v.03/14/25 (Add. #3)

NCI National Clinical Trials Network

EA5221/ACHIEVE

For Older Patients with Advanced NSCLC

Please Enroll Your Eligible Patients!

EA5221 Available Through ECOG-ACRIN Cancer Research Group

A Randomized Phase III Trial of Chemo-Immunotherapy vs Immunotherapy Alone for the Vulnerable Older Adult with Advanced Non-Small Cell Lung Cancer: The ACHIEVE Study

Patient Population

See protocol Section 3 for complete eligibility criteria

Eligibility Criteria– Step 1 Registration:

- Age ≥ 70 years, ECOG PS of 2, adequate lab values
- English/Spanish speaking in order to complete the Geriatric Assessment and QOL questionnaires
- Histologically/cytologically confirmed NSCLC with PD-L1 TPS range of 1-49%
- Must have Stage IIIB, IIIC, or IV disease and not be a candidate for combined chemo-radiation (note: prior chemo-RT for stage III with recurrence allowed)
- 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 TKI
- No symptomatic CNS disease metastases; history of CNS metastases/cord compression eligible per criterion 3.1.4; asymptomatic CNS metastases permitted
- No prior cytotoxic chemotherapy for metastatic disease; chemotherapy in the setting of adjuvant therapy or locally advanced disease allowed if completed and recovered from treatment-related AEs prior to Step 1 registration
- No prior immunotherapy for metastatic disease; immunotherapy in setting of adjuvant therapy or locally advanced disease allowed if completed > 6 months prior to step 1 registration
- No history of uncontrolled autoimmune conditions (exceptions per criterion 3.1.17)
- Must not be on immunosuppressive medication, including steroids (if > than equivalent of prednisone 10 mg QD); short courses of steroids discontinued prior to randomization are acceptable; patients on inhaled, intranasal, and/ or topical steroids are allowed
- Baseline imaging of all measurable and non-measurable sites of disease ≤ 45 days prior to Step 1 registration
- Arm B: Investigator must declare intended chemo regimen (platinum doublet vs. single agent per Section 5.1.3)

Eligibility – Step 2 Randomization: Must have completed the baseline Geriatric Assessment (GA) per protocol (after Step 1 registration and before Step 2 randomization)

Treatment Plan

See protocol Section 5 for complete treatment details

- At Step 1 registration, investigators will select the chemotherapy regimen (per protocol) believed to be most appropriate should the patient be randomized to Arm B (chemo-immunotherapy)
- After Step 1 registration, patients will complete the GA and then enroll to Step 2 to be randomized (must occur within 5 days of Step 1 registration)
- See Section 5.4 for dose mods and 5.5 for supportive care recommendations

Arm A– Pembrolizumab:

- Induction (Cycles 1-4): Pembro 200 mg IV over 30 minutes, every 3 weeks (cycle = 21 days +/- 3)
- Maintenance (Cycles 5+): Pembro 200 mg IV every 3 weeks (cycle = 21 days +/- 3) or 400 mg IV every 6 weeks (cycle = 42 days +/- 3)

Arm B– Pembrolizumab + Chemotherapy (platinum doublet or single agent):

- Baseline GA results should be reviewed prior to final chemotherapy selection (investigator may modify original selected treatment plan)
- Induction (Cycles 1-4): Pembro 200 mg IV every 3 weeks (cycle = 21 days +/- 3) AND investigator's choice of chemo: pemetrexed + carboplatin (for non-squamous cell patients only); nab-paclitaxel + carboplatin; paclitaxel + carboplatin; nab-paclitaxel only; paclitaxel only; pemetrexed only 9
  - ◊ See Section 5.1.3 for chemo dosing
- Maintenance (Cycles 5+): Discontinue chemo and continue pembro alone at either 200 mg IV every 3 weeks (21 days +/- 3) OR 400 mg IV every 6 weeks (42 days +/- 3) [may continue pemetrexed with pembro per investigator discretion]

Maintenance treatment– Both Arms

- Continue until disease progression, unacceptable toxicity, or 2 years (after 2 years, investigator must assess whether patient should continue therapy or go on treatment break)

Study Chair:
Megan Baumgart, MD

Study Co-Chair:
Balazs Halmos, MD

NCTN Study Champions:
- ***Alliance:*** Apar Kishor Ganti, MD
- ***SWOG:*** Mohammed Al-Jumayli, MD

Patient Enrollment (Oncology Patient Enrollment Network [OPEN])

https://open.ctsu.org/open 1-888-823-5923

Protocol Information (ECOG-ACRIN Operations – Boston)

http://ecog-acrin.org (Member Login) 1-857-504-2900

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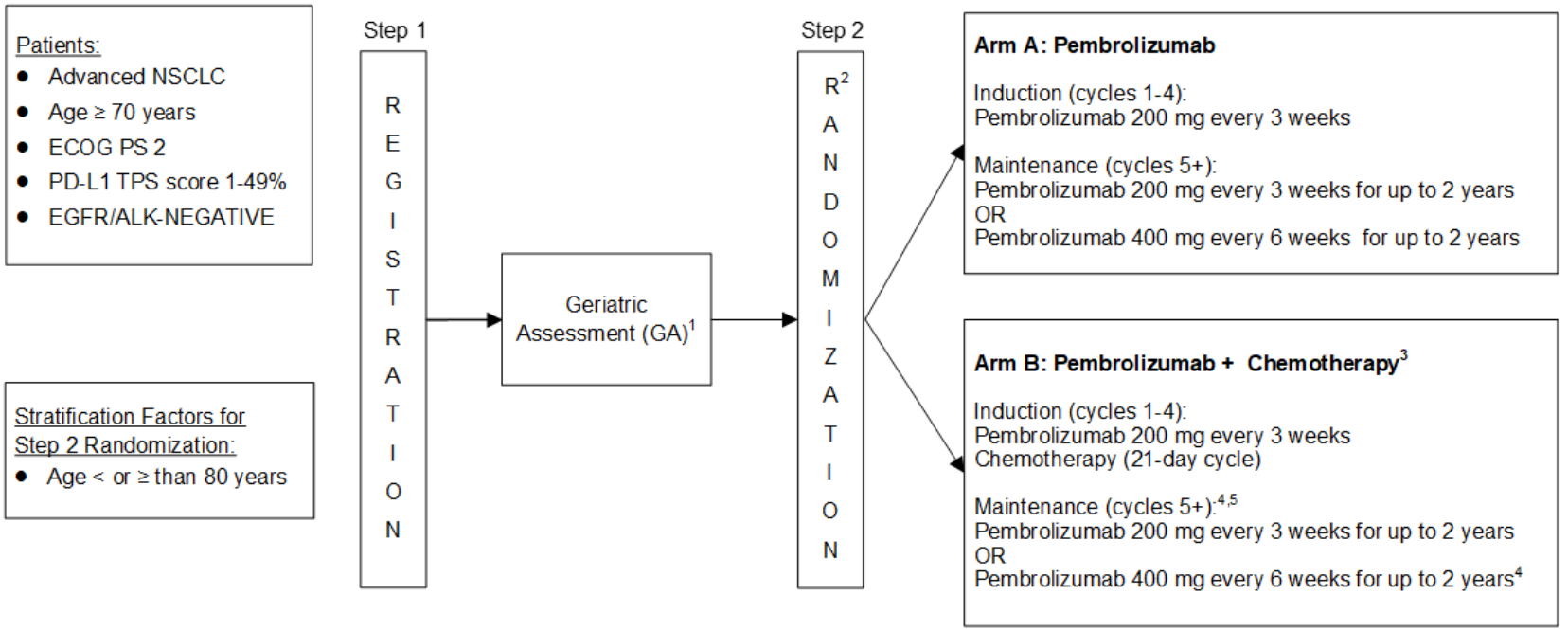
ECOG-ACRIN cancer research group

EA5221

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.