Cancer Research Consortium of West Michigan
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FAST FACTS

S1712 - A RANDOMIZED PHASE II STUDY OF RUXOLITINIB (NSC-752295) IN COMBINATION WITH BCR-ABL TYROSINE KINASE INHIBITORS IN CHRONIC MYELOID LEUKEMIA (CML) PATIENTS WITH MOLECULAR EVIDENCE OF DISEASE

ELIGIBILITY CRITERIA

Disease Related Criteria

a. Patients must have a diagnosis of chronic phase chronic myeloid leukemia without any history of progression to accelerated or blast phase CML (as defined in Section 4.0). No new bone marrow aspiration and biopsy is needed to prove diagnosis prior to randomization; however, documentation stating the patient is in chronic phase is required.
b. Patients must have detectable BCR-ABL transcripts measured by RT-PCR at a CLIA-approved laboratory and reported on the International Scale (IS) with a value of > 0.0032% IS and ≤ 1.0% IS within 21 days prior to randomization. The RT-PCR assay must have the sensitivity to detect a 4.5 log reduction in BCR-ABL transcripts from 100% IS (must be able to detect (0.0032% IS or lower).

Prior/Concurrent Therapy Criteria

a. Patients must have been on TKI therapy for CML for at least 12 months prior to randomization. Hydroxyurea prior to initiation of TKI is allowed.
b. Patients must be currently receiving treatment with bosutinib (within the allowable dose range of 200-500 mg daily), nilotinib (within the allowable dose range of 150-400 mg BID or a cumulative daily dose of 300-800 mg), imatinib (within the allowable dose range of 300-400 mg daily), or dasatinib (within the allowable dose range of 40-140 mg daily). They must have received their current TKI for a minimum of 6 months prior to randomization and must be expected to remain on the same TKI for the next 12 months.
c. Patient must not have a history of resistance to any prior TKI drug. If patient has received more than one TKI, the reason for changing treatment must have been something other than resistance or inadequate response to the prior TKI (for example, intolerance to the prior TKI and the treatment change must have occurred ≥6 months prior to randomization.
d. Patients must not be receiving any other investigational agents.

Clinical/Laboratory Criteria

a. Patients must be ≥ 18 years of age.
b. Patients must have complete history and physical examination within 28 days prior to randomization.
c. If clinically indicated, patients must have QTcF interval < 500 ms (by Fridericia calculation) on a 12-lead EKG within 7 days prior to randomization.
   QTcF = QT/(RR)0.33
   (QTcF = QT interval divided by the cube root of the RR [heart rate] in seconds)
d. Patients must have platelets ≥ 100,000/mm3 (100.0 x 109/L), ANC > 1,000/mm3 (1.0 x 109/L), and hemoglobin ≥ 8 g/dL within 7 days prior to randomization.
e. Patients must have ALT and AST ≤ 2.5 x IULN within 7 days prior to randomization.

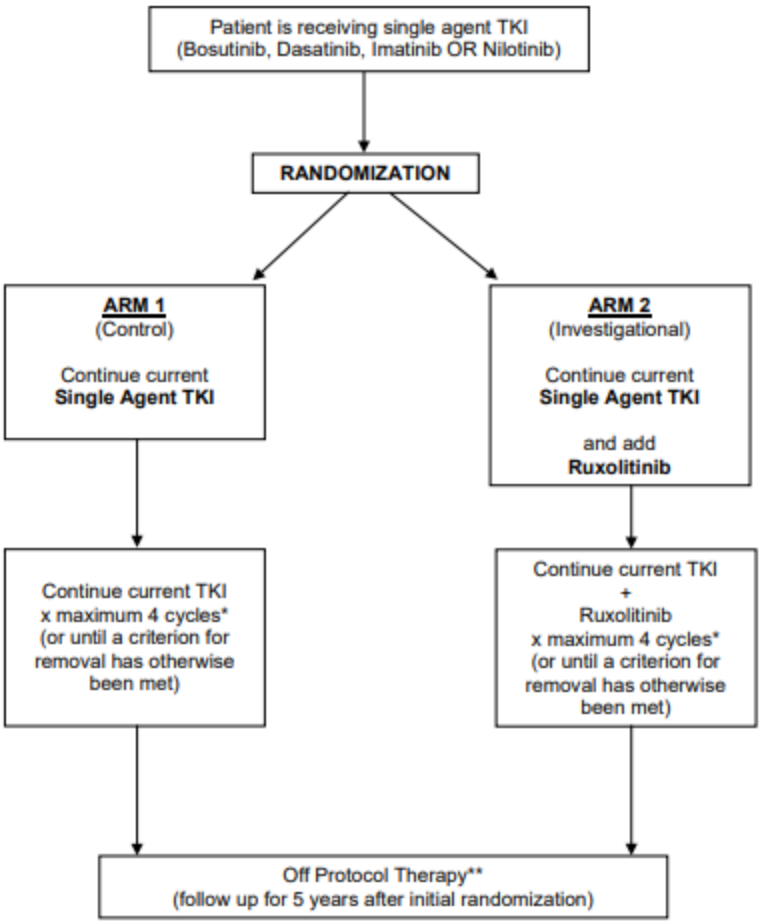
f. Patients must have total bilirubin ≤ 1.5 x IULN within 7 days prior to randomization (unless the patient has a known diagnosis of Gilbert's Syndrome).
g. Patients must have a serum creatinine ≤1.5 x IULN within 7 days prior to randomization.
h. Prior malignancy is allowed providing it does not require concurrent therapy. ***Exception:*** Active hormonal therapy is allowed.
i. Patients must not be pregnant or nursing due to the teratogenic potential of the drugs used on this study. Women of child-bearing potential must have a negative serum pregnancy test within 7 days prior to randomization. Women/men of reproductive potential must have agreed to use an effective contraceptive method during treatment and for 30 days after discontinuation of study drug. A woman is considered to be of "reproductive potential" if she has had menses at any time in the preceding 12 consecutive months. In addition to routine contraceptive methods, "effective contraception" also includes heterosexual celibacy and surgery intended to prevent pregnancy (or with a side-effect of pregnancy prevention) defined as a hysterectomy, bilateral oophorectomy or bilateral tubal ligation. However, if at any point a previously celibate patient chooses to become heterosexually active during the time period for use of contraceptive measures outlined in the protocol, he/she is responsible for beginning contraceptive measures.
j. Patients known to be HIV+ are eligible provided they meet all other eligibility criteria and have undetectable HIV viral loads on their most recent viral load test which must have been performed in the last 6 months.

Specimen Submission Criteria

Specimens for 5.4a (local BCR-ABL quantification) and 5.4b (central BCR-ABL quantification) must be drawn together.

a. Specimens (peripheral blood) must be collected and submitted to a CLIA-approved laboratory as outlined in Section 15.1, within 21 days prior to randomization. BCR-ABL transcripts must be measured using RT-PCR and results must be reported using the International Scale. The RT-PCR assay must have the sensitivity to detect a 4.5 log reduction in BCR-ABL transcripts from 100% IS (must be able to detect0.0032% IS or lower).
b. Patients must be offered participation in submission of specimens for central BCR-ABL quantification. This submission is highly encouraged as an important protocol endpoint. With patient's consent, specimens must be collected as outlined in Section 15.2, within 42 days prior to randomization.

SCHEMA



* One Cycle = 90 days.

** After Cycle 4 of protocol therapy, patients will be removed from protocol therapy. After removal from protocol therapy, the patient may remain on single-agent TKI therapy at the discretion of the treating physician; however, it will not be considered "protocol therapy." Treatment during follow-up will be at the discretion of the treating physician.