For Patients with Melanoma

EA6183 Available Through ECOG-ACRIN Cancer Research Group
A Phase II Neoadjuvant Study of Encorafenib with Binimetinib in Patients with Resectable Locoregional Metastases from Cutaneous or Unknown Primary Melanoma
(Stages III N1B/C/D)

Patient Population
See Section 3.0 for Complete Eligibility Details

- Age ≥18 years, ECOG PS 0-1, & adequate lab values
- Must have histologically proven melanoma that is clinically evidence (macroscopic LAD) stage III B/C/D (AJCC 8th ed.) of cutaneous origin or unknown primary; must have at least 1 clinically evident lymph node metastasis (N1c/stage IV melanoma patients are not eligible)
- Must have measurable disease on baseline imaging scans (defined per protocol; target tumor must be completely resectable); no evidence of distant metastases
- BRAF V600 mutation positive (CLIA certified lab)
- Must be medically fit to undergo surgery; must be able to take oral medications
- No prior treatment with BRAFi/MEKi
- No prior adjuvant therapy at this disease presentation; prior immune therapy is permitted if ≥ 6 months from last treatment
- No prior radiation to the site of evaluable disease
- Must not have active infection requiring treatment with parenteral antibiotics
- Must be able to lie still during the 18F-FLT PET/CT scan, have no previous indication of allergic reaction to the radiotracer, and meet the size limits of the qualified PET/CT scanner (see protocol for qualification details)
- Must not have impaired cardiovascular function/clinically significant cardiovascular disease (see protocol)
- Must not have impairment of GI function or disease which may significantly alter the absorption of study drug, or recent history of a partial/complete bowel obstruction
- No known history of acute/chronic pancreatitis, no history/current evidence of RVO, or risk factors for RVO
- No concurrent neuromuscular disorder that is associated with elevated CK
- No history of thromboembolic/cerebrovascular events ≤ 12 weeks prior to registration

Treatment Plan
See Section 5.0 for Complete Treatment Details

1 cycle = 28 days

Neoadjuvant Treatment (pre-surgery):
- Must begin treatment within 14 working days of registration
- Encorafenib 450 mg po once daily x 8 weeks (2 cycles)
- Binimetinib 45 mg po twice daily x 8 weeks (2 cycles)

Surgical Resection:
- Must be performed within 2 weeks of completing neoadjuvant treatment
- Must be surgically managed with complete removal of target site of metastatic melanoma, i.e., complete lymph node dissection, as feasible by surgeon
- Wide local excision of the primary/surgical exploration and formal lymphadenectomy with excision of the primary or in transit lesions should be carried out per standard recommendations (see protocol)

Adjuvant Treatment (post-surgery):
- Treatment with encorafenib and binimetinib resumes for an additional 44 weeks (11 cycles), at the same dose that was tolerated during the initial 8 weeks
- Treatment will resume within 2-7 days after surgery
- Radiation therapy is not permitted after surgery

Imaging:
- Baseline FLT-PET/CT
- Post-neoadjuvant FLT-PET/CT

Notes:
- Do not make up dose if vomiting occurs; take with or without food

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

Protocol Information

Please Enroll Your Eligible Patients!
Cycle Length = 28 days

1. FLT-Pre1: The first FLT-Pre is to be done at baseline prior to initiation of neoadjuvant treatment. The second FLT-Pre is to be done after the neoadjuvant treatment.

2. Neoadjuvant treatment begins 15 mg po once daily x 6 weeks, concurrently with FLT-Pre1. (2 Cycles)

3. Surgical resection

4. Neoadjuvant Post (2 Cycles) at least daily x 6 weeks, concurrently with FLT-Pre2.

Baseline FLT-Pre can be completed prior to the biopsy (can be done on the day).