

A PHASE II MULTI-CENTER STUDY OF CONCOMITANT CETUXIMAB AND CISPLATIN WITH RE-IRRADIATION USING INTENSITY-MODULATED RADIOTHERAPY (IMRT) IN PATIENTS WITH RECURRENT SQUAMOUS CELL CARCINOMA OF THE HEAD-AND NECK

Principal Investigator: Lucien Nedzi, MD

Coordinator: Irma Charles, MS

Contact Number: (214) 648-5536

Primary Objective: Evaluate whether the proposed treatment with current cetuximab and cisplatin and IMRT will improve the overall survival in patients with head and neck squamous cell carcinoma who recur after previous radiation treatment.

Secondary Objective:

- To determine the progression-free survival and local-regional progression in these patients
- To identify and estimate the incidence rate of acute and late toxicities associated with the treatment
- To determine the pattern of disease progression in recurrent disease patients treated with the treatment

Study Population: Total: 50 Local: 10

Schema:

Week 1: Cetuximab loading dose (400 mg/m²)

Week 2-7: Radiation with IMRT 60 Gy (2 Gy/day, daily X 5) concurrently with weekly cisplatin (30 mg/m²) and weekly cetuximab (250 mg/m²)

Assessment:

- History and physical examination
- Performance status/weight
- Blood tests
- Pregnancy Test (if applicable)
- CT/MRI of the tumor
- Chest x-ray or thoracic CT

Inclusion Criteria:

- Individuals 18 years or older

- Patients must have pathologically confirmed recurrence squamous cell carcinoma in the upper aerodigestive tract or a second squamous cell carcinoma (excluding nasopharynx and salivary gland tumors). Patients may have experienced more than one recurrence as long as the first recurrence occurred more than 6 months following the end of previous radiation
- The recurrence or second primary must be confined to the head and neck above the clavicles (loco-regional recurrence)
- The majority ($\geq 75\%$) of the recurrent tumor must have been in the areas previously irradiated to ≥ 45 Gy. The previous irradiation must not exceed a maximum of 75 Gy
- Patients with measurable recurrent disease after attempted surgical resection are eligible if they have completely healed wounds, and meet all other eligibility criteria. Patients must not have any signs of carotid exposure
- Patients previously treated with cisplatin and cetuximab are allowed, but must be at least 6 months from prior radiation and chemotherapy
- Patients may have received prior chemotherapy as a component of their primary treatment, but not for recurrent disease
- Karnofsky status ≥ 70
- Adequate bone marrow function and laboratory parameters, defined as follows:
 - Absolute neutrophil count (ANC) $\geq 2,000$ cells/mm³ based upon CBC/differential obtained within 4 weeks prior to registration on study
 - Platelets $\geq 100,000$ cells/mm³ based upon CBC/differential obtained within 4 weeks prior to registration on study
 - Hemoglobin ≥ 8.0 g/dl based upon CBC/differential obtained within 4 weeks prior to registration on study (Note: The use of transfusion or other intervention to achieve Hgb ≥ 8.0 g/dl is acceptable)
- Adequate hepatic function with bilirubin < 1.5 mg/dl, AST or ALT < 2 x the upper limit of normal within 4 weeks prior to registration
- Abdominal CT, if abnormal LFTs are noted (must be done in presence of > 1.5 x upper limit of normal of alkaline phosphatase, AST, bilirubin, or other clinical indicator)
- Adequate renal function, defined as follows:
 - Creatinine clearance ≥ 50 ml/min within 4 weeks prior to registration determined by 24-hour collection or estimated by Cockcroft-Gault formula:

$$\text{CrCl male} = [(140 - \text{age}) \times (\text{wt in kg})] / [(s\text{CR}) \times (72)]$$

$$\text{CrCl female} = 0.85 \times (\text{CrCl male})$$

- Other laboratory studies within 4 weeks prior to study entry also include sodium, potassium, glucose, calcium, magnesium, BUN, total protein and albumin
- CT or MRI of the head and neck within 4 weeks of study entry. For postoperative re-irradiation, preoperative imaging studies are acceptable
- Chest CT scan within 4 weeks prior to registration; patients with equivocal pulmonary nodules that are < 1 cm, that cannot be safely biopsied, or that are negative on PET imaging are eligible
- Must be able submit previous radiation records in order to assure that the cord tolerance is not exceeded
- Patients must sign a study-specific informed consent form prior to study entry
- For persons of childbearing potential:

Sexually active women of childbearing potential must use an effective method of birth control during the course of the study, in a manner such that risk of failure is minimized.

Prior to study enrollment, women of childbearing potential (WOCBP) must be advised of the importance of avoiding pregnancy during trial participation and the potential risk factors for an unintentional pregnancy. In addition, men enrolled on this study should understand the risks to any sexual partner of childbearing potential and should practice an effective method of birth control.

All WOCBP MUST have a negative pregnancy test within 7 days prior to first receiving investigational product. If the pregnancy test is positive, the patient must not receive investigational product and must not be enrolled in the study.

In addition, all WOCBP should be instructed to contact the Investigator immediately if they suspect they might be pregnant (e.g., missed or late menstrual period) at any time during study participation.

Exclusion Criteria:

- Primary in the nasopharynx or of the salivary gland
- Distant metastasis

- Other concurrent invasive malignancies
- History of other invasive malignancies unless disease free at least 2 years
- Pregnant and nursing women are excluded
- Prior severe infusion reaction to a monoclonal antibody
- Intercurrent medical illnesses which would impair patient tolerance to therapy or limit survival
- Active cardiac disease defined as unstable angina, uncontrolled hypertension, myocardial infarction in the last six months (unless successfully treated with CABG or PTCA), uncontrolled arrhythmia, or congestive heart failure; ≥ 3 heart-related hospitalization in the past year
- Severe COPD requiring ≥ 3 hospitalization in the past year
- Pre-existing grade ≥ 2 peripheral sensory neuropathy
- Prisoners or subjects who are compulsorily detained (involuntarily incarcerated) for treatment of either a psychiatric or physical (e.g. infectious) illness
- Recurrent head and neck cancers previously treated with concurrent cisplatin, cetuximab, and radiation. (New primary head and neck cancers whose previous primary head and neck cancer was treated with concurrent cisplatin, cetuximab, and radiation more than six months previously are eligible)