NRG ONCOLOGY
RTOG 0848

A PHASE II-R AND A PHASE III TRIAL EVALUATING BOTH *ERLOTINIB (PHII-R) AND CHEMORADIATION (PH III) AS ADJUVANT TREATMENT FOR PATIENTS WITH RESECTED HEAD OF PANCREAS ADENOCARCINOMA

*(PH II-R ERLOTINIB RANDOMIZATION COMPLETED, ARM 2 CLOSED TO ACCRUAL EFFECTIVE 4/02/14)

SCHEMA (2/19/14)

FIRST STEP:
ADJUVANT SYSTEMIC TREATMENT

Arm 1:
Gemcitabine x 5 cycles

Arm 2:
Gemcitabine + Erlotinib x 5 cycles
(Arm 2 closed to accrual effective 4/02/14)

Evaluate to Confirm No Progression

If no progression, then:

Nodal Status:
1: involved
2: uninvolved

CA19-9 result:
1: $\leq$ 90
2: $> 90 - 180$

Surgical margins:
1: positive (R1)
2: negative (R0)

First Randomization Treatment
Arm: (For patients registered prior to 4/02/14)
1. Arm 1 gemcitabine vs.
2. Arm 2 gemcitabine + erlotinib

SECOND STEP:
RT RANDOMIZATION
For Non-Progressing Patients

Arm 3:
1 cycle of chemotherapy

Arm 4:
1 cycle of chemotherapy followed by XRT with either capecitabine or 5-FU
RTOG 0848/LU203586: A Phase II-R and A Phase III Trial Evaluating both *Erlotinib (PH IIIR) and Chemoradiation (PH III) as Adjuvant Treatment for Patients with Resected Head of Pancreas Adenocarcinoma.

Eligibility:

1. Histologic proof of primary head of pancreas invasive adenocarcinoma managed with a potentially curative resection (i.e., removal of all gross tumor) involving a classic pancreaticoduodenectomy (Whipple) or a pylorus preserving pancreaticoduodenectomy. Patients with invasive adenocarcinoma that also contains a of intraductal papillary mucinous neoplasm (IPMN) are eligible: The operating surgeon must document in the operative note that a complete gross excision of the primary tumor was achieved. The pathology report must include documentation of the margin status and the size of the tumor. The pathology report must also include the status of the three major margins—bile duct, pancreatic parenchyma, and retroperitoneal (uncinate).
2. Interval between definitive tumor-related surgery and 1st step registration between 21-70 days.
3. Patients will be staged according to the 6th edition AJCC staging system with pathologic stage T1-3, N0-1, M-0 being eligible. Pathologic reporting using the CAPS format is strongly encouraged.
4. Age ≥ 18.
5. Zubrod performance status 0 or 1.
6. Complete history and physical examination including weight and Zubrod status within 31 days of study entry.
7. Before starting therapy the patient should be able to maintain adequate oral nutrition of > or = 1500 calories estimated calorie intake per day and be free of significant nausea and vomiting.
8. CBC/differential obtained within 21 days of registration on study, with adequate bone marrow function.
9. Post resection serum CA19-9 ≤ 180 units/mL within 21 days of registration on study.
10. Patients must have:
    · Serum total bilirubin ≤ twice the institutional upper limit of normal within 21 days of registration on study.
    · Creatinine levels ≤ twice the institutional upper limit of normal within 21 days of registration on study.
    · SGOT must be ≤ 2.5 x the institutional upper limit of normal within 21 days on
11. Negative serum pregnancy test for women of childbearing potential within 14 days of study registration.
12. Abdominal/pelvic CT scan with contrast is preferred. Abdominal CT alone is acceptable only if insurance restrictions are experienced. Chest CT/x-ray (CT of chest preferred) within 31 days of registration on study. Patients allergic to IV contrast can have MRI of abdomen/pelvis instead.
13. Women of childbearing potential and male participants must practice adequate contraception.
14. Patients with active HIV infection are eligible if their CD4 count is > 499/cu mm and their viral load is < 50 copies/ml; use of HAART is allowed.
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PHASE II-R and A PHASE III TRIAL EVALUATING BOTH *ERLOTINIB (PH II-R) AND CHEMORADIATION (PH III) AS ADJUVANT TREATMENT FOR PATIENTS WITH RESECTED HEAD OF PANCREAS ADENOCARCINOMA

Exclusion Criteria:

1. Patients with non-adenocarcinomas, adenosquamous carcinomas, islet cell (neuroendocrine) tumors, cystadenomas, cystadenocarcinomas, carcinoid tumors, duodenal carcinomas, distal bile duct, and ampullary carcinomas. Patients with tumors largely intraductal papillary mucinous neoplasms (IPMN) with a minimal or component of invasive carcinoma are not eligible. Patients with acinar are not eligible. Patients with IPMN’s that contain some secondary (minor) foci of adenocarcinoma are also not eligible.

2. Patients managed with a total pancreatectomy, a distal pancreatectomy, or central Pancreatectomy.

3. Prior systemic chemotherapy for pancreas cancer; note that prior chemotherapy for a cancer is allowable.

4. Prior radiotherapy to the region of the study cancer that would result in overlap of radiation therapy fields

5. Previous history of invasive malignancy (except non-melanoma skin cancer) unless the patient has been disease free for at least 2 years prior to study entry (Patients with a previous history of carcinoma in situ are eligible.

8. 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 3 months of study registration
   - Acute bacterial or fungal infection requiring intravenous antibiotics at the time of registration
   - Chronic Obstructive Pulmonary Disease exacerbation or other respiratory illness hospitalization or precluding study therapy at the time of registration

9. Pregnant or lactating women

10. Women of childbearing potential and men who are sexually active and not willing/able use medically acceptable forms of contraception; this exclusion is necessary because the treatment involved in this study may be significantly teratogenic.

11. If surgical margin status cannot be determined after consultation with the operating