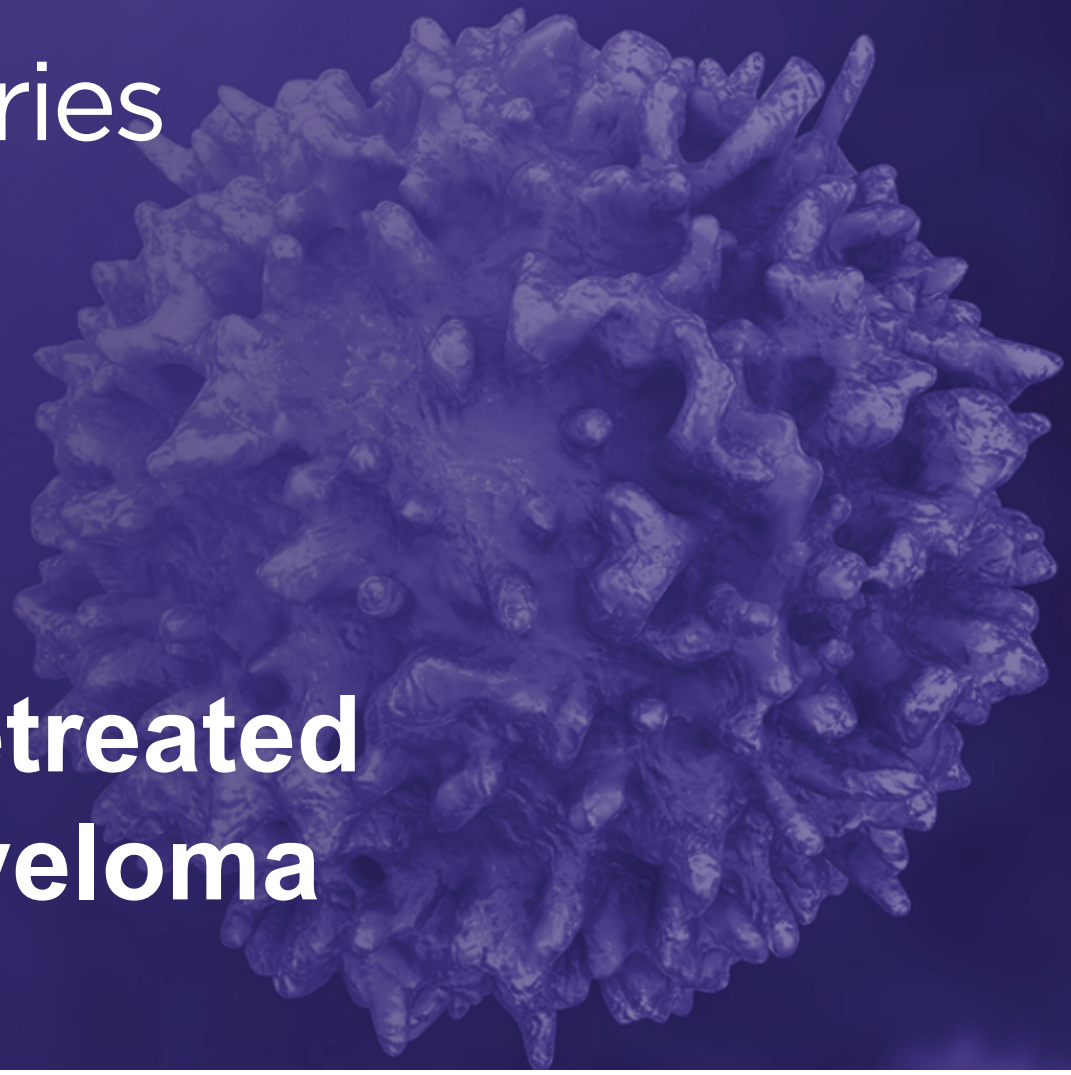
JADPRO Clinical Case Series

Key Principles in Safely Prescribing Bispecific Antibodies in Heavily Pretreated Patients With Multiple Myeloma



SUPPORTED BY

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PHARMACEUTICAL COMPANIES OF Johnson & Johnson

PRESENTER

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Program Goals

- Understand the importance of consistent observation and progressive clinical interventions in order to successfully manage CRS associated with teclistamab.
- Apply the process of ruling out other factors while concurrently treating patients for CRS associated with teclistamab.
- Describe the tenets of appropriate coordination and education between the initiating center and the community setting when managing patients on teclistamab.

Monitoring for Teclistamab-Associated Cytokine Release Syndrome

Introduction

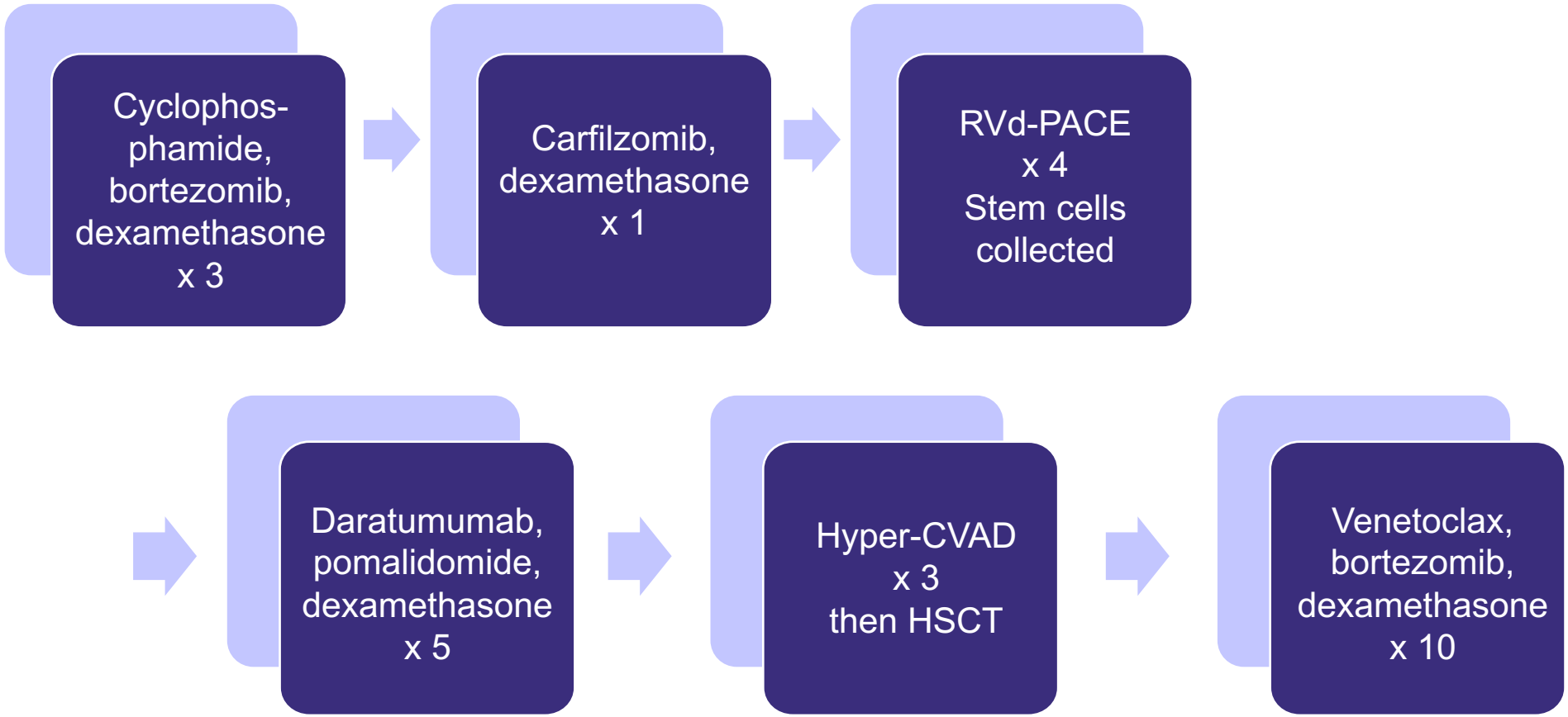
- Mrs. L is 53-year-old woman with R-ISS stage II MM
  - Initial presentation included lightheadedness and fatigue
- CT C/A/P showed multiple skeletal lesions
- SPEP: 2.9 g/dL IgG lambda
  - Kappa free light chain of 0.37 mg/dL
  - Lambda free light chain of 201 mg/dL
- Bone marrow biopsy: 75% lambda-restricted plasma cells
  - Standard risk cytogenetics, t(11;14)
- Hemodialysis initiated

Laboratory Values at MM Diagnosis

Parameter	Value at Diagnosis
Creatinine	20.7 mg/dL
Hemoglobin	2.2 g/dL
Hematocrit	6.7%
Platelets	101,000 U/L
Beta-2 microglobulin	5.4 mg/L
Albumin	3.8 g/dL
LDH	222 U/L

LDH, lactate dehydrogenase; MM, multiple myeloma; R-ISS, Revised International Staging System

Mrs. L's Treatment



Initiation of Teclistamab

- Upon relapse after venetoclax, bortezomib, and dexamethasone, Mrs. L began **teclistamab**

First 3 doses typically given inpatient
- Step-up dosing
- Monitor for CRS

Teclistamab Step-Up Dosing

#	Day	Dose
1	1	0.06 mg/kg
2	4	0.3 mg/kg
3	7	1.5 mg/kg

Teclistamab Weekly Dosing

Schedule	Dose
1 per week	1.5 mg/kg

TECVAYLI (teclistamab-cqyv) injection, for subcutaneous use. [Prescribing information]. Horsham, PA: Janssen Biotech, Inc.; October 2022.

Cytokine Release Syndrome

- Teclistamab causes release of IFN-γ or TNF-α, which can activate bystander immune and non-immune cells
  - Release of proinflammatory cytokines, which can trigger cascade reaction

MajesTEC study

72.1% of patients developed any-grade CRS
- Only 1 case was grade 3
- No grade 4

- CRS onset was median 2 days
- Duration was median 2 days

Moreau P, et al.. *N Engl J Med*. 2022;387:495-505.

Mild CRS

- On day 2 of hospital observation, Mrs. L developed a fever of 38.0°C
  - Decreased within 1 hour of intervention
  - Blood cultures and x-ray show no growth or abnormalities
- No additional CRS or ICANS symptoms
- Remaining doses administered outpatient
- After 3 cycles, free light chains normalized and SPEP too small to quantify

Polling Question

How do you typically manage mild to moderate CRS?

A. Hold the next dose and wait for resolution of symptoms

B. Hold the next dose and administer tocilizumab

C. Administer tocilizumab and continue treatment as planned, as long as symptoms improve

D. Administer a medication other than tocilizumab

Polling Question

How do you typically manage mild to moderate CRS?

A. Hold the next dose and wait for resolution of symptoms **33%**

B. Hold the next dose and administer tocilizumab **8%**

C. Administer tocilizumab and continue treatment as planned, as long as symptoms improve **50%**

D. Administer a medication other than tocilizumab **8%**

Key Takeaway

Successful management of CRS associated with teclistamab requires consistent observation and implementation of progressive clinical interventions.

Management of Teclistamab-Associated Cytokine Release Syndrome

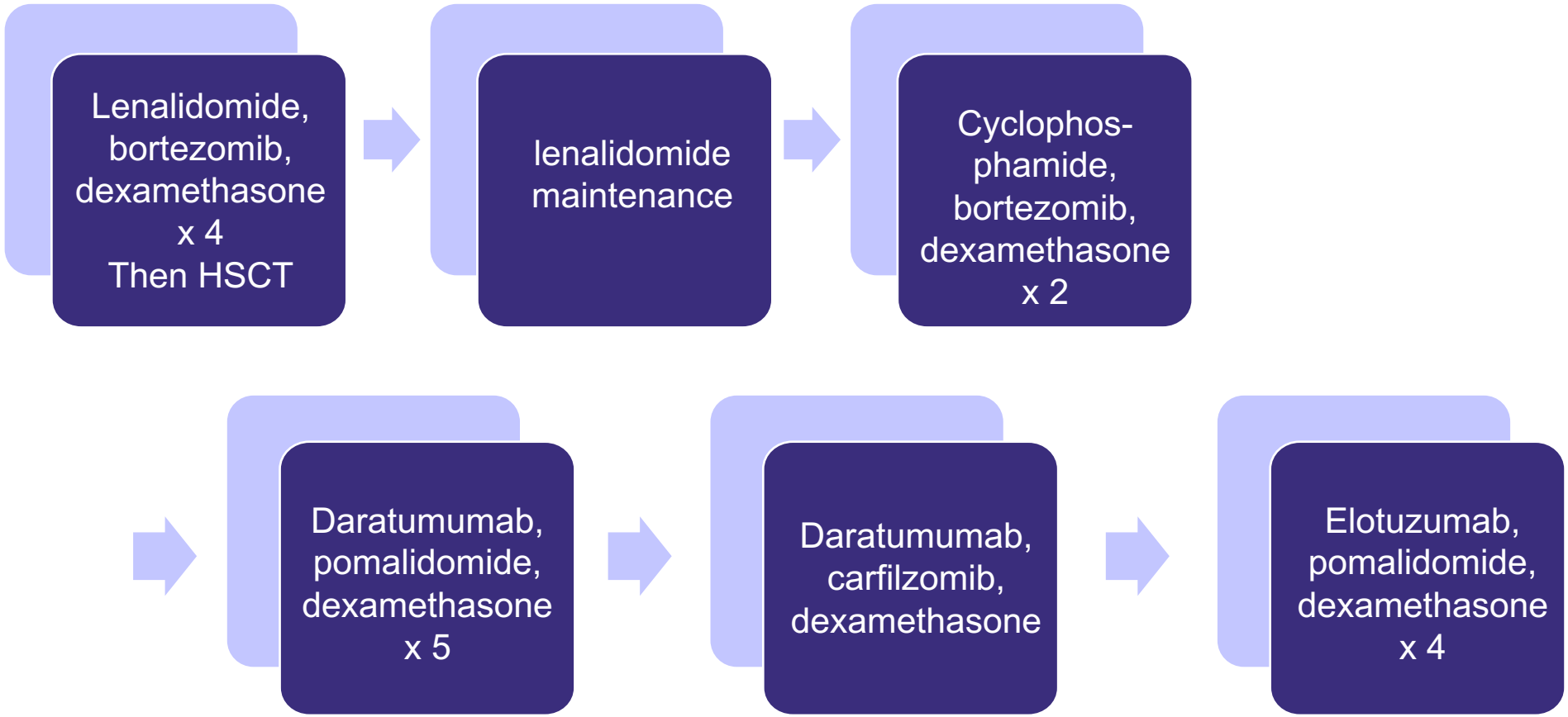
Introduction

- Mr. O is 64-year-old man with MM
  - Initial presentation to PCP for persistent back pain
- PET-CT showed no abnormal FDG uptake, no lytic lesions
- SPEP: 4.11 g/dL IgG kappa
  - Kappa free light chain of 8.7 mg/dL
  - Lambda free light chain of 0.83 mg/dL
- Bone marrow biopsy: 65-70% plasma cells
  - Standard risk cytogenetics

Laboratory Values at MM Diagnosis

Parameter	Value at Diagnosis
Calcium	9 mg/dL
Creatinine	0.98 mg/dL
Hemoglobin	13.8 mg/dL
Total protein	10 g/dL
Beta-2 microglobulin	2.57 mg/L
Albumin	3 g/dL
LDH	200 U/L

Mr. O's Treatment



Initiation of Teclistamab

- Upon relapse after elotuzumab, pomalidomide, and dexamethasone, Mr. O began **teclistamab**
- Develops signs and symptoms of CRS
  - 6 hours following Mr. O's day 4 dose (0.3 mg/kg)

Mr. O's Signs and Symptoms
Fever of 39°C
Blood pressure of 89/54 mmHg
Tachycardia of 106 bpm

TECVAYLI (teclistamab-cqyv) injection, for subcutaneous use. [Prescribing information]. Horsham, PA: Janssen Biotech, Inc.; October 2022.

Treatment of CRS

- Fluid bolus
- Blood cultures, chest x-ray
  - Returned unremarkable
- 650 mg acetaminophen with IV antibiotics
- Second bolus and 8 mg/kg IV tocilizumab
  - Symptoms resolved

ASTCT CRS Grading System

Grade	Description
1	• ≥38°C • No hypotension • No hypoxia
2	• ≥38°C • Hypotension, but vasopressors not required • Hypoxia requiring low-flow nasal cannula or blow-by
3	• ≥38°C • Vasopressor ± vasopressin • And/or require high-flow nasal cannula, face mask, non-breather mask, Venturi mask
4	• ≥38°C • Multiple vasopressors (excl. vasopressin) • Require positive pressure

Lee DW, et al. *ASTCT Biol Blood Marrow Transplant*. 2019;25:625-638.

Continued Treatment

- CRS resolved with no further episodes
- After day 7 dose, Mr. O was able to receive teclistamab outpatient
- Achieved a very good partial response

Polling Question

Which grade CRS do you most commonly see in your practice?

A. Grade 1

B. Grade 2

C. Grade 3

D. Grade 4

Polling Question

Which grade CRS do you most commonly see in your practice?

A. Grade 1 **36%**

B. Grade 2 **55%**

C. Grade 3 **9%**

D. Grade 4 **0%**

Key Takeaway

Successful management of CRS associated with teclistamab requires ruling out other factors while concurrently treating for CRS.

Transferring Patients Receiving Teclistamab From an Academic Center to a Community Clinic

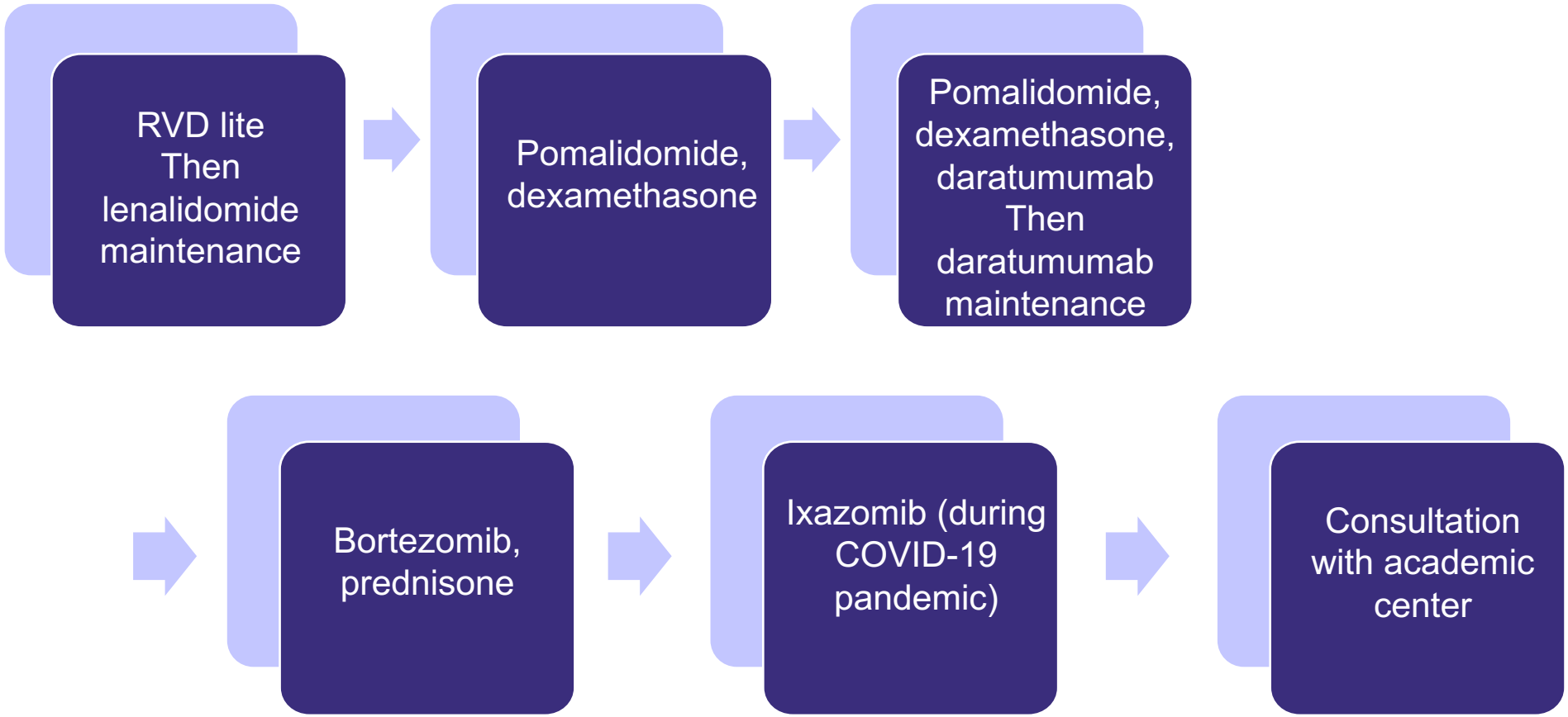
Introduction

- Mrs. T is 67-year-old female with R-ISS stage II IgA lambda MM
  - Initial presentation of severe hip pain
- PET-CT showed multiple sites of metabolically active lytic lesions in axial skeleton, compression fracture L3, fracture in right femoral neck
- SPEP: 3.5 g/dL IgA lambda
  - Kappa free light chain of 0.61 mg/dL
  - Lambda free light chain of 117.4 mg/dL
- Bone marrow biopsy: 80% plasma cells
  - Standard risk cytogenetics

Laboratory Values at MM Diagnosis

Parameter	Value at Diagnosis
Calcium	10.3 mg/dL
Creatinine	1.39 mg/dL
Hemoglobin	8.5 g/dL
Beta-2 microglobulin	4.1 mg/L
Albumin	4.0 g/dL
LDH	199 U/L

Mrs. T's Treatment at the Community Clinic



Initiation of Teclistamab

- Upon consultation at an academic center, Mrs. T was switched to teclistamab
- CRS grade 1 developed during second dose, but unremarkable otherwise
- Achieved a complete response
- Requested continuing teclistamab at her community clinic

Teclistamab in the Community

Facilities

- CRS specific training
- Clinical monitoring plan
- Clinical intervention plan
- ICU availability
- Anti – IL- 6 availability
- Transition of care outpatient → inpatient and back

Patients and Caregivers

- Know the s/s
- Know who to call and when
- Know where to go

Providers

- Be aware of risk factors
- Educate the patient and caregiver
- Mitigate risk with corticosteroids, antipyretics, antihistamines, antimicrobials (per protocol)
- Monitor: Watch for changes in hemodynamic and respiratory status, bleeding/bruising, lab values
- Maintain a broad differential diagnosis
- Know the s/s of CRS and timeframe
- Manage CRS with appropriate interventions as outlined in established guidelines

Polling Question

When you consider the transitions of care between community and academic settings for patients receiving bispecific antibody therapy, which of the following statements is most applicable?

A. Patients are generally referred for bispecific therapy and transferred back to community care at appropriate times in their treatment trajectory.

B. Patients are generally referred for bispecific therapy at appropriate times, but the transition back to the community providers is not as consistent.

C. Patients are often not referred for bispecific therapy at times that they should be, but once they do get access to this treatment modality, they are transitioned back to community care at appropriate intervals.

D. Transitions of care between academic and community settings, both pre and post bispecific antibody therapy, remain one of the most difficult aspects of care coordination.

Polling Question

When you consider the transitions of care between community and academic settings for patients receiving bispecific antibody therapy, which of the following statements is most applicable?

A. Patients are generally referred for bispecific therapy and transferred back to community care at appropriate times in their treatment trajectory. **0%**

B. Patients are generally referred for bispecific therapy at appropriate times, but the transition back to the community providers is not as consistent. **0%**

C. Patients are often not referred for bispecific therapy at times that they should be, but once they do get access to this treatment modality, they are transitioned back to community care at appropriate intervals. **0%**

D. Transitions of care between academic and community settings, both pre and post bispecific antibody therapy, remain one of the most difficult aspects of care coordination. **100%**

Key Takeaway

With appropriate coordination and education between the initiating center and community cancer facility, teclistamab can provide a safe and effective regimen for heavily pretreated patients.

Q & A

Please type your questions for Josh Epworth
into the **question box**.

Thank You