ID: UMCC 2010.101	Chemotherapy AND Bcl-xL Inhibitor (AT-101) For Organ Preservation In Adults With Advanced Laryngeal Cancer	NCT01633541

UNIVERSITY OF MICHIGAN

CONSENT TO BE PART OF A RESEARCH STUDY

INFORMATION ABOUT THIS FORM

You may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of the study, and the risks and possible benefits of participating in the study.

Please take time to review this information carefully. After you have finished, you should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or other doctors) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. *Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.*

1. GENERAL INFORMATION ABOUT THIS STUDY AND THE RESEARCHERS

1.1 Study title:

Concomitant Chemotherapy and Bcl-xL Inhibitor (AT-101) for Bioselection™ for Organ Preservation in Patients with Advanced Laryngeal Cancer

1.2 Company or agency sponsoring the study:

University of Michigan Head and Neck SPORE Grant

1.3 Names, degrees, and affiliations of the researchers conducting the study:

Principal Investigator:

Francis Worden, M.D., Department of Hematology/Oncology; Medical School

2. PURPOSE OF THIS STUDY

2.1 Study purpose:

The purpose of this study is to evaluate a new treatment approach for patients with advanced laryngeal cancer: induction chemotherapy with platinum and docetaxel plus AT-101. AT-101 is an investigational drug for the treatment of advanced cancer. It is hoped that the combination of this chemotherapy regimen will allow you to keep your voice box and to improve your voice-related quality of life. The ultimate goal of this study is to prevent having to perform the surgery to remove your voice box.

This study will help the researchers learn what effects, if any, the combination of AT-101 and induction chemotherapy with platinum and docetaxel has on your cancer. For instance, will the combination cause your tumor(s) to shrink or stop growing? The researchers will also learn about the safety of the combination of AT-101 and chemotherapy. For instance, are there any side effects? If so, what kind of side effects does the combination cause? How severe are the side effects, and how often do they occur?

3. INFORMATION ABOUT STUDY PARTICIPANTS (SUBJECTS)

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

If you are at least 18 years of age and have been diagnosed with advanced (Stage III or IV) squamous cell carcinoma of the larynx (voice box) and you are a candidate for surgical resection you might qualify to participate in this study. There are other eligibility requirements involving your health history and laboratory values which your doctor will review and discuss with you.

3.2 How many people (subjects) are expected to take part in this study?

53 patients will participate in this study at the University of Michigan over the next 3-4 years.

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?

Screening Procedures

If you agree to participate in this study, you will be asked to sign this informed consent document. This document demonstrates your willingness to be a study participant. It does not guarantee or require study participation.

Your study doctor will then review the following with you:

- Demographic information – this includes things like your name, birthday, race and ethnicity, etc.
- Medical history - this may include diseases you have had in the past, conditions other than your cancer that you currently have (e.g., diabetes, hypertension, asthma), any signs or symptoms from any current illness you have, and all of the medications you have taken in the past 7 days. Your study doctor will also take a history of the prior treatments, including surgeries, that you have received for your cancer and any ongoing side effects from those prior treatments
- Physical examination – this will include things like measuring your weight, height, blood pressure, heart rate, temperature, and a complete dental evaluation.
- Performance status - this evaluates how well you are able to complete daily activities such as dressing and eating
- Endoscopic Laryngoscopy – this test involves looking into your larynx with a lighted tube called an endoscope and will help measure your tumor and evaluate the deep extensions of your tumor. At the time of your Endoscopic Laryngoscopy, the lymph nodes in your neck will be evaluated to determine if they have been affected by your disease.
- Electrocardiogram (EKG) – this test will evaluate the electric activity of your heart
- Computed tomography (CT) scan or Chest X-Ray – this procedure makes a series of detailed pictures of your neck and chest (including your lymph nodes), and possibly your abdomen and pelvic area if the study doctor feels it's necessary. These procedures will measure the extent of your cancer. A CT/PET scan may be used as an alternative to or in addition to the diagnostic CT at the discretion of the investigator.
- Diagnostic CT scan with perfusion. A perfusion is a special CT scan that looks at the blood vessels in your tumor. It determines your tumor's extent and vascularity, the map of its blood vessels. This is not considered routine care.
- Audiogram – will be conducted to evaluate patients with hearing complaints or hearing loss (at the discretion of the prescribing physician)
- Quality of Life Assessments – these questionnaires will help the study team determine how much your cancer affects your quality of life and if the study treatments changes how you are feeling
- Laboratory assessments - about one (1) tablespoon of blood will be drawn to test for blood cell counts (numbers of each type of blood cell) and chemistries (elements and minerals in your

blood). These blood tests are routine and will help your doctor monitor your blood for any changes.

- Pregnancy test – for women capable of bearing children
- Blood sample – this blood sample (about 1 tablespoon) will be used to look for certain biomarkers (proteins). This analysis will help the study team learn who may or may not benefit from treatment in future studies with AT-101. Please discuss any questions regarding biomarker research with your study doctor.
- Bone Scan (if clinically warranted) – A special bone x-ray where dye is injected into your vein followed by an x-ray to look for cancer that has spread to your bones

There is an optional process that involves additional blood and tumor sample sent for analysis or stored for future research. You will be asked to give permission separately within this consent.

1. Tumor Specimen: If you give permission, a specimen of your tumor will be sent to the Head and Neck Cancer Research Laboratory for related studies. This research is optional.
2. Blood sample: Also, if you give permission, a blood sample will be stored to create cell lines for harvesting DNA. The sample will be sent to the Head and Neck Cancer Research Laboratory for related studies. This research is optional.

It is possible that abnormal screening test results will exclude you from this study. There may be other reasons why you cannot be in this study. These reasons will be discussed with you by your study doctor or the clinic staff.

Study Procedures

Following enrollment, you will be randomized (by chance, like the flip of a coin) to one of two arms of induction chemotherapy: platinum/docetaxal + AT-101 **or** platinum/docetaxel alone. The platinum you receive will either be cisplatin or carboplatin as deemed best by your medical oncologist.

Your chance of receiving the AT-101 is 50:50.

On Day 1, you will undergo induction chemotherapy with platinum/docetaxal. Induction chemotherapy is the use of drug therapy as the initial treatment for patients presenting with advanced cancer that cannot be treated by other means.

Days #1-3, those in the AT-101 arm will receive AT-101.

On Day 14, you will have about one (1) tablespoon of blood drawn for laboratory assessments.

On Day 23 (+/- 3 days), you will undergo an endoscopic laryngoscopy (DL) with biopsy of your tumor and blood will be drawn for laboratory assessments. You will undergo a repeat CT scan of the neck with perfusion within a week of your biopsy.

Prior to chemotherapy, you will be treated with medications to control nausea. These medications will be given by IV or taken by mouth. These medications may also cause constipation.

Depending on your response to induction chemotherapy, you may undergo a repeat cycle of platinum/docetaxel and AT-101. After induction chemotherapy, some patients, following clinical evaluation and CT imaging of the neck, will undergo treatment with radiation therapy in combination with weekly chemotherapy with platinum.

Twelve weeks following the completion of radiation therapy, you will undergo a repeat office laryngoscopy and a PET scan. The primary tumor site will be biopsied if clinically indicated. Lymph nodes in the neck that are persistent, or clinically suspicious nodes including PET positive nodes, will be removed. If you have positive laryngeal biopsies following chemotherapy and radiation therapy you will undergo salvage laryngectomy. This surgery will remove your voice box if chemotherapy and radiation therapy does not cure your cancer.

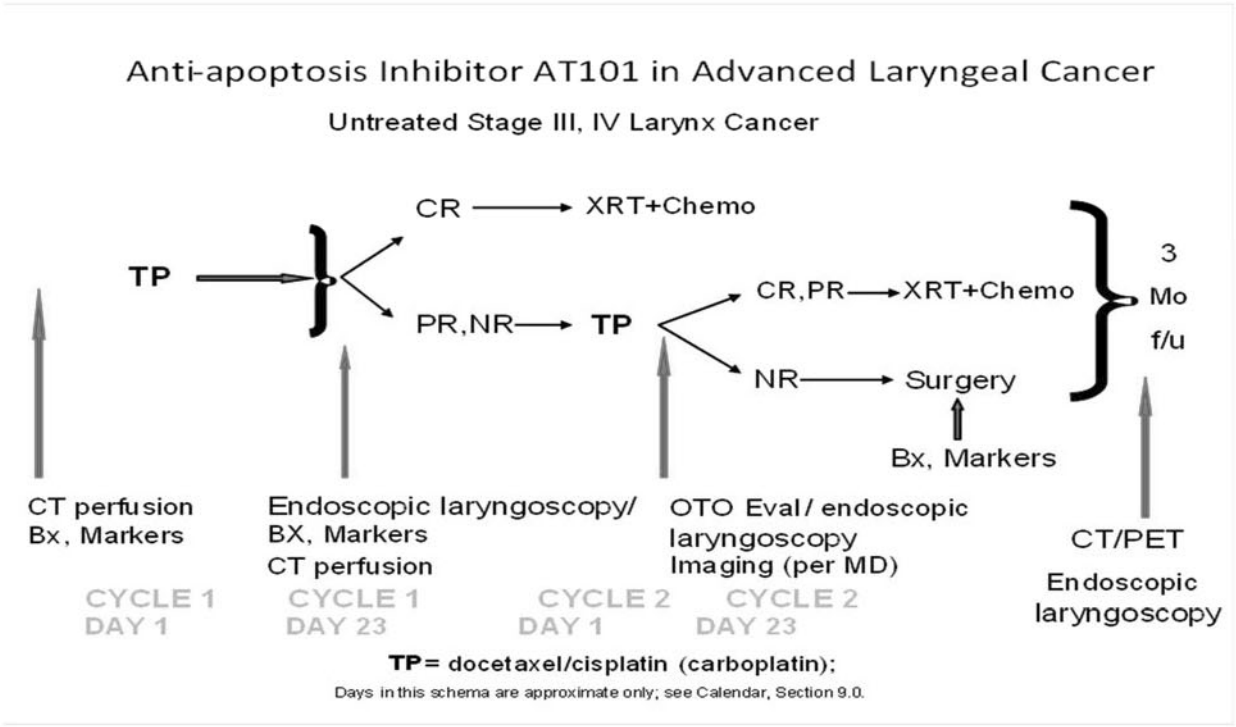
If the laryngeal (voice box) biopsy is negative but clinically or PET positive neck lymph nodes remain, you will undergo neck nodal dissection alone, which is a surgical procedure to evaluate the lymph nodes in your neck to see if cancer is present. Patients with PET negative necks and no clinically suspicious adenopathy (lymphnodes in your neck that do not look like they are involved with cancer) may have the neck observed.

If your cancer does not respond after 2 cycles of induction chemotherapy, you will be treated with salvage laryngectomy (described above) followed by radiation therapy. Platinum will be added to radiation therapy if your surgical pathology reveals high-risk features such as evidence of spreading to lymph nodes or invasion of surrounding areas.

Once you are disease-free following chemoradiation and nodal neck dissections (if needed), you will be followed at regular intervals as prescribed by your treating surgeon.

Outpatient clinical examinations will be performed at the completion of radiation therapy, at 6-8 week intervals during 1 year of follow-up, every two months during the year 2 follow-up, and every three months during the year 3 follow-up. If during this time, your physical examination or imaging studies look like your cancer is coming back, you will have a biopsy. If the biopsy is positive, you will undergo salvage laryngectomy as described above.

AT-101, Docetaxel, and Platinum may cause side effects. During the study, you will be monitored for any adverse changes that could be caused by these drugs (also known as “toxicities” or side effects). If you experience severe side effects, your treatment will be stopped until they improve enough that you may be safely treated again. If necessary, your dose of AT-101 and/or Docetaxel/platinum may be reduced. If you have side effects that are too severe, treatment with AT-101 Docetaxel/platinum may be stopped permanently. You and/or a family member will be asked to call your study doctor if you experience any mental or physical side effects or if you have any questions about AT-101 or Docetaxel/platinum.



BX = Biopsy
CR = complete response; **PR =** partial response; **NR =** no response
Chemo = induction chemotherapy
Endoscopic laryngoscopy
OTO Eval = Clinical Evaluation
CT perf. = CT Scan with perfusion
CT/PET = CT Scan and/or PET scan
Surgery = Salvage Laryngectomy

All patients will receive one cycle of chemotherapy. It may or may not include study drug. After this cycle, all patients undergo endoscopic laryngoscopy with biopsy. If you show a complete response at this point, you will receive weekly chemoradiation. If you do not show a complete response, you will receive another cycle of chemotherapy that includes the study drug. At this point there will be an exam by the surgeon, and if you have at least a partial response to the treatment, you will receive weekly chemoradiation. If you do not respond to treatment, you will proceed to surgery.

4.2 How much of my time will be needed to take part in this study?

You will need to come to clinic at the start of the study, at 3 weeks, and possibly weekly for 2 months depending on your treatment. Each clinic visit will last 1-2 hours. Regardless of your treatment plan, you will come to clinic for a follow up visit at 3 months and for additional follow up visits that are recommended by your study doctor.

4.3 When will my participation in the study be over?

Including the follow-up appointments, it is possible that you could participate in this study for approximately 3 years, provided that your disease does not get worse, and you are not experiencing any serious side effects.

4.4 What will happen with my information and/or biospecimens used in this study?

Your biospecimens and collected information may be shared with the University of Michigan Head and Neck SPORE Grant program. With appropriate permissions, your samples and collected information may also be shared with other researchers, here, around the world, and with companies. Your identifiable private information or identifiable biospecimens may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies without additional informed consent.

5. INFORMATION ABOUT RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?

AT-101 Risks

When you begin taking AT-101, you may experience a number of side effects, also called "toxicities". You should discuss these with your study doctor. Some of the possible risks of AT-101 can be predicted from the past experience of people who have received AT-101. However, there may be other side effects that we cannot predict. Standard medical care, including available drugs and other treatments, will be given to help manage the side effects. Most of these side effects are expected to be mild, but some could be severe, and it is possible that life-threatening side effects could occur. Based on the information from past studies of people who were given AT-101, most side effects will probably go away shortly after AT-101 is stopped. In some cases it is possible that these adverse effects could be long lasting or permanent.

We do not know all of the side effects of AT-101 that could occur when it is combined with other drugs or alcohol. You should always discuss the use of alcohol or any drugs (over-the-counter, prescription, herbal supplements, or illegal drugs) with your study doctor while you are participating in this study.

You should also notify any other doctors or healthcare providers who examine you that you are participating in this study, especially if you are about to undergo a surgical procedure, dental procedure, or any other drug therapy.

Medications Prohibited From Use with AT-101:

Patients may not take any of the following medications or therapies while receiving study treatment:

- Other investigational drugs are not to be used within 4 weeks of initial dosing or while receiving treatment.
- Concurrent approved or investigational anti-cancer therapy (e.g., chemotherapy, immunotherapy, targeted therapy, biologic therapy) other than protocol therapies.

Side Effects:

Likely (10-25%)

- Fatigue or tiredness
- Loss of appetite
- Diarrhea
- Nausea
- Vomiting
- Abdominal pain
- Ileus/small bowel obstruction

Less Likely (1-10%)

- Anemia or decrease in a red blood cell protein (hemoglobin) that carries oxygen in the body
- Decrease of the total number of white blood cells
- Fever
- Difficulty sleeping or falling asleep
- Weight loss
- Increased cardiac proteins indicative of heart damage (Cardiac Troponin I; Cardiac Troponin T)
- Dry skin
- Itching
- Rash/flaking or shedding of outer layer of skin
- Constipation
- Dehydration
- Feeling of fullness and tightness in the belly
- Dry mouth
- Inflammation of the stomach lining
- Gas-filled pocket in the intestinal lining
- Heartburn
- Abnormally slow bowel contraction
- Taste changes
- Infection(s) somewhere in the body
- Swelling of the arms and legs
- Abnormal liver or bone enzyme level (alkaline phosphatase)
- Increased level of a liver enzyme (ALT/SGPT; AST/SGOT)
- Elevated levels of a liver pigment (bilirubin) in the blood indicative of liver dysfunction

- Decreased blood calcium level
- Increased blood level of creatinine, a substance normally eliminated by the kidneys into the urine
- Decreased blood magnesium level
- Decreased blood potassium level
- Dizziness
- Back pain
- Leg and/or arm pain
- Headache
- Cough
- Shortness of breath
- Infertility/Inability to produce children
- Irregular menstrual periods
- Decrease in sexual desire

Rare but serious (<1%):

Events that have been reported on AT101 clinical trials but with an undetermined relationship to AT101.

- Cardiac ischemia/myocardial infarction: This means not enough blood and oxygen are flowing into the heart.
- Pancreatitis which is an inflammation or infection of the pancreas
- Blood clots

Docetaxel Risks(standard treatment):

Likely (10-25%):

- Low blood counts: Low red blood cell counts (anemia) can make you feel fatigued, weak, or short of breath. Low white blood cell counts (neutropenia) can increase your risk of infection.
- Low platelet counts can increase the risk of bruising or bleeding. If your red blood cells or platelets become too low, you may need a blood transfusion.
- Gastrointestinal side effects: including nausea, vomiting, diarrhea, constipation, or decreased appetite.
- Mouth sores.
- Hair loss.
- Fatigue, weakness.
- Skin damage at the site of the IV.
- Fluid retention (edema) can occur in your arms, legs, abdomen, or lungs.

Less likely (1-10%):

- Muscle and joint aches.
- Skin rash, peeling, or itching.
- Changes in the fingernails/toenails.
- Eye irritation or watery eyes.
- Abdominal pain.

Rare, but serious side effects include (<1%) :

- Allergic reactions, which may include itching, fevers, chills, flushing, swelling, or chest tightness. Rarely, serious allergic reactions may occur including lowering of blood pressure or shortness of breath causing you to pass out.
- Neurologic side effects: Numbness, tingling, or pain in the hands and feet, decreased deep tendon reflexes, weakness, or seizures.
- Heart side effects: Heart failure or weakening of the heart muscle, abnormal heart rhythm, or fluid around the heart.
- Liver damage or failure.
- Damage to your colon (large intestine).
- Development of acute leukemia (cancer of the blood).
- Death from severe bleeding or infection is possible, but very unlikely.

Carboplatin Risks (standard treatment):

Likely (10-25%):

- Low white blood cell counts - this may make you more open to infection
- Low platelet count - this may make you bruise more easily and bleed longer if injured
- Low red blood cell count which may cause tiredness or shortness of breath or fatigue
- Tiredness
- Loss of appetite and weight loss
- Diarrhea, constipation, nausea and vomiting, and abdominal pain
- Complete hair loss
- Skin rash
- Changes in taste
- Changes in minerals in the blood such as magnesium and potassium

Less likely, but serious (1-10%):

- Numbness or tingling in fingers or toes
- Ringing in the ears and hearing loss
- Allergic reactions
- Chills and fever with aches and pains
- Decrease in kidney or liver function
- Sores in mouth and throat (that can lead to difficulty swallowing and dehydration)
- Changes in vision

Rare, but serious (<1%):

- Seizures
- Other cancers such as acute leukemia

- Kidney failure requiring dialysis
- Deafness
- Death

Cisplatin Risks (standard treatment):

Likely (10-25%):

- Nausea
- Vomiting
- Mild to moderate decreases in kidney function,
- Imbalances in the level of some minerals in the blood (especially magnesium);
- Decreased white blood cells which can lead to infection
- Decreased red blood cells which can lead to anemia (feelings of being tired and loss of energy)
- Decreased platelet count, which can lead to bruising and bleeding after injury

Less likely (1-10%):

- Numbness and loss of taste
- Heart problems
- Thinning or loss of body hair
- Mouth sores
- Abnormal liver function tests (blood tests to show how your liver is working)
- Hearing loss
- Eye problems

Rare but Serious (<1%):

- Allergic reactions, kidney failure, and possible death

Reproductive Risks:

If there is ANY chance that you can get pregnant, you must either agree to not have vaginal intercourse or use TWO types of birth control (one from each list below) AT THE SAME TIME.

You must use two types of birth control at the same time for medical reasons all during treatment (including during temporary breaks from treatment), and for at least 3 months after treatment has stopped. You must talk to the doctor before changing any birth control methods you have already agreed to use.

Primary forms
- tubal sterilization (tubes tied)
- partner's vasectomy
- intrauterine device

Secondary forms
- male latex condom with or without spermicide
- diaphragm with spermicide
- cervical cap with spermicide
- vaginal sponge (contains spermicide)

Any birth control method can fail. The reports of birth control failing are more frequent for female patients who use only a single form of birth control. Using two forms of birth control at the same time greatly reduces the chances of pregnancy.

Females who become pregnant while in this study or within 3 months after stopping study medication, will be discontinued from the study. The study doctor will remain in contact with you to determine the outcome of your pregnancy. Males must take adequate precautions to avoid fathering a child. You must inform the study doctor if your partner becomes pregnant during the study or within 3 months after stopping study medication. The study doctor will remain in contact with you to determine the outcome of the pregnancy.

MEN

All men must use an acceptable form of birth control while taking part in the study because the effects on sperm are not known. Acceptable forms of birth control are male latex condom (with or without spermicide) or vasectomy. (IF APPLICABLE) Also, men should not donate sperm or semen while taking part in the study because the effects on sperm are not known.

Scan Risks:

CT scans will expose you to controlled amounts of radiation. The amount of radiation exposure from one CT scan is about the same as the amount of radiation a person would get from natural surroundings in 3 years. CT scan with perfusion is the same radiation exposure and risk as a standard CT scan.

In very rare cases, contrast or radioactive agents used as part of the CT scan process cause allergic reactions. Some people experience mild itching or hives. Signs of a more serious allergic reaction include shortness of breath and swelling of the throat or other parts of the body, abdominal pain, or vomiting. You will be monitored closely for these allergic reactions and will be treated immediately should one occur. If you are allergic to iodine, notify your doctor. The contrast substance injected during the CT scan may cause pain, burning feeling, sweating and rarely a serious allergic reaction that can be serious - if you know you're allergic to iodine; you must inform your doctor immediately. The contrast agent used in the CT scan may cause kidney damage, especially if you're diabetic, dehydrated and if you're older. In addition your thyroid function may be affected. Please inform your doctor if this is the case.

Endoscopic laryngoscopy with or without Biopsy Risks

There are some risks associated with a endoscopic laryngoscopy including injury to teeth, lips and/or gums, bleeding after biopsy, failure of the vocal cord to heal after biopsy, and a risk of swelling that can become severe enough to block the air passages although with proper care this is unlikely. There is also a risk for the airway to become blocked from inflammation of the back of the throat. As with any type of surgery done under general anesthesia there are risks including infection, a reaction to the drugs, breathing difficulties and even death.

Blood Draw and Injection risks

The collection of your blood and injection of dyes into your veins may cause the following: pain, swelling, bruising, irritation or redness at the site, feeling faint or light-headed, infection at the site of the needle puncture.

Genetic Risks:

The federal Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Under this law:

- Health insurance companies and group health plans may not request your genetic information that we obtain from this research
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums
- Employers with 15 or more employees may not use your genetic information that we obtain from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment

GINA does not apply to the following groups, however these groups have policies in place that provide similar protections against discrimination:

- Members of the US Military receiving care through Tricare
- Veterans receiving care through the Veteran's Administration (VA)
- The Indian Health Service
- Federal employees receiving care through the Federal Employees Health Benefits Plans

5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?

The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. It is important that you report any illnesses or side effects to your study doctor as soon as possible. You should not wait until your next scheduled visit. If you need immediate treatment and are unable to return to the clinic/hospital where the study drugs were given, your study doctor should be contacted as soon as possible.

5.3 If I take part in this study, can I also participate in other studies?

Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?

If you agree to be in this study, there may or may not be direct medical benefit to you. Your cancer may shrink and you may feel better, but this cannot be guaranteed. We hope the information learned from this study will benefit other patients with cancer in the future.

5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?

Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. OTHER OPTIONS

6.1 If I decide not to take part in this study, what other options do I have?

Your study doctor will discuss the benefits and side effects of other treatments; including the treatment of only your symptoms should you choose not to have any further cancer therapy. Other investigational studies with chemotherapy, hormones, radiation therapy, or other anti-cancer drugs may be available for your disease. Please ask any questions you may have and take as much time as you need to make your decision.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?

You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to continue being in this study. When you withdraw your permission, no new health information that might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

7.2 Could there be any harm to me if I decide to leave the study before it is finished?

You should tell the study doctor if you decide to stop your participation and you will be advised whether any additional tests may need to be done for your safety.

7.3 Could the researchers take me out of the study even if I want to continue to participate?

If you fail to comply with the instructions of your study doctor, or if your study doctor feels it is in your best interests, he/she may withdraw you from the study at any time and without your consent. Your participation in this study will also be stopped if it is felt at any time that your participation could be harmful to your health. Your participation in this study may be ended at any time for medical reasons or because the sponsor finds it necessary to limit or terminate this study.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?

AT-101 will be provided free of charge by Ascentage Pharma Group Corporation (APGC).

The study will cover all costs that are not considered a part of the routine/standard care for your condition. Taking part in this study may result in added costs to you, such as transportation to the clinic/hospital for the increased number of visits. All procedures, such as routine blood tests, diagnostic studies (i.e. CT scans), doctor visit charges, lab charges, and Docetaxel/Platinum which are standard of care for the treatment of your cancer will be charged to you or your insurance carrier in the usual way.

Examples of standard of care items that you or your health plan will pay for are:

- Health care given during the study as part of your regular care

- Items or services needed to give you study drugs or devices
- Monitoring for side effects or other problems
- Treatment of complications
- Deductibles or co-pays for these items or services.

If you do not have a health plan, or if you think your health plan may not cover these costs during the study, please talk to the researchers listed in Section 10 below or call your health plan's medical reviewer. If you get a bill you think is wrong, call the researchers' number listed in section 10.

If you are injured or become ill as a result of participation in this study, contact Dr. Frank Worden immediately. You can tell the doctor in person or call him at 734-647-8902.

The study team has given you instructions about this research study. It is important that you follow these instructions carefully. If you get sick, have a medical complication, or are injured as a result of your being in the study, call Dr. Francis Worden immediately at 734-647-8902. The doctor will either treat you or send you to another doctor for treatment.

You will get free medical care at the UMHS for any complication, injury, or illness caused by the study drug, device, or procedure. The UMHS and the study doctor are responsible for determining whether your condition was the result of your participation in the study.

The UMHS will pay for your treatment only if the need for treatment has been caused by the study drug, device or procedure. This means that you or your health plan must pay for any treatment that is part of your usual medical care or that is related to a medical condition you had before participating in the study.

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

8.2 Will I be paid or given anything for taking part in this study?

You will not be paid for participating in this study.

8.3 Who could profit or financially benefit from the study results?

Ascentage Pharma Group Corporation (APGC), the company who makes AT-101, could benefit financially from the study results. The University of Michigan, and Dr. Shoameng Wang, a researcher in the Cancer Center, also have a financial interest in the company and in the inventions being studied. They might one day profit if this and other studies show that this approach helps against cancer. Dr. Wang is not involved in this study.

Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the use of the data or discoveries. You will not have rights to these discoveries or any proceeds from them.

9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how your privacy and the confidentiality of your research records will be protected in this study.

9.1 How will the researchers protect my privacy?

Patient confidentiality is a top priority. We shall put the information collected about you during the study into a computerized research record. Your name and identifying information will be kept in this record, but only study team individuals will have access to this information. Your record will be assigned a unique code which will be used to link your treatment data with the data obtained from analysis of your specimens. We shall keep your research record confidential as required by law and institutional policy. You will not be individually identified in any reports of this study. Information that directly identifies you will be shared with investigators or study team members that are involved in this study.

If you agree to have some of your blood and tumor specimens stored for futures use, investigators involved in the SPORE program to study head and neck cancer biology, treatment and prevention will be able to withdraw specimens or data as required by their individual projects. Investigators not involved in this program must secure an appropriate Institutional Review Board (ethics board) approval in order to be permitted access to specimens. Specimens will be distributed, and any data provided will have all personal identifying information removed.

9.2 What information about me could be seen by the researchers or by other people? Why? Who might see it?

Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study. Information about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- Mental health care records (except psychotherapy notes not kept with your medical records)
- Alcohol/substance abuse treatment records
- Your AIDS/HIV status
- All records relating to your condition, the treatment you have received, and your response to the treatment
- Billing information

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.
- University, Food and Drug Administration (FDA), and/or other government officials may need the information to make sure that the study is done in a safe and proper manner.
- Study funders, or safety monitors or committees, may need the information to:
    - Make sure the study is done safely and properly
    - Learn more about side effects
    - Analyze the results of the study
- Insurance companies or other organizations may need the information in order to pay your medical bills or other costs of your participation in the study.
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your regular UMHS medical record.

- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article, but would not include any information that would let others know who you are.

A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by US law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

9.3 What happens to information about me after the study is over or if I cancel my permission?

As a rule, the researchers will not continue to use or disclose information about you, but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over. Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help University and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan Notice of Privacy Practices. This information is also available on the web at http://www.med.umich.edu/hipaa/npp.htm. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

9.4 When does my permission expire?

Your permission expires at the end of the study, unless you cancel it sooner. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below).

10. CONTACT INFORMATION

10.1 Who can I contact about this study?

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator: Francis Worden, M.D.
Mailing Address: University of Michigan Health System
Internal Medicine/ Hematology/Oncology
[redacted]

Telephone: [redacted]

You may also express a concern about a study by contacting the Institutional Review Board listed below, or by calling the University of Michigan Compliance Help Line at 1-866-990-0111.

University of Michigan Medical School Institutional Review Board (IRBMED)
2800 Plymouth Rd
Building 520, Room 3214
Ann Arbor, MI 48109-2800
Telephone: 734-763-4768
Fax: 734-615-1622
e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy, contact the University of Michigan Health System Privacy Officer at 1-866-990-0111.

When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?

Your signature in the next section means that you have received copies of all of the following documents:

- This "Consent to be Part of a Research Study" document. (*Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.)*

12. CONSENT FOR PARTICIPATING IN OPTIONAL RESEARCH

Please mark your choice regarding participation in optional research studies below.

1. A specimen of my tumor will be sent to the Head and Neck Cancer Research Laboratory for additional research for related studies. I understand that it is my choice whether or not to take part in this testing.

   Initial: _____ Date: _____ I **agree** to having a specimen of my tumor sent to the above research lab for additional research for related studies

   Initial: _____ Date: _____ I **do not agree** to having a specimen of my tumor sent to the above research lab for additional research for related studies.

2. A sample of my blood will be sent to the Head and Neck Cancer Research Laboratory and stored to create cell lines for harvesting DNA. I understand that it is my choice whether or not to take part in this testing.

   Initial: _____ Date: _____ I **agree** to having my blood sample stored to create cell lines for harvesting DNA.

   Initial: _____ Date: _____ I **do not agree** to having my blood sample stored to create cell lines for harvesting DNA.

13. SIGNATURES

Research Subject:

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with _____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Signature of Subject: _____ Date: _____

Name (Print legal name): _____

Patient ID: _____ Date of Birth: _____

Principal Investigator (or Designee):

I have given this research subject (or his/her legally authorized representative, if applicable) information about this study that I believe is accurate and complete. The subject has indicated that he or she understands the nature of the study and the risks and benefits of participating.

Name: _____ Title: _____

Signature: _____ Date of Signature: _____

PERSONAL CENSUS FORM

Name _____ Date _____

The National Cancer Institute requires that The University of Michigan Comprehensive Cancer Center report race and ethnicity information about people who participate in clinical research to ensure that all populations are offered the opportunity to participate.

☐ Check here if you do not wish to provide some or all of the information below.

1. What race do you consider yourself to be? (Please select *one or more*)
   - ☐ American Indian/Alaska Native[a]
   - ☐ Asian[b]
   - ☐ Black or African American[c]
   - ☐ Native Hawaiian or Other Pacific Islander[d]
   - ☐ White[e]
   - ☐ More than one race[f]

2. Do you consider yourself to be Hispanic[g]? ☐ Yes ☐ No

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[a] American Indian or Alaska Native- A person having origins in any of the original peoples of North, Central, or South America, and who maintains tribal affiliation or community attachment.

[b] Asian- A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent, including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand and Vietnam.

[c] Black or African American- A person having origins in any of the black racial groups of Africa. (Terms such as "Haitian" or "Negro" are sometimes used in addition to "Black" or "African American.")

[d] Native Hawaiian or Other Pacific Islander- A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.

[e] White- A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.

[f] More than one race- (It is preferred that this be selected in addition to the selection of the specific races listed above, but this may also be solely selected.)

[g] Hispanic or Latino- A person of Mexican, Puerto Rican, Cuban, Central or South American, or other Spanish culture or origin, regardless of race. The term "Spanish origin" is sometimes used in addition to "Hispanic" or "Latino."