

REAL-WORLD EXPERIENCE WITH VENETOCLAX-BASED REGIMENS FOR THE TREATMENT OF ACUTE MYELOID LEUKEMIA

Giusy Ceparano ^{1, 2*} , Mariarita Sciumè ² , Sonia Fabris ² , Enrico Barozzi ^{1, 2} , Nicolò Rampi ^{1, 2} , Pasquale De Roberto ² , Luca Baldini ^{1, 2} , Nicola Stefano Fracchiolla ²
¹ Università degli Studi di Milano, Milan, Italy,
² Hematology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy



INTRODUCTION

Prognosis of acute myeloid leukemia (AML) still represents a clinical challenge, especially in elderly patients. Venetoclax is a selective, potent, orally bioavailable BCL-2 inhibitor that has demonstrated single-agent activity both in relapse/refractory (R/R) and newly diagnosed AML. Though, the efficacy and safety of venetoclax combinations regimens in the “real-life” setting have not been extensively described. We aimed to report our single-center experience of venetoclax alone or in combination approach for AML patients not eligible for standard induction therapy.

METHODS AND RESULTS

A retrospective analysis has been performed on 39 consecutive patients affected by treatment-naïve (n=13) or R/R AML (n=26) treated with venetoclax alone (n=4) or in association with azacitidine (n=31), decitabine (n=3) or cytarabine (n=1). Median age was 71 years, with 67% older than 65 years. The majority showed an intermediate genetic risk. Sixteen patients (41%) were treated in the salvage-2 setting or later and 7 (18%) had received a prior allogeneic stem cell transplantation. Venetoclax was administered at a dose of 400 mg daily (n=22), with dose reductions to 200 mg (n=9) or 100 mg (n=8) in case of concurrent therapy with CYP3A4 inhibitors. Most common grade 3 or 4 toxicities were hematological or infectious (49% and 51%). Nineteen patients (49%) achieved a complete response, with median time to best response of 1 month. Six-month OS in treatment-naïve and R/R group were 92% and 45%, respectively (p=0.0186), with no differences among genetic risk groups. Median disease free survival was 5 months (range, 1-15 months). The estimated 6-month OS was markedly higher in patients with CR (100%), CRi (75%) and PR (75%) compared to patients with no response to therapy (18%), regardless of disease status at the time of starting treatment (p<0.0001). Seven patients underwent allogenic stem cell transplantation after venetoclax combination therapy as consolidation strategy.

CONCLUSIONS

Our real-world data confirmed that venetoclax-based regimens are a viable and safe option for AML patients unfit for intensive chemotherapy both in first line and in the salvage setting. Furthermore, the association of venetoclax and hypomethylating agents (HMAs) proved to be a feasible bridging therapy to transplantation in elderly AML patients.

CHARACTERISTIC	TOT (n=39)	Treatment-naive AML (n=13, 33%)	Relapsed/Refractory AML (n=26, 67%)
	N (%)	N (%)	N (%)
Median age (range), years	71, 30-84	76, 65-84	68, 30-78
> 65 – no. (%)	26 (67)	11 (85)	15 (58)
Male – no. (%)	20 (51)	7 (54)	13 (50)
Risk ELN – no. (%)			
adverse	13 (33)	5 (38)	8 (31)
intermediate	20 (51)	7 (54)	13 (50)
favorable	6 (15)	1 (8)	5 (19)
Molecular mutations – no. (%)			
RUNX1-RUNX1T1	0	0	0
CBFB-MYH11	0	0	0
FLT3 ITD	4 (10)	1 (8)	3 (12)
FLT3 TKD	1 (3)	0	1 (4)
NPM1	7 (18)	2 (15)	5 (19)
MLL rearrangement	0	0	0
CEBPA biallelic	1 (3)	0	1 (4)
IDH1	1 (3)	1 (8)	0
IDH2	4 (10)	3 (23)	1 (4)
Venetoclax combination regimen – no. (%)			
Azacitidine	31 (79)	12 (92)	19 (73)
Decitabine	3 (8)	1 (8)	2 (8)
ARA-C	1 (3)	0	1 (4)

CHARACTERISTIC	TOT (n=39)	Treatment-naive AML (n=13, 33%)	Relapsed/Refractory AML (n=26, 67%)
Response evaluation – no. (%)			
CR	10 (26)	4 (31)	6 (23)
Cri	9 (23)	4 (31)	5 (19)
NR	11 (28)	0	11 (42)
SD	2 (5)	1 (8)	1 (4)
PR	4 (10)	3 (23)	1 (4)
Time to best response in CR+CRi, months (median, range)	1, 1-3	1, 1-3	1, 1-3
Duration of response in CR+CRi, months (median, range)	4, 1-15	4, 1-7	4, 1-15
N° of cycles to achieve best response in CR+Cri – no. (%)	N= 19	N=8	N=11
1	16 (84)	7 (88)	9 (82)
2	1 (5)	0	1 (9)
>2	2 (11)	1 (13)	1 (9)
Relapsed status – no. (%)			
First line	13 (33)		
Salvage 1	10 (26)		
Salvage >= 2	16 (41)		
Prior allogenic SCT – no. (%)	7 (18)		
Dose of Venetoclax – no. (%)			
100 mg	8 (21)	5 (38)	3 (12)
200 mg	9 (23)	2 (15)	7 (27)
400 mg	22 (56)	6 (46)	16 (62)