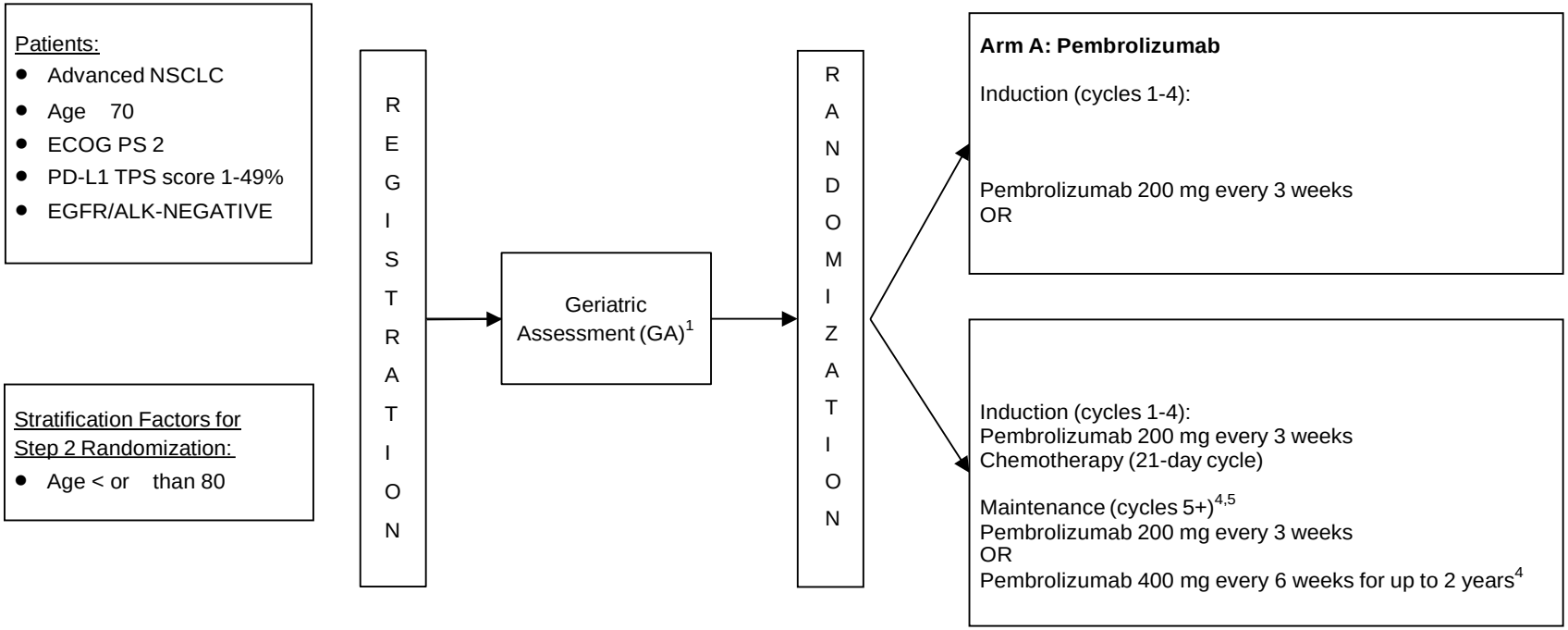
Schema



1. A baseline Geriatric Assessment (GA) will be completed following Step 1 registration and prior to Step 2 randomization. Refer to Section 7.3 and Appendix V for more information.
2. 1:1 Randomization
3. Investigator s choice of either platinum doublet or single agent chemotherapy regimen as outlined in Section 5.1.3 Chemotherapy Regimen Options
4. Arm B Cycle 5+: Patients will discontinue chemotherapy and continue Pembrolizumab alone.
5. Arm B: Patients who initiate treatment with pemetrexed may continue pemetrexed in the maintenance phase at the discretion of the treating investigator as outlined in Section 5.1.3.2.

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, and require reporting to the IRB of record as non-compliance.

All questions regarding clarification of eligibility criteria must be directed to the Group's Executive Officer (EA.ExecOfficer@ecog-acrin.org) or the Group's Regulatory Officer (EA.RegOfficer@ecog-acrin.org).

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.

3.1 Eligibility Criteria (Step 1 Registration)

_____ 3.1.1 Patient must be ≥ 70 years of age.

_____ 3.1.2 Patient must have histologically or cytologically confirmed non-small cell lung cancer (NSCLC) with PD-L1 TPS range of 1-49%.

_____ 3.1.3 Patient must have Stage IIIB, IIIC or IV disease and not be candidates for combined chemo-radiation. NOTE: Prior chemo-RT for stage III with recurrence is allowed.

_____ 3.1.4 Patient must have a tumor that is negative for EGFR mutation/ALK translocations or other actionable first line mutations in which patients would receive first-line oral tyrosine kinase inhibitors.

_____ 3.1.5 Patient must have an ECOG Performance Status of 2.

_____ 3.1.6 Patient must agree not to father children while on study and for 6 months after the last dose of protocol treatment.

_____ 3.1.7 Patient must have the ability to understand and the willingness to sign a written informed consent document. Patients with impaired decision-making capacity (IDMC) who have a legally authorized representative

(LAR) or caregiver and/or family member available will also be considered eligible.

_____ 3.1.8 Patient must have adequate organ and marrow function as defined below (these labs must be obtained within 14 days prior to Step 1 registration):

_____Absolute neutrophil count (ANC) ≥ 1,500/mcL

ANC:_____ Date of Test:_____

_____Platelets ≥ 75,000/mcL

Platelets:_____ Date of Test:_____

_____ Hemoglobin (Hgb) ≥ 8.0 g/dL

Hgb _____ Date of Test _____

_____Total bilirubin ≤ 1.5 x institutional upper limit of normal (ULN)

Total bilirubin:_____ Institutional ULN:_____

Date of Test:_____

_____AST(SGOT)/ALT(SGPT) ≤ 3.0 × institutional ULN

AST:_____ Institutional ULN:_____

Date of Test:_____

ALT: _____Institutional ULN:_____

_ Creatinine clearance (CrCL) ≥ 45 mL/min (estimated using Cockcroft-Gault method with actual body weight or measured)

Creatinine clearance _____Date of Test:_____

_____ 3.1.9 Human immunodeficiency virus (HIV)-infected patients on effective antiretroviral therapy with undetectable viral load within 6 months of Step 1 registration are eligible for this trial.

_____3.1.10 For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated.

_____3.1.11 Patients with a history of hepatitis C virus (HCV) infection must have been treated and cured. For patients with HCV infection who are currently on treatment, they are eligible if they have undetectable HCV viral.

_____3.1.12 Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial.

_____ 3.1.13 Patient must be English or Spanish speaking to be eligible for the QOL component of the study.

NOTE: Sites cannot translate the associated QOL forms.

_____3.1.14 Patient must not have symptomatic central nervous system disease (CNS) metastases. Patients with a clinical history of CNS metastases or cord compression are eligible if they have been definitively treated

and are clinically stable for at least 14 days prior to Step 1 registration and off all steroids for at least 24 hours prior to Step 1 registration. Patients with asympotmatic CNS metastases are eligible.

_____3.1.15 Patient must not have had any prior cytotoxic chemotherapy regimen for metastatic disease. Chemotherapy given in the setting of adjuvant therapy or locally advanced disease is allowed as long as treatment was completed, and they have fully recovered from treatment related adverse events prior to Step 1 registration.

_____ 3.1.16 Patient must not have had any prior immunotherapy for metastatic disease. Immunotherapy given in the setting of adjuvant therapy or locally advanced disease is allowed as long as treatment was completed greater than 6 months prior to Step 1 registration.

_____ 3.1.17 Patient must not have a history of uncontrolled autoimmune conditions with the following exceptions, which are allowed: alopecia, vitiligo, rheumatoid arthritis, psoriasis/psoriatic arthritis, Hashimoto's thyroiditis, lupus, inflammatory bowel disease.

_____ 3.1.18 Patient must not be on immunosuppressive medication, including steroids (if doses exceed the equivalent of prednisone 10 mg daily). Short courses of steroids which are discontinued prior to randomization are acceptable. Patients on inhaled, intranasal and/or topical steroids are eligible.

3.1.19 Investigator must declare their intended chemotherapy regimen should their patient be randomized to Arm B (doublet vs singlet) from the options outlined in Section 5.1.3.

Doublet?_____ (Yes/No)

Singlet?_____(Yes/No)

_____ _____

Physician Signature Date

OPTIONAL: This signature line is provided for use by institutions wishing to use the eligibility checklist as source documentation.

3.2 Eligibility Criteria (Step 2 Randomization)

3.2.1 Patient must have completed the baseline Geriatric Assessment (GA) as outlined in Section 7.3, after Step 1 registration and prior to Step 2 randomization.

_____ _____

Physician Signature Date