title: Tailoring Maintenance Therapy to CD5+ Regulatory B Cell Recovery in ANCA vasculitis

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University of North Carolina at Chapel Hill
Consent to Participate in a Research Study
Adult Participants

Consent Form Version Date: October 22, 2024

IRB Study # 18-2015
Title of Study: Tailoring Maintenance Therapy to CD5+ Regulatory B Cell Recovery in ANCA vasculitis
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Concise Summary

This is a study for adult patients with anti-neutrophil cytoplasmic antibody (ANCA) vasculitis who are in remission after initial treatment. The purpose of this research study is to learn if a special blood test can help us identify which patients with ANCA vasculitis could be monitored without additional immunosuppressive maintenance treatment. This study is NOT testing new medications. Any treatment will use the same medications that are currently routinely used for maintenance treatment in ANCA vasculitis.

The study will last 2 years. Your initial treatment has eliminated certain immune cells (called "B lymphocytes" or "B cells") from your blood. When we can detect the B cells again in your blood, it is time to decide if you need maintenance therapy. This is the time you can start in the study. At that stage, we believe that the number of a special type of B cells (called CD5+) can give us an indication of your risk of having a relapse of ANCA vasculitis in the future. If the number of CD5+ B cells is near normal, we believe that the risk of relapse is significantly lower than if that number is still abnormally low.

Therefore, if your CD5+ B cells are low, you will receive maintenance treatment as is usually done, using the same medications you would receive if you were not participating in this trial.

If your CD5+ B cells are near normal, you will be selected by chance (like flipping a coin) to either receive the same maintenance treatment or be monitored in clinic without additional maintenance treatment.

From that point forward, you will have clinic visits scheduled depending upon which study group you are assigned, for a total of 24 months or 2 years.

Potential benefit: Research is designed to benefit society by gaining new knowledge. There is little chance you will benefit from being in this research study.

Potential risk: If we think that you are at risk for relapse, you will receive maintenance therapy. If we think you are in the "low-risk-of-relapse" group, you will be randomized to receive or not receive maintenance therapy. Being in the "low-risk-of-relapse" group does not mean you will never have a relapse. It is possible that being

placed into the group receiving no maintenance therapy will put you at risk for relapsing or for relapsing sooner than if you had received maintenance therapy. However, you will be monitored closely throughout the study period so that if you do have a relapse of disease, we will be able to treat it promptly.

What are some general things you should know about research studies?

You are being asked to take part in a research study. To join the study is voluntary. You may choose not to participate, or you may withdraw your consent to be in the study, for any reason, without penalty.

Research studies are designed to obtain new knowledge. This new information may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study.

You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

Patients with anti-neutrophil cytoplasmic antibody (ANCA) vasculitis are routinely treated with medications that decrease their immune system function ("immunosuppression"). The treatments last several months and are divided in two phases: an "induction" phase is the initial phase aimed at stopping the inflammation, and a "maintenance" phase aimed at decreasing the risk of relapse. The risk of relapse varies considerably between patients, and we believe that some patients have a relatively low risk of relapse and may not need continued maintenance immunosuppression.

The purpose of this research study is to learn if a special blood test can help us identify some patients with anti-neutrophil cytoplasmic antibody (ANCA) vasculitis who are in remission after initial treatment could be monitored without additional immunosuppressive maintenance treatment. By collecting health information and laboratory samples, our goal is to learn more about this disease and find better ways to tailor treatment of ANCA vasculitis to an individual patient's needs. New knowledge will be shared with researchers and the public.

You are being asked to be in the research study because you are between 18-85 years old and have been diagnosed with ANCA glomerulonephritis or vasculitis, you have been treated for 3 months or more and you have not had any symptoms of vasculitis for at least 1 month.

Are there any reasons you should not be in this study?

You should not be in this study if any of the following are true:

1) You do not wish to participate in this research study
2) You have already been sick with ANCA vasculitis 3 times or more (had 2 relapses or more)

3) You are participating in another clinical trial that determines your treatment of ANCA vasculitis

4) You have ANCA vasculitis that has been caused by a drug you were taking

5) You have active tuberculosis, human immunodeficiency virus (HIV, the virus that causes AIDS), hepatitis C virus or hepatitis B virus infections, or another active infection requiring IV antibiotics within 3 months of starting this research study.

6) You are a woman of child-bearing age and are unwilling or unable to use birth control

7) You are unable to come your scheduled appointments

How many people will take part in this study?

There will be approximately 40 people in this research study.

How long will your part in this study last?

Your participation in this research study will last 2 years. The treatment you have received for ANCA vasculitis decreases the function of your immune system. If you are enrolled in this study, it means that you have already completed the initial (induction) phase of treatment for ANCA vasculitis, and your disease is currently not active. The treatment you have received had eliminated certain immune cells (called "B lymphocytes" or "B cells") from your blood but now, those B cells have returned.

At that stage, we believe that the number of a special type of B cells (called CD5+) can give us an indication of your risk of having a relapse of ANCA vasculitis in the future. If the number of CD5+ B cells is near normal, we believe that the risk of relapse is significantly lower than if that number is still abnormally low.

When the B cells are detectable in the blood, if your CD5+ B cells are low, you will receive maintenance treatment as is usually done, using the same medications you would receive if you were not participating in this trial. If your CD5+ B cells are near normal, you will be selected by chance (like flipping a coin) to either receive the same maintenance treatment or be monitored in clinic without additional maintenance treatment.

If you are in the group on maintenance therapy, you will have a clinic visit with a study physician every 8- 12 weeks, for a maximum of 24 months.

If you are randomized to NOT receive maintenance therapy and to be watched closely, you will be seen for clinic visits every 4 weeks for the first four months, then every 6 weeks for a total of 24 months of follow-up. You will also receive a phone call by a research coordinator about 2-3 weeks after every clinic visit to ask about any symptoms of infection or relapse.

This study is NOT testing new medications. Any treatment will use the same medications that are currently routinely used for maintenance treatment in ANCA vasculitis. This study is testing whether some patients whose CD5+ B cells return to near normal levels can be followed without receiving additional maintenance treatment.

You should be aware that the use of CD5+ B cells to guide treatment decisions is NOT currently approved by the FDA. These tests are to only be used in the *investigational* setting as noted below.

CAUTION – Use of an Investigational device. Limited by United States law to investigational use. Enumeration of B-cells for guiding management of ANCA vasculitis or other disease conditions has yet to be validated in clinical trials and should not be utilized to guide clinical therapy outside of a regulated, investigational study. This test was developed, and its performance characteristics determined by the McLendon Clinical Flow Cytometry Laboratory. The Flow Laboratory is CLIA certified and CAP accredited to perform high complexity testing.

What will happen if you take part in the study?

Enrollment visit

This visit can occur the day of your scheduled appointment in the UNC Kidney and Hypertension clinic. A member of the research team will tell you why we do this study, will explain how many study visits would happen and what will be done at each visit, and will see if you want to participate. You will be given several documents (called consent forms) to review. You will be given time to ask questions. You can read these at your visit or decide to take them home to read and discuss with your loved ones. If you choose to participate in the study, you will sign the consent forms. You will be given signed copies for your records. This process should take 20-30 minutes extra during your regular scheduled appointment.

If you decide to wait to consent, we can schedule another visit (Screening visit) where you can ask any further questions before you sign the consent. We would like this visit to be scheduled within 2 weeks of your regular visit so that we can make sure you are not in relapse before you consent.

Screening (Visit 0)

This visit can be done during your regular scheduled visit or at a future date. During this visit, you will have a physical examination by the doctor. The research coordinator will collect information about you, your medications and your previous medical history. We will need to draw an extra 24 mL of blood (a little less than 2 tablespoons) along with your standard of care blood tests.

If this visit takes place within 2 weeks of your regular Nephrology visit, we will only need to draw the 24 mL of blood for the research study and you will not need to repeat the physical exam at that visit.

We will measure the level of the special CD5+ B cells. If these are low, you will be started on maintenance treatment with rituximab. If you cannot take rituximab (500 mg by vein every 6 months), you will receive treatment with either azathioprine (Imuran) or mycophenolate mofetil (Cellcept) by mouth every day. These three medications are currently routinely used for maintenance treatment of ANCA vasculitis. The choice of which one will be prescribed to you will depend on how you tolerated them in the past, or whether your insurance company will cover the cost.

If your CD5+ B cells are near normal, you will be randomized, which means selected by chance (like flipping a coin) to either be in **the Maintenance Therapy group** where you will receive a maintenance treatment or to be in the **WATCH group** in which you will be monitored without maintenance treatment. If you are randomized to receive maintenance treatment, you will receive rituximab (500 mg by vein every 6 months). If you cannot take rituximab, you will receive treatment with either azathioprine (Imuran) or mycophenolate mofetil (Cellcept) by mouth every day.

Test Information: After consent, we will collect blood and urine samples from you at all study visits.

Total Amount of blood drawn: You will have between 10 to 16 tablespoons of blood (144 to 240 mL) taken for research during the study.

For the Maintenance Therapy Group

The maintenance treatment will start as soon as possible after we know that you are in the Maintenance Therapy group.

If you can receive rituximab: An appointment to have the rituximab infusion will be scheduled to be given at the UNC Infusion clinic. This medication is given by vein through an IV catheter. The infusion will take between four and six hours. At the time of each infusion you will be given a dose of "steroid" by vein and an antihistamine before the rituximab infusion to reduce the risk of allergic reaction. This is according to the standard protocol for the use of rituximab. This will minimize infusion reactions.

If you cannot tolerate Rituximab or if you cannot access rituximab (for example if your insurance does not agree to pay for it), your doctor will prescribe another maintenance drug: azathioprine or mycophenolate mofetil. Azathioprine and mycophenolate mofetil are oral drugs that you must take every daily.

You will have a research study visit at your infusion or at the start of the other medication. This visit will include:

- a physical exam
- vital signs (blood pressure, weight, temperature, respiration rate)
- you will give a urine sample
- you will have a blood drawn, for your care and sometimes for research (see the schedule of visits table for more info- each research blood draw is 24 mL = a bit less than 2 tablespoons)
- if you are a woman who could become pregnant, we will do a urine pregnancy test
- the doctor will review your medications and how you feel
- about every 4 months you will fill out a questionnaire about your quality of life

After the infusion or start of medication, the Maintenance Therapy group will have clinic visits for the study every 8-12 weeks for the doctor to make sure you are well and watch for relapse symptoms and the return of the B cells. The actual schedule will vary and depend upon your health and the doctor's guidance. These visits will be very similar to the visit mentioned above. You will receive further Maintenance medication for relapse symptoms or the return of the B cells. If you do not have a standard of care visit scheduled during one of the 12 week visit windows, a visit will be done remotely by phone or video to collect information.

In-between visits - surveillance phone calls

Between the study visits, you will receive a phone call from the study doctor or the study coordinator to check how you are doing and see if you have any symptoms that might be a sign of relapse or infection. They will ask you a series of questions about your health and if you have any symptoms. If, after talking with you, they think that you might be relapsing or having an infection that should be treated, you will be asked to come to the clinic within the following week for a visit.

For the WATCH group (those patients not receiving maintenance therapy) after randomization

You will have monthly clinic visits with a study doctor.

At every visit,

- you will have a physical exam
- we will take your vital signs (blood pressure, weight, temperature, respiration rate)
- you will give a urine sample
- you will have a blood draw done, for your care and sometimes for research (see the schedule of visits table for more info- each research blood draw is 24mls = a bit less than 2 tablespoons)
- if you are a woman who could become pregnant, we will do a urine pregnancy test
- the doctor will review your medications and how you feel
- every 4 months you will fill out a questionnaire about your quality of life

After Visit 5 (Week 16), the visits will decrease to every 6 weeks.

In-between visits - phone calls

Approximately two to three weeks after each study visit, you will receive a phone call from the study doctor or the study coordinator to check how you are doing. They will ask you a series of questions about your health and if you have any symptoms that might be a sign of relapse. If, after talking with you, they think that you might be relapsing, you will be asked to come to the clinic within the following week for a visit.

If you have a relapse when you are in the WATCH group, you will exit that surveillance group and be treated as needed by the doctor treating you for vasculitis. However, we would like to follow you and collect information and blood as scheduled during the rest of the study.

SCHEDULE OF VISITS for Maintenance Therapy group

	Physical exam	Review of your medications and how you feel	Quality of Life questionnaire	Blood draw for research	Urine pregnancy women only	Rituximab infusion *
Enrollment/ Screening visit	**X**	**X**	**X**	**X**	**X**	
Visit 1 Week 0	**X**	**X**	**X**	**X**	**X**	**X**

Visit 2 (8-12 weeks after V1)	**X**	**X**			**X**	
Visit 3 (8-12 weeks after V2)	**X**	**X**			**X**	
Visit 4 (8-12 weeks after V3)	**X**	**X**		**X[a]**	**X**	**X[a]**
Visit 5 (8-12 weeks after V4)	**X**	**X**			**X**	
Visit 6 (8-12 weeks after V5)	**X**	**X**	**X**		**X**	
Visit 7 (8-12 weeks after V6)	**X**	**X**		**X[a]**	**X**	**X[a]**
Visit 8 (8-12 weeks after V7)	**X**	**X**			**X**	
Visit 9 (8-12 weeks after V8)	**X**	**X**			**X**	
Visit 10 (8-12 weeks after V9 if months 24 not	**X**	**X**				
	Physical exam	**Review of your medications and how you feel**	**Quality of Life questionnaire**	**Blood draw for research**	**Urine pregnancy women only**	**Rituximab infusion ***

Visit 10 (8-12 weeks after V9 if months 24 not yet reached at V9)	**X**	**X**	**X**	**X[a]**	**X**	**X[a]**
Visit 11 (8-12 weeks after V10 if months 24 not yet reached at V10)	**X**	**X**			**X**	
Visit 12 (8-12 weeks after V11 if months 24 not yet reached at V11)	**X**	**X**			**X**	
Visit 13 (8-12 weeks after V12 if months 24 not yet reached at V11)	**X**	**X**		**X[a]**	**X**	**X[a]**

[a] Future rituximab infusion schedules will occur approximately every 6 months but timing will vary depending upon B cell levels and relapse symptoms. Research blood samples will be collected before the rituximab infusion.

SCHEDULE OF VISITS for WATCH (No maintenance therapy group)

Phone calls will occur approximately 2 to 3 weeks after study visits.

	Physical exam	Review of your medications and how you feel	Quality of Life questionnaire	Blood draw for research	Urine pregnancy women only
Enrollment/ Screening visit	**X**	**X**	**X**	**X**	**X**
Visit 1 Week 0	**X**	**X**	**X**	**X**	**X**
Visit 2 Week 4	**X**	**X**			**X**
Visit 3 Week 8	**X**	**X**			**X**
Visit 4 Week 12	**X**	**X**		**X**	**X**
Visit 5 Week 16	**X**	**X**			**X**
Visit 6 Week 22	**X**	**X**	**X**	**X**	**X**
Visit 7 Week 28	**X**	**X**			**X**
Visit 8 Week 34	**X**	**X**		**X**	**X**
Visit 9 Week 40	**X**	**X**			**X**
Visit 10 Week 46	**X**	**X**	**X**	**X**	**X**
Visit 11 Week 52	**X**	**X**			**X**

	Physical exam	Review of your medications and how you feel	Quality of Life questionnaire	Blood draw for research	Urine pregnancy women only
Visit 12 Week 58	**X**	**X**		**X**	**X**
Visit 13 Week 64	**X**	**X**			**X**
Visit 14 Week 70	**X**	**X**	**X**	**X**	**X**
Visit 15 Week 76	**X**	**X**			**X**
Visit 16 Week 82	**X**	**X**		**X**	**X**
Visit 17 Week 88	**X**	**X**			**X**
Visit 18 Week 94	**X**	**X**	**X**	**X**	**X**
Visit 19 Week 100	**X**	**X**			**X**
Visit 20 Week 106	**X**	**X**	**X**	**X**	**X**

What are the possible benefits from being in this study?

Research is designed to benefit society by gaining new knowledge. You will not benefit personally from being in this research study.

What are the possible risks or discomforts involved from being in this study?

You might be treated with rituximab, azathioprine or mycophenolate mofetil.

Side Effects of Rituximab

Infusion Reactions

Rituximab can cause infusion reactions at the time of the treatment (1 in 5 patients are affected) and you may develop fever, chills and shivering. Other side effects uncommonly seen during the infusion are itching of the skin, sickness, tiredness, headache, breathing difficulties, sensation of the tongue or throat swelling, a runny nose, flushing, back pain and an irregular heart rate, although the nurses looking after you will be monitoring you closely. You will be given glucocorticoids and antihistamines through a vein prior to receiving the infusion, to minimize these side effects. Pre-existing conditions such as heart disease may be also be affected. The frequency of these reactions decreases during subsequent infusions. This drug rarely leads to a reduction in the level of healthy antibodies or white blood cells. Rituximab may rarely also cause abnormalities of your blood and affect liver function. In patients with autoimmune diseases, use of rituximab has been associated with two rare, but quite serious, skin reactions called toxic epidermal necrolysis and Stevens- Johnson syndrome. These skin reactions can be fatal. Some of the skin reactions occurred on the day of the infusion or within a few days of the infusion. However, in some cases, the event occurred weeks or months after infusion. You will be monitored for such reactions.

Other rare adverse effects which have been recorded after administration of rituximab include: rashes, difficulty sleeping, pain in muscles and joints, pain at the infusion site, anxiety, dizziness, tingling or numbness in hands or feet, sweating, abnormal taste, cough, reactivation of viral infection (for example, cold sores), heart problems.

Other Side Effects

Some patients developed new serious viral infections or had a worsening of chronic viral infections. Most, but not all, of these patients had cancer and they were on other anti-cancer treatments which made them more at risk. In some cases, these viral infections occurred over one year after rituximab treatment and resulted in death. A rare and severe viral infection called PML (progressive multifocal leukoencephalopathy), which can cause brain damage, such as memory loss, trouble thinking and blindness, is almost always fatal and has occurred in patients who received rituximab. The majority of these patients received rituximab in combination with chemotherapy (drugs that treat cancer) or as part of a bone marrow transplant. PML is currently believed to be very rare in vasculitis patients. Tell your doctor immediately if you, your family members or a health care provider notices if you are having any new or worsening medical

problems, such as a new or sudden change in thinking, walking, strength, vision, or other problems that have lasted over several days. There are no known effective treatments for PML.

Your study doctor will discuss with you whether you are at high risk for exposure to Hepatitis B. One patient (of approximately 1000 rheumatoid arthritis patients treated with rituximab) developed a new infection with Hepatitis B virus and had symptoms of tiredness and yellow coloration of the skin. It is uncertain whether treatment with rituximab increased the risk for this infection. If you have Hepatitis B, you are not eligible for participation in this study.

Some patients with cancer who were treated with rituximab and chemotherapy had bowel problems including blockage and, in some cases, the bowel developed holes, which sometimes resulted in death.

Rituximab may lessen your body's ability to respond to live viral vaccinations (for example; measles, mumps or rubella). If you believe that it is necessary to have a non-live vaccination, you should have the vaccination 4 weeks before the first dose of study treatment.

Side Effects of Azathioprine

Azathioprine may cause nausea, diarrhea, vomiting, poor appetite, abdominal discomfort, headaches or liver upset. This drug can also cause rash, bone marrow suppression (and therefore increased risk of infection), or anemia (a low blood count). You should report any sore throat, abnormal bleeding or bruising to your study doctor. Azathioprine may also cause mouth ulcerations, and rarely gastrointestinal ulcerations, or sensitivity reactions such as fever, chills, muscle aches, and dizziness. It may also cause some hair loss.

You should wear sunscreen and avoid sunbathing, as there is an increased risk of skin cancer with this drug. Please avoid anyone with chicken pox or shingles while taking this drug.

Side Effects of Mycophenolate Mofetil

The most common side effects of mycophenolate mofetil are mild stomach upset (including diarrhea, nausea, vomiting, abdominal pain, constipation, loss of appetite and indigestion). This drug can also cause rash, bone marrow suppression (and therefore increased risk of infection), or anemia (a low blood count).

Risks Associated with Pregnancy

Because of the effects of these drugs there could be serious harm to unborn children or children who are breast-feeding. It is also possible that harmful side effects that are not yet known could happen to both the mother and unborn or breast-feeding child. If you are currently pregnant, it is important that you inform the investigator because you will not be able participate in the study. If you are able to become pregnant, you will be given a urine pregnancy test before entry into the study. You are asked to use a medically accepted method of birth control (such as implants, injectables, combined oral contraceptives, diaphragm, condom, spermicidal foam or the combination of any of the above) while you participate in the study. You should not become pregnant while you are taking these drugs. If you do become pregnant, you must tell the investigator and consult an obstetrician or maternal-fetal specialist immediately.

Pregnancy tests will be done on all women who are able to get pregnant at the start of the study. This is part of the regular care for ANCA vasculitis, which means that you will have to pay for the pregnancy tests.

Risks of relapse

If we think that you are at risk for relapse, you will receive maintenance therapy. If we think you are in the "low-risk-of-relapse" group, you will be randomized to receive or not receive maintenance therapy. However, being in the "low-risk-of-relapse" group does not mean you will never have a relapse. It is possible that being placed into the group receiving no maintenance therapy will put you at risk for relapsing or for relapsing sooner than if you had received maintenance therapy. However, you will be monitored closely throughout the study period so that if you do have a relapse of disease, we will be able to treat it promptly.

Possible signs of relapse

Please call your study doctor or your treating doctor if you experience fever, severe joint pains, persistent nose bleeds, blood in the urine, coughing up blood or any other symptoms that you may find concerning.

Other Study Risks

Blood Draws and IV Therapy

The risks for blood drawing and insertion of an IV catheter are minimal and rare. They include:

• Minor discomfort, bleeding, and bruising at the site of the needle stick

• Feeling faint (like "passing out") during the blood draw or placing of the IV. If this occurs, the technician or nurse and other trained staff will be available to help you

• Infection, like redness, warmth, pain, swelling or foul-smelling discharge at the needle site

• Irritation or clotting of the vein (called superficial phlebitis) where the IV was can rarely occur with pain, redness, firmness at the needle site

• You may have some restriction of movement during the infusion time

Risks of Research Blood Samples

The risks of drawing blood include pain, bruising, lightheadedness, and/or fainting, or rarely, infection at the site of the needle stick. However, usually, the research blood tubes will be taken at the same time as the other tubes, requiring no extra stick.

There may be uncommon or previously unknown risks. You should report any problems to the researcher.

Live Virus Vaccinations

You should not receive ANY live virus vaccinations while in the study OR while receiving medications for maintaining suppression of your immune system. If for some reason you have received a live virus vaccine in the 4 weeks prior to, or after starting the study, administration of any maintenance immunosuppression medicines for your disease will be delayed by 4 weeks.

If you choose not to be in the study, what other treatment options do you have?

You do not have to be in this research study in order to receive treatment. Participants who receive treatment as part of the study will get the same treatment they would have if they were not part of the study. The only difference in being in the study is that we will use a new, unproven laboratory test to decide if you need maintenance therapy or not. Currently, there are no strict guidelines helping your kidney doctor to decide if you need maintenance therapy or not.

What if we learn about new findings or information during the study?

You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

Will I receive any clinical results?

You will see all your lab results in your MyChart. The results from the CD5+ B cells tests are not validated yet and there will be a warning label about that in our MyChart when that result is provided.

Will you receive results from research involving your specimens?"

Tests may be done on these samples by study-approved researchers. You will not be informed of any of the results of the research testing.

The use of your samples may result in commercial profit. You will not be compensated for the use of your samples other than what is described in this consent form.

How will information about you be protected?

Your personal information will be stored in a locked cabinet and in a secure password protected database.

You will not be identified in any report or publication about this study. Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed

by representatives of the University, research sponsors, or government agencies (for example, the FDA) for purposes such as quality control or safety.

We may use de-identified data and/or specimens from this study in future research without additional consent.

What is a Certificate of Confidentiality?
This research is covered by a Certificate of Confidentiality. With this Certificate, the researchers may not disclose or use information, documents or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings in the United States, for example, if there is a court subpoena, unless you have consented for this use.

The Certificate cannot be used to refuse a request for information from personnel of a federal or state agency that is sponsoring the study for auditing or evaluation purposes or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law, such as mandatory reporting requirements for child abuse or neglect, disabled adult abuse or neglect, communicable diseases, injuries caused by suspected criminal violence, cancer diagnosis or benign brain or central nervous system tumors or other mandatory reporting requirement under applicable law. The Certificate of Confidentiality will not be used if disclosure is for other scientific research, as allowed by federal regulations protecting research subjects or for any purpose you have consented to in this informed consent document.

You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

By signing this informed consent document, you agree that some of the information generated by participating in this study and/or a copy of the consent form may be included in your medical record and that this information may be viewed by other physicians or caregivers who provide healthcare services to you. This will allow the doctors caring for you to know what study medications or tests you may be receiving as part of the study and know how to take care of you if you have other health problems or needs during the study. Additionally, the information may be shared with your medical insurance plan if the research services provided are billed to your insurance.

What will happen if you are injured by this research?

All research involves a chance that something bad might happen to you. This may include the risk of personal injury. In spite of all safety measures, you might develop a reaction or injury from

being in this study. If such problems occur, the researchers will help you get medical care, but any costs for the medical care will be billed to you and/or your insurance company. The University of North Carolina at Chapel Hill has not set aside funds to pay you for any such reactions or injuries, or for the related medical care. You do not give up any of your legal rights by signing this form.

What if you want to stop before your part in the study is complete?

You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

If you would like to withdraw from this study, you can contact the study staff listed on page 1. However, any samples or data that already have been placed in the research databases cannot be withdrawn. We recommend that you first talk with your treating nephrologist before stopping maintenance therapy.

If you are in the maintenance group and decide to stop maintenance therapy, we would like to follow you and collect information and blood during the rest of the study. We would like to be allowed to access your medical records to collect data for the study until the end of the study.

We may ask you for research blood samples during your routine clinic visits if you are followed at UNC, and if your visit is more or less at the same time as one of the study timepoints: week 22, week 46, week 70 or week 94. Per visit, the maximum volume that would be draw for research is an extra 24 mL of blood (a little less than 2 tablespoons) along with your standard of care blood tests.

Will you receive anything for being in this study?

You will be receiving parking coupons for each study visit.

Will it cost you anything to be in this study?

You will not have to pay to be in this study. You or your insurance company will be billed for the cost of all routine care provided during appointments when study visits are conducted. This means you and your insurance company will be billed for the visits, the lab tests, the treatment drug, the infusion costs, the pregnancy test (if applicable). You will not be billed for any additional research related tests.

When we take extra tubes of blood for research, you will not be billed for those tests.

If your study visit is conducted in the research unit, you will not be billed for an office visit.

If you receive a bill that you think is wrong, contact a researcher or study coordinator.

Who is sponsoring this study?

This research is funded by the National Institutes of Health (NIH). This means that the research team is being paid by the NIH for doing the study. The researchers do not, however, have a direct financial interest with the NIH or in the results of the study.

What if you have questions about this study?

You have the right to ask, and have answered, any questions you may have about this research. If you have questions about the study (including payments), complaints, concerns, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.

A description of this clinical trial will be available on www.clinicaltrials.gov, 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 website at any time.

What if you have questions about your rights as a research participant?

All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

IRB Study # 18-2015

Title of Study: Tailoring Maintenance Therapy to CD5+ Regulatory B Cell Recovery in ANCA Vasculitis

Principal Investigator: Vimal K. Derebail

Participant's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

_____ _____

Signature of Research Participant Date Time

_____

Printed Name of Research Participant

_____ _____

Signature of Research Team Member Obtaining Consent Date Time

_____

Printed Name of Research Team Member Obtaining Consent