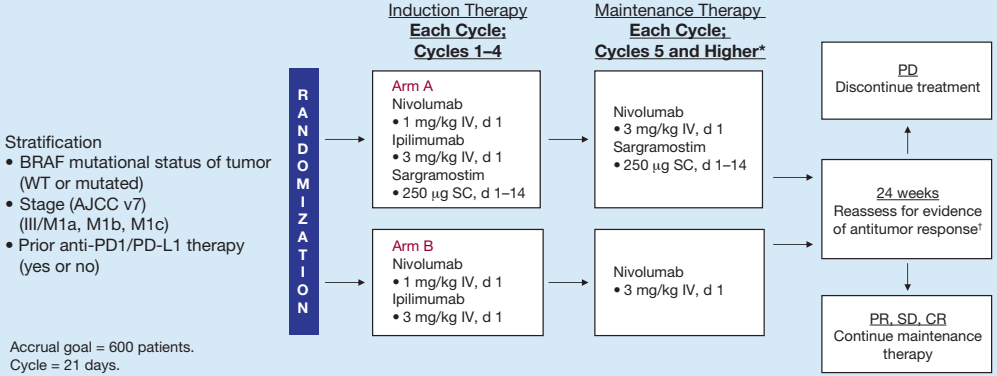
EA6141

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

Study Schema



Accrual goal = 600 patients.
Cycle = 21 days.
Doses are based on actual body weight.
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.
*Patients will receive protocol therapy until progressive disease, non-protocol therapy, or up to 2 years, whichever comes first.
†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.
CR = complete response; PD = progressive disease; PR = partial response; SD = stable disease; WT = wild type.

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Overall EA6141 Study Objectives

To determine whether the addition of sargramostim (granulocyte-macrophage colony-stimulating factor; GM-CSF) to the combination of nivolumab and ipilimumab improves efficacy of the agents, therefore providing a prolonged survival benefit, and whether it improves tolerability by decreasing high-grade adverse events

Study Objectives

Primary Objective

- Compare the overall survival of patients treated with nivolumab/ipilimumab/GM-CSF versus nivolumab/ipilimumab

Secondary Objectives

- Evaluate progression-free survival of patients treated with nivolumab/ipilimumab/GM-CSF versus nivolumab/ipilimumab
- Assess for differences in tolerability, specifically the rate of grade 3 or higher adverse events, between nivolumab/ipilimumab/GM-CSF versus nivolumab/ipilimumab
- Evaluate and compare immune-related response rate (based on immune-related response criteria) and response rate (RECIST criteria)

Exploratory Tobacco Use Objectives

Refer to protocol Section 2.1.3

Eligibility Criteria*

Main Inclusion Criteria

- ≥ 18 years of age
- ECOG performance status 0–1
- Unresectable stage III or IV melanoma (AJCC v7); histologic or cytologic confirmation of melanoma that is metastatic or unresectable and clearly progressive
- Known BRAF mutational tumor status; wild-type or mutated, prior to randomization
- Measurable disease per RECIST 1.1 criteria; all sites of disease must be evaluated within 4 weeks prior to randomization
- May have had:
  - Prior systemic therapy in the adjuvant setting (eg, interferon, BRAF, or MEK agents)

*When evaluating patients for this study, please refer to the full protocol for the complete list of eligibility criteria.

  - Prior anti-CTLA-4 or prior anti-PD-1/PD-L1 agent in the adjuvant setting, if at least one year from the last dose has passed before beginning treatment
- Discontinued chemotherapy, immunotherapy, or other investigational agents used in the adjuvant setting ≥ 4 weeks prior to randomization and recovered from adverse events due to those agents
  - Mitomycin and nitrosoureas must be discontinued ≥ 6 weeks, and radiation therapy ≥ 2 weeks, prior to study entry with recovery from adverse events due to treatment
  - Prior surgery must be ≥ 4 weeks from randomization with full recovery from post-surgical complications
- Adequate hematologic, hepatic, and renal function within 4 weeks prior to randomization

Main Exclusion Criteria

- Prior ipilimumab and/or PD-1/PD-L1 agent in the metastatic setting
- Receiving other investigational agents while on study or within 4 weeks prior to randomization
- Receiving any live vaccine within 30 days prior to randomization, while participating on study, and for 28 days after the last dose of protocol treatment
- Active central nervous system (CNS) metastases
- Any serious or unstable pre-existing medical conditions, including but not limited to, ongoing or active infection requiring parenteral antibiotics on day 1, history of bleeding diathesis or need for concurrent anticoagulation, or psychiatric illness/social situations that would limit compliance with study requirements or interfere with patient's safety or obtaining informed consent
- Active hepatitis B or C viral infection
- HIV positivity
- Autoimmune disorders or conditions of immunosuppression that require current ongoing treatment with systemic corticosteroids (or other systemic immunosuppressants), including oral steroids or continuous use of topical steroid creams/ointments or ophthalmologic steroids
- History of symptomatic autoimmune disease, motor neuropathy considered of autoimmune origin or other CNS autoimmune disease (examples per protocol)
- History of inflammatory bowel disease or diverticulitis (history of diverticulosis is allowed)

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