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Comparison of regimens targeting complete remission in the first-line treatment of acute myeloid leukemia patients

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Abstract. – OBJECTIVE: Standard treatment for adults with acute myeloid leukemia (AML) involves anthracycline and cytarabine, while alternative regimens are necessary for elderly and frail patients. This study aims to compare the effectiveness and safety of various induction regimens in AML patients.

PATIENTS AND METHODS: The retrospective study included 130 adult AML patients treated at a tertiary care center from January 2014 to December 2022. Patients received one of the following induction regimens: anthracycline and cytarabine (n = 82), azacitidine and venetoclax (n = 11), etoposide and cytarabine (n = 22), or reduced-dose anthracycline and cytarabine (n = 15). Data on demographics, clinical characteristics, treatment-related toxicities, and infectious complications were collected. Outcomes included overall survival and remission rates.

RESULTS: The anthracycline and cytarabine regimen demonstrated the highest overall survival rate, although remission rates did not significantly differ among the treatment groups. Patients receiving azacitidine and venetoclax experienced a significantly longer duration of neutropenia. The use of antiviral prophylaxis increased over the study period, reflecting improved management strategies. Infection remained the leading cause of mortality.

CONCLUSIONS: Effective management of prolonged neutropenia and infections is crucial for improving patient outcomes. Future research should focus on optimizing prophylactic and infection treatment strategies to further enhance survival in AML.

Key Words:
AML, Induction, Complete remission.

Introduction

The standard therapeutic approach for patients with acute myeloid leukemia (AML) encompasses post-induction consolidation therapy. The induction phase involves the administration of high doses of an anthracycline, such as daunorubicin, in conjunction with cytarabine, a nucleoside analog, aimed at substantially reducing the myeloblast population. Upon achieving remission, treatment transitions to the consolidation phase, typically comprising a multi-day course of cytarabine, and may also include hematopoietic stem cell transplantation (HSCT)[1]. Although the precise mechanisms underlying the cytotoxic effects of cytarabine and anthracycline are not fully elucidated, these agents are postulated to induce DNA damage, resulting in mitochondrial dysfunction and apoptosis[2]. Despite the efficacy of induction and consolidation regimens in AML treatment, these protocols are associated with significant morbidity and mortality, rendering them inappropriate for many elderly patients, particularly those with comorbid conditions, unfavorable genotypes, or treatment-resistant malignancies. Alternative therapeutic options for these patients include low-dose induction therapy or targeted therapies; however, these alternatives generally confer a reduced likelihood of achieving remission and are associated with shorter overall survival compared to intensive chemotherapy[1,3]. Notably, the period from 1971 to 2017 witnessed a paucity of new treatment approvals for AML[3]. In recent years, several innovative therapeutic agents have been introduced, including CPX-351, a liposomal formulation of cytarabine and daunorubicin; ivosidenib, an isocitrate dehydrogenase inhibitor; gilteritinib, a tyrosine kinase inhibitor; glasdegib, a sonic hedgehog pathway inhibitor; and venetoclax, a Bcl-2 inhibitor[4]. Many of these new treatments exploit the metabolic vulnerabilities of tumor cells. In this study, we aim to compare the effectiveness, safety, and

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side effects of first-line treatment regimens administered to patients with AML at our center, with the primary objective of achieving complete remission.

Patients and Methods

Patient Selection

Adult patients diagnosed with AML and followed up at our tertiary care center between January 1, 2014, and December 31, 2022, were included in this study. Exclusion criteria comprised incomplete medical records regarding necessary evaluations (blood count follow-ups, bone marrow results pre- and post-induction chemotherapy, chemotherapy regimens used), patients who did not receive induction chemotherapy at our institution, and those diagnosed with acute promyelocytic leukemia. The study was approved by the local ethics board (date: January 24, 2023, decision No.: 2023/01-08).

Researched Data

Data on patients' sex, age at diagnosis, comorbid conditions, Eastern Cooperative Oncology Group performance status (ECOG-PS), AML subtypes, European LeukemiaNet (ELN) cytogenetic subtypes, time from diagnosis to initiation of induction therapy, induction regimens, infection prophylaxis and treatments, as well as HSCT history were extracted from the hospital's electronic database. Complete remission, incomplete hematological recovery, and morphological non-leukemia state were collectively defined as remission. Unresponsive disease and partial remission were classified as non-remission. The need for respiratory support or intensive care admission, the occurrence of death, and the date and causes of death were documented. The interval from diagnosis to death from any cause or to the last follow-up visit was defined as overall survival (OS).

Study Outcomes

The primary outcome of the study was to compare the demographic and clinical characteristics, treatment-related toxicities, infectious complications, and remission rates of patients receiving different induction regimens. The secondary aim was to evaluate the induction treatments, clinical management strategies, and survival outcomes across three distinct follow-up periods: 2014-2017, 2017-2020, and 2020-2022.

Statistical Analysis

Statistical analyses were conducted using IBM® SPSS version 27.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics for categorical variables were presented as frequencies and percentages, and for continuous variables as mean±standard deviation (SD) or median (minimum-maximum). The normality of continuous variables was assessed visually and analytically. Categorical variables were compared using the χ^2 test. Independent continuous variables were compared using the Kruskal-Wallis test for three or more groups. The log-rank test assessed the relationship between parameters and overall survival, and survival rates were calculated with the Kaplan-Meier method. A p-value < 0.05 was considered statistically significant.

Results

Patient Characteristics, Management, and Endpoints

The study included 130 patients [78 (60%) men and 52 (40%) women] with a mean age at diagnosis of 53.6 ± 16.1 years. The baseline demographic and clinical characteristics of the patients are detailed in Table I. The median time from diagnosis to the start of the first induction therapy was 4 days (range: 0-72 days). For induction therapy, 82 patients (63.1%) received anthracycline and cytarabine, 22 patients (16.9%) received etoposide and cytarabine, 15 patients (11.5%) received a reduced dose of anthracycline and cytarabine, and 11 patients (8.5%) received azacitidine and venetoclax. From the beginning of treatment, 123 patients (94.6%) received antibiotics, 117 patients (90%) received antifungals, and 86 patients (66.2%) received antiviral prophylaxis or treatment for active infections. Fifty-four patients (41.5%) underwent allogeneic HSCT (Table II). After induction therapy, complete remission was achieved in 36.2% of patients, partial remission in 8.5%, incomplete hematological recovery in 4.6%, and morphological leukemia-free status in 2.3%. No response was observed in 32.3% of patients, and 16.2% could not be evaluated due to early death or other reasons. Treatment-related mortality occurred in 7.7% of patients, while 20% required intensive care and 21.5% required respiratory support. During a median follow-up period of 16.4 months (range: 0.4-98.7 months), 77 patients (59.2%) died (Table III). The OS

Table I. Baseline demographic and clinical characteristics of patients (130 patients in total).

Characteristics	Frequency, n (%)
Age at diagnosis, mean ± SD, years	53.6 ± 16.1
≥ 65 years	39 (30)
Male sex	78 (60)
ECOG-PS	
0	56 (43.1)
1	53 (40.8)
2	21 (16.2)
Comorbid diseases	
Hypertension	28 (21.5)
Diabetes mellitus	18 (13.8)
Malignancy	14 (10.8)
Coronary artery disease	11 (8.5)
Atrial fibrillation	5 (3.8)
Chronic obstructive pulmonary disease	5 (3.8)
Chronic kidney disease	3 (2.3)
Hyperlipidemia	2 (1.5)
Others	49 (37.7)
AML subtypes	
De novo	90 (69.2)
Secondary	40 (30.8)
Myelodysplastic syndrome related	29 (22.3)
Myeloproliferative disease related	7 (5.4)
Treatment related	4 (3.1)
WHO classification	
AML, not otherwise specified	60 (46.2)
AML with recurrent genetic abnormalities	35 (26.9)
AML with myelodysplasia-related changes	31 (23.8)
Therapy-related myeloid neoplasms	3 (2.3)
Myeloid sarcoma	1 (0.8)
Extramedullary involvement	6 (4.6)
Active infection at diagnosis	42 (32.3)
ELN cytogenetic risk category	
Favorable	15 (11.5)
Intermediate	68 (52.3)
Adverse	21 (16.2)
N/A	26 (20)

AML: acute myeloblastic leukemia, ECOG-PS: eastern cooperative oncology group-performance status, ELN: European LeukemiaNet, N/A: not applicable, SD: standard deviation, WHO: World Health Organization.

rate was 31.1% (95% CI: 20.7-41.5), with an estimated median survival of 21.1 months (95% CI: 11.9-30.5). The one-year and three-year OS rates were 62.1% (95% CI: 53.7-70.5) and 41.1% (95% CI: 31.9-50.3), respectively.

Comparison of Induction Regimens

In our study, induction regimens were compared based on patients' demographic and clinical characteristics, as well as HSCT and remission rates. Among patients, 6.1% in the anthracycline and cytarabine group, 77.3% in the azacitidine and venetoclax group, 68.2% in the etoposide and cytarabine group, and 53.3% in the reduced anthracycline and cytarabine group were 65 years or older ($p < 0.001$, Figure 1). Treatment groups did not differ by sex ($p = 0.361$). ECOG-PS scores of 0 were seen in 64.6% of patients receiving anthracycline and cytarabine, whereas all patients receiving azacitidine and venetoclax, 90.9% receiving etoposide and cytarabine, and 93.3% receiving reduced anthracycline and cytarabine had scores of 1-2 (Figure 2). While 22% of secondary AML patients received anthracycline and cytarabine treatment, this proportion was 54.5% in the azacitidine and venetoclax group, 40.9% in the etoposide and cytarabine group, and 46.7% in the reduced anthracycline and cytarabine group ($p = 0.033$) (Figure 3). There were no significant differences between treatment groups in terms of ELN cytogenetic risk categories ($p = 0.32$), presence of active infection at diagnosis (p

Table II. AML management and treatment responses (130 patients in total).

Parameters	Frequency, n (%)
Time from diagnosis to induction*, days	4 (0-72)
Treatments	
Anthracycline and cytarabine	82 (63.1)
Idarubicin	70 (53.8)
Daunorubicin	10 (7.7)
Mitoxantrone	2 (1.5)
Etoposide and cytarabine	22 (16.9)
Reduced anthracycline and cytarabine	15 (11.5)
Idarubicin	9 (6.9)
Mitoxantrone	6 (4.6)
Azacitidine and venetoclax	11 (8.5)
Prophylaxis/treatment of infection	
Antibiotics	123 (94.6)
Levofloxacin and TMP-SMX	46 (35.4)
Levofloxacin	44 (33.8)
Others	33 (25.4)
Antifungals	117 (90)
Posaconazole	97 (74.6)
Fluconazole	16 (12.3)
Others	4 (3.1)
Antivirals	86 (66.2)
Valacyclovir	83 (63.8)
Acyclovir	3 (2.3)
Allogeneic hematopoietic stem cell transplantation	54 (41.5)

*Median (minimum-maximum). TMP-SMX: trimethoprim-sulfamethoxazole.

= 0.37), or remission rates (p = 0.751). The median time from diagnosis to the initiation of the first induction therapy was significantly longer in patients receiving azacitidine and venetoclax compared to other treatment groups ($p < 0.001$) (Figure 4). The frequency of allogeneic HSCT was 53.7% in the anthracycline and cytarabine group but only 18.2% in the azacitidine and venetoclax group, 22.7% in the etoposide and cytarabine group, and 20% in the reduced an-

Table III. Treatment response and clinical endpoints (130 patients in total).

Parameters	Frequency, n (%)
Treatment response	
Remission	56 (43.1)
Complete remission	47 (36.2)
Incomplete hematological recovery	6 (4.6)
Morphological non-leukemia state	3 (2.3)
No remission	53 (40.8)
Unresponsive disease	42 (32.3)
Partial remission	11 (8.5)
N/A	21 (16.2)
Intensive care necessity	26 (20)
Respiratory support necessity	28 (21.5)
Exitus	77 (59.2)
Causes of death	
Infection	35 (26.9)
Infection and bleeding	21 (16.2)
Nephrotoxicity	2 (1.5)
Bleeding	1 (0.8)
N/A (other center)	11 (8.5)
Treatment-related mortality	10 (7.7)

N/A: not applicable.

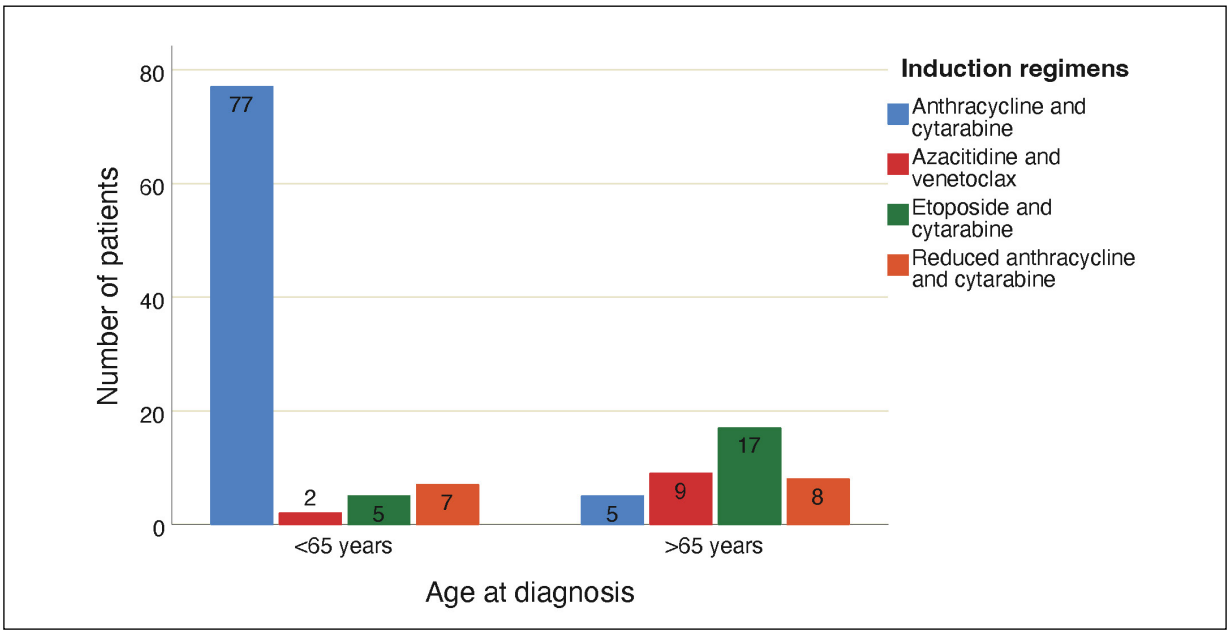

Figure 1. Induction regimens according to age groups.

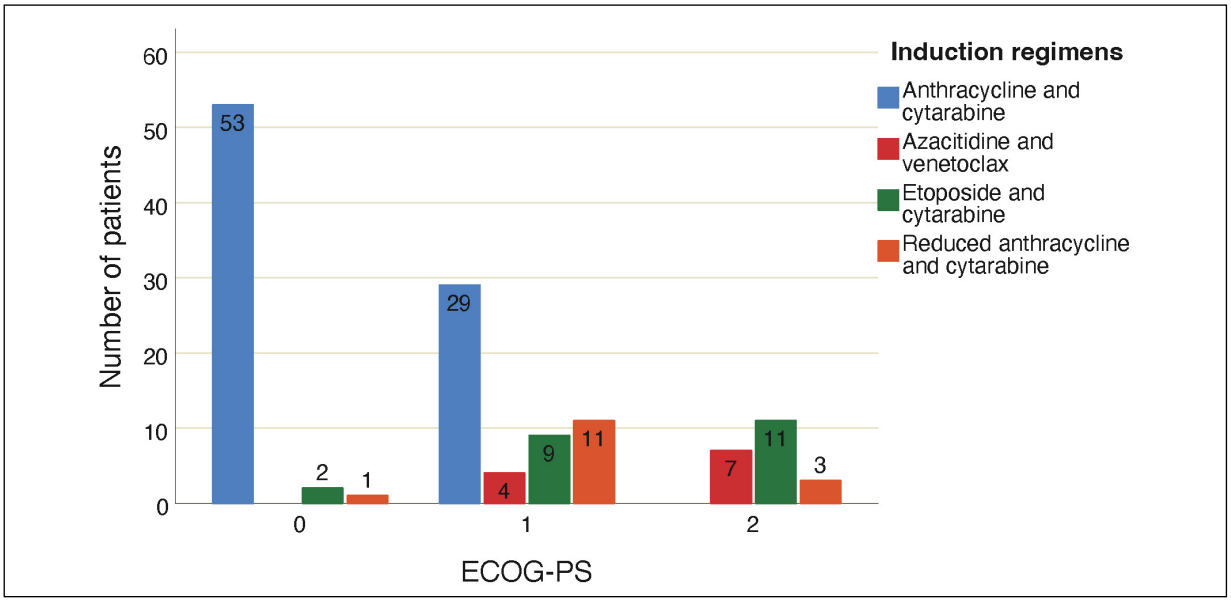

Figure 2. Induction regimens according to ECOG-PS groups.

thracycline and cytarabine group (p = 0.004), (Table IV). The frequency of febrile neutropenia (p = 0.486), diarrhea (p = 0.449), hepatotoxicity (p = 0.487), and nephrotoxicity (p = 0.142) did not significantly differ across the treatment groups. Similarly, no significant differences were observed between groups regarding skin or soft tissue infections (p = 0.941), pneumonia (p = 0.218), bacteremia (p = 0.648), mucositis (p = 0.085), gastroenteritis/colitis (p = 0.611), or fungemia (p = 0.615). However, the sepsis rate was significantly lower in the anthracycline and cytarabine group compared to the other regimens (p = 0.001). The median recovery times from

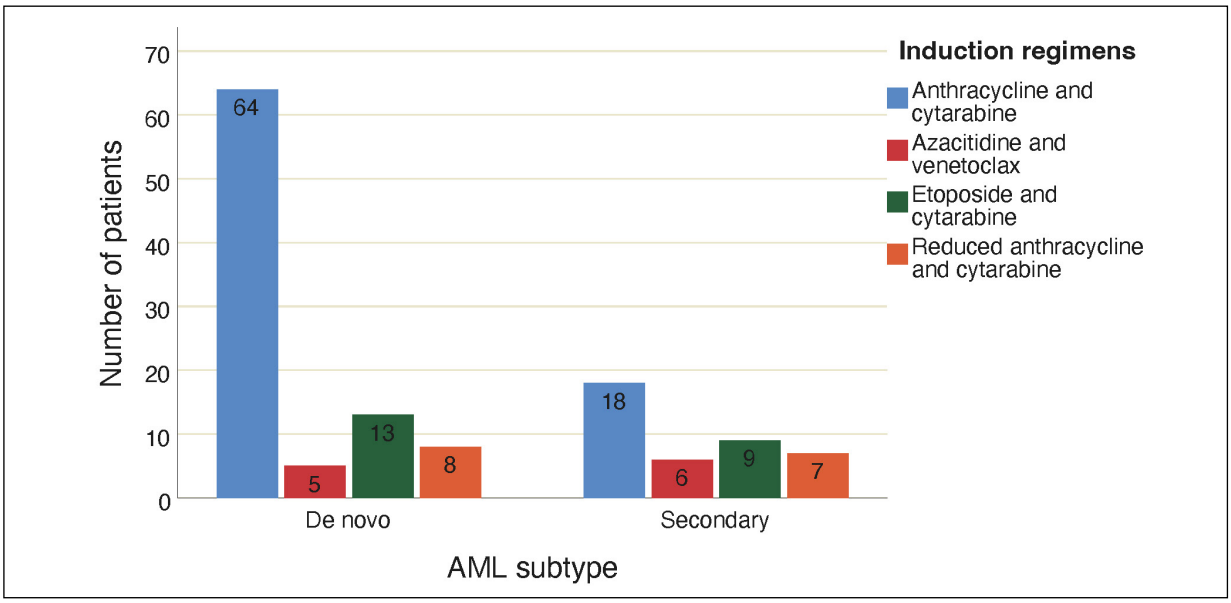

Figure 3. Induction regimens according to AML subtypes.

post-aplasia neutropenia and thrombocytopenia were as follows: 25 days (range: 16-35) and 23 days (range: 10-61) in the anthracycline and cytarabine group; 37 days (range: 25-102) and 18.5 days (range: 18-19) in the azacitidine and venetoclax group; 27 days (range: 0-37) and 28.5 days (range: 13-50) in the etoposide and cytarabine group; and 23 days (range: 19-30) and 26 days (range: 22-31) in the reduced anthracycline and cytarabine group (Figure 5, Table V).

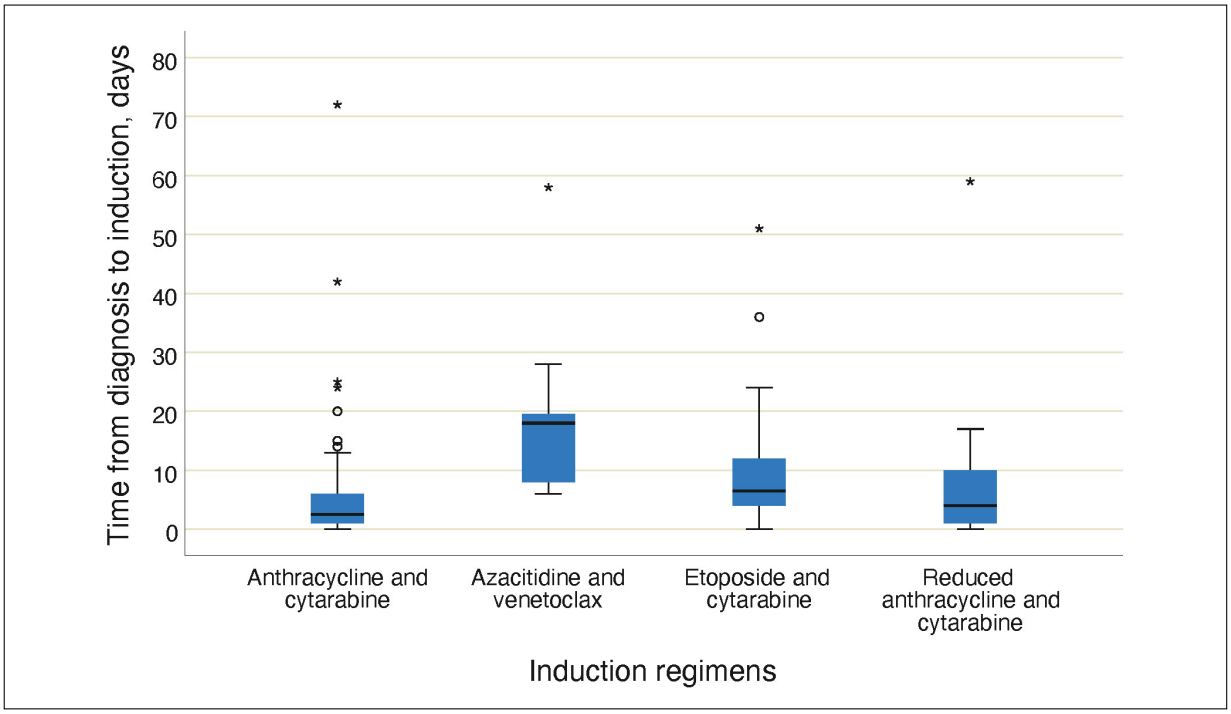

Figure 4. Comparison of time from diagnosis to initiation of induction therapy across different regimens. *represents outliners.

Table IV. Comparison of baseline demographic and clinical characteristics of treatment groups, as well as HSCT and remission rates.

Parameters		Anthracycline and cytarabine, n = 82 (%)	Azacitidine and venetoclax, n = 11(%)	Etoposide and cytarabine, n = 22 (%)	Reduced anthracycline and cytarabine, n = 15 (%)	*p*-value
Age at diagnosis ≥ 65 years		5 (6.1)	9 (81.8)	17 (77.3)	8 (53.3)	**< 0.001**
Male sex		50 (61)	7 (63.6)	15 (68.2)	6 (40)	0.361
ECOG-PS	0 1 2	53 (64.6) 29 (35.4) 0 (0)	0 (0) 4 (36.4) 7 (63.6)	2 (9.1) 9 (40.9) 11 (50)	1 (6.7) 11 (73.3) 3 (20)	**< 0.001**
AML subtype	*De novo* Secondary	64 (78) 18 (22)	5 (45.5) 6 (54.5)	13 (59.1) 9 (40.9)	8 (53.3) 7 (46.7)	**0.033**
ELN cytogenetic risk category	Favorable Intermediate Adverse	12 (16.7) 42 (58.3) 18 (25)	1 (16.7) 5 (83.3) 0 (0)	2 (13.3)* 11 (73.3) 2 (13.3)	0 (0) 10 (90.9) 1 (9.1)	0.320
Active infection at diagnosis		22 (26.8)	5 (45.5)	9 (40.9)	6 (40)	0.370
Time from diagnosis to induction*, days		2.5 (0-72)	18 (6-58)	6.5 (0-51)	4 (0-59)	**< 0.001**
Remission		40 (54.1)	4 (44.4)	6 (40)	6 (54.5)	0.751
HSCT		44 (53.7)	2 (18.2)	5 (22.7)	3 (20)	**0.004**

*Median (minimum-maximum). AML: acute myeloblastic leukemia, ECOG-PS: eastern cooperative oncology group-performance status, ELN: European LeukemiaNet, HSCT: hematopoietic stem cell transplantation.

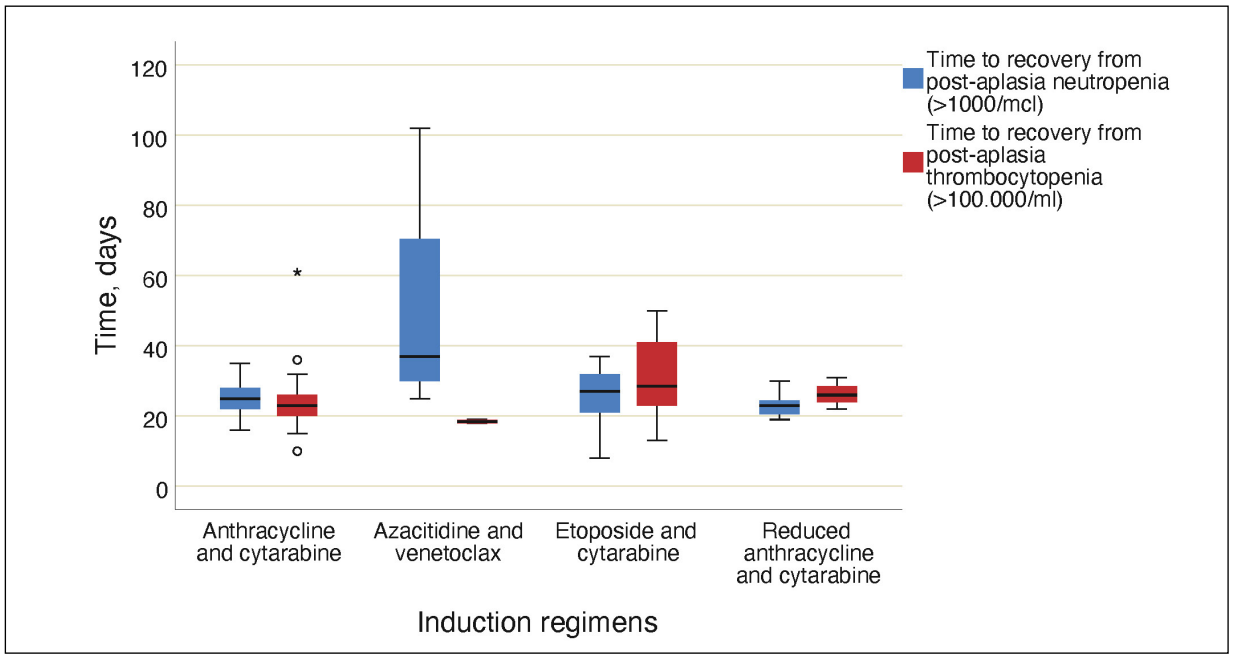

Figure 5. Comparison of time to recovery from post-aplasia neutropenia (> 1,000/mcl) and thrombocytopenia (>100,000/ml) according to induction regimens. *represents outliners.

Comparison of Temporal Treatment Periods

In our study, 23 patients (17.7%) were diagnosed between 2014-2017, 56 patients (43.1%) between 2017-2020, and 51 patients (39.2%) between 2020-2022. All patients diagnosed between 2014 and 2017 received anthracycline and cytarabine (standard or reduced dose). From 2017-2020, 12.5% received etoposide and cytarabine. Between 2020-2022, 29.4% received etoposide and cytarabine, and 21.6% received azacitidine and venetoclax. The rates of antibiotic (p = 0.053) and antifungal (p = 0.052) prophylaxis did not significantly differ over the years, but antiviral prophylaxis significantly increased from 47.8% (2014-2017) to 92.2% (2020-2022) (p < 0.001). There were no significant differences in treatment-related infectious complications (p = 0.6), induction-related mortality (p = 0.702), need for intensive care (p = 0.403), need for respiratory support (p = 0.340), remission rates (p = 0.077), or HSCT rates (p = 0.062) across the periods (Table VI). In patients who received induction therapy between 2014 and 2017, the one-year OS rate was 68.4% in the standard dose anthracycline and cytarabine group, compared to 50% in the reduced dose group (p = 0.05, Figure 6a). Similarly, for the period 2017-2020, the one-year OS rate for patients receiving anthracycline and cytarabine was significantly higher than for those receiving etoposide and cytarabine or reduced anthracycline and cytarabine (67.5%, 42.9%, and 33.3%, respectively; p = 0.007) (Figure 6b). No significant difference in OS was observed between treatment groups from 2020 to 2022 (p = 0.461) (Figure 6c). Overall, for the entire period from 2014 to 2022, the OS rate for patients treated with anthracycline and cytarabine was significantly higher than for other treatment groups (p = 0.001) (Figure 6d).

Discussion

In this study, we compared the characteristics and clinical outcomes of AML patients who underwent different induction therapies. We also examined the association of induction regimens with overall survival during different temporal treatment periods.

Treatment of AML is standardized for non-frail adults and consists of a combination of cytarabine and anthracycline, a remission induction therapy known as "7 + 3"[5]. While complete remission is achieved in 60-70% of cases with this treatment, the 5-year OS rate is only 20-30%[6]. There is no standard approach for treating elderly and frail AML patients who are not suitable for intensive

Table V. Comparison of treatment groups in terms of toxicity and infectious complications.

Parameters	Total n = 130 (%)	Anthracycline and cytarabine, n = 82 (%)	Azacitidine andvenetoclax, n = 11 (%)	Etoposide and cytarabine, n = 22 (%)	Reduced anthracycline and cytarabine, n = 15 (%)	*p*-value
Febrile neutropenia	127 (97.7)	81 (98.8)	11 (100)	21 (95.5)	14 (93.3)	0.486
Diarrhea	57 (43.8)	36 (43.9)	6 (54.5)	11 (50)	4 (26.7)	0.449
Hepatotoxicity	28 (21.5)	17 (20.7)	1 (9.1)	7 (31.8)	3 (20)	0.487
Nephrotoxicity	3 (2.3)	2 (2.4)	0 (0)	0 (0)	1 (6.7)	0.142
Infectious complications						
SSTI	41 (31.5)	25 (30.5)	3 (27.3)	8 (36.4)	5 (33.3)	0.941
Pneumonia	33 (25.4)	18 (22)	2 (18.2)	6 (27.3)	7 (46.7)	0.218
Bacteremia	27 (20.8)	20 (24.4)	1 (9.1)	4 (18.1)	2 (13.3)	0.648
Mucositis	27 (20.8)	19 (23.2)	0 (0)	7 (31.8)	1 (6.7)	0.085
Sepsis	26 (20)	8 (9.8)	3 (27.3)	8 (36.4)	7 (46.7)	**0.001**
Gastroenteritis/colitis	13 (10)	9 (11)	0 (0)	3 (13.6)	1 (6.7)	0.611
Fungemia	3 (2.3)	3 (3.7)	0 (0)	0 (0)	0 (0)	0.615
Time to recovery from post-aplasia neutropenia (> 1,000/mcl)*, days	25 (8-102)	25 (16-35)	37 (25-102)	27 (0-37)	23 (19-30)	**0.041**
Time to recovery from post-aplasia thrombocytopenia (> 100,000/ml)*, days	24 (10-61)	23 (10-61)	18.5 (18-19)	28.5 (13-50)	26 (22-31)	**0.010**

*Median (minimum-maximum). SSTI: skin and soft tissue infection.

Table VI. Comparison of different temporal periods in terms of applied treatments and clinical endpoints.

Parameters	Treatment periods, n (%)			*p*-value
	2014-2017, n = 23	2017-2020, n = 56	2020-2022, n = 51	
Treatments				
Anthracycline and cytarabine	19 (82.6)	40 (71.4)	23 (45.1)	**< 0.001**
Azacitidine and venetoclax	0 (0)	0 (0)	11 (21.6)	
Etoposide and cytarabine	0 (0)	7 (12.5)	15 (29.4)	
Reduced anthracycline and cytarabine	4 (17.4)	9 (16.1)	2 (3.9)	
Prophylaxis				
Antibiotics	20 (87)	52 (92.9)	51 (100)	0.053
Antifungals	21 (91.3)	54 (96.4)	42 (82.4)	0.052
Antivirals	11 (47.8)	28 (50)	47 (92.2)	**< 0.001**
Infectious complications	15 (65.2)	41 (73.2)	39 (76.5)	0.600
Induction-related mortality	1 (4.3)	4 (7.1)	5 (9.8)	0.702
Intensive care necessity	3 (13)	10 (17.9)	13 (25.5)	0.403
Respiratory support necessity	3 (13)	11 (19.6)	14 (27.5)	0.340
Remission	9 (42.9)	30 (63.8)	17 (41.5)	0.077
HSCT	10 (43.5)	29 (51.8)	15 (29.4)	0.062

HSCT: hematopoietic stem cell transplantation.

therapy. For decades, low-dose etoposide, cytarabine, hydroxyurea, or combinations of these drugs have been used based on clinical experience. Recently, the hypomethylating agents azacitidine and decitabine have been recommended as alternative initial and rescue treatments for AML patients. Numerous studies[7,8] have demonstrated that azacitidine prolongs survival in AML patients. Hypomethylating agents can be used in combination with cytarabine[9]. Additionally, etoposide is a widely preferred agent in combination therapies for elderly AML patients[10]. Venetoclax combination therapy has been approved for the treatment of newly diagnosed AML in the elderly or those deemed unfit for intensive therapy. Clinical studies[11,12] have demonstrated that venetoclax, in conjunction with hypomethylating agents or low-dose cytarabine, yields impressive response rates. Notably, a large phase 3 study[13] revealed that the combination of azacitidine and venetoclax significantly improved survival compared to azacitidine monotherapy. As a result, venetoclax-based combination regimens have been established as a new standard of care for the initial treatment of AML in this patient population. Despite these advances, primary resistance to initial therapy and disease relapse remain significant challenges in the treatment of AML. The majority of AML patients ultimately experience disease progression, underscoring the urgent need for further advancements.

Following the literature, in our cohort, combinations such as azacitidine and venetoclax, etoposide and cytarabine, and reduced-dose anthracycline and cytarabine were more frequently administered to patients aged 65 years or older, as well as to those with poorer performance status, compared to the standard anthracycline and cytarabine protocol[14]. The patients' sex, ELN cytogenetic risk category, and presence of active infection at diagnosis were not determinants in the selection of the induction regimen. However, standard anthracycline and cytarabine chemotherapy were administered less frequently to patients with secondary AML compared to other regimens. This is because secondary AML is often associated with advanced age and poor cytogenetic features, making some patients unsuitable for intensive chemotherapy[15,16]. In our study, the time to recovery from post-aplasia neutropenia was significantly longer in patients receiving azacitidine and venetoclax compared to other treatment groups. Prolonged neutropenia is a well-documented side effect of the Bcl-2 inhibitor venetoclax, often leading to its discontinuation[17].

The estimated median OS in AML is 8.5 months. According to the literature, the 2-year and 5-year OS rates are 32% and 24%, respec-

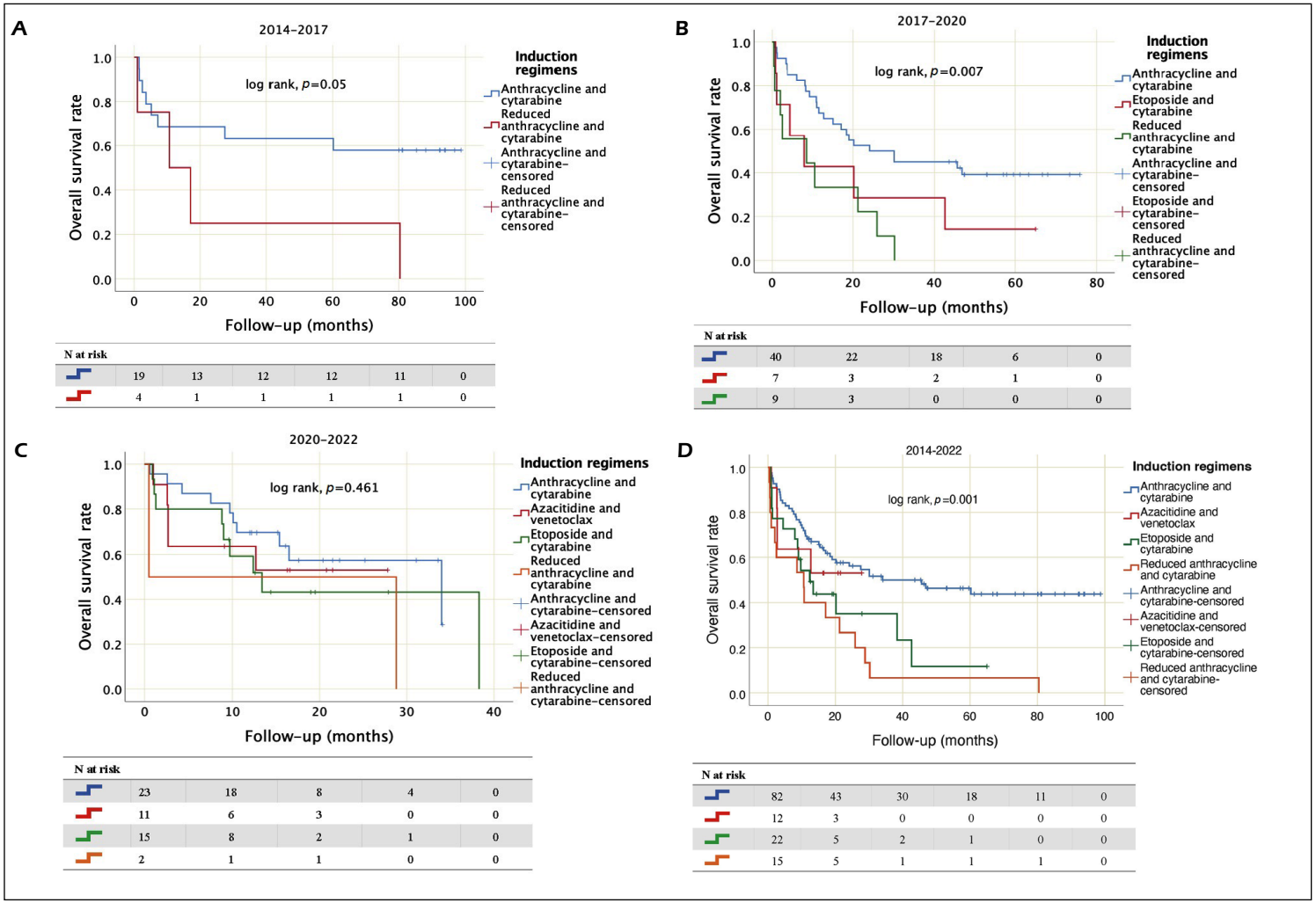

Figure 6. Association of induction regimens with overall survival in 2014-2017 (**A**), 2017-2020 (**B**), 2020-2022 (**C**) and 2014-2022 (**D**) treatment periods - Kaplan-Meier analyses.

tively[18]. The longer OS observed in patients at our center may be attributed to the lower median age at diagnosis and the presence of an active transplant unit, which attracts patients with higher survival expectations from remote areas. In addition, consistent with previous studies[19,20], the overall survival rate of patients treated with anthracyclines and cytarabine was found to be significantly higher than that of other treatment groups. Until 2017, all patients received anthracycline and cytarabine (standard or reduced dose). However, since then, a gradual increase in the utilization of alternative induction regimens has been observed. No significant differences were noted between the periods regarding treatment-related infectious complications, treatment-related mortality, need for intensive care, need for respiratory support, remission rates, or HSCT rates. While antibiotic and antifungal prophylaxis rates remained consistent across treatment periods, the frequency of antiviral prophylaxis increased over the years. This trend may be attributed to the growing literature on prophylactic antiviral treatments, which has heightened awareness. Improved management of infectious complications in AML has significantly contributed to treatment success over the past 50 years[21].

Limitations

The study has several limitations. The most significant limitation is its retrospective design. Additionally, the small sample size represents another critical constraint. The recent introduction of treatments such as oral etoposide with subcutaneous cytarabine and azacitidine with venetoclax has resulted in a heterogeneous patient distribution. Consequently, it is imperative to conduct similar studies with larger sample sizes to validate these findings.

Conclusions

In our study comparing four different AML induction treatments, the anthracycline and cytarabine regimen demonstrated the highest overall survival rate, although no significant differences in remission rates were observed between the groups. When deciding on optimal induction therapy, prioritizing the minimization of complications by considering the patient's performance status, age, and comorbidities rather than solely treatment efficacy may improve clinical outcomes. The duration of neutropenia during venetoclax and azacitidine treatment was significantly longer compared to other treatments, highlighting the importance of managing complications associated with prolonged neutropenia. The fact that infection remains the leading cause of mortality underscores the need for further research in prophylaxis and infection management.

Authors' Contributions

Conceptualization: S.Y. and U.Y.M.; formal analysis: S.Y.; funding acquisition: S.Y.; investigation: S.Y., and U.Y.M.; methodology: S.Y.; project administration: U.Y.M; resources: S.Y. and U.Y.M.; supervision: U.Y.M.; validation: U.Y.M.; visualization: U.Y.M.; writing-original draft: S.Y.; writing-review and editing, U.Y.M. All authors have read and agreed to the published version of the manuscript.

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Informed Consent

Informed consent was obtained from all study participants.

Conflict of Interest

The authors declare that they have no conflict of interest.

Data Availability

All data that support the findings of this study are available within the article and from the corresponding author.

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AI Disclosure

We utilized AI software to enhance the English language. However, no AI or other assisted technologies were used in the development of the study, including the creation of figures.

Ethics Approval

All procedures performed in the study involving human participants were in accordance with the 1964 Helsinki Declaration and its later amendments. The study was approved by Hacettepe University Ethics Board (date: 24.01.2023, decision No.: 2023/01-08).

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