Cover page of Informed Consent for Study

M16-298 Date: 23 October 2018

Title of Study	A Randomized, Double-Blind, Placebo-Controlled Phase 3 Study of Rovalpituzumab Tesirine as Maintenance Therapy Following First-Line Platinum-Based Chemotherapy in Subjects with Extensive Stage Small Cell Lung Cancer (MERU)
Protocol Number	M16-298
Clinicaltrials.gov	NCT03033511
Study Sponsor	AbbVie Phone: (800) 633-9110 Email: abbvieclinicaltrials@abbvie.com

Department of Veterans Affairs

RESEARCH CONSENT FORM

Title of Study: A Randomized, Double-Blind, Placebo-Controlled Phase 3 Study of Rovalpituzumab Tesirine as Maintenance Therapy Following First-Line Platinum-Based Chemotherapy in Subjects with Extensive Stage Small Cell Lung Cancer (MERU)
Title of Consent (if different from Study Title):
Principal Investigator: [redacted]

Are you participating in any other research studies? _____ yes _____no

PURPOSE OF RESEARCH

You are invited to participate in a research study of an investigational drug called Rovalpituzumab Tesirine (Rova-T) in subjects with Small Cell Lung Cancer (SCLC). An investigational drug is one that has not been approved by the regulatory authorities in your country. The purpose of this study is to: learn if the drug called rovalpituzumab tesirine taken after platinum-based chemotherapy will prolong the time your cancer is not getting worse; evaluate the safety and tolerability of rovalpituzumab tesirine; and understand why some subjects respond or experience side effects while others do not, despite receiving the same treatment.

Rovalpituzumab tesirine is a type of drug called an antibody drug conjugate or ADC. ADCs usually have 2 parts: a part that targets tumor cells (the antibody) and a cell-killing part (the toxin). Antibodies are proteins that are part of your immune system. They can stick to and attack specific targets on cells.

If you decide to be in the study, you will be randomly assigned (like flipping a coin) to one of two groups. You will either receive rovalpituzumab tesirine and dexamethasone, or you will receive placebos (a placebo is a dummy medication that looks like the real medication but has no active ingredients). Neither you nor your study doctor will be able to pick if you receive rovalpituzumab tesirine and dexamethasone, or if you receive the placebos. You will have an equal chance of being in either study group. This is a double-blinded study, which means neither you nor your study doctor will know to which study group you were assigned. In case of an emergency, your study doctor can find out this information.

This research study is looking for approximately [redacted] people with small cell lung cancer (SCLC) at approximately [redacted] research centers worldwide. The [redacted] expects to enroll up to [redacted] research study subjects. If the target number of subjects has been enrolled, and you are in screening, there is a possibility that you will not be enrolled.

Department of Veterans Affairs

RESEARCH CONSENT FORM

Title of Study: A Randomized, Double-Blind, Placebo-Controlled Phase 3 Study of Rovalpituzumab Tesirine as Maintenance Therapy Following First-Line Platinum-Based Chemotherapy in Subjects with Extensive Stage Small Cell Lung Cancer (MERU)	
Title of Consent (if different from Study Title):	
Principal Investigator: [redacted]	VAMC: [redacted]

VOLUNTARY PARTICIPATION

Your participation in this study is entirely voluntary. Your decision not to participate will not have any negative effect on you or your medical care. You can decide to participate now, but withdraw your consent later and stop being in the study without any loss of benefits or medical care you are entitled to.

DURATION OF STUDY INVOLVEMENT

Your participation in this study will last until your disease worsens or you no longer tolerate rovalpituzumab tesirine and dexamethasone or placebo treatment and may last approximately 12 months and include 12 study visits to the [redacted]

PROCEDURES

Screening

In order to determine if you are eligible to participate in the study you will complete the screening procedures (activities, tests and evaluations) described in this form. Such tests and evaluations are completed during a 21 day screening period that takes place before participation in the main part of the study. Most of these procedures are the same or similar to those that are normally performed as part of your regular cancer care.

- Informed consent– You will be asked to sign this consent form document.
- Medical/Oncology History – (including questions regarding your health problems, list of prescribed and over the counter medications/supplements that you are taking, details of your lung cancer diagnosis and previous treatment and questions regarding tobacco and alcohol use).
- Physical Exam– Complete physical exam.
- Vital Signs (blood pressure, heart rate, and temperature), Weight, and Height
- ECG (a test which records the electrical activity of your heart)
- Blood and urine tests to monitor your health –
    - Routine blood tests (approximately 2 teaspoons or 10 mL of blood) to check your blood counts (numbers of each type of blood cell),

chemistries (elements and minerals in your blood), blood clotting, and how well your organs are functioning.
    - Routine urine tests
- Blood collection for biomarker and/or exploratory research- (approximately 2.5 teaspoons or 12 mL of blood)
- Pregnancy Test (only for females who are able to get pregnant)-(blood; approximately 1 teaspoon or 5 mL of blood)— For post-menopausal women 55 years old or younger, a serum pregnancy test including FSH levels (a hormone) will be collected at screening. If confirmed post-menopausal, no additional pregnancy testing is required.
- Review of any medications you are taking
- Performance status evaluation (what type of daily activities you can do).
- Computed tomography (CT) scan, Magnetic Resonance Imaging (MRI), (this must be performed within 28 days before the start of study drug administration).
- Patient Reported Outcomes (PRO)- Ask you to answer questions about your health, your quality of life, and how you feel.
- Submission of tumor material from a previous surgery or biopsy, or collection of tumor material from a biopsy.

Treatment

If you choose to participate, you will receive rovalpituzumab tesirine or placebo as an approximately 30 minute infusion on Day 1 of each cycle. Each cycle is 6 weeks and every third cycle; you will not have any treatment. Dexamethasone or placebo will be taken twice a day orally (by mouth), and dosing should occur such that there are approximately 12-hours (i.e., 10 – 14 hours) between AM and PM doses on the day before you receive your infusion, the day of your infusion, and the day after your infusion. If the dose of dexamethasone or placebo is vomited within 15 minutes of taking the medication, the subject should retake the medication.

You will have a clinic visit on Days 1 and 22 of each treatment cycle and will be contacted by telephone by someone at the clinic on Days 8, 15, 29, and 36 of each cycle. You will also have a clinic visit on Day 1 of the non-treatment cycle and will be contacted by someone at the clinic on Days 8, 15, 22, 29, and 36 of the non-treatment cycle.

Your doctor will monitor the effect the study drugs have on your cancer.

After every 6 weeks of study treatment your tumor(s) will be measured to see if it (they) has become smaller, stayed the same or has grown (progressed). If your disease has not progressed and you are not experiencing side effects that in the opinion of your study doctor require stopping treatment, you may continue to receive treatment.

If you discontinue rovalpituzumab tesirine and dexamethasone or the placebos before your disease worsens, you will remain in the study and have Post-Treatment Follow Up (PTFU) visits every 6 weeks until your disease worsens. If your disease worsens, you will no longer have clinic visits, but someone from the clinic will contact you every 6 weeks to see how you are doing and if you have started any new anti-cancer treatments. Your study doctor can discuss additional anti-cancer treatment options with you.

If you are eligible to participate in this study, you will undergo one or more of the study procedures described below at each study visit. Some of these procedures may no longer be necessary. Your doctor will let you know if you are not required to do a procedure.

A table listing the Study Visits and Procedures appears later in the document. Please note that you may be asked to repeat a procedure or test and/or have additional procedures if your study doctor feels it is needed to evaluate your condition. Your doctor may ask you to come in early for some procedures because of scheduling or because of how your body is responding to the drug.

- Blood collection for biomarker and/or exploratory research
- Blood and urine tests to monitor your health:
  - Routine blood tests (approximately 2 teaspoons or 10 mL of blood) to check your blood counts (numbers of each type of blood cell), chemistries (elements and minerals in your blood), blood clotting, and how well your organs are functioning.
  - Routine urine tests
- CT Scan: A CT scan uses radiation (x-rays) to make pictures of the inside of your body. The scan can show more details or even larger areas to show organs and structures in 3 dimensions (“3-D”).

  - The study doctor or study staff may give you a contrast dye, either by mouth or with a needle. The study doctor or study staff can tell you more about contrast dye.
- Echocardiogram: An echocardiogram uses sound waves to make pictures of your heart, which helps show how well your heart pumps blood. It is very similar to the ultrasound procedure that many pregnant women take. You will be asked to lie on your left side while a technician places a wand (probe) with a cool gel on your chest.
- Electrocardiogram: An electrocardiogram (ECG) measures the electrical activity of your heart
- MRI of brain (only required after screening if you have active disease in your brain): For the MRI, part of the body will be passed into a long, narrow tube scanner, which is open at both ends. An MRI uses powerful magnets and radio waves to make pictures of body tissues and structure.
  - The study doctor or study staff may give you a contrast dye, either by mouth or with a needle. The study doctor or study staff can tell you more about contrast dye.
- Performance status: Your doctor will assess and assign a score based on your ability to perform daily tasks by asking questions.
- Pharmacogenetic (PGt): PGt testing uses blood tests to look at how someone's genes may influence if and how well the study drug may affect the disease.
- Pharmacokinetic (PK): PK testing uses blood tests to measure the amount of study drug in the body at different time points.
- Physical Exam: You should ask the study doctor or study staff about what will happen during this exam
- Pregnancy Testing: Test your blood or urine to see if you are pregnant. You will only have pregnancy testing if you are a woman and can have children.
  - The study doctor or study staff will tell you if the pregnancy test results are positive.
  - The results of the pregnancy testing must be negative in order for you to be in the study.
- Patient Reported Outcomes (PRO): Ask you to answer questions about your health, your quality of life, and how you feel.

- Health Resource Utilization: Asks you questions about your use of healthcare resources and services. For example, if you have made any visits to other doctors or hospitals.
- Study Drug: You will be given an infusion of rovalpituzumab tesirine or placebo at the study center.
    - We will give you a supply of dexamethasone or placebo and tell you how to take it.
    - We will ask you to bring back all unused dexamethasone or placebo to each visit.
- Vital Signs - Check your blood pressure by putting a band around your arm (this will squeeze your arm for about a minute), count the number of heartbeats over time, and take your temperature
- Study Diary: We will give you a study diary to record your dexamethasone or placebo dosing and daily weight. You will be instructed you how to use it and ask you to bring the completed diary back to the study center at each visit.
- Fluid Retention Questionnaire (included in the study diary): You will be asked to keep a daily weight dairy. On Days 8, 15, 29, and 36 someone from the clinic will contact you by telephone to review your diary and questionnaire. On Day 22, you will bring the questionnaire with you to your clinic visit.
- Survival Status: After your disease worsens, you will no longer have clinic visits for the study. Someone from the clinic will contact you every 6 weeks to see how you are doing and if you have started any new anti-cancer treatments.
- At every study visit, you will be asked about:
    - Any changes to the medications you are taking;
    - Any side effects you are experiencing, which may or may not be related to the study.
- Potential for Photographs: One aspect of this study involves possibly taking photographs of your skin if you develop any skin reactions while participating in the study. Your study doctor will keep the photographs in your medical chart/patient record until your participation in the study is finished, and they may be sent to the sponsor, AbbVie Inc. for later review of the reaction. Only your affected skin area will be photographed. The study doctor and the research team will take measures to protect your identity when sharing photographs of skin reactions with the sponsor.

These measures include taking the photograph very close to the affected skin region to exclude facial features, or if facial features cannot be excluded due to the location of the skin reaction, covering identifying features (such as your eyes) with a black rectangle.

Tumor Tissue Collection and Testing Consent

If you are interested in participating in the research study and sign this consent form, you agree to provide archived or fresh tumor samples for testing to see how much Delta-like protein (DLL3) your tumor has and for on-going development of biomarker-related tests and research pertaining to Rovalpituzumab Tesirine and Small Cell Lung Cancer.

These tests and procedures may be performed before the rest of the study tests and procedures so that the test results are available if you elect to enroll in the research study.

Your tumor sample will be tested at a different laboratory than your doctor's facility. Your tumor does not have to have high levels of DLL3, but knowing your DLL3 status is important if you decide to participate in the main research study.

If archived tumor material is available from a previous biopsy that you have had, we can use these samples for the tests. If not, you will be asked to have a biopsy so we can obtain the samples.

Regardless of the test results, AbbVie will keep a portion of your sample for on-going development of biomarker-related tests and research pertaining to Rova-T and Small Cell Lung Cancer. Biomarker research can help to improve our understanding of how individuals respond to drugs and our ability to predict, detect, and monitor diseases and their progression. Your samples may be used to study genetic material (instructions for cells to work that is in the form of DNA and RNA), proteins or parts of proteins (a part of all cells), and/or other molecules of cell metabolism (e.g. sugars) and fats.

The purpose of this tumor tissue collection and testing research is:

- To find out why some patients with the disease being studied respond better or worse to the study drug or drugs of the same or similar class

- To possibly find out how the disease being studied and related conditions develop and progress and how they can be diagnosed, monitored, or treated
- To possibly develop tests to identify which patients are likely to have specific diseases, respond to the study drug or drugs of the same or similar class, or to predict the progression of the disease being studied
- To possibly develop new therapies, research methods or technologies

AbbVie (or people or companies hired by AbbVie) will store the samples in a secure storage space with adequate measures to protect confidentiality. While the research continues, the samples will be stored for up to, but no longer than 20 years from the end of the research study and then destroyed. Each sample will be assigned a code and no personally identifiable information about you will be stored with the sample.

Collection and Testing Procedures

If you agree to participate in the research study, the following procedures/tests will be performed. These procedures will be required before you can participate in the main study.

- Submission of tumor material from a previous surgery or biopsy. You had surgery or biopsy in past and tissue was saved. This saved tissue will be sent to a laboratory and analyzed

OR

- Collection of tumor material from a biopsy. After the biopsy is over, a sample of your tumor material (saved from your biopsy) will be sent to a laboratory and analyzed.

Analysis of the tumor material will look for DLL3 status at a central laboratory chosen by AbbVie or their designee.

If you want the rest of your tumor material sample to be returned after the portion needed for DLL3 testing and ongoing research described above has been collected, please inform your study doctor.

Optional Research Samples

You may volunteer to participate in optional research that is separate from the main study. You do not have to participate in any of the optional research if you don't want to. You may still participate in the main study if you decide to not participate in the optional research. There is no penalty or loss of benefits if you don't want to participate, and your decision won't affect your regular medical care.

- Optional Tumor Material at Time of Progression Biopsy for Exploratory Research- If you choose to participate in this optional assessment, a tissue sample from your tumor will be taken by biopsy at the time of progression. The tissue sample will be used in order to do tests. This will involve the collection of 2 cores of tissue from your tumor for this study.

_____ Yes. I volunteer to provide my material sample(s) for the optional research described in this consent form.

_____ I **DO NOT** volunteer to provide my material sample(s) for the optional research described in this consent form.

Title of Study: A Randomized, Double-Blind, Placebo-Controlled Phase 3 Study of Rovalpituzumab Tesirine as Maintenance Therapy Following First-Line Platinum-Based Chemotherapy in Subjects with Extensive Stage Small Cell Lung Cancer (MERU)

Title of Consent (if different from Study Title):

Principal Investigator: [redacted]

Study Activities Table

Category	Procedures	Screening	Treatment (Each Cycle)								Non-Treatment Cycle Visit		End of Treatment	PTFU	Survival FU
		Day –21 to Day –1	Day –1	Day 1	Day 2	Day 8	Day 15	Day 22	Day 29	Day 36	Day 1	Weekly (Day 8, 15, 22, 29, 36)	within 7 days of decision to discontinue treatment	q6 weeks	q6 weeks
Location	Clinic Visit	X		X				X			X		X	X	
	Phone Contact					X	X		X	X		X			X
Safety Assessments	Informed Consent	X													
	Medical and Surgical History	X													
	Physical examination	X		X				X			X		X		
	Vital Signs	X		X				X			X		X		
	Routine Blood Tests (up to 10mL or 2 tsp)	X		X				X			X		X		
	Urine	X		X				X			X		X		
	Pregnancy Test^	X 5mL or 1 tsp of blood		X urine							X urine		X urine	X urine	
	Electrocardiogram (ECG)	X		X									X		
	Echocardiogram			X									X		
	Performance Status	X		X							X		X		
	Fluid Retention Questionnaire (including daily weight diary)			X		X	X	X	X	X	X	X	X		

Department of Veterans Affairs

RESEARCH CONSENT FORM

Title of Study: A Randomized, Double-Blind, Placebo-Controlled Phase 3 Study of Rovalpituzumab Tesirine as Maintenance Therapy Following First-Line Platinum-Based Chemotherapy in Subjects with Extensive Stage Small Cell Lung Cancer (MERU)
Title of Consent (if different from Study Title):
Principal Investigator: [redacted]

Category	Procedures	Screening	Treatment (Each Cycle)								Non-Treatment Cycle Visit		End of Treatment	PTFU	Survival FU
		Day –21 to Day –1	Day –1	Day 1	Day 2	Day 8	Day 15	Day 22	Day 29	Day 36	Day 1	Weekly (Day 8, 15, 22, 29, 36)	within 7 days of decision to discontinue treatment	q6 weeks	q6 weeks
	SAE/Adverse Events	SAE		X		X	X	X	X	X	X	X	X	X	X
	Concomitant Medications			X		X	X	X	X	X	X	X	X	X	X
Treatment	Rovalpituzumab tesirine or Placebo Infusion			X											
	Dexamethasone or Placebo (orally twice daily approximately 12 hours apart)		X	X	X										
Response Assessment	Disease/Response Assessment (CT Imaging)	X		X							X		X	X	
	MRI/CT of the Brain (may be repeated if doctor feels necessary)	X													
	Patient Reported Outcome (PRO)	X		X (only C2D1)							X (1st NTC)		X	X	
	Heath Resource Utilization			X				X			X		X	X	
	Survival Status														X

Category	Procedures	Screening	Treatment (Each Cycle)								Non-Treatment Cycle Visit		End of Treatment	PTFU	Survival FU
		Day –21 to Day –1	Day –1	Day 1	Day 2	Day 8	Day 15	Day 22	Day 29	Day 36	Day 1	Weekly (Day 8, 15, 22, 29, 36)	within 7 days of decision to discontinue treatment	q6 weeks	q6 weeks
Pharmacokinetic (PK), Biomarkers, and Pharmacogenetic (PG)	Pharmacokinetics (PK) (6 mL or 1.2 tsp of blood)			X pre-infusion and post-infusion							X		X		
	Tumor Material at Screening (Archived or Fresh)	X													
	Optional Tumor Material at Time of Disease Progression												X	X*	
	Blood for Inflammatory Markers (6 mL or 1.2 tsp of blood)	X		X pre-infusion									X	X*	
	Blood for Tumor & Soluble Markers (6 mL or 1.2 tsp of blood)	X		X pre-infusion									X	X*	
	Circulating Tumor Cells (8 mL or 1.6 tsp of blood)			X C1only pre-infusion									X		
	Pharmacogenetics (4mL or 1 tsp of blood)			X C1only pre-infusion									X		

Title of Study: A Randomized, Double-Blind, Placebo-Controlled Phase 3 Study of Rovalpituzumab Tesirine as Maintenance Therapy Following First-Line Platinum-Based Chemotherapy in Subjects with Extensive Stage Small Cell Lung Cancer (MERU)

Title of Consent (if different from Study Title):

Principal Investigator: [redacted]

Category	Procedures	Screening	Treatment (Each Cycle)								Non-Treatment Cycle Visit		End of Treatment	PTFU	Survival FU
		Day –21 to Day –1	Day –1	Day 1	Day 2	Day 8	Day 15	Day 22	Day 29	Day 36	Day 1	Weekly (Day 8, 15, 22, 29, 36)	within 7 days of decision to discontinue treatment	q6 weeks	q6 weeks
	Serosal Fluid* (if available)			Cycle 1 Day 1 through 70 days after last blinded study treatment											

^For post-menopausal women 55 years old or younger, a serum pregnancy test including Follicle-stimulating hormone (FSH) levels will be collected at screening. If confirmed post-menopausal at screening, no additional pregnancy testing is required. For women of child-bearing potential, urine pregnancy tests will be performed at Day 1 of each cycle, End of Treatment Visit, and PTFU until 6 months after the last dose of blinded investigational product.
*These samples may not be performed. Your doctor will let you know.

Table Abbreviations:
NTC=Non-Treatment Cycle; PTFU=Post-Treatment Follow up; q=every; SAE=Serious Adverse Events; C=cycle

Tissue Banking for Future Research

Biomarker and exploratory research can help to improve our understanding of how individuals respond to drugs and our ability to predict, detect, and monitor diseases and their progression. If you agree to participate, tumor material from a previous biopsy procedure used to diagnose your cancer or a fresh biopsy you consent for will be collected. Biomarkers are tests used to determine who may respond to drug, your body's possible response to treatment or to help explain how to improve the treatment of cancer. Blood and urine will also be collected for biomarker analysis. If required as part of your standard medical care, serosal fluid (fluid from body cavities, including the fluid surrounding the heart or lungs) may also be collected for research purposes. Your samples may be used to study biomarkers that are genetic material (instructions for cells to work that is in the form of DNA and RNA), proteins or parts of proteins (a part of all cells), and/or other molecules of cell metabolism (e.g. sugars) and fats.

The purpose of this research is:

- To find out why some patients with the disease being studied respond better or worse to the study drug or drugs of the same or similar class;
- To possibly develop tests to identify which patients are likely to respond to the study drug or drugs of the same or similar class, or to predict the progression of the disease being studied;
- To possibly develop new therapies, research methods or technologies.

AbbVie (or people or companies working with AbbVie) will store your samples at a designated laboratory with adequate measures to protect confidentiality which may be located outside of your country. The samples and data may be analyzed and used by AbbVie or people or companies working with AbbVie while research continues. Samples will be stored for up to, but no longer than, 20 years from the end of the main study. AbbVie will not use your samples or data generated from those samples for any purpose other than what is described in this form. Your samples will not be sold to other people or companies.

The research we conduct with your samples being done for research purposes only and we will not tell you or your doctor about the results of the research.

The research we conduct using your samples may result in inventions or discoveries that could be used to make new products or diagnostic or therapeutic

agents. These inventions and discoveries may become financially valuable. You will not receive any money or other benefits from any commercial or other products that are made using your specimens.

The main study risks are detailed in the main consent form and every precaution will be taken to secure participants' personal information by assigning a unique code to your sample that is collected. Potential risks may include breach of confidentiality, which may lead to discrimination in the areas of employment, insurability, social stigmatization, or psychological stress caused by disclosure of adverse information to the subject or the subject's family:

We will protect the confidentiality of your samples and information about you. Your samples will be stored in a locked area and all information about you will be stored in a locked file cabinet or on a password protected secure computer.

PARTICIPANT RESPONSIBILITIES

As a participant, your responsibilities include:

- Follow the instructions of the investigators and study staff.
- Take the study drug as instructed.
- Keep your study appointments. If it is necessary to miss an appointment, please contact the investigators or research study staff to reschedule as soon as you know you will miss the appointment.
- Tell the investigators or research study staff about any side effects, doctor visits, or hospitalizations that you may have.
- Tell the study doctor if you have any changes in medications during the study, or if you are planning to change any medications during the study.
- Do not change any of your medications or start any new medications without checking with your study doctor
- Tell the investigators or research staff if you believe you might be pregnant or gotten your partner pregnant.
- Keep the study drug in a safe place, away from children and for your use only.
- Refrain from participation in other research studies while you are subject in this study.

- Fill out your dosing sheet, questionnaires and diary completely and honestly and bring it to the study doctor's office at each visit.
- Complete the subject diary as instructed and bring with you to each clinic visit.
- Do not share your study drug with anyone. You are the only person allowed to take the study drug.
- Keep the study drug and study supplies out of the reach of children and persons of limited ability to read or understand.
- Ask questions as you think of them.
- Tell the investigators or research staff if you change your mind about staying in the study.

WITHDRAWAL FROM STUDY

If you first agree to participate and then you change your mind, you are **free to withdraw** your consent and stop your participation at any time. If you decide to withdraw from the study, you will not lose any benefits to which you would otherwise be entitled and your decision will not affect your ability to receive medical care for your condition.

If you want to stop being in the study you should tell the investigators or study staff. You can do this by phone by calling the principal investigator, [redacted], or by calling the study coordinator at [redacted]

You may withdraw from the main study and optional research at any time and may request that your samples be withdrawn at any time by notifying the study doctor in writing. There will be no consequences or penalties if you do this.

If you withdraw from the main study, your samples will continue to be stored and analyzed for exploratory research as described in this form unless you specifically withdraw from the optional research. Once AbbVie is notified that you have changed your mind about the optional research, no new research will be started, and your samples will be destroyed unless the FDA requires the sponsor to keep the samples. However, data and results that are generated from testing on your samples before the sponsor is notified will still be used.

The study may be stopped early by AbbVie, the investigator, the IRB or the FDA. You could be withdrawn from the study without your consent, at any time and for any reason. These include, but are not limited to, the following:

- Failure to follow the instructions of the investigators and/or study staff.
- The investigators decide that continuing your participation could be harmful to you.
- Pregnancy (if applicable).
- You need treatment not allowed in the study.
- The study is cancelled.
- Other administrative reasons.
- Unanticipated circumstances.

POSSIBLE RISKS, DISCOMFORTS, AND INCONVENIENCES

This study involves risks, discomforts, and possible inconveniences.

Rovalpituzumab Tesirine Discomforts and Risks:

You may experience certain side effects and discomforts from taking rovalpituzumab tesirine. You may have all, some, or none of the potential side effects. There is also a possibility that you may experience other rare or unknown side effects. Your doctors and nurses will check you closely for side effects, and may give you medicines or other treatments to stop or reduce some of these effects. Some side effects may go away soon after the study drug is stopped, but in some cases, side effects may be serious, long lasting, and/or permanent. There is even a chance that a side effect may cause death.

Rovalpituzumab tesirine has been tested in approximately 100 adult patients with cancer. The side effects listed below are those that have been observed and may or may not be related to rovalpituzumab tesirine. You may experience some of these side effects whether or not you are taking rovalpituzumab tesirine.

The following side effects have been observed in >10% of patients receiving rovalpituzumab tesirine:

- Fatigue (49%)
- Fluid buildup around the lung(s) (34%)

- Shortness of breath (31%)
- Swelling of the legs or other areas of the body (30%)
- Decreased Appetite (26%)
- Nausea (26%)
- Constipation (26%)
- Diarrhea (22%)
- Vomiting (22%)
- Low red blood cell count (18%)
- Low albumin blood level (18%)
- Low platelet blood count (17%)
- Joint pain (17%)
- Cough (16%)
- Rash (15%)
- Fever (15%)
- Photosensitivity – an increased sensitivity of skin (e.g. rash or other reaction) to sunlight exposure (13%)
- Abdominal pain (13%)
- Abnormal fluid buildup around the heart (13%)
- Superficial reddening of the skin (13%)
- Increased level of lipase (an enzyme found in the pancreas) in the blood (11%)

<u>Fluid around the lungs or heart, or in the abdomen, and swelling in the limbs:</u>
Some patients treated with rovalpituzumab tesirine have experienced a buildup or worsening of fluid surrounding the lungs, and heart or in the abdomen. Shortness of breath, fatigue, and swelling of the limbs were sometimes reported with the excess fluid. Tell your doctor immediately if you experience any of these symptoms. These side effects may interfere with your daily activities. The side effects may be life threatening, such as when too much fluid accumulates around your heart, preventing it from pumping blood effectively. You will be monitored throughout the study for these side effects. If any side effects develop, you may undergo procedures to drain the extra fluid and/or be prescribed corticosteroids or other drugs to try to reduce the fluid. In some serious cases, and if buildup of fluid is not medically treated through drainage procedures, steroids and other drugs, it may lead to death.

Skin Side Effects:
Some patients treated with rovalpituzumab tesirine have experienced rashes, typically associated with an increased sensitivity to the sun or ultraviolet light. This is called photosensitivity. You are instructed to wear sun protective clothes, sunscreen, and otherwise avoid direct sun exposure. Other skin reactions observed in patients include redness, swelling and pain of the palms of the hands and soles of the feet, or a rash consisting of target-shaped spots. If you notice any of these symptoms, tell your doctor. You will be monitored for this throughout the study and may be evaluated by a dermatologist if any of these symptoms appear.

Hematological Side Effects:
Some patients who have received rovalpituzumab tesirine have had decreases in platelets, red blood cells, and/or white blood cells, which may have consequences such as prolonged bleeding, feeling tired or weak, and being more sensitive to infections. The level of these blood cells will be checked regularly.

Inflammation of the lungs:
One patient treated with rovalpituzumab tesirine experienced progressive inflammation and thickening of the lungs, which led to death. Tell your doctor immediately if you experience a shortness of breath and difficulty breathing. You will be monitored for any clinical symptoms that may be consistent with inflammation of the lungs.

Liver Side Effects:
In rare cases, patients who have been treated with rovalpituzumab tesirine have reported elevations in certain enzymes (proteins) found in the blood which may reflect an injury to liver cells. Sometimes these elevations are associated with fatigue, weakness, abdominal pain, loss of appetite, yellowing of the skin, itching, abnormal bruising, fluid accumulation, or confusion. Your liver enzymes will be routinely monitored throughout the study, but it is important that you report any of these symptoms to your doctor as soon as you notice them.

Risks Associated with Dexamethasone:

The most common side effects (occurring in ≥ 10% of patients) reported in subjects treated with dexamethasone are listed below. Additional risks outlined in

your local label (if applicable) should also be discussed. Common events include but are not limited to:

- Nausea
- Muscle pain or weakness
- Fatigue
- Headache
- Swelling (edema)
- Confusion or mood changes
- High blood sugar (hyperglycemia)
- Stomach pain
- Weight gain
- Vision changes
- Sleep problems (insomnia)
- Skin changes (hair growth, acne, slow wound healing, rash)

Pregnancy, Breastfeeding and Birth Control:

If you are pregnant or currently breast feeding, you may not participate in this study. You understand that if you are pregnant, if you become pregnant, or if you are breast-feeding during this study, you or your child may be exposed to an unknown risk. To confirm to the extent medically possible that you are not pregnant, you agree to have a pregnancy test done before beginning this research study.

If you are female, you must not get pregnant while in this research study and for at least 6 months after the last dose of the drug. The only certain way to not get pregnant is to not have sex. If you are a male or female able to have children and choose to have sex, you must use effective birth control while in this research study from screening until at least 6 months after the end of the study. If you are male, you must agree not to donate sperm for at least 6 months after the last dose of drug.

Effective birth control for female patients includes (a) combined, estrogen and progestogen containing, hormonal contraception (oral, intravaginal, transdermal) associated with the inhibition of ovulation, initiated at least 1 month prior to Study Day 1 (randomization); (b) progestogen-only hormonal contraception (oral, injectable, implantable) associated with the inhibition of ovulation, initiated at

least 1 month prior to Study Day 1 (randomization); (c) intrauterine device; (d) intrauterine hormone-releasing system; (e) bilateral tubal occlusion; (f) vasectomized partner; and (g) sexual abstinence (refraining from heterosexual intercourse) only when this is in line with your preferred and usual lifestyle.

Male patients who are sexually active with females who are able to have children must use condoms (even if they are vasectomized) and his female partner (s) must use at least one of the birth control methods described in the above paragraph.

Even if you use birth control during the research study, there is a chance you could become pregnant. If you are pregnant or become pregnant during the research study, the study drug will be discontinued. The study drug or procedure may involve risks to the unborn baby, which are currently unforeseeable.

The study drug has not been studied in pregnant women, so its effects are unknown.

Because rovalpituzumab tesirine is investigational, all of its side effects may not be known. There have been additional toxicity seen in animal studies, such as kidney and liver toxicity. There may also be rare and unknown side effects, some of which may be irreversible and/or life threatening.

There are no well-controlled studies on dexamethasone use in pregnant women. Dexamethasone is only recommended during pregnancy when there are no alternatives and benefits outweigh the risk.

Please contact your study doctor if you become pregnant while taking dexamethasone.

It is not known whether dexamethasone is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants, you should not nurse a baby while taking dexamethasone.

If you think you are or your partner becomes pregnant during the study, you must tell the study doctor or study staff immediately. You are responsible for informing your partner(s) of the risk and for reporting any pregnancy to your study doctor.

If your partner becomes pregnant, information will be provided to the pregnant partner about known effects of study drug(s) on the unborn child and a Consent Form for Pregnant Partners will also be provided to request information about your partner's pregnancy and the health of the baby at birth.

Risks related to Study Procedures:

- Tumor Material Biopsy: Having biopsies performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site. Ask your doctor or study staff of other potential effects on the area being sampled.
- Blood Testing: Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.
- Echocardiogram: there are no special risks of this test, apart from some discomfort from laying in the correct position to get test results
- Electrocardiogram (ECG): Skin irritation is rare but could occur during an ECG from the electrodes or gel that is used. To do the ECG, you will have pads placed on different parts of your body. There is no pain or discomfort during an ECG; however, removing the pads may cause some irritation to your skin.
- MRI: For most people, there is no danger associated with having an MRI scan. However, an MRI could be very dangerous if you have certain objects or devices (usually metal) implanted in your body, such as a pacemaker, insulin pump, ear implant, joint replacement, permanent dentures, piercings, or shrapnel. You must tell the study doctor or study staff about any objects that you know are implanted or embedded in your body. Some people may feel claustrophobic, so tell the study staff if you are claustrophobic.
- Physical Exam: there are no special risks with an exam. It will be similar to examinations you have had in your doctor's office in the past.
- Pregnancy Testing: the risks are similar with any blood test

- Patient Reported Questionnaires (PRO): Filling out the questionnaires could lead you to feel uncomfortable or upset. Please tell the study doctor or study staff if you feel uncomfortable or upset while filling out a questionnaire. You have the right to refuse to answer any questions.
- Risks to DLL3 (Delta-like protein) testing: The test to determine your DLL3 status is new and is investigational use only at this time.

MRI (Magnetic Resonance Imaging)

MRI machines use a strong magnet and radiofrequency magnetic fields to make images of the body interior. The scanning procedure is very much like an X-ray or CT scan. You will be asked to lie on a long narrow couch for a certain amount of time (about an hour) while the machine gathers data. During this time you will not be exposed to x-rays, but rather a strong magnetic field and radiofrequency magnetic fields, which you will not feel. You will, however, hear repetitive tapping noises that arise from the Magnetic Resonance (MR) scanner. We will provide earplugs or headphones that you will be required to wear. The space within the large magnet in which you lie is somewhat confined, although we have taken many steps to relieve the "claustrophobic" feeling.

Magnetic fields do not cause harmful effects at the levels used in the MRI machine. However, the MR scanner uses a very strong magnet that will attract some metals and affect some electronic devices. If you have a cardiac pacemaker or any other biomedical device in or on your body, it is very important that you tell the operator/investigator immediately. As metallic objects may experience a strong attraction to the magnet, it is also very important that you notify the operator of any metal objects (especially surgical clips), devices, or implants that are in or on your body before entering the magnet room. All such objects must be removed (if possible) before entering the magnet room. In some cases, having those devices means you should not have an MRI scan performed. In addition, watches and credit cards should also be removed as these could be damaged. You will be provided a way to secure these items. If you have any history of head or eye injury involving metal fragments, if you have ever worked in a metal shop, or if you could be pregnant, you should notify the operator/investigator. You should also notify the operator/investigator if you have any tattoos on your body. Tattoos could become warm and irritated during the scan and remain so for several days.

If you would prefer not to participate in the MR scan due to the presence of tattoos on your body, please inform a research team member.

If you have had a previous reaction to Gadolinium-based contrast agents or a history of severe allergies, please notify the operator/investigator. If you have kidney problems, please tell the operator.

It has been observed that deposits of Gadolinium-based contrast agent (GBCA) remain in the brains of some people who undergo four or more contrast enhanced MRI scans, long after the last administration. It is not yet known whether these Gadolinium deposits are harmful or can lead to adverse health effects. You should talk to the study doctor if you have any questions about the use of GBCAs with MRIs.

IF YOU FEEL DISCOMFORT AT ANY TIME, NOTIFY THE OPERATOR AND YOU CAN DISCONTINUE THE EXAM AT ANY TIME.

POTENTIAL BENEFITS

You may or may not benefit from being in this study but your participation in this research study may benefit future patients with your disease or condition. Your condition may get better, it may get worse, or it may stay the same.

ALTERNATIVES

You do not have to participate in this study to get help for your condition. Alternatives to this study for the treatment of your condition may include drugs already approved or being used for treatment of your condition, surgery or other experimental drugs. Your study doctor can discuss the risks and advantages of these alternative treatment methods with you. In addition, you may discuss your options with your regular health care provider.

PARTICIPANT'S RIGHTS

You should not feel obligated to agree to participate. Your questions should be answered clearly and to your satisfaction.

You will be told of any important new information that is learned during the course of this research study, which might affect your condition or your willingness to continue participation in this study.

ClinicalTrials.gov

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

CONFIDENTIALITY

We will keep your name and all the information about you used in this study as confidential as possible. We may publish the results of this study for others to read about, but you will not be identified in any articles about the study by name, social security number, address, telephone number, or any other direct personal identifier. Also, other federal agencies as required, such as the VA Office of Research Oversight and the VA Office of the Inspector General may have access to your information.

Because this study involves an investigational drug, the Food and Drug Administration may also have access to information about you collected in this study.

FINANCIAL CONSIDERATIONS

Payment/Reimbursement

You will not be paid for taking part in this study.
The sponsor and people or companies working with the sponsor may use your biological samples when developing new tests, procedures and commercial products. If this happens, the sponsor does not plan to share any profits with you.

Costs

There will be no costs to you for any of the treatment or testing done as part of this research study. However, medical care and services provided by the VA that are not part of this study (e.g., normal hospital and prescription expenses which are not part of the research study) may require co-payments if your VA-eligibility category requires co-payment for VA services.

Sponsor

The sponsor for the research study is AbbVie. AbbVie is providing financial support and/or material for this study.

COMPENSATION for Research Related Injury

If you are injured as a direct result of being in this study, medical treatment will be available. If you are eligible for veteran's benefits, the cost of such treatment will be covered by the VA. If not, the cost of such treatments may still be covered by the VA depending on a number of factors. In most circumstances, the treatment must be provided in a VA medical facility. In addition, if you are injured directly from a properly performed study procedure, the sponsor of this study will pay for the costs of medical care. No other form of compensation for injuries is available. However, by signing this form you have not released the VA or the sponsor from liability for negligence. For further information, you may call the Human Protections Administrator at [redacted] or the V.A. Regional Counsel at ([redacted]

CONTACT INFORMATION

Questions, Concerns, or Complaints: If you have any questions, concerns or complaints about this research study, its procedures, risks and benefits, or alternative courses of treatment, you should ask the principal investigator, [redacted]. You should also contact her at any time if you feel you have been hurt by being a part of this study.

Independent Contact: If you are not satisfied with how this study is being conducted, or if you have any concerns, complaints, or general questions about the research or your rights as a participant, please contact the Stanford

Title of Study: A Randomized, Double-Blind, Placebo-Controlled Phase 3 Study of Rovalpituzumab Tesirine as Maintenance Therapy Following First-Line Platinum-Based Chemotherapy in Subjects with Extensive Stage Small Cell Lung Cancer (MERU)
Title of Consent (if different from Study Title):
Principal Investigator: [redacted] [redacted] [redacted]

Institutional Review Board (IRB) to speak to someone independent of the research team at [redacted] or toll free at [redacted] You can also write to the [redacted].

Appointment Contact: If you need to change your appointment, please contact the study coordinator at [redacted].

Alternate Contact: If you cannot reach the principal investigator, please contact the study coordinator at [redacted]

Title of Study: A Randomized, Double-Blind, Placebo-Controlled Phase 3 Study of Rovalpituzumab Tesirine as Maintenance Therapy Following First-Line Platinum-Based Chemotherapy in Subjects with Extensive Stage Small Cell Lung Cancer (MERU)
Title of Consent (if different from Study Title):
Principal Investigator: [redacted] [redacted]: [redacted]

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

As a research participant you have the following rights. These rights include but are not limited to the participant's right to:

- be informed of the nature and purpose of the experiment;
- be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
- be given a description of any attendant discomforts and risks reasonably to be expected;
- be given an explanation of any benefits to the subject reasonably to be expected, if applicable;
- be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;
- be informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should arise;
- be given an opportunity to ask questions concerning the experiment or the procedures involved;
- be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice;
- be given a copy of the signed and dated consent form; and
- be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

Department of Veterans Affairs

RESEARCH CONSENT FORM

Title of Study: A Randomized, Double-Blind, Placebo-Controlled Phase 3 Study of Rovalpituzumab Tesirine as Maintenance Therapy Following First-Line Platinum-Based Chemotherapy in Subjects with Extensive Stage Small Cell Lung Cancer (MERU)
Title of Consent (if different from Study Title):
Principal Investigator: [redacted] [redacted] [redacted]

Signing your name means you agree to be in this study and that you will receive a copy of this signed and dated consent form.

_____ _____
Signature of Participant Date

_____
Print Name of Participant

_____ _____
Signature of Legally Authorized Representative Date

_____
Print Name of Legally Authorized Representative

_____
Representative's Authority to Act for Subject

_____ _____
Signature of Person Obtaining Consent Date

_____
Print Name of Person Obtaining Consent

HIPAA regulations require the participant to give separate written permission (signature) for the use of their protected health information.

Person Obtaining Consent HIPAA Authorization confirmation:

☐ Confirm the participant signed the VA HIPAA Authorization (VA 10-0493)