

SINTOMA 2026

Flash Clinical Cases

Mantle Cell Lymphoma

Day 2 · Friday May 15, 2026

MCL · Frontline · BTKi · Transplant · Relapse

2 Cases · 3–5 min discussion each

 PATIENT

- 52M, MCL classical variant, newly diagnosed
- ECOG PS 0; asymptomatic (incidental CBC)
- MIPI: High (2.8); TP53: WT; complex karyotype

 DIAGNOSTICS

- Cyclin D1+, SOX11+; Ki-67 28%
- Karyotype: t(11;14) + 3 additional abnormalities
- PET: Diffuse LAD, spleen 16cm; CNS negative

 PRIOR THERAPY

- Treatment-naïve; transplant-eligible
- Discussed with patient: R-CHOP/R-DHAP + ASCT · ibrutinib + CHOP + ASCT (TRIANGLE) · ibrutinib + venetoclax chemo-free

 CLINICAL DILEMMA

High-MIPI, complex karyotype, TP53-WT MCL at 52. TRIANGLE showed BTKi integration superior. Does ASCT still add value when ibrutinib is included — or is the chemo-free era arriving?

 MANAGEMENT OPTIONS — no single correct answer

- A. R-CHOP/R-DHAP + ASCT** — established efficacy; TP53 WT; MCL Younger standard
- B. Ibrutinib + R-CHOP/R-DHAP + ASCT (TRIANGLE)** — BTKi integration; superior PFS; emerging standard
- C. Ibrutinib + venetoclax fixed-duration (CLARITY)** — chemo-free; deep MRD; ASCT avoidable if uMRD
- D. Acalabrutinib monotherapy** — complex karyotype argues against indefinitely deferring ASCT
- E. Acalabrutinib + venetoclax** — lower cardiac toxicity; combination without ASCT

PATIENT

- 64M, MCL — 2nd relapse after ibrutinib; blastoid features
- ECOG PS 1; BTK C481S+ (ibrutinib resistance confirmed)
- TP53 new mutation (VAF 24%); CAR-T center 2 hours away

DIAGNOSTICS

- Biopsy: MCL, Ki-67 62% (blastoid); complex karyotype (5 abnormalities)
- LDH 3.2× ULN; PET: Multiple FDG-avid sites, SUVmax 14

PRIOR THERAPY

- L1: BR × 6 → CR × 22 months
- L2: Ibrutinib × 18 months → BTK C481S resistance
- No prior venetoclax; no prior CAR-T; no pirtobrutinib

CLINICAL DILEMMA

Ibrutinib-refractory blastoid MCL with new TP53 mutation. Rapid progression. Pirtobrutinib, venetoclax, or intensive salvage — what is the next step, and when do you refer for CAR-T?

MANAGEMENT OPTIONS — no single correct answer

- A. Pirtobrutinib** — overcomes C481S resistance; ORR ~50% in BTKi-refractory MCL; outpatient
- B. Venetoclax ± ibrutinib** — venetoclax activity in BTKi-resistant MCL; different mechanism
- C. Acalabrutinib** — different covalent BTKi; limited activity post-C481S but used in practice
- D. Intensive salvage (FLAG-IDA)** — blastoid TP53+: cytoreduction; bridge to CAR-T if available
- E. CAR-T referral now + pirtobrutinib bridge** — plan CAR-T; pirtobrutinib as outpatient bridge