For Patients with Chronic Myeloid Leukemia

EA9171 Available Through ECOG-ACRIN Cancer Research Group

BLAST MRD CML 1: Blockade of PD-1 Added to Standard Therapy to Target Measurable Residual Disease (MRD) in Chronic Myeloid Leukemia (CML)
- A Phase II Study of Adding the Anti-PD-1 Pembrolizumab to Tyrosine Kinase Inhibitors in Patients with CML and Persistently Detectable MRD

**Patient Population**
- See Section 3.0 for Complete Eligibility Details

- Pre-registration (Step 0); peripheral blood must be collected for registration to Step 1:
  - Age ≥ 18; pathologically-confirmed chronic phase-CML per protocol (accelerated/blast phase CML not eligible)
  - Patient has been on TKI therapy (1st, 2nd, and 3rd line) for at least 2 years (starting from when 1st TKI initiated) prior to Step 0 pre-registration (see protocol)
  - No prior therapy with an anti-PD-1/L1/L2
  - No prior allogeneic transplant

- Registration to Treatment (Step 1 & Step 2):
  - MRD+ status confirmed per protocol
    - Step 2: MRD+ following Step 1 treatment
    - Any patient who has previously confirmed UMRD, even if reverted back to MRD+ is ineligible
  - ECOG PS 0-1 and adequate lab values
  - No active hemolytic anemia requiring immunosuppressive therapy/other pharmacologic treatment
  - No diagnosis of immunodeficiency/can’t be receiving systemic steroid therapy/other form of immunosuppressive therapy within 7 days of treatment
  - Cannot receive corticosteroids (exception per protocol)
  - No history of active TB/non-infectious pneumonitis
  - No history of hypersensitivity to pembrolizumab or any of its excipients
  - No prior anti-cancer mAb within 4 weeks of registration
  - No prior chemotherapy, targeted small molecule therapy (except imatinib/dasatinib/bosutinib/nilotinib), or RT within 2 weeks prior to Step 1 registration
  - No active CNS metastases/carcinomatous meningitis/autoimmune disease that required systemic treatment in the past 2 years (Step 1 only)
  - No active infection requiring systemic therapy; no live vaccines within 30 days of registration
  - HIV and Hep C positive patients permitted per protocol

**Treatment Plan**
- See Section 5.0 for Complete Treatment Details

- Cycle = 21 days; drugs per actual body weight

**Arm A- Pembrolizumab with TKIs (Cycle 1-18):**
- Pembrolizumab 200 mg IV over 30 mins day 1; TKIs (Imatinib, Dasatinib, Bosutinib, or Nilotinib; see protocol for starting doses) per treating physician
- If BCR-ABL becomes undetectable, the patient will discontinue pembrolizumab after cycle 18, otherwise the patient will continue on to Arm B
- Patients who achieve UMRD, but convert back to MRD+ should continue pembrolizumab and 1 year of further TKI from the date of confirmed URMD; patients without confirmed UMRD that remain MRD+ at the end of cycle 18 will go to Arm B
- Maintenance: 1 year of TKI from date of confirmed UMRD

**Arm B- Pembrolizumab with TKIs (Cycle 19-36):**
- Pembrolizumab 200 mg IV over 30 mins day 1; TKIs per treating physician
- If BCR-ABL becomes undetectable and remains so for 1 year after the first negative assay, the patient will discontinue TKI therapy
- Maintenance: 1 year of TKI from date of confirmed UMRD

For patients who achieve UMRD, but convert back to MRD+ before discontinuing TKI:
- If the conversion to MRD with loss of MMR is confirmed on 2 occasions and/or there is any other evidence of cytogenetic, hematologic, or clinical progression, the patient should be taken off treatment
- If the conversion to MRD does not reach level of loss of MMR and there is no evidence of cytogenetic, hematologic, or clinical progression, the patient may remain on current therapy plan

Note: All protocol treatment is administered on an outpatient basis (+/- 3 days from day 1); window of −5 and +10 minutes for pembrolizumab administration

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

**Protocol Information**

Please Enroll Your Eligible Patients!