

# Long-term effects of multidisciplinary team recommendations on adult patients with acute myeloid leukemia

Jingtao Huang<sup>1,2,§</sup>, Yiwen Wu<sup>3,§</sup>, Yunxiang Zhang<sup>1,§</sup>, Chuanhe Jiang<sup>1,§</sup>, Min Wu<sup>1</sup>, Zengkai Pan<sup>1</sup>, Qiusheng Chen<sup>1</sup>, Huijin Zhao<sup>1</sup>, Yu Zheng<sup>1</sup>, Yang Shen<sup>1</sup>, Yang He<sup>1,\*</sup>, Jiong Hu<sup>1,\*</sup>, Junmin Li<sup>1,\*</sup>, Xiaoxia Hu<sup>1,\*</sup>

<sup>1</sup> Shanghai Institute of Hematology, State Key Laboratory of Medical Genomics, National Research Center for Translational Medicine at Shanghai, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China;

<sup>2</sup> State Key Laboratory of Experimental Hematology, National Clinical Research Center for Blood Diseases, Haihe Laboratory of Cell Ecosystem, Institute of Hematology and Blood Diseases Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Tianjin, China;

<sup>3</sup> Haihe Laboratory of Cell Ecosystem, Tianjin Medical University, Tianjin, China.

**SUMMARY:** Optimal post-remission therapy is crucial for long-term survival in patients with acute myeloid leukemia (AML). Multidisciplinary team (MDT) conferences address this challenge by providing comprehensive, patient-centered consultations that support individualized treatment decision-making. We evaluated the effectiveness of MDT conferences in guiding post-remission treatment decisions in adults with de novo AML. We enrolled 653 adult patients with de novo AML who were treated at our center between January 2017 and December 2022. Of the 591 eligible patients (90.5%), 501 (84.8%) attended a scheduled MDT evaluation. Allogeneic hematopoietic cell transplantation (allo-HCT) was recommended for 315 patients (62.9%), of whom 251 (79.7%) subsequently underwent transplantation. Survival analyses showed that MDT attendees had superior 3-year overall survival (68.9% vs. 53.5%,  $p < 0.0001$ ) and a lower 3-year cumulative incidence of relapse (30.7% vs. 44.9%;  $p < 0.0001$ ) compared with patients who did not attend MDT conferences. Patients most likely to benefit from allo-HCT following MDT recommendations included those with intermediate- or adverse-risk disease according to the European LeukemiaNet 2017 classification, and those with favorable-risk disease who showed a suboptimal response to induction therapy. The main barriers to allo-HCT were persistent or relapsed disease and patient preference. Overall, MDT conferences effectively identified patients who were most likely to benefit from allo-HCT and were associated with higher transplantation rates within a modern healthcare system.

**Keywords:** acute myeloid leukemia, multidisciplinary team, allogeneic hematopoietic stem cell transplantation, long-term outcomes

## 1. Introduction

Allogeneic hematopoietic stem cell transplantation (allo-HCT) is a potentially curative treatment for several hematologic malignancies, with acute myeloid leukemia (AML) representing the most common indication for allo-HCT in adult patients (1-4). AML accounts for approximately 37% of allo-HCT procedures, a proportion that continues to increase in China (5). Current consensus guidelines recommend allo-HCT as standard post-remission therapy for patients with AML who are at high risk of relapse (6-9). Results from previous studies, however, have shown that only a minority of patients who are likely to benefit from allo-HCT ultimately undergo transplantation (10-14). Delays

in human leukocyte antigen (HLA) typing and referral to an allo-HCT program represent major barriers, even within academic centers, and these challenges may be exacerbated when eligible patients receive induction therapy at institutions without an established allo-HCT program (6,15,16).

Multidisciplinary team (MDT) conferences provide comprehensive, patient-centered consultations by integrating expertise across specialties, facilitating collaborative decision-making, and supporting individualized treatment strategies. MDT-based care has been shown to influence patient management practices and has been increasingly adopted across cancer centers in developed countries (17,18), where it has contributed to higher rates of allo-HCT in patients with AML (11,19,20).

In China, MDT evaluation remains at a relatively early stage, owing to the substantial time, effort, and human resources required, as well as existing disciplinary boundaries (21). At our center, MDT conferences are used to assess the suitability of individual patients with AML for allo-HCT; however, their impact on long-term survival among transplant-eligible patients remains unclear (19).

In this single-center, retrospective study, we enrolled patients with newly diagnosed AML at the time of diagnosis and followed them throughout their treatment course to assess the rate of allo-HCT among patients who did and did not undergo MDT evaluation. We evaluated the effectiveness of MDT conferences in guiding consolidation decisions, particularly recommendations regarding transplantation.

## 2. Methods

### 2.1. Study design and patient enrollment

This single-center, retrospective study screened patients with newly diagnosed AML who were admitted as inpatients between January 2017 and December 2022. Patients aged  $\geq 14$  to  $\leq 65$  years with non-acute promyelocytic leukemia (APL) AML, diagnosed according to the fourth edition of the WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues (22), were eligible. Patients with incomplete medical information or a diagnosis of APL were excluded.

AML risk stratification (favorable, intermediate, or adverse) was performed according to the European LeukemiaNet (ELN) 2017 classification (23). Clinical data were retrospectively extracted from the institutional AML and transplant database. In total, 653 patients with complete follow-up information were screened; 62 patients (9.5%) were excluded due to early death (within 3 months of diagnosis), leaving 591 patients available for analysis. The last follow-up date was December 31, 2024.

The primary objective was to determine the rate of allo-HCT among patients with newly diagnosed AML. Secondary objectives were to assess the concordance between post-remission therapies initially recommended and those ultimately administered, and to evaluate survival outcomes in patients who attended MDT conferences compared with those who did not.

This study was approved by the institutional review board of Shanghai Ruijin Hospital (RJ-2024-08) and was conducted in accordance with the Declaration of Helsinki. The requirement for written informed consent was waived because of the retrospective, non-interventional study design.

### 2.2. Measurable residual disease detection and relapse definition

Measurable residual disease (MRD) detection using multiparameter flow cytometry (MFC) and/or real-time quantitative polymerase chain reaction (qRT-PCR) was performed as previously described (24). Leukemia-associated aberrant immunophenotypes and/or "different-from-normal" approaches were applied for MRD assessment by MFC, with a threshold of 0.01% used to define MRD positivity (25). Complete remission (CR) in AML was defined as  $< 5\%$  bone marrow blasts, recovery of peripheral blood counts (absolute neutrophil count  $\geq 1.0 \times 10^9/L$  and platelet count  $\geq 100 \times 10^9/L$ ), absence of circulating blasts, no extramedullary disease, and transfusion independence. Relapse was defined as the recurrence of bone marrow blasts  $> 5\%$ , reappearance of blasts in peripheral blood, development of extramedullary disease, or recurrence of pre-transplantation chromosomal abnormalities.

### 2.3. Inclusion and exclusion criteria for allo-HCT recommendation

#### (I). Allo-HCT recommendation criteria:

- a) AML in first CR(CR1):
  - (i). Patients who achieved CR1 after  $> 2$  cycles of induction (7,8);
  - (ii). Intermediate- or adverse-risk AML according to the ELN 2017 risk stratification (23);
  - (iii). Myelodysplasia-related AML or therapy-related AML (7,8);
  - (iv). Favorable-risk AML with any of the following features (6): failure to attain major molecular remission (MMR; *RUNX1::RUNX1T1* decrease  $< 3$  log units) after two consolidation cycles, or loss of MMR within 6 months; recurrence of *CBFB::MYH11/ABL* transcript levels  $> 0.1\%$  at any time after two consolidation cycles; presence of the *KIT* D816 mutation in *CBF*-AML (26); biallelic mutated *CEBPA* (*CEBPA*<sup>bi+</sup>) AML with positive MFC-MRD after two consolidation cycles (27); AML with an *NPM1* mutation and positive MFC-MRD or detectable *NPM1* transcripts by qRT-PCR (Ct  $< 40$  in at least 2 of 3 replicates) after two consolidation cycles (24);
- b)  $\geq$  CR2 (7,8);
- c) Relapsed or refractory AML, or AML with extramedullary disease (7,8).

#### (II). Allo-HCT exclusion criteria:

- a) Patients aged  $> 70$  years and/or with overt contraindications to transplantation;
- b) No available donor;
- c) Severe comorbidities, including active central nervous system leukemia, severe cardiovascular disease, or active uncontrolled infection.

### 2.4. MDT process

Each patient underwent MDT evaluation at two separate visits. The MDT was required to include at least

two adult leukemia specialists, two HCT specialists, one psychologist, one dietitian, and two full-time coordinators from the leukemia/HCT program.

The first MDT visit was scheduled after one or two cycles of induction therapy. Treatment recommendations were based on baseline disease characteristics and the patient's physical condition. During this visit, post-remission treatment strategies were discussed and evaluated. Allo-HCT was recommended for patients with intermediate- to adverse-risk AML, whereas chemotherapy and/or targeted therapy was reserved for patients with favorable-risk disease. For patients with intermediate- to adverse-risk AML, HLA typing of patients and eligible immediate relatives was performed, and a preliminary unrelated donor search was initiated to identify potential donor sources in advance.

The second MDT visit was scheduled after two cycles of consolidation therapy. At this visit, a comprehensive assessment of treatment response and optimal timing of allo-HCT was performed, and individualized recommendations were made. Patients with intermediate- to adverse-risk AML were recommended to proceed to allo-HCT within the subsequent few weeks. Recommendations for allo-HCT in patients with favorable-risk AML were limited to those who met the allo-HCT recommendation criteria described above.

For patients who agreed to the recommended allo-HCT plan, an HCT coordinator organized and coordinated the transplant procedure. Follow-up was conducted by MDT coordinators within 3 months after the second MDT visit to determine whether patients proceeded with the planned allo-HCT. Reasons for failure to proceed to transplantation were documented.

### 2.5. Best available therapy

Best available therapy (BAT) was provided for all transplant-ineligible patients and included chemotherapy, targeted therapy, immunotherapy, traditional Chinese medicine therapy, and palliative care (28,29).

### 2.6. Statistical analysis

Continuous variables were compared using unpaired, two-tailed Student's *t* test for between-group comparisons. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate.

Propensity score weighting (PSW) with overlap weighting was applied to minimize confounding and improve covariate balance between MDT and non-MDT groups, based on propensity scores estimated from a logistic regression model. Covariate balance before and after weighting was assessed using standardized mean differences (SMDs).

For MDT-related outcome analyses, a landmark time point of 3 months after diagnosis was defined to evaluate whether MDT involvement was associated with

a reduced risk of mortality, as this corresponds to the period during which patients would have attended MDT evaluation and received treatment recommendations. In the overlap-weighted cohort, overall survival (OS) was estimated using the Kaplan–Meier method and compared using the log-rank test. The cumulative incidence of relapse (CIR) was estimated using the Fine–Gray subdistribution hazard model, with death treated as a competing event.

Logistic regression analyses were performed to identify factors associated with MDT transplant recommendations. Cox proportional hazards regression models were used to evaluate the association between MDT evaluation and survival outcomes. All analyses were performed using R software version 4.3.1. Statistical significance was defined as a two-sided *P* value < 0.05.

To evaluate the robustness of OS estimates to loss to follow-up, sensitivity analyses were conducted under extreme assumptions. Specifically, best-case and worst-case scenarios were considered, in which all patients lost to follow-up were assumed to be alive until the end of follow-up or to have died at the time of last contact, respectively. Overlap weighting was applied consistently across all sensitivity analyses.

All analyses were performed in a blinded manner, such that investigators conducting the data analyses were unaware of ELN risk classification and treatment assignments.

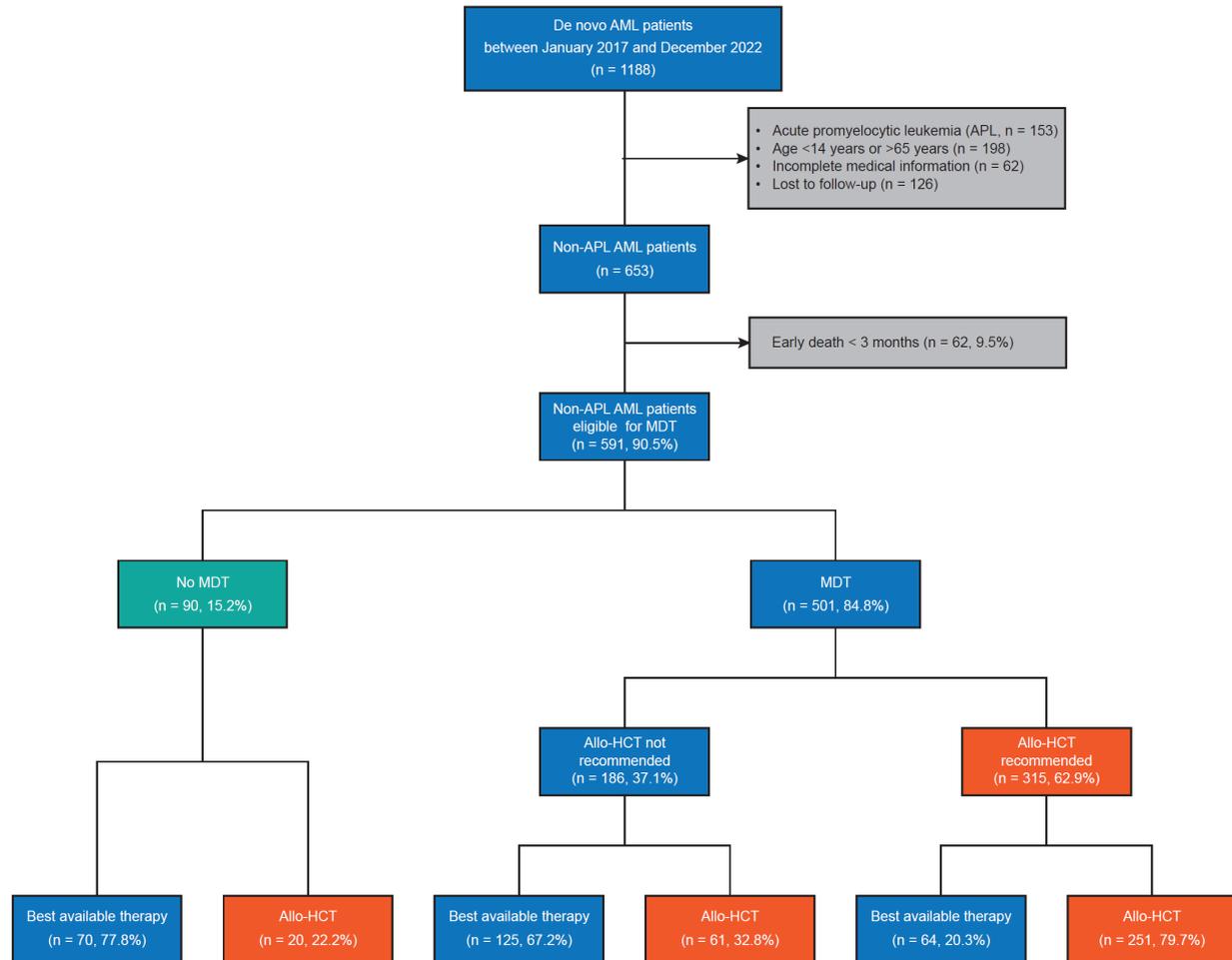
## 3. Results

### 3.1. Patients

In total, 653 patients met the eligibility criteria and consented to participate in this study. Of these, 62 patients (9.5%) died within 3 months of diagnosis and were thus excluded from further analysis. The remaining 591 patients were considered eligible for MDT evaluation to support individualized treatment planning. Among them, 501 patients (84.8%) attended at least one MDT visit following the recommendation of their attending physicians (Figure 1), and 372 patients (74.3%) attended two MDT evaluations (Table 1).

The median age of the entire cohort was 45 years (range, 15–65 years). According to the ELN 2017 risk stratification, 48.2% of patients had favorable-risk disease (*n* = 258), 24.7% had intermediate-risk disease (*n* = 146), and 27.1% had adverse-risk disease (*n* = 160). The most common AML subtype was AML with *NPM1* mutation (20.5%), followed by AML with *CEBPA* mutation (20.1%), AML with other defined genetic lesions (16.6%), and AML with myelodysplasia-related changes (10.7%).

The distribution of ELN risk categories did not significantly differ between patients who attended MDT evaluation and those who did not (favorable: 48.70% vs. 45.55%; intermediate: 25.35% vs. 21.11%;



**Figure 1. Flowchart of MDT consultation and transplant utilization.** Abbreviations: APL, acute promyelocytic leukemia; allo-HCT, allogeneic hematopoietic cell transplantation; AML, acute myeloid leukemia; MDT, multidisciplinary team.

adverse: 25.95% vs. 33.34%;  $p = 0.3373$ ; Figure 2A). Compared with non-MDT patients, MDT attendees had a higher CR rate after one cycle of induction therapy ( $p < 0.001$ ), whereas rates of MRD negativity were comparable between the two groups (55.1% vs. 45.5%). After application of PSW with overlap weighting, all covariates included in the model (age, sex, ELN 2017 risk stratification, AML subtype, and MRD status after induction therapy) were well balanced, with standardized mean differences  $< 0.01$ . Outcome analyses demonstrated that MDT attendees had superior 3-year OS compared with non-MDT patients (68.9% vs. 53.5%;  $p < 0.0001$ ; Figure 2B), as well as a lower 3-year CIR (30.7% vs. 44.9%;  $p = 0.001$ ; Figure 2C).

### 3.2. MDT and transplantation recommendation

The number of patients who participated in MDT evaluation was higher in 2020–2022 ( $n = 354$ ) than in 2017–2019 ( $n = 147$ ). Baseline characteristics of patients who attended MDT evaluation are summarized in Supplementary Table S1 (<https://www.biosciencetrends.com/action/getSupplementalData.php?ID=285>).

The median age of MDT attendees was 44 years (range, 15–65 years), with a significant increase observed in 2020–2022 compared with 2017–2019 (45.5 years [range, 15–59] vs. 42 years [range, 15–65];  $p = 0.015$ ).

In the overlap-weighted cohort, allo-HCT was associated with superior 3-year OS compared with BAT (73.8% vs. 51.9%,  $p < 0.0001$ ; Supplementary Figure S1A, <https://www.biosciencetrends.com/action/getSupplementalData.php?ID=285>) and a lower 3-year CIR (28.0% vs. 45.5%;  $p < 0.0001$ ; Supplementary Figure S1B, <https://www.biosciencetrends.com/action/getSupplementalData.php?ID=285>). Among the 501 patients who attended MDT evaluation, 315 (62.9%) were recommended for allo-HCT, of whom 251 (79.4%) proceeded to transplantation (Figure 1). This transplantation rate was significantly higher than that observed in the non-MDT group (22.2%,  $p < 0.001$ ). Among patients recommended for allo-HCT, transplantation rates were higher in those aged  $< 55$  years (82.4%;  $n = 250$ ) than in those aged  $\geq 55$  years (69.2%;  $n = 65$ ) ( $p = 0.0243$ ). Of the 186 patients (37.1%) who were

**Table 1. Comparison of MDT and non-MDT patients**

	Before weighting				After weighting			
	Total (n = 591)	MDT (n = 501)	Non-MDT (n = 90)	SMD	Total (n = 138.76)	MDT (n = 69.38)	Non-MDT (n = 69.38)	SMD
Diagnosis year								
2017-2019	175 (29.6%)	147 (29.3%)	28 (31.1%)	0.831	40.20 (29.0%)	20.10 (29.0%)	20.10 (29.0%)	< 0.001
2020-2022	416 (70.4%)	354 (70.7%)	62 (68.9%)		98.56 (71.0%)	49.28 (71.0%)	49.28 (71.0%)	
Age, n (%)				0.435				< 0.001
1-39 years	229 (38.8%)	199 (39.7%)	30 (33.3%)		49.27 (35.5%)	24.64 (35.5%)	24.64 (35.5%)	
40-54 years	229 (38.8%)	193 (38.5%)	36 (40.0%)		54.66 (39.4%)	27.33 (39.4%)	27.33 (39.4%)	
55-65 years	133 (22.4%)	109 (21.8%)	24 (26.7%)		34.83 (25.1%)	17.42 (25.1%)	17.42 (25.1%)	
Sex, n (%)				0.166				< 0.001
Male	305 (51.6%)	252 (50.3%)	53 (58.9%)					
Female	286 (48.4%)	249 (49.7%)	37 (41.1%)					
ELN 2017 stratification, n (%)				0.325				< 0.001
Favorable risk	285 (48.2%)	244 (48.7%)	41 (45.6%)		58.93 (42.5%)	29.46 (42.5%)	29.46 (42.5%)	
Intermediate risk	146 (24.7%)	127 (25.3%)	19 (21.1%)		66.35 (47.8%)	33.18 (47.8%)	33.18 (47.8%)	
Adverse risk	160 (27.1%)	130 (26.0%)	30 (33.3%)		30.18 (21.8%)	15.09 (21.8%)	15.09 (21.8%)	
AML subtype, n (%)				0.143				< 0.001
AML with defining genetic abnormalities								
AML with <i>RUNX1::RUNX1T1</i> fusion	46 (7.8%)	37 (7.4%)	9 (10.0%)		13.35 (9.6%)	6.68 (9.6%)	6.68 (9.6%)	
AML with <i>CBFB::MYH11</i> fusion	56 (9.5%)	51 (10.1%)	5 (5.6%)		9.08 (6.5%)	4.54 (6.5%)	4.54 (6.5%)	
AML with <i>BCR::ABL1</i> fusion	4 (0.7%)	4 (0.8%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	0 (0.0%)	
AML with <i>KMT2A</i> rearrangement	48 (8.1%)	44 (8.8%)	4 (4.4%)		7.47 (5.4%)	3.74 (5.4%)	3.74 (5.4%)	
AML with <i>NUP98</i> rearrangement	6 (1.0%)	6 (1.2%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	0 (0.0%)	
AML with <i>NPM1</i> mutation	121 (20.4%)	97 (19.7%)	24 (26.7%)		34.95 (25.2%)	17.47 (25.2%)	17.47 (25.2%)	
AML with <i>CEBPA</i> mutation	119 (20.1%)	105 (20.9%)	14 (15.6%)		24.77 (17.9%)	12.38 (17.9%)	12.38 (17.9%)	
AML, myelodysplasia-related	63 (10.7%)	51 (10.1%)	12 (13.3%)		17.32 (12.5%)	8.66 (12.5%)	8.66 (12.5%)	
AML with other defined genetic alterations	98 (16.6%)	84 (16.7%)	14 (15.6%)		21.10 (15.2%)	10.55 (15.2%)	10.55 (15.2%)	
AML, defined by differentiation	27 (4.6%)	19 (3.8%)	8 (8.9%)		10.72 (7.7%)	5.36 (7.7%)	5.36 (7.7%)	
Myeloid sarcoma	3 (0.5%)	3 (0.6%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	0 (0.0%)	
MRD status after induction therapy, n (%)				< 0.001				< 0.001
CR after one cycle of induction								
Negative MRD	317 (53.6%)	276 (55.1%)	41 (45.6%)		68.91 (49.7%)	34.45 (49.7%)	34.45 (49.66%)	
Positive MRD	145 (24.5%)	127 (25.4%)	18 (20.0%)		30.88 (22.3%)	15.44 (22.3%)	15.44 (22.25%)	
CR after two cycles of induction								
Negative MRD	15 (2.5%)	12 (2.4%)	3 (3.3%)		4.44 (3.2%)	2.22 (3.2%)	2.22 (3.20%)	
Positive MRD	44 (7.5%)	39 (7.8%)	5 (5.6%)		8.66 (6.2%)	4.33 (6.2%)	4.33 (6.24%)	
NR	54 (9.1%)	39 (7.8%)	15 (16.7%)		20.36 (14.7%)	10.18 (14.7%)	10.18 (14.67%)	
NA	16 (2.7%)	8 (1.6%)	8 (8.9%)		5.52 (4.0%)	2.76 (4.0%)	2.76 (3.98%)	

Abbreviations: allo-HCT, allogeneic hematopoietic cell transplantation; AML, acute myeloid leukemia; CR, complete response; ELN 2017 European LeukemiaNet 2017; MDT, multidisciplinary team; MRD: measurable residual disease; NA, not available; NR: non-remission; SMD, standardized mean difference.

Table 1. Comparison of MDT and non-MDT patients (continued)

	Before weighting				After weighting			
	Total (n = 591)	MDT (n = 501)	Non-MDT (n = 90)	SMD	Total (n = 138.76)	MDT (n = 69.38)	Non-MDT (n = 69.38)	SMD
Allo-HCT, n (%)								
No	259 (43.8%)	189 (37.7%)	70 (77.8%)	< 0.001	83.01 (59.8%)	29.31 (42.3%)	53.70 (77.41%)	0.768
Yes	332 (56.2%)	312 (62.3%)	20 (22.2%)		55.75 (40.2%)	40.07 (57.7%)	15.68 (22.59%)	0.254
Relapse, n (%)	175 (29.6%)	139 (27.7%)	36 (40.0%)	0.026	45.95 (33.1%)	18.85 (27.2%)	27.09 (39.05%)	0.038
Death, n (%)	175 (29.6%)	132 (26.4%)	43 (47.8%)	< 0.001	52.73 (38.0%)	22.21 (32.0%)	30.52 (43.98%)	0.248

Abbreviations: allo-HCT, allogeneic hematopoietic cell transplantation; AML, acute myeloid leukemia; CR, complete response; ELN 2017 European LeukemiaNet 2017; MDT, multidisciplinary team; MRD: measurable residual disease; NA, not available; NR: non-remission; SMD, standardized mean difference.

not recommended for allo-HCT, 61 (32.8%) nevertheless underwent transplantation.

### 3.3. Long-term impact of MDT on survival

Within the MDT program, 79.7% of patients (n = 251) received allo-HCT as recommended, and 67.2% of patients (n = 125) received BAT as recommended. Among patients who adhered to MDT recommendations, outcome analyses showed comparable 3-year OS (78.5% vs. 67.8%; p = 0.26; Supplementary Figure S2A, <https://www.biosciencetrends.com/action/getSupplementalData.php?ID=285>) and CIR (20.2% vs. 33.0%; p = 0.61; Supplementary Figure S2B, <https://www.biosciencetrends.com/action/getSupplementalData.php?ID=285>) between those receiving allo-HCT and those receiving BAT.

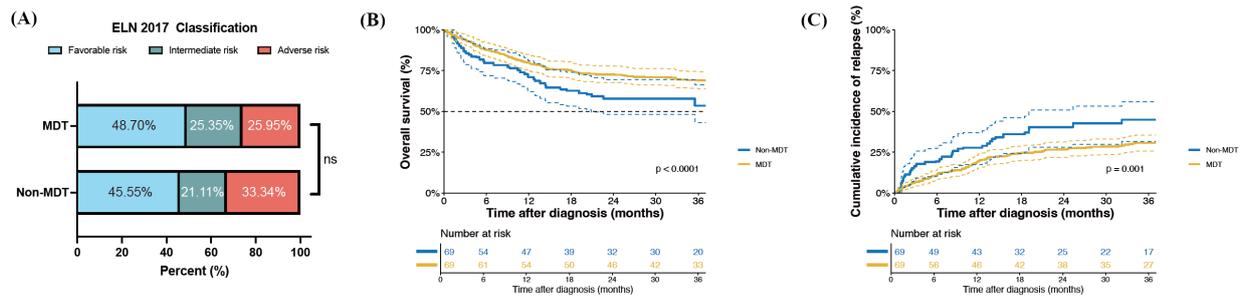
Among patients who were recommended for allo-HCT, those who proceeded to transplantation had significantly improved 3-year OS (78.6% vs. 34.8%; p < 0.0001; Figure 3A) and lower 3-year CIR (20.2% vs. 62.0%; p = 0.0011; Figure 3D) compared with those who did not undergo allo-HCT. By contrast, among patients who were not recommended for allo-HCT, allo-HCT and BAT were associated with similar 3-year OS (77.6% vs. 67.8%; p = 0.21; Figure 3B), while allo-HCT was associated with a higher 3-year CIR compared with BAT (41.7% vs. 33.0%; p = 0.025; Figure 3E).

Among non-MDT attendees, neither allo-HCT nor BAT was associated with significant differences in clinical outcomes (3-year OS: 61.6% vs. 49.2%, p = 0.38; three-year CIR: 37.5% vs. 47.8%, p = 0.32) (Figure 3C and 3F). Notably, 95.1% of patients who underwent allo-HCT contrary to MDT recommendations were classified as favorable-risk according to the ELN 2017 criteria (Supplementary Figure S3A, <https://www.biosciencetrends.com/action/getSupplementalData.php?ID=285>).

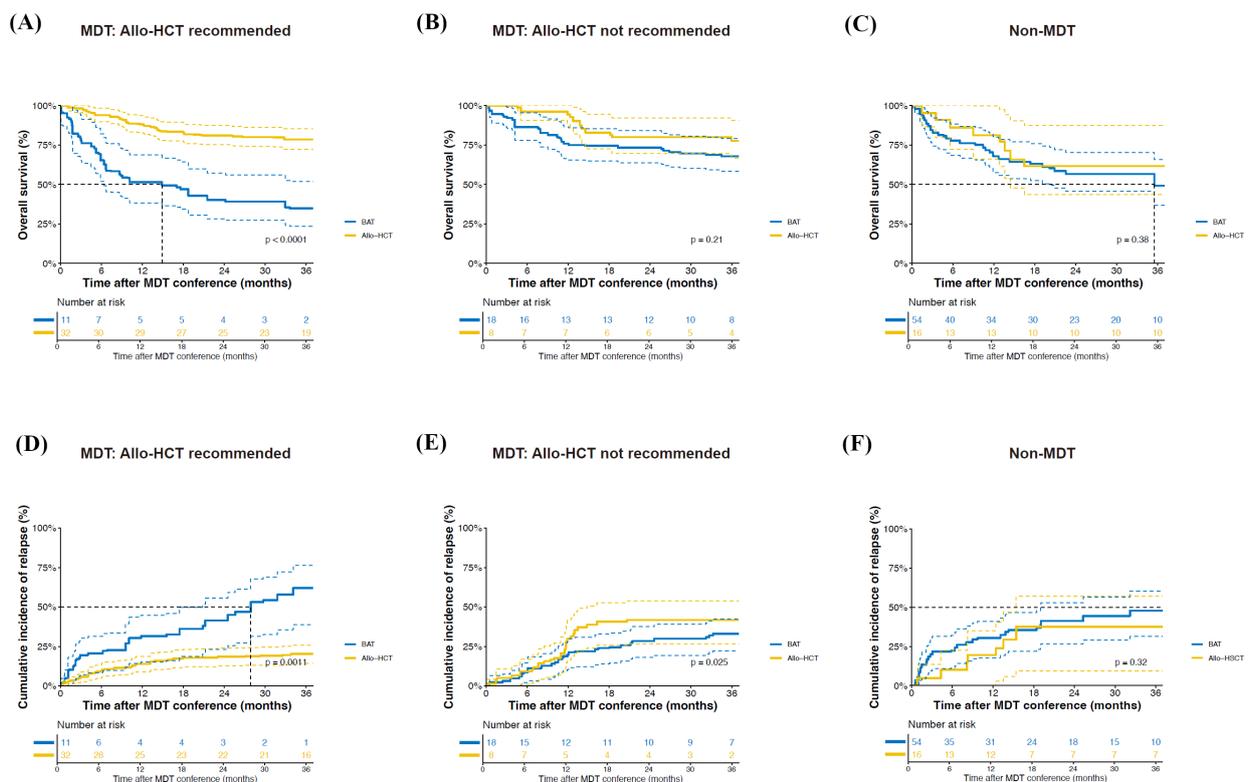
Among transplant recipients in the non-MDT, MDT-not-recommended, and MDT-recommended groups, patients in the non-MDT group had the lowest 3-year OS (61.6% vs. 77.6% vs. 78.6%, p = 0.02) (Supplementary Figure S3B, <https://www.biosciencetrends.com/action/getSupplementalData.php?ID=285>), whereas patients in the MDT-recommended group had the lowest 3-year CIR (37.5% vs. 41.7% vs. 20.2%, p = 0.01) (Supplementary Figure S3C, <https://www.biosciencetrends.com/action/getSupplementalData.php?ID=285>).

### 3.4. Identification of transplant beneficiaries by MDT evaluation

During MDT evaluation, experts assessed the potential benefit of allo-HCT based on ELN risk stratification and response to induction therapy. Logistic regression analysis revealed that intermediate-risk (OR [95% CI], 63.252 [5.758–3385.266]; p = 0.006) and adverse-risk disease (OR [95% CI], 28.128 [3.222–768.62];



**Figure 2. Overall survival (OS) of patients who attended multidisciplinary team (MDT) conferences and those who did not. Distribution of ELN 2017 risk stratification (A), and comparison of OS (B) and cumulative incidence of relapse (CIR) (C) between MDT attendees and non-attendees.**



**Figure 3. Impact of multidisciplinary team (MDT) recommendations on survival outcomes in patients with acute myeloid leukemia (AML). Comparison of overall survival (OS) among patients who were recommended for allogeneic hematopoietic cell transplantation (allo-HCT) (A), not recommended for allo-HCT (B), or who declined MDT evaluation (C) and underwent different treatment modalities. Comparison of cumulative incidence of relapse (CIR) for patients with AML who were recommended for allo-HCT (D), who were not recommended for allo-HCT (E), and who refused MDT (F), and underwent different treatment modalities.**

$p = 0.011$ ) were the main factors associated with MDT recommendations for transplantation (Table 2). Among patients who were recommended for allo-HCT, transplantation was associated with improved 3-year OS compared with BAT in those with intermediate- or adverse-risk disease (favorable risk: 81.3% vs. 61.6%,  $p = 0.16$ ; intermediate risk: 78.5% vs. 25.5%,  $p < 0.0001$ ; adverse risk: 76.8% vs. 32.6%,  $p < 0.0001$ ; Figures 4A-C). Allo-HCT was also associated with a lower 3-year CIR across all ELN risk categories (favorable risk: 20.0% vs. 60.9%,  $p = 0.022$ ; intermediate risk: 17.8% vs. 64.5%,  $p = 0.00012$ ; adverse risk: 22.8% vs. 58.6%,

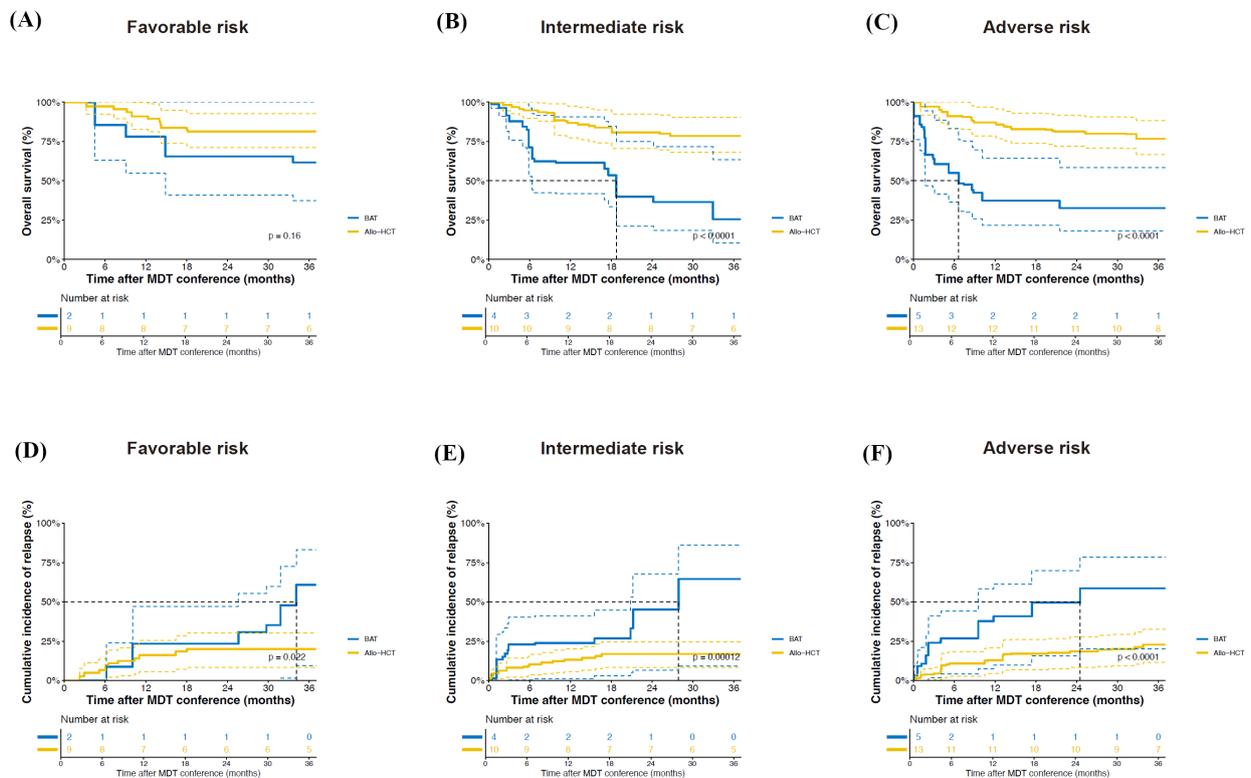
$p < 0.0001$ ; Figures 4D-F). By contrast, we found no significant differences in outcomes between allo-HCT and BAT among patients who were recommended for BAT across different risk stratifications (Supplementary Figure S4, <https://www.biosciencetrends.com/action/getSupplementalData.php?ID=285>) or among patients who declined MDT evaluation (Supplementary Figure S5, <https://www.biosciencetrends.com/action/getSupplementalData.php?ID=285>).

Factors associated with survival outcomes were further examined using Cox proportional hazards regression analysis (Table 3). MDT involvement (HR

**Table 2. Logistic regression analysis of transplantation recommendation by MDT**

Variable	Univariate			Multivariable		
	OR	95%CI	p value	OR	95%CI	p value
Diagnosis year						
2017-2019	1.0	Ref		1.0	Ref	
2020-2022	3.342	0.952-12.472	0.063	3.342	0.952-12.472	0.063
Sex						
Male	1.0	Ref		1.0	Ref	
Female	2.037	0.658-6.598	0.223	2.037	0.658-6.598	0.223
Age						
15-39	1.0	Ref		1.0	Ref	
40-54	0.621	0.150-2.377	0.492	0.621	0.150-2.377	0.492
55-65	0.403	0.084-1.794	0.237	0.403	0.084-1.794	0.237
ELN 2017 stratification						
Favorable	1.0	Ref		1.0	Ref	
Intermediate	29.249	4.317-795.899	0.005	29.249	4.317-795.899	0.005
Adverse	18.610	3.296-244.077	0.004	18.610	3.296-244.077	0.004
MRD status after induction therapy						
CR after one cycle of induction						
Negative MRD	1.0	Ref		1.0	Ref	
Positive MRD	1.748	0.453-7.678	0.430	1.748	0.453-7.678	0.430
CR after two cycles of induction						
Negative MRD	3.104	0.088-6138.122	0.587	3.104	0.088-6138.122	0.587
Positive MRD	9.017	0.680-4981.675	0.212	9.017	0.680-4981.675	0.212
NR	1.047	0.095-14.548	0.969	1.047	0.095-14.548	0.969
NA	3.445	0.026-Inf	0.662	3.445	0.026-Inf	0.662

Abbreviations: AML, acute myeloid leukemia; CI: confidence interval; CR: complete response; ELN 2017 European LeukemiaNet 2017; MDT, multidisciplinary team; MRD: measurable residual disease; NA, not available; NR: non-remission, OR: odds ratio.



**Figure 4. Long-term outcomes of multidisciplinary team (MDT) consultation attendees who were recommended for allogeneic hematopoietic cell transplantation (allo-HCT) and received different consolidation strategies.** Comparison of overall survival (OS) in patients with favorable-risk acute myeloid leukemia (AML) (A) and intermediate- or adverse-risk AML (B–C) who underwent allo-HCT or best available therapy (BAT). Comparison of cumulative incidence of relapse (CIR) in patients with favorable-risk AML (D) and intermediate- or adverse-risk AML (E–F) who underwent allo-HCT or BAT. \*\*\*\* $p < 0.0001$ .

[95% CI], 0.647 [0.450–1.008];  $p = 0.055$ ) and allo-HCT (HR [95% CI], 0.425 [0.269–0.672];  $p < 0.001$ ) were associated with improved long-term survival. Among MDT attendees, the distribution of ELN risk differed markedly between patients who were recommended for allo-HCT (favorable risk, 23.49%; intermediate risk, 37.78%; adverse risk, 38.73%) and those who were not (favorable risk, 91.40%; intermediate risk, 4.30%; adverse risk, 4.30%;  $p < 0.0001$ ; Supplementary Table S2, <https://www.biosciencetrends.com/action/getSupplementalData.php?ID=285>). Among MDT attendees, ELN risk category was not independently associated with survival after accounting for treatment allocation (intermediate risk: HR [95% CI], 1.408 [0.780–2.542],  $p = 0.257$ ; adverse risk: HR [95% CI], 1.340 [0.754–2.382],  $p = 0.318$ ).

### 3.5. Post-induction MRD and MDT transplant recommendations

Logistic regression analysis did not identify post-induction MRD as a significant factor influencing transplant recommendations made by the MDT (Table 2). Cox analysis revealed that achieving CR beyond one cycle of induction and non-remission (NR) status were

associated with poorer long-term survival outcomes in the overall cohort (Table 3). These findings suggest that post-induction MRD status warrants closer consideration in MDT decision-making.

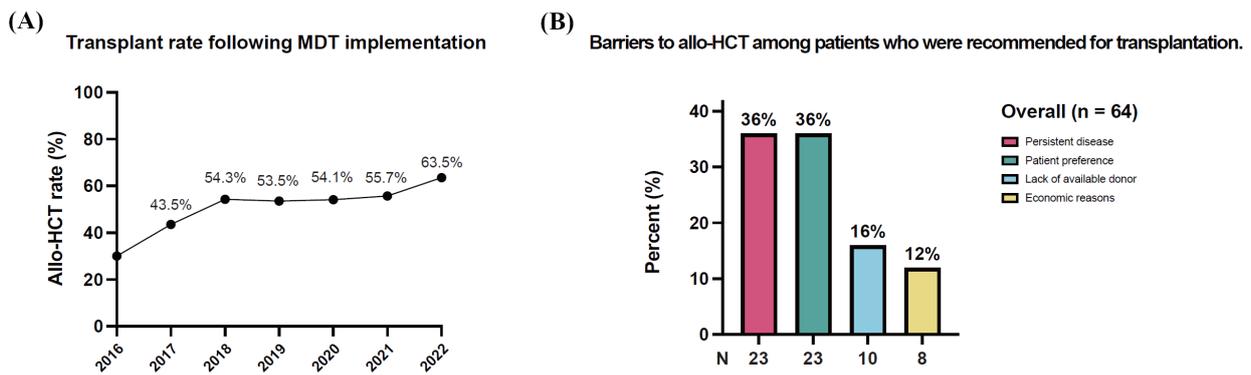
Among MDT attendees with favorable-risk disease, the effectiveness of BAT declined progressively in patients who achieved CR after one cycle of induction, after two cycles of induction, or who remained in NR status (3-year OS: 74.1% vs. 38.3% vs. 0%,  $p < 0.0001$ ; 3-year CIR: 29.6% vs. 61.7% vs. 38.8%,  $p = 0.00021$ ) (Supplementary Figures S6A and S6C, <https://www.biosciencetrends.com/action/getSupplementalData.php?ID=285>). By contrast, allo-HCT was associated with relatively stable outcomes across different post-induction response categories in favorable-risk patients (3-year OS: 79.2% vs. 69.4% vs. 100%,  $p = 0.58$ ; 3-year CIR: 30.7% vs. 30.6% vs. 0%,  $p = 0.70$ ) (Supplementary Figures S6B and S6D, <https://www.biosciencetrends.com/action/getSupplementalData.php?ID=285>).

Among MDT attendees with intermediate- or adverse-risk disease, allo-HCT was associated with higher 3-year OS compared with BAT across all response categories (CR after one cycle of induction: 80.1% vs. 52.6%,  $p < 0.0001$ ; CR after two cycles of induction: 87.7% vs. 25.6%,  $p < 0.0001$ ; NR: 64.4% vs. 0%,  $p <$

**Table 3. Cox analysis of survival following initial diagnosis in our patients**

Variable	Univariate			Multivariable		
	HR	95%CI	<i>p</i> value	HR	95%CI	<i>p</i> value
Diagnosis year						
2017-2019	1.0	Ref		1.0	Ref	
2020-2022	0.921	0.616-1.377	0.689	1.080	0.704-1.657	0.724
Sex						
Male	1.0	Ref		1.0	Ref	
Female	0.785	0.529-1.165	0.229	0.778	0.507-1.192	0.249
Age						
15-39	1.0	Ref		1.0	Ref	
40-54	1.579	0.953-2.618	0.076	1.412	0.831-2.400	0.202
55-65	2.340	1.388-3.946	0.001	1.340	0.754-2.382	0.318
ELN 2017 stratification						
Favorable	1.0	Ref		1.0	Ref	
Intermediate	2.128	1.299-3.487	0.003	1.408	0.780-2.542	0.257
Adverse	2.728	1.732-4.298	< 0.001	1.567	0.890-2.756	0.119
MRD status after induction therapy						
CR after one cycle of induction						
Negative MRD	1.0	Ref		1.0	Ref	
Positive MRD	1.334	0.738-2.411	0.340	1.436	0.778-2.649	0.247
CR after two cycles of induction						
Negative MRD	3.303	1.256-8.688	0.015	3.150	1.263-7.859	0.014
Positive MRD	3.346	1.882-5.947	< 0.001	3.420	2.051-5.701	< 0.001
NR	9.249	5.714-14.971	< 0.001	10.045	5.305-19.019	< 0.001
NA	3.560	1.599-7.925	0.002	3.478	1.444-8.376	0.005
MDT						
No	1.0	Ref		1.0	Ref	
Yes	0.635	0.438-0.920	0.017	0.674	0.450-1.008	0.055
Treatment						
BAT	1.0	Ref		1.0	Ref	
Allo-HCT	0.491	0.330-0.730	< 0.001	0.425	0.269-0.672	< 0.001

*Abbreviations:* allo-HCT, allogeneic hematopoietic cell transplantation; AML, acute myeloid leukemia; BAT, best available therapy; CI: confidence interval; CR: complete response; ELN 2017 European LeukemiaNet 2017; HR: hazard ratio; MDT, multidisciplinary team; MRD: measurable residual disease; NA, not available; NR: non-remission.



**Figure 5. Transplantation practice in the multidisciplinary team (MDT) era. (A)** Increase in allogeneic hematopoietic cell transplantation (allo-HCT) rates following MDT implementation. **(B)** Barriers to allo-HCT among patients who were recommended for, but did not undergo, allo-HCT.

0.0001) and with lower 3-year CIR (CR after one cycle of induction: 20.7% vs. 55.3%,  $p < 0.0001$ ; CR after two cycles of induction: 27.2% vs. 100%,  $p = 0.0028$ ; non-remission: 19.5% vs. 100%,  $p = 0.022$ ) (Supplementary Figures S7, <https://www.biosciencetrends.com/action/getSupplementalData.php?ID=285>).

### 3.6. MDT increases allo-HCT availability

The allo-HCT rate in the overall cohort showed a sustained annual increase, reaching 63.5% of all non-APL AML patients by 2022 and 79.4% among patients enrolled in the MDT program (Figure 5A). The most common reasons for failure to proceed to allo-HCT were persistent or relapsed disease (36%) and patient preference (36%), followed by lack of available donors (16%) and economic factors (12%) (Figure 5B).

Comparison of baseline characteristics between patients who were recommended for and underwent allo-HCT ( $n = 251$ ) and those who were recommended for but did not undergo allo-HCT ( $n = 64$ ) showed no significant differences in age, sex, or ELN 2017 risk stratification between the two groups (Supplementary Table S3, <https://www.biosciencetrends.com/action/getSupplementalData.php?ID=285>). These findings indicate that baseline clinical characteristics were broadly comparable between patients who did and did not proceed to transplantation following MDT recommendation.

## 4. Discussion

In this retrospective study, we evaluated the effectiveness of MDT evaluation in guiding optimal post-remission therapy for 653 patients with non-APL AML. Patients who attended MDT conferences had superior 3-year OS (68.9% vs. 53.5%,  $p < 0.0001$ ) and a lower 3-year CIR (30.7% vs. 44.9%;  $p < 0.0001$ ) compared with those who did not attend MDT. The higher rate of allo-HCT among MDT attendees is likely a key contributor to this survival difference. Among patients who were initially

recommended for allo-HCT following MDT evaluation, the transplantation rate reached 79%, and remained high at 66.9% among those with intermediate- to adverse-risk AML. The most common reason for failure to proceed to transplantation was persistent or relapsed disease, consistent with findings from prior studies (11,19).

Previous reports have highlighted substantial attrition between eligibility for allo-HCT and actual transplantation. In a prospective analysis conducted between 2001 and 2003, 38% of patients achieved CR after induction therapy, of whom 54% were referred for transplant consultation; however, only 26% of those referred ultimately underwent allo-HCT (10). Similarly, a retrospective analysis from the Fred Hutchinson Cancer Research Center conducted in 2013 reported that 67% of newly diagnosed patients with intermediate- to adverse-risk AML in first CR underwent allo-HCT (11). When accounting for patients who did not proceed to transplantation because of early death, failure to achieve remission, or loss to follow-up, the overall transplant rate declined to 48% (11). More recent studies have reported utilization rates of approximately 57–66% among patients with acute leukemia who were recommended for allo-HCT (19,20).

An important factor contributing to the higher allo-HCT rate observed in our study may be the widespread use of haploidentical donors (HIDs), which accounted for up to approximately 80% of transplants in our cohort. Routine use of HIDs was not reported in a comparable study by Pagel *et al.* (11) and most earlier reports (10,19). However, because HID transplantation is not yet widely implemented in many primary hospitals, increasing timely referral of eligible patients with AML to transplant-capable centers might further improve cure rates. Consistent with the growing availability of HLA-mismatched donor sources, including HIDs, only 16% of patients in our study cited lack of a suitable donor as a barrier to allo-HCT. Recent data from the Chinese Blood and Marrow Transplantation Registry Group show that the number of haploidentical transplants has increased steadily since 2008 and that HID transplantation has

become the predominant transplant modality for AML across major transplant centers in China (31). In this context, further improvements in induction regimens (particularly through the incorporation of targeted agents and immunotherapy) might increase the proportion of patients who are able to proceed to allo-HCT. Patient preference was the second most common reason for not undergoing transplantation. We expect that enhancing patient education and confidence regarding the safety and benefits of allo-HCT would help increase transplant utilization and, ultimately, improve long-term outcomes for patients with AML.

Many factors can hinder the implementation of MDT programs, including not only material and resource limitations but also less visible barriers to intra- and inter-professional collaboration (21). In our MDT process, recommendations regarding patient suitability for allo-HCT as consolidation therapy were comprehensively discussed during two MDT visits within a 4-month period, taking into account disease characteristics, donor availability, performance status, and response to therapy.

An important observation from the present study was that MDT attendees experienced better survival outcomes than non-attendees. Several factors might contribute to this difference. First, patients who attended MDT evaluation may have demonstrated better treatment adherence, which could translate into improved survival. Second, the utilization rate of allo-HCT was substantially higher in the MDT group (79.7%) than in the non-MDT group (22.2%). As shown in our analyses, allo-HCT was associated with favorable outcomes across risk stratifications, with a 3-year OS of up to 78.6% and a 3-year CIR as low as 20.2% among patients who underwent transplantation following MDT recommendation. These findings might explain, in part, the survival advantage observed among MDT attendees. Taken together, our experience suggests that patients with intermediate- or high-risk AML should be prioritized for allo-HCT during consolidation therapy, whereas in patients with favorable-risk disease, transplantation should be considered primarily for those with suboptimal responses to induction therapy.

This study has several limitations to consider. First, owing to its retrospective design, 16.1% of patients (126/779) were lost to follow-up, primarily because of missing or incorrect contact information. Sensitivity analyses using best-case and worst-case assumptions for patients lost to follow-up yielded results consistent with the primary analysis, with no material change in the direction or significance of the estimated treatment effects (Supplementary Table S4, <https://www.biosciencetrends.com/action/getSupplementalData.php?ID=285>). Second, MRD data during induction or consolidation therapy and before allo-HCT were insufficient to allow a detailed analysis of the impact of MRD on MDT decision-making. Third, as a referral center, our cohort included a higher proportion of patients with intermediate- and

adverse-risk disease, resulting in an ELN risk distribution that differs from those reported in other AML cohorts (32-34), which may introduce selection bias. Fourth, only patients admitted to our center for induction therapy were enrolled, whereas patients initially treated at community centers were referred to our institution primarily for allo-HCT evaluation. This referral pattern may limit the generalizability of our findings and highlights the need to further develop coordinated strategies and partnerships with community centers. In addition, although approximately 7.2% of patients with AML harbor *NUP98* rearrangements (35), only six such cases were identified in our cohort. This finding likely reflects the fact that RNA sequencing for genetic abnormalities was implemented at our center only in 2019, indicating incomplete molecular characterization in earlier years. Accordingly, MDT-based recommendations for patients with AML may benefit from further refinement as more comprehensive molecular profiling becomes available.

## 5. Conclusions

In summary, we demonstrate that MDT evaluation can support optimized treatment decision-making, particularly with respect to allo-HCT recommendations for patients with intermediate- and adverse-risk AML. Early disease progression and patient preference remained major barriers to transplantation. Our findings suggest that further improvements in allo-HCT utilization in China may depend on expanding MDT implementation to facilitate earlier and more efficient transplant workup, broader use of HLA-mismatched donors, continued refinement of induction regimens, and optimization of allo-HCT strategies for patients with AML who do not achieve remission.

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**Conflict of Interest:** The authors have no conflicts of interest to disclose.

**Availability of data and materials:** The datasets generated during and analyzed during the current study are available from the corresponding author (hu\_xiaoxia@126.com) on reasonable request.

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- §These authors contributed equally to this work.
- \*Address correspondence to:  
 Xiaoxia Hu, Junmin Li, Jiong Hu, and Yang He, Shanghai Institute of Hematology, State Key Laboratory of Medical Genomics, National Research Center for Translational Medicine at Shanghai, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, 197 Ruijin Er Road, Shanghai 200025, China.  
 E-mail: hu\_xiaoxia@126.com (HX), lijunmin@medmail.com.cn (LJ), hj10709@rjh.com.cn (HJ), hy21369@rjh.com.cn (HY)
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