

SINTOMA 2026

Flash Clinical Cases

MDS & AML

Day 1 · Thursday May 14, 2026

Myelodysplastic Syndromes · Acute Myeloid Leukemia

5 Cases · 3–5 min discussion each



 PATIENT

- 67M, fatigue, transfusion-dependent (2u/month)
- HTN, T2DM; ECOG PS 1
- No infections or bleeding

 DIAGNOSTICS

- MDS with ring sideroblasts, 4% blasts
- IPSS-R: Intermediate (3.5) | IPSS-M: High (6.2)
- SF3B1 mut (VAF 42%), TET2 mut (VAF 18%)
- del(5q), +8; TP53 wild-type

 PRIOR THERAPY

- ESA × 12 wks → no response
- Lenalidomide (del5q) → partial response, d/c at 8 mo (cytopenias)
- No HMA, no luspatercept

 CLINICAL DILEMMA

IPSS-R = Intermediate; IPSS-M = High. Does molecular upstaging mandate HMA therapy or transplant evaluation now — or does SF3B1+ biology argue for a gentler first step?

 MANAGEMENT OPTIONS — no single correct answer

- A. Azacitidine now** (treat per IPSS-M High)
- B. Luspatercept first** — SF3B1+; defer HMA
- C. Direct transplant evaluation** — IPSS-M High warrants allo-SCT
- D. Venetoclax + azacitidine** — molecular complexity favors intensification
- E. Observe** — IPSS-M is prognostic, not prescriptive

PATIENT

- 72F, MDS-EB2, ECOG PS 1
- CAD (stent 2019), CKD stage 2
- Lives alone; strongly prefers outpatient management

DIAGNOSTICS

- 12% blasts; del(17p), complex karyotype
- TP53 biallelic: R248W (VAF 52%) + del(17p)
- IPSS-M: Very High; RUNX1 co-mutation

PRIOR THERAPY

- Treatment-naïve
- Transplant eval: 'borderline eligible' (CKD + cardiac)
- Patient: strong outpatient preference

CLINICAL DILEMMA

Biallelic TP53, IPSS-M Very High, age 72, borderline transplant eligibility, patient preferring outpatient management. Allo-SCT vs. HMA — or goals-of-care discussion first?

MANAGEMENT OPTIONS — no single correct answer

- A. Azacitidine alone (SC)** — palliative; outpatient; aligns with preference
- B. Decitabine IV** — standard HMA
- C. Oral decitabine/cedazuridine** — outpatient HMA
- D. RIC allo-SCT after first response** — only curative option
- E. Goals-of-care discussion first** — before any treatment decision

IDH1 + NPM1 AML in MRD-Negative CR1: Transplant or Maintenance?

PATIENT

- 68M, de novo AML, ECOG PS 1
- Sibling donor available (10/10 HLA)
- Hypertension; motivated for cure

DIAGNOSTICS

- NPM1-mutant, IDH1 R132H; ELN 2022: Favorable
- Normal karyotype; No FLT3-ITD
- Post-cycle 4: CR, NPM1 PCR undetectable (10^{-5})

PRIOR THERAPY

- Azacitidine + venetoclax → CR after cycle 2
- Continued aza + ven × 2 additional cycles
- MRD: NPM1 undetectable post-cycle 4; no stem cells collected

CLINICAL DILEMMA

68-year-old with NPM1+/IDH1 AML in MRD-negative CR1 after azacitidine + venetoclax. ELN Favorable. Sibling donor available. Does IDH1 co-mutation mandate allo-SCT — or is continued therapy sufficient at this age?

MANAGEMENT OPTIONS — no single correct answer

- A. AlloSCT in CR1** — IDH1 co-mutation raises relapse risk
- B. Continue azacitidine + venetoclax** — ELN Favorable + uMRD + age 68
- C. Add ivosidenib to maintenance** — IDH1-targeted therapy to deepen and sustain remission
- D. MRD-guided approach** — sustained uMRD × 6 months: defer SCT

FLT3-ITD AML at 67: Intensive Induction or Venetoclax-Based Frontline?

PATIENT

- 67M, FLT3-ITD AML, newly diagnosed
- Fatigue, petechiae, WBC $42 \times 10^9/L$
- HTN, T2DM well-controlled; ECOG PS 1
- No prior hematologic malignancy

DIAGNOSTICS

- FLT3-ITD high allelic ratio (AR 0.72)
- NPM1 co-mutant; ELN 2022: Intermediate
- Normal karyotype; No TP53, no CBF
- BM: 68% blasts; LDH $2.8 \times ULN$

PRIOR THERAPY

- Treatment-naïve
- Institution offers intensive (7+3 + midostaurin) or non-intensive (aza + venetoclax)
- Cardiology clearance obtained; ECHO EF 55%
- Family support available

CLINICAL DILEMMA

67-year-old with FLT3-ITD high allelic ratio AML, ECOG PS 1, fit for intensive therapy. Does FLT3-ITD mandate 7+3 + midostaurin — or is azacitidine + venetoclax (\pm midostaurin) a valid frontline alternative?

MANAGEMENT OPTIONS — no single correct answer

- A. 7+3 + midostaurin** — FLT3-ITD high AR; intensive induction standard; RATIFY data
- B. Azacitidine + venetoclax** — VIALE-A FLT3 subgroup
- C. Azacitidine + venetoclax + midostaurin** — combine HMA/VEN backbone with FLT3 inhibition
- D. CPX-351 + midostaurin** — liposomal formulation
- E. Clinical trial** — FLT3-ITD frontline in older/fit patients: HMA-based vs. intensive is an open question

PATIENT

- 52F, KMT2A::MLLT3 AML, 1st relapse
- Fatigue, progressive cytopenias
- ECOG PS 1; no significant comorbidities
- Patient refused alloSCT after CR1 — personal decision

DIAGNOSTICS

- KMT2A::MLLT3 (t(9;11)); monocytic differentiation retained
- ELN 2022: Intermediate (at diagnosis); Adverse at relapse
- FLT3, NPM1, IDH: WT; BM: 38% blasts
- No new cytogenetic evolution at relapse

PRIOR THERAPY

- L1: 7+3 → CR1 after cycle 1
- HiDAC consolidation × 3 cycles
- Relapse 9 months after completing consolidation
- No prior menin inhibitor; no prior venetoclax
- AlloSCT offered and declined by patient

CLINICAL DILEMMA

KMT2A-rearranged AML at 1st relapse. Patient has refused alloSCT. No prior menin inhibitor exposure. Which salvage strategy offers the best disease control — and does the absence of SCT change the therapeutic goal?

MANAGEMENT OPTIONS — no single correct answer

- A. Revumenib monotherapy** — AUGMENT-101: KMT2A-r ORR ~50%
- B. FLAG-IDA salvage** — intensive cyto-reduction
- C. Azacitidine + venetoclax** — lower intensity
- D. Revumenib + azacitidine** — combine menin inhibition with HMA
- E. Goals-of-care discussion** — SCT declined