Oncology Clinical Pathways
Acute Promyelocytic Leukemia (APL)

June 2024 – V1.2024

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Acute Promyelocytic Leukemia – Presumptive Conditions

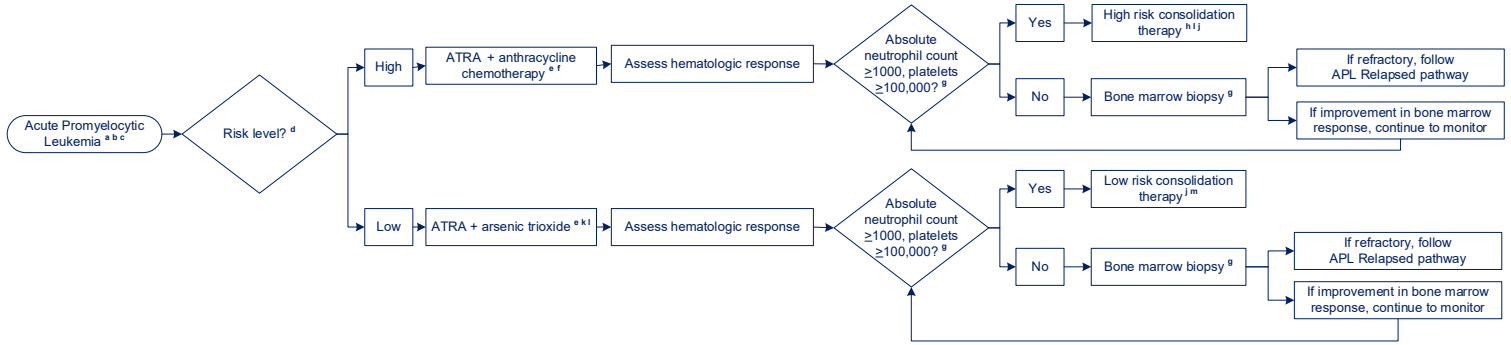
VA automatically presumes that certain disabilities were caused by military service. This is because of the unique circumstances of a specific Veteran's military service. If a presumed condition is diagnosed in a Veteran within a certain group, they can be awarded disability compensation.

Atomic Veterans – Exposure to Ionizing Radiation

- All forms of leukemia, except chronic lymphocytic leukemia

For more information, please visit U.S. Department of Veterans Affairs - Presumptive Disability Benefits (va.gov)

Acute Promyelocytic Leukemia



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

[a] **Acute Promyelocytic Leukemia** all trans retinoic acid (ATRA) should be started even prior to results of confirmatory testing; while awaiting diagnostic confirmation, begin ATRA in any patient with clinical suspicion for APL:
- Auer rods on smear, promyelocytes in excess
- Evidence of coagulopathy (low fibrinogen, bleeding)
- Hypo granular morphology (bilobed nuclei, minimal granules)
- APL-like flow cytometry profile (CD33+, CD34-, HLA-DR-, CD117+)

[b] **Initial Evaluation** includes coagulation studies, PT/INR, aPTT, fibrinogen, CBC with differential, peripheral blood smear, bone marrow biopsy with aspirate smear, flow cytometry, FISH (STAT for PML::RARA), karyotype, rapid molecular studies for FLT3 mutation, and myeloid NGS panel; if index of suspicion for APL is very high, quantitative PCR for PML::RARA can also be performed at initial workup; echocardiogram to assess left ventricular function, EKG with measurement of QTc

[c] **DIC** transfuse cryoprecipitate to keep fibrinogen ≥150 and platelet transfusion to keep platelet ≥50,000/mm^3; FFP can be used in addition for clinical significant bleeding; invasive procedures must be avoided; monitoring of DIC may need to be as frequent as q6-8h in the acute phase

[d] **Risk Levels** high risk is WBC >10,000/mm^3 and low risk is WBC ≤10,000/mm^3

[e] **ATRA** monitor for differentiation syndrome characterized by fever, hypoxia, and often transaminitis; prophylactic prednisone steroids can be used to prevent differentiation syndrome; treatment for differentiation syndrome involves holding ATRA and giving dexamethasone 10 mg every 6 hours until symptoms resolve

[f] **Anthracycline Chemotherapy** for patients who are not candidates for anthracycline chemotherapy, an alternative regimen is ATRA + arsenic trioxide + gemtuzumab ozogamicin

[g] **Absolute Neutrophil Count** and platelets can take up to 10 weeks for a hematologic response

[h] **High Risk Consolidation** ATRA + arsenic trioxide should be included in consolidation

[i] **CNS prophylaxis** is appropriate for patients who initially presented with high risk disease and who have entered into a complete remission after consolidation therapy; CNS prophylaxis prior to consolidation therapy is not recommended

[j] **Molecular remission** should be documented by obtaining PCR for PML::RARA at the conclusion of consolidation therapy; patients who are PCR negative should be monitored every 3 to 4 months for 2 years after consolidation therapy; PCR positive patients should have the PCR measured again 4 weeks later to confirm positivity; those are persistently positive should be treated per the relapsed APL pathway

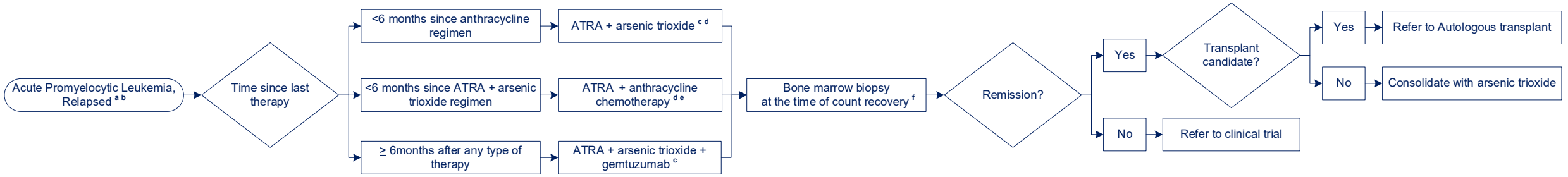
[k] **Arsenic Trioxide** should be monitored with twice weekly EKGs to measure the QTc; baseline EKG for QTc interval assessment, serum electrolytes (K, Ca, Mg) and SCr, LFTs, blood glucose; correct baseline electrolyte abnormalities; pregnancy test is recommended prior to initiation in patients with childbearing potential and patient partners who are of childbearing potential; consider thiamine level in patients at risk for deficiency due to risk of Wernicke encephalopathy; during therapy, maintain K and Mg in normal range; avoid concurrent use of drugs that prolong QTc interval; monitor for differentiation syndrome, neurologic symptoms, and nutritional status

[l] **Hydroxyurea** should be initiated if the WBC count increased to >50,000/mm^3; if hydroxyurea cannot control the WBC count then adding cytotoxic chemotherapy should be considered

[m] **Low risk consolidation** arsenic trioxide and ATRA should be included in consolidation

APL Acute Promyelocytic Leukemia
ATO Arsenic Trioxide
ATRA All Trans Retinoic Acid
CBC Complete Blood Count
CNS Central Nervous System
DIC Disseminated Intravascular Coagulation
FISH Fluorescence In Situ Hybridization
INR International Normalized Ratio
PCR Polymerase Chain Reaction
PT Prothrombin Time
aPTT, Activated Partial Thromboplastin Time
WCB White Blood Count

Acute Promyelocytic Leukemia – Relapsed



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[f] **Count Recovery** absolute neutrophil count ≥1000/mm^3, platelets ≥100,000/mm^3

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PT Prothrombin Time
aPTT, Activated Partial Thromboplastin Time

Acute Promyelocytic Leukemia – Molecular Testing Table

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Acute Leukemia (Mixed Phenotype or Undifferentiated Leukemia)	Flow Cytometry	Leukemia/lymphoma panel	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Karyotyping	Karyotyping	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
	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	RNA and DNA based CGP	Foundation Medicine	Yes	Bone Marrow Biopsy, Blood