Study Title: NATIENS: A Phase III Randomized Study to Determine the Mechanisms and Optimal Management of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis

Version Date: January 19, 2022

Part 1 of 2: MASTER CONSENT

Name of participant: _____ Age: _____

You are being invited to take part in a research study. This study is a multi-site study, meaning it will take place at several different locations. Because this is a multi-site study this consent form includes two parts. Part 1 of this consent form is the Master Consent and includes information that applies to all study sites. Part 2 of the consent form is the Study Site Information and includes information specific to the study site where you are being asked to enroll. Both parts together are the legal consent form and must be provided to you.

Key Information:

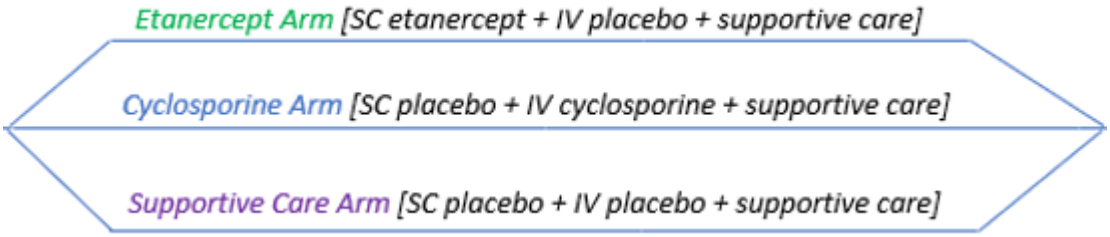
- The first section of this document contains some key points that the research team thought you would find important.
- The study is described in more detail after this section.

Key information about this study:

You are being asked to take part in this research study because you have been hospitalized with Stevens Johnson syndrome (SJS) or Toxic Epidermal Necrolysis (TEN). This study is funded by the National Institutes of Health and will enroll about 267 people at up to 22 sites in the United States. The Vanderbilt Coordinating Center is the coordinating center for this study. The Sponsor Investigator of the study is Dr. Elizabeth Phillips from Vanderbilt University Medical Center.

The purpose of this study is to determine the best treatment for patients with SJS or TEN. In this study we want to see if two different drugs, cyclosporine or etanercept are better treatment options than standard supportive care alone.

When you enroll, you will be placed into one of three treatment groups:



SC = subcutaneous injection (injection with small needle) IV = Intravenous (through a vein in your arm)

Etanercept is a drug given by injection under your skin (a shot) on study day 1 and on study day 4. Cyclosporine is a drug given by IV (into a vein in your arm) twice a day for 14 days. Standard supportive care is treating your skin, wounds, eyes, and other areas affected by SJS or TEN with care to support your natural healing without the use of does special medication to treat SJS and TEN.

Once you are placed into one of these three groups, you will be treated for 14 days. During the treatment period, since little is known about why some people get SJS or TEN, our study team will collect samples from your skin, saliva, and blood and take daily pictures of your skin to learn more about this rare reaction. If you agree to be in the study, you will be on treatment for 14 days, and followed for 12 months.

Is there any way this research can hurt me?
Cyclosporine may cause high blood pressure or may put stress on your kidneys. Etanercept may put you at higher risk for getting an infection. The study team will review your medical history to make sure it is safe for you to be in the trial to help lower your chances of having problems with either treatment. In addition, your study team and doctors will watch you for these symptoms.

Will being in the research study help me in anyway?
You will not receive any direct benefit from your taking part in this study. Your taking part may help the researchers to better understand of the treatment of SJS or TEN which may help future patients.

What other choices do I have besides taking part in this study?
You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services, or other rights. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study.

Detailed Information:
The rest of this document includes detailed information about this study
(in addition to the information listed above).

Introduction and Study Background:
SJS and TEN are the same disease but different levels of severity based on how much of your skin is involved (see below).

- Steven Johnson Syndrome (SJS): is when less than 10% of the body surface is involved and detached.

- Toxic Epidermal Necrolysis (TEN): is when greater than or equal to 10% of the body surface is involved and detached.

They are both rare and serious skin conditions that are considered to be the same disease across a spectrum of severity. Both are usually caused by a reaction to a drug. SJS and TEN start with flu-like symptoms, followed by a painful rash that spreads and blisters. This turns into the main symptom which is severe skin detachment (flaking), peeling and blistering. The peeling spreads quickly, resulting in large raw areas that may ooze or weep.

There is currently little information about the best way to treat SJS and TEN. We are asking you to participate in this trial so we can determine the best way to treat SJS and TEN and help patients like you.

Study Components:
This study is a randomized, double-blind, placebo-controlled trial. To help you better understand the study design, we will talk about what those words mean.

- Randomized: means you will be placed into a group by chance. It's like flipping a coin.
- Double-blind: means neither you, nor your doctor/study team will know what treatment group you are in.
- Placebo Controlled: Placebo is made to look like the study drug but does not have any study drug in it. Researchers use a placebo to see if the study drug works better or is safer than not taking any active drug. In this study we use normal saline (saltwater solution) as placebo.

For this study you will be placed into one of three groups. Each group will be given study drug by IV (into a vein in your arm) twice a day for 14 days and a shot of study drug on study day 1 and study 4. Each group will also receive standard supportive care for your skin, eyes, mouth, and other areas.

Cyclosporine is an FDA approved drug that has been used since the early 1980s to prevent organ rejection after an organ transplant. It is also used to treat autoimmune conditions such as rheumatoid arthritis (RA) or psoriasis.

Etanercept is an FDA approved drug used to treat inflammatory conditions such as rheumatoid arthritis (RA), plaque psoriasis, psoriatic arthritis, polyarticular juvenile idiopathic arthritis (JIA), and ankylosing spondylitis (AS).

Although cyclosporine and etanercept are approved by the FDA, they are being used in this study "off label". Off label means that the FDA has not specifically approved the use of cyclosporine or etanercept for the treatment of SJS or TEN.

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Study Visits:
You will be in the study for approximately 12 months. During that time, you will complete the following visits:

Study Activity Tables:

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Procedures	Enrollment and Randomization	Treatment Phase	Post Treatment Phase	Re-Epithelialization (RE)	3-Month & 12-Month Follow Up
Study Day	*Day 0*	*Days 1 – 14*	*Day 15 – Discharge*	*n/a*	*3 & 12 Months*
Pregnancy Test	X				
Etanercept / Placebo		X			
Standard Care		X	X		
Cyclosporine / Placebo		X			
Full Body Photography		X	X	X	X
Punch Biopsies – (4) Baseline Samples	X				
Punch Biopsies Previously Affected Skin					X
Saliva Collection	X				
Blister Fluid collection	X	X Days 1-4 only			

Blood Draws	Enrollment and Randomization	Treatment Phase	Post Treatment Phase	Re-Epithelialization (RE)	3-Month & 12-Month Follow Up
Study Day	*Day 0*	*Days 1 – 14*	*Day 15 – Discharge*	*n/a*	*3 & 12 Months*
PBMCs (*4 tbsp)*	X	Day 4 (ONLY)		X	X
Hematology and Chemistry *(< 1 tbsp)*	X	X	X	X	

Plasma (*< 1 tbsp)*	X	QOD[1]	QOD[1]	X	X
Serum (*< 1 tbsp)*	X	Day 4 only		X	X
Whole Blood *(< 1 tbsp)*	X	QOD[1]	QOD[1]	X	X
Cyclosporine Trough (< 1 tbsp)		Day 3,6,8,11 Then as Needed			
Cyclosporine Peak (<*1 tbsp*)		Day 6 only			

[1] *QOD: Every other day*

[2] *Tbsp: Tablespoon*

Enrollment: (Day 0)

On the day of enrollment, the study team will explain the study in detail and if you agree to be a part of the study, you will sign this consent form. Once the consent form is signed, the study team will ask you questions about your medical history, health, demographics, and contact information. The study team will also look at your medical records to review medications and procedures that were part of your SJS or TEN treatment prior to being part of this study. This information is needed to make sure you are eligible for the study.

On the day of enrollment, we will also collect the following samples and assessments:

- Full Body Photography
- Health and Medical Information
- Skin Punch Biopsies
- Slough Skin Collection
- Saliva Collection
- Blister Fluid collection
- Blood Sample Collection:
  - Blood collection for research purposes: (total – 75mLs or 5 tablespoons)
  - Blood collection as part of standard care: (total 11mLs or < 1 tablespoon)
- Pregnancy Test, if applicable.

The skin, saliva, blister, and blood collections are described in detail in the Study Procedures section.

Randomization: (Day 0)

Randomization may occur the same day as the enrollment visit. If you are eligible for the study, you will be randomly assigned to one of three groups described below.

Group 1: Active Etanercept injection, placebo Cyclosporine IV infusion and Standard Supportive Care

Group 2: Placebo Etanercept injection, active Cyclosporine IV infusion and Standard Supportive Care

Group 3: Placebo Etanercept injection, placebo Cyclosporine IV infusion and Standard Supportive Care

As a reminder, neither you, your doctors or study team will know which group you are assigned to.

Treatment Phase (Days 1 – 14)

Once you complete randomization, you will be start the treatment phase. The planned treatment period for all groups is 14 days.

Each group will follow the treatment schedule below:

Group 1
At baseline (day1) and on day 4 you will get 50 mg of Etanercept using a needle placed under the skin in your stomach or arm. You will also get normal saline by IV (needle in your vein) in your arm two times a day for 14 days.

Group 2
You will get 2.5mg/kg of cyclosporine by an IV (needle in your vein) in your arm 2 times a day for 14 days. At baseline (day 1) and on Day 4 you will also get normal saline by a needle placed under the skin in your stomach or arm.

Group 3
You will get placebo by IV (needle in your vein) in your arm 2 times a day for 14 days. At baseline (Day 1) and Day 4 you will also get normal saline by a needle placed under the skin in your stomach or arm.

All groups will get standard supportive care for 14 days or treatment allocation as well as during the follow-up periods. Standard supportive care includes best care of your skin, wounds and eyes and other areas affected by SJS or TEN.

Additional Study Assessments and Activities During the Treatment Phase:

In addition to the treatment above, you will have daily assessments of your skin, eyes, and mouth and we will record any treatment or medication you may have received. We will also collect samples, and perform activities as outlined below.

- Full body photography *(daily)*
- Blood collection for research purposes
- Blood collection as part of standard care

Cyclosporine and Etanercept Blood Draws:

Blood will also be collected to measure the lowest level of cyclosporine in your blood on study days 3,6,8 and 11 and the maximal level (peak level) on day 6. We collect this blood to ensure the level of study drug is not too high or too low in your body. We may need to lower the dose of cyclosporine if the level comes back too high, or if your lab values continue to rise, we may need to take additional blood to measure cyclosporine levels. If after repeat blood draws with high values, there is a chance the study doctor will stop your study treatment and take you out of the study. Before this happens, the study doctor will let you know. The cyclosporine levels will be collected on every participant, even if you are getting placebo to so that neither you or your study doctor know what group you are in.

Blood will also be drawn to assess levels of cyclosporine and etanercept at various timepoints throughout treatment. These results will not be available until the end of the study. Blood will be drawn at the timepoints listed below.

Timepoint	Pre-dose	6 hours	24 hours	48 hours	50 hours	56 hours	60 hours
Volume	5 ml	5 ml	5 ml	8 ml	5 ml	5 ml	8 ml

(Blue Text = optional draws) (1 ml = 0.068 tablespoons)

Lastly, during your treatment, the study team will receive the results of the skin biopsy that was collected at enrollment. If the results show that you have something other than SJS/TEN you will be taken out of the study. If this happens the study team will let you and your clinical doctors know.

Post Treatment Phase (Day 15 – Discharge):

After the treatment period is over, you will continue with daily study assessments until all your skin has completely healed or "re-epithelialized". We expect this to happen by Day 21 but depending on the severity (i.e., how bad) of your skin involvement it may be longer.

During the Post Treatment Phase, the following assessments/procedures will occur daily until you are discharged from the hospital:

- Full body photography
- Supportive care and documentation
- Blood collection as part of standard care: (total = 11mLs or < 1 tablespoon)

During the Post Treatment Phase, the following procedures will occur every-other-day until you are discharged from the hospital:

- Blood collection for research: (total = 12.5mLs or < 1 tablespoon)

Re-epithelialization Visit (RE)

On the day the study team determines your skin has fully healed or "re-epithelialized", the following will occur.

- Full body photography
- Supportive care and documentation
- Blood collection for research purposes: (70mLs or about 5 tablespoons)

If your skin completely heals before the end of the treatment period, your study treatment will be stopped, and samples will be collected. If you remain in the hospital after your skin fully heals, we will collect the samples listed above in the "Post Treatment Phase" every 7 days until you are discharged from the hospital.

Pre-Discharge Visit:

Prior to being discharged from the hospital, your study team will collect samples and additional information from you as outlined below.

- Contact Information
- SJS/TEN treatment medication review
- % body surface area of affected skin
- Questionnaires related to your quality of life and health

The study team will also discuss plans for your 3-month and 12-month follow up visits and ensure your contact information is up to date.

3-Month and 12-Month Follow-up Visits: *(Outpatient – 45 minutes to complete)*

We will follow-up with you at 3-months and 12-months after your enrollment date. You will be given the choice to come back to an outpatient clinic or the original hospital where you were treated for SJS or

TEN (preferred). If you choose to return to your hospital where you received care, we will compensate you for travel expenses.

At the follow-up visits the following activities will occur:

- Medical history review/update
- Patient contact information review/update
- Full body photography
- SJS/TEN treatment medication review
- Questionnaires related to your quality of life and health
- Medication Review
- Supportive care documentation review
- Skin Punch biopsy from previously affected skin
- Blood collection for research purposes

Study Procedures and Risks:

Study Procedure / Assessment	Associated Risk
Urine Pregnancy Test: Collected on day 0. If you are a woman and are able to become pregnant, you will have a urine pregnancy test to make sure that you are not pregnant before you start treatment in this study	There are no known risks to a pregnancy test. However, there is risk to becoming pregnant while you are in the study. **Pregnancy Risks:** This treatment may hurt an unborn child. If you take part in this study, you and any person you have sex with must use approved birth control such as birth control pills, birth control shots, IUD, diaphragm, or condoms while you are in this study. If you become pregnant while you are in this study, you must tell your doctor at once. Also, women must not breast feed while in this study.
Full Body Photography: (see activity table for timing) We will take photos of your skin for research purposes. Any photos taken will not have any information about you or show any features that specifically identify you. They will be stored in a secure database and may be used in research publications. These research pictures will not be a part of your medical record. Additional photos may be	**Full Body Photography Risks:** There are no known physical risks associated with full body photography. However, there is always a risk of loss of confidentiality. To minimize this risk, your full body photographs will be collected in frames and coded with a number and not with your name so

taken by your clinical (non-research) medical team as part of your medical record.	although it is unlikely someone will be able to identify you.
Punch Biopsies with Lidocaine: At enrollment (Study Day 0), 3 skin biopsies will be taken from an affected area of your skin and 1 skin biopsy on an unaffected area of your skin. Two of the collected biopsies will be analyzed to help diagnose SJS or TEN and to be sure that it is appropriate for you to stay in the study. The other two biopsies (one from affected skin and one from unaffected skin) will be used for research. In addition, at the 3-month and 12-month follow up visits, one punch biopsy will be taken from an area of previously affected skin. Procedure: We will give you a shot of a small amount of lidocaine to numb your skin before the biopsy. A disposable 4mm (less than ¼ inch) punch biopsy tool will be used to take a small part of skin. Two to four stitches will be placed at each site and a bandage placed on top. You will be given instructions on caring for the wound and how to remove your stitches. This will take about 10-20 minutes to complete.	**Punch biopsy risks**: Pain, redness, soreness, bruising, bleeding, or infection may occur at the biopsy site. Rarely some people faint. **Lidocaine risks**: Lidocaine, a numbing drug given in a shot that may burn or cause a rash, redness, or soreness where you get the shot. There is a risk that this drug may cause problems with heart rhythm.
Blister Fluid Aspiration: During the first 1-3 days we will collect fluid from any blisters you may have. This involves sticking a needle into the blister and removing the fluid with a syringe. This should take about 10-20 minutes of your time.	**Blister fluid aspiration (removal of fluid using a needle) risks**: Pain, redness, soreness, bruising, or infection may occur at the needle stick site. Rarely some people faint
Sloughed Skin: We would also like to collect the top layer of the skin that will naturally separate off during your wound care. This skin which is called sloughed skin is extra tissue that is	**Sloughed Skin Risks:** There are no known risks associated with sloughed skin removal. We will take skin that is naturally separating so you should not feel any additional discomfort from the removal.

normally removed and will be collected by us for research purposes only.	
Blood Draws: (see activity table for timing) We will collect blood for this study for research purposes. All of the blood can usually be collected in one stick, but if the sample is lost, damaged or need to be repeated we may ask for additional blood draws. Timing of Blood Collection: Over the course of your hospital stay, we will collect 5-6 tablespoons of blood three different times (Day 0, 4 and Reepithelization). On the other days, we will collect between 1-2.5 tablespoons of blood. At the 3-month, and 12-month visit, we will collect 5 tablespoons of blood. The timing of blood draws can be found in the activity table at the end of the consent form. Each blood collection should take about 10 minutes. Why do we need to collect blood? All of the blood that is collected will help us answer important questions related to SJS/TEN or as part of your routine care: An explanation of how your blood will be used for is listed below. ○ PMBC (Peripheral Blood Mononuclear Cells), Whole Blood and Plasma are collected as part of this study and will help us understand more about why some people may get SJS/TEN and what happens in their body when they do. ○ Hematology and chemistry: these tests are part of routine care, and measure things like red blood	**Blood draw**: Pain, redness, soreness, bruising, or infection may occur at the needle stick site. Rarely some people faint.

cells, white blood cells and platelets in your blood. The results will give the study team a better understanding of how the body reacts to SJS/TEN. ○ Cyclosporine Levels: If you are randomized to receive cyclosporine, this test is collected to make sure that the level of cyclosporine is not too high or too low in your body. If the cyclosporine level it too high and does not come down over a period of time, the study team may discontinue you from the study. ○ Cyclosporine and Etanercept PK (Pyruvate kinase) levels: These tests will help the study team better understand how cyclosporine and etanercept are absorbed by your body. The study team is interested if this is different in people with SJS/TEN. The timing of these tests is above.	
Standard Supportive Care: Standard supportive care includes best care of your skin, wounds and eyes and other areas affected by SJS or TEN. We will work with your medical team and outline what is considered standard supportive care as part of this protocol.	**Standard supportive care side effects** Possible discomfort with dressing changes, eye exam or urogenital (urine and genital) exam.
Saliva Sample: The study team will ask you to provide a sample of saliva by spitting into a sample collection cup. This should take about 5 minutes to complete.	**Saliva sample**: There are no significant risks associated with the saliva samples being collected. In those with SJS/TEN there may be irritation or a small amount of discomfort while giving a sample or it may not be possible to immediately produce a sample.

Treatment and procedures in this research study may involve risks that are not possible to predict. You will be informed of any new risks that may be identified during the study. Please ask your study doctor or the research staff to explain any procedure you do not understand.

Risks Associated with the Investigational Products:

In this study we will use two different investigational products. The first is cyclosporine and the other is etanercept. Depending on what group you are placed into you may receive one of these or none, you will never receive both.

Cyclosporine

If you take part in this study, you will receive an IV infusion of cyclosporine or placebo twice a day for 14 days. If you receive the active drug, you may experience the side effects below.

Common side effects (greater than 10%):

- Hypertension (increased blood pressure), Antihypertensive therapy may be required.
- Renal dysfunction, (changes in kidney function that may require a change of dose)
- Tremor (involuntary shaking of body parts)
- Headache (pain in the head)
- Nausea (feeling sick to the stomach)
- Vomiting
- Diarrhea (loose stools)
- Hirsutism (abnormal growth of hair on a person's face and body, especially on a woman)

Uncommon (less than 10%):

- Gum hyperplasia (swollen/red/painful gums)
- Hypomagnesemia (low magnesium)
- Acne (skin infection)
- Elevated Blood Levels such as: urea nitrogen, creatinine, bilirubin and aspartate transaminase (AST) and alanine aminotransferase (ALT) liver enzymes
- Hyperkalemia (increased potassium in the blood)

Etanercept

If you take part in this study, you will receive 2 doses of etanercept or placebo. One will be given at Day 1, and the other will be given on Day 4. If you are on active drug, you may experience the side effects below.

Common side effects (greater than 10%)

- Injection site reactions erythema (redness and swelling of the skin, itching, pain, bleeding, bruising. This does not usually prevent the second dose from being given.
- New serious infections or worsening of infections you already have. These may lead to hospitalization or death. In this study you will only receive 2 doses. There have been no reports of increased risk of infection in patients who have only received 2 doses.

- Hepatitis B can become active if you already have had it.
- Patients who take etanercept regularly see more frequent cold-like symptoms, diarrhea (loose stools), and dizziness.
- Patients with multiple sclerosis, nervous system problems, or pre-existing severe heart failure can see a worsening of these. For this reason, patients with these conditions will not be allowed to take part in this study.

Patients only receiving 2 doses are less like to have serious sides effects than patients who take etanercept regularly.

Cyclosporine Placebo:
If you take part in this study and are assigned to group 1, or group 3, you may receive normal saline by IV as a placebo for cyclosporine. Some people who have heart failure may have difficulty breathing if too much IV fluid is added to their body. People who have heart failure will be excluded for this study. If during your hospitalization the doctors think you may be at risk for heart failure, the study team may remove you from the study.

Etanercept Placebo:
There are known no risks associated with the etanercept placebo injection. However, since giving etanercept placebo involves receiving a shot, your skin may be irritated at the injection site; however, this should quickly resolve.

Good effects that might result from this study:

The benefits to science and humankind that *might* result from this study.
This research may inform and improve the safety of current drug use and future drug development, aid preventative measures and result in improved safety for people taking medicines for common and uncommon illnesses.

The benefits you *might* get from being in this study.
You will not receive any direct benefit from your taking part in this study. Your taking part may allow the researchers to advance their understanding of the treatment of SJS or TEN which may benefit future patients.

We may learn information about your health as part of the study that we think you and your clinical team should know about. For example, if we draw blood and one of the values comes back high or low, we may share these results with you and with your clinical team as it may be important for your care. Information that we collect for research purposes only will not be shared with you or your clinical team.

Other treatments you could get if you decide not to be in this study:
This is a treatment study. You can choose not to take part in this study. If you choose not to take part, you will not receive the study drugs that are part of this study.

Your participation in this study is voluntary. You may decide not to be in this study, or to be in the study now, and then change your mind later without affecting the medical care, education, or other services to which you are entitled or are presently receiving at this institution.

Reasons why the study doctor may take you out of this study:
Your taking part in the study may be stopped for any of the following reasons:

- Your skin biopsy is not consistent with the diagnosis of SJS/TEN
- You are found to have active COVID infection
- The study doctor feels it is in your best interest
- The Sponsor Investigator cancels the study
- You require treatment that would interfere with the study
- You withdraw consent
- You are unable to complete the required study treatment

If you are removed from the study, your study doctor will discuss study stopping procedures and future care with you and your clinical team.

What will happen if you decide to stop being in this study?
You may decide not to take part or to leave the study at any time. If you decide to leave the study, there is no penalty or loss of benefits in your routine medical care or any other benefit(s) that you would otherwise be entitled to receive. In addition, you should talk to your study doctors who will discuss future treatment and procedures for your continued care.

Pregnancies, Breastfeeding and Birth Control

<u>You cannot participate in this study if:</u>

- You are currently pregnant or breastfeeding
- You or your partner plan to get pregnant in the next month (during the active treatment period).

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Treatments and procedures involved in this research project may involve unexpected risks to your unborn or nursing child. If you are female of childbearing potential, a pregnancy test will be performed prior to your enrollment.

If you or your partner should become pregnant, or suspect that you have become pregnant, after the treatment period and before your 12-month follow up visit, you must the study doctor immediately.

Clinical Trials Registry.

A description of this clinical trial will be available on www.clinicaltrials.gov (https://clinicaltrials.gov/ct2/show/NCT02987257) as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this web site at any time.

Privacy:

Any information about you may be made available to others to use for research. To protect your privacy, we will not release your name, address, date of birth or other information that could identify you. You will not receive any benefit as a result of the data collected. This data may help us, or other researchers learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Your study data may be used to make new products or tests. This data may have value and may be developed and owned by the study staff, Vanderbilt University Medical Center, and/or others. If this happens, there are no plans to provide money to you.

Study Results:

Study results will not be shared directly with participants but will be available through www.clinicaltrials.gov and publication in medical journals

Institutional Review Board
Informed Consent Document for Research
STUDY SITE INFORMATION

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Part 2 of 2: STUDY SITE INFORMATION

Site Name:	Vanderbilt University Medical Center (VUMC)
Site Principal Investigator:	Elizabeth J. Phillips, MD
Site Principal Investigator Contact:	elizabeth.j.phillips@vumc.org (615) 322-2035
Site Study Coordinator:	Ramya Botta
Site Study Coordinator Contact:	ramya.k.botta@vumc.org

This part of the consent form includes information about the site that is asking you to participate in this study and is specific to participation at your site only. Before making your decision, both the site-specific information and the general study information should be reviewed with you. Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

Payments for your time spent taking part in this study or expenses:
You or your insurance provider will not have to pay for any procedures or samples collected that are directly related to this research study. You or your insurance provider will not have to pay for any medications administered as a part of this research study.

Costs to you if you take part in this study:
If you agree to take part in this research study, you and/or your insurance will not have to pay for the tests and treatments that are being done only for research. However, you are still responsible for paying for the usual care you would normally receive for the treatment of your illness. This includes treatments and tests you would need even if you were not in this study. These costs will be billed to you and/or your insurance.

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You have the right to ask what it may cost you to take part in this study. If you would like assistance, financial counseling is available through the Vanderbilt Financial Assistance Program. The study staff can help you contact this program. You have the right to contact your insurance company to discuss the costs of your routine care (non-research) further before choosing to be in the study. You may choose not to be in this study if your insurance does not pay for your routine care (non-research) costs and your doctor will discuss other treatment plans with you.

Payment in case you are injured because of this research study:
If it is determined by Vanderbilt and the Investigator with Division of Allergy, Immunology, and Transplantation/ National Institute of Allergy and Infectious Diseases (DAIT/NIAID) input that an injury occurred, then you and/or your insurance may be billed for the cost of medical care provided at Vanderbilt to treat the injury. You will be responsible for any copayments or deductibles associated with the treatment of that injury.

There are no plans for Vanderbilt or DAIT/NIAID to pay for the costs of any additional care. There are no plans for Vanderbilt or the Sponsor to give you money for the injury.

Who to call for any questions or in case you are injured:
If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact Dr. Elizabeth Phillips at (615) 322-9174 or (615) 310-0339 or Ramya Botta (615) 322-2035.

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the Vanderbilt University Medical Center Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

Genetic Research
One of the purposes of this study is to look at genes (DNA) and how they affect health and disease. Genes are the instruction manual for your body. The genes you get from your parents decide what you look like and how your body behaves. They can also tell us a person's risk for certain diseases and how they will

respond to treatment. You are being asked to give a blood, saliva, blister fluid and/or skin samples for genetic research for research. We are also requesting consent to obtain DNA from stored tissue specimens such as a skin or liver biopsy. What we learn about you from this sample will not be put in your health record. No one else (like a relative, boss, or insurance company) will be given your test results.

One risk of giving samples for this research may be the release of your name that could link you to the stored samples and/or the results of the tests run on your samples. To prevent this, these samples will be given a code. Only the study staff will know the code. The name that belongs to the code will be kept in a locked file or in a computer with a password. Only the sponsor of the study, Dr. Elizabeth Phillips, MD or her research staff will have access to your name.

Your sample will be kept for an unknown length of time (maybe years) for future research. The sample will be destroyed when it is no longer needed.

Your samples may be used to make new products or tests. These may have value and may be developed and owned by the study staff, Vanderbilt University Medical Center, and/or others. If this happens, there are no plans to provide money to you.

Your samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name, address, date of birth or other information that could identify you.

You will not receive any immediate benefit because of the tests done on your samples. These tests may help us learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Giving samples for research is your free choice and you may be in the study even if you do not want your samples used or stored for future research.

At any time, you may ask to have your sample destroyed. You should contact the study doctor to have your sample destroyed and no longer used for research. We will not be able to destroy research data

that has already been gathered using your sample. Also, if your identity was removed from the samples, we will not be able to locate and destroy them.

There will be no costs to you for any of the tests done on your samples. You will not be paid for the use of your samples.

Please check Yes or No to the questions below:

My blood/tissue sample may be used for research.

☐ Yes ☐ No

My blood/tissue sample may be stored/shared for future gene research in drug hypersensitivity and shared with specialty centers outside of Vanderbilt

☐ Yes ☐ No

My blood/tissue sample may be stored/shared for future research for other health problems (such as cancer, heart disease, etc.).

☐ Yes ☐ No

Confidentiality:
Vanderbilt University Medical Center may share your information and/or samples, without identifiers, to others or use it for other research projects not listed in this form. The sponsor, Vanderbilt University

Medical Center, Dr. Phillips and his staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

You will not be identified by name in any published reports about this study or in any other scientific publication or presentation.

There is a risk that if people outside the study get your health data, they could misuse it for purposes other than those outlined in this consent. The study team has strict privacy and confidentiality protection procedures in place to prevent this from occurring so the chance of this happening to you is extremely small.

It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

Authorization to Use/Disclose Protected Health Information
To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both VUMC and others) may release your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

Who will see, use or share the information?
The people who may request, receive or use your private health information include the researchers and their staff. Additionally, we may share your information with other people at Vanderbilt, for example if

needed for your clinical care or study oversight. By signing this form, you give permission to the research team to share your information with others outside of Vanderbilt University Medical Center. This may include the sponsor of the study and its agents or contractors, outside providers, study safety monitors, government agencies, other sites in the study, data managers and other agents and contractors used by the study team. We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

Do you have to sign this Authorization?
You do not have to sign this Authorization, but if you do not, you may not join the study.

How long will your information be used or shared?
Your Authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future research studies.

What if you change your mind?
You may change your mind and cancel this Authorization at any time. If you cancel, you must contact the Principal Investigator in writing to let them know by using the contact information provided in this consent form. Your cancellation will not affect information already collected in the study, or information that has already been shared with others before you cancelled your authorization.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

Institutional Review Board
Informed Consent Document for Research
STUDY SITE INFORMATION

Study Title: NATIENS: A Phase III Randomized Study to Determine the Mechanisms and Optimal Management of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis
Version Date: January 19, 2022

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally.
All my questions have been answered, and I freely and voluntarily choose to take part in this study.

Participant's Name (print): _____

Signature (if able to consent): _____ Date: ____/ _____/ ____

(If Required) Witness's Name (print): _____

Signature (if able to consent): _____ Date: ____/ _____/ ____

Witness to: □ Discussion □ Signature

Study Representative Statement

Date of IRB Approval: 01/31/2022
Date of Expiration: 01/17/2023

Institutional Review Board

VANDERBILT

Institutional Review Board
Informed Consent Document for Research
STUDY SITE INFORMATION

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Version Date: January 19, 2022

I have explained the purpose of the research, the study procedures, the possible risks and discomforts, the possible benefits, and have answered all questions to the best of my ability.

Study Representative's Name (print): _____

Signature: _____ Date: ____/ ____/ ____

Time Consent Obtained _____: _____ AM / PM

You will receive a copy of this form after it has been signed and dated.

Surrogate Consent Rider

Institutional Review Board
Informed Consent Document for Research
STUDY SITE INFORMATION

Study Title: NATIENS: A Phase III Randomized Study to Determine the Mechanisms and Optimal Management of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis
Version Date: January 19, 2022

I, _____[name of decision-maker/surrogate], am the _____[state relationship to participant] of _____ [state participant's name]. I have read the informed consent document, or it has been explained to me. I have had the opportunity to ask any questions and all my questions have been answered. I have been informed that a blood draw, saliva sample, blister fluid extraction, and/or punch biopsies will be performed to _____ _____ [participant's name]. I believe providing a blood sample, saliva sample, blister fluid sample, and/or punch biopsies would be in the interests of _____ [participant's name] and is consistent with what he/she would have decided had he/she been able to do so.

Your decision to allow your family member/friend to participate in this research study is voluntary. You may choose not to allow his/her participation. You are also free to withdraw him/her from this study at any time. In the event new information becomes available that may affect the risks or benefits associated with this research study or your willingness to allow continued participation in this research study, you will be notified so that you can make an informed decision whether to continue your family member/friend's participation in this study.

Your family member/friend will periodically be re-evaluated for the capacity to give consent. If he/she is found to be capable, continued participation in this study would only occur with his/her consent.

_____ ___/___/___
Signature of Health Care Decision-Maker/Surrogate Date

_____ ___/___/___
Signature of Witness Date

_____ ___/___/___
Name and Signature of person obtaining consent Date