RADIATION NRG ONCOLOGY

RTOG 1010

A Phase III Trial Evaluating the Addition of Trastuzumab to Trimodality Treatment of HER2-Overexpressing Esophageal Adenocarcinoma

SCHEMA (2/22/12)

STEP 1 REGISTRATION

HER2 Testing

Mandatory submission of tissue for HER2 testing

NOTE: Tumor tissue must be received and patients must have confirmed HER2 positivity before randomization can occur. Patients with confirmed HER2 negativity will not be randomized.

STEP 2 REGISTRATION

STRATIFY

Presence of adenopathy: No vs Yes—celiac absent vs. Yes—celiac present ≤ 2 cm

RANDOMIZE

<table>
<thead>
<tr>
<th>Arm 1</th>
<th>Arm 2</th>
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</thead>
<tbody>
<tr>
<td>Radiation (50.4 Gy), paclitaxel, carboplatin, and trastuzumab</td>
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<tr>
<td>Followed by surgery 5-8 weeks after completion of radiation</td>
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<tr>
<td>Then maintenance trastuzumab, every 3 weeks for 13 treatments</td>
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Note: 3D-CRT and IMRT credentialing is required for this protocol; see Section 5.1.

Patient Population: (See Section 3.0 for Eligibility) (11/5/14)

Pathologically confirmed HER2 expressing adenocarcinoma of the esophagus, centrally assessed, involving the mid (up to 25 cm), distal and/or esophagogastric junction.

Required Sample Size: 197
RTOG 1010/LU203315 - A Phase III Trial Evaluating the Addition of Trastuzumab to Trimodality Treatment of HER2-Overexpressing Esophageal Adenocarcinoma

Eligibility:

1. Pathologically confirmed primary adenocarcinoma of the esophagus that involves the mid (up to 25 cm), distal, or esophagogastric junction. The cancer may involve stomach up to 5 cm

2. Endoscopy with biopsy.

3. Stage T1N1-2, T2-3N0-2, according to the American Joint Committee on Cancer (AJCC) 7th edition staging, based upon the following minimum diagnostic work-up.

4. Age ≥ 18


6. Adequate bone marrow function defined

7. For women of childbearing potential, a negative serum pregnancy test within 14 days prior to Step 2 registration

8. Women of childbearing potential and sexually active male participants must agree to practice adequate contraception while on study and for at least 60 days following the last dose of chemotherapy or trastuzumab.
surgery and the institutional pathologist, the patient will be ineligible.

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A PHASE III TRIAL EVALUATING THE ADDITION OF TRASTUZUMAB TO TRIMODALITY TREATMENT OF HER2-OVEREXPRESSING ESOPHAGEAL ADENOCARCINOMA

Exclusion Criteria:

1. Patients with cervical esophageal carcinoma
2. Patients with T1N0 disease, T4 disease, and proximal esophageal cancers (15-24 cm)
3. Prior systemic chemotherapy for esophageal cancer; note that prior chemotherapy for a different cancer is allowable
4. Prior radiation for esophageal cancer or prior chest radiotherapy
5. Prior anthracycline or taxane
6. Evidence of tracheoesophageal fistula or invasion into the trachea or major bronchi
7. Prior invasive malignancy (except non-melanomatous skin cancer), unless disease free for a minimum of 2 years (e.g., carcinoma in situ of the breast, oral cavity, or cervix are permissible.
8. Medical contraindications to esophagectomy
9. Prior therapy with any agent targeting the HER2 pathway or HER1 (EGFR) pathway
10. Prior therapy with trastuzumab
11. Prior allergic reaction to the study drugs involved in this protocol or to a monoclonal antibody
12. Previous history of congestive heart failure
13. Severe, active comorbidity, defined as follows:
   - Unstable angina in the last 6 months
   - Transmural myocardial infarction within the last 6 months
   - Acute bacterial or fungal infection requiring intravenous antibiotics 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 immunosuppressive. Protocol-specific requirements may also exclude immunocompromised patients.
14. Pregnant or nursing women 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.