



# REGIONAL

## COMMUNITY WORKSHOP

Saturday, October 10, 2020 | 10:00 AM-12:30 PM CT



*with support from:*

Amgen, Bristol Myers Squibb, Janssen, Karyopharm Therapeutics,  
The Binding Site, and Takeda Oncology



# INTERNATIONAL MYELOMA FOUNDATION

Improving Lives. **Finding the Cure.**

# Southern USA Virtual Regional Community Workshop (RCW)

Times listed are in Central Daylight Time (CDT)

- |                      |   |
|----------------------|---|
| <b>10:00 - 10:15</b> | Welcome and Announcements from Kelly Cox  |
| <b>10:15 - 10:35</b> | “Myeloma 101” and “Frontline Therapy”<br>Kelly Godby, MD - University of Alabama Birmingham                           |
| <b>10:35 - 10:55</b> | Question and Answer Session with Panel  |
| <b>10:55 - 11:15</b> | “Relapsed Therapy” and “Emerging Therapies & Clinical Trials”<br>Luciano Costa, MD - University of Alabama Birmingham |
| <b>11:15 - 11:35</b> | Question and Answer Session with Panel  |
| <b>11:35 - 11:55</b> | “Living Well with Myeloma”<br>Beth Faiman, PhD, NCP - IMF Nurse Leadership Board                                      |
| <b>11:55 - 12:30</b> | Question and Answer Session with Experts  |



# INTERNATIONAL MYELOMA FOUNDATION

Improving Lives. **Finding the Cure.**

# Welcome and Announcements

Kelly Cox

IMF Senior Director, Regional  
Community Workshops

# Thank you to our sponsors!





# INTERNATIONAL MYELOMA FOUNDATION

Improving Lives. **Finding the Cure.**

# **“Myeloma 101”**

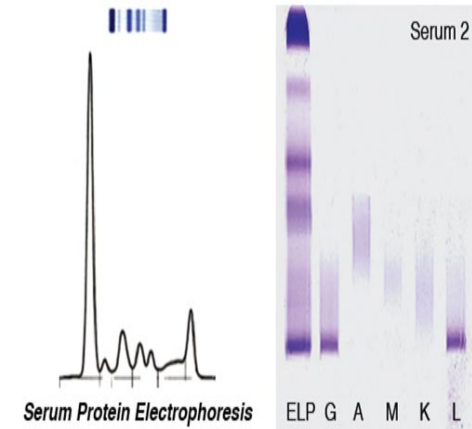
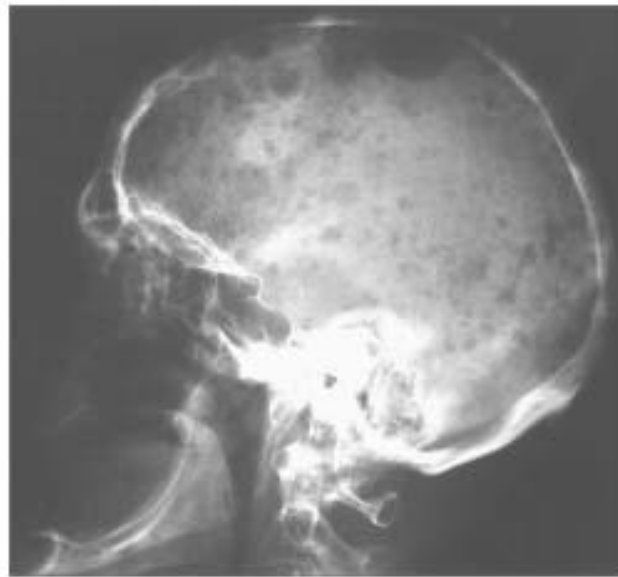
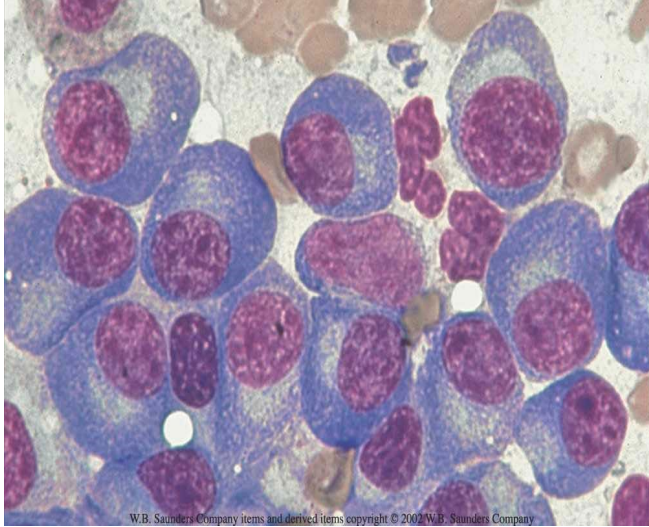
## **“Frontline Therapy”**

**Kelly Godby, MD**

**University of Alabama  
Birmingham**

# Multiple Myeloma

## The Basics & Newly Diagnosed

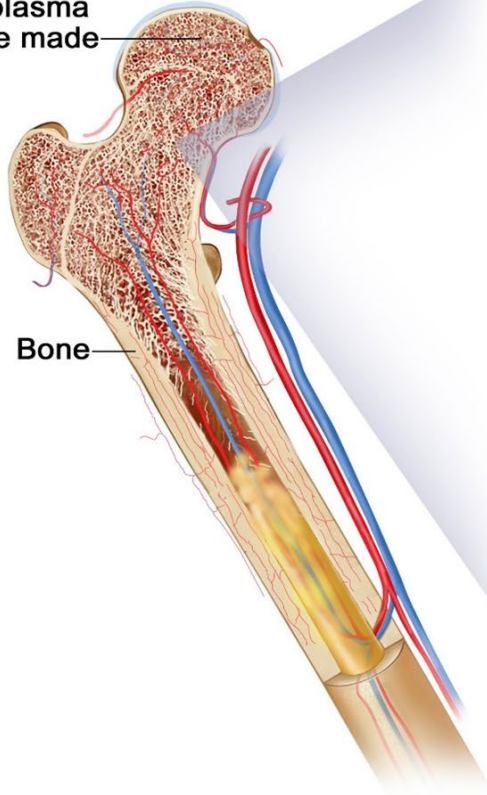


Source: Kantarjian HM, Wolff RA, Koller CA: *The MD Anderson Manual of Medical Oncology*, 2nd Edition: [www.accessmedicine.com](http://www.accessmedicine.com)  
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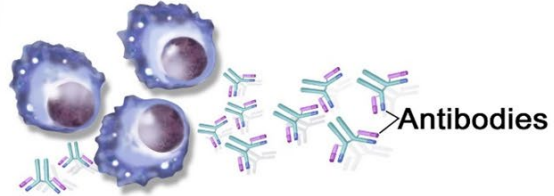
**Kelly Godby, MD**  
**Associate Professor of Medicine**  
**University of Alabama at Birmingham**  
**October 2020**

## Multiple Myeloma

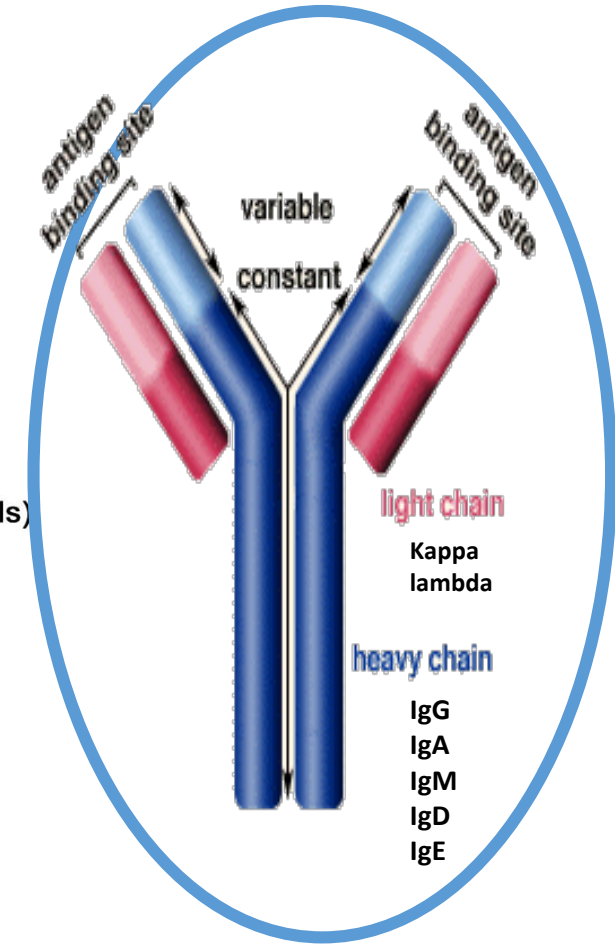
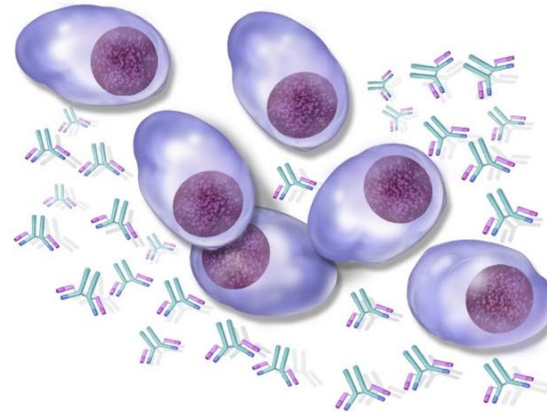
Red marrow  
where plasma  
cells are made



Normal plasma cells



Multiple myeloma cells (abnormal plasma cells)



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# Diagnostic Criteria

## MGUS

✓ Clonal protein in serum or urine

1% per year → MM

## Smoldering MM

✓ Clonal protein in serum or urine

✓ Plasmocytosis in BM (10%+) or

✓ M spike > 3g/dl

10% per yr → MM

## Symptomatic MM

✓ Clonal protein in serum or urine

✓ Clonal plasmocytosis in BM (10%+ )

✓ Morbidity (CRAB or MDE)

Sixty % PC

Light chain ratio >100

MRI (lytics)

Calcium

Renal failure

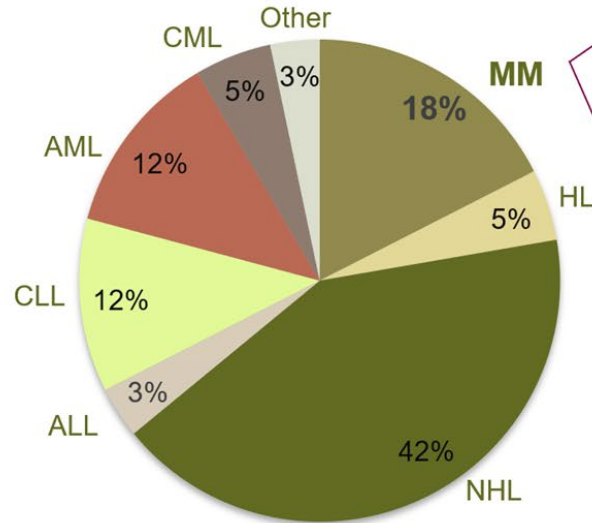
Anemia

Bone disease

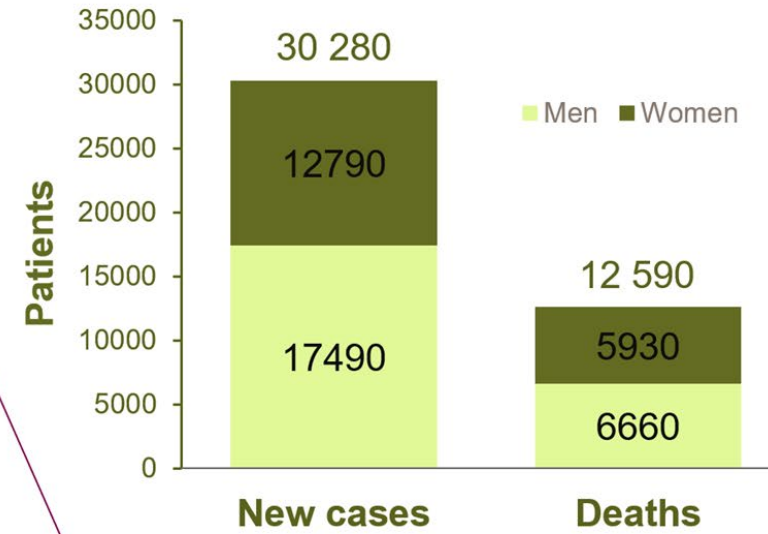
← No Treatment

→ Treatment

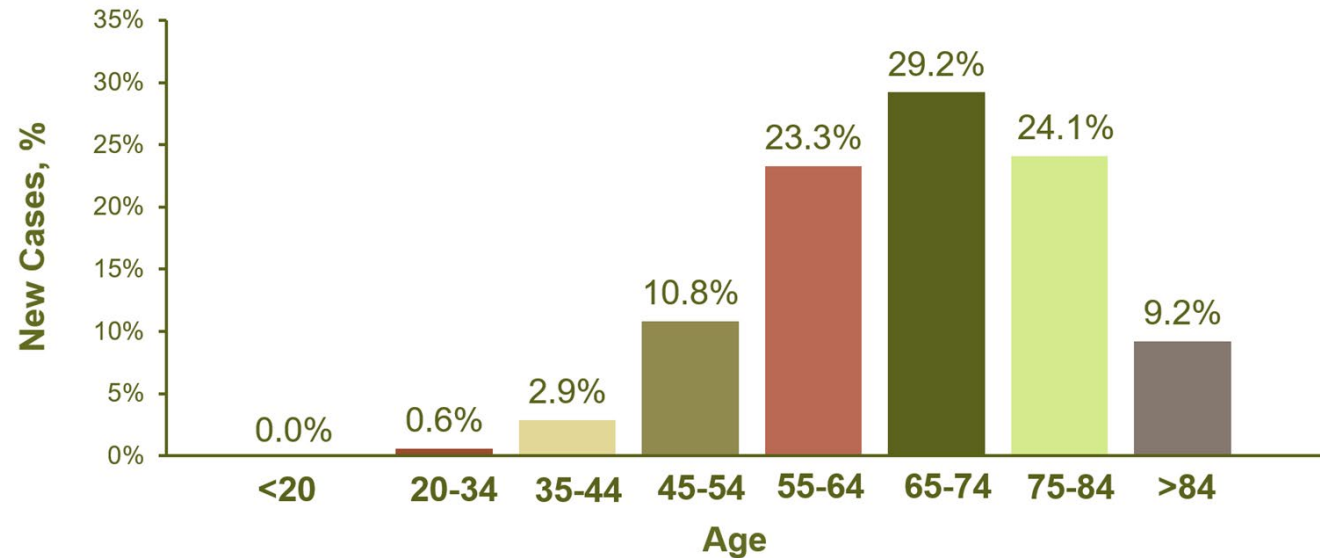
## Hematologic Malignancies in the US



## Estimated US MM Incidence and Mortality



## New Cases of MM by Age Group



**MGUS – 3% pts over 50**

# How are patients diagnosed (CRAB)?

## ➤ Bone Pain (58%)

- Bone plasmacytomas
- Compression fractures
- Fractures in legs, arms, ribcage

## ➤ Kidney (Renal) problems (48%)

- Kidney failure
- Protein in urine
- Nausea, fatigue, confusion in extreme cases

## ➤ Anemia (73%)

- Asymptomatic (found on blood test)
- Fatigue

## ➤ High Calcium (28%)

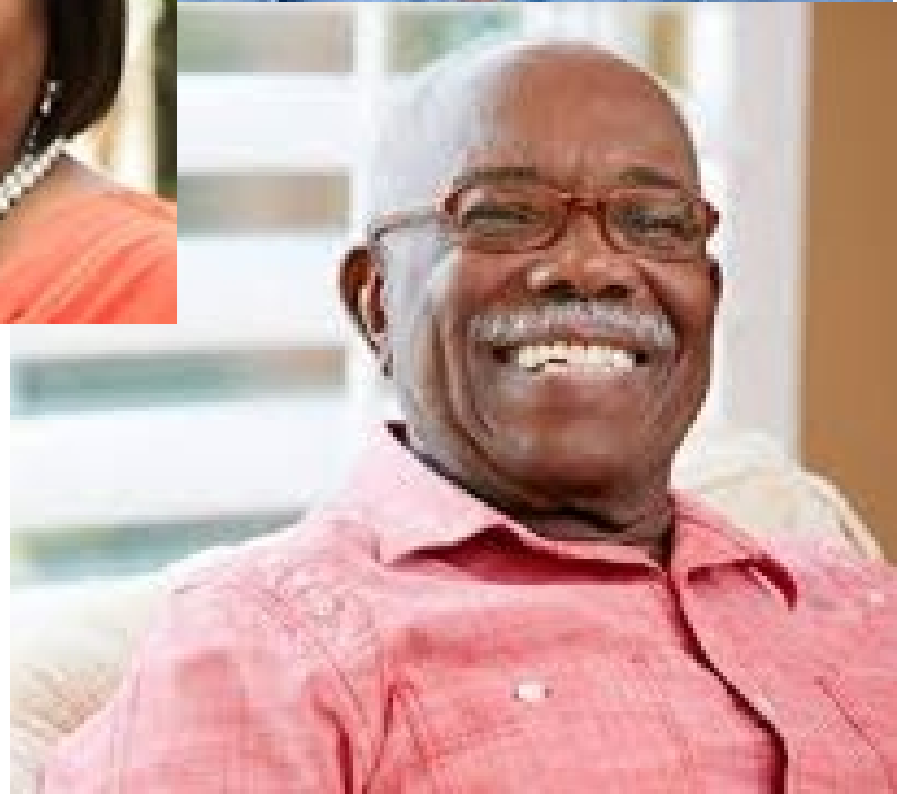
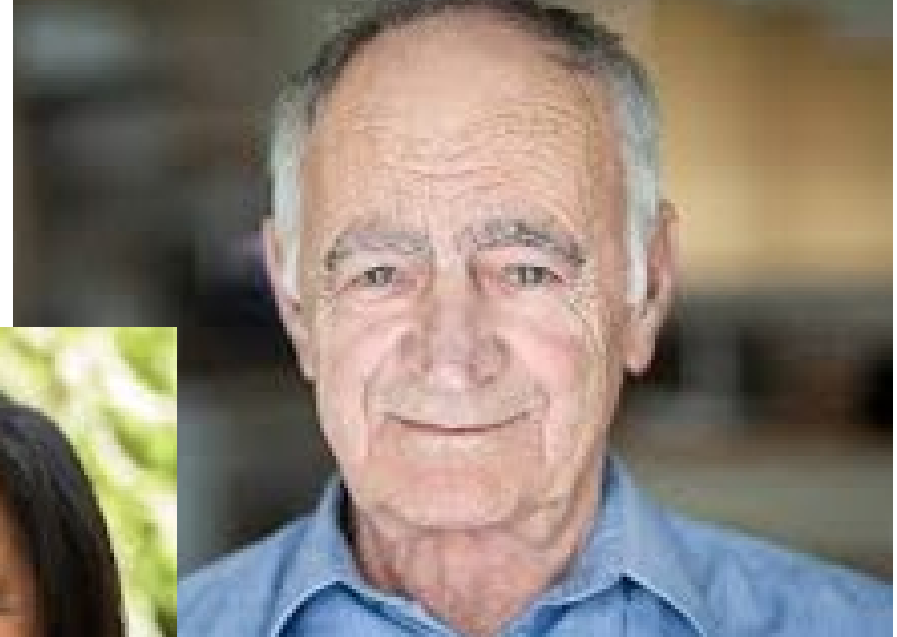
- Blood test finding
- Fatigue
- Increase urination
- Confusion/coma

## ➤ No Symptoms

- Abnormality found on routine tests

# Risk Factors

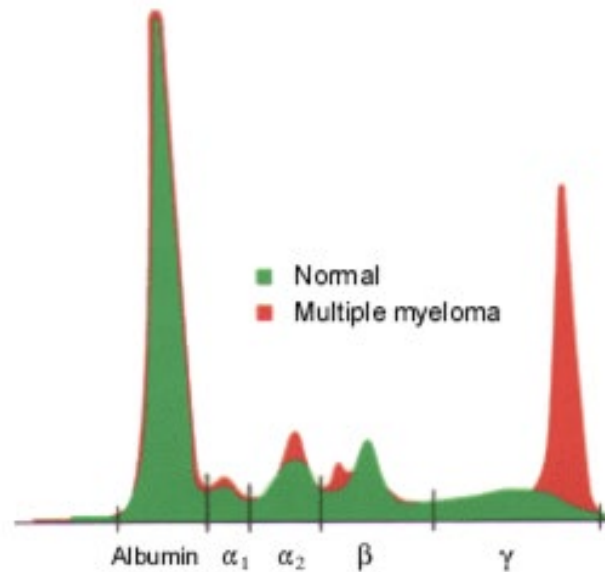
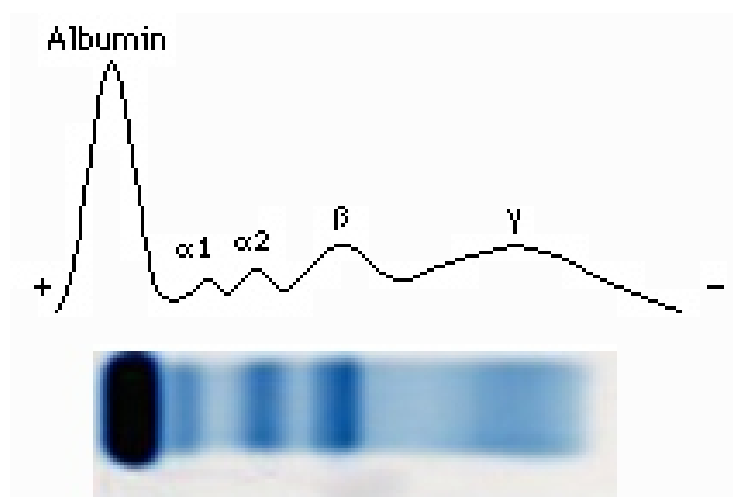
- Age
- Sex
- Race
- Family History
- Environment?



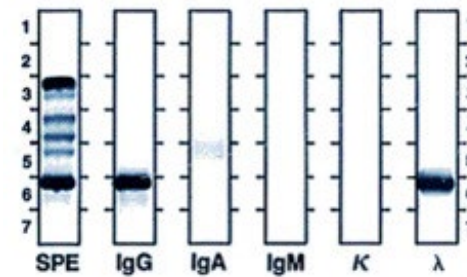
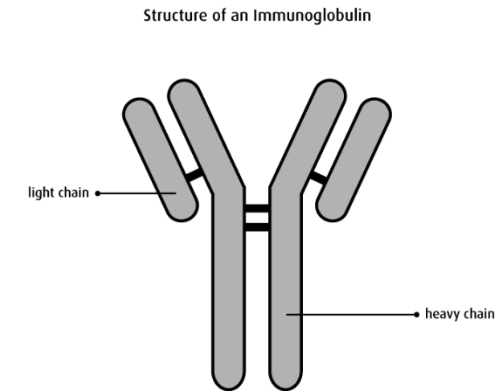
# Initial testing and assessment

- CBC– blood counts. Indicates anemia, level of white cells and platelets
- Chemistry- Indicates renal and liver problems, levels of minerals (calcium, potassium, etc) in blood
- LDH- Lactic dehydrogenase- Important for prognosis
- Albumin – Important for prognosis
- Beta 2 microglobulin- Important for prognosis
- Level of antibodies (IgG, IgA, IgM)
- SPEP, SIFE, UPEP, UIFE, serum free light chains

# Initial Testing and Assessment (SPEP and IFE)

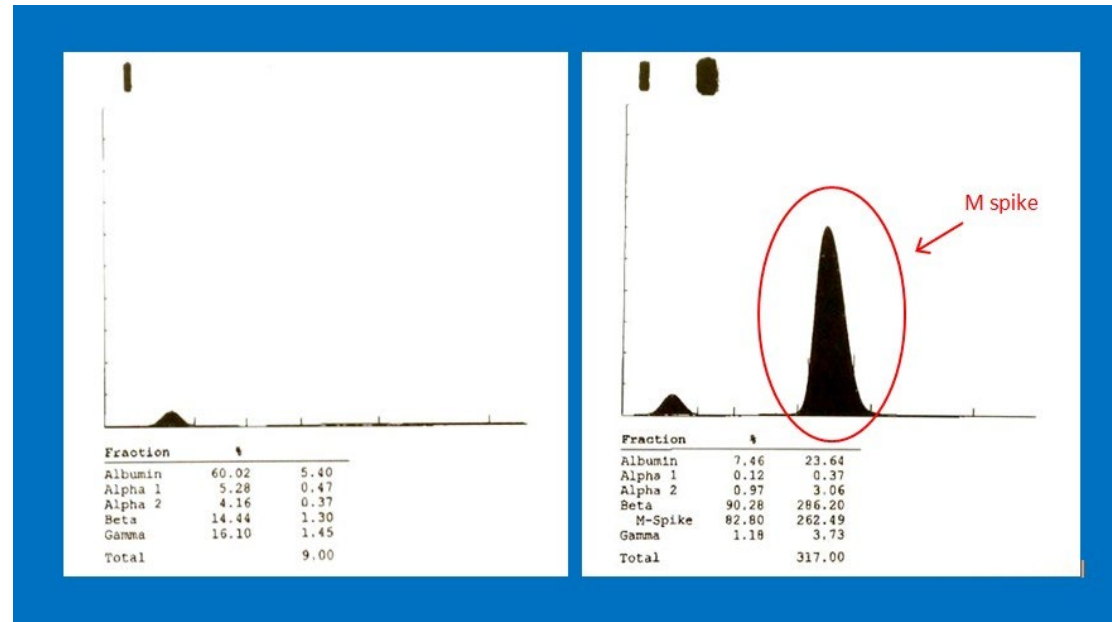


## The “M” Protein in Blood



# Initial Testing and Assessment

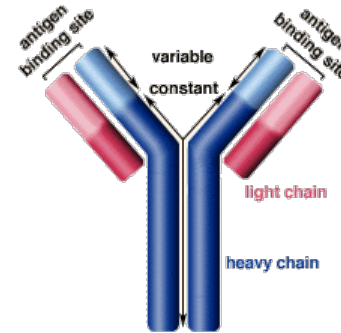
## The “M” Protein in Urine



$$\text{Concentration} \times \text{Volume} = \text{Amount}$$

## Free Light Chains

- Heavy chains and light chains produced separately in PC then assembled
- PC produce more LC than need
- Excess unbound
- **15-20% Light chain Only MM**
- Quantitates plasma cell burden and response to treatment in MM in conjunction with SPEP
- LC elevated in renal dysfunction so absolute numbers must always be taken in context of free lc ratio

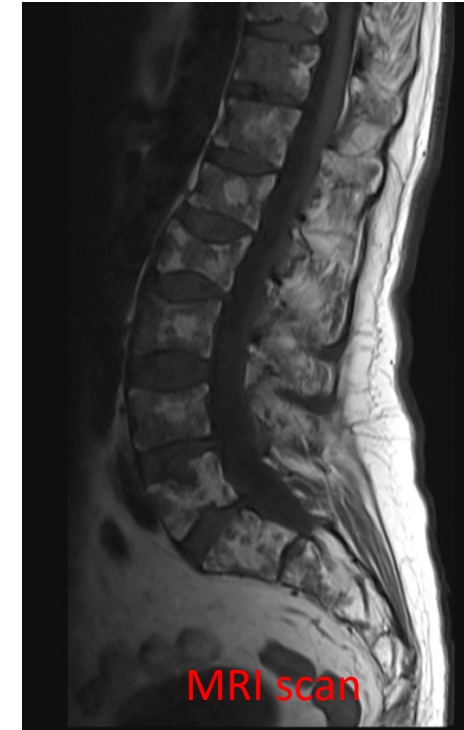
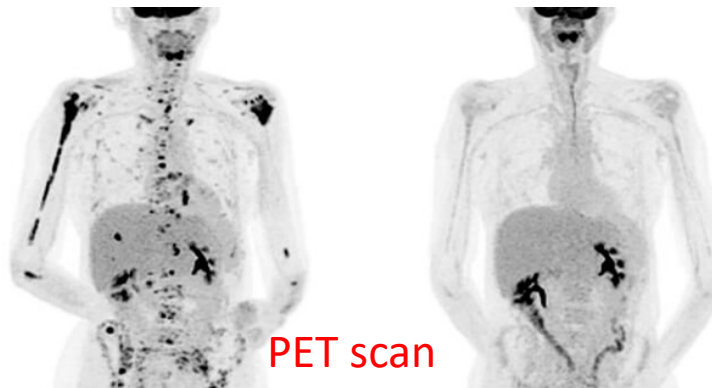


Kappa  
lambda

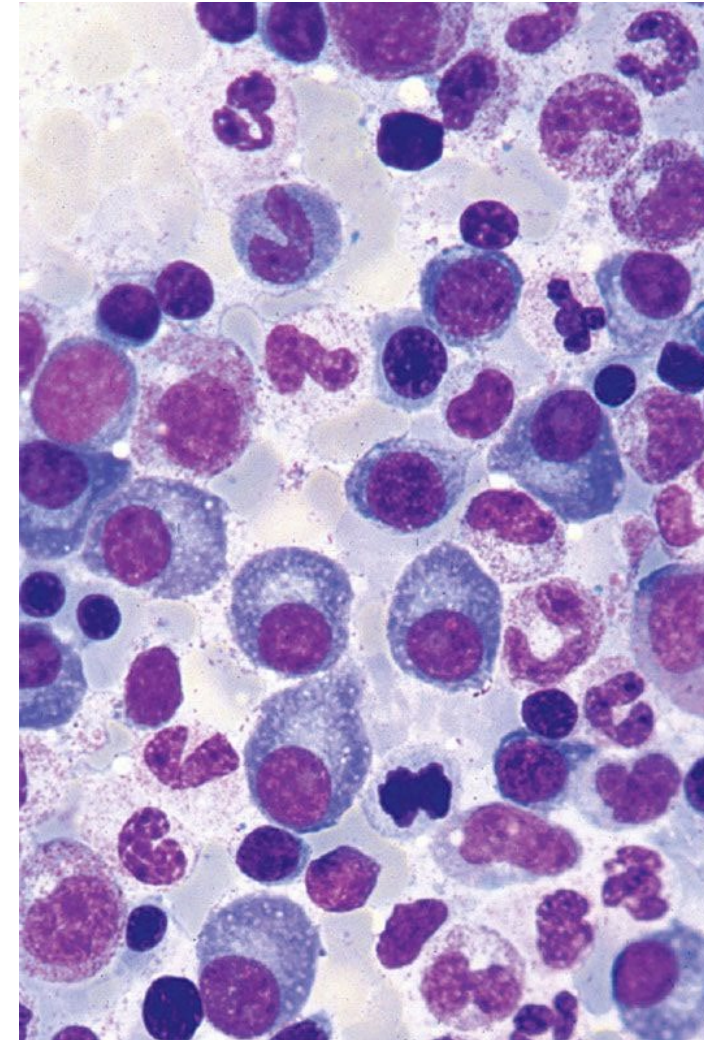
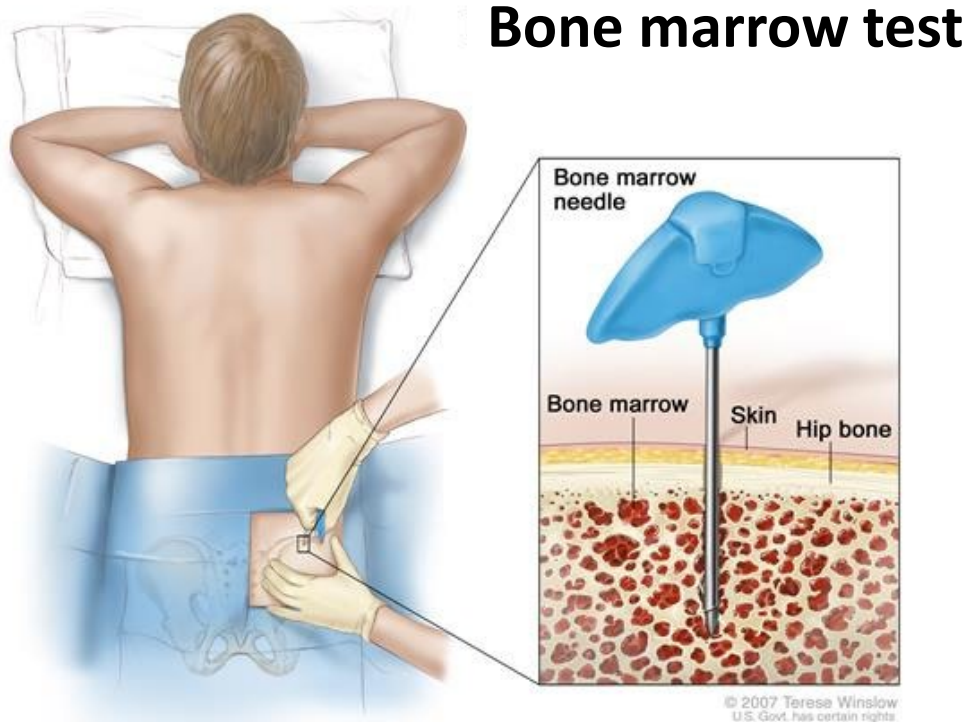
IgG  
IgA  
IgM  
IgD  
IgE

# Initial testing and assessment

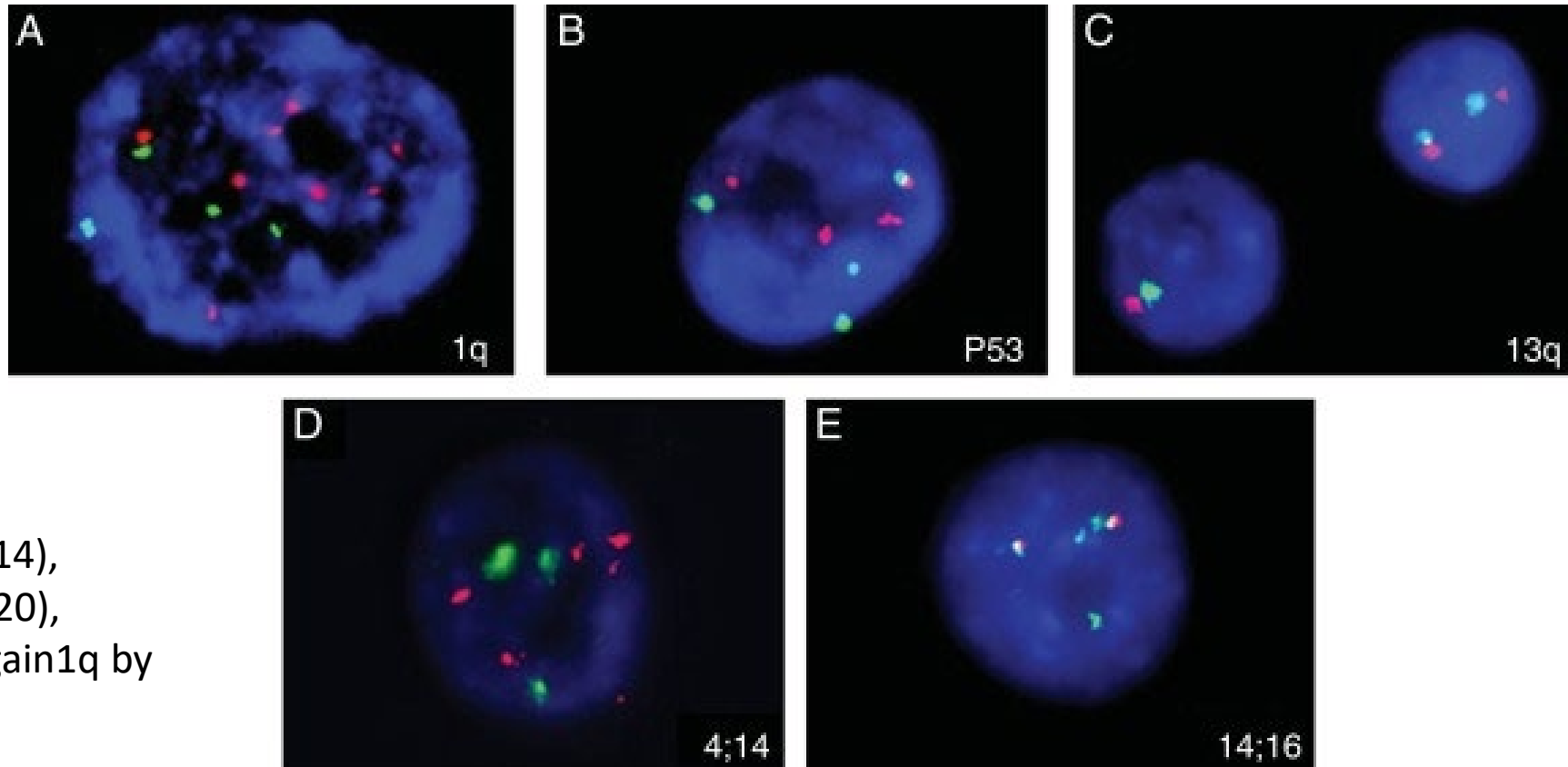
## Radiology tests



# Initial Testing and Assessment



# Fluorescence InSitu Hybridization



**High-risk** -t(4;14),  
t(14;16), t(14;20),  
del17p13, or gain1q by  
FISH

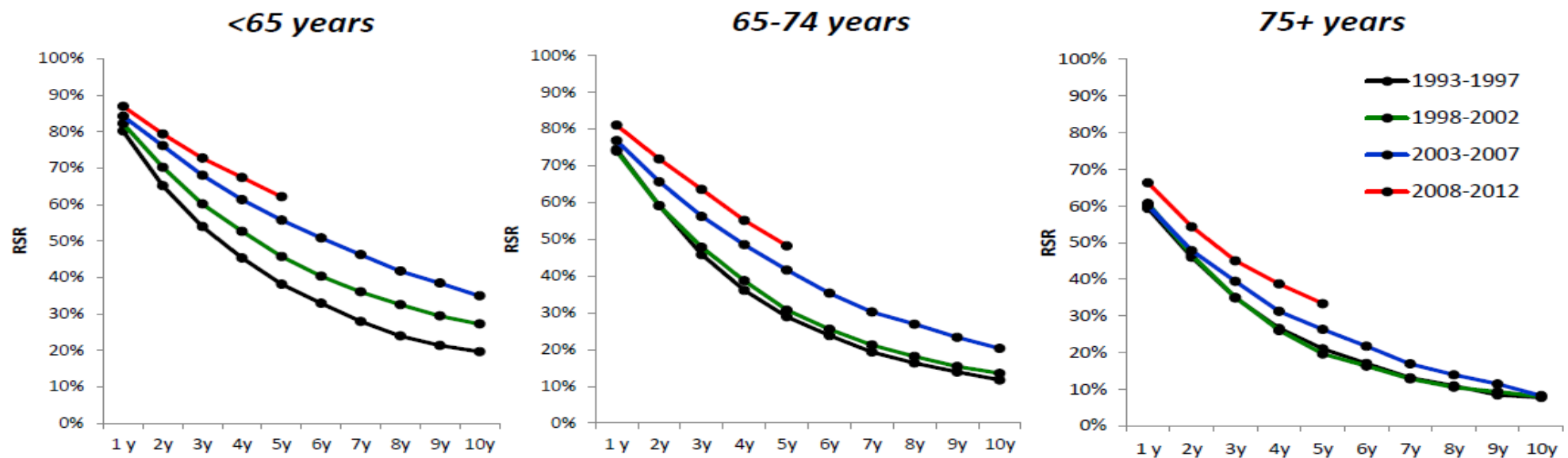
# Revised International Staging System

## Revised International Staging System (R-ISS) for MM

- R-ISS I (n = 871)
  - Including ISS stage I (serum  $\beta_2$ -microglobulin level < 3.5 mg/L and serum albumin level  $\geq$  3.5 g/dL)
  - No high-risk CA [del(17p) and/or t(4;14) and/or t(14;16)]
  - Normal LDH level (less than the upper limit of normal range)
- R-ISS III (n = 295)
  - Including ISS stage III (serum  $\beta_2$ -microglobulin level > 5.5 mg/L)
  - High-risk CA or high LDH level
- R-ISS II (n = 1,894)
  - Including all the other possible combinations

	5-Year OS*	5-Year PFS*
R-ISS I	82%	55%
R-ISS II	62%	36%
R-ISS III	40%	24%

## Improvement in 5- and 10-year relative survival rate of patients diagnosed with myeloma in the US.



# Current Treatment Landscape

## ➤ IMiDs

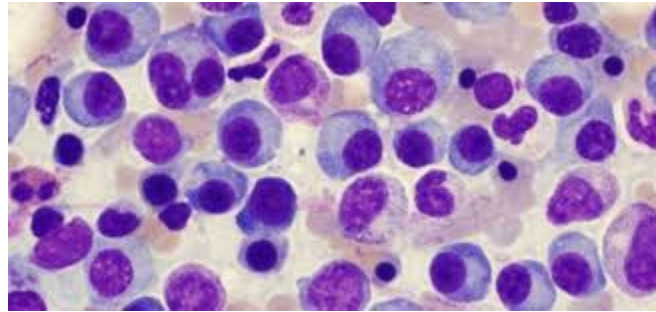
- Thalidomide
- Lenalidomide
- Pomalidomide

## ➤ Monoclonal antibodies

- Elotuzumab
- Daratumumab
- Isatuximab
- Blenrep

## ➤ Alkylators

- Melphalan (high dose)
- Cyclophosphamide
- Bendamustine



## ➤ Anthracycline

- Doxil

## ➤ Proteasome Inhibitors

- Bortezomib
- Carfilzomib
- Ixazomib

## ➤ HDAC inhibitor

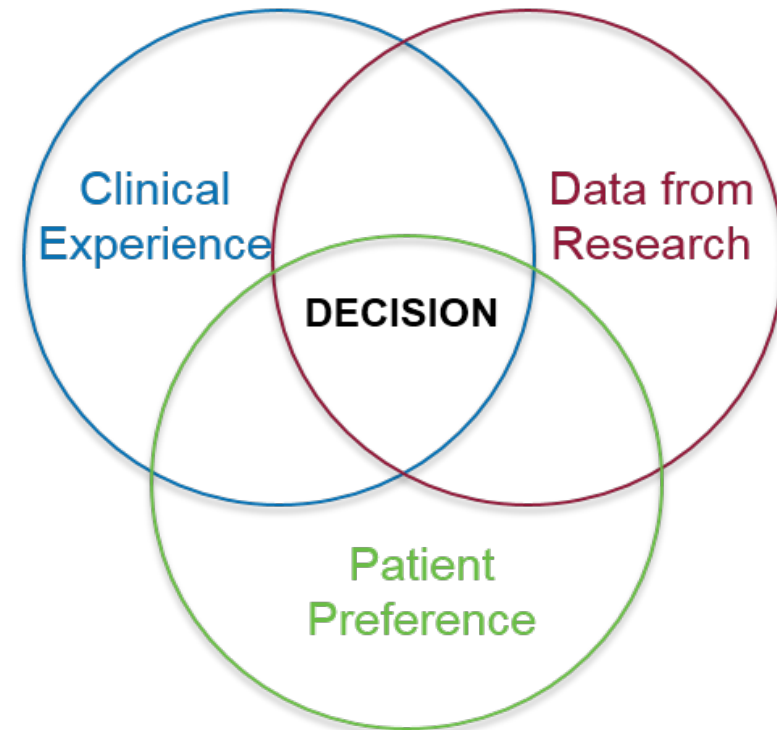
- Panobinostat

## ➤ Nuclear export inhibitor

- Selinexor

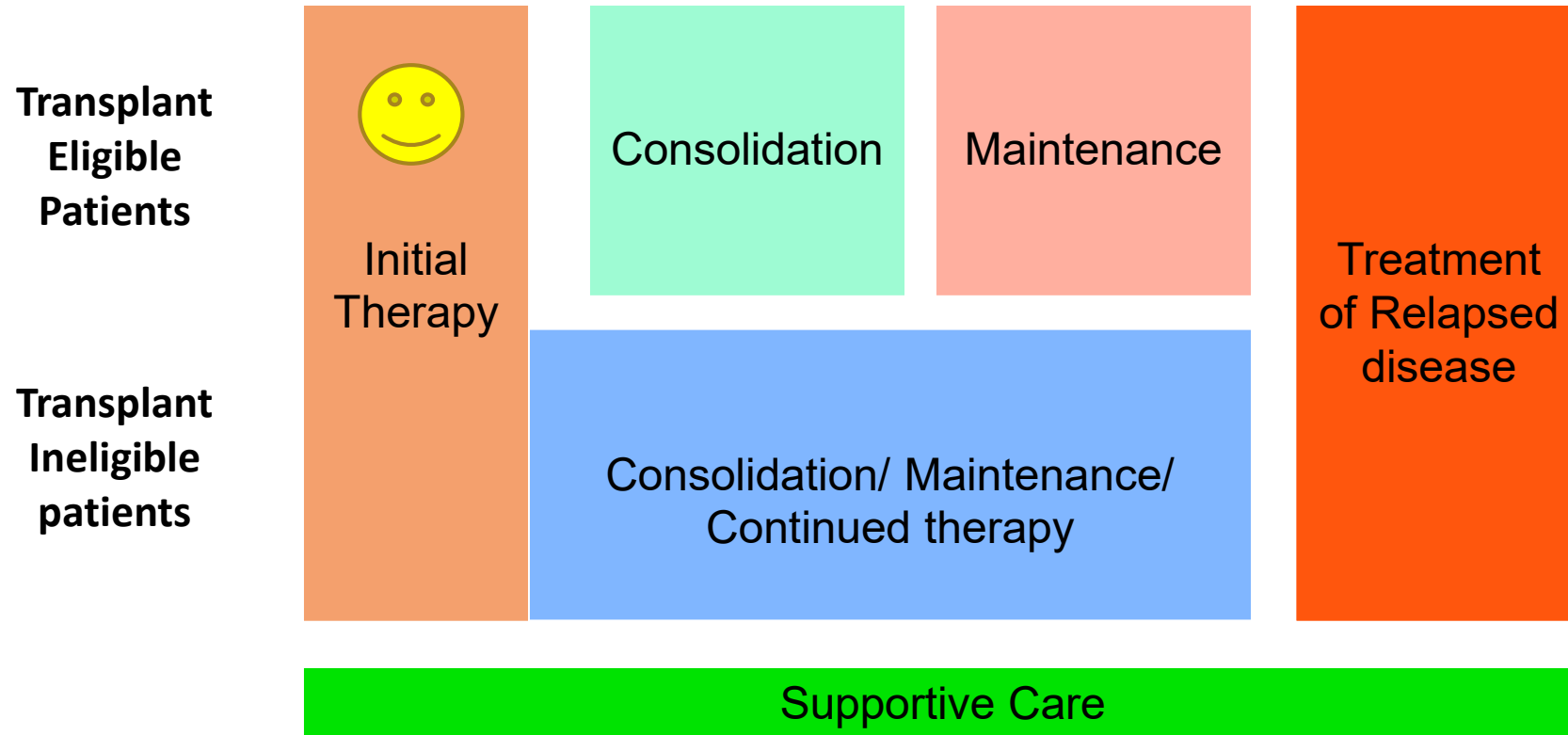
# Guiding Principles and Goals

- ▶ **Response Matters, but so does...**
- ▶ **Functional Status**
- ▶ **Side effects of therapy**
- ▶ **Co-morbidities**
- ▶ **Quality of life**
- ▶ **Cost**
- ▶ **Distance to Care Center**

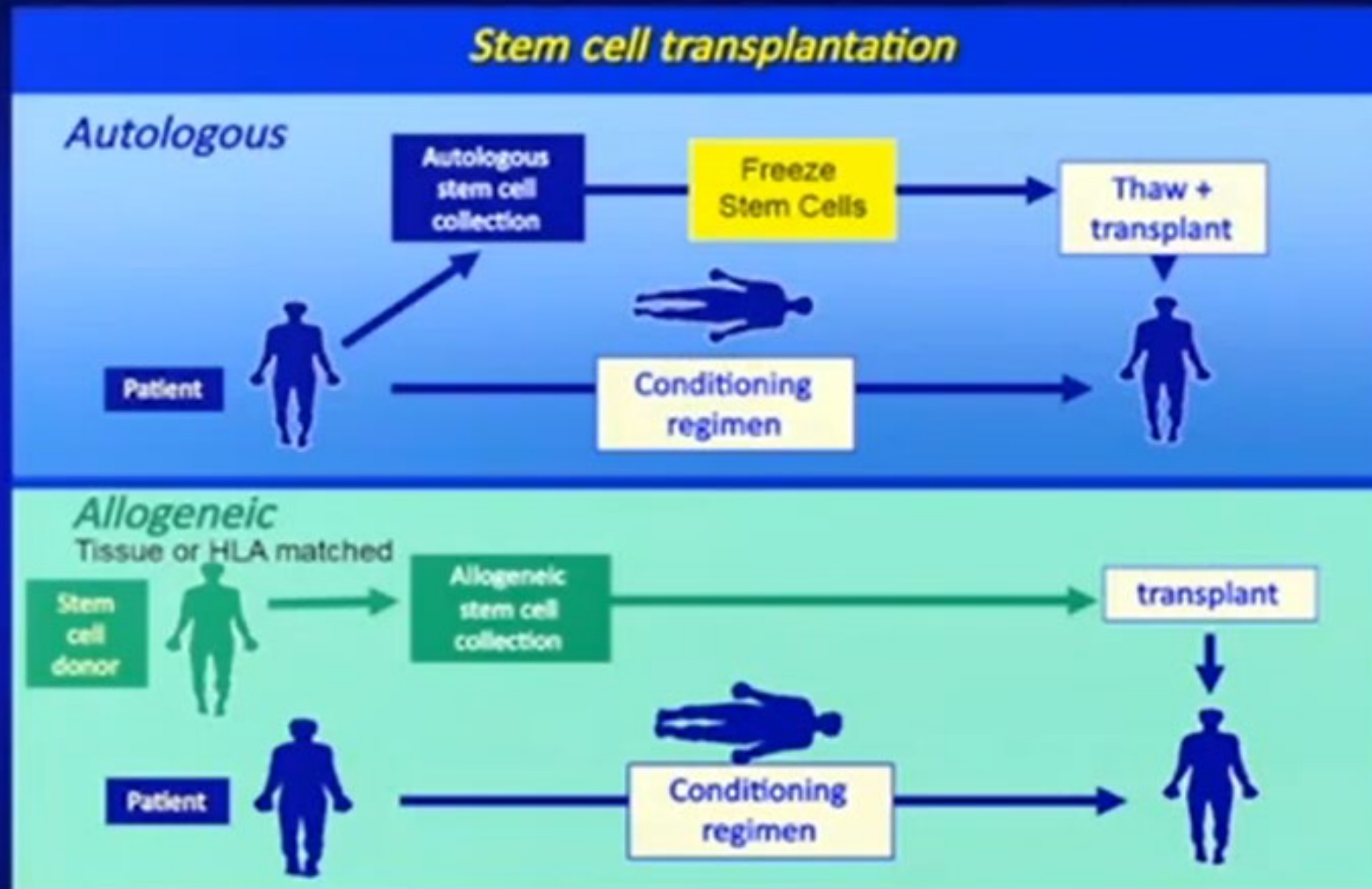


Philippe Moreau, ASH 2015

# Treatment Approach for Newly Diagnosed MM



# Stem Cell Transplant & Multiple Myeloma



Courtesy of R. Childs, NIH

Callander, Natalie, Univ. of Wisconsin, Medical grand rounds 2/10,

# What is autologous HCT?

- ▶ High dose **Melphalan**
- ▶ 1 cycle consolidative therapy
- ▶ Feasible outpatient or ~2 week hospitalization
- ▶ Requires transfusion support, median 0-2 units blood product
- ▶ <1% mortality in 100 days
- ▶ Own cells to support one time treatment with high dose chemotherapy
- ▶ Patients up to mid 70s
- ▶ Most common side effects diarrhea, transient hair loss, fever, fatigue, need for blood transfusion.
- ▶ No need for "anti rejection" meds, normal life style afterwards.

# ASCT

- 4 randomized trials of ASCT vs novel drug have consistently demonstrated a PFS advantage for ASCT

	GIMEMA <sup>[a]</sup>		Multicenter <sup>[b]</sup>		IFM 2009 <sup>[c]</sup>		EMN/H095 <sup>[d]</sup>	
	ASCT	No ASCT	ASCT	No ASCT	ASCT	No ASCT	ASCT	No ASCT
≥VGPR, %	63	59	54	50	88	78	85	74
Median PFS, mo	43	22	43	29	43	34	NR	44

- ASCT leads to deeper responses in more patients
- MRD has been added as a response category in the new IMWG response criteria
- A single high-dose melphalan-conditioned ASCT is standard

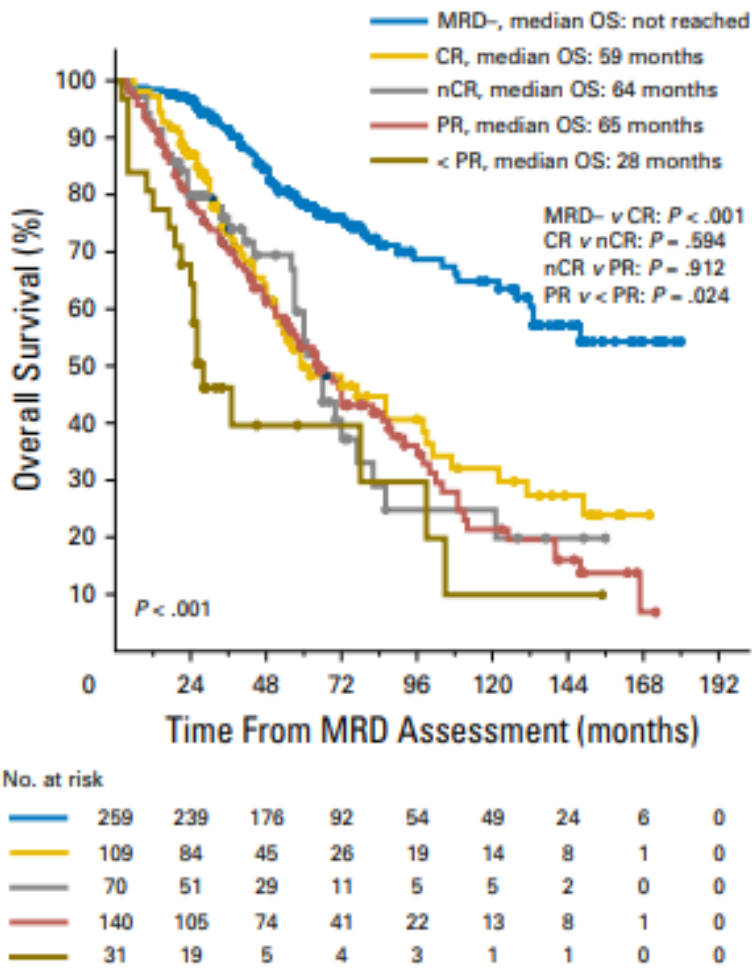
a. Palumbo A, et al. *N Engl J Med*. 2014;371:895-905; b. Gay F, et al. *Lancet Oncol*. 2015;16:1617-1629; c. Attal M, et al. *Blood*. 2015;126. Abstract 391; d. Cavo M, et al. *J Clin Oncol*. 2016;34. Abstract 8000.

# Depth of Response

Table 1. Measuring response to myeloma therapy.

Response type	Abbreviation	Tests					
		M protein reduction		Bone marrow			Freelite ratio
		Blood	Urine	Immuno-fixation	Plasma cells	Immuno-fluorescence	
Stringent complete response	sCR	0	0	Negative	0	Negative	Normal
Complete response	CR	0	0	Negative	<5%	—	—
Very good partial response	VGPR	≥90%	<100 mg/24 hrs	—	—	—	—
Partial response	PR	≥50%	≥90%	—	—	—	—
Minimal response	MR	≥25–49%	50–89%	—	—	—	—
Stable disease	SD	Does not meet criteria for response or progressive disease					
Progressive disease	PD	An increase of 25% (and 0.5 g/dL) in M protein; an increase of 10% in bone marrow plasma cells					

Degree (or depth) of response is usually associated with better prognosis.  
Some patients do well despite never achieving a CR.



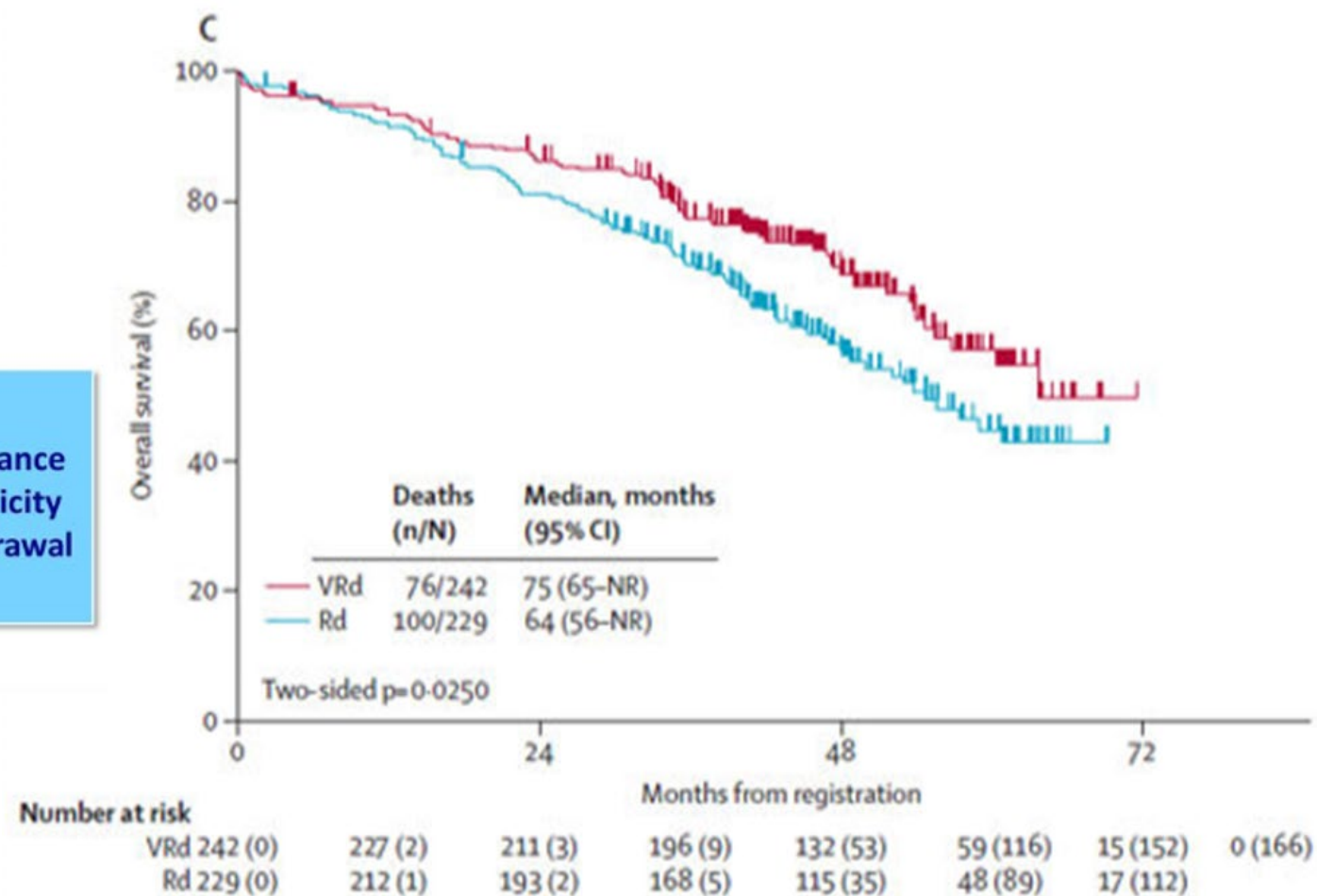
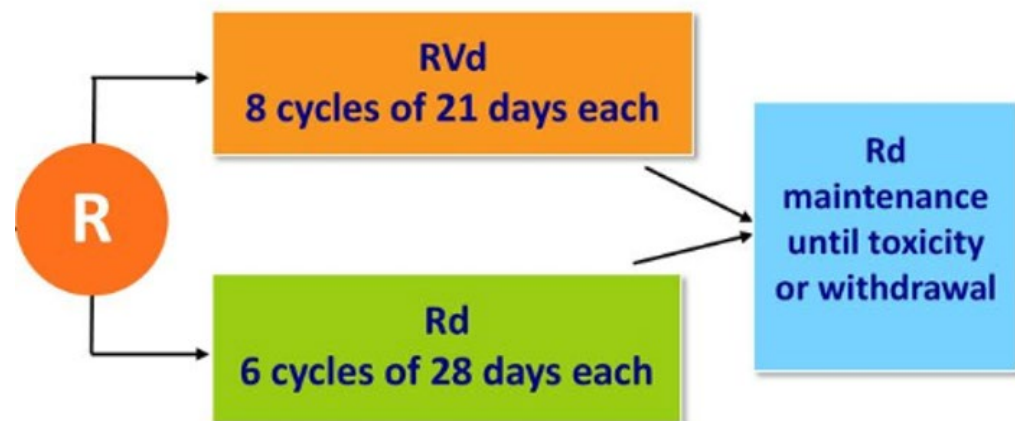
Reprinted with permission © 2014 American Society of Clinical Oncology. All rights reserved. Palumbo A et al: *J Clin Oncol* 32(6), 2014:587-600.

Landgren, O. & Iskander, K. *Journal of Internal Medicine* 281, 365–382 (2017)  
 Lahuerta, J.-J. et al. *J. Clin. Oncol.* 35, 2900–2910 (2017)

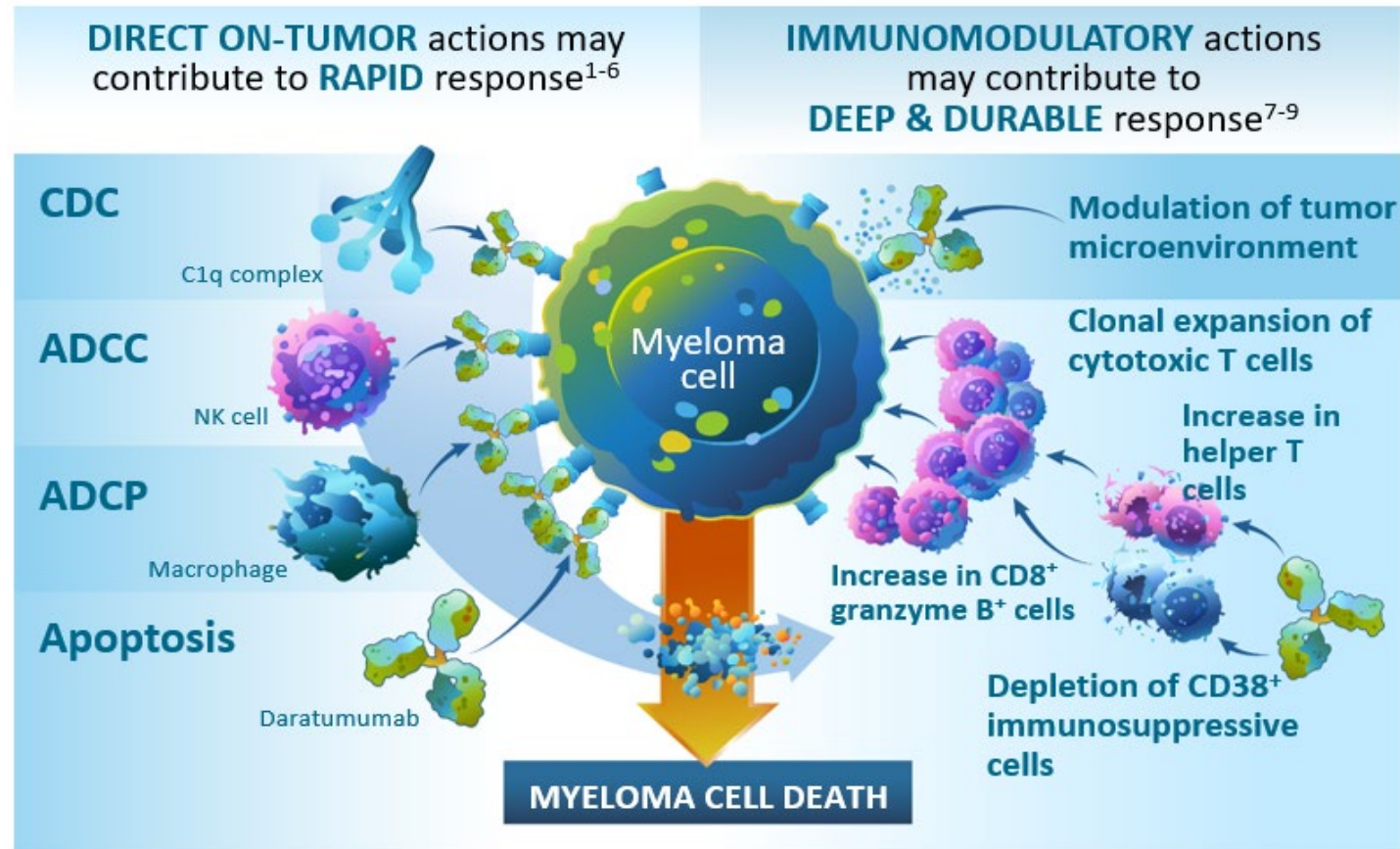
Triplet  
(3 drugs)

# Triplet (VRd) improves overall survival vs. Doublet (Rd) S0777

NDMM



# 3 drugs + Monoclonal Antibody (Daratumumab)



1. DARZALEX® US PI; 2019. 2. Liszewski MK, et al. *Adv Immunol.* 1996;61:201-283. 3. Debets JM, et al. *J Immunol.* 1988;141(4):1197-1201. 4. Overdijk MB, et al. *mAbs.* 2015;7(2):311-321. 5. Lokhorst HM, et al. *N Engl J Med.* 2015;373(13):1207-1219. 6. Plesner T, et al. *Blood.* 2012;120:73. 7. Krejci J, et al. *Blood.* 2016;128(3):384-394. 8. Adams HC III, et al. *Cytometry A.* 2019;95(3):279-289. 9. Chiu C, et al. Poster presented at: ASH 2016; San Diego, CA.

# Clinical Trials using Daratumumab NDMM (quadruplet)

- Cassiopeia

- NDMM transplant eligible, phase III
- D-VTD vs. VTD
- Improvement ORR and PFS

- Griffin

- NDMM transplant eligible, phase II
- D-VRD vs. VRD
- Improvement depth of response

- Acylone

- NDMM transplant ineligible, phase III
- D-VMP vs. VMP
- ORR and PFS benefit



### MYELOMA THERAPY<sup>a-d</sup>

#### PRIMARY THERAPY FOR TRANSPLANT CANDIDATES

##### Preferred Regimens

- Bortezomib/lenalidomide/dexamethasone (category 1)
- Bortezomib/cyclophosphamide/dexamethasone<sup>e</sup>

##### Other Recommended Regimens

- Carfilzomib/lenalidomide/dexamethasone
- Daratumumab<sup>f</sup>/lenalidomide/bortezomib/dexamethasone
- Ixazomib/lenalidomide/dexamethasone (category 2B)

##### Useful In Certain Circumstances

- Bortezomib/doxorubicin/dexamethasone
- Carfilzomib/cyclophosphamide/dexamethasone<sup>g</sup>
- Ixazomib/cyclophosphamide/dexamethasone<sup>g</sup>
- Bortezomib/thalidomide/dexamethasone (category 1)
- Cyclophosphamide/lenalidomide/dexamethasone
- Daratumumab<sup>f</sup>/cyclophosphamide/bortezomib/dexamethasone
- Daratumumab<sup>f</sup>/bortezomib/thalidomide/dexamethasone
- Dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide/bortezomib<sup>h</sup> (VTD-PACE)



### MYELOMA THERAPY<sup>a-d</sup>

PRIMARY THERAPY FOR NON-TRANSPLANT CANDIDATES
<b><u>Preferred Regimens</u></b> <ul style="list-style-type: none"><li>• Bortezomib/lenalidomide/dexamethasone (category 1)<sup>j</sup></li><li>• Daratumumab<sup>f</sup>/lenalidomide/dexamethasone (category 1)</li><li>• Lenalidomide/low-dose dexamethasone (category 1)<sup>k</sup></li><li>• Bortezomib/cyclophosphamide/dexamethasone<sup>e</sup></li></ul>
<b><u>Other Recommended Regimens</u></b> <ul style="list-style-type: none"><li>• Carfilzomib/lenalidomide/dexamethasone</li><li>• Ixazomib/lenalidomide/dexamethasone</li><li>• Daratumumab<sup>f</sup>/bortezomib/melphalan/prednisone (category 1)</li><li>• Daratumumab<sup>f</sup>/cyclophosphamide/bortezomib/dexamethasone</li></ul>
<b><u>Useful In Certain Circumstances</u></b> <ul style="list-style-type: none"><li>• Bortezomib/dexamethasone</li><li>• Cyclophosphamide/lenalidomide/dexamethasone</li><li>• Carfilzomib/cyclophosphamide/dexamethasone<sup>g</sup></li></ul>

# Initial treatment patients: summary

- **Three-drug combinations are recommended for induction**  
“ Standard of Care”
- **Regimens for newly diagnosed patients should include at least 3 of the following: steroids, IMiD, PI, or monoclonal antibody**
- **Doublets appropriate for frail patients**
- **Inclusion of a monoclonal antibody (4<sup>th</sup> drug) as part of induction therapy is a reasonable option**
  - **Data is emerging supporting Daratumumab use in 1<sup>st</sup> line**
- **Explore clinical trial options**

# Thank you!

[kgodby@uabmc.edu](mailto:kgodby@uabmc.edu)





# INTERNATIONAL MYELOMA FOUNDATION

Improving Lives. **Finding the Cure.**

# **“Relapsed Therapy” “Emerging Therapies and Clinical Trials”**

**Luciano Costa, MD  
University of Alabama  
Birmingham**

# Management of Relapsed Myeloma

**Luciano J. Costa, MD, PhD**  
Professor of Medicine  
University of Alabama at Birmingham

ljcosta@uabmc.edu

 @End\_myeloma

# When to change therapy?

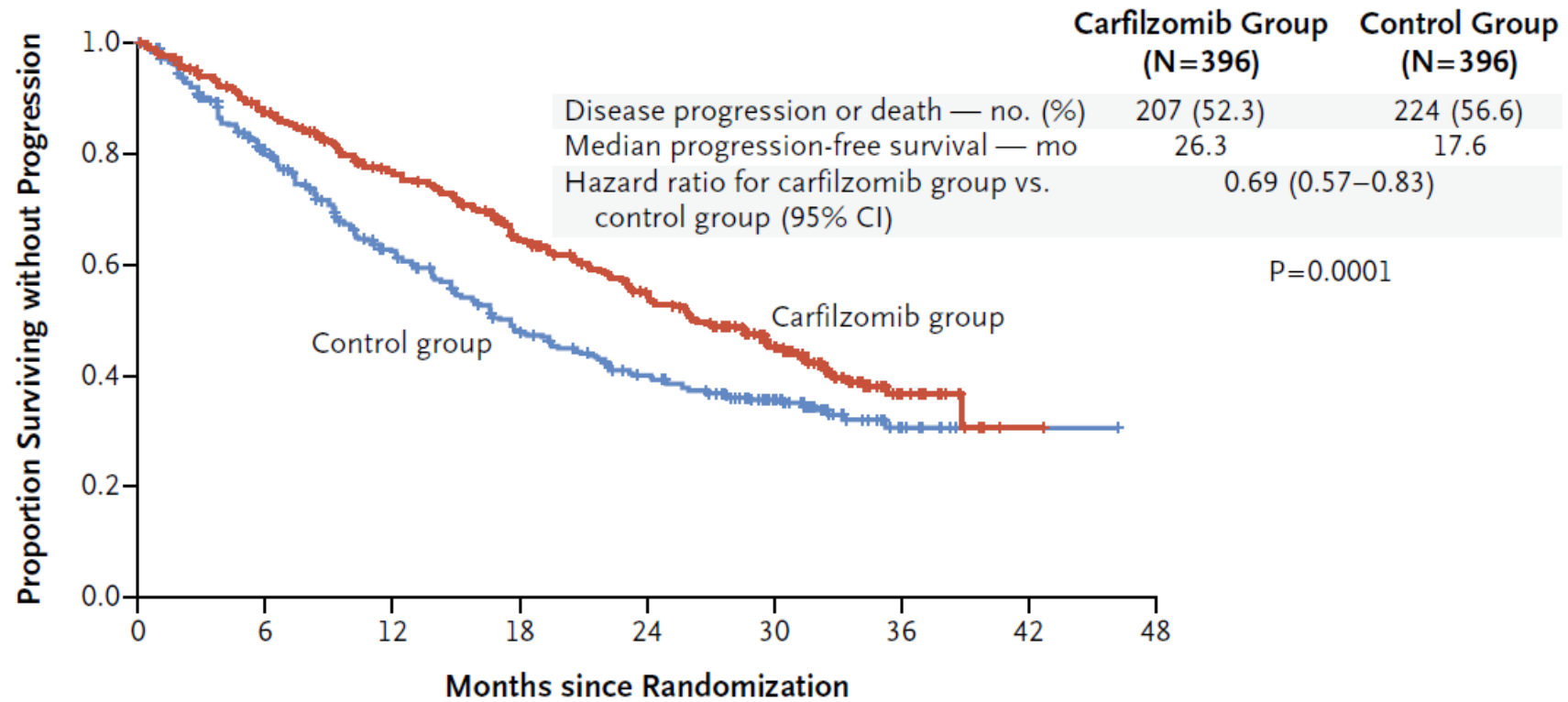
- Development of new signs and symptoms of disease
- Increase in “M” spike
- Unmanageable toxicity from current regimen
- Goals:
  - ✓ Regain control of myeloma, for the longest possible time
  - ✓ Alleviate current symptoms
  - ✓ Prevent myeloma serious events (severe anemia, renal failure, fracture, etc)
  - ✓ Prolong survival

# How to chose a regimen

- NOT one size fits all.
- Pillars are IMiDs and Proteasome inhibitors
- Consider Clinical Trial
- Factors:
  - ✓ Disease characteristics
  - ✓ Prior therapies
  - ✓ Unresolved toxicities from prior regimens
  - ✓ Coexisting diseases (heart disease, neuropathy)
  - ✓ Frailty
  - ✓ Convenience (oral vs. injectable agents)

# New Proteasome Inhibitors

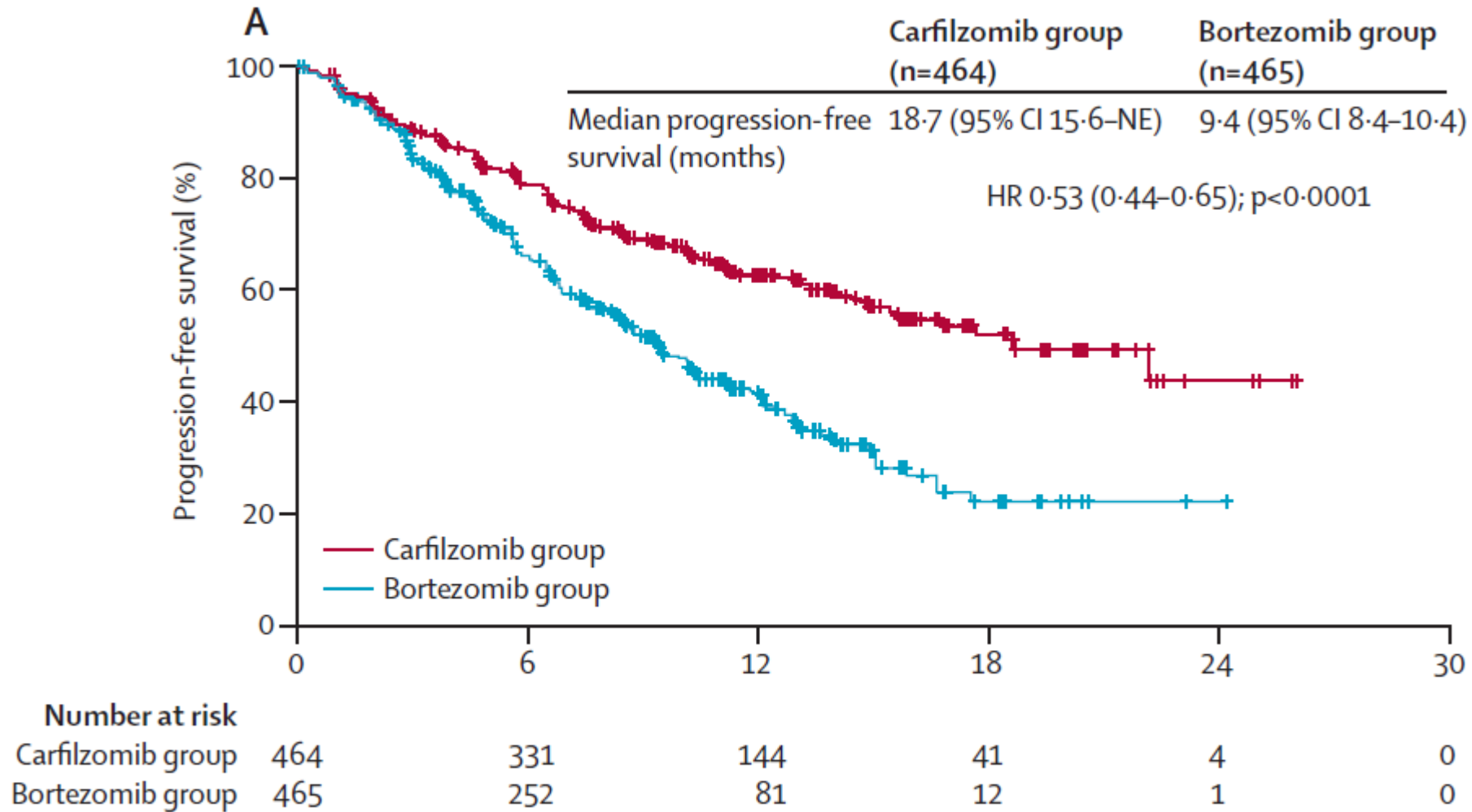
# PFS- Aspire



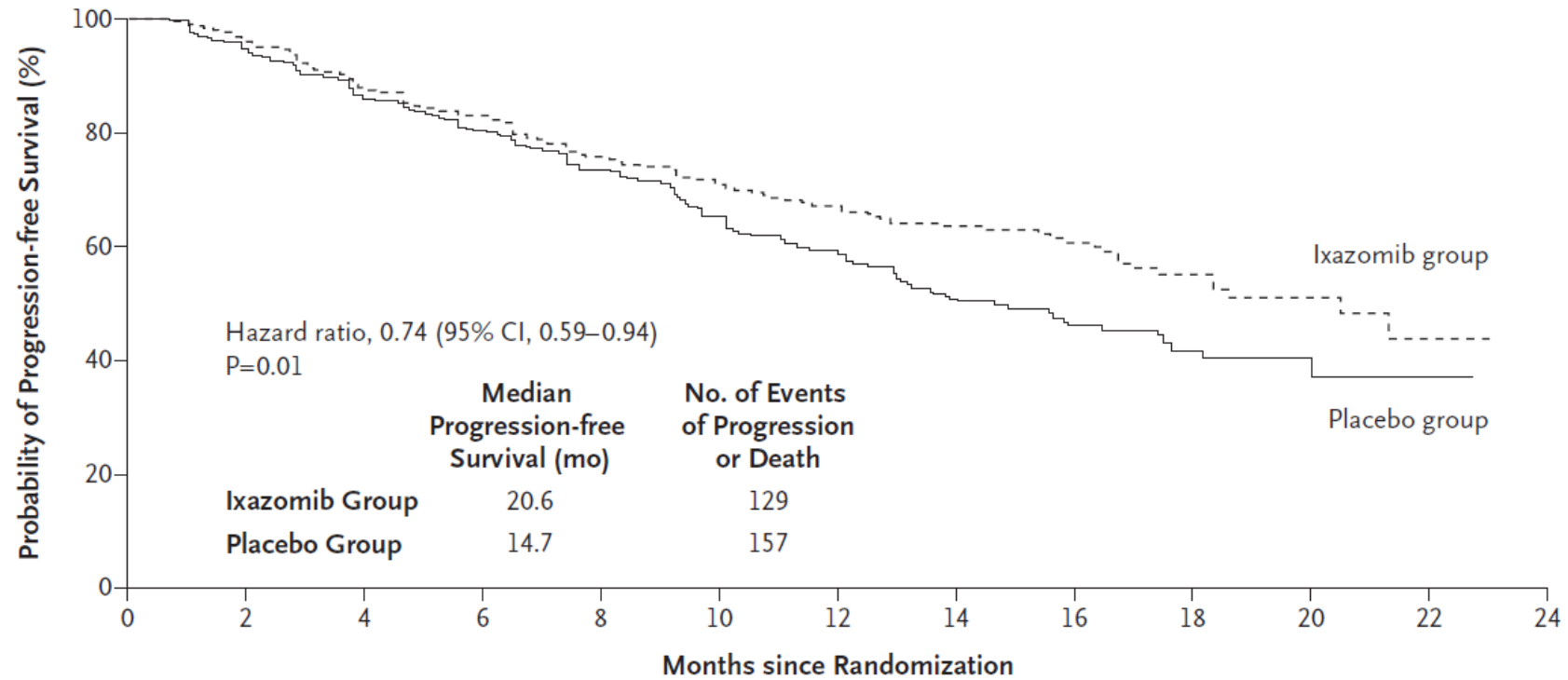
## No. at Risk

Carfilzomib group	396	332	279	222	179	112	24	1
Control group	396	287	206	151	117	72	18	1

# PFS- Endeavor



# PFS- Tourmaline MM1

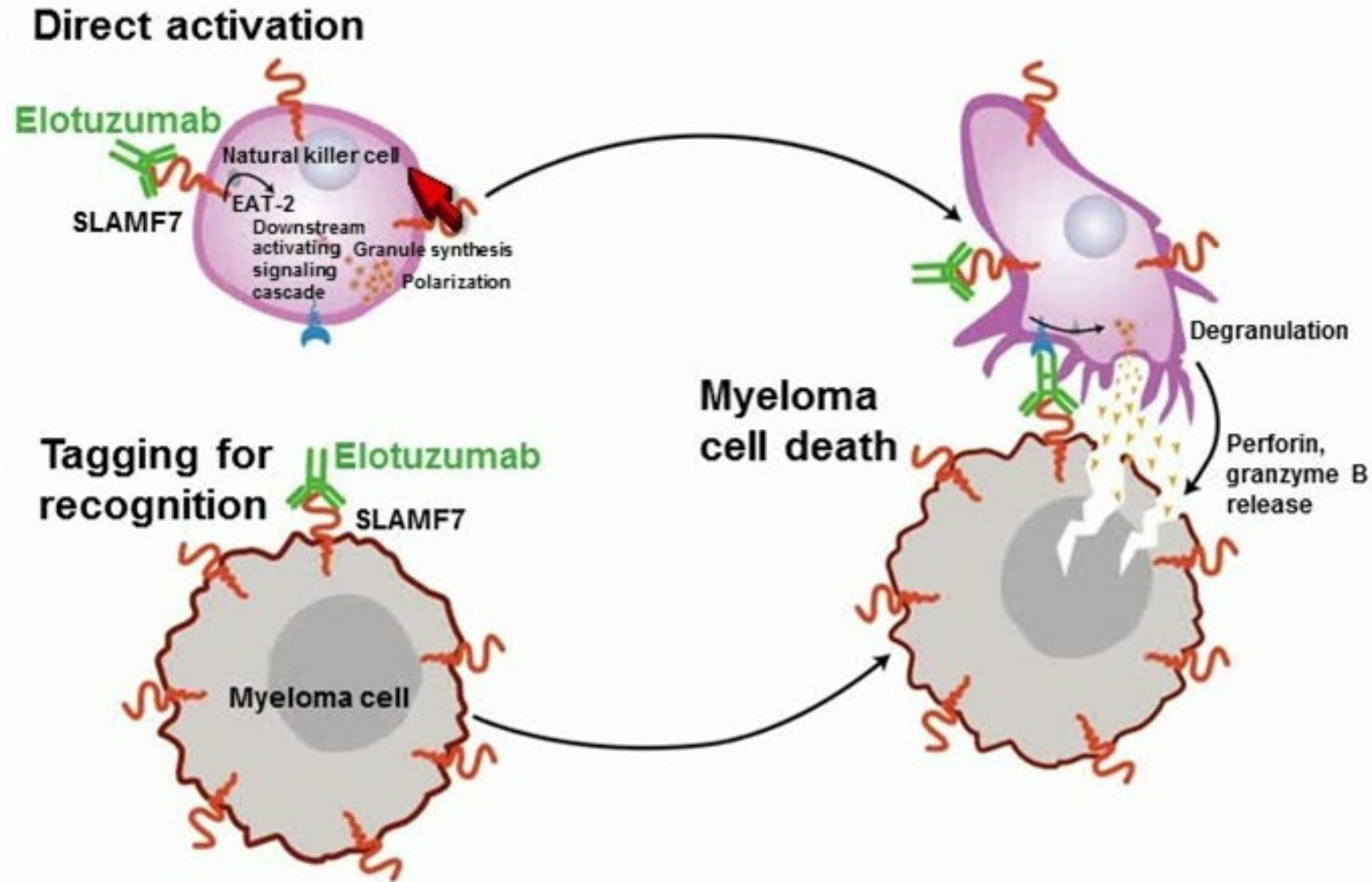


## No. at Risk

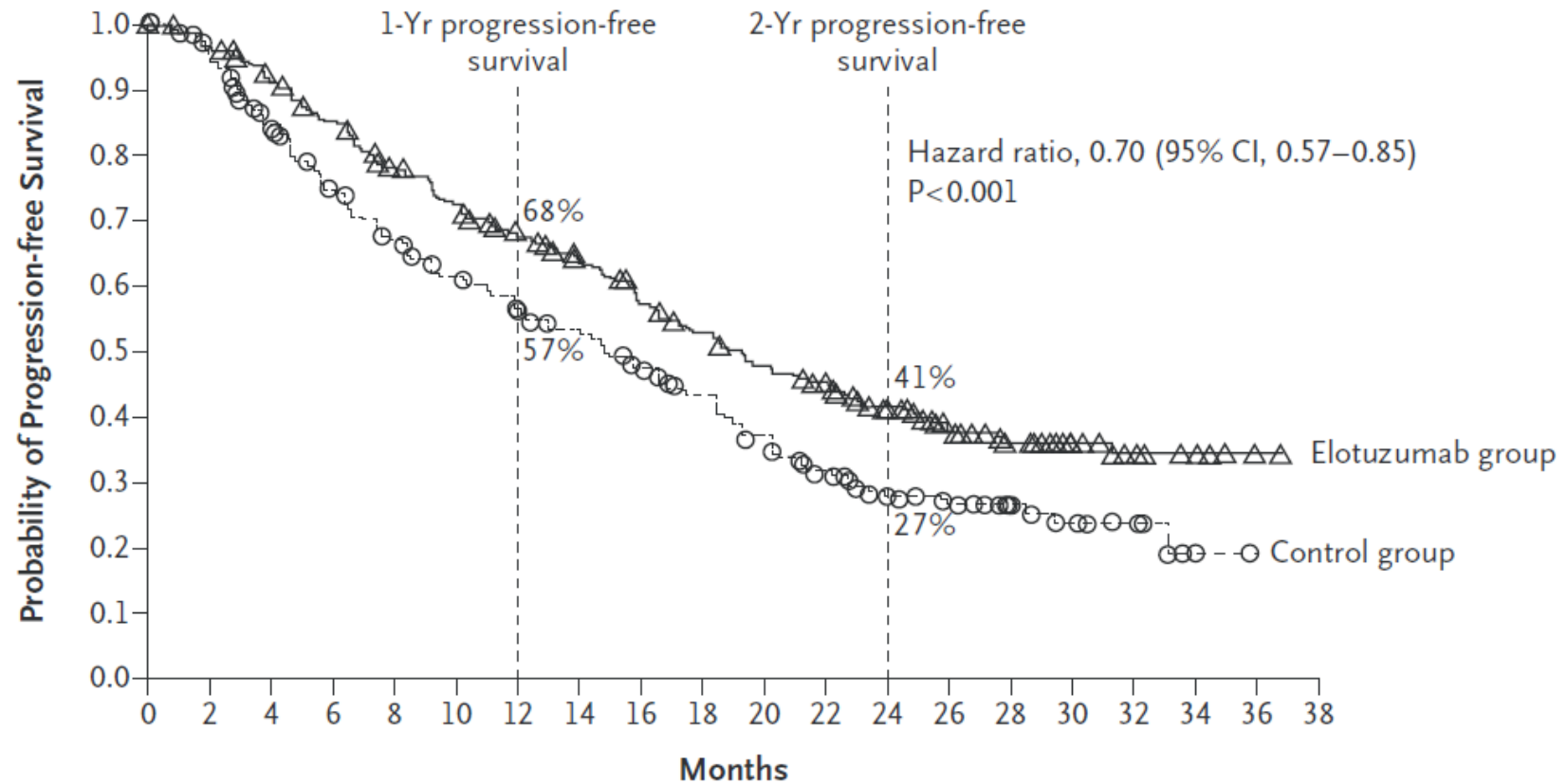
Ixazomib group	360	345	332	315	298	283	270	248	233	224	206	182	145	119	111	95	72	58	44	34	26	14	9	1	0
Placebo group	362	340	325	308	288	274	254	237	218	208	188	157	130	101	85	71	58	46	31	22	15	5	3	0	0

# Monoclonal Antibodies

# Elotuzumab, First MoAb Available for Treatment of Multiple Myeloma



# PFS- Eloquent 2

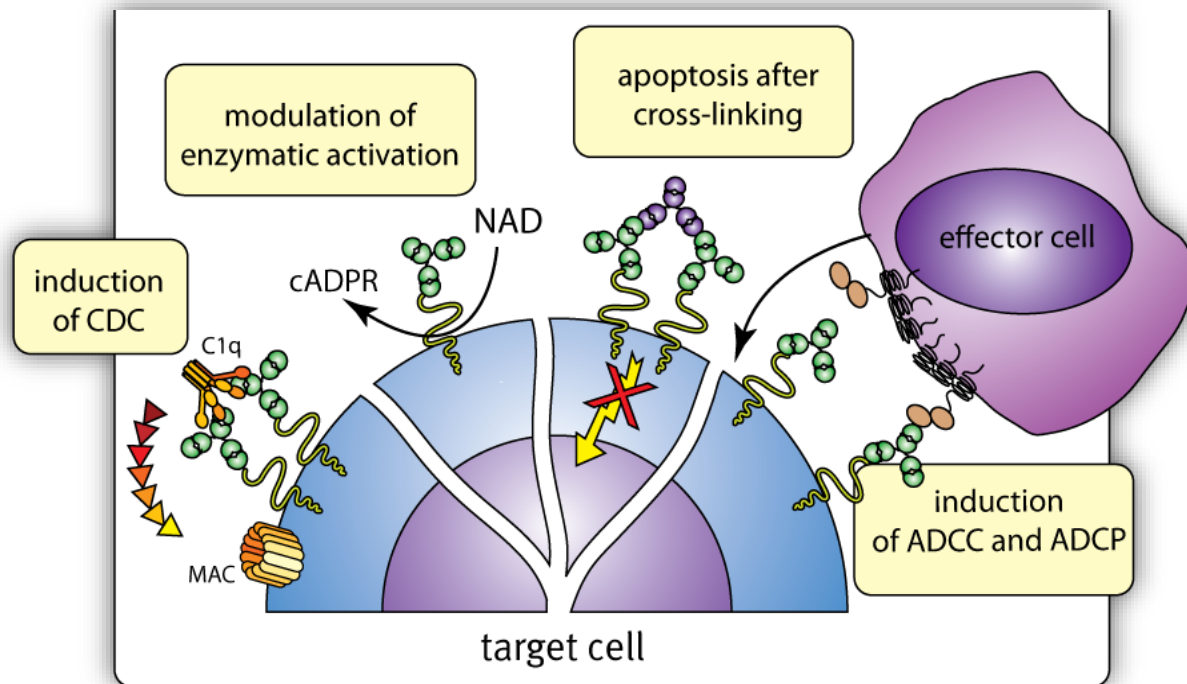


## No. at Risk

Elotuzumab group	321	303	279	259	232	215	195	178	157	143	128	117	85	59	42	32	12	7	1	0
Control group	325	295	249	216	192	173	158	141	123	106	89	72	48	36	21	13	7	2	0	0

## Daratumumab

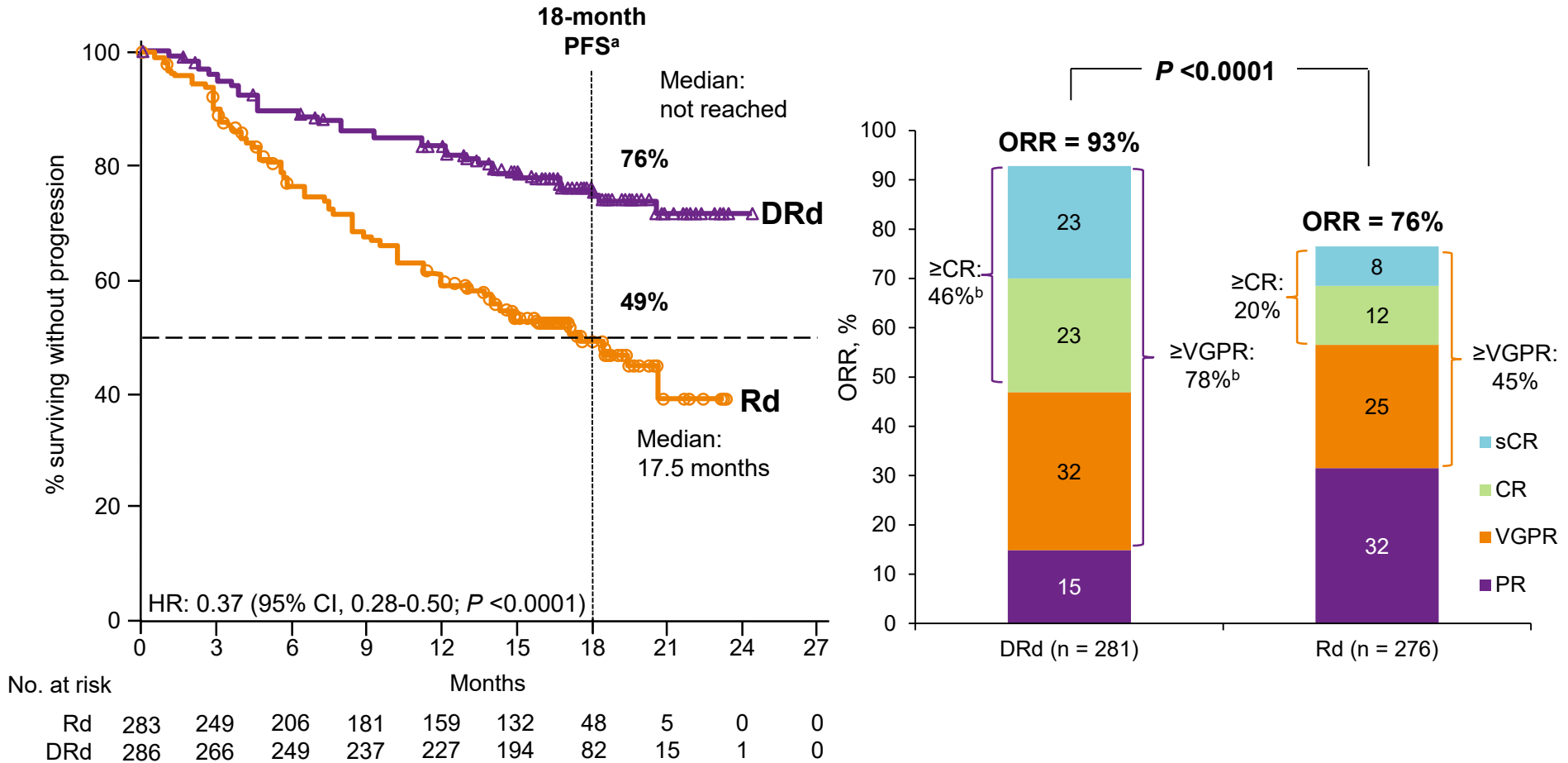
- A human mAb that targets CD38-expressing tumor cells
- DARA+LEN enhanced killing of MM cells *in vitro* and lead to synergistically higher efficacy in clinical setting



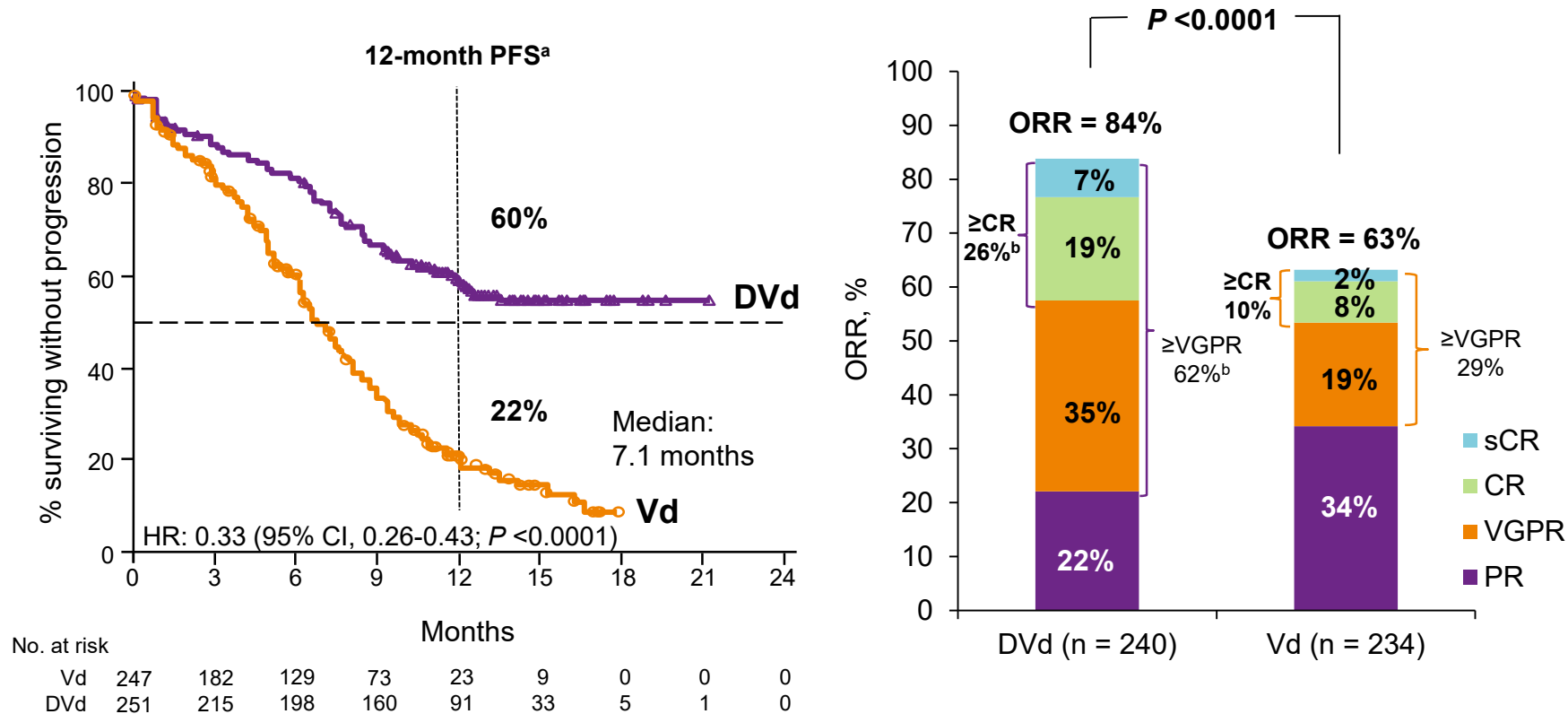
- ◆ Antibody-dependent cell-mediated cytotoxicity (ADCC)
- ◆ Antibody-dependent cellular phagocytosis (ADCP)
- ◆ Complement-dependent cytotoxicity (CDC)
- ◆ Apoptosis

DARA: daratumumab; LEN: lenalidomide; mAb: monoclonal antibody; MM: multiple myeloma

# Efficacy

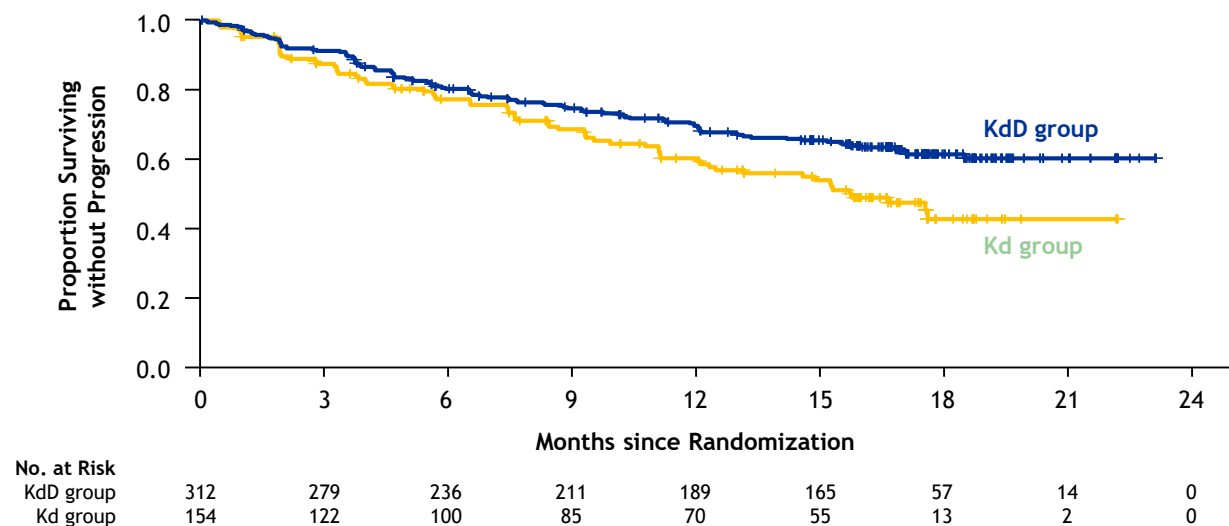


# Efficacy



- Median (range) follow-up: 13.0 (0-21.3) months
- An additional 7% of patients receiving DVd achieved ≥CR with longer follow up

## CANDOR Trial – Improved PFS



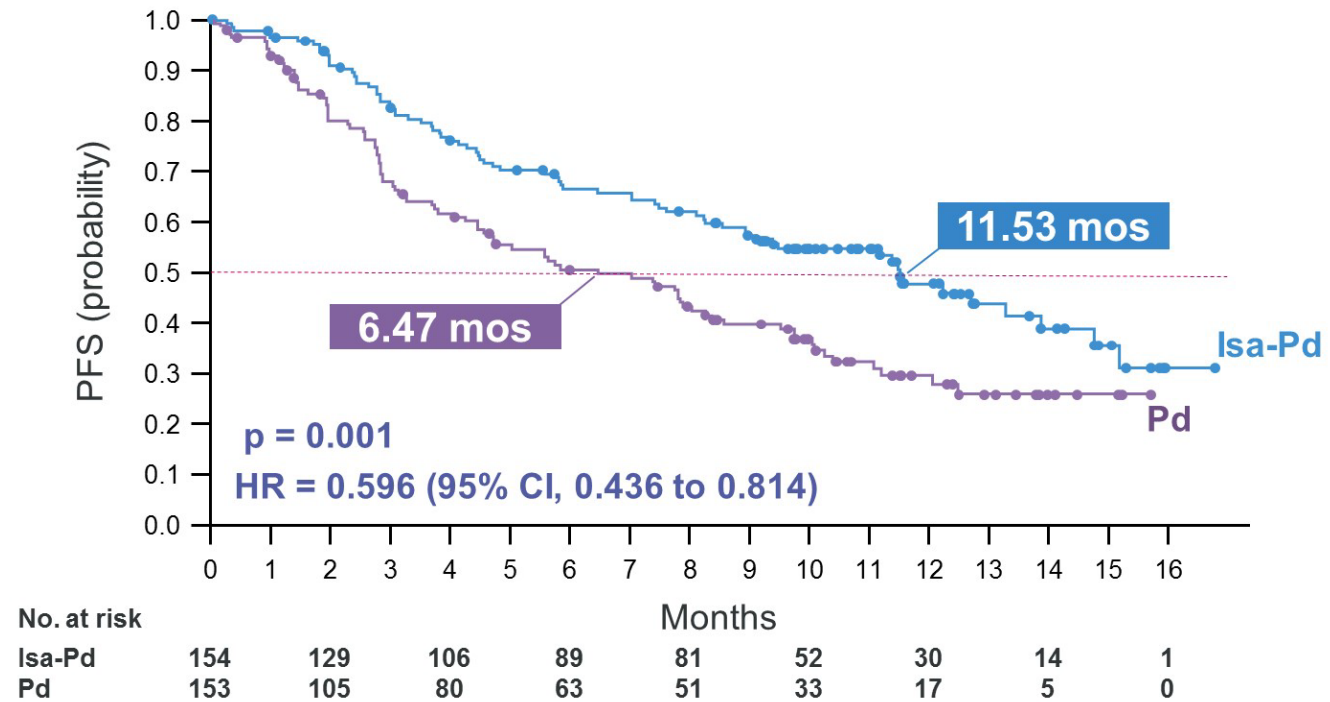
	KdD (n=312)	Kd (n=154)
Median follow-up time, months	16.9	16.3
Progression/Death, n (%)	110 (35%)	68 (44%)
Median PFS, months	NE	15.8
HR (KdD/Kd) (95% CI)	0.63 (0.46-0.85)	
p-value (1-sided)	0.0014	

Dimopoulos M, Lancet 396:186, 2020

## ICARIA (Isa-Pd vs. Pd) -

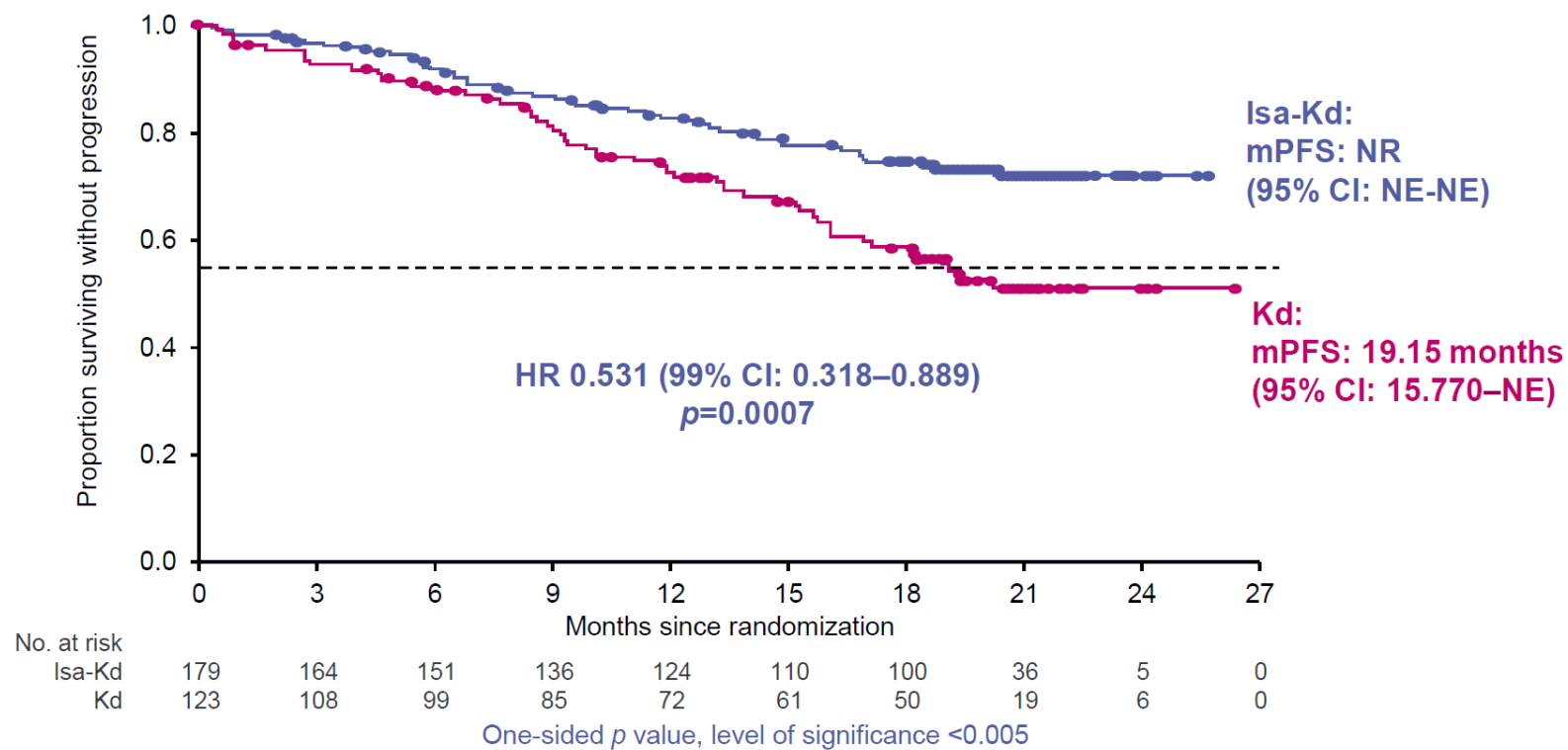
>90% Len refractory  
72% PI refractory

ORR: 60.4% vs. 35.3%  
≥VGPR: 31.8% vs. 8.5%



Attal M, Lancet 394:2096, 2019

## IKEMMA Trial

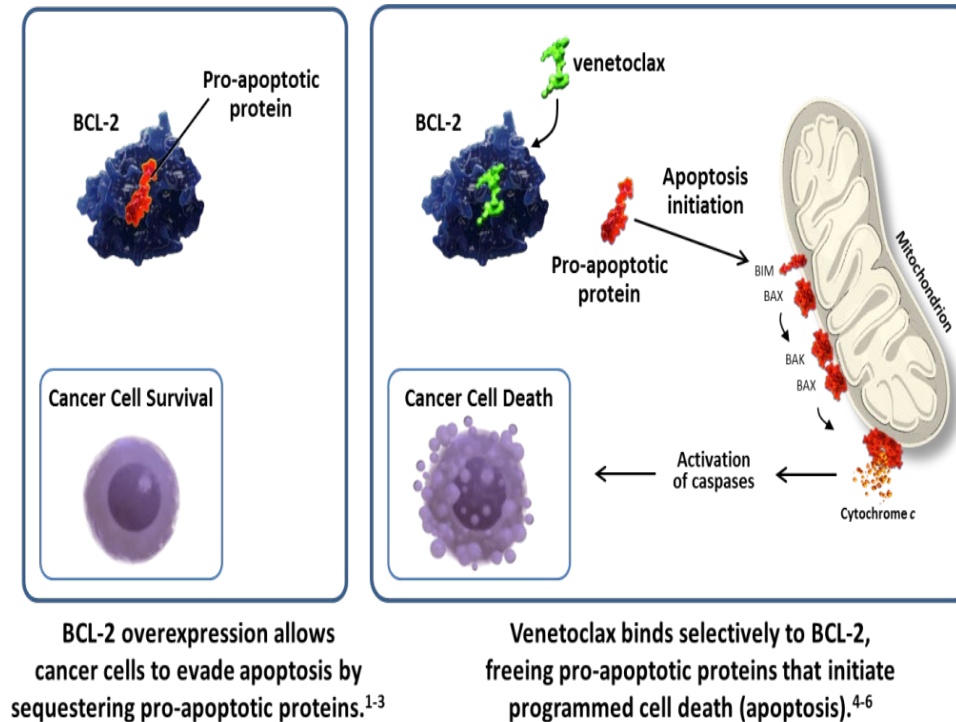


Moreau P et al. EHA 2020

# Emerging Therapies

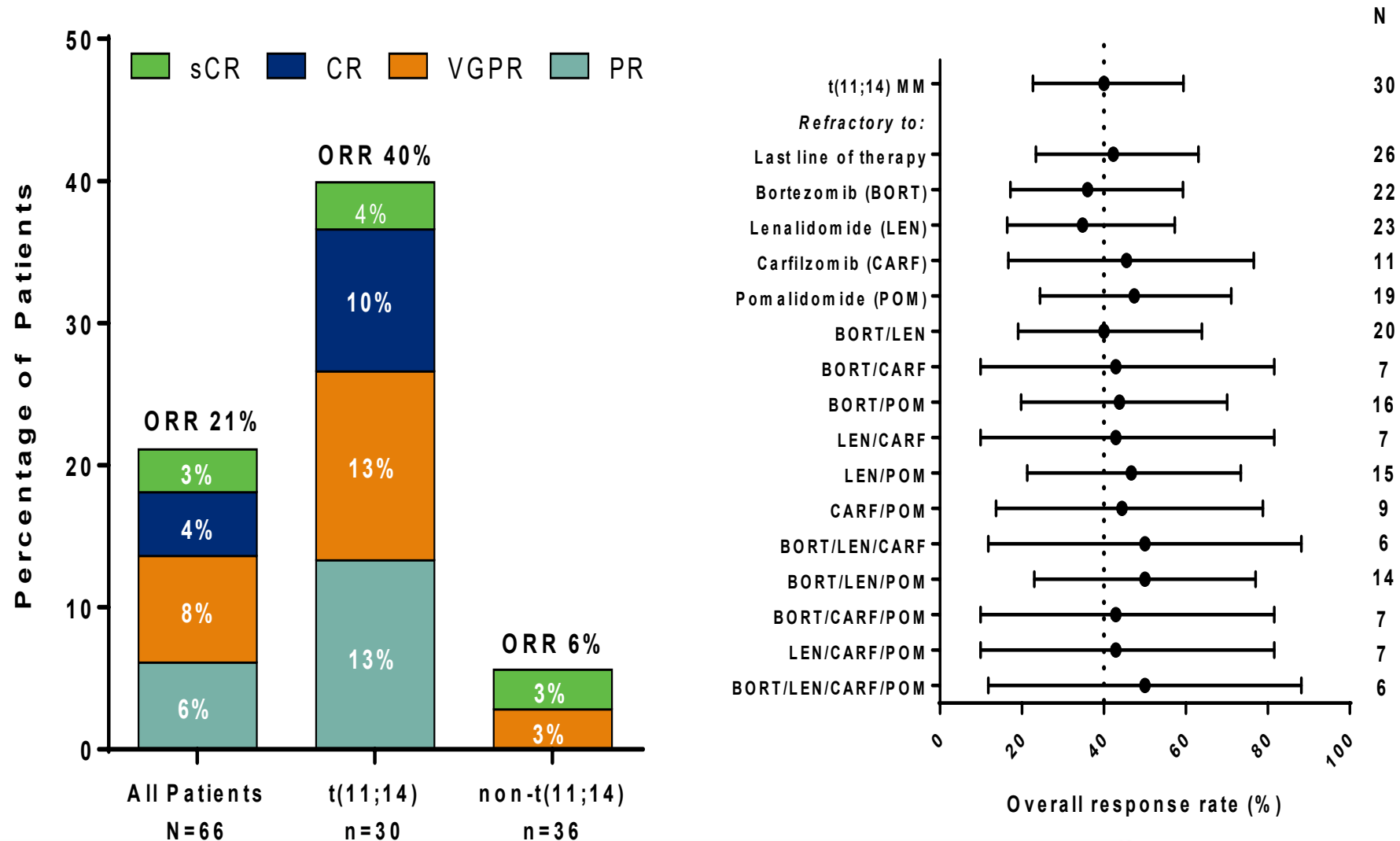
# Venetoclax

- Anti-apoptotic proteins BCL-2 and MCL-1 promote multiple myeloma (MM) cell survival<sup>1</sup>
- Venetoclax induces cell death in multiple myeloma (MM) cell lines and primary samples, particularly those positive for the translocation t(11;14), which correlates with higher ratios of *BCL2* to *MCL1* and *BCL2* to *BCL2L1* (*BCL-X<sub>L</sub>*) mRNA<sup>1,2</sup>

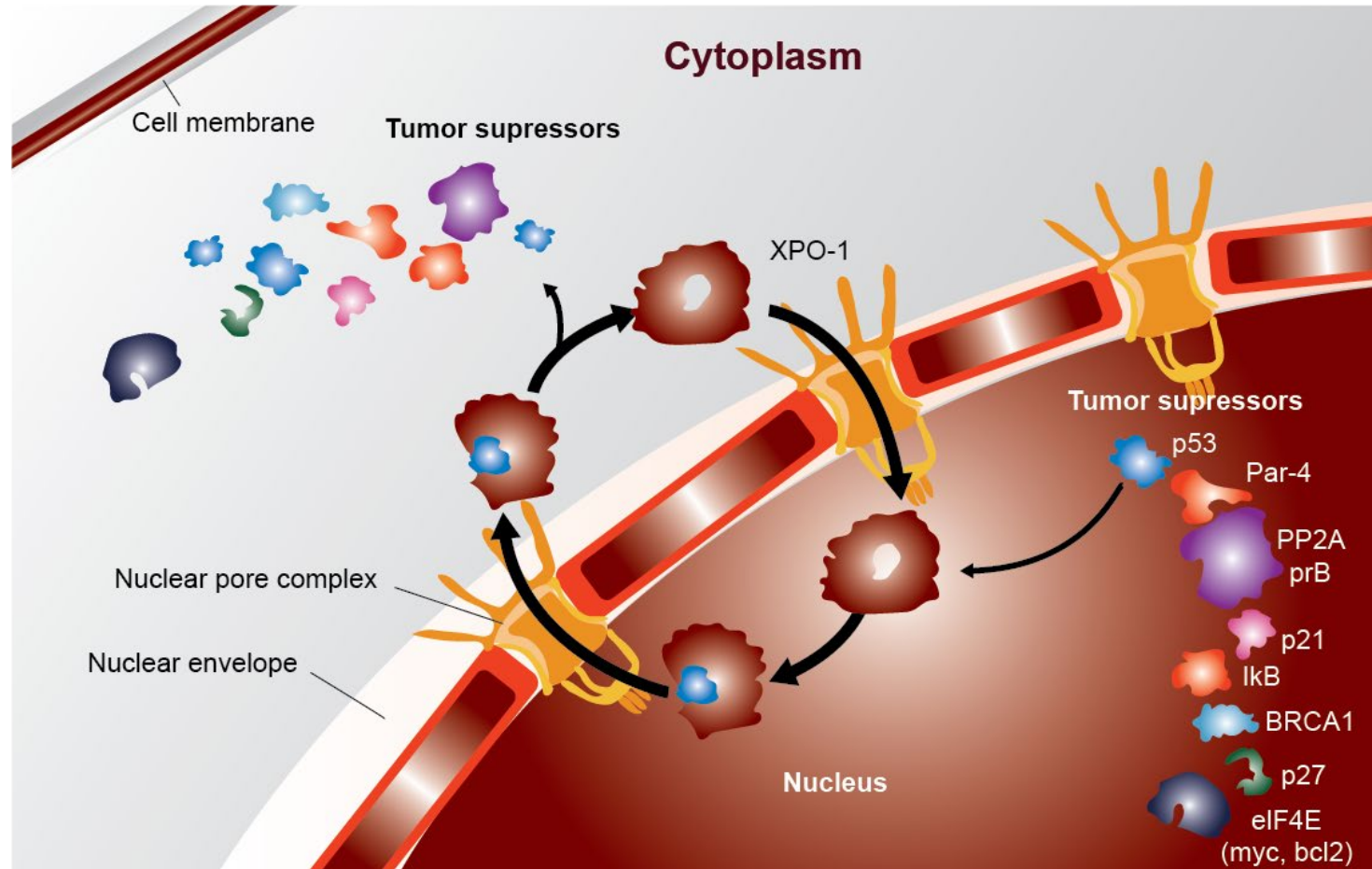


1. Levenson JD, et al. *Sci Transl Med* 2015; 7:279ra40. 2. Czabolat, et al. *Nature Reviews* 2014;15:49-63. 3. Plati J, Bucur O, Khosravi-Far R. *Integr Biol (Camb)* 2011;3:279-296.  
4. Certo M, et al. *Cancer Cell*. 2006;9(5):351-65. 5. Souers AJ, et al. *Nat Med*. 2013;19(2):202-8. 6. Del Gaizo Moore V et al. *J Clin Invest*. 2007;117(1):112-21.

# Venetoclax



# Selinexor

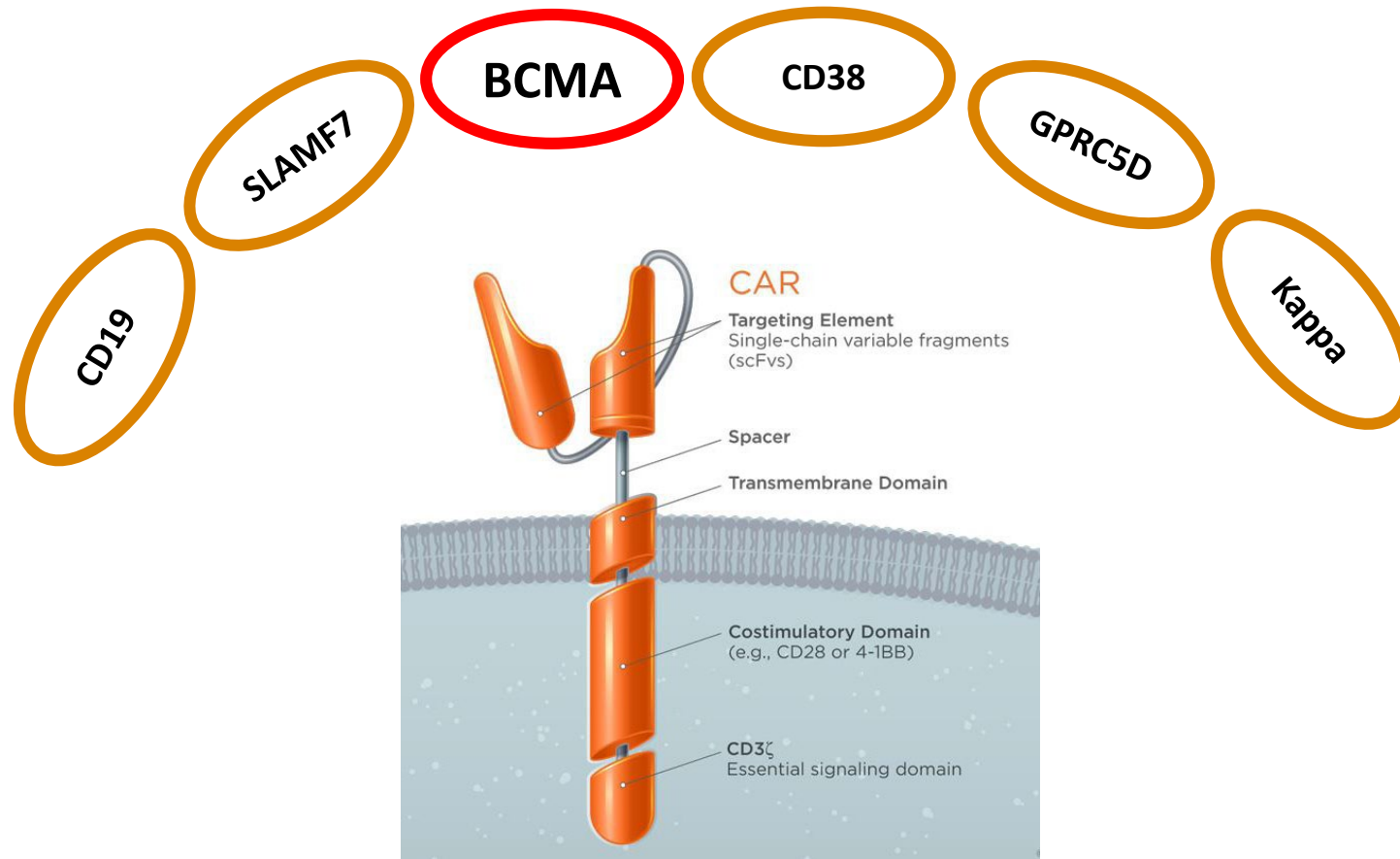


## 122 Patients refractory to PI, IMiD and Daratumumab

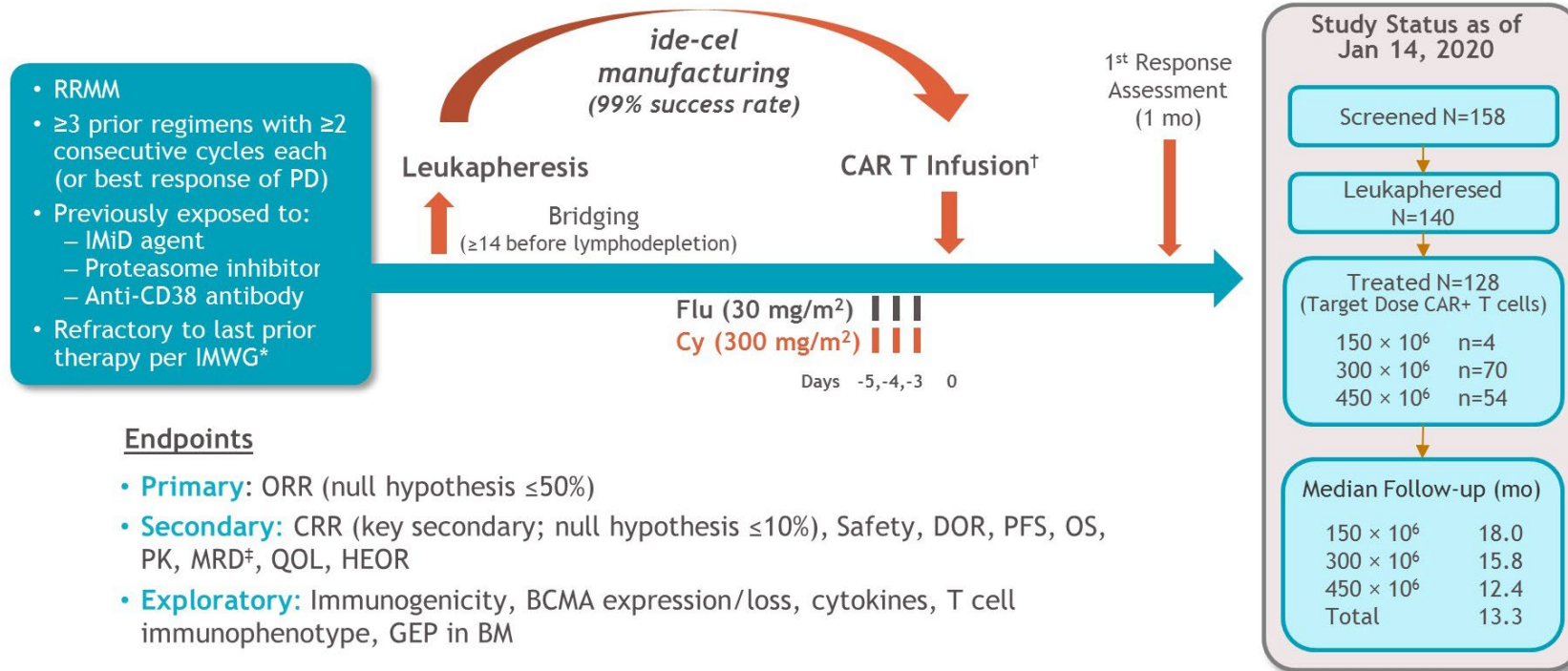
Efficacy Endpoint	
ORR	26.2%
sCR	2 pts
≥ VGPR	6.5%
VGPR	6 pts
PR	24 pts
Median DOR	4.4 mo
≥ SD	78.7%
Median PFS	3.7 mo
Median OS	8.6 mo

	No. of Patients, %				
Adverse Event	Grade 1	Grade 2	Grade 3	Grade 4	Total
Nausea	32 (41)	20 (25)	6 (8)	--	58 (73)
Thrombocytopenia	5 (6)	6 (8)	20 (25)	27 (34)	58 (73)
Fatigue	12 (15)	26 (33)	12 (15)	--	50 (63)
Anemia	2 (3)	15 (19)	21 (27)	1 (1)	39 (49)
Decreased appetite	15 (19)	22 (28)	2 (3)	--	39 (49)
Vomiting	24 (30)	8 (10)	3 (4)	--	35 (44)
Diarrhea	27 (34)	3 (4)	4 (5)	--	34 (43)
Hyponatremia	16 (20)	--	17 (22)	--	33 (42)

## CAR-T Cells Structure and Targets in MM

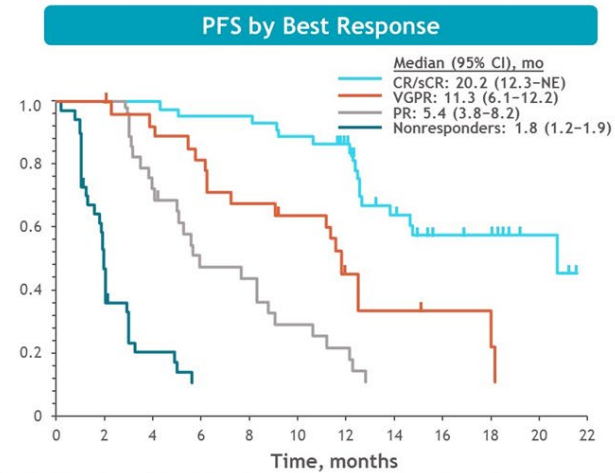
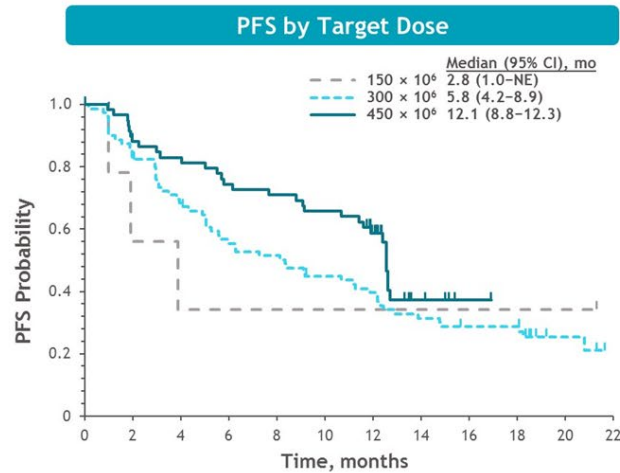
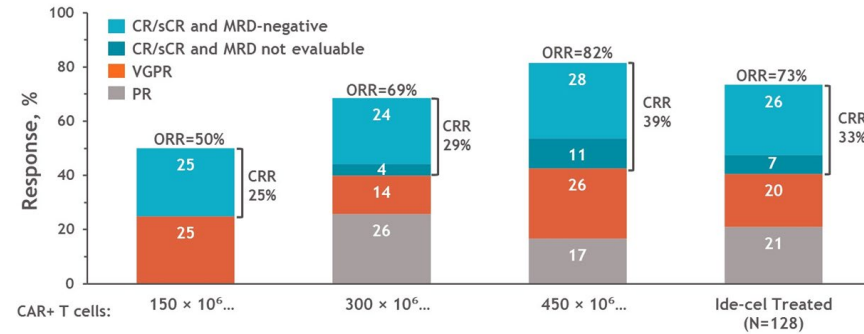


## Bb2121 (ide-cel) KarMMa 2 study



Munshi et al. ASCO 2020

## Bb2121 (ide-cel) KarMMa 2 study

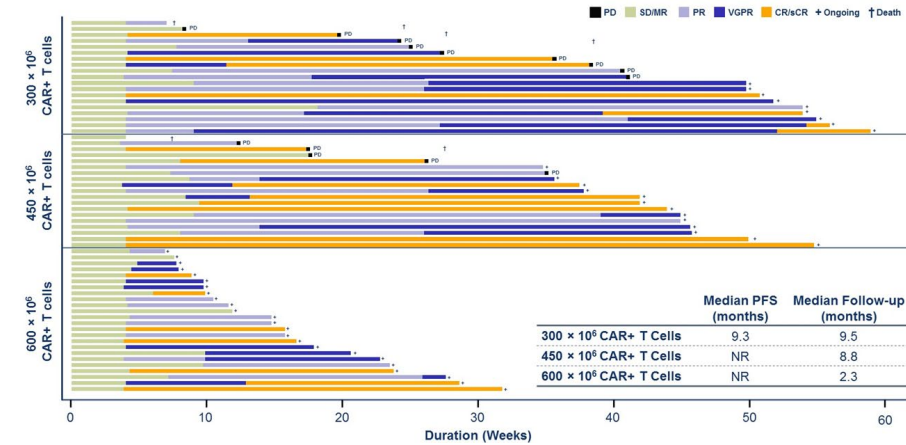
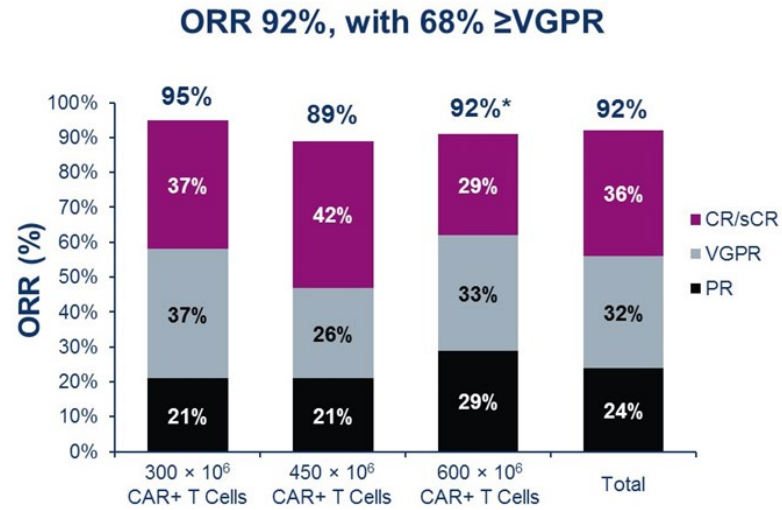


Munshi et al. ASCO 2020

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ALABAMA AT BIRMINGHAM  
Knowledge that will change your world

## JCARH125 (Orva-cel) EVOLVE study



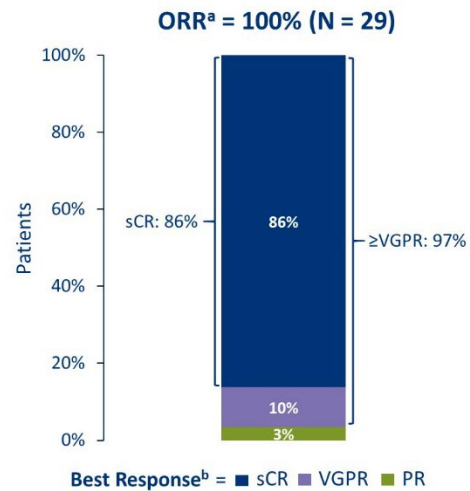
*Mailankody et al. ASCO 2020*

## JCARH125 (Orva-cel) EVOLVE study

	300 × 10 <sup>6</sup> CAR+ T Cells (n=19)	450 × 10 <sup>6</sup> CAR+ T Cells (n=19)	600 × 10 <sup>6</sup> CAR+ T Cells (n=24)	Total (N=62)
<b>Any SAE, n (%)</b>	<b>4 (21)</b>	<b>5 (26)</b>	<b>8 (33)</b>	<b>17 (27)</b>
<b>AEs of special interest grade ≥3, n (%)</b>				
Neutropenia	15 (79)	19 (100)	22 (92)	56 (90)
Anemia	8 (42)	8 (42)	14 (58)	30 (48)
Thrombocytopenia	6 (32)	10 (53)	13 (54)	29 (47)
Infections	3 (16)	4 (21)	1 (4)	8 (13)
Cytokine release syndrome (CRS)	0	1 (5)	1 (4)	2 (3)
Neurological events (NE)	1 (5)	1 (5)	0	2 (3)
MAS/HLH	0	2 (11)	1 (4)	3 (5)

*Mailankody et al. ASCO 2020*

## JNJ-4528, CARTITUDE-1 study



- 25 of 29 (86%) patients achieved sCR
- ORR and depth of response were independent of BCMA expression on myeloma cells at baseline
- Median time to first response = 1 mo (1 – 3)
- Median time to CR = 3 mo (1 – 13)

- 3% grade 3 neurotoxicity
- 7% CRS grade 3 or higher
- 9-month PFS rate 86%

*Berdeja et al. ASCO 2020*

## CAR-T – The good, the bad and the ugly

### Good

- Very active, near all patients respond
- One time treatment
- Responses are fast
- Active in very refractory disease
- “Treatment holiday”
- No “transplant-type” toxicities (GI, alopecia)

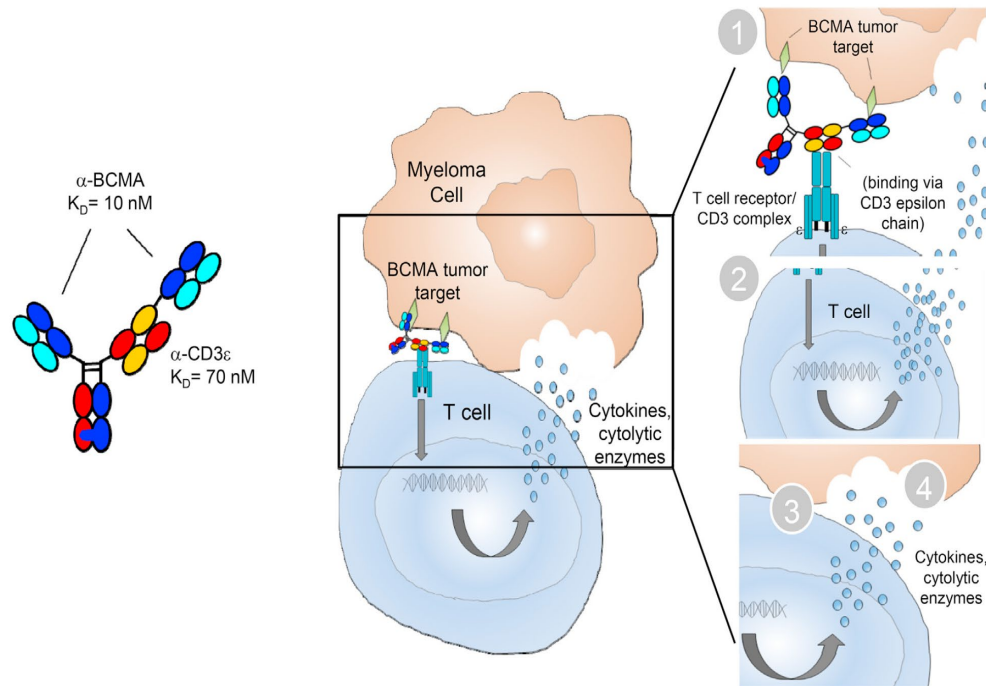
### Bad

- Manufacturing time
- Cytopenias may be persistent
- Hypogammaglobulinemia
- Most patients will be hospitalized
- Duration of response?

### Ugly

- Immuneeffective cells associated neurotoxicity syndrome (ICANS)
- Cytokine Release Syndrome (CRS)
- Access

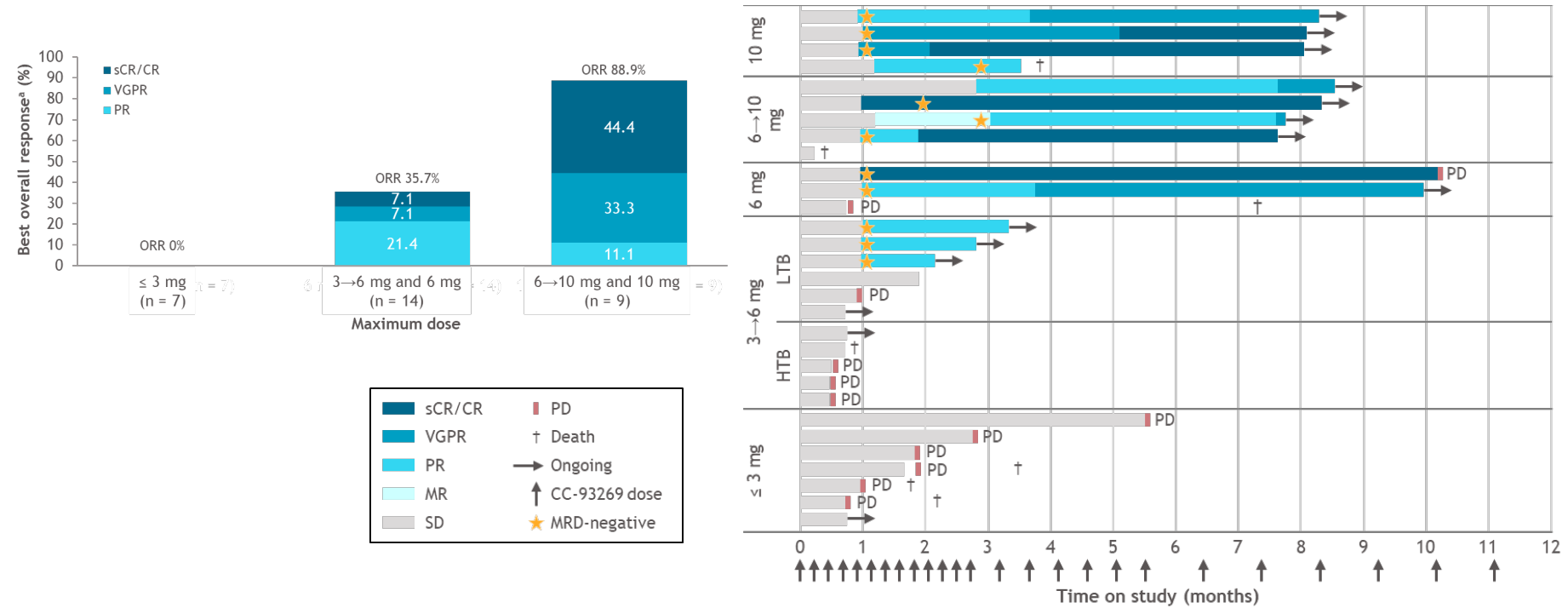
## T-Cell Engagers- Mechanism of Action



- Simultaneous binding to tumor antigen and effector-cell antigen
- Recruitment/retention of effector cells in tumor microenvironment
- T-cell activation, release of cytokines and cytolytic enzymes

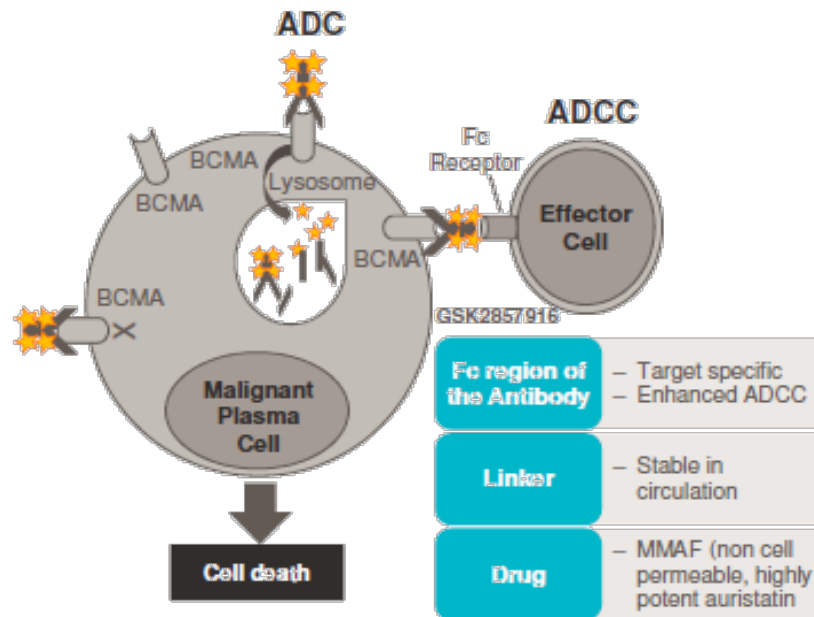
Seckinger A. *Cancer Cell* 31:1, 2017

## CC-93269- A BCMA 2+1 TCE



Costa LJ et al. EHA 2020

## Belantamab Mafodotin (GSK'916) BCMA-targeted ADC



- Prior PI, IMiD and CD38+ monoclonal antibody
- 3+ prior lines of therapy
- 2.5 mg/kg or 3.4 mg/kg q3weeks
- ORR 31% (2.5 mg) and 34% (3.4 mg)
- 24% grades 3 and 4 keratopathy
- Median PFS 2.9 and 4.9 months
- Frequent dose omissions and interruptions
- Unknown duration of keratopathy
- Complex co-management with ophthalmology

*Lonial S. et al. Lancet Oncology 2020 21:207*

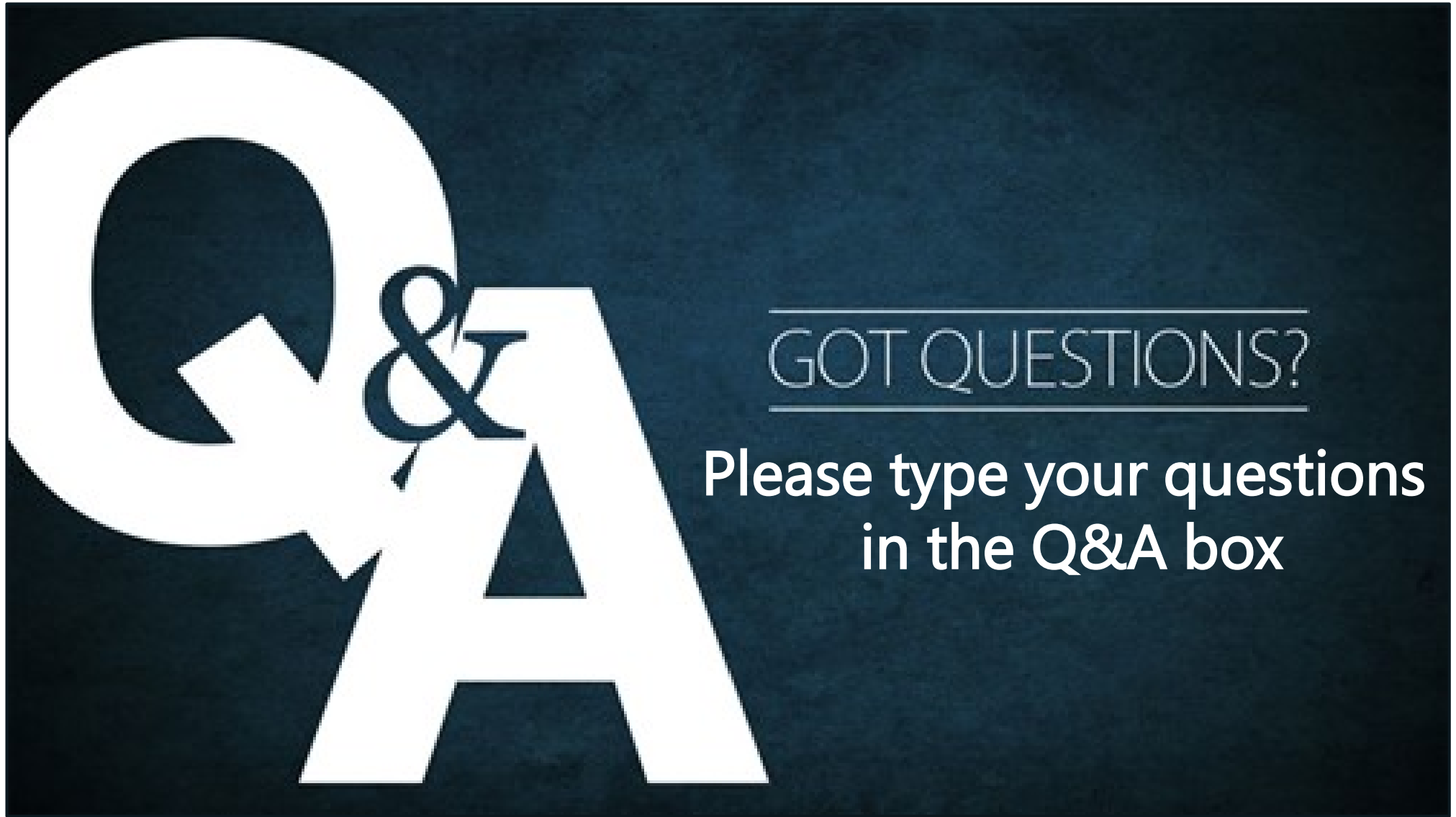
## BCMA targeting strategies

	Response	Safety	Considerations
T-cell Engagers	<ul style="list-style-type: none"> <li>• ?, likely &gt;70%</li> </ul>	<ul style="list-style-type: none"> <li>• CRS, cytopenias, infections</li> </ul>	<ul style="list-style-type: none"> <li>• Optimal dose and schedule of administration unclear.</li> <li>• Potential for prolonged and combined therapy.</li> </ul>
CAR-T cells	<ul style="list-style-type: none"> <li>• &gt;80% in dara-refractory patients</li> </ul>	<ul style="list-style-type: none"> <li>• CRS, Neurotoxicity, infections, cytopenias</li> </ul>	<ul style="list-style-type: none"> <li>• Hospital-based treatment,</li> <li>• Few centers able to deliver treatment, scalability .</li> <li>• Possibly short-living remissions</li> </ul>
ADC	<ul style="list-style-type: none"> <li>• 32% in Dara-refr</li> </ul>	<ul style="list-style-type: none"> <li>• Corneal toxicity</li> <li>• Thrombocytopenia</li> </ul>	<ul style="list-style-type: none"> <li>• Amenable to outpatient non-hospital setting treatment.</li> <li>• Ophthalmologist co-management can get complex.</li> </ul>

**Near absent data on employing different BCMA-targeting strategy after treatment failure.**

# Thank you!

[ljcosta@uabmc.edu](mailto:ljcosta@uabmc.edu)



GOT QUESTIONS?

Please type your questions  
in the Q&A box



# INTERNATIONAL MYELOMA FOUNDATION

Improving Lives. **Finding the Cure.**

# “Living Well with Myeloma”

Beth Faiman, PhD, CNP  
Cleveland Clinic Taussig  
Cancer Institute



# Be the Commander of Your Galactic Journey Constellation of Symptoms

**Presenter: Beth Faiman**

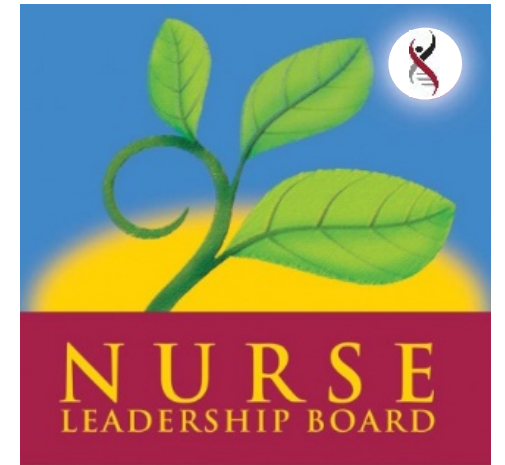
**PhD, RN, MSN, APRN-BC, AOCN®**

**Cleveland Clinic Taussig Cancer Institute**

***Location: Southern USA, RCW***

***Date: October 10, 2020***

**You are in the  
Commander's Chair**



# Myeloma and Treatments Both Contribute to How You Feel

Constellation of Symptoms

## Myeloma cells in excess can cause symptoms

- Calcium elevation
- Renal dysfunction
- Anemia
- Bone pain
- Fatigue
- Infection
- Other symptoms

## Treatments for myeloma kill myeloma cells but can cause symptoms

- Myelosuppression
- Peripheral neuropathy
- Diarrhea
- Fatigue
- Deep vein thrombosis
- Infection (eg, shingles)
- Other symptoms

How You Feel



# Common Side Effects of Myeloma Drugs

(page 1 of 3)

Constellation  
of Symptoms

	“Mides” Immunomodulatory drugs (IMiDS)			“Mibs” Proteasome Inhibitors		
	Thalomid® (thalidomide)	Revlimid® (lenalidomide)	Pomalyst® (pomalidomide)	Velcade® (bortezomib)	Kyprolis® (carfilzomib)	Ninlaro® (ixazomib)
Neuropathy (PN)	✓			✓*		✓
Thrombosis (DVT, PE)	✓ more with dex	✓ more with dex	✓ more with dex		✓	
Myelosuppression	✓ neutropenia	✓ anemia, neutropenia, thrombocytopenia	✓ neutropenia	✓ thrombocytopenia	✓ neutropenia, thrombocytopenia	✓ thrombocytopenia
Cardiopulmonary	✓ slow heart rate		✓ shortness of breath	✓ hypotension	✓ shortness of breath, hypertension	
Fatigue, weakness	✓ (incl sedation)	✓	✓	✓	✓	✓ (incl sedation)
Renal	✓	✓	✓		✓	
Rash	✓	✓	✓			
GI disturbance	✓ constipation	✓ diarrhea, constipation	✓ diarrhea, constipation	✓ nausea, vomiting, diarrhea	✓ nausea, vomiting, diarrhea, constipation	✓ diarrhea, constipation, nausea

\*Subcutaneous administration reduces rates of PN

dex = dexamethasone; DVT = deep vein thrombosis; GI = gastrointestinal PE = pulmonary embolism; PN = peripheral neuropathy

Prescribing Information: thalidomide, lenalidomide, pomalidomide, bortezomib, carfilzomib, ixazomib.



# Common Side Effects of Myeloma Drugs

(page 2 of 3)

Constellation  
of Symptoms

	"mAbs" Monoclonal Antibodies			mAb drug conjugate	HDAC inhibitor	SINE Compound
	Darzalex® (daratumumab)	Empliciti® (elotuzumab)	Sarclisa® (Isatuximab)	Blenrep® (Belantamab Mafodotin)	Farydak® (panobinostat)	Xpovio® (selinexor)
<b>Neuropathy (PN)</b>						
<b>Infusion reaction</b>	✓	✓	✓	✓		
<b>Myelosuppression</b>	✓ neutropenia, thrombocytopenia		✓ neutropenia	✓ neutropenia, thrombocytopenia	✓ neutropenia, thrombocytopenia	✓ thrombocytopenia
<b>Cardiopulmonary</b>					✓ arrhythmias, ischemia	
<b>Fatigue, weakness</b>	✓	✓			✓	✓
<b>Rash</b>						✓ hyponatremia
<b>GI disturbance</b>	✓ diarrhea	✓ diarrhea, nausea	✓ diarrhea, nausea	✓ nausea	✓ severe diarrhea, nausea, vomiting	✓ anorexia, nausea, vomiting, diarrhea

GI = gastrointestinal; neutropenia = low white blood cell count; PN = peripheral neuropathy; thrombocytopenia = low platelets.

Prescribing Information: daratumumab, elotuzumab, isatuximab, belantamab mafodotin, panobinostat, selinexor.

# Common Side Effects of Myeloma Drugs

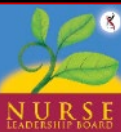
(page 3 of 3)

Constellation  
of Symptoms

	Anthracycline	Alkylating Agents	
	Doxil® (liposomal doxorubicin)	Cytosan® NEOSAR® (cyclophosphamide)	ALKERAN® EVOMELA® (melphalan)
<b>Neuropathy (PN)</b>			
<b>Infusion reaction</b>	✓ acute infusion reactions	✓ hypersensitivity	✓ hypersensitivity
<b>Myelosuppression</b>	✓ neutropenia	✓ anemia, myelosuppression, immunosuppression	✓ severe bone marrow suppression
<b>Cardiopulmonary</b>		✓ myocarditis, arrythmias, pneumonitis	
<b>Fatigue, weakness</b>	✓	✓	✓
<b>Rash</b>	✓	✓	
<b>GI disturbance</b>	✓ diarrhea, nausea, vomiting, constipation	✓ nausea, vomiting, diarrhea	✓ nausea, vomiting, diarrhea, oral mucositis


GI = gastrointestinal; neutropenia = low white blood cell count; PN = peripheral neuropathy; thrombocytopenia = low platelets.

Prescribing Information: doxorubicin, cyclophosphamide, melphalan.



# Steroid Side Effects and Management

## Steroid Side Effects

- 
- Irritability, mood swings, depression
  - Difficulty sleeping (insomnia), fatigue
  - Increased risk of infections, heart disease
  - Muscle weakness, cramping
  - Blurred vision, cataracts
  - Flushing/sweating
  - Stomach bloating, hiccups, heartburn, ulcers, or gas
  - Weight gain, hair thinning/loss, skin rashes
  - Increase in blood sugar levels, diabetes
  - Increase in blood pressure, water retention

## Managing Steroid Side Effects

- Consistent schedule (AM vs. PM)
- Take with food
- Stomach discomfort: Over-the-counter or prescription medications
- Medications to prevent shingles, thrush, or other infections

**Steroids help kill myeloma cells. Do not stop or adjust steroid doses without discussing it with your health care provider.**



# Fatigue, Depression, and Anxiety

- All can effect quality of life and relationships
- Sources include anemia, pain, reduced activity, insomnia, treatment toxicity, bone marrow suppression

## Management

- Exercise (walking, yoga, etc)
- Proper rest
- Support (social network, support group, professional counseling, etc)
- Prayer, meditation, spiritual support
- Mindfulness-based stress reduction
- Medications
- Massage, aroma therapy
- Supplements: ginseng
- Transfusion, if indicated
- Effective management of other symptoms

**At least 70% of patients experience fatigue, but only 20% tell their provider. Let your provider know about symptoms that are not well controlled or thoughts of self harm.**

# Infection Prevention & Treatment

- Compromised immune function comes from multiple myeloma and from treatment
- Good personal hygiene (skin, oral)
- Environmental control (wash hands, avoid crowds and sick people, etc)
- Growth factor (Neupogen [filgrastim])
- Immunizations (NO live vaccines)
- Medications (antibacterial, antiviral)
  - New research: for patients receiving active myeloma therapy, levofloxacin 500 mg once daily for 12 weeks reduced infection (fevers, death) (ASH 2017 #903)

**Report fever of more than 100.4°F, shaking chills even without fever, dizziness, shortness of breath, low blood pressure to HCP as directed.**  
**Infection is serious for myeloma patients!**



# Deep Vein Thrombosis (DVT ) and Pulmonary Embolism (PE)

Constellation  
of Symptoms

- Risk Factors

- Personal or family history
- Lifestyle (obesity, smoking, inactivity)
- Medical (medications, surgery)

- Symptoms

- Swelling, tightness, ache/pain, change in color or temperature
- Chest or shoulder pain
- Shortness of breath, difficult/labored breathing
- Anxiety
- Rapid heart rate

- Provider Management

- Adjusting medications and schedules (weekly steroids, types of chemo)
- Prescribing blood-thinning medications according to assessed risk (aspirin, warfarin, heparin or Direct Oral Anticoagulant[DOAC])
- Anti-embolism stockings (elastic stockings)

- Self Management

- Lifestyle changes (stop smoking, weight mgmt)
- Activity; Moving frequently when sitting long periods; Travel precautions

**Report DVT and PE symptoms immediately!**  
**These are considered a medical emergency & require immediate care.**



# GI Symptoms: Prevention and Management

Constellation  
of Symptoms

- **Diarrhea potential causes**
  - Laxatives, antacids with magnesium
  - Antibiotics, antidepressants, others
  - Milk thistle, aloe, cayenne, saw palmetto, ginseng
  - Sugar substitutes in sugar free gum
- **Take anti-diarrheal medication**
  - Imodium®, Lomotil®, or Colestid if recommended
  - Fiber binding agents – Metamucil®, Citrucel®, Benefiber®
  - Welchol® if recommended
- **Increase fluid intake:** Avoid caffeinated, carbonated, or heavily sugared beverages; works with fiber; also good for kidneys
- **Constipation potential causes**
  - Opioid pain relievers, antidepressants, heart or blood pressure medications, others
  - Supplements: Calcium, Iron, vitamin D (rarely), vitamin B-12 deficiency
- **Increase fiber**
  - Fruits, vegetables, high fiber whole grain foods
  - Fiber binding agents – Metamucil®, Citrucel®, Benefiber®
- **Nausea potential causes**
  - Supplements: Iron, Multi (iron-containing), others
- **Management**
  - Antiemetics, if prescribed
  - Frequent small meals
  - Avoid fatty, fried, spicy, or very sweet foods
  - Increase high-calorie foods to avoid weight loss

**Discuss GI issues with health care providers to identify causes of and make adjustments to medications and supplements.**

# Understanding Changes to Kidney/ Renal Function

Constellation  
of Symptoms

## Risk Factors

- Active multiple myeloma (light chains, high calcium)
- Other medical issues (ex: Diabetes, dehydration, infection)
- Medications (MM treatment, antibiotics, contrast dye)

## Prevention

- Drink, Drink, Drink
- Avoid medications that can cause further kidney injury, when possible (examples: contrast dyes, NSAIDs)



## Treatment

- Treatment for myeloma
- Hydration
- Dialysis



**Many myeloma patients will experience kidney function problems at some point; it is important to protect your kidney function early and over time.**

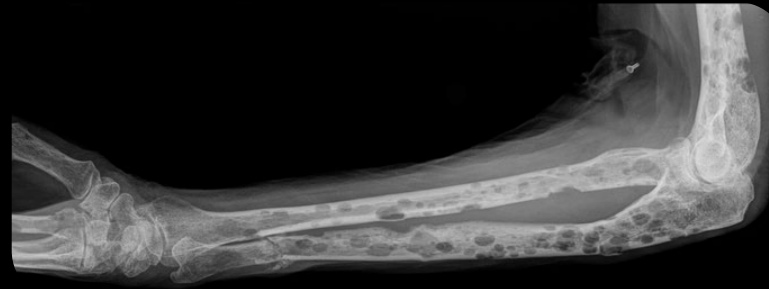
NSAID = non-steroidal anti-inflammatory.

Brigle K, et al. *CJON*. 2017;21(5)suppl:60-76. Faiman B, et al. *CJON*. 2017;21(5)suppl:19-36. Faiman B, et al. *CJON*. 2011;15suppl:66-76.

# Myeloma Cells Can Lead to Bone Damage

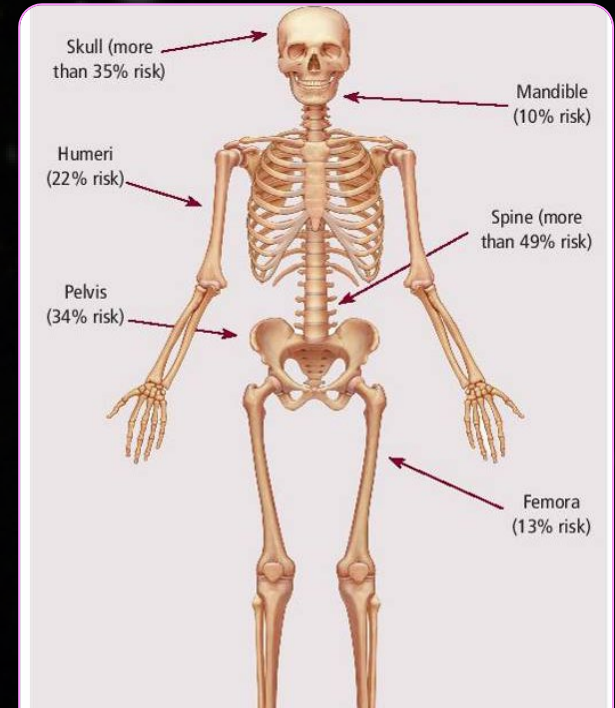
Approximately 85% of myeloma patients develop bone disease

- Protecting bone health
  - Nutrition
  - Weight-bearing activity
  - Medications
    - Vitamin D
    - Calcium (if approved by doctor)
    - Bone strengthening agents: Zometa® zoledronic acid, Aredia (pamidronate), or Xgeva® denosumab
- Report new pain to your health care provider



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**Most myeloma patients will experience bone involvement at some point; it is important to protect your bone health**



**Figure 1. Bones at Highest Risk of Being Affected by Multiple Myeloma**

# Peripheral Neuropathy (PN) Management

- Peripheral neuropathy: damage to nerves in extremities (hands, feet, or limbs)
  - Numbness
  - Tingling
  - Prickling sensations
  - Sensitivity to touch
  - Muscle weakness
  - Burning pain or cold sensation
- Prevention / management:
  - Bortezomib once-weekly or subcutaneous administration
  - Massage area with cocoa butter regularly
  - Supplements:
    - B-complex vitamins (B1, B6, B12)
    - Folic acid, and/or amino acids but do not take on day of Velcade® (bortezomib) infusion
  - Safe environment: rugs, furnishings, shoes
- If PN worsens, your HCP may:
  - Change your treatment
  - Prescribe oral or topical pain medication
  - Suggest physical therapy

**Report symptoms of peripheral neuropathy early to your health care provider; nerve damage from PN can be permanent if unaddressed**



# Pain Prevention and Management

- Pain can significantly compromise quality of life
- Sources of pain include bone disease, neuropathy and medical procedures
- Management
  - Prevent pain when possible
    - Bone strengtheners to decrease fracture risk; antiviral to prevent shingles; sedation before procedures
  - Intervention depends on source of pain
  - May include medications, activity, surgical intervention, radiation therapy, etc
  - Complementary and integrative medicine (supplements, acupuncture, etc)

**Tell your health care provider about any new bone pain or chronic pain that is not adequately controlled**



# You are Not Alone



INTERNATIONAL  
**MYELOMA**  
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## Questions?



GOT QUESTIONS?

Please type your questions  
in the Q&A box



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# REGIONAL

## COMMUNITY WORKSHOP