NRG ONCOLOGY
RTOG 1203

A RANDOMIZED PHASE III STUDY OF STANDARD VS. IMRT PELVIC RADIATION FOR POST-OPERATIVE TREATMENT OF ENDOMETRIAL AND CERVICAL CANCER (TIME-C)

SCHEMA

<table>
<thead>
<tr>
<th>STRATIFY</th>
<th>XRT Dose</th>
<th>RANDOMIZE</th>
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<tbody>
<tr>
<td></td>
<td>1. 45 Gy</td>
<td>Arm 1</td>
</tr>
<tr>
<td></td>
<td>2. 50.4 Gy</td>
<td>IMRT pelvic radiation treatment</td>
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<tr>
<td>Chemotherapy</td>
<td>1. No Chemotherapy</td>
<td>Arm 2</td>
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<tr>
<td></td>
<td>2. 5 cycles of weekly</td>
<td>4-field pelvic radiation treatment</td>
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<tr>
<td></td>
<td>cisplatin at 40mg/m2</td>
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<tr>
<td>Disease Site</td>
<td>1. Endometrial</td>
<td></td>
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<td></td>
<td>2. Cervix</td>
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See Section 5.0 for pre-registration requirements, Section 6.0 for details of radiation therapy, and Section 7.0 for details of drug therapy.

Patient Population: (See Section 3.0 for Eligibility)
Pathologically proven diagnosis of endometrial and cervical cancer who require post-operative radiation or chemoradiation; Zubrod performance status of 0–2.

Required Sample Size: 281 patients
Eligibility:

1. Pathologically proven diagnosis of endometrial or cervical cancer.
2. Patients must have undergone a hysterectomy (total abdominal hysterectomy, vaginal or radical hysterectomy or total laparoscopic hysterectomy) for carcinoma of the cervix or endometrium within 49 days prior to registration. Performance of a bilateral salpingooophorectomy will be at the treating surgeon’s discretion.
3. Appropriate stage for protocol entry, including no distant metastases, based upon the following minimum diagnostic workup:
   - History/physical examination within 45 days prior to registration
   - CT, MRI or PET-CT including the abdomen and pelvis should be performed for initial radiological staging. This may be performed pre- or post-surgery within 90 days prior to registration. Imaging performed post-operatively should show no evidence of residual disease. Any evidence of malignancy identified on pre-operative imaging should have been completely resected surgically prior to protocol treatment.
   - Chest CT or chest x-ray must be performed within 90 days prior to registration (unless a -CT has been performed)
4. Zubrod Performance Status 0-2
5. Age ≥ 18;
6. CBC/differential obtained within 14 days prior to registration on study, with adequate bone marrow function defined as follows:
   - Absolute neutrophil count (ANC) ≥ 1,500 cells/mm3;
   - Platelets ≥ 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.)

For patients receiving chemotherapy:

- Within 14 days prior to registration, serum creatinine ≤ 1.5 mg/dL and calculated creatinine clearance ≥ 50 cc/min. Both tests must be within these limits. The creatinine clearance should be calculated using the Cockcroft-Gault formula:
  - AST ≤ 2 x ULN
  - Bilirubin ≤ 2 x ULN
  - Alkaline phosphatase, Mg, BUN and electrolytes must be obtained and recorded
Exclusion Criteria:

1. Patients with para-aortic nodal disease or who require extended field radiotherapy beyond the pelvis.
2. Patients with histology consisting of endometrial stromal sarcoma, leiomyosarcoma or malignant mixed mullerian mixed tumor (MMMT or carcinosarcoma)
3. Patients who exceed the weight/size limits of the treatment table or CT scanner.
4. Mental status changes or bladder control problems that make the patient unable to comply with bladder-filling instructions.
5. Patients with evidence of metastatic disease outside of the pelvis.
6. Patients with positive or close (< 3 mm) resection margins
7. Prior invasive malignancy (except non-melanomatous skin cancer) unless disease free for minimum of 3 years.
8. Prior radiation therapy to the pelvis
9. Patients with active inflammatory bowel disease.
10. Severe, active co-morbidity, defined as follows
    - Unstable angina and/or congestive heart failure requiring hospitalization within 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
    - Other major medical illness which requires hospitalization or precludes study therapy at the time of registration
    - Hepatic insufficiency resulting in clinical jaundice and/or coagulation defects; note, however, that laboratory test coagulation parameters are not required for entry into this protocol
    - 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.
11. Patients with prior treatment with platinum-based chemotherapy
12. Women who are breastfeeding