# Initial Therapy for Patients with Multiple Myeloma Not Eligible for Transplant

A Case Study

- Mrs. T is a 77-year-old African American female with a past medical history of poorly controlled hypertension and chronic kidney insufficiency (CKI). She requires assistance with many instrumental activities of daily living
- Despite her CKI, her renal function dropped from a glomerular filtration rate (GFR) of 45 ml/min/kg to 30 ml/min/kg and she became more anemic
- She was found to have 6.1 g/dL lgG κ M-protein, 34% plasma cells in her bone marrow (42% t(6;14) by FISH), a hemoglobin on 7.4 g/dL, and bone lesions confirming a diagnosis of multiple myeloma
- Her plasma cell labeling index was 1.5% and her CRAB analysis shows hypercalcemia, anemia, renal dysfunction, a skeletal survey finds widespread osteoporosis and lytic lesions in the proximal left femur
- Based upon her frailty and comorbidities, Mrs. T is not a candidate for autologous stem cell transplant

What are the initial myeloma therapies that Mrs. T should consider?

## Work-up for Suspected Multiple Myeloma

History and physical examination				
Blood	<ul> <li>CBC with differential</li> <li>Basic metabolic panel including, BUN, creatinine, electrolytes, calcium, albumin, lactate dehydrogenase (LDH)</li> <li>Serum quantitative immunoglobulins</li> <li>Serum protein electrophoresis and immunofixation (SPEP)</li> <li>β<sub>2</sub>microglobulin</li> <li>Serum free light chain analysis</li> </ul>			
Urine	<ul> <li>24-hr protein</li> <li>Protein electrophoresis with immunofixation (UPEP)</li> </ul>			
Bone Marrow	<ul> <li>Unilateral bone marrow aspirate and biopsy evaluation with immunohistochemistry or flow cytometry, cytogenetics, and FISH</li> </ul>			
Imaging	<ul> <li>Skeletal survey</li> <li>MRI and PET/CT as clinically indicated</li> </ul>			

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#### Case Study: Laboratory Values

Lab/Normal Reference Range	Value	Lab/Normal Reference Range	Value
WBC 3.0–11.0 k/µL	10.5	BUN 8–25 mg/dL	34H
Plt Ct 150–400 k/µL	155	Creatinine 0.7–1.4	1.25
Hgb 13.0–17.0 g/dL	10.7L	mg/dL	
Hct 39.0–51.0%	32.1L	Calcium 8.5–10.5 mg/dL	9.1
MCV 80–100 fL	78L	Albumin 3.5–5.0 g/dL	<b>2.2L</b>
RDW-CV 11.5–15.0%	15.8	Alk Phos 40–150 U/L	320H
Neut % 38.5–75.0%	68	Noto: Pody woight 120 lbs	
Abs Neut 1.00–7.50 k/µL	7.1	Height 64"	

WBC = white blood cell, Plt Ct = platelet count, Hgb = hemoglobin, Hct= hematocrit, MCV = mean corpuscular volume, RDW-CV = red cell distribution width–coefficient variation, Neut = neutrophils, Abs Neut = absolute neutrophils, BUN = blood urea nitrogen, Alk Phos = alkaline phosphatase

## Case Study: Laboratory Values (continued)

SPEP: Lab/Normal Reference Range	Value
Alpha-1 0.11–0.22 g/dL	0.15
Alpha-2 Globulin 0.6–1 g/dL	0.7
Beta G 0.50–1.00 g/dL	0.65
Gamma Glob 0.60–1.35 g/dL	2.6
M-Spike (g/dL)	1.3

Gamma Glob = gamma globulin; SPEP = serum protein electrophoresis

Lab/Normal Reference Range	Value
Serum IgG	6100
717–1,411 mg/dL	
Serum IgA	17
78–391 mg/dL	
Serum IgM	12
53–334 mg/dL	
Serum Kappa	47520
534–1,267 mg/dL	
Serum Lambda 253–653 mg/dL	210

## Possible Regimens for Patients Not Eligible for Transplant

#### **NCCN Preferred Regimens (Category 1)**

Lenalidomide/low-dose dexamethasone

Melphalan/prednisone/bortezomib

Melphalan/prednisone/lenalidomide

Melphalan/prednisone/thalidomide

**Category 2A recommendations** 

Bortezomib/dexamethasone

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#### **Risk-Stratification for Multiple Myeloma**

Standard-risk

1. Trisomies (hyperdiploidy)

2. t(11;14)

3. t(6;14) ← Mrs. T had 42% t(14;16) by FISH

B. Intermediate-risk 1. t(4;14)

C. High-risk

17p deletion
t(14;16)
t(14;20)
High-risk gene expression profiling signature (unless trisomies are present, then standard risk)

Mrs. T has standard risk multiple myeloma.

Rajkumar, et al., Am J Hematol. 2013;88:226-235.

# Approach to Initial Treatment Plan By Risk Stratification

Risk	Initial Treatment	Further therapy
High	Bortezomib/lenalidomide/dexamethasone	Bortezomib maintenance
Intermediate	Bortezomib/cyclophosphamide/dexamethasone	Bortezomib maintenance
Standard	Lenalidomide and low-dose dexamethasone	

Mrs. T has standard risk multiple myeloma, so she could receive lenalidomide and low-dose dexamethasone except:.

- Lenalidomide would require dose reduction due to renal dysfunction
- VTE prophylaxis would be required (10 mg once daily)
- Lenalidomide may cause neutropenia and thrombocytopenia

Mrs. T may benefit from bortezomib-based therapy to quickly improve renal function. Melphalan, prednisone, and bortezomib is a NCCN Category I therapy that may be a good choice for this patient in addition to a bone-protective therapy. Care should be taken with Melphalan in renal impaired patients. Dose adjust as required. Bortezomib/cyclophosphamide/dexamethasone also a good option.

Rajkumar S., *Am J Hematol.* 2013;88:226-235; Revlimid (lenalidomide) PI, 2013; Roussou M., *Leukemia Res.* 2010;34:1395-1397; NCCN. Clinical practice guidelines in oncology: multiple myeloma. v.1.2013.