

**MEMORANDUM via email**

To: ClinicalTrials.gov Protocol Registration and Results System (PRS)

Subject: **ClinicalTrials.gov Record (ClinicalTrials.gov Identifier: NCT03389893)** titled,  
*Effect of Dupilumab (Anti-IL4Ra) on the Host-Microbe Interface in Atopic Dermatitis, Dupilumab Study (ADRN-09)*

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Submitted for posting is an IRB approved informed consent form version of ADRN-09 (Version 3.0, August 29, 2019).

**TITLE:** Effect of Dupilumab (anti-IL4R $\alpha$ ) on the Host-Microbe Interface in Atopic Dermatitis

**PROTOCOL NO.:** ADRN 09  
[REDACTED]

**SPONSOR:** National Institute of Allergy and Infectious Diseases (NIAID)

**INVESTIGATOR:**  
[REDACTED]

**STUDY-RELATED  
PHONE NUMBER(S):**  
[REDACTED]

#### **YOUR PARTICIPATION IS VOLUNTARY**

We will explain this research study to you. You may ask as many questions as you need.

- Taking part in this study is your decision.
- You may change your mind at any time.
- You will be given a signed copy of this consent form for your records.

You are being asked to participate in this study because you have moderate-to-severe atopic dermatitis (AD for short, and also called eczema), and you currently have active areas (lesions) on your skin.

#### **INTRODUCTION/BACKGROUND**

AD is a disease with dry, scaly, itchy skin. People with AD often have problems with repeat bacterial and viral skin infections. These repeat infections are often caused by a specific bacteria known as, *Staph aureus*, or just *Staph*.

People with chronic AD often use long-term topical or oral treatments to help control their disease symptoms. Using these medications over long periods of time can have side effects on the body. For this reason, new treatment options are being researched, especially for patients whose symptoms are not controlled by existing medications.

Dupilumab is a new treatment recently approved by the Food and Drug Administration (FDA). It is for the treatment of moderate-to-severe AD in adults whose AD symptoms are not well-controlled with topical medications.

#### **PURPOSE OF THE STUDY**

The purpose of this study is to determine how dupilumab affects the amount of bacteria on the skin, the skin's water loss, and the immune system.

## STUDY COMPONENTS

This study is funded and sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), through the Atopic Dermatitis Research Network (ADRN).

This study will enroll 99 participants, 18 to 75 years of age. Participants will be enrolled from up to 16 centers across the United States. All participants will have chronic moderate-to-severe AD.

This study has two main portions. In the first portion of the study, you will be randomly assigned, like flipping a coin, to receive either the active study medication or the placebo (a placebo does not contain active study medication). Neither you nor your study doctor and team, will know which treatment you are receiving. During this portion, 2 out of 3 participants will receive dupilumab, the active study medication, and 1 out of 3 participants will receive placebo. You will not be able to choose which treatment you receive. The first portion of this study will last for 6 weeks. During this first portion of the study, you will receive your treatment by injection, just under the skin every other week (three doses). Two injections (loading dose) will be given on the first day of treatment; the rest of your doses during this portion of the study will only require one injection.

The second portion of the study will last for 10 weeks. During the second portion of the study, all participants will receive dupilumab, the study medication. This portion is called an open-label extension, because everyone will know that you are receiving dupilumab and no one will be receiving the placebo. Dupilumab will be given every other week for five doses. On the first day of the open-label portion of the study, two injections will be given in the clinic (loading dose). The rest of the doses will only require one injection and may be given at home by you or a caregiver that you choose. Your study doctor will teach you and/or your caregiver how to inject the study medicine during the first portion of the study. It is given just like diabetics give themselves insulin at home, with a tiny needle into a pinched up part of your skin. If you are not comfortable administering injections to yourself at home you will have the option to return to [Site Name] to have the study doctor or another qualified medical staff member perform the injection for you.

Your participation in the study will last about six to seven months. The study will require 10 visits to [Site Name] and 1 telephone visit. If you are using certain medications/therapies at your first clinic visit, you may be asked to return for another clinic visit after you have stopped using those medications/therapies. The study doctor will review the medications/therapies you are currently using to decide if they are safe to stop using while participating in the study. You must agree to stop using any prohibited medications/therapies while participating in the study.

If you agree to participate in the study, you will be asked to avoid showering within 24 hours of your clinic visits. You will also be asked to avoid using hot tubs during your participation in the study and to avoid using chlorinated swimming pools within 24 hours of your clinic visits. The study staff will provide you with a card that lists these reminders for you to take home.

If you are of reproductive potential and sexually active, you will be asked to use birth control during this study because of unknown risks to your unborn child. Acceptable methods of birth control for females include hormonal contraceptives, intrauterine device, double barrier contraception (i.e., condom plus diaphragm), surgical sterilization or surgically sterilized partner. Acceptable methods of birth control for males include barrier methods with vaginal spermicide, surgical sterilization or surgically sterilized partner, or having a female partner practicing an approved birth control method for females, as described previously. If you do become pregnant or you are a male participant and your partner becomes pregnant during the study, we ask that you report the pregnancy to the study staff. If you are a male and you and your partner conceive a child, you may continue your participation in the study; we will ask you, and your partner if she agrees, to provide information regarding the pregnancy and the birth and health of your child. If you are a female and you become pregnant, you may no longer participate in the study; you will however be asked to provide information regarding your pregnancy and the birth and health of your child. This information about pregnancy, birth, and child health is important because it helps researchers better understand potential effects of dupilumab on pregnant women and their fetuses. You may provide this

information yourself, or give permission to your health care provider or obstetrician to give it directly to your study doctor.

If you agree to provide this information, you will be contacted until two weeks after your child's birth. You will be asked to report any medical problems that you (if you are a female), your partner (if you are a male), or your baby experience during this time to your study doctor. If you decide at any time that you would no longer like to provide information regarding the pregnancy and the birth and health of your child, you may withdraw your consent.

You (if you are a female) or your partner (if you are a male) and your child will not be asked to undergo any tests besides those that your health care provider, obstetrician, or pediatrician would normally perform in providing care during pregnancy, or taking care of your newborn child. If your study doctor believes that additional tests are needed to ensure the safety of you (female), your partner (male), and your child, you will be notified, and you will have the right to agree to or refuse these additional tests.

The following procedures will occur during the screening, treatment, and follow-up portions of this study:

#### **Screening Visit**

Your initial visit to the center will take about 2 hours to complete. During the visit, the following will occur:

- **Consent: We will explain the study to you.** You will be given time to read the consent form and ask questions. Once all of your questions are answered you will sign the consent form, if you want to participate in the study.
- **Questionnaires:** If you consent, then you will answer some questions about your contact information. The study team will then ask you some questions to determine whether you are eligible for this study. The questionnaires are not tests. There are no right or wrong answers to the questions. If you do not understand certain questions, you may ask the study staff members for more information.
- **Physical Exam:** You will receive a physical exam by a study doctor or another qualified staff member. The purpose of the exam is to make sure that you meet the health requirements for the study. During the exam, a member of the study staff will ask you questions about your health and your AD.
- **Medication/Therapy Use Review:** A member of the study staff will ask about the medications you have recently taken and therapies you have used. The use of certain medications/therapies may mean that your study visit will need to be rescheduled. You can come back for your visit after you come off those certain medicines/therapies for a set amount of time, which is called a "washout" period. If you are unwilling or unable to washout of certain medications/therapies, you will not be eligible to participate in the study.
- **Pregnancy Test:** If you are a female participant of child-bearing potential, you will be asked to give a small sample of urine for a pregnancy test. Results of the pregnancy test will be given to you. If your pregnancy test is positive, you will not be allowed to participate in the study.
- **Vital Signs and Growth Parameters:** A member of the study staff will check your vital signs (blood pressure, heart rate, breathing rate, and temperature), height, and weight.

- **Blood Collection:** About half of a tablespoon of blood will be collected. All of the blood can usually be collected in 1 needle stick. Your blood samples will be labeled with a number only, and not your name. Several types of tests will be performed on your blood. One test, called a complete blood count, or CBC, gives important information about the kinds and numbers of cells in the blood, especially red blood cells, white blood cells, and platelets. Another test, called a complete metabolic panel, or CMP, provides your study doctor with information on your metabolism and the health of your kidneys and liver. These tests will help to determine if you are eligible to participate in the study. You will receive the results of these two tests.
- **Moisturizer Use:** If you are eligible for the study, you will be asked to use a moisturizer at least twice a day for at least 7 days before your next visit. The study team will tell you which moisturizers can be used.

**Treatment Initiation Visit**

After you finish the Screening Visit, if you are eligible, you will be asked to complete the Treatment Initiation Visit procedures. The Treatment Initiation Visit will occur 8-28 days after the Screening Visit, when you have finished the 7 days of moisturizer use. This visit will take about 2.5 hours to complete. During the visit, the following will occur:

- Questionnaires
- Physical Exam
- Medication/Therapy Use Review
- Pregnancy Test
- Vital Signs
- Adverse event assessment
- **Blood collection:** About 4 tablespoons of blood will be collected. All of the blood can usually be collected in 1 needle stick. Your blood samples will be labeled with a number only, and not your name. Several types of research tests will be performed on your blood throughout this study. Blood tests will be done to look at your blood before and after you take the study medicine to see how the treatment affects your immune system's response. Additional tests will look at markers in your blood related to the severity of your AD. We will not give you the results of these blood tests, which are for research and not for diagnostic purposes. Blood will be collected to see how your genes and other inherited traits affect your response to the study medicine. If you provided blood for genetic studies under a previous ADRN or ADVN study and agreed that your samples or data could be used for future studies, additional blood will not need to be collected for these genetic studies. We will not give you the results for your genetic tests which are exploratory and not for diagnostic purposes.
- **Skin Swab Collection:** Skin swab samples will be collected from your arm, leg or trunk. These samples will be collected by rolling a sterile swab over the skin. The procedure will take about a minute and does not hurt. Up to 6 skin swabs will be collected during your study visit. The swabs will be used to look at bacteria on your skin. Your skin swabs that are collected before you receive any medication or placebo will be compared to your skin swabs that are collected after you take the study medication/placebo. We will not give you the results of these tests which are for research and not for diagnostic purposes.
- **Skin Tape Stripping:** Skin tape strip samples will be collected from your arm, leg or trunk. If you have a history of serious or life threatening reactions to latex, tape, or adhesives, please tell the study team as you will not be eligible for the study. Up to 20 tape strip samples will be collected during your study visit. To collect these samples, your skin will be held tight and the tape strip applied. Light pressure will be applied, and then the tape strip will be slowly removed. The first 5 tape strips will be collected from a single lesional location. The remaining 15 strips will be taken from a single non-lesional location that is next to the lesional location. A different tape strip will be used each time. Skin tape strips will be used to determine the composition of your skin. Your skin tape strips that are collected before you receive any medication or placebo will be compared to your skin tape strips that are collected after you receive medication or placebo. We will not give you the results of these tests which are for research and not for diagnostic purposes. This procedure may be slightly uncomfortable due to the irritation to the skin from

the tape strips being applied and removed many times in the same place.

- **Skin Barrier Assessments:** Study staff will use a machine, called an Aquaflux, to measure water loss from your skin. The procedure will involve the study staff placing a small probe on your skin for a few seconds. This procedure does not hurt. The study staff will take measurements with the Aquaflux machine before and during skin tape stripping. We will not give you the results of the skin barrier assessment test, which is for research and not for diagnostic purposes.
- **Skin Biopsy Collection:** If you are allergic to numbing medications such as Lidocaine or Novocain or have a history of keloid-like scars (keloids are extra scar tissue that can appear after your skin is injured or becomes swollen, they usually appear as lumpy skin with a smooth surface), you will not be eligible to participate in the study. **[URMC** One piece of your skin up to 3 mm in diameter or the size of 3 pin heads, will be collected. **Non-URMC** Up to 2 pieces of your skin, up to 2.5 mm in diameter or the size of ~3 pin heads, will be collected]. Biopsy sample(s) will be taken from your arm, leg or trunk. The area will first be cleaned and numbed by injecting a numbing medicine through a tiny needle. Next the biopsies will be taken with an instrument called a sterile biopsy punch, which is tube-shaped. The instrument is rotated downward through the skin using a twirling motion. The procedure is quick and does not hurt since the skin is numbed first. The biopsy site(s) will need to be kept dry for the first 24-48 hours after the procedure. The study staff will provide you with instructions on caring for the biopsy site(s) at home. Skin biopsy samples will be used to look at how your skin responds to the study medication or the placebo. Your skin biopsies that are collected before you receive any medication or placebo will be compared to your skin biopsies that are collected after you receive medication or placebo.
- **Photographs of collection sites:** Photographs will be taken of the sites where the skin swabs, tape strips, and biopsies will be collected. This will allow the study staff to identify the collection sites at later visits. Your face will not be included in any photos that are taken so you cannot be identified.
- **Injection of study medication or placebo:** **The injection of the study medication/placebo will be given subcutaneously (just under your skin, and not in your muscle).** You will be randomly assigned to receive either the study medication or placebo. There will be a 2-in-3 chance that you will receive study medication and a 1-in-3 chance you will receive a placebo. Neither you nor the study staff will know which group you are assigned to. Two subcutaneous injections of either the study medication or placebo will be injected into either the skin of your belly, thighs, or upper arms by the study doctor or another qualified medical staff member. This procedure may be slightly uncomfortable due to the needle stick. The study staff will teach you or your caregiver how to inject the study medicine so that you can inject it at home during the open-label portion of the study, if you choose to do so.

### **Day 3 Visit**

You will be asked to return to the clinic about 3 days after you begin your treatment. The Day 3 Visit will take about 1.5 hours to complete. During this visit, the following will occur:

- Questionnaires
- Physical Exam
- Medication/Therapy Use Review
- Confirmation of Pregnancy Status
- Vital Signs
- Skin Swab Collection, up to 6 skin swabs
- Skin Barrier Assessment
- Photographs
- Adverse event assessment

### **Day 7 (Week 1) Visit**

You will be asked to return to the clinic about 7 days after you begin your treatment. The Day 7 Visit will take about 2.5 hours to complete. During this visit, the following will occur:

- Questionnaires

- Physical Exam
- Medication/Therapy Use Review
- Confirmation of Pregnancy Status
- Vital Signs
- Adverse event assessment
- Blood Collection, about one and a half tablespoons for research tests. We will not give you the results of these blood tests, which are for research and not for diagnostic purposes.
- Skin Swab Collection, up to 6 skin swabs
- Skin Tape Stripping, up to 15 non-lesional skin tape strips
- Skin Barrier Assessment before and after tape stripping
- Skin Biopsy Collection, [URMC 1 skin biopsy non-URMC up to 2 skin biopsies]
- Photographs

**Day 14 (Week 2) Visit**

You will be asked to return to the clinic about 14 days after you begin your treatment. The Day 14 Visit will take about 2.5 hours to complete. During this visit, the following will occur:

- Questionnaires
- Physical Exam
- Medication/Therapy Use Review
- Pregnancy Test
- Vital Signs
- Adverse Event assessment
- Blood Collection, about 4 tablespoons for research tests. We will not give you the results of these blood tests, which are for research and not for diagnostic purposes.
- Skin Swab Collection, up to 6 swabs
- Skin Tape Stripping, up to 15 non-lesional and 5 lesional skin tape strips
- Skin Barrier Assessment before and after tape stripping
- Photographs
- Injection of study medication or placebo (1 injection)
  - The study staff will teach you or your caregiver how to inject the study medicine so that you can inject it at home during the open-label portion of the study, if you choose to do so. At this visit you may choose to give the injection yourself, or have your caregiver give the injection, under the supervision of a qualified staff member.

**Day 21 (Week 3) Visit**

You will be asked to return to the clinic about 21 days after you begin your treatment. The Day 21 Visit will take about 2.5 hours to complete. During this visit, the following will occur:

- Questionnaires
- Physical Exam
- Medication/Therapy Use Review
- Confirmation of Pregnancy Status
- Vital Signs
- Adverse Event Assessment
- Blood Collection, about one and a half tablespoons for research tests. We will not give you the results of these blood tests, which are for research and not for diagnostic purposes.
- Skin Swab Collection, up to 6 swabs
- Skin Tape Stripping, up to 15 non-lesional skin tape strips
- Skin Barrier Assessments before and after tape stripping
- Skin Biopsy Collection, [URMC 1 skin biopsy non-URMC up to 2 skin biopsies]

- Photographs

**Day 28 (Week 4) Visit**

You will be asked to return to the clinic about 28 days after you begin your treatment. The Day 28 Visit will take about 2.5 hours to complete. During this visit, the following will occur:

- Questionnaires
- Physical Exam
- Medication/Therapy Use Review
- Pregnancy Test
- Vital Signs
- Adverse Event assessment
- Blood Collection, about 4 tablespoons for research tests. We will not give you the results of these blood tests, which are for research and not for diagnostic purposes.
- Skin Swab Collection, up to 6 swabs
- Skin Tape Stripping, up to 15 non-lesional and 5 lesional skin tape strips
- Skin Barrier Assessments before and after tape stripping
- Photographs
- Injection of study medication or placebo (1 injection)
  - The study staff will teach you or your caregiver how to inject the study medicine so that you can inject it at home during the open-label portion of the study, if you choose to do so. At this visit you may choose to give the injection yourself, or have your caregiver give the injection, under the supervision of a qualified staff member.

**Day 42 (Week 6) Visit**

You will be asked to return to the clinic about 42 days after you begin your treatment. The Day 42 Visit will take about 2 hours to complete. During this visit, the following will occur:

- Questionnaires
- Physical Exam
- Medication/Therapy Use Review
- Pregnancy Test
- Vital Signs
- Adverse Event assessment
- Blood Collection, about one and a half tablespoons for research tests. We will not give you the results of these blood tests, which are for research and not for diagnostic purposes.
- Skin Swab Collection, up to 6 swabs
- Skin Tape Stripping, up to 15 non-lesional skin tape strips
- Skin Barrier Assessments before and after tape stripping
- Photographs
- Two injections of study medication or placebo. Participants who were previously receiving the placebo will receive two injections of the study medication. Participants who were previously receiving the study medication will receive one injection of the study medication and one injection of placebo. This will help make sure you and your study team do not know which treatment you were receiving during the first portion of the study.
  - The study staff will teach you or your caregiver how to inject the study medicine so that you can inject it at home during the open-label portion of the study. The study staff will ask you or your caregiver to give your injection at this visit, so that they can ensure you are able to safely complete injections at home during the open-label extension portion of the study, if you choose to do so.
- If you choose to administer study medication at home, you will be provided with two doses of study medication to take home for administration on Days 56 and 70.

**Day 56 (Week 8) Home Study Medication Injection**

You or your caretaker will give one injection of study medication. If you are not comfortable administering injections to yourself at home, you will have the option to return to [Site name] to have the study doctor or another qualified medical staff member perform the injection for you.

**Day 70 (Week 10) Home Study Medication Injection**

You or your caretaker will give one injection of study medication. If you are not comfortable administering injections to yourself at home, you will have the option to return to [Site name] to have the study doctor or another qualified medical staff member perform the injection for you.

**Day 77 (Week 11) Visit**

You will be asked to return to the clinic about 77 days after you begin treatment for the first portion of the study (35 days after you begin the open-label portion of the study). The Day 77 Visit will take about 2 hours to complete. During this visit, the following will occur:

- Questionnaires
- Physical Exam
- Medication/Therapy Use Review
- Pregnancy Test
- Vital Signs
- Adverse Event Assessment
- Blood collection, about one and a half tablespoons for research tests. We will not give you the results of these blood tests, which are for research and not for diagnostic purposes.
- Skin Swab Collection, up to 6 skin swabs
- Skin Tape Stripping, up to 15 non-lesional skin tape strips
- Skin Barrier Assessments before and after tape stripping
- Photographs
- If you choose to administer study medication at home, you will be provided with two doses of study medication to take home for administration on Days 84 and 98.

**Day 84 (Week 12) Home Study Medication Injection**

You or your caretaker will give one injection of study medication. If you are not comfortable administering injections to yourself at home, you will have the option to return to [Site name] to have the study doctor or another qualified medical staff member perform the injection for you.

**Day 98 (Week 14) Home Study Medication Injection**

You or your caretaker will give one injection of study medication. If you are not comfortable administering injections to yourself at home, you will have the option to return to [Site name] to have the study doctor or another qualified medical staff member perform the injection for you.

**Day 112 (Week 16) Visit**

You will be asked to return to the clinic about 112 days after you begin treatment in the first portion of the study (10 weeks after you begin your open label treatment). The Day 112 Visit will take about 2 hours to complete.

During this visit, the following will occur:

- Questionnaires
- Physical Exam
- Medication/Therapy Use Review
- Pregnancy Test
- Vital Signs
- Adverse Event Assessment

- Blood collection, about one and a half tablespoons for research tests. We will not give you the results of these blood tests, which are for research and not for diagnostic purposes.
- Skin Swab Collection, up to 6 skin swabs
- Skin Tape Stripping, up to 15 non-lesional and 5 lesional skin tape strips
- Skin Barrier Assessments before and after tape stripping
- Photographs

**Day 182 (Week 26) Follow-Up Phone Call**

A study staff member will call you about 182 days after you begin treatment (12 weeks after you receive your last dose of study medication). The call will take about 30 minutes. You will be asked about your AD, any new symptoms you have experienced since your last clinic visit, and any medications/therapies you have used since your last visit. You will be asked if you have consistently used birth control and if you have tested positive to a pregnancy test since your last visit if you are a female participant. You will be asked if your partner has tested positive to a pregnancy test since your last clinic visit if you are a male. If you have asthma, you will be reminded not to change your asthma medications without approval from your doctor.

**Unscheduled Visit**

You may be asked to return for an Unscheduled Visit as needed, if your AD worsens or other concerns arise between regularly scheduled visits. The site staff may also ask you to return to the clinic to provide additional samples for more detailed testing, or if samples were lost or destroyed, or if the amounts of samples collected at a previous visit were not enough to complete the testing. The type and amount of each sample may vary at each Unscheduled Visit, and will be explained prior to your clinic visit.

If an Unscheduled Visit occurs, the following procedures will occur:

- Questionnaires
- Physical Exam
- Medication/Therapy Use Review
- Pregnancy Test, per investigator discretion
- Vitals

The following items may occur based on the reason for your Unscheduled Visit:

- Skin Barrier Assessments
- Blood Collection: Up to 4 tablespoons of blood may be collected
- Skin Tape Stripping: Up to 15 non-lesional and 5 lesional skin tape strips may be collected
- Skin Swab Collection: Up to 6 skin swabs may be collected
- Skin Biopsy Collection: [URMC 1 skin biopsy may be collected non-URMC Up to 2 skin biopsies may be collected]

**RISKS and DISCOMFORTS**

Procedures in this research study may involve risks that are not possible to predict. You will be informed of any new risks that may be identified during the study. Below is a description of the risks we know about for each procedure. Please ask your study doctor or the research staff to explain any procedures or risks that you do not understand.

**Questionnaires**

You may find that some of the questions are too personal. You do not have to answer any questions that make you feel uncomfortable. There is also a possibility that your answers may be read by others outside of the study. Your participant identification number, not your name, is put on the questionnaires.

**Physical Exam**

There are no known risks for the physical exam.

**Stopping Medication/Therapy Use**

Stopping medications/therapies during this study may cause your AD to get worse.

**Pregnancy Test**

There are no known risks for the pregnancy test.

**Vital Signs and Growth Parameters**

There are no known risks for having your vital signs and growth parameters checked.

**Skin Barrier Assessments**

There are no known risks for the skin barrier assessments.

**Blood Collection**

The risks of having blood taken may include pain, bleeding, or bruising. Lightheadedness and fainting rarely occur. A numbing agent may be placed on the skin before the blood draw to numb the area and reduce the pain of the stick. Side effects of the numbing agent (mainly skin rash) are unlikely, but may occur.

**Skin Swab Collection**

There are no known risks for the skin swab collection.

**Skin Tape Stripping**

Skin tape stripping may cause mild redness and irritation of the skin where the tape was applied. Redness and irritation should disappear after about 12 hours. There is a small risk of infection at the tape stripping site. There is also a possible risk of rare allergic reactions to the tape. If you have a history of serious or life-threatening allergic reactions to tape, or adhesives, you will not be able to participate in the study.

**Skin Biopsy Collection**

The risks of a skin biopsy include pain and the possibility of swelling, bleeding, and infection. A tiny scar may form at the biopsy site. In very rare instances, injection of the lidocaine to numb the skin can cause allergic reactions, which can be mild to life-threatening. These can range from hives, itching, swelling of the throat, mouth, or lips, difficulty breathing or significant drop in blood pressure. If you are allergic to lidocaine or have a history of keloid-like scars, you will not be eligible to participate in the study.

**Injection of Study Medication and/or Placebo**

The most common risks (occurring in greater than or equal to 1% of participants) associated with injection of the study treatment are:

- Injection site reactions including:
  - Pain
  - Tenderness
  - Bruising
  - Swelling
  - Redness
  - Rash
  - Hives
  - Itch
  - Inflammation (swelling)
- Eye conditions including:
  - Conjunctivitis (redness and swelling of the outermost layer of the white part of the eye and the inner surface of the eyelid)

- Blepharitis (inflammation or swelling of the eyelid)
- Keratitis (inflammation or irritation of the cornea covering the iris and pupil)
- Eye pruritus (itching)
- Dry eye
- Oral herpes and other herpes simplex infections

Rare risks (occurring in less than 1% of participants) include hypersensitivity and cardiovascular thromboembolic events. For AD patients, increased eosinophil count (eosinophils are a type of white blood cell that are linked to inflammation) is also rare although it is found to be more common in patients with asthma and chronic rhinosinusitis.

Hypersensitivity is a condition in which your body's immune system over-reacts to receiving the study treatment. Hypersensitivity may result in serum sickness (an allergic response from your body) or serum sickness-like reaction with fever, rash, and joint symptoms. Hypersensitivity may result in an allergic reaction. Allergic reactions can be mild to life-threatening. These can range from hives; itching; swelling of the throat, mouth, or lips; difficulty breathing or significant drop in blood pressure. Sometimes life-threatening allergic reactions are called anaphylaxis. If you have a history of serious or life-threatening allergic reactions (anaphylaxis) to any of the ingredients in the study medication or placebo, you will not be able to participate in the study.

Some people on study treatment may have an increase in the number of eosinophils in their blood. The increase in eosinophils is temporary.

Cardiovascular thromboembolic events are events such as heart attack and stroke. These events are caused by a blood clot which blocks blood flow through an artery in the heart or brain.

If you have asthma you will be asked to continue taking your current asthma treatment medications as prescribed by your doctor. Stopping or decreasing your asthma medications while on study treatment could cause you to have an asthma attack.

It is not known whether the immune response to a parasite infection is affected by study treatment, but this is a possible risk. The study team will explain to you the types of situations that could put you at high risk for getting a parasite infection.

#### **Genetic Studies**

As part of this study, we will be collecting genetic information about you and the resulting data will be sent to the National Institutes of Health (NIH) repository (a repository is a place where data and/or specimens are stored, maintained and shared for future use). Genetic data will be shared with other researchers at many institutions through a central repository kept at the National Center for Biotechnology Information at the National Institutes of Health. Because data is shared, other researchers may use the data to study other diseases or conditions.

The data from this study will be coded and traditional identifiers (name, birth date, initials, etc.) will be removed. Your study doctor may keep the key to the code that links your name to the data. However, the National Institutes of Health will never receive this code or any other information that could identify you. The clinical sites involved in this study will not be told what types of research will be done with the data that is sent to the repository.

Any researcher who uses the data will follow rules on confidentiality restrictions. Even though we will remove traditional identifying information (name, birth date, initials, etc.), there is a very small chance this information could accidentally become known to you, the study doctor, or others.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic

information. Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination if you have already been diagnosed with the genetic disease being tested.

Although we have made every effort to protect your identity, there is a small risk of loss of confidentiality. If the results of these studies of your genetic makeup were to be accidentally released, it might be possible that the information we will gather about you as part of this study could become available to an insurer or an employer, or a relative, or someone else outside the study. Even though there are discrimination protections in both state and Federal law, there is still a small chance that you could be harmed if a release occurred.

#### **POTENTIAL BENEFITS**

If you agree to take part in this study, there may be no direct medical benefit to you. Your AD may or may not improve while in this study. There is a possibility that your disease symptoms will improve while you are receiving the study medication. Given 33% of participants will receive placebo during the first portion of the study, and you will be asked to withhold your current AD management medications, your disease may get worse. The information learned from this study may someday benefit the future treatment and care of people with AD.

#### **ALTERNATIVES TO PARTICIPATION**

There are other options available for you if you decide not to enroll in this study. You may receive treatment from a doctor without participating in this study. Your doctor may prescribe dupilumab for you since it is an FDA approved medication that is available to the public. You may choose to enroll in another study. You do not have to participate in this study in order to receive treatment at [Site Name].

#### **VOLUNTARY WITHDRAWAL FROM STUDY**

You may decide not to take part in the study or to leave the study at any time. If you decide not to participate, or to leave the study, there is no penalty or loss of benefits in your routine medical care or any other benefit(s) that you would otherwise receive.

If you leave the study prior to completion, we may ask you to complete a final assessment by phone. This phone call will be to confirm that any ongoing signs and symptoms related to your participation in the study are resolved. Study staff will be able to answer any questions you may have about your AD.

If you decide to leave the study or if you decide you do not want us to keep your contact information, you can call [Number] to remove your information from our list. You can also write to us at [Site Address] to let us know that you want to leave the study.

#### **REASONS WHY YOU MAY BE TAKEN OFF STUDY WITHOUT YOUR CONSENT**

You may be removed from the study without your consent at any time. Reasons why you may be removed from the study include, but are not limited to, the following:

- The study doctor feels it is not in your best interest to continue in this study.
- You are unable to complete required study procedures. This may be due to the development of a new disease, becoming pregnant, or starting treatment(s) not allowed for study participants.
- The study is stopped by [Site Name], the National Institute of Allergy and Infectious Diseases, or other health authorities.
- You do not comply with study procedures or follow study rules.

#### **COSTS TO THE PARTICIPANT (YOU)**

There will be no charge to you or your health insurance company for any costs for the study medication or placebo. There will be no cost to you or your health insurance company for costs which are directly related to this study's procedures:

- Blood draw

- Skin Swab Collection
- Skin Tape Stripping
- Skin Barrier Assessments
- Skin Biopsy Collection

The normal costs related to your AD care during the course of the study will be up to you and/or your insurer:

- Physician visits outside of study visits
- Emergency room or urgent care visits
- Hospitalizations

#### **PAYMENTS (REIMBURSEMENT)**

You will be compensated for the time and effort that you put into this study.

You will receive \$35 for completing questionnaires, the physical exam, and pregnancy testing (if applicable) at each visit. You will receive \$25 (per visit) if you complete the blood collection, \$10 (per visit) if you complete the skin swab collection (up to 6 skin swabs), \$25 (per visit) if you complete the skin tape strip collection (up to 20 tape strips), and \$15 (per visit) if you complete the skin barrier assessments. You will receive \$50 (per visit) per skin biopsy. Refer to the Table below for payments for each study visit.

	Screening	Treatment Initiation	Day 3	Day 7	Day 14	Day 21	Day 28	Day 42	Day 77	Day 112	Day 182	Unscheduled Visit
Questionnaires, physical exam, pregnancy testing (as applicable), vital signs	\$35	\$35	\$35	\$35	\$35	\$35	\$35	\$35	\$35	\$35		\$35
Blood Collection	\$25	\$25		\$25	\$25	\$25	\$25	\$25	\$25	\$25		\$25
Skin Swab Collection		\$10	\$10	\$10	\$10	\$10	\$10	\$10	\$10	\$10		\$10
Skin Tape Strip Collection		\$25		\$25	\$25	\$25	\$25	\$25	\$25	\$25		\$25
Skin Barrier Assessments		\$15	\$15	\$15	\$15	\$15	\$15	\$15	\$15	\$15		\$15
[URMC Skin Biopsy Collection]		\$50		\$50		\$50						\$50
[non-URMC Skin Biopsy Collection]		\$50/bx*		\$50/bx*		\$50/bx						\$50/bx*
Study Drug Injection		\$25			\$25		\$25	\$25				
Phone Call											\$10	
[URMC Total]	\$60	\$185	\$60	\$160	\$135	\$160	\$135	\$135	\$110	\$110	\$10	Up to \$160
[non-URMC Total]	\$60	\$235	\$60	\$210	\$135	\$210	\$135	\$135	\$110	\$110	\$10	Up to \$210

\*Up to 2 biopsies (bx) will be collected at this visit

If you are asked to return for an Unscheduled Visit to provide additional blood, skin swabs, skin tape strips, or skin biopsies, you will be compensated per sample. If you are requested to provide multiple sample types at the Unscheduled Visit, you will be compensated for each sample you provide. The table above outlines the compensation you will receive per sample.

In the event you are asked to return to clinic for an Unscheduled Visit due to experiencing increased disease activity, adverse reactions to the study medication or placebo, or other concerns, you will receive \$35 for each visit.

If you choose to, or are asked to, leave the study before it is finished, you will only be compensated for the activities you complete.

It is important to know that payment for participation in a study may be taxable income.

#### **RESEARCH-RELATED INJURY**

If you are injured or become ill because of taking part in this study, it is important to tell your study doctor [Site Name]. Emergency medical treatment will be available to you, through [Site Name]. You or your health insurance provider will be billed for the payment for any treatment you require as a result of a study-related injury. No other form of reimbursement is available. [Site Name] and the National Institutes of Health, including the Division of Allergy, Immunology, and Transplantation do not have programs to pay if you are hurt or have other bad results that are not the fault of the study doctors. You may contact [Name] at [Number] for more information or to report study-related injuries.

In case of injury resulting from this study, you will not lose any legal rights by signing this form.

#### **CONFIDENTIALITY**

Your medical and research records will be confidential to the extent permitted by law. Efforts will be made to keep your personal information private. However, we cannot guarantee complete confidentiality. You will be identified by a code, and personal information from your records will not be released without your written permission. You will not be identified in any publication or in the sharing of your data about this study.

Your records may be reviewed by the United States agency financially sponsoring the research (the National Institute of Allergy and Infectious Diseases). This includes National Institute of Allergy and Infectious Diseases representatives, agents, employees, contractors, and other persons assisting in conducting, monitoring or analyzing the study. [This includes the study monitors from Rho, Inc., [insert local IRB, if applicable], Western Institutional Review Board, Principal Investigator, the U.S. Food and Drug Administration (FDA), and research staff at [Site Name]. Your records may also be looked at by companies that are providing support for this study; this includes Regeneron Pharmaceuticals, Inc., Sanofi ULC, and their affiliates. All of these people are required to keep your identity and information confidential.]

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. Data may also be entered into other databanks; however, no information will be included that can identify you.

#### **CERTIFICATE OF CONFIDENTIALITY**

We will do everything we can to keep others from learning about your participation in this study. To help us protect your privacy, we have obtained a Certificate of Confidentiality from the United States Department of Health and Human Services (DHHS).

With this Certificate, we cannot be forced (for example by court order or subpoena) to disclose information that may identify you in any federal, state, local, civil, criminal, legislative, administrative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except to prevent serious harm to you or others, and as explained below.

You should understand that a Certificate of Confidentiality does not prevent you, or a member of your family, from voluntarily releasing information about yourself, or your involvement in this study.

If an insurer or employer learns about your participation, and obtains your consent to receive research information, then we may not use the Certificate of Confidentiality to withhold this information. This means that you and your family must also actively protect your own privacy.

A Certificate of Confidentiality does not represent an endorsement of the research study by the Department of Health and Human Services or the National Institutes of Health.

#### PROBLEMS OR QUESTIONS

 I can call	 At	 If I have questions or concerns about
[Pr. Name]	Phone: [Phone number] [24 hour number]	General study questions Research-related injuries or emergencies Any research-related concerns or complaints
	Phone: [REDACTED]	Rights of a research participant Any research-related questions, concerns or
		If investigator/study contact cannot be reached If I want to speak with someone other than Investigator, Study Contact or research staff

#### STORAGE OF SAMPLES and/or INFORMATION FOR FUTURE USE

We are asking your permission to store and share your unused blood, skin swabs, skin tape strips, and skin biopsies collected during the course of this study. This will include any secondary samples created from them. Storing and sharing your unused samples will mean they are available for use in future research studies. Stored samples may be used for tests not currently planned and new scientific discoveries may lead to new tests. Future studies may help researchers learn more about AD or other immunological diseases.

**IRB Approved Informed Consent Form**

The results of tests performed on stored samples or reports resulting from the analysis of your samples will not be given to you or your doctor, and they will not be put in your medical record. They will not identify you in traditional ways (name, birth date, initials, etc.) and will not affect your routine medical care.

There is no anticipated potential benefit to you from the collection, storage, and sharing of your samples. The purpose of storage and sharing data is to make information available for use in health research. Collecting, storing, sharing information and making it available to other researchers for other studies may help people in the future. Although your stored research samples will not be sold, the information obtained from the research performed on your samples may in the future lead to the development of commercial products. You will not receive any money from research using your stored samples and information.

Samples will be stored [REDACTED]

[REDACTED]. If you decide to allow storage, your samples and information may be stored for an unknown length of time.

There may be a risk of loss of confidentiality associated with the storage and analysis of samples or the information resulting from the analysis of your samples.

You can change your mind at any time and ask to have your samples destroyed. This request should be made in writing to the study doctor. If you make this request, all remaining stored samples will be destroyed. However, the results of any previous tests using your stored samples will be used. Your decision regarding the storage of samples or the information resulting from the analysis of your samples will not affect your ability to participate in this study.

**Please indicate your response below:**

I agree to the storage and sharing of my blood, skin swabs, skin tape strips, and skin biopsies for genetic tests not currently planned.

Yes     No

Initials of Research Participant

I agree to the storage and sharing of blood, skin swabs, skin tape strips, skin biopsies, and information resulting from the analysis of my samples for other tests not currently planned.

Yes     No

Initials of Research Participant

**SIGNATURE PAGE**

Please sign below if you agree to take part in this study.

- You have read the informed consent and had it explained to you
- You were given the opportunity to ask questions about the information
- You understand the risks and benefits of this study as explained in this consent form
- You voluntarily agree to take part in the study

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Research Participant's Name  
(Please print)

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Research Participant's Signature

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Date

Signature of person explaining and obtaining the consent:

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Name and Title  
(Please Print)

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Signature

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Date

(NOTE: This consent form with the original signatures MUST be retained on file by the principal investigator. A signed copy must be given to the research participant. A signed copy should be placed in the research participant's medical record, if applicable.)