Clinical, Molecular, and Treatment Characteristics of Long-Term Survivors Amongst Older Adults with IDH1/2-Mutated Acute Myeloid Leukemia Treated with IDH Inhibitors

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INTRODUCTION

- Prognosis for patients age ≥ 65 with acute myeloid leukemia (AML) is dismal; estimated five-year survival rates range anywhere from 5-18% for this age group.
- Ivosidenib and enasidenib are approved oral targeted therapies for patients with IDH1- or IDH2-mutated AML. Both agents have been shown to induce meaningful rates (30-40%) of complete remission or complete remission with partial hematologic recovery.
- After FDA approvals in 2017 and 2018, initial studies for these targeted therapies reported median overall survival ranging anywhere from 6-12 months.

AIMS

- Explore the clinical, molecular, and treatment characteristics of long-term survivors (≥ 2 years) treated with IDH inhibitors to identify which patients may benefit most from these therapies.
- Provide updated survival analyses 5-6 years post drug approval.

METHODS

- We conducted a retrospective cohort study of all AML patients age ≥ 60 treated with IDH1/2-targeted therapies at our institution.
- Patients were required to have at least 2 years of follow up to be included.
- Estimated overall survival (OS) was calculated from diagnosis to date of death or last follow-up. Estimated event-free survival (EFS) was calculated as time from diagnosis to progression, relapse, or death. The Kaplan-Meier method was used to estimate the survival functions and 95% confidence intervals.

RESULTS

BASELINE CHARACTERISTICS (total n = 9)	
Sex, % (n)	
Male	67 (6)
Female	33 (3)
Race	
White	100 (9)
Ethnicity	
Hispanic/Latino	11 (1)
non-Hispanic/Latino	78 (7)
Unknown	11 (1)
Median age at dx (range)	71 (64 – 84)
ECOG	
0	22 (2)
1	78 (7)
Primary AML	56 (5)
Secondary AML	44 (4)
Prior MDS	11 (1)
Prior MPN	11 (1)
Therapy-related	22 (2)
2022 ELN risk	
Favorable	22 (2)
Intermediate	33 (3)
Adverse	44 (4)
Cytogenetics	
Normal	78 (7)
IDH therapy started at	
Front-line	44 (4)
Relapse	44 (3)
Progression	0
Maintenance	22 (2)

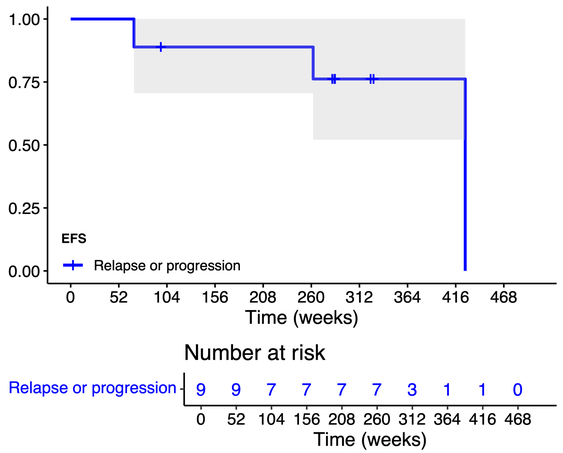


Figure 1. Kaplan-Meier curve for event-free survival. Estimated 5-year event free survival was 89%.

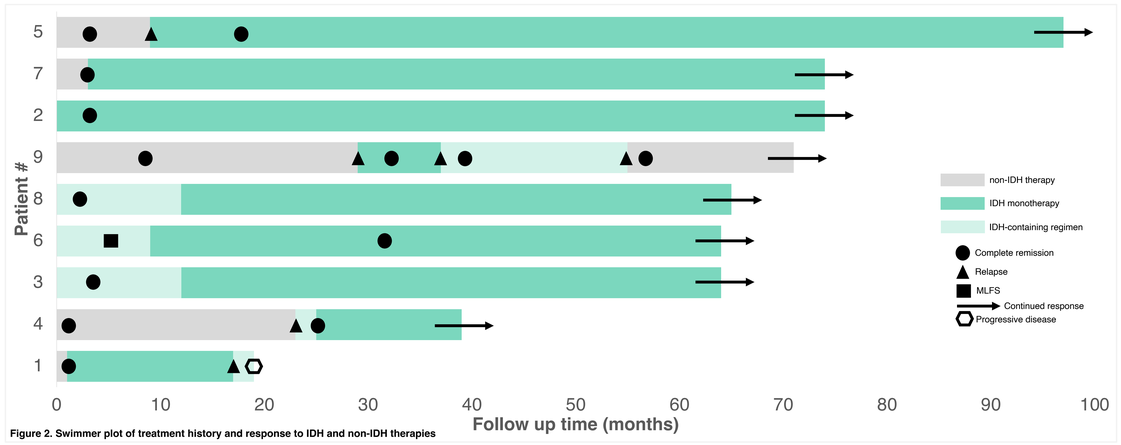


Figure 2. Swimmer plot of treatment history and response to IDH and non-IDH therapies

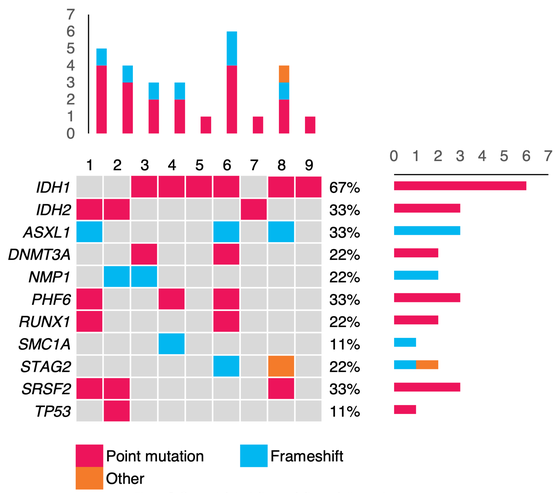


Figure 3. Oncoprint depicting mutations at diagnosis

- Median follow up time was 5.5 years (range: 1.5 – 8.3).
- All patients eventually achieved or maintained complete remission. Five of 9 patients (55%) had clearance of their IDH mutation.
- All patients are alive at the time of this report. One patient has relapsed. The rest remain in complete remission.

CONCLUSIONS

- We show here that IDH therapy received in various treatment settings can achieve long-term control of AML in a select cohort of older patients, including those with adverse risk disease, arguably “curing” those in CR for ≥ 5 years.
- Most long-term survivors had normal cytogenetics (78%). MDS-related gene mutations and number of mutations did not correlate with worse outcomes.
- A larger study would help validate our findings and evaluate other predictors of survival in these patients.

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