

# How I Treat Myeloma: Transplant Ineligible Patient

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- **No conflicts to disclose**

# How I Treat

## *Transplant Ineligible Newly Diagnosed MM*

**High Risk**



**Intermediate Risk**



**Standard Risk**



## New MM

- No melphalan
- No thalidomide
- No high-dose dex
- **No twice-weekly or IV bortezomib**
- Target CR only in high risk



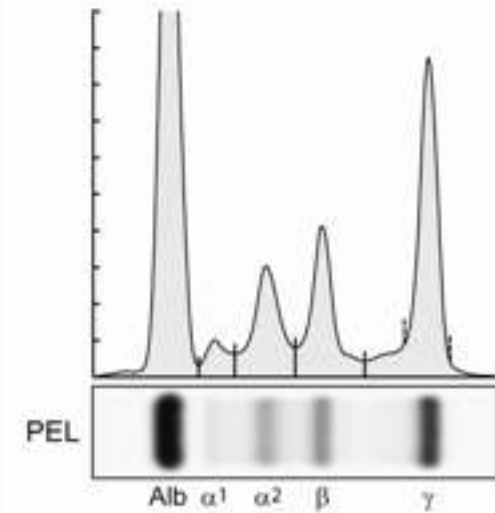
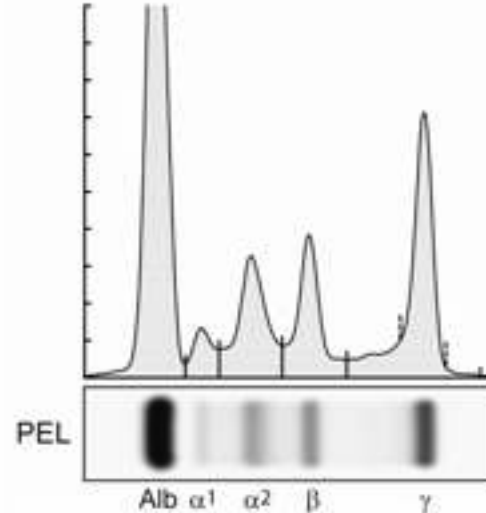
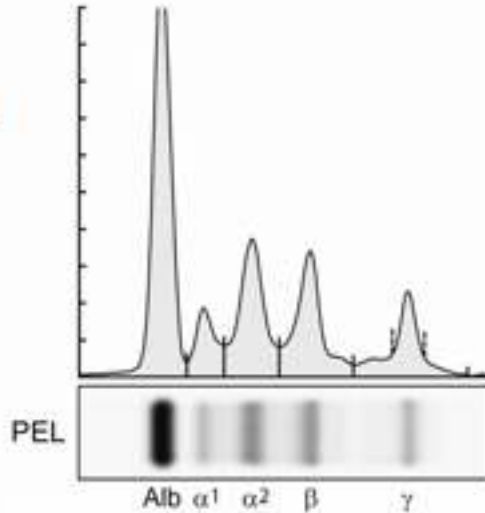
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MGUS

SMM

MM

Monoclonal Protein



Bone Marrow/ M Protein

<10% plasma cells  
**AND** <3gm/dL M protein

≥10% plasma cells **OR** ≥3 gm/dL M protein

≥10% plasma cells

Clinical Picture

Asymptomatic  
No end-organ damage\*

Asymptomatic  
No end-organ damage

Symptomatic  
End-organ damage present

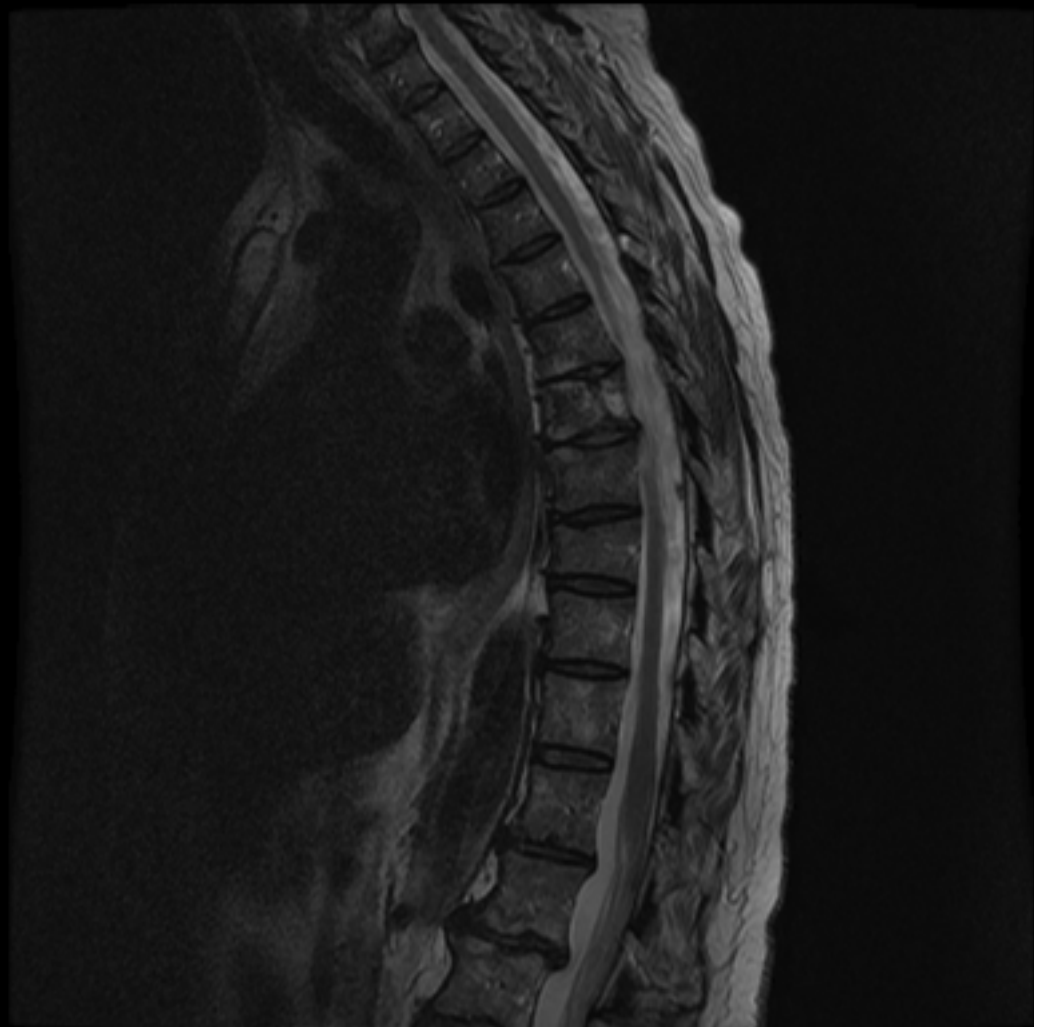
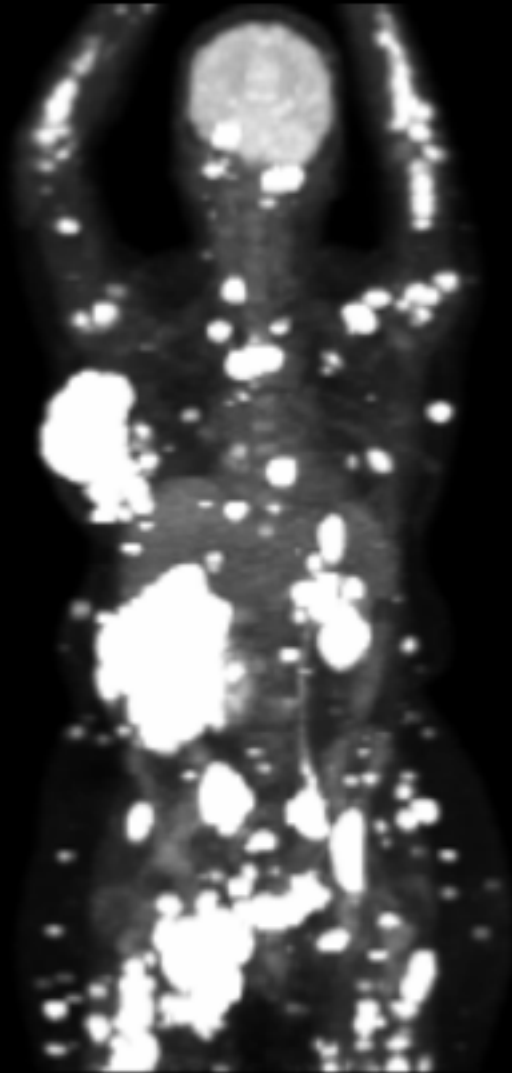
Therapy

Observation only

Observation only

Therapy required

\*Hypercalcemia, anemia, renal failure or lytic bone lesions attributable to plasma cell disorder



## mSMART 2.0 Risk Stratification

### High-Risk

- FISH
  - Del 17p
  - t(14;16)
  - t(14;20)
- GEP defined high-risk

### Intermediate-Risk

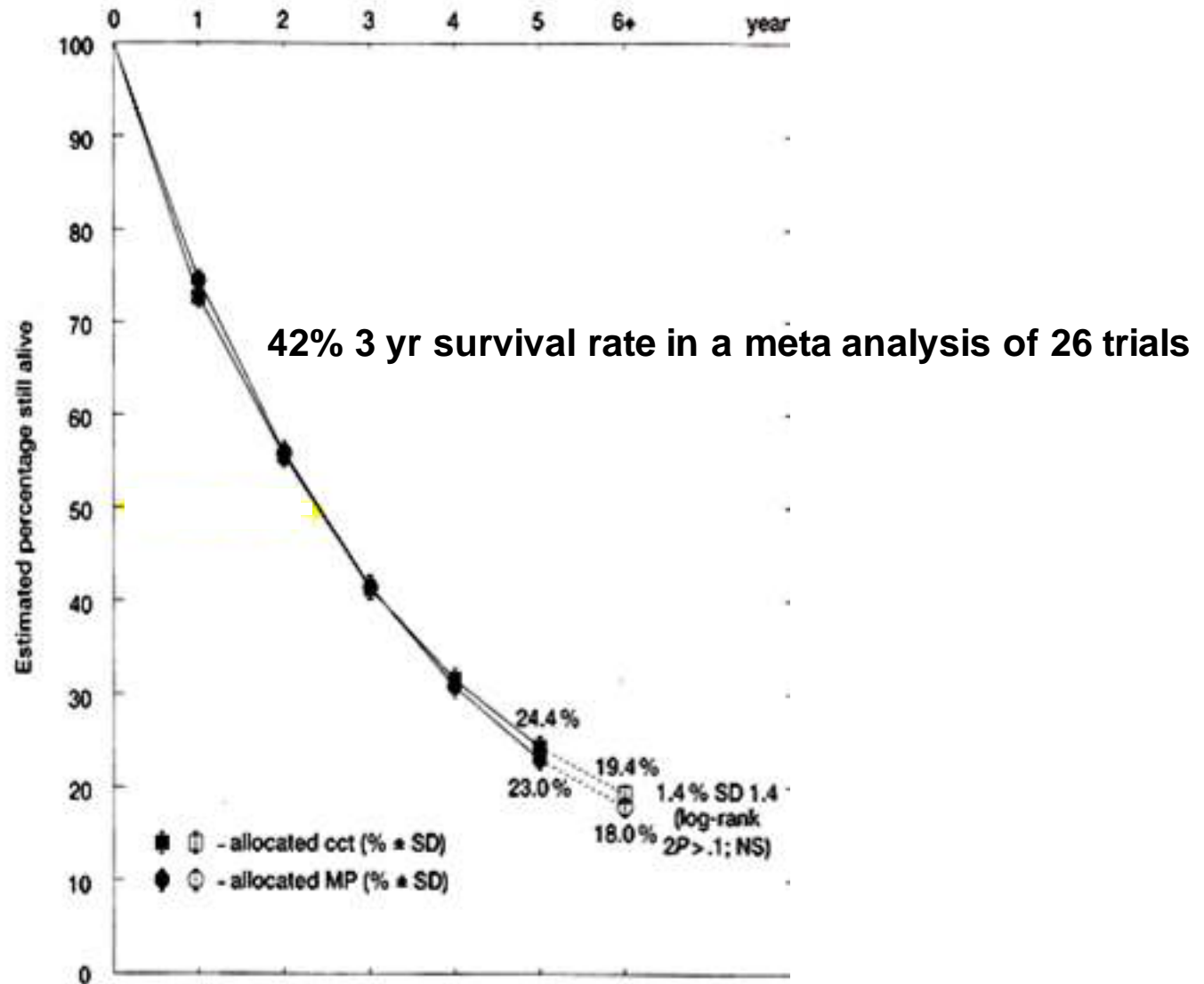
- FISH
  - t(4;14)
- Cytogenetic Deletion 13 or hypodiploidy
- PCLI  $\geq 3\%$

### Standard-Risk

- All others including:
- Hyperdiploid
  - t(11;14)
  - t(6;14)



## MP: No longer an option



# What are the current options?

# Alkylator-Steroid + IMiD

- **MPT**
- **MPR**
  
- **CTD**
- **CRD**

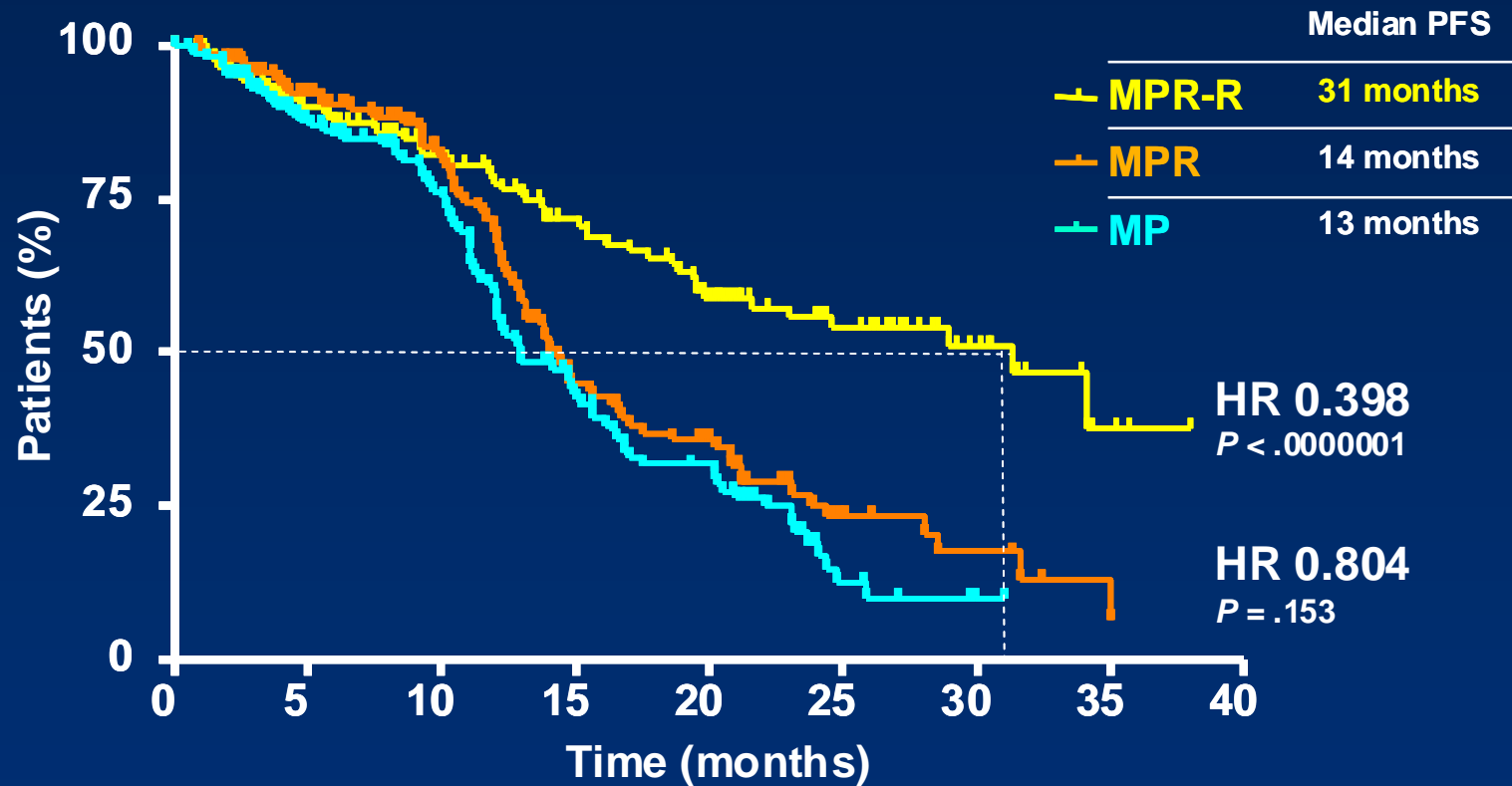
## Treatment of elderly MM patients (MPT vs MP)

<b>Study</b>	<b>Regimen</b>	<b>N</b>	<b>TTP PFS/EFS</b>	<b>Overall Survival (months)</b>	<b>3 year OS (%)</b>
<b>Palumbo (Blood 2008)</b>	<b>MPT MP</b>	<b>129 126</b>	<b>22 15</b>	<b>45 vs 48 P=0.79</b>	<b>~65% (MPT)</b>
<b>Facon (Lancet 2007)</b>	<b>MPT MP</b>	<b>125 196</b>	<b>28 18</b>	<b>52 vs 33 P=0.0006</b>	<b>~65% (MPT)</b>
<b>Hulin (JCO 2009)</b>	<b>MPT MP</b>	<b>113 116</b>	<b>24 19</b>	<b>44 vs 29 P=0.03</b>	<b>~55% (MPT)**</b>
<b>Wijermans (JCO 2010)</b>	<b>MPT MP</b>	<b>165 168</b>	<b>13 9</b>	<b>40 vs 31 P=0.05</b>	<b>~55% (MPT)</b>
<b>Waage (Blood 2010)</b>	<b>MPT MP</b>	<b>182 175</b>	<b>15 14</b>	<b>29 vs 32 P=0.46</b>	<b>~43% (MPT)</b>
<b>Beksac (Eur J Hematol 2011)</b>	<b>MPT MP</b>	<b>58 57</b>	<b>21 14</b>	<b>26 vs 28 P=0.65</b>	<b>~30% (MPT)</b>

## Adverse Events with MPT in the Elderly

	MP	MPT
Grade $\geq 2$ neuropathy	5%	21%

# MP versus MPR



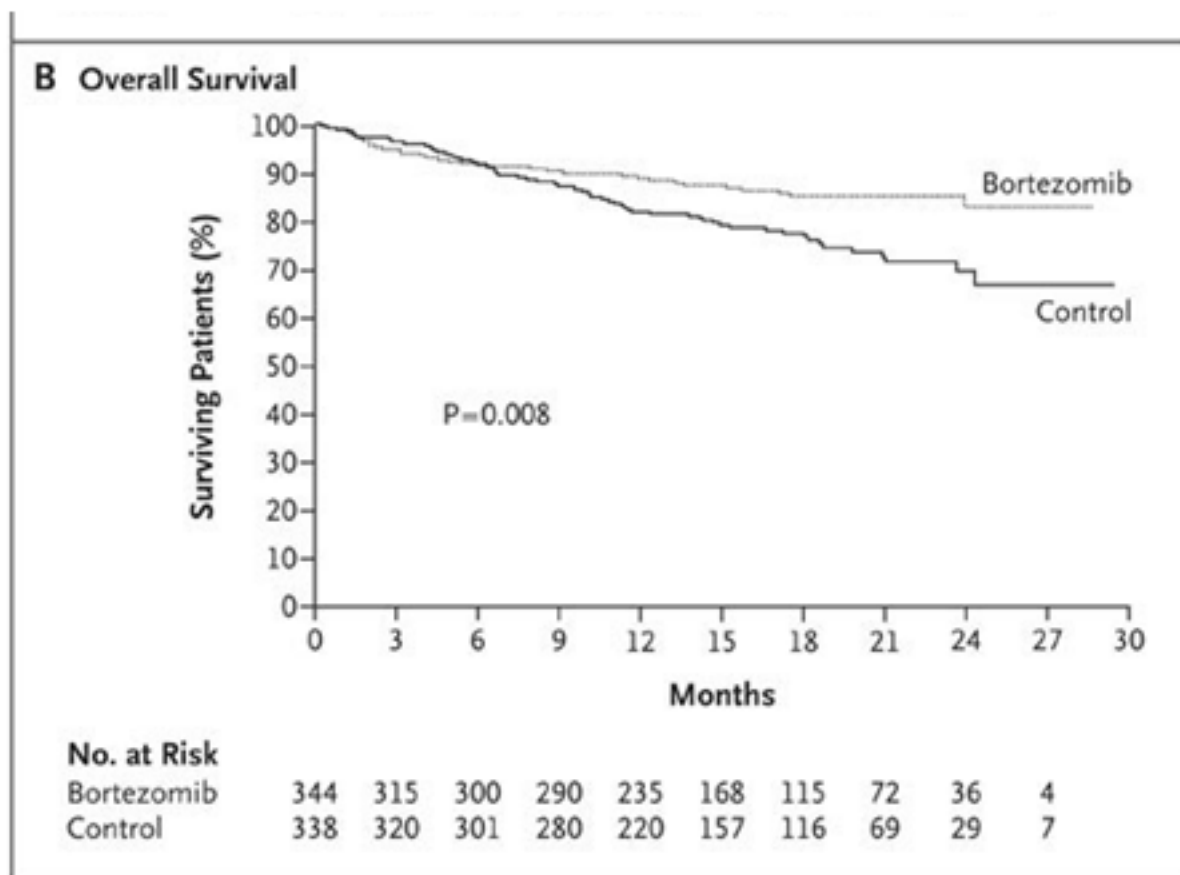
Median follow-up 25 months

\*Analysis based on data up to May 2010

# Alkylator-Steroid + Bortezomib

- **VMP**
- **VCD (CyBorD)**

### VISTA Trial: VMP vs MP: Overall Survival



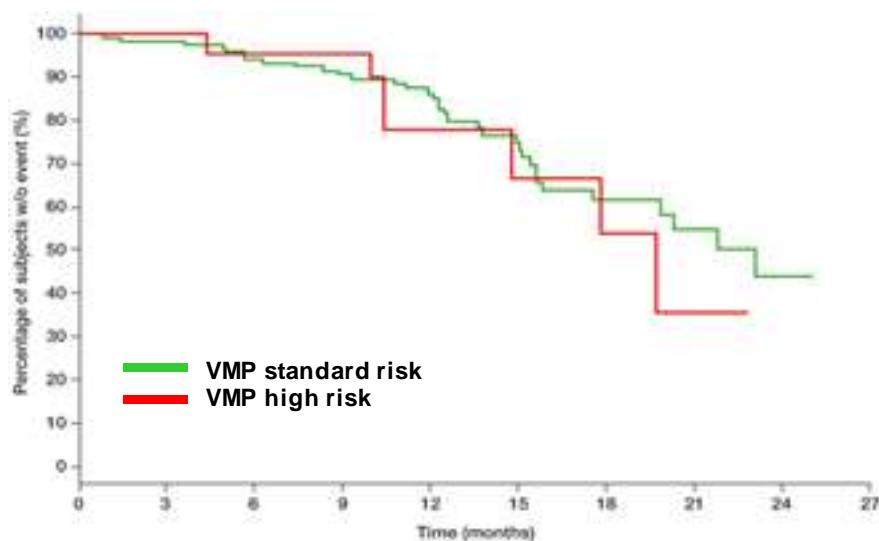


## VISTA TRIAL: Adverse Events (Safety Population)

		VMP		MP		
Peripheral sensory neuropathy	151 (44)	43 (13)	1 (<1)	16 (5)	0	0
Neuralgia	121 (36)	28 (8)	2 (1)	5 (1)	1 (<1)	0
Dizziness	56 (16)	7 (2)	0	37 (11)	1 (<1)	0
Other conditions						
Pyrexia	99 (29)	8 (2)	2 (1)	64 (19)	6 (2)	2 (1)
Fatigue	98 (29)	23 (7)	2 (1)	86 (26)	7 (2)	0
Anorexia	77 (23)	9 (3)	1 (<1)	34 (10)	4 (1)	0
Asthenia	73 (21)	20 (6)	1 (<1)	60 (18)	9 (3)	0

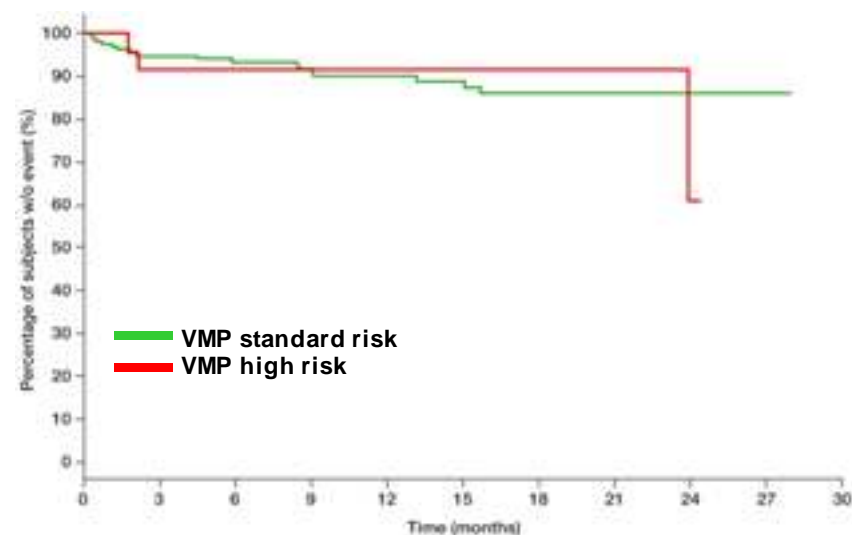
# VMP in High/Intermediate Risk MM

## TTP



VMP standard risk (N=142): 23.1 months (34 events)  
 VMP high risk (N=26): 19.8 months (7 events)  
 HR = 1.297 (95% CI: 0.55, 3.06)

## OS



VMP standard risk (N=142): not reached (16 events)  
 VMP high risk (N=26): not reached (3 events)  
 HR = 1.009 (95% CI: 0.278, 3.663)

# Non-Melphalan Containing Regimens

- **Rd**
- **VRD, VTD, VTP**

## Treatment of elderly MM patients (Phase III trials)

Study	Regimen	N	TTP PFS/EFS	Overall Survival (months)	3 year OS (%)
Palumbo (Blood 2008)	MPT MP	129 126	22 15	45 vs 48 <i>P</i> =0.79	~60% (MPT)
Facon (Lancet 2007)	MPT MP	125 196	28 18	52 vs 33 <i>P</i> =0.0006	~65% (MPT)
Hulin (JCO 2009)	MPT MP	113 116	24 19	44 vs 29 <i>P</i> =0.03	~55% (MPT)**
Wijermans (JCO 2010)	MPT MP	165 168	13 9	40 vs 31 <i>P</i> =0.05	~55% (MPT)
Waage (Blood 2010)	MPT MP	182 175	15 14	29 vs 32 <i>P</i> =0.46	~43% (MPT)
San Miguel (JCO 2010)	VMP MP	344 338	24 17	NR* vs 43 <i>P</i> <0.001	69% (VMP)
Rajkumar (Lancet Oncol 2010)	Rd RD	222 223	25 19	NR*	75% (Rd age ≥65)

## Overall survival with Rd in patients $\geq 70$

Toxicity	3 yr OS	3 yr OS excluding SCT
Jacobus, EHA 2010	73%	70%
Gay, EHA 2010	70%	65%

## VRD

- 66 evaluable pts

CR	29%	}	67%*
nCR	11%		
VGPR	27%		

PR (33%)

- Overall response rate: 100%

## VCD (CyBorD)

Response, %	EVOLUTION		Mayo Clinic
	VRD (n = 42)	VCD (n = 49)	VCD (n = 63)
CR/nCR	40%	37%	41%
≥ VGPR	50%	45%	60%
ORR (≥ PR)	83%	84%	90%

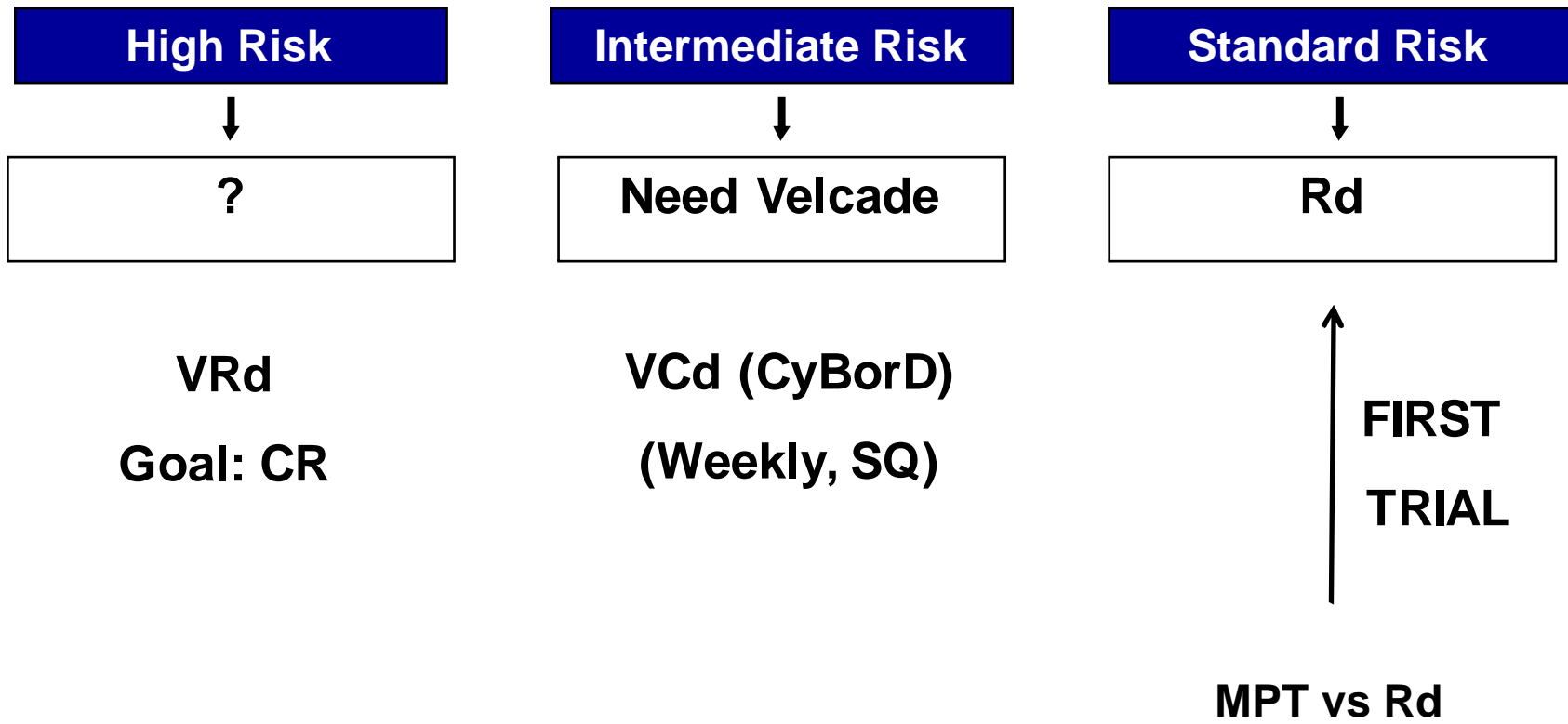
# Choice of Initial Therapy Non-Transplant Candidates

Regimen	Route	DVT Risk	Neuropathy risk
MPT/CTDa	Oral	Yes	Yes
VMP/VCD	IV	No	Yes
Rd	Oral	Yes	No
VRd, VTD, VTP	IV	Yes	Yes



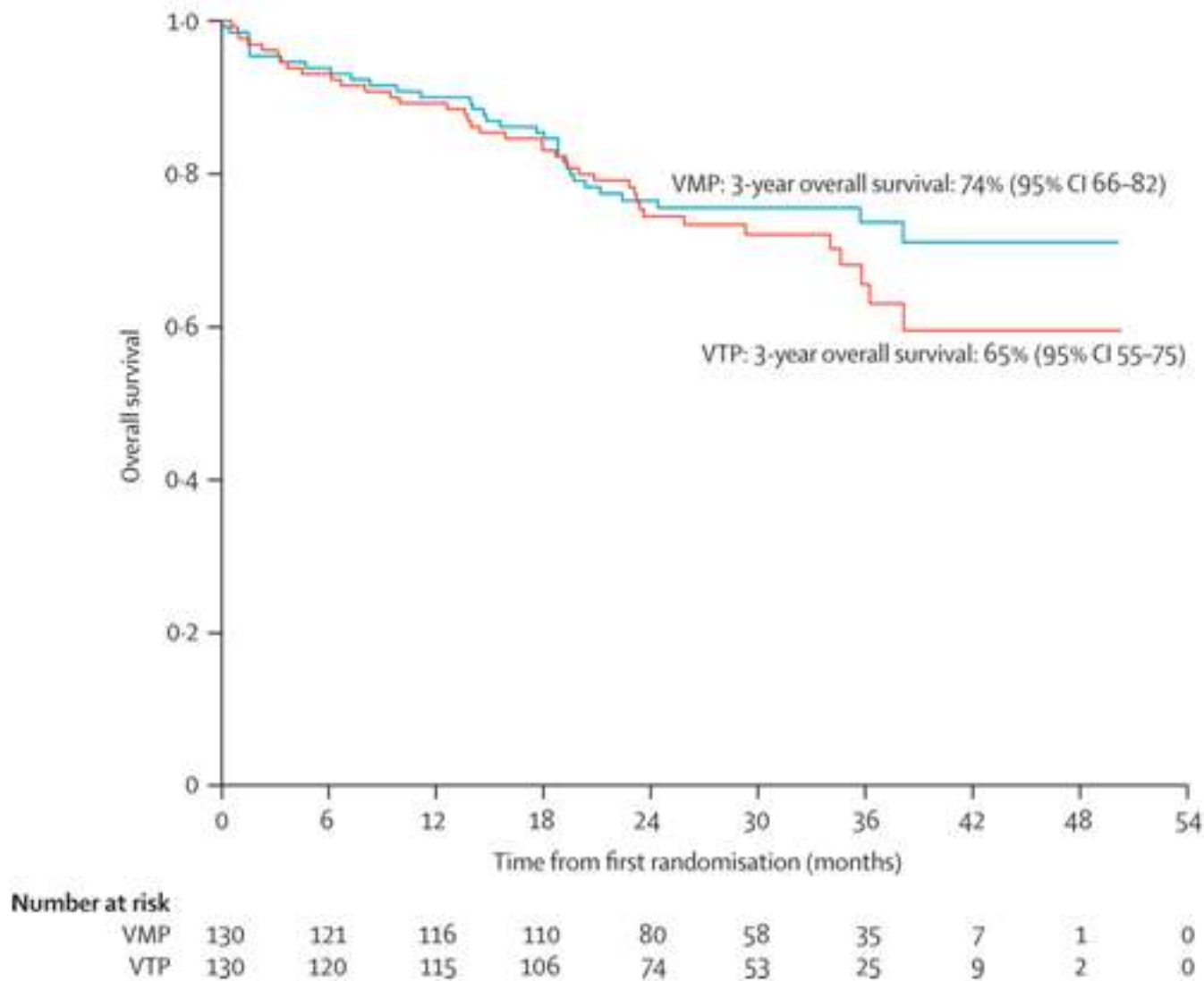
# How I Treat

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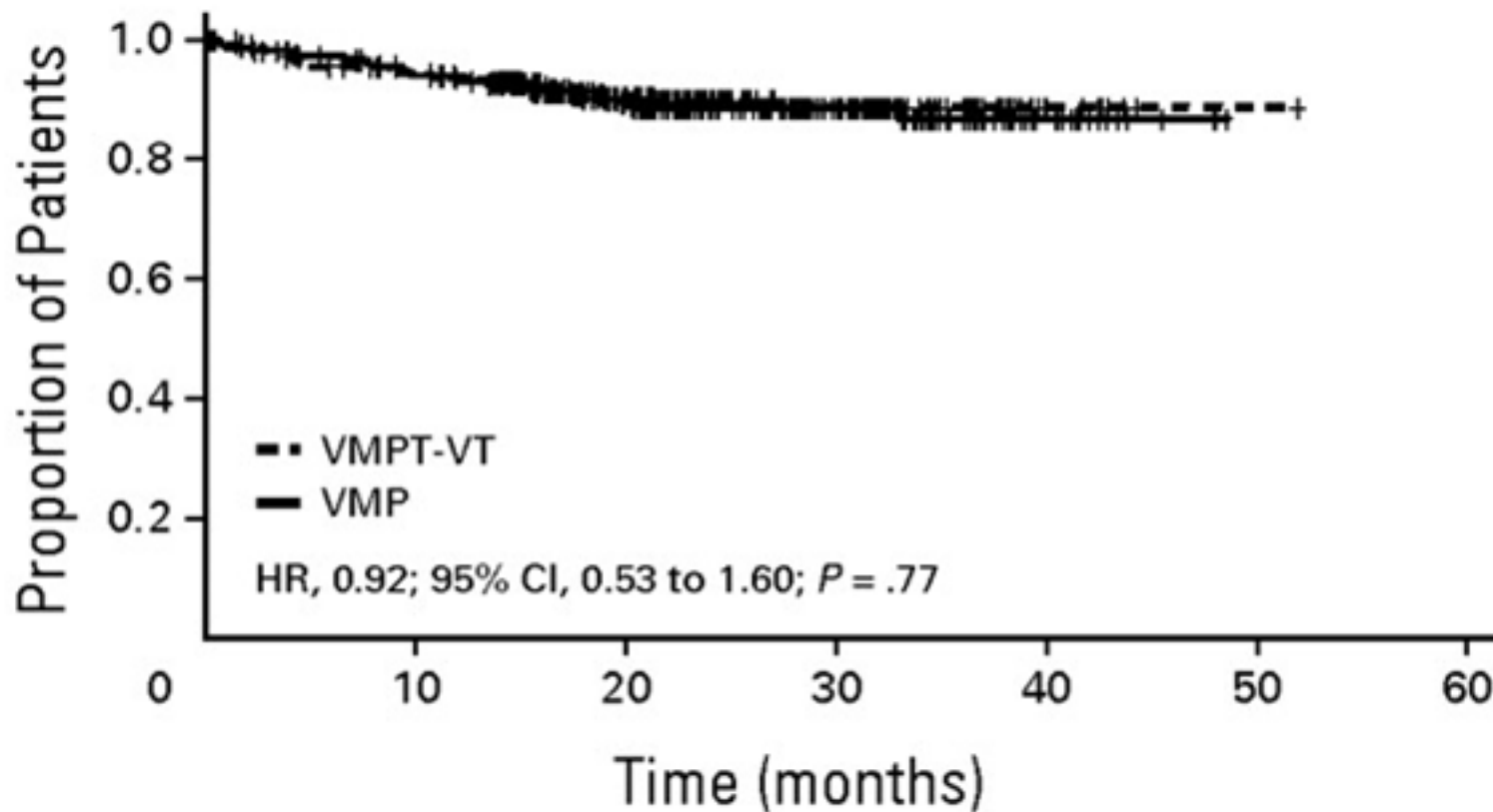
# What schedule of bortezomib?

# Excellent results with once-weekly Bortezomib



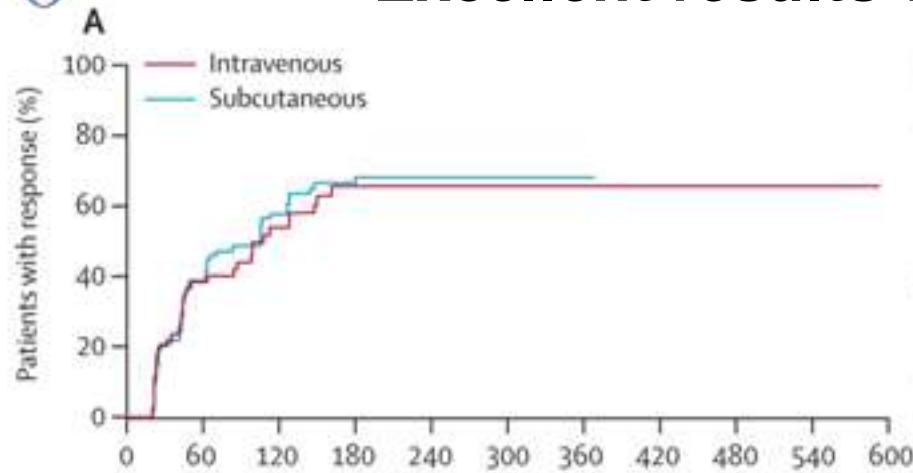
# Excellent results with once-weekly Bortezomib

## VMP versus VMPT



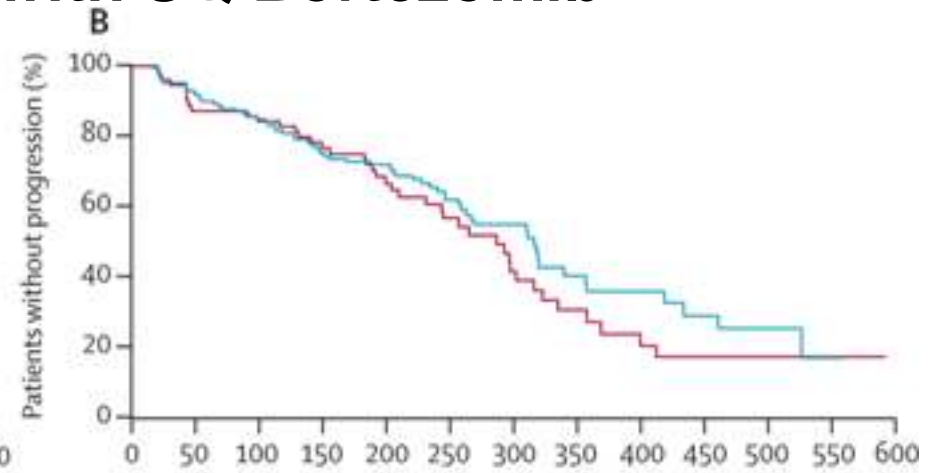
No. at risk					
VMPT-VT	254	225	148	68	8
VMP	257	225	157	76	18

# Excellent results with SQ Bortezomib

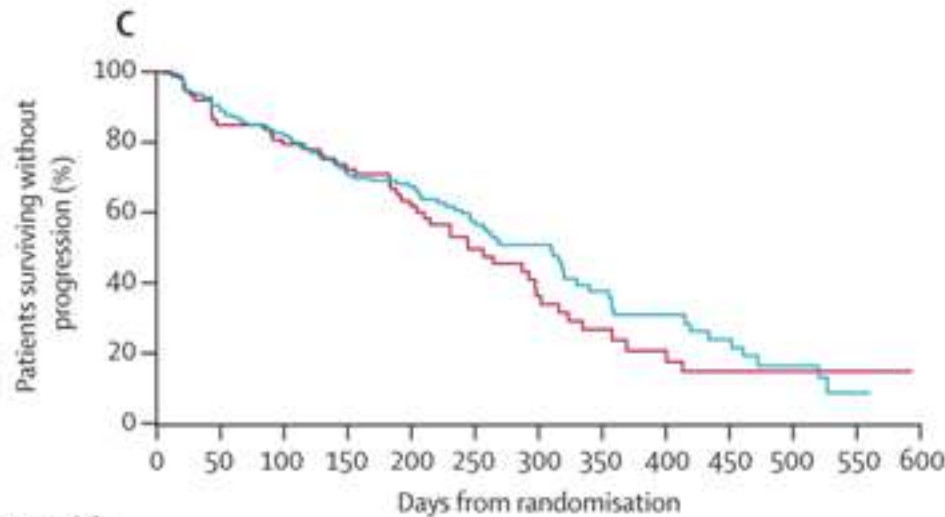


**Number at risk**

Intravenous	73	35	22	12	7	4	2	2	2	2	0
Subcutaneous	145	70	32	19	11	3	1	0	0	0	0

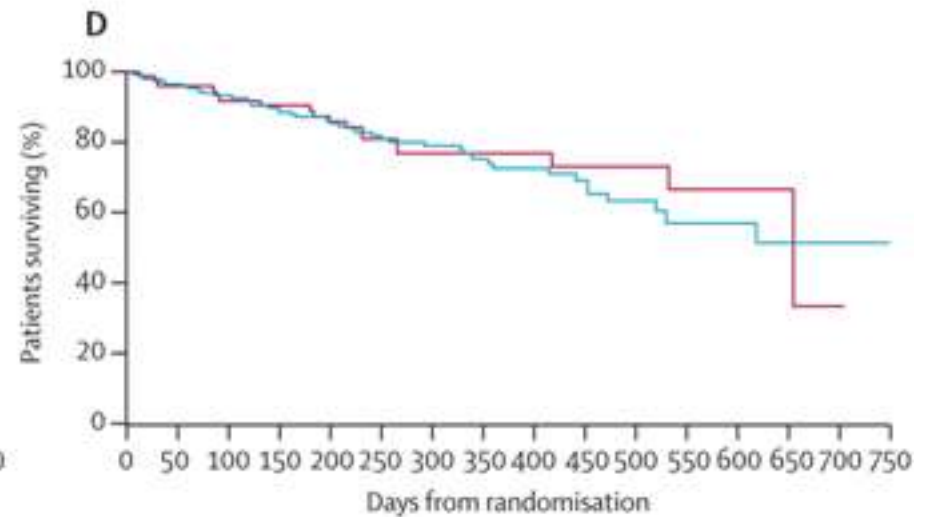


	74	60	56	50	36	24	16	10	7	5	4	3	1
	148	126	109	93	72	51	32	18	13	8	5	2	1



**Number at risk**

Intravenous	74	61	57	51	38	24	16	10	7	5	4	3	1
Subcutaneous	148	129	116	97	76	55	36	22	16	10	6	2	1

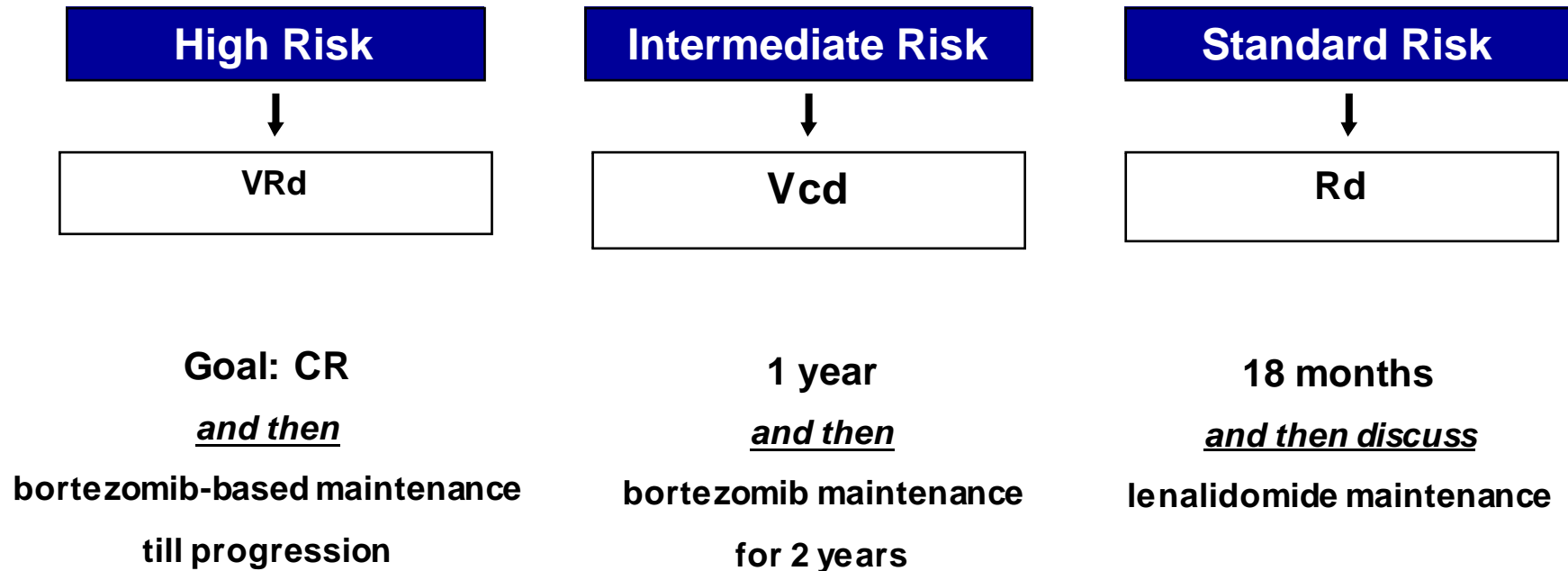


	74	70	67	64	53	42	33	29	26	19	12	9	4	2	1	0
	148	141	136	125	107	88	71	59	47	37	26	15	12	4	2	0

# How long to treat?

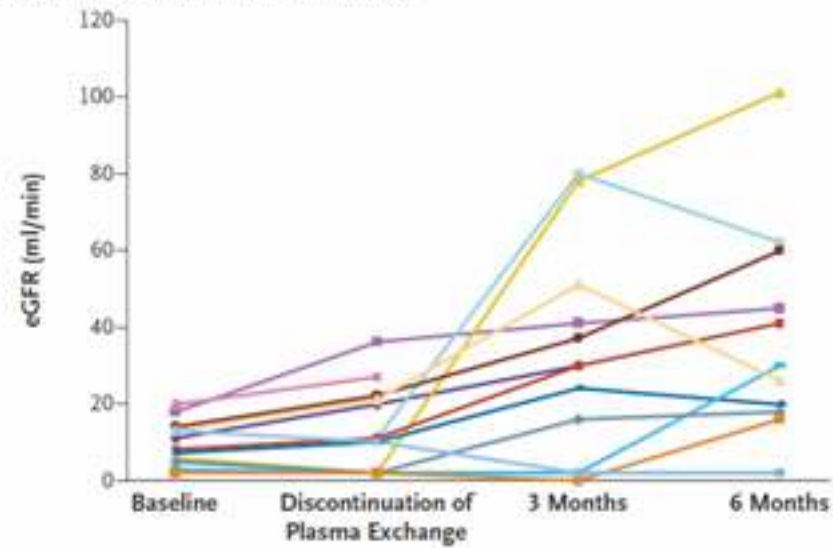
# How I Treat

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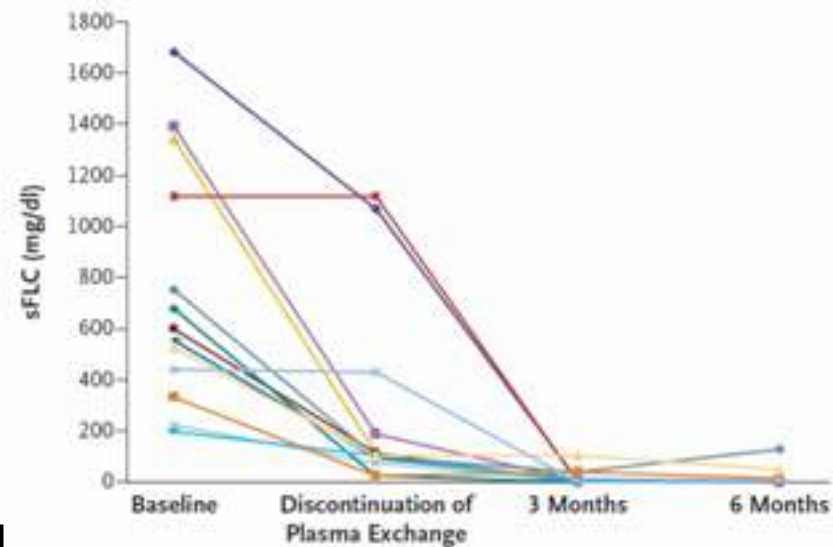


# Acute Renal Failure

**A Estimated Glomerular Filtration Rate**



**B Serum Free Light Chains**





# Supportive Care

- **Pamidronate (Aredia) or Zoledronic acid (Zometa)**
- **Antibiotics**
- **Anticoagulants**
- **Prevention of gastritis**
- **Pain control**
- **Kyphoplasty or Vertebroplasty**
- **Radiation**

**The FINAL slide**