Preliminary Pharmacokinetic and MRD Results from AML Patients Treated with 7 and 14 Day Dosing Schedule of Emavusertib added to Combination therapy with Azacitidine and Venetoclax

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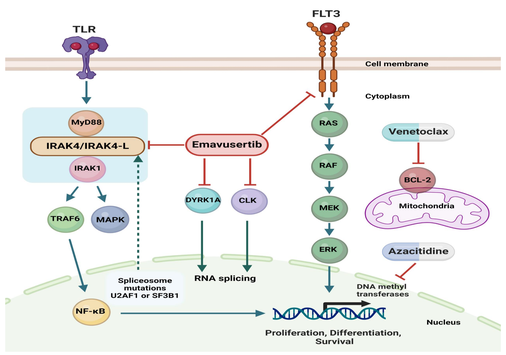
INTRODUCTION

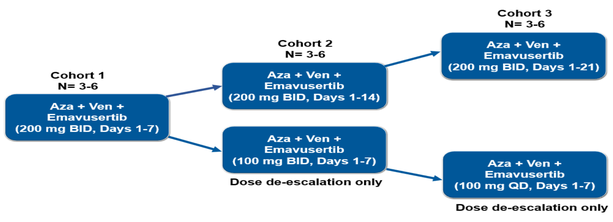
- Acute myeloid leukemia (AML) is a heterogenous disease and exhibits a dynamic mutational landscape as the disease progresses[1].
- In the VIALE-A study[2], 67 of 164 (41%) of patients who achieved composite complete response (CRc) and were evaluable for MRD achieved undetectable MRD by flow cytometry using established ELN guidelines (uMRD < 10^{-3}).
- Studies have shown that primary and adaptive resistance in venetoclax-based combinations are often associated with FLT3-ITD mutations[3].
- Emavusertib is a novel, potent oral inhibitor of interleukin-1 receptor-associated kinase 4 (IRAK4) with additional inhibitory activity against FLT3 and CDC-like kinases (CLK1/2/4).
- As of October 12, 2025, the ongoing TakeAim Leukemia trial (EUCTR#2023-505828-58) has enrolled 10 patients who achieved CRc with Aza/Ven and had detectable MRD.
- Emavusertib was given for either 7 (n=4) or 14 days (n=6) of each 28-day schedule.
- Here we present preliminary efficacy including MRD conversion, safety and PK data. MRD assays were performed by flow cytometry using established ELN guidelines (uMRD < 10^{-3}).

MECHANISM OF ACTION



The mechanism of action of emavusertib in combination with azacitidine and venetoclax

STUDY DESIGN

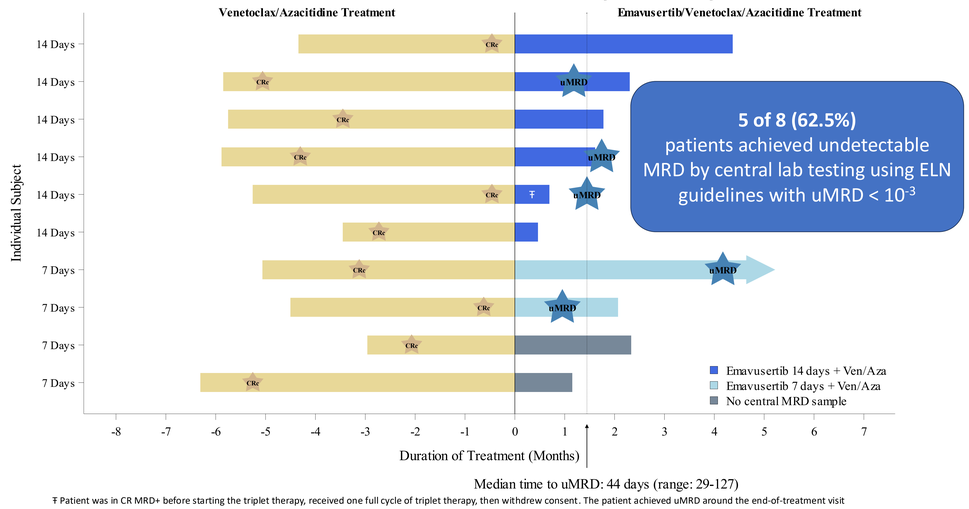


RESULTS

Baseline Characteristics

		Emavusertib (200 mg BID) 7 days + Aza + Ven (n=4)	Emavusertib (200 mg BID) 14 days + Aza + Ven (n=6)
Female n (%) : Male n (%)		1 (25) : 3 (75)	5 (83) : 1 (17)
Age (yrs): median (range)		69.5 (67, 72)	74 (69, 81)
ELN Risk Classification, n (%)	Adverse	1 (25)	2 (33)
	Favorable	1 (25)	1 (17)
	Intermediate	2 (50)	3 (50)
Number of Cycles Aza + Ven Received, n (%)	2	1 (25)	0
	3	1 (25)	1 (17)
	4	1 (25)	1 (17)
	5	0	3 (50)
	6	1 (25)	1 (17)
Most Recent Response on Aza + Ven, n (%)	CR	3 (75)	5 (83)
	CRh	1 (25)	1 (17)

Duration on Treatment (Months)

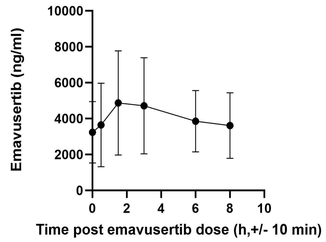


Median time to uMRD: 44 days (range: 29-127)

Ŧ Patient was in CR MRD+ before starting the triplet therapy, received one full cycle of triplet therapy, then withdrew consent. The patient achieved uMRD around the end-of-treatment visit

Pharmacokinetics

Mean (+/-SD) Plasma Emavusertib Concentration (C1D4)



Dose	Cmax (ng/mL)	AUC0_8 (h*ng/mL)
7d	1719.0	12260.8
7d	3742.2	27733.0
7d	3477.8	16794.4
7d	4331.7	33447.3
14d	8949.7	55073.2
14d	9430.3	56892.0
14d	4581.3	27688.4
14d	8642.5	55435.3
14d	2475.1	18676.6
14d	3521.8	23983.3
mean	**5087.1**	**32798.4**

C1D4 data is consistent with PK data across the emavusertib program

- **Mean AUC_{0-8}** = 32798 h*ng/ml, observed
- **Mean Cmax** = 5087 ng/ml

Treatment-related adverse events Grade ≥ 3 in all treated patients

Grade 3+ Treatment-Related Adverse Events N (%)	200 mg BID Emavusertib 7 day + Aza + Ven (n%)	200 mg BID Emavusertib 14 day + Aza + Ven n (%)	Total n (%)
Any Grade 3 or higher Emavusertib related Adverse Events	4 (100)	6 (100)	10 (100)
Neutropenia	3 (75)	5 (83)	8 (80)
Thrombocytopenia	3 (75)	3 (50)	6 (60)
Febrile Neutropenia	2 (50)	1 (17)	3 (30)
Anemia	1 (25)	1 (17)	2 (20)
Asthenia	0	1 (17)	1 (10)
Blood Creatine phosphokinase increased	0	1 (17)	1 (10)
Neutrophil count decreased	1 (25)	0	1 (10)
Pneumonia	0	1 (17)	1 (10)

CONCLUSIONS

- The addition of emavusertib to azacitidine and venetoclax improved MRD conversion in AML patients (62.5% of patients treated with the triplet achieved uMRD) and is a promising option for AML patients, where uMRD is associated with better PFS and OS
- Emavusertib PK values are consistent with our monotherapy leukemia studies
- Additional regimens with this triplet combination continue to be investigated to determine the optimal dosing schedule for safety and efficacy
- These initial findings support further investigation of this triple combination to improve patient outcomes in a difficult to treat population

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