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Prolonged Cytopenias After First-Line Treatment With Venetoclax and Hypomethylating Agent in Newly Diagnosed AML/MDS-IB

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CONTEXT

Venetoclax (VEN) + hypomethylating agents (HMA) have proven to be an effective treatment for unfit patients diagnosed with acute myeloid leukemia (AML) or myelodysplastic syndrome with increased blasts (MDS-IB). However, a proportion of VEN+HMA responders have prolonged hematological recovery, resulting in life-threatening infectious complications.

OBJECTIVE

To identify patient and disease characteristics associated with prolonged neutropenia or thrombocytopenia after treatment with VEN+HMA.

DESIGN

A single-center retrospective study was conducted (2020-2024). We analyzed time to absolute neutrophil count (ANC) >1000 cells/mm^3 and platelet (PLT) count >100,000 cells/mm^3 recovery and factors associated with prolonged myelosuppression in patients with newly diagnosed AML/MDS-IB who achieved CR/CRi/MLFS after VEN+HMA therapy.

PATIENTS

Fifty-eight previously untreated AML (n=49; 84.5%) or MDS-IB (n=9; 15.5%) patients aged 70.5±8.9 years were divided according to ANC and PLT recovery time counting from day 1 of the best-response-inducing VEN+HMA cycle.

Patients in the “early recovery” cohort recovered in less than 35 days (ANC group n=19, PLT group n=27), and those in the “prolonged recovery” cohort recovered in 35 or more days/not recovered (ANC group n=39, PLT group n=31).

RESULTS

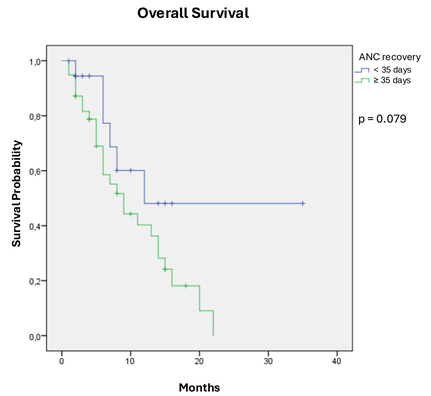
82.2% (n=48) patients have achieved CR/CRi, and 17.2% (n=10) had MLFS lacking hematological recovery.

The most common mutations were *RUNX1* (22.4%), *TP53* (20.7%), and *FLT3* (19%), although they were not associated with prolonged neutropenia (*P*=0.572, *P*=0.608, *P*=0.310, respectively).

Prior chemotherapy/therapy-related disease (*P*=0.023) and VEN dosing for >14 days (*P*=0.044) were associated with longer (≥35 days) ANC recovery.

OS did not differ significantly and was 12 months (95% CI, N/A) in the recovered and 9 months (95% CI, 5.7-12.3, *P*=0.079) in the prolonged ANC recovery cohort.

Prior MDS/MPN (*P*=0.001) and baseline ANC level ≥1000 cells/mm^3 (*P*=0.021) resulted in longer PLT recovery.



Characteristics	ANC recovery in <35 days (N=19)	ANC recovery in ≥35 days (N=39)	P-value
Age, years			
Mean ± SD	71.4 ± 7.19	69.6 ± 9.7	0.460
ECOG ≥2, No. (%)	13 (68.4)	22 (56.4)	0.380
ELN adverse group, No. (%)	15 (78.9)	28 (71.8)	0.752
Ven duration >14 days, No. (%)	0 (0)	8 (20.5)	**0.044**
Baseline blasts BM, %			
Median (IQR)	30.5 (19.6-50)	26 (14.8-52.5)	0.624
Flow MRD negativity, %	8 (42.1)	8 (20.5)	0.084
G-CSF, days	9 (7.8-12.3)	5 (3-21)	0.553
Adverse karyotype, No. (%)	8 (42.1)	19 (48.7)	0.636
Prior MDS/MPN, No. (%)	6 (31.6)	14 (35.9)	0.745
Prior chemotherapy, No. (%)	1 (5.3)	13 (33.3)	**0.023**
Prior radiotherapy, No. (%)	1 (5.3)	6 (15.4)	0.407
Secondary disease, No. (%)	8 (42.1)	22 (56.4)	0.306
Febrile neutropenia, No. (%)	10 (34.5)	19 (48.7)	0.780
Documented infection, No. (%)	9 (47.4)	19 (48.7)	0.923
Further alloSCT, No. (%)	6 (31.6)	8 (20.5)	0.514

CONCLUSIONS

Prior chemotherapy exposure and venetoclax dosing for >14 days are associated with prolonged ANC recovery, whereas prior MDS/MPN diagnosis and a higher baseline ANC level resulted in longer PLT recovery after VEN+HMA therapy.

REFERENCES

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