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ELEVENTH ANNUAL MEETING

Sequential Salvage Chemotherapy and Lintuzumab-Ac225 in Relapsed/Refractory AML Results in Deep Responses and Prolonged Survival in Adverse Risk AML and in AML Patients that Received Prior Venetoclax Therapy

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INTRODUCTION

Lintuzumab-Ac225 is a humanized CD33 antibody conjugated to the alpha emitting isotope, Actinium225. In addition to targeted radiation delivery, preclinical studies indicate Lintuzumab-Ac225 depletes the anti-apoptotic protein MCL-1. We performed a Phase I study where Lintuzumab-Ac225 was administered after CLAG-M salvage chemotherapy.

AIM

We report the outcomes of **high-risk** patients enrolled to this study.

High-risk was defined as patients with AML with ELN adverse risk disease and/or patients with relapsed/refractory disease after venetoclax-based therapies, as contemporary studies report poor outcomes in these patients, with median survival around 3-4 months[1,2].

METHOD

This Phase I study enrolled R/R AML fit pts, with adequate organ function, and with CD33 expression on >25% of leukemic blasts.

Induction consisted of G-CSF, 300mcg/d, given D1-6, cladribine 5mg/m2, given D2-6, cytarabine 2g/m2, given D2-6, and mitoxantrone 10mg/m2, given D2-4. Lintuzumab-Ac225 was administered once on day 8 ±1 day.

The trial enrolled to 4 cohorts, with Lintuzumab-Ac225 at doses ranging from 0.25 uCi/kg to 1.0 uCi/kg. Response is descriptively reported, and Kaplan Meier estimator was used to report overall survival (OS).

RESULTS

Characteristic	High Risk N=19	All N=23
Age, Median (range)	65y(40-73)	62y(20-73)
ELN Risk, n(%)		
Favorable	1(5%)	2(9%)
Intermediate	1(5%)	4(17%)
Adverse	17(90%)	17(74%)
TP53 Abnormality	**12(63%)**	12(52%)
Mutation, VAF<20%	1(9%)	1(4%)
Mut, VAF>20% or TP53mut+CC	11(91%)	11(48%)
Prior Therapies, median(range)	2(1-5)	2(1-5)
CD33 expression, Median(range)	82%(32-100)	82%(29-100)
Prior HSCT, n(%)	11(58%)	13(57%)
Prior Venetoclax, n(%)	13(68%)	13(57%)

Table 1. Baseline Characteristics

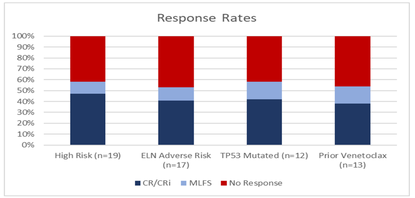


Figure 1. Responses. CR/CRi and MLFS.

Patients	ORR	MRD negativity	1 yr OS	Median OS if HCT (mo)
All (n=23)	65%	75%	48%	24
High-risk (n=19)	**58%**	**75%**	**42%**	**24**
ELN Adverse risk (n=17)	53%	67%	35%	24
TP53 mutated (n=12)	**58%**	**80%**	42%	26
Prior Venetoclax (n=13)	**54%**	**100%**	**46%**	**30**

Table 2. Response and Survival. MRD assessed by MFC.

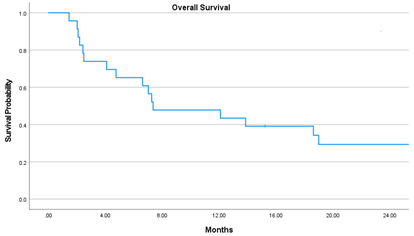


Figure 2. Overall Survival

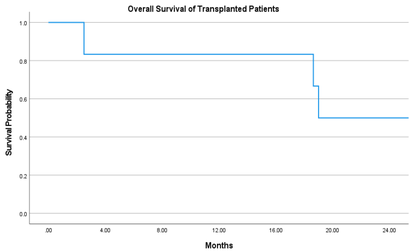


Figure 3. Overall Survival after 1st Allo HCT

CONCLUSIONS

Compared to historically reported outcomes, CLAG-M followed by Lintuzumab-Ac225 yielded higher clinical responses in high-risk populations, including patients previously treated with Venetoclax.

Furthermore, this regimen yields high MRD negative responses and serves as a promising bridge to allogeneic HCT.

Taken together, these results further support late-stage clinical development of Lintuzumab-Ac225 in combination with CLAG-M in the contemporary R/R AML setting.

REFERENCES

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