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Real-World Outcomes of Decitabine + Venetoclax with IDH inhibition for AML

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BACKGROUND

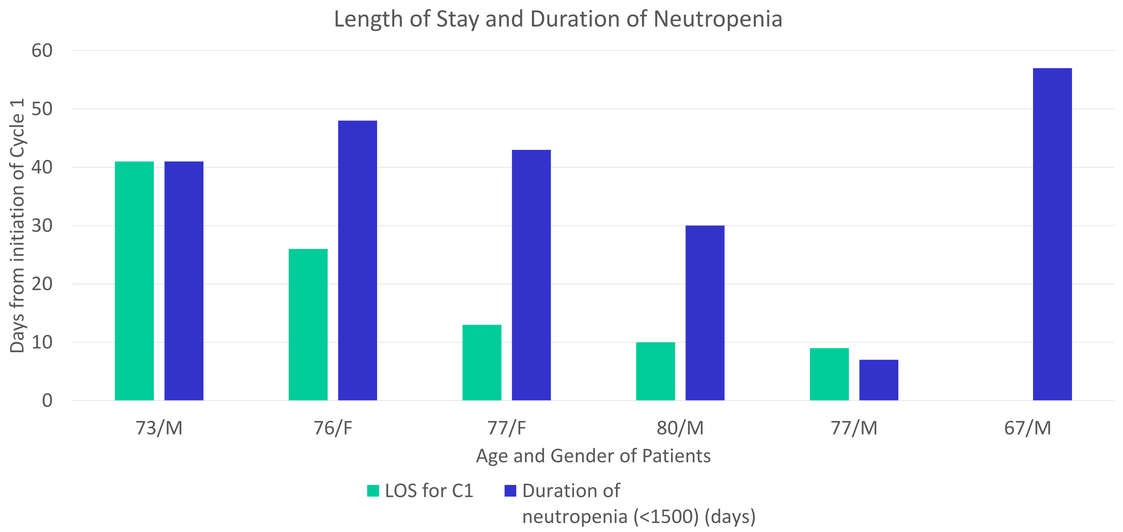
- Treatment with a hypomethylating agent (HMA) and venetoclax is a common regimen for older/unfit patients with acute myeloid leukemia (AML).
- Approximately 20% of AML harbors mutations in *isocitrate dehydrogenase 1/2* (*IDH1/2*), which promotes oncogenesis and dependence on the BCL-2 pathway.
- In the VIALE-A trial, venetoclax and azacitidine showed a complete remission (CR) with incomplete count recovery (CR/CRi) rate of 75% in newly diagnosed *IDH1/2*^{mut}AML (median overall survival of 24.5 months).
- *IDH1/2* inhibitors (IDHi) are approved both as monotherapy and with an HMA for AML.
- Pre-clinical data studying venetoclax and IDHi in combination indicates a synergistic effect, though limited clinical data is available.

AIM

To Assess outcomes in *IDH1/2*^{mut} AML treated with "triplet regimen" of 10-day decitabine, venetoclax, and IDHi (DAC+VEN+IDHi).

METHODS

- Retrospective case series of patients with *IDH1/2*^{mut}AML treated at a tertiary-care hospital.
- The primary outcome was response rate and secondary outcomes included duration of response, overall survival, and adverse events.



Age/Gender	Best Response to C1 Dac Ven	Best Response to Dac-Ven-IDHi	Infections?	LOS for C1	Duration of neutropenia (<1500) (days)
73/M	Refractory/residual disease	Dead	Bacteremia	41	41
76/F	CRi	CRi	Unspecified	26	48
77/F	CR (MRD-)	CR (MRD -)	Pneumonia	13	43
80/M	Refractory/residual disease	Refractory/residual disease	no	10	30
77/M	PR	PR	no	9	7
67/M	CR (MRD+)	CR (MRD -)	no	0	57

RESULTS

- Six patients were included (4 male; median age 76.5). Five patients had newly diagnosed AML (3 were de novo; 2 were secondary to myelodysplastic or myeloproliferative neoplasms). One patient had refractory AML treated with 2 cycles of CPX-351. Three patients had CR after cycle 1 of DAC+VEN+IDHi (1 CR/CRi, 1 minimal residual disease [MRD]+ CR, 1 MRD-CR). Two patients had refractory disease after cycle 1. One patient had PR after cycle 1. Best responses to DAC+VEN+IDHi were unchanged after cycle 1. Five patients were alive at last follow-up (median of 409 days from cycle 1, day 1 of DAC+VEN+IDHi); 4 were in CR and 1 in PR. Four patients at last follow-up were greater than 1-year from cycle 1, and one patient was 8-months from cycle 1. The median length of hospitalization was 13 days; the median duration of neutropenia was 48 days. One patient died at day 41 from infectious-related complications. One patient underwent an allogeneic bone marrow transplantation on day 76 and remained in CR (MRD-) at last follow-up.

CONCLUSIONS

- Patients with IDH1/2 mutant AML may benefit from addition of IDH inhibitor in combination with an HMA and venetoclax. This regimen merits further evaluation.

REFERENCES

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