VAAAHS Research IRB
IRB NUMBER: IRB-2019-1156
IRB APPROVAL DATE: 11/12/2020

VA INFORMED CONSENT CHECKLIST

Complete this checklist for each consent obtained and file with the original informed consent document

RESEARCH STUDY IDENTIFICATION (Required information)
STUDY TITLE: **Induction of Senescence using Dexamethasone to Re-sensitize NSCLC to Anti-PD1 Therapy** PI: **Dr. Nithya Ramnath** NAME OF STUDY TEAM MEMBER OBTAINING CONSENT:_____ ROLE OF STUDY TEAM MEMBER OBTAINING CONSENT: _____

RESEARCH SUBJECT IDENTIFICATION: (Required information)

			| | |	/ /
Last Name	First Name	Mid. Init.	Last-4 SSN	Todays Date (mm/dd/yy)

A.	Date ALL required SIGNATURES (Subject, Witness (If required by IRB) and Person Obtaining Consent), their PRINTED NAMES and the DATES they signed the informed consent document (ICD) have been Checked and Verified Accurate and appear in the proper location
B.	DATE AND TIME (ICD) WAS REVIEWED AND DEEMED COMPLETE AND VALID **Must be prior to date/time of Subject's First Study Activity**
C.	DATE AND TIME OF THE SUBJECT'S FIRST STUDY ACTIVITY OR INVOLVEMENT
	Verify and Initial each requirement below.
1.	Informed consent and HIPAA Authorization, if required by VA-IRB was obtained from this subject prior to study participation.
2.	A VA Scope of Practice Form has been signed by the PI and approved by the VA IRB which designates me as an authorized agent of the PI and qualified to obtain consent for this study.
3.	This prospective subject was given adequate time necessary to carefully and fully read the Informed consent document (ICD) and all questions were answered to his/her satisfaction.
4.	All aspects of this subject's study involvement, including the purpose of the study, known and potential risks, possible benefits and alternatives to study participation were explained and discussed prior to subject signing the ICD.
5.	If required, a scanned image of the Research Enrollment Note, Consent Form and/or HIPAA Authorization will be entered into the subject's electronic medical record (CPRS).
6.	*Subject has been consented using the most recently approved, VA date-stamped version of the consent form (VA Form 10-1086) and HIPAA Authorization Form (VA Form 10-0493).*
7.	A copy of the completed and signed, original informed consent document has been issued to this subject and the subject was instructed to retain that copy for reference and to ask any and all questions that might arise throughout their study involvement.
8.	The subject has been shown where in the ICD to locate study team phone number(s) and the phone number of the VAAAHS IRB Coordinator. The subject has been reminded to call with any questions or concerns. Cathy Kaczmarek @ 734.845.3439
9.	The subject has been informed that participation is entirely voluntary and that they may withdraw their participation at any time and for any reason.
10.	Original ICDs and all copies are printed and issued as single-sided documents and that the original signed ICD must be kept in the investigator's project files on VA property.
11.	Upon completion of the Informed Consent Process, this subject's name was added to the Master List of All Subjects. [Per revised VHA Handbook 1200.05 (11/12/14) a MLS is no longer required, but a list of all enrolled participants is considered good research practice.]
12.	I know I can contact the VAAAHS IRB Coordinator at 734.845.3439 or the Research Compliance Officer at 734.845.4013 if I have questions or concerns regarding the consent of this or any individual considering study participation.

Department of Veterans Affairs Research Consent Form

Title of Study:	Induction of Senescence using Dexamethasone to Re-sensitize Non-Small Cell Lung Cancer (NSCLC) to Anti-PD1 Therapy	
Principal Investigator:	**Dr. Nithya Ramnath**	VAMC: **VA Ann Arbor Healthcare System**

Key Information

WHAT IS THE STUDY ABOUT AND WHY ARE WE DOING IT?

The purpose is to determine whether giving a 7 to13-day course of Dexamethasone (a steroid), should be usual care when we use immunotherapy to treat patients with non-small cell lung cancer (NSCLC). Right now, immunotherapy is given without any steroids – or given if patients' immune systems are too weak. We are trying to see if the dexamethasone will improve the body's immune system, , perhaps allowing future immunotherapy to work better. The study is being funded by the Department of Veterans Affairs.

WHAT DOES THE STUDY INVOLVE AND HOW LONG WILL IT LAST?

Your participation in this study may last up to 6 years.

CT scans will be completed as your physician would regularly order them - approximately every 3 months.

Additional research procedures will include:

- 2 FLT-PET scans at the University of Michigan to determine steroid uptake prior to giving immunotherapy
- Extra tubes of blood at time of routine blood draw to look at correlation of your blood samples, Dexamethasone uptake on FLT PET scans, and response to treatment.
- Short course of Dexamethasone (steroid) before your first three immunotherapy infusions.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

You may choose to volunteer to see if you will respond to immunotherapy again, or if your immunotherapy course will work better with the addition of Dexamethasone. It may help your body's immune system tolerate immunotherapy again to treat your lung cancer.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

This treatment may not help, and your disease could grow. There have been studies showing that the addition of dexamethasone with immunotherapy produced worse outcomes. Dexamethasone may weaken your immune system putting you at a higher risk for infections that could make you feel worse. An example is pneumonia.

You may want to try a different treatment to target your cancer, choose palliative, or comfort care.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you understand the risks and potential benefits and would like to volunteer. Your participation in this study is voluntary, and you will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS? The person in charge of the study is Dr. Nithya Ramnath of the VA Ann Arbor Healthcare System. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study please contact Brittany Pannecouk (study coordinator) at (734) 845-3966.

RESEARCH SUBJECT IDENTIFICATION: (Required information)

			| | |	/ /
Last Name	First Name	Mid. Init.	Last-4 SSN	Todays Date (mm/dd/yy)

Title of Study:	Induction of Senescence using Dexamethasone to Re-sensitize Non-Small Cell Lung Cancer (NSCLC) to Anti-PD1 Therapy	
Principal Investigator:	**Dr. Nithya Ramnath**	VAMC: **VA Ann Arbor Healthcare System**

RESEARCH DETAILS

WHAT IS THE PURPOSE OF THIS STUDY?
You are being asked to join a research study. As you read this form about the study, ask any questions you have. Feel free to take this document with you and talk the study over with your family, friends, and doctor before you decide. Being in the study is voluntary. You may decide not to join, and you may stop at any time. No matter what you decide to do, none of your VA benefits will be affected in any way. When all your questions are answered and if you decide to join the study, you will then be asked to sign this form to begin the study. By signing this form, it means you understand the study, risks, and you want to join the study. You will be given a copy of this consent form.

You are being asked to join this study because you have Non-Small Cell Lung Cancer (NSCLC). You are eligible because you have progressed on an FDA-approved therapy for lung cancer called immunotherapy. These therapies help your body's own immune system fight cancer. Some examples are: pembrolizumab (Keytruda), or nivolumab (Opdivo), durvalumab (Imfinzi). We are trying to find out if giving a strong steroid (dexamethasone) for 7-13 days and then stopping it (at least 72 hours before resuming immunotherapy) will jump start your immune system to respond to immunotherapy again, perhaps allowing the immunotherapy to work better. Our study is based on rigorous laboratory experiments where we have noted such an effect.

HOW LONG WILL I BE IN THE STUDY?
We plan to enroll up to 39 patients at the VA Ann Arbor Healthcare System. The study will last a total of 6 years: 1 year of treatment and 5 years of follow up, until withdrawal of consent or death. If you decide you no longer want to participate you may withdraw consent at any time.

WHAT WILL HAPPEN AND WHAT CAN I EXPECT IF I TAKE PART IN THIS STUDY?
During this study there will be a screening/baseline period to make sure you are able to be involved in the study. Once we know you are eligible you will begin the treatment phase. If you progress, or no longer want to be in the study, we will complete end-of-treatment tests. Once you have finished the end-of-treatment tests, we will follow your medical record for survival status. If you decide to withdraw consent, we will not contact you or look at your medical record any further, but we will keep the information already collected.

SCREENING / BASELINE: The following will happen within 28 days of enrolling into the study:

1. You will need to sign consent before any screening procedures.
2. The following information will be reviewed from your medical record collected during your routine standard of care visits:
    a. Review of your medical history, past treatments, medications, vitals, physical exam.
    b. Review of lab results from your routine blood draw.
    c. Review of a routine standard CT scan of the chest, abdomen, and pelvis.
    d. Review of a routine FDG-PET scan.
3. The following will be completed as research only:
    a. If you have tumor tissue left over from a previous biopsy (archival tissue), the study team will request a sample of the tissue to send for research testing. We will be looking at the genes in the tissue that control immune response.
    b. An FLT-PET scan will be completed at the University of Michigan with a research blood collection (approx. 6 teaspoons).

c. Begin steroid, Dexamethasone. How long you will take the steroid will depend on which group you are assigned to.
d. Undergo a second FLT-PET scan at the University of Michigan with another research blood sample collection (approx. 6 teaspoons) the same day you restart your immunotherapy infusion.

Treatment:
During the treatment phase you will be assigned to one of the below groups. Group assignment depends on how the subject before you tolerated the treatment. Each group will have different dexamethasone (steroid) tapers. This will happen before your 1st, 2nd, and 3rd infusions only. You will be given a drug diary, so you know when to start, stop, and how much steroid to take daily, depending on which group you are in.

Group 1: Dexamethasone 4mg twice a day for 7 days,
2mg twice a day for 2 days,
1mg twice a day for 1 day,
3 days off steroid,
Immunotherapy infusion

Group 2: Dexamethasone 4mg twice a day for 10 days,
2mg twice a day for 2 days,
1mg twice a day for 1 day,
3 days off steroid,
Immunotherapy infusion

Group 3: Dexamethasone 4mg twice a day for 13 days,
2mg twice a day for 2 days,
1mg twice a day for 1 day,
3 days off steroid,
Immunotherapy infusion

Research blood samples (approx. 6 teaspoons) will be taken at the same time as your routine labs before your 1st, 2nd, and 3rd infusions. These samples will have all our personal identifiers removed and a special code will be given to them. The samples will then be delivered to Karmanos Cancer Institute (Dr. Ratnam's laboratory) at Wayne State University to look and see if there are any markers that could cause activation of your cancer. We are sending your samples outside of the VA because they have a specific machine to be able to analyze your samples that we do not have here at the VA.

Your immunotherapy infusion will be given every 3 weeks (21 days) or every 4 weeks (28 days). The infusion runs over 30 minutes, but you can expect your appointment to be at least 1 hour to account for time to put in the IV for the infusion and to disconnect you after the infusion is done. These infusions can be given for up to 1 year.

As part of routine care the study team will do the following:
- Collect your clinical information from your medical record such as lab values, scan results, medications, adverse events, and any toxicities.
- You will have routine CT scans about every 12 weeks (3 months) to see how you are responding to treatment.

For the research portion study

- Your information will be given a unique study code and entered in VA Redcap. This is a password protected database behind the VA firewall.

End of Treatment / Follow Up

If you stop getting immunotherapy for any reason, you will then enter follow up. The study team will review your medical record or call you every 6 months for 5 years to see if you started any new treatments and check your survival status.

Risks of Immunotherapy (pembrolizumab, durvalumab, nivolumab): The pharmacist will discuss the risks with you and will give you an information sheet. Below are some side effects. This is routine clinical care and not research:

Most Common: at least 1 out of 10 people may experience the following

- Inflammation of organs (Hepatitis, pancreatitis, esophagitis, etc.)
- Rash
- Shortness of breath
- Chest Pain, pressure, or fast heartbeat
- Unexplained bruising or bleeding
- Change in eyesight
- Very bad joint and/or muscle pain
- Weakness
- Dizziness
- Fever or chills
- Flushing
- Excessive sweating
- Burning, numbness or tingling
- White patches on skin
- Loose Stools (diarrhea)
- Change in taste
- Not able to sleep

Least Common: at least 1 out of 100 people may experience the following

- Pyrexia
- Cough
- Increased liver enzymes
- Low red blood cell count (anemia)
- Increased creatinine
- Hypoglycemia
- Headache
- Neuropathy
- Weight loss
- Nausea
- Vomiting

Risks of Dexamethasone (Steroid) – This drug is given as research
Most Common: at least 1 out 10 people may experience the following

- Increased appetite
- Swelling of face, fingers, hands, feet, or lower legs
- Weight gain
- Agitation
- Anxiety
- Headache
- Nervousness
- Nausea
- Vomiting
- Abdominal Pain
- Diarrhea
- Acne
- Mood changes
- Increased thirst

Least Common: at least 1 out of 100 people may experience the following

- Signs of infection
- Bone/joint pain
- Irregular heartbeat
- Eye pain/pressure
- Heartburn
- Black stools
- Puffy face
- Swelling of ankles/feet
- Pain/redness/swelling of arms and legs
- Tiredness

Blood drawing
There may be some discomfort, bruising, or bleeding at the site where the blood is drawn. Rarely, fainting occurs because of drawing blood.

FLT-PET Scan
The research FLT PET exposes you to small amounts of radiation because of the radiotracer and scanner that is used. We do everything we can to make sure it is the least amount of radiation possible. You could also experience some claustrophobia because the scanner is small. The total radiation that is involved for both scans is 21.7 mSv which is equivalent to 7 years of natural background radiation that you are exposed to in your everyday life.

Confidentiality Risk
There is also a risk of a breach of confidentiality. VA Approved research staff assigned to this study will be looking at your medical record for data collection. The University of Michigan will be doing the PET scan and drawing extra blood, which could cause a breach. To protect your confidentiality, you will be given a unique code to link you to the research data collected from your medical record. Your personal information will be removed from the blood samples that are sent to Wayne State and will only be labeled with your unique code, date of draw and time of draw.

Women of Childbearing Potential
The safe use of immunotherapy in pregnant women and nursing mothers has not been established. Consequently, there may be risks to you (or to your embryo or fetus) if you are or may become pregnant that are unknown. Women of childbearing potential enrolling in this study must (i) have been using a birth control measure (an intrauterine device (IUD), birth control pills, a condom, diaphragm, or abstinence) for the previous three months, (ii) must have a negative pregnancy test, and (iii) must agree to continue to use a birth control measure for the duration of the study. If, while participating in the study, you suspect you have become pregnant, please contact the study physician immediately. Women are of childbearing potential unless they have been surgically sterilized (for example tubal ligation or hysterectomy) or are post-menopausal, that is, no menstrual period for more than 6 months. Nursing mothers may not participate in this study.

WHAT ARE THE POSSIBLE BENEFITS OF THIS STUDY?
We do not know if you will get any benefits from taking part in this research study. However, there is a possible benefit of you re-responding to immunotherapy to treat your cancer.

The information we get from this study might help others with your same condition if we see subjects re-respond to immunotherapy treatments with the addition of the steroids.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT WANT TO JOIN THIS STUDY?
You may choose not to participate in this study. If this is your decision, depending on the extent of your disease there may be other cancer treatments available that you haven't tried yet. You may also choose to be seen by palliative care, or choose hospice help as well.

You may discuss these options with your doctor.

HOW WILL MY PRIVATE INFORMATION BE PROTECTED?
Your personal information will be removed from the data we collect from your medical record and blood samples. You will be assigned a unique code to link you to your samples and research record. Only the research staff will know this link. This information will be kept on a secure drive located on the VA server. We will enter your coded data into a database that is password protected, behind the VA firewall. Your information and samples collected as part of the research, will not be used or distributed for future research studies.

We will include information about your study participation in your medical record.

While this study is being conducted, you will not have access to your research related health records.

This will not affect your VA healthcare including your doctor's ability to see your records as part of your normal care and will not affect your right to have access to the research records after the study is completed.

If results of this study are reported in medical journals or at meetings, you will not be identified by name, by recognizable photograph, or by any other means without your specific consent.
No information by which you can be identified will be released or published unless required by law.

We will let you and your physician know of any important discoveries made during this study which may affect you, your condition, or your willingness to participate in this study.

Federal Oversight agencies and offices may have access to your records.

Health Information Portability and Accountability Act (HIPAA)

There are rules to protect your private health information. Federal and state laws and the federal medical law, known as the HIPAA Privacy Rule, also protect your privacy. By signing this form, you provide your permission called your 'authorization,' for the use and disclosure of information protected by the HIPAA Privacy Rule.

Dr. Ramnath (Principal Investigator) and her Study Team study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records such as medical history, past treatments, lab results, scan results. Your unique study code and medical information will be shared with Wayne State, but no personal identifiers will be shared with them. The university of Michigan will be given personal information, so they can arrange for the PET scan to be done.

The research team may also need to disclose your health information and the information it collects to others as part of the study progress. Others may include the VA Clinical Science Research & Development (CSR&D); the VA Clinical Science Research & Development Data Monitoring Committee (DMC); Institutional Review Board and local Research & Development Committee, Office of Human Research Protections (OHRP), the VA Office of Research Oversight (ORO). This study is being funded by a VA merit grant.

Your health information disclosed pursuant to this authorization may no longer be protected by Federal laws or regulations and may be subject to re-disclosure by the recipient.

You can revoke this authorization, in writing, at any time. To revoke your authorization, you must write to the Principal Investigator of this study or you can ask a member of the research team to give you a form to revoke the authorization. Your request will be valid when the Principal Investigator receives it. If you revoke this authorization, you will not be able to continue to participate in the study. This will not affect your rights as a VHA patient to treatment or benefit outside of the study. If you revoke this authorization, Dr. Nithya Ramnath and her research team can continue to use information about you that was collected before receipt of the revocation. The research team will not collect information about you after you revoke the authorization.

Treatment, payment or enrollment/eligibility for benefits cannot be conditioned on you signing this authorization. This authorization will expire at the end of the research study unless revoked prior to that time.

WHAT ARE THE COSTS TO ME IF I TAKE PART IN THIS STUDY?
You will not be charged for any treatments or procedures that are part of this study. If you usually pay co-payments for VA care and medications, you will still pay these co-payments for VA care and medications that are not part of this study.

WILL I BE REIMBURSED FOR MY PARTICIPATION?
You will be given $25 each time you go to the University of Michigan for the FLT-PET Scan, or $50 total for the two scans needed for the study. This is to help offset the cost of parking and to help with meals or gas. This payment will be given in the form of a check or electronic transfer of funds (EFT) directly into your account that is set up with the VA if you have one – you can tell us which payment method you prefer.

WHAT WILL HAPPEN IF I AM INJURED BECAUSE OF MY BEING IN THE STUDY?
If you become injured because of the study, the VA will provide treatment for research related injury in accordance with applicable federal regulations (38 CFR 17.85). However, there will be no compensation should you be injured while on study.

If you should have a medical concern or get hurt or sick because of taking part in this study, call:

DURING THE DAY:

Ms. Brittany Pannecouk at (734) 845-3966 and

AFTER HOURS:

Call the VA Operator at (734) 769-7100 or (800) 361-7387 and ask then to page the on-call Hematology/Oncology doctor.

Emergency and ongoing medical treatment will be provided as needed.

DO I HAVE TO TAKE PART IN THE STUDY?
Study participation is voluntary. If you do not want to take part in the study, there will be no penalty or loss of benefits that you are entitled to. You may withdraw at any time and still receive the same routine care that you would otherwise have received.

Data already collected prior to the withdrawal, will be reviewed for the study but we will not collect further information, except from public records, such as survival data. Specimens already collected cannot be withdrawn.

RIGHT OF INVESTIGATOR TO TERMINATE MY PARTICIPATION
The investigator may take you off study if you are not tolerating the treatment, have progressed, or feel it is no longer in your best interest. If you do come off study for any of those reasons, we would like to follow your medical record for new treatments and survival status.

WHO DO I CONTACT ABOUT THIS STUDY IF I HAVE QUESTIONS?

Title of Study:	Induction of Senescence using Dexamethasone to Re-sensitize Non-Small Cell Lung Cancer (NSCLC) to Anti-PD1 Therapy	
Principal Investigator:	**Dr. Nithya Ramnath**	VAMC: **VA Ann Arbor Healthcare System**

If you have any questions, complaints, or concerns about the research or related matters you may contact any of the below individuals
Dr. Ramnath, Principal Investigator, (734) 845-5800
Brittany Pannecouk, Study Coordinator, (734) 845-3966
Dr. Kemp Cease Co-Investigator (734) 845-5800
Dr. Paul Swiecicki Co-Investigator (734) 845-5800
If you have questions about your rights as a study participant, or you want to make sure this is a valid VA study, you may contact the Institutional Review Board (IRB). This is the Board that is responsible for overseeing the safety of human participants in this study. You may call the IRB Coordinators at (734) 845-3440 if you have questions, complaints or concerns about the study or if you would like to obtain information or offer input.

WILL I BE TOLD NEW INFORMATION ABOUT THIS STUDY?
You will be notified of any new findings developed during the research study that may affect your willingness to continue participation.

Any clinically relevant research results will be disclosed to you by study staff either over the phone or at your next clinic visit.

AGREEMENT TO PARTICIPATE IN THE RESEARCH STUDY

Dr./Mr./Ms._____ has explained the research study to me. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me. I have been given the chance to ask questions and obtain answers.

By signing this document below, I voluntarily consent to participate in this and authorize the use and disclosure of my health information for this study. I also confirm that I have read this consent, or it has been read to me. I will receive a copy of this consent after I sign it.

I agree to participate in this research study as has been explained in this document.		
_____ Participant's Name (Print)	_____ Participant's Signature	_____ Today's Date

Person Obtaining Informed Consent		
_____ Name (Print)	_____ Signature	_____ Today's Date