STUDY SUBJECT INFORMATION AND CONSENT FORM

Study Title: A Multicentre, Randomised, Double-blind, Placebo-controlled, Phase 3 Study Evaluating the Efficacy and Safety of Two Doses of Anifrolumab in Adult Subjects with Active Systemic Lupus Erythematosus

Protocol #: D3461C00005

Sponsor: AstraZeneca AB

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You should keep a copy of this form. If you have any questions or problems during the study, call the phone number(s) above.

INTRODUCTION

You are being asked to take part in a research study of an experimental drug called Anifrolumab (MEDI-546), which is being developed as a drug for treating Lupus. "Experimental" means the drug has not been approved by any Authority that regulates new medications, including the United States (US) Food and Drug Administration (FDA) or any other international regulatory/government agencies. Therefore this study is part of a research project. The study is sponsored by AstraZeneca AB (AstraZeneca; "the Sponsor").

Information about this study is made available on public websites to follow the applicable law to ensure that the Sponsor provides clear and open information about this clinical research to the public. These sites include but are not limited to http://www.clinicaltrials.gov, which is a registry and a results database of clinical studies conducted in the US and around the world.

Your Study doctor is a researcher for this study. As a researcher, he/she is interested both in your health and how this study is carried out. The Study doctor is being paid by AstraZeneca to conduct this study. You will continue to receive medical care even if you choose not to take part in this study.

Before you decide if you want to take part in this study it is important for you to understand why the research is being done, how your information will be used, what the study will involve and the possible benefits, risks and discomforts. Please take time to read the following information carefully and discuss it with your doctor. Your participation is voluntary and your decision will not effect any medical care received by you or your partner. If you do not sign this consent form, you cannot take part in this study.

WHY IS THIS STUDY BEING DONE?

You have been asked if you would like to participate in this experimental research study because you have Lupus (also known as Systemic Lupus Erythematosus or SLE). This study is being carried out to see whether the addition of Anifrolumab (MEDI-546) to your current Lupus treatment is effective in reducing Lupus disease activity.

Lupus is an autoimmune disease, which means that your immune system not only attacks bacteria and viruses but also attacks your healthy cells and organs, affecting many parts of the body. Lupus can cause fever, joint pain, rash (redness of the skin), sensitivity of the skin to sunlight, as well as other symptoms, and may lead to inflammation and organ damage.

Current treatments for Lupus are mainly drugs that suppress the immune system such as cortisone-like drugs (such as prednisone) and cyclophosphamide (a drug sometimes used in treating certain types of cancer), and drugs commonly used to treat or prevent malaria (called antimalarials) such as hydroxychloroquine. Many of these treatments may have serious side effects if used for a long time. Therefore, there is a need for new and effective treatments for Lupus.

Interferons are a family of proteins produced by the body that help protect us against viral and other types of infections. Proteins are some of the building blocks that form cells, tissues, and organs and help to carry out all the functions of the body. One family of related proteins, called type I interferons, is a group of small proteins in the body that are involved in the control of inflammation. These proteins are thought to be involved in the chronic inflammation seen in subjects with Lupus. Therefore, by blocking the action of type I interferons it may help to reduce the symptoms of inflammation in Lupus.

Anifrolumab (MEDI-546), the drug being tested in this study, is a man-made human monoclonal antibody that blocks the actions of type I interferons. An antibody is a type of protein that exists naturally in the body that helps you to fight infections. A monoclonal antibody is a protein that is artificially made in a laboratory, and acts like an antibody found normally in the body.

This study will evaluate two doses of Anifrolumab (MEDI-546) to see how they compare with placebo (an inactive substance that looks identical to the drug being tested). The purpose of this study is to determine if Anifrolumab (MEDI-546) is effective at the dose tested in reducing the signs (for example skin rash/redness, joint inflammation) and symptoms (such as joint pain) of Lupus in subjects with moderate to severe disease and to collect information about the safety of Anifrolumab (MEDI-546). This study will also measure levels of Anifrolumab (MEDI-546) in the blood, and test your blood to see if your body forms antibodies against Anifrolumab (MEDI-546). This study will also look at whether Anifrolumab (MEDI-546) can improve control of your disease to the point that the dose of any cortisone-like medications (such as prednisone) you were on at the start of the study can be reduced.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

There will be approximately 450 subjects in this study. The study is being conducted in approximately 173 locations throughout approximately 18 countries around the world.

DO I HAVE TO TAKE PART?

It is up to you to decide whether or not to take part in this study. If you decide not to participate in the clinical study, your decision will not affect the medical treatment and care you are otherwise entitled to receive. If you do decide to take part after reading this Informed Consent Form and asked any questions you might have about the study, you will be asked to indicate your consent to participate in this study by signing and dating this Informed Consent Form and initialing each page before any study procedures are performed.

If you decide to take part, you are still free to withdraw your consent from study assessments (procedures) and/or study treatment (medication) at any time. This is described in more detail in a later section of this document.

Your primary physician/family doctor and/or gynecologist (for women only) will be informed about your participation in this study with your agreement.

WHO CAN BE IN THE STUDY?

In order to be allowed in this study, you must be between the ages of 18 and 70 years at the time of the screening visit with moderately-to-severely active Lupus, and require therapy in addition to your standard of care treatment.

If you are a female, you must not be pregnant or breast-feeding and you must not become pregnant during the study. If you are a male who is sexually active with a female partner of childbearing potential, 2 acceptable methods of birth control must be used simultaneously throughout the study. Acceptable methods for birth control for males and females are described later in this document.

HOW LONG WILL I BE IN THE STUDY?

The planned length of time you will be in the study is approximately 64 weeks (up to 30 days for screening, 52 weeks treatment period (total of 13 doses, from Week 0 to Week 48, evaluation at Week 52, and additional 8 weeks for follow-up).

WHAT WILL HAPPEN TO ME IF I TAKE PART?

If you decide to participate in this research study, you will be asked to make a total of 17 or 18 study visits (depending on whether screening visit is done during one or two visits) during the next 16 months. This includes study visits for screening, a treatment period, and a follow-up period.

This study will evaluate two doses of Anifrolumab (MEDI-546), 150 mg and 300 mg, to see how they compare with placebo.

SCREENING

During the screening period, some tests and procedures will be done to determine if you are eligible to participate in the study. The screening visit may take place over more than 1 day, but the tests and procedures should be done within a maximum of 30 days before you receive the first dose of study drug.

During the screening time, you will discuss your medical history and Lupus history with your Study doctor. It is important for your own safety that you tell your Study doctor about any medications you are taking for Lupus and for any other conditions (including medications taken some time ago), nonprescription medication (over-the-counter medication, such as aspirin, for example), and any herbal or dietary supplements. You should also tell your Study doctor about any allergies that you have so that he or she can check that you are not allergic to anything in the study drug.

You will not be able to enter this study if you are currently participating in any other study that has an investigational product (study drug). If you had major surgery within the past 8 weeks prior to signing this consent, or if you plan to have any surgery during this study period, you should inform the Study doctor and he will determine if you are able to be considered for this study.

The following assessments and procedures will be performed at screening:

- A general health check and physical examination (including height, weight, blood pressure, heart rate, breathing rate, and temperature). This will include questions about your health (such has HIV status) and your medications.
- An electrocardiogram (ECG) to check the health of your heart. This will involve sticky pads being stuck to your chest, wrist and legs.
- A chest X-ray. A machine will take a picture of your chest and lungs. This test may not need to be done if you have had a normal chest x-ray within the 12 weeks before first administration of study drug.
- Tuberculosis (TB) test. TB is a type of bacterial infection that affects the lungs and on rare occasions can be fatal. A blood sample is required to perform this test.
- If you are a woman, you will have tests to see if you are pregnant or if you are postmenopausal.
- Women are required to have a Pap smear (also known as a cervical smear) unless they have previously had their cervix surgically removed. This test is to confirm that you do not have cervical cancer. This test may not need to be done if you have had a Pap or cervical smear performed within the past 2 years that showed no signs of cancer.
- If you are a woman, you may be asked to have a mammogram according to the local guidelines.
- Your Study doctor may check your oral cavity and review your dental health carefully during the screening process.
- You will have some tests to assess your Lupus:

    - Your Study Doctor will ask you questions about your disease.
    - The Study Doctor will check your skin for signs of disease. If you have active skin lesions due to Lupus at the beginning of the study, and consent to optional study photography, photographs of your skin lesions will be taken to evaluate how study drug affects your skin lesions over time.
    - The Study Doctor will check your joints to see if they are tender or swollen, and will also check if you have any organ damage caused by your Lupus or findings such as skin cancer that might disqualify you from entering the study.
    - You will have blood samples collected and urine sample collected (about one-half cup) to measure certain chemicals that may be in your body that are related to your disease.

- You will also have other blood tests and urine tests to check that you are healthy and that you are eligible for the study; these include tests for liver and kidney damage, diabetes, and blood counts and tests for certain infections such as hepatitis B and C. If you have positive test results for hepatitis B or C, we will notify you. We are required to notify state health authorities of positive results. If these tests are positive you cannot take part in this research study. If you do not want to be tested you should not take part in this research study.
- A blood sample will be taken to measure the amount of type I interferon activity (type I interferon signature) in your blood. Your blood cells contain a type of molecule called ribonucleic acid, or RNA for short. RNA helps make proteins

such as the type I interferon group that controls inflammation. This blood test will measure the RNA that is made when levels of type I interferon increase and may indirectly measure Lupus activity or inflammation. This test is experimental meaning that it has not been approved by the U.S. FDA. The results will not be given to you or your study doctor.

The results from the screening assessments will allow your Study doctor to decide if you are eligible to take part in the study. It is possible that the results of one or more assessments may mean that your Study doctor decides that you cannot take part.

DURING THE STUDY
If you are eligible and you choose to take part in this study, then you will be included in 1 of 3 treatment groups:

- Treatment Group 1: Anifrolumab (MEDI-546) 150 mg (approximately 90 subjects)
- Treatment Group 2: Anifrolumab (MEDI-546) 300 mg (approximately 180 subjects)
- Treatment Group 3: Placebo (approximately 180 subjects)

You have a two in five (40%) chance of receiving Anifrolumab (MEDI-546) 300mg (the study drug), a one in five (20%) chance of receiving Anifrolumab (MEDI-546) 150mg (the study drug) and a two in five (40%) chance of receiving placebo. Which treatment you receive is decided at random by a computer (purely by chance, like drawing straws). You will remain on the same treatment throughout the study. This study is known as “double-blind,” which means that neither you nor your Study doctor will know which treatment you have received. In the event of an emergency, your Study doctor will have the ability to find out which treatment you have been given if he/she feels that knowing that information will affect your care during an emergency.

While you are in the study, you will receive the treatment (either study drug or placebo) every 4 weeks for 48 weeks (13 doses in all). The treatment will be given to you in your vein over a minimum of 30 minutes. This is called an intravenous or IV infusion. You will be monitored for at least 1-2 hours after each study drug infusion.

When you have finished taking part in this study, you and your Study doctor will discuss your options for managing your Lupus.

Study Visits
After the screening period, you will return to the study site for assessments and treatments, for 14 visits. The visits will occur every 4 weeks. You will receive study drug at Visits 1 through 13. At Visit 14 you and your Study doctor will decide if long term treatment through participation in another study is appropriate. If it is decided that you will no longer continue the study medication you will return for two more follow-up visits; at 8 weeks and 12 weeks after your last dose. If you meet eligibility criteria and participate in an extension study after week 52, you will be asked to review and sign another informed consent form that will give information about that study.

At each visit, you will be asked about your general health, medications you are taking, and any side effects that you may have experienced. You will also be asked to answer questions about your Lupus, including recent visits to your family doctor and emergency room and if you have had any days off work. You will be instructed to call the Study Team to report any abnormalities or side effects that may occur between study visits and to come to the study site if medical evaluation is needed.

The following assessments and procedures will be performed at your study visits.

- At Visits 1, 7, and 14 a blood sample will be collected to check the lipids (fats) in your blood. You will need to fast for at least 8 hours before this test. This means that you should not have anything to eat or drink, other than water, before these visits. You will be allowed to take your prescribed medications during this time.
- Questionnaires. You will be asked to complete some questionnaires at some visits only. Please see below for more details.
- You will have an ECG to check the health of your heart at Visits 1 and 14.
- Your weight, temperature, blood pressure, heart rate, and breathing rate will be measured at every visit.
- You will have physical examination and Lupus assessments at every visit. (The Study Doctor will check your skin for signs of disease and your joints to see if they are tender or swollen. Your Study Doctor will also check if you have any organ damage caused by your Lupus.).
- If you are eligible and if you provide consent, photographs of any active skin lesions will be taken at Visits 1, 2, 3, 4, 7, 10, 14, and final follow-up visit to see if there has been any change.
- If you are a woman of childbearing potential, you will have a urine pregnancy test before receiving study drug at every visit and during follow-up visits.
- Blood and urine samples for the following laboratory tests will be collected during the study.

    - Routine tests to monitor your general health throughout the study (including urine) at every visit, to measure certain chemicals that are related to your disease. These are tests to verify liver and kidney damage, and blood counts.
    - To see if you are making type I interferons (Visits 1, 4, 7, 10, 14, and final follow-up visit).
    - To measure inflammation based on your RNA levels (Visits 7 and 14), and certain cells and proteins in your blood (Visits 1, 4, 7, 10, 14, and final follow-up visit).
    - To measure levels of study drug in your blood and how the study drug is utilized in your body (Visits 1, 4, 7, 10, 13, 14, and during follow-up visits).
    - To see if your immune system is making antibodies to Anifrolumab (MEDI-546) (Visits 1, 4, 7, 10, 13, 14, and final follow-up visit).
    - To test for TB (Visit 14). Additional testing may be performed if the result obtained at screening is inconclusive (Visits 3, 7, and 10).

The total amount of blood that will be collected over the course of this 16-month study is approximately 545 ml. At Visit 14, women are required to have a Pap smear (also known as a cervical smear which is part of a routine gynecological checkup) unless they have previously had their cervix (lower part of the uterus) surgically removed. This test is to confirm that you do not have cervical cancer. This test should be done at screening (note: it may not need to be done if you have had a Pap or cervical smear performed within the past 2 years that showed no signs of cancer) and then, sometime between weeks 48 and 52 you should have one additional Pap smear performed to make sure that there are no new findings.

If you experience abnormal vaginal bleeding or pain on intercourse during the study, please ensure that you report this to the study staff who may recommend a gynecological evaluation.

Questionnaires
Throughout the study, you will be asked to complete several questionnaires. The questionnaires will ask you:

- about your general health to assess your overall health state
- to measure the fatigue you may be experiencing
- to measure your pain you may be experiencing
- how you are feeling related to overall mood,
- how you feel your Lupus affects your daily well-being
- a single question that asks how your illness affects you
- how Lupus affects your work productivity
- if you have needed unscheduled medical care

Most of these forms will take about 5 to 10 minutes to complete and will be given to you electronically, in an electronic notepad. Some of the questionnaires will ask you if you are having thoughts of suicide. If you are having thoughts of hurting yourself, your study doctor will immediately refer you to the Emergency room or a mental health specialist

Current Lupus Medication
It is important for your own safety that you tell your Study doctor about any medications you are taking for Lupus. If you are randomized to receive Anifrolumab (MEDI-546), it may take some time to see improvement in your symptoms. During this time the medications you were on at the beginning of the study will remain the same unless your Lupus is much better or much worse. Your current medications for Lupus will be assessed during your study participation, and will be adjusted by your Study doctor according to the study plan, especially if there are safety reasons that would require a change in treatment.

At each visit, you will be checked to see if your Lupus is better or worse. If your Lupus gets much worse and you need more medications to control your Lupus, your Study doctor may prescribe additional medications to help control your Lupus or you may stop

receiving the study drug, have some tests done, and you have the option to remain in or leave the study as some medications might not be permitted in the study for safety reasons, including possible interactions with the study drug.

While on study, your Study doctor will decrease your cortisone-like drug (such as prednisone) dose as a part of this study. If your disease activity worsens after decreasing the dose of cortisone-like drug (such as prednisone) you receive, your doctor will evaluate and may return the cortisone-like drug (such as prednisone) dose up to previous levels administered when you entered the study.

Lupus Assessments
You will have some tests to assess your Lupus at every visit. The Study doctor will check your skin for signs of disease and your joints to see if they are tender or swollen. Your Study doctor will also check if you have any organ damage caused by your Lupus.

Photographs of any active skin rash/redness will be taken at each visit for some subjects, in some countries that are participating in this study. If your Study Doctor is participating in the photography portion of the study, you will be given a separate consent to review for medical photography.

If you have an adverse event or side effect that is identified at your final study visit, then your Study doctor may wish to contact you if further follow-up information is needed. The Sponsor may also ask your Study doctor for this information.

WHAT DO I HAVE TO DO?

You must be willing to attend the scheduled visits as described in this Informed Consent Form. It is also important that you take your medications as directed by the Study doctor. You must inform the Study doctor as soon as possible about any medical treatment you receive outside of your participation in the study.

It is also important that you provide accurate and complete information about your medical history and your present condition and tell the medical staff about any other medication you are taking before and during the study. Do not start taking any new medications (prescription, non-prescription or herbal supplements) without confirming with the Study doctor. This is important because any new medication may potentially cause a problem in combination with your other medications, including the study drug. Also, do not take any illegal drugs during the study.

You must also be willing to report any undesirable, unwanted or unusual symptoms you may experience as well as report any worsening of conditions you have now.

You must not take part in any other studies using other experimental drugs, while you are taking part in this study.

Women who are pregnant or nursing mothers are not allowed to be in the study as the safety of the study drug in pregnancy and to nursing children is unknown. If you are currently pregnant or if you are a nursing mother, being in the study may involve risk to

you, your unborn child, or nursing child. You must tell your Study doctor immediately if you become pregnant. If you become pregnant during the study, you will not be given any more study drug.

It is very important that you use an acceptable method of birth control to prevent pregnancy during this study. Sustained abstinence is an acceptable practice; however, periodic abstinence, the rhythm method, and the withdrawal method are not acceptable methods of contraception. Please discuss acceptable methods of birth control with your Study doctor.

If you are a woman of childbearing potential (that is, you are not surgically sterile or you are not at least 1 year postmenopausal), you must avoid becoming pregnant and you must use 2 of the following methods of birth control, only one of which can be a barrier method, from screening and for at least 12 weeks after your last dose of study drug:

- Barrier methods
    - Male condom plus spermicide
    - Cervical cap (plus spermicidal cream or jelly) plus male condom
    - Diaphragm (plus spermicidal cream or jelly) plus male condom
- Intrauterine devices (IUDs)
    - Copper T plus condom or spermicide
    - Progesterone T plus condom or spermicide
- Hormonal contraceptives
    - Implants
    - Hormone shot/injection
    - Combined pill (contains a combination of estrogen and progestin)
    - Minipill
    - Contraceptive patch

If you are a man and your partner is of childbearing potential, unless you are surgically sterile (for example have had a vasectomy [a surgery that cuts and seals tubes that carry sperm]), you and your partner must use 2 of the above methods of birth control during the entire time you are in the study from screening and for at least 12 weeks after your last dose of study drug.

If you or your partner becomes pregnant during the study, or if you later learn that you or your partner became pregnant during the study or follow-up period, you must contact the Study doctor immediately for further instructions about follow-up. The Study Team will ask you about any pregnancy during the study and follow-up visits. If at any time you report a pregnancy of your partner, the Study Team will ask for your partner's

consent and attempt to collect information about the results of the pregnancy and/or birth and will schedule any follow-up visits that may be necessary. This health information will become part of the clinical trial records and will be shared with the Sponsor so that the Sponsor may determine if there are any effects of the study drug upon unborn children.

WHAT IS KNOWN ABOUT THE SAFETY OF ANIFROLUMAB (MEDI-546)?

In total, 291subjects have received Anifrolumab (MEDI-546) in research studies.

Thirty-four adults with Systemic slerosis (an autoimmune disease that affects the body's connective tissue and causes hardening of the skin), were enrolled in a previous study (Study MI-CP180) with Anifrolumab (MEDI-546). All of the subjects were followed for 84 days following the last dose of Anifrolumab (MEDI-546).

An ongoing study (Study CD IA MEDI 546 1013) has included 307 subjects with chronic, moderately-to-severely active Lupus who did not improve with standard of care treatment for Lupus. Another study with Anifrolumab (MEDI-546) is CD-IA-MEDI 546-1145. In this study subjects who took the study drug or placebo in Study CD IA MEDI 546 1013 receive Anifrolumab for an extended period of time to evaluate the long-term safety of Anifrolumab. At the time of developing this informed consent document, seventy-eight (78) subjects have been enrolled and continue in this study.

On another ongoing study (Study D3461C00002) adult Japanese subjects with active Lupus are taking different doses of Anifrolumab (MEDI-546) to evaluate the safety and tolerability of the study drug. At the time of developing this informed consent document, seventeen (17) subjects have been enrolled and continue in this study.

WHAT ARE THE POSSIBLE SIDE EFFECTS, RISKS, AND DISCOMFORTS OF TAKING PART?

RISKS FROM STUDY DRUG

Side Effects

The study drug may cause some side effects. The information on side effects from one completed study and 3 ongoing studies with Anifrolumab (MEDI-546) in humans is limited. You may experience none, some, or all of the same side effects reported in the previous studies, and there may be side effects that have not been previously reported.

The most common side effects (adverse events) in Study MI-CP180 (study in subjects with Systemic sclerosis (an autoimmune disease that affects the body's connective tissue and causes hardening of the skin)) were:

- Upper respiratory tract infection (a cold or runny nose); (29.4%)
- Headache (20.6%)
- Diarrhea and nausea (upset stomach) (17.6%, each)

Arthralgia (pain in a joint), fatigue, and pruritus (itchiness) (11.8%, each).The most common side effects (adverse events) in Study CD-IA-MEDI-546-1013 (subjects were receiving study drug or placebo), have been:

- Headache (11.1%); (10.8% of subjects on study drug and 11.9% of subjects on placebo)
- Upper respiratory tract infection (a cold or runny nose) (10.1%); (10.8% of subjects on study drug and 8.9% of subjects on placebo)
- Urinary tract infection (9.5%); (8.8% of subjects on study drug and 10.9% of subjects on placebo)
- Nasopharyngitis (a common cold) (8.2%); (11.3% of subjects on study drug and 2.0% of subjects on placebo)
- Herpes zoster (reactivation of the chickenpox virus resulting in pain and painful blisters on the skin in specific areas of the body and rarely involving organs in the body) (shingles) (5.2%) (7.4% of subjects on study drug and 1.0% of subjects on placebo)
- Bronchitis (inflammation in the lungs) (5.2%) (5.9% of subjects on study drug and 4.0% of subjects on placebo)
- Diarrhea (5.2%) (5.9% of subjects on study drug and 4.0% of subjects on placebo)

One adverse event of transverse myelitis, disorder of the nervous system caused by inflammation of the spinal cord, was reported along with a positive herpes zoster laboratory test. The patient recovered with routine treatments. Symptoms of the condition may include pain, muscle weakness, or abnormal physical sensations that may progress to more severe symptoms, including loss of use of arms and/or legs, or decreased ability to control urine and bowel movements.

The most common side effects (adverse events) in Study CD-IA-MEDI-546-1145 (study to evaluate the long-term safety of Anifrolumab [MEDI-546]) have been:

- Flu and nasopharyngitis (a common cold) (4.0%)

The most common side effects in Study D3461C00002 (study in adult Japanese subjects with active SLE for 48 weeks) have been:

- Nasopharyngitis (a common cold) (41.2%)
- Pain in the abdomen (23.5%)
- Upper respiratory tract infection (a cold or runny nose), headache, and SLE (each 17.6%)
- Herpes zoster (reactivation of the chickenpox virus resulting in pain and painful blisters on the skin in specific areas of the body and rarely involving organs in the body) (shingles) was observed (11. 8 %) subjects in this study

4 out of 8 patients who continued this study beyond week 48 experienced Upper respiratory tract infection (a cold or runny nose).

There was 1 death in Study CD-IA-MEDI-546-1013. A 60-year-old white female with no relevant medical history, was admitted to the hospital and was diagnosed with colitis (inflammation of the intestine), 26 days after receiving the first dose of investigational product. Her condition got worse despite intensive treatment, with possible spread of the infection, and she died on Day 34.

The investigator (Study doctor) did not think the subject's death was caused by the study drug Anifrolumab (MEDI-546).

There may be risks involved in taking this study drug that have not been identified. There is always a risk involved in taking a new medication in development but you will be closely monitored and you are encouraged to report anything that is troubling you.

Hypersensitivity Reactions
There is a remote chance that you may have a serious hypersensitivity reaction (anaphylaxis) or allergic reaction to the study drug. Anaphylaxis may cause a serious drop in blood pressure, difficulty in breathing, severe hives, and sometimes death. Your Study doctor will monitor you very closely for at least 2 hours after you receive the study drug at visits 1-4 and for at least 1 hour for visits 5-13. Your Study doctor will have medications available to treat any allergic reactions that might occur.

Less serious allergic reactions, such as skin rash with or without itching and swelling, may also occur within hours to days after receiving the study drug. These effects may get better without treatment.

One subject in the previous study with Anifrolumab (MEDI-546) experienced a reaction limited to a skin rash with itching during the first infusion of study drug. The subject successfully finished the infusion after receiving treatment for the reaction and received the remaining 3 infusions of study drug without any further reaction.

Possible Risks Based on Nonhuman Studies
The effects of Anifrolumab (MEDI-546) on the unborn fetus are not known. Results of a reproductive study in monkeys showed no changes to the mother or fetus that were considered to be related to Anifrolumab (MEDI-546) after receiving 30 or 60 mg/kg of Anifrolumab (MEDI-546) every 14 days.

Possible Risk of Infections
Because Anifrolumab (MEDI-546) blocks the actions of type 1 interferons that help defend us against viral infections, the ability of your immune system to fight off infections may be suppressed by the study drug. Your Study doctor may have prescribed additional medicines that can also suppress the immune system. Suppression of the immune system could increase your risk of developing infections, decrease your natural defenses to limit the severity of infections, or result in a slower recovery from infection. This suppression of the immune system could also increase your risk of developing a viral infection or allow it to become more severe or life threatening. The overall risk of developing or worsening infection may depend on the

doses and combinations of drugs being given to you to suppress the immune system, including Anifrolumab (MEDI-546). In ongoing Anifrolumab (MEDI-546) studies, infections are the most frequently reported type of side effects. These events are common in the population being studied and it is currently not known if they are related to Anifrolumab (MEDI-546).

More subjects dosed with Anifrolumab (MEDI-546) than subjects dosed with placebo developed herpes zoster (reactivation of the chickenpox virus resulting in pain and painful blisters on the skin in specific areas of the body and rarely involving organs in the body) (shingles) infections, but these have occurred in only a few subjects (17 out of 291). All of the subjects with shingles responded to antiviral medication and some needed to have Anifrolumab (MEDI-546) stopped. It is important that you notify your Study doctor as soon as possible if you experience a painful or itching blistering or red rash on your skin so that you can be treated.

More subjects dosed with Anifrolumab (MEDI-546) than placebo developed colds, the flu or mild viral infections which did not require special care.

Because blocking interferon might lower your resistance to viral infections, if you are a woman it is important that you have pap smears before starting the study and during study participation. Most cases of cervical cancer appear to be caused by the papilloma virus, which you may have been exposed to without knowing.

The Pap smear can detect early changes in your cervix which may be treatable. Although we have seen no cases of cervical cancer in subjects treated with Anifrolumab (MEDI-546) to date, having a pap smear regularly is important for your safety in this study.

During your participation in this study, you will be asked to report problems that might be due to viruses such as cold sores or shingles. If you are ill with an infection, you should still, if at all possible, come to the clinic for an assessment. If you have an infection or fever you should bring it to the attention of the Study doctor or Study Team as soon as possible.

You should also not receive any live vaccines, such as the nasal flu vaccine or the ZOSTAVAX Shingles Vaccine, during your participation in this study. You should speak with your study doctor before receiving any vaccine.

Possible Risk of Cancer

Type 1 interferons may have a role in the ability of your immune system to control cancers and suppressing their action may increase your risk of developing a cancer. Cases of various types of cancers were reported in subjects who received anifrolumab in clinical studies. These included, for example cancers of blood cells (leukemia), lymph nodes (lymphoma), breast cancer and lung cancer. No cancer was reported among patients who received placebo in these studies but the number of patients receiving placebo was lower than those who received Anifrolumab (MEDI 546). At this point, there is not enough

information to know whether or not receiving Anifrolumab (MEDI 546) will increase, decrease, or have no effect on the risk of developing cancer in an individual with Lupus. If you have any further questions about the risk of cancer you may discuss them with your study doctor.

Other Possible Side Effects
Some serious side effects have been observed with the drugs that belong to the same class as the study drug. Your Study doctor will closely monitor your condition and will actively search for any signs or symptoms of those conditions. Those events are called Adverse Events of Special Interest (AESI). Those events include:

- Serious infections, or opportunistic infections (infections caused by bacteria, virus, fungal or protozoa (parasites that can cause infections) which normally do not cause an infection in individuals with normal body defenses but that may cause severe infections in individuals with compromised body defenses).
- Hypersensitivity reactions including anaphylaxis (serious allergic reaction that is rapid in onset and includes a number of symptoms such as an itchy rash, throat swelling, breathing difficulty and low blood pressure that is sometimes fatal) and infusion-related reactions.
- Cancer (malignant tumor development).
- Herpes zoster (reactivation of the chickenpox virus resulting in pain and painful blisters on the skin in specific areas of the body and rarely involving organs in the body) (shingles).
- Tuberculosis (new infection or reactivation of dormant disease) and latent tuberculosis.
- Flu (severe infection caused by virus with fever, headache, muscle pain, fatigue, vomiting, diarrhea).
- Non Lupus vasculitis (inflammation of blood vessels).
- Major cardiovascular (heart) events (MACE) (this includes stroke, heart attack, severe chest pain, death due to cardiovascular events).

RISKS FROM STUDY PROCEDURES
You will be required to see your Study doctor more frequently than you would if you were receiving standard care. This may cause some disruption to your normal activities and home life and this should be discussed with your family and friends if it will have an impact on them.

Risks from Chest X-ray
A chest x-ray is a commonly used diagnostic procedure. The test exposes you to a small dose of radiation. The amount of radiation exposure from one chest x-ray is similar to the amount of radiation exposure a person experiences in our natural surroundings in 10 days.

Risks associated with Venipuncture/Intravenous (IV) Needle Insertion:
You may experience pain, bleeding, and/or bruising when your IV is started or when blood is taken from you, occasional light-headedness and, rarely, fainting. Rarely, you may develop an infection with redness, irritation or a blood clot of the vein at the site of the IV or where blood is taken. There is a very small potential for a skin or serious blood infection

each time the IV is started or a blood sample is drawn. The Study Team is highly trained and will make every effort to minimize these risks. A Study doctor will supervise the administration of the study drug, and you will be closely observed after each infusion. Your blood pressure, pulse, temperature and respiratory rate will be measured before, during, and after you receive the study drug and checked closely by the Study Team to see if you are having symptoms from the study drug. If you have symptoms, they will be treated to reduce any discomfort.

Risks Associated with ECG
You will also have an ECG which is a painless test that looks at the electrical activity of your heart by putting small sticky patches on your chest, arms and legs. These patches have thin wires that connect to a machine which will read and print a report. The test takes about 5-10 minutes. Some areas, where the patches will be placed, may need to be shaved. After the test, there may be a small amount of irritation where the patches were attached and some discomfort when the patches are removed.

Risks Associated with Questionnaires
The questionnaires may contain questions that are sensitive in nature and you may feel uncomfortable. If you have concerns after completing the questionnaire, you should contact your Study Doctor.

OTHER RISKS
The study treatment and procedure may involve risks to you (or to an embryo or fetus if the subject should become pregnant) which are currently unknown. In order to identify any potential complications you will be asked to report any changes or problems you may have noticed between study visits. It is important to remember this includes any new gynecological symptoms, such as unusual vaginal bleeding and painful intercourse. You will be followed closely throughout your involvement with the study by your Study doctor who will evaluate any changes or problems that develop.

WHAT IF NEW INFORMATION BECOMES AVAILABLE?
You will be told if any new information on the study medication becomes available which may influence your decision to continue in the study.

ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?
It is hoped that study treatments will help you. However, this cannot be guaranteed. Even if there is no benefit to you, what is learned in this study may help us to better understand Lupus and be of future benefit to those with the disease.

WHAT OTHER TREATMENTS ARE AVAILABLE?
If you do not want to take part in the study there are other medications which are available to treat your Lupus. You should discuss with your Study doctor other alternatives for treatment for your condition. Current treatments for Lupus include a variety of drugs that suppress the immune system, such as cortisone-like drugs (such as prednisone), cyclophosphamide, methotrexate, and mycophenolate mofetil and nonsteroidal anti-inflammatory drugs (NSAIDs) such as naproxen or ibuprofen and paracetamol (or acetaminophen) which can be used for fever, joint pain, and arthritis.

Belimumab is a drug that has recently been approved by the FDA for the treatment of Lupus, which targets another protein involved in activating the immune cells that attack your tissues. Topical sunscreens are used to minimize rashes or skin conditions resulting from exposure to sunlight (photosensitivity). Antimalarial agents (such as hydroxychloroquine) can also be used to treat Lupus. Your Study doctor can explain these treatments to you in more detail if you choose not to take part in this study.

CAN I STOP BEING IN THE STUDY?

At any time during the course of the study and for any reason, you can withdraw from the study without any penalty or loss of benefits to which you are otherwise entitled. Your decision to leave the study will have no effect on your future care or treatment by physicians or by this institution.

If you leave the study early, it is recommended that you go through the final study procedures that the Study doctor considers necessary, which may include safety follow-up visits. Even if you stop receiving study drug, you are encouraged to continue to participate in the study and to complete study visits as scheduled, as the collected safety data will be of importance for the better understanding of the effects of the study drug.

If you decide to withdraw your consent, no further study-related contacts or data collection will then occur.

If you have an adverse event or side effect that is identified at your final study visit or withdrawal visit then your Study doctor may wish to contact you and ask you about this, until it has completely resolved. The Sponsor may also ask the Study doctor for this information.

The Study doctor may also decide that it is best that you leave the study without your consent. The study may also be ended by the Sponsor for any reason without your consent.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

There will be no cost to you for any expenses related to this study.

You will continue to receive your current standard of care during the study. You or your insurance company will still be charged for your standard care. Neither you nor your insurance company will be charged for the following items:

- Study drug
- Study visits
- Study procedures
- Study laboratory tests

Therefore, you should not claim these costs from your insurer.

WILL I BE COMPENSATED (MONEY OR OTHER) FOR TAKING PART IN THE STUDY?

You will not be paid for being in this study. You will not be paid for lost wages or other damages or losses. However, reasonable and necessary expenses in connection with the study, such as travel and parking, will be reimbursed if you have receipts for these expenses. You will be reimbursed only for those visits you have completed should you leave the study early.

WHAT HAPPENS IF I HAVE AN INJURY RESULTING FROM THIS STUDY?

If you suffer any side effect or other physical injury as a direct result of taking part in the study, the Sponsor will pay for the reasonable costs of medical treatment in accordance with applicable laws.

The Sponsor has insurance to cover these costs.

The Sponsor will make these payments where the side effect or other physical injury probably resulted from:

- a drug being tested or administered as part of the study; or
- any test or procedure you received as part of the study.

These payments will only be available if:

- you received the study drug as directed by your study doctor, and followed all of the instructions given to you by your study doctor;
- your injury was not deliberately caused;
- you immediately told your study doctor about your injury; and
- the medical advice of your study doctor was followed.

The Sponsor will only pay for the medical costs that are not covered by your insurance or other programs. In addition, the Sponsor may not pay for medical treatment or any compensation, or any amount may be reduced, if the injury is connected to your underlying medical condition (lupus).

If you have medical insurance please check with your insurance company that taking part in this study will not affect your policy.

You do not give up any legal rights by signing this consent form.

WHO IS ORGANIZING THE FUNDING OF THE RESEARCH?

The Sponsor of this study is paying for the research. The Sponsor is paying the Study doctor and/or the Study doctor's institution to carry out the study.

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?

In case of a study-related injury or whenever you have questions about the study or your study medication, please contact:

Study Doctor/Contact Name: Barry E Shibuya MD

Daytime Telephone Number(s): 510-791-1300

24-hour Contact Number(s): 510-449-5413

You may ask questions about this study at any time, even if you are no longer receiving study drug. Answers to questions about this research study can be obtained from the study doctor.

If you experience any symptoms you think might be related to taking part in this study, or any other medical problems, be sure to report them quickly to the study doctor.

If you have any questions about your rights as a research subject, or complaints about this research, you should contact:

Please call Copernicus Group IRB at 1-888-303-2224 if:

- You want to talk to someone other than the study doctor or study staff.
- You have a hard time reaching the study doctor or study staff.
- You have questions about your rights as a research subject.

Please visit the Copernicus Group IRB website www.cgirb.com for more information about research studies and the role of a research subject.

WILL MY MEDICAL INFORMATION BE KEPT PRIVATE?

Your study doctor and study staff will collect and use information about you for the study. This can include birthdate, sex, race, information about your health, and data obtained from any donated blood or tissue samples (this is known as “Personal Data”).

So that you cannot be identified, your Personal Data is protected by a code. This coded data is referred to as “Study Data” and your study doctor controls the code key. Personal Data will not be disclosed to anyone unless necessary to conduct the study, if necessary for your health and wellbeing, or that of another subject, or if required by law.

AstraZeneca AB Sweden (The Sponsor) needs to collect and use the Study Data to carry out the study, learn about the study drug and support applications for approval of the study drug. We may use Study Data for research on other diseases and to develop other drugs, diagnostic tests or medical aids. Lab specimens that are analyzed for the study can be stored and sent to third party vendors for analysis for up to 15 years for this study. AstraZeneca is organizing this study as the study sponsor and is responsible for your personal data.

To aid this and future research and to improve science, patient care and public health the Sponsor may share the Study Data with other companies in our group, service providers, contractors, other researchers, Copernicus Group Independent Review Board (CGIRB), and health authorities such as the U.S. FDA.

You may have the right to see your Study Data held by your study doctor and to correct mistakes in your data. The results of the study may be published in the medical literature.

In all situations described above, when using and sharing your Study Data and publishing results, strict controls are in place to ensure that the information does not reveal who you are.

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.

WHAT OTHER INFORMATION WILL BE AVAILABLE?

You will receive a summary of the study results when the study ends. To allow for full analysis of all participants' data, this will be about 12 months after the last person completes their participation in the study.

CONSENT FORM

A Multicentre, Randomised, Double-blind, Placebo-controlled, Phase 3 Study Evaluating the Efficacy and Safety of Two Doses of Anifrolumab in Adult Subjects with Active Systemic Lupus Erythematosus

By signing this consent form, I agree to the following:

- I have received verbal information on the above study and have read the attached written information. I confirm that I have read and understand this consent form and any information sheets. I have had a chance to consider the information, ask questions, and discuss the study.
- I consent to take part in the study and I am aware my participation is entirely voluntary. I understand that I am free to withdraw at any time, without giving a reason, without my medical care or legal rights being affected and without this affecting my future care. I understand that by signing this informed consent I am not waiving any legal rights that I otherwise have.
- I understand that relevant sections of my medical notes, and data collected during the study, may be looked at by responsible individuals representing the company sponsoring the study (the Sponsor), auditors, supervisory bodies, or regulatory authorities where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.
- I agree that my regular doctor (for example family doctor, primary physician or gynecologist) can be informed of my participation in the study.
- I understand I will receive a copy of this information and consent form. I understand that the signed original will remain on file with the Study doctor.
- I have received a copy of the Experimental Subjects Bill of Rights.
- I agree to take part in this study.

_____	_____	_____
Signature of Subject	Date of Signature	Time of Signature

_____
Printed Name of Subject (BLOCK CAPITALS)

The information about the study was described to the subject in a language he/she understood.

_____	_____
Signature of Person Conducting Informed Consent Discussion	Date of Signature

_____
Printed Name of Person Conducting Informed Consent Discussion (BLOCK CAPITALS)

AUTHORIZATION TO USE AND DISCLOSE HEALTH INFORMATION

How is my health information collected, used, and disclosed (shared)?

During the course of the study, the study doctor will collect health information about you, which will be used to learn about the safety and effectiveness of the study drug. This will include information that identifies you. You must give your authorization (permission) before the study doctor can use or share your health information with others. If you decide not to give permission to use and share your health information, then you will not be able to be in this research study. This section will describe how your health information will be collected, used, and disclosed and describes your rights, including the right to see your health information.

Definition of Health Information

Your health information includes your medical records such as your medical records made by any doctor, hospital, or other healthcare provider not part of the study. It also includes information about you collected during the study. This information may include the dates or results of different tests or examinations. The study doctor may need this information to watch, review and report on the safety of the study drug.

Some of the information that may identify you includes:

- Your name
- Your address
- Your telephone number
- Your photograph
- Your date of birth
- Your social security number
- Other details about you, such as your race/ethnicity or gender

The Persons who will get your Health Information

If you sign this form, you allow the study doctor to collect and use your health information to carry out this study. You also give your permission to disclose your health information without personal identifiers (unless required by law) to all of the following groups:

- The study sponsor and its related companies, which are located around the world. These companies may use and disclose your health information to carry out the study, to apply for approval of the study drug, both in the United States and in foreign countries.
- All the people at the study doctor's site who help the study doctor to carry out the study or help with the paperwork for the study.
- People and companies who work with the study sponsor on the study (for example, the sponsor may hire another company to help oversee the study, or it may hire a laboratory to do lab tests or to check your health information and the data collected during the study). These companies may be located around the world.
- Other doctors and health care workers who help with the study.
- Copernicus Group Independent Review Board (CGIRB, a research ethics committee, that watches over the study.
- The Food and Drug Administration (FDA), other Department of Health and Human Services agencies and other government agencies in the United States and in foreign countries that watch over the study.
- The people you have named as emergency contacts (if any) in case you do not show up for your appointments with the study doctor and the study team has not been able to reach you.

If you sign this form, you are also allowing healthcare providers that treat you outside of the study to share your health information with the study doctor. This will allow the study doctor to have all the information needed to carry out, watch and review the study and to report to regulatory authorities on the safety of the study drug. This includes disclosure in the event of your death. Your study doctor may ask you to sign a separate authorization form to obtain this information.

The study site (where the study is taking place) and the study sponsor are each responsible for their handling of your study-related health information in accordance with applicable data protection laws.

Possible Transfer of Your Health Information Out of the Country
As explained above, the study sponsor may send your study data (with your initials and a code number, but not your name) outside of the United States for the reasons described in this form.

Please know that the laws in other countries may not provide the same level of data protection and may not stop your study data from being disclosed to others. When your study data is processed in Sweden by the Sponsoring Company, AstraZeneca AB is responsible for your personal data.

Notice on Redisclosure of Your Health Information and Confidentiality
The researchers conducting this research can disclose your protected information only to the persons whom you have permitted to see it, and only in the ways you have permitted. However, if you sign this form it is possible that those persons may share your protected information with other persons. Federal law does not protect you against this, but the laws of your state may provide additional protection.

Your Right to See and/or Copy Your Study-Related Health Information
You may see and copy your study-related health information as long as the study doctor keeps this information. You may also, under data protection laws, have the right to ask that any mistakes in your study-related health information be corrected. However, you may not be able to see, or copy, your study-related health information until after the study has been completed, otherwise, it could affect the study.

Cancelling Your Authorization (Withdrawing Your Permission)
You may cancel your authorization (withdraw your permission) that you have given in this form at any time. To do this, you need to write to the study doctor at the following address:

Barry E Shibuya MD
Fremont Rheumatology (Barry Shibya MD Inc)
3775 Beacon Ave Ste 100
Fremont CA 94538

If you withdraw your permission, the study doctor will no longer use your health information or share it with others, unless the study doctor needs to do so to protect the study data and research results. However, the study sponsor may still use or disclose information about you that was shared with the study sponsor before you cancelled your authorization, if allowed under state law. If you have provided biological samples, you may withdraw your consent to the use of your samples at any time. If a link between you and your samples exists and the samples have not been anonymized, the Study Sponsor and the Study Doctor will make sure that your biological sample(s) will be destroyed. However, if any analysis or research has already been performed on the samples, the Study Sponsor does not have to destroy the results of this analysis or research.

Expiration of Your Authorization (Permission)
Your permission will expire December 31, 2060, unless you withdraw it in writing before then.

Your decision to withdraw your Authorization or not to participate will not involve any penalty or loss of access to treatment or other benefits to which you are entitled.

AUTHORIZATION
I AUTHORIZE THE COLLECTION, USE AND DISCLOSURE OF MY HEALTH INFORMATION IN ACCORDANCE WITH THIS FORM, INCLUDING TRANSFER TO COUNTRIES OUTSIDE OF THE UNITED STATES.

_____

Printed Name of Subject

_____

Signature of Subject **Date**