A PHASE I STUDY OF GEMTUZUMAB OZOGAMICIN ADDED TO CYTARABINE, DAUNORUBICIN, AND MIDOSTAURIN INDUCTION IN NEWLY DIAGNOSED FLT3-MUTATED ACUTE MYELOID LEUKEMIA

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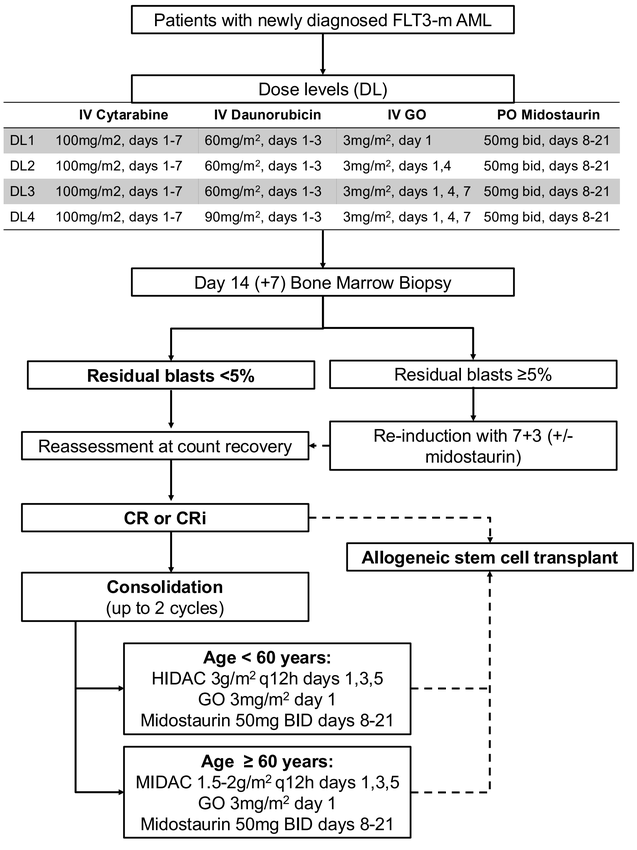
Introduction

- Approximately 30% of patients with acute myeloid leukemia (AML) have FLT3 mutations
- Standard treatment for newly diagnosed FLT3-mutated (FLT3-m) AML in fit patients consists of 7+3+FLT3 inhibitor[1,2]
- FLT3-m AML appears to have a higher CD33 expression
- Gemtuzumab ozogamicin (GO) is an anti-CD33 antibody drug conjugate

Objectives

- **Primary outcome:** determine the maximum tolerated dose (MTD), guided by a Bayesian toxicity probability interval "keyboard" design
- **Secondary outcome:** preliminary efficacy analysis

Methods



Results

Table 1. Baseline Characteristics

	No (%)
Age Group	
Mean (range)	51 (20-73)
Sex	
Male	11 (52.38)
Race	
White	21 (100)
Ethnicity	
Non-Hispanic	21 (100)
ECOG at screening	
0	10 (48)
1	8 (38)
2	3 (14)
FLT3 Status	
FLT3- ITD+	15 (71)
FLT3- TKD+	4 (19)
FLT3- ITD+, FLT3-TKD+	2 (10)
ELN 2022	
Favorable	2 (10)
Intermediate	15 (71)
Adverse	4 (19)

Results (cont'd)

Table 2. DLT summary

DL	Patients, N (%)	DLT, N	Event(s)
1	3 (14%)	0	
2	9 (43%)	2	One patient without count recovery by day 42; another patient with grade 3 bilirubin increase and EF decrease
3	6 (29%)	2	GI toxicity resulting in <50% of midostaurin administration (2 patients)
4	3 (14%)	0	

Most frequent adverse events: diarrhea (76%), nausea (76%)
Most frequent grade 3+ AEs:
- **Hematologic:** WBC decrease (62%), plt count decrease (57%)
- **Non-hematologic**: sepsis (38%), dyspnea (19%)

Count recovery (of the 18 completing induction):
- **Median time to plt recovery:** 26 days (range, 19-54)
- **Median time to ANC recovery:** 27 days (range, 19-68)

Table 3. Treatment best response and transplant utilization

Best response	**N (%)**
CR + CRi	16 (76%)
Stable disease	2 (10%)
No assessment	3 (14%)
Transplant	**N (%)**
Yes	13 (62%)
No	8 (38%)

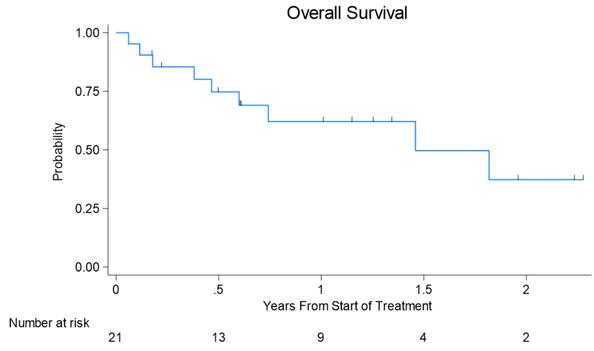


Figure 1. Overall survival

Discussion

- DL2 was identified as the MTD, with two doses of GO (3mg/m² on days 1, 4)
- Prospective study by Röllig et al. also supported the use of two doses of GO[3]
- MIDOTARG clinical trial found higher rates of negative measurable residual disease in NPM1-mutated patients with two doses of GO[4]
- Response rates appear promising in this dose-finding study

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