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Treatment Patterns and Outcomes With Olutasidenib After Venetoclax in *IDH1*-Mutated AML Using Real-World Data From Chart Review

Poster # AML - 792

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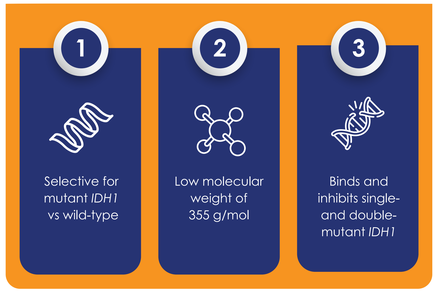
Introduction

- Olutasidenib is a potent and selective oral small-molecule inhibitor of mutated isocitrate dehydrogenase 1 (*mIDH1*) that is FDA approved for patients with relapsed or refractory (R/R) m*IDH1* acute myeloid leukemia (AML)



- In the final 5-year results from a phase 2 trial, olutasidenib achieved 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[2]

Objectives

The objectives of this study were to describe the clinical characteristics, treatment patterns, safety, and real-world effectiveness of adults with R/R m*IDH1* AML receiving olutasidenib following venetoclax in routine practice

Methods

- ***Data source***: This retrospective cohort study used data from a physician-based chart review. Treating oncologists abstracted data from medical records into an electronic case report form
- ***Eligibility criteria***: Eligible patients were ≥18 years of age, had R/R AML with an *IDH1* mutation, had prior treatment with venetoclax, and started olutasidenib from December 2022 to March 2025. Patients were excluded if they received prior IDH1-targeted therapy or >1 additional therapy between receipt of venetoclax and olutasidenib. All patients were required to have a response evaluation and at least 1 full 28-day cycle of olutasidenib

Results

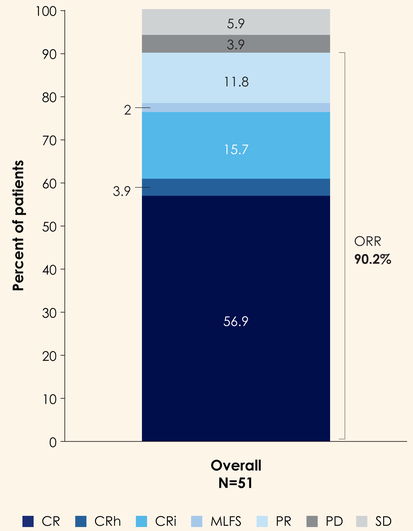
- Physician site characteristics:
  - 18 treating oncologists
  - 9 academic, 9 community
- Key patient characteristics (**Table 1**):
  - The median patient age at diagnosis was 61 years and 78% were male
  - ECOG was 0–1 in 60.8% and 2–3 in 39.2% of patients at the time of olutasidenib initiation, and 15.7% had AML with antecedent MDS
- Patients were evenly distributed geographically across the United States
- Treatment patterns:
  - 72.5% of olutasidenib use was in the second line, 27.5% in the third line
  - Olutasidenib was administered as monotherapy (96.1%) and in combination with azacitidine (3.9%)
  - Most patients (90.2%) received venetoclax-based therapy in the first-line setting; overall response rate (ORR) in response to venetoclax was 81.3% and CR/CR with incomplete hematologic recovery (CRi) was 47.9%

Table 1. Key Patient Characteristics

Patient Characteristics	N=51 n (%)
Median age, y (IQR)	61 (57, 69)
Male sex	40 (78.4)
Antecedent MDS	8 (15.7)
***IDH1* mutation type**	
R132C	22 (43.1)
R132G	13 (25.5)
R132H	3 (5.9)
R132L	4 (7.8)
R132S	1 (2.0)
Unknown	8 (15.7)
ECOG PS	
0	3 (5.9)
1	28 (54.9)
2	13 (25.5)
3	7 (13.7)
Unknown	0
Type of co-mutation	
DNMT3A	22 (43.1)
FLT3	18 (35.3)
NPM1	18 (35.3)
RUNX1	4 (7.8)
None	20 (39.2)
RBC/Platelets transfusion dependence at olutasidenib start	
Yes	36 (70.6)
No	15 (29.4)
Olutasidenib duration (months)	
Median estimated via KM (IQR)	32.4 (22.2, NR)
Follow-up time from olutasidenib start (days)	
Mean (SD)	401.2 (274.7)
Median (Q1, Q3)	265 (226.0, 693.0)

- Clinical response (**Figure 1**):
  - **The ORR with olutasidenib was 90.2% (46/51)**, with a CR rate of 56.9% (29/51) and a CR/CRh rate of 60.8% (31/51)
  - In first-line venetoclax and second-line olutasidenib, ORR was 89.2% (33/37) and CR was 54.1% (20/37)

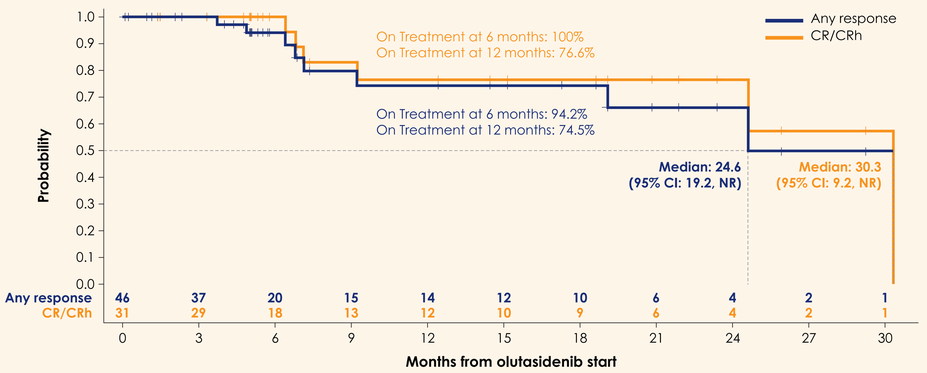
Figure 1. Clinical Response to Olutasidenib Following Venetoclax



CR, complete remission; CRh, complete remission with partial hematologic recovery; CRi, complete remission with incomplete hematologic recovery; MLFS, morphologic leukemia-free state; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

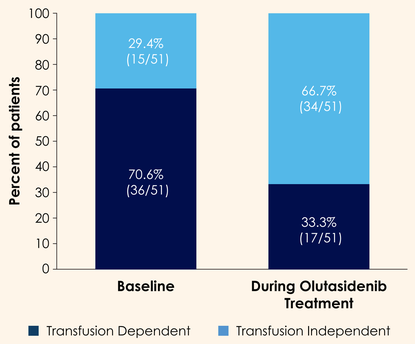
- Response duration (**Figure 2**):
  - The median duration of response for all responders (CR, CRh, CRi/p, MLFS, PR) was 24.6 months (95% CI: 19.1, NR)
  - The median duration of CR/CRh was 30.3 months (95% CI: 9.2, NR)
- Red blood cell (RBC) and/or platelet transfusion dependence (**Figure 3**):
  - At baseline, 36/51 patients (70.6%) were RBC and/or platelet dependent. During olutasidenib treatment, **34/51 patients (66.7%) achieved or remained transfusion independent**
  - Of the 36 (70.6%) patients who were RBC and/or platelet transfusion dependent at baseline, **20 (55.6%) achieved transfusion independence** while on olutasidenib

Figure 2. Duration of Response



Note: All patients censored at the end of data were on olutasidenib treatment at the time of censoring.
CR, complete remission; CRh, complete remission with partial hematologic recovery; NR, not reached.

Figure 3. RBC and/or Platelet Transfusion Dependence



RBC, red blood cell.

- Treatment discontinuation
  - Of the 12 patients discontinuing olutasidenib, the primary reason was disease progression (41.7%). The most common adverse events were fatigue (11.8%), infection, neutropenia, and nausea (each 7.8%)
- Limitations
  - Charts were not selected through randomized sampling, limiting the generalizability of results
  - Physicians were asked to provide sequential charts; however, physicians could have selected patients through biased sampling

Conclusions

- **Olutasidenib demonstrated robust real-world effectiveness** in adults with R/R m*IDH1* AML previously treated with venetoclax, a subgroup with historically very poor outcomes
- **Substantial reductions in transfusion dependence** further support olutasidenib as a viable post-venetoclax therapeutic option
- These findings **suggest early sequencing of olutasidenib after prior treatment with venetoclax-based therapy may optimize treatment outcomes**
- Results from a cohort of patients from the United States support olutasidenib as an important treatment option in this clinically challenging setting and warrant confirmation in larger, prospectively defined real-world cohorts[2,3]

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ACKNOWLEDGMENTS

This study was conducted by Inizio Ignite Putnam and was funded by Rigel Pharmaceuticals, Inc. (South San Francisco, California, USA). Creative assistance was provided by Oxford PharmaGenesis Inc (Wilmington, Delaware, USA) and was funded by Rigel Pharmaceuticals, Inc.
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Presented at the 2026 Society of Hematologic Oncology Annual Meeting, September 9-12, 2026, Houston, Texas, USA
Originally presented at the 2026 European Hematology Association Annual Meeting, June 11-14, 2026, Stockholm, Sweden