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Venetoclax in Combination With low-Dose Cytarabine and/or Actinomycin D In Relapsed or Refractory (R/R) Acute Myeloid Leukemia (AML) Patients With IDH1 or IDH2 Mutations

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INTRODUCTION

IDH1/2 inhibitors (IDHi) are US FDA-approved salvage therapies for IDH-mutated (IDHm) R/R AML. Nevertheless, IDHi have limited accessibility. Herein, we report the real-life results of venetoclax (Ven) in combination with low-dose cytarabine and actinomycin D (ACTIVE triplet therapy) for IDHm R/R AML.

AIM

To evaluate the safety and efficacy of ACTIVE triplet therapy for IDHm R/R AML.

METHOD

- Observational, single-center, retrospective study.
- Patients were treated during 2018-2023.
- 27 R/R patients were included.

Characteristics	
Diagnosis, n/N (%)	
AML	26/27 (96.3)
MDS-IB2	1/27 (3.7)
IDH mutation n/N (%)	
IDH1	8/27 (29.6)
IDH2	19/27 (70.4)
Median ange, years (range)	65 (34-80)
Eastern Cooperative Oncology Group performance status (range)	1 (0-3)
Median number of previous treatment lines, n (range)	1 (1-4)
Previous Ven exposure, n/N (%)	3/27 (11.1)
European LeukemiaNet 2022 risk group, n/N (%)	
Adverse	14/27 (51.9)
Favorable/Intermediate	13/27 (48.1)

Table 1. *Patients' characteristics. 3 patients relapsed post-allogeneic stem cell transplant (alloSCT). 3 patients had adverse cytogenetics*

Most common co-mutations	n/N (%)
DNMT3A	13/27 (48.1)
ASXL1	9/27 (33.3)
FLT3-ITD	8/27 (29.6)
RUNX1	5/27 (18.5)
SRSF2	3/27 (11.1)

Table 2. *The most common co-mutations.*

RESULTS

- Median RFS was 9.2 months (95% CI: 0-–20.8).
- Median OS was 16 months (95% CI: 7.9-–19.5).
- 12- and 24- month OS was 55% and 39%, respectively.
- The ORR (complete remission (CR) + incomplete count recovery (CRi) + morphological leukemia-free state (MLFS) was 81%. CR, CRi, and MLFS rates were 63%, 11% and 7%, respectively.
- MRD negativity rate was 55% among CR/CRi patients.
- 41% were bridged to alloSCT.
- 30- and 60-day mortality rates were 11% and 19%, respectively.

3-5 grade adverse events	n/N (%)
Infectious complications	
Febrile neutropenia	16/27 (59.3)
Sepsis	5/27 (18.5)
Pneumonia	5/27 (18.5)
Catheter-related infections	3/27 (11.1)
Non-infectious complications	
Tumor lysis syndrome	4/27 (14.8)
Diarrhea	3/27 (11.1)
Multi-organ failure	2/27 (7.4)

Table 3. *3-5 grade by Common Terminology Criteria for Adverse Events (CTCAE) adverse events of the treatment.*

CONCLUSION

ACTIVE regimen demonstrated high antileukemic efficacy in R/R IDHm AML. Most common AEs were infectious complications with incidence of tumor lysis syndrome.

REFERENCES

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