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NCI National Clinical Trials Network

EA6141

ECOG-ACRIN cancer research group

For Patients with Unresectable Melanoma

EA6141 Available Through ECOG-ACRIN Cancer Research Group

Randomized Phase II/III Study of Nivolumab plus Ipilimumab plus Sargramostim versus Nivolumab plus Ipilimumab in Patients with Unresectable Stage III or Stage IV Melanoma

Patient Population

See Section 3 for Complete Eligibility Details

- Age ≥ 18, ECOG PS 0-1, and adequate lab values
- Must have known BRAF mutational status of tumor; Wild-type or mutated, prior to randomization
- Must have unresectable stage III/IV melanoma (AJCC v7); histological/cytological confirmation of melanoma that is metastatic or unresectable and clearly progressive
- Must have measurable disease (RECIST 1.1)
- May have had prior systemic therapy in the adjuvant setting (i.e., interferon, BRAF, MEK agents); may have had prior anti-CTLA-4 or anti-PD-1/anti-PD-L1 in the adjuvant setting, if at least 1 year from last dose of treatment
- May not have had any prior ipilimumab and/or anti-PD-1/PD-L1 agent in the metastatic setting
- Must have discontinued chemotherapy, immunotherapy, or other investigational agents used in the adjuvant setting ≥ 4 weeks prior to randomization; ≥ 6 weeks for mitomycin/nitrosoureas; ≥ 2 weeks for RT; ≥ 4 weeks for surgery
- Must not have had any live vaccine per protocol timeline (see protocol for details)
- No currently active CNS metastases; patients with only whole brain irradiation for CNS are ineligible
- No serious/unstable pre-existing medical conditions (see protocol for examples)
- Must not have HIV or active HBV/HCV infection
- No autoimmune disorders/conditions of immunosuppression that require current ongoing treatment with systemic corticosteroids (exceptions permitted per protocol); no history of symptomatic autoimmune disease, motor neuropathy of autoimmune origin, or other CNS autoimmune disease
- No history of inflammatory bowel disease; no diverticulitis (history of diverticulosis is allowed)

Treatment Plan

See Section 5 for Complete Treatment Details

Cycle = 21 days

Arm A:

- Induction (Cycles 1-4):
  - ◊ Nivolumab 1 mg/kg IV, day 1 of each cycle
  - ◊ Ipilimumab 3 mg/kg IV, day 1 of each cycle
  - ◊ Sargramostim (GM-CSF) 250 ug subQ days 1-14 of each 21 day cycle
- Maintenance (starting with cycle 5; until excessive toxicity, progression, or for 2 years):
  - ◊ Nivolumab 3 mg/kg IV, day 1 of each cycle
  - ◊ Sargramostim (GM-CSF) 250 ug subQ days 1-14 of each 21 day cycle

Arm B:

- Induction (Cycles 1-4):
  - ◊ Nivolumab 1 mg/kg IV, day 1 of each cycle
  - ◊ Ipilimumab 3 mg/kg IV, day 1 of each cycle
- Maintenance (starting with cycle 5; until excessive toxicity, progression, or for 2 years):
  - ◊ Nivolumab 3 mg/kg IV, day 1 of each cycle

Notes:

- *Doses are based on actual body weight. If the patient's weight on the day of dosing differs by > 10% from the weight used to calculate the previous dose, the dose must be recalculated*
- *Nivolumab is infused over 30 minutes, followed by a saline flush; Ipilimumab is then infused over 30 minutes*
  - ◊ *Separate infusion bags and filters must be used for each infusion*

Study Chair:
F. Stephen Hodi, MD

Co-Chair:
Ahmad Tarhini, MD, PhD

Patient Enrollment

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

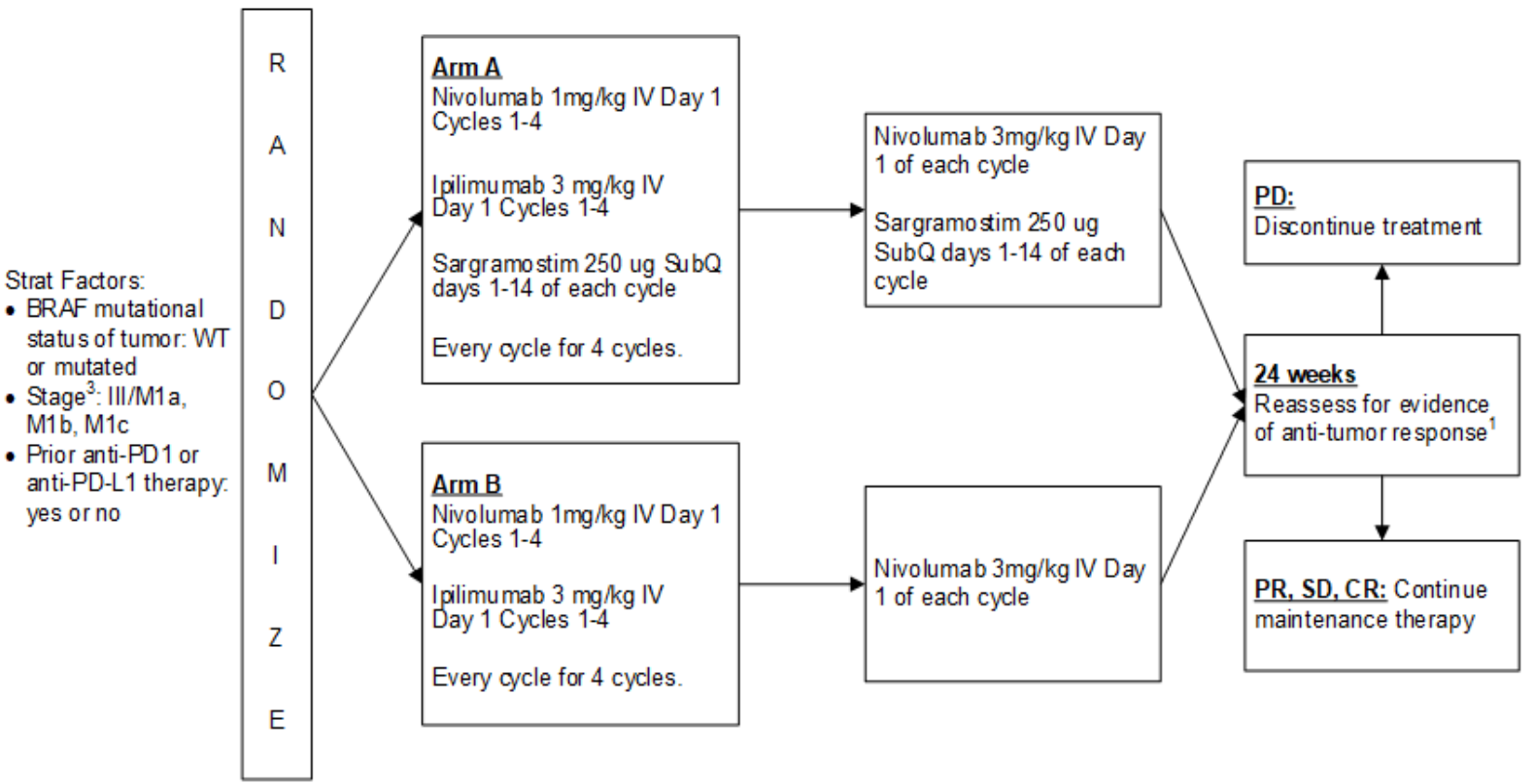
Protocol Information

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

Please Enroll Your Eligible Patients!

EA6141

Schema



Accrual Goal= 600
1 cycle= 21 days

1. Scans will be done at week 12 but treatment should continue until week 24 regardless of progression unless treatment is contraindicated by Section 5.4.
2. Patients will receive protocol therapy until progressive disease, non-protocol therapy, or up to two years, whichever comes first.
3. All patients must be assessed according to AJCC v7 criteria to determine eligibility and stratification for this trial.