For Patients with Advanced Melanoma

EA6192 Available Through ECOG-ACRIN Cancer Research Group
A Phase II Study of Biomarker Driven Early Discontinuation of Anti-PD-1 Therapy in Patients with Advanced Melanoma (PET-Stop)

Patient Population
See Section 3 for Complete Eligibility Details

Step 0 Pre-registration Eligibility Criteria:
- Age ≥18 years, ECOG PS 0-2, and adequate lab values
- Must have active advanced melanoma, defined as unresectable stage IIIIB-IV (AJCC 8); exception per protocol
- Must have melanoma originating from cutaneous, acral-lentiginous, or mucosal primary sites (ocular primary site is not eligible; unknown primary site is eligible)
- Must have had measurable disease (imRECIST) prior to start of initial anti-PD-1 therapy, defined per protocol
- Must be actively receiving standard of care anti-PD-1 therapy, currently be 52 weeks (+/- 2 weeks) from start of anti-PD-1 therapy, and have not experienced a toxicity that prevents them from continuing (see protocol for details/permited systemic anti-PD-1 therapy regimens)
- Must not be receiving concurrent anti-tumor therapies in addition to the standard of care anti-PD-1 regimens (patients receiving bisphosphonates and RANKL inhibitors for management of bone metastases are eligible)
- HIV/HBV/HCV patients are eligible per protocol
- Patients with brain metastases are eligible per protocol
- Patients with known history/current symptoms of cardiac disease, or history of treatment with cardiotoxic agents should be NYHA class 2B or better
- Must have experienced complete/partial response, or stable disease on restaging scans (imRECIST) that is maintained on the PET/CT scan at week 52 (+/- 2 weeks) from start of initial anti-PD-1 therapy

Step 1 Registration Eligibility Criteria:
- Must register within 4 weeks of registration to Step 0, and meet one of: 1) Had no positive hypermetabolic lesions on week 52 PDG-PE/T/CT 2) if positive, either a representative lesion was biopsied (core needle, punch, or excisional) and subsequent pathology determines the presence/absence of viable tumor within 28 days of registration to Step 0, OR documentation states the patient is not able to undergo biopsy

Treatment Plan
See Section 5 for Complete Treatment Details

Prior to Step 0 registration, patient must have been actively receiving standard of care anti-PD-1 therapy. All enrolled patients will continue their standard of care anti-PD-1 therapy through 52 weeks (+/- 2 weeks) from start of initial anti-PD-1 therapy, then proceed to Arm A or B:
- Arm A– Negative FDG-PET/CT scan or positive FDG-PET/CT scan, but negative biopsy for viable tumor:
  - Discontinue anti-PD-1 based therapy after week 52 (+/- 2 weeks) from start of initial anti-PD-1 therapy and be monitored by active surveillance
- Arm B– Positive FDG-PET/CT scan and positive biopsy for viable tumor (or biopsy not performed):
  - Continue the same anti-PD-1 based therapy for an additional 48 weeks beyond week 52 (+/- 2 weeks) from the start of initial anti-PD-1 therapy, with one of the following standard FDA approved regimens (maintenance; no switching allowed):
    - Nivolumab 240 mg IV Q 2 weeks or 480 mg IV Q 4 weeks
    - Pembrolizumab 200 mg IV Q 3 weeks or 400 mg IV Q 6 weeks
    - Nivolumab 480 mg/Relatlimab 160 mg FDC IV Q 4 weeks
  - Weight-based dosing or different dosing schedules are permissible as long as dosing is similar/equivalent to the standard flat dosing schedules
  - If disease progression or dose limiting toxicity is not experienced, patients will continue on anti-PD-1 therapy for 2 years total treatment, then discontinue anti-PD-1 and undergo FDG-PET/CT scan
  - If patients experience disease progression (either arm), therapeutic management will be at the discretion of the treating physician

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

Protocol Information

Please Enroll Your Eligible Patients!
1. Patient must be actively receiving standard of care anti-PD-1-based therapy and continue for at least 2 weeks (4+ of 2 weeks) from start of study.

2. Patients assigned to Arm B will continue the same anti-PD-1-based therapy (Nivolumab, Pembrolizumab, or Nivolumab/Pembrolizumab, FDC).

**Schema**

- **Step 0**: Restart with advanced melanoma and FDC.
- **Step 1**: Monitor with serial CT scans every 2 weeks. Discontinue therapy if no lesions appear.
- **Study**: Biopsy all residual lesions of FDG-PET/CT scan.
- **Monitor of treatment**: 
  - If positive, repeat the same anti-PD-1-based therapy (Nivolumab, Pembrolizumab, or Nivolumab/Pembrolizumab, FDC).
  - If negative, repeat the same anti-PD-1-based therapy (Nivolumab, Pembrolizumab, or Nivolumab/Pembrolizumab, FDC).

AmB: PD-1 based therapy.