Case-based Panel: Management of Patients with Relapsed or Refractory MM

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Clinical Case #1

- December 2014: 65 yo African American male psychiatrist presented with back pain and pancytopenia, found to have a sacral mass with paramedullary extension- biopsied and consistent with plasma cell neoplasm, received radiation.
- 1/2015: BMBx 20% kappa-restricted BMPC, PET/CT showed focal uptake in sternum and lytic lesion with pathologic fracture of 9th right rib. FISH t(11;14), trisomy 4. SPEP no M-protein, KLC 1340 mg/L, ratio >1000.
- April 2015 VTD-PACE in Little Rock, Arkansas, followed by mel 200mg/m2 and ASCT June 2015, achieved VGPR, followed by RVd maintenance
- Jan 2016 changed to Ixazomib, lenalidomide, dex for maintenance due to peripheral neuropathy
- May 2019 progression based on rising light chains and 8% BMPC on repeat marrow. Started DPd. Progressive dose-reductions in pomalidomide due to intolerance.
- Feb 2022 PET/CT showing marrow replacing lesions at T11 and T12 that were new. BMBx negative.

Clinical Case #1 continued…

- 8/2022 KPd followed by apheresis, no need for bridging and SOC Idecel. sCR at day 100. Monitored with annual PET scans as lesions typically preceded marrow involvement and light chain rise.
- Feb 2025 PET/CT showing new L4 lesion, biopsy proven plasma cell neoplasm, with one additional lytic lesion on left 8th rib. BMBx negative, but light chains rising – by March 2025 up to 56mg/L with ratio 44.

Summary: 77 yo retired psychiatrist with no significant past medical history who was diagnosed with KLC MM in 2014 with t(11;14), now refractory to IMiD, PI, anti-CD38, and BCMA-directed CART. Walks about 2-3 miles per day with his husband.

Clinical Case #2

- 74 yo male with history of stroke in 2016, atrial fibrillation, multi-vessel coronary artery disease s/p CABG 10/3/2025 while myeloma was actively progressing. Despite significant cardiac history, prior to CABG walking 2-3 miles per day and post CABG about 1 mile per day and attending cardiac rehab.
- 12/2007 IgG kappa MGUS
- 8/2017 progressed to IgG kappa MM based on K/L ratio >100, 30% BMPC, and one lytic lesion. FISH +1q and monosomy 13.
- 10/2017: RVd x 6 followed by Len maintenance with best response VGPR.
- August 2021 rising light chains and bone marrow biopsy showing 20% BMPC. DVd with best response PR but stable so treatment was not changed.
- March 2025 Admitted with new onset CHF and acute renal insufficiency thought to be due to cardiorenal syndrome. All treatment held.

Case #2 continued…

- August 2025 light chains rising up to 500mg/L and started on DPVd. Progressive dyspnea so LHC performed and showed multivessel CAD so he was planned for CABG while myeloma was actively progressing. Placed on PCd with some stabilization in light chain trajectory. Then treatment held for 1 month for CABG.
- 10/3/2025 underwent 3-vessel CABG which was complicated by readmission for CHF and need for medical optimization.
- 12/1/2025 KLC up to 2200mg/L. BMBx showed 60% BMPC and PET/CT showing 2 new lesions in lumbar spine.

Summary: 74 yo male with multivessel CAD and recent 3-vessel CABG, triple-class refractory with no history of T-cell redirection. Able to walk up to 1 mile at a time, attending cardiac rehab. No social support at home as his family mostly lives in El Salvador.

Clinical Case #3

- August 2025: 65 yo male who presented with abdominal pain, found to have multifocal retroperitoneal, and intra-abdominal soft tissue masses and scattered lucent lesions throughout the axial and appendicular skeleton on CTAP.
- Transferred to UCSF for further work-up. On arrival, had leukocytosis with WBC 40.5. Flow cytometry revealed 80% circulating plasma cells. **LLC:** 13,331 mg/L, KLC 4.3 mg/L. **M protein:** 0.4 g/dL **IFE:** IgD lambda. **Serum IgD:** 1120 mg/dL. **Calcium:** 10.8; **Creatinine:** 3.49; **Hemoglobin:** 10.6 g/dL.
- 8/20/2025: Initiated PLEX and Dara-CyBorD Inpatient. Course was complicated by afib with RVR and cardiac hypokinesis
- 8/21/2025: **PET/CT:** infiltrative thoracic and abdominopelvic lymphadenopathy with low level activity. Large bilateral pleural effusions. Thoracentesis, pleural fluid + for plasma cells.
- 8/22/2025: Bone marrow biopsy: 95% cellularity with sheets of atypical lambda-restricted, plasma cells with anaplastic morphology. High Ki-67 (60-70%), CD138+ plasma cells comprising 90% of the marrow cellularity. **FISH:** gain 1q, monosomy 13, gain or rearrangement of 14q32.

Case #3 Continued…

- Initial decline in light chains from 13,000→ 608 mg/L, then started to rise again.
- 9/30/2025: VDCEP inpatient chemotherapy with initial drop in LLC to 120mg/L
- 11/6/2025: DKRd initiated as outpatient. LLC 2400mg/L → 341.4mg/L → 1226 mg/L

Summary: 65 yo male with IgD lambda PCL with extramedullary disease and gain 1q, monosomy 13 and complex karyotype, refractory to Dara-CyBorD and DKRd with short term response to VDCEP. Performance status is generally excellent, though with some deconditioning due to prolonged hospitalization and readmissions, with no major comorbidities aside from atrial fibrillation with no recurrent events since initial hospital admission.

Case #3 continued…

- Insurance issues with CART collection and administration – had to go to Los Angeles
- 2/4/26: Admitted for Talquetamab bridging. After Step up dose #1 had grade 2 CRS and ICANS. After step up dose #2, had recurrent CRS and grade 2 ICANS without return to baseline with steroids and tocilizumab.
- 2/11/26: MRI brain showed scattered leptomeningeal enhancement throughout the supra and infratentorial brain with more focal area along left parietal lobe with associated vasogenic edema – favored to represent leptomeningeal myelomatous involvement.
- 2/13/26: LP with concern for plasma cells on flow cytometry of CSF. Received triple IT chemotherapy – cytarabine, methotrexate and hydrocortisone. CSF cleared.
- 3/2026: continued talquetamab bridging with LLC normalized and M protein undetectable, IgD unmeasurable.
- 4/6/2026: planned ciltacel infusion