Official Title	A Proof-of-Concept Study of Combination Therapy with INCMGA00012 (Anti–PD-1), INCAGN02385 (Anti–LAG-3), and INCAGN02390 (Anti–TIM-3) in Participants with Advanced or Metastatic PD-(L)1 refractory Merkel Cell Carcinoma
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University of Washington
Fred Hutchinson Cancer Center
RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE: A Study of Combination Therapy with INCMGA00012 (Anti-PD-1), INCAGN02385 (Anti-LAG-3) and INCAGN02390 (Anti-TIM-3) in Participants with Advanced or Metastatic PD(L)-1 refractory Merkel Cell Carcinoma (MCC)

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SUMMARY

You are being asked to take part in this research study ("Study") because you have advanced Merkel Cell Carcinoma (MCC) that has travelled to other parts of your body. Prior treatment with an immune-stimulating drug targeting PD-1 or PD-L1 did not work or has stopped working to treat your cancer.

Up to 20 people will take part in the study.

This study is being conducted at the University of Washington and Fred Hutchinson Cancer Center.

Take your time and read the information carefully and discuss it with anyone, including friends and family. If you have questions, please ask the Study Doctor or Study staff to answer them.

Things to know before deciding to take part in a research study:

- The main goal of a research study is to learn things to help patients in the future.
- The main goal of regular medical care is to use standard treatments to help each patient.
- Your participation in this Study is voluntary. You will be joining the Study out of your own free will, without any kind of pressure, and you may leave the Study any time you wish.

The decision to join or not join the study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will still continue to treat you.

- Parts of this study may involve standard medical care. Standard care is the treatment usually given for a certain condition or illness.
- Other parts of this study may involve experimental (investigational) drugs, or procedures that are being tested for a specific condition or illness. An investigational drug is one that has not been approved by the U.S. Food & Drug Administration (FDA) for the disease being studied.
- After reading the consent form and talking with the research staff, you should know which parts of the study are experimental and which parts are standard medical care. You should also know what parts you would receive even if you weren't in the study.
- Your medical records may become part of the research record. If that happens, your medical records may be looked at. They may also be looked at or copied by government agencies or other groups associated with the study.
- Your medical insurance may be billed for any standard medical care you receive during the study. If your insurance company is billed then it may have access to the research records. Insurance companies may not pay for treatment that is part of a study. Taking part in a study could affect your current or future insurance coverage.

If you take part in this research study, you will be given a copy of this signed and dated consent form.

PURPOSE OF THE STUDY

We are doing this study to find out how the study drugs work in subjects who have advanced MCC that has stopped responding to currently approved medications. We are studying the combination of three medications, which have been designed to help the immune system kill cancer cells. These three medications are: Retifanlimab or INCMGA00012 (Anti-PD-1), INCAGN02385 (Anti-LAG-3) and INCAGN02390 (Anti-TIM-3). Throughout this document, when combinations of INCMGA00012 (Anti-PD-1), INCAGN02385 (Anti-LAG-3) and INCAGN02390 (Anti-TIM-3) are mentioned, they will collectively be called "Investigational Agents."

You may be eligible for this study because your cancer did not respond or stopped responding to an immunotherapy drug that worked by targeting PD-1 or PD-L1 (including pembrolizumab, avelumab or nivolumab, drugs which are thought to be very similar to retifanlimab). Unfortunately, there are no FDA-approved drugs or other therapies yet shown to work for patients like you. We hypothesize that combining three drugs that all stimulate the immune system, similar to retifanlimab but with slightly different mechanisms, will slow down the growth of or even shrink your tumors. We also will be closely monitoring the safety of the Investigational Agents. Retifanlimab has been tested in MCC patients, but this will be the first time the other two drugs will be given to patients with MCC. All three of these agents have been tested in other patients with advanced cancers alone and in combination. Early studies show that these three drugs have similar types of side-effects as the anti-PD-1 or anti-PD-L1 drug you have already received, although there may be somewhat greater chance of developing side-effects with the combination. More details can be found in the "Risks and Side Effects" section below. Clinical trials are in process to fully assess the safety and anti-tumor effect of the Investigational Agents. The US Food and Drug Administration ("FDA") has not approved these agents for use as a prescription or over-the-counter medication.

PROCEDURES

Screening Phase
Before you begin any part of this study, we will ask you to review and sign this consent form. After signing this consent form, the study will begin with the screening phase. During this phase, we will do some tests and procedures to find out if you meet all the requirements to take part in this research study. These will have to be completed within 30 days of your first dose of the Investigational Agents.

Some of these tests and procedures may be considered part of your regular cancer care and would have been done even if you were not taking part in the research study. If you already had some of these tests and procedures done recently, they may not need to be repeated again. The Study Doctor will let you know what needs to be done. You may be asked to have more examinations and/or tests if the Study Doctor thinks they are necessary in order to ensure your safety and health.

It is possible that after the results of the screening tests are reviewed, you will not be considered eligible to take part in this study. If this happens, the Study Doctor will tell you the reasons for ineligibility. They will discuss other treatment options with you, as available.

Treatment Phase
If you are found to be eligible, you will enter the treatment phase. We will ask you to come to the clinic for study treatments. When you come to the clinic, we will perform tests and procedures. If you are able to continue taking part in the study, we will give you an infusion of the Investigational Agents. All subjects will receive the same Investigational Agents. There are no sham or placebo treatments in this trial.

The study treatment phase will be done in 2 parts:

Induction Phase: During this period, you will get treatment every 2 weeks. Two of the three Investigational Agents will be given once every 2 weeks; these include INCAGN02385 (Anti-LAG-3) and INCAGN02390 (Anti-TIM-3). The third drug, retifanlimab or INCMGA00012 (Anti-PD-1), will be given every 4 weeks. This phase of treatment will continue for a total of 24 weeks or approximately 6 months.

Maintenance Phase: During this period, you will get all three Investigational Agents once every 6 weeks. This phase of treatment will continue from 6 months up to 2 years total after starting the study treatments. Reducing the frequency of drug treatments has the potential to reduce their effect on controlling the cancer, though we think this is unlikely given our experiences with immunotherapy. Benefits to reduced frequency of visits include less travel and treatment time, which may improve your quality of life.

Tests and Procedures
These tests and procedures will be done at the screening visit and throughout the treatment period.

- We will review your medical history, including your cancer history.
- We will do a physical examination of major body systems.

- We will collect vital signs measurements including blood pressure, pulse rate, respiratory rate, and body temperature.
- We will collect blood for safety tests. We will test your blood to look at your kidney, liver, thyroid and adrenal function, and blood cell counts.
- We will collect blood for research tests periodically. This could help researchers better understand how the investigational agents work on your immune cells and against the cancer.
- The study doctors will discuss with you about two optional blood tests, called AMERK and circulating tumor DNA (ctDNA). Both these tests can help detect the presence of cancer in your body. These tests will be done at the time of the scans as described below. The results of this test can be used to help your study doctor learn more about the levels of cancer present in your body at different time points. These tests are considered optional tests and you can choose not to get it done.
- If you are a woman who is able to have children, we will test your urine or blood to see if you are pregnant. If you are pregnant, planning to become pregnant, or breastfeeding, it will not be safe to take part in this study.
- We will ask you how you are feeling, if your level of activity has changed, and if you have any side-effects from the treatment.
- We will review any medications that you take, including over-the-counter drugs, vitamins, and herbal products.
- We will look at places where your cancer is in your body. We will use one of the tests described below. Your Study Doctor will decide which test is best for you. These images will include your chest, abdomen and pelvis. If you have cancer in your head, neck, arms and legs, we may scan these areas too. The frequency of the scans will be every 8 weeks in the first 6 months followed by every 12 weeks up to 2 years.

    - Computed Tomography (CT) Scan: This is the most commonly used scan. This test uses a small amount of radiation (x-ray) to take pictures of the inside of your body. If can show a cross section, like a thin “slice” of your body, or it can show the body tissues and structures in “3-D”. For this test, the study doctor or staff may give you a contrast dye, either by mouth or injected into a vein with a needle. The study doctor or staff can tell you more about the contrast dye.
    - Magnetic Resonance Imaging (MRI) Scan: This test uses powerful magnets and radio waves to make pictures of body tissues and structures. During an MRI, you must lie on your back in the MRI scanner without moving. The inside of the MRI scanner is a tight space. You may have a contrast dye given by mouth or injected into a vein with a needle. The study doctor or staff can tell you more about the contrast dye.

We will collect a research biopsy of your tumor tissue to study cancer cells in the body. This procedure is a required part of the study, unless the Study Doctor thinks that it is unsafe or too challenging based on location of your tumor(s). This procedure will be done several times during the study. The first biopsy will be done during the screening phase to get a baseline sample. It will be repeated approximately 2 weeks after starting the treatment phase. A biopsy will also be done later in the study if your cancer starts growing. Studying your cancer cells will help the

researchers learn more about how the Investigational Agents work on the immune system and against the cancer cells.

Safety Follow-up
After receiving the last treatment in the study, you will have two "Safety Follow-up" assessments. These will take place approximately 30 and 90 days after you have finished taking the Investigational Agents. We will repeat some of the procedures listed above to make sure that you are not having delayed side-effects from the study treatments.

Long-Term Follow-Up
After completion of the treatment phases, the Study Doctor or staff will contact you once every 6 months up to 5 years total to assess your well-being and disease status. You likely do not need to come in person for these updates.

Disease Progression
If at any point on the study your tumor grows significantly in size, you will stop receiving the investigational agents. At that time, we will collect blood and tissue samples for research unless it is unsafe or not feasible, to help us understand why some cancers do not respond to this treatment**.**

Study Length
If you join this study, you will get the Investigational Agents for a maximum of 2 years or until your cancer is no longer responding to treatment. After completing the treatment, the study team will continue to contact you once every 6 months up to a total of 5 years after starting the study treatment.

The study doctor can remove you from taking part in the study at any time. This may happen if:

- They think it is in your best interest not to continue in the study.
- You are not able or willing to follow study procedures.
- You are pregnant.
- The whole study is stopped.

If you withdraw from the study for any reason, previously collected information would remain in the study records and would be included in the analysis of results. This information could not be removed from the study records.

RISKS AND SIDE EFFECTS

The side effects or risks of taking Investigational Agents:

- are not yet fully known and may vary depending on the disease you are being treated for and other medical conditions you may have.
- may have occurred in participants taking the Study Drug or might have been related to Study Drug.
- may go away after the Investigational Agents is stopped
- may be serious, long lasting, and/or permanent (such as nerve damage or Type 1 diabetes)

- may even cause death.

You will receive information from the Study staff:

- before your participation about all the known side effects/ risks.
- during your participation about any new information that may affect your willingness to continue to participate in the Study.

If you experience any side effects or have any other problems, you must immediately tell the appropriate Study staff or your Study Doctor. If you feel that your symptoms or side effects are life-threatening, call 911 right away or seek medical help immediately. Contact your study doctor when the medical emergency is over or as soon as you can.

Investigational Agents
Retifanlimab has been tested in many participants in other clinical studies, both as on its own as well as in combination with other drugs. INCAGN02385 and INCAGN02390 have been tested on their own in a small number of humans. Additionally, the combination of retifanlimab and INCAGN02385, and retifanlimab with INCAGN02385 and INCAGN02390 have been tested in very few humans. Therefore, **little is known about the risks of giving these compounds in combination.** The details of the risks of these drugs are listed below.

These compounds are drugs that works through the immune system; therefore, possible symptoms or side effects (called “adverse events”) that could occur may be immune-related effects such as inflammation of tissues of the skin (e.g., itching, redness, rash) or bowels (e.g., diarrhea), and fatigue or lack of energy. Because they are foreign proteins, they can also cause an allergic reaction when they are infused though this is rare. Many side effects are likely to go away after the Study Drug is stopped, or after some medical intervention. As seen with other immune therapies, there have been rare cases of serious, long lasting, and/or permanent side effects; some of which may even cause death.

If you experience any side effects listed below, or have any other problems, you must immediately tell the appropriate Study Staff or your Study Doctor so that you can receive the necessary treatment. If you do not understand what any of these side effects mean, please ask the Study Doctor or study staff to explain these terms to you. If you feel that these symptoms or side effects are life threatening, seek medical assistance immediately.

During your participation, you will be given any new information that may affect your willingness to participate in the Study. You should discuss the possible side effects with your Study Doctor.

Risk of Allergic Reaction
Sometimes people have allergic reactions to drugs. If you have a very bad allergic reaction, you could die. Some things that happen during an allergic reaction that could be a sign or symptom of a life-threatening allergic reaction (anaphylaxis) are:

- a rash
- having a hard time breathing
- wheezing
- a sudden drop in blood pressure (making you feel dizzy or lightheaded)
- swelling around the mouth, lips, throat, tongue, eyes and/or neck
- a fast pulse

- sweating
- a feeling of dread
- inability to breathe without assistance

If an allergic reaction occurs, it is likely to happen during your infusion or soon after your infusion is complete. You will be monitored by your Study Doctor after your infusion for signs of allergic reaction or other side effects. If you have signs or symptoms of an allergic reaction after you leave the clinic, you should get medical help and contact the Study Doctor or Study staff immediately.

Risks associated with Retifanlimab given alone
The risks (possible side effects) of taking retifanlimab are not yet fully known and may vary depending on the cancer you are being treated for and other medical conditions you may have. Therefore, you will be informed of the symptoms or medical events (called "side effects" or "adverse events" below) that have occurred in participants treated with retifanlimab only in clinical studies. During your time on the study, you will be given any new information about retifanlimab that becomes available which could affect your willingness to continue to participate in the study.

Retifanlimab works by helping your immune system to fight your cancer. However, retifanlimab can also cause your immune system to attack normal organs and tissues in your body and can affect the way they work, which can result in side effects. You should discuss the possible side effects listed below with your study doctor. Some of the side effects listed below occurred in participants taking retifanlimab but may not be caused by retifanlimab itself, but instead may be due to your cancer being treated, other ongoing illnesses, or other medications. Some of these side effects may be serious, life-threatening, long lasting, or permanent, and may lead to death. You may be given medications such as steroids to help with the treatment of these side effects.

The following side effects occurring in 727 participants treated with retifanlimab were as noted:

Very Common (occurring in ≥ 10% of participants); some may be serious (i.e., causing hospitalization, life-threatening, or may cause death)
• Anemia (low red blood cell count) which may make you feel tired and weak • Asthenia (lack of energy, weakness or poor physical condition) • Constipation • Decreased appetite • Diarrhea • Fatigue (extreme tiredness) • Fever • Itching (itchy skin) • Joint pain • Nausea • Urinary tract infection
Common (occurring in < 10 % and ≥ 1% of participants); some may be serious (i.e., causing hospitalization, life-threatening, or may cause death)
• Abdominal swelling • Abnormal taste

- Acute kidney injury (kidney problems) that may have either no symptoms or may cause decreased urine output, cause you to have blood in urine and/or may cause tiredness, shortness of breath, or swelling of legs, ankles and/or feet
- Bleeding in the rectum or vagina
- Blood in the urine
- Blurry vision
- Chills
- Colitis (inflammation of the bowels/gut) which may cause severe pain in your belly with loose or watery stools, and black, tarry, sticky stools or stools with blood or mucus
- Confusion
- Cough
- Decreased albumin (blood protein) which can cause swelling, weakness, or fatigue
- Decreased calcium which can cause weakness or cramping
- Decreased lymphocyte and/or neutrophil counts (white blood cells) which may have no symptoms but can make it hard for your body to fight infections
- Decreased magnesium which may cause weakness, muscle ramping, and/or abnormal heart rhythm
- Decreased phosphate which may cause muscle weakness, bone pain, confusion, and muscle breakdown
- Decreased potassium which may cause tiredness, muscle cramping and/or abnormal heart rhythm
- Decreased sodium which can cause nausea, vomiting, headache, confusion, loss of energy, irritability, muscle weakness, spasms or cramps, seizures and/or coma
- Dehydration
- Depression
- Difficulty sleeping (insomnia)
- Dizziness
- Dry mouth
- Dry skin or skin inflammation
- Eye redness and irritation
- Headache
- Herpes zoster (a viral infection) that can cause itchy skin rashes, fever and/or chills
- Hypertension (increased blood pressure) that can cause headache, anxiety and/or shortness of breath
- Hyperthyroidism (overactive thyroid gland) that may cause you to feel anxious and nervous, sick to your stomach, shaky, hot or sweaty, irritable, weak, have difficulty sleeping and/or lose weight or hair
- Hypothyroidism (underactive thyroid gland) that can make feel cold or tired, gain weight, be constipated, have dry skin or hair, lose hair and/or have muscle weakness, aches, tenderness or stiffness
- Increased amylase (enzyme or special protein made by the pancreas to help your body digest food) which may cause severe upper abdominal pain that is worse after eating, fever, loss of appetite, yellowing of the eyes or skin and/or rapid pulse
- Increased blood sugar which may mean you have diabetes

- Increased creatinine that indicates acute kidney injury that may have no symptoms or may cause muscle cramps, weakness, changes in frequency of urination and/or fluid retention
- Increased lipase (enzyme or special protein made by the pancreas that helps your body absorb fats) that may not cause any symptoms or may be due to signs of acute pancreatitis (inflammation to the pancreas) such as abdominal or back pain, fever, nausea, vomiting, loss of appetite and/or swelling of the abdomen
- Increased liver enzymes and/or bilirubin that indicate inflammation or damage to cells in the liver, which may cause pain or swelling in the abdomen, light headedness, weakness, nausea, poor appetite and/or jaundice (yellowing of the eyes or skin)
- Increased potassium which can cause heart problems
- Increased uric acid which can cause pain in the joints and decreased kidney function
- Inflammation of the lining of the stomach
- Influenza-like illness (flu-like illness)
- Infusion related reaction which may make you feel dizzy or faint, flushed, get a rash, have a fever and/or feel short of breath
- Low blood pressure
- Mouth sores
- Muscle pain or spasms
- Muscle weakness
- Pain in single or combined parts of the body including arms, abdomen, back, bone, groin, legs, neck, throat, and tumor
- Paresthesia or peripheral neuropathy (abnormal feeling of pins and needles) which may mean there is nerve damage
- Peripheral edema (swelling of lower legs or hands)
- Pneumonia (lung infection) which can cause fever, cough, shortness of breath, chest pain, chills, nausea and/or vomiting
- Pneumonitis (lung inflammation with possible difficulty in breathing)
- Protein in the urine
- Rash (such as rash all over the body, or rash that is itchy or looks like a flat, and/or red area on the skin that is covered with small merging bumps)
- Redness of the skin
- Shortness of breath
- Upset stomach or heartburn
- Vomiting
- Weight loss
- Weight increase

Uncommon (occurring in <1% and ≥0.1% of participants); some may be serious (i.e. causing hospitalization, life-threatening, or may cause death)

- Adrenal insufficiency (a condition where the adrenal glands found on top of each kidney do not produce enough “stress” hormones (such as cortisol) needed for bodily functions) which can cause fatigue, muscle weakness, loss of appetite, weight loss or abdominal pain
- Dermatitis (skin irritation) that may be itchy, be dry or is a rash on swollen, reddened skin

- Diabetic ketoacidosis causing increased thirst, frequent urination, lack of appetite, weakness, fruity scented breath, drowsiness and/or blurred vision
- Hepatitis (inflammation of the liver) or hepatocellular injury (liver injury) that may make you feel sick to your stomach and vomit, feel like not eating, feel tired, have a mild fever, have a pain in the right side of your belly, yellow eyes and skin, and/or dark urine
- Hypophysitis (inflammation of pituitary gland) which causes low levels of hormones produced by the pituitary gland that may cause decreased appetite, headaches, vision problems, thirstiness, tiredness, unexplained weight gain or loss, and/or sensitivity to cold
- Infection in the bile duct
- Interstitial lung disease (scarring and inflammation of the lungs) which makes the lungs be stiff and can make breathing difficult
- Iritis or keratitis (inflammation of the iris or cornea of the eye) that may cause eye redness, blurred vision, sensitivity to light, eye pain, see floaters and/or have headaches
- Muscle inflammation which may make you feel weak or have pain in the muscles
- Myocarditis (inflammation of the heart) that may cause your heart to have difficulty pumping blood throughout your body, which can cause chest pain, shortness of breath and/or swelling of the legs. You may experience a fast or irregular heartbeat that may cause dizziness or fainting.
- Nephritis (inflammation of the kidney) and/or kidney injury or failure so you may pass less urine or have cloudy or bloody urine, swelling and/or low back pain
- Palmar-plantar erythrodysesthesia syndrome (hand-foot syndrome) which can cause redness, swelling, and pain on the palms of the hands and/or the soles of the feet
- Pancreatitis (inflammation of the pancreas) which can cause pain or swelling in your upper abdomen with pain spreading to your back and include fever, nausea, vomiting and/or rapid heartbeat
- Pericarditis (inflammation of the sac around the heart) which can cause chest pain, fever, cough, or palpitations
- Polyarthritis (arthritis in multiple joints)
- Radiculopathy (pinching of a nerve root in the spinal column) and can cause pain, numbness, tingling, and/or weakness in the arms and legs
- Rash (includes different types of rash such as itchy rash or rash all over the body or rash that looks like a flat, and/or bumpy red area on the skin; and/or rash that may have bumpy areas with liquid or ulceration)
- Raynaud's phenomenon (disorder that causes blood vessels to turn red, pale, and then blue when exposed to cold)
- Severe blistering skin condition which may lead to loss of skin, usually caused by a drug reaction and can be life threatening
- Skin color loss or change
- Thyroiditis (inflammation of the thyroid gland, an organ that makes and stores thyroid hormones). This condition may cause changes in your heart rate, blood pressure, body temperature, and/or the rate at which food is converted into energy
- Tissue under the skin and over the muscle becomes swollen, inflamed, and thick
- Toxic skin eruption which is a rash caused by certain drugs

- Type 1 diabetes, a condition that can cause too much sugar in your blood, feeling thirstier than usual, frequent urination and/or weight loss. You may need to be given insulin shots
- Uveitis (inflammation of the uvea which is the pigmented layer of the eye) that may cause eye redness, blurred vision, sensitivity to light, eye pain, see floaters and/or have headaches
- Vocal cord paralysis (lack of control over the muscles that control your voice) which can make it hard to speak or breathe

Risks associated with INCAGN02385 given alone
As of 21-March-2022, 22 participants with advanced solid tumors have received INCAGN02385 given every 2 weeks at doses of up to 750 mg. Possible symptoms or side effects that have been reported to date in more than 10% of participants with human testing of INCAGN02385 are included in the table below.

Some of the side effects listed below occurred in participants taking INCAGN02385 but may not be due to INCAGN02385 itself; instead, they may be due to the disease being treated, other ongoing illnesses, or other medications.

Very Common (more than 10%) side effects observed in participants receiving INCAGN02385 alone:	
• Fatigue (extreme tiredness)	• Joint pain
• Cough	• Increased creatinine in the blood
• Decreased potassium in the blood	• Constipation
• Nausea	• Dyspnea (shortness of breath)
• Tumor pain	• Headache
• Anemia (low red blood cell count)	• Decreased sodium
• Pain in arms or legs	• Prolonged time for blood clotting
• Vomiting	• Protein in the urine
• Increased uric acid in blood	

In addition, some serious adverse events (a side effect that resulted in hospitalization or death, or otherwise required rapid reporting to Incyte Biosciences International Sàrl) occurred in patients given INCAGN02385, however no serious adverse events were observed in more than one participant.

One participant taking INCAGN02385 had an adverse event leading to discontinuation of study drug (transient ischemic stroke; not related to INCAGN02385).

Risks associated with INCAGN02390 given alone
As of 28-June-2022, 40 unique participants with advanced cancer have received INCAGN02390 given every 2 weeks at doses of up to 1600 mg. All participants had at least 1 side effect after treatment; those occurring in ≥ 10% of participants are presented in the table below.

Some of the side effects listed below occurred in participants taking INCAGN02390 but may not be due to INCAGN02390 itself; instead, they may be due to the disease being treated, other ongoing illnesses, or other medications.

Very Common (more than or equal to 10%) side effects observed in participants receiving INCAGN02390 alone:	
• Anemia (low red blood cell count)	• Diarrhea
• Back pain	• Tumor pain
• Fatigue	• Abdominal pain
• Abdominal pain	• Bone pain
• Headache	• Constipation
• Decreased sodium in the blood	• Dizziness
• Nausea	• Dyspnea (shortness of breath)
• Increased liver enzymes	• Hydronephrosis (enlarged kidney)
• Chills	• Pleural effusion (fluid between lungs and chest wall)
• Decreased appetite	• Pruritis (itching)
• Dehydration	• Fever
• Cough	

In addition, 18 participants had at least 1 serious adverse event. 1 participant died of multiple organ dysfunction syndrome due to disease recurrence which was considered not treatment-related. Six participants had at least 1 adverse event that led to study discontinuation (sepsis, acute respiratory failure, fluid collection in the lungs, irregular heartbeat, and abnormal vaginal openings). 4 participants had at least 1 adverse event due to increased activity in the immune system (insufficient adrenal hormones, low thyroid hormonal levels, kidney injury and skin rashes). 1 participant had an infusion-related adverse event (fever).

Risks Associated with Combination Therapy (INCAGN02385 + INCAGN02390 or Retifanlimab + INCAGN02385 + INCAGN02390)
As of 28-June-2022, 27 participants with different types of cancer have received INCAGN02390 in combination with INCAGN02385, or INCAGN02385 and retifanlimab. Overall, 19 participants (90.5%) had at least one side effect. Side effects occurring in ≥10% of patients are presented in the table below.

Some of the side effects listed below occurred in participants taking INCAGN02385 + INCAGN02390 or retifanlimab + INCAGN02385 + INCAGN02390 but may not be due to taking the drugs; instead, they may be due to the disease being treated, other ongoing illnesses, or other medications.

Very Common (more than or equal to 10%) side effects observed in participants receiving INCAGN02385 + INCAGN02390, or Retifanlimab + INCAGN02385 + INCAGN02390	
• Anemia (low number of red blood cells)	• Blood creatinine increased
• Diarrhea	• Chills
• Fatigue	• Nausea
• Fever	• Pain
• Abdominal pain	• Pain in arms or legs
• Joint Pain	• Tumor pain
• Back Pain	

INCAGN02385 + INCAGN02390
9 participants (90.0%) had at least one adverse event. 5 participants (50.0%) taking INCAGN02385 in combination with INCAGN02390 had at least 1 serious adverse event, but only one participant had a serious adverse event considered to be related to this study combination (inflammation of the blood vessels). 1 participant had a side effect that led to death, due to sepsis (an infection in the blood) as a result of COVID-19 and was not considered related to the study treatment.

Retifanlimab + INCAGN02385 + INCAGN02390
16 participants (94.1%) reported at least 1 adverse event. Three participants receiving the combination of retifanlimab + INCAGN02385 + INCAGN02390 (17.6%) had at least 1 serious adverse event (fluid collection in the heart, inflammation of the heart, inflammation of the lungs). 2 participants (11.8%) reported at least 1 adverse event due to increased activity in the immune system that led to study discontinuation (inflammation of the heart, inflammation of the lungs, and skin rash). These adverse events were related to this triplet combination. No participants given this triplet combination reported adverse events leading to death.

Pregnancy Related Risks/ Use of Birth Control
All of the risks to an unborn or a nursing child from the Investigational Agents are not and may harm the unborn or nursing child. **You cannot be in this study if you are pregnant, breastfeeding a child, are trying to get pregnant, or intend to father a child during the study.**

If you become pregnant during the study, you must tell the Study Doctor and stop the Investigational Agents immediately. If you are no longer pregnant and meet the treatment continuation period within 28 days of stopping the Investigational Agents, study treatment may be resumed after approval has been received from your Study Doctor. If you remain pregnant, your participation in this Study will end. The Study Doctor will report the pregnancy to Incyte Biosciences International Sàrl (drug manufacturer). The Study Doctor will ask to medically follow the pregnancy outcome and follow up to the first well-baby visit to monitor you and your child's safety.

Males: **If your partner becomes pregnant, you must notify the Study Doctor immediately.** The Study Doctor will report the pregnancy to Incyte Biosciences International Sàrl. The Study Doctor will ask your partner for her permission to follow her pregnancy until delivery and follow-up to the first well-baby visit to monitor your partner's and your child's safety. Your partner will be

provided with a separate consent form describing what information will be collected, why it is collected and how it is used, shared, and stored. It will also explain her rights. She does not have to provide this information if she does not want to.

You must take appropriate precautions to avoid pregnancy including donating oocytes (eggs) or to avoid fathering a child including donating sperm, from screening through 180 days after your last dose of the Investigational Agents. The Study Doctor will talk to you about the types of birth control that you can use while taking part in this study. They will help you select birth control that is the best choice for you. The study doctor will instruct you in correct use of your selected birth control methods. They will review your responsibility to use this birth control consistently and correctly at each visit.

Birth control methods, even when used properly, are not perfect. **If you or your partner becomes pregnant during the study, or you want to stop using birth control during the study, you should tell the study doctor immediately.**

Other Risks

Blood draws/ blood tests	Momentary discomfort, soreness, bruising, and in rare cases, infection at the draw site or excess bleeding; rarely light headedness or fainting.
Biopsy	Procedure risks (depending on location): Pain, bleeding, bruising, dizziness, scarring, and a small risk of infection. Side effects from numbing medication: Mild irritation where medication is applied. There may be additional risks depending on where your biopsy is performed. Your Study Doctor will discuss these additional risks with you.
CT scan	Contrast material risks: Allergic reactions (from itching/rash to allergic reaction (from mild itching/rash to severe difficulty breathing, shock, rarely death), and kidney problems (if dehydration or poor kidney function). Some of the tests that you will have in this research study will expose you to radiation. Everyone receives a small amount of radiation every day called “background radiation”. This radiation is natural and comes from space, air, water, soil, and the food you eat. Each year you are exposed to about 3 milliSieverts (mSv) of this background radiation. A milliSievert is a unit of radiation dose. For comparison, the estimated radiation dose from each of these tests is listed below. The risk to your health from this level of radiation exposure is too low to be detectable and may be nonexistent. • Chest CT: 7 mSv • Abdomen CT: 8 mSv • Pelvis CT: 6 mSv • CT Biopsy: 5 mSv
MRI	Enclosed space risks: Claustrophobia (fear of being closed in), nervousness, sweating, and loud sound. An MRI cannot be performed if you have metal in your body (eg, pacemakers, infusion pumps, aneurysm clips, metal prostheses, joints, rods, some implanted metallic or electrical devices, or plates). You need to tell your Study Doctor or Study staff if you have metal in your body.

Genetic Research Risks	The pharmacogenomics and biomarker research that may be performed using your tissue and blood samples may involve genetic testing. Procedures have been put into place to make sure that any results from genetic research cannot be linked to you. However, there is a possibility that information from your participation in this study could negatively affect you or your family in some way if a genetic disorder were discovered.

Since the study drug combinations are investigational, we don't know all of the risks of this treatment. It is important that you tell us about all symptoms and side effects that you have as soon as they happen, whether or not you think they are caused by the study treatment. The phone numbers for the study team are on the first page of this document.

BENEFITS

It is possible that your condition or health may improve because you are taking part in this study. However, there is no guarantee that you will benefit in any way. Your participation in this research may help future cancer patients.

ALTERNATIVE TREATMENT

It is important to speak with your Study Doctor about all of your treatment options prior to deciding to participate in this Study.

You do not have to join this study. You are free to say "yes" or "no". Your regular medical care would not change if you decide to say "no."

You may choose to have treatment with other cancer drugs or treatment methods. These options may include any current standard treatment for your type of cancer. Your study doctor will talk with you about alternate treatments available for your form of cancer. They will talk with you about the risks and benefits of the alternative treatments.

If you think you might prefer comfort care, please discuss this with your family, friends and your doctor. Enrollment in this study may exclude you from other research studies.

PAYMENT FOR PARTICIPATION

You will not be paid for participating in this Study. You may be reimbursed for your travel expenses for this Study.

COSTS

During your participation in this Study, standard medical care will be provided. You would not be billed for:

- The cost of the Investigational Agents (INCAGN02385, INCAGN02390, and INCMA00012). However, the cost of infusing the medications will be considered as regular medical care and billed to you or insurance.

- Research blood tests
- Research tumor biopsies

You may also have some extra costs, listed below. Your insurance company might pay these costs, but some insurance policies do not cover these costs. We could help find out whether your insurance company would cover these costs. The extra costs are:

- Cost of tests that are given more often than usual.
- Cost of standard doctor visits, the costs of giving you the Investigational Agents, scans, AMERK serology and ctDNA tests (if you choose to get them done) and blood testing for safety.
- Cost of any other medical care needed, including treatment of side effects because of this study.

COMPENSATION FOR INJURY

For a life-threatening problem, call 911 right away or seek help immediately. Contact your study doctor when the medical emergency is over or as soon as you can. For all other medical problems or illness related to this research, immediately contact the study staff listed below. They will treat you or refer you for treatment.

You or your health insurance will have to pay for the treatment. **The study team does not have funds to pay you for a research-related injury, added medical costs, loss of a job, or other costs to you or your family.** State or national law may give you rights to seek payment for some of these expenses. You do not waive any right to seek payment by signing this consent form.

You or your insurer will be billed for treatment of problems or complications that result from your condition or from standard clinical care.

SOURCE OF FUNDING FOR THE STUDY

The study team and/or the University of Washington is receiving the study drugs and financial support from the sponsor, Incyte Biosciences International Sàrl.

CONFIDENTIALITY

Your participation in this study will be noted in your UW medical record. A copy of this consent form will be placed in your medical record.

If you join this study, some people or organizations might need to look at your medical records and research records for quality assurance or data analysis. They include:

- Researchers involved with this study.
- Incyte Biosciences International Sàrl (the drug manufacturer) and their agents.
- Institutional Review Boards (IRB), including the Fred Hutchinson Cancer Center IRB. An IRB is a group that reviews the study to protect the rights and welfare of research participants.

- Fred Hutchinson Cancer Center and University of Washington
- Office for Human Research Protections, Food and Drug Administration, and other regulatory agencies as required.

We will do our best to keep personal information confidential. But we cannot guarantee total confidentiality. Personal information may be given out if required by law. For example, workplace safety rules may require health workers to contact you about lab tests. Or a court may order study information to be disclosed. Such cases are rare.

We will not use personal information in any reports about this study, such as journal articles or presentations at scientific meetings.

If you join this study, information about your participation would be made part of your permanent medical record. This information would include a copy of this consent form. If you authorize others to see your medical record, they would see a copy of this consent form.

How is my genetic information protected?
The Biological Samples that you provide will not be given or sold to anyone, nor will they be used for purposes other than the research described in this form.

A federal law called the Genetic Information Nondiscrimination Act (GINA) helps protect genetic information about people who join research studies. GINA restricts access to genetic information so that it cannot be used for health insurance coverage decisions. GINA prevents health insurance companies or group health plans from:

- Asking for genetic information obtained in research studies, or
- Using genetic information when making decisions regarding your eligibility or premiums

GINA *does not* help or protect against genetic discrimination by companies that sell life, disability or long term care insurance. ‘

WHAT WILL MY INFORMATION AND TISSUE SAMPLES BE USED FOR?

Your information and tissue samples (such as blood and cancer cells) will be used for laboratory studies by our team at the University of Washington and Fred Hutchinson Cancer Center. These studies will help researchers learn more about how the Investigational Agents and your cancer work.

During this study, if the researchers learn new information that may be important to your general health or to your disease or condition, they will share that information with you. There is a possibility that you may be asked to sign a new consent form if this occurs.

WILL MY INFORMATION AND TISSUE SAMPLES EVER BE USED FOR FUTURE RESEARCH?

After performing the studies planned above, there may be blood or tumor tissue left over. Researchers would like to keep your unused blood and tissue for future research to learn more about Merkel cell carcinoma. In the future, new tests may become available in areas such as genetics, molecular and cellular biology, or immunology to study the nature of disease. Your

samples will be stored for future research in a secure location at the University of Washington. Any test results or data gathered from this research in the future may not be available to you. If any discoveries, patents, or products come from these future tests, you will not have any rights to payment or given credit for them.

This choice is optional and is not required for you to participate in the treatment portion of the study. If you say "no," your tissue and information (even if made anonymous) will not be used in future research. If you choose to allow storage of your leftover samples, we will keep them for an unlimited period of time. If you decide you do not want to have your samples used for this research at a later point, you will need to contact the University of Washington in writing. We could not return donated tissue to you or your doctor, but we might be able to destroy the donated tissue.

FUTURE GENETIC RESEARCH DATABASES

Several genetic databases are available to help researchers understand different diseases. These databases contain DNA code and medical information from participants who have various diseases.

It is possible that in the future, genetic information may be available from the blood and tumor samples. In this event, we would like to release DNA code and information about your medical condition into a genetic database in order to help future research. The genetic database would not contain names, addresses, or other information that could be used to identify you.

The DNA code in a genetic database cannot be used by itself to identify any specific person. A researcher who already has DNA code about you could use information from a genetic database to learn more about you. Once we release information to a genetic database, we no longer have any control over the use of this information.

YOUR RIGHTS

Taking part in this study is your choice. You can change your mind and drop out (withdraw) at any time. If you do not to participate or decide to withdraw, there will be no penalty. You won't lose any benefits you receive now or have a right to receive.

The research study team will also tell you if we learn new information that could change your mind about taking part or continuing in this research study.

If you want to drop out, you need to tell the study team so that you end the study in the safest way. The study team will also talk to you about follow-up care, if needed. They will discuss the different withdrawal options and your responsibilities with you. The study doctor may ask you to have more tests for safety reasons. You may also be asked if you would agree to take part in the follow up portion of the research study. If you agree to continue with the follow up part of the study, we will continue to collect information about your health as described above.

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.

YOUR RESPONSIBILITY

If you join this study, you would have some responsibilities:

- Follow the schedule of study visits and procedures.
- Take study medications as directed.
- Prevent pregnancy
- Tell us about your side effects.

FOR MORE INFORMATION

If you have questions or concerns about this study, you could talk to your doctor anytime. Other people you could talk to are listed below:

If you have questions about:	**Call:**
This study (including complaints and requests for information)	206-606-2015 (Dr. Shailender Bhatia)
If you get sick or hurt in this study	206-598-6190 (Dr. Bhatia or Oncology Fellow on-call)
Your rights as a research participant	206-667-5900 or email irodirector@fredhutch.org (Director of Institutional Review Office, Fred Hutchinson Cancer Center) 206-543-0098 (Human Subjects Division, University of Washington)
Your bills and health insurance coverage	206-606-6226 (Patient Finance)

Emergency number (24 hours): 206-598-6190

Do not sign this consent form unless you have had a chance to ask questions and have gotten satisfactory answers.

If you agree to be in this study, you will receive a signed and dated copy of this consent form for your records.

CONSENT

I agree to allow samples of my blood to be collected for research testing for this study.

(Indicate initials next to your choice)

Yes _____ **No_____**

I permit my leftover samples to be stored and used for future Merkel cell cancer research.

(Indicate initials next to your choice)

Yes _____ **No_____**

Signatures

I have read this consent form (or it has been read to me). All my questions about the study and my part in it have been answered. I freely consent to be in this research study.

By signing this consent form, I have not given up any of my legal rights.

_____
Subject (age 18+) /Printed Name

_____ _____
Subject (age 18+) Signature Date

RESEARCHER'S STATEMENT

I have discussed the research study, including procedures and risks, with the person signing above. A copy of the signed consent form will be given to the participant.

_____
Name of Person obtaining consent (printed)

_____ _____
Signature of Person obtaining consent Date

---------- Use this witness section only if applicable ----------

If this consent form is read to the subject because the subject is unable to read the form, an impartial witness not affiliated with the research or investigator must be present for the consent.

If you were a witness for a participant who was not able to read this written consent form, sign below to indicate (1) you were present at the consent discussion in person, (2) you witnessed the verbal presentation of the written consent form, and (3) the participant had the opportunity to ask questions and agreed to take part in the study.

_____
Name of Impartial Witness

_____ _____
Signature of Impartial Witness Date

Copies to: Researcher's file
Subject
Subject's medical record (if applicable)