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# Current Concepts in Consolidation & Maintenance Therapy for Multiple Myeloma

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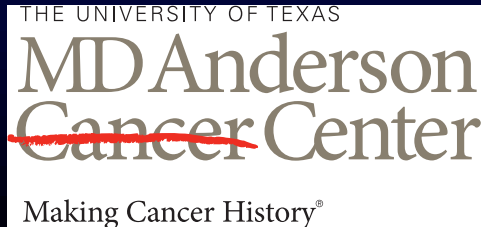
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Chair, SWOG Myeloma Committee

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# Disclosures

<b>Advisory Committee and Consulting Agreements</b>	Bristol-Myers Squibb Company, Celgene Corporation, Takeda Oncology
<b>Contracted Research</b>	Bristol-Myers Squibb Company, Celgene Corporation, Forma Therapeutics, Karus Therapeutics, Onyx Pharmaceuticals, an Amgen subsidiary, Spectrum Pharmaceuticals Inc, Takeda Oncology

# Case presentation 3: Dr Favaro

## 68-year-old man

- Fall 2015: Incidental diagnosis of multiple myeloma
- Cytogenetics: t(11;14), monosomy 13, 1q21
- RVD x 4
  - Developed severe sensory and motor neuropathy after cycle 4
- Jan 2017: Autologous transplant → Len 2.5 mg for 2 months
- Patient stops Len due to ongoing sensory and motor neuropathy requiring physical therapy; gabapentin and pregabalin ineffective



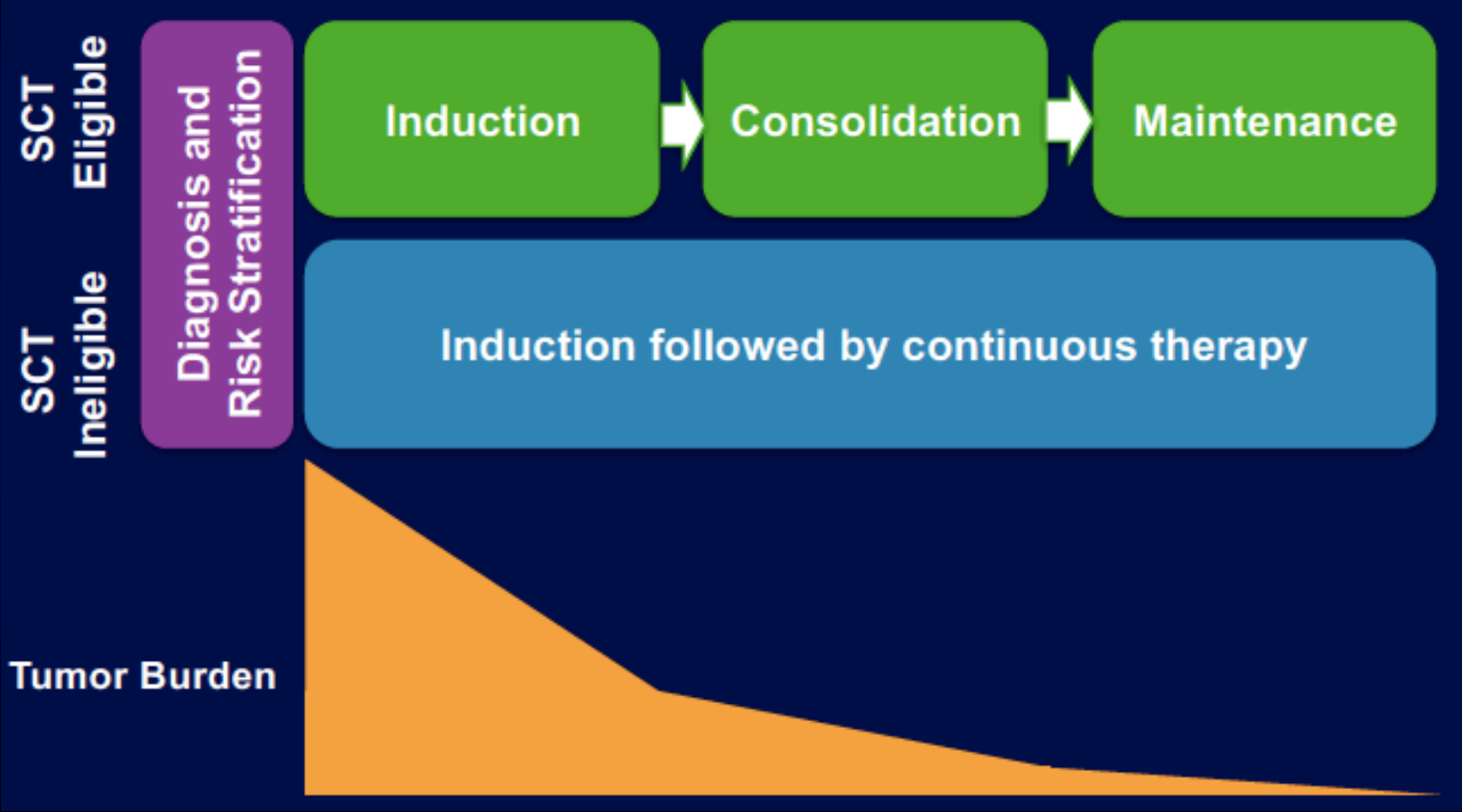
# Case presentation 4: Dr Morganstein

## 55-year-old woman

- 2016: Back pain, imaging: Lytic lesions; found to have t(4;14) MM
- RVD x 4
- Autologous transplant
- Lenalidomide maintenance initiated at 10 mg qd
  - Changed to Len 10 mg 21/28 due to cytopenias
- Ixazomib at 3 mg added to Len maintenance for 2 months → unable to tolerate due to nausea



# Definitions



SCT Eligible

SCT Ineligible

Diagnosis and Risk Stratification

Induction

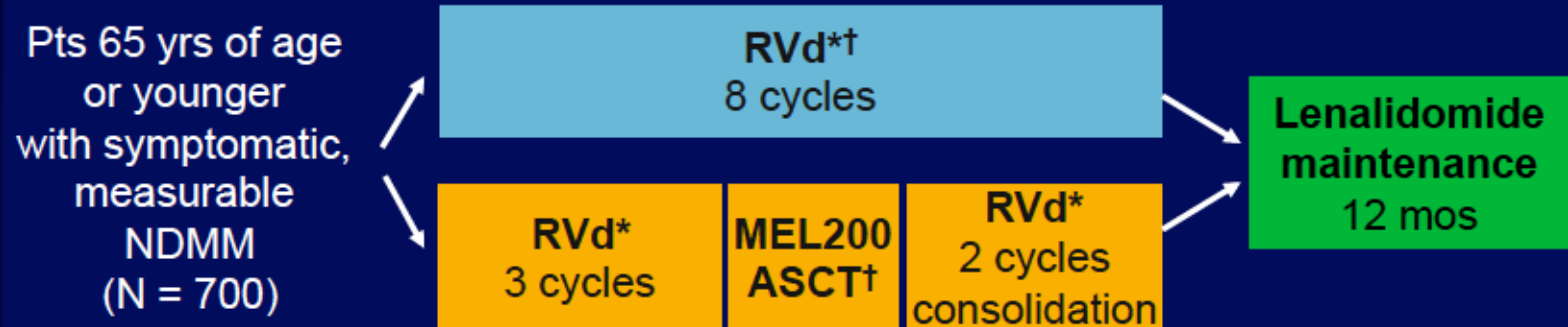
Consolidation

Maintenance

Induction followed by continuous therapy

Tumor Burden

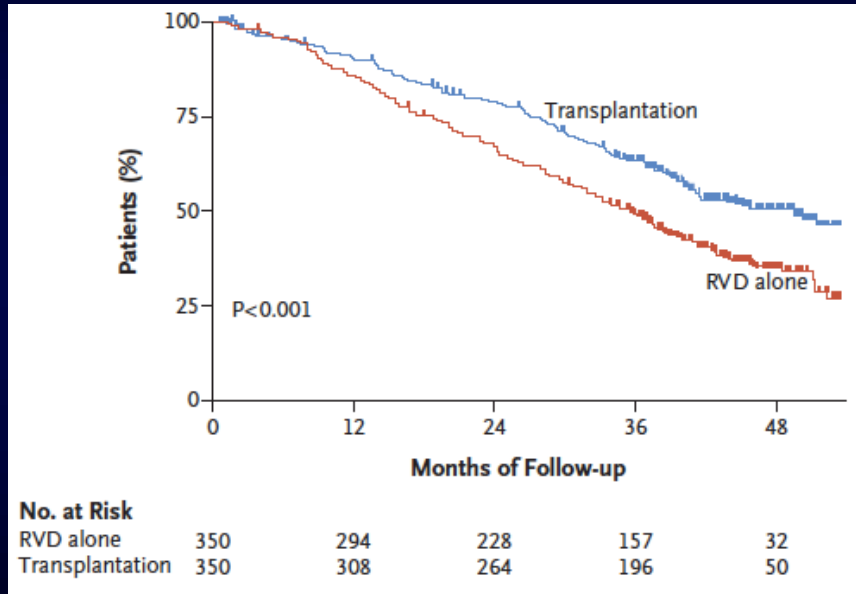
# IFM/DFCI 2009 Study



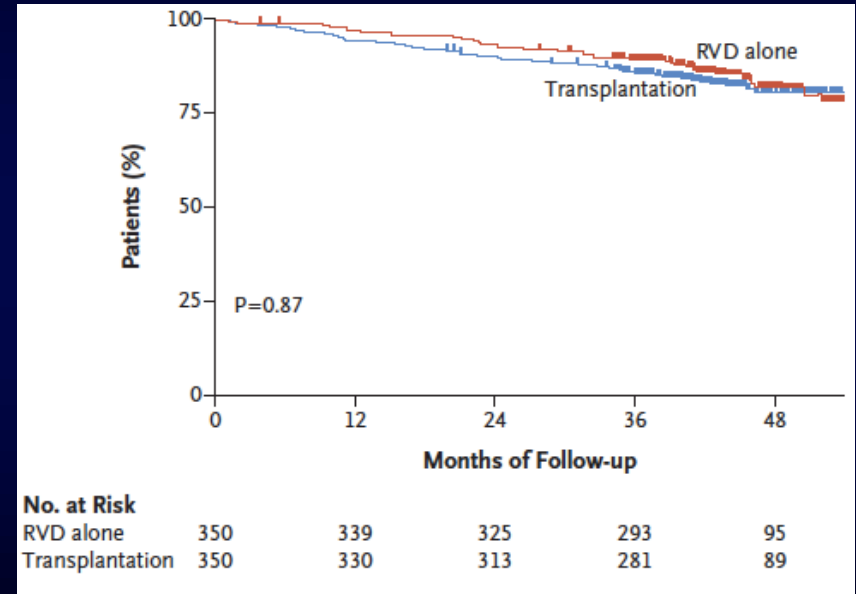
- Primary objective: PFS
- Secondary objectives: ORR, MRD, TTP, OS, Safety

# PFS & OS Data

## PFS

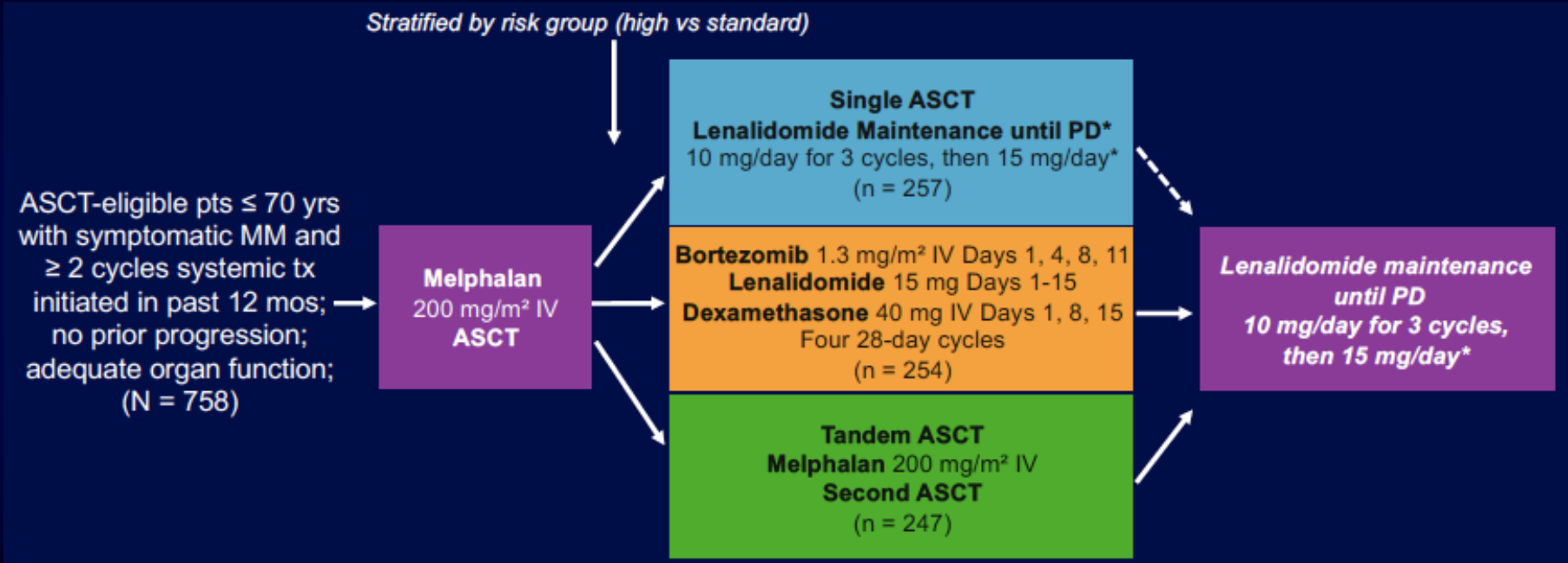


## OS

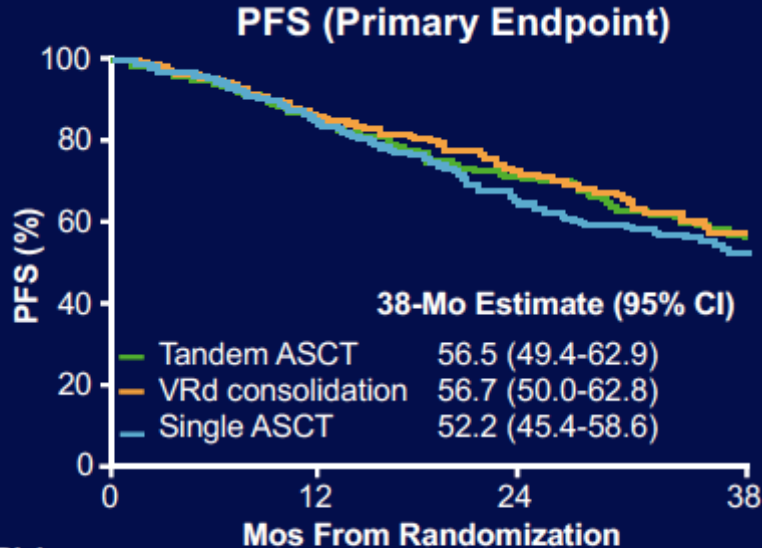




# BMT CTN STaMINA Trial

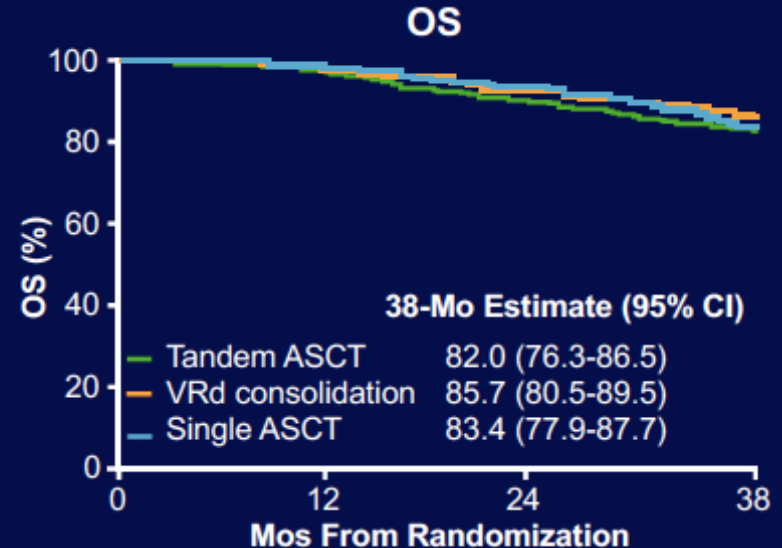


# PFS & OS Data



**Pts at Risk, n**

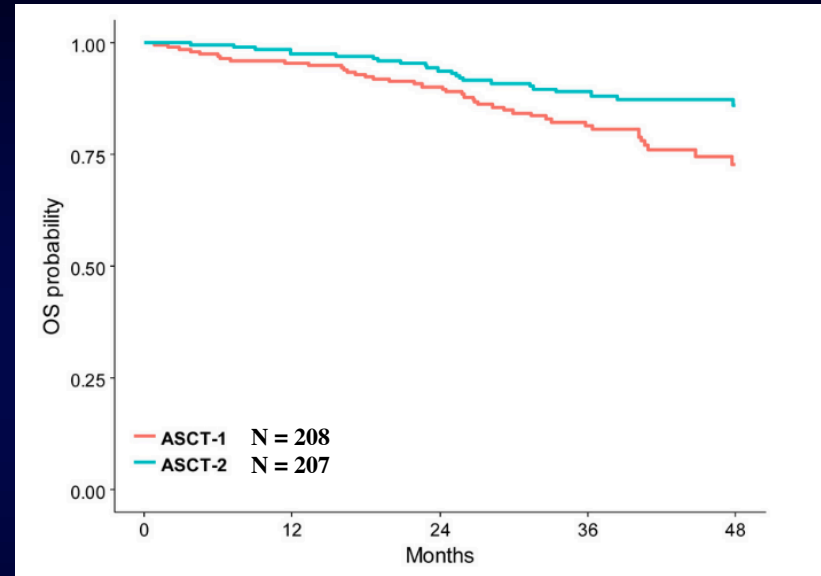
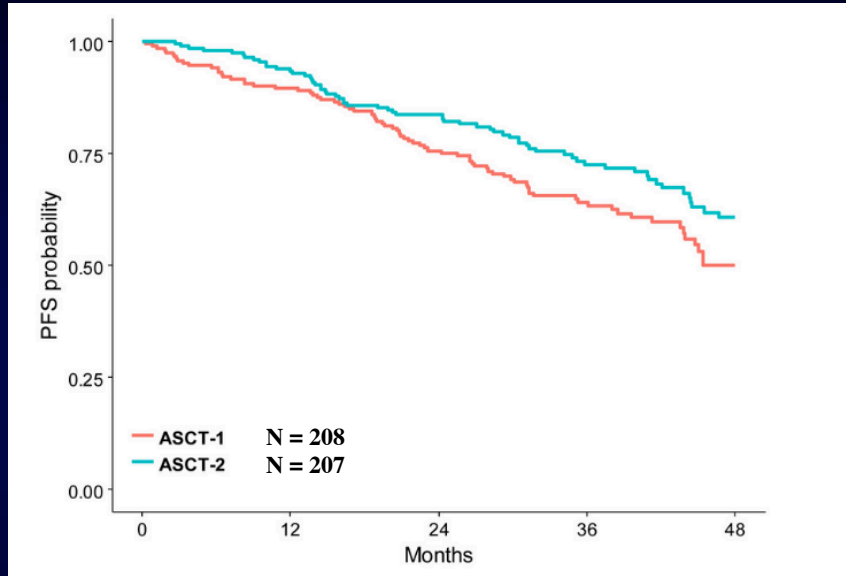
	0	12	24	38
Tandem ASCT	247	200	153	87
VRd	254	215	172	99
Single ASCT	257	213	158	80



**Pts at Risk, n**

	0	12	24	38
Tandem ASCT	247	231	204	147
VRd	254	246	229	166
Single ASCT	257	247	227	148

# 2nd Transplant May Still Be Alive

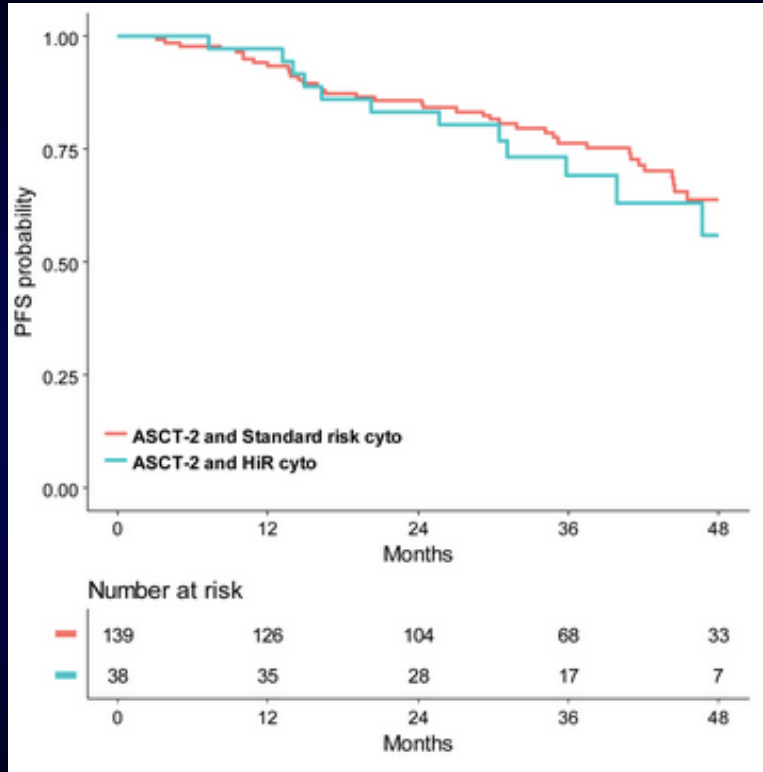


- Phase III EMN02/H095: CyBorD → R1. VMP vs. ASCT1 vs. ASCT2 (some centers)
- Later R to consolidation & len maintenance

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Cavo, M et al. ASH 2017 Abstract #401.

# 2nd Transplant May Still Be Alive

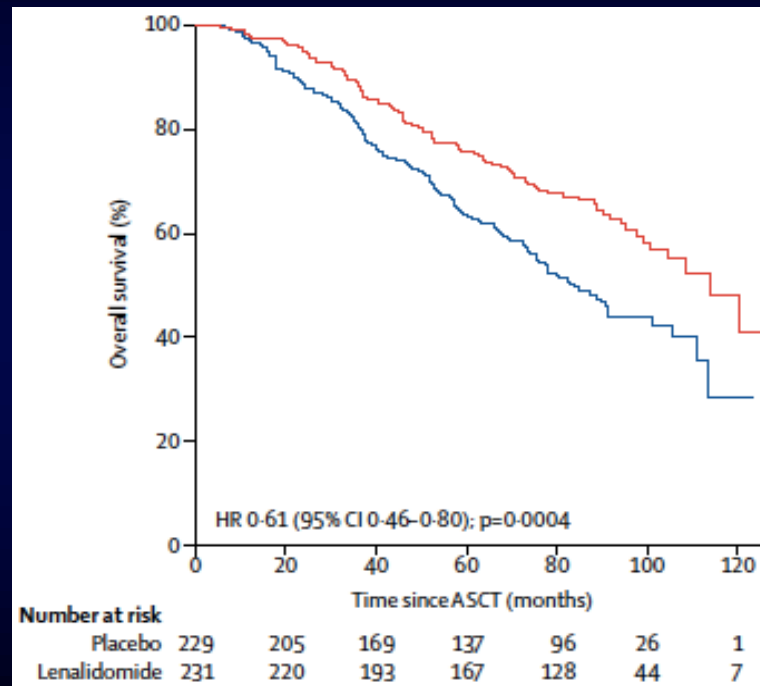
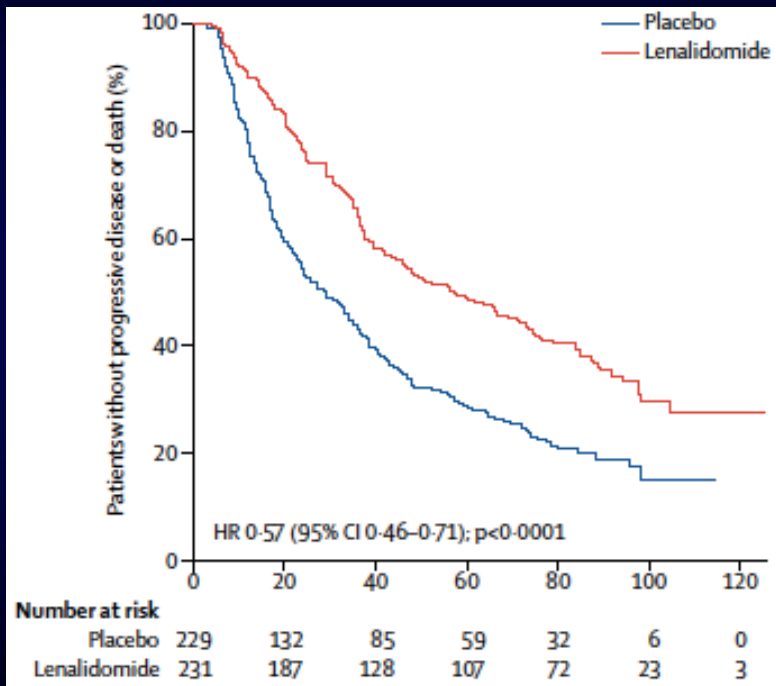


- Phase III EMN02/H095
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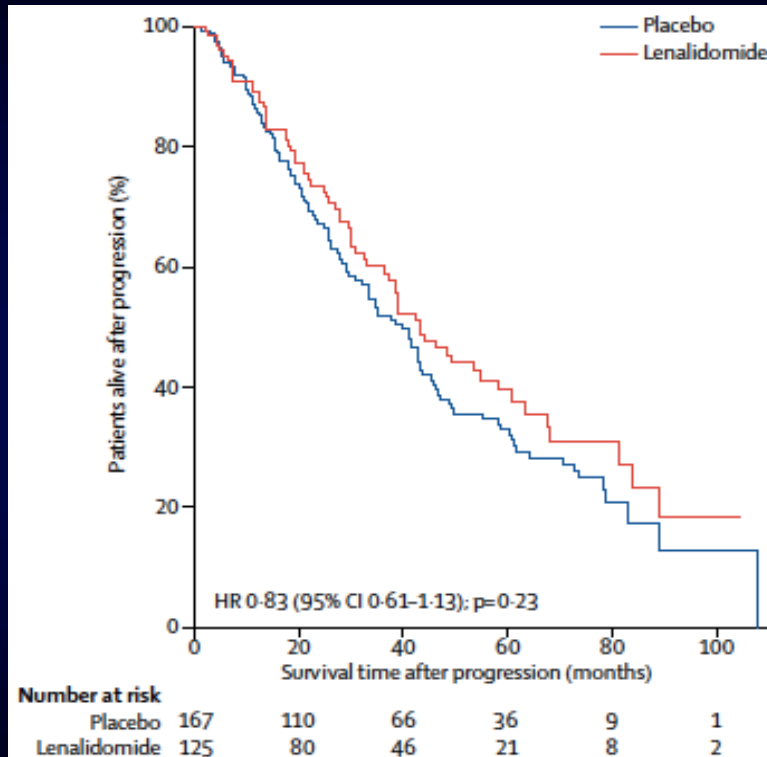
# Len Maintenance: Updated CALGB Data

## Better PFS

## Better OS



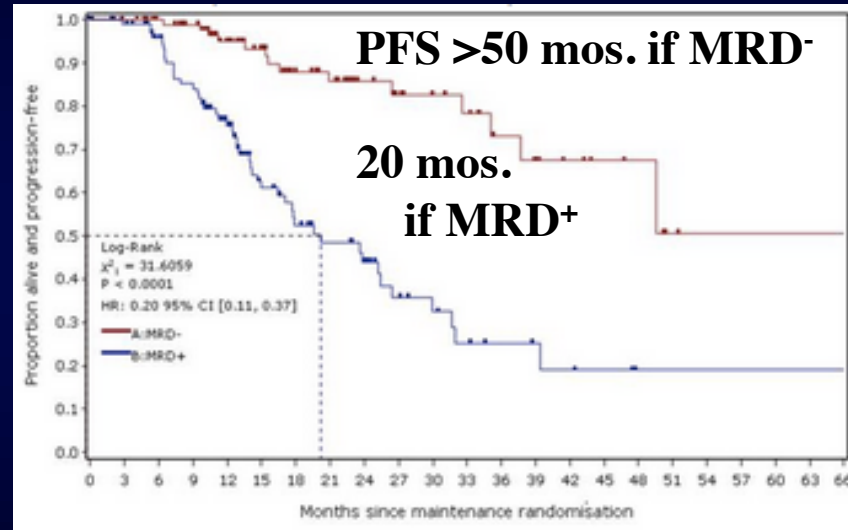
# Len Maintenance: Updated CALGB Data



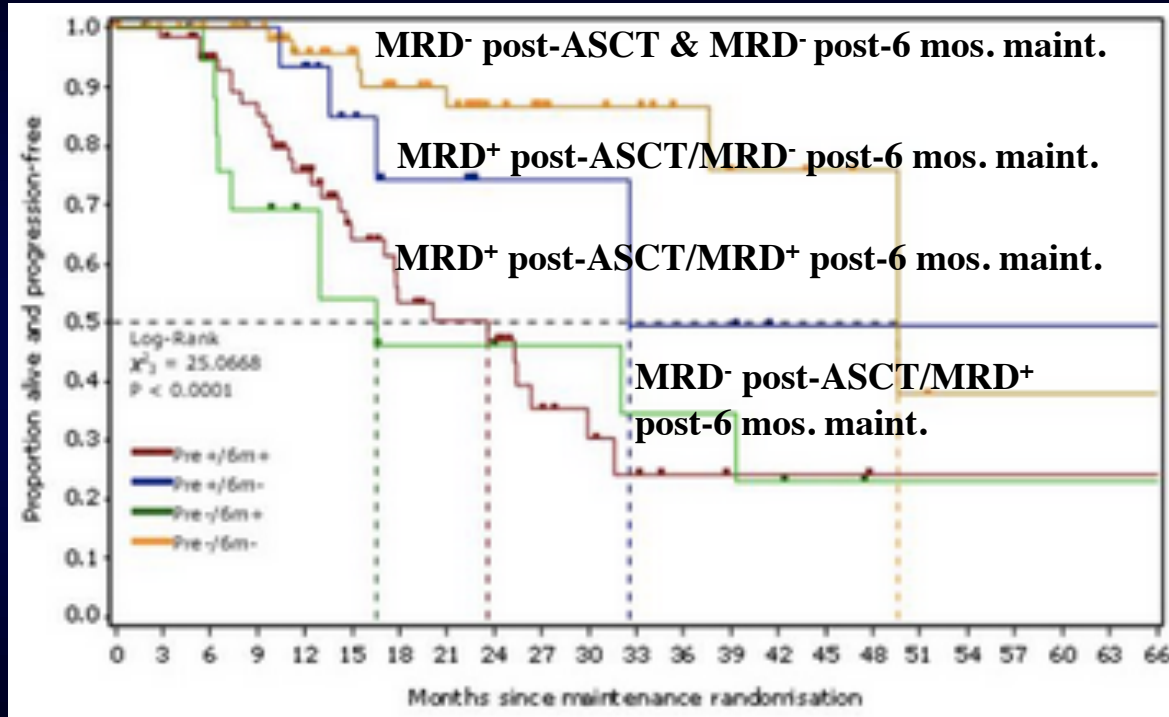
- No difference in OS after progression, so does not impact on later therapies

# Role of MRD Testing

- Myeloma XI trial of CTD vs. RCD, CVD if sub-optimal response, then obs/len/len + vorinostat



# Role of MRD Testing





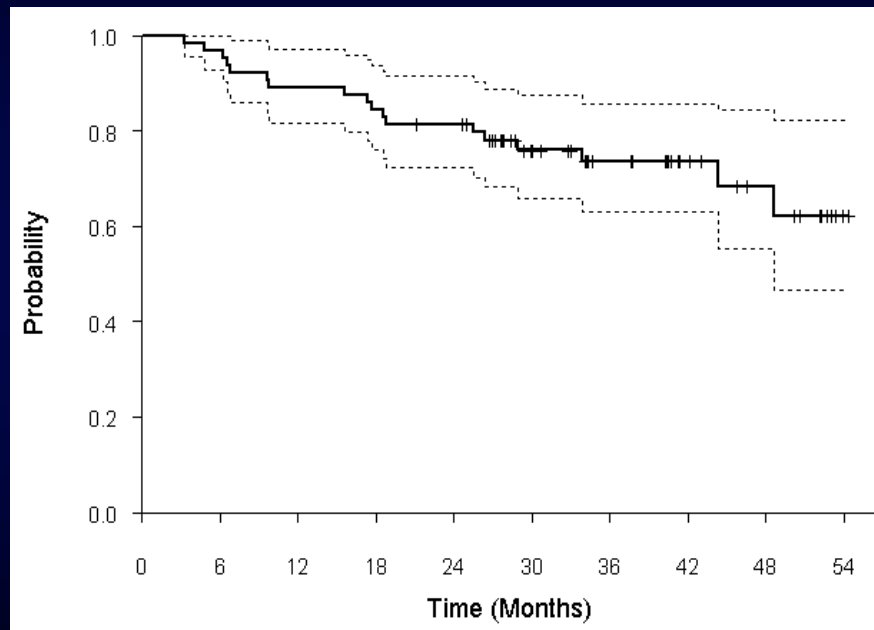
## Does Risk Matter?

- Myeloma XI trial: Len (10 mg for 21/28 days) vs. observation in all myeloma patients

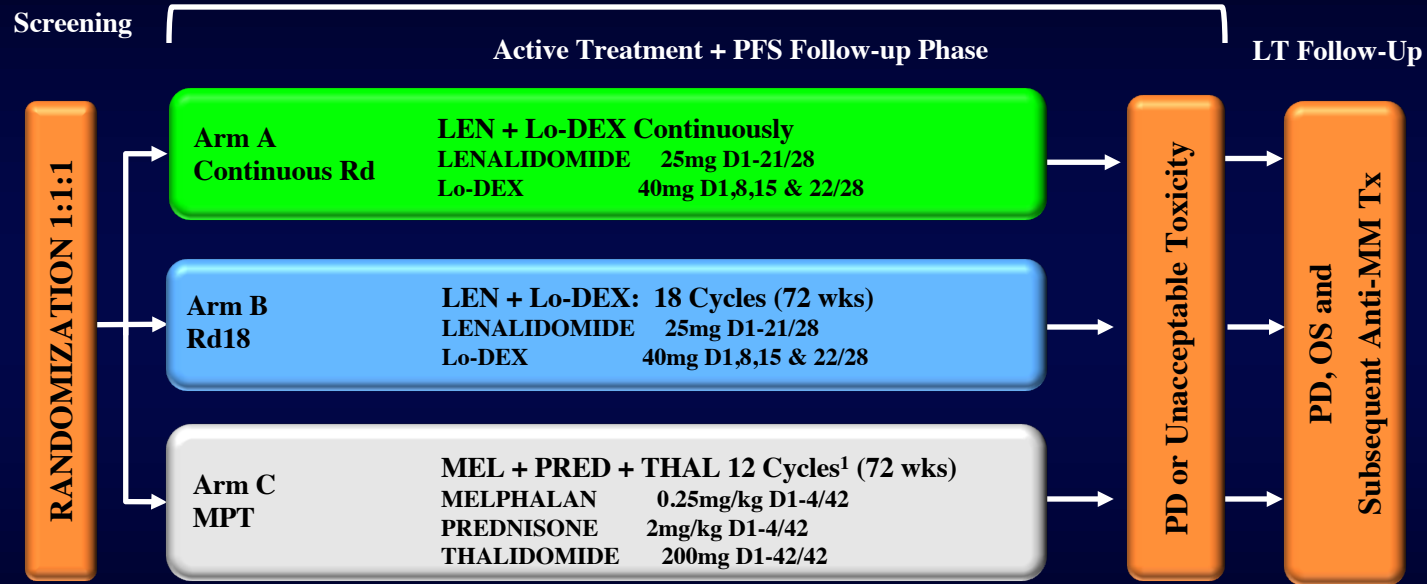
	Lenalidomide	Observation
All patients	39.1 months (HR 0.46; p<0.0001)	19.9 months
del(17p) or t(4;14) <sup>+</sup>	24.7 months	10.5 months
del(17p) or t(4;14) <sup>-</sup>	60.4 months	30.7 months
High risk (t(4;14), t(14;16), t(14;20), del(17p), gain(1q)	HR 0.30 95% CI [0.19, 0.48]	
Ultra-high risk	HR 0.31 95% CI [0.15, 0.66]	

# Pilot of Ixazomib/Lenalidomide

- Median f/u 37.8 months
- Median PFS not yet reached
- Estimated 2 year PFS 81%



# FIRST Trial Design



*Pts > 75 yrs: Lo-DEX 20 mg D1, 8, 15 & 22/28; THAL<sup>2</sup> (100 mg D1-42/42); MEL<sup>2</sup> 0.2 mg/kg D1-4*

# Updated Analysis

## PFS

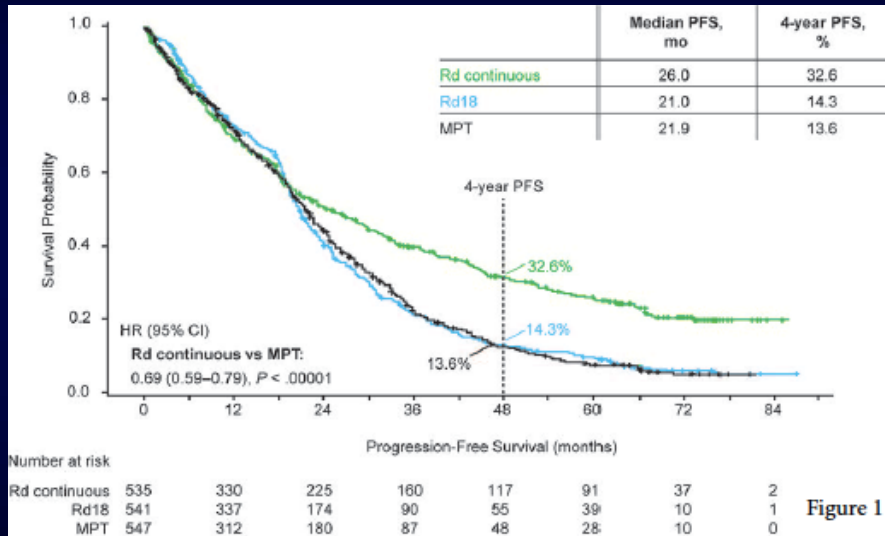


Figure 1

## OS

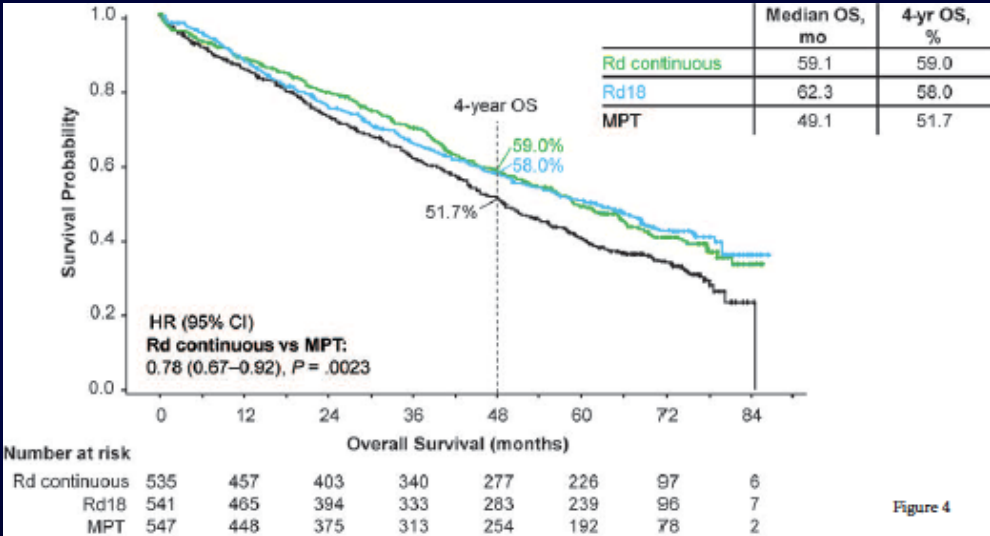


Figure 4

# Updated Analysis

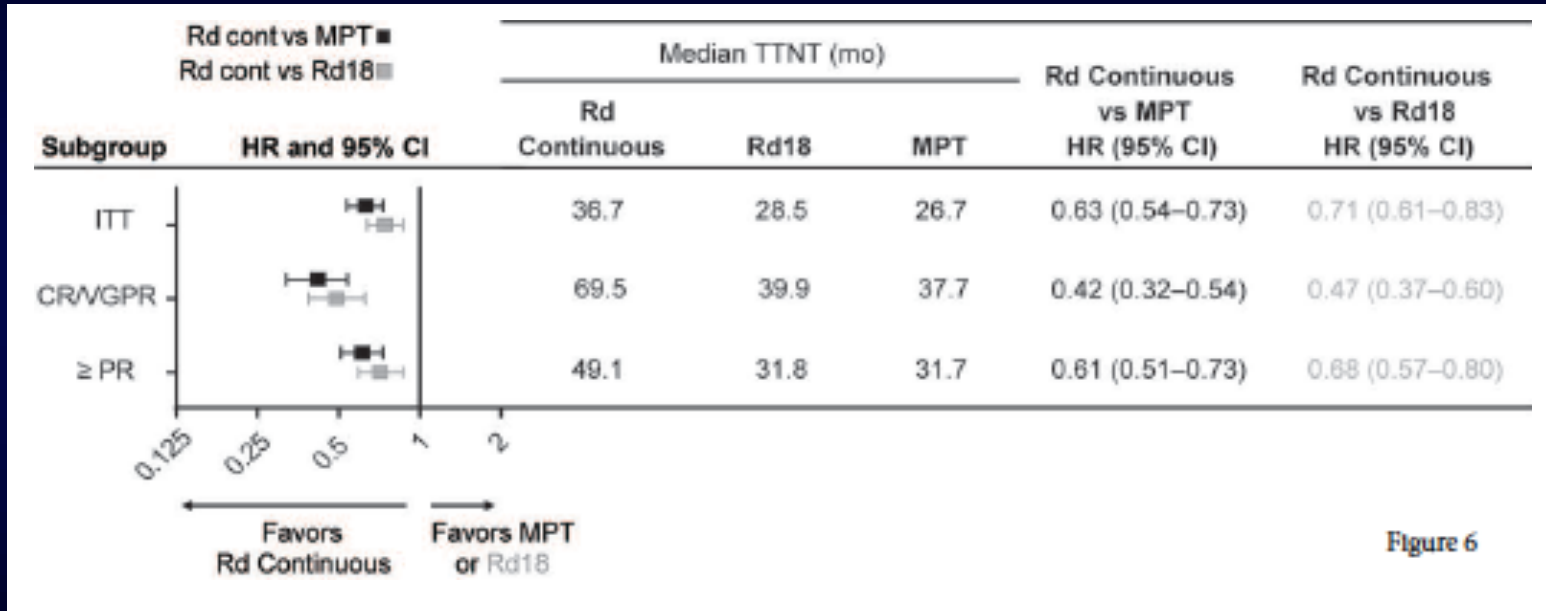
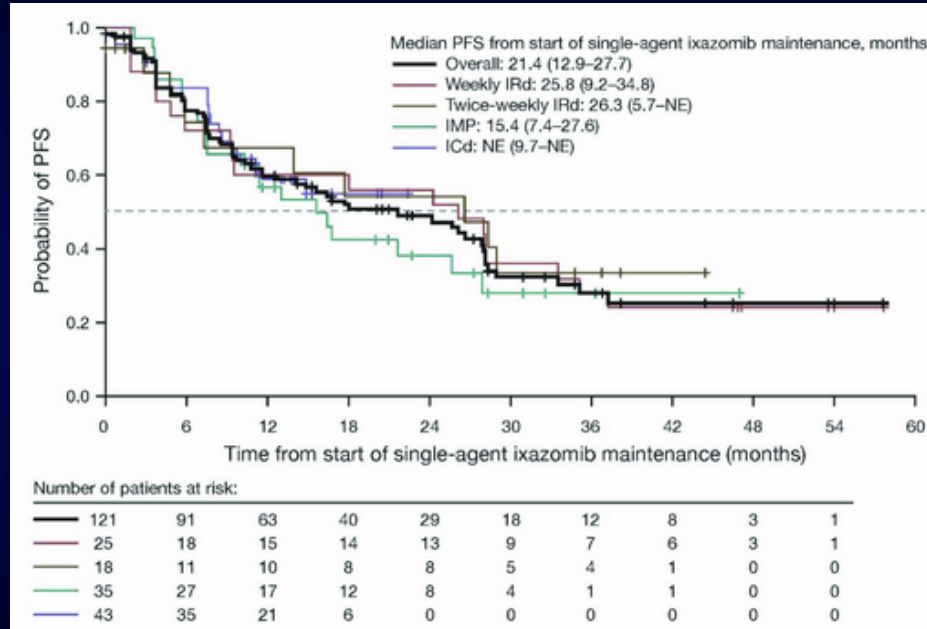


Figure 6

# Other Options: Ixazomib

- Integrated analysis of 4 trials using ixazomib maintenance after ixa-based induction



# Other Options: Ixazomib Adverse Events

**Table:** Most common any-grade, all-cause AEs and grade  $\geq 3$  drug-related AEs ( $\geq 2\%$  of pts) during induction and during maintenance

n (%)	Incidence during induction (N=121)		Incidence during maintenance (N=121)	
	Any-grade AEs	Grade $\geq 3$ AEs	Any-grade AEs	Grade $\geq 3$ AEs
<b>Hematologic</b>				
Thrombocytopenia	42 (35)	20 (17)	17 (14)	3 (2)
Neutropenia	41 (34)	27 (22)	11 (9)	3 (2)
Lymphopenia	20 (17)	11 (9)	4 (3)	3 (2)
Anemia	30 (25)	5 (4)	16 (13)	2 (2)
<b>Non-hematologic</b>				
Rashes, eruptions, and exanthems NEC*	57 (47)	8 (7)	24 (20)	2 (2)
Nausea	53 (44)	2 (2)	21 (17)	2 (2)
Peripheral neuropathies NEC*	52 (43)	2 (2)	16 (13)	1 (<1)
Diarrhea	51 (42)	3 (2)	33 (27)	3 (2)
Arthralgia	18 (15)	0	21 (17)	2 (2)
Dizziness	16 (13)	1 (<1)	13 (11)	2 (2)

\*NEC, not elsewhere classified, high-level term incorporating multiple preferred terms

## Take Home Messages

- Consolidation therapy
  - Non-transplant consolidation is not a current standard after induction
  - Consolidation does not seem to benefit patients in the post-transplant setting
  - Single ASCT is a standard, and some may benefit from a second ASCT (high risk?)
  - Role of MRD testing to identify optimal candidates for consolidation is currently under study



## Take Home Messages

- Maintenance therapy
  - Lenalidomide is the standard of care
  - Addition of steroids may be warranted
  - Single-agent ixazomib maintenance data pending
  - Combination therapy with addition of bortezomib or ixazomib may be helpful in high-risk setting
  - MRD is of prognostic benefit, but insufficient data are available to use this to determine length or intensity of maintenance