EA5142 Available Through ECOG-ACRIN Cancer Research Group

For Patients with NSCLC

Adjuvant Nivolumab in Resected Lung Cancers (ANVIL)-
A Randomized Phase III Study of Nivolumab After Surgical Resection and
Adjuvant Chemotherapy in Non-Small Cell Lung Cancers

Patient Population
See Section 3.0 for Complete Eligibility Details

- Age ≥ 18 years, ECOG PS 0-1, and adequate lab values
- Must have undergone complete surgical resection of their stage IB (≥ 4 cm), II, or IIIA NSCLC (AJCC 7th ed.) and have had negative surgical margins
- Baseline chest CT must be performed within 30 days prior to randomization to ensure no evidence of disease
- Must be registered to the ALCHEMIST-SCREEN (A151216) trial prior to randomization; tumors must have PD-L1 tested centrally as part of A151216
- Non-squamous tumors must not be positive for EGFR Exon 19 deletion/Exon 21 L858R mutation and ALK rearrangement (see protocol for details)
- No uncontrolled intercurrent illness (see protocol); no prior treatment with an immune checkpoint inhibitor
- Must follow minimum and maximum time between surgery and randomization per protocol
- Must have completed and recovered from any adjuvant chemotherapy 2 or more weeks prior to randomization (6 weeks for mitomycin/nitrosoureas; 4 weeks for postoperative RT)
- Must have recovered to Grade ≤ 1 non-hematologic toxicity except for alopecia, ototoxicity and neuropathy
- No known/suspected autoimmune disease, or condition requiring systemic corticosteroids equivalent to > 10 mg prednisone per day (or other immunosuppressive medications) within 2 weeks of randomization; see protocol
- No known interstitial lung disease that is symptomatic or may interfere with the detection/management of suspected drug-related pulmonary toxicity
- No known history of HIV, hep B, or hep C that is untreated and/or with a detectable viral load
- No history of allergic reactions attributed to compounds of similar chemical/biologic composition to nivolumab

Treatment Plan
See Section 5.0 for Complete Treatment Details

All patients must have undergone complete resection of their lung cancer and completed all planned adjuvant chemotherapy and radiation therapy; Cycle = 28 days

Nivolumab Arm:
- Patients will receive their first dose within 14 working days of randomization
- Nivolumab is administered at a flat dose of 480 mg IV (30-minute [+/- 5 min]) on day 1 (+/- 2 days), q4 weeks for up to 1 year
- Note: for patients on nivolumab at the time of Add#4 activation, the following transitionary instructions applied:
  - Current 4-week cycle should be completed at the 240 mg IV q2 weeks dosing schedule
  - The next cycle (2 weeks after last 240 mg dose) will begin the 480 mg IV q4 week schedule
- Subjects may be dosed no sooner than 26 days from the previous infusion (or 12 days during the 240 mg q2 weeks schedule)
  - If toxicity is encountered, nivolumab can be interrupted, delayed, or discontinued (delays may be no longer than 10 weeks)
  - Dose reductions are not permitted
- Premedications are not given prior to the first dose of nivolumab; if a grade 1 or 2 infusion related reaction occurs, patients may be administered premedication prior to future nivolumab infusions

Observation Arm:
- Patients will be followed serially with CT imaging as outlined in Section 7
- The duration of observation should not exceed 1 year

Patient Enrollment
All Sites: Oncology Patient Enrollment Network (OPEN) https://open.ctsu.org

Protocol Information

Please Enroll Your Eligible Patients!
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### Eligibility
- Patient registered to ALCHEMIST screening trial (A151216)
- If non-squamous, no ALK rearrangement or EGFR Exon 19 deletion/Exon 21 L858R mutation
- No contraindication to nivolumab

### Stratification
- Stage AJCC 7th edition: IB/IIA vs IIIB/IIIA
- Histology: squamous vs. non-squamous
- Prior adjuvant treatment for lung cancer (none vs chemotherapy vs chemotherapy + radiation)
- PD-L1 status: positive ($\geq 1\%$) vs. negative ($< 1\%$)/non-evaluable membranous expression determined centrally

### Schema

**Randomize**

- **ARM A**
  - Nivolumab 480 IV q4 weeks for up to 1 year

- **ARM B**
  - Observation per standard of care for up to 1 year

### Cycle
- 4 weeks (28 days)

### Accrual Goal
- 903 patients

1. If Stage 1B, then tumor must be $\geq 4cm$
2. Adenosquamous should be grouped as non-squamous
3. PD-L1+ is defined as $\geq 1\%$ by IHC
4. Patients will be followed for recurrence and survival for 10 years