Hematopoietic stem cell transplantation for acute myeloid leukemia: Brazilian Society of Cell Therapy and Bone Marrow Transplantation Consensus

Mariana Pinto Pereira[1], Maura Rosane Valério Ikoma-Colturato[2], Vaneuza Araujo Funke[3], Beatriz Stela Gomes de Souza Pitombeira[4], Eduardo Jose de Alencar Paton[5], Adriano Arantes[6], Karine Sampaio Nunes Barroso[4], Miriam Perlingeiro Beltrame[7], Gustavo Bettarello[8], Camila de Pádua Coelho Hugo[5], Tharsis Cardoso Ferreira dos Santos[9], Felipe Magalhaes Furtado[10], Elizabeth Xisto Souto[6], Fernando Barroso Duarte[4], Lucia Silla[1*]

1. Hospital de Clínicas de Porto Alegre – Porto Alegre (RS), Brazil.
2. Hospital Amaral Carvalho – Jaú (SP), Brazil.
3. Universidade Federal do Paraná – Hospital de Clínicas – Curitiba (PR), Brazil.
4. Hospital Universitário Walter Cantídio – Fortaleza (CE), Brazil.
5. Oncoclínicas – Cancer Center – Nova Lima (MG), Brazil.
6. Hospital Israelita Albert Einstein – São Paulo (SP), Brazil.
7. Hospital Erasto Gaertner – Curitiba (PR), Brazil.
8. Hospital DF Star – Brasília (DF), Brazil.
9. Hemocentro – São José do Rio Preto (SP), Brazil.
10. Hospital da Criança – Brasília (DF), Brazil.

***Corresponding author:** dralucia.silla@gmail.com

Section editor: Abrahão Elias Hallack Neto

Received: July 30, 2026 • **Accepted:** Aug. 28, 2026

ABSTRACT

This document updates the 2023 Brazilian Society of Cell Therapy and Bone Marrow Transplantation (SBTMO) consensus on allogeneic hematopoietic stem cell transplantation (HSCT) for acute myeloid leukemia (AML), incorporating the 2022 and 2024 European LeukemiaNet (ELN) risk classifications, the 2025 ELN-DAVID measurable residual disease (MRD) recommendations, recent induction trials, and the 2025 European Society for Blood and Marrow Transplantation (EBMT) transplant indications. MRD monitoring, assessed by quantitative polymerase chain reaaction, next-generation sequencing, or multiparameter flow cytometry, now guides transplant timing alongside ELN risk category, refining decisions in intermediate-risk patients and informing pre- and post-transplant management. Allogeneic HSCT remains indicated for adverse-risk AML and second complete remission regardless of MRD status, while favorable-risk patients generally avoid transplant unless MRD persists after consolidation. For elderly patients, chronological age alone should not exclude HSCT candidacy; comprehensive geriatric assessment and alternative donor sources have expanded access, supported by Brazilian regulatory changes raising the eligibility age to 75. Conditioning strategy, graft-*versus*-host disease prophylaxis with post-transplant cyclophosphamide, stem cell source selection, and donor immunogenetic screening are addressed, alongside emerging post-transplant maintenance therapies for high-risk molecular subgroups. Novel cellular therapies—CAR-T and CAR-NK cells—remain investigational, limited by antigen escape and short persistence, requiring consolidation with allogeneic HSCT. This consensus provides evidence-graded recommendations to standardize transplant decision-making for AML across Brazilian centers, reflecting the rapidly evolving therapeutic and diagnostic landscape.

Keywords: Leukemia, Myeloid, Acute, Hematopoietic Stem Cell Transplantation, Brazil.

INTRODUCTION

This document constitutes the update to the Brazilian Society of Bone Marrow Transplantation (SBTMO) recommendations on allogeneic hematopoietic stem cell transplantation (HSCT) for acute myeloid leukemia (AML). The previous version, published in the *Journal of Bone Marrow Transplantation and Cellular Therapy* in 2023[1], already incorporated the European LeukemiaNet (ELN) 2022 recommendations[2]. The present update integrates data from the ELN 2024 guidelines[3]—specifically developed for less-intensive therapies—, the most recent induction clinical trials, new evidence on measurable residual disease (MRD) according to ELN David for AML MRD working party 2025, and the 2025 European Society for Blood and Bone Marrow Transplantation (EBMT) recommendations for transplant indications[4].

In recent years, there have been significant advances in the field of HSCT for AML: approval of new targeted agents (midostaurin, gilteritinib, enasidenib, ivosidenib, gemtuzumab ozogamicin) and consolidation of azacitidine + venetoclax as the standard regimen for patients ineligible for intensive chemotherapy[5]. In parallel, MRD monitoring has established itself as an essential tool for HSCT decision-making, going beyond the ELN risk category as the sole criterion[4,6].

It is equally important to emphasize that the HSCT indication should be considered at the time of diagnosis, based on the estimated relapse risk for each risk category, MRD status throughout treatment, the patient's clinical condition, and donor availability. HSCT remains the gold standard for patients with intermediate- and adverse-risk AML, being the only modality with sustained curative potential in these populations.

DIAGNOSIS AND RISK STRATIFICATION

Diagnostic criteria and classification

AML diagnosis is currently guided by two parallel classification systems: the 5th edition of the World Health Organization's document[7] and the International Consensus Classification[8], which differ in certain diagnostic criteria despite a shared molecular basis.

The diagnosis of AML by the WHO[8] is based on the identification of ≥ 20% blasts in the bone marrow or peripheral blood. Exceptions include AML with the defining genetic abnormalities—including *PML-RARA*, *RUNX1-RUNX1T1*, *CBFB-MYH11*, *RBM15-MRTFA*, *DEK-NUP214*, rearrangements of *KMT2A*, *MECOM*, or *NUP98*, and *NPM1* mutation—, meaning these diagnoses can be made regardless of blast percentage. The exceptions that still require the full 20% threshold are *BCR-ABL1* fusion and *CEBPA*-mutated AML. According to the ICC[8], in patients with defining mutations—such as NPM1, in-frame bZIP *CEBPA* mutations, or recurrent translocations—, the diagnosis is confirmed with ≥ 10% blasts (with the exception of BCR-ABL1, which still requires 20%).

Complete diagnostic workup must include bone marrow morphology, multiparameter flow cytometry immunophenotyping, conventional cytogenetics (karyotype), fluorescence *in-situ* hybridization when indicated, and a comprehensive molecular panel by polymerase chain reaction and/or next-generation sequencing (NGS) for the main mutations: *FLT3-ITD/TKD*, *NPM1*, *IDH1*, *IDH2*, *CEBPA*, *TP53*, *RUNX1*, *ASXL1*, *SF3B1*, *SRSF2*, and other prognostically relevant genes. The *FLT3-ITD* allelic ratio must be quantified, as it impacts risk stratification.

The WHO[7] recognizes the following AML categories: AML with recurrent genetic abnormalities (renamed from "recurrent genetic abnormalities"[9]), AML, myelodysplasia-related (defined by cytogenetic or gene mutation criteria—not morphologic dysplasia alone), secondary myeloid neoplasms (including those following cytotoxic therapy), myeloid neoplasms with germline predisposition, and AML not otherwise specified.

Hereditary myeloid malignancy syndromes (HMMS), including germline mutations in *DDX41*, *RUNX1*, *CEBPA*, *TP53*, and DNA repair genes, should be actively investigated when there is a personal or family history of cytopenias, hematological malignancies, or suggestive mutations in the somatic molecular profile[7].

European LeukemiaNet 2022 risk stratification: intensive therapy

The ELN 2022 is the reference standard for risk stratification in patients receiving intensive chemotherapy, being widely validated in multicenter studies. It encompasses cytogenetic abnormalities and molecular mutations[2] (Table 1).

Table 1. European LeukemiaNet risk stratification: intensive therapy.

Risk category	Genetic abnormality
Favorable	t(8;21)(q22;q22.1); *RUNX1::RUNX1T1* inv(16)(p13.1q22) or t(16;16)(p13.1;q22); *CBFB::MYH11* Mutated *NPM1* without *FLT3-ITD* bZIP in-frame mutated *CEBPA*
Intermediate	Mutated *NPM1* with *FLT3-ITD* Wild-type *NPM1* with *FLT3-ITD* (without adverse-risk genetic lesions) t(9;11)(p21.3;q23.3); *MLLT3::KMT2A* Cytogenetic and/or molecular abnormalities not classified as favorable or adverse
Adverse	t(6;9)(p23;q34.1); *DEK::NUP214* t(v;11q23.3); *KMT2A* rearranged t(9;22)(q34.1;q11.2); *BCR::ABL1* t(8;16)(p11;p13); *KAT6A::CREBBP* inv(3)(q21.3q26.2) or t(3;3); *GATA2, MECOM*(EVI1) t(3q26.2;v); MECOM(EVI1)-rearranged -5 or del(5q); -7; -17/abn(17p) Complex karyotype, monosomal karyotype Mutated *RUNX1*; *ASXL1*; *SF3B1*; *SRSF2*; *STAG2*; *U2AF1*; *ZRSR2*; *BCOR*; *EZH2*; *TP53**

ITD: internal tandem duplication; high/low: allelic ratio; *TP53 mutation at a variant allele fraction of at least 10%, irrespective of the TP53 allelic status (mono- or biallelic mutation). Source: Adapted from Döhner et al.[2].

European LeukemiaNet 2024 risk stratification: less-intensive therapies

In 2024, the ELN published a risk classification specifically for AML patients receiving less-intensive therapies (hypomethylating agent ± venetoclax)[3], recognizing that the ELN 2022 stratification[2], developed for intensive chemotherapy, does not adequately discriminate outcomes in this population (Table 2). The Beat-AML 2024 model demonstrated that the ELN 2022 does not differentiate favorable from intermediate risk in patients ≥ 60 years old receiving less-intensive therapy (two-year overall survival = 47 *versus* 50%, respectively; $p = 0.71$)[10]. In this new classification, *IDH1*, *IDH2*, *NPM1*, and *DDX41* mutations are categorized as favorable in the absence of co-occurring adverse mutations, whereas *TP53*-mutated AML is always adverse regardless of *FLT3* status. The model was developed from pooled data from the VIALE-A phase 3 trial and a phase 1b study of azacitidine + venetoclax[11]. The limitations of this study include its inapplicability to patients with prior hypomethylating agent exposure or antecedent myeloproliferative neoplasms, as well as its inability to characterize rare gene rearrangements. Therefore, prospective validation in clinical trials and real-world datasets is still needed.

Table 2. European LeukemiaNet 2024 risk stratification: less-intensive therapy.

Risk category	Genetic abnormality (less-intensive therapy)	Key condition
Favorable	*IDH1**, *IDH2*, *NPM1*, or *DDX41* mutations (without co-occurring adverse-risk mutations) AML with MR gene mutations (*FLT3-ITD*neg, *NRAS*wt, *KRAS*wt, *TP53*wt)	*FLT3-ITD* negative No *NRAS or KRAS* or *TP53* mutation.
Intermediate	AML with MR gene mutations (*FLT3-ITD*pos and/or *NRAS*mut and/or *KRAS*mut; *TP53*wt) Other cytogenetic and molecular abnormalities (*FLT3-ITD*pos and/or *NRAS*mut and/or *KRAS*mut; *TP53*wt)	*TP53*wt - signaling comutations shift favorable → intermediate
Adverse	Mutated *TP53* (VAF ≥10%)	Universal poor prognosis: all regimens

AML: acute myeloid leukemia; MR: myelodysplasia-related; VAF: variant allele frequency; ITD: internal tandem duplication; wt: wild-type. This classification does not apply to patients who have received prior treatment with a hypomethylating agent; *favorable risk applies specifically to patients treated with AZA + IVO, regardless the presence of activating signaling gene mutations. Source: Adapted from Döhner H et al.[3].

Measurable residual disease and the transplant decision

MRD guides transplant decisions in AML, both before HSCT for risk stratification (Tables 3 and 4) and after HSCT for relapse monitoring (Table 5). ELN-DAVID 2025 consensus recommends the assay types, time points, sample types, and thresholds to optimize the use of MRD for decision making[12]. While pretransplant MRD positivity does not preclude proceeding to transplant (Table 3), post-HSCT MRD can tailor target epigenetic and immune-based interventions to reduce relapse risk while managing graft-*versus*-host disease (GVHD).

Table 3. Recommendations for the applicability of measurable residual disease in patients eligible for hematopoietic stem cell transplantation.

Recommendation	Level of evidence	Grade of recommendation
For clinical decision-making, MRD should be assessed following the specific recommendations for the assay type, time point, and tissue, according to the ELN 2025 consensus[12] (Table 4).	I	A
For clinical decision making, MRD assessment should be performed with a qualified assay as based on the guidelines for rare events in MFC[6,12].	?	A
Clinical interpretations of MRD response are termed optimal, warning, and high risk of treatment failure, according to MRD cutoff values: negative (MRD-), low-level positive (MRD-LL), and positive (MRD+). These cutoff values vary according to the method used and the AML molecular group[12] (Table 5).	II	A
Patients with ELN favorable risk and optimal MRD response (MRD-) do not require HCT.	I	A
For ELN intermediate risk patients with optimal MRD response, the value of alloHSCT may be discussed with the patient, although deferring transplantation for these patients in first remission is associated with a higher relapse incidence[13–17].	I	A
Patients in the warning category (primarily MRD-LL) should continue their planned treatment including alloHSCT, if indicated. These patients should be closely monitored for MRD relapse.	III	B
Patients with MRD+, in the categories "high risk of treatment failure" and "MRD relapse", should be considered for HSCT if eligible, regardless of the genetic risk.	II	A
ELN adverse risk patients are eligible for HSCT regardless of early MRD response, due to the high risk of relapse. Maintenance therapy after alloHSCT and post-transplant monitoring may be instructed by MRD assessment in these patients.	II	A
Pretransplant MRD positivity is not a contraindication to HSCT. It is recommended not to delay HSCT for patients who have achieved clinical remission. It improves the outcome of patients who test MRD positive compared with continued chemotherapy or observation.	IV	B
In patients with detectable MRD before HSCT, myeloablative conditioning should be considered.	II	B

MRD: measurable residual disease; ELN: European LeukemiaNet; MFC: multiparametric flow cytometry; AML: acute myeloid leukemia; alloHSCT: allogeneic hematopoietic stem cell transplantation. Source: Adapted from Heuser et al.[6] and Cloos et al.[12].

Measurable residual disease in the pre-hematopoietic stem cell transplantation setting

The methodology underlying MRD interpretation is detailed in Table 4, which specifies, marker by marker, which assay and sample type should be used, at what time point in treatment, and the cutoffs that separate negative, low-level positive and positive results. Table 5 then defines what counts as MRD relapse for each of these markers, based on conversion from undetectable to detectable or on crossing the specified threshold.

Targeted therapy for measurable residual disease in the pre-hematopoietic stem cell transplantation setting

There are discussions about the benefit from additional therapy to eradicate persistent MRD pre-HSCT for some populations, but there is no consensus, and prospective studies are needed to define this issue[20]. It must be stressed that *NPM1* mutated patients with persistent MRD at HSCT have high incidence of relapse may benefit from further treatment designed to eradicate MRD prior to HSCT. Another issue to consider is that patients who are unable to tolerate intensive conditioning may benefit from additional therapy targeting MRD.

Table 4. Recommendations for measurable residual disease assay type, time point and tissue, according to the European LeukemiaNet 2025 consensus in patients eligible for hematopoietic stem cell transplantation[15].

Marker	Assay	Time point	Tissue	MRD %	MRD burden	Qualitative MRD response
RUNX1::RUNX1T1 and *CBFB::MYH11*	qPCR	After two cycles Cht or pre-HSCT	BM	≥ 3-log10 reduction from diagnosis	Low-level/ negative	Optimal
				< 3-log10 reduction from diagnosis	Positive	Warning
		EOT (after consolidation/ HSCT)	BM	≥ 3-log10 reduction from diagnosis	Low-level/ negative	Optimal
				< 3-log10 reduction from diagnosis	Positive	High risk of failure
NPM1	qPCR	After two cycles Cht or pre-HSCT	PB	< 0.001% or undetectable (A)	Negative	Optimal
				≥ 0.001% to < 0.01% and detectable (B)	Low level positive	Warning
				≥ 0.01% and B	Positive	Warning
		EOT (after consolidation/ HSCT)	BM	< 0.001% or A	Negative	Optimal
				≥ 0.001% to < 0.1% and B	Low level positive	Warning
				≥ 0.1% and B	Positive	High risk of failure
PML::RARA	qPCR	EOT (after consolidation/ HSCT)	BM	< 0.001% or A	Negative	Optimal
				≥ 0.001% and B	Positive	Warning
FLT3-ITD	NGS	After two cycles ChT or pre-HSCT	PB or BM	< LOD (10^{-3}/10^{-4})	Negative	Optimal
				≥ LOD (10^{-3}/10^{-4})	Positive	High risk of failure
		EOT (after consolidation/ alloHSCT)	PB or BM	< LOD (10^{-3}/10^{-4})	Negative	Optimal
				≥ LOD (10^{-3}/10^{-4})	Positive	High risk of failure
MFC (LAIP or DfN)	MFC	After two cycles Cht or pre-HSCT	BM	< 0.01% or < LOD	Negative	Optimal
		EOT (after consolidation/ alloHSCT)	BM	≥ 0.01% to < 0.1% and > LOD	Low level positive	Warning
				≥ 0.1%	Positive	High risk of failure

MRD: measurable residual disease; qPCR: quantitative polymerase chain reaction; NGS: next generation sequencing; MFC: multiparametric flow cytometry; Cht: chemotherapy; HSCT: allogeneic hematopoietic cell transplantation; EOT: end of treatment; allo-HSCT: allogeneic hematopoietic stem cell transplantation; BM: bone marrow; PB: peripheral blood; LAIP or DfN: leukemia-associated immunophenotype or different from normal immunophenotype; LOD: limit of detection. Source: Adapted from Cloos et al.[12].

Table 5. Definition of measurable residual disease relapse.

Marker	Assay	Tissue	MRD relapse definition
General definition			**Conversion from undetectable to detectable MRD with the following thresholds**
NPM1	qPCR	PB	≥ 0.01% or ≥ 1log$_{10}$ if MRD+ previously
NPM1	qPCR	BM	≥ 0.1% or ≥ 1log$_{10}$ if MRD+ previously
RUNX1::RUNX1T1 and CBFB::MYH11	qPCR	PB and BM	≥ 0.1% or ≥ 1log$_{10}$ if MRD+ previously
PML::RARA	qPCR	BM	≥ 0.001% or ≥ 1log$_{10}$ if MRD+ previously
FLT3-ITD	UHS NGS	PB or BM	> LOD*
LAIP/DfN	MFC	BM	≥ 0.1%
Other gene mutation	UHS NGS	PB or BM	≥ 0.01% or ≥ 1log^{10} if MRD+ previously

MRD: measurable residual disease; qPCR: quantitative polymerase chain reaction; PB: peripheral blood; BM: bone marrow; UHS: ultra-high sensitivity; NGS: next generation sequencing; LOD: limit of detection; *not require a repeat sample as it is associated with imminent relapse. However, low-level FLT3-ITD MRD ≥ LOD but < 0.01% VAF should be promptly confirmed in a repeat sample, particularly when the FLT3-ITD clone differs from that detected at diagnosis; LAIP/DfN: leukemia-associated immunophenotype/different from normal immunophenotype; MFC: multiparameter flow cytometry. Source: Adapted from Cloos et al.[12].

Measurable residual disease in the post-hematopoietic stem cell transplantation setting

Relapse remains the leading cause of treatment failure after HSCT in AML. The identification of patients at imminent risk of relapse through MRD monitoring is essential to enable timely therapeutic intervention[4,21–25]. The median interval between molecular MRD detection by NGS and overt relapse is approximately three months, whereas MRD detection by multiparameter flow cytometry appears to precede morphologic relapse by a shorter interval, approximately two months[24,25]. A systematic compilation of available evidence was undertaken by EBMT in 2025, providing the framework for current post-transplant MRD management strategies[4].

Time points

Timing, sample source, and assay-specific considerations have been addressed in the 2025 ELN-DAVID recommendations (Table 4). For flow cytometry-based assays, bone marrow monitoring should be performed every three months for 12 months. Patients with defined molecular targets should be monitored every four to six weeks for 24 months[12]. A suggested schedule includes assessments at D+30, D+60, D+90, D+180, D+270, and D+365[12,23,26,27].

INDICATIONS FOR ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN ACUTE MYELOID LEUKEMIA

Hematopoietic stem cell transplantation in first complete remission

The indication for allogeneic HSCT in first complete remission (CR1) is based on the relapse risk estimated by ELN category, MRD status, and the patient's clinical condition (including HCT-comorbidity index and EBMT comorbidity scores)[28,29].

Recommendations are[30]:

- Adverse risk: allogeneic HSCT in CR1 is strongly indicated (A1). This is the highest priority, regardless of MRD. HSCT should be performed as soon as possible after achieving complete remission, minimizing the number of consolidation cycles;
- Intermediate risk: allogeneic HSCT in CR1 is indicated (A1), particularly in the presence of MRD positivity. In patients with MRD-negative status and low-allelic-ratio *FLT3-ITD* (per ELN 2022/2024)[2,3], the decision may be individualized through multidisciplinary discussion;
- Favorable risk: allogeneic HSCT in CR1 is not routinely indicated. High-dose cytarabine consolidation (HiDAC) is the preferred strategy. Exception: persistently MRD-positive after consolidation warrants reassessment of the HSCT indication.

The HSCT indication should be considered from the time of diagnosis, anticipating human leukocyte antigen (HLA) typing of the patient and potential family donors, so that transplantation is not delayed beyond the optimal window.

Hematopoietic stem cell transplantation in second complete remission and refractory/relapsed disease

Allogeneic HSCT should be offered to all AML patients in second complete remission (CR2) (level of evidence A1). In refractory/relapsed (R/R) disease, median overall survival is less than six months without re-induction followed by HSCT. The goal of re-induction is to achieve CR2 and consolidate with HSCT—the only strategy with curative potential in this setting. Main re-induction options include:

- FLAG-IDA: standard re-induction regimen for patients eligible for intensive therapy. CR ~45–55%[31,32];
- Gilteritinib: indicated in *FLT3-ITD/TKD*+ R/R AML. Median overall survival 9.3 *versus* 5.6 months *versus* chemotherapy (CR 21%)[33]. U.S. Food and Drug Administration/Brazilian Health Regulatory Agency approved;

- Enasidenib / ivosidenib: for *IDH2*+ / *IDH1*+ relapsed AML, respectively. May serve as a bridge to HSCT[34];
- Azacitidine + venetoclax (rescue): increasingly used as non-intensive re-induction. CR ~20–30%[35];
- For R/R AML patients: FLAMSA-RIC: sequential regimen consisted with high-dose chemotherapy followed by reduced-intensity conditioning (RIC) with three-year overall survival of ~40% and three-year disease-free survival (DFS) of ~39% (meta-analysis)[36]; or FLAMSA-BuMel[37]: two-year overall survival of 89% and two-year DFS of 68% in the HLA-matched group *versus* 34 and 34% in the haploidentical group, respectively.

In patients with active AML at the time of allogeneic HSCT, outcomes are substantially worse. Achieving CR prior to HSCT should therefore be the primary objective whenever feasible.

Hematopoietic stem cell transplantation for elderly patients

The incidence of AML increases with age, with a median age at diagnosis of 68 years old. In patients with intermediate- and high-risk, once CR is achieved, the allogeneic HSCT is considered a therapeutic strategy with a chance of cure[38]. Chronological age alone should not be considered a limiting factor for HSCT eligibility, as advances in conditioning regimens, supportive care, and the use of alternative donor sources have enabled HSCT to become a feasible therapeutic option for older patients[39,40].

Therefore, an appropriate selection process should be performed to identify patients who are most likely to benefit from HSCT, considering the toxicity associated with transplant protocols, the high risk of relapse, and challenges related to access to transplantation[41]. The decision to perform allogeneic HSCT in older adults should be based on a comprehensive multidimensional and multidisciplinary assessment, including physical fitness, comorbidities, physiological reserve, and frailty, in order to identify pre-transplant vulnerabilities, support decision-making regarding patient suitability for the procedure, and tailor post-transplant supportive care strategies to improve outcomes.

Currently, there are no standardized and validated geriatric assessment scales specifically designed for HSCT. The comprehensive geriatric assessment (CGA) is a well-established tool that evaluates all patients older than 60 years old, considering functional status, frailty, comorbidities, disease status, previous therapies, and psychosocial and socioeconomic factors[39,41,42]. Other parameters may also assist in transplant decision-making. The HCT-CI is widely used to assess comorbidity burden, while the composite health risk assessment model (CHARM) score, originally developed to predict the risk of non-relapse mortality, has also been associated with increased frailty, disability, cognitive decline, and severe organ toxicities, outcomes that are particularly relevant in older allogeneic HSCT recipients. In addition, the Montreal cognitive assessment (MoCA) evaluates cognitive function and may provide important information during pre-transplant evaluation. Other tools are also available to assess frailty in older adults[42–44].

In Brazil, the Ordinance No. 1,813, dated July 22, 2020, expanded the age limit for eligibility for allogeneic HSCT to up to 75 years old, thereby increasing access to treatment, particularly for patients with AML and MDS[45]. In 2018, the incorporation of a comprehensive geriatric assessment to evaluate the eligibility of older patients for HSCT became widely adopted[39], and the ordinance GM/MS No. 8,041, dated September 25, 2025, strengthened the organization of the National Transplant Policy in Brazil and established that older patients must undergo a CGA prior to transplantation as a requirement for safety and eligibility[46].

It is essential to carefully consider RIC and non-myeloablative regimens, and donor selection should take into account donor age, as advanced donor age may be associated with less favorable outcomes[47].

A Brazilian study[39] evaluated the outcomes of HSCT in patients aged 60 years old or older treated for AML, MDS, and myeloproliferative neoplasms over an 11-year period. The study demonstrated a progressive increase in the use of allogeneic HSCT in elderly group in Brazil. AML was the main indication for transplantation, accounting for 52% of cases. Overall survival in patients older than 60 years old with AML was 52% (95% confidence interval 46–59).

Since 2018, the use of haploidentical donors in older patients has increased, but haploidentical transplantation has been associated with lower overall survival and a higher risk of mortality in the elderly population[39]. In elderly patients with R/R AML, the prognosis remains poor in the absence of allogeneic HSCT. Only a small proportion of older patients with R/R AML proceed to allogeneic HSCT, and the presence of active disease at the time of transplantation is the strongest predictor of post-transplant relapse.

In this context, the two-year overall survival after HSCT is below 10% in older patients with active disease and adverse cytogenetic features[48]. The phase III SIERRA trial evaluated a targeted pre-transplant conditioning strategy using the anti-CD45 radioimmunoconjugate ^{131}I-apamistamab. It was well tolerated and resulted in higher durable complete response rates compared with conventional care in older patients with active R/R AML who are typically ineligible for standard transplantation, addressing an important unmet clinical need in this population[48].

CONDITIONING REGIMENS AND IMMUNOPROPHYLAXIS

Myeloablative and reduced-intensity conditioning

Myeloablative conditioning is indicated for young patients (< 55–60 years old) without significant comorbidities (HCT-CI ≤ 2), while RIC is indicated for those over 60 years old or with comorbidities contraindicating MAC (B2)[4].

Long-term Gruppo Italiano Trapianto di Midollo Osseo (GITMO) results showed no difference in leukemia-free survival (LFS) or overall survival between the BuFlu and BuCy2 arms (2B)[49]. Among busulfan-based regimens, Bu4/Flu has been shown to be preferable to Bu4/Cy, offering lower toxicity without compromising antileukemic efficacy[49]. Treosulfan-fludarabine, in turn, appears to be a more effective and safer conditioning regimen than busulfan-fludarabine for AML patients undergoing allogeneic HSCT, particularly those at higher risk[50]. A meta-analysis further shows that adding decitabine to the conditioning regimen is associated with significantly better overall survival, reduced relapse risk, and improved DFS, without increasing non-relapse mortality or grade II–IV acute GVHD[51].

Although MAC is associated with a higher rate of treatment-related mortality, this is offset by the substantially higher relapse rate seen with RIC, and overall, MAC leads to improved survival in patients with AML undergoing allogeneic HSCT (1A)[52]. In *FLT3*-positive AML specifically, MAC appears superior to RIC in preventing relapse only among patients who are *NPM1* wild-type at diagnosis and *FLT3-ITD* MRD-positive before HSCT (1A)[53]. Center for International Blood and Marrow Transplant Research (CIBMTR) data (2022; N = 3,113) demonstrated that the number of chemotherapy cycles required to achieve CR and pre-transplant MRD status—rather than the conditioning regimen *per se*—significantly influence outcomes in RIC-HSCT[54].

Immunoprophylaxis

Post-transplant cyclophosphamide (PTCy)-based HSCT, typically 50 mg/kg/day on days +3 and +4, is associated with favorable outcomes in patients with AML who remain leukemia-free two years after the transplant, and long-term results after haploidentical HSCT with PTCy-based GVHD prophylaxis are comparable to those achieved with 10/10 matched unrelated donor (MUD) and matched sibling donor (MSD)[55].

Consistent with this, a recent study found that haploidentical HSCT with PTCy is not inferior to 9/10-MUD HSCT[56]. In MUD using PTCy, DPB1-permissive mismatching reduces relapse in high-risk AML/MDS without increasing GVHD or non-relapse mortality, supporting DP-permissive mismatching as an actionable criterion for donor selection[57]. For AML patients in CR2, haploidentical PTCy-HSCT is associated with lower relapse incidence and chronic GVHD, translating into superior GVHD-free/relapse-free survival compared with MUD HSCT[58]. Regarding prophylactic regimens, PTCy/CNI/MMF and ATG/CNI/MTX appear to offer similar outcomes as alternatives for GVHD prophylaxis in AML patients[59], while the combination of PTCy and ATG seems superior to either approach used alone (2B)[60].

Stem cell source

Mobilized peripheral blood stem cells (PBSC) are the most used source nowadays, associated with faster neutrophil and platelet engraftment. In MUD-MAC transplants, PBSC is associated with a higher incidence of severe chronic GVHD compared with bone marrow[61]. In the Brazilian experience, PBSC in myeloablative related transplants was associated with higher chronic GVHD incidence, supporting the SBTMO GVHD Study Group recommendation to individualize stem cell source based on chronic GVHD risk[61]. For RIC transplants, PBSC is the preferred source. For haploidentical, the pioneering Baltimore protocol (which utilizes PTCy to prevent GVHD) historically preferred BM[62]. However, substituting PBSC for BM as the graft source in the Hopkins' protocol for haploidentical transplantation following RIC was shown to be feasible and does not affect outcomes adversely[63,64].

Notes on donor selection

The immunogenetic donor selection strategies for AML HSCT are described in a specific chapter of the SBTMO guidelines. Relevant considerations include:

- In haploidentical transplants, HLA loss by the leukemic clone may render donor lymphocyte infusion (DLI) and retransplantation from the same donor ineffective. At relapse, HLA loss evaluation is recommended by flow cytometry, HLA-KMR, or NGS before deciding on the salvage strategy[65];
- Donors with donor-specific anti-HLA antibodies positive for recipient HLA antigens must be screened. If positive and the only available donor, the patient should be desensitized prior to transplantation[66];
- Germline myeloid predisposition (HMMS) must be ruled out in all potential family donors, particularly when there is a personal or family history of cytopenias, hematological malignancies, or germline mutations identified in the patient's somatic profile. Donors with pathogenic or likely pathogenic mutations in HMMS-related genes should be avoided, even if asymptomatic[2].

Unrelated donor transplantation

CIBMTR and EBMT data in MRD and MUD transplants demonstrate comparable overall survival and relapse-free survival (RFS) for AML. Younger MUDs resulted in improved DFS compared with older MSD recipients across both the PTCy- and CNI-based GVHD prophylaxis strategies[67]. Of note, the presence of a single-allele mismatch did not influence outcomes, and no difference was observed between older-aged MSD and younger mismatched unrelated donors (MMUDs) when PTCy-based GVHD prophylaxis is used[67]. MUD is associated with higher rates of grade II–IV acute GVHD and transplant-related mortality (TRM) compared to MRD. In the absence of a 10/10 MUD, an 8/8 HLA-matched donor may be acceptable, and 7/8 mismatched donors carry higher TRM and should be critically evaluated[67].

Haploidentical hematopoietic stem cell transplantation with post-transplant cyclophosphamide

Haploidentical HSCT with PTCy (Baltimore protocol) represents a consolidated alternative for patients lacking an HLA-identical donor[62]. Retrospective CIBMTR (N > 10,000)[67] and EBMT data have not demonstrated a significant difference in relapse probability between haplo-PTCy and MUD transplants. TRM in haploidentical transplants is comparable to 8/8 MUD. An EBMT registry cohort with 852 R/R AML patients demonstrated two-year overall survival of 30% and two-year DFS of 25% with haploidentical HSCT (A2)[68]. In relapse after haploidentical-PTCy HSCT, DLI may be ineffective when leukemic clones have lost HLA molecules (HLA loss), observed in ~33% of relapses[69].

Autologous hematopoietic stem cell transplantation

Autologous HSCT as consolidation in first CR is indicated in specific subgroups:

- Favorable-risk AML after one consolidation cycle, MRD-negative, no available donor (C4);

- AML in CR1: an option per Brazilian experience in the absence of an HLA-compatible donor (C4);
- Acute promyelocytic leukemia in second complete molecular remission (B2): autologous HSCT is superior to allogeneic HSCT in second acute promyelocytic leukemia remission[70].

POST-HEMATOPOIETIC STEM CELL TRANSPLANTATION MAINTENANCE THERAPY

Post-HSCT maintenance therapy represents an area of growing evidence, particularly in patients at high relapse risk (MRD-positive pre-HSCT, *FLT3-ITD*, *BCR-ABL1*). The immediate post-transplant period is complex, requiring antimicrobial and antiviral prophylaxis, transfusion support, and GVHD management, all which demand caution in initiating maintenance.

Among the agents studied:

- Sorafenib: the randomized SORMAIN trial demonstrated RFS benefit in *FLT3-ITD*+: one-year cumulative incidence of relapse was 7% in the sorafenib group (400 mg orally twice daily) and *versus* 38.5% in the control group, $p = 0.0010$)[71];
- Midostaurin: it failed to show a statistically significant improvement in RFS or overall survival compared to standard of care in a phase 2 randomized trial, partly due to gastrointestinal toxicities[72];
- Azacitidine: non-randomized phase I/II studies show favorable results; a randomized study of 187 patients showed no difference in RFS (RELAZA trial)[73]. Oral azacitidine (CC-486—QUAZAR AML-001) demonstrated LFS benefit in patients ≥ 55 years old not eligible for HSCT, but post-HSCT data require confirmation[74];
- Gilteritinib: it may improve RFS in patients with detectable *FLT3-ITD* MRD pre- or post-HCT, though larger trials are still needed[75];
- Venetoclax-azacitidine (NCT04161885) and IDH1/2 inhibitors (ivosidenib/enasidenib, NCT03839771) are under active clinical investigation as post-transplant maintenance strategies in AML.

The SBTMO recommendation is that post-HSCT maintenance should preferably be performed within the context of clinical trials. Outside of trials, sorafenib may be considered in high-risk *FLT3-ITD*+ patients, starting from D+30–60, after engraftment stabilization.

OTHER TYPES OF CELLULAR THERAPY IN ACUTE MYELOID LEUKEMIA

Cellular immunotherapy for AML remains experimental, with no product currently available on the market. A more comprehensive review of cellular therapy for hematological cancers is provided elsewhere in this consensus.

CAR-T cells

CAR-T cell therapy for AML, as noted above, remains experimental[76]. Most AML studies have focused on CD33, CD123, and CLL-1, while newer targets, including FLT3, CD7, NKG2D, CD70, TIM3, and CD38, have also been tested[76–80]. Although meaningful responses have been observed, they are usually neither deep nor durable. Antigen overlap between AML cells and healthy progenitors, antigen escape, and the immunosuppressive bone marrow niche appear to be the central barriers[81,82]. The major toxicities are cytokine release syndrome and myeloablation with prolonged cytopenias; neurotoxicity appears less frequent in AML than in some other settings. To date, responses obtained with CAR-T cell therapy should be consolidated with allogeneic HSCT because of both the short-lived nature of the response and profound myeloablation. Dual-target CAR-T cells are being tested in preclinical and early clinical studies[82].

Natural killer cells

Natural killer (NK) cell therapy appears promising compared with T-cell therapy. In fact, the initial studies of cellular immunotherapy for AML used NK cells, mostly haploidentical NK cells. The rationale for these studies relies

on HSCT data using T-cell-depleted haploidentical grafts. The authors observed long-term LFS without GVHD in patients who received haploidentical mismatched NK cells[83]. In addition, in HSCT, NK cells lead lymphocyte immune recovery, and the number and rate of NK-cell recovery are directly correlated with HSCT success[84]. However, several aspects remain unresolved, including the *ex-vivo* production platform for NK cells, the intensity of the lymphodepletion regimen, and, most importantly, their very short persistence in peripheral blood[85].

For some authors, NK cells should behave like T cells, since successful CAR-T cell therapy is associated with persistence and expansion in peripheral blood[86]. The uncertainty around this behavior comes from animal studies of NK-cell physiology, particularly antiviral responses[87], in which the tissue-resident characteristics of innate lymphocytes, among which NK cells are the best-known population, were recently reaffirmed. According to these authors, in virus-infected animal models, NK cells undergo modest expansion followed by considerable contraction, but they develop memory, which is important for tissue protection against viral recrudescence. There is no reason to assume that they would behave differently in the tumor setting. Studies using *ex-vivo*-activated NK cells generated in the presence of genetically modified feeder cells and infused into patients after high-dose myeloablation/lymphodepletion are not enrolling patients yet (NCT06783478).

CAR-NK cells are promising and may be safer than anti-AML CAR-T cells[88,89]. CD33-targeted CAR-NK cells were able to induce MRD-negative complete remissions with low toxicity compared with CAR-T cells, but the clinical response was also short-lived[90], which has been attributed to the known low persistence of NK cells in peripheral blood. Several other targets are being tested, including CD123, FLT3, CLL-1, TIM3, CD70, and NKG2D/NKG2D-ligand pathways[91–98]. Compared with CAR-T cells, CAR-NK cell therapy appears to exhibit less myelosuppression and a less pronounced exhaustion phenotype[99].

RECOMMENDATIONS

Allogeneic hematopoietic stem cell transplantation: related or unrelated

- Allogeneic HSCT is indicated in high-risk AML in CR1 (A1);
- Allogeneic HSCT is indicated in AML in CR2 (A1);
- Allogeneic HSCT is indicated in intermediate-risk AML in CR1, particularly in MRD-positive patients (A1);
- Allogeneic HSCT is indicated in R/R AML (C4);
- MRD status must be evaluated before HSCT and integrated into the therapeutic decision; post-HSCT MRD monitoring is mandatory.

The recommendations for HSCT in AML, including donor type and conditioning intensity, are summarized with their levels of evidence and recommendation grades in Table 6.

Table 6. Hematopoietic stem cell transplantation recommendations in acute myeloid leukemia.

Indication	Level of evidence	Recommendation grade
Allogeneic HSCT (related or unrelated) in high-risk AML (CR1)	A1	Strong
Allogeneic HSCT in AML in second complete remission (CR2)	A1	Strong
Allogeneic HSCT in intermediate-risk AML with MRD-positive CR1	A1	Strong
Allogeneic HSCT in refractory/relapsed AML	C4	Moderate
Haploidentical HSCT (PTCy) — alternative when no HLA-identical donor available	A2	Moderate (B)
Autologous HSCT — favorable-risk AML, MRD-negative post-consolidation, no available donor	C4	Weak
Myeloablative conditioning — young patients, no significant comorbidities (HCT-CI ≤ 2)	A1	Strong
Reduced-intensity conditioning — patients > 60 years old or with comorbidities	B2	Moderate

HSCT: hematopoietic stem cell transplantation; AML: acute myeloid leukemia; MRD: measurable residual disease; PTCy: post-transplant cyclophosphamide; HLA: human leukocyte antigen; HCT-CI: hematopoietic stem cell transplantation-comorbidity index. Source: Adapted from Greco et al.[30].

Conditioning regimens

- MAC is indicated in young patients without significant comorbidities (age < 55 years old, HCT-CI ≤ 2) (A1);
- Older patients or those with comorbidities should prefer RIC (B2).

Haploidentical hematopoietic stem cell transplantation

Level of evidence A2 — Recommendation grade B.

Autologous hematopoietic stem cell transplantation

- Indicated in favorable-risk AML after one consolidation cycle, MRD-negative, no available donor (C4);
- Indicated in AML in CR1 per Brazilian experience in the absence of an HLA-compatible donor (C4);
- Indicated in APL in CR2 (B2).

CONCLUSION

Allogeneic HSCT remains the only curative option for patients with intermediate- and adverse-risk AML. MRD status, assessed before and after transplant, is now central to the decision: it refines who among intermediate-risk patients truly benefits from HSCT and shapes how post-transplant surveillance and maintenance are conducted. Advances in conditioning regimens, PTCy-based GVHD prophylaxis, and more permissive donor and age criteria have broadened access to HSCT. Novel cellular therapies such as CAR-T and CAR-NK cells remain investigational. As the diagnostic and therapeutic landscape for AML continues to evolve rapidly, these recommendations should be revisited periodically, guided by prospective data and by real-world outcomes captured through the SBTMO registry.

CONFLICT OF INTEREST

Nothing to declare.

DATA AVAILABILITY STATEMENT

All datasets were generated or analyzed in the current study.

AUTHORS' CONTRIBUTIONS

Substantive scientific and intellectual contributions to the study: Pinto MP, Ikoma-Colturato MRV, Funke VA, Pitombeira BSGS, Paton EJA, Arantes A, Barroso KSN, Beltrame MP, Bettarello G, Coelho Hugo CP, Ferreira dos Santos TC, Furtado FM, Souto EX, Duarte FB and Silla L; **Conception and design:** Pinto MP, Ikoma-Colturato MRV, Funke VA, Pitombeira BSGS, Paton EJA, Arantes A, Barroso KSN, Beltrame MP, Bettarello G, Coelho Hugo CP, Ferreira dos Santos TC, Furtado FM, Souto EX, Duarte FB and Silla L; **Acquisition of data:** Pinto MP, Ikoma-Colturato MRV, Funke VA, Pitombeira BSGS, Paton EJA, Arantes A, Barroso KSN, Beltrame MP, Bettarello G, Coelho Hugo CP, Ferreira dos Santos TC, Furtado FM, Souto EX, Duarte FB and Silla L; **Manuscript preparation:** Pinto MP, Ikoma-Colturato MRV, Funke VA, Pitombeira BSGS, Paton EJA, Arantes A, Barroso KSN, Beltrame MP, Bettarello G, Coelho Hugo CP, Ferreira dos Santos TC, Furtado FM, Souto EX, Duarte FB and Silla L; **Manuscript writing:** Pinto MP, Ikoma-Colturato MRV, Funke VA, Pitombeira BSGS, Paton EJA, Arantes A, Barroso KSN, Beltrame MP, Bettarello G, Coelho Hugo CP, Ferreira dos Santos TC, Furtado FM, Souto EX, Duarte FB and Silla L; **Critical revision:** Pinto MP and Silla L; **Final approval of the version to be published:** Silla L.

FUNDING

Not applicable.

DECLARATION OF USE OF ARTIFICIAL INTELLIGENCE TOOLS

During the preparation of this manuscript, the authors used [Claude (Anthropic)] to assist with grammar and spelling review of the English text and to support drafting of the abstract. After using this tool, the authors reviewed, edited, and take full responsibility for the content of the manuscript.

ACKNOWLEDGEMENTS

Not applicable.

REFERENCES

1. Silla LMR, Ikoma-Colturato MRV, Funke VA, Pitombeira BSGS, Paton EJA, Hamerschlak N, Arantes A, Astigarraga C, Barroso KSN, Beltrame MP, Bettarelo G, Campregher P, Furtado FM, Souto EX, Torres MA, Duarte FB. Hematopoietic stem cell transplantation for acute myeloid leukemia: consensus update. JBMTCT. 2023;4(1):14-8. https://doi.org/10.46765/2675-374X.2023v4n1p184

2. Döhner H, Wei AH, Appelbaum FR, Craddock C, DiNardo CD, Dombret H, Ebert BL, Fenaux P, Godley LA, Hasserjian RP, Larson RA, Levine RL, Miyazaki Y, Niederwieser D, Ossenkoppele G, Röllig C, Sierra J, Stein EM, Tallman MS, Tien HF, Wang J, Wierzbowska A, Löwenberg B. Diagnosis and management of AML in adults: 2022 ELN recommendations. Blood. 2022;140(12):1345-77.

3. Döhner H, DiNardo CD, Appelbaum FR, Craddock C, Dombret H, Ebert BL, Fenaux P, Godley LA, Hasserjian RP, Larson RA, Levine RL, Miyazaki Y, Niederwieser D, Ossenkoppele G, Röllig C, Sierra J, Stein EM, Tallman MS, Tien HF, Wang J, Wierzbowska A, Wei AH, Löwenberg B. Genetic risk classification for adults with AML receiving less-intensive therapies: the 2024 ELN recommendations. Blood. 2024;144(21):2169-73.

4. Sanz J, Bug G, Ciceri F, Craddock C, Dillon R, Esteve J, Porta MGD, Heuser M, de Leeuw DC, Nagler A, Onida F, Roboz GJ, Ruggeri A, Sánchez-Ortega I, Srour M, Yakoub-Agha I, Buccisano F. Measurable residual disease-guided interventions in patients with acute myeloid leukaemia undergoing allogeneic haematopoietic cell transplantation: best practice recommendations from the European Society for Blood and Marrow Transplantation Practice Harmonisation and Guidelines Committee. Lancet Oncol. 2025;26(11):e586-96. https://doi.org/10.1016/s1470-2045(25)00426-7

5. DiNardo CD, Jonas BA, Pullarkat V, Thirman MJ, Garcia JS, Wei AH, Konopleva M, Döhner H, Letai A, Fenaux P, Koller E, Havelange V, Leber B, Esteve J, Wang J, Pejsa V, Hájek R, Porkka K, Illés Á, Lavie D, Lemoli RM, Yamamoto K, Yoon SS, Jang JH, Yeh SP, Turgut M, Hong WJ, Zhou Y, Potluri J, Pratz KW. Azacitidine and venetoclax in previously untreated AML (VIALE-A). N Engl J Med. 2020;383(7):617-29.

6. Heuser M, Freeman SD, Ossenkoppele GJ, Buccisano F, Hourigan CS, Ngai LL, Tettero JM, Bachas C, Baer C, Béné MC, Bücklein V, Czyz A, Denys B, Dillon R, Feuring-Buske M, Guzman ML, Haferlach T, Han L, Herzig JK, Jorgensen JL, Kern W, Konopleva MY, Lacombe F, Libura M, Majchrzak A, Maurillo L, Ofran Y, Philippe J, Plesa A, Preudhomme C, Ravandi F, Roumier C, Subklewe M, Thol F, van de Loosdrecht AA, van der Reijden BA, Venditti A, Wierzbowska A, Valk PJM, Wood BL, Walter RB, Thiede C, Döhner K, Roboz GJ, Cloos J. 2021 Update on MRD in AML: A Consensus Document from the ELN MRD Working Party. Blood. 2021;138(26):2753-67.

7. Khoury JD, Solary E, Abla O, Akkari Y, Alaggio R, Apperley JF, Bejar R, Berti E, Busque L, Chan JKC, Chen W, Chen X, Chng WJ, Choi JK, Colmenero I, Coupland SE, Cross NCP, De Jong D, Elghetany MT, Takahashi E, Emile JF, Ferry J, Fogelstrand L, Fontenay M, Germing U, Gujral S, Haferlach T, Harrison C, Hodge JC, Hu S, Jansen JH, Kanagal-Shamanna R, Kantarjian HM, Kratz CP, Li XQ, Lim MS, Loeb K, Loghavi S, Marcogliese A, Meshinchi S, Michaels P, Naresh KN, Natkunam Y, Nejati R, Ott G, Padron E, Patel KP, Patkar N, Picarsic J, Platzbecker U, Roberts I, Schuh A, Sewell W, Siebert R, Tembhare P, Tyner J, Verstovsek S, Wang W, Wood B, Xiao W, Yeung C, Hochhaus A. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms. Leukemia. 2022;36(7): 1703-19. https://doi.org/10.1038/s41375-022-01613-1

8. Arber DA, Orazi A, Hasserjian RP, Borowitz MJ, Calvo KR, Kvasnicka HM, Wang SA, Bagg A, Barbui T, Branford S, Bueso-Ramos CE, Cortes JE, Dal Cin P, DiNardo CD, Dombret H, Duncavage EJ, Ebert BL, Estey EH, Facchetti F, Foucar K, Gangat N, Gianelli U, Godley LA, Gökbuget N, Gotlib J, Hellström-Lindberg E, Hobbs GS, Hoffman R, Jabbour EJ, Kiladjian JJ, Larson RA, Le Beau MM, Loh ML, Löwenberg B, Macintyre E, Malcovati L, Mullighan CG, Niemeyer C, Odenike OM, Ogawa S, Orfao A, Papaemmanuil E, Passamonti F, Porkka K, Pui CH, Radich JP, Reiter A, Rozman M, Rudelius M, Savona MR, Schiffer CA, Schmitt-Graeff A, Shimamura A, Sierra J, Stock WA, Stone RM, Tallman MS, Thiele J, Tien HF, Tzankov A, Vannucchi AM, Vyas P, Wei AH, Weinberg OK, Wierzbowska A, Cazzola M, Döhner H, Tefferi A. International consensus classification of myeloid neoplasms and acute leukemias: integrating genetic, clinical, and morphologic information. Blood. 2022;140(11):1200-28. https://doi.org/10.1182/blood.2022015850

9. Arber DA, Orazi A, Hasserjian R, Thiele J, Borowitz MJ, Le Beau MM, Bloomfield CD, Cazzola M, Vardiman JW. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016;127(20):2391-405. https://doi.org/10.1182/blood-2016-03-643544

10. Hoff FW, Blum WG, Huang Y, Welkie RL, Swords RT, Traer E, Stein EM, Lin TL, Archer KJ, Patel PA, Collins RH, Baer MR, Duong VH, Arellano ML, Stock W, Odenike O, Redner RL, Kovacsovics T, Deininger MW, Zeidner JF, Olin RL, Smith CC, Foran JM, Schiller GJ, Curran EK, Koenig KL, Heerema NA, Chen T, Martycz M, Stefanos M, Marcus SG, Rosenberg L, Druker BJ, Levine RL, Burd A, Yocum AO, Borate UM, Mims AS, Byrd JC, Madanat YF. Beat-AML 2024 ELN-refined risk stratification for older adults with newly diagnosed AML given lower-intensity therapy. Blood Adv. 2024;8(20):5297-305. https://doi.org/10.1182/bloodadvances.2024013685

11. Pratz KW, Jonas BA, Pullarkat V, Thirman MJ, Garcia JS, Döhner H, Récher C, Fiedler W, Yamamoto K, Wang J, Yoon SS, Wolach O, Yeh SP, Leber B, Esteve J, Mayer J, Porkka K, Illés Á, Lemoli RM, Turgut M, Ku G, Miller C, Zhou Y, Zhang M, Chyla B, Potluri J, DiNardo CD. Long-term follow-up of VIALE-A: Venetoclax and azacitidine in chemotherapy-ineligible untreated acute myeloid leukemia. Am J Hematol. 2024;99(4): 615-24. https://doi.org/10.1002/ajh.27246

12. Cloos J, Valk PJM, Thiede C, Döhner K, Roboz GJ, Wood BL, Walter RB, Wang S, Wierzbowska A, Wei AH, Wu D, Vergez F, Venditti A, van der Reijden BA, van de Loosdrecht AA, Tiong IS, Thol FR, Subklewe M, Roumier C, Reuvekamp T, Ravandi F, Preudhomme C, Plesa A, Othman J, Ossenkoppele GJ, Ofran Y, Mimoun A, Maurillo L, Majchrzak A, de Leeuw D, Kern W, Kim DDH, Ikoma-Colturato MRV, Haaksma LH, Guzman ML, Feuring M, Depreter B, Czyz A, Bücklein V, Baer C, Bachas C, Freeman SD, Buccisano F, Hourigan CS, Dillon R, Heuser M. 2025 update on MRD in acute myeloid leukemia: a consensus document from the ELN-DAVID MRD Working Party. Blood. 2026;147(11):1147-67. https://doi.org/10.1182/blood.2025031480

13. Venditti A, Piciocchi A, Candoni A, Melillo L, Calafiore V, Cairoli R, de Fabritiis P, Storti G, Salutari P, Lanza F, Martinelli G, Luppi M, Mazza P, Martelli MP, Cuneo A, Albano F, Fabbiano F, Tafuri A, Chierichini A, Tieghi A, Fracchiolla NS, Capelli D, Foà R, Alati C, La Sala E, Fazi P, Vignetti M, Maurillo L, Buccisano F, Del Principe MI, Irno-Consalvo M, Ottone T, Lavorgna S, Voso MT, Lo-Coco F, Arcese W, Amadori S. GIMEMA AML1310 trial of risk-adapted, MRD-directed therapy for young adults with newly diagnosed acute myeloid leukemia. Blood. 2019;134(12):935-45. https://doi.org/10.1182/blood.2018886960

14. Löwenberg B, Pabst T, Maertens J, Gradowska P, Biemond BJ, Spertini O, Vellenga E, Griskevicius L, Tick LW, Jongen-Lavrencic M, van Marwijk Kooy M, Vekemans MC, van der Velden WJFM, Beverloo B, Michaux L, Graux C, Deeren D, de Weerdt O, van Esser JWJ, Bargetzi M, Klein SK, Gadisseur A, Westerweel PE, Veelken H, Gregor M, Silzle T, van Lammeren-Venema D, Moors I, Breems DA, Hoogendoorn M, Legdeur MJC, Fischer T, Kuball J, Cornelissen J, Porkka K, Juliusson G, Meyer P, Höglund M, Gjertsen BT, Janssen JJWM, Huls G, Passweg J, Cloos J, Valk PJM, van Elssen CHMJ, Manz MG, Floisand Y, Ossenkoppele GJ. Addition of lenalidomide to intensive treatment in younger and middle-aged adults with newly diagnosed AML: the HOVON-SAKK-132 trial. Blood Adv. 2021;5(4):1110-21. https://doi.org/10.1182/bloodadvances.2020003855

15. Tettero JM, Ngai LL, Bachas C, Breems DA, Fischer T, Gjertsen BT, Gradowska P, Griskevicius L, Janssen JJWM, Juliusson G, Maertens J, Manz MG, Pabst T, Passweg J, Porkka K, Valk PJM, Löwenberg B, Ossenkoppele GJ, Cloos J. Measurable residual disease-guided therapy in intermediate-risk acute myeloid leukemia patients is a valuable strategy in reducing allogeneic transplantation without negatively affecting survival. Haematologica. 2023;108(10):2794-8. https://doi.org/10.3324/haematol.2022.282639

16. Han L, Li Y, Wu J, Peng J, Han X, Zhao H, He C, Li Y, Wang W, Zhang M, Li Y, Sun H, Cao H, Sang L, Jiang Z, Yu J. Post-remission measurable residual disease directs treatment choice and improves outcomes for patients with intermediate-risk acute myeloid leukemia in CR1. Int J Hematol. 2022;116(6):892-901. https://doi.org/10.1007/s12185-022-03441-6

17. Othman J, Potter N, Ivey A, Jovanovic J, Runglall M, Freeman SD, Gilkes A, Thomas I, Johnson S, Canham J, Cavenagh J, Kottaridis P, Arnold C, Ommen HB, Overgaard UM, Dennis M, Burnett A, Wilhelm-Benartzi C, Dillon R, Russell NH. Postinduction molecular MRD identifies patients with NPM1 AML who benefit from allogeneic transplant in first remission. Blood. 2024;143(19):1931-6. https://doi.org/10.1182/blood.2023023096

18. Appelbaum FR. Hematopoietic cell transplantation as treatment of patients with acute myeloid leukemia with measurable residual disease after consolidation therapy. Best Pract Res Clin Haematol. 2018;31(4):405-9. https://doi.org/10.1016/j.beha.2018.09.009

19. Versluis J, Kalin B, Zeijlemaker W, Passweg J, Graux C, Manz MG, Vekemans MC, Biemond BJ, Legdeur MJC, Kooy MVM, de Weerdt O, Wijermans PW, Hoogendoorn M, Bargetzi MJ, Kuball J, Schouten HC, van der Velden VHJ, Janssen JJWM, Pabst T, Lowenberg B, Jongen-Lavrencic M, Schuurhuis GJ, Ossenkoppele G, Cornelissen JJ. Graft-versus-leukemia effect of allogeneic stem-cell transplantation and minimal residual disease in patients with acute myeloid leukemia in first complete remission. JCO Precis Oncol. 2017;1:1-13. https://doi.org/10.1200/po.17.00078

20. Shaffer BC, Kebriaei P, Lima M, Jimenez AMJ. Measurable residual disease testing and allogeneic hematopoietic cell transplantation for AML: adapting PreMEASURE to clinical practice. BMT. 2025;60:128-34. https://doi.org/10.1038/s41409-024-02481-2

21. Aitken MJL, Ravandi F, Patel KP, Short NJ. Prognostic and therapeutic implications of measurable residual disease in acute myeloid leukemia. J Hematol Oncol. 2021;14(1):137. https://doi.org/10.1186/s13045-021-01148-5

22. Gang M, Othus M, Walter RB. Significance of measurable residual disease in patients undergoing allogeneic hematopoietic cell transplantation for acute myeloid leukemia. Cells. 2025;14(4):290. https://doi.org/10.3390/cells14040290

23. Geramita E, Hou JZ, Shlomchik WD, Ito S. Maintenance strategies for relapse prevention and treatment. Hematology. 2024;2024(1):635-43. https://doi.org/10.1182/hematology.2024000589

24. Shah MV, Jorgensen JL, Saliba RM, Wang SA, Alousi AM, Andersson BS, Bashir Q, Ciurea SO, Kebriaei P, Marin D, Patel KP, Popat UR, Rezvani K, Rondon G, Shpall EJ, Champlin RE, Oran B. Early post-transplant minimal residual disease assessment improves risk stratification in acute myeloid leukemia. Biol Blood Marrow Transplant. 2018;24(7):1514-20. https://doi.org/10.1016/j.bbmt.2018.02.003

25. Wienecke CP, Heida B, Venturini L, Gabdoulline R, Krüger K, Teich K, Büttner K, Wichmann M, Puppe W, Neziri B, Reuter M, Dammann E, Stadler M, Ganser A, Hambach L, Thol F, Heuser M. Clonal relapse dynamics in acute myeloid leukemia following allogeneic hematopoietic cell transplantation. Blood. 2024;144(3): 296-307. https://doi.org/10.1182/blood.2023022697

26. Spyridonidis A. How I treat measurable (minimal) residual disease in acute leukemia after allogeneic hematopoietic cell transplantation. Blood. 2020;135(19):1639-49. https://doi.org/10.1182/blood.2019003566

27. Tavares RCB, Pelegrina PRD, Breviglieri CNM, Rodrigues ALM, Zamperlini G, Sousa AM, Horn PRCB, Darrigo Jr LG, Daudt L. Management of pediatric acute leukemias relapse after hematopoietic cell transplantation. J Bone Marrow Transplant Cell Ther. 2025;6(1):e285. https://doi.org/10.46765/2675-374X.2025v6n1e285

28. 2 Wildes TM, Stirewalt DL, Medeiros B, Hurria A. Hematopoietic stem cell transplantation for hematologic malignancies in older adults: geriatric principles in the transplant clinic. J Natl Compr Canc Netw. 2014;12(1):128-36. https://doi.org/10.6004/jnccn.2014.0010

29. Gratwohl A. The EBMT risk score. Bone Marrow Transplant. 2012;47(6):749-56. https://doi.org/10.1038/bmt.2011.110

30. Greco R, Ruggeri A, McLornan DP, Snowden JA, Alexander T, Angelucci E, Averbuch D, Bazarbachi A, Hazenberg MD, Kalwak K, Kenyon M, Mekelenkamp H, Neven B, Pedrazzoli P, Peric Z, Risitano AM, Sánchez-Ortega I, Ciceri F, Sureda A. Indications for haematopoietic cell transplantation and CAR-T for haematological diseases, solid tumours and immune disorders: 2025 EBMT practice recommendations. Bone Marrow Transplant. 2025;60(11):1499-525. https://doi.org/10.1038/s41409-025-02701-3

31. Steinmetz HT, Schulz A, Staib P, Scheid C, Glasmacher A, Neufang A, Franklin J, Tesch H, Diehl V, Dias Wickramanayake P. Phase-II trial of idarubicin, fludarabine, cytosine arabinoside, and filgrastim (Ida-FLAG) for treatment of refractory, relapsed, and secondary AML. Ann Hematol. 1999;78(9):418-25. https://doi.org/10.1007/s002770050541

32. Anžej Doma S, Sever M, Jakoš G, Podgornik H. FLAG/FLAG-Ida regimen in secondary and relapsed/refractory acute myeloid leukemia—even in the era of new treatment modalities still a significant player. J. Clin Med. 2024;13(7):1842. https://doi.org/10.3390/jcm13071842

33. Perl AE, Martinelli G, Cortes JE, Neubauer A, Berman E, Paolini S, Montesinos P, Baer MR, Larson RA, Ustun C, Fabbiano F, Erba HP, Di Stasi A, Stuart R, Olin R, Kasner M, Ciceri F, Chou WC, Podoltsev N, Recher C, Yokoyama H, Hosono N, Yoon SS, Lee JH, Pardee T, Fathi AT, Liu C, Hasabou N, Liu X, Bahceci E, Levis MJ. Gilteritinib or chemotherapy for relapsed or refractory FLT3-mutated AML. N Engl J Med. 2019;381(18):1728-40. https://doi.org/10.1056/nejmoa1902688

34. Stein EM, DiNardo CD, Fathi AT, Mims AS, Pratz KW, Savona MR, Stein AS, Stone RM, Winer ES, Seet CS, Döhner H, Pollyea DA, McCloskey JK, Odenike O, Löwenberg B, Ossenkoppele GJ, Patel PA, Roshal M, Frattini MG, Lersch F, Franovic A, Nabhan S, Fan B, Choe S, Wang H, Wu B, Hua L, Almon C, Cooper M, Kantarjian HM, Tallman MS. Ivosidenib or enasidenib combined with intensive chemotherapy in patients with newly diagnosed AML: a phase 1 study. Blood. 2021;137(13):1792-803. https://doi.org/10.1182/blood.2020007233

35. Sui J, Xu Z, Zhang L, Jiao Y, Bian R, Pan D, Yan X. Early replacement of re-induction therapy following failed intensive induction treatment enhances the therapeutic efficacy of newly diagnosed AML. Sci Rep. 2025;15(1):20022. https://doi.org/10.1038/s41598-025-04139-5

36. Garcia JS, Kim HT, Murdock HM, Cutler CS, Brock J, Gooptu M, Ho VT, Koreth J, Nikiforow S, Romee R, Shapiro R, Loschi F, Ryan J, Fell G, Karp HQ, Lucas F, Kim AS, Potter D, Mashaka T, Stone RM, DeAngelo DJ, Letai A, Lindsley RC, Soiffer RJ, Antin JH. Adding venetoclax to fludarabine/busulfan RIC transplant for high-risk MDS and AML is feasible, safe, and active. Blood Adv. 2021;5(24):5536-45. https://doi.org/10.1182/bloodadvances.2021005566

37. Jondreville L, Roos-Weil D, Uzunov M, Boussen I, Grenier A, Norol F, Morel V, Nguyen S, Souchet L. FLAMSA-busulfan-melphalan as a sequential conditioning regimen in HLA-matched or haploidentical hematopoietic stem cell transplantation for high-risk myeloid diseases. Transplant Cell Ther. 2021;27(11):915.e1-e8. https://doi.org/10.1016/j.jtct.2021.07.018

38. Sackstein P, Williams A, Zemel R, Marks JA, Renteria AS, Rivero G. Transplant eligible and ineligible elderly patients with AML—a genomic approach and next generation questions. Biomedicines. 2024;12(5):975. https://doi.org/10.3390/biomedicines12050975

39. Duarte FB, Garcia YDO, Hamerschlak N, Funke VAM, Moreira MCR, Paz AA, Filho JS, Astigarraga CC, da Silva RL, de Molla VC, Silvério A, Rocha VG, Feliciano JVP, Barros GMN, Colturato VAR, Nabhan SK, Farias JSH, Maia ACA, Atalla Â, Chiattone R, Macedo MCMA, Aranha MAF, Zogbi YAN, Lener D, Soares RDA, Scheinberg P, Calixto RF, Teixeira GM, Colella MP, Rodrigues CA, Simione AJ, Silva CC, Martin PJ, Flowers ME. Allogeneic hematopoietic cell transplantation in elderly patients in a Latin American country: analysis of 11 year of data from the Brazilian Registry SBTMO/CIBMTR. Transplant Cell Ther. 2025;31(2):79.e1-e9. https://doi.org/10.1016/j.jtct.2024.12.003

40. Wall SA, Devine S, Vasu S. The who, how and why: Allogeneic transplant for acute myeloid leukemia in patients older than 60years. Blood Rev. 2017;31(6):362-9. https://doi.org/10.1016/j.blre.2017.07.002

41. Lima YCSF, Duarte BA, Duarte Filho FB, Duarte IA, Duarte JVAD, Santos ACF, Colturato VAR, Souza MP, Simione AJ, Campos SEVC, Barroso F. Allogeneic hematopoietic stem cell transplantation in elderly patients in Brazil. J Bone Marrow Transplant Cell Ther. 2023;4(2):198. https://doi.org/10.46765/2675-374X.2023v4n2p198

42. Salas MQ, Alfaro Moya T, Pasic I, Baile González M, Acera Gómez M, Fox L, Pérez Artigas MDM, Santamaría A, Quintela González MDC, Sánchez Salinas A, Salmerón Camacho JM, Illana Álvaro V, Abdallahi-Lefdil Z, Cornago Navascues J, Pardo L, Fernández-Luis S, Vega Suárez LP, Villar S, Beorlegui-Murillo P, Esquirol A, Izquierdo García I, Mussetti A, Lavilla E, Lopez-Marín J, Filaferro S, Basalobre P, Bento L, Law A, Viswabandya A, Michelis FV, Mattsson J, Alibhai SMH, Rovira M, Kim DDH, Sureda A, Kumar R. HCT Frailty Scale (HCT-FS) for assessing frailty in adult candidates for allogeneic haematopoietic cell transplantation: an international prospective, observational cohort. eClinicalMedicine. 2026;91. https://doi.org/10.1016/j.eclinm.2025.103753

43. Sorror ML, Saber W, Logan B, Geller N, Bellach A, Kou J, Wood W, McCarty JM, Knight TG, Runaas L, Johnston L, Walston J, Nakamura R, Jarrett L, Mishra A, Uberti J, Dahi PB, Saultz JN, McCurdy SR, Morris LE, Imus PH, Hogan WJ, Nadiminti K, Bhatt VR, Olin R, Maakaron J, Sobecks R, Wall SA, Mattila D, Protz B, Devine SM, Horowitz MM, Artz AS. Novel composite health assessment risk model for older allogeneic transplant recipients: BMT-CTN 1704. Blood Adv. 2025;9(13):3268-80. https://doi.org/10.1182/bloodadvances.2025015793

44. Sarmento ALR. Montreal Cognitive Assessment (MoCA): versão experimental brasileira. Recife: Neuropsicologia Brasil; 2012.

45. Brasil. Ministério da Saúde. Portaria GM/MS n. 1.813, de 22 de julho de 2020. Diário Oficial da União. 2020.

46. Brasil. Ministério da Saúde. Portaria GM/MS n. 8.041, de 25 de setembro de 2025. Diário Oficial da União. 2025.

47. Duarte RF, Sánchez-Ortega I. HCT in elderly patients. In: Sureda A, Corbacioglu S, Greco R, Kröger N, Carreras E (Eds.). The EBMT handbook: Hematopoietic cell transplantation and cellular therapies. 8th ed. Cham, Switzerland: Springer; 2024.

48. Gyurkocza B, Nath R, Seropian S, Choe H, Litzow MR, Abboud C, Koshy N, Stiff P, Tomlinson B, Abhyankar S, Foran J, Hari P, Chen G, Al-Kadhimi Z, Kebriaei P, Sabloff M, Orozco JJ, Jamieson K, Silverman M, Van Besien K, Schuster M, Law AD, Larkin K, Pandit-Taskar N, Rowley SD, Munshi P, Cook R, Levy MY, Lazarus HM, Sandmaier BM, Pagel JM, Reddy V, MacDougall J, McNamara K, Spross J, Haeuber E, Vusirikala M, Nahar A, Desai A, Giralt S. Randomized phase III SIERRA trial of 131|-apamistamab before allogeneic hematopoietic cell transplantation versus conventional care for relapsed/refractory AML. J Clin Oncol. 2025;43(3):201-13. https://doi.org/10.1200/jco.23.02018

49. Rambaldi A, Grassi A, Masciulli A, Boschini C, Micò MC, Busca A, Bruno B, Cavattoni I, Santarone S, Raimondi R, Montanari M, Milone G, Chiusolo P, Pastore D, Guidi S, Patriarca F, Risitano AM, Saporiti G, Pini M, Terruzzi E, Arcese W, Marotta G, Carella AM, Nagler A, Russo D, Corradini P, Alessandrino EP, Torelli GF, Scimè R, Mordini N, Oldani E, Marfisi RM, Bacigalupo A, Bosi A. Busulfan plus cyclophosphamide versus busulfan plus fludarabine as a preparative regimen for allogeneic haemopoietic stem-cell transplantation in patients with acute myeloid leukaemia: an open-label, multicentre, randomised, phase 3 trial. Lancet Oncol. 2015;16(15):1525-36. https://doi.org/10.1016/s1470-2045(15)00200-4

50. Stölzel F, Stelljes M, Beelen DW, Markiewicz M, Reményi P, Luft T, Ciceri F, Wagner-Drouet EM, Junghanss C, Scheid C, Patriarca F, Socié G, Hilgendorf I, Rambaldi A, Schaefer-Eckart K, Russo D, Wulf G, Glass B, Labussiere-Wallet H, Stuhler G, Bieniaszewska M, Casper J, Holler E, Benedetti F, Iori AP, Kunadt D, Mihajlović J, Schild B, Khan I, Li X, Bethge W. GVHD and GRFS in patients with acute myeloid leukemia undergoing allogeneic HCT with treosulfan- versus reduced-intensity busulfan-based conditioning: a subgroup analysis of a randomized phase 3 trial. Haematologica. 2026. https://doi.org/10.3324/haematol.2025.288770

51. Luo C, Zhang J, Huang X, Wu G, Huang Y, Ding Y, Huang Z, Song Q, Chen J, Li X, Xu S. The effects of adding decitabine to conditioning regimen for patients with acute myeloid leukemia or myelodysplastic syndrome undergoing allogeneic hematopoietic stem cell transplantation: a systematic review and meta-analysis. Ann Hematol. 2025;104(12):6175-86. https://doi.org/10.1007/s00277-025-06342-w

52. Scott BL, Pasquini MC, Fei M, Fraser R, Wu J, Devine SM, Porter DL, Maziarz RT, Warlick E, Fernandez HF, Soiffer RJ, Alyea E, Hamadani M, Bashey A, Giralt S, Geller NL, Leifer E, Hourigan CS, Gui G, Mendizabal A, Horowitz MM, Deeg HJ, Horwitz ME. Myeloablative versus reduced-intensity conditioning for hematopoietic cell transplantation in acute myelogenous leukemia and myelodysplastic syndromes-long-term follow-up of the BMT CTN 0901 clinical trial. Transplant Cell Ther. 2021;27(6):483.e1-e6. https://doi.org/10.1016/j.jtct.2021.02.031

53. Levis MJ, Hamadani M, Logan BR, Jones RJ, Singh AK, Litzow MR, Wingard JR, Papadopoulos EB, Perl AE, Soiffer RJ, Ustun C, Oshima MU, Uy GL, Waller EK, Vasu S, Solh M, Mishra A, Muffly LS, Kim HJ, Stelljes M, Najima Y, Onozawa M, Thomson K, Chen C, Hasabou N, Rosales M, Hill JE, Gill SC, Nuthethi R, King D, Mendizabal A, Devine SM, Horowitz MM, Chen YB. Impact of transplant conditioning, NPM1 mutations, and measurable residual disease in FLT3-ITD acute myeloid leukemia. Blood Adv. 2025;9(20):5123-33. https://doi.org/10.1182/bloodadvances.2025016306

54. Boyiadzis M, Zhang MJ, Chen K, Abdel-Azim H, Abid MB, Aljurf M, Bacher U, Badar T, Badawy SM, Battiwalla M, Bejanyan N, Bhatt VR, Brown VI, Castillo P, Cerny J, Copelan EA, Craddock C, Dholaria B, Perez MAD, Ebens CL, Gale RP, Ganguly S, Gowda L, Grunwald MR, Hashmi S, Hildebrandt GC, Iqbal M, Jamy O, Kharfan-Dabaja MA, Khera N, Lazarus HM, Lin R, Modi D, Nathan S, Nishihori T, Patel SS, Pawarode A, Saber W, Sharma A, Solh M, Wagner JL, Wang T, Williams KM, Winestone LE, Wirk B, Zeidan A, Hourigan CS, Litzow M, Kebriaei P, de Lima M, Page K, Weisdorf DJ. Impact of pre-transplant induction and consolidation cycles on AML allogeneic transplant outcomes: a CIBMTR analysis in 3,113 AML patients. Leukemia. 2023;37(5):1006-17. https://doi.org/10.1038/s41375-022-01738-3

55. Rodríguez-Arbolí E, Ferhat AT, Raiola AM, Morsink L, Blaise D, Versluis J, Sica S, Kwon M, López-Corral L, Nur E, Kulagin A, Bramanti S, Rovira M, Forcade E, Martino M, Vydra J, Piemontese S, Sanz J, Mohty M, Ciceri F. Late outcomes after posttransplant cyclophosphamide-based GVHD prophylaxis in patients with AML: an ALWP-EBMT study. Blood Neoplasia. 2026;3(2):100199. https://doi.org/10.1016/j.bneo.2026.100199

56. Gantner A, Labuhn S, Fürst D, Mannes S, Flossdorf S, Ayuk FA, Schroeder T, Stelljes M, Zeiser R, Dreger P, Eder M, Blau IW, Schetelig J, Brecht A, Burchert A, Edinger M, Wais V, Schrezenmeier H, Döhner H, Schmeller S, Fleischhauer K, Kröger N, Sala E, German Registry for Hematopoietic Stem Cell Transplantation and cell Therapy (DRST). Haploidentical transplantation with post-transplant cyclophosphamide is not inferior to 9/10-MUD transplantation with ATG in patients with myeloid malignancies. Bone Marrow Transplant. 2026;61:694-701. https://doi.org/10.1038/s41409-026-02827-y

57. Smallbone P, Cao K, Saliba RM, Carmarzzi Y, Al-Atrash G, Alvarez M, Rondon G, Fingrut WB, Aljawai YM, Olson AL, Alousi AM, Chen GL, Tanner MR, Zou J, Ramdial JL, Champlin RE, Shpall EJ, Oran B. Reduced relapse in high risk acute myeloid leukemia and myelodysplastic neoplasms with permissive HLA-DPB1 mismatches and post-transplant cyclophosphamide. Leukemia. 2026;40(5):934-45. https://doi.org/10.1038/s41375-026-02907-4

58. Ye Y, Labopin M, Yakoub-Agha I, Socié G, Blaise D, Gedde-Dahl T, Blau IW, Raiola AM, Byrne J, Daguindau E, Labussière-Wallet H, Huynh A, Bazarbachi A, Nagler A, Brissot E, Li L, Luo Y, Shi J, Mohty M, Huang H, Ciceri F. Superior GVHD-free, relapse-free survival for haploidentical transplant with PTCy than matched unrelated donor for AML patients transplanted in second complete remission: a study from the acute leukemia working party of the European Society for Blood and Marrow Transplantation. Am J Hematol. 2025;100(10):1760-71. https://doi.org/10.1002/ajh.70008

59. Sanz J, Labopin M, Blaise D, Raiola AM, Busca A, Vydra J, Tischer J, Chevallier P, Bramanti S, Fanin R, Socié G, Forcade E, Kröger N, Koc Y, Itäla-Remes M, Zecca M, Nagler A, Brissot E, Spyridonidis A, Bazarbachi A, Giebel S, Piemontese S, Mohty M, Ciceri F. Haploidentical stem cell donor choice for patients with acute myeloid leukemia: a study from the ALWP of the EBMT. Blood Adv. 2024;8(10):2332-41. https://doi.org/10.1182/bloodadvances.2023012133

60. Bazarbachi AH, Labopin M, Raiola AM, Blaise D, Arcese W, Santarone S, Koc Y, Bramanti S, Kulagin A, Kwon M, Sica S, Sanz J, Brissot E, Nagler A, Ciceri F, Mohty M. Posttransplant cyclophosphamide versus anti-thymocyte globulin versus combination for graft-versus-host disease prevention in haploidentical transplantation for adult acute myeloid leukemia: A report from the European Society for Blood and Marrow Transplantation Acute Leukemia Working Party. Cancer. 2024;130(18):3123-36. https://doi.org/10.1002/cncr.35365

61. Byrne M, Savani BN, Mohty M, Nagler A. Peripheral blood stem cell versus bone marrow transplantation: A perspective from the Acute Leukemia Working Party of the European Society for Blood and Marrow Transplantation. Exp Hematol. 2016;44(7):567-73. https://doi.org/10.1016/j.exphem.2016.04.005

62. Luznik L, O'Donnell PV, Symons HJ, Chen AR, Leffell MS, Zahurak M, Gooley TA, Piantadosi S, Kaup M, Ambinder RF, Huff CA, Matsui W, Bolaños-Meade J, Borrello I, Powell JD, Harrington E, Warnock S, Flowers M, Brodsky RA, Sandmaier BM, Storb RF, Jones RJ, Fuchs EJ. HLA-haploidentical bone marrow transplantation for hematologic malignancies using nonmyeloablative conditioning and high-dose, posttransplantation cyclophosphamide. Biol Blood Marrow Transplant. 2008;14(6):641-50. https://doi.org/10.1016/j.bbmt.2008.03.005

63. Campregher PV, Hamerschlak N, Colturato VA, Mauad MA, de Souza MP, Bouzas LF, Tavares Rde C, Barros JC, Chiattone R, Paz A, Silla L, Vigorito AC, Miranda E, Funke VA, Flowers ME. Survival and graft-versus-host disease in patients receiving peripheral stem cell compared to bone marrow transplantation from HLA-matched related donor: retrospective analysis of 334 consecutive patients. Eur J Haematol. 2015;95(5):421-5. https://doi.org/10.1111/ejh.12508

64. Raj K, Pagliuca A, Bradstock K, Noriega V, Potter V, Streetly M, McLornan D, Kazmi M, Marsh J, Kwan J, Huang G, Getzendaner L, Lee S, Guthrie KA, Mufti GJ, O'Donnell P. Peripheral blood hematopoietic stem cells for transplantation of hematological diseases from related, haploidentical donors after reduced-intensity conditioning. Biol Blood Marrow Transplant. 2014;20(6):890-5. https://doi.org/10.1016/j.bbmt.2014.03.003

65. Tsirigotis P, Byrne M, Schmid C, Baron F, Ciceri F, Esteve J, Gorin NC, Giebel S, Mohty M, Savani BN, Nagler A. Relapse of AML after hematopoietic stem cell transplantation: methods of monitoring and preventive strategies. A review from the ALWP of the EBMT. Bone Marrow Transplant. 2016;51(11):1431-8. https://doi.org/10.1038/bmt.2016.167

66. Ciurea SO, Lima M, Cano P, Korbling M, Giralt S, Shpall EJ, Wang X, Thall PF, Champlin RE, Fernandez-Vina M. High risk of graft failure in patients with anti-HLA antibodies undergoing haploidentical stem-cell transplantation. Transplantation. 2009;88(8):1019-24. https://doi.org/10.1097/tp.0b013e3181b9d710

67. Nath K, Zhang MJ, Bye M, Abid MB, Benjamin C, Betts B, Bhatt NS, Arrieta Bolaños E, Bolon YT, Gadalla SM, Grunwald MR, Krem MM, Lee SJ, Marsh SGE, Martino R, Mehta PA, Milano F, Prestidge T, Saultz JN, Shaw BE, Spellman SR, Choe H, Shaffer BC. Transplant outcomes using older matched sibling donors compared with young alternative donors: a CIBMTR analysis. Blood Adv. 2025;9(14):3469-78. https://doi.org/10.1182/bloodadvances.2024014858

68. Lee CJ, Savani BN, Mohty M, Labopin M, Ruggeri A, Schmid C, Baron F, Esteve J, Gorin NC, Giebel S, Ciceri F, Nagler A. Haploidentical hematopoietic cell transplantation for adult acute myeloid leukemia: a position statement from the Acute Leukemia Working Party of the European Society for Blood and Marrow Transplantation. Haematologica. 2017;102(11):1810-22. https://doi.org/10.3324/haematol.2017.176107

69. Crucitti L, Crocchiolo R, Toffalori C, Mazzi B, Greco R, Signori A, Sizzano F, Chiesa L, Zino E, Lupo Stanghellini MT, Assanelli A, Carrabba MG, Marktel S, Marcatti M, Bordignon C, Corti C, Bernardi M, Peccatori J, Bonini C, Fleischhauer K, Ciceri F, Vago L. Incidence, risk factors and clinical outcome of leukemia relapses with loss of the mismatched HLA after partially incompatible hematopoietic stem cell transplantation. Leukemia. 2015;29(5):1143-52. https://doi.org/10.1038/leu.2014.314

70. Chakrabarty JLH, Rubinger M, Le-Rademacher J, Wang HL, Grigg A, Selby GB, Szer J, Rowe JM, Weisdorf DJ, Tallman MS. Autologous is superior to allogeneic hematopoietic cell transplantation for acute promyelocytic leukemia in second complete remission. Biol Blood Marrow Transplant. 2014;20(7):1021-5. https://doi.org/10.1016/j.bbmt.2014.03.025

71. Burchert A, Bug G, Fritz LV, Finke J, Stelljes M, Röllig C, Wollmer E, Wäsch R, Bornhäuser M, Berg T, Lang F, Ehninger G, Serve H, Zeiser R, Wagner EM, Kröger N, Wolschke C, Schleuning M, Götze KS, Schmid C, Crysandt M, Eßeling E, Wolf D, Wang Y, Böhm A, Thiede C, Haferlach T, Michel C, Bethge W, Wündisch T, Brandts C, Harnisch S, Wittenberg M, Hoeffkes HG, Rospleszcz S, Burchardt A, Neubauer A, Brugger M, Strauch K, Schade-Brittinger C, Metzelder SK. Sorafenib maintenance after allogeneic hematopoietic stem cell transplantation for acute myeloid leukemia with FLT3 –internal tandem duplication mutation (SORMAIN). J Clin Oncol. 2020;38(26):2993-3002. https://doi.org/10.1200/jco.19.03345

72. Maziarz RT, Levis M, Patnaik MM, Scott BL, Mohan SR, Deol A, Rowley SD, Kim DDH, Hernandez D, Rajkhowa T, Haines K, Bonifacio G, Rine P, Purkayastha D, Fernandez HF. Midostaurin after allogeneic stem cell transplant in patients with FLT3-internal tandem duplication-positive acute myeloid leukemia. Bone Marrow Transplant. 2021;56(5):1180-9. https://doi.org/10.1038/s41409-020-01153-1

73. Platzbecker U, Wermke M, Radke J, Oelschlaegel U, Seltmann F, Kiani A, Klut IM, Knoth H, Röllig C, Schetelig J, Mohr B, Graehlert X, Ehninger G, Bornhäuser M, Thiede C. Azacitidine for treatment of imminent relapse in MDS or AML patients after allogeneic HSCT: results of the RELAZA trial. Leukemia. 2012;26(3):381-9. https://doi.org/10.1038/leu.2011.234

74. Wei AH, Döhner H, Pocock C, Montesinos P, Afanasyev B, Dombret H, Ravandi F, Sayar H, Jang JH, Porkka K, Selleslag D, Sandhu I, Turgut M, Giai V, Ofran Y, Kizil Çakar M, Botelho de Sousa A, Rybka J, Frairia C, Borin L, Beltrami G, Čermák J, Ossenkoppele GJ, La Torre I, Skikne B, Kumar K, Dong Q, Beach CL, Roboz GJ. Oral azacitidine maintenance therapy for acute myeloid leukemia in first remission. N Engl J Med. 2020;383:2526-37. https://doi.org/10.1056/NEJMoa2004444

75. Levis MJ, Hamadani M, Logan B, Jones RJ, Singh AK, Litzow M, Wingard JR, Papadopoulos EB, Perl AE, Soiffer RJ, Ustun C, Ueda Oshima M, Uy GL, Waller EK, Vasu S, Solh M, Mishra A, Muffly L, Kim HJ, Mikesch JH, Najima Y, Onozawa M, Thomson K, Nagler A, Wei AH, Marcucci G, Geller NL, Hasabou N, Delgado D, Rosales M, Hill J, Gill SC, Nuthethi R, King D, Wittsack H, Mendizabal A, Devine SM, Horowitz MM, Chen YB; BMT-CTN 1506/MORPHO Study Investigators. Gilteritinib as post-transplant maintenance for AML with internal tandem duplication mutation of *FLT3*. J Clin Oncol. 2024;42(15):1766-75. https://doi.org/10.1200/jco.23.02474

76. Lloret-Madrid P, Chorão P, Guerreiro M, Montesinos P. CAR-T cell therapy for acute myeloid leukemia: where do we stand now? Curr Oncol. 2025;32(6):322. https://doi.org/10.3390/curroncol32060322

77. Damiani D, Tiribelli M. CAR-T cells in acute myeloid leukemia: where do we stand? Biomedicines. 2024;12(6):1194. https://doi.org/10.3390/biomedicines12061194

78. Cummins K, Gill S. Chimeric antigen receptor T cells in acute myeloid leukemia. Hematol Oncol Clin North Am. 2023;37(6):1125-47. https://doi.org/10.1016/j.hoc.2023.06.004

79. Wang X, Zhang Y, Xue S. Recent progress in chimeric antigen receptor therapy for acute myeloid leukemia. Ann Hematol. 2024;103(6):1843-57. https://doi.org/10.1007/s00277-023-05601-y

80. Saito S, Nakazawa Y. CAR-T cell therapy in AML: recent progress and future perspectives. Int J Hematol. 2024;120(4):455-66. https://doi.org/10.1007/s12185-024-03809-w

81. Sauer T, Rooney CM. Current challenges for CAR T-cell therapy of acute myeloid leukemia. Transfusion. 2019;59(4):1171-3. https://doi.org/10.1111/trf.15199

82. Hederih J, Patrick J, Gannon I, Rampotas A, Roddie C, Sellar R. CAR cellular therapies for acute myeloid leukemia: current landscape and future directions. Immunotherapy. 2026;18(7):615-32. https://doi.org/10.1080/1750743X.2026.2689849

83. Ruggeri L, Capanni M, Urbani E, Perruccio K, Shlomchik WD, Tosti A, Posati S, Rogaia D, Frassoni F, Aversa F, Martelli MF, Velardi A. Effectiveness of donor natural killer cell alloreactivity in mismatched hematopoietic transplants. Science. 2002;295(5562):2097-100. https://doi.org/10.1126/science.1068440

84. McCurdy SR, Radojcic V, Tsai HL, Vulic A, Thompson E, Ivcevic S, Kanakry CG, Powell JD, Lohman B, Adom D, Paczesny S, Cooke KR, Jones RJ, Varadhan R, Symons HJ, Luznik L. Signatures of GVHD and relapse after posttransplant cyclophosphamide revealed by immune profiling and machine learning. Blood. 2022;139(4):608-23. https://doi.org/10.1182/blood.2021013054

85. Silla L. Peripheral blood persistence and expansion of transferred non-genetically modified Natural Killer cells might not be necessary for clinical activity. Immunother Adv. 2023;3(1):ltac024. https://doi.org/10.1093/immadv/ltac024

86. Cichocki F, Felices M, Matson AW, Lee MJ, Miller JS. Can natural killer cells cure leukemia? Leukemia. 2026;40(8):1600-3. https://doi.org/10.1038/s41375-026-02992-5

87. Wethington D, Ahmad S, Potempa M, Giuliani G, Aguilar OA, Poudel M, Grassmann S, Stewart W, Adams NM, Sun JC, Lanier LL, Das J. Clonal stochasticity in early NK cell response to mouse cytomegalovirus is generated by mature subsets of varying proliferative ability. bioRxiv [Preprint]. 2025:2023.09.07.556760. https://doi.org/10.1101/2023.09.07.556760

88. Gurney M, O'Dwyer M. Realizing innate potential: CAR-NK cell therapies for acute myeloid leukemia. Cancers (Basel). 2021;13(7):1568. https://doi.org/10.3390/cancers13071568

89. Rana S, Thomas L, Kirkham AM, Shorr R, Visram A, Maganti H, Seftel M, Allan DS. CAR-NK cells to treat patients with cancer: a systematic scoping review of published studies and registered clinical trials. Cytotherapy. 2025;27(10):1179-89. https://doi.org/10.1016/j.jcyt.2025.06.006

90. Bahramloo M, Shahabi SA, Kalarestaghi H, Rafat A, Mazloumi Z, Samimifar A, Asl KD. CAR-NK cell therapy in AML: Current treatment, challenges, and advantage. Biomed Pharmacother. 2024;177:117024. https://doi.org/10.1016/j.biopha.2024.117024

91. Mansour AG, Teng KY, Li Z, Zhu Z, Chen H, Tian L, Ali A, Zhang J, Lu T, Ma S, Lin CM, Caligiuri MA, Yu J. Off-the-shelf CAR-engineered natural killer cells targeting FLT3 enhance killing of acute myeloid leukemia. Blood Adv. 2023;7(20):6225-39. https://doi.org/10.1182/bloodadvances.2022007405

92. Dong H, Ham JD, Hu G, Xie G, Vergara J, Liang Y, Ali A, Tarannum M, Donner H, Baginska J, Abdulhamid Y, Dinh K, Soiffer RJ, Ritz J, Glimcher LH, Chen J, Romee R. Memory-like NK cells armed with a neoepitope-specific CAR exhibit potent activity against NPM1 mutated acute myeloid leukemia. Proc Natl Acad Sci U S A. 2022;119(25):e2122379119. https://doi.org/10.1073/pnas.2122379119

93. Klaihmon P, Luanpitpong S, Kang X, Issaragrisil S. Anti-TIM3 chimeric antigen receptor-natural killer cells from engineered induced pluripotent stem cells effectively target acute myeloid leukemia cells. Cancer Cell Int. 2023;23(1):297. https://doi.org/10.1186/s12935-023-03153-9

94. Christodoulou I, Ho WJ, Marple A, Ravich JW, Tam A, Rahnama R, Fearnow A, Rietberg C, Yanik S, Solomou EE, Varadhan R, Koldobskiy MA, Bonifant CL. Engineering CAR-NK cells to secrete IL-15 sustains their anti-AML functionality but is associated with systemic toxicities. J Immunother Cancer. 2021;9(12):e003894 https://doi.org/10.1136/jitc-2021-003894

95. Morgan MA, Kloos A, Lenz D, Kattre N, Nowak J, Bentele M, Keisker M, Dahlke J, Zimmermann K, Sauer M, Heuser M, Schambach A. Improved activity against acute myeloid leukemia with chimeric antigen receptor (CAR)-NK-92 cells designed to target CD123. Viruses. 2021;13(7):1365. https://doi.org/10.3390/v13071365

96. Wang Y, Yu Y, Wang S, Qu J, Song Y. From innate immunity to precision cancer therapy: the clinical advancement of NK cell therapy. Int Immunopharmacol. 2026;174:116373. https://doi.org/10.1016/j.intimp.2026.116373

97. Bexte T, Albinger N, Al Ajami A, Wendel P, Buchinger L, Gessner A, Alzubi J, Särchen V, Vogler M, Rasheed HM, Jung BA, Wolf S, Bhayadia R, Oellerich T, Klusmann JH, Penack O, Möker N, Cathomen T, Rieger MA, Imkeller K, Ullrich E. CRISPR/Cas9 editing of NKG2A improves the efficacy of primary CD33-directed chimeric antigen receptor natural killer cells. Nat Commun. 2024;15(1):8439. https://doi.org/10.1038/s41467-024-52388-1

98. Li YR, Shen X, Chen Y, Zhu Y, Huang J, Oliai C, Yang L. Synergizing hypomethylating agents with off-the-shelf CD70-targeted chimeric antigen receptor-engineered natural killer T cells for the treatment of acute myeloid leukemia. Leukemia. 2026;40(5):880-93. https://doi.org/10.1038/s41375-026-02930-5

99. Li YR, Chen Y, Yang L. Exploring CAR cell therapies beyond CAR-T for myeloid malignancies. J Biomed Sci. 2026;33(1):60. https://doi.org/10.1186/s12929-026-01265-8