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617.ACUTE MYELOID LEUKEMIAS: BIOMARKERS, MOLECULAR MARKERS AND MINIMAL RESIDUAL DISEASE IN DIAGNOSIS AND PROGNOSIS

Differences within the Immune Microenvironment May Account for Poorer Outcomes in African American AML Patients Compared to European American Patients with AML

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Background: Acute myeloid leukemia (AML) is an aggressive hematological malignancy arising from an immature myeloid progenitor with notoriously poor outcomes. A critical factor responsible for the difficulty in treating this disease evasion of the host immune system by AML. Both the innate and adaptive immune systems have been shown to be dysfunctional in AML with poor type I interferon responses, decreased STING signaling and increased populations of granulocytic and monocytic myeloid derived suppressor cells ultimately leading to poor adaptive response. Studies in solid tumors have demonstrated that variation in immunity contributes to racial disparities in cancer and outcomes. This is felt to be due to variation in geographic ancestry leading to differences in the innate immune genome required due to the need for protection against environmental pathogens. However, no data exists comparing innate and adaptive immunity by race in patients (pts) with AML. Here we sought to characterize the immune microenvironment with treatment outcomes in racially diverse AML pts.
Methods: Adults with newly diagnosed AML were identified who had corresponding cryopreserved bone marrow mononuclear cells available within Roswell Park Hematologic Procurement bank. Pts were matched as closely as possible for age, gender, cytogenetic risk per ELN 2017 and molecular profile. Transcriptional differences between African American (AA, n=26) and European American (EA, n=26) AML pts and healthy controls (n=10) were analyzed using transcriptomics data from NanoString Pan Cancer Immune Profile panels. AA and EA AML samples were compared to each other, as well as their race-matched healthy controls. The 'Limma' package in R was utilized for differential gene expression analysis. Research was conducted according to the Declaration of Helsinki in accordance with the Institutional Review Board regulated protocol.
Results: The median age of the entire cohort (n=52) was 65 years (range: 28-92), with 28 female patients (53.8%) (**Table 1**). Within the AA cohort, the majority of pts had intermediate risk cytogenetics per ELN 2017 (n=19; 73.1%, and 6 pts had FLT3 *mut* (26.1%). Three pts (11.5%) underwent allogeneic stem cell transplant, with a median overall survival (OS) censoring for transplant of 5 months (range; 0.5-68 months) (**Figure 1**). Within the EA cohort, most pts had poor risk cytogenetics (n=15; 57.7%). Six pts had FLT3 *mut* (26.1%), and three pts had TP53 *mut* (12%). Five pts underwent allogeneic stem cell transplant (19.2%), with a median OS of 16.4 months (range; 0.8-67 months). Sixty-nine significantly ($p<0.05$, $|logFC|>1.5$) differentially expressed genes in AA vs. EA pts were identified. Gene set enrichment analysis (GSEA) revealed alterations to Interferon, Jun kinase and STAT signaling pathways in AA pts. In contrast, EA pt samples were enriched for pathways related to amyloid metabolism and other T and B cell immune pathways. Master regulator analysis using LISA highlighted transcriptional dysregulation attributed to PDGB5, CTCF, AR, and NOTCH in AA pts and to GLIS2, SMAD1 and NFE2 in EA pts.
Conclusions: As previously reported, we found that a clinically matched cohort of AA AML patients experienced significantly worse OS as compared to EA counterparts. We have identified several significant alterations within the immune microenvironment between cohorts, which may potentially explain this discrepancy in survival in AA patients. These differences could potentially serve as targetable alterations for therapeutic purposes. This work represents the first of its kind evaluating the immune microenvironment by race in AML patients and are awaiting confirmation in a larger cohort.

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Table 1. Baseline demographics of cohort.

	African American (n=26)	Eastern European (n=26)
Age (median; years) (range)	64.5 (33 - 92)	65.5 (28 - 90)
Male	13 (50%)	11 (42.3%)
Female	13 (50%)	15 (57.7%)
Favorable Cytogenetics	1 (3.8%)	1 (3.8%)
Intermediate Cytogenetics	19 (73.1%)	10 (38.5%)
Poor Cytogenetics	6 (23.1%)	15 (57.7%)
FLT3*mut*	6 (n=23; 26.1%)	6 (n=26; 26.1%)
TP53*mut* (n=33)	0 (n=6; 0%)	3 (n=25; 12%)

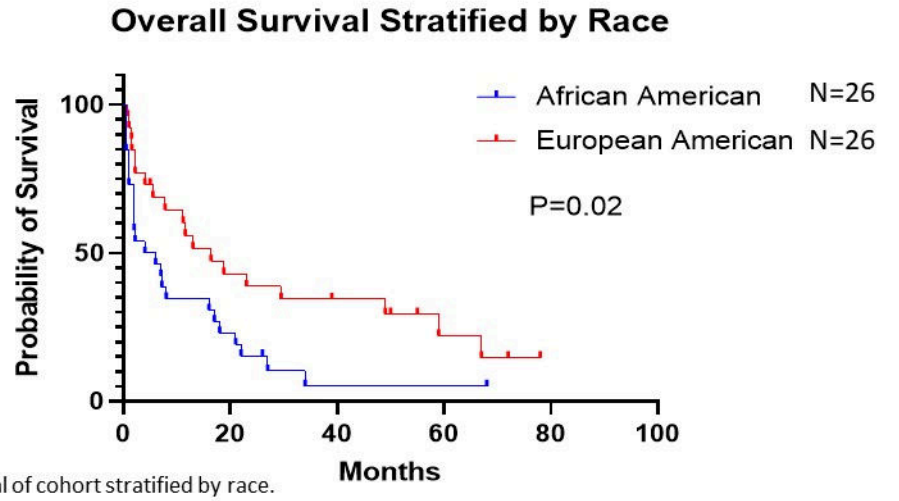

Figure 1. Overall survival of cohort stratified by race.

Figure 1

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