Real-World Treatment Patterns and Outcomes With Olutasidenib After Venetoclax in *IDH1*-Mutated Acute Myeloid Leukemia Using Electronic Health Record Data

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Introduction

- Olutasidenib is a potent and selective oral small-molecule inhibitor of mutated *isocitrate dehydrogenase 1* (m*IDH1*) that is FDA approved for patients with relapsed or refractory (R/R) m*IDH1* acute myeloid leukemia (AML)

Properties of Olutasidenib

1. Selective for mutant *IDH1* vs wild-type
2. Low molecular weight of 355 g/mol
3. Binds and inhibits single- and double-mutant *IDH1*

- In the final 5-year results from the pivotal phase 2 trial, olutasidenib achieved a complete remission (CR) or CR with partial hematologic recovery (CRh) in 35% of patients with a median CR/CRh duration of 25.3 months[1]
- Venetoclax in combination with a hypomethylating agent is a standard first-line regimen for patients with AML who are ineligible for intensive chemotherapy; while this regimen is initially effective, most patients ultimately relapse or become refractory and require additional treatment options such as olutasidenib[2]
- While clinical trials have shown encouraging results for olutasidenib in the post-venetoclax setting, real-world data on its utilization and outcomes are limited

Methods

- ***Data source:*** This retrospective cohort study analyzed data derived from the Loopback Platform, a multisource electronic health record-based real-world database of US patients, incorporating structured clinical data and abstracted data from physician notes
- ***Eligibility criteria:*** Adults (≥18 years of age) with a confirmed diagnosis of R/R m*IDH1* AML, who received a venetoclax regimen prior to olutasidenib, were not enrolled in clinical trials, had available physician notes, received at least 25 days of olutasidenib treatment, and had a documented clinical response assessment
- ***Treatment response:*** Patients with a response were categorized as CR, CRh, CR with incomplete blood count recovery (CRi), or morphologic leukemia-free state (MLFS). Response status was determined based on explicit documentation in physician notes or laboratory values consistent with established criteria

REFERENCES

1. Cortes J, et al. *J Hematol Oncol*. 2025;18(1):102.
2. Abaza Y, et al. *Am J Hematol*. 2024;99(4):606-14.

ACKNOWLEDGMENTS

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Results

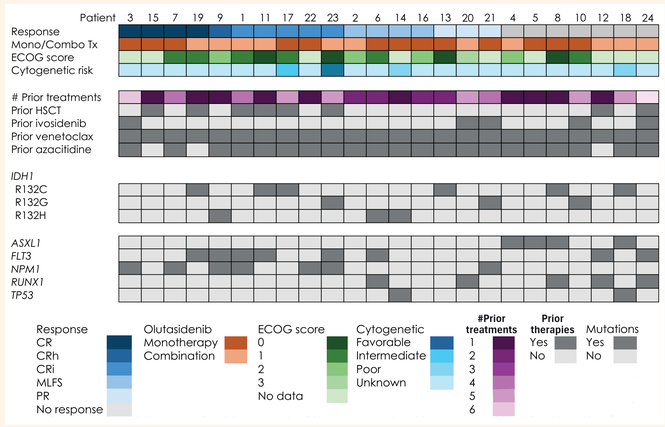
Table 1. Key Patient Characteristics

Patient Characteristics	N=24
Median age (IQR)	65.0 (55-74)
Male sex, n (%)	15 (62.5)
Prior HSCT for AML, n (%)	8 (33.3)
***IDH1* mutation type, n (%)**	
R132C	6 (25.0)
R132G	3 (12.5)
R132H	3 (12.5)
Unknown	12 (50.0)
ECOG PS, n (%)	
0	4 (16.7)
1	6 (25.0)
2	4 (16.7)
3	1 (4.2)
Unknown	9 (37.5)
Number of co-mutations, n (%)	
0	6 (25.0)
1	10 (41.7)
2	8 (33.3)
Type of co-mutation, n (%)	
FLT3	8 (33.3)
NPM1	7 (29.2)
RUNX1	5 (20.8)
ASXL1	4 (16.7)
TP53	2 (8.3)
Olutasidenib duration (months)	
Mean (SD)	5.3 (4.9)
Median (IQR)	4.0 (1.7–6.5)
Index olutasidenib treatment, n (%)	
Monotherapy	13 (54.2)
Combination therapy	11 (45.8)

Treatment patterns (Figure 1):

- All patients received prior venetoclax (58% in the frontline), with 67% (16/24) receiving it immediately prior to olutasidenib. Median venetoclax duration was 5.3 months (IQR 2.5–12.4) among all patients and 3.5 months (IQR 1.9–5.8) among 14 responders
- Median olutasidenib duration was 4.0 months (IQR 1.7–6.5). Disease progression was the main reason for olutasidenib discontinuation

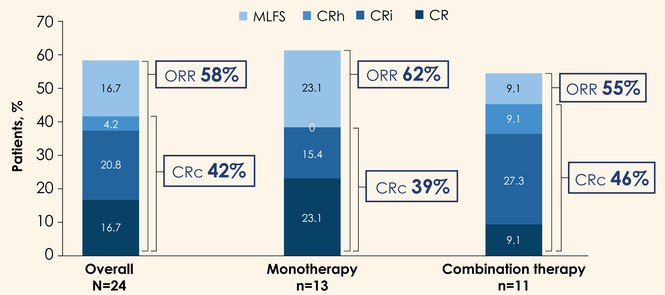
Figure 1. Oncoprint for All Patients



Response rates (Figure 2):

- **The overall response rate (ORR) was 58% (14/24)**, with a composite complete remission (CRc) rate of 42% (10/24). Among patients who received venetoclax immediately prior to olutasidenib, ORR was 63% (10/16)
- ORR was 62% among 13 patients treated with olutasidenib monotherapy, and 55% in 11 patients treated with combination therapy
- Ten patients (42%) received olutasidenib as the next line of therapy after first-line venetoclax. Among these patients, ORR was 60% and CRc was 50%; responses included 2 CR, 2 CRi, 1 CRh, and 1 MLFS
- Five patients (21%) received ivosidenib prior to olutasidenib, and among these patients, 1 achieved a CR and 2 achieved a PR

Figure 2. Patient Response Outcomes



Note: 3 patients in the analysis set were "reported" as having a partial response but were excluded from ORR calculations.

Partial response:

- Three patients were identified in physician notes as potential partial responders, but insufficient documentation to confirm their status led to their exclusion from these analyses, resulting in a more conservative estimate of response

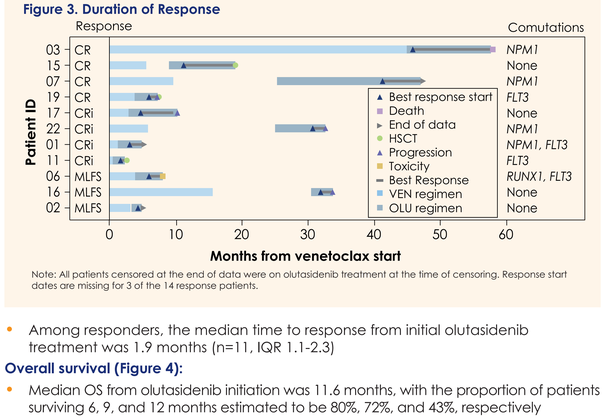
Transfusion independence:

- Thirteen patients (54%) were transfusion dependent at olutasidenib initiation, defined as ≥1 transfusion in the 8 weeks prior to treatment. Among these patients, 2 (15%) achieved 8-week transfusion independence after starting olutasidenib

Response duration (Figure 3):

- Median duration of CRc was 11.9 months among 8 patients with evaluable DoR data

Figure 3. Duration of Response



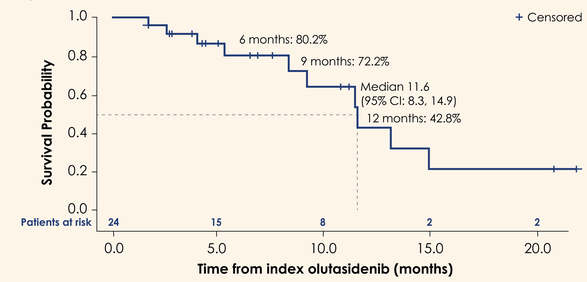
Note: All patients censored at the end of data were on olutasidenib treatment at the time of censoring. Response start dates are missing for 3 of the 14 response patients.

- Among responders, the median time to response from initial olutasidenib treatment was 1.9 months (n=11, IQR 1.1-2.3)

Overall survival (Figure 4):

- Median OS from olutasidenib initiation was 11.6 months, with the proportion of patients surviving 6, 9, and 12 months estimated to be 80%, 72%, and 43%, respectively

Figure 4. Overall Survival



Note: Overall survival was calculated from the start of olutasidenib.

Conclusions

- This study provides real-world evidence on treatment patterns and outcomes of patients treated with olutasidenib for R/R m*IDH1* AML after prior venetoclax
- Olutasidenib was most frequently used as monotherapy immediately after venetoclax
- The ORR of 58% and CRc rate of 42% observed in this small real-world analysis are consistent with the efficacy data reported in the olutasidenib pivotal phase 2 trial;[2] responses were also observed in patients harboring deleterious co-mutations
- These findings support olutasidenib as a viable therapeutic option in post-venetoclax treatment settings, where outcomes are typically poor. A prospective single-arm, phase 2 study is underway in this treatment setting (NCT07471841)