Concordance Between Bone Marrow and Peripheral Blood Samples for Assessment of FLT3 Internal Tandem Duplication (ITD) Mutations: Data From Patients Screened for Participation in QUANTUM-R, a Global, Randomized, Open-Label, Phase 3 Study

Examining the Effect of Quizartinib Monotherapy vs Salvage Chemotherapy on Overall Survival in Patients With FLT3-ITD–Mutated AML Who Are Refractory to or Have Relapsed After First-Line Therapy

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INTRODUCTION

Acute myeloid leukemia (AML) is a heterogeneous disease characterized by clonal evolution with multiple factors driving its biology and resistance to therapy. Patients with FLT3 internal tandem duplication (ITD) mutations are a frequent subset of patients with AML who are refractory to or have relapsed after first-line therapy. Quizartinib, an investigational FLT3 inhibitor, has shown activity in patients with AML, including those with FLT3-ITD mutations. The QUANTUM-R trial was a global, randomized, open-label, phase 3 study comparingquizartinib to salvage chemotherapy in patients with relapsed or refractory AML who had FLT3-ITD mutations.

OBJECTIVE

To examine the concordance of FLT3 ITD assessment between bone marrow (BM) and peripheral blood (PB) samples from patients enrolled in the QUANTUM-R trial.

METHODS

Patient Selection

Patients with FLT3-ITD mutant bone marrow and/or blood were selected at the time of screening in the phase 3 study. Patient selection criteria included being 18 to 75 years of age, having AML with FLT3-ITD mutation, and receiving quizartinib as first-line therapy or salvage therapy with quizartinib versus salvage chemotherapy (estimated enrollment, n = 363).

RESULTS

Blast Count and Presence of ITD

In 88 patients with ITD, the ITD ratio ranged from 1% to 80%. The ITD ratio was similar in both specimen types for most patients; however, a trend toward lower ITD ratios in peripheral blood samples was observed.

Equivalency Study Statistics

Length and Number of ITDs

In 10 patients with both BM and PB ITD, the length of ITD was between 20 and 100 bases. A second ITD was present in both specimen types for all cases.

CONCLUSIONS

Our results show a high degree of concordance between BM and PB when assessing FLT3 ITD mutations. Of 23% of patients showed agreement in BM and PB, the blast count in BM was higher than that in PB in 78% of patients. No correlation between blast count and PB allele ratio was found in any ITD subtypes. We recommend that concordance between BM and PB ITD specimens should be confirmed in patients with myeloid neoplasms.

Bland-Altman Difference Plot (Figure 3)

Table 1: Length of ITD in Bone Marrow and Peripheral Blood in Representative Patients

Table 2: Length and Ratio of ITD in Bone Marrow and Peripheral Blood in Representative Patients

Table 3: Length and Ratio of ITD in Bone Marrow and Peripheral Blood in Representative Patients

Figure 1: Quizartinib RIT study design. Patients receiving either 40 or 60 mg daily in a 1:1 randomization to evaluate the effects of quizartinib on transfusion requirements, tumor burden, and overall survival in patients with FLT3-ITD–mutated AML. Treatment was stopped if the patient met criteria for withdrawal of consent or progression of disease.

Figure 2. Scatter plot with Deming fit.