

SINTOMA 2026

Flash Clinical Cases

Multiple Myeloma

Day 2 · Friday May 15, 2026

NDMM · RRMM · Smoldering · MRD · Maintenance

5 Cases · 3–5 min discussion each

 PATIENT

- 59M, NDMM, newly diagnosed; back pain, fatigue
- ECOG PS 1; ISS Stage II; transplant-eligible
- No significant comorbidities; creatinine normal

 DIAGNOSTICS

- BM: 60% PCs, IgG kappa; R-ISS Stage II
- Cytogenetics: t(4;14) — high risk; no del(17p), no 1q gain
- M-protein: 4.2 g/dL; LDH normal; PET: 3 focal lesions

 PRIOR THERAPY

- Treatment-naïve
- Discussed with patient: VRd · Dara-VRd · Isa-VRd
- Stem cell mobilization planned

 CLINICAL DILEMMA

Transplant-eligible NDMM with t(4;14) high-risk cytogenetics. Quadruplet induction is now the standard — but which one? And does t(4;14) change the PI choice between bortezomib and carfilzomib?

 MANAGEMENT OPTIONS — no single correct answer

- Dara-VRd (PERSEUS)** — daratumumab quadruplet; superior PFS + MRD; emerging global standard
- Isa-VRd (GMMG-HD7)** — isatuximab quadruplet; superior MRD negativity; alternative CD38
- Isa-KRd (carfilzomib)** — t(4;14) high-risk: carfilzomib may overcome PI resistance; less neuropathy
- VRd triplet + ASCT** — GRIFFIN data; still valid if quadruplet access limited
- Dara-VTd (CASSIOPEIA)** — thalidomide-based quadruplet; European standard; widely used in Brazil

PATIENT

- 62M, NDMM, transplant-eligible; back pain, Hgb 10.2
- ECOG PS 1; standard risk cytogenetics (del13q only)
- Asks: 'Do I really need a stem cell transplant?'

DIAGNOSTICS

- BM: 65% PCs, IgG lambda; ISS Stage II; R-ISS II
- No t(4;14), t(14;16), del(17p), or 1q gain
- Post-DaraVRD × 4: sCR — BM negative, sFLC normalized
- MRD by NGS (IGH): Undetectable at 10^{-5} ; stem cells collected

PRIOR THERAPY

- Induction: DaraVRD × 4 cycles → sCR
- MRD: NGS (IGH) undetectable at 10^{-5}
- Stem cells collected (10.2×10^6 CD34+/kg)
- Decision point: ASCT vs. continued DaraVRD consolidation

CLINICAL DILEMMA

Standard-risk NDMM achieving sCR + MRD-negative after DaraVRD. Stem cells collected. Does this patient need ASCT — or can MRD-negative sCR with DaraVRD consolidation substitute?

MANAGEMENT OPTIONS — no single correct answer

- Proceed to ASCT** — PERSEUS: DaraVRD + ASCT superior even in MRD-negative patients; deepen further
- Continue DaraVRD, no ASCT** — sCR + uMRD; standard-risk; reserve ASCT for relapse
- MRD-guided ASCT** — if sustained uMRD × 6 months, defer; if MRD turns positive, transplant
- Escalate to 10^{-6} MRD testing before deciding** — 10^{-5} may still harbor residual disease
- Lenalidomide + bortezomib maintenance** — 1q gain intermediate risk; PI may add benefit

 PATIENT

- 55F, NDMM, transplant-eligible; hip pain, hypercalcemia
- ECOG PS 1; mild CKD (creatinine 1.4)
- ISS Stage III; R-ISS Stage III

 DIAGNOSTICS

- BM: 80% PCs, IgG kappa
- High-risk: t(4;14) + del(17p) — double hit
- 1q gain+; LDH elevated (2.1× ULN)
- M-protein: 5.6 g/dL; skull lesions on MRI

 PRIOR THERAPY

- Treatment-naïve
- Tandem ASCT planned at institution
- Induction choice under discussion: VRd vs. Dara-VRd vs. Dara-VKd vs. Isa-VRd

 CLINICAL DILEMMA

Double-hit NDMM (t(4;14) + del(17p)), R-ISS III. Multiple quadruplet options available. Does double-hit cytogenetics mandate the most intensive available therapy — and is tandem ASCT justified?

 MANAGEMENT OPTIONS — no single correct answer

- Dara-VRd + tandem ASCT + Dara-len maintenance** — most intensive proven approach (PERSEUS + tandem)
- Isa-KRd (carfilzomib)** — carfilzomib may overcome del(17p) PI resistance; less neuropathy
- VRd + single ASCT + len maintenance** — standard backbone; tandem ASCT benefit in quadruplet era unclear
- Isa-VRd + single ASCT + Isa maintenance** — isatuximab quadruplet; alternative CD38 to daratumumab
- Dara-KRd (carfilzomib + daratumumab + Rd)** — maximum intensity; double-hit justifies most aggressive quadruplet

PATIENT

- 67F, RRMM — 2nd relapse; lenalidomide-refractory
- ECOG PS 1; mild CKD (eGFR 52); no prior BCMA therapy
- Best corrected visual acuity: normal; ophthalmology cleared

DIAGNOSTICS

- BM: 40% PCs, IgG lambda; del(13q); no del(17p)
- R-ISS Stage II; LDH normal; M-protein: 2.8 g/dL
- Prior len exposure: refractory (progressed on len maintenance)

PRIOR THERAPY

- L1: VRd × 8 → ASCT → len maintenance → progression
- L2: Dara-len-dex → PR × 14 months → progression (len-refractory)
- No prior BCMA therapy; no prior pomalidomide; no prior carfilzomib

CLINICAL DILEMMA

Len-refractory RRMM after 2 lines. No prior BCMA therapy. Belantamab mafodotin combinations (DREAMM-7 and DREAMM-8) now approved. Which combination — and how do you manage the corneal toxicity?

MANAGEMENT OPTIONS — no single correct answer

- Belantamab + bortezomib + dex (DREAMM-7)** — PI-based combo; superior PFS vs. DVd
- Belantamab + pomalidomide + dex (DREAMM-8)** — IMiD switch; pom-based; DREAMM-8 data
- Daratumumab + carfilzomib + dex (DVKd)** — switch PI + CD38 re-exposure; no BCMA
- Isatuximab + carfilzomib + dex (IsaKd)** — IKEMA data; CD38 + carfilzomib; no BCMA
- Teclistamab or elranatamab (BCMA bispecific)** — BCMA-naive; deepest responses; outpatient

PATIENT

- 68M, RRMM — penta-refractory (dara, bortezomib, carfilzomib, len, pom)
- ECOG PS 2; HTN, CKD 3a; recent pneumonia (resolved)
- CD4 180/ μ L (immune-compromised); IgG 320 mg/dL

DIAGNOSTICS

- BM: 55% PCs, IgG kappa; del(17p) + gain(1q)
- LDH 3.1 \times ULN; calcium 11.8 mg/dL (mildly elevated)
- No extramedullary disease by PET

PRIOR THERAPY

- L1–3: VRd + ASCT \rightarrow Dara-len-dex \rightarrow KPd
- L4: Teclistamab (BCMA \times CD3) \rightarrow VGPR \times 8 months, then progression
- Now: 5th-line relapse after BCMA-targeted bispecific
- No prior CAR-T; no prior GPRC5D-targeted agent

CLINICAL DILEMMA

Triple-class exposed RRMM after BCMA bispecific failure. Four approved options available: GPRC5D bispecific, BCMA re-challenge, BCMA ADC, BCMA CAR-T. All active. How do you choose — and in what order?

MANAGEMENT OPTIONS — no single correct answer

- Talquetamab (GPRC5D \times CD3)** — non-BCMA target; MonumentAL-1 ORR ~75%; active post-BCMA bispecific
- Teclistamab (BCMA \times CD3) re-challenge or switch to elranatamab** — different BCMA bispecific; class re-challenge responses reported
- Belantamab mafodotin (BCMA ADC)** — different BCMA mechanism (ADC vs. bispecific); DREAMM-7/8 data
- CARVYKTI (ciltacabtagene) CAR-T** — BCMA CAR-T post-bispecific: deepest responses; eligibility and logistics
- Goals-of-care reassessment** — PS 2, del(17p), CKD, immune-compromised: is disease control still the goal?

 PATIENT

- 59F, NDMM, post-ASCT; 1q gain + del(13q)
- Feeling well, returned to work; ECOG PS 0
- Day +100 assessment: VGPR → MRD positive (10^{-4})
- Asks: 'Which maintenance gives me the best chance?'

 DIAGNOSTICS

- ISS Stage II; 1q gain (3 copies) + del(13q) — intermediate risk
- Post-ASCT day +100: BM morphologically clear
- MRD by NGS: Positive at 10^{-4} (1 in 10,000 cells)
- M-protein: Trace (0.2 g/dL)

 PRIOR THERAPY

- Induction: DaraVRD × 4 → PR
- ASCT (melphalan $200\text{mg}/\text{m}^2$) → VGPR
- Day +100: VGPR; MRD positive 10^{-4}
- Maintenance options under discussion

 CLINICAL DILEMMA

Post-ASCT NDMM, 1q gain, MRD-positive at 10^{-4} on day +100. AURIGA directly addresses this scenario. Does MRD positivity mandate daratumumab-containing maintenance — or is lenalidomide monotherapy sufficient?

 MANAGEMENT OPTIONS — no single correct answer

A. Lenalidomide monotherapy — IFM/DFCI/CALGB standard; PFS + OS benefit; MRD may convert over time

B. Lenalidomide + daratumumab (AURIGA protocol) — MRD-positive post-ASCT: daratumumab addition superior MRD conversion

C. DaraVRD consolidation × 2 more cycles first — MRD positive at +100: consolidate before maintenance

D. MRD-guided intensification — if MRD persists at +180, add daratumumab; if converts, len alone

E. Lenalidomide + bortezomib maintenance — 1q gain may benefit from PI maintenance