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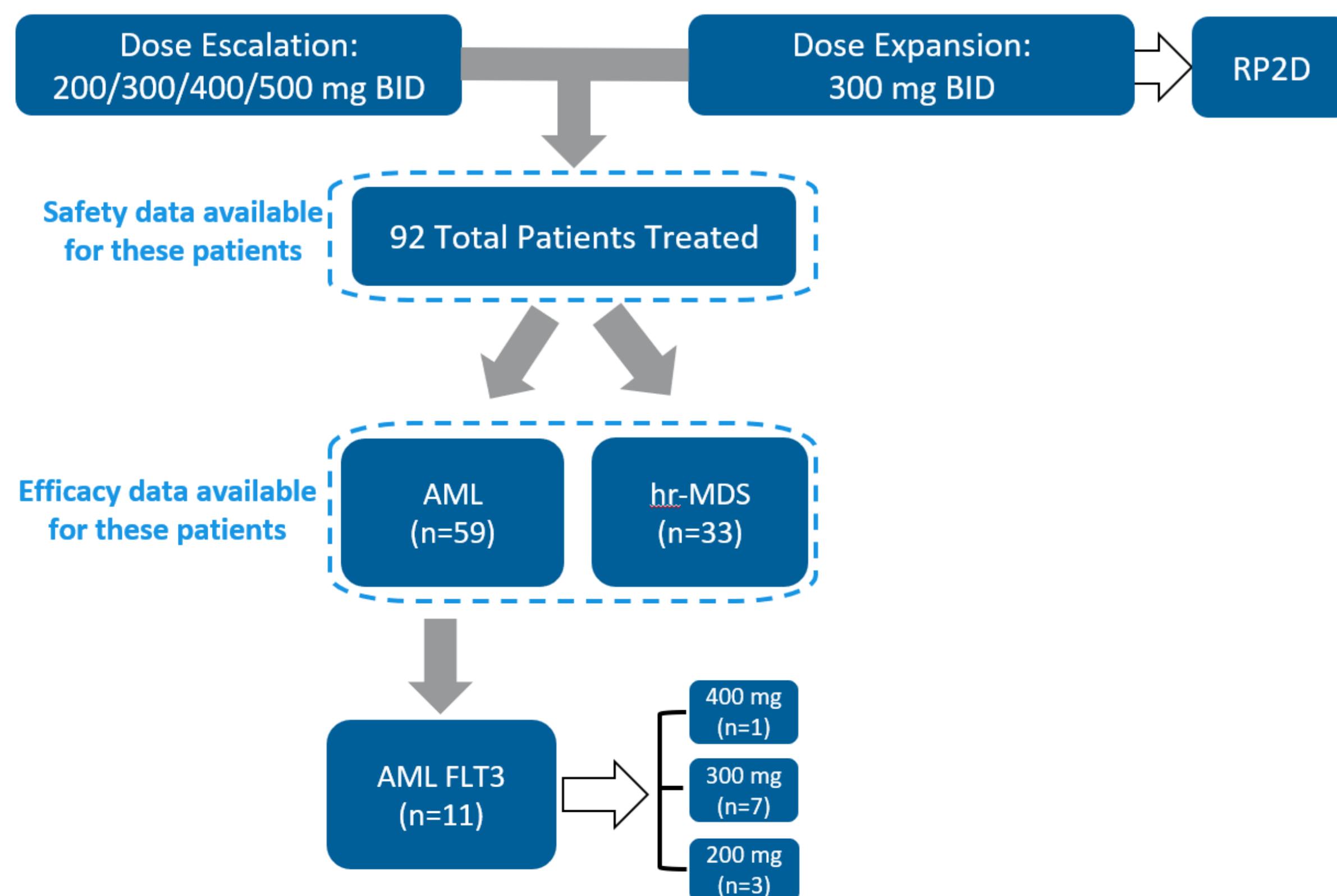
INTRODUCTION

- Acute myeloid leukemia (AML) is a heterogenous disease and exhibits a dynamic mutational landscape as the disease progresses.
- Internal tandem duplication (ITD) of *FLT3* is considered an acquired late-event mutation and is associated with a poor prognosis in AML.
- Emavusertib dual targeting of IRAK4 and *FLT3* (ITD and TKD) confers potential efficacy advantages compared to other IRAK4 and *FLT3* inhibitors.
- IRAK4 is upregulated during anti-*FLT3* or other cytotoxic therapies, which could drive a resistance pathway of early relapse and progression.^{1,2,3}
- As of June 12, 2023, the ongoing TakeAim Leukemia trial (NCT04278768) has 92 patients (11 with *FLT3* mutation) treated with emavusertib monotherapy.

METHOD

- The safety, clinical activity, and potential biomarkers of emavusertib in relapsed/refractory (R/R) AML and higher-risk myelodysplastic syndrome (hr-MDS) are being investigated. The dosing was escalated in 3+3 fashion and followed by dose expansion.
- Here we present preliminary safety and efficacy data in the subset of enrolled AML patients who carried *FLT3* mutation (*FLT3m*) at enrollment and were treated with emavusertib monotherapy.
- Mutational profiles of patients were documented based on local testing results. Bone marrow and peripheral blood of enrolled patients were collected at the baseline and on treatment.
- Mutations were also documented based on patients' molecular pathology reports provided by trial sites.

STUDY POPULATION

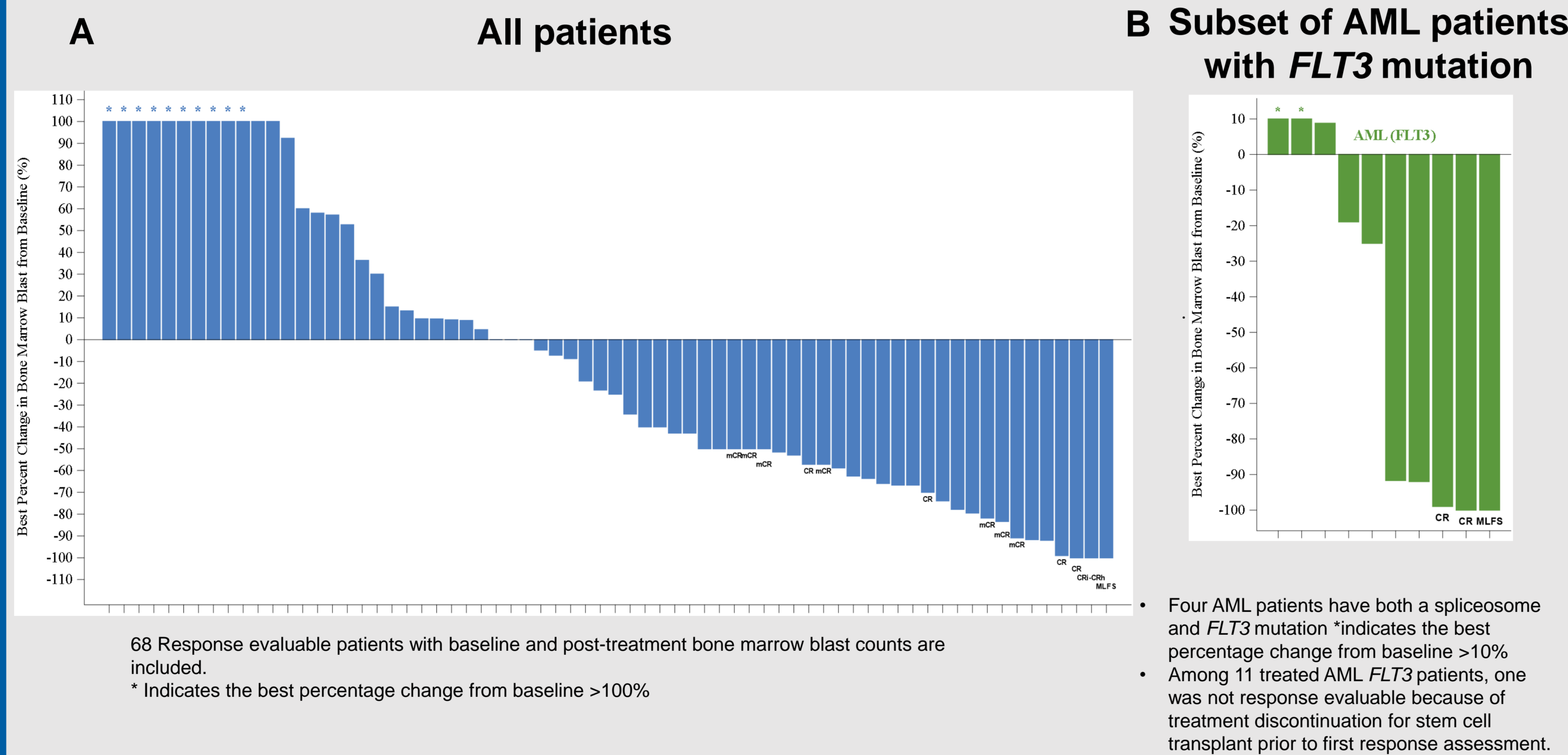


RESULTS

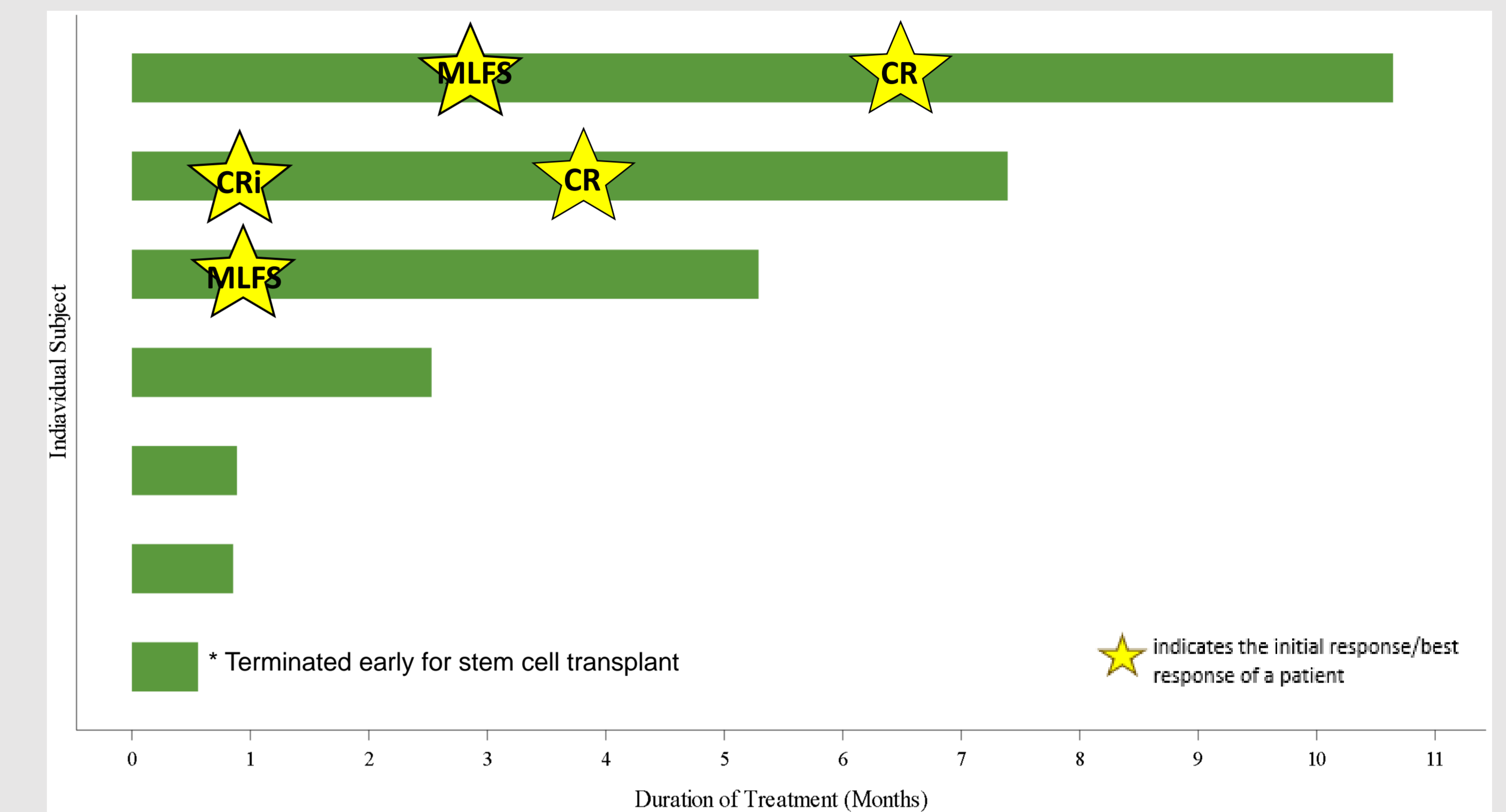
Baseline Characteristics

	All patients (AML and hr-MDS) (n=92)	AML – <i>FLT3</i> (n=11)
Female n (%) : Male n (%)	30 (32.6) : 62 (67.4)	5 (45.5) : 6 (54.5)
Age (yrs): median (range)	74 (32, 88)	78 (61, 87)
Race n (%)	Asian	2 (2.2)
	Black or African American	2 (2.2)
	White	80 (87)
	Others	3 (3.3)
	Not reported	5 (5.4)
Median platelets ($10^3/mm^3$) (range)	25.5 (1, 275)	21 (1, 38)
Median bone marrow blast (%) (range)	33.5 (4, 98) (AML) 10.0 (2, 19) (hr-MDS)	50 (4, 98)
Median lines of prior therapy (range)	2 (1, 7)	2 (1, 6)

Single-agent activity in R/R AML and hr-MDS



Duration of treatment in R/R AML patients with *FLT3* mutations at 300 mg BID



Clinical activity in R/R AML with *FLT3* Mutation at 300mg BID

	# prior therapy	Prev. <i>FLT3</i> i	<i>FLT3</i> mutation	Co-mutations At Baseline	Best response	Best <i>FLT3</i> response
Patient 1	1	N	ITD	SRSF2, DNMT3A	CR	Negative by PCR
Patient 2	1	N	ITD	BCOR, U2AF1, WT1 (These mutations disappeared under Tx)	CR	Negative by PCR
Patient 3	2	Y	ITD	None Reported	MLFS	Positive by PCR
Patient 4	4	Y	TKD	NRAS, PTPN11, RAD21, RUNX1, SF3B1, TET2, GATA2, STAT3	SD	N/A
Patient 5	4	N	ITD	BCOR, ETV6, KRAS, NRAS, RUNX1, U2AF1	PD	N/A
Patient 6	3	Y	ITD	NPM1, TET2 x 2	SD	N/A
Patient 7	4	Y	ITD	DNMT3A, KRAS, NRAS, SBDS	NE	N/A

CONCLUSIONS

- Emavusertib has an acceptable and manageable safety profile in R/R AML and hr-MDS patients.
- No dose-limiting myelosuppression was reported.
- Changes in mutational profiles are suggestive of disease-modifying activity of emavusertib.
- Emavusertib has demonstrated strong anti-cancer activity in patients with *FLT3m*, including patients who have progressed on a prior *FLT3* inhibitor.
- Enrollment in this trial is continuing at the RP2D dose of 300 mg BID (phase 2 expansion cohort) in patients with ≤ 2 prior therapies.

REFERENCES

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CONTACT INFORMATION

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

Grade 3+ Treatment-Related Adverse Event reported in > 1 patients	200 mg BID (N = 24)	300 mg BID (N = 50)	400 mg BID (N = 15)	500 mg BID (N = 3)	Total (N=92)
	n (%)	n (%)	n (%)	n (%)	n (%)
Number of patients having grade 3+ TRAEs	4 (16.7)	14 (28.0)	7 (46.7)	2 (66.7)	27 (29.3)
Platelet count decreased	1 (4.2)	2 (4.0)	2 (13.3)	0	5 (5.4)
Blood creatine phosphokinase increased	0	3 (6.0)	0	0	3 (3.3)
Neutrophil count decreased	0	2 (4.0)	1 (6.7)	0	3 (3.3)
Alanine aminotransferase increased	2 (8.3)	0	0	0	2 (2.2)
Anemia	0	2 (4.0)	0	0	2 (2.2)
Lipase increase	0	2 (4.0)	0	0	2 (2.2)
Neutropenia	0	1 (2.0)	1 (6.7)	0	2 (2.2)
Syncope	0	1 (2.0)	0	1 (33.3)	2 (2.2)

Note: After discussion with regulatory authorities of investigator-reported AEs, objective laboratory criteria for the determination of rhabdomyolysis were adopted from existing approved drug labels (CPK >10 x ULN and SCr ≥ 1.5 x ULN). Previously, reported events of rhabdomyolysis were determined by subjective criteria. Using the objective criteria, rhabdomyolysis was reported in 1/92 patients.