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Precision management of acute myeloid leukemia: A unified guideline of international and regional standards

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INTRODUCTION

Acute myeloid leukemia (AML) is a molecularly heterogeneous malignancy with poor prognosis, especially in elderly and relapsed/refractory (R/R) patients. Key advances, including molecular testing, targeted therapies, MRD monitoring, and allo-HSCT, have driven AML management into the personalized era. This guideline integrates frameworks from ELN (2022/2024) for genetic risk stratification, NCCN (v3.2026) for clinical protocols, Children's Oncology Group (COG) for pediatric standards, and Chinese guidelines and consensus (2023-2025) for regional adaptations. While global diagnostic standards have harmonized, we address therapeutic divergences necessitated by drug accessibility and population-specific data (Figure 1).

DIAGNOSIS AND RISK STRATIFICATION

AML diagnosis is consistent across major guidelines. Diagnosis requires ≥ 20% blasts in bone marrow or peripheral blood, or ≥10% for subtypes with genetic abnormalities (*e.g.*, t(8;21), inv(16), t(15;17), *NPM1*, and *KMT2A*). ELN 2022 refines the 2017 framework by prioritizing molecular precision. Favorable-risk features include in-frame *CEBPA*-bZIP mutations (replacing the 2017 biallelic requirement) and *NPM1* mutations without *FLT3*-ITD. The *FLT3*-ITD is reclassified as intermediate-risk regardless of allelic ratio. Adverse-risk encompasses *TP53* mutations (VAF ≥10% denoting very adverse risk), myelodysplastic syndrome (MDS)-related mutations (*e.g.*, *ASXL1*, *RUNX1*, *SRSF2*, *BCOR*, *EZH2*, *SF3B1*, *STAG2*, *U2AF1*, *ZRSR2*), complex karyotypes, and *KMT2A* rearrangement.

Building on this, the ELN 2024 update introduces a context-dependent model specifically for low-intensity therapy, identifying *NPM1*, *IDH1/2*, and *DDX41* as favorable markers. MRD assessment remains essential for dynamic risk evaluation. Complementing global standards, Chinese Adult AML Guideline (2023) integrates region-specific adverse markers, such as *NUP98* rearrangements, to optimize local clinical decision-making.

COMPARATIVE GUIDELINES FRAMEWORK

To reconcile global standards with regional practice, key divergences among NCCN (v3.2026), ELN (2022/2024), and Chinese (2023) guidelines are summarized: 1) NCCN/ELN removed *FLT3*-ITD allelic ratio from risk assessment, whereas the Chinese guideline retains it for favorable-risk stratification; 2) ELN 2024 tailors genetic risk for less-intensive therapy, while NCCN/Chinese guidelines primarily based on intensive-chemotherapy-derived cohorts; 3) NCCN/ELN adopt a 10% blast cutoff for specific molecular subtypes, versus 20% in China; 4) The Chinese framework uniquely incorporates region-specific markers such as *NUP98*-rearrangements.

TREATMENT STRATEGIES

Initial treatment in adults

Patients eligible for intensive therapy. Standard "7+3" regimen remains the backbone for fit adults (complete remission (CR) 70-75%). For *FLT3*-ITD AML, NCCN (V3.2026) elevated quizartinib plus "7+3" to Category 1 recommendation (QuANTUM-First; OS 31.9 *vs* 15.1 months), alongside midostaurin (RATIFY; OS 74.7 *vs.* 25.6 months). For *CD33*-positive/core-binding factor (CBF) AML, fractionated gemtuzumab ozogamicin (GO) improves survival and reduces relapse risk by ~20% (ALFA-0701/AML15). In patients aged ≥ 60 with secondary/therapy-related AML (s-AML/t-AML), CPX-351 is the NCCN-recommended standard induction, demonstrating superior OS over "7+3" (NCT01696084; 9.56 *vs.* 5.95 months). As quizartinib, midostaurin, GO, and CPX-351 are commercially unavailable in China, homoharringtonine (HHT)-based regimens serve as local alternatives. For younger patients, FLAG-Ida may be considered (UK-NCRI AML15/AML19), although it is not yet a first-line recommendation.

Patients ineligible for intensive therapy (unfit and elderly patients). Venetoclax plus an HMA is the established standard for unfit and elderly patients. Azacitidine plus venetoclax is the frontline choice (VIALE-A; OS 14.7 *vs* 9.6 months). While treatment for elderly AML generally aligns with this population, the venetoclax duration may be shortened to 14–21 days.[1] In China, this combination is graded as Level 1a evidence, although CAG regimen (cytarabine, aclarubicin, G-CSF) remains a common regional alternative. For *IDH1*-mutated AML, ivosidenib plus azacitidine is recommended (AGILE; OS 29.3 *vs.* 7.9 months). Notably, NCCN (v3.2026) has elevated decitabine plus venetoclax to preferred status for this subgroup (NCT03404193; CR/CRi >80%). While enasidenib plus HMA targets *IDH2* (AG221-AML-005), it awaits first-line inclusion and remains unavailable in China. Investigational triplet regimens (HMA + venetoclax + *IDH*-inhibitor) demonstrated promising CR rates (92%) (NCT03471260 and NCT04774393),[2] representing a potent future direction. For very elderly or frail patients, HMA monotherapy (azacitidine or decitabine) or low-dose cytarabine (LDAC) ± glasdegib (BRIGHT-AML-1003, unavailable in China) may be considered. Uniquely, the 2025 Chinese Consensus on Elderly AML emphasizes integrating traditional Chinese medicine with standard supportive care, recommending agents such as Huang Lian Jie Du Tang (Level 1a evidence) and Qing Wen Bai Du Yin (Level 2b evidence).

Management of pediatric AML (pAML)

Standard induction (DA/DAE/ADE) and HiDAC-based consolidation are utilized globally. Adding GO (AAML0531) to CD33+ pAML reduces relapse (32.8% *vs.* 41.3%) and improves EFS (53.1% *vs.* 46.9%), particularly in *KMT2A*-rearranged and CBF-AML, though toxicity offsets OS benefits. In China, HHT-based regimens (CCLG-AML) are commonly used, achieving higher CR (79.9% *vs.* 73.9%) than etoposide-based protocols. Both COG and the 2024 Chinese pAML Consensus adopt molecular genetics and MRD (≥ 0.1% adverse-risk threshold) for risk stratification, recommending allo-HSCT in CR1 for high-risk or MRD-positive patients.

Post-remission management hematopoietic stem cell transplantation

Following the achievement of CR, high-dose cytarabine (HiDAC) remains the post-remission cornerstone. For *FLT3*-ITD AML, NCCN (v3.2026) solidifies TKI-combined consolidation as Category 1. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is prioritized for intermediate- or adverse-risk patients in CR1, with candidacy determined by physiological fitness (*e.g.*, HCT-CI score or Comprehensive Geriatric Assessment) rather than age. MRD monitoring remains crucial for guiding allo-HSCT decisions. Chinese guidelines further recommend CR1 transplantation if MRD remains

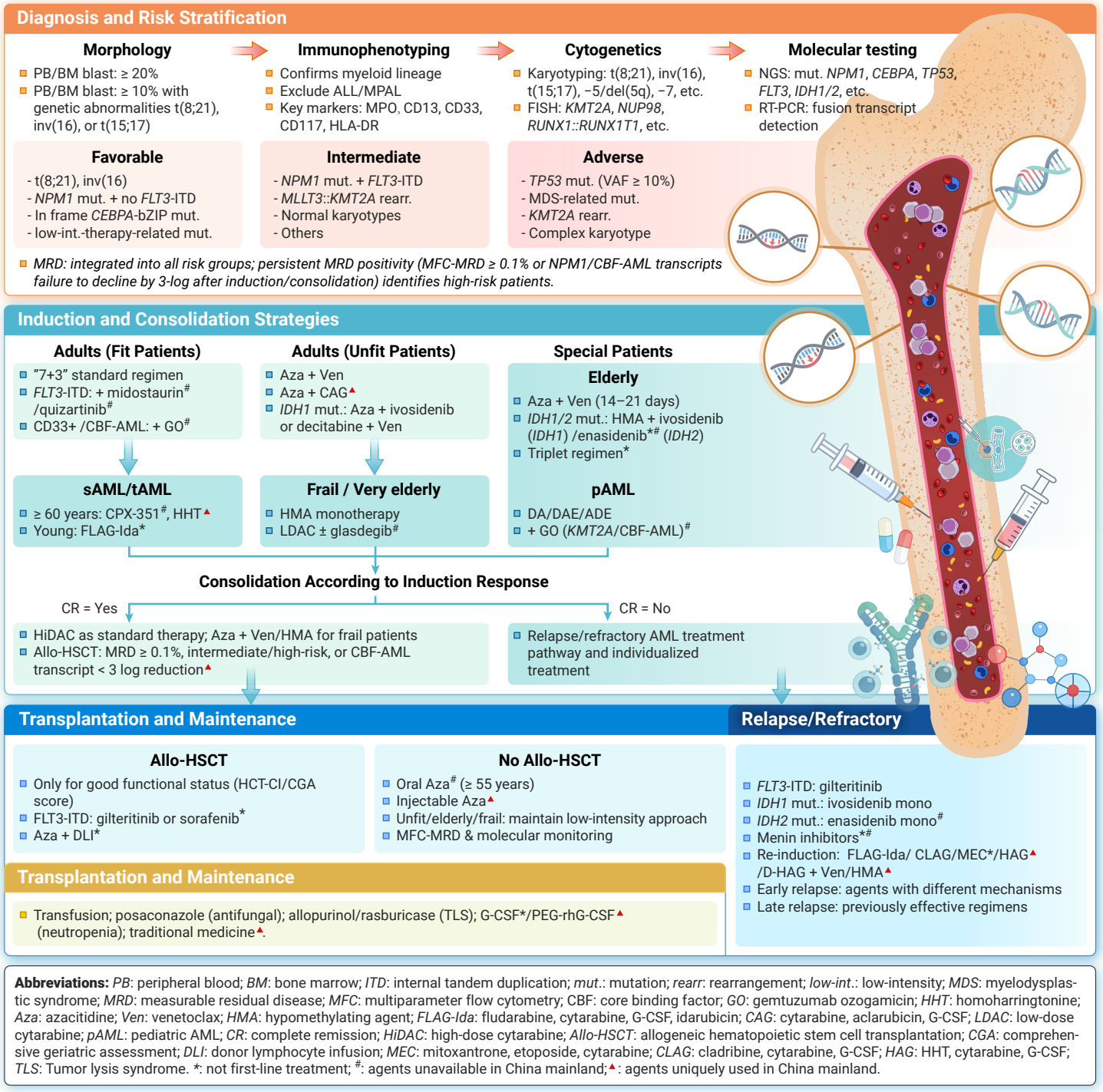

Figure 1. Management of acute myeloid leukemia.

persistently positive or CBF-AML transcript levels fail to decline by ≥ 3 log.

Maintenance therapy. Post-transplant maintenance is molecularly stratified. For *FLT3*-ITD-mutated AML, gilteritinib is the preferred standard, especially in peri-transplant MRD-positivity (MORPHO). Sorafenib remains a viable alternative (SORMAIN), with a Chinese Phase 3 trial (NCT02474290) reporting significantly reduced cumulative relapse (7% *vs.* 24.5%). Other *FLT3* inhibitors (midostaurin/quizartinib) are not yet established in this setting. For *IDH* mutations, ivosidenib and enasidenib remain under clinical evaluation for maintenance. For MRD-positive patients, azacitidine ± donor lymphocyte infusion has shown potential in high-risk patients (HOVON-105) or those with imminent relapse (RELAZA), although it is not yet first-line recommendation.

Non-transplant maintenance. For patients not undergoing transplant or those unable to tolerate further consolidation, oral azacitidine (CC-486) is the standard therapy for patients ≥ 55 years (QUAZAR-AML-001; OS 24.7 *vs.* 14.8 months), though its efficacy in favorable-risk AML (*e.g.,* CBF-AML) is less established. Due to limited accessibility in China, injectable azacitidine serves as the practical alternative. For patients initially on low-intensity regimens, continuous therapy with schedule adjustments is recommended to ensure long-term tolerability.

Management of R/R AML

The management of R/R AML is increasingly biomarker-driven, aiming to achieve remission as a bridge to allo-HSCT. Targeted therapies form the cornerstone for patients with actionable mutations. For *FLT3*-ITD, gilteritinib is the preferred standard (ADMIRAL; OS 9.3 *vs.* 5.6 months). For *IDH*-mutations, ivosidenib (AG120-C-001; *IDH1*) and enasidenib (AG221-AML-004;

IDH2) monotherapies are recommended. While ivosidenib is approved in China (AG120-C-001; CR+CRh 30.4%), enasidenib is unavailable, making venetoclax-based regimens a regional alternative. NCCN (v3.2026) has incorporated menin inhibitors – ziftomenib (KOMET-001; CR/CRh 22%)[3] and revumenib[4] (AUGMENT-101; CR/CRh 22.8%, for *KMT2A*-rearranged or *NPM1*-mutated AML) – as targeted options, although they await approval in China.

For fit patients, intensive salvage chemotherapy, including FLAG-Ida (UK-NCRI-AML15), MEC (mitoxantrone + etoposide + cytarabine), or CLAG (cladribine + LDAC + G-CSF), remains an option. NCCN (v3.2026) emphasizes combining FLAG-Ida/CLAG with venetoclax as a potent reinduction strategy for adverse-risk cases. Uniquely in China, the HAG (or D-HAG plus venetoclax/HMA) regimen is a widely adopted salvage strategy for its accessibility. Therapeutic strategy is also guided by relapse timing. Early relapse (≤ 12 months) requires switching to agents with different mechanisms, along with transplantation evaluation. For late relapse (> 12 months), re-induction with prior effective therapy may be considered. For molecular relapse (MRD-conversion), early intervention is recommended prior to hematologic relapse, as per Chinese guidelines.

In recent years, low-intensity triplet regimens (*e.g.*, tuspetinib + venetoclax + azacitidine; TUSCANY) have shown promising CR rates (78%), although phase III validation is still lacking. Annamycin, when combined with cytarabine, has demonstrated prolonged survival without cardiotoxicity (MB-106; CR 40%), and the phase III MIRACLE trial is ongoing (NCT05319587). These advancements signify a shift toward more potent, low-toxicity salvage framework.

Supportive care

Supportive care principles are largely consistent across global guidelines. Blood transfusions are recommended when hemoglobin < 70 g/L or platelets < 10×10^9/L. For antifungal prophylaxis, NCCN recommends posaconazole (POSA) during induction (Grade 1a), echoed by COG and the 2024 Chinese pAML Consensus for intermediate/adverse-risk pAML. Tumor lysis syndrome prophylaxis is managed with allopurinol, reserving rasburicase for high-tumor-burden cases, as recommended by NCCN. In addition, G-CSF (*e.g.*, filgrastim) remains optional to stimulate neutrophil production in neutropenia; innovative long-acting formulations (PEG-rhG-CSF) are widely utilized in China. Uniquely, Chinese guidelines emphasize integrating traditional medicine with standard nutritional care to reduce chemotherapy-induced toxicities, enhance immune recovery, and improve patient well-being.

CONCLUSION AND FUTURE PERSPECTIVES

AML management has entered the precision medicine era, yet a one-size-fits-all global guideline remains impractical. While international frameworks are largely harmonized, regional adaptations are not merely substitutes for inaccessible agents; rather, they represent evidence-based, parallel standards of care tailored to local socioeconomic and pharmacogenetic realities. Looking ahead, emerging therapies, including bispecific antibodies, immune checkpoint inhibitors, and CAR-T/NK cell therapies, hold great promise, but currently lack evidence from large-scale trials.[5] Future advancements must therefore balance the integration of novel agents with the optimization of regionally accessible regimens to maximize survival for AML patients worldwide.

REFERENCES

1. Gangat N. and Tefferi A. (2025). Venetoclax schedule in AML: 7 vs 14 vs 21 vs 28 days. *Blood Cancer J.* **15**:56. DOI:10.1038/s41408-025-01270-4
2. DiNardo C.D., Marvin-Peek J., Loghavi S., et al. (2025). Outcomes of frontline triplet regimens with a hypomethylating agent, venetoclax, and isocitrate dehydrogenase inhibitor for intensive chemotherapy-ineligible patients with isocitrate dehydrogenase-mutated AML. *J. Clin. Oncol.* **43**:2692–2699. DOI:10.1200/JCO-25-00640
3. Wang E.S., Montesinos P., Foran J., et al. (2025). Ziftomenib in relapsed or refractory NPM1-mutated AML. *J. Clin. Oncol.* **43**:3381–3390. DOI:10.1200/JCO-25-01694
4. Issa G.C., Aldoss I., Thirman M.J., et al. (2025). Menin inhibition with revumenib for KMT2A-rearranged relapsed or refractory acute leukemia (AUGMENT-101). *J. Clin. Oncol.* **43**:75–84. DOI:10.1200/JCO.24.00826
5. Sun W. and Huang X. (2024). CAR-T cell therapy shines as a beam of hope in the fight against acute leukemia. *Holist. Integ. Oncol.* **3**. DOI:10.1007/s44178-024-00117-5

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Y.X.: Conceptualization, Methodology, Investigation, Formal analysis, Visualization, Writing – original draft, Writing – review & editing, Funding acquisition. H.Y1,4: Conceptualization, Methodology, Investigation, Formal analysis, Writing – review & editing, Funding acquisition. Y.S: Investigation, Writing – review & editing. H.Y3: Conceptualization, Supervision, Writing – review & editing, Funding acquisition.

DECLARATION OF INTERESTS

The authors declare no competing interests.