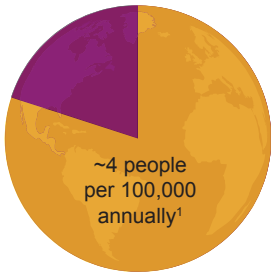
Acute Myeloid Leukemia (AML)

Overall AML survival rates have improved over the last several years, but new therapies are needed, particularly in patients with poor prognostic factors

United States incidence of AML



AML represents approximately

80%
of all acute leukemia cases in adults in the United States[2]

31%
of all leukemia cases in adults in the United States[3]

AML is predominantly a disease of older adults[1]

60%
diagnosed at ⩾65 years of age

34%
diagnosed at ⩾75 years of age

Median age at diagnosis:
69
years

Despite improvements in treatment of AML, patients ⩾70 years of age with AML have particularly poor outcomes[4]

Kaplan–Meier-Estimated 5-Year Overall Survival in the United States (2010-2017)[4]

t-AML refers to the development of AML as a consequence of prior cytotoxic therapy for another disease[5,6]

t-AML may develop through several mechanisms[5]

1. **Mutational events caused by cytotoxic therapy (eg, alkylating agents or radiation)**
2. **Abnormal recombination caused by topoisomerase II inhibitors**
3. **Selection of pre-existing chemotherapy-resistant clones**

AML arising from prior therapy is described differently in the ICC and WHO 2022 classifications[7,8]:

- **ICC 2022:** "therapy-related AML" is a diagnostic qualifier and not a stand-alone entity
- **WHO 2022:** "myeloid neoplasms post cytotoxic therapy" replaces "therapy related" and requires full diagnostic workup; exposure to PARP inhibitors is included as a qualifying criterion

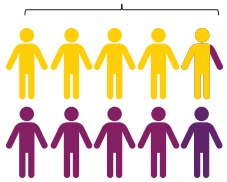
t-AML and AML-MRC are both associated with poor outcomes[9–13]

Up to 48% of adult AML cases are AML-MRC[9,14,19]

Complete remission rates[11,12,16-18,a]:

AML–MRC:
24%[18]-61%[12]

t-AML:
30%[18]-63%[16,b]



Median overall survival[12,20,21,a]:

AML-MRC:
10 months

t-AML:
6 months

~5%-10% of AML cases are t-AML[11,13,14,16,17]

It is important to consider AML subtype when determining diagnosis and customizing a treatment plan

AML-MRC was defined in the WHO 2016 classification as a distinct category of AML determined by clinical history, cytogenetics, or morphology[6]

Defined as **patients with AML who have ⩾20% blasts** in the peripheral blood or bone marrow and any of the following[6,22]:

- Previously documented MDS or MDS/MPN
- MDS-related cytogenetic abnormalities
- Multilineage dysplasia in ⩾50% of ⩾2 cell lineages in the absence of *NPM1* or biallelic *CEBPA* mutations

Excluding factors[6,22]:

- Any of the cytogenetic abnormalities qualifying for diagnosis of AML with recurrent genetic abnormalities, such as inv(3), t(6;9), or *NPM1* mutation
- Prior cytotoxic therapy for unrelated disease

AML-MRC is not included as a category in the ICC and WHO 2022 classifications[7,8]:

- **ICC 2022: prior MDS or MDS/MPN is used as a diagnostic qualifier**, AML with myelodysplasia-related cytogenetic abnormality and AML with myelodysplasia-related gene mutation are separate categories, and multilineage dysplasia is not included
- **WHO 2022:** a type of AML with defining genetic abnormalities **"AML-MR" replaces AML-MRC** and includes AML transformation of MDS or MDS/MPN and AML with MDS-related cytogenetics or gene mutations; multilineage dysplasia is not included

AML treatment decisions are guided by a range of factors[5]

The goal of AML treatment is to control, and if possible, eradicate disease, ideally using induction therapy to achieve complete remission, and then consolidation and/or maintenance therapy to deepen and prolong the response. HCT should be considered during first remission according to the benefit:risk ratio

The results of genetic analyses should be available as rapidly as possible (eg, 3-5 days) to guide treatment decisions. A short delay in starting treatment to establish the best treatment option is recommended to optimize outcomes

There are no generally accepted or validated criteria to consider a patient ineligible for intensive chemotherapy; however, criteria used in clinical trials have included[5,23,24]:

- **Age ⩾75 years** (but not as an absolute criterion as some may still derive benefit from intensive treatment)
- **DLCO ⩽65% (or FEV_1 ⩽65%)**
- **Inadequate performance status**
- **Presence of significant comorbidities**

Abbreviations: AML = acute myeloid leukemia, AML-MR = acute myeloid leukemia – myelodysplasia-related, AML-MRC = acute myeloid leukemia with myelodysplasia-related changes, DLCO = diffusion capacity of the lungs for carbon monoxide, FEV_1 = forced expiratory volume in the first second, HCT = hematopoietic cell transplantation, ICC = International Consensus Classification, MDS = myelodysplastic syndrome, MPN = myeloproliferative neoplasm, PARP = poly (ADP ribose) polymerase; t-AML = therapy-related acute myeloid leukemia, WHO = World Health Organization.

Footnote: [a]Data for complete remission rates and overall survival are from different studies with different patient populations. [b]Complete remission rates for t-AML in the literature: 30%,[18] 54%,[17] 61%,[11] and 63%.[16]

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