NCI National Clinical Trials Network

EA9171/BLAST MRD CML 1

For Patients with 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; bone marrow aspirate and/or biopsy confirmed chronic phase CML per protocol
  - ◊ Step 2: MRD+ following Step 1 treatment
- ECOG PS 0-2 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 from time of consent to registration (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 prior to study registration/not recovered from earlier AEs (Step 1 only); 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

Arm A- Pembrolizumab with TKIs (Cycle 1-18):

- Pembrolizumab 200 mg IV over 30 mins day 1; TKIs (Imatinib, Dasatinib, Bosutinib, or Nilotinib) 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; if BCR-ABL remains undetectable for 1 year after the first negative assay, the patient will discontinue TKI therapy

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

TKI recommended starting doses (see protocol):
Imatinib 400 mg PO once daily days 1-21, Dasatinib 100 mg PO once daily days 1-21, Nilotinib 300 mg PO twice daily days 1-21, Bosutinib 400 mg PO once daily days 1-21

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

Notes:

- *Drugs are administered according to actual body weight*
- *All protocol treatments will be administered on an outpatient basis (+/- 3 days from day 1)*
- *There is a window of –5 minutes and +10 minutes for pembrolizumab administration*

Study Chair:
Amer M. Zeidan, MD

Patient Enrollment

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

Protocol Information

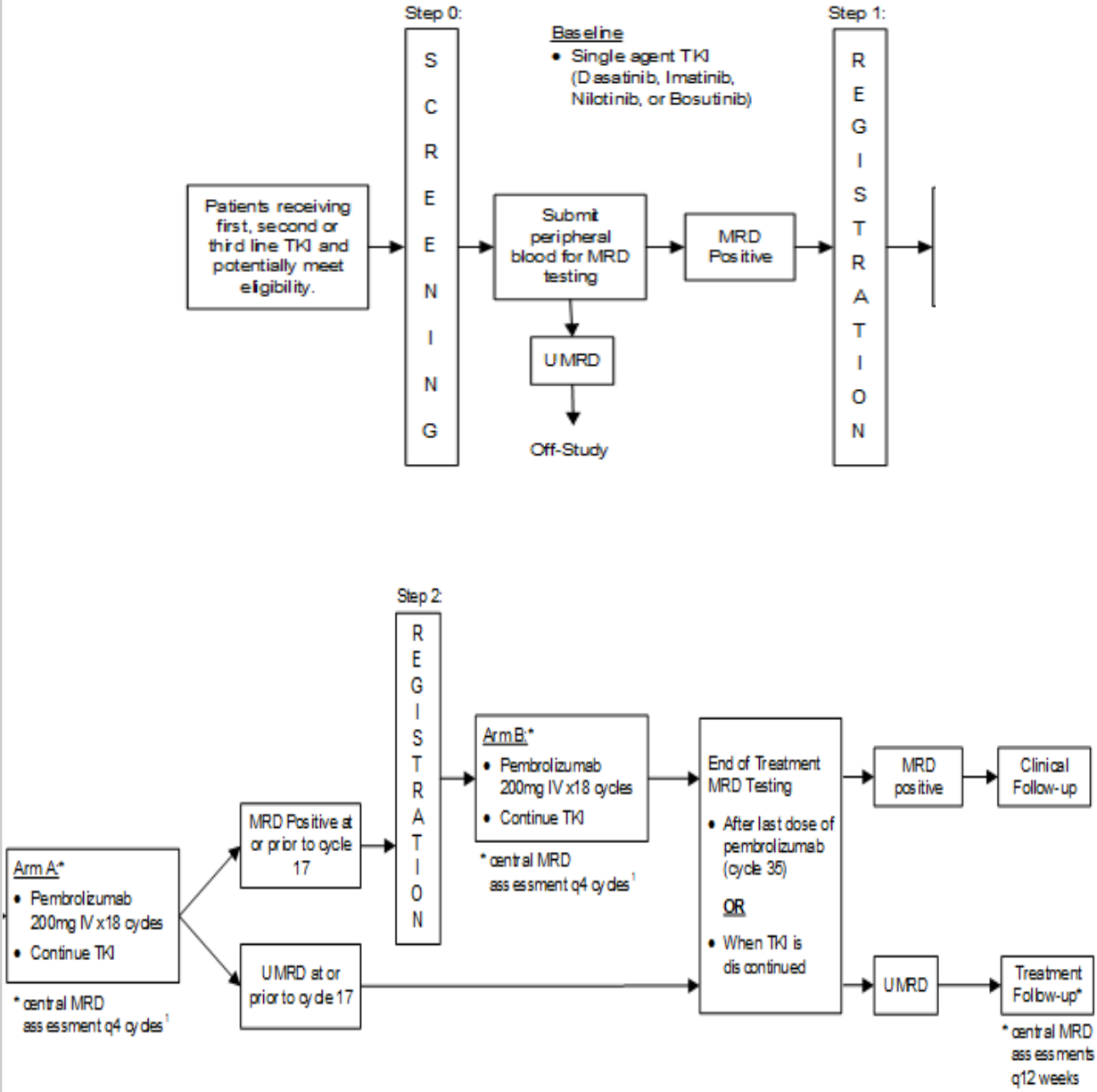
ECOG-ACRIN Operations-Boston: 857-504-2900, http://ecog-acrin.org (Member Login)

Please Enroll Your Eligible Patients!

EA9171

ECOG-ACRIN cancer research group

Schema



1. Assessed at cycles 5, 9, 13, 17 (Arm A) and 21, 25, 29, 33 (Arm B) prior to pembrolizumab dose. For patients who discontinue TKI, MRD will be assessed centrally q4 weeks for the first 6 months post TKI discontinuation; q8 weeks for the subsequent 6 months post TKI discontinuation; then q12 weeks for 12 months.