MC1365 / 14-000428

A Randomized Phase II Trial of a Genetically Engineered NIS-Expressing Strain of Measles Virus Versus Investigator's Choice Chemotherapy for Patients With Platinum-Resistant Ovarian, Fallopian, or Peritoneal Cancer

NCT02364713

Document Date: 08/18/2022

MAYO CLINIC

Name and Clinic Number
Protocol #: MC1365 **Version #: non-bulky disease** **Version Date: 14Aug2020**

Approval Date: **August 18, 2022**
Not to be used after: **August 17, 2023**

RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: MC1365, Randomized Phase II Trial of a Genetically Engineered NIS-Expressing Strain of Measles Virus Versus Investigator's Choice Chemotherapy for Patients with Platinum-Resistant Ovarian, Fallopian, or Peritoneal Cancer

IRB#: 14-000428

Principal Investigator: Dr. Evanthia Galanis and Colleagues

Please read this information carefully. It tells you important things about this research study. A member of our research team will talk to you about taking part in this research study. If you have questions at any time, please ask us.

Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision.

To help you decide if you want to take part in this study, you should know:

- Taking part in this study is completely voluntary.
- You can choose not to participate.
- You are free to change your mind at any time if you choose to participate.
- Your decision won't cause any penalties or loss of benefits to which you're otherwise entitled.
- Your decision won't change the access to medical care you get at Mayo Clinic now or in the future if you choose not to participate or discontinue your participation.

For purposes of this form, Mayo Clinic refers to Mayo Clinic in Arizona, Florida and Rochester, Minnesota; Mayo Clinic Health System; and all owned and affiliated clinics, hospitals, and entities.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you a copy of this form to keep. A copy of this form will be put in your medical record.

CONTACT INFORMATION

You can contact …	At …	If you have questions about …
Principal Investigators: Dr. Evanthia Galanis Dr. Matthew Block Dr John Camoriano Dr Gerardo Colon-Otero	**Phone:** (507) 285-2411 **Institution Name and Address:** Mayo Clinic 200 1st Street SW Rochester, MN 55905 **Phone:** (480) 301-8000 **Institution Name and Address:** Mayo Clinic Arizona 13400 E. Shea Boulevard Scottsdale, AZ 85259 **Phone:** (904) 953-7291 **Institution Name and Address:** Mayo Clinic Florida 4500 San Pablo Road, Jacksonville, FL 32224	▪ Study tests and procedures ▪ Research-related injuries or emergencies ▪ Any research-related concerns or complaints ▪ Withdrawing from the research study ▪ Materials you receive ▪ Research-related appointments
Mayo Clinic Institutional Review Board (IRB)	**Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681	▪ Rights of a research participant
Research Participant Advocate (The RPA is independent of the Study Team)	**Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** researchparticipantadvocate@mayo.edu	▪ Rights of a research participant ▪ Any research-related concerns or complaints ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information ▪ Withdrawing from the research study

You can contact …	At …	If you have questions about …
Patient Account Services	**Toll-Free:** (844) 217-9591	▪ Billing or insurance related to this research study

Other Information:

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.

1. Why are you being asked to take part in this research study?

You are being asked to take part in this research study because you have recurrent, persistent, or progressive epithelial ovarian, fallopian tube, or primary peritoneal cancer.

The plan is to have about 60 people take part in this study at Mayo Clinic.

2. Why is this research study being done?

The idea of using measles virus strains as anticancer therapy has emerged from the observation that natural measles infection may result in an antitumor effect (cancer fighter).

This study is being done:

- To test the safety, tolerability and efficacy of an engineered strain of measles virus compared to standard chemotherapy and to see what effects (good and bad) it has on you and your disease
- To assess the virus' effects in the body using blood, urine, throat gargle specimen(s), and tissue samples

3. Information you should know

Who is Funding the Study?

This research study is supported by the Schulze Foundation.

Information Regarding Conflict of Interest:

This research has been reviewed by the Mayo Clinic Conflict of Interest Review Board and is being conducted in compliance with Mayo Clinic Conflict of Interest policies.

Both the Mayo Clinic Conflict of Interest Review Board and the Institutional Review Board have reviewed the Financial Conflict of Interest for one or more of the investigators and/or Mayo Clinic related to this research and they have determined that this Financial Conflict of Interest poses no additional significant risk to the welfare of participants in this research project or to the integrity of the research.

Additional information is available to any interested study participant regarding the details of this Financial Conflict of Interest and how it is being managed by contacting the study coordinator or the Office of Conflict of Interest Review at 507-284-0075.

One or more of the investigators associated with this project and Mayo Clinic have a Financial Conflict of Interest in technology used in the research and that the investigator(s) and Mayo Clinic may stand to gain financially from the successful outcome of the research.

4. How long will you be in this research study?

You will be in the study until your cancer grows, you develop significant side effects from your cancer treatment, or you choose to stop participating in the research study.

5. What will happen to you while you are in this research study?

This is a randomized trial. You will be assigned by chance (like a coin toss) to receive either measles virus (Arm A) or standard chemotherapy (Arm B). A computer program will place you in one of the study groups. You and the Principal Investigator can't choose your study group. You will have a two in three chance of receiving the measles virus and a one in three chance of receiving standard chemotherapy. However, if you are assigned to the chemotherapy arm (Arm B), you and your provider can choose from a list of chemotherapy options which one to receive while on the clinical trial.

Prior to randomization, you will have a surgical evaluation to determine if a peritoneal port placement (catheter in the abdomen) is feasible. If it cannot be done, you will not be entered in the study. If it can be done, you will be randomized to either Arm A or Arm B. You will be told which arm you are in.

Additional tests you will have before randomization include:

- A complete physical exam, during which the researchers will look at your past medical history and look at how you are doing now
- Measurement of your height and weight, blood pressure, temperature, and pulse
- Blood tests as part of your regular medical care
- CA-125 blood test
- A chest x-ray to exclude the presence of tumor in your lungs
- Blood tests just for this research study
- An echocardiogram or MUGA to assess the function of your heart

If it is not known if you have HIV you will need to have a blood test done. If your HIV test result is positive you will need to have a second test done to make sure the results are the same. The researcher will tell you how to find medical help and counseling, as needed, and you may not be able to take part in the study. Your health insurer or you will have to pay for the cost of the repeat test, any follow-up medical care, or counseling.

If the HIV test result is positive, it is state law that they be reported to the State Department of Health. The test results will also be put in your medical record.

Patients who are HIV positive or have other immune impairment will be ineligible for the trial.

In this study, each 4-week period will be called a treatment "cycle".

If you are randomized to Arm A, you will have a peritoneal port placed surgically. A tumor sample will be submitted for research purposes at the time of surgery. About 4 weeks after surgery, you will start treatment on the trial, and you will have the following tests performed:

When	What you do
Prior to Cycle 1 Day 1-	• Complete physical exam, including height, weight, blood pressure, temperature and pulse. • Blood tests as part of your regular medical care • CA-125 blood test • Research blood draws • SPECT scan (Cycle 1 only; if this scan is positive the SPECT scan will be repeated again during Cycle 2) • CT or MRI or PET/CT exam of abdomen and pelvis • Complete questionnaire • Urine Sample • Peritoneal aspirate • Mouth gargle specimen
Prior to Cycle 1 Day 1	• Admission to Mayo Clinic Hospital for two overnight stays at CRTU, St Mary's Campus in Rochester, MN OR Check in for pretreatment at Mayo Clinic in Arizona OR Mayo Clinic in Florida
Cycle 1, Day 1	• Treatment with MV-NIS at Mayo Clinic You will stay overnight in Rochester, MN You will be observed for at least 8 hours after receiving MV-NIS in Arizona and Florida
Cycle 1, Day 3 and Day 8	• Mouth gargle specimen • Peritoneal aspirate • Urine sample • Research blood draw • SPECT scan (If this scan is positive, the SPECT scan will be repeated again during Cycle 2.)
Day 1 (≤3 days prior) of every cycle thereafter-	• Complete physical exam, including height, weight, blood pressure, temperature and pulse. • Blood tests as part of your regular medical care • CA-125 blood test • Complete questionnaire • Treatment with MV-NIS on Day 1 of each cycle (Treatment will take place in the outpatient setting)

When	What you do
Cycle 1, Day 15-Gonda Building	• Research blood draw • SPECT (If this scan is positive, the SPECT scan will be repeated again during Cycle 2)
Cycle 3, Day 1 or ≤3 days prior to Day 1 (and Day 1 of every odd cycle thereafter: Cycle 3, 5, 7, etc.)	• CT or MRI or PET/CT exam of abdomen and pelvis

If the virus is found in your urine or throat samples, then your family members may also be offered testing for immunity against the measles virus. If your family members are not immune to the measles virus, they will be offered the measles vaccine.

If you are randomized to Arm B, you will have the following tests performed:

When	What you do
Cycle 1 Day 1 or ≤7 days prior (and Day 1 of every odd cycle thereafter: Cycle 3, 5, 7, etc.)	• A complete physical exam • Measurement of your height and weight, blood pressure, temperature, and pulse • Blood tests as part of your regular medical care; • CA-125 blood test • Research blood draw • CT or MRI or PET/CT exam of abdomen and pelvis • Complete Questionnaire • Treatment with standard chemotherapy on day 1 of each cycle*
Cycle 1 Day 8 and Day 15 ± 3 days (and Days 8 and 15 of every cycle thereafter)**	• Blood tests as part of your regular medical care* • Treatment with chemotherapy*
Cycle 2 Day 1 ± 3 days (and Day 1 of every even cycle thereafter)	• Blood tests as part of your regular medical care* • Treatment with chemotherapy*
*Blood tests and treatments may be performed by another oncologist, provided results and records are forwarded to Mayo Clinic. Research blood samples must be sent to Mayo Clinic. **Day 8 and Day 15 blood tests and treatments are required for patients received gemcitabine (GEM), topotecan (TOPA), or paclitaxel (TAXOL), but not for patients receiving liposomal doxorubicin (DOXIL).	

6. What are the possible risks or discomforts from being in this research study?

ARM A Risks

Peritoneal Port Placement

Placement of the peritoneal port:

You will need to have a catheter (like a plastic tube) placed into your abdomen in a way that will keep it secure for long-term use. This port placement will be done to make it easier to administer the measles virus and to remove fluid for testing from the abdomen. This procedure is done by a surgeon and under general anesthesia (put to sleep) and must be done before you start the study. A small pump will be used to pump the measles virus into your abdomen. The use of the peritoneal port in the abdomen is a new way to use this device. It is more commonly put into a large blood vessel. You will need to return to Mayo Clinic when you get the measles virus and for the frequent blood collections. When the study is done the port will be removed with a minor procedure.

Risks related to the peritoneal port:

Placement of the catheter (plastic tube) in to your abdomen could involve mild or life-threatening risk. You will receive anesthesia during the placement of the tube, which usually will take less than 1 hour. This placement will usually be done as same-day (outpatient) surgery. You will be admitted for surgery the day of the procedure. This procedure involves making a small incision that goes down into the abdomen where the catheter can be inserted. The catheter is then attached to a small reservoir (container) about the size of screw cap on a soda bottle. This reservoir is inserted under the skin and remains there throughout the study. The risks from the procedure include infection, bleeding and intestinal (bowel) injury: these are very rare but if they occur they will require hospitalization to treat, and an intestinal injury can even be life threatening. At the same time that the doctor puts this catheter in, a small piece of tumor will be collected. This procedure is called a tumor biopsy. You should expect pain around the incision site that will require treatment with oral pain medication to last 3-5 days. After returning to your hospital room after the procedure you will be observed and discharged after 2-4 hours.

If there are any concerns about your condition you will be admitted for overnight observation. Long-term complications could include infection of the peritoneal cavity, local discomfort, and catheter malfunction.

MV-NIS

While you are taking part in this study, you are at risk for these side effects. You should talk to your study doctor and/or your medical doctor about these side effects. The safety of administering MV-NIS is not known. The side effects discussed below are based upon the illness seen with measles infection and common reactions seen after measles vaccination. Although the strain of the virus used in this study was derived from the vaccine lineage, it is not known if this virus is more or less attenuated than other vaccine strains. The route of administration is different, and the doses of virus used in this study can be significantly higher than those given at the time of vaccination. Therefore, there may be other side effects that are not known. Other drugs may be given to lessen side effects. Many side effects go away shortly after the viral treatment is stopped, but in some cases side effects can be serious, long lasting, or may never go away. There may be a risk of death

Common side effects of the virus:

- Abdominal discomfort resulting from administration of the viral solution into the peritoneal cavity
- Fatigue

Less common side effects:

- Moderate to high fever lasting 1-2 days, starting within a day or two of the virus administration
- Low white blood cell count (the blood cells that fight infection)

Rare side effects:

- An acute allergic reaction with shortness of breath, rash, wheezing, and low blood pressure, which in rare cases can be fatal
- Reactions at the injection site such as wheal, flare or urticaria
- Reaction or infection of the lining of the abdomen (peritoneum) after administration of the virus in the abdominal cavity (peritonitis), or spleen infection
- A decrease in the number of platelets in the blood, resulting in the potential for increased bleeding and decreased ability for clotting
- Diarrhea
- Auto-immune or immune-complex disease
- Infection with measles outside the abdomen
- Prolonged fever
- Joint pain
- Cough and runny nose

- Skin rash
- Decrease in delayed type-hypersensitivity skin test responses, which can increase your susceptibility to certain types of infection

In addition, people rarely develop pneumonia or encephalitis after exposure to measles virus, although this is unlikely in subjects with measles immunity.

Should you develop a measles systemic infection, treatments of potential benefit, although not FDA approved, include immune globulin and ribavirin.

SPECT (Single-Photon Emission Computed Tomography): you will receive an oral radioactive substance (I-123) then you will lie on a bed while the SPECT machine takes pictures of your body. The pictures take quite a long time. During the pictures you should remain as still as possible but please breathe normally. You will be exposed to radiation during the SPECT procedure. The amount of radiation you will receive has a low risk of harmful effects.

Cytomel® (liothyronine sodium)
The risks of Cytomel® may include:

- Irregular heartbeats
- Sweating
- Headaches
- Shortness of breath
- Vomiting

Blood Draw
The risks of drawing blood include pain, bruising, lightheadedness, and/or fainting, or rarely, infection at the site of the needle stick.

Echocardiogram (ECHO)
This test uses sound waves to look at your heart. The person doing the test will press on your chest with a machine to obtain the pictures. The pressure may be uncomfortable.

MUGA
If you have a MUGA scan performed, you will receive an injection of radioactive material. The amount of radiation you will receive has a low risk of harmful effects."

Pregnancy/birth control
Pregnancy and birth control measures will not be addressed, for in order for the subject to be included in the study, they must have had a prior bi-lateral oophorectomy (removal of the ovaries). A person cannot get pregnant if this is surgery was done.

In the unlikely event that death occurs, irrespective of the cause, permission for an autopsy will be requested of your family. This is important so that the researchers can further document the safety and effectiveness of this treatment. The researchers encourage you to talk to your family regarding this issue.

ARM B Risks
Note: You will only receive ONE of the following four chemotherapy drugs while on the clinical trial if you are randomized to Arm B. You and your provider will determine which of the drugs you will be treated with.

Gemcitabine

Likely risks of gemcitabine *(events occurring greater than 20% of the time)*
- Decrease in white blood cells (may increase chance of developing an infection)
- Decrease in red blood cells (may cause feelings of being tired)
- Decrease in platelets (may increase the chance of bruising or bleeding after injury)
- Nausea (feeling sick to your stomach)
- Vomiting (being sick)
- Flu-like symptoms, including fever, headaches, mild chills, muscle soreness, fatigue, weakness, lethargy, loss of appetite, cough, runny nose, and sweating
- Changes in liver function tests (tests that show how your liver is working). These changes are usually mild and non-progressive and rarely require stopping treatment with gemcitabine.
- Diarrhea
- Temporary red itchy rash
- Tingling, prickling, or creeping feeling on the skin
- Shortness of breath
- Fluid retention (usually seen as swelling of the hands, feet, or face)

Less likely risks of gemcitabine *(events occurring less than or equal to 20% of the time)*
- Mild effect on the kidneys (blood or protein in the urine)
- Mild hair loss
- Inflammation of the mucous membranes of the mouth and throat
- Loss of appetite

- Sleepiness
- Agitation (feeling restless)
- Inability to sleep

Rare but serious risks of gemcitabine *(events occurring less than 2-3% of the time)*

- Fast or irregular heartbeat
- Decreased blood pressure
- Severe changes in liver function tests (including changes that may cause jaundice)
- Severe difficulty breathing
- Severe effects on the kidneys, sometimes leading to kidney failure
- Heart failure
- Confusion
- Convulsions
- Coma
- Severe allergic reactions. Symptoms may include rash, changes in blood pressure, swelling and increased fluid in the tissues, increases in heart rate, difficulty breathing and collapse.
- Blood vessel inflammation and gangrene (death of soft tissue due to lack of blood supply)
- Capillary leak syndrome, which can cause low blood pressure or reduced the amount of oxygen getting to tissue
- Severe skin reactions, including peeling of the skin
- Blistering red sores in the mucous membranes or larger areas of the body)

<u>Liposomal Doxorubicin</u>

Likely risks of Liposomal Doxorubicin (Doxil®)

- Swelling of the arms and legs (Peripheral edema)
- Fever
- Headache
- Pain
- Loss of hair from body and head (Alopecia)
- Redness or sores of the palms of the hands or soles of the feet (palmar-plantar erythrodysesthesia/hand-foot syndrome)
- Rash
- Mouth sores (Stomatitis)
- Throwing up (Vomiting)
- Feeling sick to your stomach. (Nausea)

- Inflammation and/or sores in the mouth that make swallowing difficult and are painful (Mucositis)
- Difficulty passing stool (Constipation)
- Uncontrolled loss of appetite or not feeling hungry (Anorexia)
- Loose stool (Diarrhea)
- Indigestion or heartburn (Dyspepsia)
- Intestinal obstruction
- Decreased production within the bone marrow that causes decreased production of the red cells, white cells or platelets (Myelosuppression)
- A low number of white blood cells, which are the infection fighting cells, which could put you at risk for infection (Neutropenia)
- Leucopenia
- Decreased number of blood cells (platelets) that help to clot the blood, which could put you at increased risk of bleeding (Thrombocytopenia)
- Decrease in red blood cells, which are the oxygen carrying cells, which can make you feel tired (Anemia)
- Weakness
- Back pain
- Sore throat (Pharyngitis)
- Shortness of breath or difficulty breathing (Dyspnea)
- Infection

Less likely risks of Liposomal Doxorubicin (Doxil®)

- Heart stops beating which can cause death (Cardiac arrest)
- Chest pain
- Swelling in arms or legs (edema)
- Low blood pressure (hypotension)
- Pallor tachycardia
- Widening of the blood vessels, especially the arteries, leading to increased blood flow or reduced blood pressure (Vasodilation)
- Agitation
- Anxiety
- Chills
- Confusion
- Feeling sad or blue (Depression)
- Sensation of lightheadedness or vertigo (spinning sensation) (Dizziness)
- Difficulty falling or staying asleep (insomnia)
- Excessive sleepiness (somnolence)

- Loss of balance (Vertigo)
- Acne
- Bruising (Contusion)
- Dry skin
- Inflammation of the skin from any cause, resulting in a range of symptoms such as redness, swelling, itching, or blistering (Dermatitis)
- A medical condition in which large areas of the skin are covered in persistent boils (furunculosis)
- A flat, red area on the skin that is covered with small bumps (maculopapular rash)
- Itching sensation (pruritus)
- Skin discoloration
- Vesiculobullous rash
- Excessive or abnormal loss of body fluids (Dehydration)
- Elevation of a liver pigment (bilirubin) in the blood indicating liver dysfunction (Hyperbilirubinemia)
- Abnormally high calcium in the blood stream, which can result in fatigue, confusion, feeling sick to your stomach, throwing up, difficulty passing stool, abnormal heartbeat, coma and death (Hypercalcemia)
- High blood sugar (Hyperglycemia)
- Low potassium levels in the body (Hypokalemia)
- Decrease sodium levels in the blood (Hyponatremia)
- Abdomen enlarged
- Uncontrolled loss of appetite or not feeling hungry (Anorexia)
- Collection of fluid in the abdominal area (Ascites)
- Muscle wasting, unintentional weight loss (Cachexia)
- Indigestion or heartburn (Dyspepsia)
- Difficulty swallowing (Dysphagia)
- Inflammation of the esophagus (the tube that carries food from the mouth to the stomach) (Esophagitis)
- Too much gas passed from the rectum (Flatulence)
- Gingivitis
- Inflammation of the tongue (Glossitis)
- Inability of the intestines to pass food or drink normally (Ileus)
- Mouth ulceration
- Thrush (oral moniliasis)
- Rectal bleeding
- Taste perversion
- Weight loss

- Dry mouth (xerostomia)
- Cystitis
- Dysuria
- Leucorrhea
- Pelvic pain
- Polyuria
- Urinary urgency
- Vaginal bleeding
- Vaginal moniliasis
- Damage to the red blood cells resulting in a reduction in the blood's ability to transport oxygen (Hemolysis)
- Prothrombin time increased
- Abnormal liver function test which may indicate that your liver is not functioning properly (ALT increased)
- Inflammation of a vein with the formation of a blood clot (Thrombophlebitis)
- Joint pain (Arthralgia)
- Increased tension (Hypertonia)
- Muscle pain (Myalgia)
- Neuralgia
- Neuritis (peripheral)
- Neuropathy
- Tingling, burning or prickling sensation (paresthesia)
- Pathological fracture
- Infection around the eye, also called pink eye (Conjunctivitis)
- Dry eyes
- Retinitis
- Ear pain
- Albuminuria
- Blood in the urine (Hematuria)
- Apnea
- Cough
- Nose bleed (Epistaxis)
- Collection of fluid in the space around the lung (pleural effusion)
- Pneumonia
- Cold symptoms, such as runny or stuffy nose. (rhinitis)
- Sinusitis
- Allergic reaction

- Infusion-related reactions
- Moniliasis
- Diaphoresis

Rare but serious risks of Liposomal Doxorubicin (Doxil®)

- Abscess
- Acute brain syndrome
- Abnormal vision
- Acute myeloid leukemia (secondary)
- Alkaline phosphates increased
- Anaphylactic or anaphylactoid reaction
- Asthma
- Blindness
- Bone pain
- Bronchitis
- BUN increased
- Bundle branch block
- Cardiomegaly
- Cardiomyopathy
- Infection of the skin and surrounding tissue (cellulitis)
- Decrease in the ability of the heart to pump blood, because of a weakening of the heart muscle [congestive heart failure, (CHF)]
- Inflammation in the colon (Colitis)
- Creatinine increased
- An infectious disease that affects parts of the body, especially the brain and central nervous system, with lesions or abscesses caused by the fungus Cryptococcus neoformans (Cryptococcosis)
- Diabetes mellitus
- Erythema multiforme
- Erythema nodosum
- An increase in the number of granular white blood cells that stain with the dye eosin, occurring in some allergies and parasitic diseases (Eosinophilia)
- Fecal impaction
- Flu-like syndrome
- Inflammation of the stomach (gastritis)
- Glucosuria
- Hemiplegia
- Hemorrhage

- Hepatic failure
- Kind of infection of the liver which causes inflammation and can cause liver damage (hepatitis)
- Hepatosplenomegaly
- Elevated potassium in the blood (hyperkalemia)
- Elevated sodium in the blood (hypernatremia)
- Increased uric acid in the blood (hyperuricemia)
- Hyperventilation
- Low blood sugar (hypoglycemia)
- Hypolipidemia
- Low levels of magnesium in the blood (hypomagnesemia)
- Decreased level of phosphorus in the blood (hypophosphatemia)
- Hypoproteinemia
- Hypothermia
- Injection site hemorrhage
- Injection site pain
- Yellow skin and increase in certain blood tests indicating damage to the liver. (jaundice)
- Ketosis
- Lactic dehydrogenase increased
- Kidney failure
- Swelling of the lymph nodes (lymphadenopathy)
- Lymphangitis
- Migraine
- Inflammation of the muscles with rising muscle enzyme levels in the blood. (myositis)
- Optic neuritis
- Palpitation
- Pancreatitis
- Pericardial effusion
- Small purple or red dots on the skin (petechia)
- Abnormal accumulation of air in the chest between the lung and chest wall, which may make it difficult to breathe (pneumothorax)
- Blood clots in the lungs which could be life threatening or cause death (pulmonary embolism)
- Radiation injury
- Sclerosing cholangitis
- Involuntary changes in body movement or function, sensation, awareness or behavior (seizure)

- Infection that has spread to the bloodstream and can cause low blood pressure, fever and/or death (sepsis)
- Skin necrosis
- Skin ulcer
- Fainting. (syncope)
- Tenesmus
- Thromboplastin decreased
- Thrombosis
- Ringing in the ears. (tinnitus)
- Dark red, raised, itchy bumps or hives (urticaria)
- Visual field defect
- Ventricular arrhythmia

Topotecan

Likely risks of Topotecan

- Feeling tired (Fatigue)
- Fever
- Pain
- Headache
- Hair loss (Alopecia)
- Rash
- Feeling sick to your stomach (Nausea)
- Throwing up (Vomiting)
- Loose stools (Diarrhea)
- Trouble passing stools (Constipation)
- Stomach pain (Abdominal pain)
- Loss of appetite or not feeling hungry (Anorexia)
- Mouth sores (Stomatitis)
- A low number of white blood cells, which are the infection fighting cells, which could put you at risk for infection (Neutropenia)
- Decreased white blood cells, which are the infection fighting cells, which could put you at risk for infection (Leukopenia)
- Decrease in red blood cells, which are the oxygen carrying cells, which could make you feel tired (Anemia)
- Decreased number of blood cells (platelets) that help to clot the blood (which could put you at increased risk of bleeding) (Thrombocytopenia)
- Fever with dangerously low white blood cell count (Neutropenic fever)

- Infection that has spread to the bloodstream and can cause low blood pressure, fever, and/or death (Sepsis)
- Weakness
- Shortness of breath (Dyspnea)
- Cough

Less likely risks of Topotecan

- Temporary increase in liver enzymes
- Tingling, burning, or prickling sensation (Paresthesia)

Rare but serious of Topotecan

- Stomach pain (Abdominal pain)
- Fever, chills, swelling of body, shortness of breath (Allergic reactions)
- Serious allergic reaction to the medication which can cause hives, itching, shortness of breath, swelling of the lips or throat, difficulty breathing , and could be life threatening (Anaphylactoid reactions)
- Abnormal swelling below the skin usually around the lips and eyes (Angioedema)
- Bleeding (severe, associated with thrombocytopenia)
- Redness, flaking or sloughing of skin (Dermatitis (severe)
- Injection site reactions (redness of the skin (Mild erythema) and/or bruising)
- Serious infection starting from the bowel if you have had bad diarrhea and low blood counts. This may lead to death (Neutropenic colitis)
- Reduction in the number of red blood cells (which could make you feel tired), white blood cells (which could put you at risk for infection), and platelets (which could put you at risk for bleeding) (Pancytopenia)
- Severe itching (Pruritus)
- Low potassium levels in the blood (Hypokalemia)

<u>Paclitaxel</u>

Likely risks of Paclitaxel

- Flushing, cardiovascular
- Hair loss (alopecia)
- ECG abnormal
- Feeling sick to your stomach (nausea)
- Loose stools (diarrhea)
- Throwing up (vomiting)
- Irritation or sores in the Gastrointestinal tract (stomatitis)

- Inflammation and/or sores in the mouth that may make swallowing difficult and are painful (mucositis)
- Abdominal pain (with intraperitoneal paclitaxel)
- Decreased white blood cells, which are the infection fighting cells, which could put you at risk for infection (leukopenia)
- A low number of white blood cells, which are the infection fighting cells, which could put you at risk for infection (neutropenia)
- Decrease in red blood cells, which are the oxygen carrying cells, which could make you feel tired (anemia)
- Abnormal Liver function tests which may indicate that your liver is not functioning properly (alkaline phosphatase/AST increased)
- Neuromuscular & skeletal weakness
- Muscle pain (myalgia)
- Joint pain (arthralgia)
- Elevated levels of a byproduct normally filtered out by the kidneys that when elevated could indicate kidney damage (creatinine increased)
- Infection
- Numbness, tingling, or inflammation of the nerves (usually in the hands and feet), which may be painful (peripheral neuropathy)
- Hypersensitivity reaction (includes chest pain, dyspnea, flushing, hypotension)
- Fluid retention (edema)
- Low blood pressure (hypotension)
- Decreased number of blood cells (platelets) that help to clot the blood (which could put you at increased risk of bleeding) (thrombocytopenia)
- Redness, flaking or sloughing of skin in the radiation treatment area (rash)
- Hematologic bleeding (hemorrhage)
- Pain, redness, bruising, pressure, swelling, and/or hardness of the skin at the infusion/injection site (injection site reaction)

Less likely risks of Paclitaxel

- Slow heart rate (bradycardia)
- High blood pressure (hypertension)
- Cardiovascular rhythm abnormalities
- Fainting (syncope)
- Formation or presence of a blood clot inside a blood vessel (venous thrombosis)
- Fever with dangerously low white blood cell count (febrile neutropenia)
- Rapid heartbeat (tachycardia)
- Nail changes

- Abnormal level of bilirubin in the blood - Bilirubin is a bile pigment found in the liver (Bilirubin increased)
- Shortness of breath (dyspnea)

Rare but serious of Paclitaxel

- Rapidly developing and serious allergic reaction that affects a number of different areas of the body at one time (anaphylaxis)
- Loss of muscle coordination (ataxia)
- Abnormal heartbeat (atrial fibrillation, AV block, cardiac conduction abnormalities)
- Back Pain
- Infection of the skin and surrounding tissue (cellulitis)
- Chills
- Infection around the eye, also called pink eye (conjunctivitis)
- Dehydration
- Inflammation of the the small intestin and the colon (enterocolitis)
- Hardening of the skin and connective tissues (induration)
- Mechanical or functional obstruction of the intestines (intestinal obstruction)
- Development of hole or tear in the intestine, which can cause damaging intestinal fluids to leak into the abdominal cavity, resulting in bleeding, severe pain, fever, nausea, vomiting, infection and possibly death (intestinal perforation)
- Inflammation and injury of the large intestine result from inadequate blood supply (ischemic colitis)
- Flat, red area on the skin that is covered with small confluent bumps (maculopapular rash)
- General feeling of being unwell (malaise)
- Increase in production or shedding of tears (lacrimation increased)
- A heart attack is when blood vessels that supply blood to the heart are blocked, preventing enough oxygen from getting to the heart. The heart muscle dies or becomes permanently damaged. (MI)
- Poison or toxin affecting organs or nerves involved with hearing or balance (ototoxicity)
- Inflammation of the pancreas (pancreatitis)
- Inflammation of the veins (phlebitis)
- Itching sensation (pruritus)
- Blood clots in the lungs which could be life threatening or cause death (pulmonary embolism)
- Scarring of the lungs (pulmonary fibrosis)
- Pain, redness or skin breakdown at the sites where there has been exposure to radiation therapy (radiation recall)

- Inflammation of the lungs due to radiation therapy (radiation pneumonitis)
- Involuntary changes in body movement or function, sensation, awareness, or behavior (seizure)
- Peeling of the skin (skin exfoliation)
- Death of the skin tissue (skin necrosis)
- A disorder characterized by less than 10% total body skin area separation of dermis. The syndrome is thought to be a hypersensitivity complex affecting the skin and the mucous membranes. (Stevens-Johnson syndrome)
- Irregular heartbeat (supraventricular tachycardia and ventricular tachycardia)
- A disorder characterized by greater than 30% total body skin area separation of dermis. The syndrome is thought to be a hypersensitivity complex affecting the skin and the mucous membranes. (toxic epidermal necrolysis)
- Thickening and tightening of the skin (skin fibrosis)
- Kidneys fail to adequately filter toxins and waste products from the blood (renal insufficiency)
- Obstruction of the intestine due to paralysis of the intestinal muscles (paralytic ileus)
- Congestive heart failure (CHF)
- Extravasation recall
- Necrotic changes and ulceration following extravasation
- Hepatic encephalopathy
- Death of liver tissue (hepatic necrosis)
- Interstitial pneumonia
- Neuroencephalopathy
- Neutropenic enterocolitis
- Visual disturbances

U.S. Boxed Warning: Bone marrow suppression is the dose-limiting toxicity; do not administer if baseline absolute neutrophil count (ANC) is less than1500 cells/mm^3 (1000 cells/mm^3 for patients with AIDS-related KS); reduce future doses by 20% for severe neutropenia.

U.S. Boxed Warning: Severe hypersensitivity reactions have been reported.

Bevacizumab

If you are receiving liposomal doxorubicin, topetecan, or paclitaxel your doctor may decide to also give you bevacizumab.

Common risks of bevacizumab (occurring more than 20% of the time)

- Diarrhea (loose stools)
- Nausea
- Vomiting
- Sores in the mouth and throat (stomatitis)
- Fatigue
- Joint pain (arthralgia)
- Muscle pain (myalgia)
- Pain in extremity
- Back pain
- Abdominal pain
- Headache
- Shortness of breath (dyspnea)
- Nosebleed (epistaxis)
- High blood pressure (hypertension)
- Platelet count decreased – may lead to bleeding
- Decreased blood cell counts, including white blood cells (leukopenia) and neutrophils (neutropenia), which may lead to infection
- Trouble sleeping (insomnia)
- Abnormal protein levels in urine (proteinuria)
- Cough
- Dizziness
- Decreased appetite
- Increased blood sugar (hyperglycemia)
- Increased magnesium level in blood (hypomagnesemia)
- Rash
- Urinary tract infection

Less common risks of bevacizumab (occurring less than 20% of the time)

- Muscle weakness (asthenia)
- Speech disorder (dysarthria or dysphonia)
- Nasal mucosal disorder
- Rhinitis allergic
- Mucosal inflammation
- Runny nose (rhinorrhea)
- Stuffy nose (sinusitis, sinus congestion)
- Infection
- Numbness or tingling in hands and feet (peripheral sensory neuropathy)

- Hand-foot syndrome (palmar-plantar erythrodysesthesia)
- Hemorrhoids
- Bleeding gums (gingival bleeding)
- Bruising (contusion)
- Pain in mouth or throat (oropharyngeal pain)
- Weight loss
- Low blood sodium levels (hyponatremia)
- Low blood calcium (hypocalcemia)
- Low blood protein (hypoalbuminemia)
- High blood potassium (hyperkalemia)
- Lymphocytes count decreased (lymphopenia)
- Abnormal liver function tests (AST)
- Abnormal kidney function tests (creatinine increased)
- Swelling in hands and feet (peripheral edema)
- Nail disorder
- Dry skin
- Blood clots (thrombosis)
- Deep vein thrombosis (DVT)
- Anxiety
- Chest pain
- Pelvic pain
- Neck pain

Rare but serious risks of bevacizumab (occurring less than 3%

- Perforation or fistula – a hole or opening that allows leaking between organs
- Blood clots or stroke
- Life threatening bleeding
- Posterior Reversible Encephalopathy Syndrome (PRES) – a condition usually caused by severe high blood pressure that results in headache, seizures, visual disturbances, altered consciousness
- Kidney damage (nephrotic syndrome)
- Infusion reaction
- Congestive heart failure

Blood Draw

The risks of drawing blood include pain, bruising, lightheadedness, and/or fainting, or rarely, infection at the site of the needle stick.

Echocardiogram (ECHO—patients receiving Liposomal Doxorubicin only)
This test uses sound waves to look at your heart. The person doing the test will press on your chest with a machine to obtain the pictures. The pressure may be uncomfortable.

Pregnancy/birth control
Pregnancy and birth control measures will not be addressed, for in order for the subject to be included in the study, they must have had a prior bi-lateral oophorectomy (removal of the ovaries). A person cannot get pregnant if this surgery was done.

7. Are there reasons you might leave this research study early?

You may decide to stop at any time. You should tell the Principal Investigator if you decide to stop and you will be advised whether any additional tests may need to be done for your safety.

In addition, the Principal Investigator, Dr. E. Galanis, Dr M. Block or Mayo Clinic may stop you from taking part in this study at any time:

- if it is in your best interest,
- if you don't follow the study procedures,
- if the study is stopped.

If you leave this research study early, or are withdrawn from the study, no more information about you will be collected; however, information already collected about you in the study may continue to be used.

We will tell you about any new information that may affect your willingness to stay in the research study.

8. What if you are injured from your participation in this research study?

Where to get help:

If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research related injuries?

If you have side effects from the study treatment, you need to report them to the researcher and your regular physician, and you will be treated as needed. Mayo will bill you or your insurer for these services at the usual charge. Mayo will not offer free medical care or payment for any bad side effects from taking part in this study.

9. What are the possible benefits from being in this research study?

There is no guarantee that this study will make your health better. However, the information gained in this study may help doctors' better treat cancer patients in the future.

10. What alternative do you have if you choose not to participate in this research study?

You do not have to be in this study to receive treatment for your condition. Other choices of treatment for your disease include other investigational treatments, radiation therapy, biotherapy, and chemotherapy. You should talk to the researcher and your regular physician about each of these choices before you decide if you will take part in this study. You also have the option of choosing no treatment.

11. What tests or procedures will you need to pay for if you take part in this research study?

You will not need to pay for any tests and procedures which are done just for this research study, nor for the investigational drug. Mayo will pay for the measles virus (MV-NIS) that you receive during this study. The tests and exams done just for the research study include the blood tests done just for research purposes, baseline HIV testing, a baseline echocardiogram or MUGA scan, the peritoneal aspirates and tumor biopsy, the placement of the catheter in the abdomen and the surgical assessment of the effect of the treatment if necessary. This research coverage includes the Cytomel®, I-123, and the SPECT scans.

Rochester patients only: You will not be billed for room and board or nursing charges while in the Clinical Research Unit. However, you may be billed for other expenses such as medications prescribed at the time of discharge.

All patients: You and/or your health plan will need to pay for all other tests and exams that you would normally have as part of your regular medical care. These tests and exams include standard blood tests, x-rays, and CT scans that measure your tumors. Should side effects occur, you and/or your health plan might also have to pay for other drugs or treatments which are given to help control side effects.

If you have billing or insurance questions call Patient Account Services at the telephone number provided in the Contact Information section of this form.

12. Will you be paid for taking part in this research study?

You won't be paid for taking part in this study.

13. What will happen to your samples?

We would like to keep your sample for future research. You can still take part in this current study even if you don't want your sample used for future research. If you agree to give your sample, it will be the property of Mayo Clinic.

Other researchers at Mayo Clinic who aren't involved with this study may ask to use your sample for future research. Researchers at other institutions may also ask for a part of your sample for future studies. Your sample will be sent to researchers in a coded format, which protects your identity.

Some future studies may examine your DNA, which is the genetic information you inherited from your parents (genetic testing). The Principal Investigator may contact you if there are findings which may be useful for your health care. You would be given general information on the potential risks, benefits, and costs of choosing to learn about the findings.

Please read the following statements and mark your choices:

1. I permit my sample to be stored and used in future research of Cancer at Mayo Clinic:

☐ Yes ☐ No Please initial here: _____Date: _____

2. I permit my sample to be stored and used in future research at Mayo Clinic to learn about, prevent, or treat any other health problems:

☐ Yes ☐ No Please initial here: _____Date: _____

3. I permit Mayo Clinic to give my sample to researchers at other institutions:

☐ Yes ☐ No Please initial here: _____Date: _____

There is a very small chance that some commercial value may result from the use of your donated sample. If that happens, you won't be offered a share in any profits.

You may request to have your sample destroyed by writing to the Principal Investigator. The address is found in the "Contact Information" section of this consent form.

Because we cannot predict how your sample will be used in the future, we cannot promise that samples can be retrieved and destroyed.

14. How will your privacy and the confidentiality of your records be protected?

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study. Various methods are used to safeguard confidentiality. Some or all of the following may be used in this study: assigning a specific code or registration number to each participant's data and samples, research materials stored in locked areas, password protected data stored on a computer. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form. If the results of the research are made public, information that identifies you will not be used.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and

why they may need to do so. Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to Mayo Clinic.

Health information may be collected about you from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

Why will this information be used and/or given to others?

- To do the research.
- To report the results.
- To see if the research was done correctly.

Who may use or share your health information?

- Mayo Clinic research staff involved in this study.

With whom may your health information be shared?

- The Mayo Clinic Institutional Review Board that oversees the research.
- Other Mayo Clinic physicians involved in your clinical care. Researchers involved in this study at other institutions.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.
- The sponsor(s) of this study and the people or groups it hires to help perform this research.
- A group that oversees the data (study information) and safety of this research.

In addition, individuals involved in study oversight and <u>not</u> employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, or copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule.

Your Privacy Rights

You do not have to sign this form, but if you do not, you cannot take part in this research study.

If you cancel your permission to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

If you choose not to take part or if you withdraw from this study, it will not harm your relationship with your own doctors or with Mayo Clinic.

You can cancel your permission to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Participant Subject Advocate at: researchparticipantadvocate@mayo.edu

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission lasts forever, unless you cancel it. Because research is an ongoing process, we cannot give you an exact date when the study will end.

ENROLLMENT AND PERMISSION SIGNATURES

Your signature documents your permission to take part in this research

	/ /	: AM/PM
Printed Name	Date	Time

Signature

Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

	/ /	: AM/PM
Printed Name	Date	Time

Signature