Protocol Title: Randomized Phase III Trial of Dabrafenib + Trametinib Followed by Ipilimumab + Nivolumab at Progression vs. Ipilimumab + Nivolumab Followed by Dabrafenib + Trametinib at Progression in Patients with Advanced BRAFV600 Mutant Melanoma

Target Population: Stage III-IV Melanoma
- BRAF V600 Mutant Melanoma
- Recurrent or Metastatic Melanoma

Summary: To determine whether initial treatment with either combination Ipilimumab + Nivolumab (with subsequent Dabrafenib in combination with Trametinib) or Dabrafenib in combination with Trametinib (with subsequent Ipilimumab + Nivolumab) significantly improves 2-Year Overall Survival (OS) in patients with Unresectable Stage III or Stage IV BRAF V600 Mutant Melanoma.

Key Inclusion Criteria:
- **STEP 1:**
  - Patients must have Unresectable Stage III or Stage IV disease.
  - Measurable disease.
  - Melanoma that is metastatic or unresectable and clearly progressive.
    - NOTE: Any patient with BRAF V600 Mutant Melanoma (whether Cutaneous, Acral, or Mucosal Primary) who meets the eligibility criteria is eligible for participation in this trial.
    - Patients with Uveal Melanoma are NOT eligible for this trial.
  - Patients must have BRAF V600 Mutation.
  - Patients may have had prior systemic therapy in the adjuvant setting.
    - However, this adjuvant treatment must not have included a CTLA4 or PD1 Pathway Blocking Antibody or a BRAF/MEK Inhibitor.
    - Patients may not have had any prior systemic treatment for advanced (measurable metastatic) disease.
  - Patients must have discontinued chemotherapy, immunotherapy or other investigational agents used in the adjuvant setting ≥ 4 Weeks prior to entering the study and recovered from adverse events due to those agents.
    - Mitomycin and Nitrosoureas must have been discontinued ≤ 6 Weeks prior to entering study.
    - Patients must have discontinued radiation therapy ≥ 2 Weeks prior to entering the study and recovered from any adverse events associated with treatment.
  - Patients are ineligible if they have any currently active Central Nervous System (CNS) Metastases.
- **STEP 2 (CROSSOVER ARM FOR PATIENTS WITH PROGRESSIVE DISEASE):**
  - The patient must have met all eligibility criteria (except as detailed below) at the time of crossover:
    - Measurable disease is not required.
    - Only prior systemic therapy as part of Step 1 is allowed.
  - Patients must have Melanoma that is metastatic and clearly progressive.

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For additional information: https://clinicaltrials.gov/ct2/show/study/NCT02224781