Oncology Clinical Pathways
Acute Myeloid Leukemia (AML)

April 2025 – V1.2025

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Acute Myeloid Leukemia – Presumptive Conditions

VA automatically presumes that certain disabilities were caused by military service. This is because of the unique circumstances of a specific Veteran's military service. If a presumed condition is diagnosed in a Veteran within a certain group, they can be awarded disability compensation.

Atomic Veterans – Exposure to Ionizing Radiation

- All forms of leukemia

Gulf War and Post 9/11 Veterans

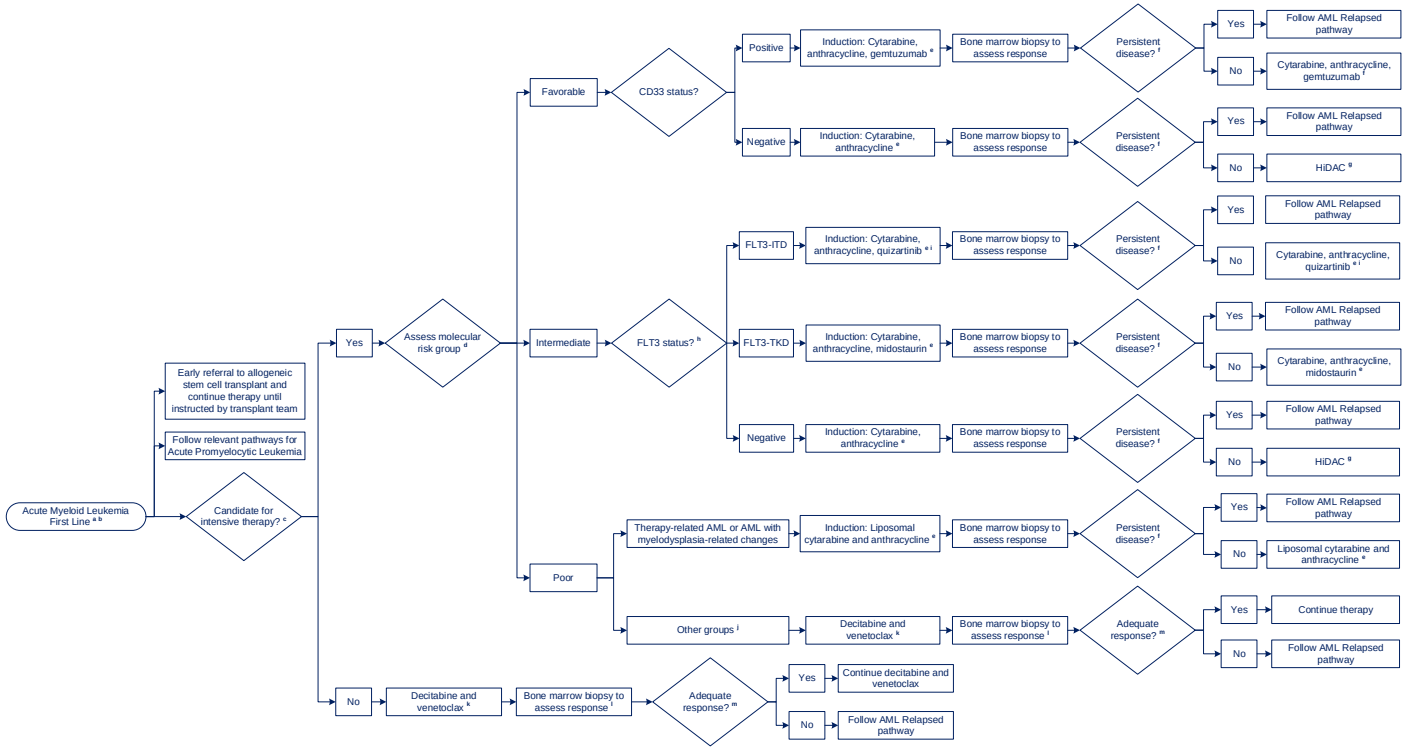
If the patient served on or after Sept. 11, 2001, in Afghanistan, Djibouti, Egypt, Jordan, Lebanon, Syria, Uzbekistan, or Yemen or if the patient served in the *Southwest Asia theater of operations, or Somalia, on or after Aug. 2, 1990, specific conditions include:

- Acute leukemias

*The Southwest Asia theater of operations refers to Iraq, Kuwait, Saudi Arabia, the neutral zone between Iraq and Saudi Arabia, Bahrain, Qatar, the United Arab Emirates, Oman, the Gulf of Aden, the Gulf of Oman, the Persian Gulf, the Arabian Sea, the Red Sea, and the airspace above these locations.

For more information, please visit U.S. Department of Veterans Affairs - Presumptive Disability Benefits (va.gov); VA makes several cancers presumptive for service connection Jan 08 2025; eCFR :: 38 CFR 3.320b -- Presumptive service connection for leukemias, multiple myelomas, myelodysplastic syndromes, and myelofibrosis.

Acute Myeloid Leukemia – First Line



Clinical trial(s) always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Diagnosis** must include flow cytometry, karyotype, rapid order (<72 hours) molecular tests (to include: FLT3, NPM1, IDH1, and IDH2), and myeloid NGS test (at minimum must include: ASXL1, BCOR, CEBPA, EZH2, FLT3, IDH1, IDH2, NPM1, RUNX1, SF3B1, SRSF2, STAG2, TP53, U2AF1, and ZRSR2); additional optional genes include: CBL, DDX41, KIT, KRAS, NRAS, and other genes associated with myeloid neoplasms; AML FISH testing can also be performed, either up front, or at the discretion of the pathologist (can include: -5/5q, -7/7q, KMT2A, t(8;21) RUNX1::RUNX1T1, t(15;17) PML::RARA, t(16:16) or inv(16) CBFB::MYH11, t(9;22) BCR::ABL1, and TP53)

[b] **Supportive Care** includes transfusions with leukocyte depleted/irradiated units for patients who are transplant candidates; platelet transfusion for platelet ≤ 10 per 10,000/mm^3, pRBC transfusion for Hgb < 7 g/dL, cryoprecipitate for fibrinogen < 150 mg/dL; tumor lysis syndrome monitoring, allopurinol and IV fluid prophylaxis, and rasburicase treatment if needed for patients with high WBC, hyperuricemia, and/or renal dysfunction; infection prophylaxis is recommended e.g., fungal, HSV/VZV, and bacterial

[c] **Candidate for Intensive Therapy** assess by age, performance status, comorbidities, and social factors; useful tool is the Fred Hutch Treatment Related Mortality Calculator; echocardiogram is required if considering intensive therapy; candidates for intensive therapy assumes that the patient is a transplant candidate; early HLA typing recommended

[d] **Risk Group Classification** determined via guidelines such as European LeukemiaNet (ELN) or National Comprehensive Care Network (NCCN)

[e] **Anthracycline** either daunorubicin or idarubicin is appropriate

[f] **Persistent Disease** second induction may be appropriate based on depth of response and regimen used

[g] **HiDAC** "High Dose" Cytarabine Consolidation; dosing schedule may be on days 1-3 or days 1, 3, and 5; monitoring for neurologic (cerebellar) toxicity required; supportive care with steroid eye drops required

[h] **FLT3 Status** mutation defined as point mutation in the TKD or ITD mutation

[i] **Quizartinib** has a boxed warning for risk of QT prolongation, Torsades de pointes, and cardiac arrest; perform EKG at baseline, weekly during induction and consolidation phases and weekly for at least the first month of maintenance, then periodically; refer to prescribing information for EKG monitoring recommendations; monitor serum electrolytes (magnesium, potassium) at baseline and as clinically indicated

[j] **Other Groups** includes AML secondary to myeloproliferative neoplasms as well as unfavorable molecular features

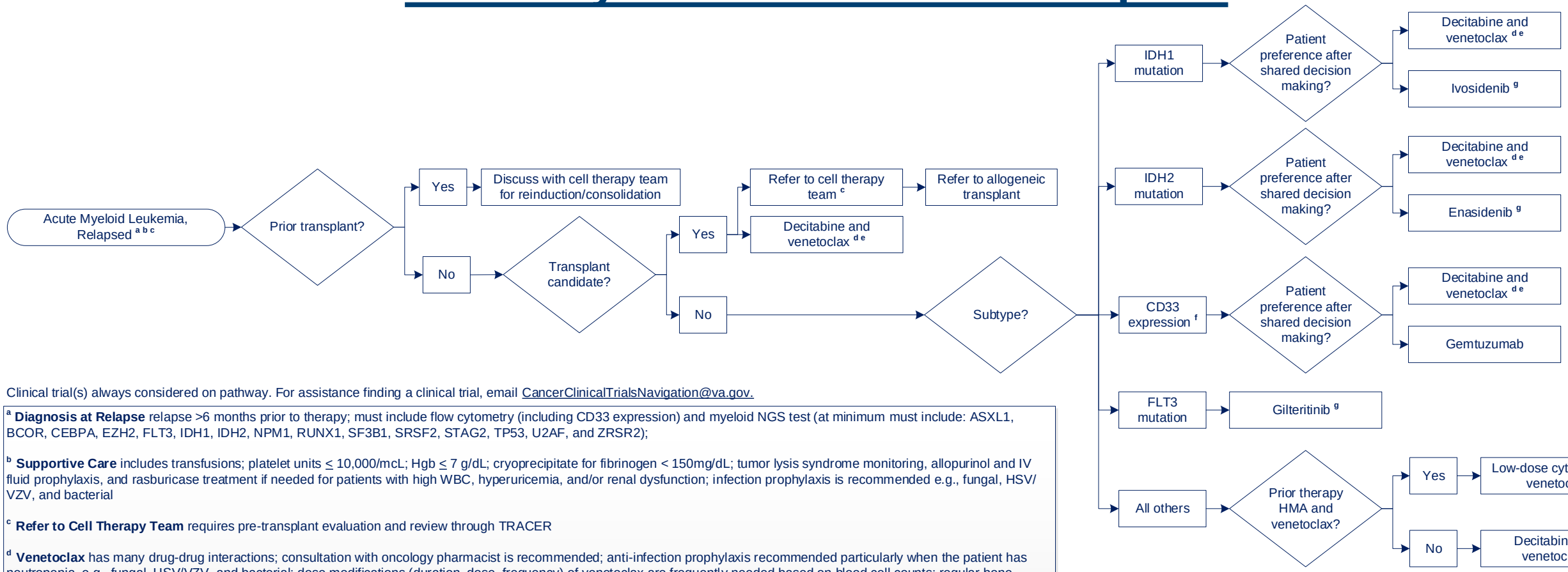
[k] **Venetoclax** has many drug-drug interactions; consultation with oncology pharmacist is recommended; anti-infection prophylaxis recommended particularly when the patient has neutropenia, e.g., fungal, HSV/VZV, and bacterial; dose modifications (duration, dose, frequency) of venetoclax are frequently needed based on blood cell counts; regular bone marrow biopsies to assess and follow response are needed with this continuous therapy

[l] **Bone Marrow Biopsy** after decitabine and venetoclax variability in response times

[m] **Adequate Response** defined as at minimum a partial remission

AML Acute Myeloid Leukemia
ITD Internal Tandem Duplication
TKD Tyrosine Kinase Domain

Acute Myeloid Leukemia – Relapsed



Clinical trial(s) always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Diagnosis at Relapse** relapse >6 months prior to therapy; must include flow cytometry (including CD33 expression) and myeloid NGS test (at minimum must include: ASXL1, BCOR, CEBPA, EZH2, FLT3, IDH1, IDH2, NPM1, RUNX1, SF3B1, SRSF2, STAG2, TP53, U2AF, and ZRSR2);

[b] **Supportive Care** includes transfusions; platelet units ≤ 10,000/mcL; Hgb ≤ 7 g/dL; cryoprecipitate for fibrinogen < 150mg/dL; tumor lysis syndrome monitoring, allopurinol and IV fluid prophylaxis, and rasburicase treatment if needed for patients with high WBC, hyperuricemia, and/or renal dysfunction; infection prophylaxis is recommended e.g., fungal, HSV/VZV, and bacterial

[c] **Refer to Cell Therapy Team** requires pre-transplant evaluation and review through TRACER

[d] **Venetoclax** has many drug-drug interactions; consultation with oncology pharmacist is recommended; anti-infection prophylaxis recommended particularly when the patient has neutropenia, e.g., fungal, HSV/VZV, and bacterial; dose modifications (duration, dose, frequency) of venetoclax are frequently needed based on blood cell counts; regular bone marrow biopsies to assess and follow response are needed with this continuous therapy

[e] **Refractoriness to Hypomethylating agents** decitabine or azayctidine: to avoid HMA + venetoclax combinations if previously refractory to HMA and can consider other options or reinduction with chemotherapy

[f] **CD33 Expression** in absence of other targets

[g] **Ivosidenib, Enasidenib, and Gilteritinib** require special monitoring for and treatment of differentiation syndrome

AML Acute Myeloid Leukemia
HMA Hypomethylating Agent

Acute Myeloid Leukemia – Molecular Testing Table

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Acute Myeloid Leukemia (AML)	Flow cytometry	Leukemia/lymphoma panel	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	FISH	-5/-5q, -7/-7q, KMT2A, t(8;21) RUNX1::RUNX1T1, t(15;17) PML::RARA, t(16;16) or inv(16) CBFB::MYH11; t(9;22) BCR::ABL1; TP53	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Karyotyping	Karyotype	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Rapid Molecular Tests (<1 week TAT)	FLT3 ITD and TKD, IDH1/2, NPM1 (quantitative preferred), CEBPA (optional)	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Somatic NGS	NGS panel ASXL1, BCOR, CEBPA, EZH2, FLT3, IDH1, IDH2, NPM1, RUNX1, SF3B1, SRSF2, STAG2, TP53, U2AF1, and ZRSR2. Optional genes include: CBL, DDX41, KIT, KRAS, NRAS, and other genes associated with myeloid neoplasms.	GLA	GLA Grant*	Bone Marrow Biopsy, Blood
	Somatic NGS	Consider CGP if no driver mutation detected	Foundation Medicine	Yes	Bone Marrow Biopsy, Blood
	Germline NGS	Consider germline testing and genetic counseling if VAF >40% in AML predisposition genes (CEBPA, DDX41, RUNX1, ANKRD26, ETV6, GATA2, SAMD9, SAMD9L, BLM, NF1, CBL)	Local VA or locally contracted vendor	No	Blood
* Reach out to GLA for information on use of NGS testing under a VA sponsored grant, with no cost to your local facility					