Protocol Version Date: 02/10/2023

NCI National Clinical Trials Network

E4512 ALCHEMIST

For Patients with Non-Small Cell Lung Cancer

E4512 Available Through ECOG-ACRIN

A Randomized Phase III Trial for Surgically Resected Early Stage Non-Small Cell Lung Cancer: Crizotinib versus Observation for Patients with Tumors Harboring the Anaplastic Lymphoma Kinase (ALK) Fusion Protein

Patient Population

See Section 3.0 for Complete Eligibility Details

- Age ≥ 18 years, ECOG PS 0 or 1, and adequate lab values.
- Must have undergone complete surgical resection of their stage IIA, IIB, IIIA or IIIB non-squamous or squamous b NSCLC per AJCC 8th and have negative margins. N3 disease is not allowed.
- Baseline chest CT must be performed within 6 months (180) days prior to randomization to ensure no evidence of disease. If clinically indicated additional imaging must be performed to rule out metastatic disease.
- Must be registered to A151216 prior to randomization.
- Must test positive for translocation or inversion events involving the ALK gene locus as determined by the Vysis Break Point FISH assay and defined by an increase in the distance between 5' and 3' ALK probes or the loss of the 5' probe (See protocol section 3.1.6. for more details).
- Must not have uncontrolled intercurrent illness (i.e., serious ongoing/active infection, symptomatic CHF, unstable angina pectoris, uncontrolled cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements.
- No known interstitial fibrosis or interstitial lung disease.
- No prior treatment with crizotinib or another ALK inhibitor.
- No ongoing cardiac dysrhythmias of Grade ≥ 2 CTCAE v.4.0, uncontrolled A-fib (any grade), or QTc interval > 470 msec.
- No use of medications, herbals, or foods that are known potent CYP3A4 inhibitors/inducers (see Appendix V).
- Must be adequately recovered from surgery at time of randomization (see protocol for details).
- Must have completed any prior adjuvant chemotherapy/RT 2 or more weeks (6 or more weeks for mitomycin/nitrosoureas) prior to randomization and be adequately recovered.

Treatment Plan

See Section 5.0 for Complete Treatment Details

In order to be eligible for this trial, all patients must have undergone complete resection of the cancer prior to enrollment. Accepted types of resection (with negative margins) will consist of lobectomy, sleeve lobectomy, bi-lobectomy, pneumonectomy, intrapericardial pneumonectomy, wedge resection or segmentectomy. Adjuvant chemotherapy and post-operative RT are permitted as indicated prior to study enrollment.

Cycle = 3 weeks (21 days).

Arm A
Crizotinib:

- 250 mg PO BID, Days 1-21.
- Repeat cycles every 21 days.
- Maximum duration of treatment is 2 years.
- Patients enrolled in Arm A will continue to receive crizotinib open-label.

Arm B
Observation:

- Patients randomized to observation will be followed serially with CT imaging as outlined in Section 7.2.

Number of Participants: 168

Study Chair:
David E. Gerber, M.D.

Co-Chair:
Corey J. Langer, M.D.

Thoracic Surgery Co-Chair:
Onkar Khullar, M.D.

Patient Enrollment

All Sites: Oncology Patient Enrollment Network (OPEN) https://open.ctsu.org/open

Protocol Information

CTSU Help Desk: 1-888-823-5923, CTSUcontact@westat.com, www.ctsu.org

Please Enroll Your Eligible Patients!

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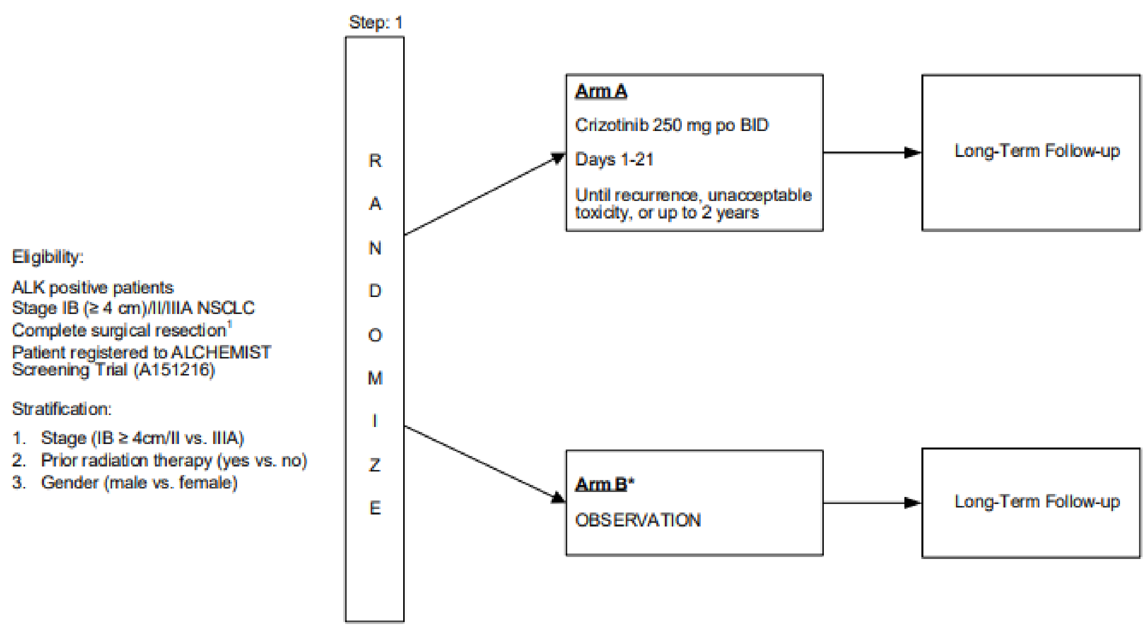
Schema



Accrual Goal: 168 patients
Cycle= 3 weeks (21 days)

1. Patients must have completed any prior surgery 4 or more weeks prior to randomization and be adequately recovered at time of randomization. Maximum time between surgery and randomization is 4 months if no adjuvant chemotherapy was administered, 9 months if adjuvant chemotherapy was administered, and 11 months if adjuvant chemotherapy and radiation therapy were administered.

*Prior to activation of Addendum 8, Arm B patients were receiving placebo
*Patients enrolled on previous addendums will have been enrolled based on AJCC v7 and patients enrolled after amendment #12 and on will be based on AJCC v8

ECOG-ACRIN cancer research group

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