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ORAL ABSTRACTS

906.OUTCOMES RESEARCH-MYELOID MALIGNANCIES

Intensification of Therapy and Pharmacogenetic Personalization Mitigate Racial Disparities in Pediatric Acute Myeloid Leukemia Outcomes

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Introduction

Recent reports have highlighted disparities in outcomes for black children, adolescents, and young adults with acute myeloid leukemia (AML) compared to their non-Hispanic white counterparts. An analysis of pediatric AML patients treated from 1996-2013 revealed that black race was associated with inferior event-free survival (EFS) and overall survival (OS) (Conneely 2021). In a study of adolescent and young adult patients with AML, black race was a predictor of poor outcome, particularly among patients 18-29 years old (Larkin 2022). Addressing these outcome disparities and developing treatment strategies to overcome them is crucial. In this study, we evaluated the interactions between outcomes by race and cytarabine pharmacogenomics in pediatric AML patients treated on two multi-institutional clinical trials.

Methods

Pediatric patients with newly diagnosed AML treated on AML02 (NCT00136084) or AML08 (NCT00703820) were included. Patients received high-dose cytarabine, daunorubicin, and etoposide (HDAC), low-dose cytarabine, daunorubicin, and etoposide (LDAC), or clofarabine and cytarabine (Clo/AraC) as initial therapy. The pharmacogenomics ACS10 scores, derived from combination of 10 single nucleotide polymorphisms, were calculated as reported (Elsayed 2022).

Results

Overall, 86 patients were black and 359 were white; 68 had other or unknown racial backgrounds and were not included in this analysis. Complete remission rates after two courses of induction therapy did not differ between black and white patients (92.6% vs 95.0%, p=0.63), nor did the rates of MRD negativity after one course of therapy (55.8% vs 55.4%, p=0.85). The EFS rates of black and white patients were nearly identical, with 5-year estimates of 58.3% (95% CI = 48.8%-69.8%) and 58.2% (95% CI = 53.2%-63.6%; p=0.89, Fig 1). Likewise, OS did not differ between black and white patients (63.8%; 95% CI = 54.3%-74.8% vs 69.4%; 95% CI = 64.7%-74.5%; p=0.24). The cumulative incidence (CI) of relapse did not differ by race (26.0% vs 26.1%, p=0.99), nor did the CI of treatment-related mortality (7.0% vs 6.8%, p=0.78). The prevalence of core binding factor (CBF) leukemia was higher in black patients as compared with white patients (30% vs 19%, p=0.04), but we did not find differences in EFS between black and white patients with or without CBF AML.

We recently showed that low ACS10 scores were associated with worse outcomes in patients treated with low-dose cytarabine-based induction. In the present study, there was a significant difference in the distribution of ACS10 scores according to race, with low scores occurring in 73% of black patients compared with 30% of white patients (p<0.001). When patients on all treatment regimens were considered, there were no differences in EFS between black and white patients with low (p=0.88)

or with high ACS10 scores (p=0.72). However, black patients with low ACS10 scores had significantly better outcomes after treatment with Clo/Ara-C induction compared with LDAC induction (p=0.01 for EFS and p=0.04 for OS, Fig 2). In multivariable model adjusting for age, risk group, and leukocyte count, Clo/Ara-C induction was identified as the best treatment option for black patients with low ACS10 scores (EFS: HR = 0.2, p=0.03).

Discussion

Our findings contrast with recent reports, as we did not observe significant outcome differences between black and white patients in terms of complete remission rates, EFS, OS, CI of relapse, or CI of treatment-related mortality. The higher prevalence of low ACS10 scores in black patients compared with white patients likely contributes to outcome disparities observed among patients treated with LDAC in the present study and those in the literature, which have included patients who almost exclusively received low-dose cytarabine-based induction therapy. In the present study, black patients with low ACS10 scores had significantly worse outcomes compared to those with high scores when treated with LDAC. However, these differences in outcome were eliminated by the use of HDAC or Clo/Ara-C induction. By contrast, black patients with high ACS10 scores did not appear to benefit from HDAC or Clo/Ara-C induction. Our results suggest that pharmacogenomics differences between black and white patients should be considered when tailoring induction regimens to improve outcomes of black patients and bridge the racial disparity gap in AML treatment.

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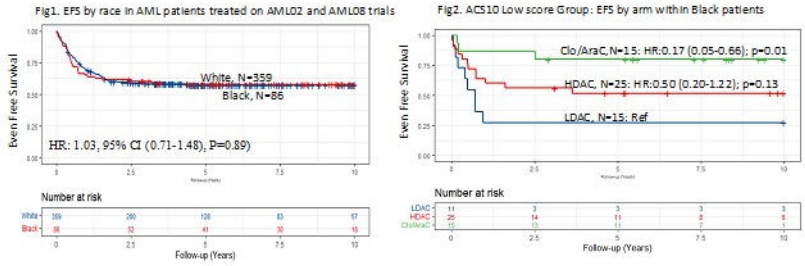

Figure 1

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