v.04/16/25

NCI National Clinical Trials Network

EA5231/CLEAR

For Patients with Non-Small Cell Lung Cancer

Please Enroll Your Eligible Patients!

EA5231 Available Through ECOG-ACRIN Cancer Research Group

A Randomized Phase III Trial of Checkpoint blockade in Lung cancEr patients in the Adjuvant setting based on pathologic Response following neoadjuvant therapy (CLEAR)

Patient Population

See protocol Section 3 for complete eligibility criteria

Patients will be consented and registered to Step 0 at any point from initiation of neoadjuvant chemo-immunotherapy through post-surgery. **Patients without pCR after surgery will continue to Step 1 on EA5231**. Patients with pCR after surgery will be offered enrollment in SWOG study S2414/INSIGHT instead (if available at the site)

Step 0 (Registration) Eligibility Criteria:

- ≥ 18 years of age; Stage II to select stage IIIB (N2 but excluding N3) NSCLC of any histology (IASLC 8th ed.)
- Must be one of the following: 1) planning to undergo/ currently undergoing/ recently completed any SOC neoadjuvant chemoimmunotherapy with plans to undergo surgical resection, 2) recently completed any SOC neoadjuvant chemoimmunotherapy AND completed surgical resection (awaiting pCR status), ***or*** 3) completed any SOC neoadjuvant chemo-immunotherapy AND completed surgical resection with confirmed non-path CR status

Step 1 (Randomization) Eligibility Criteria:

- Must have completed R0 resection after SOC ≥ 3 cycles of neoadjuvant treatment; must have non-pathological CR status post-surgery
- ECOG PS 0-2/Karnofsky ≥ 60%; adequate lab values ≤ 28 days prior to Step 1 randomization; body weight > 30 kg
- No known EGFR/ALK genetic alterations
- Must have chest CT after surgery and ≤ 28 days prior to Step 1 randomization
- Must not have experienced a toxicity that led to the permanent discontinuation of prior immunotherapy
- Must not be receiving ongoing steroids at a dose of 10 mg prednisone or higher (or equivalent); no history of treatment-related pneumonitis per protocol
- Must not have received/plan to receive post-op RT
- No history of interstitial lung disease, active primary immunodeficiency, or allogenic organ transplant
- Must not have a diagnosis of ataxia telangiectasia

Treatment Plan

See protocol Section 5 for complete treatment details

For patients without a pathologic complete response after surgery (Step 1 randomization 1:1):

- 1 cycle = 28 days
- **Arm A:** Durvalumab alone for 12 cycles
  - ◊ Durvalumab 1500 mg IV on Day 1 of each cycle
- **Arm B:** AZD6738 (ceralasertib) + Durvalumab for 12 cycles
  - ◊ AZD6738 (ceralasertib): 240 mg (2 x 120 mg tablets) PO BID, Days 1-7 of each cycle
  - ◊ Durvalumab 1500 mg IV on Day 8 of each cycle

Note:

- *Patients must initiate treatment (C1D1) within 4-12 weeks following surgery*
- *Interruption of > 12 weeks between 2 consecutive cycles will result in discontinuation of study treatment*
- *If durvalumab is permanently discontinued, AZD6738 (ceralasertib) must also be discontinued*
- *There are no permitted dose modifications for durvalumab or dose re-escalations for AZD6738 (ceralasertib)*
- *If one agent is temporarily held due to toxicity related to that agent alone, treatment with the other agent may continue*

Study Chair:
Dwight Owen, MD, MSc

Study Co-Chair:
Charu Aggarwal, MD, MPH

NCTN Study Champions:
- ***SWOG:*** Jeremy Cetnar, 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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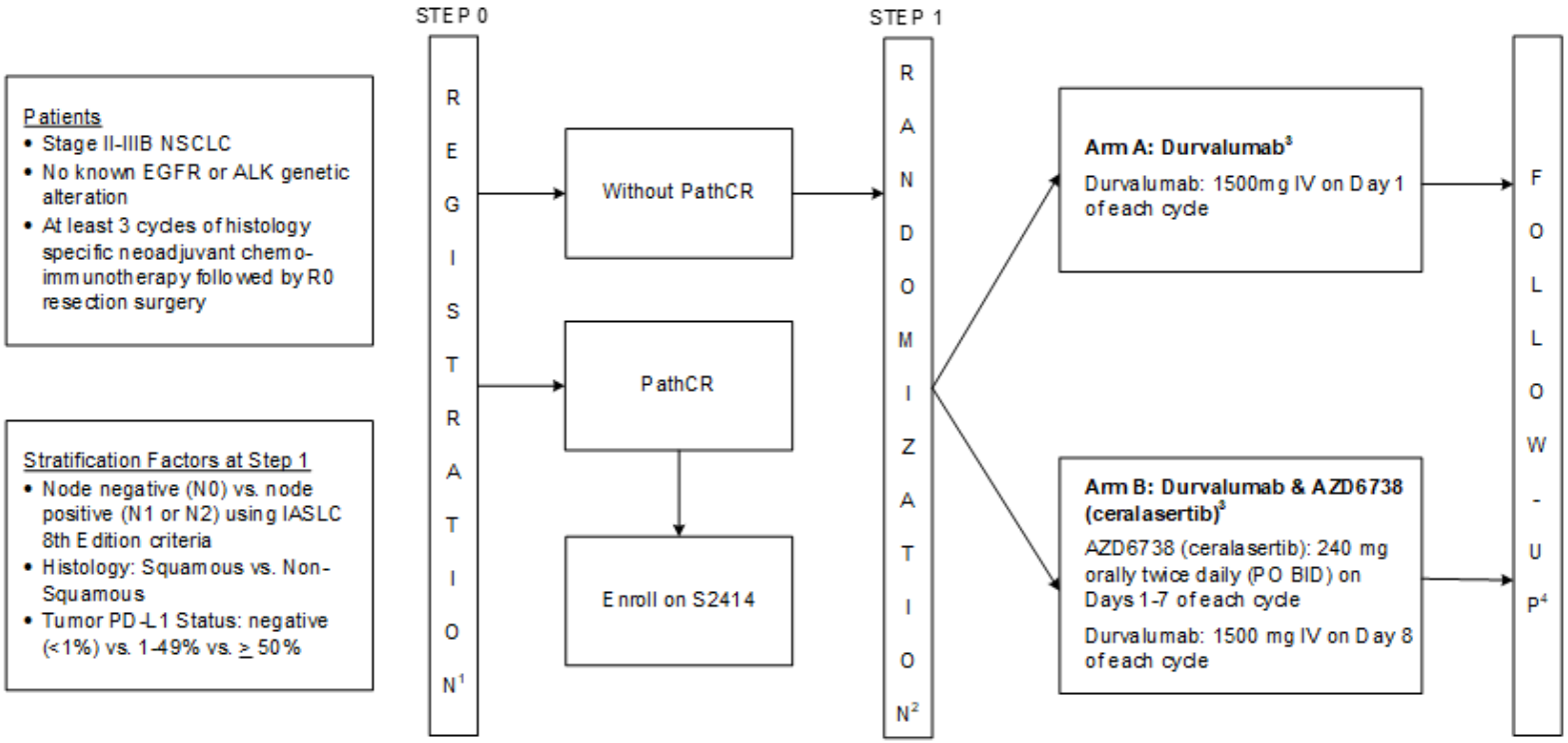
ECOG-ACRIN cancer research group

EA5231

Schema



Patients
- Stage II-IIIB NSCLC
- No known EGFR or ALK genetic alteration
- At least 3 cycles of histology specific neoadjuvant chemo-immunotherapy followed by R0 resection surgery

Stratification Factors at Step 1
- Node negative (N0) vs. node positive (N1 or N2) using IASLC 8th Edition criteria
- Histology: Squamous vs. Non-Squamous
- Tumor PD-L1 Status: negative (<1%) vs. 1-49% vs. ≥ 50%

N = 630
1 Cycle = 28 days

1. Step 0 Registration can occur at any time from initiation of neoadjuvant chemotherapy to post surgery. Patients will then either enroll to Step 1 on EA5231 if they do not have a pathologic complete response (pathCR) post-surgery or be offered enrollment on SWOG protocol S2414 if they have pCR post-surgery. Patient must initiate EA5231 treatment (i.e., D1 of Cycle 1) within 4-12 weeks following surgery
2. Randomization is 1:1
3. Treatment is given for a total of 12 cycles. 1 Cycle = 28 days
4. Patients will be followed for response until progression and for survival for 10 years from the date of Step 1 randomization