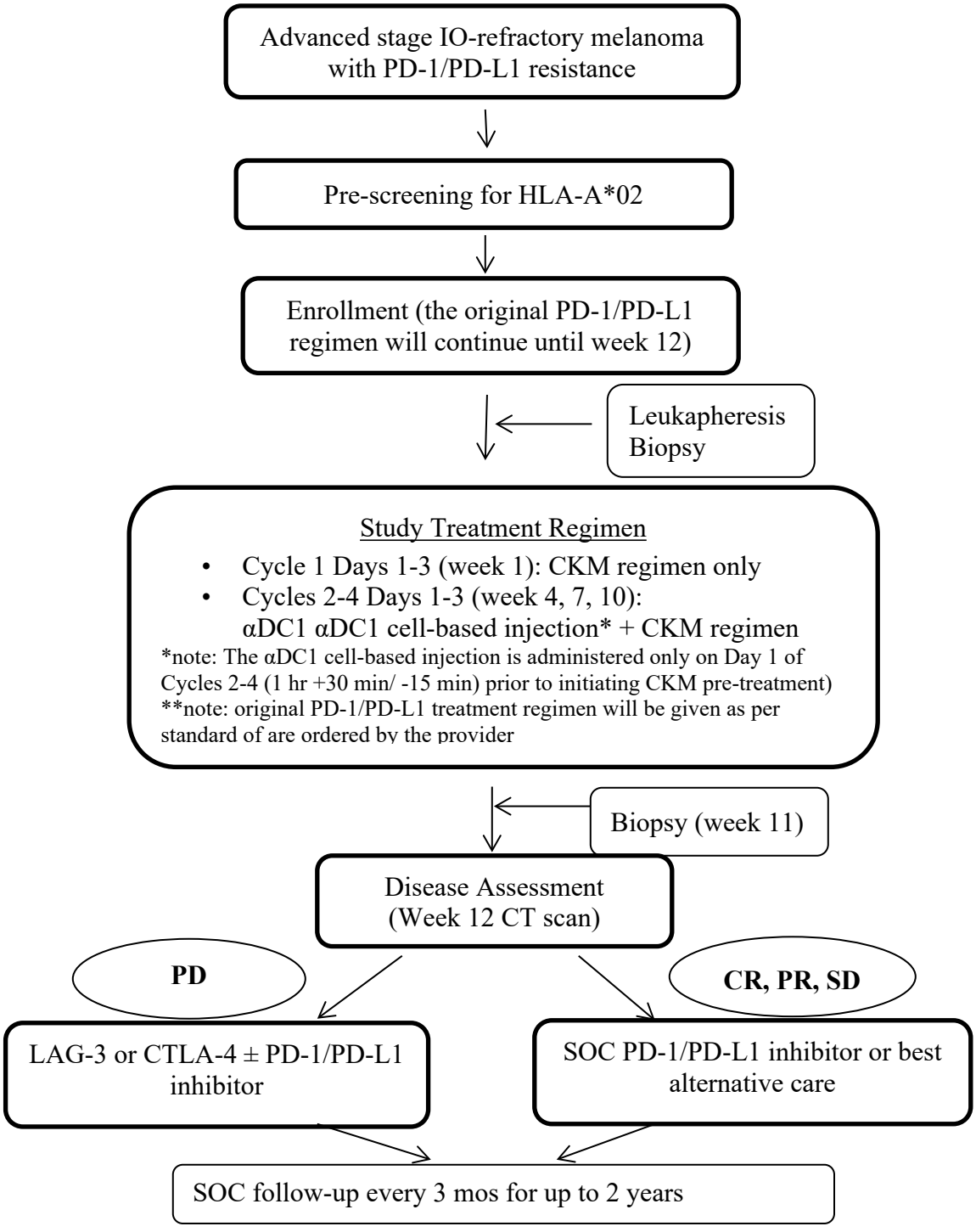
All study participants will get the same study intervention.

Once you have satisfactorily met all the inclusion and exclusion criteria, you will undergo leukapheresis or apheresis). Leukapheresis is a procedure to separate and collect the white blood cells from your blood. These white blood cells will be used make the cell-based treatment that you will be receiving as part of your treatment.

Prior to starting the treatment regimen (Cycle 1 will only be CKM – the 3 cycles to follow will be the cell-based treatment along with the CKM), a biopsy of your melanoma tissue and a sample of non-cancer tissue close to the cancerous tissue, will be performed. This same procedure will be performed after you complete the 4 cycles (1 cycle = 3 weeks) of the treatment regimen.

In each of the 4 cycles of the combination immunotherapy (on Days 1-3), each participant will receive a three-day-long course of CKM (IFN-α2b, IV, over 30 minutes followed by rintatolimod IV, over 2.5 hours and celecoxib (celecoxib will be taken orally, before IFN-a2b and after IFN-a2b) on days 1-3. In addition, on Day 1of cycles 2-4, participants will receive the αDC1 cell-based treatment intradermally (i.e., just under the skin).

Another way to find out what will happen to you during this study is to read the chart below.



CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease; SOC, standard of care

All treatment will be administered on an outpatient basis.

Response to the treatment regimen will be evaluated by a CT scan, performed as a part of standard of care at week 12 (± 1 week). At that time point, a participant whose scan shows stable disease or partial response will be offered the opportunity to restart on PD-1 blockade drug treatment:

- PD-1 is a protein that is found on some of your immune cells which helps to keep the body's immune responses in check. When PD-1 comes together with another protein (called PD-L1), it can prevent your immune cells from being able to kill cancer cells. So, if the PD-1 protein is blocked, the ability of your immune system to kill cancer cells is increased.

If your disease has progressed, you will be offered an opportunity to switch to CTLA4 blockade (Ipilimumab) ± PD-1/PD-L1 inhibitor (unless contra-indicated) or to LAG3 blockade (another, more recently developed, factor allowing an improved immune response) ± PD-1/PD-L1 inhibitor (unless contra-indicated) and will be assessed as per standard of care guidelines. If you have either a complete or partial response to the treatment or your disease has stabilized, you will be offered PD-1 blockade (according to the approved standard of care regimen) or best alternative care. Thereafter, you will be contacted by phone every 3 months for up to 2 years by medical record review/telephone call for survival status and other anti-cancer therapies.

3. If I take part in this study, what tests and procedures will I have done?

Prior to being enrolled in the study, you will be screened to ensure that you meet the eligibility criteria to take part in the study.

Pre-Screening Evaluation (HLA-A2 Testing)

- Blood will be taken (approximately 6ml) or a buccal swab (swab of inner check) to determine the presence or absence of the HLA-A2 gene.

Screening/ Baseline Evaluations: Unless otherwise specified, the following will be performed within 28 days prior to starting the treatment regimen:

- Your doctor will perform a physical exam and check your vital signs. This will include recording your height and weight, a general evaluation of your clinical condition, your blood pressure, pulse rate, respiratory rate and body temperature
- Your medical history will be obtained, especially relating to your cancer
- Performance Status Assessment: You will be asked about how well you are able to perform ordinary tasks and carry out daily activities
- Concomitant medications: You will be asked to list any medications that you take on a regular basis (prescription and non-prescription and, any medications that you may be taking that will start or stop within 1 week of starting on the study treatment regimen
- You will undergo some routine blood tests in order to check your blood cell counts, electrolytes, heart, kidneys, and thyroid
- Urine pregnancy test for women of child-bearing potential to be performed within 7 days prior to starting the treatment regimen

- You will have an electrocardiogram (EKG) done. This is a recording of the electrical activity of your heart
- Baseline Tumor/Disease Assessment: A CT scan of the chest abdomen and pelvis

Within 1 Week before Starting CKM Treatment Regimen

- A biopsy of your tumor tissue.

Your white blood cells will be collected in a process called a leukapheresis or apheresis. The cells will be collected by inserting a needle into each arm. Your blood will be drawn through sterile tubing into a sterile bowl inside a machine that separates your white blood cells from the rest of your blood. Your cells will be collected into a sterile collection bag. During the procedure, the machine works in cycles. In one cycle the machine is drawing blood into the sterile bowl to collect your cells. In the second cycle the machine is returning your red blood cells and platelets (cells that help your blood clot) back to you. The procedure ends with the machine in the return cycle. A solution call acid-citrate-dextrose (ACD) and salt solution (saline) is used during the process to prevent your blood from clotting within the tubing of the machine. A small amount of the solution will also be returned to you along with your red blood cell and platelets. The procedure usually takes between 2-3 hours to complete and trained personnel in the Apheresis Unit supervise the procedure.

CKM and αDC1/TBVA Cell-Based Treatment Regimen

- Your doctor will perform a physical exam and check your vital signs (as described in the Screening/ Baseline Evaluations).
- Concomitant medications assessment (as described in the Screening/ Baseline Evaluations)
- You will undergo some routine blood tests in order to check your blood cell counts, electrolytes, heart, kidneys, and thyroid

End of Treatment

- Your doctor will perform a physical exam and check your vital signs (as described in the Screening/ Baseline Evaluations).
- Concomitant medications assessment (as described in the Screening/ Baseline Evaluations)
- End of Treatment Disease Assessment: A CT scan of the chest abdomen and pelvis

Follow-Up

- Your study coordinator will call you once a month for the first three months following end of treatment.
- Concomitant medications assessment (as described in the Screening/ Baseline Evaluations)

4. Will I be informed of research results?

If we learn new information from research tests or analyses during this study that may be important to your health or to your disease or condition or your clinical care, we will share that information with you. Such information will be provided to you as part of your clinical care.

5. Why would I be taken off the study early?

You may be taken off the study for any of the following reasons:

- Your medical condition changes
- New information becomes known to us that would influence your decision to remain on the study
- The treatment is no longer helpful to you. Other options for your condition will then be discussed with you.
- The sponsor of the study may decide to stop or change the study
- You do not follow the study schedule or requirements
- You experience unacceptable side effects
- You no longer want to participate

6. What risks and discomforts are involved?

While you take part in this study, you may be at risk for side effects. The side effects may be mild, moderate, or severe. Many side effects go away shortly after the treatment stops, but occasionally, side effects can be serious, long lasting, or may be permanent.

It is not possible to tell which side effect will affect you or how mild or severe the side effect might be. We can only tell you what other people have experienced.

It is very important that you notify your doctor right away about **any** side effects, problems, or unusual experiences you may have while taking this medication and related study procedures. This will decrease the chance that the side effects continue or become worse. Sometimes there are other medications that we can give you to make the side effects better or make you more comfortable. If severe side effects do develop, you and your doctor may decide it is in your best interest to stop taking part in the study.

There may be other side effects of the drugs/procedures that we do not know of yet.

Notify the study coordinator or study doctor before taking any new over-the-counter drugs or other medications to assure it is safe to take the new medication while on this study.

The drug(s)/procedures used in this study may cause all, some, or none of the side effects listed.

The risks and side effects for the drugs in this study are listed below.

For **Celecoxib**:

Unlikely Side Effects: Those that occur in approximately 5% to 9% of persons who receive this drug:

- Indigestion, stomach upset
- Blockage of the airway which may cause shortness of breath, cough, wheezing
- Elevated liver enzymes in blood
- Abnormal heartbeat which may cause fainting
- Diarrhea, nausea
- Headache
- High blood pressure which may cause dizziness, blurred vision
- Kidney damage which may cause swelling
- Sores in stomach which may cause belly pain
- Swelling of the stomach
- Stroke which may cause paralysis, weakness

Rare but Serious Side Effects: Those that occur in less than 5% of persons who receive this drug:

- Heart attack which may cause chest pain
- Swelling of the legs
- Belly pain
- Vomiting
- Severe liver enzyme elevation which may cause yellow eyes and skin, tiredness
- Bowel perforation
- Internal bleeding which may cause belly pain, black tarry stool, or blood in vomit
- Severe skin rash
- Severe allergic reaction with low blood pressure or trouble breathing
- Blood clot

For **Interferon Alpha-2b, The following side effects have been reported:**

Very Common Side Effects: In 10 people who received this drug, more than 1 experienced the following:

- Pain
- Swelling and redness or skin damage at the injection site
- Hair loss
- Dizziness
- Changes in appetite
- Stomach or abdominal pain, diarrhea, nausea (feeling sick)
- Viral infection
- Depression, mood swings
- Insomnia
- Anxiety
- Sore throat and painful swallowing
- Fatigue
- Chills and shivering
- Fever
- Flu-like reaction
- Feeling of general discomfort
- Headaches
- Weight loss
- Vomiting
- Irritability
- Weakness
- Changes in mood
- Cough (sometimes severe)
- Shortness of breath
- Itching, dry skin, rash
- Sudden and severe muscle pain, joint pain, muscle and/or bone pain
- Changes in laboratory blood values including decreased white blood cell count.

Common Side effects: In 100 people who received this drug, between 1 to 10 patients experienced the following:

- Thirst

- Dehydration
- High blood pressure
- Migraines
- Swollen glands
- Flushing
- Menstrual problems
- Decreased sexual drive
- Vaginal problem
- Breast pain
- Pain in testicle
- Problems with thyroid gland
- Red gums, dry mouth, red or sore mouth or tongue
- Tooth ache or dental disorders
- Herpes simplex (fever blisters)
- Taste disorders
- Upset stomach
- Heartburn
- Constipation
- Liver enlargement (liver disorders, sometimes severe)
- Loose stools
- Sinus infection
- Lung inflammation
- Eye pain
- Disorders in the tear ducts
- Irritation and redness of the thin membrane covering the eye
- Agitation
- Sleepiness
- Sleepwalking
- Behavioral disorders
- Nervousness
- Stuffy or runny nose
- Sneezing
- Rapid breathing
- Pale or reddened skin
- Bruising
- Skin or nail disorders
- Red, dry, scaly patches of thickened skin (psoriasis)
- Increased sweating
- Increased need to pass urine
- Slight tremors
- Decreased sensitivity to touch, and
- Joint inflammation and swelling.

Uncommon Side Effects: In 1,000 people who received this drug, between 1 to 10 patients experienced the following:

- Bacterial infection
- Tingling feeling, and
- Inflammation of the tissue around the heart (possible chest pain).

Rare Side Effects: In 10,000 people who received this drug, between 1 to 10 patients experienced the following:

- The study treatment may cause an increased risk of infection, such as pneumonia (an infection of the lungs). A low number of white blood cells may increase the risk of infection. It may become life-threatening. Symptoms of infection may include fever, pain, redness, and/or difficulty breathing.

Very Rare Side Effects: In 10,000 people who received this drug, less than 1 patient experienced the following:

- Low blood pressure
- Puffy face
- Diabetes
- Leg cramps
- Back pain
- Kidney disorders
- Nerve alteration
- Bleeding gums
- A disorder caused by decreased production of red blood cells, white blood cells and platelets which may cause severe anemia, infection and bleeding may occur. This may be serious or life-threatening without treatment.
- Pure red cell aplasia, a condition where the body stopped or reduced the production of red blood cells, has been reported. This condition causes severe anemia, symptoms which would include unusual tiredness and lack of energy.
- Sarcoidosis, (a disease characterized by persistent fever, weight loss, joint pain and swelling, skin lesions and swollen glands) has been very rarely reported.
- Loss of consciousness has occurred very rarely, mostly in elderly patients treated at high doses.
- Cases of stroke (cerebrovascular events) have been reported. Seek your doctor immediately if you have any of these symptoms.

Side Effects of Unknown Frequency:

- Gum disease and dental disorders
- Change in color of the tongue
- Altered mental condition
- Loss of consciousness
- Acute hypersensitivity reactions including hives, swelling of hands, feet, ankles, face, lips, mouth, or throat which may cause difficulty in swallowing or breathing, difficulty breathing due to narrowing of the airways and a severe, whole-body allergic reaction have been reported (at unknown frequency).
- Vogt-Koyanagi-Harada syndrome (an autoimmune inflammatory disorder affecting the eyes, skin and the membranes of the ears, brain and spinal cord)

- Thoughts about threatening the life of others
- Mood disorder with extremes of happiness and sadness
- Heart failure
- Pericardial effusion (a fluid collection that occurs between the heart lining and the heart itself, scarring of the lungs that can affect the ability to breathe and may make you short of breath, and reactivation of hepatitis B infection (liver damage) have been reported with interferon alpha 2b use.

Pulmonary arterial hypertension – a disease of severe narrowing of the blood vessels in the lungs resulting in high blood pressure in the blood vessels that carry blood from the heart to the lungs may occur particularly in patients with risk factors such as HIV infection or severe liver disorders (cirrhosis). The episodes were reported at different time points during the treatment, typically several months after starting treatment with interferon alpha 2b.

For **Rintatolimod**:

Likely Side Effects: Those that occur in at least 15% of people who receive this drug:

- Mild, short-lived pain at the infusion site
- Flu-like symptoms which may include, but not limited to: fever, chills, mild muscle or joint aches, headache, fatigue, and possibly nausea and vomiting
- Diarrhea
- Pruritus (itching)
- Dilation of blood vessels which decreases blood pressure

Less likely side effects: Those occurring in 5 -15% of people who receive this drug:

- Flushing (redness of the face, neck, and chest), occasionally, it can be accompanied by a tightness of the chest, increased heart rate, anxiety, shortness of breath, reports of "feeling hot", excessive sweating, and nausea
- A more pronounced fever with chills and fatigue in response to a single infusion. This typically resolves over 12 to 24 hours, responds to acetaminophen (pain and fever reducing medication), and does not recur on subsequent dosing.
- Hives
- Syncope, temporary loss of consciousness due to drop in blood pressure
- Ear disorder
- Migraine
- Sensitivity to light
- Rash
- Irregular heart rate
- Vision problems

Rare Side Effects: Those occurring in <5% of people who receive this drug:

- Alopecia, hair loss
- Temporary increased swelling around the tumor or even increased enhancement of the tumor
- Complications from the infusion that include infection, bleeding, or nerve damage
- Decreased liver function

The risks and side effects for the intradermal (injection under the skin) **αDC1 cell-based treatment** are listed below.

Likely Side Effects: Those that occur in approximately 15% - 30% of people who receive this drug.

- Minor discomfort and skin redness at the site of injection

Less likely Side Effects: Those that occur in approximately 10%-14% of people who receive this drug.

- Minor swelling at the site of injection

Unlikely Side Effects: those that occur in approximately 5% to 9% of persons who receive this drug.

- Skin rashes
- Transient flu like symptoms

Rare but Serious Side Effects: Those that occur in less than 5% of people who receive this drug.

- Allergic reaction
- Autoimmunity
- Infection

We do not yet know the side effects the use of these drugs together may cause. There may be unknown and unexpected side effects as a result of using these drugs together.

Procedure Risks:

Tumor Biopsy:
You may experience pain, discomfort, and/ or soreness at the site where biopsy was done. The soreness is generally diminished within 48 hours of the procedure

Leukapheresis:
Common risks associated with blood donations may also occur occasionally with leukapheresis procedures. The risks are related to the use of needles to puncture the veins of the donor and include pain, bleeding, bruising of the skin, infection at the needle insertion site and minor damage to the nerves in the skin. Dizziness and fainting may also occur occasionally, as well as chills, abdominal cramps, nausea and vomiting.

If the veins in your arms are not adequate for the procedure, a special apheresis catheter may be inserted into the large vein in your neck for the collection. The risks associated with this procedure include pain, bleeding, bruising of the skin, infection at the needle insertion site, minor damage to the nerves in the skin, potential nerve pain, and risk of puncturing the lung. You may also experience an allergic reaction to the medicine that will be used to numb the skin where the needle will be inserted.

Tingling in the fingers and around the mouth may occur when the red blood cells are returned to the donor. This is due to the infusion of citrate (which is mixed with the blood in the collection set to prevent clotting) with the red blood cells. Citrate is used as a fuel by the body and is rapidly removed from the blood stream, making this a very brief phenomenon. It can generally be overcome by slowing the rate of return of the red blood cells or by taking calcium supplements or intravenous calcium replacement for more severe symptoms.

Blood Draw:
You may experience mild pain, discomfort, bruising at the needle insertion site, inflammation of the vein, possible infection and bleeding

7. Reproductive risks:

This study may involve risks to you or your unborn child that are not known at this time therefore, you should not become pregnant or father a baby while you are participating in this study. Also, you should not nurse your baby while on this study. Women of childbearing potential will be required to take a pregnancy test before being allowed to take part in this study. You may also be asked to take pregnancy tests while receiving the study treatment. The pregnancy test must be negative before you enter this study.

You will be asked to practice an effective method of birth control while you are on this study and for a time after your treatment ends. This includes, but is not limited to, oral birth control pills, an IUD, condoms with spermicide, or abstinence. In women of childbearing potential, birth control should continue for six (6) months after the last treatment to ensure the drug/treatment has cleared from the body. Since interactions between the study drug and oral birth control pills cannot be ruled out, a "barrier" method of contraception (condom, diaphragm) must be used as well. In certain cases, oral birth control pills cannot be used for birth control. Please discuss this with your doctor.

When you sign this consent form, to the best of your knowledge, you are not pregnant and do not plan to become pregnant while taking part in this study. Should you become pregnant during this study, you need to immediately tell your study doctor and obstetrician. If you wish you may request a referral for counseling or ask about counseling (such as genetic counselor, social worker, or psychologist.) to discuss this further.

Male patients must use an effective method of birth control. This can include, but is not limited to, condoms with spermicide, abstinence, or having a vasectomy. When taking part in this study, you should continue use of birth control and should not donate sperm for three months after receiving the last dose of the drug to be sure the drug has cleared from the body. Discuss birth control measures with your doctor.

8. 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.
- Keep the study medication out of the reach of children and do not share the study drug with any other person.
- Write down in your medication diary when you take the study drug (only applicable for celecoxib) at home.

9. What will this cost?

Examinations, scans, laboratory tests, and other medical procedures and treatments that would routinely be needed to monitor and treat your illness are known as "standard of care" services.

Charges for these services will be billed to you and/or your insurance carrier in the usual manner. You will be responsible for all co-payments, deductibles, and/or account balances as determined by your individual health insurance contract.

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.

The following drugs/ treatments that you will receive as part of your clinical research study are considered research related:

- **Cytokine Modulation Therapy**
  - **Interferon-α2b**
  - **Rintatolimod**
  - **Celecoxib**
- **Intradermal αDC1 cell-based treatment**

These drugs/ treatments) will be provided to you at no cost by the study sponsor.

There are many different types of insurance plans and contracts. It is not possible to tell you in advance the exact amount your insurance will pay and what your financial responsibility will be. If you wish, a financial counselor can meet with you to help answer your questions regarding insurance coverage issues before you decide to participate in this study. A Financial Counselor can be reached at 716-845-3161.

There are certain insurance plans that will not cover charges for any care related to an experimental or investigational therapy or study. These plans may deny coverage for even the routine, standard of care medical services you will need to receive during the time you are enrolled in the study. If you have an insurance plan that does not cover participation in a clinical research study, or if you currently have no insurance coverage, a financial counselor can meet with you to provide an estimate of the costs that would be associated with participation in this study. A payment schedule can be developed if needed. A Financial Counselor can be reached at 716-845-3161.

A representative from the Patient Access Department can help you obtain authorizations from your insurance carrier when needed. A representative from the Patient Access Department can be reached at 716-845-1049.

You and /or your insurance company will be responsible for charges related to the administration of drugs used in this clinical research study and for charges for medications that may be needed to prevent or control side effects.

If you develop complications or side effects from your participation in this clinical research study, medical treatment will be provided at the usual charge. A financial counselor can be reached at 716-845-3161 to provide an explanation of coverage and to answer questions you may have regarding study related billing.

10. <u>What happens if I am injured as a result of this study?</u>

If you believe you have been injured as a direct result of your participation in this research study, notify the Roswell Park Patient Advocate at (716) 845-1365 or the Study Doctor at (716) 845-7505.

Medical diagnosis and treatment for the injury will be offered, and a determination will be made regarding appropriate billing for the diagnosis and treatment of the injury. A financial counselor can be reached at 716-845-3161 to provide an explanation of coverage and to answer questions you may have regarding study related billing.

You do not give up any legal rights by signing this form. You are not prevented from seeking to collect compensation for injury related to malpractice, fault, or blame on the part of those involved in the research.

11. Will I be paid for joining this study?

You will receive no payment for taking part in this study.

It is possible that this research project may result in developing treatments, devices, new drugs, or procedures that could be used for commercial profit by the sponsor or other entities. If this happens, you understand that you will not receive any financial payment or share in any commercial profit for the use of your information and biospecimens (such as blood or tissue samples) collected as part of this research.

12. Where can I find more information?

You may call the NCI's Cancer Information Service 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.

For accurate cancer information including Physician Data Query (PDQ), visit https://www.cancer.gov.

13. Who do I contact with questions?

You are free to ask questions at any time about this study and to ask for more information from the doctor identified on this document. If you have any questions, concerns or complaints about this study, you should contact the study doctor identified on the first page of this document. In case of an emergency after regular hospital hours, you should telephone (716) 845-2300 and ask for the medical doctor on call.

If you have questions about your rights as a research subject or you feel you have been injured as a result of your participation in this research study, you can call the Roswell Park Patient Advocate (Support) Office at (716) 845-1365. You should also feel free to contact the Patient Advocate Office at any time while considering participation, during participation or once your participation is complete. This office is unaffiliated with any specific research study. They can help you obtain additional information regarding your research participation and your rights as a research subject or how to proceed should you feel you have been injured as a result of your participation. They are available to discuss any problems, concerns, questions or input you may have.

It may be necessary to contact you at a future date regarding new information about the medication or procedures that you have received. For this reason, we ask that you notify the Patient Access office at 716-845-1049 or stop at the Registration Desk in the Lobby of Roswell Park to update us of any change in your address.

CONFIDENTIALITY AND USE OF HEALTH INFORMATION

If you volunteer to take part in this research study, and you sign this document, you give permission to the study doctor and research staff to use or disclose (release) your health information that identifies you and is collected as part of the research study described in this consent. This means that others may know or be able to find out your identity, use your health information and share it with others. We want you to know who may use this information and how they may use it. We also want to tell you about your rights before you agree to take part in the study.

If you volunteer to take part in this research study, you consent to the release of your health information from other medical facilities for any moderate to life-threatening or fatal adverse events that occur while on study treatment through 90 days after treatment ends.

Who may see this information?

- Dr. Puzanov and all the members of the study/research team and other health care professionals at Roswell Park
- The Sponsor of this study, its' affiliates, successor companies, assigns, companies that may buy information from the Sponsor, and business collaborators, individuals and organizations working with the Sponsor and their representatives, including authorized study monitors, auditors and clinical research organization representatives
- Government or Regulating Agencies such as the FDA, DHHS, NCI, NIH or other agencies worldwide
- Government agencies that must receive reports about certain diseases and conditions
- Institutional Review Boards or Data Safety and Monitoring Boards at Roswell Park and its affiliates or outside of Roswell Park

What information may be collected, used and shared?

Health information that identifies you and relates to your participation in this study will be collected and created. This may include the following:

- Health information, sometimes known as "Protected Health Information" (PHI) can include your name; address, patient identification number; medical record number; date of birth; photographs; information about your health, including past medical history, treatment, diagnosis, test results and any other information about your health or medical condition; or about payment of charges for medical treatment found in your medical record or other records maintained by Roswell Park.

- Information from the procedures used to find out whether you are eligible to take part in this study. This may include physical examinations, blood and urine tests, x-rays and other procedures or tests, and any other information that you may release to us, including information about your health history.

- Information obtained in the course of the study including information about your response to any treatments you receive, information related to study visits and phone calls, physical examinations, blood and urine tests, genomic or genetic tests, x-rays and other procedures or tests, and any other information about your participation in this study.

Why will this information be used and/or shared?

PHI and other information that may identify you will be used and given out to others to carry out the research study. The sponsor will analyze (test) and evaluate the results of the study. The sponsor, its agents, assigns, government agencies, and others may visit the research site to follow how the study is being done and may review your information for this purpose.

This information may be given to the FDA. It may also be shared with other governmental agencies in this country and in other countries. This is done for participant protection and so the sponsor can receive marketing approval for any new products that may result from this research. The information may also be used to meet the reporting needs of the governmental agencies.

The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed (shared).

Your health information may also be stored in a research database or repository. This information may then be used for other research, either de-identified or identified, with or without further IRB review and approval. This information will be kept indefinitely.

What if I decide not to give permission to use and give out my health information?

If you refuse to authorize the collection, use and disclosure of your health information as indicated above, you will not be able to be in this research study.

Your decision not to sign this authorization or to withdraw from the study will not involve any penalty or loss of benefits to which you are otherwise entitled and will not affect your access to non-research related health care here.

What happens if I want to withdraw my authorization?

You may change your mind and revoke (take back) this authorization at any time, except to the extent that Roswell Park has already acted (used or disclosed health information) based on this authorization. To revoke/withdraw this authorization, you must write to the study doctor (name and address is on the first page of this form) and let the doctor know that you are withdrawing your authorization to use and disclose your information.

If you should die while enrolled in or after taking part in this study, your health information may be used or disclosed solely for research purposes without getting any added authorization.

The results of clinical tests or therapy performed as part of the research may be included in your medical record and will not be removed from the record if you withdraw.

If all information that does or can identify you is removed from your health information or biospecimens (such as blood or tissue samples), the remaining information or biospecimens will no longer be subject to this authorization and may be used or disclosed for other purposes, including use for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

May I review or copy the information obtained from me or created about me?

You will not have the right to review or copy aspects of your Protected Health Information (PHI) that are considered to impact the integrity (truthfulness) of this research study. At the end of this research study and at your written request, you may have access to your health information that relates to the research study. This information is kept in your medical record, which is a set of data that includes medical information or billing records used in whole or in part by your doctors or other health care providers at Roswell Park to decide about care and treatment. Access to your health information in your medical record is described in the Notice of Privacy Practices provided to you by Roswell Park. If it is necessary for your care and/or treatment, your PHI will be provided to you or your referring or primary care doctor. You will not have access to your blood, tissue, and diagnostic research study results that are performed in a laboratory/facility that is not approved to report clinical results.

If it is necessary for your care and/or treatment, your health information will be provided to you or your referring or primary care doctor.

When does this authorization end?

This authorization does not have an end date.

What happens to my health information after it is given to others?

If you sign this form, the health information collected from you and shared as indicated above, may be re-disclosed to third parties who are not subject to the same laws as those in the United States and may no longer be protected. There is a risk that your information will be given to others without your permission; however, the Sponsor also has protections in place to assure the security of your health information.

Authorization

As a participant in this study, you agree to allow the use of your health information for research purposes. You understand that your health information will be used/ disclosed by Roswell Park as indicated in this document. You understand that you have a right to withdraw your authorization for use of your health information in writing, but the information which has already been used or disclosed before your written withdrawal will continue to be used for research purposes. Finally, you understand your health information that has been disclosed by Roswell Park through this authorization to the study sponsor, government agencies, or others may be further disclosed by them, as the health information will no longer be protected by the federal privacy laws.

Statement of Investigator/Person Conducting the Informed Consent Discussion:

I certify that the nature and purpose, the potential benefits and possible risks associated with participation in this research study have been explained and that any questions about this information have been answered. A signed copy of this consent will be given to the participant.

SIGNATURE_____ **DATE**_____ **TIME**_____

PRINTED NAME_____

Participant's Statement of Consent:

By signing below, you agree that:

- You have been told of the reasons for this study.
- You have had the study explained to you.
- You have had all of your questions answered, including those about areas you did not understand, to your satisfaction.
- You have carefully read this consent form and will receive a copy of this form.
- You do **not** waive any **legal** rights you have under federal or state laws and regulations.
- You willingly give your consent to voluntarily join in this research study.

Participant:

SIGNATURE_____**DATE**_____ **TIME**_____

PRINTED NAME_____

Witness Signature is needed in the following circumstances – check below:

☐ Not Applicable
☐ The person consenting cannot write – mark must be made as appropriate.
☐ The person consenting cannot read - consent has been read to him/her.
☐ The person consenting cannot understand English and the consent has been verbally interpreted (The witness should be fluent in both English and the language of the person consenting).

Witness Statement:

The person consenting has signed this document in my presence.

SIGNATURE_____**DATE**_____**TIME**_____

PRINTED NAME _____

RELATIONSHIP TO PARTICIPANT_____

CONSENT HANDLING
Original to CRA-Regulatory with Race/ Ethnicity if applicable
Copy to:
- Patient
- Medical Records