

## COG-AAML18P1: Stopping Tyrosine Kinase Inhibitors (TKI) to Assess Treatment-Free Remission (TFR) in Pediatric Chronic Myeloid Leukemia - Chronic Phase (CML-CP)

### FAST FACTS

Eligibility Reviewed and Verified By \_\_\_\_\_

MD/DO/RN/LPN/CRA Date \_\_\_\_\_

MD/DO/RN/LPN/CRA Date \_\_\_\_\_

Consent Version Dated \_\_\_\_\_

### PATIENT ELIGIBILITY:

**Important note:** The eligibility criteria listed below are interpreted literally and cannot be waived (per COG policy posted 5/11/01). All clinical and laboratory data required for determining eligibility of a patient enrolled on this trial must be available in the patient's medical research record which will serve as the source document for verification at the time of audit.

All clinical and laboratory studies to determine eligibility must be performed within 7 days prior to enrollment unless otherwise indicated. Most recent RQ-PCR result to confirm remission may be up to 30 days old from the date drawn.

\_\_\_ 1. Timing

Patients must be enrolled before treatment is discontinued. The date TKI is planned to be discontinued must be no later than **ten (10)** calendar days after the date of study enrollment. **Patients who discontinue treatment prior to study enrollment will be considered ineligible.**

\_\_\_ 2. Age

Patient must have been diagnosed with CML-CP at < 18 years of age.

- Patient must be < 25 years of age at enrollment

\_\_\_ 3. Diagnosis

- Patient must have histologic verification of CML-CP at original diagnosis.
- Patient must be in molecular remission (MR) with a BCR-ABL1 level of  $\leq 0.01\%$  BCR-ABL1 as measured using the International Scale (IS) by RQ-PCR for  $\geq 2$  consecutive years at the time of enrollment. See [Section 8.2.2](#) for definitions of MR status.

**Please Note:** The lab evaluating disease status and molecular response for this study must be College of American Pathology (CAP) and/or Clinical Laboratory Improvement Amendments (CLIA) certified (US only), sites in other countries must be certified by their accredited authorities. All labs must use the International Scale guidelines with a sensitivity of detection assay  $\leq 0.01\%$  BCR-ABL1 and be able to report results in  $\leq 2$  weeks.

\_\_\_ 4. Prior Therapy

Patient must have received any TKI for a minimum of 3 consecutive years at time of enrollment.

\_\_\_ 5. Patient agrees to discontinue TKI therapy.

The required age of assent is 14.

### EXCLUSION CRITERIA

- \_\_\_ 1. Known T3151 mutation.
- \_\_\_ 2. Additional clonal chromosomal abnormalities in Ph<sup>+</sup> cells at any time prior to enrollment that include "major route" abnormalities (second Ph, trisomy 8, isochromosome 17q, trisomy 19), complex karyotype or abnormalities of 3q26.2.
- \_\_\_ 3. History of accelerated phase or blast crisis CML. See [Section 8.2.6](#) and [Section 8.2.7](#) for the definitions of accelerated phase and blast crisis.
- \_\_\_ 4. Female patients who are pregnant.
- \_\_\_ 5. Lactating females are not eligible unless they have agreed not to breastfeed their infants.
- \_\_\_ 6. Female patients of childbearing potential are not eligible unless a negative pregnancy test result has been obtained.

## **REQUIRED OBSERVATIONS:**

### **Required Tests**

- Physical exam including spleen measurement
  - Height, weight, BMI
  - Tanner stage
  - RQ-PCR for BCR-ABL1 (IS) (peripheral blood)<sup>B, R</sup>
  - CBC with diff and platelets
  - Creatinine, total bilirubin, AST, ALT, albumin, BUN, sodium, potassium, chloride, bicarbonate, calcium, phosphate, magnesium
  - Urinalysis
  - Pregnancy test for females of childbearing potential
- <sup>B</sup> The baseline/pre-TKI discontinuation RQ-PCR for BCR-ABL1 does not need to be repeated if the test was done within 21-days prior to TKI discontinuation.
- <sup>R</sup> If the patient needs to re-start TKI per study guidelines, another BCR-ABL1 test is not required prior to re-starting TKI if the test was done within 21 days of re-starting TKI.

**Recommended Tests** – may be performed 6 weeks before and up to 6 weeks after discontinuation of TKI

- T, NK and B-cell quantification, IgA, IgG, IgM, IgE, IgD
- Parathyroid hormone, alkaline phosphatase, vitamin D
- T4, TSH
- Fasting blood glucose, HbA1c, total cholesterol, HDL-C, LDL-C, triglycerides
- **Females**-FSH, LH, estradiol, AMH for patients who are age > 8 years or if patient has started puberty
- **Males**-FSH, LH, testosterone for patients who are age > 10 years or if patient has started puberty
- ECG
- MUGA or ECHO
- DEXA scan, growth hormone, IGF1, IGFBP3 (**These tests are recommended, please upload results if available**)

## **TREATMENT PLAN:**

### **Discontinuation of TKI**

After the patient is enrolled, the patient should be instructed to stop taking their TKI medication within 10 calendar days after the enrollment. The date the patient first stopped taking their TKI medication will serve as the date to measure the time points for study observations and disease evaluations.

### **Required Reporting:**

See Section 10 for patient reported outcomes

See Section 11 for neurocognitive outcomes

## **OPTIONAL SPECIMEN REQUIREMENTS:**

10mL of whole blood per Section 12