# Testing What Happens When an Immunotherapy Drug (Pembrolizumab) is Given by Itself Compared to the Usual Treatment of Chemotherapy With Radiation After Surgery for Recurrent Head and Neck Squamous Cell Carcinoma

**Status:** RECRUITING

## Eligibility Criteria

**Age:** 18 years to 79 years old

This study is NOT accepting healthy

**Healthy Volunteers:** volunteers

**Inclusion Criteria:**

* Patient must be between 18 and 79 years of age * Patient must have locoregionally recurrent or second primary HNSCC (oral cavity, oropharynx, larynx, hypopharynx) in a previously radiated field * Patient must have undergone surgery with gross total resection and must be randomized within 8 weeks of surgery * Patients must have high risk disease defined as: * Positive margins and/or extra nodal extension (ENE) * Positive margins are defined as malignancy at or within 1 mm of the margin. High grade dysplasia (i.e. carcinoma in situ) at the margin is also considered positive * ENE may be either gross or microscopic * Patient must have a PD-L1 Combined Positive Score (CPS) \>= 1 in a Clinical Laboratory Improvement Act (CLIA) certified laboratory. Testing can be done locally as long as it is done in a CLIA certified laboratory. This testing must be on the tumor specimen from the resection of the patient's recurrent or second primary HNSCC * Patient must have had prior radiation to the area of recurrent or second primary tumor. This is defined as \> 50% of the presurgical tumor volume having previously received a dose of \> 45 Gy as determined by the treating radiation oncologist * Patient must have completed prior radiation a minimum of 6 months prior to randomization * Patient must not have any evidence of distant disease based on baseline imaging done within 28 days prior to randomization * Patient must not have received anti-PD-1/PD-L1 therapy for recurrent disease. If the patient received anti-PD-1/PD-L1 therapy as part of initial upfront curative intent treatment (either as part of definitive non-surgical therapy or in the adjuvant setting) in the past, the last dosage of anti-PD-1/PD-L1 therapy must have been given greater than one year prior to randomization * Patient must have an Eastern Cooperative Oncology Group (ECOG) performance status 0-1 * Patient must have the ability to understand and the willingness to sign a written informed consent document. Patients with impaired decision-making capacity (IDMC) who have a legally authorized representative (LAR) or caregiver and/or family member available will also be considered eligible * Patient must not be pregnant or breast-feeding due to the potential harm to an unborn fetus and possible risk for adverse events in nursing infants with the treatment regimens being used. All patients of childbearing potential must have a blood test or urine study within 14 days prior to randomization to rule out pregnancy. A urine or serum pregnancy test must be repeated within 72 hours prior to receiving the first dose of pembrolizumab or chemotherapy if the test done for eligibility/randomization is done outside of this 72 hour window. If the urine test is positive or cannot be confirmed as negative, a serum pregnancy test will be required. A patient of childbearing potential is someone, regardless of whether they have undergone tubal ligation, who meets the following criteria: 1) has achieved menarche at some point, 2) has not undergone a hysterectomy or bilateral oophorectomy; or 3) has not been naturally postmenopausal (amenorrhea following cancer therapy does not rule out childbearing potential) for at least 24 consecutive months (i.e., has had menses at any time in the preceding 24 consecutive months) * Patient must not expect to conceive or father children by using by using accepted and effective method(s) of contraception or by abstaining from sexual intercourse while on study treatment, and continue for 120 days after the last dose of study treatment * Absolute neutrophil count (ANC) \>= 1,500/mcL (obtained =\< 28 days prior to protocol randomization) * Platelets \>= 100,000/mcL (obtained =\< 28 days prior to protocol randomization) * Total bilirubin =\< 1.5 x institutional upper limit of normal (ULN) (obtained =\< 28 days prior to protocol randomization) * Aspartate aminotransferase (AST) (serum glutamic oxaloacetic transaminase \[SGOT\])/alanine aminotransferase (ALT) (serum glutamic pyruvic transaminase \[SGPT\]) =\< 3.0 x institutional ULN (obtained =\< 28 days prior to protocol randomization) * Creatinine clearance \> 30 ml/min using the Cockcroft-Gault formula (obtained =\< 28 days prior to protocol randomization) * Patient must not have a current active infection that requires systemic treatment at time of randomization * Patient must not have a history of non-infectious pneumonitis requiring steroids within 3 years prior to randomization * Patient must not have a history of solid organ transplant or stem cell transplant * Patient must not be on immunosuppressive medication within 7 days prior to randomization, EXCEPT for the following: a) intranasal, inhaled, topical steroids, or local steroid injection (e.g., intra-articular injection); b) systemic corticosteroids at physiologic doses =\< 10 mg/day of prednisone or equivalent; c) steroids as premedication for hypersensitivity reactions (e.g., CT scan premedication) * Patients with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, should have a clinical risk assessment of cardiac function using the New York Heart Association Functional classification. Patients with New York Heart Association class III or IV heart failure are not eligible * Patient must not have received a live vaccine within 30 days prior to the first dose of study drug. Examples of live vaccines include, but are not limited to, the following: measles, mumps, rubella, varicella/zoster (chicken pox), yellow fever, rabies, Bacillus Calmette-Guerin (BCG), and typhoid vaccine. Seasonal influenza vaccines for injection are generally killed virus vaccines and are allowed; however, intranasal influenza vaccines (e.g., FluMist \[registered trademark\]) are live attenuated vaccines and are not allowed * Patient must not have severe hypersensitivity (\>= grade 3) to pembrolizumab and/or any of its excipients * Patient must not have an active autoimmune disease that has required systemic treatment in past 2 years (i.e., with use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (e.g., thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency) is not considered a form of systemic treatment and is allowed * Patient must not have a known psychiatric or substance abuse disorder that would interfere with the participant's ability to cooperate with the requirements of the study * Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial as long as they have not been HIV-infected with a history of Kaposi sarcoma and/or multicentric Castleman disease * Patient must not have a known history of hepatitis B (defined as hepatitis B surface antigen \[HBsAg\] reactive) or known active hepatitis C virus (defined as HCV ribonucleic acid \[RNA\] \[qualitative\] is detected) infection * NOTE: No testing for hepatitis B and hepatitis C is required unless mandated by a local health authority

## Conditions & Interventions

**Interventions:**

DRUG: Carboplatin, DRUG: Cisplatin, PROCEDURE: Computed Tomography, RADIATION: Intensity-Modulated Radiation Therapy, PROCEDURE: Magnetic Resonance Imaging, BIOLOGICAL: Pembrolizumab, RADIATION: Proton Beam Radiation Therapy

**Conditions:**

Recurrent Head and Neck Squamous Cell Carcinoma, Recurrent Hypopharyngeal Squamous Cell Carcinoma, Recurrent Laryngeal Squamous Cell Carcinoma, Recurrent Oral Cavity Squamous Cell Carcinoma, Recurrent Oropharyngeal Squamous Cell Carcinoma

## More Information

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**Phase:** PHASE2

**IRB**

**Number:** HM20022077

**System ID:** NCT04671667

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