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Blood 142 (2023) 5180–5182

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

906.OUTCOMES RESEARCH-MYELOID MALIGNANCIES

Treatment Challenges in Acute Myeloid Leukemia in Lower-Middle-Income Countries: Navigating Intensity, Affordability, and Infections

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Introduction:
Acute Myeloid Leukemia (AML) is a highly aggressive and genetically heterogeneous hematologic malignancy with a potentially fatal outcome if left untreated. The standard treatment, the 7+3 regimen, involving intensive chemotherapy, has been the cornerstone of therapy for decades. However, this approach poses challenges, especially for older patients and those with comorbidities. In lower-middle-income countries like India, managing AML becomes even more complex due to delayed diagnosis, increased infections, financial constraints and limited access to newer targeted therapies.
Methods:
This retrospective study aimed to investigate treatment scenarios and outcomes for two induction regimens, the standard 7+3 and Azacitidine+Venetoclax (Aza+ven), in newly diagnosed AML patients in a lower-middle-income setting from January 2018 to May 2023, conducted after institute ethical clearance. Included were treatment-naïve AML patients aged 14 years and above undergoing induction treatment with either regimen. Exclusion criteria comprised Acute promyelocytic leukemia, relapsed/refractory cases, prior chemotherapy, and incomplete records. Baseline data, ELN prognostic scores, and treatment responses were recorded. Morphological remission and multiparametric flowcytometry based measurable residual disease (MRD) were assessed after one induction. Cytarabine 100mg/m2 I.V. continuous infusion x 7 days; Daunorubicin 60mg/m2 I.V. x 3 days; Azacitidine 75 mg/m2 I.V. x 7 days; Venetoclax 100mg x 14-28 days. Both groups received posaconazole antifungal prophylaxis. Complications were graded according to CTCAE Version 5. The data were analyzed using SPSS Statistics 20. Continuous variables presented as mean ± SD, categorical variables as frequency (%). Normality was checked with the Kolmogorov-Smirnov test, using T-tests for continuous variables and chi-square for categorical variables. Kaplan-Meier for survival. Cox PH regression for prognostic factors ($p < 0.05$, two-tailed).
Results:
A total of 422 new patients were diagnosed with AML; 212 (50.2%) patients opted for treatment, and 210 (49.8%) patients opted out. The most common reason was economic constraint (39%), followed by distance to the treatment centre (19%). Out of 212, only 138 (32.7%) received either of the induction regimens; still, 13 (9.3%) of patients were not included for analysis in accordance with the exclusion criteria. The study included 99 AML patients, with 71 on 7+3 and 28 on Aza+ven. Both groups were comparable in gender distribution, AML type, ELN prognostic risk, molecular mutations, and extramedullary disease.

However, the Aza+ven group had significantly older patients (56.6 years vs. 41.8 years in 7+3, p <0.001) and exhibited more baseline infections (2.8% vs. 60%, p = 0.001), and poorer ECOG performance scores (p = 0.001). Despite these differences, the Aza+ven group had reduced complications like febrile neutropenia (53.6% vs. 93%, p<0.001), bacterial sepsis (14.3% vs. 39.4%, p = 0.012), gastric intolerance grade 2 and above (7% vs. 46.5%, p<0.001), decreased transfusion requirements(p<0.001), and a comparable complete remission rate of 63.7% in Aza+ven vs. 64.8% in 7+3 (p = 0.96), Patients achieving remission (CR) regardless of regimen used led to overall survival benefits (43 ± 4.5 months vs. 25 ± 4.3 months in patients not achieving remission, p=0.012) shown in figure 1, similarly stem cell transplantation had survival benefit over other consolidation chemotherapies (47 ± 5.9 months vs. 30 ± 3.9 months, p=0.009), The average unaided treatment cost per cycle of Aza+ven was 7352 ± 4530 USD vs. 9237 ± 5939 USD, p= 0.229. Table 1 enlist the baseline characteristics and outcomes summary between the two groups.

Conclusion:

This study highlights treatment challenges in AML management in lower-middle-income countries, with a significant number of patients unable to access timely care at the diagnosis center. The Aza+ven regimen showed promise, offering benefits over the standard 7+3, especially for unfit and older patients. Addressing barriers to treatment accessibility and affordability is vital to improve AML outcomes in resource-limited regions. Further research, including larger prospective studies, is needed to validate the Aza+ven regimen's efficacy and long-term outcomes in this context, offering hope for a better outlook for AML patients facing this aggressive malignancy.

Disclosures No relevant conflicts of interest to declare.

Table 1: Baseline characteristics and outcomes of newly diagnosed AML patients treated with 7+3 and Azacitidine venetoclax regimens.			
Parameters	7+3 n (%)	Aza+ven n (%)	p Value
Total case received induction therapy	71 (100%)	28 (100%)	
Male Female	36 (50.7%) 35 (49.3%)	18 (64.3%) 10 (35.7%)	0.22
Age in years-Mean Standard deviation, Range	41.86 13.23, 14-65	56.68 12.33, 16-69	**<0.001**
ECOG Score:0-1 2-4	67 (94.4%) 4 (5.6%)	13 (46.4%) 15 (53.6%)	**0.001**
ELN Risk-Favorable Intermediate Adverse Can not categorize	15 (21.1%) 24 (33.8%) 11 (15.5%) 21 (26.9%)	4 (14.3%) 12 (42.9%) 9 (32.1%) 3 (10%)	0.08
AML with recurrent genetic mutation AML NOS Secondary/MDS related Therapy related	18 (25.4%) 49 (69%) 2 (2.8%) 2 (2.8%)	7 (25%) 16 (57.1%) 4 (14.3%) 1 (3.6%)	0.185
Baseline infection	2 (2.8%)	17 (60.7%)	**0.001**
FLT3-ITD	16 (30.1%)	6 (24%)	0.42
Febrile neutropenia	66 (93%)	15 (53.6%)	**<0.001**
GI Intolerance	33 (46.5%)	2 (7.1%)	**<0.001**
ICU admission	23 (33%)	2 (7.1%)	**0.005**
Transfusion requirements Packed RBCs- Mean, (range) Single donor platelets- Mean, (range)	 6 (0-17) 6 (1-24)	 3.5 (0-12) 3 (0-10)	 **<0.001** **<0.001**
Patients required Granulocyte	24 (35.8%)	0	**<0.001**
Invasive fungal infection-Probable -Proven	9 2	0 0	0.07
Bacterial culture positive sepsis	28 (39.4%)	4 (14.3)	**0.012**
Remission (CR1+CRh)	46 (64.8%)	18 (63.7%)	0.96
MRD negative	22 (38.6%)	9 (36%)	0.82
Transplant	24 (33.8%)	5 (17.9)	0.116
Relapse	36 (50.7%)	9 (32.1%)	**0.05**
Median OS (Months) ± SD	30 ± 5.2	16 ± 3.44	0.448
Average cost per cycle ± SD USD (1USD=81.9 INR)	9237 ± 5939	7352 ± 4530	0.229

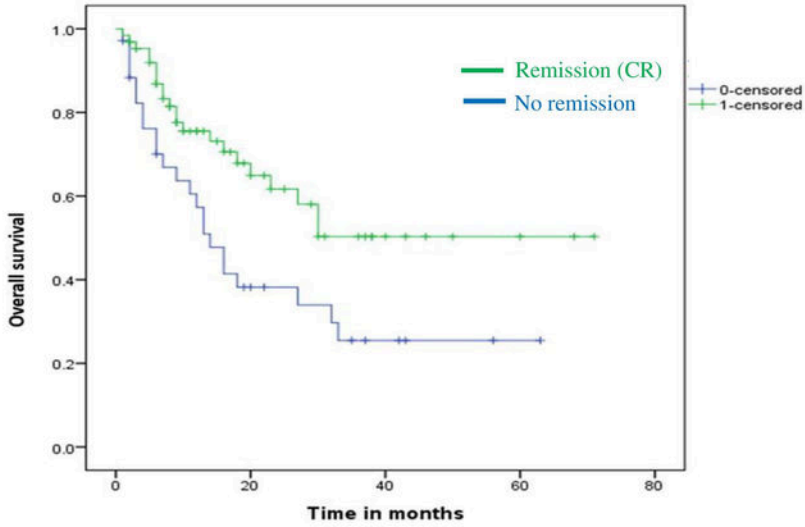

Figure1: Kaplan-Meier curve shows Patients achieved remission (CR) experienced improvement in overall survival, median OS 43 ± 4.5 vs. 25 ± 4.3 months for those who did not achieve remission (p= 0.012), both treatment regimens had similar remission rates.

Figure 1

https://doi.org/10.1182/blood-2023-186818