CME OUTFITTERS

Real-World Tactics to Address Health Inequities in Multiple Myeloma Care

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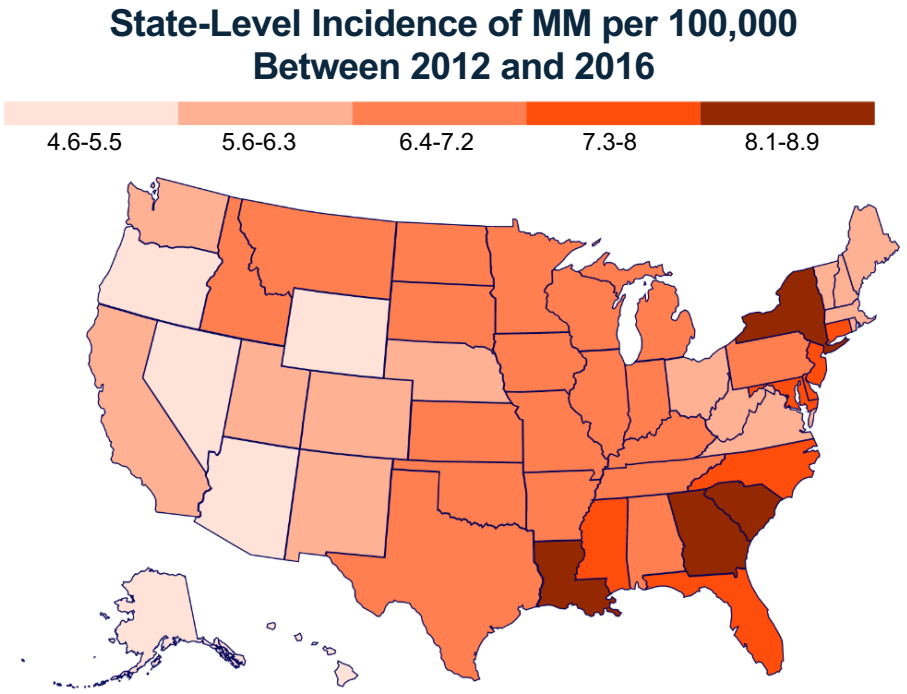
Learning Objective

Recognize the impact of health inequities on patients with multiple myeloma and develop individual treatment strategies for optimal clinical outcomes

Multiple Myeloma: A Systemic Plasma Cell Malignancy

- Estimated new cases and deaths in 2022 in the United States:
  - New cases: 34,470
  - Deaths: 12,640
- Percentage of patients surviving 5 years: 55.6%
- Median age at diagnosis: 69 years
- MM is most common in men and Black adults



Siegel RL, et al. CA Cancer J Clin. 2022;72(1):7-33. SEER Cancer Stat Facts: Myeloma. National Cancer Institute website. http://seer.cancer.gov/statfacts/html/mulmy.html. Accessed May 6, 2021.

Patient Case: Daniel

- Daniel is a 55-year-old Black man
  - Overweight, mild (untreated) hypertension
- Visits his primary care physician with complaints of fatigue, thirst, and frequent urination
  - Diagnosed with prediabetes (A1C 6.2%)
  - Given instructions on weight control and exercise
- 6 months later, returns with same symptoms including a lingering sinus infection and general aches
  - Told his prediabetes makes him prone to infections that are made worse by seasonal allergies
  - His PSA is checked but is normal (0.6 ng/mL)

PSA = prostate-specific antigen

Realities of Health Care Access

- Black people have a twofold higher incidence of and mortality from myeloma compared with White people.
  - Many disparities in outcomes can be attributed to delays in diagnosis due to misdiagnosis (e.g., diabetes)
- Black and Hispanic patients with myeloma are less likely to utilize stem cell transplantation or bortezomib treatment compared with White patients; they also receive novel treatments later after their diagnosis compared with White patients.
- Notably, new studies show that Black patients may have a higher survival rate than White patients when all patients have equal access to novel treatments.

American Association for Cancer Research. AACR Cancer Disparities Progress Report. https://cancerprogressreport.aacr.org/disparities/. Published 2022. Accessed June 15, 2022.

Audience Response

How does the biology of myeloma affect outcomes?

a. Immune checkpoint inhibitors have dramatically improved outcomes for patients with myeloma.
b. The rate of myeloma progression is very consistent between patients, making it easy to plan subsequent therapies.
c. The best depth of response in the first year of diagnosis is extremely important.
d. Improved management of adverse effects has been important to improving outcomes, since there have been only small changes to active therapies in the past decade.
e. I'm not sure

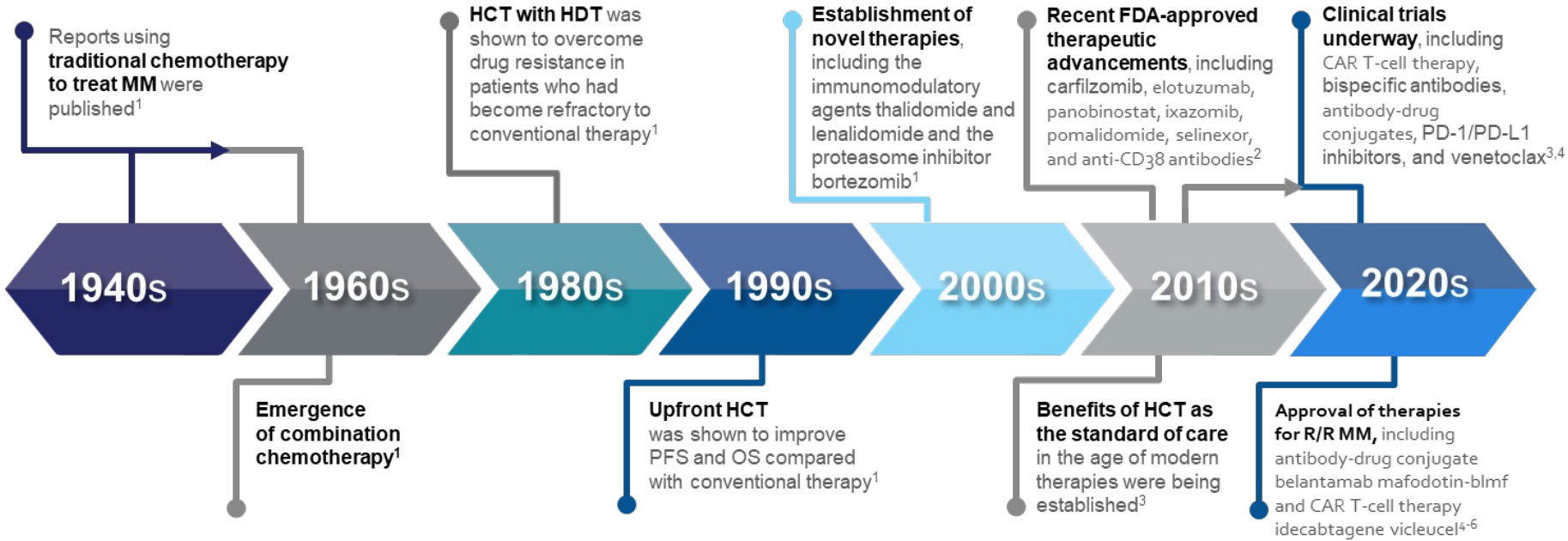
Not One Disease

- MGUS to active MM transition period is different among patients. Diagnosis is made at variable time points during the transition, so degree of end organ damage is different
- Management strategies have improved MM survival from 2-3 years in the 2000s to > 10 years in the 2020s
- Advances in understanding myeloma biology has led to new therapeutic targets
- MM Pathways
- Bone marrow microenvironment
- Immune regulation and modulation
- Picking the right strategy that gives the highest likelihood of the best depth of response in the first year of diagnosis is extremely important for survival outcomes

MGUS = monoclonal gammopathy of undetermined significance; MM = multiple myeloma

Martinez-Lopez J, et al. Blood. 2011;118(3):529-534. Usmani SZ, et al. Leukemia. 2013;27(1):226-232. Usmani SZ, et al. Leukemia. 2012;26(11):2398-2405.

History of MM Treatments



CAR = chimeric antigen receptor; HDT = high-dose therapy; OS = overall survival; PD-1 = programmed cell death 1; PD-L1 = programmed cell death-ligand 1; PFS = progression-free survival; R/R = relapsed/refractory

1. Laubach J, et al. Annu Rev Med. 2011;62:249-264. 2. Rajkumar SV. Am J Hematol. 2020;95(5):548-567. 3. Palumbo A, et al. N Engl J Med. 2014;371(10):895-905. 4. Zanwar S, et al. Blood Cancer J. 2020;10(8):84. 5. US Food and Drug Administration. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-granted-accelerated-approval-belantamab-mafodotin-blmf-multiple-myeloma. Accessed Sept 12, 2022. 6. US Food and Drug Administration. https://www.fda.gov/news-events/press-announcements/fda-approves-first-cell-based-gene-therapy-adult-patients-multiple-myeloma. Accessed Sept 12, 2022.

The Four T's

- **T**riplets
- **T**ransplants
- Clinical **T**rials
- CAR **T**-cell therapy

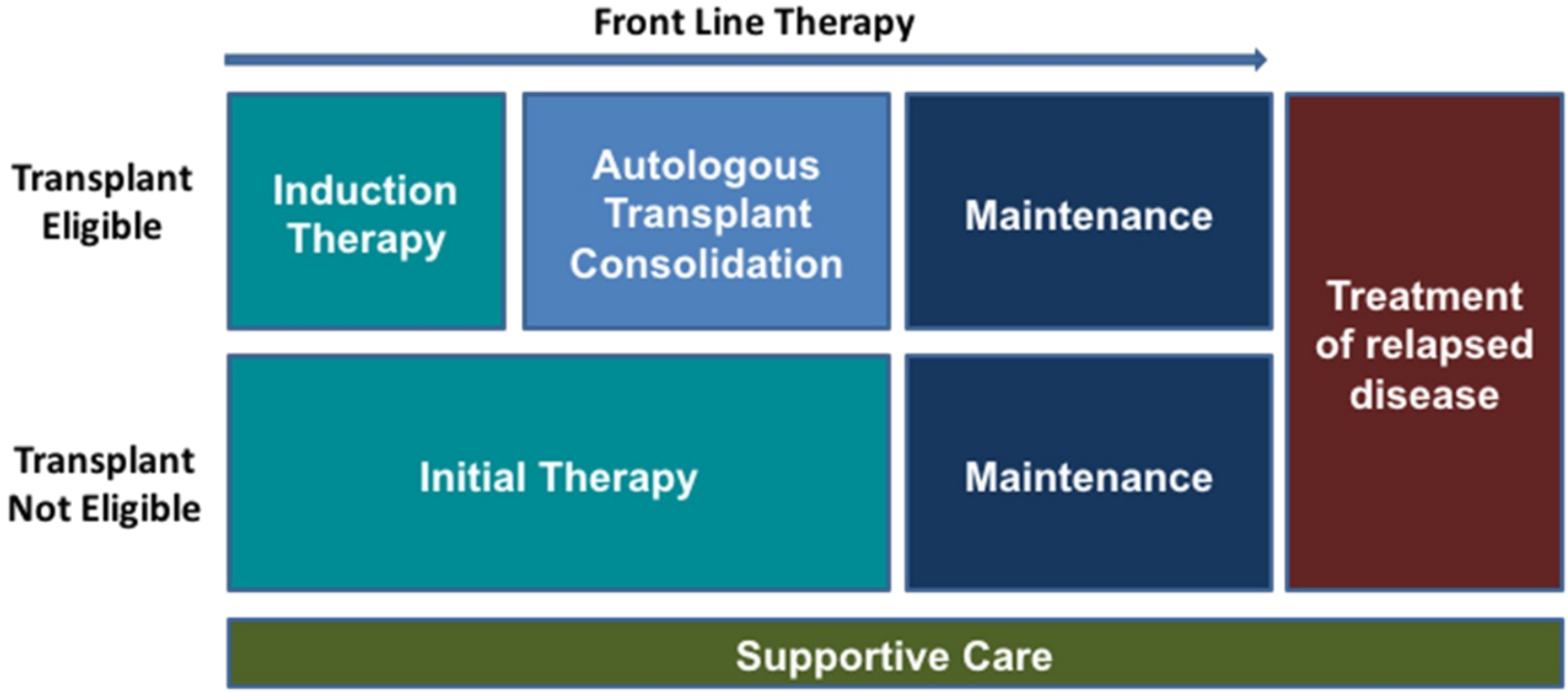
CAR = chimeric antigen receptor

Blind Spots

- Poor assessment of MM disease biology at diagnosis and relapse:
  - Highly dependent on the quality of random pelvic bone biopsy
    - Can fix by creating SOP for sample ‘pecking order’
  - No assessment of focal bone lesions or extramedullary disease
    - Can fix by concomitant biopsy of such lesions as ‘routine’ practice, not patient friendly
  - Only examine at finite timepoints
    - Harder fix as biopsies are not patient friendly, this is not CLL
  - This leads to the ‘unexpected’ poor responders or unexpected ‘early relapse’ we see in the clinics.
- Incorporation of immunome and bone marrow microenvironment status in MM patient assessment
- Assessing depth of response/detect MRD status

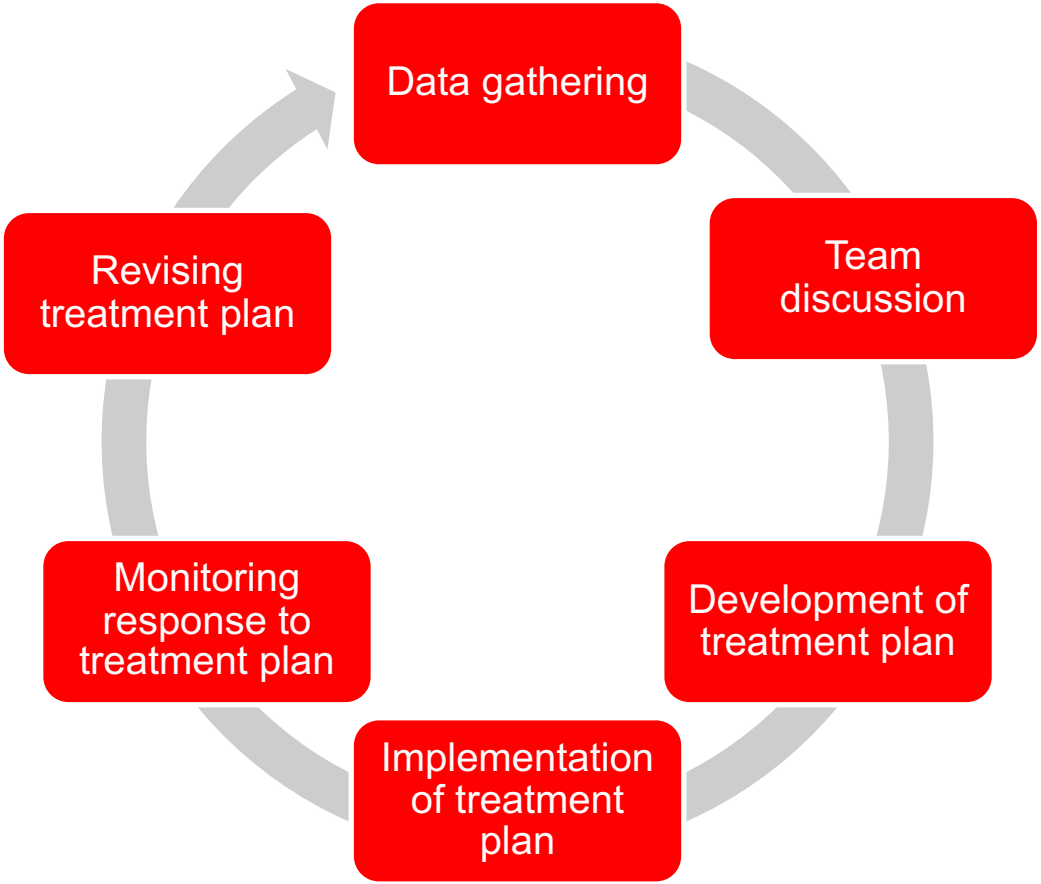
CLL = chronic lymphocytic leukemia; MRD = minimal residual disease; SOP = standard operating procedure

Treatment Paradigm For NDMM



NDMM = newly diagnosed multiple myeloma

Ongoing Management Process During Care

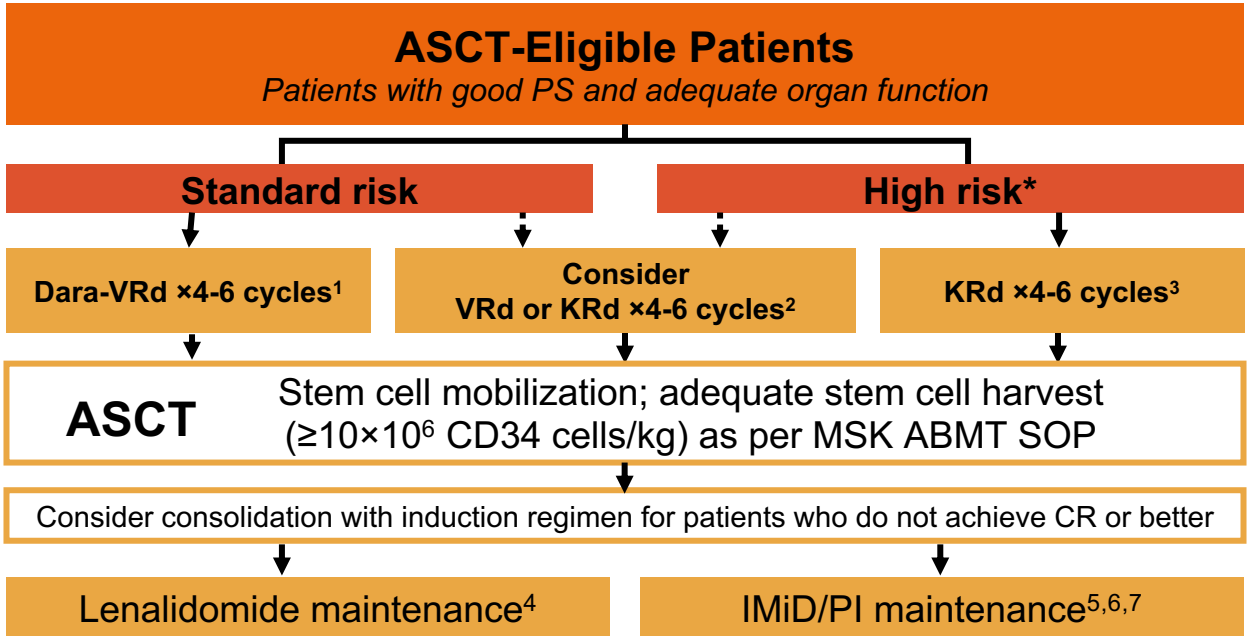


Patient Case: Daniel

- Daniel receives a diagnosis of multiple myeloma
  - IgA lambda, standard risk
- He receives VRd, followed by ASCT, no maintenance therapy
  - He achieves a complete response
  - However, within 2 years, he experiences serologic progression
  - Imaging studies reveal new lytic bone disease

ASCT = autologous stem cell transplant; VRd = bortezomib, lenalidomide, and dexamethasone

MSK Approach to Transplant Eligible NDMM



CR = complete response; DVRd = daratumumab, bortezomib, lenalidomide, and dexamethasone; IMiD = immunomodulatory drug; KRd = carfilzomib, lenalidomide, and dexamethasone; PI = proteasome inhibitor; PS = performance status; Tx = treatment

*By R-ISS staging (R-ISS II/III) and/or cytogenetics (t[4;14], t[14;16], or del[17p]), elevated LDH, primary plasma cell leukemia

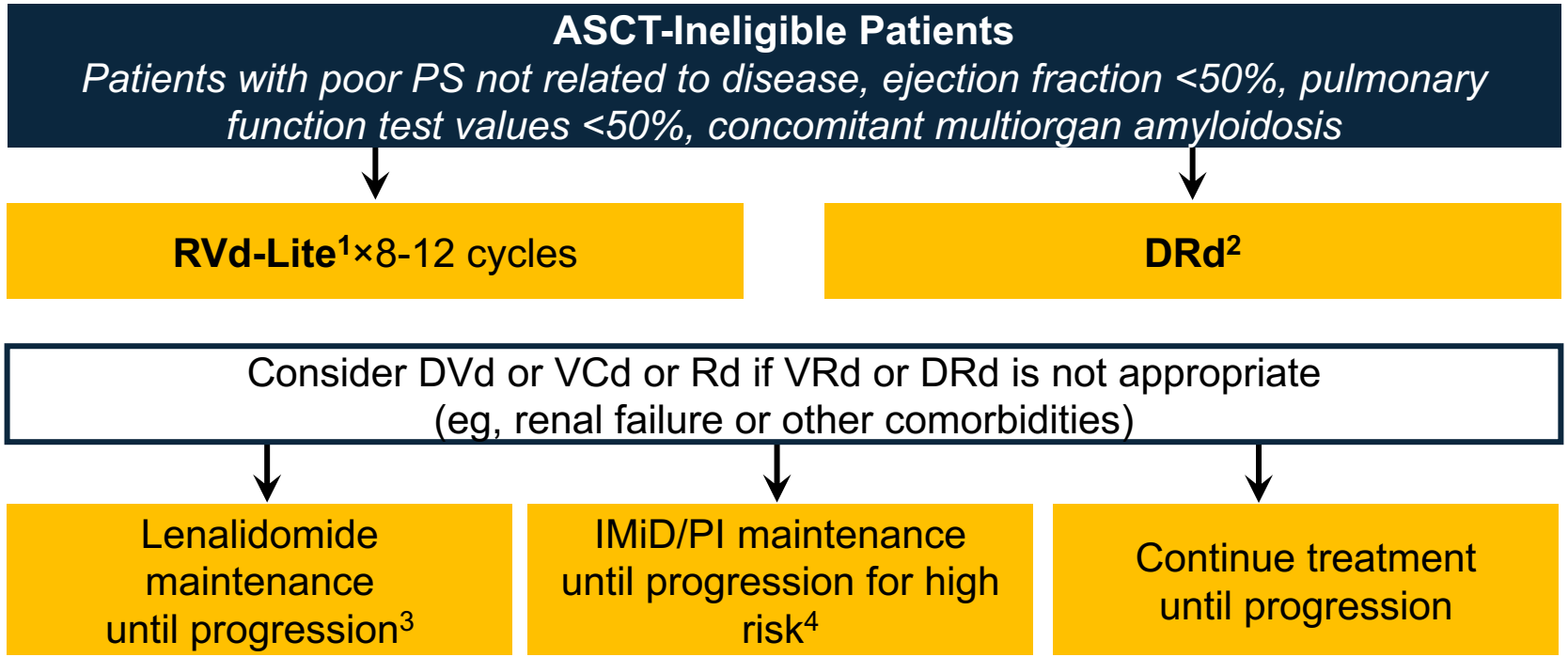
1. Attal. NEJM. 2017;376:1311. 2. Voorhees PM. Blood 2020. 3. Gay. ASH 2020. Abstr 294. 4. McCarthy. J Clin Oncol. 2017;35:3279. 5. Nooka. Leukemia. 2014;28:690. 6. Dimopoulos. ASH 2018. Abstr 301. 7. Usmani. Lancet Haematol. 2021 Jan;8(1):e45-e54.

Patient Case: Daniel

- Daniel receives treatment with DaraKd
  - His hypertension worsens, but can be controlled with medication
  - Unfortunately, he experiences progressive disease after 18 months
- He receives pomalidomide/cyclophosphamide/dex
  - Attains a short-lived PR
- He receives ciltacabtagene autoleucel
  - He develops grade 3 cytokine release syndrome, mild headache
  - AEs managed with fluids, acetaminophen, tocilizumab
- He maintains an ongoing CR (9 months)

AE = adverse event; DaraKd = daratumumab, carfilzomib, and dexamethasone; PR = partial response

MSK Approach to Transplant Ineligible NDMM



DRd = daratumumab, lenalidomide, and dexamethasone; DVd = daratumumab, bortezomib, and dexamethasone; VRd-Lite = modified VRd regimen

1. O'Donnell. Br J Haematol. 2018;182:222. 2. Facon. ASH 2018. Abstr LBA-2. 3. Larocca. ASH 2018. Abstr 305. 4.Usmani. Lancet Haematol. 2021 Jan;8(1):e45-e54.

Key Questions Towards Curing Myeloma

- What is the molecular and immunobiology of disease evolution and progression in MM?
  - Can we recognize patients at precursor state and intervene early?
  - Can we pick different strategies for different disease biology and immune status?
- How to accurately assess sustained MRD negativity:
  - Can we utilize novel imaging and novel peripheral blood assessments?
- Can MRD guide treatment time and treatment strategy?
  - Sustained MRD at which threshold, how far apart? Use the same for high-risk vs standard-risk disease?
- Optimal sequencing of existing therapies and incorporation of select novel MoAs based on disease biology:
  - Pay attention to supportive care, short-term and long-term sequelae of treatments

MoA = mechanism of action; MRD = minimal residual disease

Coming Down the Pike

- Quadruple combinations
- Small Molecules
  - XPO1 inhibitors: Selinexor combinations
  - CELMoDs: Iberdomide, CC-480
  - BCL2/MCL1 Pathway: Venetoclax and its combinations, several MCL1 inhibitors
- Novel Antibody Drug conjugates
  - Belantamab mafodotin combinations
- Bispecific Antibodies
  - BCMAxCD3
  - GPRC5DxCD3
- CAR T-cell therapy
  - BCMA-directed therapies

BCMA = B-cell maturation antigen

Practical Points to Addressing Disparities

- Awareness of the disparities and their multiple causes
- The importance of building trust in the clinic
- Supporting efforts of community engagement
- Culturally sensitive care – recognizing differences, listening to patients and meeting them where they are, especially in communication
- Leveraging the whole health care team of social work, nurses, pharmacists, etc.
- Advocating and facilitating better access to therapies and insurance coverage
- Pointing patients to the resources that can help them
  - https://m-powernewyork.myeloma.org/

Summary

- Early detection is important to disease control
- Black patients with myeloma are diagnosed at a later time
- As a group, Black patients have a shorter overall survival than White patients
- Black patients are less likely to receive ASCT, bortezomib, or early use of novel agents than White patients
- However, when the same treatments are received by both groups, Black patients do as well, or better, than White patients

SMART Goals

Specific, Measurable, Attainable, Relevant, Timely

- Do not discount symptoms consistent with myeloma or quickly attribute to another cause
- Adhere to guideline recommendations for treatment planning
- Encourage clinical trial participation

To Receive Credit

To receive CME/CE credit for this activity, participants must complete the post-test and evaluation online.

Participants will be able to download and print their certificate immediately upon completion.

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Oncology Hub

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Diversity and Inclusion Hub

Free resources and education to educate health care providers and patients on health-related inequities
https://www.cmeoutfitters.com/diversity-and-inclusion-hub/