ELSEVIER

Blood 142 (2023) 2442–2444

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

906.OUTCOMES RESEARCH-MYELOID MALIGNANCIES

Real-World Outcomes with Intensive Chemotherapy in Acute Myeloid Leukemia Patients Deemed "Unfit" for Remission Induction By Landmark Trials' Criteria

Thomas Eipe, PharmD[1], Hasmukh Jain, MDDM[2], Manju Sengar, MD DM[3], Bhausaheb Bagal, MD DM[2], Lingaraj Nayak, MBBS, MD DM[4], Alok Shetty, MD DM[2]

[1]Department of Clinical Pharmacology, Tata Memorial Centre, Mumbai, India
[2]Department of Medical Oncology, Tata Memorial Centre, Mumbai, India
[3]Department of Medical Oncology, Tata Memorial Centre, Homi Bhabha National Institute, Mumbai, India
[4]Department of Medical Oncology, Tata Memorial Centre, MUMBAI, India

Background:
Induction mortality rates in acute myeloid leukemia (AML) ranges from 7.1% to 40% across Indian tertiary care centers (Kayal S, ASH 2022) exceeding those in the western countries, possibly due to treatment delay, multidrug resistant infections, and inadequate social support. Furthermore, patients seen in our clinics are not representative of those in landmark clinical trials, as a majority of them would be considered unfit for intensive induction based on the trial criteria. Consequently, these patients are left with treatment options, such as less intensive hypomethylating agents, BCL2 inhibitors, and newer targeted therapies. However, these drugs often remain unfeasible due to high out-of-pocket costs and regulatory approval delays, so a majority of patients receive intensive induction with antibiotics. In this retrospective study, we evaluate the effectiveness and toxicities associated with the utilization of such a strategy in the Indian context.

Method:
This retrospective study was conducted at a single tertiary care cancer center in India. It included patients aged ≥15 years, with acute myeloid leukemia, who received intensive induction chemotherapy as decided by the multidisciplinary joint clinic between January 01, 2017, and December 31, 2019. Patient data were extracted from the Indian acute leukemia research database [INwARD], which is a prospective registry of multiple centers, maintained and audited by the Clinical Data Management Center [CDMC], Vellore for the Hematology cancer consortium and is compliant with ICH-GCP regulations. Ethical approval was obtained from the institutional ethics committee, and the study was registered in the Clinical Trial Registry - India (CTRI/2020/02/023455). Patients were categorized based on the established criteria for "unfit for intensive chemotherapy" derived from landmark trials (VIALE-A, NCT02203773, VIALE-C), and subsequent analyses were performed. Outcomes assessed included 30-day induction mortality, documented infection at diagnosis (defined as fever with radiological, microbiological, or clinical focus of infection) and fungal infections according to EORTC and MSG classifications. Post-induction bone marrow response was defined as complete response/complete response with incomplete marrow recovery (CR/CRi) with ≤5% BM blasts, platelet count $<100 \times 10^9$/L, and absolute neutrophil count $<1.0 \times 10^9$/L. Kaplan-Meier analyses were conducted to assess event-free survival and overall survival.

Results:
Among 1326 eligible patients, 385 received intensive chemotherapy during the study period (49 received less intensive therapy, 442 referred outside, 210 on palliative care, 212 lost to follow up and 28 died). Demographic and baseline characteristics are detailed in Table 1. Cytarabine and daunorubicin (98.9%) were the most common first-line treatments. Of the 385 patients receiving intensive chemotherapy, 188 were categorized as unfit according to the study criteria (Refer Table 1). The unfit cohort exhibited higher 30-day induction mortality compared to the fit cohort (20.5% vs. 6%, P<0.0001) with a trend for higher incidence of proven and probable fungal infections (18.4% vs. 11.2%, P=0.054). Complete remission rates (CR+CRi) were lower in the unfit cohort (52.4% vs. 68%, P<0.001), while no difference in documented bloodstream infections was observed (P=0.754). Univariate analysis revealed that induction mortality was most influenced by age>50 (P=0.019), ECOG ≥2 (P=0.002) and infection at diagnosis (P<0.0001). However, upon conducting multivariate analyses, infection at diagnosis emerged as the strongest predictor of induction mortality (OR:2.91, 95%CI, 1.51 to 5.59, P=0.001). The median follow up was 15.7 months (range, 0.2-73.8). The 2-year estimated event-free survival (EFS) and overall survival (OS) of the entire cohort was 42.9% and

69.2% respectively. For the unfit and fit cohort, the 2-year EFS was 42.2% vs 43.9% (P=0.065), and the 2-year OS was 62.5% vs 75.1% (P=0.001) respectively.

Conclusion:

Unfit patients who received intensive chemotherapy had higher induction mortality and lower overall survival. Furthermore, it underscores the importance of improving accessibility to novel therapies, to provide a safe and viable alternative for nearly half of our AML patient population.

Disclosures Jain: *ImmunoACT:* Research Funding; *Zydus Pharmaceuticals:* Research Funding; *Intas Pharmaceuticals:* Research Funding.

Table 1: Baseline characteristics of all patients treated with intensive chemotherapy

Characteristic, n (%)	Unfit cohort (N=188)	Fit cohort (N=197)	Overall cohort (N=385)
Age at diagnosis, Median (min-max)	32.5 (15-60)	33 (15-61)	33 (15-61)
Age, years; n (%)			
<30	85 (45.2)	85 (43.1)	170 (44.2)
30-50	78 (41.5)	93 (47.2)	171 (44.4)
>50ǂ	25 (13.3)	19 (9.6)	44 (11.4)
Sex, n (%)			
Female	74 (39.4)	84 (42.6)	158 (41)
Male	114 (60.6)	113 (57.4)	227 (59)
ECOG performance-status score, n (%)			
0-1	84 (44.7)	188 (95.4)	272 (70.6)
2-4†	101 (53.7)	-	101 (26.2)
Unknown	3 (1.6)	9 (4.6)	12 (3.1)
TLC at diagnosis, n (%)			
<100,000 cells/mm^3	158 (84)	173 (87.8)	331 (86)
>100,000 cells/mm^3	30 (16)	24 (12.2)	54 (14)
Albumin at diagnosis, median	3.83	4.1	4.0
ELN risk group, n (%)			
Favorable risk	82 (43.6)	83 (42.1)	165 (42.9)
Intermediate risk	64 (34)	72 (36.5)	136 (35.3)
Poor risk	16 (8.5)	13 (6.6)	29 (7.5)
Unknown	26 (13.8)	29 (14.7)	55 (14.3)
Comorbidities, n (%)			
None	159 (84.6)	162 (82.2)	321 (83.4)
At least one	29 (15.4)	35 (17.8)	64 (16.6)
Ejection fraction, n (%)			
≤50%†	5 (2.7)	-	5 (1.3)
>50%	172 (91.5)	191 (97)	363 (94.3)
Unknown	11 (5.9)	6 (3)	17 (4.4)
Creatinine clearance ≤45 ml/min, n (%)±	8 (4.3)	-	8 (2.1)
Total bilirubin > 1.5 x ULN, n (%)±	21 (11.2)	-	21 (5.4)
Infection at diagnosis, n (%)±	131 (69.7)	-	131 (34.0)
Mortality, n (%)			
Alive	127 (67.6)	158 (80.2)	285 (74)
Dead	61 (32.4)	39 (19.8)	100 (26)

Criteria to be 'unfit' for intensive chemotherapy is defined as age≥75 yearsǂ (0 patients) or <75 years with any of the specified criteria†

Figure 1: Kaplan-Meier curves for Overall survival (OS) between the 2 cohorts

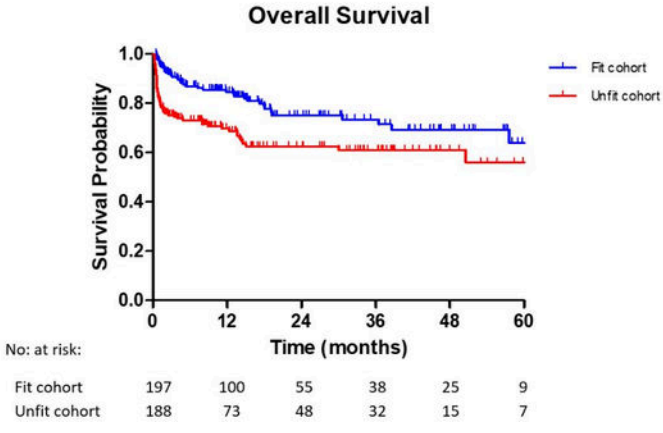

Figure 1

https://doi.org/10.1182/blood-2023-188787