Hypomethylating agents plus venetoclax *versus* intensive chemotherapy prior to transplant in high-risk acute myeloid leukemia

High-risk acute myeloid leukemia (AML) defined by cytogenetics and molecular alterations in the European LeukemiaNetwork 2022 (ELN-2022) classification has a poor prognosis.[1] Allogeneic stem cell transplantation (allo-SCT) in first remission is associated with a significant reduction of relapse risk and improved survival compared to intensive chemotherapy (IC) only.[2] Older AML patients between 60-74 years of age represent a high-risk population, as they frequently have ELN high-risk AML predicting disease resistance to IC.[3] In this age group, IC is associated with low complete remission (CR) rates (approximately 40-50%) and poor overall survival (OS).[1,4]

Thus, there is a need for new therapeutic strategies aimed at decreasing toxicities and improving efficacy in this population. The less-intensive regimen combining the hypomethylating agent (HMA) azacitidine (AZA) and the BCL-2 inhibitor venetoclax (VEN) has considerably changed the treatment paradigm for older subjects with newly-diagnosed AML.[5] Allo-SCT after VEN-AZA appears feasible,[6] with emerging evidence of post allo-SCT sustained remission.[7] Yet it still remains an open question whether HMA-VEN is equivalent to IC on post-transplant outcomes in high-risk AML patients.

Therefore, we assembled a retrospective cohort of consecutive patients aged 60-74 years newly diagnosed with ELN-2022 adverse-risk AML[1] treated with allo-SCT after prior intensive or less-intensive remission induction therapy. All patients were diagnosed between April 2014 and May 2024 at three US centers (DFCI, MSKCC, Yale Cancer Center) and five European centers (France: IPC-Marseille; CHU-Nice; HCL-Lyon; CHU-Bordeaux; Lithuania: Vilnius University-Hospital Santaros-Klinikos). Less-intensive treatment consisted of standard HMA-VEN including 7 days of AZA 75 mg/m² or 5-10 days of decitabine (DEC) 20 mg/m². IC induction consisted of conventional 7+3 or CPX-351 plus additional treatment with *FLT3*-inhibitors per local standards for *FLT3*-mutated patients. Patients in the IC arm could receive consolidation therapy with Cytarabine per local standards.

Data were collected from patients' electronic medical records. Institutional review boards of all the participating sites approved the study. We used ELN-2022 response criteria.[1] Composite CR (cCR) was defined as CR + CR with incomplete count recovery (CRi). Overall response (OR) was defined as cCR + morphologic leukemia-free state (MLFS). Time-to-event outcomes were defined from the date of allo-SCT. OS was defined as the time to death from any cause. RFS was the time to either relapse or death. CIR was defined as the time to relapse, with non-relapse mortality (NRM) considered a competing risk. All statistical tests were two-sided and $P<0.05$ was considered statistically significant. Survival rates were estimated using the Kaplan-Meier method. Log-rank test was used to compare OS and RFS. RI and NRM were compared with Gray's test. Survival analyses were performed using a Cox proportional hazards regression or a Fine-Gray model in competing risks setting. Multivariable regression models included baseline factors present in >10% of patients and factors significant in univariable analyses ($P<0.10$).

We included 139 patients with newly diagnosed adverse-risk AML per ELN-2022 who consecutively underwent allo-SCT after first-line therapy between September 2014 and July 2024 (*Online Supplementary Figure S1*). The median age at diagnosis was 66 years (range, 60-74). Eighty-four patients (60%) had received IC as induction therapy, including 64 (76%) with 7+3 and 20 (24%) with CPX-351 (Table 1). Five patients received *FLT3* inhibitors during induction therapy. AML treated with HMA-VEN were more likely to harbor monosomal or complex karyotype (54% *vs*. 28%; $P=0.002$), chromosome 5q (del5q, 32% *vs*. 16%; $P=0.032$) and 7q deletions (del7q, 28% *vs*. 9%; $P=0.003$), or chromosome 17p abnormalities (27% *vs*. 6%; $P=0.001$). Twenty-nine patients had *TP53* mutations (20.8%), including 23 (16.5%) with a *TP53*m variant allele frequency (VAF) >10%. HMA-VEN-treated patients had *TP53*-mutated AML in 32% *versus* 13% in the IC group ($P=0.005$).

In the HMA-VEN group, CR, CRi, and MLFS rates were 58.5%, 19%, and 13%, respectively. cCR and OR rates were 77% and 91%. In the IC group, responses were achieved after one (N=53, 83%) or two (N=11, 17%) cycles of induction chemotherapy. CR, CRi, and MLFS rates were 66%, 5%, and 6%, respectively. cCR and OR rates were 71% and 77%. Measurable residual disease (MRD) status at time of best response was available for 68 of 112 patients who achieved OR during induction. In the HMA-VEN group, 22 patients (73%) were MRD negative (MRD^-), while eight (27%) were MRD postive (MRD^+). In the IC group, 24 (63%) were MRD^- and 14 (37%) MRD^+.

Seven patients who achieved response relapsed prior to allo-SCT (all in the IC group). When adding patients who never achieved remission, a total of 31 patients were transplanted with active disease, five (9%) in the HMA-VEN group and 26 (31%) in the IC group ($P=0.003$).

With a median follow-up of 52.3 months (95% confidence

Table 1. Patient and disease characteristics by treatment type.

	Overall N=139	HMA-VEN N=55	Intensive chemotherapy* N=84	*P*
Patients characteristics				
Median age, years (range)	66.6 (60-74)	67.3 (60-74)	66 (60-74)	0.13
Age < 70 years, N (%)	101 (73)	36 (65.5)	65 (77)	0.12
Prior HMA, N (%)	9/138 (6.5)	0/54	9 (11)	0.013
Missing data,# N	1	1	-	-
Treatment center, N (%)				
DFCI	82 (59)	17 (31)	65 (77)	-
MSKCC	16 (12)	3 (5)	13 (15)	
YALE	6 (4)	6 (11)	0	
IPC	8 (6)	6 (11)	2 (2)	
CHU Nice + HCL	16 (12)	16 (29)	0	
CHU Bordeaux	5 (4)	5 (9)	0	
Vilnius	6 (4)	2 (4)	4 (5)	
Disease characteristics, N (%)				
Prior myeloid malignancy	41/138 (30)	19/54 (35)	22/84 (26)	0.26
Missing data#	1	1	-	-
Prior MDS	26 (19)	13 (23)	13 (15)	0.26
Therapy related†	21/138 (15)	6/54 (11)	15 (18)	0.28
Missing data#	1	1	-	-
Cytogenetics,‡ N (%)				
Complex karyotype	51/134 (38)	29/54 (54)	22/80 (28)	0.002
Missing data#	5	1	4	-
Del5q	29/131 (22)	16/50 (32)	13/81 (16)	0.032
Missing data#	8	5	3	-
Del7q	21/131 (16)	14/50 (28)	7/81 (9)	0.003
Missing data#	8	5	3	-
Chr17p abnormalities	18/130 (14)	13/49 (27)	5/81 (6)	0.001
Missing data#	9	6	3	-
MECOM rearrangement	8/133 (6)	4/52 (8)	4/81 (5)	0.5
Missing data#	6	3	3	-
Monosomal caryotype	39/135 (29)	24/54 (44)	15/81 (19)	0.001
Missing data#	4	1	3	-
Mutations,§ N (%)				
ASXL1	39 (28)	17 (31)	22 (26)	0.55
BCOR	14/134 (10)	0	14/79 (18)	0.001
Missing data#	5	0	5	-
DNMT3A	32 (23)	10 (18)	22 (26)	0.27
FLT3	7 (5)	1 (2)	6 (7)	0.16
IDH1	12 (9)	2 (4)	10 (12)	0.08
IDH2	21 (15)	6 (11)	15 (18)	0.26
JAK2	10/134 (7)	6/50 (12)	4 (5)	0.12
Missing data#	5	5	-	-
N/KRAS	17 (12)	6 (11)	11 (13)	0.7
PTPN11	11/129 (9)	5/50 (10)	7/79 (9)	0.83
Missing data#	10	5	5	-
RUNX1	36 (26)	14 (25)	22 (26)	0.92
SF3B1	9 (6)	6 (11)	3 (4)	0.09
SRSF2	22/134 (16)	10 (18)	12/79 (15)	0.65
Missing data#	5	-	5	-
STAG2	15/134 (11)	3 (5)	12/79 (15)	0.08
Missing data#	5	-	5	-
TET2	29 (21)	11 (20)	18 (21)	0.84
TP53	29 (21)	18 (32)	11 (13)	0.005
VHRcm	63/134 (47)	32/54 (59)	31/80 (39)	0.02
Missing data#	5	1	4	-
ELN24 risk group, N (%)				
Favorable	87 (63)	32 (58)	55 (65)	0.38
Intermediate	15 (11)	5 (9)	10/75 (12)	0.78
Adverse	28 (20)	18 (33)	10 (12)	0.028
Missing data#	9 (6)	-	9 (11)	-

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*Composite of 7 + 3 and liposomal cytarabine/daunorubicin. †Therapy-related disease was defined as receipt of chemotherapy and/or radiation for a prior nonmyeloid neoplasm. ‡Cytogenetic analysis was available in 121 of 139 patients (87%). §Only mutations present in ≥5% of patients included. VHRcm (very high-risk cytogenetic and molecular alterations): complex karyotype, monosomal karyotype, MECOM rearrangement and/or *TP53* mutation #Variables without "Missing data" specification had no missing data, i.e., statistical analyses were performed on N=139 patients, N=55 in the hypomethylating agents-ventoclax (HMA-VEN) cohort and N=84 in the intensive-chemotherapy cohort.

interval [CI]: 44.4-63.7), post allo-SCT OS was 34.4 (95% CI: 16.1-not reached [NR]) and 28.3 months (95% CI: 14.9-56.3) in the HMA-VEN and IC groups, respectively (*P*=0.636). RFS was 29.2 (95% CI: 14.7-NR) and 21.1 months (95% CI: 10.7-48.7) in the HMA-VEN and IC groups, respectively (*P*=0.959; Figure 1A, B). NRM and CIR were similar between both groups (NRM at 6 and 12 months: 8% and 11% in the HMA-VEN group *vs*. 5% and 18% in the IC group; *P*=0.632; CIR at 6 and 12 months: 11% and 25% in the HMA-VEN group, 13% and 23% in the IC group; *P*=0.643). We evaluated survival for patients in cCR at time of allo-SCT and compared it with patients transplanted without achieving cCR. In the HMA-VEN group, post allo-SCT OS was 38.8 (95% CI: 22.2-NR) *versus* 6.6 months (95% CI: 2.73-NA) respectively (*P*=0.022). In the IC group, post allo-SCT OS was 48.7 (95% CI: 27.0-NR) *versus* 12.8 months (range, 8.8-38.7; *P*=0.010). For these patients, outcome was not impacted by induction type (*P*=0.55; Figure 1C, D). MRD status was not predictive of post allo-SCT OS or RFS in univariable analysis (hazard ratio [HR]=1.39; 95% CI: 0.70-

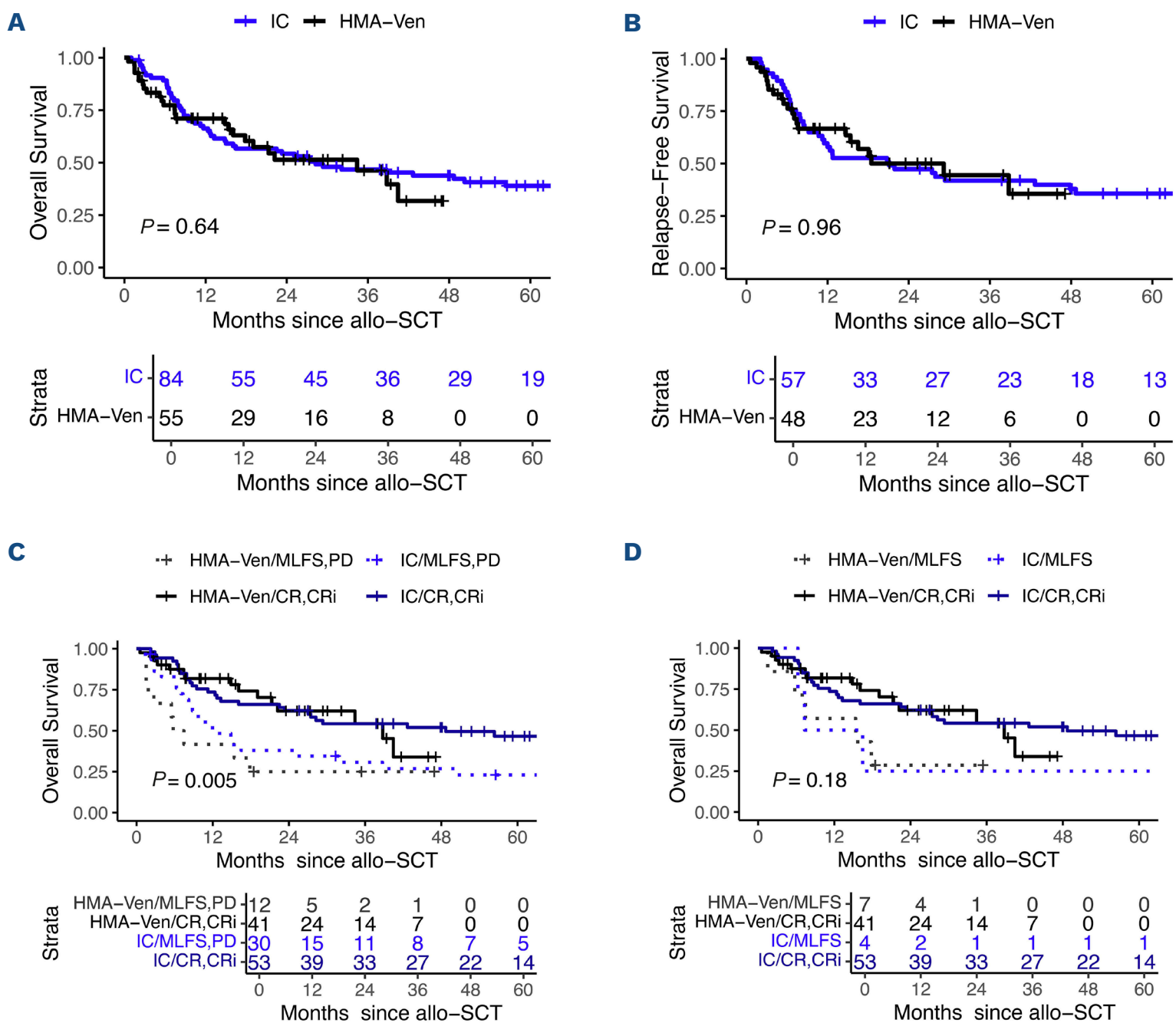


Figure 1. Overall survival and relapse-free survival in patients treated with allogeneic stem cell transplant after prior induction with hypomethylating agents plus venetoclax or intensive chemotherapy. (A) Comparison of post allogeneic stem cell transplant (allo-SCT) overall survival (OS) for patients treated with either hypomethylating agents plus venetoclax (HMA-VEN) or intensive chemotherapy (IC). (B) Comparison of relapse-free survival (RFS) for patients treated with either HMA-VEN or IC. (C) Comparison of patients in complete response (CR) and CR with incomplete hematological recovery (CRi) with patients in morphologic leukemia free-state (MLFS) and progressive disease (PD) for both treatment type. (D) Comparison of patients in CR-CRi with patients in MLFS after excluding patients treated by allo-SCT with an active disease, for both treatment types.

2.79; *P*=0.347 and HR=0.81; 95% CI: 0.38-1.73; *P*=0.583, respectively).

Multivariable analyses found that induction type (HMA-VEN *vs*. IC) did not impact post allo-SCT OS (HR=0.95; 95% CI: 0.54-1.68; *P*=0.864). The only factor associated with better survival was the achievement of cCR at allo-SCT (HR=0.43; 95% CI: 0.26-0.69; *P*=0.001). Monosomal karyotype was predictive of worse survival (HR=2.29; 95% CI: 1.34-3.92; *P*=0.003; Table 2). Treatment type did not impact RFS (HR=0.49; 95% CI: 0.22-1.08; *P*=0.08). Achievement of CR/CRi at allo-SCT was associated with improved RFS (HR=0.29; 95% CI: 0.12-0.72; *P*=0.0075) while *N/KRAS* mutation and del7 were associated with worse RFS (HR=2.39; 95% CI: 1.10-5.19; *P*=0.028 and HR=3.82; 95% CI: 1.68-8.67; *P*=0.0014, respectively; *Online Supplementary Table S1*).

In exploratory subgroup analyses, patients with AML harboring del5q and *TP53* mutations had better OS with HMA-VEN + allo-SCT compared to IC (HR=0.31; 95% CI: 0.12-0.88; *P*=0.027, and HR=0.39; 95% CI: 0.16-0.98; *P*=0.044, respectively). When analyzing RFS, we found that in patients with monosomal karyotype (HR=0.31; 95% CI: 0.12-0.78; *P*=0.013), del5q (HR=0.23; 95% CI: 0.06-0.82; *P*=0.023), del7q (HR=0.22; 95% CI: 0.06-0.82; *P*=0.024) or 17p.abn (HR=0.15; 95% CI: 0.03-0.94; *P*=0.042), HMA-VEN before allo-SCT was associated with prolonged survival compared to IC (*Online Supplementary Figure S2*).

Allo-SCT after VEN-based treatment is feasible, with low rates of NRM and acceptable OS.[6-8] Recent classifications have demonstrated major differences in the prognostic determinants for intensive and less-intensive therapies.[9] For example, complex cytogenetics without *TP53* mutations, usually associated with resistance to IC, allow for high response rates with HMA-VEN.[10] In multivariable analyses, first-line regimen did not impact OS nor RFS in this cohort of selected patients who underwent allo-SCT. Although no definitive conclusions should be drawn from our subgroup analyses, which are only hypothesis-generating, we found that chromosome 5 and 17p deletions as well as *TP53* mutations favored HMA-VEN compared to IC. Although HMA-VEN has yielded poor results in *TP53*-mutated AML in the VIALE-A cohort,[11] most patients were not consolidated with allo-SCT because of age or comorbidities. Interestingly, in a cohort of *TP53*-mutated AML, a recent report found that induction therapy containing VEN was associated with an increased rate of patients proceeding to allo-SCT, most likely owing to reduced toxicity.[12]

Our study has several limitations. The present cohort was constructed with consecutive patients who reached allo-SCT after either intensive or less-intensive induction, meaning that patients who did not reach transplant in the study period were not included. Therefore, this study does not report the initial number of patients aged 60-74 who began induction with either HMA-VEN or IC. Induc-

Table 2. Univariable and multivariable analyses for overall survival.

Variables	Overall survival					
	Univariable analyses			Multivariable analysis†		
	HR	95% CI	*P*	HR	95% CI	*P*
HMA-VEN *versus* IC	1.13	0.7-1.84	0.64	0.95	0.54-1.68	0.864
Age ≥70 years	0.86	0.5-1.46	0.57	-	-	-
Prior myeloid malignancies	1.46	0.90-2.35	0.12	-	-	-
Therapy related	1.2	0.67-2.15	0.54	-	-	-
Response status prior to allo-SCT (cCR *vs*. active disease)	0.47	0.30-0.75	0.001	0.43	0.26-0.69	0.001
Monosomal karyotype	2.15	1.32-3.50	0.002	2.29	1.34-3.92	0.003
Complex karyotype	1.64	1.03-2.62	0.04	-	-	-
Del5q	1.44	0.84-2.48	0.18	-	-	-
Del7	1.71	0.95-3.08	0.08	-	-	-
Chr 17p abnormalities	1.58	0.82-3.04	0.17	-	-	-
BCOR	0.37	0.13-1.02	0.054	-	-	-
IDH2	0.7	0.36-1.36	0.29	-	-	-
N/KRAS	1.53	0.8-2.9	0.2	-	-	-
TP53	1.91	1.12-3.24	0.02	-	-	-

†Final multivariable model was reached after using a stepwise regression to minimize model complexity. allo-SCT: allogeneic stem cell transplant; cCR: composite complete remission; CI: confidence interval; Chr: chromosome; HMA-VEN: hypomethylating agents plus venetoclax; HR: hazard ratio; IC: intensive chemotherapy.

tion approach was selected by the physician, possibly influenced by patient and disease characteristics. Our dataset did not include information regarding allo-SCT modalities such as conditioning regimen, donor type, stem-cell source or graft-*versus*-host disease prophylaxis, which could all influence post allo-SCT outcome. Data regarding post allo-SCT maintenance therapy was not available. Additionally, a proportion of patients in the IC cohort were treated before VEN approval.

Despite the limitations, this study is in line with recent evidence showing similar outcomes after initial treatment with HMA-VEN or IC in fit patients, in randomized trials comparing both therapies.[13] HMA-VEN may allow higher response rates and reduced toxicity, which in turn might improve survival when compared to IC.[7,13,14]

Until sufficient follow-up is reached in these studies, real-world data can provide evidence supporting the use of HMA-VEN as an alternative, less toxic induction strategy for patients with ELN-2022 adverse-risk AML who are intended to proceed to allo-SCT.

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Contributions

Conception and design by GB, MS, and SG. Provision of study materials or patients by all authors. Collection and assembly of data by GB, AI, AS, LA, PYD MH, SS, MS, and SG. Data analysis and interpretation by GB, JG, SG, and MS. Manuscript writing by GB, JG, and SG. Final approval of manuscript by all authors.

Data-sharing statement

The data that support the findings of this study are available upon request from the corresponding author.

References

1. Döhner H, Wei AH, Appelbaum FR, et al. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN. Blood. 2022;140(12):1345-1377.
2. Cornelissen JJ, Blaise D. Hematopoietic stem cell transplantation for patients with AML in first complete remission. Blood. 2016;127(1):62-70.
3. Wakita S, Yamaguchi H, Ueki T, et al. Complex molecular genetic abnormalities involving three or more genetic mutations are important prognostic factors for acute myeloid leukemia. Leukemia. 2016;30(3):545-554.
4. Short NJ, Kantarjian H. When less is more: reevaluating the role of intensive chemotherapy for older adults with acute myeloid leukemia in the modern era. J Clin Oncol. 2021;39(28):3104-3108.
5. DiNardo CD, Jonas BA, Pullarkat V, et al. Azacitidine and venetoclax in previously untreated acute myeloid leukemia. N Engl J Med. 2020;383(7):617-629.
6. Mukherjee A, Milton DR, Jabbour E, et al. Allogeneic stem cell transplantation (AlloSCT) for patients (pts) with acute leukemia following venetoclax-based therapy. J Clin Oncol. 2019;37(Suppl 15):7047.
7. Short NJ, Ong F, Ravandi F, et al. Impact of type of induction therapy on outcomes in older adults with AML after allogeneic stem cell transplantation. Blood Adv. 2023;7(14):3573-3581.
8. Ong F, Ravandi F, Popat UR, et al. Impact of induction approach on post-stem cell transplant (SCT) outcomes in older adults with newly diagnosed acute myeloid leukemia (AML). J Clin Oncol. 2022;40(Suppl 16):7038.
9. Döhner H, DiNardo CD, Appelbaum FR, et al. Genetic risk classification for adults with AML receiving less-intensive therapies: the 2024 ELN recommendations. Blood. 2024;144(21):2169-2173.
10. Xie J, Bao X, Xue SL, et al. Venetoclax with decitabine as frontline treatment in younger adults with newly diagnosed ELN adverse-risk AML. Blood. 2023;142(15):1323-1327.
11. Pollyea DA, Pratz KW, Wei AH, et al. Outcomes in patients with poor-risk cytogenetics with or without TP53 mutations treated with venetoclax and azacitidine. Clin Cancer Res. 2022;28(24):5272-5279.
12. Senapati J, Garcia-Manero G, DiNardo CD, et al. Barriers to allogeneic stem cell transplantation in responding patients with TP53-mutated acute myeloid leukemia. Bone Marrow Transplant. 2025;60(6):910-913.
13. Fathi A, Perl A, Fell G, et al. Results from paradigm - a phase 2 randomized multi-center study comparing azacitidine and venetoclax to conventional induction chemotherapy for newly diagnosed fit adults with acute myeloid leukemia. Blood. 2025;146(Suppl 1):6.
14. Lu J, Xue S li, Wang Y, et al. Venetoclax and decitabine vs intensive chemotherapy as induction for young patients with newly diagnosed AML. Blood. 2025;145(22):2645-2655.