

# Volunteers Needed for Sjögren's Syndrome Study

*Researchers at the National Institutes of Health (NIH) Clinical Center seek people with Sjogren's Syndrome to join a research study. Doctors are evaluating the safety and tolerance of tofacitinib in people with Sjogren's Syndrome. Compensation will be offered.*

## Do You Qualify?

*You may qualify for this study if you are:*

- Willing & able to sign/date the informed consent form
- Willing to comply with all study procedures and available for study visits and calls
- Male or female aged 18-75 years old
- Diagnosed with Sjögren's Syndrome
- Enrolled, or willing to enroll, in a companion study, 15-D-0051, to screen for Sjögren's Syndrome

*You may not qualify if you:*

- Are a current smoker or tobacco use within 3 months
- Are pregnant or breastfeeding
- Are on current or prior treatment with rituximab or belimumab

## Study Procedures Include:

- A total of 10 study visits
- An oral exam, medical, eye exam and history
- Blood and saliva collection
- Lip biopsy

## Compensation:

- Compensation is offered for each study visit in addition to a completion bonus.

## Location

NIH Clinical Center, in Bethesda, Maryland. On the Metro red line (Medical Center stop).

## To Learn More

- Call the Office of Patient Recruitment: 1-800-411-1222, TTY: 1-866-411-1010
- Read about the study online: [ClinicalTrials.gov](http://ClinicalTrials.gov) and search using study number: **20-D-0131**
- For more information, please call or e-mail: **Sasha Clary** 301-529-7924, [sasha.clary@nih.gov](mailto:sasha.clary@nih.gov)



National Institute of Dental  
and Craniofacial Research

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**PRINCIPAL INVESTIGATOR: Blake M. Warner, D.D.S, Ph.D., M.P.H., ABOMP**

**STUDY TITLE: Safety of Tofacitinib, an oral Janus Kinase Inhibitor, in primary Sjögren's syndrome Phase Ib-IIa placebo-controlled clinical trial and associated mechanistic studies**

**STUDY SITE: National Institutes of Health Clinical Research Center**

Cohort: *Affected Patient*

Consent Version: 06.16.2022

### WHO DO YOU CONTACT ABOUT THIS STUDY?

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### KEY INFORMATION ABOUT THIS RESEARCH

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). This section provides the information we believe is most helpful and important to you in making your decision about participating in this study. Additional information that may help you decide can be found in other sections of the document. Taking part in research at the NIH is your choice.

Sjögren's syndrome is an autoimmune disease that often involves multiple systems and organs of the body. An autoimmune disease is one in which your immune system attacks the cells and components of your own body. Sjögren's syndrome can cause dry mouth, dry eyes, fever, joint pains, rashes and many other symptoms. Sjögren's syndrome can also affect other organs, such as the kidney or the lungs and increase your risk for lymphoma.

When you have Sjögren's syndrome, your cells can produce proteins which, rather than killing bacteria or viruses, attack your body and cause damage to various organs. One such type of protein that can be found in patients with Sjögren's syndrome is called a cytokine. Patients with Sjögren's syndrome produce extra cytokines and these have been shown to cause damage to various organs of the body. Cytokines have been found in salivary gland biopsy tissue from Sjögren's syndrome patients. In addition, cytokines recruit signaling molecules, which are thought to accelerate the progression of Sjögren's syndrome.

Tofacitinib is a drug that is approved by the FDA for treating rheumatoid arthritis but has never been used to treat Sjögren's syndrome. Tofacitinib works by blocking the effect of some of the cytokines on cells. Scientists at NIH think that this drug can target the cytokines that are involved in causing damage to various organs in patients with Sjögren's syndrome. By blocking such cytokines, we may slow down or prevent organ damage in patients with Sjögren's syndrome.

### PATIENT IDENTIFICATION

#### Consent to Participate in a Clinical Research Study

NIH-2977 (4-17)

File in Section 4: Protocol Consent (1)

Version Date: 06/16/2022

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IRB NUMBER: 20D0131

IRB APPROVAL DATE: 06/21/2022

Current treatments for Sjögren’s syndrome include a variety of drugs that work by suppressing the immune system, such as hydroxychloroquine, and steroids.

There are some Sjögren’s syndrome patients for whom these medications are not beneficial. Therefore, there is a need for new treatments for Sjögren’s syndrome.

The remaining document will now describe the research study in more detail. This information should be considered before you make your choice. Members of the study team will talk with you about the information in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research interventions in which they would want to participate. Take the time you need to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

### **IT IS YOUR CHOICE TO TAKE PART IN THE STUDY**

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

### **WHY IS THIS STUDY BEING DONE?**

This is a research study. The purpose of this research study is to evaluate the safety and tolerance of tofacitinib in people with Sjögren’s syndrome

We are asking you to join this research study because you have Sjögren’s syndrome. The current medications used in Sjögren’s syndrome can be associated with serious side effects. In addition, there are Sjögren’s syndrome patients for whom these medications are not beneficial. Researchers are trying to find new, more effective and safe treatments

Through this study, we hope to learn how patients with Sjögren’s syndrome tolerate this medication. It will also help us better understand Sjögren’s syndrome. Tofacitinib has been approved by the United States Food and Drug Administration (FDA) for use in patients with rheumatoid arthritis but has never been given to patients to treat Sjögren’s syndrome. In this document, we will tell you why we think this drug may be useful to treat Sjögren’s syndrome, and what other treatments are available for you. We will also tell you what we know about tofacitinib to date, and about any risks to you from taking part in this study. We will also describe what is involved in the study. We plan to enroll 30 subjects in the study and each subject will be followed for 28 weeks or about 7 months for this study.

### **WHAT WILL HAPPEN DURING THE STUDY?**

During the study, you will continue to receive your routine medications and the study medication or placebo will be given as an additional medication. If you develop a flare of Sjögren’s syndrome during the study, only medications that are allowed by the protocol will be provided as treatment. These medications are detailed in the “Use of medication during the study” section below. If your flare needs immediate immunosuppressive treatment, you will be taken out of the study and will be treated according to standard treatment for Sjögren’s syndrome flare.



You will be asked to enroll in “Characterization of Diseases with Salivary Gland Involvement” Study (15-D-0051) to be pre-screened to determine if you may be eligible to screen for this study. If you are eligible to screen for this study, you will be asked to sign this informed consent form and undergo screening procedures/tests to see if you qualify for the study. If you qualify for the study, you will be randomly assigned (in a manner like flipping a coin) to receive either an oral dose of tofacitinib 5mg (1 tablet) twice daily or a placebo (a substance that looks like tofacitinib but contains no medication) for 168 days. Neither you nor the study staff will know who receives the drug or placebo. The study staff will find out about your treatment assignment after the last subject has completed the study and we will inform you of your treatment assignment at that time. For every two patients who receive tofacitinib, one will receive placebo; in total 20 subjects will receive drug, and 10 will receive placebo.

The first dose of tofacitinib or placebo will be given at the NIH Clinical Research Center Day hospital or Outpatient Clinic in the NIH.

Here is more information about what will happen in the study:

You will come to the NIH Clinical Center outpatient visit to see if you are able to be in this study. This visit is called a Screening visit. At this visit, a NIH study team member will review this consent form with you and discuss your medical history. During this visit you will receive an explanation of the study by the NIH study team and be given a chance to ask questions about the study. If you are interested in being in the study, you will be asked to sign this form. You will not be allowed to be in any part of the study until you have signed and dated this form. You will receive a copy of the signed and dated form.

If you are found to be eligible for this study, you will be asked to return to the NIH Clinical Center to begin study drug or placebo administration (Study Day 1). If you are a female who can become pregnant, you will have a pregnancy test done before receiving your dose of study drug or placebo. If the urine pregnancy test is positive, you will no longer be eligible for the study and will not receive a dose of study drug or placebo.

Before dosing you will be evaluated to make sure your health did not worsen since screening. Your vital signs (blood pressure, respiratory rate, heart rate, and temperature) and weight will be taken. We will give you a physical exam and ask you questions about your Sjögren’s syndrome activity. Routine blood (blood counts, safety labs, and chemistries) and urine tests will be completed. We will also ask if you have had any problems since your last visit. Throughout the study, you will be asked to complete multiple questionnaires about various aspects of your health.

After you have orally taken the first dose of study drug or placebo at NIH on Day 1, you will be provided with a 35-day supply of tablets. The tablets should be taken orally twice daily with or without food.

You will be asked, by the research nurse coordinator, to bring your bottle containing study tablets with you to the Day 28, 56, 84, 112, 140, 168 and unscheduled visits. Please be sure to bring all tablets that might be left over. We will do a tablet count to be sure you are taking the tablets as directed by the study investigator. The Day 168 visit will be the last visit during which you will take the tablets. You will also be seen on Day 196 as a final assessment after stopping the study drug.



## STUDY PROCEDURES

### EKG

An electrocardiogram (EKG) is a test that gives us a measure of the heart's electrical activity. You will be asked to lie flat on a table and several small electrode pads (like stickers) will be placed on the body. This test takes about 10 minutes.

### Vascular Studies

You will be requested to hold all your medications the morning when you come in for these studies, and to resume these medications on the same day, once these studies are completed.

- a) **Peripheral wave analysis (SphygmoCor):** This test will measure your blood pressure and the speed of your blood flow through your body's organs. It indicates the level of arterial stiffness, which could be related to the buildup of arterial plaque. This test takes 15 minutes. Blood pressure cuffs will be wrapped around your arm and thigh. The cuffs will inflate for a few seconds to record the signals in the software. The technician will also touch an electric pressure sensor to your neck (carotid artery) for a few seconds, which will record signals via the software. You will be requested to undergo this test 3 times during the study.
- b) **Peripheral Arterial Tonometry (Endopat):** This test will examine the function and reaction of your blood vessels in a noninvasive manner. A thimble-shaped cup will be placed on your finger that will place slight pressure on your finger and measure your blood flow. A pressure cuff will be placed on your arm and will be used to determine your blood pressure and flow. You will be requested to undergo this test 3 times during the study.
- c) **Cardio-ankle vascular index (CAVI):** This test will precisely measure the blood pressure and blood flow speed at various organs throughout your body. It indicates the level of arterial stiffness throughout the body, which could be related to the build-up of arterial plaque. For this procedure, electrocardiogram electrodes will be placed on both of your wrists, a microphone will be placed on your chest and a blood pressure cuff placed on each arm and leg. The discomfort should be minimal and similar to what it feels like to have your blood pressure checked on your arms and/or legs. You will be requested to undergo this test 3 times during the study.

### Saliva Collection

We will collect saliva samples 5 times at certain time points during your study participation. Prior to providing saliva samples, you will be asked:

- Medications used to increase your saliva flow (e.g., pilocarpine) should NOT be taken 24 hours before this exam.
- Not eat or drink for 90 minutes before the saliva collection.

- Subjects will be asked to spit into a cup for 5 minutes. Then, small suction cups will be placed on either side of your cheeks to collect saliva from the glands in your cheeks (parotid glands). Saliva will be collected from under your tongue. A small amount of citric acid (lemon juice) will be swabbed on your tongue to stimulate saliva flow. Saliva will again be collected from your cheeks and under your tongue.

### **Eye Exam**

You will have an eye evaluation and a test for dry eyes. This exam will take about 1.5 hours.

To test for dry eyes, we will do a Schirmer's Tear test. The test is done twice; first without numbing drops to stimulate tears and then with numbing drops to not stimulate tears. A small piece of filter paper is placed inside the lower eyelid. The paper will absorb the tears, which measures the amount.

Then you will have two colored drops placed in each eye to look at the smoothness of the surface of your eyes. We will look at the smoothness of your eyes with a special microscope called a slit-lamp. After the eye exam another small piece of filter paper will be placed inside the lower eyelid and remove, this test will be done to measure inflammation.

### **Questionnaires**

We will ask that you complete a few questionnaires about your health and its effects on your well-being.

### **Minor salivary gland lip biopsy**

You will have a biopsy of some "minor" salivary glands. First, numbing medicine is injected into the inside of your lower lip. Then a small incision (less than 1 inch) will be made and several tiny salivary glands will be removed. These glands are shallow. It is closed with several small stitches. Unless dissolvable stitches are used, you may have a follow up visit to remove them. They can be also be removed by your own doctor.

### **Plaque collection**

You may have dental plaques (a sticky, thin film that is made up of a protein substance and microorganisms that sticks to the tooth) and tongue and mucosal scrapings (the lining of the mouth) collected from various parts of the oral cavity to look for microbial flora using a small tongue depressor.

### **Ultrasound of the salivary glands**

During the study, you may have ultrasound examinations of the parotid (the large salivary glands in your cheeks) and/or submandibular (the salivary glands below the floor of the mouth) glands.

We will put some gel on your face. We will then press on your face with a smooth wand. An ultrasound uses sound waves to make a picture of a body organ.

### **Blood Collected for SARS-CoV-2**

Sjogren's syndrome patients may be at greater risk for infection with COVID- 19 and COVID- 19 is known to cause post infection complications like local effects on mouth such as taste and dry

mouth and other complaints like malaise, fatigue and joint pain. As part of this study, we will take some blood to test for prior infection with the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19). If you have antibodies to SARS-CoV-2, we will tell you what the results mean. Your participation will not be affected by the results of this test.

### **Blood and Urine Samples Collected for Research Studies**

In addition to the blood drawn for the clinical tests discussed above, we will also collect blood and urine samples for research purposes. These samples and the information obtained in interviews (such as, questionnaires, evaluations) will be used for research purposes to better understand Sjögren's syndrome and the effect of tofacitinib on patients with Sjögren's syndrome. The total amount of blood taken for research or clinical care purposes will be within current NIH guidelines and will be no more than one pint (the amount equivalent to a blood donation) in any 8-week period. Some of the blood will be used immediately for studies of various blood cells and DNA and RNA expression, which show which genes are active at a certain time-point. However, some of the blood and urine samples will be stored and analyzed in the future. We plan to use the stored samples to conduct studies to better understand the immune, cellular and molecular mechanisms involved in Sjögren's syndrome using current or future technologies.

### **USE OF MEDICATION DURING THE STUDY**

You can be taking the following medications when you begin the study:

- Prednisone less than or equal to 10 mg/day; during the study we will try to keep your prednisone dose stable but if your Sjogren's is stable we may consider lowering your prednisone dose
- Hydroxychloroquine up to 400 mg or 6.5 mg/kg/day (if >400 mg)
- Chloroquine up to 500 mg daily
- Quinacrine up to 100 mg daily

You will be given a list of medications that you cannot take while on this study. Please ask the staff if you are unsure if your medications are on the list provided. It is very important that you check with your study doctor before you start taking any medication, including over-the-counter medications and herbal preparations, or you change the dose of your existing medications.

### **HOW LONG WILL THE STUDY TAKE?**

After you complete your screening visit and you are found to be eligible for the study, you will have to come to the NIH Clinical Center for 9 additional visits over 28 weeks. Each visit will occur at the Clinical Center and is expected to take up to 5 hours. In addition, you will be contacted by phone on 5 occasions in between your on-site clinic visits. Additionally, it may be necessary for some patients to have unscheduled visits to address unanticipated issues arising during the study.

### **HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?**

We plan to have approximately 30 people participate in this study at the NIH.

**WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN THE STUDY?**

On September 1, 2021, based on a completed review of a large, randomized safety clinical trial, the FDA concluded that, although very rare, there is an increased risk of serious heart-related events such as heart attack or stroke, cancer, blood clots, and death with the arthritis and ulcerative colitis medicine Tofacitinib. This led to the requirement of a **“Boxed Warning”** as follows:

- Increased risk of serious bacterial, fungal, viral, and opportunistic infections leading to hospitalization or death, including tuberculosis (TB).
- Higher rate of deaths from any cause, including sudden cardiovascular death with Tofacitinib vs. TNF blockers in rheumatoid arthritis (RA) patients.
- Malignancies have occurred in patients treated with Tofacitinib. Higher rate of lymphomas and lung cancers with Tofacitinib vs. TNF blockers in RA patients.
- Higher rate of Major Adverse Cardiovascular Events (MACE) (defined as cardiovascular death, myocardial infarction, and stroke) with Tofacitinib vs. TNF blockers in RA patients.
- Thrombosis has occurred in patients treated with Tofacitinib. Increased incidence of pulmonary embolism, venous and arterial thrombosis with Tofacitinib vs. TNF blockers in RA patients.

Additional details regarding the risks from taking Tofacitinib:

You may develop an infection; most commonly, upper respiratory, throat, and urinary tract infections have been seen in patients who receive tofacitinib. You may develop a more serious infection, such as pneumonia, cellulitis, herpes zoster, and urinary tract infections. These types of infections are much rarer.

Rarely tears in intestinal tract have been seen; however, it is not clear what role tofacitinib had in causing these tears.

**Get emergency help right away if you have any symptoms of a heart attack or stroke while taking tofacitinib, including:**

- discomfort in the center of your chest that lasts for more than a few minutes, or that goes away and comes back
- severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw
- pain or discomfort in your arms, back, neck, jaw, or stomach
- shortness of breath with or without chest discomfort
- breaking out in a cold sweat
- nausea or vomiting
- feeling lightheaded
- weakness in one part or on one side of your body
- slurred speech

Malignancies were reported on trials of patients taking Tofacitinib. There is a small increased risk of malignancy, most commonly lung, breast cancer, and possibly lymphoma. The risk of developing lymphoma is very low and approximates the already known elevated risk of lymphoma in patients with Sjögren’s Syndrome.



Clots, (aka: thromboses), including pulmonary embolism (PE), deep venous thrombosis (DVT), and arterial thrombosis, have occurred in patients treated with Tofacitinib and other Janus kinase (JAK) inhibitors used to treat inflammatory conditions. The risk was identified in patients over the age of 50 with at least one major cardiovascular risk factor. Many of these events were serious and some resulted in death. Patients with a history of clots are excluded from participating in this study.

A small percentage of patients developed a decrease in lymphocytes (type of white blood cell important for the immune system, a decrease in neutrophils (type of white blood cell that helps fight off infections), or a decrease in hemoglobin (protein in red blood cell that carries oxygen from the lungs to your body's tissues).

Increased in liver function enzymes or lipids have also been noted. We will assess hematology and chemistry laboratory values during every scheduled visit for the study to ensure these values do not worsen.

Worsening of kidney function. Most of the time, this worsening of kidney function was very mild and reversible. You will be ineligible for this study if your kidney function is significantly abnormal at screening. We will assess your kidney function during every scheduled visit to ensure these values do not worsen.

Since we have not given this medicine to people who have Sjögren's syndrome it is uncertain if it will have no effect on your Sjögren's syndrome, or it could possibly make it worse.

Tofacitinib has not been used to treat Sjögren's syndrome before, so we do not know if it will be effective.

If this therapy does not work, or you receive placebo, your Sjögren's syndrome may worsen. If you develop a flare that needs immediate immunosuppressive treatment, you will be withdrawn from the protocol and your doctors will treat you with conventional medications. Certain lab abnormalities may require that the drug dose be reduced, or that you stop taking the drug for a short period of time or permanently.

## **RISKS FROM STUDY PROCEDURES**

### **Blood and urine collection**

Blood draws may sometimes cause pain, mild bleeding, bruising, a small risk of infection, occasional lightheadedness and, rarely fainting. The amount of blood drawn will be kept within the NIH guidelines of about 112 teaspoons or 550 mL, over any 8-week period. This is about the same as the amount you would give during a single blood donation.

### **Vascular function studies**

Minor discomfort with the blood pressure cuff may occur, but no other side effects are expected.

- 1. Peripheral wave analysis (SphygmoCor):** This test involves the non-invasive attachment of blood pressure cuff to your extremities. It should not cause you discomfort, other than the feeling of the blood pressure cuff inflating (such as what you would feel when your blood pressure is being measured) you should not experience discomfort with the vascular testing. The test will also touch an electric pressure sensor to your neck which is painless.

- 2. Peripheral arterial tonometry (Endopat):** This test involves placing a probe on your finger for a short time and use of a blood pressure cuff and is generally not associated with any discomfort.
- 3. Cardio-ankle vascular index (CAVI):** This test involves the non-invasive attachment of electrodes and blood pressure cuffs. It should not cause you discomfort. Other than the feeling of the blood pressure cuff inflating (such as what you would feel when your blood pressure is being measured) you should not experience discomfort with the vascular testing.

### **EKG**

We will do an EKG to check the function of your heart. There may be minor discomfort, like removing a bandage, when the EKG electrodes taped to your chest are removed. Rarely, a reaction to the electrodes may cause redness or swelling of the skin.

### **Saliva collection**

The sour solution may cause some discomfort or pain in your cheeks or the bottom of your mouth.

### **Eye Exam**

The filter paper used to measure tear production and inflammation may irritate your eye and cause discomfort or pain. This resolves shortly after the paper is removed. The anesthetic eye drops used in the eye evaluation sometimes cause a local allergic reaction that can be treated with eye drops.

### **Questionnaires**

There are minimal risks associated with questionnaires, but you may possibly feel uncomfortable with some of the questions.

### **Minor salivary gland lip biopsy**

Injection of the numbing medicine can cause some temporary stinging. There may be some bleeding, bruising, or swelling at the incision site. Rarely an infection can occur. There may be numbness near the incision, but this is usually temporary. An allergic reaction to the numbing medicine can occur. This is rare but can be very serious. It is important that you notify the dentist if you ever had an allergic reaction during a dental procedure. Some volunteers have developed sores near the incision area after the biopsy. This has occurred in about 5% of people. These are known to occur with surgical procedures in the mouth and generally heal rapidly. Occasionally, the incision may heal irregularly, causing a small tag or bubble (mucocele). Such defects will be corrected by an NIDCR dentist or oral surgeon.

### **Plaque collection**

Collecting plaque samples has a small risk of minor bleeding of the gums. Sampling of bacteria from your teeth, tongue and the insides of your cheek should not hurt. You may feel pressure from the instrument.

### **What are the risks related to pregnancy?**

If you can become pregnant, we will ask you to have a pregnancy test before beginning this study. We also do not know how tofacitinib will affect a pregnant woman or her fetus. Therefore, you

cannot take part in the study if you are pregnant or will not use an effective form of birth control. You must practice an effective method of birth control to prevent pregnancy during this study and 3 months after the completion of the study. Women who are nursing mothers are not allowed to be in the study because the safety of tofacitinib to nursing children is unknown. You must avoid pregnancy until 3 months after the end of the study. If you become pregnant during the study, the study drug or placebo will be stopped, and you will be asked to complete all the visits described above. The study doctor will ask to follow the outcome of your pregnancy and the condition of your newborn.

If you are a sexually active person with a partner able to become pregnant, it is important that your partner not become pregnant during your participation in this study and 3 months after the completion of the study. There may be unknown risks to a fetus or risks we did not anticipate. You and your partner must agree to use birth control if you want to take part in this study. If you think your partner has become pregnant during your participation in this study, please contact the study team as soon as possible. If you and your partner plan for your partner to become pregnant after your participation in this study, please discuss this with the study team.

### **WHAT ARE THE BENEFITS OF BEING IN THE STUDY?**

You might not benefit from being in this study.

#### **Are there any potential benefits to others that might result from the study?**

In the future, other people might benefit from this study because the knowledge gained from this study may help in developing treatment for those with Sjogren's syndrome.

### **WHAT OTHER OPTIONS ARE THERE FOR YOU?**

Before you decide whether to be in this study, we will discuss other options that are available to you. Instead of being in this study, you could choose not to participate in this study and continue your medical care with your regular doctor.

### **DISCUSSION OF FINDINGS**

#### **New information about the study**

If we find out any new information that may affect your choice to participate in this study, we will get in touch with you to explain what we have learned. This may be information we have learned while doing this study here at the NIH or information we have learned from other scientists doing similar research in other places.

#### **Return of research results**

Generally, we do not plan to return research results. However, if you choose, we will send you and your primary care provider, a notice of whether you received tofacitinib or placebo.

### **EARLY WITHDRAWAL FROM THE STUDY**

Subjects who withdraw or are withdrawn from the study after receiving tofacitinib or placebo will be asked to complete the Week 24 (end of treatment) and the Week 28 follow-up assessments. Subjects who withdraw or are withdrawn before Day 1 will resume care with their referring physician with no further evaluation in this protocol.

The doctors doing this study may decide that it is best that you leave the study. You may be asked to leave the study, for example, if there are major changes in your health status or if you are unable to comply with the study schedules. If this occurs, the investigator will talk to you about the reason for removing you from the study. The study may also be ended by the investigator without your consent.

If you leave the study early for any reason, due to the investigators or your decision, you will be encouraged to complete exit procedures that include the safety assessments used in the study and follow up visits. This will be useful to determine any long-term side effects of the tofacitinib and also to learn the effects of tofacitinib on your Sjogren's, if you received the study drug.

### **STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA**

#### **Will your specimens or data be saved for use in other research studies?**

As part of this study, we are obtaining specimens and data from you.

We will remove all the identifiers, such as your name, date of birth, address, or medical record number and label your specimens and data with a code so that you cannot easily be identified.

However, the code will be linked through a key to information that can identify you. We plan to store and use these specimens and data for studies other than the ones described in this consent form that are going on right now, as well as studies that may be conducted in the future. These studies may provide additional information that will be helpful in understanding Sjogren's syndrome, or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to the development of a commercial product by the NIH and/or its research or commercial partners. There are no plans to provide financial compensation to you if this happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you.

I give permission for my coded specimens and data to be stored and used for future research as described above.

\_\_\_\_\_ Yes      \_\_\_\_\_ No

Initials

Initials

#### **Will your specimens or data be shared for use in other research studies?**

We may share your coded specimens and data with other researchers. If we do, while we will maintain the code key, we will not share it, so the other researchers will not be able to identify you. They may be doing research in areas that are similar to this study or in other unrelated areas. These researchers may be at NIH, other research centers and institutions, or commercial entities.

I give permission for my coded specimens and data to be shared with other researchers and used by these researchers for future research as described above.

\_\_\_\_\_ Yes      \_\_\_\_\_ No  
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If you change your mind and do not want us to store and use your specimens and data for future research, you should contact the research team member identified at the top of this document. We will do our best to comply with your request but cannot guarantee that we will always be able to destroy your specimens and data. For example, if some research with your specimens and data has already been completed, the information from that research may still be used. Also, for example, if the specimens and data have been shared already with other researchers, it might not be possible to withdraw them.

In addition to the planned use and sharing described above, we might remove all identifiers and codes from your specimens and data and use or share them with other researchers for future research at the NIH or other places. When we or the other researchers access your anonymized data, there will be no way to link the specimens or data back to you. We will not contact you to ask your permission or otherwise inform you before we do this. We might do this even if you answered "no" to the above questions. If we do this, we would not be able to remove your specimens or data to prevent their use in future research studies, even if you asked, because we will not be able to tell which are your specimens or data.

NIH policies require that your clinical and other study data be placed in an internal NIH database that is accessible to other NIH researchers for future research. Usually, these researchers will not have access to any of your identifiers, such as your name, date of birth, address, or medical record number; and your data will be labeled with only a code. We cannot offer you a choice of whether your data to be placed in this database or not. If you do not wish to have your data placed in this database, you should not enroll in this study.

#### **Will your genomic data be shared outside of this study?**

As part of this study, we will put your genomic data in a large database which will be freely available to the public. These databases are commonly called data repositories. These data are intended for other researchers to use and learn from but anyone can gain access to them, including law enforcement. The information in this database will include but is not limited to genetic information, race, ethnicity and sex. If your individual data are placed in one of these repositories, they will be labeled with a code and not with your name or other information that could be used to easily identify you. This information when combined with information from other public sources could be used to identify you, though we believe it is unlikely that this will happen.

Summary information about all of the participants included in this study (including you) is being placed in a database and will be available through open access. That means that researchers and non-researchers will be able to access summary information about all the participants included in the study, or summary information combined from multiple studies, without applying for permission. The risk of anyone identifying you with this information is very low.



NIH policies require that genomic data be placed in a repository for sharing. Therefore, we cannot offer you a choice of whether your data will be shared. If you do not wish to have your data placed in a repository, you should not enroll in this study.

### **How long will your specimens and data be stored by the NIH?**

Your specimens and data may be stored by the NIH indefinitely.

### **Risks of storage and sharing of specimens and data**

When we store your specimens and data, we take precautions to protect your information from others that should not have access to it. When we share your specimens and data, we will do everything we can to protect your identity, for example, when appropriate, we remove information that can identify you. Even with the safeguards we put in place, we cannot guarantee that your identity will never become known or someone may gain unauthorized access to your information. New methods may be created in the future that could make it possible to re-identify your specimens and data.

### **PAYMENT**

#### **Will you receive any type of payment for taking part in this study?**

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will be paid \$60 for each outpatient visit if you are enrolled in the study. You will not be paid for the screening visit. You will be paid an additional \$100 at the end of study (Day 196) as a study completion bonus. If you have a second (or an extra non-diagnostic biopsy), you will be paid \$220 for each extra salivary gland biopsy.

If you are unable to finish the study, you will receive \$60/visit for the parts you completed. If you have unpaid debt to the federal government, please be aware that some or all of your compensation may be automatically reduced to repay that debt on your behalf.

With few exceptions, study compensation is considered taxable income that is reportable to the Internal Revenue Service (IRS). A "Form 1099-Other Income" will be sent to you if your total payments for research participation are \$600 or more in a calendar year.

### **REIMBURSEMENT**

#### **Will you receive reimbursement or direct payment by NIH as part of your participation?**

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

This study does not offer reimbursement for participants, or payment of, hotel, travel, or meals.

## COSTS

### Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

## CONFLICT OF INTEREST (COI)

The NIH reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a COI Guide. You may ask your research team for a copy of the COI Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines or the guidelines of their home institution, but they do not need to report their personal finances to the NIH.

No NIH investigator involved in this study receives payments or other benefits from any company whose drug, product or device is being tested.

## CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

## CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

### Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- The study Sponsor NIDCR
- Qualified representatives from Pfizer, Inc., the pharmaceutical company who produces tofacitinib.

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance that, despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.

In most cases, the NIH will not release any identifiable information collected about you without your written permission. However, your information may be shared as described in the section of this document on sharing of specimens and data, and as further outlined in the following sections.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any



information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens or data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

### **Certificate of Confidentiality**

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

### **Privacy Act**

The Federal Privacy Act generally protects the confidentiality of your NIH medical information that we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.



**POLICY REGARDING RESEARCH-RELATED INJURIES**

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

**PROBLEMS OR QUESTIONS**

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Principal Investigator, Blake Warner, DDS, PhD, MPH ([blake.warner@nih.gov](mailto:blake.warner@nih.gov), (301)-500-8063). You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

**CONSENT DOCUMENT**

Please keep a copy of this document in case you want to read it again.



**Adult Research Participant:** I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

\_\_\_\_\_  
Signature of Research Participant

\_\_\_\_\_  
Print Name of Research Participant

\_\_\_\_\_  
Date

**Investigator:**

\_\_\_\_\_  
Signature of Investigator

\_\_\_\_\_  
Print Name of Investigator

\_\_\_\_\_  
Date

**Witness should sign below if either:**

1. A short form consent process has been used to enroll a non-English speaking subject or
2. An oral presentation of the full consent has been used to enroll a blind or illiterate subject

\_\_\_\_\_  
Signature of Witness

\_\_\_\_\_  
Print Name of Witness

\_\_\_\_\_  
Date

**NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

\_\_\_\_ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

\_\_\_\_ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: \_\_\_\_\_.

