

RTOG 0436: A Phase III Trial Evaluating the Addition of Cetuximab to Paclitaxel, Cisplatin, and Radiation for Patients With Esophageal Cancer Who Are Treated Without Surgery

Fast Facts

Patient Eligibility

1. Pathologically (histologic or cytologic) proven diagnosis of primary squamous cell or adenocarcinoma of the esophagus or gastroesophageal junction within 12 weeks prior to registration. Patients with involvement of the gastroesophageal junction with Siewert type I or II tumors (tumors arising from the distal esophagus and involving the esophagogastric junction or tumors starting at the esophagogastric junction and involving the cardia) are eligible.
 - Disease must be encompassed in a radiotherapy field.
 - Patients with celiac, perigastric, mediastinal or supraclavicular adenopathy are eligible.
 - Patients with cervical esophageal carcinoma are eligible.
2. Stage T1N1M0; T2-4, Any N, M0; Any T, Any N, M1a, based upon the following minimum diagnostic work-up:
 - History/physical examination within 6 weeks prior to registration
 - PET/PET-CT scan (strongly recommended) or chest/abdominal CT within 6 weeks prior to registration
 - EKG within 6 weeks of study entry
 - Endoscopy with biopsy or cytology by fine needle aspiration (FNA) (must be able to document histologic subtype) within 12 weeks of study entry. Patients with T3-4 proximal thoracic esophageal tumors (15-25 cm) must undergo bronchoscopy to exclude fistula. (**NOTE:** Any images from endoscopic procedures up to the time of progression must be kept in the patient's confidential study file.)
3. Zubrod performance status 0-2
4. Age ≥ 18
5. CBC/differential obtained within 2 weeks prior to registration on study, with adequate bone marrow function defined as follows:
 - Absolute neutrophil count (ANC) $\geq 1,500$ cells/mm³
 - Platelets $\geq 100,000$ cells/mm³
 - Hemoglobin ≥ 8.0 g/dl (Note: The use of transfusion or other intervention to achieve Hgb ≥ 8.0 g/dl is acceptable.)
6. Additional laboratory studies obtained within 2 weeks prior to registration on study
 - Creatinine ≤ 1.5 mg/dl
 - Bilirubin ≤ 1.5 x upper limit of normal
 - AST ≤ 3 x upper limit of normal
 - Serum pregnancy test for women of childbearing potential
7. Patient's total intake (oral/enteral) must be ≥ 1500 kCal/day
8. Patient must provide study-specific informed consent prior to study entry
9. Women of childbearing potential and male participants must practice adequate contraception

Patient Ineligibility

1. Evidence of tracheoesophageal fistula, or invasion into the trachea or major bronchi. Patients with T3-4 proximal thoracic esophageal tumors (15-25 cm) must undergo bronchoscopy to exclude fistula.
2. Prior invasive malignancy (except non-melanomatous skin cancer) unless disease free for a minimum of 2 years (For example, carcinoma in situ of the breast, oral cavity, or cervix are all permissible).
3. Prior systemic chemotherapy for esophageal cancer; note that prior chemotherapy for a different cancer is allowable. See Section 3.2.2.
4. Prior radiation therapy that would result in overlap of planned radiation therapy fields.
5. Prior therapy that specifically and directly targets the EGFR pathway.
6. Prior platinum-based and/or paclitaxel-based therapy.
7. Prior allergic reaction to the study drugs involved in this protocol.
8. Prior severe infusion reaction to a monoclonal antibody.

9. Severe, active comorbidity, defined as follows:
 - Unstable angina and/or congestive heart failure requiring hospitalization within the last 3 months
 - Transmural myocardial infarction within the last 6 months
 - Acute bacterial or fungal infection requiring intravenous antibiotics at the time of registration
 - Chronic obstructive pulmonary disease exacerbation or other respiratory illness requiring hospitalization or precluding study therapy at the time of registration
 - Acquired immune deficiency syndrome (AIDS) based upon current CDC definition; note, however, that HIV testing is not required for entry into this protocol. The need to exclude patients with AIDS from this protocol is necessary because the treatments involved in this protocol may be significantly immunosuppressive. Protocol-specific requirements may also exclude immunocompromised patients.
10. Pregnancy or women of childbearing potential and men who are sexually active and not willing/able to use medically acceptable forms of contraception; this exclusion is necessary because the treatment involved in this study may be significantly teratogenic.
11. Women who are nursing.

Pre-Study Parameters

1. Histologically proven diagnosis by endoscopy w/ biopsy or cytology by FNA
2. History/physical w/ weight, PS
3. PET/PET-CT/Chest/abdominal CT (PET/PET-CT strongly recommended)
4. EKG
5. Endoscopy/biopsy (see section 11.2)
6. CBC w/diff, ANC, platelets, Hgb, Creatinine, bilirubin, AST, Magnesium, Calcium, Potassium
7. pregnancy test (if applicable)

Treatment

SCHEMA

S T R A T I F Y	<p>Histology:</p> <ol style="list-style-type: none"> 1. Adenocarcinoma 2. Squamous <p>Cancer lesion size:</p> <ol style="list-style-type: none"> 1. < 5 cm 2. ≥ 5 cm <p>Celiac nodes:</p> <ol style="list-style-type: none"> 1. Present 2. Absent 	R A N D O M I Z E	<p>Arm 1: Radiation Therapy + Paclitaxel + Cisplatin + Cetuximab</p> <p>Arm 2: Radiation Therapy + Paclitaxel + Cisplatin</p>
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