



IS ETHNICITY AN EFFECT MODIFIER BETWEEN FLT3 INHIBITORS AND SALVAGE THERAPY FOR RELAPSED AND REFRACTORY ACUTE MYELOID LEUKEMIA?

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BACKGROUND

Acute myeloid leukemia (AML), a heterogeneous hematologic malignancy, is the most common acute leukemia in adults. It is characterized by the clonal expansion of myeloid blasts in peripheral blood, bone marrow, and/or other tissues. In 2019, about 69,700 people were living with AML in the United States (USA). About 54% of cases are diagnosed after 65 years of age. The FLT3-ITD (*internal tandem duplication*) happens in 22-25% of the patients with AML and is associated with a poor prognosis. Some guidelines and health technology assessment (HTA) agencies have recently begun to recommend targeted therapy for relapsed or refractory (R/R) AML patients with an FLT3 mutation.

OBJECTIVE

To evaluate the effect of ethnicity on the efficacy of FLT3 inhibitors (FLT3i) for relapsed or refractory acute myeloid leukemia (R/R AML).

METHODS

This is a systematic review with direct meta-analysis. Structured searches were conducted on Medline, Lilacs, and Embase. Additionally, a complementary search was conducted. Studies that compared a FLT3i with salvage therapy for the treatment of R/R AML in patients with FLT3 mutation were selected. The meta-analysis was conducted through the inverse variance method and the random-effects models were calculated by the DerSimonian and Laird method. Hazard ratios (HR) and relative risks (RR) were reported with their 95% confidence interval (95%CI). The protocol of this research is available in PROSPERO (CRD42022324118).

RESULTS

Three studies were included. ADMIRAL and COMMODORE evaluated gilteritinib and QuANTUM evaluated quizartinib compared to salvage therapy. The data from ADMIRAL was quite complete regarding ethnicity, but QuANTUM did not report the HRs and 95%CIs for the Black or the “other” categories. COMMODORE only included Asian patients.

The magnitude of effect of the FLT3i compared to salvage therapy seems higher in the Asian subgroup compared to the other ethnic groups (HR=0.55, 95%CI=0.32-0.94 vs. HR=0.74, 95%CI=0.60-0.90, **Figure**). This result was driven by the effect of gilteritinib, though. There was no indication that it would be true for quizartinib as well. Further studies are necessary to evaluate this hypothesis since no difference between subgroups was observed in the random-effects model (p-value=0.32). The fixed-effects model, though, showed a p-value=0.05. There was basically no difference in magnitude of effect in the white population between ADMIRAL and QuANTUM (HR=0.72, 95%CI=0.52-1.00 and HR=0.75, 95%CI=0.57-1.01).

CONCLUSION

It is unclear whether ethnicity is an effect modifier between FLT3i and salvage therapy because of relatively small samples and the loss of randomization derived from the subgroup analysis. Nevertheless, this matter surely deserves further investigation.

Figure. Meta-analysis of overall survival stratified by ethnicity

