# EA6141

## 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/anti-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

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**Study Chair:**
F. Stephen Hodi, MD

**Co-Chair:**
Ahmad Tarhini, MD, PhD

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**Patient Enrollment**

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

**Protocol Information**

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

Please Enroll Your Eligible Patients!
1. Maintenance Therapy Cycle 2 and 3:

- Every cycle for 4 cycles
- Day 1: Cycles 1-4
- Dexamethasone 3 mg/kg IV
- Liposomal doxorubicin 1 mg/kg IV
- Cycles 1-4

2. Induction Therapy Cycle:

- Day 1: Cycles 1-4
- Dexamethasone 3 mg/kg IV
- Liposomal doxorubicin 1 mg/kg IV
- Cycles 1-4

3. 24-week treatment:

- Every cycle for 4 cycles
- Day 1: Cycles 1-4
- Dexamethasone 3 mg/kg IV
- Liposomal doxorubicin 1 mg/kg IV
- Cycles 1-4

4. Discontinue treatment if no partial or complete response or if no evidence of improvement.

5. Restart treatment every 24 weeks if no complete or partial response.

6. Duration of therapy:

- Prior to R-Mei Fd: Pemetrexed 500 mg IV or nelarabine
- Prior to cytarabine or gemcitabine
- Prior to iplaribinetin or temozolomide
- Prior to sunitinib or axitinib
- Prior to acetaminophen or ibuprofen

7. Maintenance therapy:

- Liposomal doxorubicin 1 mg/kg IV
- Dexamethasone 3 mg/kg IV