ACUTE MYELOID LEUKEMIA —PATIENT PHARMACIST PROFILE REVIEW

Cancer & Non-Cancer Medication Checklist | NCCN AML v3.2026 | ELN 2022

Patient: _____ **MRN:** _____ **DOB:** _____ **Age/Gender:** _____

Phase: ☐ Induction ☐ Consolidation ☐ Maintenance ☐ Relapse ☐ Refractory

ELN Risk: ☐ Favorable ☐ Intermediate ☐ Adverse

DIAGNOSIS & DISEASE CHARACTERISTICS (EVAL-1)

☐	AML subtype confirmed (WHO/ICC 2022)	*Subtype:*
☐	De novo vs. secondary (s-AML: prior MDS/MPN; t-AML: prior chemo/RT)	*Origin:*
☐	**APL EXCLUDED (PML::RARA / morphology)** — *fatal if no ATRA*	*Status:*
☐	BM biopsy + aspirate: blast %	*Blasts %:*
☐	Immunophenotyping: flow cytometry + IHC	*CD:*
☐	Cytogenetics / FISH result	*Karyotype:*
☐	NGS molecular panel sent	*Lab / pending?:*
☐	Prior HMA exposure (impacts Ven/HMA benefit) *HMA-exposed may have reduced benefit*	*HMA-naive?:*

MOLECULAR PROFILE — ELN 2022 RISK (AML-A)

FAVORABLE (if no co-occurring adverse markers)		
☐	NPM1 mut — without FLT3-ITD + no adverse cytogenetics *Favorable only if isolated; adverse karyotype negates benefit*	*Result:*
☐	bZIP in-frame CEBPA mut	*Result:*
☐	CBF-AML: t(8;21) or inv(16)/t(16;16) *Check KIT mutation — increases relapse risk in t(8;21)*	*Result:*
INTERMEDIATE / ACTIONABLE		
☐	**FLT3-ITD (allelic ratio no longer stratifies per ELN 2022)** *ELN: any FLT3-ITD = intermediate if no adverse co-mut*	*Result:*
☐	FLT3-TKD	*Result:*
☐	IDH1 R132H/C mutation *Ivosidenib eligible*	*Result:*
☐	IDH2 R140/R172 mutation *Enasidenib eligible*	*Result:*
☐	DNMT3A / WT1 mutations	*Result:*
ADVERSE RISK (AML-MRC gene mutations)		
☐	**TP53 mut (mono- or biallelic) — very high risk**	*Result:*
☐	**ASXL1 / RUNX1 / BCOR / EZH2 / SF3B1 / SRSF2 / STAG2 / U2AF1 / ZRSR2** *Any = adverse per ELN 2022*	*Result:*
☐	**Complex karyotype / monosomal karyotype / del(5q)/-7/inv(3)/t(6;9)**	*Result:*

PATIENT FITNESS & BASELINE ASSESSMENT

☐	Age + ECOG PS (fitness-based, not age-based eligibility) *NCCN: intensive eligibility = fitness-based*	*Age:* *ECOG:*
☐	**Cardiac: LVEF (echo or MUGA — baseline required)** *Reassess before EACH anthracycline-consolidation*	*LVEF %:*
☐	**Renal: SCr / CrCl / eGFR** *HiDAC dose risk increases if CrCl reduced*	*CrCl mL/min:*
☐	**Hepatic: bilirubin / AST / ALT** *Impacts anthracycline, Ven, GO dosing*	*Bili / AST / ALT:*
☐	CBC with differential (WBC / ANC / Plt / Hgb)	*Values:*
☐	**Coagulation: PT / PTT / fibrinogen / D-dimer (DIC screen)** *Especially if APL on differential — DIC = life-threatening*	*Values:*
☐	**BMP: electrolytes / uric acid / LDH / phos / calcium** *TLS risk assessment baseline*	*Values:*
☐	**G6PD status (if rasburicase planned)** *Rasburicase CI in G6PD def — causes hemolytic anemia*	*G6PD result:*
☐	CMV serology (IgG/IgM — if HCT candidate)	*CMV status:*
☐	**HBsAg / HBcAb / HCV (hepatitis screening)** *Reactivation risk with immunosuppressive therapy*	*Results:*
☐	HIV status	*Results:*
☐	**Pregnancy test (females of childbearing potential)**	*Beta-hCG:*
☐	**Baseline ECG / QTc interval** *Required for quizartinib, gilteritinib, ATO*	*QTc ms:*
☐	Vitamin B12 / Folate (rule out nutritional anemia mimicking AML)	*Results:*

CNS LEUKEMIA ASSESSMENT (AML-B)

☐	**CNS symptoms present? (HA, vision, cranial nerve findings)**	*Symptoms:*
☐	LP: REQUIRED if symptomatic; Category 2B if asymptomatic	*LP performed?:*
☐	IT chemotherapy if CNS involvement confirmed	*IT agent / schedule:*

⚠ *Routine LP for asymptomatic patients = Category 2B only*

AML TREATMENT PLAN VERIFICATION	
INTENSIVE INDUCTION ELIGIBLE (AML-1)	
7+3 — Ara C dose (100/200 mg/m^2 CI) + anthracycline dose confirmed *Dauno 60-90 mg/m^2 or Ida 12 mg/m^2*	*Cytarabine mg/m^2 / Anthracycline mg/m^2:*
CPX-351 — indication verified (t-AML or AML-MRC only) *NOT a replacement for standard 7+3 in de novo AML*	*Indication confirmed?:*
+ Midostaurin (FLT3+ intensive eligible) — 50 mg BID Days 8-21 *RATIFY trial | Reduce if GI intolerance*	*FLT3 confirmed?:*
+ GO gemtuzumab (CD33+, CBF-AML favorable/intermediate ONLY) *NOT beneficial in adverse-risk dx*	*CD33+ / Risk group?:*
+ Quizartinib (FLT3-ITD+ intensive eligible) — 35.4 mg PO Days 8-21 *QuANTUM-First | QTc monitoring required*	*FLT3-ITD confirmed?:*
LOWER-INTENSITY / INDUCTION INELIGIBLE (AML-4)	
Ven/Aza (VIALE-A) or Ven/LDAC — fitness criteria documented *Age ≥75 OR comorbidities per FDA label*	*Eligibility criteria:*
Venetoclax ramp-up schedule correct *CYP3A4 inhibitor co-admin MUST reduce dose*	*Ven+HMA: 100/200/400 mg D1-3 Ven+LDAC: 100/200/400/600mg D1-4:*
WBC <25x10^9/L achieved before Ven initiation *Use hydroxyurea or leukapheresis if needed per AML-J*	*WBC at start*
IDH1i (ivosidenib) / IDH2i (enasidenib) monotherapy if eligible	*Mutation confirmed:*
Gilteritinib (FLT3+ lower intensity eligible)	*Indication:*
POST-REMISSION / CONSOLIDATION (AML-6)	
HiDAC — renal function checked before EACH cycle *3 g/m2 q12h x6 doses; cerebellar tox risk if CrCl reduced*	*CrCl pre-each cycle:*
alloHCT planned? Donor search initiated? (adverse/intermediate risk)	*Timeline / Donor:*
Maintenance therapy applicable? *CC-486 in CR/CRi post-chemo (≥55y) | FLT3i maintenance*	*Agent / indication:*
⚠ *CC-486 (Onureg/oral azacitidine) NEVER equals parenteral azacitidine — different dose, schedule, indication*	

CRITICAL DRUG INTERACTIONS (PHARMACIST FLAG)	
Venetoclax + posaconazole (strong CYP3A4 inhibitor) *Voriconazole/Itraconazole (70 mg); Fluconazole (100 mg)*	*Ven dose adjusted to 70 mg?:*
Venetoclax + strong CYP3A4 INDUCER — AVOID *Markedly reduces Ven plasma levels — avoid per NCCN AML-J*	*Rifampin / phenytoin / carbamazepine?:*
FLT3i (quizartinib / gilteritinib) + QT-prolonging drugs *Correct K+/Mg2+ proactively; baseline + periodic ECG*	*QTc trend / offending drugs?:*
Posaconazole suspension + PPI (reduced absorp.) *Acidic gastric pH needed for susp.; use tabs/IV or avoid PPI*	*PPI on med list?:*
Statin + azole (CYP3A4 inhibition) *Hold or switch to pravastatin (non-CYP3A4)*	*Simvastatin/lovastatin?:*
NSAIDs — renally toxic + antiplatelet in thrombocytopenia	*NSAID present?:*
Anticoagulants — dose/risk appropriate with thrombocytopenia? *Risk-benefit at Plt <50K — individualize*	*AC agent / Plt count:*
Herbal supplements (St. John's Wort = CYP3A4 inducer)	*Discontinued?:*
Grapefruit / Seville orange (CYP3A4 inhibition)	*Patient counseled?:*

SUPPORTIVE CARE CHECKLIST (AML-F / NCCN)	
INFECTION PROPHYLAXIS	
Antibacterial prophylaxis (fluoroquinolone if prolonged neutropenia)	*Agent:*
Antiviral: acyclovir/valacyclovir (HSV/HZV) *HZV ppx especially with ATO-based therapy*	*Agent / dose:*
PJP ppx — TMP-SMX or alternative *Allergy: dapsone/atovaquone/inhaled pentamidine*	*Agent / dose:*
Antifungal ppx (agent appropr for phase?) *R/R Ven regimens: NCCN recommends antifungal*	*Agent / indication:*
CMV monitoring plan (HCT candidates) _____	*Plan documented?:*
TUMOR LYSIS SYNDROME (AML-J / AML-F)	
TLS risk stratified (WBC / LDH / uric acid / blasts)	*Risk level:*
TLS ppx: allopurinol OR rasburicase *Rasburicase: rapidly rising WBC, high UA, renal dx*	*Agent / dose:*
G6PD checked before rasburicase *If G6PD def -> use allopurinol only*	*G6PD result:*
IV hydration + diuresis ordered	*Rate:*
TLS labs Q6-8h for first 24h of Ven dose escalation (AML-J)	*Schedule defined?:*
BLOOD PRODUCTS / TRANSFUSIONS (AML-F)	
Leukocyte-depleted blood products ordered *All AML patients — aGVHD risk*	*Confirmed?:*
Transfusion thresholds defined (Hgb <= 7-8; Plt <10K or bleeding)	*Thresholds set:*
Irradiated products (HCT candidates or heavy immunosuppression)	*Indicated?:*
Alloimmunized? -> HLA-specific products	*Antibody screen:*
OTHER SUPPORTIVE CARE	
Antiemetics (per NCCN guidelines) *Dex may be omitted in AML — immunosuppressive concern*	*Regimen:*
CVAD (multi-lumen central line)	*Type / date placed:*
G-CSF — NOT routine in induction; only for life-threatening sepsis *Hold ≥ 1 week before BM assessment to avoid confounding*	*Indication documented?:*
Prednisolone 1% eye drops QID (HiDAC ≥2g/m2) *Start D1 HiDAC; until 24h post-completion*	*Ordered? Dates?:*
Mucositis management protocol in place	*Plan?:*
Palliative care referral (NCCN recommends early)	*Referral placed?:*

NON-CANCER MEDICATIONS ASSESSMENT	
Antihypertensives (dose appropriate for current fluid/BP status?)	*Agent / BP:*
Anticoag/ antiplatelets (risk vs. benefit in thrombocytopenia?) *Hold if Plt <50K*	*Agent / Plt:*
Diuretics (hypovolemia risk during TLS aggressive hydration?)	*Agent / dose:*
Diabetes medications (steroid-induced hyperglycemia?) *Dexa premedication?*	*Agent / glucose:*
PPIs / H2RAs — still indicated? *PPI reduces posaconazole suspension absorption*	*Agent / indication:*
Seizure medications — CYP3A4 inducer? AVOID with venetoclax	*Agent identified?:*
Statins — myopathy risk with azoles?	*Agent / azole?:*
NSAIDs — contraindicated in thrombocytopenia + renal compromise	*Discontinued?:*
Opioids — renal/hepatic dose adjust needed?	*Agent / function:*
All herbals / supplements assessed *St. John's Wort = AVOID; antiplatelet herbals = AVOID*	*Supplements?:*

MONITORING, COUNSELING & CLINICAL PEARLS

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RESPONSE ASSESSMENT & MRD (AML-H / AML-I)	
Day 14-21 BM biopsy (hypoplasia assessment for intensive induction)	*Date planned:*
Post-induction BM day 28-35 response classification	*CR / CRi / MLFS / PD?:*
MRD method defined: MFC (DTA) vs. PCR (NPM1, CBFB) vs. NGS *No single universal standard; method depends on mutation subtype*	*Method / marker:*
MRD+ result triggers action (consolidation intensification / alloHCT)?	*Plan if MRD+?:*
Response category documented per NCCN AML-I criteria	*Category:*
⚠ *MRD negativity correlates with improved RFS but thresholds not universally standardized per NCCN*	

ONGOING MONITORING PARAMETERS (AML-G)	
CBC + differential — frequency and trigger for BM biopsy defined	*Frequency:*
BMP / LFTs — frequency per phase of treatment	*Frequency:*
Uric acid / LDH / phos / Ca (TLS) *Q6-8h during Ven ramp-up → daily until TLS risk resolved*	*Frequency:*
Neuro check before EACH HiDAC dose (≥2 g/m2) *Nystagmus / slurred speech / dysmetria / ataxia → HOLD*	*Documented pre-dose?:*
prednisolone 1% QID for HiDAC *Through 24h post-last cytarabine dose*	*Start/stop date:*
ECG / QTc monitoring (quizartinib, gilteritinib, ATO) *Correct hypoK/hypoMg before and during therapy*	*Baseline + frequency:*
Lifetime cumulative anthracycline dose *Dauno ~550 mg/m2; Ida ~150 mg/m2*	*Dauno or Ida total mg/m2:*
G-CSF held ≥1 week before planned BM assessment *Cannot interpret marrow if G-CSF within 7 days*	*Last G-CSF date:*
Venetoclax cytopenias — dose/duration reduction criteria documented	*Plan in place?:*
IDH inhibitor differentiation syndrome monitoring (WBC, sx) *Can occur weeks-months after initiation; steroids at first sign*	*Monitoring plan:*
Renal function trend during induction (rapidly rising Cr -> hold HiDAC)	*Cr trend:*

PATIENT COUNSELING CHECKLIST	
Goals of therapy discussed (curative vs. disease control)	*GOC documented?:*
Neutropenic fever: when to call, temp threshold (38.3C / 101F)	*Patient verbalized?:*
Venetoclax: take with fatty meal, no grapefruit, pill swallow intact *Ven requires fat-containing meal for absorption; do not crush*	*Counseled?:*
Oral targeted agents: missed dose policy, storage, adherence plan	*Agent-specific?:*
No live vaccines during active treatment or immunosuppression	*Counseled?:*
Fertility preservation discussion (age-appr.)	*Documented?:*
Infection precautions (hand hygiene, food safety, crowds)	*Counseled?:*
REMS program (arsenic trioxide, GO)	*Enrolled?:*
Adherence barriers identified and addressed	*Barrier?:*

PATIENT COUNSELING CHECKLIST

CRITICAL SAFETY — DO NOT MISS

- 🔴 **APL must be excluded before starting standard AML induction — treating APL without ATRA risks fatal DIC/differentiation syndrome.**
- 🔴 **CC-486 (oral azacitidine/Onureg) is NOT interchangeable with parenteral azacitidine — different formulation, dose, schedule, and indication. NEVER substitute.**
- 🔴 **Venetoclax + posaconazole: reduce Ven to 70 mg proactively. This must be caught at order entry — missed adjustment = overdose/toxicity.**
- 🔴 **Rasburicase contraindicated in G6PD deficiency — causes severe hemolytic anemia. Check G6PD status or use allopurinol if uncertain.**
- 🔴 **G-CSF confounds BM biopsy interpretation — MUST be held >=1 week before any planned marrow assessment.**

PHARMACOKINETIC & DRUG INTERACTION PEARLS

- 🟡 Posaconazole suspension requires acidic gastric pH for absorption. PPIs blunt this — use delayed-release tablet formulation or IV if PPI cannot be stopped.
- 🟡 Strong CYP3A4 inducers (rifampin, phenytoin, carbamazepine, St. John's Wort) MUST BE AVOIDED with venetoclax, dramatically reduce plasma levels.
- 🟡 Simvastatin/lovastatin + azole antifungals = elevated myopathy risk. Switch to pravastatin or rosuvastatin (minimal CYP3A4).
- 🟡 FLT3 inhibitors (quizartinib, gilteritinib): QT prolongation risk — correct hypokalemia and hypomagnesemia before and during therapy.

REGIMEN-SPECIFIC CLINICAL PEARLS

- 🔵 HiDAC cerebellar toxicity risk rises with age >60 and renal dysfunction. Neurologic exam (nystagmus, dysmetria, slurred speech, ataxia) BEFORE EVERY DOSE.
- 🔵 Steroid eye drops (prednisolone 1% QID) with every HiDAC cycle >=2 g/m2 — commonly omitted but required per NCCN to prevent keratoconjunctivitis.
- 🔵 FLT3-ITD allelic ratio no longer stratifies ELN 2022 risk. Any FLT3-ITD = intermediate risk if no adverse co-mutations — important for treatment selection.
- 🔵 NPM1 mutation is favorable ONLY when isolated (no FLT3-ITD, no adverse cytogenetics). Adverse karyotype co-occurring with NPM1 = adverse-risk per ELN 2022.
- 🔵 CPX-351 indication is t-AML or AML-MRC only — NOT a standard replacement for 7+3 in de novo AML. Verify indication at order review.
- 🔵 GO (gemtuzumab ozogamicin) has limited benefit in adverse-risk disease — confirm favorable or intermediate CBF-AML before approving.
- 🔵 IDH inhibitors: differentiation syndrome can occur weeks to months after initiation (unlike standard chemotherapy). Monitor WBC, start steroids early.
- 🔵 Venetoclax during R/R therapy: NCCN explicitly recommends antifungal prophylaxis. Ensure it is prescribed before cycle start.
- 🔵 NCCN: intensive induction eligibility is fitness-based, not age-based. Elderly patients with ECOG 0-2 and favorable genetics may benefit from intensive therapy.
- 🔵 Dexamethasone antiemetic: inclusion as a scheduled antiemetic in AML is controversial due to immunosuppressive effects — may be omitted or modified.

CLINICAL PEARLS

● BM Biopsy + Aspirate (Blast %): The biopsy gives architecture (cellularity, fibrosis, dysplasia pattern), aspirate gives cytology and morphology of individual cells. **AML is defined as ≥20% blasts** in BM or peripheral blood (WHO 2022). However, the **ICC retains a ≥10% threshold for AML with recurrent genetic abnormalities** — this distinction matters because it determines whether your patient has AML vs. MDS-EB (excess blasts).Blast % at baseline establishes the **disease burden**, and— relevant for TLS risk stratification. High blast % + high WBC = high TLS risk → aggressive prophylaxis, possible rasburicase over allopurinol. The day 14–21 BM biopsy during intensive induction tells you if there's residual leukemia (hypoplastic = good, persistent blasts = reinduction decision per AML-3). Post-induction BM (day 28–35): Defines response — CR requires <5% blasts with count recovery. CRi ≤5% blasts but incomplete count recovery. MLFS ≤5% blasts without count recovery. Pharmacist action: High blast count at diagnosis → flag TLS risk → ensure allopurinol is started OR escalate to rasburicase if WBC rapidly rising, uric acid elevated, or renal function impaired. Also check if WBC needs to be $<25\times10^9$/L before initiating venetoclax (NCCN AML-J). Karyotype + molecular together = complete ELN 2022 risk. You cannot assign risk from cytogenetics alone or molecular alone in many cases. A normal karyotype with FLT3-ITD and no NPM1 = intermediate risk. That same patient with a concurrent ASXL1 mutation = adverse risk.

● Immunophenotyping (Flow Cytometry + IHC): A panel of surface and intracellular **markers** expressed on the leukemic blasts, used to confirm myeloid lineage and identify specific **antigen expression**. **IHC uses tissue** sections (biopsy), while **flow cytometry uses suspended cells** (aspirate) with fluorescent antibody panels.

CD33	Target for **gemtuzumab ozogamicin (GO)** in **favorable/intermediate CBF-AML with CD33+ per NCCN**.
CD34	Marks immature progenitors; associated with certain subtypes
CD117 (c-KIT)	Myeloid blast marker; KIT mutations in CBF-AML increase relapse risk
MPO (myeloperoxidase)	Confirms myeloid lineage; required for AML diagnosis
CD13, CD15	Myeloid differentiation markers
HLA-DR	Typically negative in APL (PML::RARA) — HLA-DR negativity + CD33+ + MPO+ → high suspicion for APL
CD3, CD19, CD20	If positive → raises question of biphenotypic/mixed phenotype acute leukemia (MPAL) or contamination
TdT	Lymphoid marker; if positive in AML context → workup for ALL vs. MPAL

● Cytogenetics/FISH: Used for ELN 2022 risk stratification and determines treatment pathway. **Cytogenetics** (conventional karyotyping / G-banding) looks at the full chromosome picture (all 23 pairs) and identifies structural and numerical abnormalities. **FISH** uses fluorescent probes targeted at specific chromosomal loci to detect specific translocations or deletions with higher sensitivity. **FISH is faster** than conventional karyotype (24–72h vs. 7–10 days) and more sensitive for specific targets. It is particularly useful for rapid detection of APL (PML::RARA), CBF translocations, and MLL rearrangements when morphology is suspicious and you cannot wait for full karyotype to initiate therapy. Karyotype determine if patient needs alloHCT referral urgently (adverse risk → transplant in CR1 is the standard per NCCN AML-6). Also determines if CPX-351 is appropriate (t-AML and AML-MRC), often is adverse cytogenetics.

(8;21)(q22;q22) → RUNX1::RUNX1T1	Favorable	HiDAC consolidation preferred; GO may add benefit (CBF-AML); check KIT mutation
inv(16)/t(16;16) → CBFB::MYH11	Favorable	Same as t(8;21)
Normal karyotype (NK)	Intermediate	Molecular mutations then determine risk — NPM1, FLT3, CEBPA
t(9;11) → KMT2A::MLLT3	Intermediate	
Complex karyotype (≥3 abnormalities)	Adverse	alloHCT in CR1; venetoclax-based regimens increasingly used
Monosomal karyotype	Adverse	Very poor prognosis; intensive vs. lower-intensity decision critical
-7 / del(7q) / -5 / del(5q)	Adverse	
inv(3) / t(3;3) → GATA2::MECOM	Adverset	
(6;9) → DEK::NUP214	Adverse	FLT3-ITD co-occurs frequently

● Next-generation sequencing (NGS) Molecular Panel: checks for point **mutations**, **insertions/deletions** (indels), and **gene fusions**, at far greater depth and sensitivity than Sanger sequencing. Per NCCN v3.2026 (EVAL-1, updated): The mandatory minimum genes to be tested for ELN 2022 risk stratification are: ASXL1, BCOR, KIT, EZH2, FLT3-ITD, FLT3-TKD, NPM1, bZIP CEBPA, IDH1, IDH2, RUNX1, SF3B1, SRSF2, STAG2, TP53, U2AF1, ZRSR2 — and "other mutations." Timing nuance: NGS typically takes 7–14 days. Treatment often starts before results return. For example, if FLT3-ITD comes back positive while the patient is already on 7+3, midostaurin is added starting Day 8.

FLT3-ITD	Adds **midostaurin** (intensive, RATIFY) or **quizartinib** (intensive, QuANTUM-First) or **gilteritinib** (lower intensity). QTc monitoring for all FLT3i. Allelic ratio no longer stratifies ELN 2022 — any ITD = intermediate risk if no adverse co-mutation
FLT3-TKD	**Gilteritinib** covers TKD; quizartinib does NOT cover TKD
IDH1 R132	**Ivosidenib** eligible (lower intensity or R/R). Differentiation syndrome monitoring protocol needed
IDH2 R140/R172	**Enasidenib** eligible. Also differentiation syndrome risk. R172 tends to be mutually exclusive with NPM1
NPM1	Favorable prognosis if isolated. Best MRD marker by PCR (NPM1-PCR). Now also targetable with **ziftomenib** (R/R, added in NCCN v2.2026)
TP53	Adverse, especially biallelic. Impacts eligibility for certain trials; venetoclax-based lower-intensity regimens often used
RUNX1, ASXL1, SRSF2, etc.	AML-MRC gene mutations = adverse ELN 2022. CPX-351 is FDA-approved for AML-MRC
DNMT3A, TET2, ASXL1	**CHIP-related mutations** — NOT reliable MRD markers; they persist in remission. If the team is planning MRD monitoring by NGS, the molecular oncologist needs to select the right target mutation (ideally disease-specific, not CHIP-related).
KIT	In CBF-AML (t(8;21)): KIT mutation increases relapse risk — may influence decision to pursue alloHCT even in favorable-risk CBF

● **APL exclusion is morphology + flow + FISH together. HLA-DR negativity on flow + hypergranular promyelocytes + FISH for PML::RARA is your trifecta. Never wait for full karyotype if APL is suspected — initiate ATRA empirically, because the risk of fatal DIC from delay outweighs the risk of empiric ATRA in a non-APL patient.**

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