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ORAL ABSTRACTS

613.ACUTE MYELOID LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Feasibility, Safety and Predictors of Outcomes of Patients with Newly Diagnosed Acute Myeloid Leukemia Discharged "Early" after Intensive Induction Therapy

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Background: Patients (pts) treated with intensive induction therapy for newly diagnosed acute myeloid leukemia (AML) traditionally remain admitted until an absolute neutrophil count (ANC) >0.5 x 10^3/L. Although a small number of centers reported on pt discharge with ANC <0.5 x 10^3/L via an "early" discharge (DC) program (EDP) post-intensive induction, little is known about the safety and outcomes among this group of pts, including the rates and predictors of post-DC complications (e.g., febrile neutropenia (FN), microbiologically proven infection) and both early- and long-term outcomes. We sought to describe our experience with an EDP and identify predictors of differential outcomes.

Methods: We conducted a single-center, retrospective study of pts with newly-diagnosed AML admitted to Yale Cancer Center (YCC) for intensive induction during December 2014-January 2023. Re-induced patients were excluded. Patients were eligible for the EDP if they: 1) were afebrile x 7 days, 2) required no parenteral therapies, 3) required transfusion support less than daily, 4), lived within 60 minutes of YCC with "average" traffic, and 5) had a dedicated care giver available 24 hours per day with reliable transportation to/from clinic. Chi-square and Wilcoxon rank-sum tests were applied to categorical and continuous variables, respectively. Overall survival (OS) was estimated using the Kaplan-Meier method and was compared using log-rank test. Statistical significance was determined by p-value <0.05.

Results: A total of 188 pts were evaluated. Amongst this population, 99 (52.7%) pts were DC under the EDP, while 89 (47.3%) were not. To remove confounding from peri-DC ANC kinetics, we focused on pts DC with an ANC <0.1 x 10^3/L (n=53, "EDP pts") and compared them with non-EDP pts (DC ANC >0.5 x 10^3/L). There were no significant differences in age, sex, ECOG performance status (PS), baseline LVEF on echocardiography or other comorbidities. With regards to disease-specific factors, there was no difference in pre-induction blood counts (e.g., WBC 7.2 vs. 8.1, p=0.610), serum creatinine, uric acid, lactate dehydrogenase, AML subtype, or disease biology e.g., karyotypic or molecular features (Table 1).

Pts received 7+3 without (47%) or with (27%) other therapy, while 22% received liposomal daunorubicin/cytarabine. There were no differences in the rates of regimens used between EDP and non-EDP pts. The incidence of induction-related complications like FN (81.1% vs 89.9%, p=0.220), DIC, TLS, and bleeding were similar between groups, although there was a trend toward more documented infection among non-EDP pts (48.3% vs 30.2%, p=0.052). Findings on the D14 marrow (performed in 79% of pts) were similar between groups (chemoablation, p=0.131; D14 blast %, p=0.546).

Median days admitted from induction to DC was nearly a week less for EDP pts (22 [interquartile range (IQR): 19-29] vs 28 days [IQR: 25-32], p<0.0001). Amongst EDP patients, 12 (22.6%) were re-admitted, 10 (83%) due to FN with 4 of these pts having an infectious source identified. The median duration of re-admission was 6.5 days (IQR: 4.5-13). When considering re-admissions prior to ANC/count recovery or initiation of consolidation, EDP pts still had lower time spent in hospital prior to eventual count recovery (24 vs 28, p<0.0001).

ANC at DC did not predict OS amongst the larger cohort (n=188, p=0.949), but was associated with re-admission amongst pts DC with ANC <0.5 in univariate analysis (p=0.02). Time to DC and ANC at DC were strongly associated amongst the larger cohort (n=188, p=0.01 from linear regression) and pts DC with ANC <0.5 (p<0.00001 from linear regression)(Figure 1).

Although non-EDP pts had a shorter time to first response (33 vs 36 days, p=0.020), there were no differences in rates of CR/CRi/CRh (73.0% vs 60.4%, p=0.167) when compared with EDP pts. Similarly, there were no differences in early (60- and 90-day) mortality, or median OS between EDP and non-EDP pts (32.3 vs 26.4 months, p=0.695)(Table and Figure 1).
Conclusions: Our study shows that pts treated intensively for newly-diagnosed AML and meeting several criteria can be safely DC prior to count recovery without detriment to early mortality or OS. EDP pts spent up to a week more out of hospital when compared with non-EDP counterparts. Healthcare utilization, cost effectiveness and patient satisfaction evaluations of the EDP are underway.

Disclosures Podoltsev: *Cogent Biosciences:* Other: IDMC Member; *AI Therapeutics; Arog Pharmaceuticals; Astellas Pharma, Inc.; Astex Pharmaceuticals; Boehringer Ingelheim Pharmaceuticals, Inc.; Celgene Corporation; CTI BioPharma Corp.; Daiichi Sankyo, Inc.; Genentech, Inc.; Jazz Pharmaceuticals, Inc.; Kartos Therapeuti:* Research Funding; *AbbVie Inc.; Blueprint Medicines (former); Constellation Pharmaceuticals (former); CTI BioPharma Corp. (former); Incyte Corporation (former); Novartis (former); PharmaEssentia (former):* Consultancy. **Zeidan:** *Schrödinger:* Consultancy, Honoraria; *Syndax:* Consultancy, Honoraria; *Genentech:* Consultancy, Honoraria; *Astellas:* Consultancy, Honoraria; *Gilead:* Consultancy, Honoraria; *ALX Oncology:* Consultancy, Honoraria; *Lox Oncology:* Consultancy, Honoraria; *Regeneron:* Consultancy, Honoraria; *AbbVie:* Consultancy, Honoraria; *Novartis:* Consultancy, Honoraria; *BeyondSpring:* Consultancy, Honoraria; *Agios:* Consultancy, Honoraria; *Jazz:* Consultancy, Honoraria; *Notable:* Consultancy, Honoraria; *Orum:* Consultancy, Honoraria; *Kura:* Consultancy, Honoraria; *Chiesi:* Consultancy, Honoraria; *Seattle Genetics:* Consultancy, Honoraria; *Takeda:* Consultancy, Honoraria; *Epizyme:* Consultancy, Honoraria; *Syros:* Consultancy, Honoraria; *Shattuck Labs:* Research Funding; *Otsuka:* Consultancy, Honoraria; *Daiichi Sankyo:* Consultancy, Honoraria; *Boehringer-Ingelheim:* Consultancy, Honoraria; *Servier:* Consultancy, Honoraria; *BioCryst:* Consultancy, Honoraria; *Zentalis:* Consultancy, Honoraria; *Geron:* Consultancy, Honoraria; *Ionis:* Consultancy, Honoraria; *Taiho:* Consultancy, Honoraria; *Tyme:* Consultancy, Honoraria; *Foran:* Consultancy, Research Funding; *Mendus:* Consultancy, Honoraria; *Amgen:* Consultancy, Honoraria; *Astex:* Research Funding; *Celgene/BMS:* Consultancy, Honoraria; *Incyte:* Consultancy, Honoraria; *Pfizer:* Consultancy, Honoraria; *Janssen:* Consultancy, Honoraria. **Shallis:** *Bristol Myers Squibb:* Consultancy; *Curio Science:* Consultancy; *Servier:* Consultancy; *Rigel:* Consultancy; *Gilead Sciences:* Consultancy.

Table 1. Baseline characteristics and outcomes for patients with ANC at discharge ≤ 0.1 versus ≥ 0.5

	ANC at discharge ≤ 0.1 (n=53)	ANC at discharge ≥ 0.5 (n=89)	p-value
Age at diagnosis, median (IQR)	58 (44 - 65)	61 (48 - 68)	0.176 †
Sex, n (%)			0.383 ‡
Female	25 (47.2%)	34 (38.2%)	
Male	28 (52.8%)	55 (61.8%)	
Race / Ethnicity, n (%)			0.610 ‡
White	43 (81.1%)	67 (75.3%)	
African American	4 (7.5%)	8 (9.0%)	
Hispanic	5 (9.4%)	8 (9.0%)	
Other	1 (1.9%)	6 (6.7%)	
ECOG PS, n (%)			0.844 ‡
0	33 (62.3%)	50 (56.2%)	
1	17 (32.1%)	31 (34.8%)	
2	2 (3.8%)	6 (6.7%)	
3	1 (1.9%)	2 (2.2%)	
Baseline ECHO, mean (SD)	0.621 (0.042)	0.629 (0.060)	0.439 †
AML type, n (%)			
De novo	35 / 53 (66.0%)	64 / 89 (71.9%)	0.584 ‡
Secondary	12 / 53 (22.6%)	20 / 89 (22.5%)	1.000 ‡
Therapy-related	6 / 53 (11.3%)	6 / 89 (6.7%)	0.524 ‡
Karyotype, n (%)			
Normal	21 / 53 (39.6%)	40 / 89 (44.9%)	0.657 ‡
Complex	7 / 53 (13.2%)	13 / 89 (14.6%)	1.000 ‡
CBF	6 / 53 (11.3%)	7 / 89 (7.9%)	0.697 ‡
ASXL1, n (%)	4 / 53 (8.4%)	8 / 83 (9.6%)	0.913 ‡
RUNX1, n (%)	3 / 53 (5.7%)	11 / 83 (13.3%)	0.258 ‡
NPM1, n (%)	12 / 53 (29.9%)	23 / 84 (27.4%)	0.676 ‡
TET2, n (%)	4 / 53 (7.5%)	14 / 83 (16.9%)	0.192 ‡
CEBPA, n (%)			
1xMut	0 / 53 (0.0%)	1 / 83 (1.2%)	1.000 ‡
2xMut	3 / 53 (5.7%)	4 / 83 (4.8%)	1.000 ‡
FLT3, n (%)			
ITD	13 / 53 (24.5%)	21 / 84 (25.0%)	1.000 ‡
TKD	2 / 53 (3.8%)	10 / 84 (11.9%)	0.184 ‡
IDH, n (%)			
IDH1	1 / 53 (1.9%)	7 / 83 (8.4%)	0.227 ‡
IDH2	6 / 53 (11.3%)	15 / 83 (18.1%)	0.413 ‡
DNMT3A, n (%)	9 / 53 (18.9%)	14 / 83 (16.9%)	1.000 ‡
PTPN11, n (%)	4 / 53 (7.5%)	1 / 83 (1.2%)	0.147 ‡
RAS, n (%)			
NRAS	11 / 53 (20.8%)	15 / 83 (18.1%)	0.869 ‡
KRAS	5 / 53 (9.4%)	4 / 83 (4.8%)	0.483 ‡
Splicing mut, n (%)			
SRSF2	5 / 53 (9.4%)	12 / 83 (14.5%)	0.550 ‡
SF3B1	3 / 53 (5.7%)	8 / 83 (9.6%)	0.612 ‡
U2AF1	5 / 53 (9.4%)	7 / 83 (8.4%)	1.000 ‡
TP53, n (%)	6 / 53 (11.3%)	8 / 83 (9.6%)	0.980 ‡
Induction regimen, n (%)			0.146 †
Vyxeos	14 (26.4%)	17 (19.1%)	
7+3	19 (35.8%)	48 (53.9%)	
7+3+FLT3i	13 (24.5%)	13 (14.6%)	
7+3+GO	6 (11.3%)	6 (6.7%)	
Other	1 (1.9%)	5 (5.6%)	
Baseline Lab Data			
Cr at D1, median (IQR)	0.85 (0.68 - 0.98)	0.83 (0.67 - 1.00)	0.965 †
Uric acid at D1, median (IQR)	3.7 (2.8 - 5.2)	4.2 (2.8 - 5.2)	0.918 †
LDH at D1, median (IQR)	358 (257.5 - 850.5)	360.5 (235.8 - 762.3)	0.895 †
WBC at D1, median (IQR)	7.2 (2.1 - 25.5)	8.1 (2.7 - 30.7)	0.610 †
Hgb at D1, median (IQR)	7.9 (6.9 - 8.9)	7.9 (7.3 - 9.2)	0.398 †
PLT at D1, median (IQR)	46.0 (27.0 - 85.0)	60.0 (32.0 - 97.0)	0.189 †
Induction complications			
Febrile neutropenia	43 (81.1%)	80 (89.9%)	0.220 ‡
Documented infection	16 (30.2%)	43 (48.3%)	0.052 ‡
DIC	3 (5.7%)	5 (5.6%)	1.000 ‡
Bleeding	8 (15.1%)	25 (28.1%)	0.117 ‡
Tumor lysis syndrome	2 (3.8%)	11 (12.4%)	0.157 ‡
Day 14 marrow evaluation			
If D14 marrow evaluation performed			
Chemoablated	31 / 42 (73.8%)	52 / 70 (74.3%)	0.131
Residual disease	10	17	
Inconclusive	1	1	
D14BM blast %, median (IQR)	2.5 (2.0 - 5.0)	2.5 (2.0 - 10.0)	0.546 †
Time to first response, days (IQR)	36 (31 - 42)	33 (28 - 38)	**0.020** †
First response			0.072 ‡
CR	28 (52.8%)	63 (70.8%)	
CRi	3 (5.7%)	2 (2.2%)	
CRh	1 (1.9%)	0 (0.0%)	
MLFS	8 (15.1%)	4 (4.5%)	
PR	1 (1.9%)	4 (4.5%)	
Stable	12 (22.6%)	14 (15.7%)	
Progressive	0 (0.0%)	2 (2.2%)	
Clinical outcomes			
Days admitted pre-discharge, median (IQR)	22 (19 - 29)	28 (25 - 32)	**< 0.0001** †
Days admitted pre-recovery, median (IQR)	24 (20 - 30)	28 (25 - 32)	**< 0.0001** †
Early mortality			
≤ 60 days from induction	0 (0%)	2 (2.2%)	0.717 ‡
≤ 90 days from induction	1 (1.9%)	3 (3.4%)	1.000 ‡
Median OS with 95% CI, having accounted for censoring	32.3 months (12.1 - Q3 n/a)	26.4 months (17.4 - 73.9)	0.695 *

† Wilcoxon rank sum test for each continuous variable
‡ Chi-square test for each contingency table
* Log-rank test of survival curves between groups

Figure 1. Overall survival by discharge ANC ≥500 vs ≤100 x 10^3/L

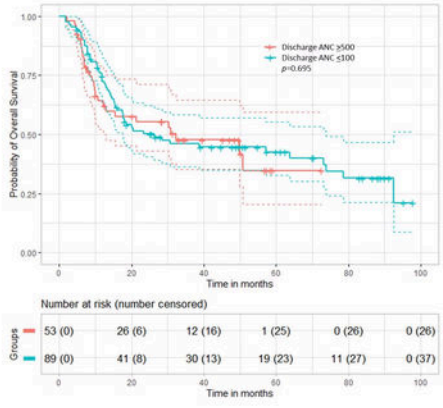

Figure 1

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