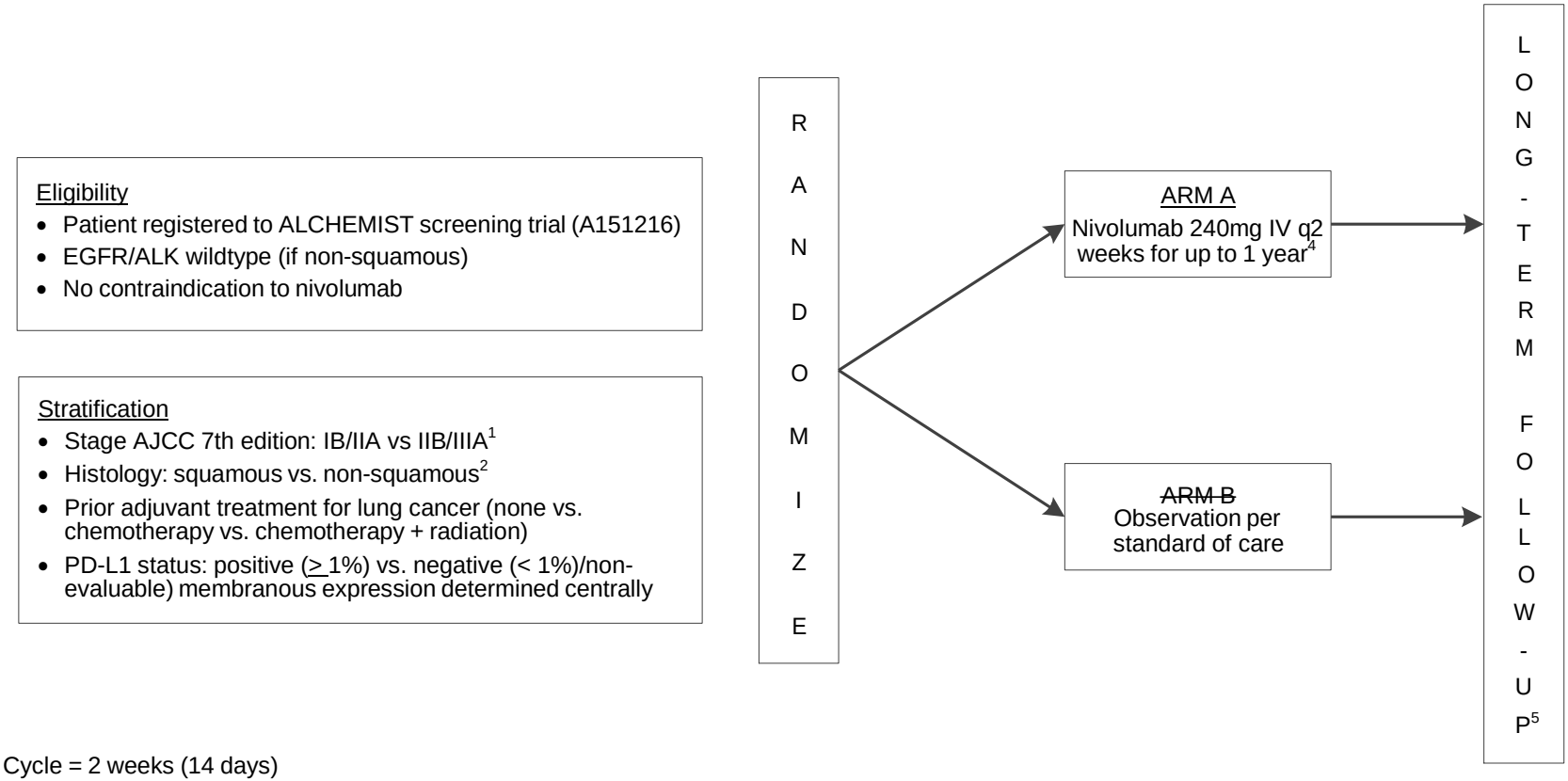
Schema



Cycle = 2 weeks (14 days)
Accrual Goal = 714 patients

1. If Stage 1B, then tumor must be ≥ 4cm
2. Adenosquamous should be grouped as non-squamous
3. PD-L1+ is defined as ≥ 1% by IHC
4. Maximum number of doses is 26
5. Patients will be followed for recurrence and survival for 10 years

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, M) _____

Physician Signature and Date _____

NOTE: CTEP Policy does not allow for the issuance of waivers to any protocol specified criteria (http://ctep.cancer.gov/protocolDevelopment/policies_deviations.htm). Therefore, all eligibility criteria listed in Section 3 must be met, without exception. The registration of individuals who do not meet all criteria listed in Section 3 can result in the participant being censored from the analysis of the study, and the citation of a major protocol violation during an audit. All questions regarding clarification of eligibility criteria must be directed to the Group's Executive Officer (EA.ExecOfficer@jimmy.harvard.edu) or the Group's Regulatory Officer (EA.RegOfficer@jimmy.harvard.edu).

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

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 IIIA NSCLC according to the AJCC 7th edition and have had negative surgical margins.

_____ 3.1.3 Baseline chest CT must be performed within 1 month (30 days) of 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 0-1.

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

_____ 3.1.6 Non-squamous tumors must be *EGFR* and *ALK* wild-type (results ascertained in centrally as part of ALCHEMIST-SCREEN protocol).

_____ 3.1.7 Tumors must have PD-L1 status tested centrally as part of the ALCHEMIST-SCREEN protocol.

_____ 3.1.8 Women must not be pregnant or breast-feeding due to unknown and potentially harmful effects of nivolumab on the developing fetus or child.

_____3.1.9 All females of childbearing potential must have a blood test or urine study within 2 weeks prior to registration 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 child bearing potential?_____(Yes or No)

Date of blood test or urine study: _____

_____ 3.1.10 Women of childbearing potential and sexually active males must be strongly advised to use an accepted and effective method of contraception or to abstain from sexual intercourse during the treatment period and for 31 weeks after the last nivolumab infusion.

_____ 3.1.11 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 situation that would limit compliance with study requirements.

_____ 3.1.12 No prior treatment with an immune checkpoint inhibitor (anti-PD-1, anti-PD-L1, anti-CTLA4 monoclonal antibody).

_____ 3.1.13 Patients must have adequately recovered from surgery and chemotherapy at the time of randomization.

_____3.1.13.1 Minimum time between date of surgery and randomization is 4 weeks

_____3.1.13.2 Maximum time allowed between surgery and randomization:

- 10 months if adjuvant chemotherapy and radiation therapy was administered
- 8 months if adjuvant chemotherapy was administered
- 3 months if no chemotherapy is administered.

_____3.1.14 Patients must have completed and recovered from any adjuvant chemotherapy 2 or more weeks prior to randomization (6 weeks for mitomycin and nitrosoureas; 4 weeks for post-operative radiation therapy).

_____3.1.15 Patients must have adequate organ function as defined by the following criteria within 2 weeks prior to randomization:

_____ 3.1.15.1 Serum aspartate transaminase (AST) and serum alanine transaminase (ALT) ≤ 2.5 x upper limit normal

AST:_____Date of Test:_____

ALT:_____Date of Test:_____

_____ 3.1.15.2 Total bilirubin ≤ 1.5 x ULN (except in subjects with Gilbert Syndrome who must have a total bilirubin < 3.0xULN)

Giblert syndrome: yes/no

Total bilirubin:_____Date of Test:_____

_____ 3.1.15.3 WBC ≥ 2000/µL

WBC:_____Date of Test:_____

_____ 3.1.15.4 Neutrophils ≥ 1000/µL:

Neutrophils:_____Date of Test:_____

_____ 3.1.15.5 Platelets ≥ $100x10^3$/µL

Platelets:_____Date of Test:_____

_____ 3.1.15.6 Hemoglobin ≥ 8 g/dL

Hemoglobin:_____Date of Test:_____

_____ 3.1.15.7 Serum creatinine ≤ 2xULN

Creatinine:_____Date of Test:_____

_____3.1.16 Prior to randomization patients with any non-hematologic toxicity from surgery, chemotherapy and radiation therapy must have recovered to Grade ≤ 1 with the exception of alopecia, ototoxicity and neuropathy.

_____3.1.17 Patients must not have any history of active malignancy within two years from randomization deemed by the investigator to pose a higher risk of recurrence than the lung cancer in question.

_____3.1.18 Patients must not be receiving any other investigational anti-cancer agents while on study.

_____3.1.19 Patients must not have known or suspected autoimmune disease. Subjects with type I diabetes mellitus, hypothyroidism requiring hormone replacement, or skin disorders not requiring systemic treatment are permitted to enroll.

_____3.1.20 Patients must not have a condition requiring systemic corticosteroids equivalent to >10 mg prednisone per day or other immunosuppressive medications within 2 weeks of randomization.

_____3.1.21 Patients must not have known interstitial lung disease that is symptomatic or may interfere with the detection or management of suspected drug-related pulmonary toxicity.