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POSTER ABSTRACTS

613.ACUTE MYELOID LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

First-Line Venetoclax and a Hypomethylating Agent or Conventional Chemotherapy in Older Adults with *IDH*-Mutated AML

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Introduction

The treatment of older adults with acute myeloid leukemia (AML) remains challenging. Although next-generation sequencing has allowed for the molecular characterization of AML at an increasing rate, relatively little is known about the outcomes of molecularly selected cohorts of older adults with AML. Up to 20% of patients with AML harbor *IDH* mutations, which confer BCL2 dependence and sensitivity to venetoclax. Therefore, we sought to compare the outcomes of intensive chemotherapy (IC) to venetoclax and a hypomethylating agent in older adults with *IDH* ^{mut}AML.

Methods

From the Project ERIS database, we analyzed 50 patients aged 60 years or older with AML and an *IDH1* or *IDH2* mutation identified on next-generation sequencing at diagnosis from January 1, 2013 to April 18, 2023 at VCU Massey Comprehensive Cancer Center. We recorded baseline patient-related and disease characteristics, including age, ECOG, Charlson comorbidity index (CCI) scores, molecular profiling and ELN 2022 cytogenetic risk, dates of regimen initiation, and survival. We separated patients by receipt of therapy type: IC with conventional 7+3 or CPX-351, venetoclax with a hypomethylating agent (decitabine or azacitidine; VEN+HMA), and HMA monotherapy as a comparison arm. We used the D'Agostino & Pearson method for normality testing and the t-test, Mann-Whitney, or ANOVA (as applicable) tests for between-group comparisons. Categorical comparisons used Fischer's exact test. We applied the Bonferroni correction if multiple comparisons were made. We analyzed survival by the Kaplan-Meier method with significance determined by the log-rank test. The event for calculating the overall survival (OS) was the date of death. Patients were otherwise censored at the date of last contact.

Results

Among 50 older patients with *IDH* ^{mut} AML, 24 (48.0%) received IC, 18 (36.0%) received VEN+HMA, and eight (16.0%) were treated with HMA monotherapy (Table A). In the overall cohort, the median *IDH1* variant allele frequency (VAF) was 41.2% (range: 8.3-48.2), and the median *IDH2* VAF was 43.8% (range: 6.8-51.0). The most common mutations in *IDH1* and *IDH2* were Arg132Cys (52.9%) and Arg140Gln (83.3%), respectively. Patients treated with IC were significantly younger compared with the VEN+HMA cohort (64 vs 74 y., $p < 0.0001$). The IC cohort also had significantly better ECOG scores compared with the VEN+HMA cohort (1 vs 2, $p = 0.0023$), but no difference in CCI scores (5 vs 6, $p = 0.163$). Consequently, significantly more patients in the IC cohort proceeded to an allogeneic stem cell transplant (alloSCT) compared with VEN+HMA (29.2% vs 0%, $p = 0.014$). Strikingly, there was no significant difference in the median overall survival between the IC and VEN+HMA cohorts (14.1 m. vs 12.2 m., $p = 0.485$). Next, we analyzed the addition of the HMA monotherapy cohort - which had no significant difference in any baseline characteristic compared with the VEN+HMA cohort. Both IC and VEN+HMA significantly prolonged overall survival compared with HMA monotherapy in *IDH* ^{mut} AML ($p = 0.043$, Figure B).

Discussion

Despite significantly older age, worse ECOG PS, and fewer patients proceeding to alloSCT in the VEN+HMA cohort compared with IC, there was no significant difference in overall survival between the two treatment modalities. These findings provide evidence suggestive of the comparable efficacy of VEN+HMA and IC in older adults with *IDH* ^{mut} AML. Both treatment strategies appear to offer significantly prolonged survival relative to HMA monotherapy. Prospective trial designs in molecularly selected cohorts are needed to confirm these findings.

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A. Demographics of VEN+HMA vs intensive chemotherapy (IC) in older adults with *IDH*^{mut} AML

	VEN+HMA (N = 18)	Intensive Chemotherapy (N=24)	Significance
Age — years (%)	74 (66–88)	64 (60–76)	p < 0.0001
Sex — male (%)	7 (38.9)	13 (54.2)	p = 0.366
Race — White (%)	13 (72.2)	19 (79.2)	p = 0.720
ECOG — (range)	2 (0–4)	1 (0–4)	p = 0.002
CCI — (range)	6 (4–12)	5 (4–14)	p = 0.163
ELN 2022 Adverse — (%)	7 (38.9)	10 (41.7)	p > 0.999
Median *IDH1* VAF — (%)	44.1 (8.3–46.8)	39.2 (9.7–48.2)	p = 0.979
Median *IDH2* VAF — (%)	43.8 (6.8–49.9)	42.7 (21.1–51.0)	p = 0.698
AlloSCT — (%)	0 (0)	7 (29.2)	p = 0.014

B. Overall survival of older adults with *IDH*^{mut} AML across differing treatment modalities

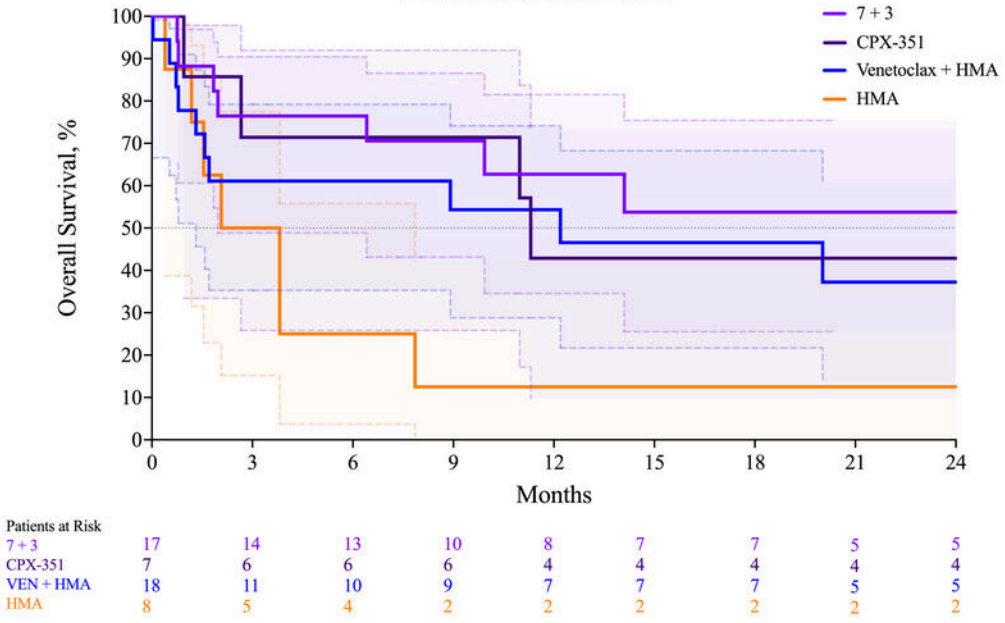

Figure 1

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