

**SWOG S0709: A Phase II Selection Design of Pharmacodynamic Separation of Carboplatin/
Paclitaxel/Erlotinib or Erlotinib Alone in Advanced Non-Small Cell Lung Cancer (NSCLC) Patients
with Performance Status 2 (PS 2) Selected by Serum Proteomics**

Fast Facts

Provided Drug: OSI-774

Eligibility Criteria

1. Patients must have histologically or cytologically proven newly diagnosed **selected** Stage IIIB (T4 lesion due to malignant pleural effusion) or Stage IV, as defined in Section 4.0, advanced primary non-small cell lung cancer (adenocarcinoma, large cell carcinoma, squamous cell carcinoma or unspecified) or recurrent disease after previous surgery and/or irradiation.
2. Potentially eligible patients will be consented for baseline specimen submission for the screening step of this trial (see Section 18.1 for the **S0709** Baseline Proteomics Specimen Consent Form). A serum sample must be submitted prior to registration to the University of Colorado for mass spectroscopic analysis (see Section 15.1). Patients must show evidence of EGFR TKI therapy benefit (i.e. qualify as "VeriStrat Positive") as determined by this analysis. Results are expected within 5 working days after receipt of specimens. Patients must not be registered before results are obtained (see Section 15.1e).
3. Patients must have measurable or non-measurable disease (see Section 10.1) documented by CT, MRI, X-ray, physical exam or nuclear exam. The CT from a combined PET/CT must not be used to document measurable disease unless it is of diagnostic quality as defined in Section 10.1a. Pleural effusions, ascites and laboratory parameters are not acceptable as the only evidence of disease. Measurable disease must be assessed within 28 days prior to registration. Non-measurable disease must be assessed within 42 days prior to registration. All disease must be assessed and documented on the Baseline Tumor Assessment Form
4. Patients must not have symptomatic brain metastasis. Patients may have previously treated brain metastasis with radiation completed at least 8 weeks prior to registration.
5. Patients must have a Zubrod Performance Status of 2 (see Section 10.4).
6. Patients may have received prior radiation therapy provided that at least 21 days have elapsed since the completion of prior radiation therapy and patients have recovered from all associated toxicities at the time of registration.
7. Patients may have received prior surgery provided that at least 21 days have elapsed since surgery (thoracic or other major surgeries) and patients have recovered from all associated toxicities at the time of registration. There must be no anticipation of need for major surgical procedures during protocol treatment.
8. Patients may have received adjuvant chemotherapy, but at least one year must have elapsed since completion of this type of therapy. Patients must not have received prior systemic hormonal therapy, chemotherapy or biologic therapy for advanced non-small cell lung cancer. Patients must not have received prior therapy with EGFR inhibitors.
9. All patients must be 18 years of age or older.
10. Patients must have a serum creatinine $\leq 2 \times$ IULN a measured or calculated Creatinine clearance ≥ 50 ml/min using the following formula. These tests (or the serum Creatinine value used to calculate the creatinine clearance) must be obtained within 28 days prior to registration.
11. Patients must not have gastrointestinal tract disease resulting in an inability to take enteral medication, malabsorption syndrome, a requirement for IV alimentation, had prior surgical procedures affecting absorption or uncontrolled inflammatory GI disease (e.g., Crohn's, ulcerative colitis).
12. Patients must be offered participation in the additional embedded translational medicine studies as outlined in Section 15.2. With the patient's consent, blood, plasma and tissue will be submitted for testing.
13. Patients must not have a significant history of cardiac disease, i.e., uncontrolled high blood pressure, unstable angina, congestive-heart failure, myocardial infarction within the last six months, or cardiac ventricular arrhythmias requiring medication.
14. Patients must be willing to provide prior smoking history as requested on the Prestudy Form.
15. No prior malignancy is allowed except for the following: adequately treated basal cell or squamous cell skin cancer, in situ cervical cancer, adequately treated Stage I or II cancer from which the patient

is currently in complete remission, or any other cancer from which the patient has been disease-free for 5 years.

16. Pregnant or nursing women may not participate in this trial because of the increased risk of fetal harm including fetal death from the chemotherapeutic agents. Women/men of reproductive potential may not participate unless they have agreed to use an effective contraceptive method.
17. Patients must be informed of the investigational nature of this study and must sign and give written informed consent in accordance with institutional and federal guidelines.
18. At the time of patient registration, the treating institution's name and ID number must be provided to the Data Operations Center in Seattle in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered into the data base.

Pre-Study Parameters

1. History and physical including weight and performance status
2. Labs including CBC with differential serum bilirubin, SGOT or SGPT, serum creatinine, creatinine clearance, albumin, LDH, Alk. Phos., PT/INR
3. Scans for disease assessment, CT or MRI brain and bone scan if clinical indicated
4. Pre-registration serum sample proteomics
See section 9.0 for details of prestudy requirements.

Treatment

Blood submission for serum proteomics screening using VeriStrat.

Proteomics negative patients are not eligible.

Proteomics positive patients are randomized to the following arms.

Arm 1

Drug	Dose	Route	Frequency
OSI-774	150 mg	PO	Daily

Arm 2 – Cycle is 21 days

Drug	Dose	Route	Frequency	Cycle
OSI-774	150 mg	PO	Days 2-16	1-4
Carboplatin	AUC = 5	IV	Day 1	1-4
Paclitaxel	200 mg/m ²	IV	Day 1	1-4
OSI-774	150 mg	PO	Daily	5+

Treatment continues until progression, unacceptable toxicity, patient refusal or treatment delay of 3 or more weeks.

OSI-774 provided.