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Squamous Cell CarcinomaSquamous Cell Carcinoma of the Head and Neck (SCCHN)

A Study to Evaluate the Efficacy and Safety of Multiple Treatment Combinations in Patients with Locally Advanced Squamous Cell Carcinoma of Head and Neck

A study to evaluate the anti-tumor effects of neoadjuvant treatment with Atezolizumab monotherapy, and combination treatments, consisting of Atezolizumab+Tiragolumab, Atezolizumab+Tiragolumab+ immune-modulating stereotactic body radiotherapy (iSBRT), and Atezolizumab+Tiragolumab+Carboplatin and Paclitaxel in Patients with Locally Advanced Squamous Cell Carcinoma of Head and Neck

Trial Status	Trial Runs In	Trial Identifier
Completed	5 Countries	NCT05459129 CO43613

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

A Phase Ib/II, Open-Label, Multicenter, Randomized Umbrella Study Evaluating The Efficacy and Safety of Multiple Treatment Combinations in Patients With Locally Advanced Squamous Cell Carcinoma of the Head and Neck (Morpheus-Head and Neck Cancer)

Trial Summary:

This is a Phase Ib/II, open-label, multicenter, randomized, umbrella study in participants with locally advanced squamous cell carcinoma of the head and neck (SCCHN). The study will enroll treatment-naive participants with resectable Stage III-IVA human papillomavirus (HPV)-negative, programmed death-ligand 1 (PD-L1)-positive SCCHN with measurable disease, as assessed by the investigator according to Response Evaluation Criteria in Solid Tumors, Version 1.1 (RECIST v1.1) who have not received systemic treatment for their disease.

Hoffmann-La Roche Sponsor	**Phase 1/Phase 2** Phase

NCT05459129 CO43613
Trial Identifiers

Eligibility Criteria:

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Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is the Morpheus Head and Neck Cancer clinical trial needed?

This Phase Ib/II, randomized umbrella study is designed to accelerate the development of treatments or treatment combinations by identifying early signals and establishing proof of concept clinical data in patients with resectable SCCHN. This study will assess the importance of simultaneously targeting multiple mechanisms of immune escape through immune cell priming and activation, tumor infiltration, and/or recognition of tumor cells for elimination.

2. How does the Morpheus Head and Neck Cancer clinical trial work?

This clinical trial is recruiting people who have a health condition called Locally Advanced Squamous Cell Carcinoma of Head and Neck (SCCHN) or Head & Neck cancer.

The purpose of this trial is to compare the effects, good or bad, of the Atezolizumab alone or treatment combinations Atezolizumab+Tiragolumab, Atezolizumab+Tiragolumab +iSBRT, and Atezolizumab+Tiragolumab+Carboplatin & Paclitaxel on patients with head and neck cancer. This study is designed with the flexibility to open new treatment arms as novel treatment combinations become available and to close existing treatment arms that demonstrate minimal clinical activity or unacceptable toxicity.

Participants will be given the clinical trial treatment in 21-day cycles for 2 cycles (6 weeks) prior to surgery to remove the primary tumor and metastatic lymph nodes. Participants will be seen by the clinical trial doctor starting 3 weeks after their surgery for a month. Hospital visits will include blood tests and assessments to see how the participant is responding to the treatment and any side effects they may be having. Participants' total time in the clinical trial will be roughly 2-3 years. Participants are free to stop trial treatment and leave the clinical trial at any time.

3. What are the main endpoints of the Morpheus Head and Neck Cancer clinical trial?

The main clinical trial endpoints (the main results that are measured in the trial to see if the medicine has worked) are to evaluate the efficacy of treatment against the head and neck cancer based on pathologic complete response (pCR) as determined by central pathologic review.

The other clinical trial endpoints are to evaluate the efficacy are Event-free survival (EFS), relapse-free survival (RFS), overall survival (OS) and objective response rate (ORR) according to RECIST v1.1 and the safety of treatment will also be evaluated.

4. Who can take part in this clinical trial?

People can take part in this trial if they are at least 18 years old and have been diagnosed with localized, advanced resectable Stage III-IVA squamous cell carcinoma (SCCHN) of head and neck.

People may not be able to take part in this trial if they have certain other medical conditions, have previously received certain treatments, eg. any prior therapy for SCCHN, including immunotherapy, chemotherapy, or RT. People may not be able to take part in this trial if they have received prior treatment with any of the drugs being used in this trial. People may not be able to take part in this trial if they are/planning to become pregnant, or are breastfeeding.

5. What treatment will participants be given in this clinical trial?

Everyone who joins this clinical trial will be split into groups randomly (like flipping a coin) and given either:

• **Atezolizumab**: administered by intravenous (IV) (in your vein) infusion over 30#60 minutes on Day 1 of each cycle, alone or in combination with any one of the following drugs:

• **Tiragolumab**: 600 mg IV on Day 1 of each cycle

• **Tiragolumab** 600 mg IV on Day 1 of each cycle + **iSBRT** 8 Gy x 3 doses - between Days 2 and 21 of Cycle 1

• **Tiragolumab** 600 mg IV on Day 1 of each cycle + **Paclitaxel** 175 mg/m2 on Day 1 of each cycle, **Carboplatin** AUC 5 mg/mL/min - IV on Day 1 of each cycle

Participants will have a 25% [e.g., equal to 1 in 4] chance of being placed in any of the treatment group.

This is a double-blinded trial, which means that neither the participant nor the clinical trial doctor can choose or know the group the participant is in, until the trial is over. This approach helps to prevent bias and expectations about what will happen. However, the participant’s clinical trial doctor can find out which group the participant is in, if their safety is at risk.

6. Are there any risks or benefits in taking part in this clinical trial?

The safety or effectiveness of the experimental treatment or use may not be fully known at the time of the trial. Most trials involve some risks to the participant, although it may not be greater than the risks related to routine medical care or the natural progression

of the health condition. Potential participants will be told about any risks and benefits of taking part in the clinical trial, as well as any additional procedures, tests, or assessments they will be asked to undergo. These will all be described in an informed consent document (a document that provides people with the information they need to make a decision to volunteer for a clinical trial). A potential participant should also discuss these with members of the research team and with their usual health care provider. Anyone interested in taking part in a clinical trial should know as much as possible about the trial and feel comfortable asking the research team any questions about the trial.

Risks associated with the clinical trial

Participants may have side effects (an unwanted effect of a drug or medical treatment) from the treatments used in this clinical trial. Side effects can be mild to severe and even life threatening, and can vary from person to person.

Atezolizumab, Tiragolumab, Paclitaxel, Carboplatin

Potential participants will be told about the known side effects of the study drugs, and where relevant, also potential side effects based on human and laboratory studies or knowledge of similar drugs.

Study drugs will be given by intravenous (IV) injection (in your vein). Participants will be told about any known side effects of intravenous injection.

Radiotherapy (iSBRT)

Participants will be told about any known side effects of immune-modulating stereotactic body radiotherapy (iSBRT) and where relevant, also potential side effects based on human and laboratory studies or knowledge of similar devices.

iSBRT will be used which is a highly focused radiation treatment that gives an intense dose of radiation concentrated on a tumor, while limiting the dose to the surrounding organs. Participants will be told about any known side effects of iSBRT and where relevant, also potential side effects based on human and laboratory studies or knowledge of similar procedures.

Potential benefits associated with the clinical trial

Participants' health may or may not improve from participation in the clinical trial, but the information that is collected may help other people who have a similar medical condition in the future.

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For more information about this clinical trial see the **For Expert** tab on the specific ForPatients page or follow this link to ClinicalTrials.gov https://clinicaltrials.gov/ct2/results?cond=&term=NCT05459129&cntry=&state=&city=&dist=1

Inclusion Criteria:

- Eastern Cooperative Oncology Group Performance Status of 0 or 1
- Histologically confirmed, resectable Stage III-IVA SCCHN
- Eligible candidate for R0 resection with curative intent at the time of screening
- HPV-negative test for oropharyngeal carcinoma, as determined locally by p16 immunohistochemistry (IHC), in situ hybridization, or polymerase chain reaction-based assay
- Measurable disease (at least one target lesion), as assessed according to RECIST v1.1
- PD-L1 expression, defined as a combined positive score (CPS) >= 1
- Adequate hematologic and end-organ function
- Negative HIV test with the following exception: patients with a positive HIV test at screening are eligible provided they are stable on anti-retroviral therapy, have a CD4 count >= 200/µL, and have an undetectable viral load.
- Negative hepatitis B surface antigen (HBsAg) test at screening
- Positive hepatitis B surface antibody (HBsAb) test at screening, or negative HBsAb at screening accompanied by either of the following: Negative total hepatitis B core antibody (HBcAb), Positive total hepatitis B core antibody (HBcAb) followed by a negative quantitative hepatitis B virus (HBV) DNA.

Exclusion Criteria:

- HPV-positive oropharyngeal cancer, as determined locally by p16 IHC, in situ hybridization, or by polymerase chain reactions-based assay
- Distantly metastasized SCCHN
- Any prior therapy for SCCHN, including immunotherapy, chemotherapy, or RT
- Prior treatment with any of the protocol-specified study treatments
- Treatment with investigational therapy within 42 days prior to initiation of study treatment
- Treatment with systemic immunostimulatory agents within 4 weeks or 5 drug-elimination half-lives (whichever is longer) prior to initiation of study treatment
- Prior allogeneic stem cell or solid organ transplantation
- Treatment with systemic immunosuppressive medication within 2 weeks prior to initiation of study treatment
- Treatment with a live, attenuated vaccine within 4 weeks prior to initiation of study treatment, or anticipation of need for such a vaccine during study treatment or within 5 months after the final dose of study treatment
- Active or history of autoimmune disease or immune deficiency
- History of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on screening chest computed tomography (CT scan)
- History of malignancy other than SCCHN within 5 years prior to screening, with the exception of malignancies with a negligible risk of metastasis or death (e.g., 5 -year OS rate>90%)
- Active tuberculosis
- Severe infection within 4 weeks prior to initiation of study treatment
- Treatment with therapeutic or prophylactic oral or intravenous (IV) antibiotics within 2 weeks prior to initiation of study treatment

- Significant cardiovascular disease such a New York Heart Association cardiac disease (Class II or greater), myocardial infarction or cerebrovascular accident within 3 months prior to initiation of study treatment, unstable arrhytmia, or unstable angina
- Major surgical procedure, other than for diagnosis, within 4 weeks prior to study initiation of study treatment, or anticipation of need for a major surgical procedure other than tumor resection, during the study
- Any of other disease, metabolic dysfunction, physical examination finding, or clinical laboratory finding that contraindicates the use of investigational drug, may affect the interpretation of the results, impair the ability of the patient to participate in the study, or renders the patient at high risk form treatment complications
- History of severe allergic reactions to chimeric or humanized antibodies or fusion proteins
- Known hypersensitivity to Chinese hamster ovary cell products or recombinant human antibodies
- Known allergy or hypersensitivity to any of the study drugs or their excipients
- Known intolerance to any of the drugs required for premedication
- Pregnancy or breastfeeding, or intention of becoming pregnant during the study
- Eligible only for the control arm
- Active EBV infection or known or suspected chronic EBV infection at screening

Specific Exclusion Criteria for Atezo+Tira+CP:

- Known severe allergy or hypersensitivity to placlitaxel, platinum or platinum-containing compounds
- Known history of severe hypersensitivity to products containing Cremophor EL
- Creatinine clearance <45m./min (Calculated using the Cockcroft-Gault formula)