A Phase 1b/2 Trial of Dupilumab Given in Conjunction With PD-1 or PD-L1 Blockade and Anakinra in the Treatment of Relapsed/Refractory Metastatic NSCLC

PI: Thomas Marron
NCT05013450
Document Date: 7/8/2025

STUDY INFORMATION:

Study Title: A Phase 1b/2 trial of Dupilumab given in conjunction with PD-1 or PD-L1 blockade and Anakinra in the treatment of relapsed/refractory metastatic NSCLC

Study site(s): Icahn School of Medicine at Mount Sinai, Mount Sinai Hospital- Chelsea

Lead Researcher (Principal Investigator): Thomas Marron, MD PhD

Physical Address: Mount Sinai Hospital/Ruttenberg Treatment Center; 1470 Madison Ave, 3rd Floor, New York, NY 10029
Mailing Address: Icahn School of Medicine at Mount Sinai, Box 1079, One Gustave L. Levy Place, New York, NY 10029
Phone: 212-824-9472

Sub-Investigator Name: Nicholas Rohs, MD
Institution: The Blavatnik Family-Chelsea Medical Center at Mount Sinai
Address: 325 West 15th Street, New York, NY 10011
Phone: 212-367-0137

SUMMARY OF THIS RESEARCH STUDY:

This document explains a research study you might be interested in joining. Participation in the study is voluntary. You can agree to join or not. Your decision will not limit your ability to receive care at Mount Sinai. You should only agree to take part if you understand the study and if all of your questions about the research study are answered. If you do join the study, the research team must share any new information with you that may change your mind about taking part.

The purpose of this research study is to test whether the use of three medications- dupilumab, anakinra, and the cancer immunotherapy you have already received are able to control cancer when given in combination. While all three of the medications are approved by the FDA, dupilumab and anakinra are not approved for treating cancer, and the combination of these three types of drugs has never been studied (or FDA approved) for the treatment of cancer. To be a candidate for this trial, you have to have a diagnosis of metastatic lung cancer, meaning lung cancer that cannot be cured with surgery or radiation, and have already received an immunotherapy—a medication that activates the immune system with the goal of killing cancer—that targets PD-1 or PD-L1. These are standard therapies used to treat cancer that take the breaks off the immune system, activating the immune system to recognize cancer as something foreign to the body and attacking it. Most commonly the standard FDA-approved immunotherapies used are pembrolizumab (Keytruda) or durvalumab (Imfinzi), though there are many

different similar medicines available that are given as a standard (FDA approved) therapy. If your cancer has returned after having used immunotherapy, or if it never disappeared and is now growing, this trial will look at adding two new medications to this standard immunotherapy (the drugs targeting PD-1 or PD-L1) that you have previously received. The goal of this is to see if the addition of two additional therapies, dupilumab (Dupixent) and anakinra will result in control or shrinkage of your tumor.

Dupilumab (Dupixent) is an FDA approved medication for the treatment of severe asthma, atopic dermatitis (or eczema), and chronic sinusitis. Based on some studies in mice, it appears that this drug given for allergic conditions may also help the immune system eliminate lung cancer. However, until recently this drug has never been specifically tested in participants with lung cancer who are receiving immunotherapy. A trial that is completed in which dupilumab was given to patients such as you, who have progressed on standard lung cancer immunotherapy, demonstrated that some—not all—patients had their tumors shrink or stop growing. In this trial, you will receive three injections of dupilumab while you receive standard lung cancer immunotherapy.

Anakinra is an FDA approved medication for the treatment of multiple inflammatory conditions like rheumatoid arthritis and rare conditions in patients with genetic defects causing excessive inflammation, and is commonly used for other conditions like gout, inflammation of the lining of the heart (known as pericarditis), and even COVID-19. However, anakinra has never been specifically tested in participants with lung cancer who are receiving immunotherapy. In this trial, if you are enrolled into Cohort B, you will be taught on the first day how to inject this drug at home, and will be provided with pre-filled syringes that you will take home and keep in the refrigerator that you will inject daily for four weeks (28 days).

If you choose to take part, you will be asked to:

- Take study drugs as directed
- Complete all visits associated with this study
- Follow your study doctor’s and nurse’s instructions
- Notify the study doctor and/or study staff of any changes that you may experience in your health (side effects)

If you choose to take part, there may be risks to taking part in this study from the study drug or from some of the procedures or tests done in this study. Also, your condition may get better but it could stay the same or even get worse. The risks dupiumab and anakinra present are described in detail later in this document.

You will not benefit directly from taking part in this research. The potential benefits of using the study medicines are still unknown. However, the information gained on this approach and how it works may help the understanding of treating cancer in the future.

If you take part in this study, you should tell the study team immediately if you have any unusual health problems, injuries, or side effects, even if you do not think these problems are caused by the study or by the study drug.

If you are interested in learning more about this study, please continue to read below.

STUDY PARTICIPATION:

You may qualify to take part in this research study because have Non-small lung cancer

Your participation in this research study is expected to last 2 years.

There are 42 people expected to take part in this research study at Mount Sinai Hospital The first 21 participants were enrolled into Cohort A and received only the dupilumab injections alongside continuing standard immunotherapy. The next 21 patients—you will be part of this cohort—will be enrolled into Cohort B that receive both dupilumab and anakinra. 11 people will be enrolled at Mount Sinai Hospital and 10 people at the Blavatnik Family-Chelsea Medical Center at Mount Sinai.

The new treatments in this trial, the dupilumab and anakinra, will be administered over the course of ~6 weeks. You will have your first imaging done after starting therapy to see how your cancer is responding about 9 weeks after starting the new treatment. If your cancer is responding (if it is not growing, or if it is shrinking) then you will continue your standard immunotherapy (the PD-1 or PD-L1 antibody you had previously received) for up to 2 years, which is the standard clinical recommendation. Your oncologist will continue to follow your clinical course for up to 5 years.

Funds for conducting this research study are provided by Icahn School of Medicine at Mount Sinai.

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

DESCRIPTION OF WHAT IS INVOLVED:

If you agree to take part in this research study, here is what may be involved:

Screening: You must meet the requirements to be in this study and sign this informed consent form to begin.

- Screening will be performed within 28 days prior to starting the trial to determine eligibility.
- You will discuss your current and past health with the study doctor/staff.
- The study doctor/staff will take your blood pressure, pulse, breathing rate, body temperature and measure the level of oxygen in your blood.
- The study doctor/staff will discuss current and past medications you have taken/are taking

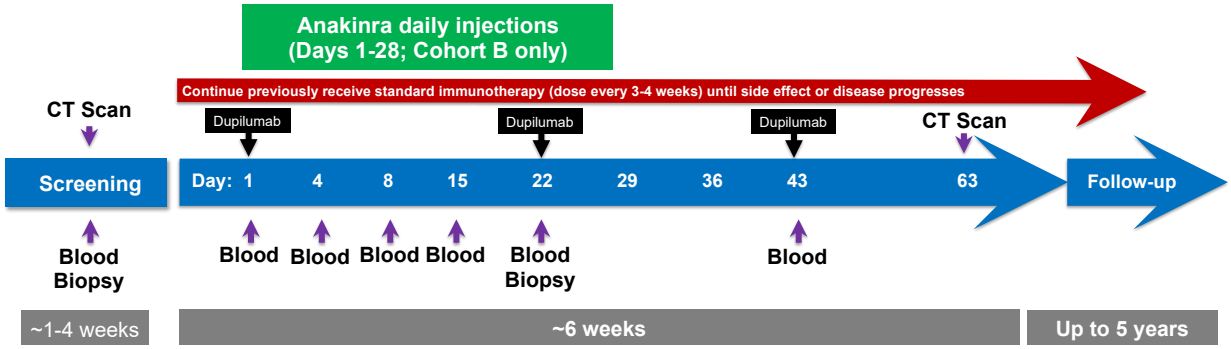
Biopsy(post treatment):

You will undergo core needle or forceps/excisional biopsy during the screening period and at around 4 weeks from the time you start treatment. This tissue will be transported to the Human Immune Monitoring Core (HIMC) where it will be analyzed.

Blood Draw:

The study doctor/staff will draw blood from a vein in your arm, approximately 100mL, or approximately 7 tablespoons, at multiple time points as noted in the figure below.

Treatment



The schematic above shows the treatment schedule for the clinical trial. You will be continued on standard immunotherapy if you are still taking it, or if you had stopped the immunotherapy you had received previously you will be started on pembrolizumab, a standard immunotherapy used for lung cancer participants with metastatic lung cancer on Day 1 (this medication is typically given every 3 weeks). Day 1 denotes the first day you will start the new medicine; you will receive an injection into your skin (subcutaneous) of the dupilumab on Days 1, 22 and 43. For participants in Cohort B, which you will be enrolled in, in addition to the dupilumab you will be treated for 28 days with anakinra. On the first day the research team will teach you how to inject this drug at home, and they will provide you with pre-filled syringes of the anakinra that you will take home and store in your refrigerator. You will inject yourself once a day with the anakinra.

Three weeks after the last dupilumab you will undergo imaging (typically a CT scan or a PET/CT) to determine how your cancer has responded to therapy. You will discuss with your oncologist the next treatment steps at this point: for most participants if your cancer is stable (not growing significantly) or shrinking you will continue the standard immunotherapy, which is most often given for up to 2 years. If the cancer is growing you will discuss with your oncologist at that point whether to try a different therapy. All subsequent treatment and imaging will be done as per the standard care a lung cancer patient receives, and will not be part of a clinical trial, however, your doctor will continue to follow your progress to know how you have responded to the dupilumab over the long-term.

Study calendar: below is a schedule of the activities described above. D1 represents the first day of the clinical trial when you will receive the first dose (injection) of the dupilumab.

	Screening	D1	D4	D8	D15	D22	D29	D43	D63
Informed Consent	X								
Medical history	X								
Physical exam	X	X				X		X	
Side effect evaluation	X	X				X		X	
CT scan or PET/CT	X								X
Standard blood test	X	X				X		X	
Tumor biopsy	X						X		
Research blood draw	X	X	X	X	X	X		X	
PD-1 or PD-L1 blockade (Standard)		X				X		X	
Dupilumab injections		X				X		X	
Anakinra		X (Days 1-28, daily injection)							

- Because this research study involves the use of study drugs, a note must be included in your electronic medical record that you are taking part in the research. This way, anyone involved in your medical care will know that you are a study participant, and they can work to avoid any problems or negative outcomes that could arise if they do not know.

Pregnancy

If you can possibly get pregnant, a blood test for pregnancy will be done before you begin the study.

You cannot be included in the study if you are or become pregnant, as the study drug could harm your fetus. You also should not be in the study if you are producing milk to feed a child as the study drug could harm your baby.

Unless you are at least one year past menopause or have had a successful operation to make pregnancy impossible, you should use effective birth control. Unless you are sexually abstinent (not having genital sex) the recommended methods of birth control are:

- The consistent use of approved hormonal birth control (pill, patches, or rings),
- An intrauterine device (IUD),
- Contraceptive injection (Depo-Provera),
- Double barrier methods (Diaphragm with spermicidal gel or condoms with contraceptive foam),
- Sexual abstinence (no sexual activity),
- Sterilization (a vasectomy, getting tubes tied, or a hysterectomy).

All birth control methods (other than abstinence and sterilization) are only effective if you use them properly, start them at least one month before you begin the research study, and continue using them

throughout the research study and for one month after the research study ends. If you are unsure whether the method of birth control you use is approved to use while you are in this study, you should ask the Lead Researcher before you begin the study. If you are less than one-year post-menopausal, you could still become pregnant. If you or your partner becomes pregnant, or may be pregnant, at any time, you must tell a person from the research team immediately. The team may stop the study drug and refer you/your partner to an obstetrician/gynecologist for follow-up.
Should you/your partner become pregnant, whether or not you/your partner have the baby, the people funding and overseeing the research may ask for information on the pregnancy, even if you are no longer part of the study. You/your partner will be asked for additional written consent to share this information if that happens.

Semen/Sperm:

Drugs can be found in semen and alter sperm. Since you are taking part in a study using experimental drugs or treatments, it is recommended that 1) you use a condom, 2) you do not get a partner pregnant or expose them to semen, and 3) you do not donate semen. These recommendations apply both while you are taking the study drug, and for 3 months after you stop taking the study drug. This is because levels of the study drug may be present in the sperm and/or semen even after you stop taking the study drug. You are encouraged to tell your partner(s) and/or their doctor(s) that you are participating in this clinical trial.

Future Contact:

The researchers may wish to use your personal contact information to contact you in the future. Do you give the researchers permission to **contact you** in the future to request the collection of additional information about you, discuss how your private information, study data and/or samples might be used, or discuss possible participation in another research study?

Please initial your choice: Yes_____ No_____

If “Yes”, please indicate your preferred method of contact: (initial all that apply)

[ ] Email [ ] Phone [ ] Letter [ ] Text

USE OF YOUR DATA AND/OR SAMPLES:

The research team will never use or share your personal information (such as, name, address, date of birth, social security number), study data and/or samples (blood, tissue, urine, saliva, or any other body matter) that are collected as part of this study for future research, even if your identity is removed. Your data and/or samples will only be used to complete this study and then they will be destroyed.

(1) Will you allow the researchers to store your data and/or samples to use in future research studies?

Please initial your choice: Yes_____ No_____

If you select No, please stop here and move to the next section, **'Your Responsibilities If You Take Part in This Research**' section below."

If yes, please continue to the next question and tell us how your personal information, study data and/or samples may be used in future research studies.

(3) Do you give the researchers permission to keep the data and/or samples, so they could use them in future studies that are **directly related** to the purpose of the current study?

Please initial your choice: Yes_____ No_____

(4) Do you give the researchers permission to keep the data and/or samples indefinitely, so they could use them for future studies that are **not related** to the purpose of the current study (for example a different area of research)?

Please initial your choice: Yes_____ No_____

(4.1) From time to time, researchers outside of medicine and related sciences would like to use data and/or samples. This might be in the fields such as anthropology, human origins, mapping human migration patterns. Do you give permission for researchers **outside the field of medicine** to use your data and/or samples?

Please initial your choice: Yes_____ No_____

a. If the future research in a different area can be done without having to know that the data and/or samples came from you personally, that will be done.
b. If the future research in a different area requires that it is known specifically who the data and/or samples came from, then one of the following will be done:

I. If you allowed the researchers to contact you in the future, they may be able to contact you to explain why your data and/or samples is needed and what will be done with it. Your permission will be asked to use your data and/or samples in that research project.
II. If you do not give permission to be contacted in the future, or if it is found that contacting you is not practical (for example, because you have moved), your data and/or samples may still be used. The Institutional Review Board (IRB) will be asked for permission to use the data and/or samples linked to your identity. The IRB can give permission for researchers to use and share identifiable health information without contacting you, but only if it determines that sharing the data and/or samples will not be more than minimal risk to you or your privacy. The IRB is a committee of doctors and scientists and nonscientists, including people not associated with this hospital or medical school, whose job it is to protect people who participate in research.

(5) Do you give permission to have your data and/or samples given **to other researchers,** including those at Mount Sinai, other medical or scientific institutions and for-profit companies, for use in research within the limits you have chosen above?

Please initial your choice: Yes_____ No_____

YOUR RESPONSIBILITIES IF YOU TAKE PART IN THIS RESEARCH:

If you decide to take part in this research study, you will be responsible for the following things:

- Attending all study visits
- Taking prescribed medications and avoiding certain medications (the study team will tell you
- what drugs to avoid and how to self-inject Anakinra).Using birth control methods as described in the Description of What's Involved section.
- You must be willing to follow study procedures and report any changes in your health that occur during the study, even if you do not think the changes in your health are related
- While participating in this research study, you should not take part in any other research project

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

There may be costs to you for taking part in this study.

Taking part in this research study may lead to added costs to you. You or your insurance company will be responsible for the costs of all items and services during the research study which you would have received for your condition if you were not enrolled in this research study. You or your insurance company will also be responsible for the costs of all services that occur during the research study that your physician believes are medically necessary to treat you. If you are uninsured, you will be billed or them. You or your insurance company will not be responsible for the costs of the items and services

associated with this research study (e.g., study drugs) which are provided to you only for research purposes and not to treat your condition. You will not be reimbursed for your travel to and from Mount Sinai or the expenses associated with travel. You will not receive money or any other form of compensation for participating in this study.

POSSIBLE BENEFITS:

This study is not designed to benefit you personally.
It is important to know that you may not get any benefit from taking part in this research. Others may not benefit either. However, because people respond differently to study treatments and because the study drugs are experimental, no one can know in advance if you will benefit. It is possible that your condition may worsen while on study treatment. The potential benefits of using the study medicines are still unknown. However, the information gained on this approach and how it works may help the understanding of treating cancer in the future.

POSSIBLE RISKS AND DISCOMFORTS:

The study doctor and research staff will monitor you to see if you have side effects.

However, your doctors do not know all the side effects that may happen, and there may be unknown side effects that could occur with this new combination of medications. Side effects can vary from mild to very serious, and there is also a risk of death. The study doctor may give you drugs to help lessen side effects that you experience. In some cases, the duration of side effects may be unknown. Depending on the stage of your disease, it is possible that you may be cured of your cancer with surgery alone. You have the option to go directly to surgery and not participate in this clinical trial.

If you experience side effects that require treatment between regular clinic/hospital visits, it is important that you make every effort to inform Mount Sinai. Some medications may interact with the study drug and with the other medications you will be taking in this study. Because of this, it is important to tell the research staff about any medications you are taking and to check with the research team before starting any new medications.

This trial involves continuation of an immunotherapy targeting PD-1 or PD-L1, and you have already received one of these medications; however, there is always the possibility of a toxicity to still occur. Additionally, this medication has not been studied when given in conjunction with the dupilumab. Below is a list of the common and uncommon side effects of the PD-1 or PD-L1 antibodies. This information is based on data from cancer participants in other clinical trials with PD-1/PD-L1 blocking antibodies such as pembrolizumab (Keytruda) or durvalumab (Imfinzi). In addition, there may be side effects that are not yet known that may occur. You should tell your doctor or nurse right away about any possible side effects you experience.

Most common side effects of PD-1/PD-L1 blocking antibodies such as pembrolizumab (Keytruda) or durvalumab (Imfinzi) (more than 10% of participants) They are grouped by location felt in the body
GENERAL
Feeling tired or lack of energy
SKIN
Rash
Itching
STOMACH & ABDOMEN
Diarrhea

Common Side Effects of PD-1/PD-L1 blocking antibodies such as pembrolizumab (Keytruda) or durvalumab (Imfinzi) (less than 10% of participants): They are grouped by location felt in the body
GENERAL
Dizziness or lightheadedness
Vertigo (feeling off balance which can lead to dizziness)
Chills
Headache
Fever
Low levels of sodium in the blood
Low platelet counts (thrombocytopenia): this may increase your risk for skin bruising, nose bleeds, and bleeding from the gums
Low red blood cell counts (anemia): this may make you feel weak and tired
Increased blood sugar
Reaction related to infusion of the medicine. The symptoms may include but not limited to fever, rash, pain, swelling
Allergic reaction/hypersensitivity (allergy)
SKIN
Dryness
Redness
Loss of color from areas
HANDS, FEET, ARMS AND LEGS
Swelling
Tingling, burning, numbness or weakness
MUSCLES AND BONES

Swelling
Pain in the muscles, bones, ligaments, tendon, and nerves
Abnormalities in bones *(determined by an increase in alkaline phosphate test (ALP))*
STOMACH AND ABDOMEN
Constipation
Stomach pain
Decreased appetite
Feeling sick
Vomiting
Inflammation of the colon (*which may include stomach pain, cramping, diarrhea, etc.*)
Inflammation of pancreas *(determined by an increased amylase and/or lipase)*
Abnormal liver function *(determined by an increase in AST or ALT enzymes, or increase in alkaline phosphate test (ALP))*
Abnormal kidney function *(determined by an increase in creatinine)*
Increase in bilirubin (liver function test) which could indicate abnormal liver function.
HEAD AND NECK
Dry mouth
Swelling of face
Inflammation of the mouth *(which may include canker sores, cold sores, flu-like symptoms, etc.)*
Thyroid gland function decreased or may be increased; increased thyroid stimulating hormone - a lab test result associated with abnormal thyroid function
CHEST
Lung inflammation (pneumonitis): it is possible that PD-1 or PD-L1 blocking drugs may cause inflammation of the tissues of the lung. This adverse effect has been reported in participants treated with PD-1/PD-L1 blocking antibodies such as pembrolizumab (Keytruda) or durvalumab (Imfinzi). While many participants with X-ray or CT abnormalities have not developed any symptoms, some participants have developed mild to severe symptoms and in rare cases, death has occurred as a result of their lung inflammation. Signs and symptoms of lung inflammation may include difficulty breathing, pain or discomfort while breathing, chest pain, cough, shortness of breath, increased rate of breathing, fever, low blood oxygen levels, or fatigue
Cough
Shortness of breath

Uncommon Side Effects of PD-1/PD-L1 blocking antibodies such as pembrolizumab (Keytruda) or durvalumab (Imfinzi) (less than 1% of participants): They are grouped by location felt in the body
GENERAL

Diabetes
low blood pressure
Pemphigoid: blistering of the skin or mouth caused by the immune system attacking healthy tissue
Joint pain and stiffness
High blood pressure
Dehydration
Low white blood cell counts (neutropenia): these put you at higher risk for infection
Difficulty falling and/or staying asleep (Insomnia)
SKIN
Hives
Skin disease with thickened patches of red skin, often silvery scales (Psoriasis)
Erythema multiforme: a skin disorder that's considered to be an allergic reaction to medicine or an infection. Symptoms may include symmetrical, red, raised skin areas that can appear all over the body, more noticeable on the fingers and toes. These patches often look like "targets" (dark circles with purple-grey centers)
STOMACH AND ABDOMEN
Decreased secretion of hormones produced by adrenal glands
Decreased thyroid stimulating hormone – a lab test result associated with abnormal thyroid function
Inflammation of the kidney, pancreas, and/or stomach
Inflammation of the liver
Kidney function failure, kidney disease
HEAD AND NECK
Dry eye
Hair Loss
Underactive function of the pituitary gland situated at the base of the brain
Inflammation of the thyroid gland
Inflammation of the eye
Blurred vision
CHEST
Bronchitis
Increased heart rate
Abnormal heart rhythm
Respiratory failure: a condition in which not enough oxygen passes from your lungs into your blood, or when your lungs cannot properly remove carbon dioxide
Upper respiratory tract infection: a common viral / bacterial infection that affects the nose, throat,

and airways

Rare Side Effects of PD-1/PD-L1 blocking antibodies such as pembrolizumab (Keytruda) or durvalumab (Imfinzi) (less than 0.1% of participants). They are grouped by location felt in the body
GENERAL
Autoimmune hemolytic anemia: a malfunction of the immune system that produces autoantibodies, which attack red blood cells as if they were foreign substances to the body
Severe allergic reaction may include but not limited to high grade fever, rash, swelling and pain
Inflammation of the heart
Damage to the protective covering of the nerves in the brain and spinal cord
Diabetes complications resulting in excess blood acids
Sarcoidosis, a disease involving abnormal collections of inflammatory cells (granulomas) in organs such as lungs, skin, and lymph nodes
Histiocytic necrotizing lymphadenitis or Kikuchi lymphadenitis: disorder of the lymph nodes which causes the lymph nodes to become enlarged, inflamed and painful, commonly affecting lymph nodes of the neck and possibly associated with fever or muscle and joint pains.
Drug induced liver injury
Polymyalgia rheumatica
Disease caused by the body's immune system attacking healthy organs
CHEST
Lung infiltrates, associated with infection or inflammation
Pericarditis: a swelling and irritation of the thin saclike membrane surrounding the heart (pericardium)
SKIN
Acne-like skin condition resulting in redness of face (Rosacea)
Inflammation of blood vessels
Toxic epidermal necrolysis: a potentially fatal disease characterized by blistering and peeling of the top layer of skin resembling a severe burn
Stevens Johnson syndrome: inflammatory disorder of skin and mucous membranes, resulting in blistering and shedding of skin
STOMACH AND ABDOMEN
Rupture of the intestine/hole in the intestine
HEAD AND NECK
Double Vision
Inflammation of the brain, potentially life threatening of fatal

Myasthenic syndrome (neurologic syndrome characterized by muscle weakness) including myasthenia gravis, a nerve disease that may cause weakness of eye, face, breathing, and swallowing muscles.
Inflammation of the lining of the brain and spinal cord
Cranial nerve disorder
MUSCLES AND BONES
Guillain-Barre syndrome, an autoimmune disorder associated with progressive muscle weakness or paralysis
Rhabdomyolysis: muscle fiber released into the blood stream which could damage your kidneys
Muscle Inflammation

Dupilumab (Dupixent) is a drug used typically to treat asthma, atopic dermatitis or other allergic conditions. It has not been studied when given in combination with cancer immunotherapy, such as you have already received. Below is a list of the potential side effects seen with long-term administration of this drug. Please contact your physician immediately if you experience any of the symptoms listed below, or any new symptoms of any sort while on this new combination of medications.

Most common side effects of dupilumab (more than 10% of participants):
Antibody development (against the drug)
Irritation at the site of injection
Common Side Effects of dupilumab (Dupixent) (less than 10% of participants):
Insomnia
Oral herpes simplex infection (activation of viral infection causing sores on mouth)
Gastritis (stomach pain)
Toothache
Eosinophilia (rise in the number of eosinophils in the blood)
Herpes simplex infection (can cause an infection in other areas such as your brain)
Joint ache
Eye irritation
Mouth pain

Uncommon Side Effects of dupilumab (Dupixent) (less than 1% of participants):
Anaphylaxis (severe life-threating allergic reaction)
Dry eye syndrome

Eosinophilic granulomatosis with polyangiitis (a condition in which the immune system is activated in varying parts of the body causing inflammation in blood vessles and organ damage)
Erythema nodosum (a type of skin inflammation causing a painful rash)
Eye inflammation (keratitis)
Serum sickness (an allergic reaction to a new drug that can cause symptoms making you feel ill like you have a virus
Significant cardiovascular events, such as a heart attack
Vasculitis, which is a term referring to inflammation of blood vessels that can cause pain or organ damage

Anakinra is an drug typically used to treat inflammatory conditions like rheumatoid arthritis and rare conditions in patients with genetic defects causing excessive inflammation, and is commonly used for other conditions like gout, inflammation of the lining of the heart (known as pericarditis), and even COVID-19. It has not been studied when given in combination with cancer immunotherapy, such as you have already received, nor with dupilumab. Below is a list of the potential side effects seen with longer-term administration of this drug. Please contact your doctor that is treating you immediately if you experience any of the symptoms listed below, or any new symptoms of any sort while on this new combination of medications.

Most common side effects of anakinra (more than 10% of patients receiving long-term treatment for inflammatory conditions):
Abnormal liver function (determined by an increase in AST or ALT enzymes, or increase in gamma-glutamyl transferase(GGT))
Vomiting
Infection
Injection site irritation
Headache
Muscle or joint aches
Fever
Common Side Effects of anakinra (less than 10% of participants):
Rash
High potassium or sodium in the blood
Constipation

Low white blood cells
Anxiety
Hypothermia (low body temperature)
Kidney injury

Uncommon Side Effects of anakinra (less than 1% of participants):
A new blood cancer (melanoma or lymphoma)
Elevated cholesterol

Please inform your study doctor or nurse IMMEDIATELY if you experience any of the following:

- Any new or increased shortness of breath;
- Any new or increased chest pain;
- Any new or increased pain/difficulty while breathing;
- Any new or increased cough or any significant change in your type of cough; for example, any new or increased mucous or blood in your cough;
- Any change in the amount of oxygen you require;
- Any fever, fatigue, or other symptoms that occur at the same time as any changes to your breathing or other lung symptoms.

If you start to develop symptoms, your study doctor will ask you to return to the clinic for additional tests, which could include a physical exam, measurement of oxygen levels, blood tests, chest x-rays, and/or CT scans. You will be monitored very closely for changes in your overall lung symptoms, monitoring may require hospitalization. You may require specific treatment in order to control pneumonitis. You may also be seen by a special doctor called a pulmonologist, who has special training to be an expert in how your lungs work. Prolonged treatment with medicines that suppress inflammation, sometimes needed to manage the side effects of cancer immunotherapy, may lower your body's ability to fight off certain infections. These infections may require treatment with antibiotic or antifungal medications and may be fatal.

In addition to these risks, this research may hurt you in ways that are not known. The unknown risks might be minor or might be major (death).

Reproductive Risks

There are unknown risks from the medications you will receive *to the development of the fetus. Therefore, if you are a woman who is able to become pregnant, you should not become pregnant during treatment with these medicines and for 180 days after completing study treatments. If you are able to become pregnant, in order to participate in this study, you must agree to use birth control to prevent pregnancy. Men with female partners who are able to become pregnant also have to use condoms during the treatment with these medicines and for 180 days after completing study treatments. Please*

read the acceptable methods of birth control found under the Description of What's Involved section of this document.

Risk of Core Needle Biopsy: *Risks of biopsy are infection, pain, and bleeding. Additionally, as a needle is going into the tumor there is a risk of an air leak, also known as a pneumothorax. If this occurs participants may need to have a tube placed into their chest to remove the air and reinflate the lung. These biopsies are done as an outpatient, however, should you have a complication you may have to be admitted to the hospital to be observed. To minimize these risks, sterile procedures, anesthesia, and careful observation of the patient post-procedure are used.*

Blood Sampling: The possible side effects of drawing blood include pain, bleeding, bruising, light-headedness, fainting and, on rare occasions, local blood clot formation or infection with redness and irritation of the vein.

Intravenous (IV) Line and injection: Infusion of the PD-1 or PD-L1 antibody, similar to what you have experienced before when receiving these agents, may cause discomfort, irritation, mild bruising, bleeding, leakage of drug solution, and rarely infection, nausea, and lightheadedness. The dupilumab is injected into the skin (subcutaneous) and can occasionally cause irritation, bruising, or bleeding at the injection site.

Privacy risks (disclosure of private information): *Risk of loss of private information; this risk is always existing, but, there are procedures in place to minimize the risk.*

During the study, we will tell you about new information or changes in the study that may affect your health or your willingness to continue on the study. When informed of this new information, if you agree to continue in the study, you will be asked to sign an updated consent form.

Genetic Information: *There is a Federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans, and most large employers to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. This law generally will protect you in the following ways:*

- *Health insurance companies and group health plans may not request your genetic information that we get from this research;*
- *Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums;*
- *Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.*

Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

OTHER OPTIONS TO CONSIDER:

You may decide not to take part in this research study. If you decide not to take part, this will not affect the clinical care you receive at Mount Sinai. The choice is totally up to you. If you have only received first line chemotherapy and immunotherapy the standard next approach may be another type of chemotherapy, and your physician will discuss if you would be a candidate for additional chemotherapy, what the chemotherapy is and what the schedule would be, and potential risks and benefits of this "standard" approach
Instead of being in this research study, your choices may include:

- Choose to receive standard treatment for your disease such as chemotherapy
- Choose to forgo further anti-cancer therapy

IN CASE OF INJURY DURING THIS RESEARCH STUDY

If you are injured or made sick from taking part in this research study, you will get medical care. Generally, it will be billed to you or your insurance. You will be responsible for all treatment costs not covered by your insurance, including deductibles, copayments, and coinsurance. This does not prevent you from seeking payment for injury related to malpractice or negligence. You can contact the Lead Researcher for more information.

ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop taking part in this study at any time. No matter what you choose, your care and benefits through Mount Sinai will not be negatively impacted.

If you decide to stop being in the study, please contact the Lead Researcher or the research staff.
You may also withdraw your permission for the researchers to use and share any of your protected information for research, but you must do so in writing to the Lead Researcher at the address on the first page. Even if you withdraw your permission, the Lead Researcher may still use the information that was already collected if that information is necessary to complete the research study. Your health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from taking part in the research study.

If you decide you don't want your data and/or samples to be used for research anymore, you can contact the researcher and ask to have your data and/or samples withdrawn or labeled so that they will not to be used in additional projects or shared. If your data and/or samples have already been shared with researchers, those researchers will be asked to stop using them. However, if any data and/or samples have already been shared without your identity or a linking code, it won't be possible to retrieve them. Data and/or samples that have already been used will not be affected by your decision. If your data

and/or samples have already been deposited in an external repository, the study team will request that your data and/or samples be removed.

Withdrawal without your consent: The Lead Researcher, the funder or Mount Sinai may stop your involvement in this research study at any time without your consent. This may be because the research study is being stopped, the instructions of the research team have not been followed, the Lead Researcher believes it is in your best interest, or for any other reason. If data and/or samples have been stored as part of the research study, they too can be destroyed without your consent.

CONTACT INFORMATION:

If you have any questions, concerns or complaints at any time about this research, or you think the research has harmed you, please contact the office of the research team and/or the Lead Researcher at phone number 212-824-9472

DISCLOSURE OF FINANCIAL INTERESTS:

Dr. Thomas Marron (the Lead Researcher in this study) is the named inventor on a patent application related to the use of dupilumab and PD-1/PD-L1 blockade for the treatment of cancer, the focus of this study.

Dr. Marron also is a paid consultant for Regeneron, the developer of dupilumab.

Additionally, Dr. Marron is a paid consultant for other companies that research and develop cancer therapies.

If you have questions regarding paid relationships that your physician/researcher may have with industry, you are encouraged you to talk with your physician/researcher, or check for industry relationships posted on individual faculty pages on our website at http://icahn.mssm.edu/.

MAINTAINING CONFIDENTIALITY – HIPAA AUTHORIZATION:

As part of this study, some of your private and/or protected health information will be obtained, used, and shared with your permission. There is a Federal Health Insurance Portability and Accountability Act (HIPAA) that makes sure this is done correctly and safely.

What is protected health information (PHI)?
PHI is the combination of two things:

1. PHI contains information that identifies you. It will be used to contact you and link you to your health information, like name, date of birth, medical record number, and address.

2. PHI also contains health information, including information about your mental and physical health from your visits to doctors or hospitals, or from study visits.

Every time you visit a hospital or your doctor, PHI is created and recorded in your medical record by your healthcare providers. In the same way, the PHI created as part of this study will be linked to who you are and your medical information.

What PHI is collected and used in this research study, and might also be shared with others?

As part of this study, the research team at the hospital(s) involved in the research will collect your name, address, telephone, date of birth, date of admission, date of discharge, date of death, social security number, medical records number, health plan numbers, and other unique codes.

During the study, the researchers will gather information by:

- Reviewing and/or taking your medical history (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc.)
- Doing a physical examination that generally also includes blood pressure reading, heart rate, breathing rate, and temperature.
- Completing the tests, procedures, questionnaires and interviews explained in the description section of this consent.
- Reviewing genetic tests.

Why is your PHI being used?
Researchers need the information that identifies you so they can contact you during the study. They need your health information and the results of any tests and procedures being collected as part of this study to answer the questions posed in the study. The purpose of the study is discussed earlier in this consent form. Before researchers analyze the data, they remove any information that would let others know who you are or that you took part in the study. If researchers publish or present study results at scientific meetings, lectures, or other events, their presentations would not include any information that would let others know who you are, unless you give separate permission to do so.

The Lead Researcher may also use and share the results of these tests and procedures with other healthcare providers at Mount Sinai who are involved in your care or treatment. The research team and other authorized members of The Mount Sinai Health System (“Mount Sinai”) workforce may use and share your information to ensure that the research meets legal, institutional or accreditation requirements. For example:

- The Mount Sinai Program for the Protection of Human Subjects is responsible for overseeing research on human participants and may need to see your information.
- If you receive any payments for taking part in this study, the Mount Sinai Finance Department may need your name, address, social security number, payment amount, and related information for tax reporting purposes.

- I*f the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.*

Who, outside Mount Sinai, might receive your PHI?
As part of the study, the Lead Researcher, research team and others in the Mount Sinai workforce may disclose your PHI, including the results of the research study tests and procedures, to the following people or organizations: (It is possible that there may be changes to the list during this research study; you may request an up-to-date list at any time by contacting the Lead Researcher.)

- The United States Department of Health and Human Services (DHHS) and the Office of Human Research Protection (OHRP) (the government organization that is responsible for protecting human research participants).
- Other collaborating research center(s) and their associated research/clinical staff who are working with the researchers on this project
- A Data Safety Monitoring Board or other committee that will monitor the study on an ongoing basis for safety.
- The United States Food and Drug Administration.

In all disclosures outside of Mount Sinai, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifier is required by law. Some records and information disclosed may be identified with a unique code number. The Lead Researcher will ensure that the key to the code will be kept in a locked file, or will be securely stored electronically. The code will not be used to link the information back to you without your permission, unless the law requires it, or rarely if the Institutional Review Board (IRB) allows it after determining that there would be minimal risk to your privacy. It is possible that a sponsor or their representatives, a data coordinating office, a contract research organization, may come to inspect your records. Even if those records are identifiable when inspected, the information leaving the institution will be stripped of direct identifiers. Additionally, when applicable, the monitors, auditors, the IRB, *OHRP, as well as the Food and Drug Administration (FDA) will be granted direct access to your medical records for verification of the research procedures and data. OHRP and FDA are authorized to remove information with identifiers if necessary to complete their task. By signing this document you are authorizing this access.* The results of this research may be published. However, your name and other identifying information will be kept confidential.

For how long will Mount Sinai be able to use or disclose your PHI? Your authorization for use of your PHI for this specific study does not expire.

Will you be able to access your records?
During your participation in this study, you will have access to your medical record and any study information that is part of that record. The research team is not required to release research information to you that is not part of your medical record.

Do you need to give the researchers permission to obtain, use or share your PHI?
NO! If you decide not to let the research team obtain, use or share your PHI, you should not sign this form, and you will not be allowed to volunteer in the research study. If you do not sign, it will not affect your treatment, payment, or enrollment in any health plans or affect your eligibility for benefits.

Can you change your mind?
If you decide to stop being in the study, please contact the Lead Researcher or the research staff. The research team may ask you whether they can continue to collect information from your medical record. You will also have to decide if you wish to limit the continued use of the information collected during the study. Under US privacy laws you may also withdraw your permission for the researchers to use and share any of your protected information for research, but you must do so in writing to the Lead Researcher at the address on the first page.

Even if you withdraw your permission, the Lead Researcher may still use the information that was already collected, but only to complete this research study. Your health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from taking part in the research study.

If you have not already received it, you will also be given The Hospital's Notice of Privacy Practices that contains more information about how The Hospital uses and discloses your PHI.

It is important for you to understand that once information is disclosed to others outside Mount Sinai, the information may be re-disclosed and will no longer be covered by the federal privacy protection regulations. However, where possible, Mount Sinai has entered into agreements with those who will receive your information to continue to protect your confidentiality.

If researchers are reviewing your medical records or asking questions about your medical history or conditions, it is possible that they may learn information related to your HIV status. If that is the case, the following information concerns you. If researchers are not reviewing your medical records or asking questions about your medical history or conditions, then you may ignore the following section.

Notice Concerning HIV-Related Information
If you are authorizing the release of HIV-related information, you should be aware that the recipient(s) is (are) prohibited from re-disclosing any HIV-related information without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (888) 392-3644 or the New York City Commission on Human Rights at (212) 416-0197. These agencies are responsible for protecting your rights.

How the Institutional Review Board (IRB) can help you:

This research has been reviewed and approved by an Institutional Review Board (IRB). You may reach a representative of the Mount Sinai Program for Protection of Human Subjects at telephone number (212) 824-8200 during regular work hours (Monday-Friday, 9am-5pm, excluding holidays) for any of the

reasons listed below. This office will direct your call to the right person within the Mount Sinai Health System:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You are not comfortable talking to the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

ADULT PARTICIPANT:

Your signature below documents your permission to take part in this research study and to the use and disclosure of your protected health information. A signed and dated copy will be given to you.

Signature of Participant	Printed Name of Participant	Date	Time

PERSON EXPLAINING STUDY AND OBTAINING CONSENT:

Signature of Consent Delegate	Printed Name of Consent Delegate	Date	Time

WITNESS SECTION:

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the participant, and that consent was freely given by the participant.

Signature of Witness	Printed Name of Witness	Date	Time