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ELEVENTH ANNUAL MEETING

Safety and efficacy of FLAG-Ida-based therapy combined with venetoclax for the treatment for newly diagnosed and relapsed/refractory patients with AML- a systematic review

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INTRODUCTION

- Intensive induction chemotherapy (IC) remains the mainstay of therapy for fit patients with acute myeloid leukemia (AML)
- Although advances in IC dosing and incorporation of targeted therapies result in improved CR rates of 70%-80%, in some specific clinical and genetic settings 50%-60% of patients will have refractory disease or ultimately relapse
- Venetoclax (VEN) in combination with IC is increasingly used to treat patients with high-risk AML

AIM

- The primary safety outcome was infection rate
- The primary efficacy outcome was response to treatment [composite complete remission (CRc) and overall response rate (ORR)].

METHODS

- We conducted an electronic search for studies that directly described treatment combination with FLAG-Ida and Venetoclax for patients with AML
- The primary safety outcome was infection, and the primary efficacy outcome was response to treatment
- Risk of bias was assessed according to the ROBINS-I tool

RESULTS

- Six studies including 221 patients with newly-diagnosed (ND) AML (n=120)) and Relapsed or refractory (R/R) AML (n=101) disease, were included in this systematic review. Pooling of results was not conducted due to major differences between studies

- Neutropenic fever ranged between 44-55% patients
- Bacteremia ranged between 24-48% patients
- Pneumonia ranged between 12-30% patients
- Invasive fungal infections ranged between 11-36% patients.
- Time to ANC and platelet recovery ranged between 23-29 and 23-31 days, respectively.
- Early death rate was 8.7% (14/160) patients: 4 patients at 30 days, additional 10 in 60 days.

- CRc rates ranged between 53 to 78% for R/R AML.
- CRc for ND was reported by one study only (89%).
- ORR were reported in 60 to 78% of patients with R/R AML.
- Only one study reported an ORR for ND patients of 98%.

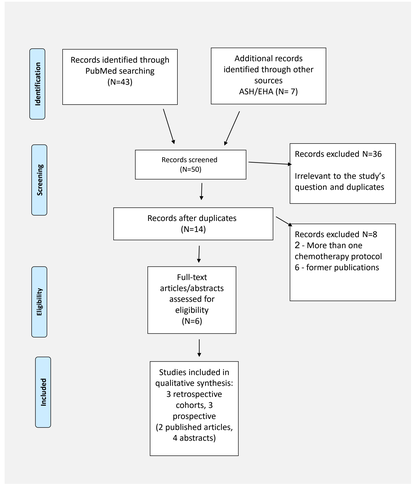


Figure 1

Author	Publication status	Design	Number patients	AML type	Age*	Post allo relapse n (%)	Previous lines of therapy*
DiNardo C.[1]	abstract 2022	Prospective	33	R/R 33	47 (18 - 68)	10 (30)	1 (1-4)
DiNardo C.[2]	Published 2022	Prospective	45	ND 45	44 (20 - 65)	NA	NA
Wolach O.[3]	Published 2022	Retrospective, real world	25	R/R 24 ND 1	53.4 (31.1-72)	11 (44)	1 (0-3)
Shahswar R.[4]	Abstract 2022	Retrospective controlled	37	R/R 37	54	8 (22)	1 (1-5)
Abaza Y.[5]	Abstract 2022	Retrospective	24	ND 17, R/R 7	48 (21-68)	1 (6)	1 (1-2)
Marconi G.[6]	Abstract 2022	Prospective	57	ND 57	54 (18 - 65)	NA	NA

Characteristics of studies

Author	Bacteremia n(%)	IFI n(%)*	Early death 30 days	Early death 60 days	Median time to Neuto>500	Median time to PLT>50K
DiNardo C. R/R	10 (43)	NA	0	4	Neuto + PLT 37 d	
DiNardo C. ND	11 (24)	4 (36)	0	0	Neuto + PLT 31d	
Wolach O.	12 (48)	8 (32)	3 (12)	3 (12)	23 (95% CI 20-28)	31 (95% CI 17.6-38.3)
Shahswar R.	10 (27)	4 (11)	NA	NA	NA	NA
Abaza Y.	NA	NA	NA	NA	ND 25 (19-42) R/R 29 (24-43)	ND 23 (17-42) R/R 31.5 (23-78)
Marconi G.	NA	NA	1	3	NA	NA

Safety Outcomes

Author	ORR definition	ORR n(%)	CRc N (%)	OS in 12 months	Proceeded to AlloSCT/DLI
DiNardo C. R/R	CR	19/32 (60)	17/32 (53)	*27 (95% CI 22.3-26.3)	13 (68)
DiNardo C. ND	CR, CRh, CrI, MLFS, PR	44 (98)	40 (89)	92% (95% CI: 84%–100%)	27 (60)
Wolach O.	CRc, MLSF	19 (76)	18 (72)	50% (95% CI 31%-69%)	10 (40)
Shahswar R.	CR, CRI and MLFS	29 (78)	CR/CRi 22/59)	*12 (95%, 7.6 - NR)	30 (81)
Abaza Y.	CR, CrI, MLFS, PR	19/24 (79)	NA	* ND 13.2 (4.3-22, 95% CI: NR) R/R 13.2 (4.3-22, 95% CI: NR)	12 (54)
Marconi G.	CR, CRh, CrI, MLFS, PR	NA	NA	NA	28 (49)

Efficacy outcomes

CONCLUSIONS

- in our systematic review, FLAG-Ida plus VEN proved to be a potentially tolerable and effective regimen in ND and R/R AML patients.
- Infections and myelosuppression pose a concern mandating prophylactic anti-bacterial and anti-fungal treatment and a proactive approach to suspected and proven infections.
- Overall, toxicity as reflected in this analysis is acceptable with promising response and remission rates for this challenging group of patients.
- We suggest to further evaluate and confirm the safety and efficacy of this new protocol in future RCTs.

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