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POSTER ABSTRACTS

615.ACUTE MYELOID LEUKEMIAS: COMMERCIALLY AVAILABLE THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

TP53-Mutated Acute Myeloid Leukemia Patients Treated with Intensive Therapies Have Superior Outcomes: A Single Institution, Retrospective Study

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Background: Mutations in *TP53*, found in 5-20% of acute myeloid leukemia (AML), confer poor prognosis and are associated with high rates of therapy resistance, high relapse rates, and dismal overall survival (OS). Recent advances have provided a variety of options for up-front AML therapy including a liposomal preparation of standard-of-care chemotherapy (CPX-351) and venetoclax-based combinations. Due to known poor outcomes with intensive chemotherapy, many providers are favoring less intense strategies for patients with *TP53* mutant AML, but these approaches have not been directly compared for this patient subgroup. Strategies for treating *TP53* mutant AML are highly heterogeneous and optimal treatment strategies have not been defined in this setting. We performed a retrospective study to compare the clinical outcomes of *TP53* mutant AML patients treated at our center.

Methods: The study was a single-center, retrospective cohort analysis conducted at the University of Minnesota. Adult patients (age ≥18 years) with the diagnosis of AML or myeloid sarcoma between January 1, 2014 and July 31, 2022 who have next-generation sequencing panel confirming a pathogenic *TP53* mutation and received front-line therapy for AML at our center were included in this study. Kaplan-Meier analysis was used to estimate the probabilities of OS, defined as the date of treatment initiation to the date of death from any cause or last follow-up.

Results: Our study includes 88 patients with *TP53* mutant AML with available clinical data in an AML registry at our institution. Baseline demographic and clinical characteristics are summarized in **Table 1**. The median age at diagnosis was 67 years (range 28-87) with male predominance (65.9%). Among this, 15/88 patients (17.1%) had therapy-related AML and 40/88 patients (45.5%) had secondary AML. The median bone marrow blast percentage at diagnosis was 31% and peripheral blast percentage was 9%. The majority of patients have high variant allelic frequency (VAF, 71.9% with VAF > 0.4 for patients with available VAF data) and *ASXL1* was the most frequent co-mutation identified followed by *KRAS* and *NRAS*.

Treatment regimens were classified as intensive or nonintensive. Intensive treatment regimens included infusional cytarabine with either daunorubicin or idarubicin (7+3), liposomal cytarabine and daunorubicin (CPX-351), and mitoxantrone, etoposide and cytarabine (MEC). Nonintensive regimens included hypomethylating agents (decitabine or azacitidine) with or without venetoclax and clofarabine with low-dose subcutaneous cytarabine.

A total of 66 patients were included in the survival analysis. There was no significant difference in OS between patients aged < 65 years and ≥ 65 years at diagnosis (2-year OS, 11% versus 5%, P=0.76). Superior 2-year OS was observed in patients who received front-line intensive (n = 31) versus nonintensive (n = 35) induction chemotherapy (2-year OS, 13% versus 3%, P=0.01, **Figure 1**). Patients who received intensive therapy for any line of treatment also demonstrated superior OS compared to those who never received intensive therapy (2-year OS, 12% versus 3%, P=0.02). The rate of achieving complete remission (CR) was higher in patients who received intensive treatment compared to non-intensive therapy in the first-line (51.6% versus 25.7%, P=0.03). Rate of CR at any time was also higher for patients who received intensive treatment for any line of treatment (50% versus 18.2%, P<0.01). Among the intensive first-line treatment group, 7+3 (n = 18) showed superior OS relative to CPX-351 (n = 12) (2-year OS, 22% versus 0%, P=0.03) although there was no significant difference in CR rate (55.6% versus

50%, P=0.77). Furthermore, significant survival benefit was shown in patients who underwent allogeneic hematopoietic cell transplantation compared to patients who had not (2-year OS, 21% versus 4%, P<0.01]).

Conclusions: In our cohort, *TP53* mutant AML patients treated with intensive chemotherapy and transplant have superior outcomes to those who do not. Since this was a retrospective study, we cannot rule out the possibility that these results are confounded by providers favoring more intensive therapies for fitter patients. However, these data imply that *TP53* mutant patients may benefit from more intensive therapy and suggests that future work to define optimal therapy regimens in this patient population may incorporate intensive strategies.

Disclosures No relevant conflicts of interest to declare.

Table 1 Baseline demographic and clinical characteristics

Total N = 88	Value Median (range) or N (%)
Age at diagnosis	67.3 (28.9-87.1)
Gender	
Male	58 (65.9%)
Female	30 (34.1%)
Therapy-related AML	15 (17.1%)
Secondary AML	40 (45.5%)
TP53m VAF	
≤ 0.4	9/32 (28.1%)
> 0.4	23/32 (71.9%)
Co-mutations	
FLT3	3 (3.4%)
IDH1/IDH2	4 (4.6%)
NPM1	1 (1.1%)
RUNX1	0 (0%)
ASXL1	14 (15.9%)
KRAS/NRAS	10 (11.4%)
KIT	1 (1.1%)
Baseline BM blast (%)	31 (1-94%)
Baseline WBC (x10³ cells/μL)	3.1 (0.1-82.8)
Baseline peripheral blast (%)	9 (0-78%)
Peripheral blast count (x10³ cells/μL)	0.2 (0-1.7)

Figure 1 Kaplan-Meier curve of 2 year-OS for patients with intensive versus non-intensive first-line treatment

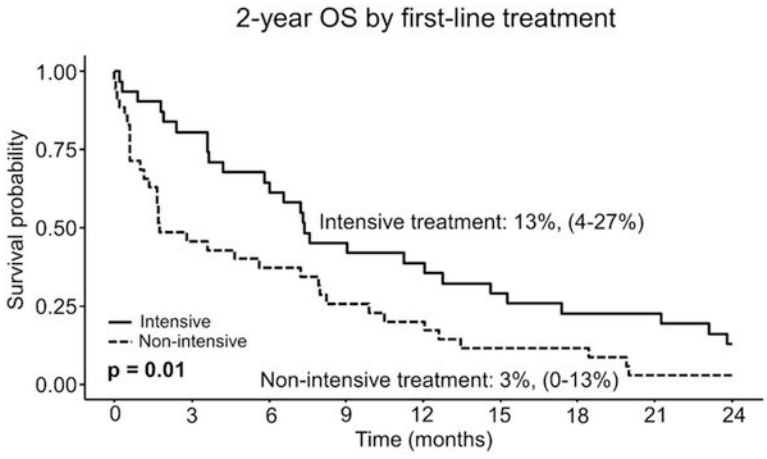

Figure 1

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