University of Wisconsin-Madison
Consent to Participate in Research
and
Authorization to Use Protected Health Information for Research

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Study Title for Participants: Study of INCB081776 with radiation therapy and other treatments for head and neck cancer

Formal Study Title: UW23121: Pilot Study of INCB081776 Together with Palliative Radiation and Anti-PD-1 Checkpoint Blockade with Pembrolizumab in Patients with Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma

Lead Researcher: *Justine Yang Bruce, MD*

Institution: *University of Wisconsin Carbone Cancer Center*

_____ _____

Participant name MR#

Key Information

The information in this section is to help you decide whether or not to be a part of this study. You can find more detailed information later on in this form.

Why are researchers doing this study?

We are doing this research because patients with recurrent head and neck cancer have limited treatment options. INCB081776 is an investigational drug which means it has not been approved by the US Food and Drug Administration (FDA) for use as a prescription or over-the-counter medication. INCB081776 blocks two proteins called Axl and Mer that may allow cancer cells to develop resistance to chemotherapy drugs. We would like to see whether blocking these proteins with the INCB081776 can activate your immune system to fight your cancer.

Anti-PD-1 therapy is known as an immune checkpoint inhibitor. This is a type of drug that targets immune “checkpoints” to reduce your body’s immune system response that could protect a tumor. This allows the cancer treatment to better treat the tumor. The anti-PD-1 therapy drug used in this study is pembrolizumab. Pembrolizumab is FDA approved for treatment of head and neck cancer but using it in combination with INCB081776 and radiation therapy is not considered standard of care.

We will be utilizing palliative radiation therapy combined with the INCB081776 and anti-PD-1 therapy. Palliative radiation therapy is used to treat metastatic tumors or tumors that are causing symptoms. Palliative radiation therapy has been shown to work well with anti-PD-1 therapy for symptom management.

We invite you to take part in a research study about INCB081776 and how it works combined with palliative radiation therapy and anti-PD-1 checkpoint blockade treatment for head and neck cancer. We are inviting you because you have a tumor that has recurred or spread after originating in the head and neck.

What will I need to do in this study?

The research team will ask you to undergo a minimum of 2 research biopsies (up to 3 research biopsies may be obtained unless previously collected tissue can be used) – once at baseline (unless tissue that was previously collected can be used), another biopsy prior to treatment with the Anti-PD-1 therapy, and after completion of palliative radiation if a fresh research biopsy was not done at baseline. You will also receive staggered treatment first – you will complete a 56 day cycle taking INCB081776 by mouth for the first 14 days, then receive Anti-PD-1 therapy via a vein in your arm on days 15 and 36. You will follow that up with palliative radiation therapy. Starting at Cycle 2, each cycle will be 21 days and you will continue to take the INCB081776 orally and receive the Anti-PD-1 therapy on day 1 of each cycle. This will continue until disease progression, if you have serious reactions to the drug combination, or if you withdraw.

You will also be required to have regularly scheduled eye exams at screening, during cycles 1-3, and follow-up at the end of treatment if abnormalities are observed.

We expect that you will be in this research study for 12 months.

You can find detailed information about the study procedures in the section called **If I take part in the study, what will I do?**

What are some reasons I might – or might not – want to be in this study?

Possible reasons you might want to participate	**Possible reasons you might not want to participate**
• I want to help researchers find out if the study treatment could help people with my condition. • I want the chance to get the study treatment, even though it may have	• I'm concerned about unknown side effects with an investigational drug. • I won't be able to take time off work to go to all the study visits.

unwanted side effects and doctors don't know if it's better. • Interested in contributing to scientific knowledge even though you won't benefit directly from the study.	

Do I have to be in the study?

No, you do not have to be in this study. Taking part in research is voluntary. If you decide not to be in this study, your choice will not affect your healthcare or any services you receive. There will be no penalty to you. You will not lose medical care or any legal rights. You can ask all the questions you want before you decide.

Instead of being in this research study, your choices may include: treatment with anti-PD-1 therapy alone (pembrolizumab), which is FDA approved for treatment of recurrent/metastatic head and neck squamous cell carcinoma. Your doctors might also offer palliative radiation therapy, which has been determined to be a standard treatment option for you.

Detailed Information

The following is more detailed information about this study in addition to the information listed above.

How is research different from health care?

When you go to a health provider for care, the provider focuses on how to help you as an individual. When you take part in a study, you are helping to answer a research question, like how safe or effective a treatment is, or what dose to use. Treatment is based on a study plan, not on you as an individual.

Who can I talk to about this study?

If you have questions, concerns, or complaints, or think that participating in the research has hurt you, talk to the research team at 608-915-0100.

If you have concerns about your rights as a research participant or have complaints about the research study or study team, call the confidential research compliance line at 1-833-652-2506. UW Staff not part of the study team will work with you to address concerns and assist in resolving any complaints.

If I take part in the study, what will I do?

If you decide to participate in this research study, the researchers will ask you to attend regular study visits for treatment, lab tests, and tumor evaluations. The visits will occur every few weeks, initially during a 56 day cycle, then consecutively after that starting at Cycle 2 consisting of a 21 day cycle. These visits may take between 2 and 6 hours,

depending on what is required at the time of your specific visit. Your study doctor will use these visits to assess if the study treatment is working and if you are having side effects. The length of time that you will be in this study will depend on how well your cancer responds to treatment. Follow up will continue after your treatment ends. You will stay in the study as long as there is evidence that your disease is not growing and you are not experiencing unacceptable side effects.

We have multiple facilities for delivering care, therefore you may have study visits in more than one location. Your study team will work closely with you when scheduling your study visits.

This study involves a screening period, treatment period, and a follow-up period. Some of the procedures performed at the research visits would be performed regardless of your participation in this study and are called “standard of care” (SOC). Others are performed solely for this study and are referred to as “research-related” (RR). All procedures that will be performed as listed below.

Screening (Day -28)

Screening/Baseline Visit (Day -28 to -1)

- Assessment of medical history [Standard of Care (SOC)]
- Physical examination including vitals, weight and height (SOC)
- Evaluation of your ability to carry out daily activities (SOC)
- Assessment of medication history (SOC)
- Blood tests to evaluate if treatment can be safely given and establish baseline levels (about 1-2 teaspoons of your blood will be taken) (SOC)
- Pregnancy (blood or urine) test if applicable (SOC)
- Tumor tissue collection for banking (SOC)
- Eye exams (RR)
- Research biopsy #1 (archival tissue or fresh research biopsy if archival tissue is not available) (RR)

Cycle one

Cycle 1 Day 1 (C1D1

- Physical examination including vitals, weight (SOC)
- Assessment of medication history (SOC)
- Evaluation of your ability to carry out daily activities (SOC)
- Blood tests to evaluate if treatment can be safely given if required per protocol (about 1-2 teaspoons of your blood will be taken) (SOC)
- Adverse event assessment (SOC)
- Begin INCB081776 therapy (home therapy Days 1- 56) (RR)

Cycle one, Day 8 (C1D8)

- Eye exams (RR)
- Research biopsy #2 (performed before treatment with pembrolizumab and palliative RT, cycle 1 days 9 to 14) (RR)

Cycle one, day 15 (C1D15)

- Adverse event assessment (SOC)
- Assessment of medication history (SOC)
- Blood tests to evaluate if treatment can be safely given (about 1-2 teaspoons of your blood will be taken) (SOC)
- Administer anti-PD-1 on Day 1 (RR)
- Eye exams (RR)
- Physical examination including vitals, weight (SOC)
- Evaluation of your ability to carry out daily activities (SOC)

Palliative Radiation Therapy (to be completed between C1D29 to C1D33)

- Radiation Therapy Treatment (SOC)

Cycle 1, Day 29 (C1D29)

- Eye exams (RR)

Cycle 1, Day 36 (C1D36)

- Physical examination including vitals, weight (SOC)
- Assessment of medication history (SOC)
- Evaluation of your ability to carry out daily activities (SOC)
- Blood tests to evaluate if treatment can be safely given (about 1-2 teaspoons of your blood will be taken) (SOC)
- Adverse event assessment (SOC)
- Administer anti-PD-1 (RR)

Cycle 1 day 37 to day 49

- Research biopsy #3 (performed after treatment with INCB081776, pembrolizumab and palliative RT **only** if just one research biopsy has been obtained) (RR)

Cycle two

Cycle two+, day 1 (C2+D1)

- Physical examination including vitals, weight (SOC)

- Assessment of medication history (SOC)
- Evaluation of your ability to carry out daily activities (SOC)
- Blood tests to evaluate if treatment can be safely given (about 1-2 teaspoons of your blood will be taken) (SOC)
- Obtain Pill Diary (RR)
- Adverse event assessment (SOC)
- Administer anti-PD-1 on Day 1 (SOC)
- Administer INCB081776 therapy (RR)
- Eye exam (RR)

Cycle 3 and every THIRD cycle, day 1

- Disease assessment
- TSH, reflex free T4
- Eye exam
- Perform disease assessments (SOC)
    - The following may be used for assessments:
        - CT of neck
        - PET scan and/or CT of Chest ± CT of Abdomen/Pelvis

Safety Follow-up (30 days after therapy completion +/- 7days)

This visit will be performed per standard of care, 30 days after the last dose of study therapy. This can be due to disease progression or due to other reasons for discontinuation as noted above.

- Adverse event assessment (SOC)
- Physical examination including vitals, weight (SOC)
- Evaluation of your ability to carry out daily activities (SOC)
- Blood tests to ensure you are recovering from any treatment side effects (about 1-2 teaspoons of blood) (SOC)
- Assessment of medication history (SOC)
- Eye exam (if previous exam was abnormal)

Study Treatment overview:

INCB081776 is administered orally via capsule daily for each cycle. The capsule should be taken in the morning with a full glass of water. You will be required to fast at least 2 hours before and 1 hour after taking the dose.

Pembrolizumab or the anti-PD-1 therapy is administered via an IV infusion once every 21 days. An IV infusion is performed via a needle and tube inserted into your vein.

Palliative Radiation therapy is radiation therapy that is administered during cycle 1 over the course of days 29-33. The radiation therapy is administered daily for 5 days.

Eye Exam Overview:

Eye exams are performed to ensure no significant changes occur while undergoing study treatment. The types of exams performed are comprehensive eye exams, the use of an Amsler grid, the Humphrey visual field test, fundus photography, and OCT.

Comprehensive eye exams consist of tests checking eye pressure, movement, clarity of vision, and eye structure.

An amsler grid will be provided to allow you to monitor your vision daily. Amsler grids are a grid with a dot in the center. They are used to monitor possible distortions in your visual field.

The Humphrey visual field test uses lights of varying intensity which light up in different parts of the testing field while you focus on a certain spot. This test can identify blind spots in your peripheral vision.

Fundus photography is the use of a specialized camera to take pictures of the inside rear part of your eye. This is used to monitor any possible changes that could take place internally in your eye.

Optical Coherence Tomography (OCT) is a non-invasive test that scans color coded images of your retina to monitor any possible changes.

Research Biopsies:

Research biopsies are being collected in order to check for changes within the tumor. The research biopsies will be collected at up to 3 timepoints – baseline (which can be fresh or previously collected tumor tissue), prior to treatment with the anti-PD-1 therapy (collected fresh), and after the completion of the palliative radiation therapy (collected fresh and only required if no fresh tissue was collected for the first biopsy). The biopsies will be collected using a cut-forceps procedure if possible or using the core needle method. Core needle biopsy procedures use a long hollow tube to obtain a sample of tissue. The cut-forceps procedure is when only a sample of the tissue is cut from the tumor area and removed for purposes of tissue testing. During the biopsy, a doctor will first numb the area and then make a small cut into the skin where either the needle is inserted or where the forceps will be used.

Protected health information (PHI) used in this study

Protected health information, also called PHI, is information about your physical or mental health that includes your name or other information that can identify you, like

your date of birth or medical record number. To do this study, we will use the following kinds of PHI:

- Results of tests or procedures done as part of the study
- Things you tell the researchers about your health
- Information currently in your medical records as well as information added to your medical records during the course of this study. This information could include your medical history; your diagnosis; lab test results. We will get this information from your health care providers.

What happens if I say yes, but I change my mind later?

You can leave the research at any time. If you choose to leave the study, your choice will not affect your healthcare or any services you receive. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

If you decide to leave the research, contact the investigator so that the investigator can tell you how to leave the study safely and we will ask you to come in for a final study visit to check your health.

If you stop being in the research, already collected data may not be removed from the study database. You may be asked whether the investigator can collect data from your routine medical care. If you agree, this data will be handled the same as research data.

Your authorization for researchers to use your protected health information (PHI) does not have an end date. However:

- You can choose to take back your authorization for researchers to use your health information. You can do this at any time before or during your participation in the research.
- If you take back your authorization, information that was already collected may still be used and shared with others, but the researchers will no longer be able to collect NEW information about you.
- If you take back your authorization, you will not be able to take part in the research study.
- To take back your authorization, you will need to tell the researchers by writing to the Lead Researcher, Justine Yang Bruce, MD, at University of Wisconsin Carbone Cancer Center (UWCCC), 1111 Highland Avenue, WIMR 3109, Madison, WI 53705

Will being in this study help me in any way?

Being in this study may relieve your symptoms. The study treatment may work better than standard care for your condition, but we cannot promise this will happen. The study treatment might not work at all, or it might have bad side effects. Even if the study does not help you directly, your participation in this study may help other people in the future by helping us learn more about how treatment with anti-PD-1 and INCB081776 in conjunction with palliative radiation therapy could better treat recurrent head and neck cancer.

What are the study risks?

Known Interventional Risks:

INCB081776 Risks

Possible Side Effects Associated with INCB081776

Not all of the side effects of INCB081776 are currently known. This study drug is investigational and is not a part of the usual approach for treating this type of cancer. Known risks for this treatment are listed below:

Very Common Risks (≥ 1/10):

- Anemia
- Fatigue
- Nausea
- Vomiting
- Eye toxicities*
    - Blurry vision
    - Decreased vision
    - Vision loss

Common Risks (≥ 1/100 to < 1/10):

- inflammation of the liver

*Based on information known regarding INCB081776, it is anticipated that eye toxicities would be temporary and would resolve once drug is stopped. The study requires frequent eye assessments to ensure safety and catch changes to vision quickly.

In addition to these risks, this research may hurt you in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death.

The research may also hurt a pregnancy or fetus in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death. You should not be

or become pregnant or participate in sex that could result in pregnancy while on this research study.

Anti- PD-1 Therapy Risks

Common risks:

- Diarrhea
- Shortness of breath
- Inflammation of the lungs
- Inflammation of the liver
- Thyroid disorders and diabetes
- Inflammation of the brain

Palliative radiation therapy Risks:
Palliative radiation therapy is utilized as a treatment for symptomatic lesions from metastatic disease.

Expected side effects and toxicities associated with radiation therapy include:

- Inflammation of the surrounding tissue
- Pain
- Bleeding
- Increased risks of fractures
- Peeling skin

Other risks from research-related procedures
Biopsy tissue collection:
Common risks include:

- Biopsy site irritation
- Bleeding
- Swelling
- Infection

Rare risks include:

- Air pressure on the lung which could cause lung collapse

Forcep biopsy risks:
Common risks include:

- Bleeding
- Infection
- Swelling
- Bruising

Blood draws for clinical laboratory testing risks include bruising, swelling at the injection site, dizziness and lightheadedness.

Optical Coherence Tomography (OCT) Eye Exam: Your ophthalmologist may put dilating drops in your eye. Your eyes may be sensitive to light for several hours after the exam.

For more information about risks and side effects, ask the study doctor.

There is a risk that your information could become known to someone not involved in this study.

In addition to these risks, this research may hurt you in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death.

Will being in this study cost me anything?

You and your insurance company will be charged for the health care services that you would ordinarily be responsible to pay such as clinic visits, all costs associated with pembrolizumab, routine lab work to monitor for safety, all costs associated with radiation therapy and scans that are used to follow your disease. You remain responsible for all deductibles, co-pays, and balances under your insurance. In some cases, insurance will not pay for services ordinarily covered because these services were performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay. A member of the study team can talk to you about what procedures would be considered standard of care and the coverage of those costs.

The study will provide the following study-related items/procedures for you at no cost during participation in the study:

- INCB081776 will be provided free of charge by the InCyte Corporation.
- All charges that are associated with obtaining the biopsies, and/or obtaining tissue from pathology for banking,
- Charges associated with eye exams obtained for study purposes.

What happens to the information collected for the research?

We have strict rules to protect your personal information and protected health information (PHI). We will limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. The study will be protected by a Certificate of Confidentiality from the National Institutes of Health. This means that even if the police or courts ask to look at the data we have collected, we will not share any information that would identify you as

a participant in the study. Once issued, the Certificate will retroactively cover information collected since the beginning of the study.

However, we cannot promise complete confidentiality. Federal or state laws may permit or require us to show information to university or government officials and to study sponsors responsible for carrying out or monitoring this study. This includes University of Wisconsin and its representatives and affiliates, including those responsible for ensuring compliance, such as the Human Research Protection Program, and the Food and Drug Administration.

We may also have to tell appropriate authorities, such as child protective services or health care providers, if we learn during the study that you or others are at risk of harm (for example, due to child or elder abuse, or suicidal thoughts).

Authorizing the research team to use your PHI means that we can release it to the people or groups listed in this form for the purposes described in this form. Once your health information is released outside UW-Madison or UW Health it may not be protected by privacy laws and might be shared with others.

If the sponsor pays any of your medical expenses, we may be required to give the sponsor your name, date of birth, and Medicare ID or social security number.

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.

Will information from this study go in my medical record?
A medical record may be created for you if you do not already have one. Your medical record might say that you participated in this study, and a copy of this consent and authorization form might go in your medical record. All of the information regarding your cancer treatment will be in your medical record. Both you and your UW Health providers will be able to see these results. Both you and your UW Health providers will be able to see these results.

Will I receive the results of research tests?
Most tests done as part of a research study are only for research and have no clear meaning for health care. No clinical information will be obtained from the research biopsies; thus you will not be informed of any results. The eye exams are considered clinical information, and you would be informed of findings in your medical record.

Can I be removed from the research without my agreement?
The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include:

- your health changes and the study is no longer in your best interest

- you do not follow the study rules or no longer meet the requirements to be in the study
- the study is stopped by the sponsor or researchers

What else do I need to know?

What happens if I am injured or get sick because of this study?
If you are injured or get sick because of this study, medical care is available to you through UW Health, your local provider, or emergency services, as it is to all sick or injured people.

- If it is an emergency, call 911 right away or go to the emergency room.
- For non-emergency medical problems, contact the study team for instructions.
- Call the Lead Researcher, Justine Yang Bruce, MD, at 608-915-0100 to report your sickness or injury.

Here are some things you need to know if you get sick or are injured because of this research:

- If the sickness or injury requires medical care, the costs for the care will be billed to you or your insurance, just like any other medical costs.
- Your health insurance company may or may not pay for this care.
- No other compensation (such as lost wages or damages) is usually available.
- UW-Madison and UW Health do not have a program to pay you if you get sick or are injured because of this study.
- By signing this consent form and taking part in this study, you are not giving up any legal rights you may have. You keep your legal rights to seek payment for care required because of a sickness or injury resulting from this study.

Will I receive anything for participating?
We will provide $70 for each of the eye exams that occur at baseline, C1D8, C1D15 and C1D29 to ease the burden of those visits.

We will provide remuneration of $100 per fresh tissue biopsy.

Permission to communicate about the study by email
We are requesting your email address so we can so we can exchange information about scheduling, etc. Email is generally not a secure way to communicate about your health as there are many ways for unauthorized users to access email. You should avoid sending sensitive, detailed personal information by email. Email should also not be used to convey information of an urgent nature. If you need to talk to someone immediately, please contact the Lead Researcher, Dr. Justine Yang Bruce at 608-915-0100. You do not have to provide your email address to participate in this study.

How many people will be in this study?
We expect about 12 people will be in this research study.

Who is funding this study?
This research is being funded by NCI through a SPORE grant with Incyte corp. providing the INCB081776 (research drug) for the study.

Will my data and samples be used for future research?

This study is collecting data and samples from you. We would like to make your data and samples available for other research studies that may be done in the future. The research may be about similar diseases or conditions to this study. However, research could also be about unrelated diseases, conditions, or other types of research. These studies may be done by researchers at this institution or other institutions, including commercial entities. Your data and samples may be shared with researchers around the world. Our goal is to make more research possible. We plan to keep your data and samples indefinitely. To get your data and samples, future researchers must seek approval from this institution and review by an IRB may be required.

Your name and identifying information will be removed from any data and samples you provide before they are shared with other researchers. Researchers cannot easily link your identifying information to the data and samples.

We will do our best to protect your data and samples during storage and when they are shared. However, there remains a possibility that someone could identify you. There is also the possibility that people who are not supposed to might access your data and samples. In either case, we cannot reduce the risk to zero.

It is your choice whether or not to let researchers share your data and samples for research in the future. If you say “yes,” you can change your mind later. If you say “no,” you can still fully participate in this study. If you change your mind and no longer wish to have us store or share your data and samples, you should contact the investigator. We will do our best to honor your request and to get back any data and samples that have been shared with other researchers. However, there may be times we cannot. For example, if we do not have a way to identify your data and samples, we will not be able to get them back. In addition, if the data and samples have already been used for new research, the information from that research may still be used. We will destroy any data and samples we have or are able to get back.

Please initial next to your choice:

_____YES, my data and samples may be used in other research studies

_____NO, my data and samples MAY NOT be used in other research studies.

Information about genetic research

Future research using your stored samples could involve genetic analysis. Some of the tests we will perform on your stored biopsy samples will be genetic testing, which is done on your DNA. DNA, or deoxyribonucleic acid, carries the genetic instructions for the cells that make up your body. Genes tell your body how to do things like form your spine, or what color your eyes should be.The Genetic Information Nondiscrimination Act (GINA) prohibits health insurance companies or health plan administrators from requesting or requiring genetic information of you or your family members or using such information for decisions regarding your eligibility for insurance or your premiums. However, this law does not provide the same protection for disability, life insurance, or long-term care insurance. GINA also prohibits most employers (with 15 employees or more) from using genetic information when making decisions on your employment, including decisions related to hiring, firing, promotion, pay, and job assignments.

Agreement to participate in the research study

You do not have to sign this form. If you refuse to sign, however, you cannot take part in this research study. If you sign the line below, it means that:

- You have read this consent and authorization form.
- You have had a chance to ask questions about the research study, and the researchers have answered your questions.
- You want to be in this study.
- You give authorization for your protected health information to be used and shared as described in this form.

Signature of participant	Date

Printed name of participant

Signature of person obtaining consent	Date

Printed name of person obtaining consent

The following witness line is to be signed only if this consent form is provided as a written summary and accompanied by a short form foreign language consent, or if this consent form is read aloud to a participant unable to read.

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the participant, that the participant's questions were answered, and that consent was freely given by the participant.

Signature of witness to consent process

Date

Printed name of person witnessing consent process