Children's Hospital of Philadelphia

Informed Consent and HIPAA Authorization Form

Study Title: Efficacy of dupilumab on facilitated food introduction in Eosinophilic Esophagitis

Version Date: October 19, 2023

Principal Investigator: Jonathan Spergel, MD Telephone: (215) 590-2549

Emergency Contact: Jonathan Spergel, MD Telephone: (215) 590-2549
On nights or weekends telephone the CHOP Operator at 215-590-1000 and ask to speak to the Allergy attending on call

You, or your child, may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of this research study, and the risks and possible benefits of participating.

In the sections that follow, the word "we" means the study doctor and other research staff. If you are a parent or legal guardian who is giving permission for a child, please note that the word "you" refers to your child.

Study Overview

Why are you being asked to take part in this study?

You are being asked to take part in this research study because you have been diagnosed with eosinophilic esophagitis (EoE) and are between the ages of 6-25 years old. To be eligible for the study, you will also need to have identified that either milk, egg, soy or wheat triggers your EoE.

What is the purpose of this research study?

The purpose of this research study is to see if Dupilumab can allow successful reintroduction of allergic EoE foods into the diet. Researchers want to understand if dupilumab relieves EoE symptoms and reduces esophageal inflammation when EoE-allergic foods are introduced back into the diet.

The goal will be to expand your diet without making your esophageal symptoms or inflammation worse.

Dupilumab is a type of drug called a "monoclonal antibody". An antibody is a special kind of protein that your immune system normally makes to fight bacteria and viruses. Scientists can now make antibodies in the laboratory and produce them for the treatment

of many different diseases. Dupilumab has been shown to target specific molecules that play a role in inflammatory allergic diseases such as eczema and asthma.

Dupilumab has been approved by regulatory agencies including the United States (US) Food and Drug Administration (FDA) for the treatment of moderate-to-severe atopic dermatitis (eczema) in children greater than 6 years of age and adults in the US and European Union (EU). Dupilumab is also approved as an add-on treatment in patients with moderate-to-severe asthma in children greater than 6 years of age and adults in the US and EU, and for the add-on maintenance treatment of nasal polyps with chronic rhinosinusitis in adults in the US.

Dupilumab is being studied for treatment of EoE. Dupilumab is investigational in this study, because it has not been approved by any health authority for individuals under the age of 12 years old, and not as a conjunctive therapy for food reintroduction. It has also been studied in Eosinophilic Esophagitis with positive results for ages > 12. It has also been studied for 1-11 years of age, but no studies have been released..

If you agree to take part, your participation will last for up to 52 weeks and will involve 17 study visits. You will need to take the dupilumab for up to 51 weeks. There is one follow-up week after you complete the study medication. There are differences between this study and your usual care. As a participant in the research you will:

- Receive a study drug;
- Have 17 extra research clinic visits;
- Have an initial research esophageal endoscopy with biopsy, followed by up to a further three such procedures done as part of clinical care;
- During the endoscopy, you will have additional research biopsies of the esophagus
- Have research blood tests

The main risks of this study are from dupilumab. These include: eye inflammation called conjunctivitis. The risks from endoscopy are bleeding and pain.

You may benefit from participation in this study if dupilumab allows you to add back allergic trigger foods to your diet.

If there is anything in this form you do not understand, please ask questions. Please take your time. You do not have to take part in this study if you do not want to. If you take part, you can leave the study at any time. If you do not choose to take part in this study, you can discuss treatment options with your doctor.

How many people will take part?

This study will take place in a single outpatient site at Children's Hospital of Philadelphia. There will be approximately 30 subjects aged 6 to 25 years with known food induced Eosinophilic Esophagitis.

What is the current standard of treatment for this disease?

The two main treatment options are, 1) Dietary therapy: this involves removal of the one or more of the common trigger foods (milk, egg, soy and wheat) and, 2) Medical therapy: this involves use of steroids taken by mouth and or medications to reduce stomach acid (proton pump inhibitors), which helps reduce the esophageal inflammation.

What is involved in the study?

Everyone in this study will get study drug. You will be treated with study drug for 12 weeks to see if you respond. If you respond then a trigger food will be introduced into your diet. A second food may be introduced 12 weeks after that, and then a third food at week 36. You will remain on study drug throughout this period.

Initial phase:

In the initial phase, we will examine if you respond to study drug by examining esophageal inflammation at 12 weeks by a research endoscopy with biopsy.

At this visit, there are 3 possibilities:

1. If your endoscopy and biopsy shows no disease you will proceed to the trigger food introduction phase.
2. If your endoscopy and biopsy shows mild disease you will continue on study drug for another 12 weeks. If that biopsy shows no disease then you will proceed to the trigger food introduction phase. If the biopsy still shows disease then you will exit from the study.
3. If your biopsy shows active disease, meaning you did not respond to the study drug you will exit from the study.

Food introductory phase

A trigger food will be introduced as one serving size per day at week 13. If repeat esophageal biopsy at week 24 shows no inflammation then you can increase the serving size to 2 servings per day of that trigger food or you can choose to add in a second trigger food. If the week 24 biopsy show mild inflammation your diet will remain the same. If active disease is present then the trigger food will decrease to ½ serving size a day.

At the week 36 esophageal endoscopy with biopsy you will have three options. If there is no inflammation you may increase the serving size to ad lib (if eating one trigger food) or you may increase the serving size of the 1st and 2nd trigger foods to 2 serving size a day or you may add a 3rd trigger food. If the biopsy shows mild inflammation your diet will

remain the same. If active disease is present then the trigger food/s will decrease to ½ a serving size a day

What are the study procedures?

Some of the procedures in this study will be repeated several times. Tests that are part of your regular, routine medical care will continue to be performed. Additional tests may be performed if any of your initial test results are not normal. The study doctor or study staff will do the things listed below when you come in for study visits. If you would like more information about which tests and procedures will be done at each study visit, you can ask the study doctor or study staff.

Samples (Esophageal biopsies and blood samples) will be collected as part of this study for study related analysis. They will be analyzed during the course of the study to examine how you respond to introduction of trigger food.

The first endoscopy will be considered research as it looks your response to dupilumab (a research medication). The remaining endoscopies will be standard of care as it is normal practice to do upper endoscopy and biopsy after each food introduction.

The study involves the following tests and procedures:

Experimental Procedures:

Food introduction: You will be add one serving size of a known EoE trigger food. It can be either milk, egg, wheat or soy. Depending on the results of your next endoscopy, you can either add a new food, decrease the amount of food or increase the amount of food as listed above.

Study Drug Administration: The study medication is given by injection under the skin (subcutaneous) in the upper arms, stomach, or upper thighs, avoiding the navel and waist areas. The same site should not be injected twice in a row. The amount of study drug you receive will depend on your age and weight. If a study drug injection is done in the clinic you will be asked to stay for at least 30 minutes after the injection for observation.

During the first 2 study visits you will be trained by the site staff to give an injection or how to inject yourself with study drug at scheduled time points throughout the study. You will also be provided with written instruction about how to do the injections. If you do not want to inject study drug you can have it done in the clinic.

Quality of Life Questionnaires: Questionnaires related to your EoE to be completed by you and your parent.

Symptoms Questionnaires: Questionnaires related to your EoE symptoms to be completed by you

Diet Diary: To indicate that you are eating the new foods.

Administration Dosing Diary: If you choose to self-administer the injections, you will need to record study treatment administration at home.

Receive and Return Drug: Used and unused dupilumab will be returned for accountability.

Routine Clinical Trial Procedures:

Upper Endoscopy and Biopsy: Endoscopy ("EGD") is a test where an instrument is inserterted into your mouth and looks into your esophagus, which is the "tube" your food passes through to your stomach. Biopsy is when a very tiny piece of tissue is taken from your esophagus. A total of at least 4 samples will be collected from your esophagus. Tissue samples from the stomach and/or small intestine may be taken as well. You will be given some medication for this procedure, which will make you feel sleepy, this is called conscious sedation. Upper endoscopy will be performed at visits 4, 8, 12 and 16. The endoscopy at visit 4 is research. The endoscopy at week 8, 12 and 16 are standard of care. There will be six research biopsies at week 4, 8, 12 and 16.

Endoflip: If you agree, the EndoFLIP, a device approved by the Food and Drug Administration (FDA) will be used to take measurements in your esophagus. A catheter (thin flexible tube) will be inserted through the endoscope channel or alongside the endoscope to obtain measurements of your esophagus. These measurements will be used to determine if the EndoFLIP device is a good method to measure inflammation and stiffness of the esophagus in children with EoE. More information related to the EndoFLIP procedure will be discussed at the end of this consent form.

Medical and Medication History: The study doctor or study staff will ask you to give personal information, such as your name, age, race, and ethnicity. The study team will also review your medical records and medications during the study and ask you how you feel. It is very important that you answer these questions to the best of your ability. Your study doctor may ask questions related to your asthma and/or allergic rhinitis and/or atopic dermatitis if you have these conditions. If required, the study doctor, with your permission, may contact your personal physician to collect additional medical information or past medical history. You will also be asked questions about any new medical problems since your last visit.

Physical Examination: This will involve an examination of your body, e.g. the doctor may look at your skin, eyes, throat, and listen to your heart and lungs.

Vital Signs: The study doctor or study staff will check your blood pressure and pulse, and take your body temperature. Your weight and height will also be checked.

Blood Testing: You will complete blood draws at visits 1,4,8,12 and 16. We will collect one tablespoon of blood at the time of each upper endoscopy (visits 4,8,12,16).

Pregnancy Testing: If you are pregnant or nursing, you will not be allowed to participate in this study. If you are a female and have already started having periods, you will be asked to take blood or urine pregnancy tests at various specified visits. The results will be shared with you and not with your parent(s). We strongly encourage you to share the results with your parents. If you are found to be pregnant, you will not be able to continue participation in the study.

Birth Control for Female Subjects: If you are old enough to become pregnant, you must use effective birth control methods during the study and up until 12 weeks after the last dose of the study drug. Your study doctor can explain the types of birth control that should be used.

Visit Schedule

The table below provides a brief description of the purpose and duration of each study visit.

At each visit, we will do a physical exam and collect vital signs

After the first visit, we will collect health information to determine if any adverse events occurred and questionnaires will be given.

Visit Schedule

The table below provides a brief description of the purpose and duration of each study visit.

Visit	Purpose	Main Procedures0	Duration
Visit 1	Screening visit	Consent,Medical history, Physical exam, blood, diary training, pregnancy test (if applicable), drug dispensation/ Injection training	2.5 hours
Visit 2 Visit 3 Visit 6 Visit 10 Visit 14	Study Drug Administration	Physical exam, Questionnaire, drug dispensation/ Injection training (V2 & 3)/ drug administration	1.5 hours

Visit 4 Visit 8 Visit 12 Visit 16	Endoscopy with Biopsies	EGD, EndoFLIP, bloodwork, questionnaires, Physical exam	4 hours
Visit 5 Visit 9 Visit 13	Food Introduction	Physical exam, questionnaire, food introduction, blood work, drug dispensation	3 hours
Visit 7 Visit 11 Visit 15	Symptom Evaluation	Questionnaire, Advese Events	1 hour
Visit 17	End of Treatment	Physical exam, Questionnaires, Adverse Events	1.5 hours

What are the risks of this study?

Study drug (Dupilumab) has been studied in more than 12,000 individuals in completed and on-going studies, including healthy volunteers, patients with eczema (atopic dermatitis), asthma, nasal polyps and eosinophilic esophagitis. In these studies, some patients were treated with study drug while others received placebo. In completed studies approximately 7000 patients have received study drug, including children and adolescents with eczema and asthma down to 6 months of age.

The risks involved in giving study drug are not fully known. A side effect is an undesirable effect of a drug or medical treatment. In clinical studies of study drug in adults with eczema, side effects reported more often in patients treated with study drug compared to those receiving placebo, and which were possibly related to study drug, are listed in the table below.

Most Common (More than 1 in 10)	**Common** (between 1 and 10 out of 100)	**Rare** (less than 1 out of 100)

Atopic Dermatitis (Eczema) Only: Conjunctivitis: 'Pink eye' due to allergy, infection or other cause Both Asthma and Atopic Dermatitis (Eczema): Injection site reaction: including redness, swelling, pain, itching at the site of study drug injection	Asthma, Atopic Dermatitis and Allergic upper airway inflammation: Eosinophilia: an increase in a certain kind of white blood cells as detected in a blood test Asthma only: Oropharyngeal pain: Sore throat CRSwNP (a disease of interior of the nose and the sinus) only: Arthralgia: Joint Pain Gastritis: Stomach pain and inflammation Toothache Insomnia: Sleep difficulities Infection: Enterobiasis (pin worm): A type of intestinal worm infection Injection site reactions including pain, bruising or swelling at the site of study drug injection Conjunctitivitis: 'Pink eye' due to allergy, infection or other causes Atopic Dermatitis only: Headache Herpes simplex infection of mouth, lips (cold sores, also known as fever blisters), genitals or ears Blepharitis: Inflammation (swelling and redness) of the eyelid	Asthma, Atopic Dermatitis, and Allergic upper airway inflammation: Anaphylactic reaction: A type of serious allergic reaction, symptoms may include skin flushing, rash or hives, sneezing, runny nose, difficulty breathing, wheezing, a sense of choking, sudden change in blood pressure (causing dizziness or lightheadedness), swelling around the mouth, throat, or eyes, fast pulse or sweating, abdominal cramps, diarrhea Serum sickness like reaction, serum sickness: A type of reaction where symptoms may include fever, rash, joint swelling, joint pain, muscle pain, headache, nausea, diarrhea, swollen glands and blurred vision

	Eye pruritus: Itching in eye Dry eye: Dryness of the eyes Keratitis: Swelling and redness of the cornea (the outer clear layer in front of the eyeball) due to any cause including herpes infection	

The higher risk of pink eye, swelling of the eyelid or outer layer of eyeball, and herpes sores in dupilumab treated patients has been seen in eczema patients and not in asthma patients. You should let your study doctor know about any new or worsening eye symptoms or if your eye symptoms get worse.

Post – marketing information Some additional side effects beyond those identified in clinical trials have been identified from reports received after study drug was placed on the market:

- Joint pain
- Angioedema (a condition that causes puffiness or swelling in the tissue under the skin; areas that may be affected include but are not limited to, the face, eyelids, mouth, tongue and hands)
- Ulcers on the cornea (the outer clear layer in front of the eyeball)
- Facial rash

Risk of allergic or hypersensitivity reaction:
As with any drug, there is a slight chance that you may experience a local or generalized allergic reaction (also known as a hypersensitivity reaction) – including anaphylactic reactions. An anaphylactic reaction can happen immediately (within minutes or hours) after taking study drug.

Symptoms of anaphylactic reaction or other allergic reaction may include:

- skin flushing
- rash or hives
- sneezing
- runny nose
- difficulty breathing, wheezing a sense of choking
- sudden change in blood pressure (causing dizziness or lightheadedness)
- swelling around the mouth, throat, or eyes
- fast pulse or sweating
- abdominal cramps, diarrhea, etc.

The severity of this type of immediate reaction ranges from mild to severe. A mild reaction may progress to a more severe one, so you should contact the study personnel if you experiences any new symptoms occurring within a couple of hours after study drug injection. You should not be given any further study drug injections if you have had a generalized or serious or severe allergic reaction to study drug in the past or have a known allergy to any part of this medication.

An anaphylactic or severe allergic reaction requires immediate medical treatment and could result in permanent disability or death if not treated promptly. If you believe you are having an anaphylactic or severe allergic reaction, you should immediately seek emergency medical treatment and alert the study doctor and study staff as soon as possible.

Also, it is possible that your body may develop antibodies to study drug. Formation of antibodies is a natural defense reaction of the body's immune system against the presence of foreign substances. These antibodies may sometimes work against your body, which could result in illness.

Another kind of hypersensitivity reaction called 'serum sickness' or 'serum sickness type reaction' sometimes occurs days to weeks after study drug injection and it may cause complaints of fever, skin rash, swelling and pain in joints, muscle pain, swollen glands, headache, nausea, diarrhea and blurred vision.

Risks from food introduction:

The main risk from food introduction is exacerbation of Eosinophilic Esophagitis symptoms. You will be monitored weekly by phone for increasing symptoms and study visits for worsening symptoms by validated EoE questionnaires. In addition, the other risk is increasing eosinophils in the esohagus which can lead to scarring of the esophagus if not treated. Therefore, we monitor for worsening disease at 12 weeks after food introduction by upper endoscopy with biopsy. The scarring is reversible whith further treatment.

Other Risks:

There is a risk that your Eosinophilic Esophagitis (EoE) may not get better or may get worse during the study. Pink eye (conjunctivitis) and inflammation of the outer clear layer in front of the eyeball (keratitis), possibly associated with blurred vision, have been reported with study drug, mostly in patients being treated for eczema.
You should report new onset or worsening eye symptoms to your healthcare provider. If you develop conjunctivitis that does not resolve following treatment or if your signs and symptoms are suggestive of keratitis, you need to tell your doctor, as you might need an

eye exam.

A temporary increase in the number of eosinophils (a type of white blood cell) in the bloodstream has been observed with study drug in clinical studies. This increase was not associated with clinical symptoms in most patients. However, in patients with asthma, this increase in blood eosinophils has rarely been associated with symptoms such as inflammation of blood vessels or lungs, which in some cases can be very serious. Please discuss with your study doctor if you have a history of high blood eosinophil levels or an eosinophil related disorder or experiences unexplained symptoms like numbness, tingling, weakness, rash and worsening cough or any new heart problems.

If you also have asthma, please do not adjust or stop your asthma medicines without consulting with the study doctor. Study drug should not be used to treat acute asthma symptoms.

If you are using any steroid medications (e.g., applying to the skin, taking orally or by an inhaler), talk to your doctor and do not stop using them suddenly. Steroid medications have to be stopped slowly and under doctor's instructions. Stopping or reducing steroid medications may cause withdrawal symptoms and/or cause other conditions to appear which were previously being hidden by the steroid medications.

Based on the nature of study drug and its mechanism of action, other theoretical risks might include infections with parasites (e.g. intestinal worms). The symptoms of pinworms include anal itching and related difficulty sleeping due to the itching. Other parasitic infections can cause abdominal pain, vomiting or diarrhea

In one of the studies in patients with moderate to severe asthma, more patients on study drug reported serious adverse events involving the heart than patients on placebo. A similar heart problem has not been observed in other clinical studies involving the study drug.

Tell your study doctor if you have recently had or are due to have a vaccination. In a clinical study in adult patients with eczema, study drug was shown to not interfere with the development of immune response to two non-live vaccines (Adacel and Menomune) that were tested in this study. These vaccines provide protection against infections specific to these vaccines. Dupilumab has not been tested in combination with live virus vaccines.

Based on results from a research study in patients with eczema, study drug is not expected to have an interaction with most of the drugs that are commonly prescribed by doctors. However, since data do not exist for every drug, it is possible that study drug may have some interaction with other drugs you are taking.

There is a risk that your underlying disease, for which you are in this study, may not get better or may worsen during the study.

Dupilumab has not been studied as extensively in children as in adults. There might be some currently unknown risks of study drug that are specific to children.

It is possible that there may be other side effects associated with study drug which are unknown at this time, some of which may be serious or life-threatening. There is limited long-term safety data currently available with study drug. You should tell your study doctor or a member of the study staff about any new health problems that develop while you are in this study and about any new medications you start taking (including over-thecounter medication, herbal remedies, and non-prescription drugs).

You will be given any new information as it becomes available that can help you decide whether you want to continue in the study.

Major elective surgical procedures are prohibited during study treatment (through week 52). Please talk to your study doctor if you have any planned surgeries.

Reproductive Risks:

For female subjects:

If you are a female, you must not be pregnant, breastfeeding, or become pregnant during this study and until 12 weeks after the last dose of study drug. Study drug has not been studied in pregnant or breastfeeding women. If you become pregnant while receiving study drug, there may be risks to you and your unborn baby. Nobody knows what these risks could be right now. The effect of study drugon women who are breastfeeding and their breast-fed child is also unknown.

If sexually active, you must agree to use a medically acceptable method of birth control from start of study until 12 weeks after the last dose of study drug. Please discuss acceptable birth control measures with you study doctor. These methods may include:

- Stable use of combined (estrogen- and progestogen-containing) hormonal contraception (oral, intravaginal, transdermal) or progestogen-only hormonal contraception (oral, injectable, implantable) associated with inhibition of ovulation initiated 2 or more menstrual cycles prior to screening
- Intrauterine device; intrauterine hormone-releasing system
- And/or sexual abstinence (Sexual abstinence is considered a highly effective method only if you refrain from heterosexual intercourse from the start of study until 12 weeks after the last dose of study drug, and this is your preferred and usual lifestyle.)

Females who become pregnant during the study should contact Dr. Spergel immediately and stop the study. The study doctor or study staff will ask for information about the pregnancy and the birth of the baby.

Risk from Blood Draw:

Taking blood may cause some pain, bleeding or bruising at the spot where the needle enters your body. Rarely, taking blood may cause fainting or infection.

Risk from upper GI endoscopy:

Possible risks and discomforts associated with the endoscopy procedure include gagging, nausea, vomiting, sore throat and possible reaction to the numbing medicine used during the procedure. The endoscope could puncture or pierce the intestines. This could require additional treatment or surgery. When biopsies are taken, this could lead to bleeding or infection. There are other less common riks of endoscopy. The doctor performing the endoscopy will explain these riks to you in more detail before you have the endoscopy procedure.

Risks from Sedation:

Sedative medicines may make you sleep for several hours and sometimes can have prolonged effect. Uncommon but serious complications include: irregular heartbeat, increases or decreases in blood pressure, rare reactions to medications used, and blockage of breathing passages. All of these complications are treatable but rarely, may lead to coma or even death. Emergency personnel and equipment will be be available in the event of a serious adverse reaction to sedation. You will have an opportunity to discuss thse risk and specific drugs that will be use with the nurse or doctor who will supervise the sedation.

Risk from Endoflip:

If you agree to measurements in the esophagus with the EndoFLIP, sedation time may increase from 2 to 5 additional minutes. Also, the balloon at the tip of the catheter (thin flexible tube) containing a saline solution may rupture however the solution is not harmful to you. The EndoFLIP test adds time to the clinically indicated endoscopy, which increases the time you are exposed to the risks of anesthesia. This time will be approximately 5 minutes, which is the time required to perform the EndoFLIP measurements. There is a possible risk of over inflation of the balloon. This is not expected, because the EndoFLIP device has a pressure sensor and alarm system to prevent over inflation of the balloon or rupture of the balloon. If the balloon leaks or ruptures, a saline solution may leak into the esophagus, which is not expected to be harmful to you

Risks associated with physical exams, questionnaires, diet diaries and interviews*:*

You may experience momentary embarrassment or discomfort when completing these procedures; however this is unlikely. These procedures involve minimal risk and are similar to procedures that are typically done as part of routine medical care.

Risk of breach of confidentiality:

As with any study involving collection of data, there is a possibility of breach of confidentiality of data. Every precuastion will be taken to secure participants' personal information to ensure confidentiality.

At the time of participation, each participant will be assigned a study identification number. This number will be used on data collection forms, blood samples, tissue specimens and in the database instead of names and other private information. A separate list will be maintained that will link each participant's name to the study identification number for future reference and communication.

Are there any benefits to taking part in this study?

The major benefits is the ability to eat new foods in your diet, which in the past you could not eat, which can possible lead to improvement in the quality of life. In addition, dupilumab may lead to improvement in your EoE. In addition, your participation will provide new information on the effects of dupilumab in people, and might help others with EoE in the future.

Do you need to give your consent in order to participate?

If you decide to participate in this study, you must sign this form. A signed copy will be given to you to keep as a record.

What are your responsibilities?

Please consider the study time commitments and responsibilities as a research subject when making your decision about participating in this study. You will need to follow the study doctor's instructions, keep all study appointments and take the study drug as directed.

During the study, if you need to change any of your medications or therapies, please talk to the study doctor.

What happens if you decide not to take part in this study?

Participation in this study is voluntary. You do not have to take part in order to receive care at CHOP. If you decide not to take part or if you change your mind later there will be no penalties or loss of any benefits to which you are otherwise entitled.

Can you stop your participation in the study early?

You can stop being in the study at any time. You do not have to give a reason. If you have started receiving study drug and decide to discontinue, you should let the study doctor know before you stop. You will be asked to come back for a follow-up visit. Procedures will be done to help ensure that there are no changes in your health. You will also be asked to return all unused, partially used, and/or used containers to the study site.

Can the study doctor take you out of the study early?

The study doctor may take you off of the study if:

- Your condition worsens.
- If you are experiencing unusual or serious side effects.
- The study drug is no longer available.
- You cannot meet all the requirements of the study.
- New information suggests taking part in the study may not be in your best interests.
- The study is stopped by The sponsor, Regeneron Pharmaceuticals, Inc., the investigator, or a regulatory authority such as the FDA has the right to stop your participation in the study at any time, with or without your consent.

What choices do you have other than this study?

You do not have to take part in this study to receive treatment for your EoE. There may be other alternatives such as esophageal dilatation, or being treated with diets that eliminate foods that you may be allergic to. Some subjects are treated with corticosteroids or other medications. For medical therapy, dupilumab is now an approved medication for EoE patients greater than 12 years old.The study doctor will discuss these options with you.

There are benefits and risks related to these medicines that the study doctor will discuss with you.

Your other option is for you to not take part in the study.

What about privacy, authorization for use of Personal Health Information (PHI) and confidentiality?

As part of this research, health information about you will be collected. This will include information from medical records, physical exams, questionnaires, laboratory tests, and procedures you have done as part of this study. Your research laboratory test results will not be placed in your electronic medical record here at CHOP. All laboratory results and procedures involved with this research study will only be placed in your research subject chart. Medical records are available to CHOP staff. Staff will view your records only when required as part of their job. Staff are required to keep your information private. Information that could identify you will not be shared with anyone - unless you provide your written consent, or it is required or allowed by law. We will do our best to keep your personal information private and confidential. Your name will not be attached to records or samples released for research purposes. Instead, your records and samples will only be identified by a code. However, we cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

The results of this study may be shown at meetings and published in journals to inform other doctors and health professionals. We will keep your identity private in any publication or presentation. To fulfill regulatory requirements and industry guidelines, the results from this study will also be provided to qualified researchers who request it for legitimate research purposes in a manner that does not disclose your identity.

Several people and organizations may review or receive your identifiable information. Those listed below will need your information to conduct the research, to assure the quality of the data, or to analyze the data or samples. These groups include:

- Members of the research team and other authorized staff at the Children's Hospital of Philadelphia;
- People from agencies and organizations that perform independent accreditation and/or oversight of research; such as the Department of Health and Human Services, Office for Human Research Protections.
- Regeneron Pharmaceuticals and Sanofi, its collaborators in the research study or those developing the study drug, and their affiliates, representatives, agents and contractors (the "Regeneron Parties");
- The Food and Drug Administration;
    - Public health authorities that are required by law to receive information for the prevention or control of disease.
- Other U.S. government agencies and possible government agencies of other countries

By law, CHOP is required to protect your health information. The research staff will only allow access to your health information to the groups listed above. By signing this document, you are authorizing CHOP to use and/or release your health information for this research. Some of the organizations listed above may not be required to protect your information under Federal privacy laws. If permitted by law, they may be allowed to share it with others without your permission.

The study results and coded data will be kept as long as they are needed for research purposes, any regulatory requirements, and CHOP's data retention schedule. As advancements in medical technology continue, Dr. Spergel will share deidentified data after the results are published for future research projects to find new scientific information about the study, study drug, EoE, or other related diseases.

Your permission to use and share the information and data from this study will continue until the research study ends and will not expire. Researchers continue to analyze data for many years and it is not possible to know when they will be completely done.

Will you receive any results from the tests done as part of this study?

The results produced as part of this study are for research purposes only. If, during the course of the study, the study doctor learns information related to your child's health from the study procedures, the study doctor may discuss this information and your child's options with you and your child.

Can you change your mind about the use of personal information?

You may change your mind and withdraw your permission to use and disclose your health information at any time. To take back your permission, it is preferred that you inform the investigator in writing.

Dr. Jonathan Spergel

The Children's Hospital of Philadelphia

Division of Allergy and Immunology

34th Street and Civic Center Blvd. Philadelphia, PA 19104

In the letter, state that you changed your mind and do not want any more of your health information collected. The personal information that has been collected already will be used if necessary for the research. No new information will be collected. If you withdraw your permission to use your personal health information, you will be withdrawn from the study.

Additional Information

The principal investigator (PI) will monitor adverse events and other safety concerns during the study. As the drug is approved for this age group and has been studied in this indication, little new adverse events are expected. While the study is in progress, you may not be given access to some health information that is related to the study.

You will be informed if changes to the study are needed to protect your health. You will be told about any new information that could affect your willingness to stay in the study, such as new risks, benefits or alternative treatments.

Financial Information

While you are in this study, the cost of your usual medical care – procedures, medications and doctor visits – will continue to be billed to you or your insurance.

Will there be any additional costs?

There will be no cost to you for the study drug, study doctor's time, certain procedures such as the endoscopy done at the screening visit and supplies required by this study.

You are responsible for the cost of your standard medication, in addition to any costs related to procedures and supplies not required by the study. All study drug supplies will be provided at no costs to you.

You or your insurance will be billed for the routine costs of a trial, which include procedures listed at "routine clinical trial procedures" above. This includes three endoscopies after food introduction.

We can help you understand your financial responsibilities.

Will you be paid for taking part in this study?

You/parents will be reimbursed $35 per visit for travel and expenses without receipts, and up to $250 per visit with receipts for expenses. You will be compensated $125 for each endoscopy due to extended time without receipts and $250 with receipts for travel expenses.

The study team will provide you with a debit card for you to receive the compensation for Study particpation. You will be required to register your payment card with the company that is providing the payment cards by entering personal information, including your name, date of birth, and home address.

If you receive payment using a bankcard, the bank will have access to identifiable information. The bank will not have access to any medical information. If payment exceeds $600 in a calendar year, you will receive a W9 form.

Who is funding this research study?

CHOP is sponsoring this study and it is being supported by Regeneron and Sanofi by supplying free drug for the study. Regeneron is a drug company that makes the drug being studied in this research project. Sanofi is working in collaboration with Regeneron.

You will not receive money or any other form of payment for the samples you contribute or for any medical or genetic tests, drugs or other commercial products we may develop through this research. You will not receive money or any other form of payment if an approved product is developed from the research performed in this study.

Dr. Spergel is a paid consultant for Sanofi and Regeneron, the sponsor of this study. Dr. Antonella Cianferoni, a sub-investigator working on this study, is a paid consultant for Genzyme Corporation, a subsidiary of Sanofi. Sanofi is working in collaboration with Regeneron. Both Doctor's participation has been reviewed in accordance with CHOP's Conflicts of Interest Policy. If you have any questions or concerns, you may contact Dr. Jonathan Spergel, Dr. Antonella Cianferoni or the Conflict of Interest Office at COI@email.chop.edu or 267-426-6044. Please ask Dr. Jonathan Spergel if you have any questions about how this study is funded.

What if you have questions about the study?

If you have questions about the study, call the study doctor, Dr. Jonathan Spergel at 215-590-2549. You may also talk to your own doctor if you have questions or concerns.

The Institutional Review Board (IRB) at The Children's Hospital of Philadelphia has reviewed and approved this study. The IRB looks at research studies like these and makes

sure research subjects' rights and welfare are protected. If you have questions about your rights or if you have a complaint, you can call the IRB Office at 215-590-2830.

A description of this clinical study 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.

What happens if you are injured during the study?

If you are hurt or get sick from something that was done as part of this study, doctors at the clinic or hospital can arrange for emergency care. Treatment may be billed to you or your insurer. If your injury is caused by a research procedure or the experimental drug, Regeneron may pay for treating the injury. This does not mean that a mistake happened.

The Hospital does not offer financial compensation or payment if you are injured as a result of participating in this research.

If you think you have been injured from taking part in this study, call Dr. Jonathan Spergel at (215)-590-2549. He can go over things with you, let you know of resources that may be available and give you information on what you need to do.

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

What will be done with my data when this study is over?

During this study we will collect blood, urine, and esophageal biopsy tissue from you; we will not use these samples in future research. We will use and may share data for future research. They may be shared with researchers/institutions outside of CHOP. This could include for profit companies. We will not ask for your consent before using or sharing them. We will remove identifiers from your data and/or specimens, which means that nobody who works with them for future research will know who you are. Therefore, you will not receive any results or financial benefit from future research done on your specimens or data.

Consent to Inform Your Doctors of Your Study Participation (OPTIONAL)

Please indicate whether you would like us to inform your doctor(s) of your participation in this study.

_____ (initials) I request that my doctor(s) **not** be informed of my participation in this study.

_____ (initials) I request that my doctor(s) be informed of my participation in this study.

Consent to Take Part in this Research Study and Authorization to Use and Disclose Health Information for the Research

The research study and consent form have been explained to you by:

Person Obtaining Consent	Signature of Person Obtaining Consent
	Date

By signing this form, you are indicating that you have had your questions answered, you agree to take part in this research study and you are legally authorized to consent to your child's participation. You are also authorizing the use of your/your child's health information as discussed above. If you don't agree to the collection, use and sharing of health information, you cannot participate in this study. **NOTE:** *A foster parent is not legally authorized to consent for a foster child's participation.*

Name of Subject	
Signature of Subject (18 years or older)	Date

Both Parents Must Sign this Consent Form

Name of Authorized Representative #1	Relation to subject: ☐ Parent ☐ Legal Guardian
Signature of Authorized Representative #1	Date
Name of Authorized Representative #2	Relation to subject: ☐ Parent ☐ Legal Guardian
Signature of Authorized Representative #2	Date

Child Assent to Take Part in this Research Study
For children capable of providing assent:

I have explained this study and the procedures involved to _____ in terms he/she could understand and that he/she freely assented to take part in this study.

_____
Person Obtaining Assent

_____ _____
Signature of Person Obtaining Assent Date

This study has been explained to me and I agree to take part.

_____ _____
Signature of Subject (optional) Date

For children unable to assent:

I certify that _____ was not capable of understanding the procedures involved in the study sufficiently to assent to study participation.

_____
Person Responsible for Obtaining Assent

_____ _____
Signature of Person Responsible Date