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Acute Myeloid Leukaemia

A mini review for clinicians

For postgraduate residents (medical and haematology oncology, haematology, internal medicine, emergency medicine, critical care, infectious diseases, pathology, transfusion medicine), practising clinicians and medical students

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Updated 17 October 2026. Educational summary written in our own words from current guidelines and primary trials; no drug doses; not advice for an individual patient. Verify current guidelines and Indian regulatory approvals before treatment decisions. Patients and families: please see the patient guides at drharitha.co.in.

Acute Myeloid Leukaemia

Haematological cancers, part 7 · AML in fit and unfit adults · Genetics and ELN risk · Induction, transplant and maintenance · Targeted therapy at relapse · Acute promyelocytic leukaemia · Leukaemia emergencies · Key points for clinicians · Last updated 17 October 2026

01 At a glance

- **AML is the commonest acute leukaemia of adults** (about 80% of adult acute leukaemias); median age at diagnosis 65–68 years in Western registries. It is a group of diseases defined by genetics, not one disease.
- **Suspect it from a blood count:** blasts on the smear, unexplained cytopenias, fever, bleeding or a very high white count. Fatigue and pallor often precede the diagnosis by months.
- **Stabilise before you classify:** in the first hours look for APL (bleeding, low fibrinogen: start ATRA on suspicion), leukostasis, tumour lysis and neutropenic infection (antibiotics within 60 minutes).
- **Classify by genetics** (WHO 5th edition or ICC 2022): marrow morphology and flow, karyotype, FISH and a rapid FLT3/NPM1/IDH panel plus a myeloid NGS panel. ELN 2022 sorts patients into favourable, intermediate and adverse risk ([ELN 2022](#)^[1]).
- **Fit adults:** 7+3 induction, with midostaurin or quizartinib for FLT3 mutations, gemtuzumab for CD33-positive core-binding-factor AML, and CPX-351 for therapy-related or myelodysplasia-related AML; then consolidation or allogeneic transplant by risk and MRD.
- **Unfit adults:** venetoclax with azacitidine improves survival over azacitidine alone ([VIALE-A](#)^[2]); IDH1-mutated AML: ivosidenib with azacitidine ([AGILE](#)^[3]).
- **APL is an emergency and one of the most curable leukaemias:** ATRA plus arsenic trioxide gives 72-month event-free survival of about 97% in low/intermediate-risk disease ([APLO406](#)^[4]).
- **Relapse:** repeat the genetics; targeted drugs (gilteritinib, IDH inhibitors, menin inhibitors) or salvage chemotherapy bridge to allogeneic HCT, the only cure.
- **India:** patients are younger (median 40 years in Vellore) and arrive after weeks of symptoms from far away; cost decides who is treated, multidrug-resistant infections drive induction deaths, and APL early deaths remain high ([Philip 2015](#)^[5]; [Mamlekar 2025](#)^[6]).

AML in one picture: suspect, stabilise, classify, then treat by fitness and genetics

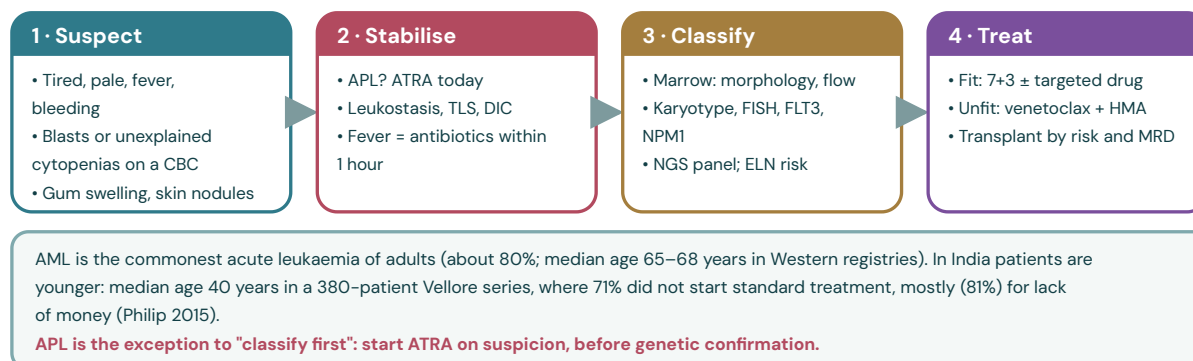
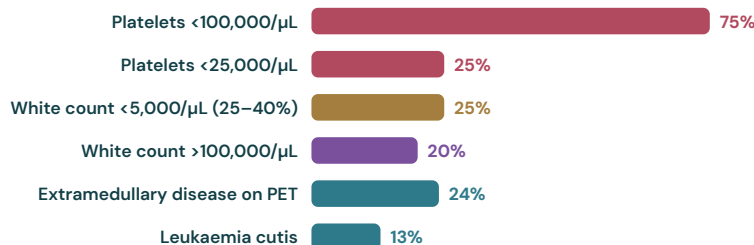


Figure 1. The four steps (UpToDate AML overview, diagnosis and induction reviews; Philip 2015 for India).

02 Clinical presentation, common traps & causes

What the first blood count shows (adults with newly diagnosed AML)



Look for

- Pallor, bruises, petechiae
- Gum hypertrophy (monocytic)
- Violaceous skin nodules
- Mass: myeloid sarcoma
- Sternal tenderness
- Fundal bleeds

Median white count about 15,000/μL: a normal or low count does not exclude AML. The smear shows blasts in nearly all patients; Auer rods are pathognomonic. Fever in a neutropenic patient is infection until proved otherwise. Bone pain and lymph nodes are uncommon (think ALL).

Figure 2. Presenting findings (UpToDate AML diagnosis review; extramedullary disease on PET in 3,522 patients). Leukaemia cutis is mostly monocytic AML.

Who gets it, and why

- **Age:** incidence rises with age; about 4 per 100,000 adults a year in the USA. AML is under 10% of acute leukaemias in children under 10 (where ALL dominates) but about 80% in adults.
- **Causes:** unknown in most. Known risks: previous chemotherapy (alkylating agents, topoisomerase II inhibitors) or radiotherapy (therapy-related AML), an earlier MDS or MPN, benzene, smoking (greatest risk above 60), and obesity (especially APL). Most AML arises from clonal haematopoiesis that has gathered further mutations.
- **Inherited predisposition:** familial disorders may underlie 5–10% of AML/MDS in older adults and 10–20% in young adults. Clues: relatives with blood cancers, long-standing cytopenias, a germline-type variant (DDX41, RUNX1, GATA2, biallelic CEBPA) on NGS. This matters when a sibling is the planned donor ([Klco 2021^{\[7\]}](#)).
- **APL:** 5–20% of AML depending on region; peaks in young adults (median age 40–50 years in Western series; 33 years in Lucknow).
- **India:** in a 2-year prospective Vellore series of 380 adults and children with non-APL AML, median age was 40, symptoms had lasted a median of 4 weeks, patients travelled a median of 580 km, and only 29% started standard treatment, 81% of the rest for lack of money ([Philip 2015^{\[5\]}](#)). At AIIMS, 480 patients aged 8–60 treated with 3+7 and high-dose cytarabine had 18.4% induction mortality ([Bahl 2015^{\[8\]}](#)).

Common traps

- **"Viral fever" treated for weeks.** Fever with pallor, bruises or gum bleeding needs a CBC with a smear the same day.
- **A normal or low white count read as "not leukaemia".** A quarter to two-fifths of patients have fewer than 5,000 white cells; the smear, not the count, makes the diagnosis.
- **Gum swelling sent to the dentist.** Gingival hypertrophy and violaceous skin nodules suggest monocytic AML.
- **Bleeding treated with plasma alone while the diagnosis waits.** Bleeding with low fibrinogen and granular cells is APL until proved otherwise: ATRA the same day.

- **A red cell transfusion in a breathless patient with 200,000 white cells.** It raises blood viscosity and can precipitate leukostasis: cytoreduce first, transfuse slowly if essential.
- **"Hyperkalaemia" treated in a patient with a huge white count.** Potassium leaks from cells in a clotted sample; check a heparinised (plasma) sample.
- **A mass biopsied and called "small round cell tumour" or lymphoma.** Myeloid sarcoma needs myeloid immunostains; it is AML whatever the marrow shows.

SHARE WITH PATIENTS: SYMPTOMS AND SUSPICION

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

Leukaemia occurs only in children?

Leukaemia always causes a very high white blood cell count?

Frequent fever always means an ordinary infection?

A normal haemoglobin level rules out leukaemia?

If there are no swollen lymph nodes, leukaemia is impossible?

03 Diagnosis, workup & staging essentials

The first 24 hours: four emergencies to look for before the marrow report

Bleeding / APL

- Smear: abnormal promyelocytes
- PT, aPTT, fibrinogen, D-dimer
- ATRA at once if APL suspected
- Platelets + cryo; no heparin

Leukostasis

- WBC >100,000 (or less with many blasts)
- Breathless, confused, visual change
- Start cytoreduction now
- Slow or withhold red cells

Tumour lysis

- K, PO₄, Ca, urate, creatinine
- High WBC or high LDH = high risk
- IV fluids; allopurinol or rasburicase
- G6PD before rasburicase

Infection

- Fever with ANC <500
- Cultures, then antibiotics <60 min
- Antipseudomonal beta-lactam
- Do not wait for the diagnosis

Spurious results: a huge white count lowers glucose and oxygen in the tube and releases potassium from clotting cells (pseudohyperkalaemia). Send the blood gas on ice and check potassium on a heparinised sample before treating a "high" value.

Figure 3. Emergencies at presentation (UpToDate AML diagnosis, complications, hyperleukocytosis, TLS and neutropenic fever reviews).

Making the diagnosis

- **Blood:** CBC with differential and smear review; PT, aPTT and fibrinogen; metabolic panel with LDH, urate and phosphate. When many blasts circulate, flow cytometry and genetics can be done on blood.
- **Marrow:** unilateral aspirate (500–cell count) and biopsy from the posterior iliac crest; the sternum is acceptable for aspiration only. Warn the laboratory: fresh samples are needed for flow, karyotype, FISH and molecular tests. Bleeding or infection at the site is unusual even with low counts.
- **Lineage:** myeloblasts are large with prominent nucleoli; Auer rods are pathognomonic. Flow cytometry (CD13, CD33, CD117, MPO; CD34 often) confirms myeloid lineage and sets the baseline for MRD.
- **Genetics:** banding karyotype (FISH does not replace it), rapid FLT3 (ITD and TKD), NPM1 and IDH1/2, and a myeloid NGS panel including TP53, CEBPA, RUNX1, ASXL1 and splicing genes; PML::RARA by PCR or FISH when APL is possible.
- **Diagnosis:** ≥10% myeloid blasts with a defining genetic lesion (APL, CBF fusions, KMT2A, DEK::NUP214, MECOM, CEBPA), any blast count with mutated NPM1 (WHO), ≥20% for BCR::ABL1 and for most AML without a defining lesion; myeloid sarcoma counts as AML at any marrow blast count ([WHO 2022](#)^[9]; [ICC 2022](#)^[10]).
- **CNS and imaging:** brain CT for suspected bleeding, MRI and lumbar puncture only for neurological symptoms (CNS involvement is found in about 1–3% at diagnosis and does not by itself worsen outcome) ([Ganzel 2021](#)^[11]); PET-CT for suspected myeloid sarcoma.

Work-up of suspected AML: what each test adds

Blood	Marrow	Genes	The patient
• CBC, smear review • PT, aPTT, fibrinogen • Metabolic panel, LDH, urate, phosphate • Flow on blood if many blasts	• Aspirate (500-cell count) + biopsy • Flow cytometry: lineage • Karyotype (banding) ± FISH • Tell the lab before the procedure	• FLT3 (ITD + TKD), NPM1, IDH1/2: fast • Myeloid NGS panel incl. TP53, CEBPA • PML::RARA by PCR or FISH if APL • Germline clues: DDX41, RUNX1, GATA2	• HLA type patient and siblings • Echo before anthracycline • HBV, HCV, HIV; pregnancy test • Fertility advice, central line

CT or MRI of the brain and a lumbar puncture only for neurological symptoms (correct platelets and clotting first; defer the LP in APL until the coagulopathy is corrected). PET-CT only for suspected myeloid sarcoma. Results that change induction (FLT3, CBF fusions, APL) should be available within days.

Figure 4. Work-up (ELN 2022 recommendations, Döhner 2022; UpToDate AML diagnosis and induction reviews).

Naming the AML: genetics first, blast count second (WHO 5th edition and ICC 2022)

≥10% blasts + a defining lesion	Usually ≥20% blasts	Qualifiers and look-alikes
• APL: PML::RARA • CBF: RUNX1::RUNX1T1, CBFB::MYH11 • KMT2A (MLLT3), DEK::NUP214, MECOM • Mutated CEBPA (bZIP) • NPM1-mutated: no blast threshold • BCR::ABL1: needs ≥20%	• Mutated TP53 • Myelodysplasia-related mutations or karyotype • Acute erythroid leukaemia • No defining abnormality • (ICC: 10–19% = MDS/AML)	• Therapy-related, post-MDS/MPN, germline • Myeloid sarcoma = AML at any blast % • Not AML: B12/folate lack, aplasia, leukaemoid reaction • Mixed phenotype, BPDCN, CML blast phase

The two classifications agree for the defining genetic subtypes and differ mainly in labels and blast cut-offs for TP53-mutated and myelodysplasia-related AML. Report both where your laboratory can.

Figure 5. Classification (Khoury 2022; Arber 2022; UpToDate AML classification and diagnosis reviews). Simplified.

Not AML: the differentials to exclude

- **ALL, mixed phenotype acute leukaemia, blastic plasmacytoid dendritic cell neoplasm and CML in blast phase:** flow cytometry and BCR::ABL1 testing separate them (ALL and CML are parts 8 and 9).
- **MDS:** blasts below the AML threshold with dysplasia; ICC calls 10–19% blasts MDS/AML. **MPNs** can transform; ask about earlier high counts or a large spleen.
- **Megaloblastic anaemia** (B12, folate, copper deficiency) can mimic AML with severe cytopenias: measure vitamin levels. **Aplastic anaemia:** hypocellular marrow without blasts.
- **Leukaemoid reaction** in severe infection: few blasts, no maturation block, a clear cause. **Inherited marrow failure** (Fanconi anaemia, telomere disorders): somatic clues and germline testing.

SHARE WITH PATIENTS: TESTS AND DIAGNOSIS

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

A routine blood test alone can identify every type of leukaemia?

A bone marrow test makes leukaemia spread?

All leukaemias are the same disease?

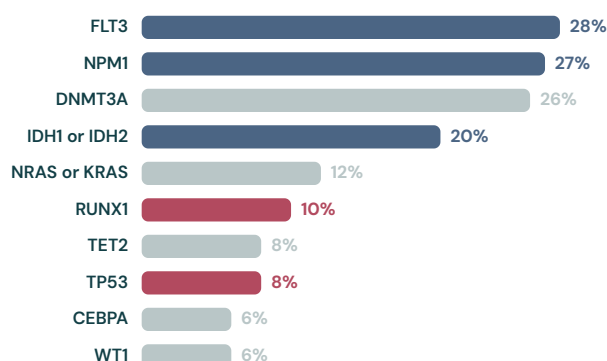
Blood cancer is always hereditary?

04 Biology and biomarkers that change treatment

Biology in brief

- **A clonal disease of stem and progenitor cells:** AML usually grows out of age-related clonal haematopoiesis (DNMT3A, TET2, ASXL1) after further mutations; on average 13 mutations per genome, about five in recurrently mutated AML genes ([TCGA 2013^{\[12\]}](#)).
- **Two kinds of hit:** lesions that drive proliferation (FLT3, KIT, RAS) cooperate with lesions that block differentiation (CBF fusions, CEBPA, NPM1). Leukaemic cells suppress normal haematopoiesis rather than simply crowding it out.
- **Clones evolve:** relapse may come from the dominant clone gaining mutations or from a minor clone that survived treatment, so genetics must be repeated at relapse.
- **IDH1/2 mutations** (about 20%) make the oncometabolite 2-hydroxyglutarate and block differentiation: ivosidenib, olutasidenib and enasidenib release the block, which is why they can cause differentiation syndrome.

How often each gene is mutated in adult AML (200 genomes)



Drug-targetable

- FLT3: midostaurin, quizartinib, gilteritinib
- IDH1: ivosidenib, olutasidenib
- IDH2: enasidenib
- NPM1 or KMT2A: menin inhibitors (revumenib, ziftomenib)
- CD33 (CBF AML): gemtuzumab ozogamicin
- BCL2: venetoclax (any genotype)

Navy = a drug exists for the change; rose = adverse risk. NGS should report every result within the time needed to choose induction; repeat it at relapse, because the clone often changes.

Figure 6. Mutation frequencies from The Cancer Genome Atlas (Ley 2013), as reported in the UpToDate molecular genetics review; drug list from the treatment reviews.

ELN 2022 genetic risk (for intensive treatment) and ELN 2024 (for venetoclax + HMA)

Favourable

- t(8;21) RUNX1::RUNX1T1
- inv(16)/t(16;16) CBFB::MYH11
- NPM1 mutated, no FLT3-ITD
- In-frame bZIP CEBPA

Intermediate

- FLT3-ITD (any NPM1)
- t(9;11) MLLT3::KMT2A
- Anything not favourable or adverse

Adverse

- t(6;9), KMT2A-r, BCR::ABL1, MECOM
- -5/del(5q), -7, 17p; complex
- ASXL1, BCOR, EZH2, RUNX1, SF3B1, SRSF2, STAG2, U2AF1, ZRSR2
- TP53 mutated

ELN 2024 with venetoclax + azacitidine: median overall survival (months)

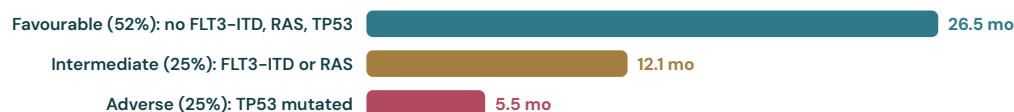


Figure 7. Genetic risk (Döhner 2022; Döhner 2024; UpToDate AML risk factors and prognosis review). Myelodysplasia-related mutations count as adverse.

Markers that change treatment

Marker	Frequency	What it changes
FLT3-ITD / TKD	~28% (all FLT3)	Midostaurin or quizartinib with induction; gilteritinib at relapse; ITD = intermediate risk
NPM1	~27%	Favourable without FLT3-ITD; PCR MRD guides transplant; menin inhibitors at relapse
CBF fusions (t(8;21), inv(16))	t(8;21): 1–7% of adults, median age 25–30	Gemtuzumab if CD33+; favourable; MRD by PCR
IDH1 / IDH2	~20%	Ivosidenib + azacitidine (unfit); IDH inhibitors at relapse
TP53	~8% (more in older and therapy-related)	Adverse in every model; poor response to all current therapy; trials
Myelodysplasia-related genes	Common in older adults	Adverse (ELN 2022); CPX-351 if fit; transplant in CR1
KMT2A rearrangement	Uncommon	Adverse (except t(9;11)); menin inhibitor at relapse
PML::RARA	APL: ≥95% of cases	ATRA + arsenic; PCR monitoring to molecular remission
CD33	Nearly all CBF AML	Gemtuzumab ozogamicin

- **MRD:** after induction and consolidation, measurable residual disease by flow or PCR is a strong predictor: in a meta-analysis, MRD-negative patients had 5-year OS of 68% vs 34% ([Short 2020](#)^[13]). NPM1 transcripts measured by PCR predict relapse ([Ivey 2016](#)^[14]).
- **ELN 2024 for lower-intensity therapy:** with venetoclax and azacitidine, median survival was 26.5 months (no FLT3-ITD, RAS or TP53 mutation), 12.1 months (FLT3-ITD or RAS) and 5.5 months (TP53) ([ELN 2024](#)^[15]).

05 Local therapy: radiotherapy, surgery & procedures

Radiotherapy

- **Myeloid sarcoma** compressing a vital structure, or persisting after recovery from induction: add RT (about 20 Gy is generally enough) to systemic treatment, which remains the main therapy.
- **CNS disease:** leptomeningeal AML without deficits is treated with intrathecal methotrexate, cytarabine or triple therapy; cranial nerve palsies or other deficits need RT (for example 18–25 Gy to the brain, field down to C2), started as soon as CNS involvement is suspected because nerve recovery falls with delay. Cranial rather than craniospinal RT spares the marrow; avoid high-dose systemic chemotherapy for two weeks before, during and after cranial RT.
- **Spinal cord compression by a chloroma:** dexamethasone, urgent MRI and RT and/or decompression with surgical and radiation oncology input.

Procedures and their pitfalls

- **Lumbar puncture:** only for neurological symptoms in adults (no routine CNS prophylaxis); image first if there are focal signs or altered mentation; correct platelets and clotting; the most experienced operator; many centres give one dose of intrathecal chemotherapy at the diagnostic tap. In APL, defer the LP until the coagulopathy is corrected.
- **Leukapheresis:** no proven benefit on its own; used with hydroxyurea only for symptomatic leukostasis when induction cannot start at once ([Oberoi 2014](#)^[16]).
- **Central venous catheters:** needed for induction, but avoid insertion in APL until the coagulopathy is controlled; most AML-related clots are line-related.
- **Allogeneic HCT:** the main "procedure" of curative AML care. Type HLA of the patient and siblings at diagnosis in fit patients; eligibility depends on performance status and heart, lung, liver and kidney function, not age alone.

o6 Systemic therapy: indications & options

Fit adults: induction

Fit or unfit? Decide on function and comorbidity, not on age alone

Fit

- ECOG 0–2 and Charlson 0–2
- No severe heart, lung, liver or kidney disease
- Intensive induction
- Transplant if indicated

Unfit, not frail

- ECOG 3 or Charlson 3
- Or age >75 (Ferrara)
- Venetoclax + HMA
- IDH1: ivosidenib + azacitidine

Frail

- ECOG ≥3 and Charlson ≥3
- Dependent in daily activities
- Supportive care first
- Gentle therapy if wished

Assess: ECOG or Karnofsky, basic and instrumental daily activities, a short physical performance test, Charlson or HCT–CI, cognition, and what the patient wants. Talk frankly about prognosis, quality of life, resuscitation and intensive care before starting.

Figure 8. Fitness (Ferrara 2013; UpToDate medically unfit adults and older adults pretreatment evaluation reviews).

Induction for fit adults: one backbone, add-ons chosen by the genes

7+3: seven days of cytarabine with an anthracycline on days 1–3 (daunorubicin or idarubicin)

FLT3 mutated

- Add midostaurin (ITD or TKD)
- or quizartinib (ITD)
- RATIFY · QuANTUM–First

CBF, CD33+

- Add gemtuzumab ozogamicin
- t(8;21) or inv(16)
- Meta-analysis: fewer relapses

t-AML / AML–MR

- CPX–351 (liposomal daunorubicin + cytarabine)
- Then transplant if fit

Other paths

- Comorbid: venetoclax + HMA
- Weak heart: no anthracycline
- Sarcoma: add RT ~20 Gy

Day 14–21 marrow (nadir)

Hypoplastic with <5% blasts → wait for counts

Day ~28 marrow (recovery)

CR: <5% blasts, no blasts in blood; MRD status

Pregnancy: first trimester → termination, then treat; later → discuss urgent induction versus temporary measures.

Azacitidine–venetoclax gave more complete remissions and more transplants than 7+3 in a randomised trial (Fathi 2026) but not longer survival; most experts await more data.

Figure 9. Induction (Stone 2017; Erba 2023; Hills 2014; Lancet 2018; Fathi 2026; UpToDate induction and therapy-related neoplasm reviews). Regimen names only, no doses.

- **7+3** (seven days of cytarabine with daunorubicin or idarubicin on days 1–3) gives complete remission in about three-quarters of fit younger adults; higher daunorubicin exposure improved outcomes in younger adults ([Fernandez 2009](#)^[17]).
- **FLT3–mutated**: add midostaurin (ITD or TKD; RATIFY: median OS 75 vs 26 months, 4–year OS 51% vs 44%) or quizartinib (ITD; QuANTUM–First: median OS 32 vs 15 months), and continue the inhibitor in consolidation and maintenance ([RATIFY](#)^[18], [QuANTUM–First](#)^[19]).
- **CD33–positive CBF AML**: add gemtuzumab ozogamicin: fewer relapses and better 5–year survival in favourable and intermediate cytogenetics, largest in CBF AML ([Hills 2014](#)^[20]).
- **Therapy-related or myelodysplasia-related AML** (favourable or intermediate genetics): CPX–351, a liposomal daunorubicin–cytarabine, rather than 7+3: 5–year OS 18% vs 8% in patients aged 60–75, with more

patients reaching transplant ([Lancet 2018](#)^[21]; [Lancet 2021](#)^[22]). TP53-mutated therapy-related AML: CPX-351, other intensive regimens or lower-intensity therapy, ideally in a trial.

- **Azacitidine-venetoclax for fit adults:** in the PARADIGM trial it gave more composite remissions (78% vs 53%) and more transplants than 7+3, with similar overall survival ([Fathi 2026](#)^[23]): acceptable for selected intermediate- or adverse-risk patients; most experts await longer follow-up.
- **Special cases:** limited heart function → non-anthracycline induction; myeloid sarcoma → add RT; first-trimester pregnancy → termination, then treatment; later pregnancy → discuss urgent induction against temporary measures such as leukapheresis.
- **Response:** marrow at the nadir (day 14–21; <20% cellularity and <5% blasts) and at count recovery (~day 28): CR needs <5% marrow blasts, no circulating blasts and no extramedullary disease; record MRD.

Fit adults: after remission

After complete remission: consolidate or transplant? Risk group and MRD decide

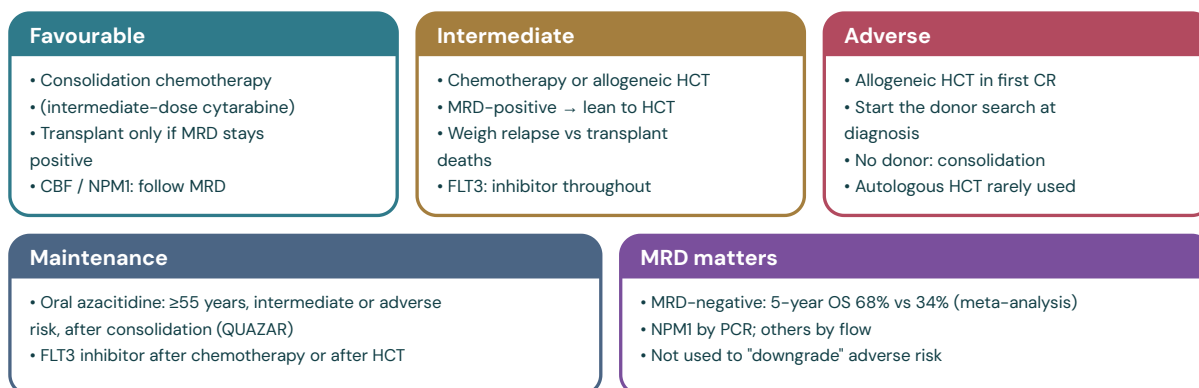


Figure 10. Post-remission choices (Koreth 2009; Wei 2020 QUAZAR; Short 2020; Ivey 2016; UpToDate post-remission review).

- **Without post-remission therapy almost everyone relapses.** Choice depends on ELN risk, MRD, age and fitness.
- **Favourable risk:** consolidation chemotherapy (intermediate-dose cytarabine is suggested over high-dose for most); transplant only for persistent or rising MRD. **Intermediate risk:** consolidation or allogeneic HCT, decided on MRD, donor and transplant risk. **Adverse risk:** allogeneic HCT in first CR ([Koreth 2009](#)^[24]).
- **Maintenance:** oral azacitidine for patients ≥55 years with intermediate- or adverse-risk AML after consolidation (QUAZAR: median OS 25 vs 15 months) ([QUAZAR](#)^[25]); an FLT3 inhibitor after chemotherapy or after HCT for FLT3-mutated AML.
- **Transplant conditioning:** myeloablative regimens give fewer relapses but more transplant deaths than reduced-intensity regimens, with similar long-term survival; the choice follows age and comorbidity.

Unfit adults

Unfit adults: what the combination trials showed**VIALE-A · venetoclax + azacitidine vs azacitidine**

Median overall survival (months)

**VIALE-A**

CR + CRi (%)

**AGILE · ivosidenib + azacitidine (IDH1) vs azacitidine**

Median overall survival (months)

**AGILE**

CR by 24 weeks (%)



Teal = combination, grey = azacitidine alone. Venetoclax brings more febrile neutropenia (42% vs 19%): check the marrow on day 14–21 of cycle 1 and pause venetoclax if the marrow is clear but counts are low. Azoles raise venetoclax levels, so the dose is adjusted. Without venetoclax: azacitidine or decitabine alone; low-dose cytarabine if an HMA is unsuitable.

Figure 11. Lower-intensity therapy (DiNardo 2020 VIALE-A; Montesinos 2022 AGILE; UpToDate medically unfit adults review). Compare within a trial, not across trials.

- **Unfit but not frail:** venetoclax with azacitidine or decitabine (VIALE-A: OS 15 vs 10 months; CR 37% vs 18%) ([VIALE-A](#)^[2]). IDH1-mutated: ivosidenib with azacitidine (AGILE: OS 24 vs 8 months) ([AGILE](#)^[3]). Without venetoclax: azacitidine or decitabine alone ([AZA-AML-001](#)^[26]; [Kantarjian 2012](#)^[27]).
- **Not suitable for an HMA** (earlier HMA for MDS, severe organ dysfunction): low-dose cytarabine (with venetoclax in VIALE-C) or a targeted drug by mutation ([VIALE-C](#)^[28]).
- **Monitoring:** with venetoclax or ivosidenib combinations, check the marrow early in cycle 1 (day 14–21) because responses are fast and counts may need time off venetoclax; then every three cycles. Venetoclax doses are adjusted when azole antifungals are given.
- **Frail:** supportive care (transfusions, antimicrobials, symptom control) is the mainstay; gentle therapy if the patient chooses it. Discuss resuscitation and intensive care early.

Relapsed or refractory AML

Relapsed or refractory AML: retest the genes, look for a donor, aim for transplant**FLT3**

- Gilteritinib
- OS 9.3 vs 5.6 months vs salvage (ADMIRAL)

IDH1 / IDH2

- Ivosidenib or olutasidenib (IDH1)
- Enasidenib (IDH2)
- Watch for differentiation syndrome

NPM1 / KMT2A

- Menin inhibitors: revumenib, ziftomenib
- FDA: NPM1 in Oct–Nov 2025
- India: availability to confirm

No target

- Salvage chemotherapy (FLAG-IDA, MEC)
- or venetoclax + HMA
- Clinical trial

Primary refractory disease affects 20–50% after intensive induction. Only allogeneic HCT (or, after a transplant, a second HCT or donor lymphocytes) can cure relapsed AML; type HLA and call the transplant team when relapse is found. Survival after HCT ranges from about 40% to under 5% depending on remission duration, genetics and disease at transplant.

Figure 12. Relapsed disease (Perl 2019; DiNardo 2018; Stein 2017; FDA notices 2025; UpToDate relapsed AML review).

- **20–50% fail to reach CR with intensive induction**, and many who do will relapse. Repeat the marrow with flow and NGS, type HLA and involve the transplant team at once.
- **FLT3:** gilteritinib beat salvage chemotherapy (median OS 9.3 vs 5.6 months; CR/CRh 34% vs 15%) ([ADMIRAL](#)^[29]). **IDH1:** ivosidenib or olutasidenib (CR in about a third) ([DiNardo 2018](#)^[30]). **IDH2:** enasidenib

(CR 19%, median OS 9 months) ([Stein 2017^{\[31\]}](#)).

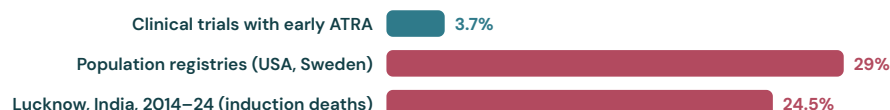
- **NPM1-mutated or KMT2A-rearranged:** menin inhibitors. Revumenib (KMT2A-rearranged acute leukaemia, and NPM1-mutated AML from October 2025) and ziftomenib (NPM1, 13 November 2025; CR+CRh 21% in 112 adults) are FDA-approved ([FDA 2025^{\[32\]}](#)); they cause differentiation syndrome and QT prolongation. Not covered by the supplied UpToDate relapse topic (updated before these approvals): web-verified; Indian availability to be confirmed.
- **No target:** salvage chemotherapy (FLAG-IDA, MEC, cladribine-based) for the fit, venetoclax with an HMA for others, and clinical trials. Transplant in CR2 (myeloablative if fit); after a transplant relapse, a second HCT or donor lymphocytes are the only curative options.

Acute promyelocytic leukaemia

APL: an emergency that is now one of the most curable leukaemias



Early deaths: the gap between trials and real life



APLO406: ATRA + ATO gave 72-month event-free survival of 97% vs 77% with ATRA + chemotherapy. Registry early death 17–29% (upper value shown). No heparin; antifibrinolytics only in selected patients. Avoid central lines, lumbar puncture and bronchoscopy before and during induction.

Figure 13. APL (Lo-Coco 2013; Cicconi 2020; Park 2011; Mamlekar 2025; UpToDate APL diagnosis and initial treatment reviews). No doses.

- **Diagnosis:** abnormal promyelocytes with dense granules and Auer rod bundles (hypergranular), or bilobed nuclei with few visible granules (microgranular, about a quarter); CD13/CD33 positive, CD34 and HLA-DR usually negative; t(15;17) PML::RARA in $\geq 95\%$. Start ATRA when APL is suspected; confirmation comes later.
- **Coagulopathy:** transfuse platelets and cryoprecipitate to keep platelets $\geq 30,000$ –50,000/ μ L and fibrinogen >150 mg/dL; no heparin; antifibrinolytics only in selected patients; avoid central lines, lumbar puncture and bronchoscopy before and during induction.
- **Low/intermediate risk (WBC $\leq 10,000/\mu$ L):** ATRA plus arsenic trioxide (APLO406: 72-month EFS 97% vs 77%; fewer relapses and no induction deaths) ([APLO406^{\[4\]}](#); [Cicconi 2020^{\[33\]}](#)). AML17 tested ATRA-ATO in all risk groups ([AML17^{\[34\]}](#)). Where ATO is not available: ATRA with an anthracycline.
- **High risk (WBC $>10,000/\mu$ L):** ATRA with an anthracycline, or ATRA plus ATO with hydroxyurea or an anthracycline for a rising white count ([Sanz 2000^{\[35\]}](#)).
- **After induction:** ATO-based consolidation; after an ATO-containing regimen and a molecular remission, no maintenance; without ATO, intermittent ATRA maintenance. Relapse occurs in 5–10% overall and 20–30% of high-risk patients: ATRA plus ATO, then autologous HCT if PCR-negative; gemtuzumab for molecular relapse where available.

- **India:** CMC Vellore showed durable remissions with single-agent arsenic trioxide in newly diagnosed APL ([Mathews 2006](#)^[36]; [Mathews 2010](#)^[37]). In 102 patients at SGPGIMS Lucknow (2014–2024; median age 33; 47% high risk; median 18 days from symptoms to diagnosis), induction mortality was 24.5%, mostly from bleeding and infection, and 34% received less platelet or cryoprecipitate support than planned because of shortages ([Mamlekar 2025](#)^[6]).

Differentiation syndrome: think of it with every differentiating drug

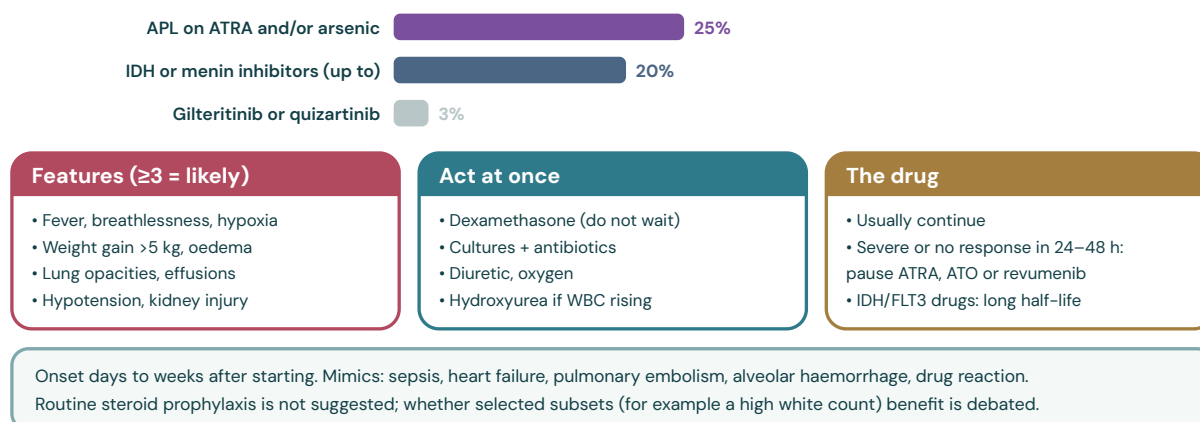


Figure 14. Differentiation syndrome (De Botton 1998; Montesinos 2009; UpToDate differentiation syndrome review). Percentages are approximate incidences.

- **Differentiation syndrome** affects about a quarter of patients with APL on ATRA and/or ATO, up to a fifth on IDH or menin inhibitors, and about 3% on gilteritinib or quizartinib ([De Botton 1998](#)^[38]; [Montesinos 2009](#)^[39]). Give dexamethasone as soon as it is suspected; continue the drug unless the syndrome is severe or does not respond in 24–48 hours.

Emergencies and supportive care (shared by acute leukaemias)

High white count: leukostasis and tumour lysis travel together

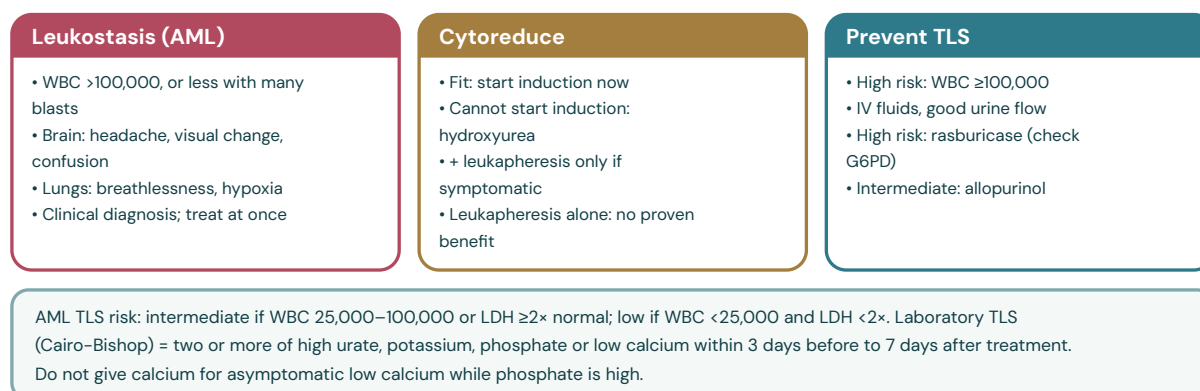


Figure 15. Hyperleukocytosis and TLS (Oberoi 2014; Cairo 2004; Coiffier 2008; UpToDate hyperleukocytosis and TLS reviews). No doses.

- **Hyperleukocytosis** (WBC >100,000/μL) occurs in 10–20% of new AML; leukostasis (brain, lungs) can occur below that threshold when blasts dominate. Fit: start induction at once. Induction delayed: hydroxyurea (plus leukapheresis only if symptomatic). Hold or slow red cell transfusion; give platelets as needed.

- **Tumour lysis:** high risk in AML with WBC $\geq 100,000/\mu\text{L}$; intermediate with 25,000–100,000 or LDH $\geq 2\times$ normal ([Montesinos 2008](#)^[40]). High risk: IV fluids plus rasburicase (not in G6PD deficiency); intermediate: fluids plus allopurinol ([Cairo 2004](#)^[41]; [Coiffier 2008](#)^[42]).
- **DIC** is common in APL and in monocytic AML with a high count: measure PT, aPTT, fibrinogen and D-dimer at diagnosis and support with platelets and cryoprecipitate ([ISTH score](#)^[43]).

Infection: prevent during neutropenia, treat fever as an emergency

Prevent

- Fluoroquinolone while ANC < 500 (expected > 7 days)
- Fluconazole from start of induction
- Second induction or no response: mould-active azole
- Aciclovir if HSV-positive

Fever = emergency

- Cultures, then antibiotic within 60 minutes
- Cefepime, meropenem or piperacillin-tazobactam
- Vancomycin only for line, skin, pneumonia or shock

Still febrile

- Stable: do not change for fever alone
- Febrile after 4–7 days: search for fungus
- Add an antifungal
- Right-sided pain: typhlitis

India: in an Indian tertiary cancer centre, multidrug-resistant organisms grew in 55% and fungal pneumonia was diagnosed in 55% of patients during induction despite prophylaxis; induction mortality 7.4% (Jain 2020). Choose empirical antibiotics from your own resistance data.

Figure 16. Infections (Freifeld 2011; Taplitiz 2018; Bucaneve 2005; Cornely 2007; Jain 2020; UpToDate neutropenic fever and prophylaxis reviews).

- **Prophylaxis** for expected ANC $< 500/\mu\text{L}$ for more than 7 days: a fluoroquinolone ([Bucaneve 2005](#)^[44], [Taplitiz 2018](#)^[45]); antifungal prophylaxis from the start of induction (fluconazole, switching to a mould-active azole for a second induction or refractory disease) ([Cornely 2007](#)^[46]); aciclovir for HSV-seropositive patients.
- **Neutropenic fever is an emergency:** cultures, then an antipseudomonal beta-lactam within 60 minutes; vancomycin only for line, skin or soft-tissue infection, pneumonia or instability; do not change antibiotics for fever alone in a stable patient; add an antifungal after 4–7 days of unexplained fever ([IDSA 2011](#)^[47]).
- **India:** multidrug-resistant organisms grew in 55% and fungal pneumonia was diagnosed in 55% of patients during induction at an Indian tertiary cancer centre, despite prophylaxis ([Jain 2020](#)^[48]). Local resistance data should drive empirical choices.
- **Blood products:** leukocyte-depleted (and in many centres irradiated) products; red cells for haemoglobin ≤ 8 g/dL in most; platelets below 10,000/ μL or higher with bleeding, fever, sepsis or coagulopathy. No erythropoiesis-stimulating agents during induction.

India: check availability and cost before planning

- Availability and cost in India change often and were not verified for this page. Before planning treatment, check current access and cost of venetoclax, azacitidine (injectable and oral), midostaurin, quizartinib, gilteritinib, ivosidenib, enasidenib, gemtuzumab ozogamicin, CPX-351, revumenib and ziftomenib, rasburicase and mould-active azoles.
- Check local access to rapid FLT3/NPM1 testing, NGS panels, flow MRD and PML::RARA PCR, HLA typing and allogeneic transplant (sibling, unrelated and haploidentical) early, so that results and donor searches do not delay treatment.

Quick reference (also as a printable PDF on the Printable Teaching Resources page)

Table A. Diagnosis and work-up tests and what they change

Test	When	What it changes	Pitfalls
CBC + smear review	Every suspected case	Blasts, Auer rods, abnormal promyelocytes (APL)	A normal or low white count does not exclude AML
PT, aPTT, fibrinogen, D-dimer	Every case, at once	DIC; APL suspicion; transfusion targets	Recheck often in APL
Potassium, phosphate, calcium, urate, creatinine, LDH	Before and during induction	Tumour lysis risk and prevention	Pseudohyperkalaemia and false low glucose/oxygen with very high counts
Marrow aspirate + biopsy; flow cytometry	All (blood alone may do if many blasts)	Myeloid lineage; blast %; baseline for MRD	Tell the laboratory first; sternum for aspirate only
Karyotype ± FISH	All	CBF, KMT2A, MECOM, complex/monosomal: ELN risk	FISH does not replace banding
FLT3, NPM1, IDH1/2 (rapid); NGS myeloid panel	All	Midostaurin/quizartinib; ELN risk; targeted drugs	Repeat at relapse; germline variants may show up
PML::RARA by PCR or FISH	Suspected APL	Confirms APL; baseline for molecular remission	Do not wait for it to start ATRA
HLA typing (patient and siblings)	Fit patients; intermediate/adverse risk	Donor search early	Exclude a familial disorder before using a sibling donor
Echo; HBV, HCV, HIV; pregnancy test	Before induction	Anthracycline choice; antiviral prophylaxis	Weak heart: non-anthracycline induction
Brain imaging + lumbar puncture	Neurological symptoms only	CNS disease → intrathecal therapy ± RT	Correct platelets and clotting first; defer in APL

Table B. Treatment by setting

Setting	Usual approach	Alternatives	Key points
Fit, FLT3 wild type	7+3 (cytarabine + daunorubicin or idarubicin)	Venetoclax + HMA in selected intermediate/adverse risk	Day 14–21 nadir marrow; remission marrow ~day 28
Fit, FLT3 mutated	7+3 + midostaurin (ITD or TKD) or quizartinib (ITD)	—	Continue the inhibitor in consolidation and maintenance
Fit, CBF AML (CD33+)	7+3 + gemtuzumab ozogamicin	—	Follow fusion transcripts (MRD) by PCR
Therapy-related or MDS-related AML	CPX-351, then allogeneic HCT	Venetoclax + HMA if less fit	Five-year OS 18% vs 8% with 7+3
In CR: favourable risk	Intermediate-dose cytarabine consolidation	HCT if MRD persists	MRD guides
In CR: intermediate risk	Consolidation or allogeneic HCT	Oral azacitidine maintenance (≥55)	MRD-positive → transplant
In CR: adverse risk	Allogeneic HCT in first CR	Consolidation if no donor	Start donor search at diagnosis

Setting	Usual approach	Alternatives	Key points
Unfit, not frail	Venetoclax + azacitidine (or decitabine)	IDH1: ivosidenib + azacitidine; HMA alone; low-dose cytarabine	Marrow day 14–21 of cycle 1; adjust venetoclax with azoles
Frail	Supportive care	Gentle therapy if the patient wishes	Transfusions, antimicrobials, symptom control at home
APL, WBC ≤10,000	ATRA + arsenic trioxide	ATRA + anthracycline if no ATO	ATRA on suspicion; no maintenance after ATO-based CR
APL, WBC >10,000	ATRA + anthracycline, or ATRA + ATO with cyto-reduction	—	Highest risk of bleeding and differentiation syndrome
Relapsed or refractory	Targeted drug by mutation, or salvage chemotherapy	Venetoclax + HMA; trial	Allogeneic HCT is the only cure

Table C. Treatment options: evidence and best fit

Option	Best fit	Evidence	Watch for
Midostaurin + 7+3	FLT3-ITD or TKD, fit	RATIFY ^[18] : 4-year OS 51% vs 44%	Nausea, mucositis
Quizartinib + 7+3	FLT3-ITD, fit	QuANTUM-First ^[19] : median OS 32 vs 15 months	QT prolongation, neutropenia
Gemtuzumab ozogamicin	CD33+ CBF AML	Hills 2014 ^[20] : fewer relapses, better OS (fav/int)	Liver sinusoidal obstruction
CPX-351	t-AML, AML-MR, 60–75 years	Lancet 2021 ^[22] : 5-year OS 18% vs 8%	Long cytopenias
Oral azacitidine maintenance	≥55 years, intermediate/adverse, in CR	QUAZAR ^[25] : OS 25 vs 15 months	Cytopenias, nausea
Venetoclax + azacitidine	Unfit adults	VIALE-A ^[2] : OS 15 vs 10 months; CR+CRi 65% vs 23%	Febrile neutropenia, TLS at start
Ivosidenib + azacitidine	IDH1-mutated, unfit	AGILE ^[3] : OS 24 vs 8 months	Differentiation syndrome, QT prolongation
Gilteritinib	Relapsed FLT3-mutated	ADMIRAL ^[29] : OS 9.3 vs 5.6 months	Differentiation syndrome, liver tests
Ivosidenib / olutasidenib; enasidenib	Relapsed IDH1; IDH2	DiNardo 2018 ^[30] , Stein 2017 ^[31]	Differentiation syndrome
Revumenib; ziftomenib	Relapsed NPM1 (revumenib also KMT2A)	FDA 2025 ^[32] : CR+CRh 21% (ziftomenib)	Differentiation syndrome, QT; India availability to confirm
ATRA + arsenic trioxide	APL, low/intermediate risk	APLO406 ^[4] : 72-month EFS 97% vs 77%	Differentiation syndrome, QT, liver
Allogeneic HCT	Adverse risk, MRD-positive, relapse	Koreth 2009 ^[24] : benefit in intermediate/adverse risk	GVHD, infection, transplant mortality

Table D. Managing problems during treatment

Problem	Prevent	Recognise	Act
Neutropenic fever	Fluoroquinolone; azole; hand hygiene	Temperature $\geq 38^{\circ}\text{C}$ with ANC < 500	Cultures; antipseudomonal beta-lactam within 60 minutes
Invasive mould infection	Mould-active azole if second induction	Fever after 4–7 days of antibiotics; lung nodules	Antifungal therapy; look for the source
Tumour lysis	Fluids; allopurinol or rasburicase by risk	Rising K, PO ₄ , urate, creatinine; low Ca	Fluids, K-lowering, dialysis; no Ca for asymptomatic low Ca
Leukostasis	Start cytoreduction early	Breathless, hypoxic, confused, visual change	Induction or hydroxyurea; leukapheresis if symptomatic
DIC / APL bleeding	ATRA early; platelets and cryoprecipitate	Low fibrinogen, oozing, headache	Keep platelets $\geq 30\text{--}50,000$ and fibrinogen > 150 ; no heparin
Differentiation syndrome	Watch weight, oxygen, creatinine daily	Fever, dyspnoea, oedema, effusions, hypotension	Dexamethasone at once; pause drug only if severe
Typhlitis	Early imaging if abdominal pain	Right-sided pain, distension, diarrhoea at nadir	Supportive care, broad antibiotics; surgery if perforation
Anthracycline heart damage	Baseline echo and ECG	Breathlessness, oedema	Echo; cardiology; non-anthracycline options
CNS disease	Not routine prophylaxis in adults	Headache, cranial nerve palsy	Intrathecal therapy; RT for deficits or masses
QT prolongation	ECG; correct K and Mg	Prolonged QTc on ECG	Hold arsenic, quizartinib, ivosidenib or menin inhibitor; correct electrolytes

SHARE WITH PATIENTS: TREATMENT AND HOPE

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

[Every leukaemia patient needs a bone marrow transplant?](#)

[Leukaemia can never be cured?](#)

[Chemotherapy is the only treatment for leukaemia?](#)

[If leukaemia returns after treatment, nothing can be done?](#)

[Blood transfusions can cure leukaemia?](#)

07 Management algorithms

Six decision paths pull together sections 02–06.

ALGORITHM 1

Suspected acute leukaemia: the first 24 hours

Blasts on the smear, unexplained cytopenias, bleeding with low fibrinogen, very high white count → CBC and smear, PT/aPTT/fibrinogen, chemistry with urate, phosphate and LDH; cultures if febrile

EMERGENCIES NOW

APL suspected (abnormal promyelocytes, DIC) → **ATRA today** + platelets and cryoprecipitate

WBC >100,000 or symptoms → cytoreduce

Fever with neutropenia → antibiotics within 60 min

APL: no heparin, no lines or LP until clotting is corrected

CONFIRM AND CLASSIFY

Marrow: morphology, flow, karyotype, FISH

Rapid → FLT3, NPM1, IDH1/2, PML::RARA

Full → myeloid NGS panel

WHO 5 / ICC name; ELN risk

Myeloid sarcoma = AML

PLAN

Fitness: ECOG, comorbidity, wishes

Fit → Algorithms 2 and 3

Unfit → Algorithm 4

APL → Algorithm 6

HLA-type patient and siblings

All: TLS prevention by risk · leukocyte-depleted blood products · echo, viral serology, pregnancy test · early referral to a leukaemia centre.

ALGORITHM 2

Fit adults: induction by genetic subgroup

Fit for intensive therapy (ECOG 0–2, no severe organ disease) → rapid genetics back within days

FLT3 MUTATED

7+3 + midostaurin (ITD/TKD) or quizartinib (ITD)

Same drug in consolidation

Then maintenance

RATIFY · QuANTUM-First

CBF OR OTHER

CBF, CD33+ → 7+3 + gentuzumab

Other → 7+3

Nadir marrow day 14–21

Weak heart → non-anthracycline

T-AML OR AML-MR

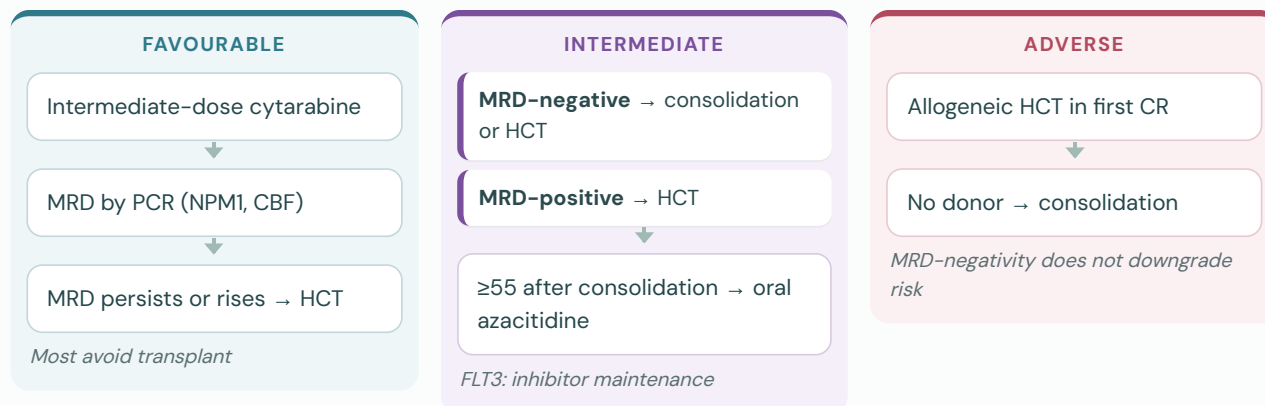
CPX-351

Early donor search

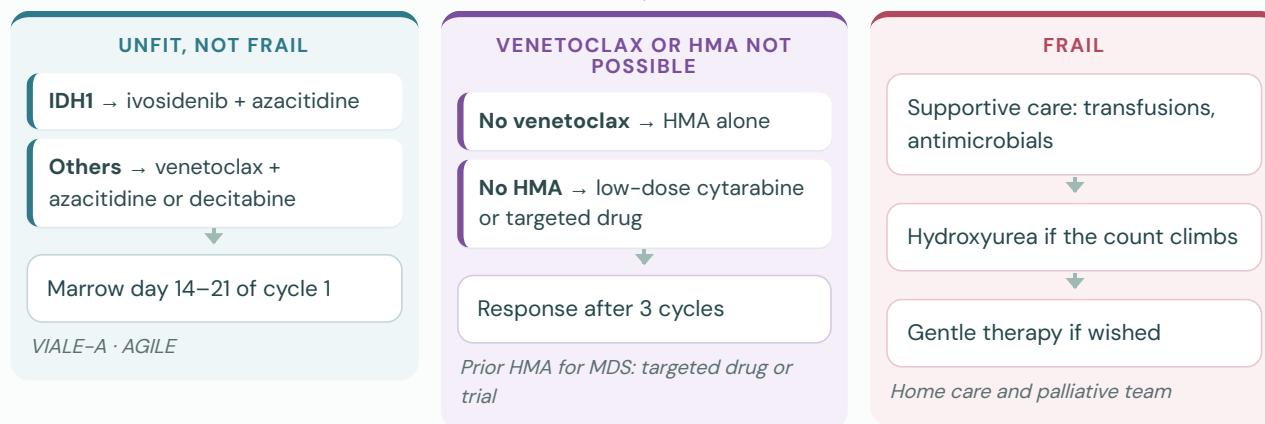
Allogeneic HCT in first CR

TP53: CPX-351, other intensive or HMA-based

All: fluoroquinolone + fluconazole prophylaxis · aciclovir if HSV-positive · remission marrow with MRD at ~day 28.

ALGORITHM 3**In first complete remission: consolidate, transplant, maintain****CR after induction** → ELN 2022 risk, MRD (PCR for NPM1 and CBF; flow for others), donor availability, fitness

All: HLA typing at diagnosis · MRD-negative 5-year OS 68% vs 34% · CBC at intervals; marrow if counts fall or MRD rises.

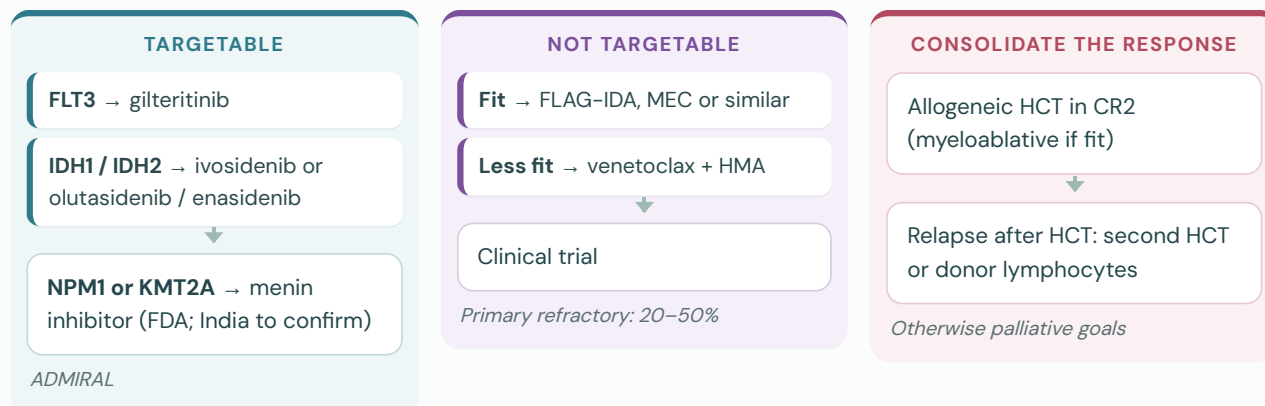
ALGORITHM 4**Unfit adults****Not fit for intensive induction** → frailty, comorbidity, goals; IDH1, FLT3, NPM1, TP53 status

All: TLS prevention at venetoclax start · adjust venetoclax with azoles · continue while responding · revisit goals each cycle.

ALGORITHM 5

Relapsed or refractory AML

Relapse, or no CR after induction → repeat marrow with flow and NGS; HLA typing; transplant consultation now

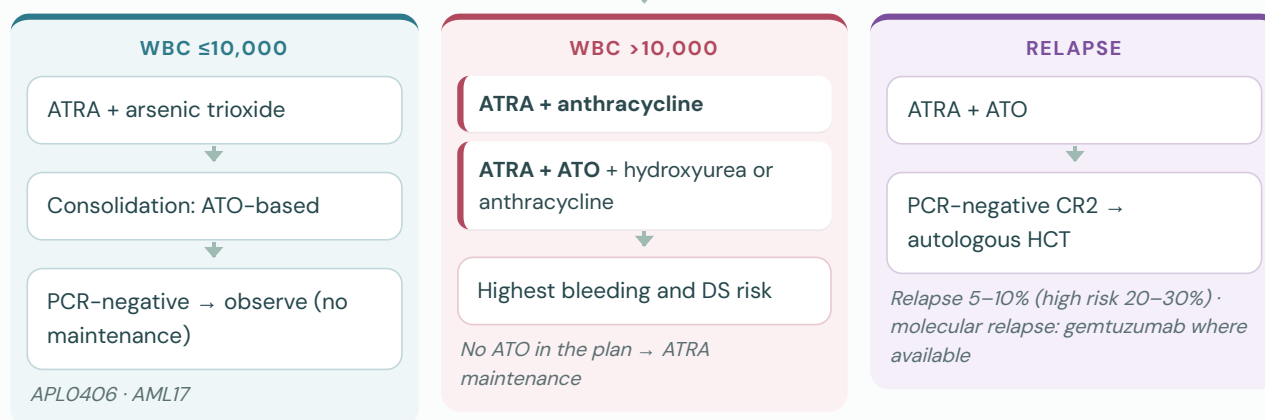


All: differentiation syndrome with IDH, FLT3 and menin drugs · antifungal cover with salvage · honest discussion of prognosis.

ALGORITHM 6

Acute promyelocytic leukaemia

Suspected APL (bleeding, DIC, abnormal promyelocytes) → **ATRA today**; platelets $\geq 30,000$ – $50,000/\mu\text{L}$ and fibrinogen >150 mg/dL; PCR or FISH for PML::RARA



All: daily weight, oxygen and creatinine (differentiation syndrome → dexamethasone at once) · ECG for QT on arsenic · no heparin · no central lines or LP during induction.

08 Survivorship, follow-up & late effects

After treatment: remission, MRD and follow-up

Complete remission

- Marrow blasts <5%
- No blasts in blood, no extramedullary disease
- CRh / CRi: partial count recovery

MRD

- NPM1, CBF fusions: PCR
- Others: multiparameter flow
- Rising MRD predicts relapse

Follow-up

- CBC at regular intervals
- Marrow if counts fall or MRD rises
- Late effects: heart, fertility, GVHD

Survival falls steeply with age: 5-year survival about 50% at 15–39 years, 33% at 40–59, 13% at 60–69 and 3% at 70–79 in England (2001–2006). Newer drugs and transplant in older adults have improved this since.

Figure 17. Response and follow-up (ELN 2022; Shah 2013 for survival by age; UpToDate induction, post-remission and prognosis reviews).

- **Response:** CR (<5% marrow blasts, no circulating blasts, no extramedullary disease), CR with partial (CRh) or incomplete (CRi) count recovery, and MRD status by flow or PCR ([ELN 2022](#)^[1]).
- **Monitoring:** clinical review and CBC at regular intervals; some experts follow MRD in blood (NPM1, CBF fusions). A falling count or a rising MRD level needs a marrow examination.
- **Outcomes:** five-year survival falls with age: about 50% under 40, 33% at 40–59, 13% at 60–69 and 3% at 70–79 in England (2001–2006) ([Shah 2013](#)^[49]); results are better in younger adults with favourable genetics and with modern targeted and transplant care.
- **Late effects:** anthracycline heart damage, infertility (offer fertility advice before treatment), chronic graft-versus-host disease and infections after transplant, second cancers, fatigue and the financial toll of treatment.
- **Living after AML:** encourage activity and normal contact with people (with sensible infection precautions while counts are low); follow the transplant team's vaccination schedule after HCT; report fever, bleeding and new tiredness promptly.

SHARE WITH PATIENTS: LIFE DURING AND AFTER TREATMENT

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

A normal blood count means leukaemia has completely disappeared?

Leukaemia patients must avoid all physical activity and social contact?

Children cured of leukaemia can't lead normal adult lives?

09 Landmark trials

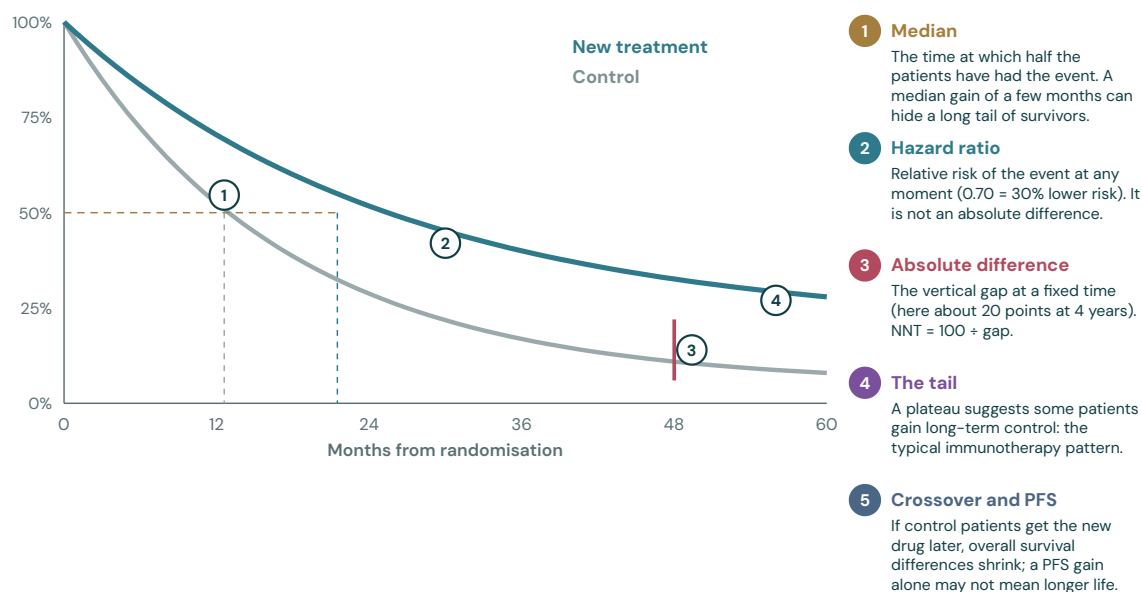


Figure 18. How to read a survival curve (illustrative). Use the absolute gap at a fixed time and overall survival, not the median or PFS alone, when weighing benefit against toxicity and cost.

The trials behind today's choices

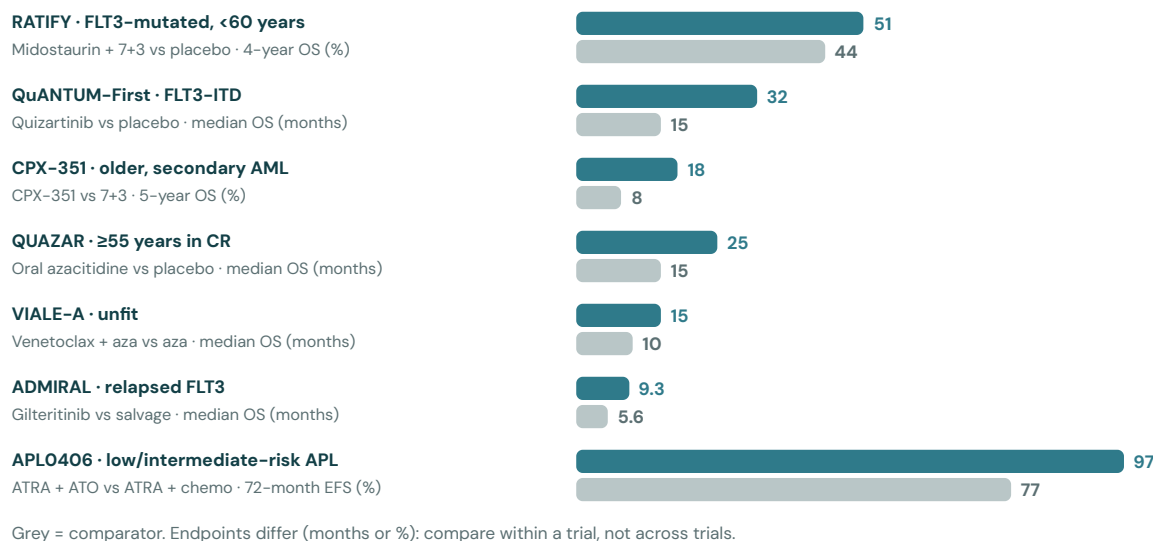


Figure 19. Landmark results as reported in the UpToDate induction, post-remission, unfit, relapsed, therapy-related and APL reviews.

- **RATIFY^[18]** and **QuANTUM-First^[19]**: an FLT3 inhibitor with 7+3 → better survival → every fit FLT3-mutated patient gets one.
- **Hills 2014^[20]**: gemtuzumab with induction → fewer relapses → standard in CD33-positive CBF AML.
- **CPX-351 phase 3^[21]**: CPX-351 vs 7+3 in older patients with secondary AML → better 5-year survival and more transplants.
- **QUAZAR^[25]**: oral azacitidine maintenance in CR (≥55 years) → longer survival.

- [VIALE-A](#)^[2] and [AGILE](#)^[3]: combinations with azacitidine → longer survival for unfit adults.
- [ADMIRAL](#)^[29]: gilteritinib vs salvage chemotherapy for relapsed FLT3-mutated AML → longer survival.
- [APLO406](#)^[4]: ATRA + arsenic trioxide vs ATRA + chemotherapy → higher cure with less toxicity.
- [MRD meta-analysis](#)^[13]: MRD negativity roughly doubles 5-year survival across ages, subtypes and methods.

10 Practice pearls & pitfalls

- Fever, pallor and bleeding: a CBC with a smear today, not another course of antibiotics for "viral fever".
- A normal white count does not exclude AML; the smear makes the diagnosis.
- Bleeding with low fibrinogen and granular cells: start ATRA the same day, before genetic confirmation.
- In APL keep platelets $\geq 30,000$ – $50,000/\mu\text{L}$ and fibrinogen >150 mg/dL; no heparin; no lines or LP during induction.
- WBC $>100,000$ with breathlessness or confusion: cytoreduce now; avoid red cell transfusion if you can.
- Neutropenic fever: cultures, then an antipseudomonal beta-lactam within 60 minutes; know your hospital's resistance pattern.
- Send FLT3, NPM1 and the karyotype on day 1: they change induction.
- Fitness, not age, decides intensive versus lower-intensity therapy.
- Type HLA of the patient and siblings at diagnosis in fit patients; check for a familial disorder before using a sibling donor.
- Repeat the genetics at relapse: the target may have changed.
- Differentiation syndrome with ATRA, ATO, IDH or menin inhibitors: dexamethasone first, questions later.

11 Case vignettes: lines of management

Nine cases from the clinic.

CASE 1 APL · bleeding · ATRA on suspicion

Gum bleeding and a "low" white count

32 years, woman

WBC 2,800/ μ L

Fibrinogen 90 mg/dL

A 32-year-old teacher from Nellore has had gum bleeding and bruises for 5 days. Haemoglobin 8.1 g/dL, white count 2,800/ μ L, platelets 18,000/ μ L; PT prolonged, fibrinogen 90 mg/dL, D-dimer high. The smear shows a few large cells with dense granules and bundles of Auer rods.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

SUSPECT

Bleeding with DIC, a low count and granular cells: APL until proved otherwise. Early bleeding death is the main threat.

2

ACT TODAY

ATRA started within hours, before PCR results; platelets and cryoprecipitate to keep platelets $\geq 30,000$ –50,000/ μ L and fibrinogen >150 mg/dL; no heparin; no central line or lumbar puncture.

3

CONFIRM

PML::RARA positive by RT-PCR. White count $\leq 10,000$ / μ L: low/intermediate risk.

4

TREAT

ATRA plus arsenic trioxide; daily weight, oxygen and creatinine; ECG for QT. ATO-based consolidation; PCR-negative remission → observation, no maintenance.

TEACHING POINTS

- Start ATRA on suspicion; do not wait for genetics.
- In APL a low white count is usual, and bleeding kills early.
- ATRA plus arsenic cures most low-risk APL.

See: Sections 03 and 06, Algorithm 6.

CASE 2 APL · differentiation syndrome

Breathless on day 9

24 years, man

High-risk APL

ATRA + ATO + anthracycline

A 24-year-old with high-risk APL (white count 38,000/ μ L at diagnosis) on ATRA, arsenic trioxide and an anthracycline develops fever of 38.6 °C, breathlessness, a 4 kg weight gain and bilateral lung opacities with small effusions on day 9. His creatinine is rising.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

RECOGNISE

Three or more features (fever, dyspnoea, weight gain, opacities, effusions, kidney injury): differentiation syndrome. Infection and fluid overload are the mimics.

2

ACT

Dexamethasone at once, without waiting for tests; cultures and broad-spectrum antibiotics; oxygen; diuretic.

3 THE DRUGS

Severe (needing intensive care) or no response in 24–48 hours: pause ATRA and arsenic, and restart when it resolves. Otherwise continue them.

4 THEN

Most patients recover. Keep watching weight, oxygen and creatinine daily through induction.

TEACHING POINTS

- Differentiation syndrome is a clinical diagnosis: treat first.
- Steroids at once; stop the drug only if severe.
- The same syndrome occurs with IDH and menin inhibitors.

See: Section O6 (APL), Algorithm 6.

CASE 3 AML · NPM1 with FLT3-ITD · fit**Fever and 62,000 white cells**

45 years, man

NPM1 + FLT3-ITD

ELN intermediate

A 45-year-old electrician has 2 weeks of fever and tiredness. White count 62,000/ μ L with 70% blasts, haemoglobin 7.9 g/dL, platelets 31,000/ μ L, LDH 2.5 times normal. Karyotype normal; NPM1 mutated; FLT3-ITD present. ECOG 1.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1 FIRST 24 HOURS

Fever: cultures, then antibiotics within the hour. White count 25,000–100,000: intermediate TLS risk → IV fluids and allopurinol. No leukostasis symptoms.

2 CLASSIFY

NPM1 with FLT3-ITD: ELN 2022 intermediate risk (FLT3-ITD removes NPM1 from the favourable group).

3 INDUCE

7+3 with quizartinib (or midostaurin); nadir marrow on day 14–21; remission marrow with NPM1 MRD by PCR.

4 AFTER CR

Consolidation with the FLT3 inhibitor; NPM1 MRD-positive → allogeneic HCT; FLT3 inhibitor maintenance. Siblings HLA-typed at diagnosis.

TEACHING POINTS

- Send FLT3 and NPM1 on day 1: they change induction.
- FLT3-ITD makes NPM1-mutated AML intermediate risk.
- PCR MRD guides transplant.

See: Sections O4 and O6, Algorithms 2 and 3.

CASE 4 AML · core binding factor · favourable**Tiredness and bruises at 28**

28 years, woman

t(8;21)

CD33 positive

A 28-year-old has 3 weeks of tiredness and bruising. White count 9,000/ μ L with 40% blasts containing Auer rods; platelets 42,000/ μ L. Karyotype t(8;21) with RUNX1::RUNX1T1; blasts CD33 positive.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

CLASSIFY

RUNX1::RUNX1T1: AML by definition ($\geq 10\%$ blasts is enough); ELN favourable.

2

BEFORE TREATMENT

Fertility counselling and pregnancy test; echo; HBV, HCV and HIV tests.

3

INDUCE

7+3 with gemtuzumab ozogamicin (CD33-positive CBF AML).

4

AFTER CR

Intermediate-dose cytarabine consolidation; follow RUNX1::RUNX1T1 transcripts by PCR; allogeneic HCT only if MRD persists or rises.

TEACHING POINTS

- CBF AML: gemtuzumab adds benefit.
- Favourable risk usually means no transplant in first CR.
- A rising transcript predicts relapse: act early.

See: Sections O4 and O6, Algorithms 2 and 3.

CASE 5 Hyperleukocytosis · leukostasis**Confused and breathless with 210,000 white cells**

52 years, man

WBC 210,000/ μ L

Monocytic AML

A 52-year-old from Gudur has 2 days of headache, blurred vision and breathlessness; oxygen saturation 88%. White count 210,000/ μ L, mostly monoblasts; gum hypertrophy. Serum potassium 6.4 mmol/L, creatinine 1.6 mg/dL, urate 11 mg/dL.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

RECOGNISE

Leukostasis (brain, lungs) with high TLS risk. Recheck potassium on a heparinised sample (pseudohyperkalaemia) and send the blood gas on ice.

2

CYTOREDUCE

Fit: start induction now. If induction cannot start at once: hydroxyurea plus leukapheresis (he is symptomatic). Leukapheresis alone has no proven benefit.

3

PROTECT

IV fluids; rasburicase after a G6PD check; avoid red cell transfusion unless essential; platelets as needed; watch for DIC; brain CT for focal signs.

4

THEN

Induction chosen by genetics; with monocytic AML, look for skin and CNS involvement if symptoms suggest it.

TEACHING POINTS

- WBC $>100,000$ with symptoms is an emergency.
- Treat the leukaemia (chemotherapy or hydroxyurea), not just the number.
- Red cell transfusion raises viscosity: avoid or go slowly.

See: Sections O3 and O6, Algorithm 1.

CASE 6 Induction · neutropenic fever**Fever on day 10 of induction**

38 years, woman

ANC 100/ μ L

Day 10 of 7+3

A 38-year-old on day 10 of 7+3 develops a temperature of 38.8 °C; blood pressure 100/60 mmHg; a central line is in place. She is on levofloxacin and fluconazole prophylaxis.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1 HOUR 1

Blood cultures (line and peripheral), then an antipseudomonal beta-lactam (cefepime, meropenem or piperacillin-tazobactam) within 60 minutes, chosen with local resistance data.

2 ADD

Vancomycin only for line or skin infection, pneumonia or haemodynamic instability.

3 DAY 4–7

Still febrile but stable: do not change antibiotics for fever alone; search for fungal infection; add an antifungal (mould-active if a second induction follows).

4 WATCH

Right-sided abdominal pain → CT for neutropenic enterocolitis (typhlitis); diarrhoea → test for *C. difficile*.

TEACHING POINTS

- Neutropenic fever: antibiotics within the hour.
- Know your hospital's resistance pattern.
- Persistent fever: think fungus.

See: Section O6 (emergencies and supportive care).

CASE 7 Therapy-related AML**Pancytopenia 5 years after breast cancer**

61 years, woman

Prior chemotherapy and RT

-7, del(5q)

A 61-year-old treated 5 years ago with anthracycline-cyclophosphamide chemotherapy and radiotherapy for breast cancer now has pancytopenia with 24% marrow blasts. Karyotype: -7 and del(5q); TP53 not mutated. ECOG 1, normal heart function.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1 CLASSIFY

Therapy-related myeloid neoplasm (AML after cytotoxic therapy) with adverse cytogenetics.

2 INDUCE

Fit: CPX-351 rather than 7+3 (5-year OS 18% vs 8% in older adults with secondary AML).

3 AFTER CR

Allogeneic HCT in first remission; start the donor search now.

4 IF LESS FIT

Venetoclax with an HMA, as for de novo AML.

TEACHING POINTS

- Ask about previous chemotherapy and radiotherapy.
- Therapy-related AML: CPX-351 and transplant.
- The prognosis is worse than for de novo AML.

See: Sections O2 and O6, Algorithm 2.

CASE 8 Unfit · venetoclax + azacitidine

A 74-year-old with heart failure

74 years, man

Heart failure, diabetes

No IDH1, FLT3 or TP53 change

A 74-year-old retired farmer with diabetes and heart failure (ejection fraction 40%) has tiredness and breathlessness. Haemoglobin 6.8 g/dL, white count 3,200/ μ L with 30% blasts, platelets 22,000/ μ L. NGS: no IDH1/2, FLT3 or TP53 mutation. He lives independently.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

ASSESS

Unfit for intensive therapy (age, heart failure, diabetes) but not frail.

2

TREAT

Venetoclax with azacitidine; TLS prevention at the start; venetoclax adjusted if an azole is used.

3

MONITOR

Marrow on day 14–21 of cycle 1: a clear marrow with low counts → pause venetoclax to let counts recover; then marrow every 3 cycles.

4

GOALS

Discuss quality of life, transfusion needs, travel for each cycle, and his wishes about resuscitation and intensive care.

TEACHING POINTS

- Fitness, not age, decides.
- VIALE-A: venetoclax with azacitidine improves survival.
- Check the marrow early in cycle 1.

See: Section O6 (unfit adults), Algorithm 4.

CASE 9 Relapse · FLT3

Relapse 10 months after consolidation

50 years, man

FLT3-ITD at relapse

Matched sibling

A 50-year-old with NPM1-mutated AML (no FLT3 mutation at diagnosis) was MRD-negative after 7+3 and consolidation and did not have a transplant. Ten months later he has cytopenias and 35% marrow blasts; NGS now shows NPM1 and a new FLT3-ITD. His brother is a full HLA match.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

RETEST

Marrow with flow and NGS: FLT3-ITD has appeared; the clone has changed.

2

TREAT

Gilteritinib (ADMIRAL) or salvage chemotherapy (FLAG-IDA); watch for differentiation syndrome. A menin inhibitor is another option for NPM1-mutated relapse where available.

3

TRANSPLANT

Second remission → allogeneic HCT from the matched brother.

4

AFTER HCT

FLT3 inhibitor maintenance.

TEACHING POINTS

- Always repeat the genetics at relapse.
- Gilteritinib beats salvage chemotherapy for FLT3-mutated relapse.
- Only a transplant can cure relapsed AML.

See: Section O6 (relapsed), Algorithm 5.

12 References & guidelines

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- Cross-checked in October 2026 against 29 UpToDate topic reviews: acute myeloid leukemia in adults: overview; clinical manifestations, pathologic features, and diagnosis; classification; cytogenetic abnormalities; molecular genetics; pathogenesis; risk factors and prognosis; induction therapy in fit, younger adults; post-remission therapy in medically fit adults; management of medically unfit adults; treatment of relapsed or refractory AML; involvement of the central nervous system; overview of complications; AML in older adults: pretreatment evaluation and prognosis; therapy-related myeloid neoplasms: management and prognosis; familial disorders of acute leukemia and myelodysplastic syndromes; allogeneic HCT: indications, eligibility, and prognosis; clinical manifestations, pathologic features, and diagnosis of APL in adults; initial treatment of APL in adults; treatment of relapsed or refractory APL in adults; differentiation syndrome associated with treatment of acute leukemia; hyperleukocytosis and leukostasis in hematologic malignancies; tumor lysis syndrome (pathogenesis, clinical manifestations, definition, etiology and risk factors; prevention and treatment); overview of neutropenic fever syndromes; treatment of neutropenic fever syndromes in high-risk adults; prophylaxis of infection during chemotherapy-induced neutropenia in high-risk adults; prevention of invasive fungal infections in adults with hematologic malignancies and HCT recipients; evaluation and management of DIC in adults; and, for contrast only, AML in children and adolescents. All trial citations below come from the reference lists of these reviews, except the four Indian papers and the FDA menin-inhibitor notices, which were found and verified by web search on 17 October 2026.
- Reviewed and approved by Dr. Haritha Chiramana, 17 October 2026.

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Educational summary for health professionals, written in our own words from current guidelines and primary trials. No drug doses are given. Hodgkin, aggressive B-cell, indolent B-cell, T-cell and cutaneous lymphomas are parts 1–5 and multiple myeloma is part 6; acute lymphoblastic leukaemia and chronic myeloid leukaemia are parts 8 and 9; CLL is covered in the indolent B-cell module; MDS and myeloproliferative neoplasms are mentioned here only as differentials. Verify current guidelines, Indian regulatory approvals and individual patient factors before treatment decisions.