

A PHASE II TRIAL OF ERLOTINIB (TARCEVA ®) IN COMBINATION WITH STEREOTACTIC BODY RADIATION THERAPY (SBRT) FOR PATIENTS WITH LOCALLY ADVANCED OR METASTATIC NON-SMALL CELL LUNG CANCER (NSCLC)

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Primary Objective: To evaluate the effect of SBRT in combination with erlotinib upon the six month progression-free survival

Secondary Objective:

- To describe the actuarial rate in-field local control and rate of out-of-field disease progression
- To evaluate the safety of SBRT in combination with erlotinib for patients with locally advanced or metastatic NSCLC after prior chemotherapy
- To evaluate overall survival after SBRT in combination with erlotinib
- To evaluate the duration of erlotinib usage and time to initiation of third line systemic agent (chemotherapy or biologic agent)

Study Population: Total: 24 -- Local: 10

Schema:

<p style="text-align: center;"><u>NSCLC</u> Progressed after first line systemic therapy; ≤6 discrete lesions eligible for erlotinib and SBRT to all lesions</p>
<p style="text-align: center;"><u>Week 1</u> Begin erlotinib</p>
<p style="text-align: center;"><u>Weeks 2-4</u> -Continue erlotinib -Begin SBRT</p>
<p style="text-align: center;"><u>Post-SBRT</u> Continue erlotinib until disease progression or unacceptable toxicity</p>

Inclusion Criteria:

- Patients must have biopsy proven NSCLC that is locally advanced or metastatic
- Patients must have had failure of at least one prior chemotherapy regimen
- Patients must not have started erlotinib therapy more than 4 weeks prior to the initiation of SBRT.
- Age \geq 18 years
- Patients must have measurable disease at baseline.
- Patients can have up to only 6 discrete active extracranial lesions (\leq 3 in the liver and \leq 3 in the lung) identified by PET scan and also seen on correlative plain film, CT scan, or MRI within 8 weeks prior to the initiation of SBRT.
 - For patients who have received prior radiotherapy to the primary site in the lung, residual PET activity is difficult to interpret and will not be considered a site of active disease if the CT appearance is stable or improved over an interval of at least three months
 - Patients who previously received radiotherapy to the primary site will be ineligible if there is CT evidence of disease progression within the past 3 months
 - Patients with previously un-irradiated primary sites will be potentially eligible, but special considerations apply
 - Up to 2 contiguous vertebral metastases will be considered a single site of disease
- Patients must have a KPS $>$ 60
- AST, ALT & Alkaline phosphates must be \leq 2.5X the upper limit of normal. Total bilirubin must be within the limit of normal.
- Patients should have adequate bone marrow function as defined by peripheral granulocyte count of \geq 1500/mm³.
- Patients should have adequate renal function (serum creatinine \leq 1.5 times the ULN).
- Females of childbearing potential should have a negative pregnancy test.
- Patients who would be receiving SBRT for lung tumors who are known or suspected by the treating radiation oncologist to have compromised lung function must have a documented forced expiratory volume in 1 second (FEV1) \geq 1L.
- Patients must provide verbal and written informed consent to participate in the study.
- Total bilirubin: within normal institutional limits

Exclusion Criteria:

- Patients who previously received radiotherapy to the primary site with CT evidence of disease progression at the primary site within 3 months following the initial radiotherapy.
- Patients with known brain metastases are ineligible.
- Patients with serious, uncontrolled, concurrent infection(s).
- Significant weight loss (>10%) in the prior 3 months.
- Because the tolerance dose of SBRT to the gastrointestinal tract is not established, patients with metastatic disease invading the esophagus, stomach, intestines, or mesenteric lymph nodes will not be eligible.
- Patients with cutaneous metastasis of NSCLC.
- Treatment for other carcinomas within the last five years, except cured non-melanoma skin and treated in-situ cervical cancer
- Patients with more than 6 discrete extra-cranial lesions.
- Participation in any investigational drug study within 4 weeks preceding the start of study treatment.
- Unwillingness to participate or inability to comply with the protocol for the duration of the study.
- Patients who are pregnant. Patients with reproductive capability will need to use adequate contraception during the time of participation in the study.
- Patients who have had prior EGFR inhibitors.