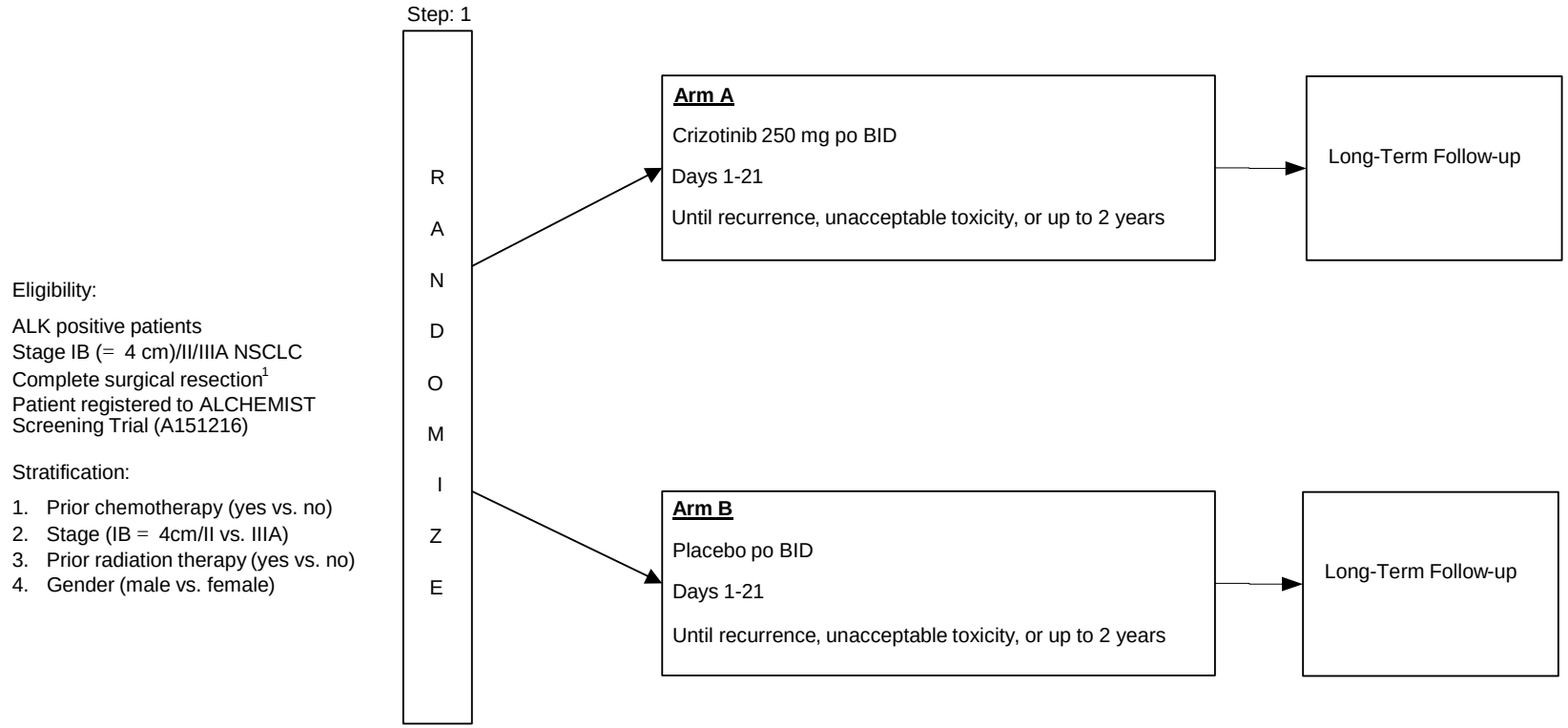
Schema



Eligibility:

ALK positive patients
Stage IB (= 4 cm)/II/IIIA NSCLC
Complete surgical resection[1]
Patient registered to ALCHEMIST Screening Trial (A151216)

Stratification:

1. Prior chemotherapy (yes vs. no)
2. Stage (IB = 4cm/II vs. IIIA)
3. Prior radiation therapy (yes vs. no)
4. Gender (male vs. female)

Accrual Goal: 378 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 3 months if no adjuvant chemotherapy was administered, 8 months if adjuvant chemotherapy was administered, and 10 months if adjuvant chemotherapy and radiation therapy were administered.

Rev. 1/16

3. Selection of Patients

Each of the criteria in the checklist that follows must be met in order for a patient to be considered eligible for this study. Use the checklist to confirm a patient's eligibility. For each patient, this checklist must be photocopied, completed and maintained in the patient's chart.

In calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test is done on a Monday, the Monday four weeks later would be considered Day 28.

ECOG-ACRIN Patient No. _____

Patient's Initials (L, F) _____

Physician Signature and Date _____

NOTE: All questions regarding eligibility should be directed to the study chair or study chair liaison.

NOTE: Institutions may use the eligibility checklist as source documentation if it has been reviewed, signed, and dated prior to randomization by the treating physician.

NOTE: **The 7th edition of the AJCC Cancer Staging Manual will be used for the disease stage criteria for E4512.**

Rev. 4/15

3.1 Randomization Eligibility Criteria

_____ 3.1.1 Age ≥ 18 years.

_____ 3.1.2 Patients must have undergone complete surgical resection of their stage IB (≥ 4 cm), II, or non-squamous IIIA NSCLC per AJCC 7th edition and have had negative margins. N3 disease is not allowed.

Rev. 7/15

_____ 3.1.3 Baseline Chest CT with or without contrast must be performed within 6 months (180 days) prior to randomization to ensure no evidence of disease. If clinically indicated additional imaging studies must be performed to rule out metastatic disease.

_____ 3.1.4 ECOG performance status 0 or 1 (Refer to Appendix IV).

_____ 3.1.5 Patients must be registered to the ALCHEMIST-SCREEN (ALLIANCE A151216) trial prior to randomization.

_____ 3.1.6 Positive for translocation or inversion events involving the ALK gene locus (e.g. resulting in EML4-ALK fusion) 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. This must have been performed:

3.1.6.1 By a local CLIA certified laboratory: Report must indicate the results as well as the CLIA number of the laboratory which performed the assay. Tissue must be available for submission for central, retrospective confirmation of the ALK fusion status via ALCHEMIST-SCREEN (ALLIANCE A151216).

OR

3.1.6.2 Patient registered to and the ALK fusion status performed centrally on the ALCHEMIST-SCREEN (ALLIANCE A151216).

_____ 3.1.7 Women must not be pregnant or breast-feeding because, based on the mechanism of action, crizotinib may cause fetal harm when administered during pregnancy. In animal studies, teratogenicity was not evident, but embryotoxic and fetotoxic effects were noted in rats at crizotinib exposures similar to and above those observed in humans at the recommended clinical dose.

_____ 3.1.8 All females of childbearing potential must have a blood or urine pregnancy test within 72 hours prior to randomization to rule out pregnancy. A female of childbearing potential is any woman, regardless of sexual orientation or whether they have undergone tubal ligation, who meets the following criteria: 1) has not undergone a hysterectomy or bilateral oophorectomy; or 2) has not been naturally postmenopausal for at least 24 consecutive months (i.e., has had menses at any time in the preceding 24 consecutive months).

Female of childbearing potential? _____(Yes or No)

Date of blood or urine test: _____

_____ 3.1.9 Women of childbearing potential and sexually active males must be strongly advised to practice abstinence or use an accepted and effective method of contraception.

_____ 3.1.10 Patients must NOT have uncontrolled intercurrent illness including, but not limited to, serious ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, uncontrolled cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements.

_____ 3.1.11 No known interstitial fibrosis or interstitial lung disease.

_____ 3.1.12 No prior treatment with crizotinib or another ALK inhibitor.

_____ 3.1.13 No ongoing cardiac dysrythmias of Grade ≥ 2 NCI CTCAE version 4.0, uncontrolled atrial fibrillation (any grade), or QTc interval > 470 msec.

_____ 3.1.14 No use of medications, herbals, or foods that are known potent CYP3A4 inhibitors or inducers, included but not limited to those outlined in Appendix V.

_____ 3.1.15 Patients must be adequately recovered from surgery at the time of randomization.

_____ 3.1.15.1 The minimum time requirement between date of surgery and randomization must be at least 4 weeks (28 days).

_____ 3.1.15.2 The maximum time requirement between surgery and randomization must be:

- 3 months (90 Days) if no adjuvant chemotherapy was administered

- 8 months (240 Days) if adjuvant chemotherapy was administered
- 10 months (300 Days) if adjuvant chemotherapy and radiation therapy were administered.

_____ 3.1.16 Patients must have completed any prior adjuvant chemotherapy or radiation therapy 2 or more weeks (6 or more weeks for mitomycin and nitrosoureas) prior to randomization and be adequately recovered at the time of randomization.

NOTE: Patients taking low dose Methotrexate for non-malignant conditions and other cytotoxic agents for non-malignant conditions are allowed to continue treatment while on study.

NOTE: Neo-adjuvant chemotherapy or radiation therapy for the resected lung cancer is not permitted.

_____ 3.1.17 Patients must have adequate organ function as defined by the following criteria within 2 weeks prior to randomization:

NOTE: It is strongly encouraged that these tests take place no more than one week prior to randomization to meet the 2 week requirement for randomization:

_____ 3.1.17.1 Serum Aspartate Transaminase (AST) and Serum Alanine Transaminase (ALT) ≤ 2.5 x upper limit of normal (ULN)

AST: _____Date of Test:_____

ALT:_____Date of Test:_____

_____3.1.17.2 Total Serum Bilirubin ≤ 1.5 x ULN

Total Bilirubin:_____Date of Test:_____

_____3.1.17.3 Absolute neutrophil count (ANC) ≥ 1500/mm^3

ANC:_____Date of Test:_____

_____3.1.17.4 Platelets ≥ 30,000/mm^3

Platelet count:_____Date of Test:_____

_____3.1.17.5 Hemoglobin ≥ 8.0 g/dL

Hemoglobin:_____Date of Test:_____

_____3.1.17.6 Serum Creatinine ≤ 2 x ULN

Serum Creatinine:_____Date of Test:_____

_____ 3.1.18 Prior to randomization patients with any non-hematologic toxicity from surgery, chemotherapy, or radiation must have recovered to Grade ≤ 1 with the exception of alopecia and the criteria outlined in Section 3.1.17.

_____ 3.1.19 Patients must not have any history of cancer within 5 years from randomization, with the exception of in-situ carcinomas and non-melanoma skin cancer.

_____ 3.1.20 Patients may not be receiving any other investigational agents while on study.