Version 06/07/22 (Add. #3)

NCI National Clinical Trials Network

EA5181

ECOG-ACRIN cancer research group

For Patients with Unresectable Stage 3 NSCLC

EA5181 Available Through ECOG-ACRIN Cancer Research Group

Randomized Phase III Trial of MEDI4736 (durvalumab) as Concurrent and Consolidative Therapy or Consolidative Therapy Alone for Unresectable Stage 3 NSCLC

Patient Population

See Section 3.0 for Complete Eligibility Details

Step 1 Eligibility– Concurrent Therapy:

- ≥ 18 years old; ECOG PS 0-1; adequate lab values; measurable disease (RECIST 1.1); must have body weight > 30 kg (no unintentional weight loss > 10% within 30 days of registration)
- Must have either newly diagnosed stage IIIA/B/C NSCLC (AJCC 8th ed.) that is unresectable and is histologically and/or cytologically confirmed OR nodal recurrence after surgery for early stage NSCLC (see protocol)
  - ◊ Patients with nodal recurrence after surgery are eligible if no prior chemotherapy/radiation was ever administered for this lung cancer, prior curative-intent surgery was at least 90 days prior to the nodal recurrence, and no prior radiation was administered to the region of study cancer that would cause overlap of treatment fields
- No active, known or suspected autoimmune disease and neuromuscular paraneoplastic syndromes (see protocol)
- No prior allogeneic bone marrow transplantation/solid organ transplant; no past radiation to the current intended treatment site; no prior systemic treatment with antibodies/drugs targeting T-cell costimulation/immune checkpoint inhibitors
- Review protocol for cardiac criteria

Step 2 Eligibility– Consolidation:

- Must not receive any non-protocol anti-cancer therapy after the end of Step 1 chemo/radiation or during Step 2 consolidation
- > Grade 2 non-hematologic or > Grade 3 hematologic toxicities must recover to Grade 2 or less within 45 days after the end of Step 1 concurrent chemo/radiation (exceptions per protocol); patients with suspected ≥ Grade 2 pneumonitis (non-infectious) are not eligible for Step 2 durvalumab and will proceed to follow-up
- Must not have disease progression on the first post-treatment chest CT scan (obtained within 14 days of the last dose of RT); patient will proceed to follow-up if so

Treatment Plan

See Section 5.0 for Complete Treatment Details

Cycle length depends on investigator's choice of chemotherapy regimens (Option 1: cisplatin and etoposide; Option 2 for non-squamous histology only: pemetrexed, cisplatin, folic acid, B12; Option 3: paclitaxel and carboplatin)

Step 1:

- Arm A: Concurrent chemotherapy/radiotherapy and durvalumab:
  - ◊ Systemic platinum double chemotherapy (investigator's choice) given concurrent with radiotherapy (60Gy in 2Gy fractions; 5 days/week)
  - ◊ Durvalumab 750mg IV every 2 weeks for 3 doses during concurrent chemo/radiation
- Arm B: Concurrent chemotherapy/radiotherapy:
  - ◊ Systemic platinum double chemotherapy (investigator's choice) given concurrent with radiotherapy (60Gy in 2Gy fractions; 5 days/week)

Step 2:

- Arm C: Consolidative durvalumab for up to 1 year (12 monthly cycles):
  - ◊ Patients from both Arm A and Arm B (Step 1) will be registered to Step 2 and receive consolidative durvalumab 1500 mg IV every 28 days for 1 year starting within 14 days after the last dose of Step 1 radiation

Notes:

- *Doses are based on the patient's actual weight*
- *Doses that are missed during the weekly RT schedule will not be made up but will be documented*
- *All treatment visits must occur +/- 3 days from the scheduled date*
- *Chemotherapy should be given prior to the radiation therapy on the day of treatment*
- *IMRT and 3DCRT are allowed*

Study Chair:
Nathan Pennell, MD, PhD

Co-Chair:
John Varlotto, MD

Patient Enrollment

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

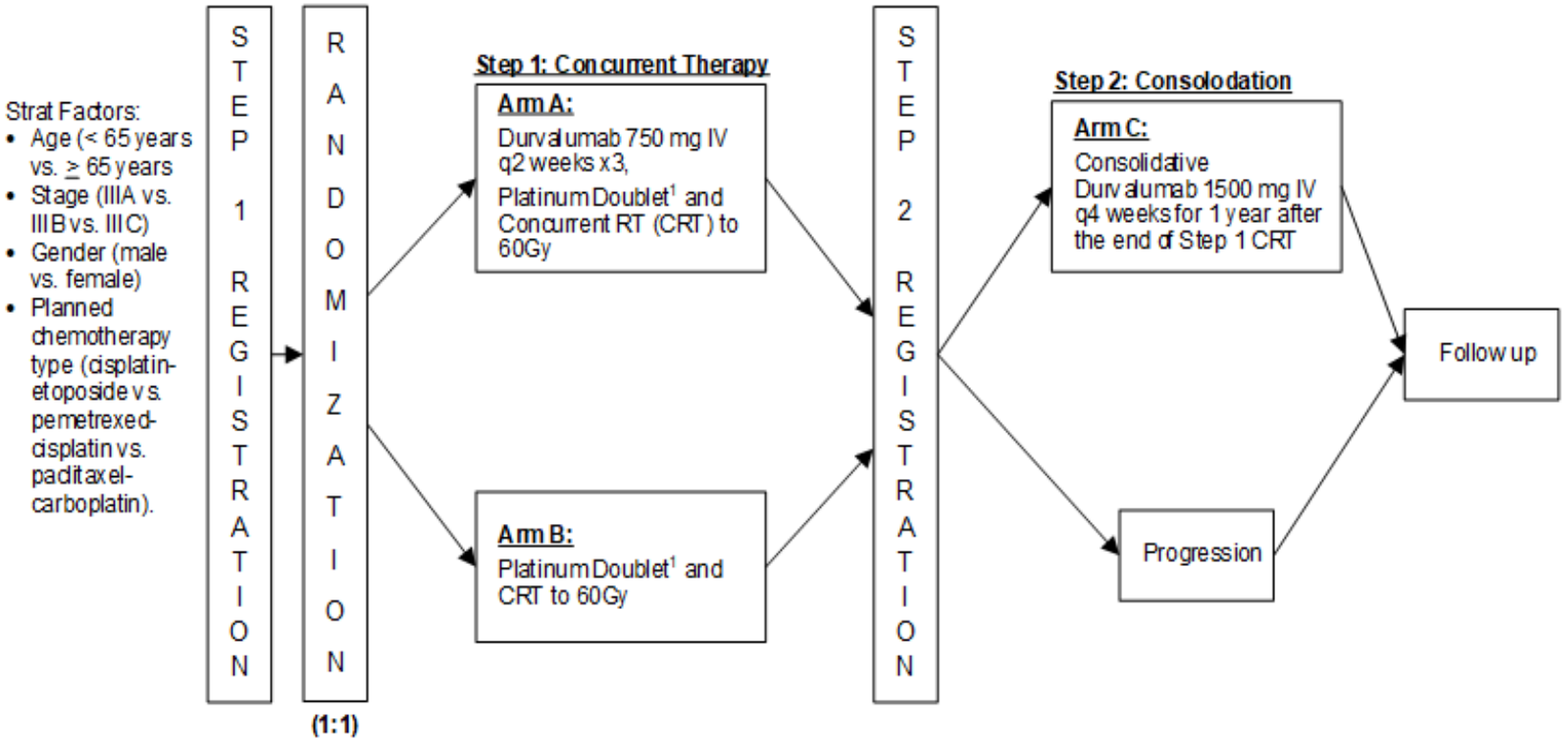
Protocol Information

ECOG-ACRIN Operations-Boston: 857-504-2900, http://ecog-acrin.org (Member Login)

Please Enroll Your Eligible Patients!

EA5181

Schema



N = 660

Cycle = Step 1 (Arms A & B): 28 days for patients receiving platinum doublet option #1 (see below)
21 days for patients receiving platinum doublet option #2 (see below)
7 days for patients receiving platinum doublet option #3 (see below)
Step 2 (Arm C): 28 days for patients on consolidative durvalumab (Arm C).

1. Investigator's Choice for Step 1 (see Section 5.1):
   a. Option #1: Cisplatin 50 mg/m2 IV on C1D1, C1D8, C2D1, C2D8; Etoposide 50 mg/m2 IV C1D1-D5; C2D1-D5 (Cycle = 28 days)
   b. Option #2: Pemetrexed 500 mg/m2 IV C1D1, C2D1; Cisplatin 75 mg/m2 IV on C1D1, C2D1 (Cycle = 21 days) (nonsquamous only)
   c. Option #3: Paclitaxel 45 mg/m2 IV on D1 of each cycle for 6 cycles; Carboplatin AUC 2 IV on D1 of each cycle for 6 cycles (Cycle = 7 days)