Gemtuzumab Ozogamicin in Patients with Newly Diagnosed Acute Myeloid Leukemia – Day 1 vs Day 1, 4 and 7 Regimen

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Abstract

Gemtuzumab ozogamicin (GO) is an antibody-drug conjugate comprising the CD33-directed monoclonal antibody covalently linked to N-acetyl gamma calicheamicin.

The mostly commonly utilized regimens include GO at 3 mg/m2 (capped at 4.5 mg) on Day 1, 4 and 7 and Day 1 (with or without cap).

To date, there has been no comparative analyses evaluating differential outcomes and MRD negativity based on dosing regimen.

Hence, we undertook this retrospective analysis to study the differences in responses and outcomes in patients treated with 1-day compared to the 3-day GO regimen.

Materials & Methods

We conducted a retrospective analysis of all patients with newly diagnosed AML that received GO in combination with 7+3 as the upfront treatment between 2017 and 2021 at Moffitt Cancer Center.

The 1-day cohort included patients that received a single dose of GO during induction while the patients that received GO on Day 1, 4 and 7 were included in the 3-day cohort.

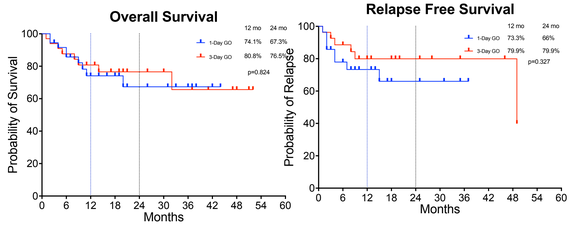
Results

Table 1. Baseline characteristics of patients included in the two cohorts

Variable		All n=72	1 Day GO n=38	GO on D1, 4, 7 n=34	p-value
Age, median (range), years		54 (20-74)	58 (24-74)	52 (20-69)	0.035
Gender					0.479
	Male	36 (50)	17 (44.7)	19 (55.9)	
	Female	36 (50)	21 (55.3)	15 (44.1)	
Race					0.225
	White	60 (83.3)	31 (81.6)	29 (85.3)	
	African American	2 (2.8)	2 (5.3)	0	
	Asian	2 (2.8)	0	2 (5.9)	
	Unknown	8 (11.1)	5 (13.2)	3 (8.8)	
Cytogenetic risk					0.172
	Favorable	26 (36.1)	14 (36.8)	12 (35.3)	
	Intermediate	43 (59.7)	24 (63.2)	19 (55.9)	
	Adverse	3 (4.2)	0	3 (8.8)	
ELN risk					0.101
	Favorable	42 (58.3)	21 (55.3)	21 (61.8)	
	Intermediate	20 (27.8)	14 (36.8)	6 (17.6)	
	Adverse	10 (13.9)	3 (7.9)	7 (20.6)	
ECOG					0.227
	0	27 (37.5)	13 (34.2)	14 (41.2)	
	1	43 (59.7)	25 (65.8)	18 (52.9)	
	2	2 (2.8)	0	2 (5.9)	
Anthracycline					0.030
	Daunorubicin	63 (87.5)	30 (78.9)	33 (97.1)	
	Idarubicin	9 (12.5)	8 (21.1)	1 (2.9)	
Was GO capped?					<0.001
	Yes	56 (77.8)	23 (60.5)	33 (97.1)	
	No	16 (22.2)	16 (39.5)	1 (2.9)	

Table 2. Responses based on GO schedule

Variable		All n=72	1 Day GO n=38	GO on D1, 4, 7 n=34	p-value
ORR (CR + CRi)		56 (77.8)	29 (76.3)	27 (79.4)	0.784
	CR	55 (76.4)	29 (76.3)	26 (76.5)	
	CRi	1 (1.4)	0	1 (2.9)	
Relapse		8 (14.3)	3 (10.3)	5 (14.7)	0.382
AlloSCT in CR1		22 (39.3)	10 (34.5)	12 (35.3)	0.445
Post induction MRD					0.084
	MRD negative	11 (19.6)	3 (10.3)	8 (29.6)	
	MRD positive	22 (39.3)	13 (44.8)	9 (33.3)	
Post consolidation MRD					0.411
	MRD negative	29 (51.8)	15 (51.7)	14 (51.8)	
	MRD positive	6 (10.7)	2 (6.9)	4 (14.8)	
30-day TRM		4 (5.5)	2 (5.3)	2 (5.8)	0.908
60-day TRM		5 (6.9)	3 (7.9)	2 (5.8)	0.737



At a median follow up of 19 months, there was no difference in the 12-month OS (74.1 vs 80.8%; p=0.824) and RFS (73.3 vs 79.9%; p=0.327) between 1-day and 3-day cohorts.

Results

- Median age at diagnosis was 54 years (20-74 years).
- 52.8% patients (n=38) received 1-day and 47.2% (n=34) received 3-day-GO.
- Patients in the 3-day cohort were younger (52 vs 58 years; p=0.035), received daunorubicin (97.1 vs 78.9%; p=0.030), and capped GO (97.1 vs 60.5%; p<0.001).
- The ORR was comparable for both cohorts (76.3 vs 79.4%, p=0.784).
- There was no difference between the two groups in terms of relapse, alloSCT, 30-day or 60-day TRM.
- MRD-negativity rates post-induction trended towards being higher (29.6 vs 10.3%; p=0.084) in the 3-day cohort, however, this difference disappeared post-consolidation (51.8 vs 51.7%; p=0.411).
- More patients in the 3-day cohort received GO in consolidation however this was not significant (60 vs 37.5%; p=0.156). MRD-negativity rates post-consolidation for patients that were MRD-positive post-induction were not different for patients that got GO in consolidation (75 vs 100%; p=0.21).
- OS and RFS (Figure 1).
- There was no difference in OS for patients that were MRD-negative post-induction or post-consolidation and for patients that attained MRD-negativity earlier. However, RFS was higher in patients that were MRD-negative post-consolidation (12-mo RFS 100 vs 80%; p=0.046).

Conclusions

- 3-day-GO led to improved MRD-negativity rates post-induction however this difference disappeared after consolidation.
- MRD-negativity post-consolidation improved RFS irrespective of regimen.
- There was no difference in OS, RFS and other outcomes between the two cohorts and earlier attainment of MRD-negativity did not affect OS. Also, use of GO in consolidation did not affect MRD-negativity post-consolidation.

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