WELCOME & INTRODUCTIONS

Multiple Myeloma: Know Your Treatment Options

To register or to view the BCC schedule, visit www.LLS.org/bcc.

Georgia Blood Cancer Conference	Wisconsin Blood Cancer Conference
Atlanta, GA	Milwaukee, WI
September 7, 2019	**September 21, 2019**

BEATING CANCER IS IN OUR BLOOD.

Program will begin shortly

LEUKEMIA & LYMPHOMA SOCIETY®

1

2

Disclosures

- Consulting: BlueBird Biotech, Bristol-Myers Squibb, Celgene, Fate Therapeutics, Janssen, Juno, Karyopharm, Magenta Therapeutics, Sanofi, Takeda
- Honoraria: BlueBird Biotech, Bristol-Myers Squibb, Celgene, Fate Therapeutics, Janssen, Juno, Karyopharm, Magenta Therapeutics, Medscape, Takeda
- I will be discussing non-FDA approved indications during my presentation.

3

Questions

- Is there a “best therapy” for multiple myeloma patients requiring therapy?
- Should a MM patient receive therapy for a fixed duration of time or until progression?
- What is the correlation, if any, between the duration of maintenance therapy and clinical benefit?
- What is the role of high dose melphalan and autologous stem cell transplant (ASCT) in MM?
- What is the role of consolidation therapy after ASCT?

4

What can be done to prolong response and improve survival after initial therapy for multiple myeloma?

- Maintenance
  - Easy to deliver, convenient for the patient, modest toxicity, improve PFS and ideally OS when compared with re-treatment at relapse , *Michelic et al Leukemia 2007*
- Does improved PFS result in improved OS?
- How long should maintenance be given?
  - Fixed time versus until progression
- Should all MM patients be given maintenance after primary therapy?

5

Definitions

- **Progression-free survival:** The length of time during and after the treatment of a disease, such as cancer, that a patient lives with the disease but it does not get worse. In a clinical trial, measuring the progression-free survival is one way to see how well a new treatment works.
- **Overall survival:** The length of time from either the date of diagnosis or the start of treatment for a disease, such as cancer, that patients diagnosed with the disease are still alive. In a clinical trial, measuring the overall survival is one way to see how well a new treatment works.

https://www.cancer.gov/publications/dictionaries/cancer-terms/

6

Definitions

- **Median overall survival:** The length of time from either the date of diagnosis or the start of treatment for a disease, such as cancer, that half of the patients in a group of patients diagnosed with the disease are still alive. In a clinical trial, measuring the median overall survival is one way to see how well a new treatment works. Also called median survival.

https://www.cancer.gov/publications/dictionaries/cancer-terms/

7

Definitions

- **Hazard Ratio:** A measure of how often a particular event happens in one group compared to how often it happens in another group, over time. In cancer research, hazard ratios are often used in clinical trials to measure survival at any point in time in a group of patients who have been given a specific treatment compared to a control group given another treatment or a placebo. A hazard ratio of one means that there is no difference in survival between the two groups. A hazard ratio of greater than one or less than one means that survival was better in one of the groups.

https://www.cancer.gov/publications/dictionaries/cancer-terms/

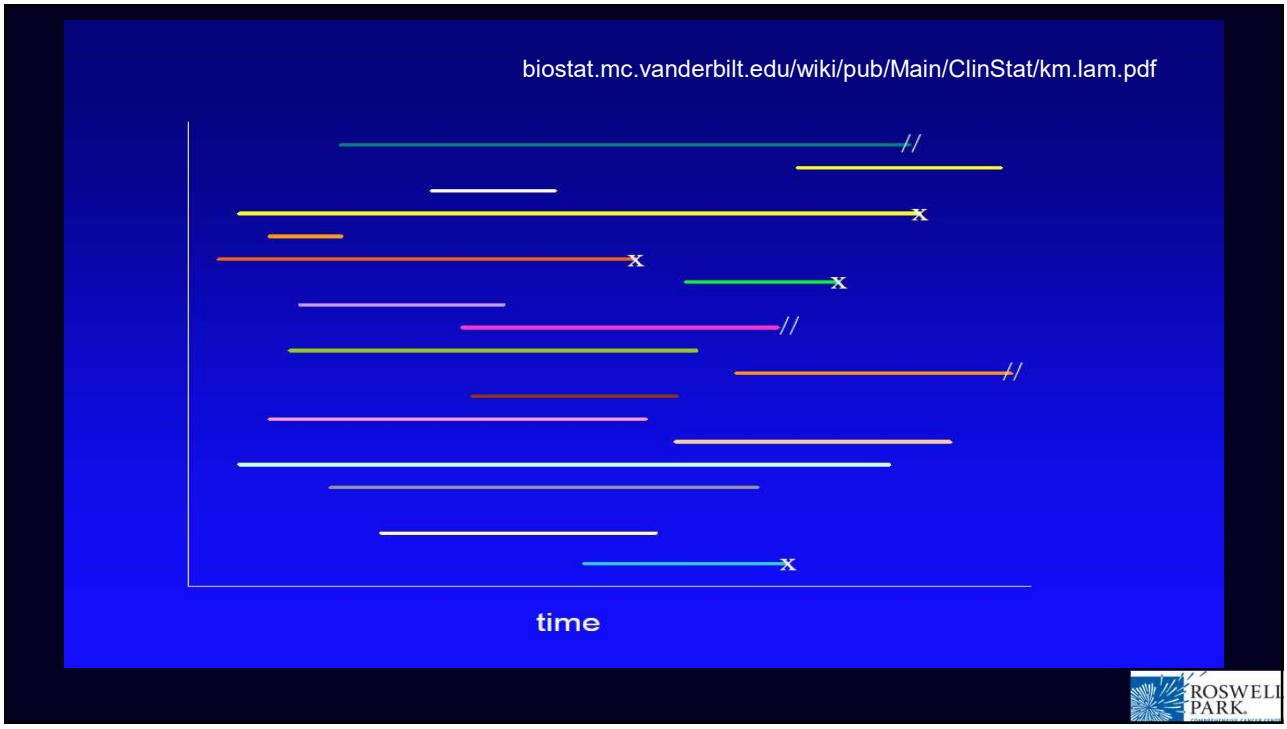
8

What is a Kaplan Meier Analysis?

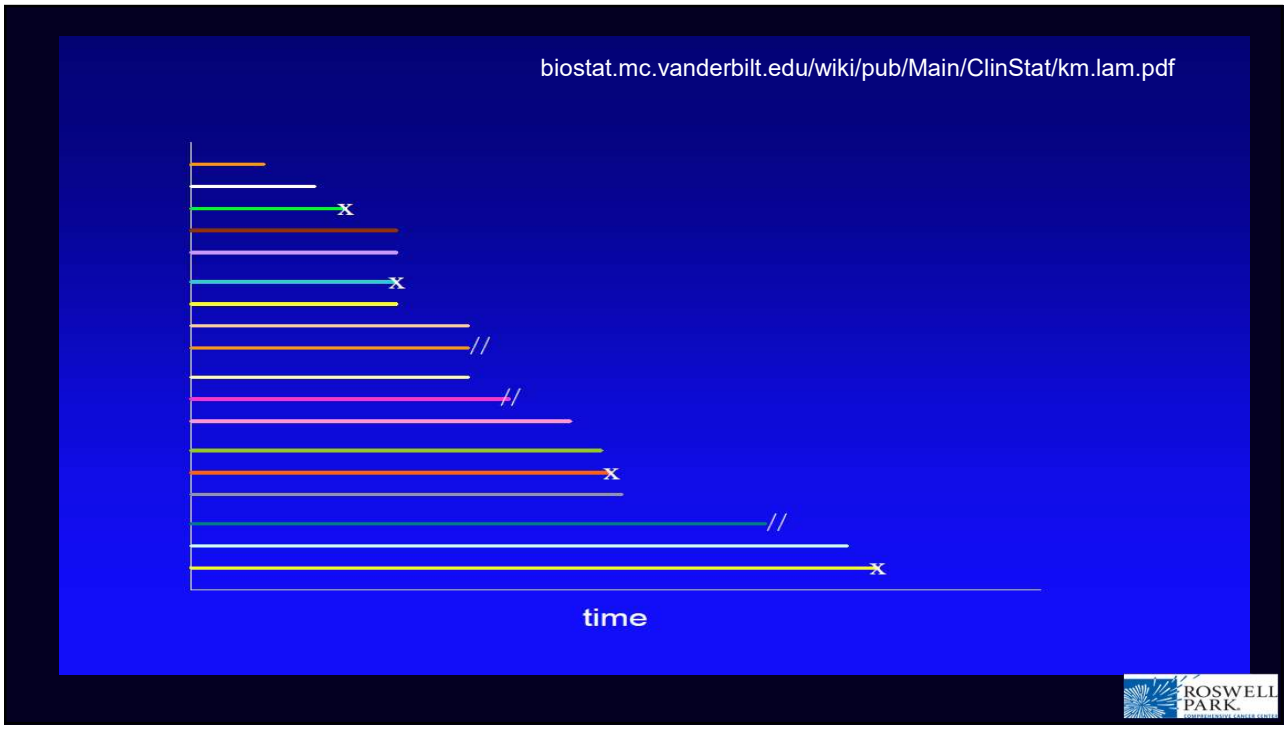
- Used to estimate a population's disease progression or survival
- If all patients are followed until progression or death, the curve is estimated by calculating the fraction of patients surviving over time
- However, patients may drop out for any reason, move away, decline therapy, have an adverse event, become lost to follow-up
- A Kaplan-Meier analysis is a way to follow survival over time and account for the patients being followed for different lengths of time

biostat.mc.vanderbilt.edu/wiki/pub/Main/ClinStat/km.lam.pdf

9

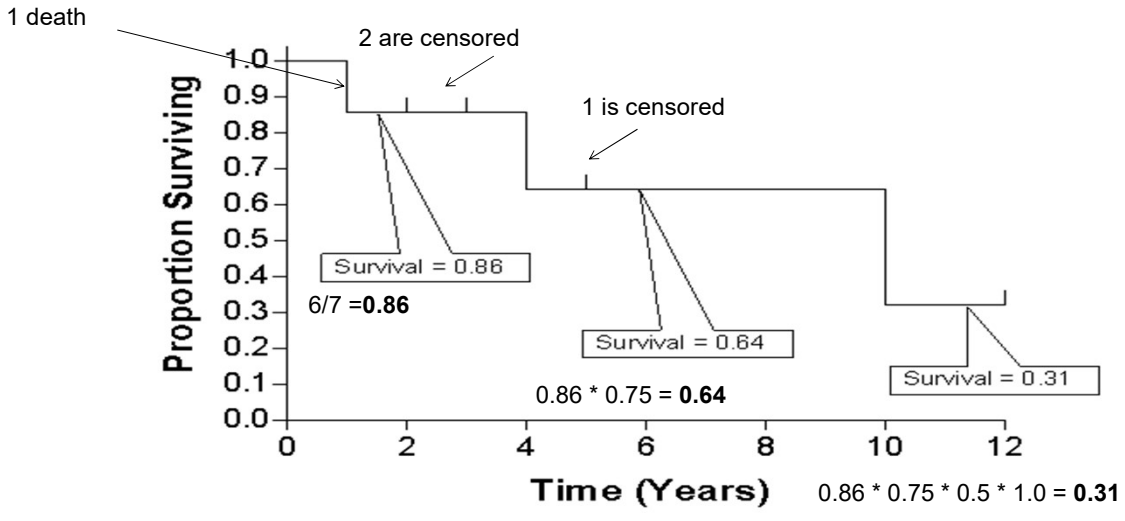


10



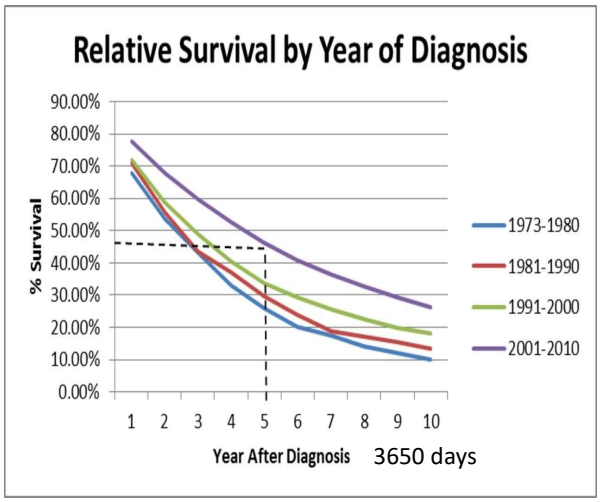
11

What is a Kaplan Meier Analysis?



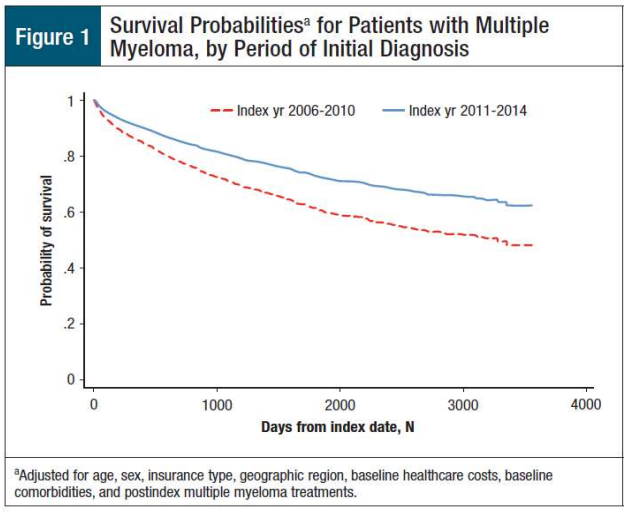
http://cancerguide.org/scurve_km.html

12



David Robinson et al. Blood 2014;124:5676

blood



Maiese EM et al Am Health Drug Benefits 2018 11:39

ROSWELL PARK COMPREHENSIVE CANCER CENTER

13

Multiple Myeloma Presentations

- CRAB Criteria
  - Bone Pain/Back Pain
  - Anemia
  - Renal Failure
    - Rising creatinine
  - Hypercalcemia
    - Fatigue and somnolence
- Myeloma Defining Events
- Age
  - Not always over 65 years old
- Family History
- Race
  - greater incidence in African Americans
- History of MGUS (Monoclonal Gammopathy of Undetermined Significance)
- Other diseases
  - Amyloidosis, unexplained neuropathies
- Asymptomatic
  - Laboratory abnormalities

14

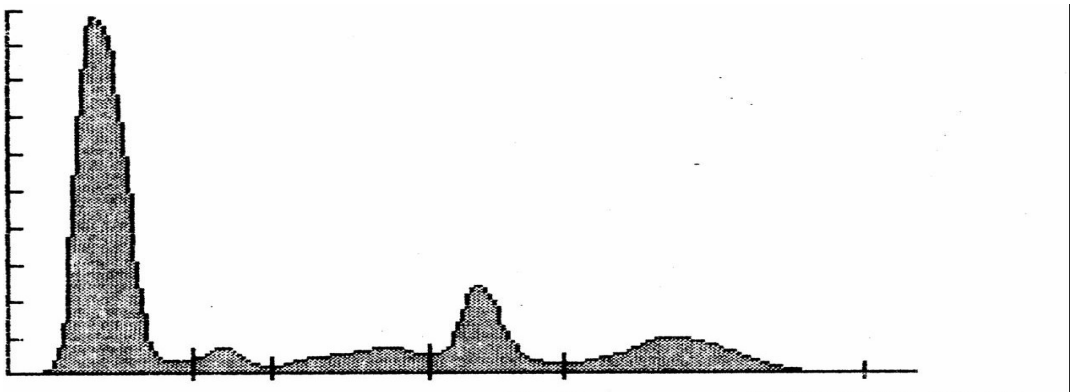
Laboratory/Radiographic Tests

- General Tests
  - Serum Total Protein
    - Not elevated in light chain disease
  - Urine Protein
  - Creatinine
  - Hemoglobin/hematocrit
  - Calcium
  - Albumin
  - LDH
- Specific Tests
  - Immunoglobulin levels
  - Serum Protein Electrophoresis
  - Urine Protein Electrophoresis
    - Random versus 24 hour urine
  - Serum and Urine Immunoelectrophoresis
  - Serum Free Light Chains (Not total light chains!)
    - IgD if Light Chains only
  - Beta-2 Microglobulin
  - Bone marrow test with CD 138 selected FISH
  - Skeletal Survey/MRI for back pain/PET CT Scan
  - Whole body low dose CT
  - Bone Density Scan?
  - Gene Expression Profiling?

ROSWELL PARK

15

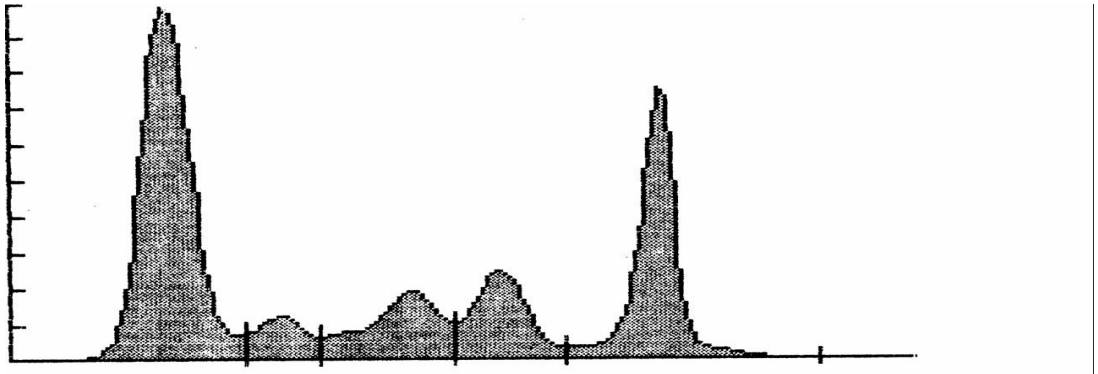
Normal Serum Protein Electrophoresis



FRACTION	%	GM/DL	REFERENCE	RANGE
ALBUMIN	58.64	4.10	3.50 --TO--	5.00
ALPHA 1	4.03	0.28	0.10 --TO--	0.50
ALPHA 2	8.56	0.60	0.50 --TO--	1.10
BETA	14.69	1.03	0.60 --TO--	1.40
GAMMA	14.08	0.99	0.70 --TO--	1.90
TOTAL		7.00	6.30 --TO--	8.20

16

IgG Monoclonal Gammopathy (Myeloma)



FRACTION	%	GM/DL	REFERENCE	RANGE	
ALBUMIN	45.27	3.71	3.50	-TO-	5.00
ALPHA 1	5.27	0.43	0.10	-TO-	0.50
ALPHA 2	12.31	1.01	0.50	-TO-	1.10
BETA	11.85	0.97	0.60	-TO-	1.40
GAMMA	25.30	2.07+	0.70	-TO-	1.90
TOTAL		8.20	6.30	-TO-	8.20

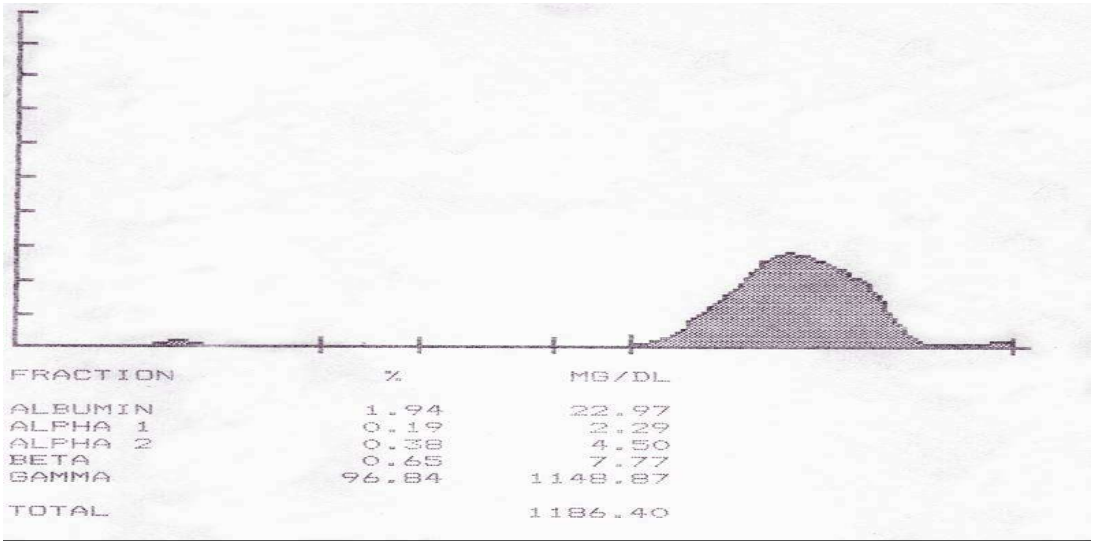
17

Normal Urine Electrophoresis

FRACTION	%	MG/DL
ALBUMIN	42.04	2.40
ALPHA 1	3.82	0.22
ALPHA 2	3.91	0.22
BETA	10.10	0.58
GAMMA	40.13	2.29
TOTAL		5.70

18

Light Chain Disease
Urine Electrophoresis

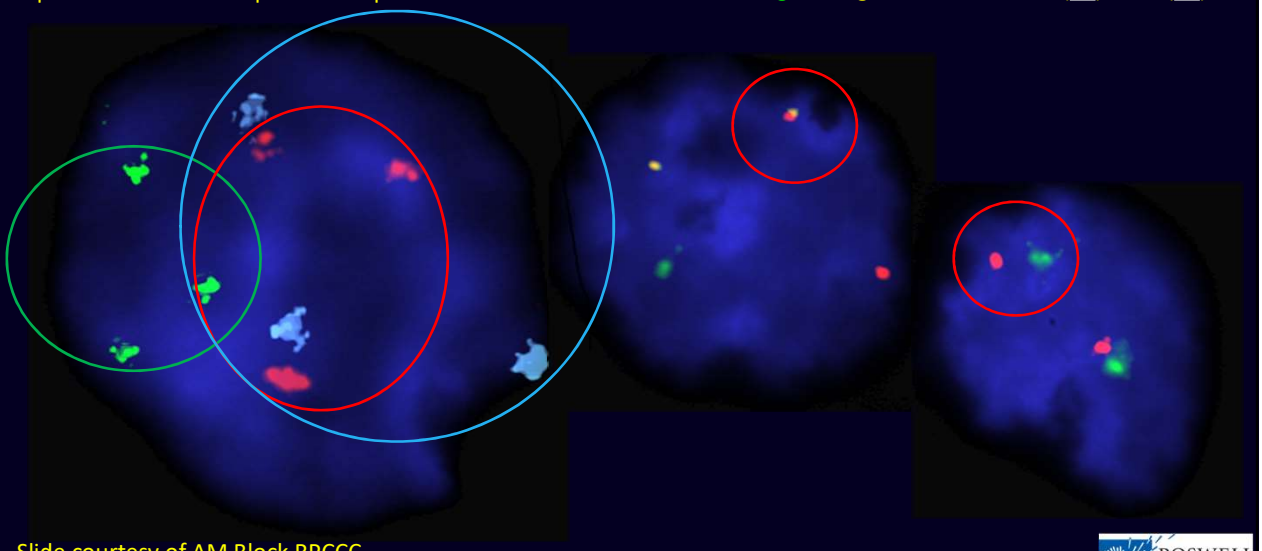


FRACTION	%	MG/DL
ALBUMIN	1.94	22.97
ALPHA 1	0.19	2.29
ALPHA 2	0.38	4.50
BETA	0.65	7.77
GAMMA	96.84	1148.87
TOTAL		1186.40

19

Hyperdiploidy: Odd numbered chromosomes are often duplicated. Probes detecting numerical changes involving #*5* (green), #*9* (aqua) and #*15* (red).
3 copies instead of the expected 2 copies.

IGH/CCND1 rearrangement. Dual color, dual fusion probes
CCND1 at *11q13*: red and IGH: green
Normal: 1 red (normal #*11*) & 1 green (normal #*14*)
2 "fusion" red/green signals: abnormal der(*11*) & der(*14*)

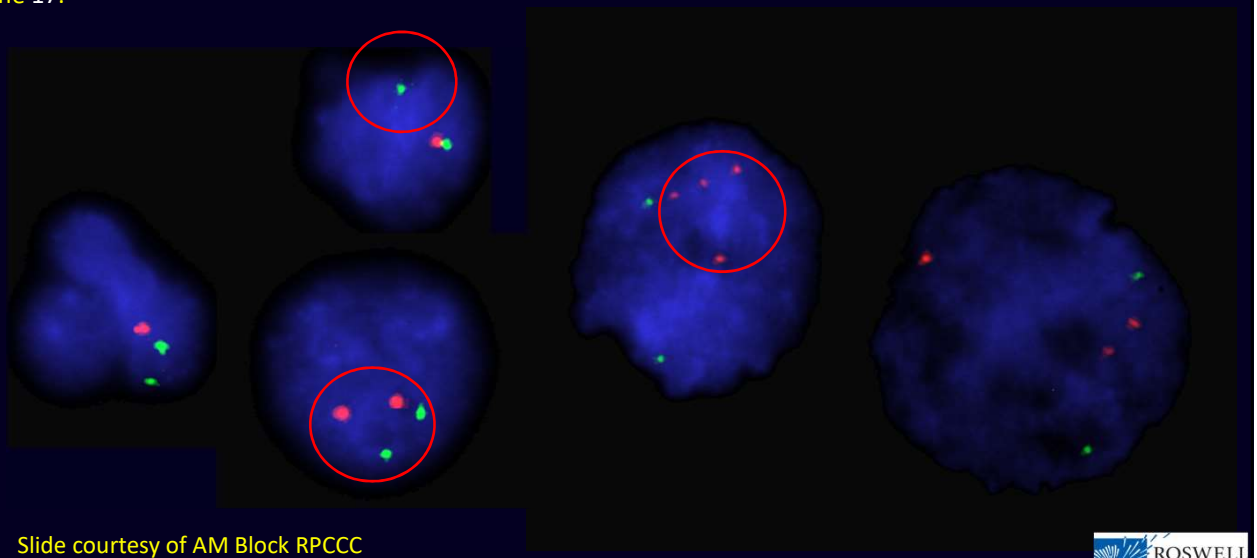


Slide courtesy of AM Block RPCCC

20

Green probe: chromosome #17 centromere, red probe: *P53*. Normal chromosome:one green/one red signal pattern. Deletion: loss of a red signal from one 17.

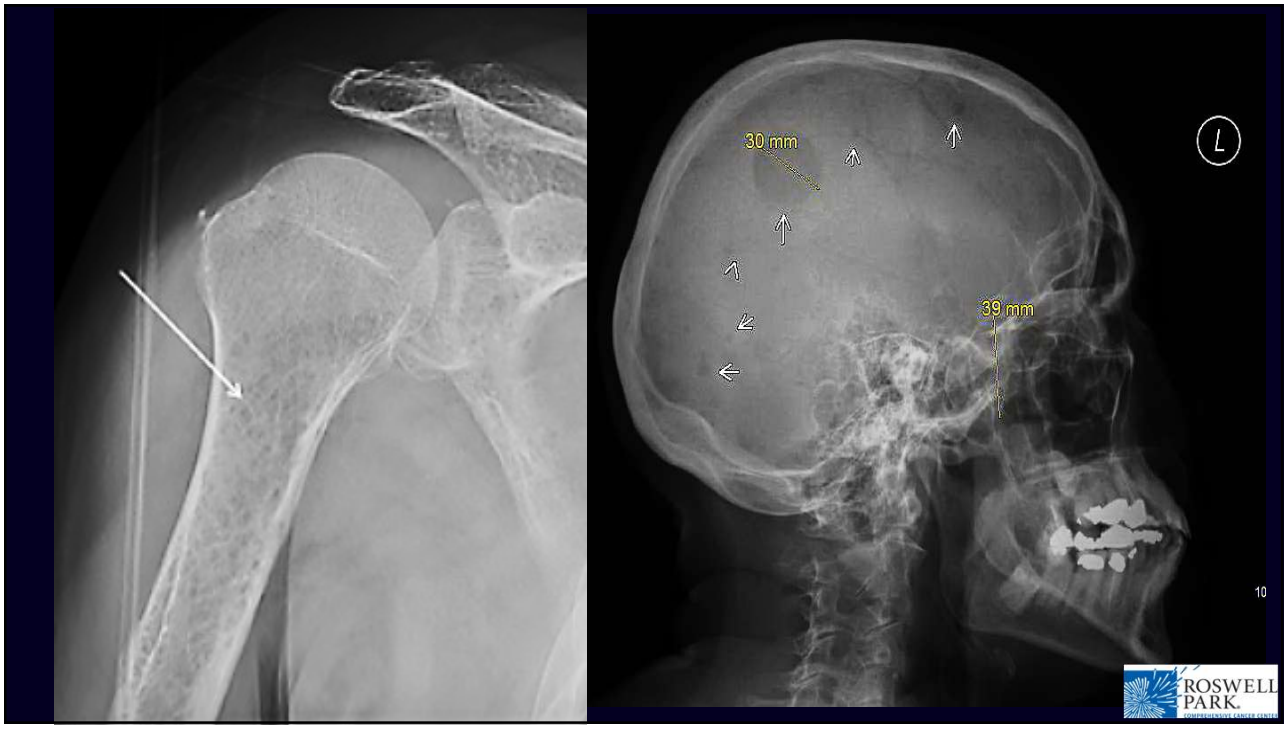
Green probe: CDKN2C; short arm at *1p32.3* & red probe: CKS1B; long arm at *1q21.3*. Gains of the long arm, show 3-4 red signals



Slide courtesy of AM Block RPCCC

ROSWELL PARK

21



22

IMWG Criteria for Diagnosis of MM

MGUS	Smoldering Myeloma	Active or Symptomatic Multiple Myeloma
▪ M protein < 3 g/dL ▪ Clonal plasma cells in BM < 10% ▪ No myeloma-defining events	▪ M protein ≥ 3 g/dL (serum) or ≥ 500 mg/24 hrs (urine) ▪ Clonal plasma cells in BM ≥ 10% to 60% ▪ No myeloma-defining events	▪ Underlying plasma cell proliferative disorder ▪ AND ≥ 1 SLiM-CRAB* features

*S: ≥ 60% (Sixty) clonal bone marrow plasma cells
Li: Serum free Light chain ratio ≥ 100 (involved kappa) or ≤ 0.01 (involved lambda)
M: MRI studies with > 1 focal lesion (> 5 mm in size)
C: Calcium elevation (> 11 mg/dL or > 1 mg/dL higher than ULN)
R: Renal insufficiency (CrCl < 40 mL/min or serum creatinine > 2 mg/dL)
A: Anemia (Hb < 10 g/dL or 2 g/dL < normal)
B: Bone disease (≥ 1 lytic lesions on skeletal radiography, CT, or PET/CT)

Watch ASCO 2019; IMWG Update Early indications for SMM progression and SMM ECOG Trial (Len vs Obs)

Rajkumar. Lancet Oncol. 2014;15:e538

Slide credit: clinicaloptions.com

23

Risk Models for SMM Stratification

Risk Model	Risk of Progression to MM	
Mayo Clinic		Median TTP
≥10% clonal BMPC infiltration	1 risk factor	10 y
≥3 g/dL of serum M-protein	2 risk factors	5 y
sFLC ratio between <0.125 or >8	3 risk factors	1.9 y
Spanish Myeloma		Median TTP
≥95% of aberrant PCs by MFC	No risk factor	NR
Immunoparesis	1 risk factor	6 y
	2 risk factors	1.9 y
Heidelberg		3-year TTP
Tumor mass using the Mayo Model	T-mass low + CA low risk	15%
t(4;14), del17p, or +1q	T-mass low + CA high risk	42%
	T-mass high + CA low risk	64%
	T-mass high + CA high risk	55%

Abbreviations: BMPC = bone marrow plasma cells; CA = cytogenetic abnormalities; eHb = evolving change in hemoglobin; eMP = evolving change in the monoclonal protein; FLC = free light chain; GEP = Gene Expression Profiling; MFC = multiparameter flow cytometry; MM = multiple myeloma; PC = plasma cell; Penn = Pennsylvania model; sFLC = serum FLC; SMM = smoldering MM; SWOG = South West Oncology Group; TTP = time to progression.

Risk Model	Risk of Progression to MM	
SWOG		2-year TTP
Serum M-protein ≥2 g/dL	No risk factor	30%
Involved FLC >25 mg/dL	1 risk factor	29%
GEP risk score >−0.26	≥2 risk factors	71%
Penn		2-year TTP
≥40% clonal BMPC infiltration	No risk factor	16%
sFLC ratio ≥50	1 risk factor	44%
Albumin ≤3.5 mg/dL	≥2 risk factors	81%
Japanese		2-year TTP
Beta 2-microglobulin ≥2.5 mg/L	2 risk factors	67.5%
M-protein increment rate >1 mg/dL/d		
Czech and Heidelberg		2-year TTP
Immunoparesis	No risk factor	5.3%
Serum M-protein ≥2.3 g/dL	1 risk factor	7.5%
Involved/uninvolved sFLC >30	2 risk factors	44.8%
	3 risk factors	81.3%

Risk Model	Risk of Progression to MM	
Barcelona		2-year TTP
Evolving pattern = 2 points	0 points	2.4%
Serum M-protein ≥3 g/dL = 1 point	1 point	31%
Immunoparesis = 1 point	2 points	52%
	3 points	80%
Mayo Clinic evolving model		
eMP	0 points	12.3 y
eHb	1 point	4.2 y
≥20% PCs	2 points	2.8 y
	3 points	1 year
Danish		3-year TTP
Serum M-protein ≥3 g/dL	No risk factor	5%
Immunoparesis	1 risk factor	21%
	2 risk factors	50%

Revised IMWG/Mayo	Risk Factors	#Risk of Prog,2yr	^Risk of Prog,2yr	*Median TTP
BMPC > 20%	0	5%	8%	110 mo
M-protein > 2g/dl	1	17%	21%	68 mo
sFLC ratio >20	≥2 (2)	46%	37%	28 mo
t(4,14), t(14,16), +1q, del13q	≥3		59%	

Mateos MV, González-Calle V Clin Lymphoma Myeloma Leuk 2017 11:716 (10 Models)
**Lakshman A et al Blood Ca J 2018, 8:59*
#San Miguel J et al ASCO 2019 A8000, ^presentation*

PRESENTED AT: 2019 ASCO ANNUAL MEETING #ASCO19 Slides are the property of the author, permission required for reuse.

PRESENTED BY: Philip McCarthy

24

24

Revised International Staging System for Multiple Myeloma: A Report From International Myeloma Working Group

Original ISS Stage	Criteria
I	Serum β2-M <3.5 mg/L, serum albumin ≥3.5 g/dL
II	Not ISS stage I or III
III	Serum β2-M ≥5.5 mg/L

Stg	Factor	Pt N (%)	5 yr PFS	5 yr OS
I	**Absence of adverse factors** (no high LDH, ISS 2 or 3, t(4;14) and/or t(14;16) and/or del(17p))	871 (28)	**55%**	**82%**
II	**Not R-ISS I or III**	1,894 (62)	**36%**	**62%**
III	**ISS 3 and high-risk CA by iFISH or high LDH**	295 (10)	**24%**	**40%**

β2-M, beta-2 microglobulin; CA, chromosomal abnormalities; iFISH, interphase fluorescent in-situ hybridization; ISS, International Staging System; LDH, lactate dehydrogenase; L, liter; mg, milligrams; MM, multiple myeloma; Pts, Patients; R-ISS, revised International Staging System. 3,060 evaluable patients

From: GIEMEMA. PETHEMA/GEM, HOVON/GMMG, IFM

Palumbo et al J Clin Oncol. 2015, 33:2863
Moreau P et al. J Clin Oncol. 2014, 32:2173.

25

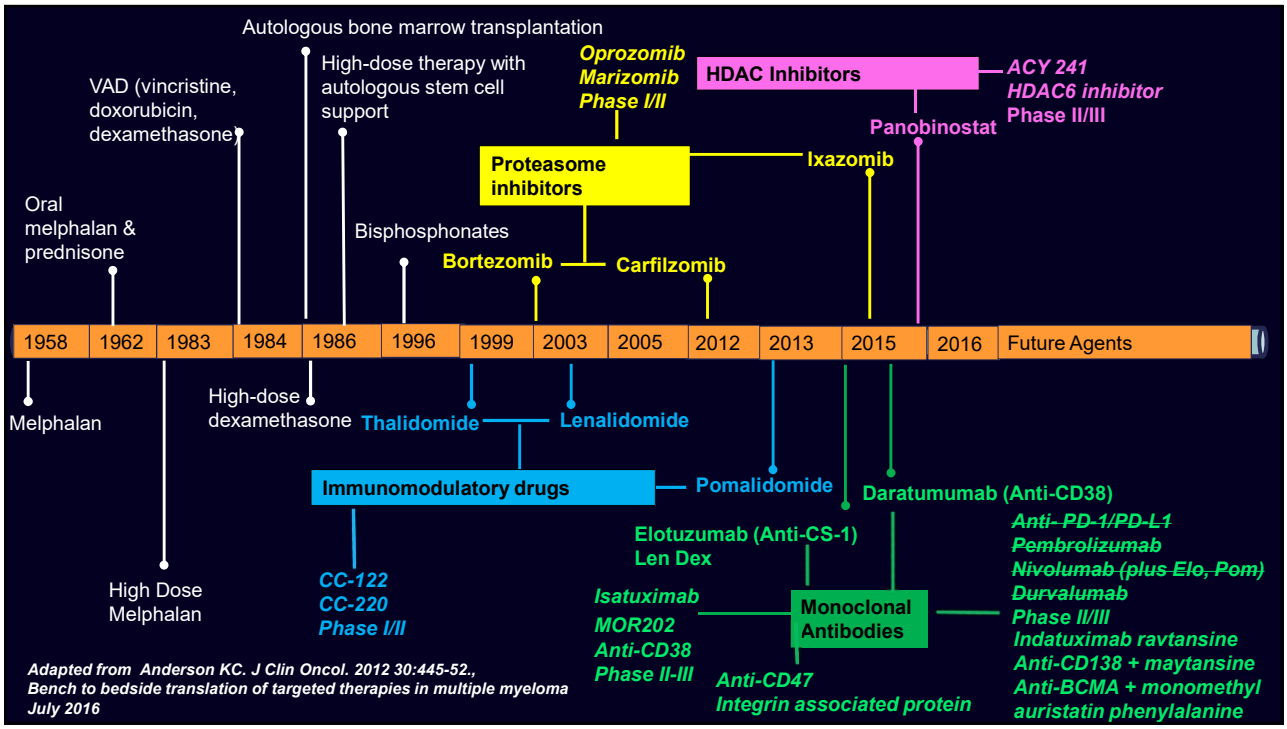
Multiple Myeloma Therapy in the Era of Novel Agents

Before the new drugs, treating Multiple Myeloma was like waiting for a taxi and none would come

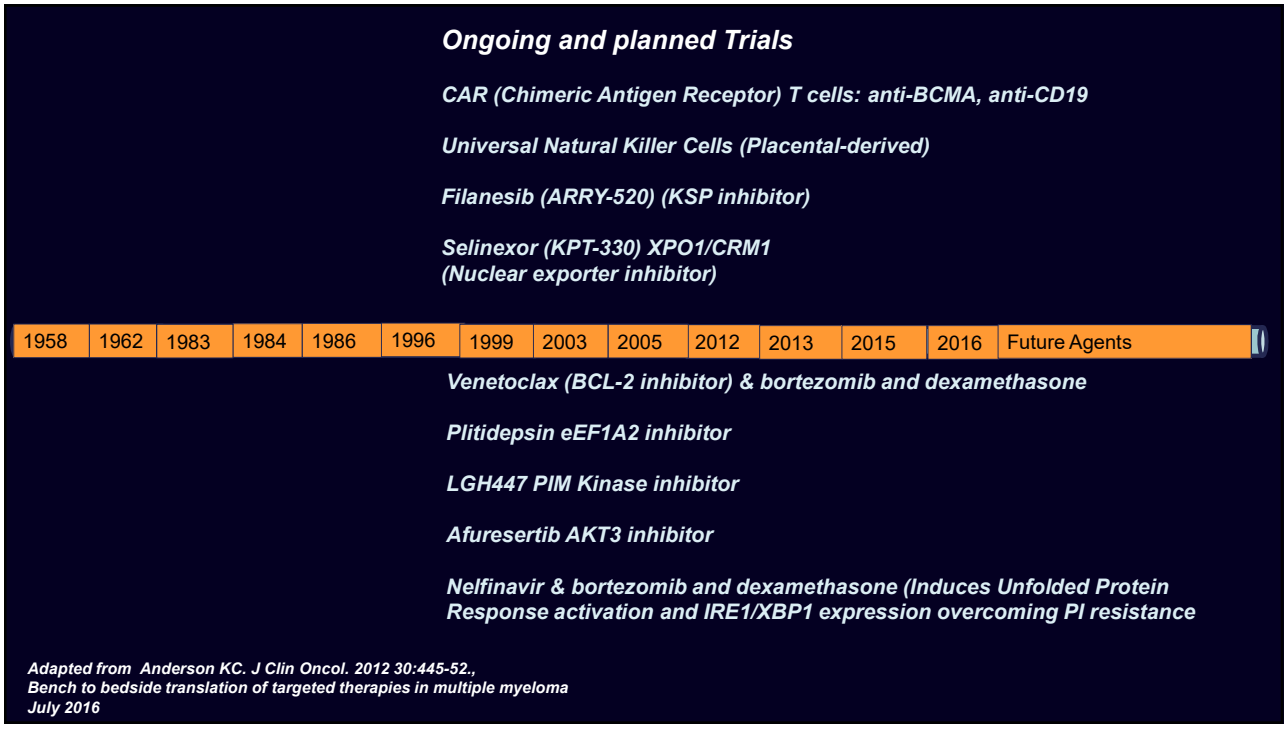
Then all of a sudden, 5 come at once

Dr. Khalid Al Hashmi
Senior Consultant Hemato - Oncologist
AFH, Oman

26

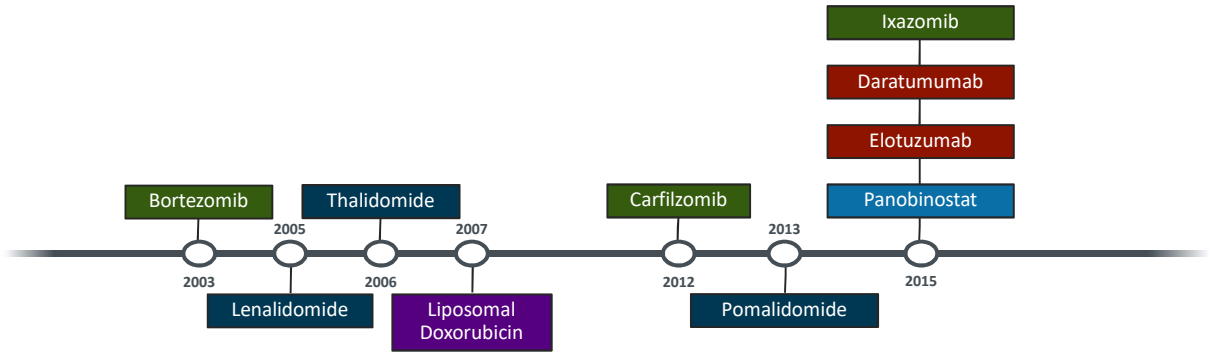

Autologous bone marrow transplantation
VAD (vincristine, doxorubicin, dexamethasone)
High-dose therapy with autologous stem cell support
Oprozomib
Marizomib
Phase I/II
HDAC Inhibitors
ACY 241
HDAC6 inhibitor
Phase II/III
Panobinostat
Proteasome inhibitors
Ixazomib
Oral melphalan & prednisone
Bisphosphonates
Bortezomib
Carfilzomib
1958
1962
1983
1984
1986
1996
1999
2003
2005
2012
2013
2015
2016
Future Agents
Melphalan
High-dose dexamethasone
Thalidomide
Lenalidomide
Immunomodulatory drugs
Pomalidomide
Daratumumab (Anti-CD38)
Elotuzumab (Anti-CS-1)
Len Dex
Anti- PD-1/PD-L1
Pembrolizumab
Nivolumab (plus Elo, Pom)
Durvalumab
Phase II/III
Indatuximab ravtansine
Anti-CD138 + maytansine
Anti-BCMA + monomethyl auristatin phenylalanine
High Dose Melphalan
CC-122
CC-220
Phase I/II
Isatuximab
MOR202
Anti-CD38
Phase II-III
Monoclonal Antibodies
Anti-CD47
Integrin associated protein
Adapted from Anderson KC. J Clin Oncol. 2012 30:445-52.,
Bench to bedside translation of targeted therapies in multiple myeloma
July 2016

27


Ongoing and planned Trials
CAR (Chimeric Antigen Receptor) T cells: anti-BCMA, anti-CD19
Universal Natural Killer Cells (Placental-derived)
Filanesib (ARRY-520) (KSP inhibitor)
Selinexor (KPT-330) XPO1/CRM1
(Nuclear exporter inhibitor)
1958
1962
1983
1984
1986
1996
1999
2003
2005
2012
2013
2015
2016
Future Agents
Venetoclax (BCL-2 inhibitor) & bortezomib and dexamethasone
Plitidepsin eEF1A2 inhibitor
LGH447 PIM Kinase inhibitor
Afuresertib AKT3 inhibitor
Nelfinavir & bortezomib and dexamethasone (Induces Unfolded Protein Response activation and IRE1/XBP1 expression overcoming PI resistance
Adapted from Anderson KC. J Clin Oncol. 2012 30:445-52.,
Bench to bedside translation of targeted therapies in multiple myeloma
July 2016

28

FDA-Approved Therapy for Multiple Myeloma Since 2000



Proteasome Inhibitor
Immunomodulatory Agent
HDAC Inhibitor
Monoclonal Antibody
Cytotoxic Chemotherapy

Most common current NDMM treatment plan:
Combine 2 classes and add dexamethasone

29

29

Treatment paths

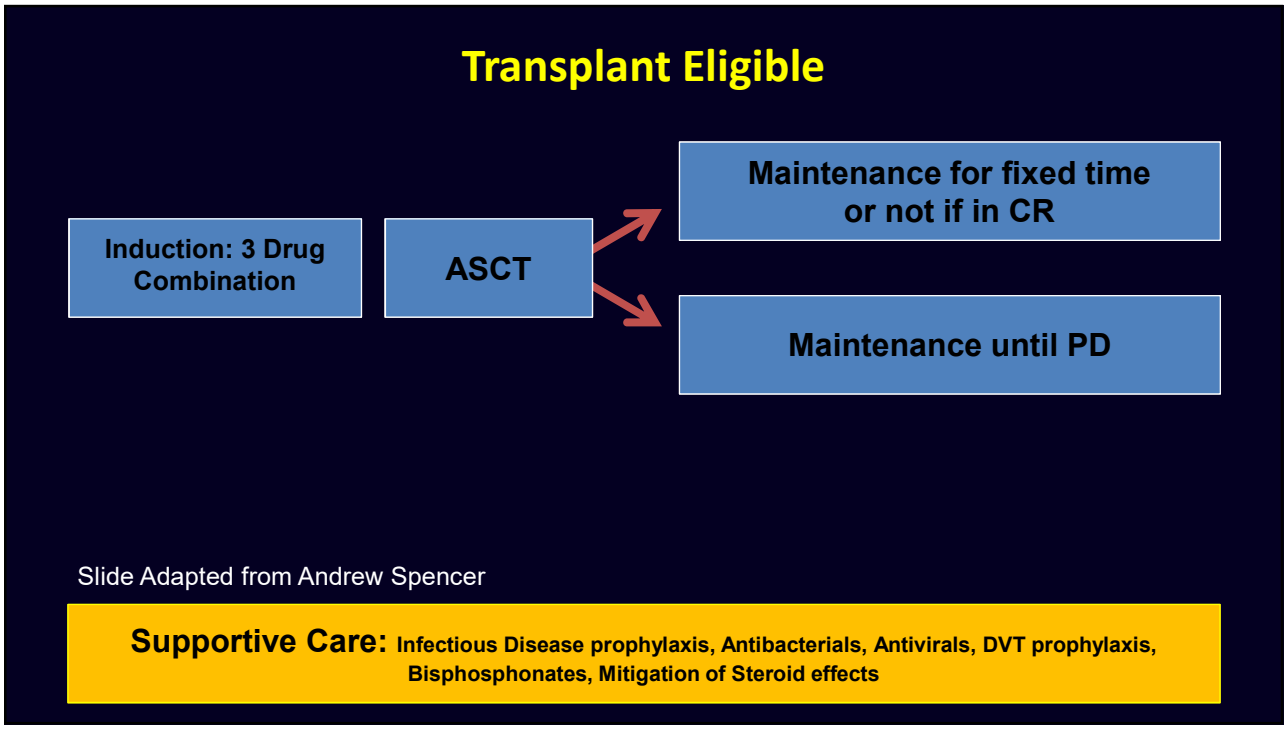
Patients with Multiple Myeloma

transplantation-eligible
- Good performance status more than age
- normal organ function
- stem cells collected
- patient choice

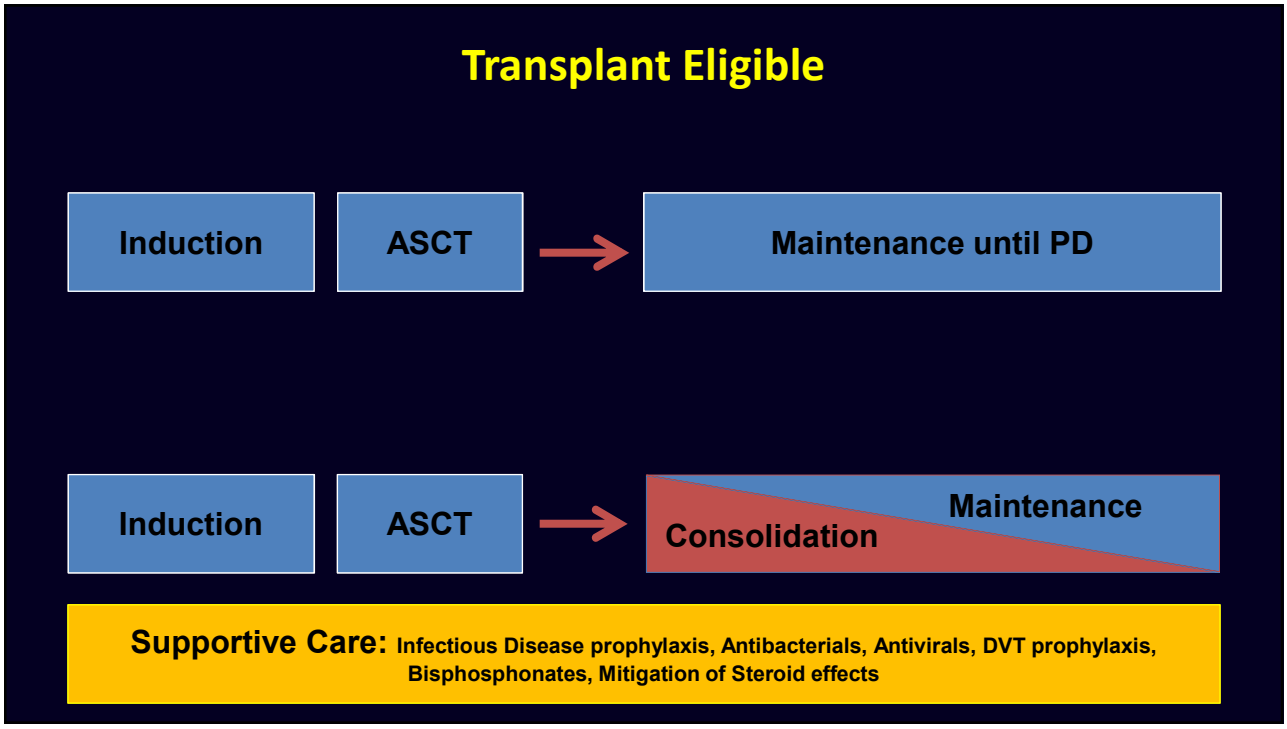
not transplant-eligible
- Poor performance status rather than age
- comorbidities
- no stem cells
- patient choice

Slide Adapted from Jens Hillengass

30

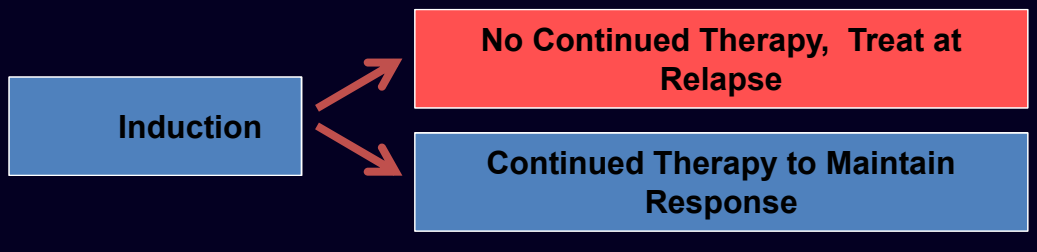

Transplant Eligible
Induction: 3 Drug Combination
ASCT
Maintenance for fixed time or not if in CR
Maintenance until PD
Slide Adapted from Andrew Spencer
Supportive Care: Infectious Disease prophylaxis, Antibacterials, Antivirals, DVT prophylaxis, Bisphosphonates, Mitigation of Steroid effects

31


Transplant Eligible
Induction
ASCT
Maintenance until PD
Induction
ASCT
Consolidation
Maintenance
Supportive Care: Infectious Disease prophylaxis, Antibacterials, Antivirals, DVT prophylaxis, Bisphosphonates, Mitigation of Steroid effects

32

Transplant-Ineligible



Slide Adapted from Andrew Spencer

Supportive Care: Infectious Disease prophylaxis, Antibacterials, Antivirals, DVT prophylaxis, Bisphosphonates, Mitigation of Steroid effects

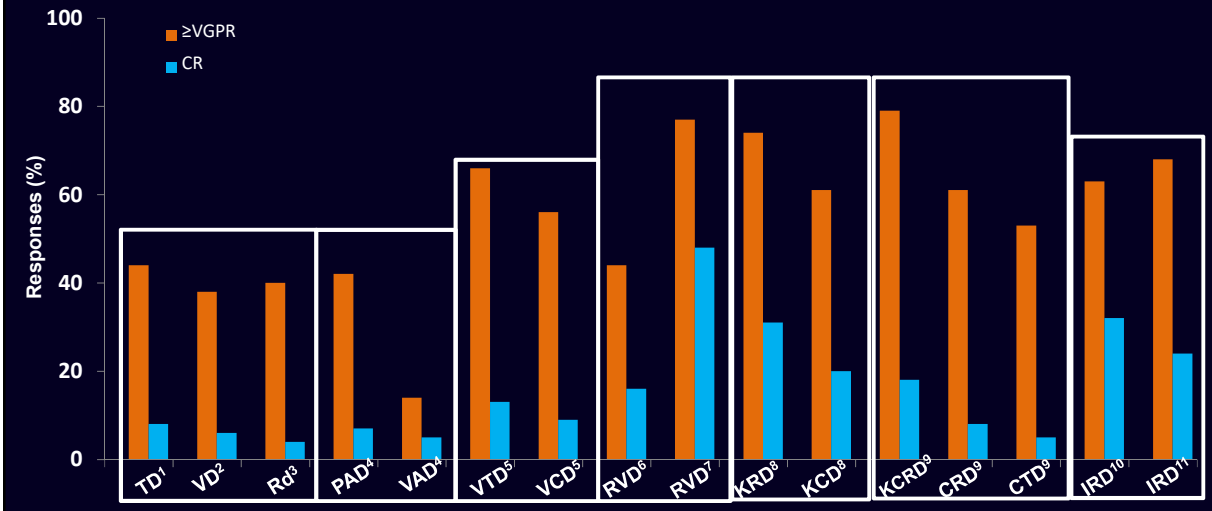
33

Transplant Ineligible

Supportive Care: Infectious Disease prophylaxis, Antibacterials, Antivirals, DVT prophylaxis, Bisphosphonates, Mitigation of Steroid effects

34

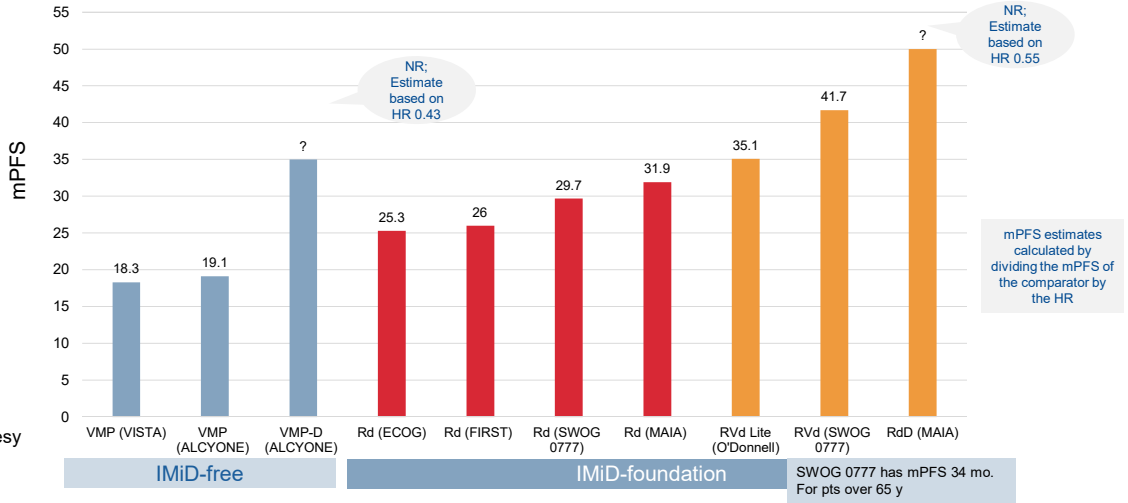
Selected induction regimens and response in MM patients



1. Rajkumar SV, et al 2008 J Clin Oncol 26:2171-77; 2. Harousseau JL, et al 2010 J Clin Oncol 28:4621-4629.; 3. Rajkumar SV, et al Lancet Oncol 2010; 11: 29–37; 4. Sonneveld P, et al J Clin Oncol 2012; 30:2946-55.; 5. Moreau P et al Blood 2016; 127:2569-257 (4 Cycles of VTD and VCD); 6. Durie et al Lancet 2017; 389:519 (8 cycles of RVD); 7. Attal et al NEJM 2017; 376:1311-1320 (8 cycles of RVD); 8. Gay et al ASCO 2017 Abs 8003 (4 cycles of KRD/KCyD; 9. Walter et al NCRI 2017 (4 cycles); 10. Kumar S, et al . Lancet Oncology 2014; 15:1503-12; EHA 2017 S408 (Ixa weekly); 11: Richardson et al BJH 2018 182:231 (Ixa 2x weekly)

35

Overview of mPFS in recent phase 3 trials in NSCT NDMM

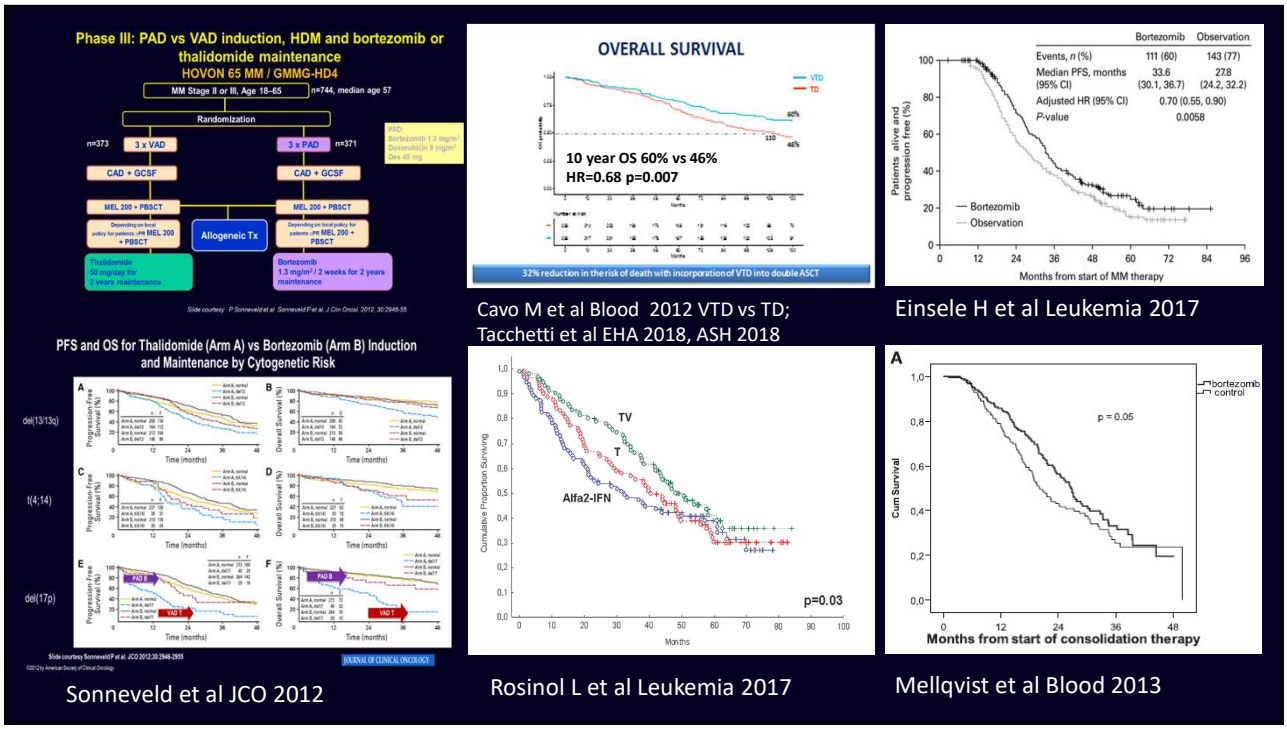


Slide courtesy T Facon

Direct comparison between trials is not intended and should not be inferred. HR, hazard ratio; NR, not reached; NSCT, non-stem cell transplant; PFS, progression-free survival; Rd, lenalidomide, low-dose dexamethasone; RdD, daratumumab, lenalidomide, dexamethasone; RVd, lenalidomide, bortezomib and dexamethasone; VMP; bortezomib, melphalan, prednisone.

1. Velcade [SmPC]. Beerse, Belgium: Janssen-Cilag International. 2014. 2. Dimopoulos M, et al. Blood. 2018;132:156. Presented at ASH 2018. 3. Rajkumar SV, et al. Lancet Oncol. 2010;11:29–37. 4. Facon T, et al.Blood.2018;131:301–310. 5. Revlimid. [SmPC]. Europe. 2019. 6. Facon T, et al. Blood. 2018;132:LBA-2. Presented at ASH 2018. 7. O'Donnell EK, et al. Br J Haematol. 2018;182:222–230

36



Cavo M et al Blood 2012 VTD vs TD; Tacchetti et al EHA 2018, ASH 2018

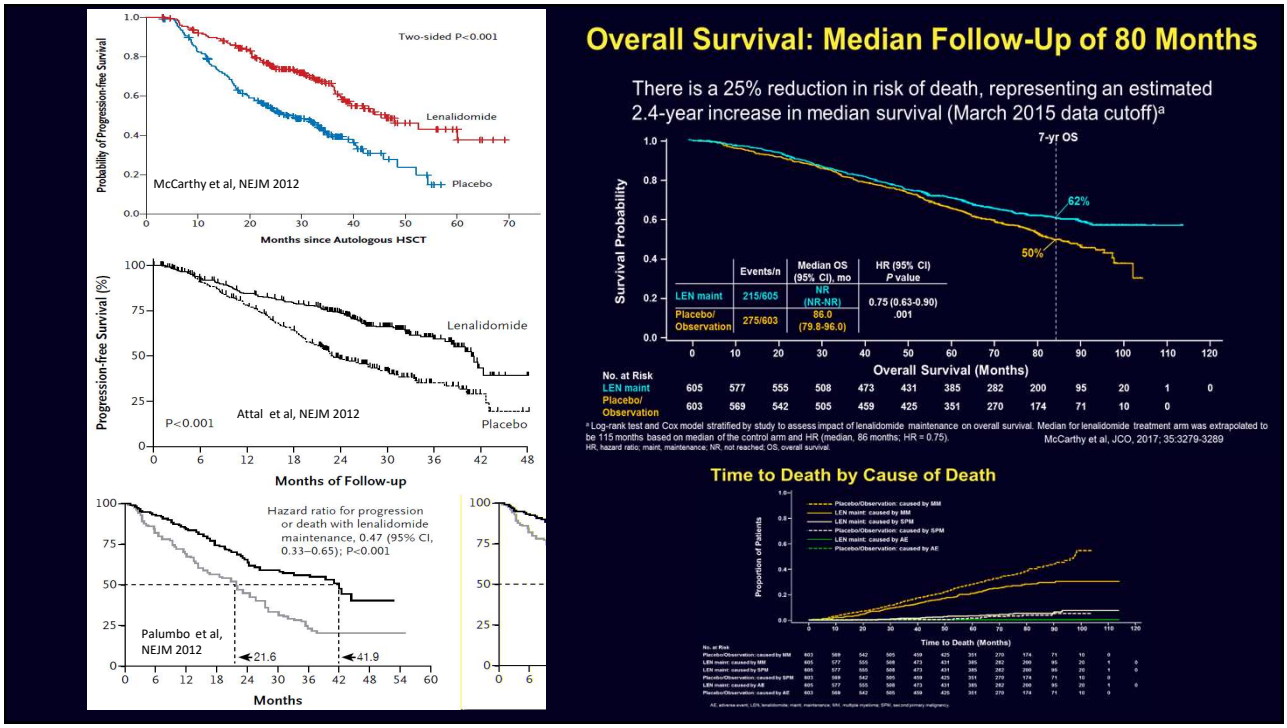
Einsele H et al Leukemia 2017

Sonneveld et al JCO 2012

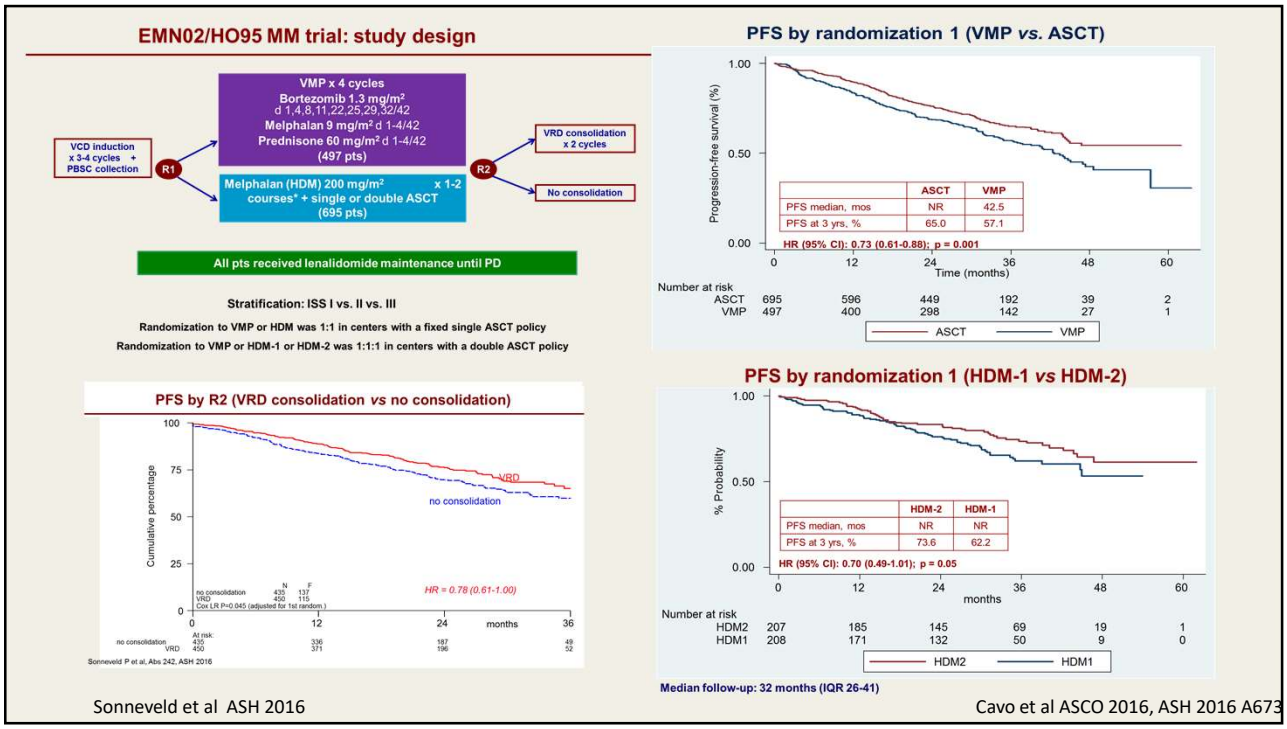
Rosinol L et al Leukemia 2017

Mellqvist et al Blood 2013

37



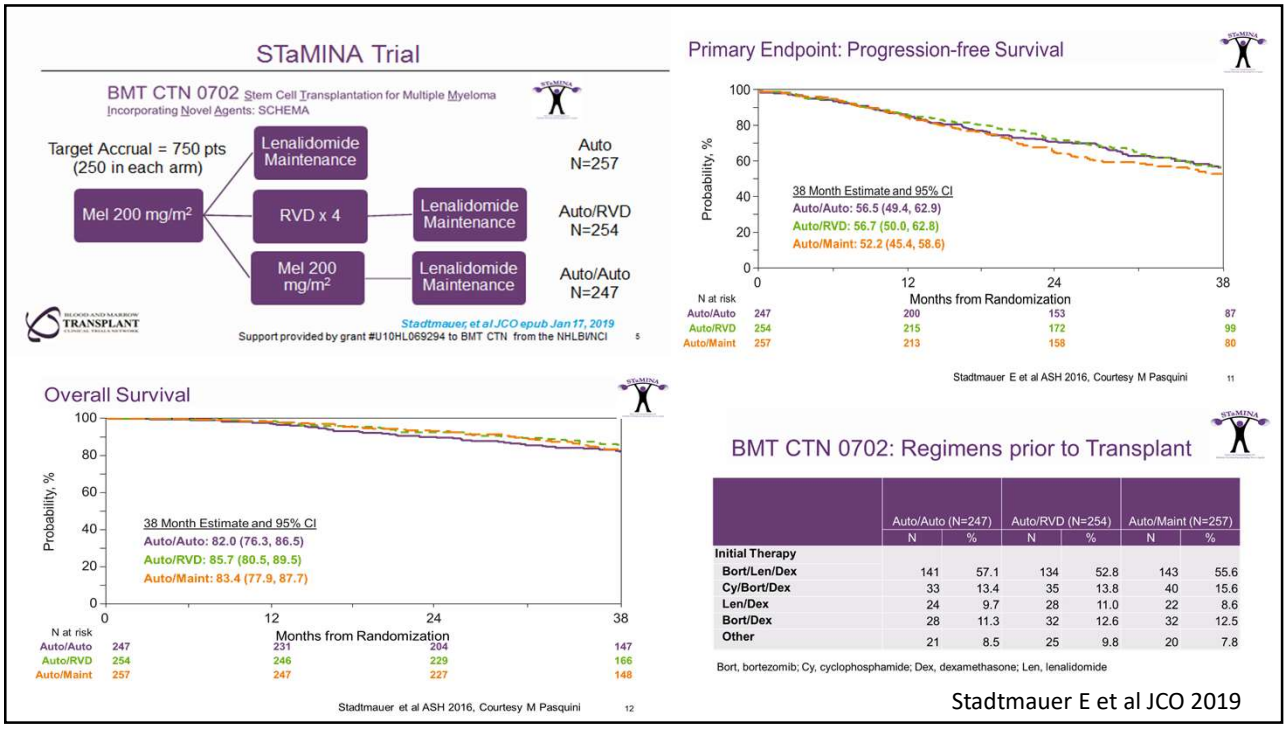
38



Sonneveld et al ASH 2016

Cavo et al ASCO 2016, ASH 2016 A673

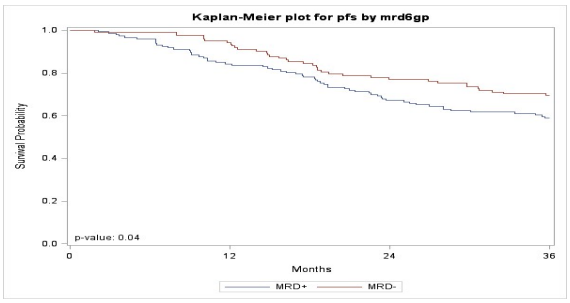
39

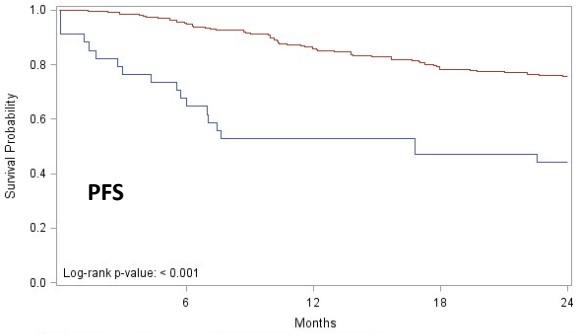


Stadtmauer E et al JCO 2019

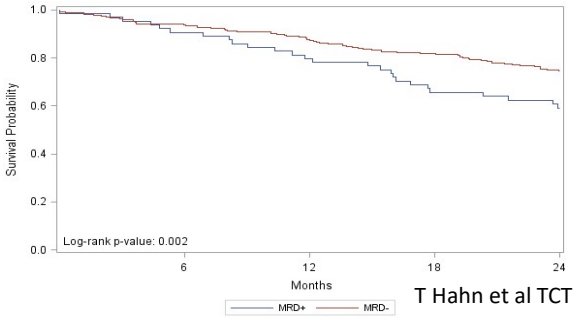
40

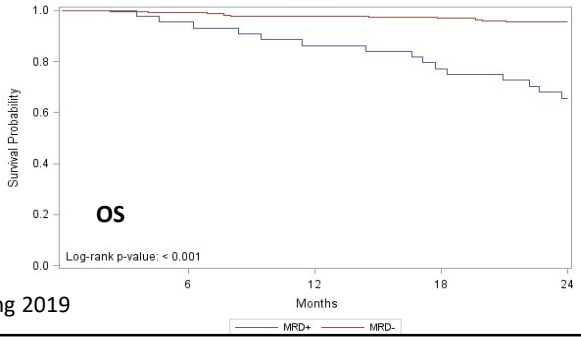
PFS by MRD status post induction BMT CTN 0702 **PFS/OS by MRD status at one year on maintenance therapy**





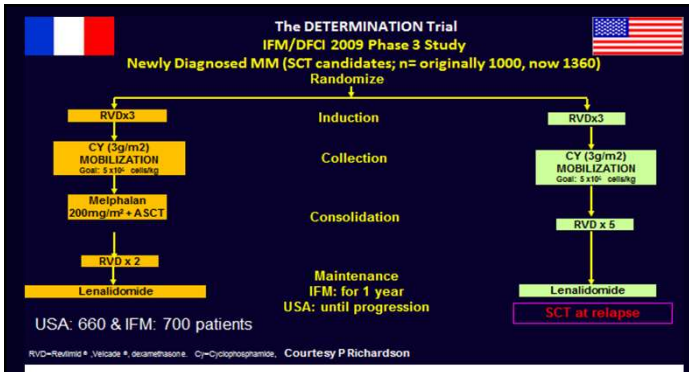
PFS by MRD status pre-maintenance

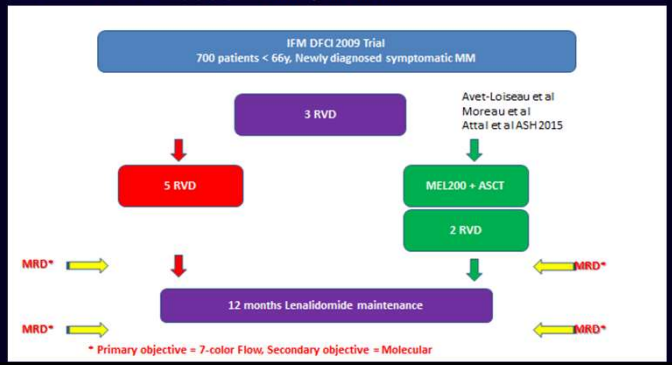


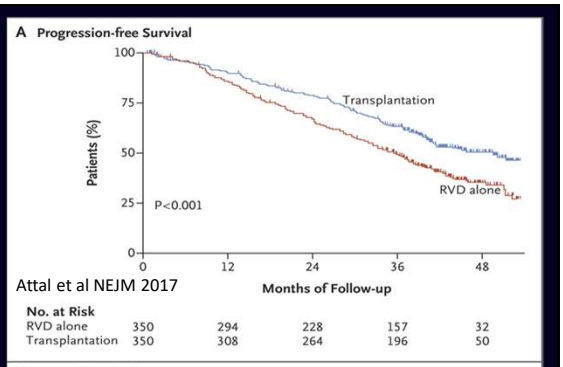


T Hahn et al TCT Meeting 2019

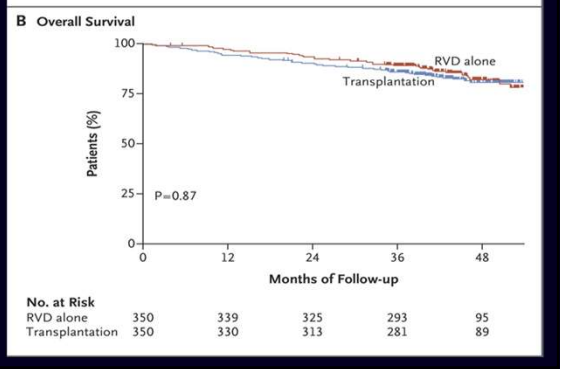
41





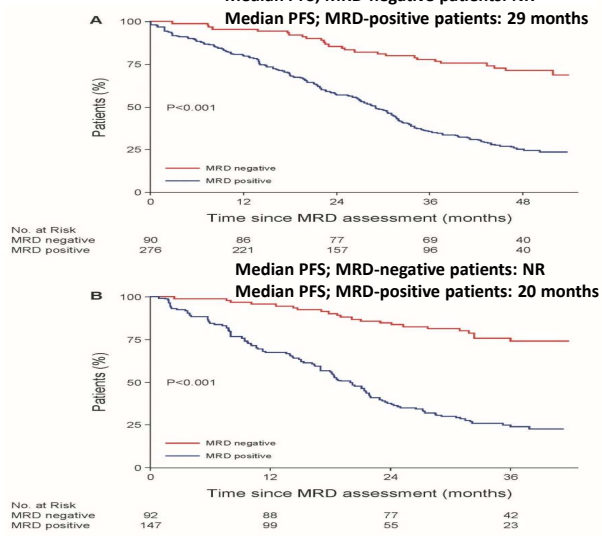


Attal et al NEJM 2017

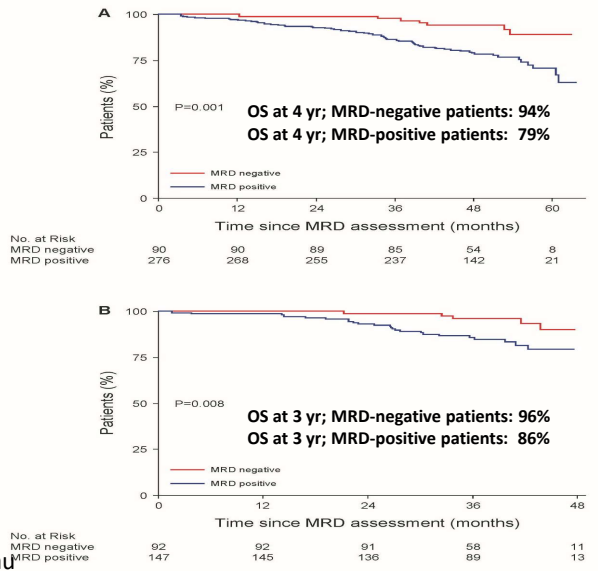


42

A: K-M Curves for PFS by MRD Status at the Start of Maintenance Therapy.
B: K-M Curves for PFS by MRD Status after 12 months of maintenance therapy.

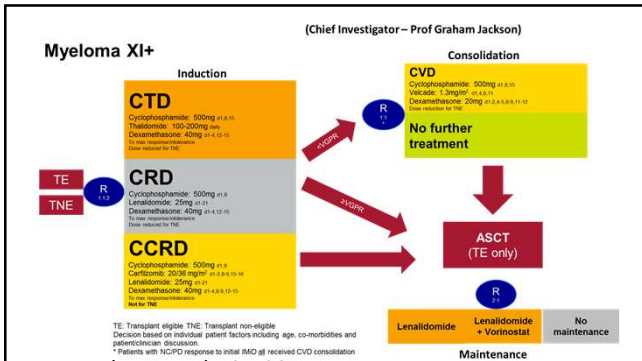


A: K-M Curves for OS by MRD Status at the Start of Maintenance Therapy.
B: K-M Curves for OS by MRD Status after 12 months of maintenance therapy.

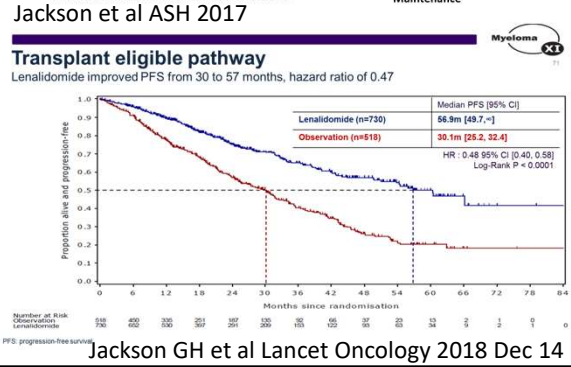


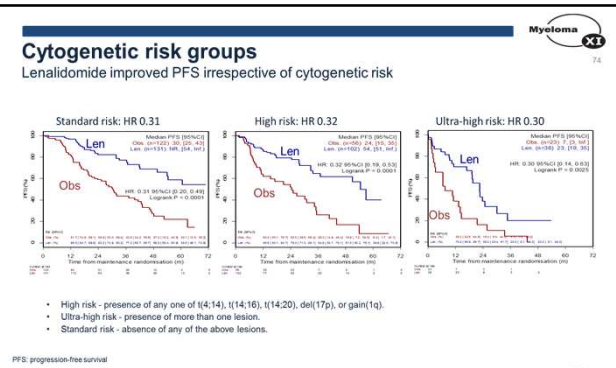
Perrot A et al Blood 2018 Sept on line, courtesy H Avet Loiseau

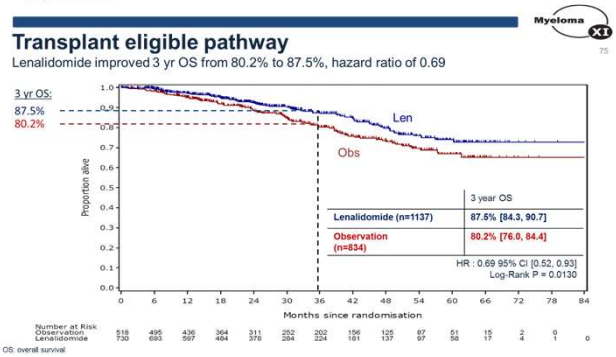
43



Jackson et al ASH 2017

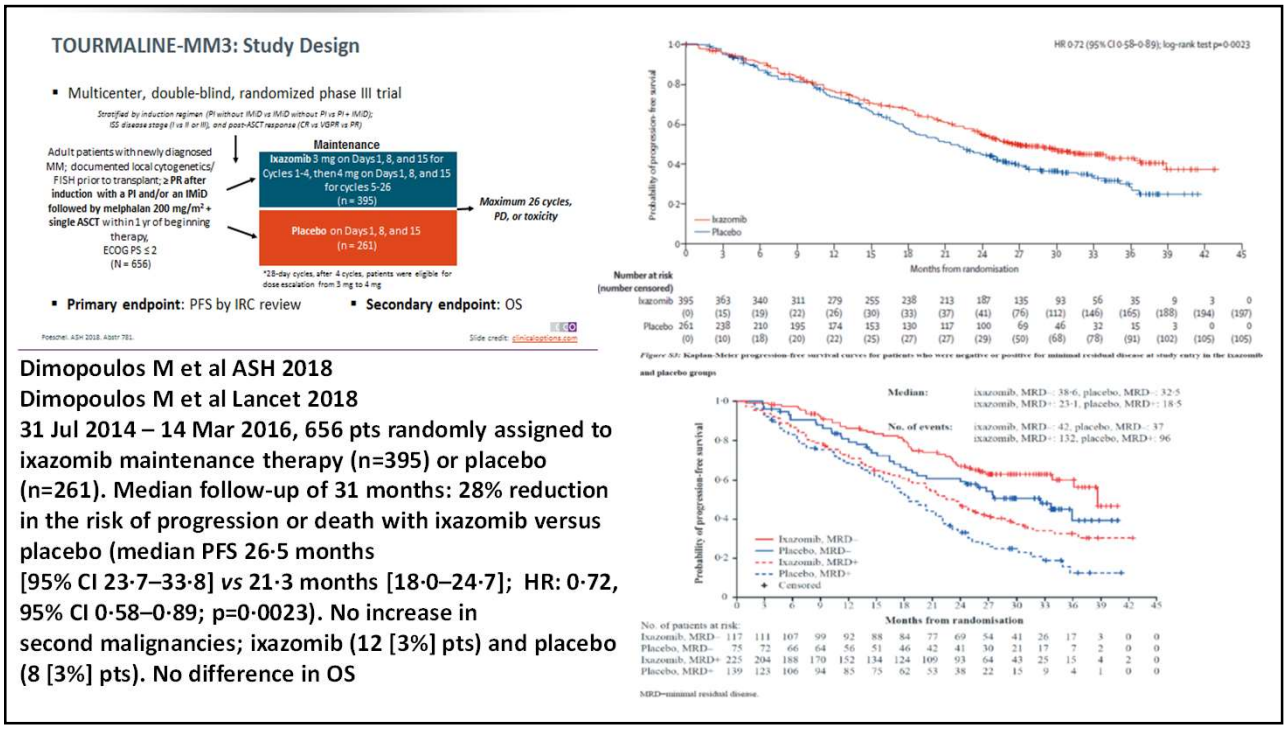






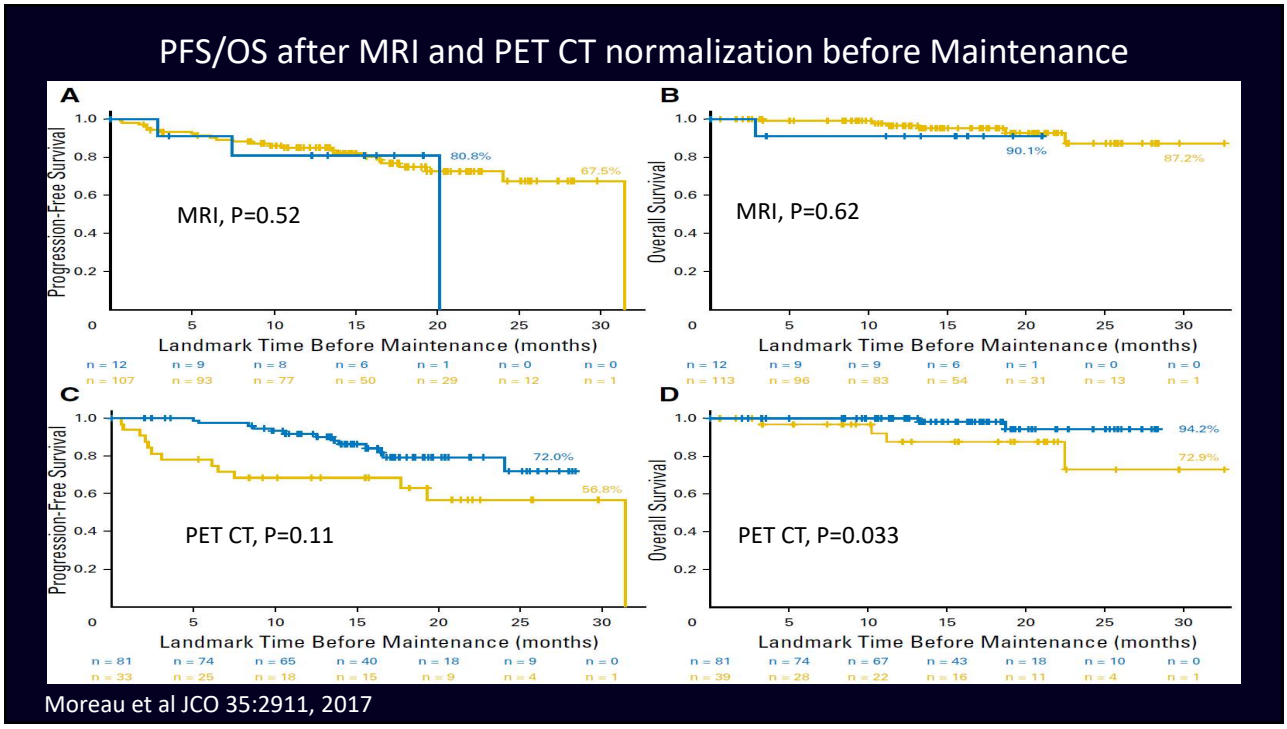
Jackson GH et al Lancet Oncology 2018 Dec 14

44



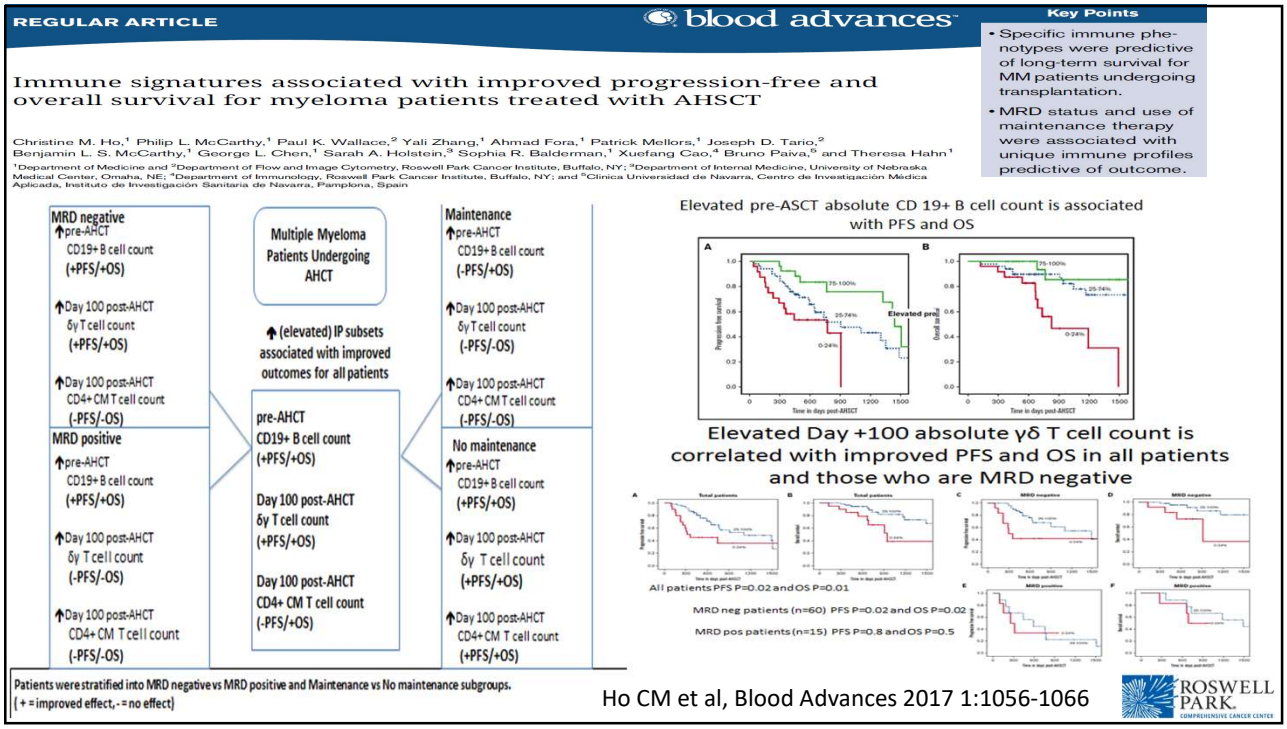
Dimopoulos M et al ASH 2018
Dimopoulos M et al Lancet 2018
31 Jul 2014 – 14 Mar 2016, 656 pts randomly assigned to ixazomib maintenance therapy (n=395) or placebo (n=261). Median follow-up of 31 months: 28% reduction in the risk of progression or death with ixazomib versus placebo (median PFS 26·5 months [95% CI 23·7–33·8] *vs* 21·3 months [18·0–24·7]; HR: 0·72, 95% CI 0·58–0·89; p=0·0023). No increase in second malignancies; ixazomib (12 [3%] pts) and placebo (8 [3%] pts). No difference in OS

45



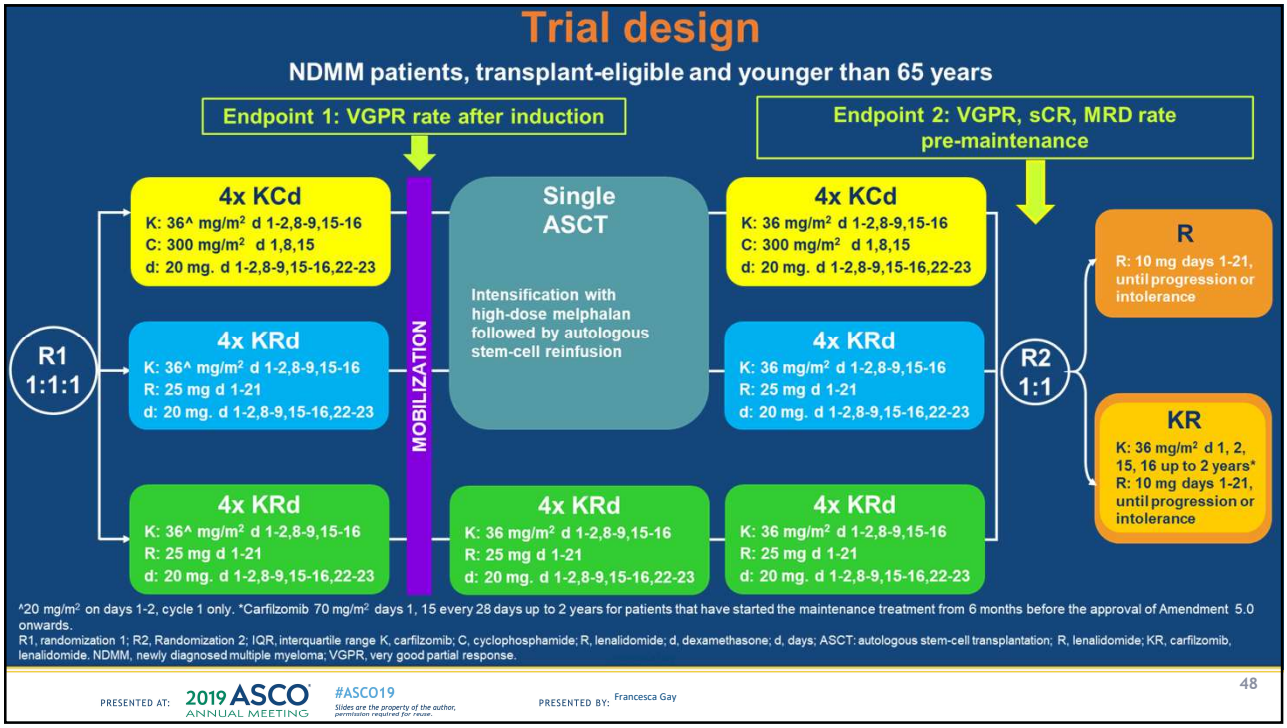
Moreau et al JCO 35:2911, 2017

46



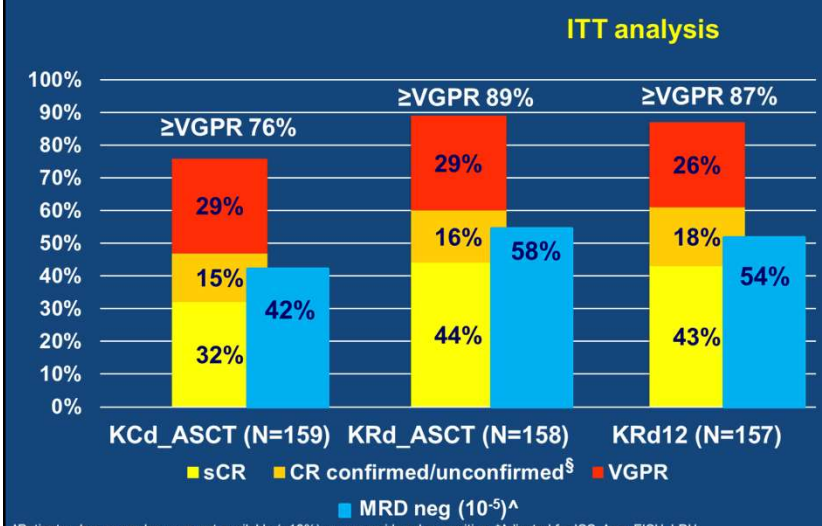
Ho CM et al, Blood Advances 2017 1:1056-1066

47



48

Pre-maintenance response rate and MRD negativity



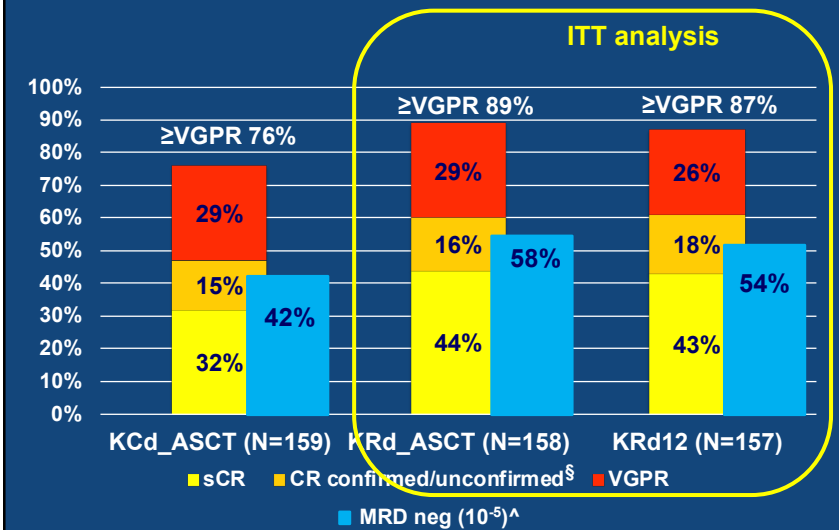
	OR>1	P value*
≥VGPR		
KRd_ASCT vs KCd_ASCT	2.53	0.004
KRd12 vs KCd_ASCT	2.11	0.015
sCR		
KRd_ASCT vs KCd_ASCT	1.65	0.035
KRd12 vs KCd_ASCT	1.60	0.048

MRD neg (10^{-5})		
KRd_ASCT vs KCd_ASCT	2.02	0.009
KRd12 vs KCd_ASCT	1.73	0.042

^Patients whose samples were not available (~10%) were considered as positive. *Adjusted for ISS, Age, FISH, LDH.
§Unconfirmed CR/sCR: patients missing immunofixation/sFLC analysis needed to confirm CR/sCR (6% in KCd_ASCT_KCd; 8% in KRd_ASCT_KRd; 6% KRd_12).
ASCT, autologous stem-cell trasplantation; K, carfilzomib; R, lenalidomide; C, cyclophosphamide; d, dexamethasone; KCd_ASCT, KCd induction-ASCT-KCd consolidation; KRd_ASCT, KRd induction-ASCT-KRd consolidation; KRd12, 12 cycles of KRd; MRD, minimal residual disease; neg, negativity; sCR, stringent complete response; CR: complete response; VGPR: very good partial response; OR: odds ratio; FISH, fluorescence in situ hybridization; LDH, lactate dehydrogenase; FLC, free light chain, ISS, International Staging System.

49

Pre-maintenance response rate and MRD negativity

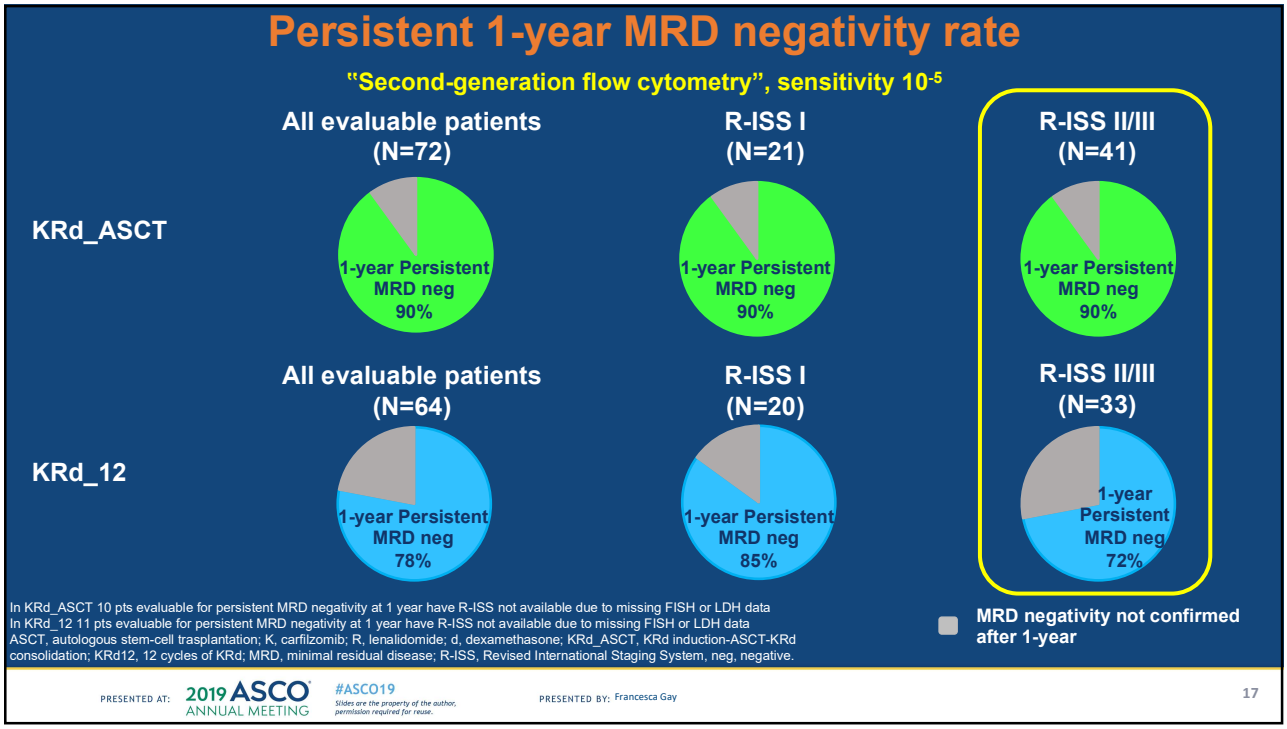


	OR>1	P value*
≥VGPR		
KRd_ASCT vs KCd_ASCT	2.53	0.004
KRd12 vs KCd_ASCT	2.11	0.015
sCR		
KRd_ASCT vs KCd_ASCT	1.65	0.035
KRd12 vs KCd_ASCT	1.60	0.048

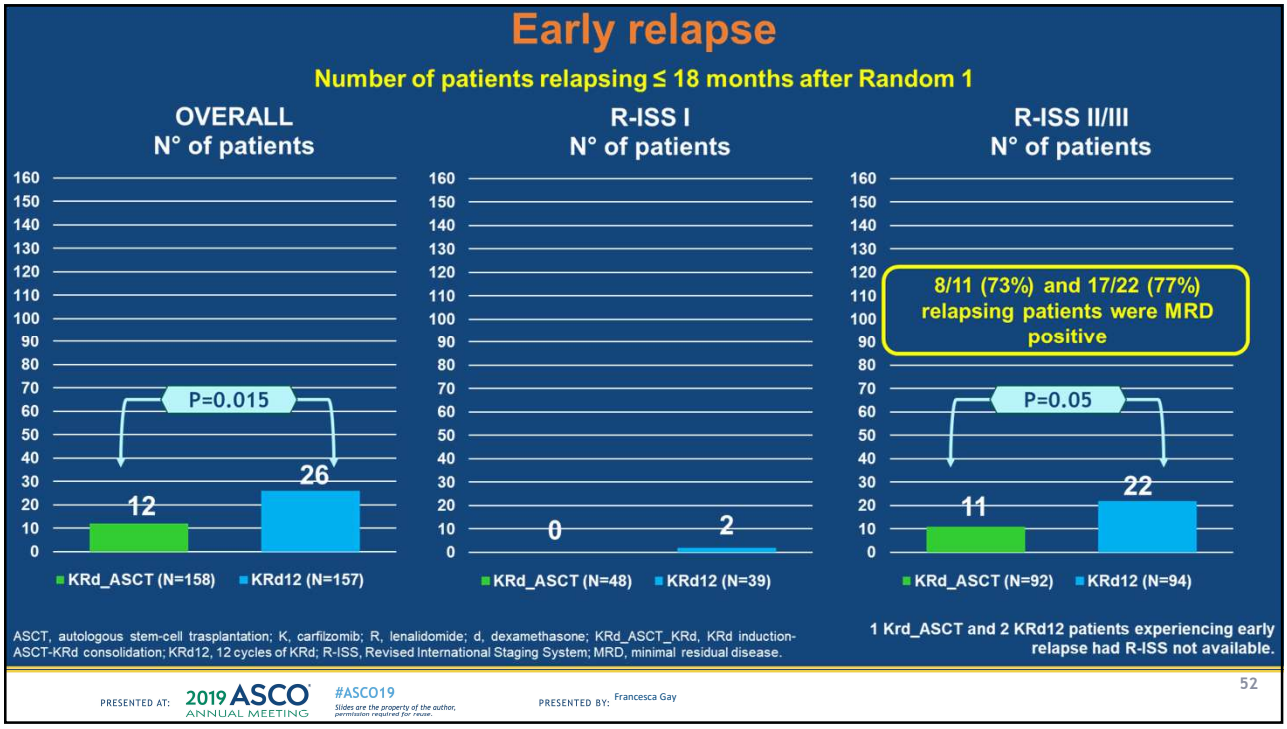
MRD neg (10^{-5})		
KRd_ASCT vs KCd_ASCT	2.02	0.009
KRd12 vs KCd_ASCT	1.73	0.042

^Patients whose samples were not available (~10%) were considered as positive. *Adjusted for ISS, Age, FISH, LDH.
§Unconfirmed CR/sCR: patients missing immunofixation/sFLC analysis needed to confirm CR/sCR (6% in KCd_ASCT_KCd; 8% in KRd_ASCT_KRd; 6% KRd_12).
ASCT, autologous stem-cell trasplantation; K, carfilzomib; R, lenalidomide; C, cyclophosphamide; d, dexamethasone; KCd_ASCT, KCd induction-ASCT-KCd consolidation; KRd_ASCT, KRd induction-ASCT-KRd consolidation; KRd12, 12 cycles of KRd; MRD, minimal residual disease; neg, negativity; sCR, stringent complete response; CR: complete response; VGPR: very good partial response; OR: odds ratio; FISH, fluorescence in situ hybridization; LDH, lactate dehydrogenase; FLC, free light chain, ISS, International Staging System.

50


Persistent 1-year MRD negativity rate
"Second-generation flow cytometry", sensitivity 10-5
All evaluable patients (N=72)
R-ISS I (N=21)
R-ISS II/III (N=41)
KRd_ASCT
1-year Persistent MRD neg 90%
1-year Persistent MRD neg 90%
1-year Persistent MRD neg 90%
All evaluable patients (N=64)
R-ISS I (N=20)
R-ISS II/III (N=33)
KRd_12
1-year Persistent MRD neg 78%
1-year Persistent MRD neg 85%
1-year Persistent MRD neg 72%
In KRd_ASCT 10 pts evaluable for persistent MRD negativity at 1 year have R-ISS not available due to missing FISH or LDH data
In KRd_12 11 pts evaluable for persistent MRD negativity at 1 year have R-ISS not available due to missing FISH or LDH data
ASCT, autologous stem-cell trasplantation; K, carfilzomib; R, lenalidomide; d, dexamethasone; KRd_ASCT, KRd induction-ASCT-KRd consolidation; KRd12, 12 cycles of KRd; MRD, minimal residual disease; R-ISS, Revised International Staging System, neg, negative.
MRD negativity not confirmed after 1-year
PRESENTED AT: 2019 ASCO ANNUAL MEETING #ASCO19
Slides are the property of the author, permission required for reuse.
PRESENTED BY: Francesca Gay
17

51


Early relapse
Number of patients relapsing ≤ 18 months after Random 1
OVERALL N° of patients
R-ISS I N° of patients
R-ISS II/III N° of patients
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
P=0.015
12
26
KRd_ASCT (N=158)
KRd12 (N=157)
0
2
KRd_ASCT (N=48)
KRd12 (N=39)
8/11 (73%) and 17/22 (77%) relapsing patients were MRD positive
P=0.05
11
22
KRd_ASCT (N=92)
KRd12 (N=94)
ASCT, autologous stem-cell trasplantation; K, carfilzomib; R, lenalidomide; d, dexamethasone; KRd_ASCT_KRd, KRd induction-ASCT-KRd consolidation; KRd12, 12 cycles of KRd; R-ISS, Revised International Staging System; MRD, minimal residual disease.
1 Krd_ASCT and 2 KRd12 patients experiencing early relapse had R-ISS not available.
PRESENTED AT: 2019 ASCO ANNUAL MEETING #ASCO19
Slides are the property of the author, permission required for reuse.
PRESENTED BY: Francesca Gay
52

52

Early relapse

Multivariate Logistic Regression Model*

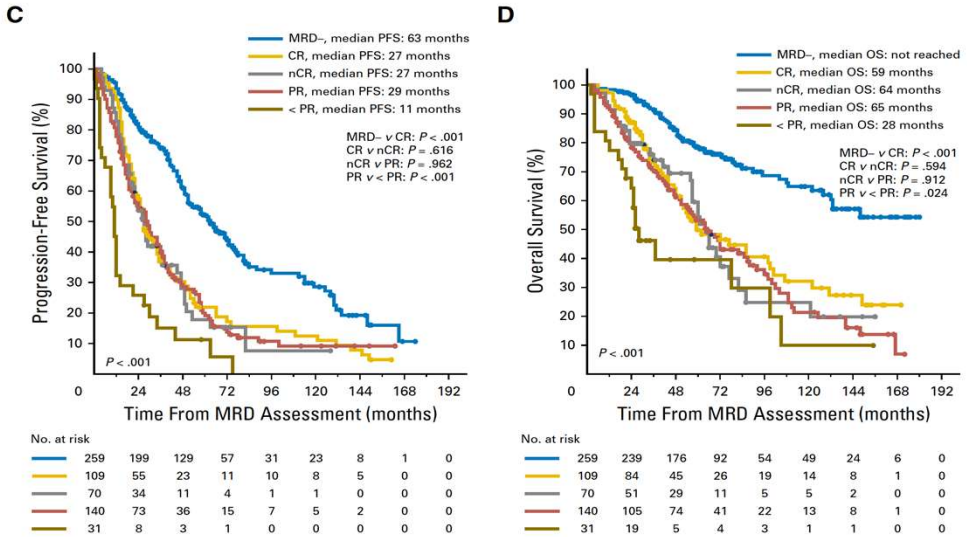
	OR	95% CI	P-value
R-ISS II/III vs R-ISS I	3.78	1.71-8.35	0.001
KRd-ASCT vs KRd12	0.41	0.19-0.88	0.022
MRD negative (10^{-5})	0.21	0.12-0.40	<0.001

Increased risk of early relapse

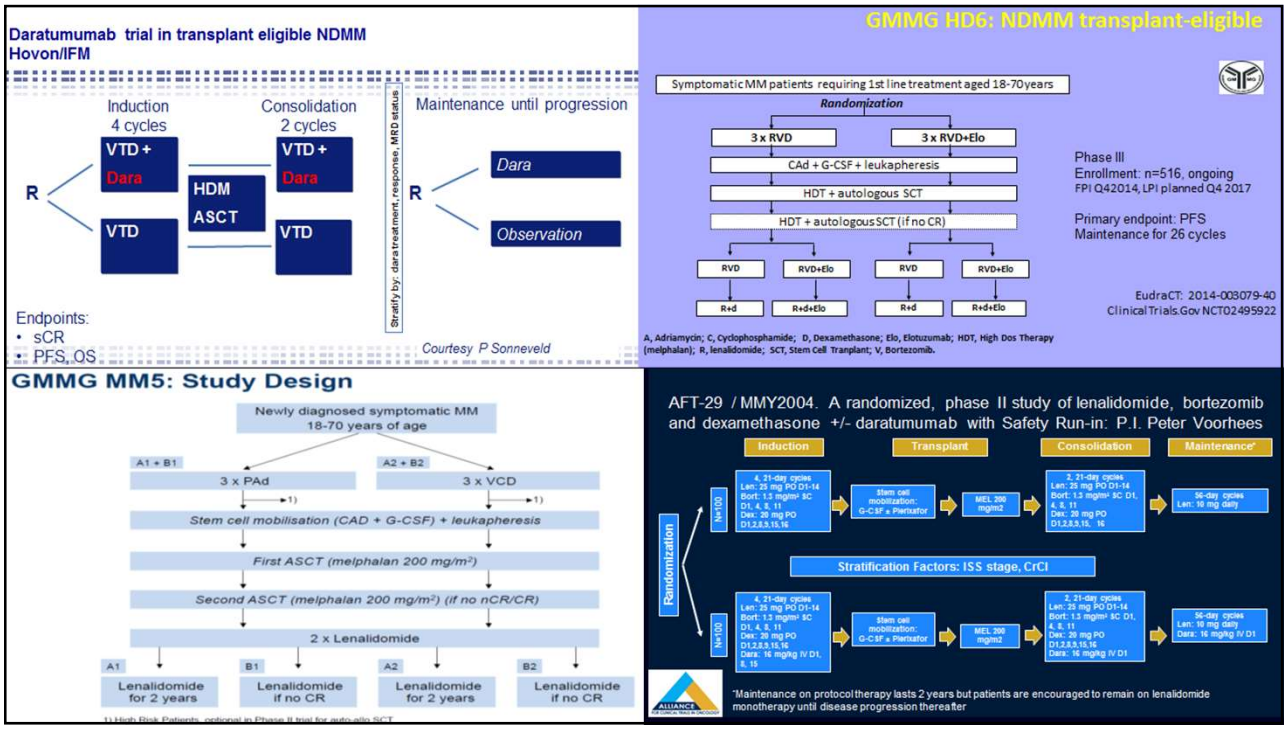
Reduced risk of early relapse

*The model was also adjusted for the presence/absence of plasmacytoma and for age as continuous variable.
ASCT, autologous stem-cell trasplantation; K, carfilzomib; R, lenalidomide; d, dexamethasone; KRd_ASCT, KRd induction-ASCT-KRd consolidation; KRd12, 12 cycles of KRd; R-ISS, Revised International Staging System; OR, odds ratio; CI, confidence interval.

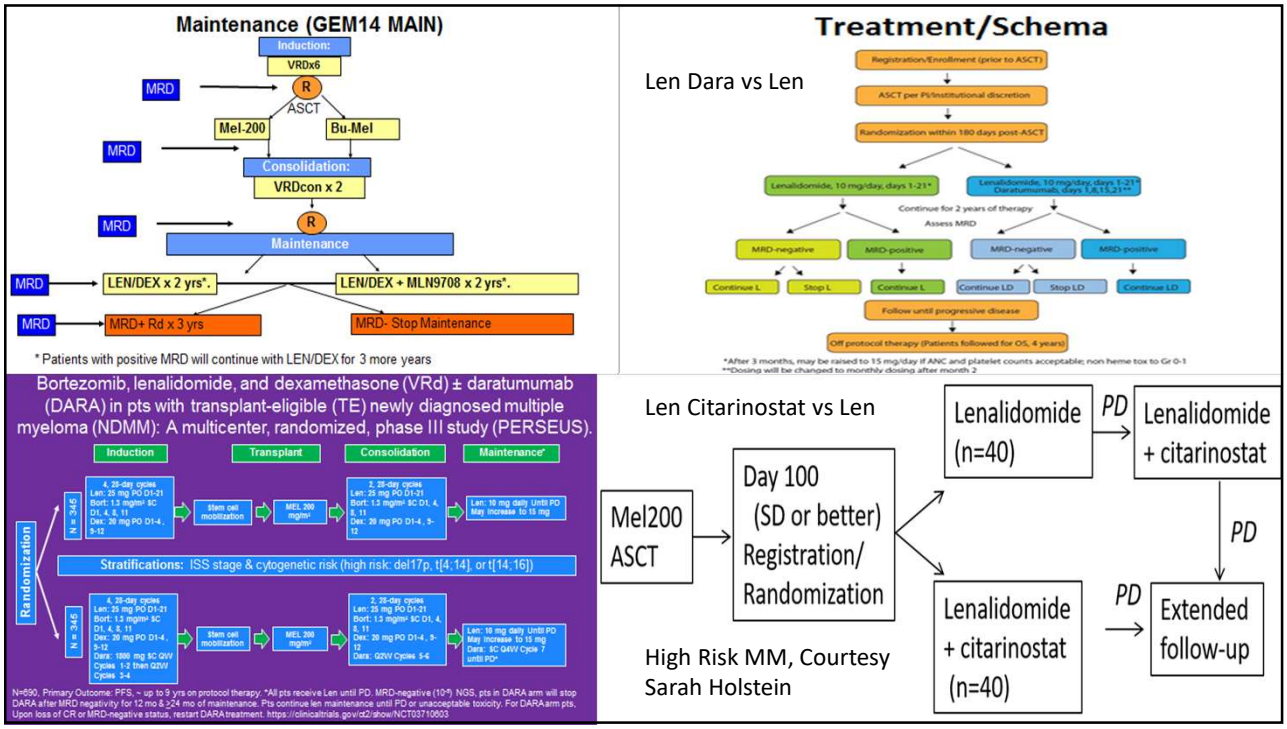
Depth of Response



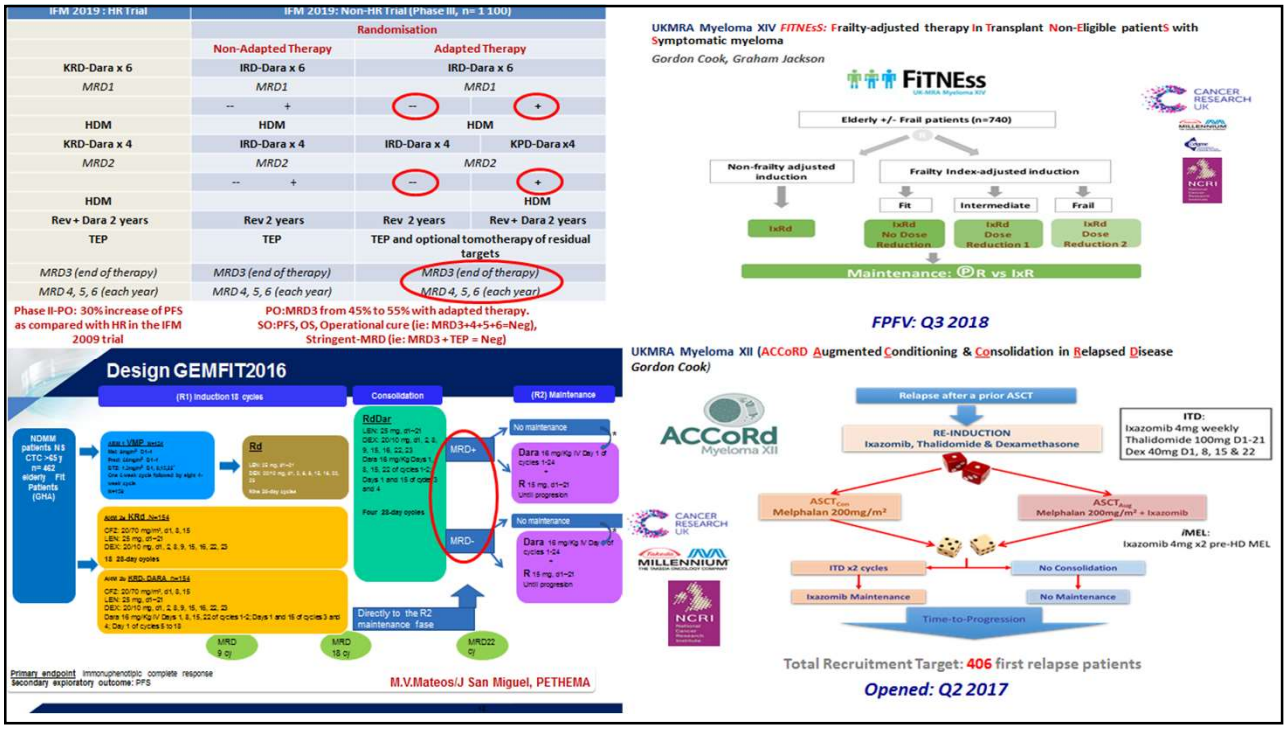
Slide courtesy J Hillengass Lahuerta 2017 JCO


Daratumumab trial in transplant eligible NDMM
Hovon/IFM
Induction
4 cycles
Consolidation
2 cycles
Maintenance until progression
R
VTD + Dara
VTD
HDM ASCT
VTD + Dara
VTD
R
Dara
Observation
Stratify by: daratreatment, response, MRD status
Endpoints:
• sCR
• PFS, OS
Courtesy P Sonneveld
GMMG HD6: NDMM transplant-eligible
Symptomatic MM patients requiring 1st line treatment aged 18-70years
Randomization
3 x RVD
3 x RVD+Elo
CAd + G-CSF + leukapheresis
HDT + autologous SCT
HDT + autologous SCT (if no CR)
RVD
RVD+Elo
RVD
RVD+Elo
R+d
R+d+Elo
R+d
R+d+Elo
Phase III
Enrollment: n=516, ongoing
FPI Q42014, LPI planned Q4 2017
Primary endpoint: PFS
Maintenance for 26 cycles
EudraCT: 2014-003079-40
Clinical Trials.Gov NCT02495922
A, Adriamycin; C, Cyclophosphamide; D, Dexamethasone; Elo, Elotuzumab; HDT, High Dos Therapy (melphalan); R, lenalidomide; SCT, Stem Cell Tranplant; V, Bortezomib.
GMMG MM5: Study Design
Newly diagnosed symptomatic MM
18-70 years of age
A1 + B1
A2 + B2
3 x PAd
3 x VCD
Stem cell mobilisation (CAD + G-CSF) + leukapheresis
First ASCT (melphalan 200 mg/m²)
Second ASCT (melphalan 200 mg/m²) (if no nCR/CR)
2 x Lenalidomide
A1
B1
A2
B2
Lenalidomide for 2 years
Lenalidomide if no CR
Lenalidomide for 2 years
Lenalidomide if no CR
AFT-29 / MMY2004. A randomized, phase II study of lenalidomide, bortezomib and dexamethasone +/- daratumumab with Safety Run-in: P.I. Peter Voorhees
Induction
Transplant
Consolidation
Maintenance*
Randomization
N=100
N=100
Stratification Factors: ISS stage, CrCl
*Maintenance on protocol therapy lasts 2 years but patients are encouraged to remain on lenalidomide monotherapy until disease progression thereafter

55


Maintenance (GEM14 MAIN)
Induction:
VRDx6
MRD
R
ASCT
Mel-200
Bu-Mel
MRD
Consolidation:
VRDcon x 2
MRD
R
Maintenance
MRD
LEN/DEX x 2 yrs*.
LEN/DEX + MLN9708 x 2 yrs*.
MRD
MRD+ Rd x 3 yrs
MRD- Stop Maintenance
* Patients with positive MRD will continue with LEN/DEX for 3 more years
Treatment/Schema
Len Dara vs Len
Registration/Enrollment (prior to ASCT)
ASCT per PI/Institutional discretion
Randomization within 180 days post-ASCT
Lenalidomide, 10 mg/day, days 1-21*
Lenalidomide, 10 mg/day, days 1-21* + Daratumumab, days 1,8,15,21**
Continue for 2 years of therapy
Assess MRD
MRD-negative
MRD-positive
MRD-negative
MRD-positive
Continue L
Stop L
Continue L
Continue LD
Stop LD
Continue LD
Follow until progressive disease
Off protocol therapy (Patients followed for OS, 4 years)
*After 3 months, may be raised to 15 mg/day if ANC and platelet counts acceptable; non heme tox to Gr 0-1
**Dosing will be changed to monthly dosing after month 2
Bortezomib, lenalidomide, and dexamethasone (VRd) ± daratumumab (DARA) in pts with transplant-eligible (TE) newly diagnosed multiple myeloma (NDMM): A multicenter, randomized, phase III study (PERSEUS).
Induction
Transplant
Consolidation
Maintenance*
Randomization
N = 345
N = 345
Stratifications: ISS stage & cytogenetic risk (high risk: del17p, t[4;14], or t[14;16])
N=690, Primary Outcome: PFS, ~ up to 9 yrs on protocol therapy. *All pts receive Len until PD. MRD-negative (10-5) NGS, pts in DARA arm will stop DARA after MRD negativity for 12 mo & ≥24 mo of maintenance. Pts continue len maintenance until PD or unacceptable toxicity. For DARA arm pts, Upon loss of CR or MRD-negative status, restart DARA treatment. https://clinicaltrials.gov/ct2/show/NCT03710603
Len Citarinostat vs Len
Mel200 ASCT
Day 100 (SD or better) Registration/ Randomization
Lenalidomide (n=40)
PD
Lenalidomide + citarinostat
PD
Lenalidomide + citarinostat (n=40)
PD
Extended follow-up
High Risk MM, Courtesy Sarah Holstein

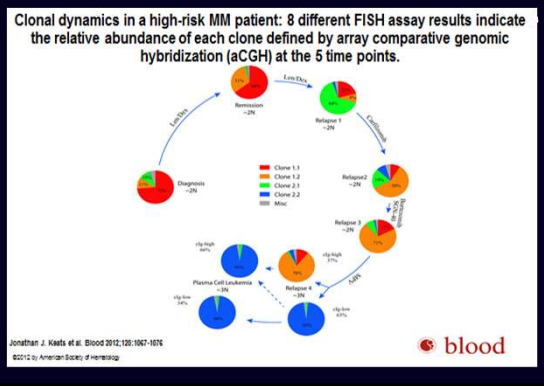
56



57

RRMM Presentation at Relapse/Progression

- Asymptomatic
  - Laboratory abnormalities
    - Treating when fulfilling criteria for PD versus earlier therapy

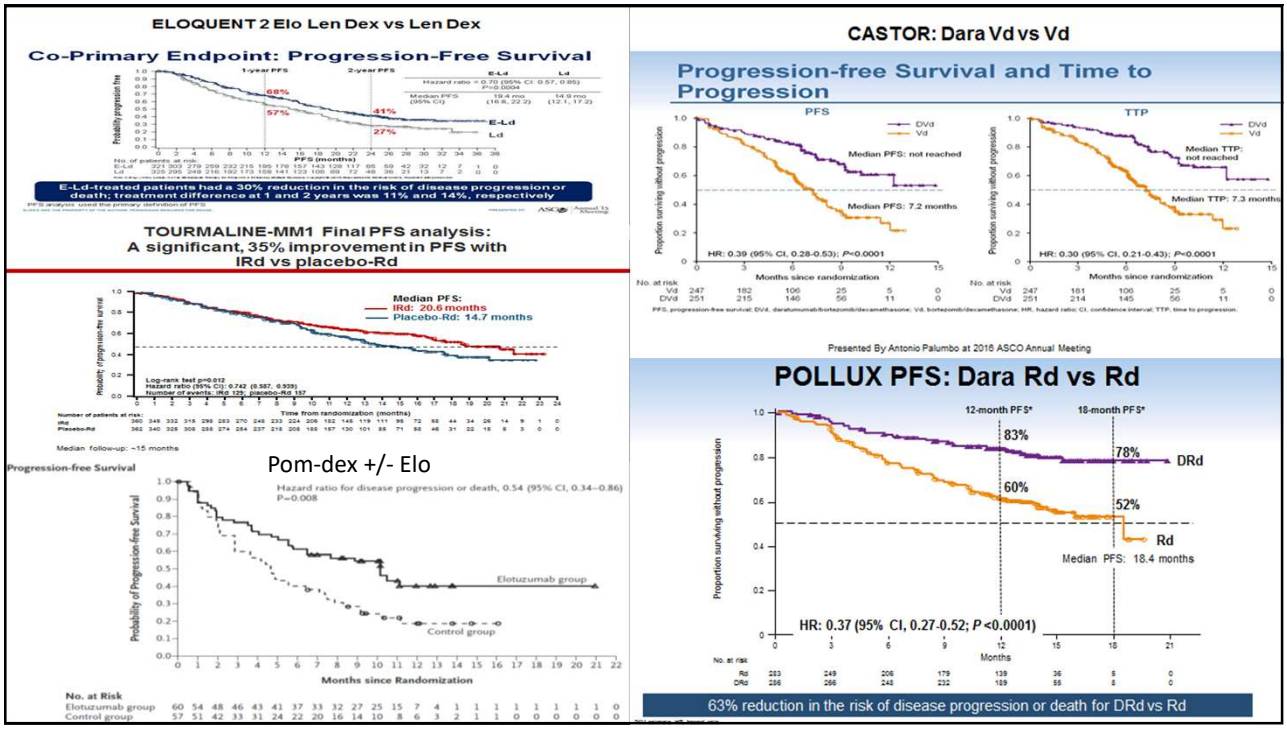


- Symptomatic
  - Need for earlier treatment
  - Progression within 6 to 9 months versus beyond 6 to 9 months
    - Previous regimen versus new regimen

Unlike many solid tumors, can re-use previous therapies especially when combining with a new therapy

- elotuzumab/len/dex
- daratumumab/len/dex
- daratumumab/bortezomib/dex
- carfilzomib/len/dex
- pomalidomide/dex
- elotuzumab/pom/dex
- panobinostat/bortezomib/dex

58



59

RRMM Randomized Salvage Therapy Studies

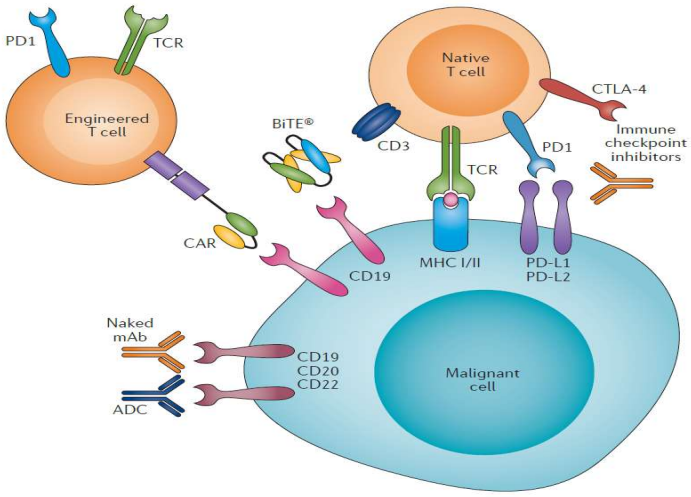
	Med Rx lines (range)	Exclusion	Study Combination versus Control PFS	OS	Benefit PFS/OS
Daratumumab Rd vs Rd# Dimopoulos et al NEJM 2016	1 (1-8)	Len refractory (refr) or intolerant (intol)	NR vs 18.4 mo; HR 0.37; P<0.001	7.4 mo median F/U; 18 mo 4 yr OS 86 vs 76% P=0.0534	+/+-
Elotuzumab Rd vs Rd^ Lonial et al NEJM 2015	2 (1-4)	Len refr or intol < 9 mo from last len dose	19.4 vs 14.9 mo; HR 0.70; P<0.001	24.5 mo median F/U; Med OS 48 vs 40 mo; HR 0.78	+/+-
Elotuzumab Pd vs Pd& Dimopoulos et al NEJM 2018	3 (2-8)	Previous P Rx, PCL, Low CrCl	10.3 mo vs 4.7 mo; HR 0.54; P=0.008	At 9.1 mo follow up Deaths:22% vs 32% HR 0.62	+/+-
Daratumumab Vd vs Vd* Palumbo et al NEJM 2016	2 (1-9)	PI refr or intol	NR vs 7.2 mo; HR 0.39; P<0.001	7.4 mo median F/U OS NR vs NR; HR 0.77; P=0.30	+/+-
Ixazomib Rd vs Rd Moreau et al NEJM 2016	2 (1-3)	Len or PI refr	20.6 vs 14.7 mo; HR 0.74; P=0.01	23 mo median F/U; OS 77.5 vs 75.2% P=ND	+/+-
Carfilzomib Rd vs Rd Stewart et al NEJM 2015@	2 (1-3)	Len or PI refr	26.3 vs 17.6 mo; HR 0.69; P=0.0001	67.1 mo median F/U; Med OS 48 vs 40 mo; HR 0.79 P=0.005	+/+
Carfilzomib 70d vs 27x2d Moreau et al Lancet Onc 2018	2-3	PCL, no PR to any Rx	11·2vs 7·6 mo HR 0·69; P=0·0029;	13.2 mo F/U One year OS 77 vs 72% P=ND	+/+-
Carfilzomib d (Kd) vs Vd Dimopoulos et al Lancet Oncol 2017	2 (1-3)	PI refr or < 6 mo from last PI Rx<PR to all Rx	18.7 vs 9.4 mo; HR 0.53; P<0.0001	37.5 mo median F/U OS 47.6 vs 40 mo HR 0.79; P=0.01	+/+
Panobinostat Vd vs Vd San Miguel et al Lancet Oncol 2014	2 (1-2)	PI or HDAC inhibitor refr	11.99 vs 8.08 mo HR 0.63 P<0.0001	6.5 mo median F/U; Median OS 33.64 vs 30.39 mos HR 0.87 P=0.26	+/+-
Pomalidomide d vs d San Miguel et al Lancet Oncol 2013	5 (2-14)	IMid intol or refr to d	4.0 vs 1.9 mo HR 0.48 P<0.0001	4.2 mo median F/U 11.9 vs 7.8 mo HR 0.53 P=0.0002	+/+

d: Dexamethasone; HR: Hazard Ratio; Len: Lenalidomide; ND: No difference; NR: Not Reached; OS:Overall Survival; PI: Proteasome Inhibitor; PFS: Progression-Free Survival; Rd: Lenalidomide/d; Vd: Bortezomib/d # Update Dimopoulos et al Haematologica 2018, *Update, Spencer et al Haematologica 2018, &Phase II study, ^Update Dimopoulos et al Cancer 2018 @Update Siegel et al JCO 2018

60

Mechanisms of Selected Immunotherapies

- Checkpoint Inhibitors (PD-1/PD-L1,PD-L2; CTLA-4;Lab-3
- Antibody agonists (CD137;GITR; CD40)
- Bi-specific T cell engagers (BITE) (blinatumumab) or other targets
  - AMG 420 Anti BCMA BITE, Topp et al Blood 2018 132: 1010 (ASH 2018)
- Naked antibodies (Rituximab, Herceptin, Anti-BCMA)
- Antibody drug conjugates (Brentuximab Vedotin, Anti-BCMA-drug conjugate (GSK2857916)
- Chimeric Antigen Receptor T cells (Engineered)
- NK cells



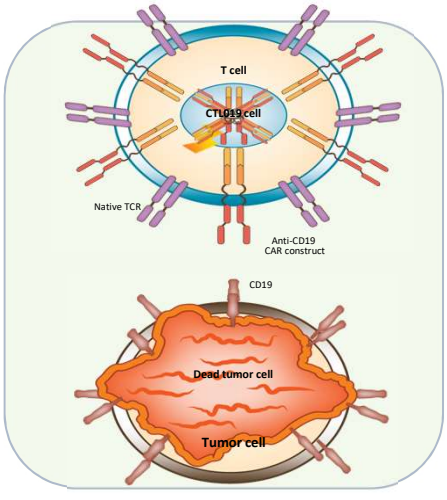
Modified from Batlevi CL et al Novel immunotherapies in lymphoid malignancies Nature Rev Clin Oncol January 2016

61

Chimeric Antigen Receptor (CAR) T cell therapy

- **Gene transfer technology stably expresses CARs on T cells[1,2]**
- **CAR T cell therapy takes advantage of the cytotoxic potential of T cells, killing tumor cells in an antigen-dependent manner[1,3,4]**
- **Persistent CAR T cells consist of both effector (cytotoxic) and central memory T cells[3,4]**
- **First human trial in resistant CLL patients[4]**
- **T cells are non-cross resistant to chemotherapy**

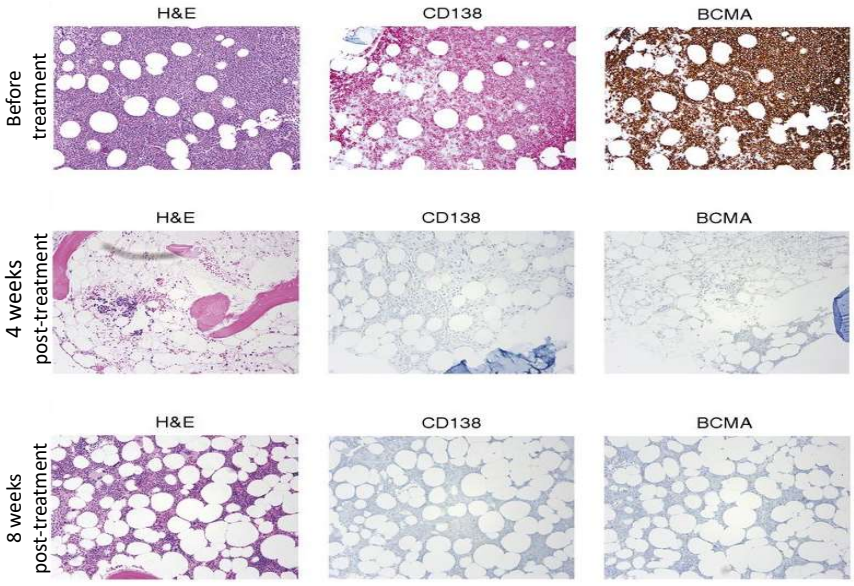
1. Milone MC, et al. *Mol Ther.* 2009;17:1453-1464.
2. Hollyman D, et al. *J Immunother.* 2009;32:169-180.
3. Kalos M, et al. *Sci Transl Med.* 2011;3:95ra73.
4. Porter DL et al. *NEJM* 2011. 365:725-33



Original Slide Courtesy of D Porter

62

BCMA+ CAR T therapy For Multiple Myeloma



Zhao ASH 2018 Abstract 955
- 88% ORR (50/57)
- 42/57 (74%) patients in CR
  Median time to response: 1 mo
  Median DoR: 16 mos
  39/57 (68%) MRD-negative

Berdeja et al ASH 2017 Abs 740
85% ORR
Raje et al ASCO 2018
Higher response rates at higher cell doses with high rate of MRD-

November 17th, 2017
FDA Breakthrough Designation

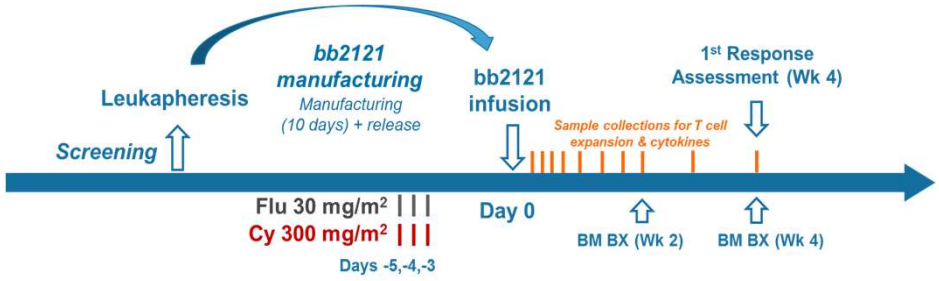
Syed Abbas Ali et al. Blood 2016;128:1688-1700

63

CRB-401 Study Design (bluebird)

3 + 3 Dose Escalation of CAR + T Cells

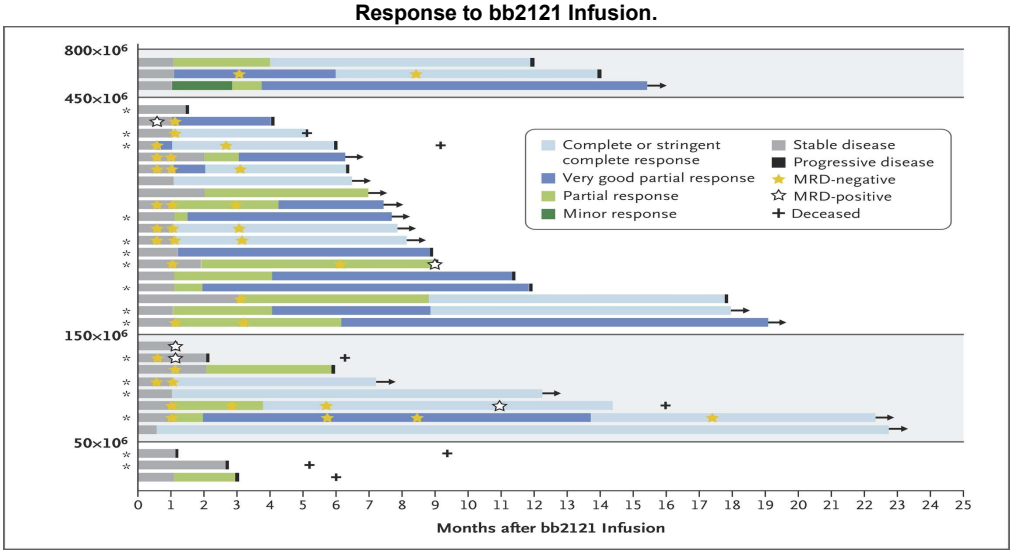
*1200 x 10^6 dose cohort no longer planned



Raje N et al. N Engl J Med 2019;380:1726-1737

64

Response to bb2121 Infusion.



N=33 patients: Objective response rate was 85%, including 15 patients (45%) with CR. 6 of the 15 CR patients have relapsed. Median PFS was 11.8 months (95% CI, 6.2 to 17.8). All 16 patients who had were ≥ PR and who could be evaluated for minimal residual disease(MRD) had MRD-negative status (≤10^{-4} nucleated cells).

Raje N et al. N Engl J Med 2019;380:1726-1737

The NEW ENGLAND JOURNAL of MEDICINE

65

JCARH125 Phase 1/2 Anti-BCMA Study

RESPONSE OVER TIME AT DOSE OF 50 × 10^6 CAR+ T CELLS (Longest Follow-up)

Responses continued to improve over time

Five of the 14 patients (36%) showed deepening of response past Day 29

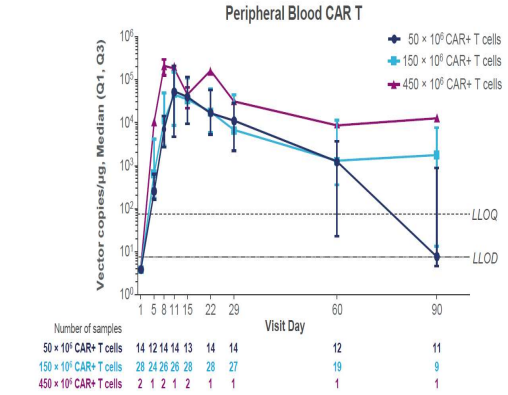
Six of nine evaluable patients were MRD-negative by NGS at Day 29[a]

[a]One patient had MRD assessment at Month 2

CR, complete response; DL, dose level; MR, minimal response; MRD, minimal residual disease; NGS, next generation sequencing; PD, progressive disease; PR, partial response; sCR, stringent complete response; SD, stable disease; VGPR, very good partial response.

11

JCARH125 EXPANSION AND LONG-TERM PERSISTENCE



- Robust expansion observed at all dose levels
- Trend for increased persistence past Month 2 at dose levels ≥150 × 10^6 CAR+ T cells

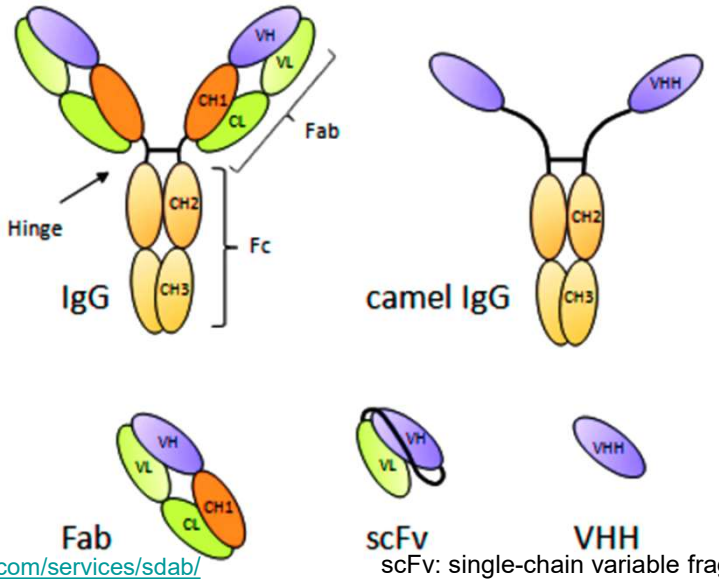
Vector copy number assessed by quantitative polymerase chain reaction, using genomic deoxyribonucleic acids extracted from whole blood.

12

Mailankody S et al ASH 2018 (Juno)

66

Single Domain Antibodies



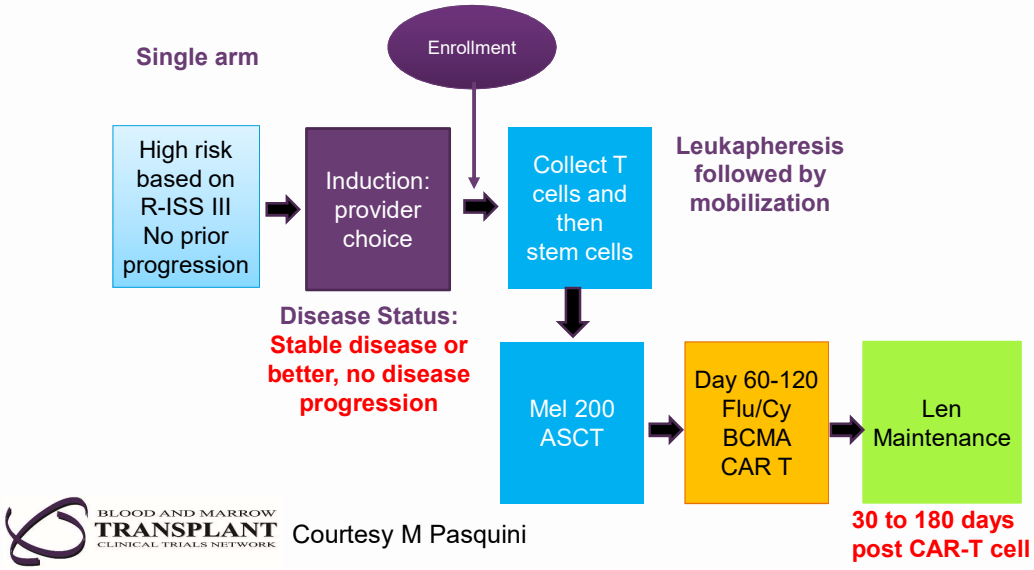
http://www.abdesignlabs.com/services/sdab/

scFv: single-chain variable fragment

Single domain antibodies, also known as VHH Janssen CAR Construct

67

Proposed Study Schema: Tandem Approach

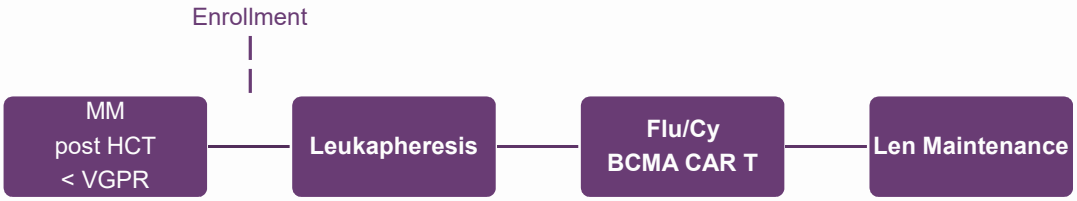


BLOOD AND MARROW TRANSPLANT CLINICAL TRIALS NETWORK

Courtesy M Pasquini

68

PROPOSED Study Schema



~9 mo post auto HCT No prior disease Progression

Day 30 -180 post CAR T-cells

CR rate at 6 months

BLOOD AND MARROW TRANSPLANT CLINICAL TRIALS NETWORK Courtesy M Pasquini

69

Drug Sequencing Strategies in RRMM
First or Slow Relapse

Slow (Indolent) Relapse or First Relapse

Participate in Clinical Trials with Novel Agents

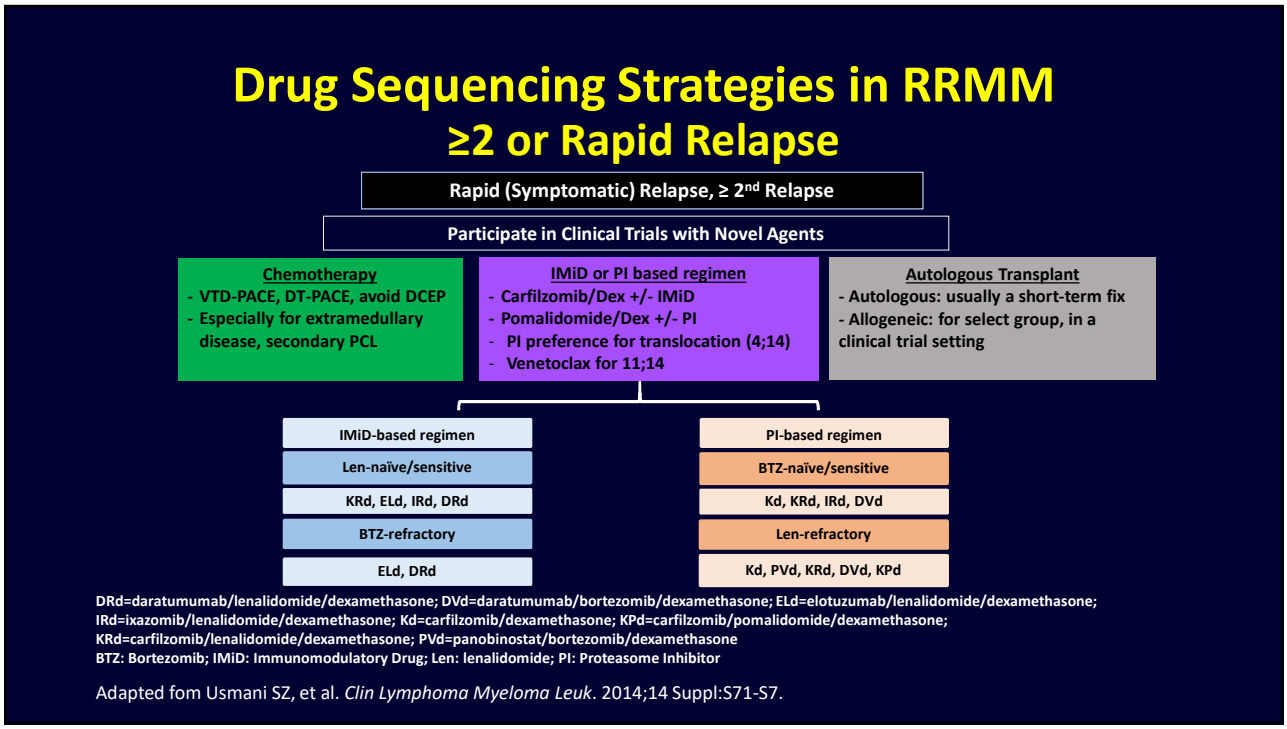
IMiD-based Regimen	PI-based Regimen	Autologous Transplant
-Underlying Peripheral Neuropathy -No prior IMiD exposure -Prior IMiD use with good tolerance, durable/deep response, and PFS -Prior bortezomib use	-Prior IMiD use -No prior PI exposure -Prior PI use with good tolerance, durable/deep response, and PFS -Translocation (4;14)	- Long remission post first transplant (>24 months without maintenance; >36 months with maintenance) - Transplant not part of primary therapy
Len-naïve/sensitive	BTZ-naïve/sensitive	
KRd, ELd, IRd, DRd	Kd, KRd, IRd, DVd	
BTZ-refractory	Len-refractory	
ELd, DRd, KRd, EPd	Kd, PVd, KRd, DVd, KPd, EPd	

DRd=daratumumab/lenalidomide/dexamethasone; DVd=daratumumab/bortezomib/dexamethasone; ELd=elotuzumab/lenalidomide/dexamethasone; IRd=ixazomib/lenalidomide/dexamethasone; Kd=carfilzomib/dexamethasone; KPd=carfilzomib/pomalidomide/dexamethasone; KRd=carfilzomib/lenalidomide/dexamethasone; PVd=panobinostat/bortezomib/dexamethasone
BTZ: Bortezomib; IMiD: Immunomodulatory Drug; Len: lenalidomide; PI: Proteasome Inhibitor

Adapted from Usmani SZ, et al. *Clin Lymphoma Myeloma Leuk*. 2014;14 Suppl:S71-7

70

Drug Sequencing Strategies in RRMM
≥2 or Rapid Relapse



DRd=daratumumab/lenalidomide/dexamethasone; DVd=daratumumab/bortezomib/dexamethasone; ELd=elotuzumab/lenalidomide/dexamethasone; IRd=ixazomib/lenalidomide/dexamethasone; Kd=carfilzomib/dexamethasone; KPd=carfilzomib/pomalidomide/dexamethasone; KRd=carfilzomib/lenalidomide/dexamethasone; PVd=panobinostat/bortezomib/dexamethasone
BTZ: Bortezomib; IMiD: Immunomodulatory Drug; Len: lenalidomide; PI: Proteasome Inhibitor

Adapted fom Usmani SZ, et al. *Clin Lymphoma Myeloma Leuk*. 2014;14 Suppl:S71-S7.

71

Summary: Upfront Therapy for the Transplant Ineligible MM Patient

- Transplant Ineligible (TI) fit patient
  - VRd for Eight 21 day Cycles patient followed by Rd until PD or AE (SWOG S0777)
- TI, frail patient
  - VRd "Lite" for 4 to 8 Cycles followed Rd or Rd alone until PD (O'Donnell et al BJH 2018, FIRST Trial)
- High Risk Cytogenetics
  - t(4;14), t(14;16), t(14;20), del 17p, +1q
    - Bortezomib containing regimen
    - PI for long term disease control (Carfilzomib or Ixazomib?)
- IMiD Intolerance
  - VCD, if less fit, VD, VMP
- PI Intolerance
- KRd for very fit patient
  - IRD for frail patient
- Outside USA
  - VMP vs VTP/VTD
  - CRD > CTD (UK)
- Future: Incorporation of Monoclonal Antibodies into Front Line Therapy?

ROSWELL PARK

72

Conclusions

- Newly Diagnosed Multiple Myeloma (NDMM) Patient
  - Transplant Eligible
    - Induction, Autologous Stem Cell Transplant (ASCT) followed by maintenance (+/- consolidation) until progression
  - Transplant Ineligible
    - Induction, followed by continuous therapy/maintenance until progression
  - Induction regimens often consist of glucocorticoids, an immunomodulatory drug (IMiD) and a proteasome inhibitor (PI)
  - Will agents such as daratumumab become part of frontline therapy?
- Improved therapy prolongs progression free and overall survival (PFS/OS)
- Understanding the control of MM proliferation and differentiation allows for new drug development

ROSWELL PARK

73

Conclusions

- The majority of patients will have progressive disease as MM is incurable
  - Relapsed and Refractory (RRMM)
  - Multiple choices and Investigational studies are ongoing and planned to test new strategies to improve outcome
  - *Early surrogate endpoints for long term outcome (PFS/OS) must be tested in clinical trials so as to prevent studies that must remain open for 10 years or longer especially for an OS endpoint (Examples include Minimal Residual Disease (MRD) testing and Immune Profiling)*
- Novel approaches to MM treatment include immunotherapy
- However immunotherapy can be a double edged sword and careful monitoring is critical

ROSWELL PARK

74

Questions for the Future

- Will KRD without ASCT suffice for induction and consolidation before maintenance and will KR will be the new standard for maintenance? (FORTE)
- Will Elo/RVD and/or Elo/Rd become new standards post ASCT for consolidation and/or maintenance respectively? (GMMG-HD6)
- Will VTD-Dara and/or Dara become new standards for consolidation and/or maintenance post ASCT respectively? (CASSIOPEIA)
- Will Len+Ixa+Dex to be the new maintenance standard post ASCT? (GEM 14)
- Will Dara-RVD will be the standard for induction pre ASCT and for consolidation followed by R-Dara maintenance? (GRIFFIN and PERSEUS)
- Will RVD generate equivalent OS to transplant even with an shorter PFS? (IFM DFCI 2009)
- How will Risk Stratification and MRD testing be used during treatment?
  - New Cytogenetic Risk Stratification, *Perrot et al, JCO 2019*

75

People and Services who make the BMT program possible

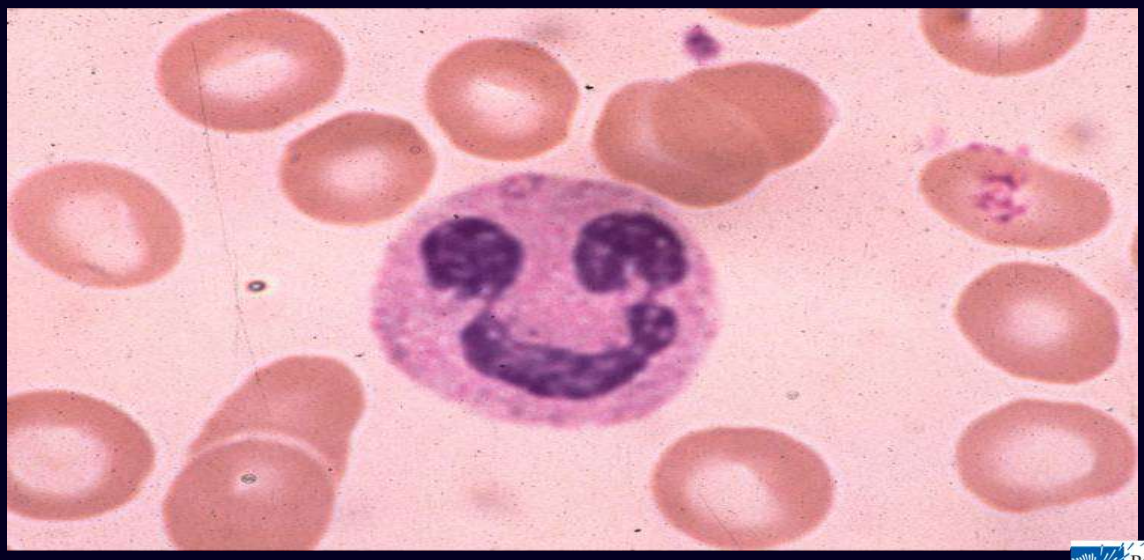
- S Balderman
- G Chen
- C Ho
- M Ross
- M Aungst
- M Burgess
- M Everett
- A Koeppel
- J Lex-Sikinoff
- A Nemmer
- S Myszka
- A Phillips-Hall
- P Paplham
- R Russell
- A Beck
- S Flavin
- D Oliansky
- F Zhang
- A Kariapper
- H Jacobson
- R McKenzie
- S Oakley
- D Manfredi
- T Hahn
- M Herr
- S Schinnagel
- L Privitere
- K West
- J Pleskow
- M Cimino
- M Steward
- D Swinnich
- K Stawicki
- D Cipolla
- K Dubel
- P Lipka
- S Siconolfi
- C Warren
- L Yoerg
- S Pry
- R De Wald
- L Markel
- R Kumpf
- K Dunn
- A Kader
- J NIchols
- H Bashaw
- T Chodon
- R Koya
- C Choi
- J Becker
- E Duman
- L Vesneske
- Rad Onc Service
- Radiology Svc
- Surgery Svc
- Pathology Svc
- Lab Medicine
- Stem Cell Lab
- Apheresis Unit
- S Szeglowski
- L Regan
- S Segal
- J Maxick-Jason
- J Kapinos
- A Singh
- ID service
- B Segal
- N Almyroudis
- D DePaolo
- Managed Care and Finance Svc
- S Randolph
- M Budd
- Medical Oncology Fellows
- Leukemia, Lymphoma and Myeloma Services
- 5 East, 5 North and 6 North Nursing and Secretarial Staff
- Hospitalist Staff
- J Hillengass
- F Hernandez
- E Wang
- M Ernstoff
- J Lau
- E Repasky and Lab
- P Torka
- P Wallace
- J Tario
- Y Zhang
- S Johnson
- C Johnson
- V Filadora
- T Schwaab
- B Kuvshinoff
- Support by RPCI Alliance, RPCI Core Grant, NCI, NHLBI and B and E McCarthy

76

Acknowledgements

- Patients and Caregivers who participated in the clinical trials
- Abstract presenters for sharing presentations and discussion: S Gay, S Lonial, MV Mateos
- Helpful discussion and/or sharing of PP presentations: S Holstein, J Hillengass, V Suman, M Attal, H Avet-loiseau, J Blade, M Boccadero, M Bustoros, M Cavo, G Cook, F Davies, O Decaux, M deLima, R de Tute, T Facon, R Gale, L Garderet, I Ghobrial, P Hari, JL Harousseau, G Jackson, S Jagannath, X Leleu, H Ludwig, M Mohty, G Morgan, P Moreau, P Neri, S Oliva, R Owen, B Paiva, A Palumbo, M Pasquini, T Plesner, P Richardson, L Rosinol, J San Miguel, P Sonneveld, E Stadtmauer, N Weinhold S Zweegman
- Roswell Park Colleagues: T Hahn, P Wallace, J Tario, J Hillengass, M Merz, A Merz, S Balderman, G Chen, F Hernandez, C Ho, K Lee, M Ross, P Torka
- Alliance, BMT CTN, ECOG, SWOG, MYSC Colleagues: S Holstein, V Suman, K Anderson, P Richardson, C Linker, K Owzar, S Jung, C Hofmeister, D Hurd, R Vij, J Moreb, NS Callander, K van Besien, T Gentile, L Isola, R Maziarz, D Gabriel, A Bashey, T Shea, S Devine, H Hassoun, D Weisdorf, T Martin, E Stadtmauer, S Giralt, M Pasquini, A Krishnan, M Horowitz, D Sargent, R Orlowski, V Rajkumar, S Kumar, M Perales, S Devine, J Omel, A Yee, C Rodriques, J Laubach, M Kwok, S Dinner, A Mahindra, T Wildes, A Rosko, B Sommers, H Cohen, C Mitsiades, C Garparetto, D Carlisle, E Faber, E O'Donnell, H Hassoun, C Mitsiades, C Rodriguez, I Galinsky, N Nathwani, P Voorhees, S Tuchman, T Kelley, Y Efebera, Y Wen, H Landau, G Bianchi, E Alyea, A Artz, C Ustin, J McCarty, C Sauter, B Andreadis, M Hamadani, K Komanduri, S Nathan, A Sung, S Vasu, W Basen, C Brunstein, M Wieduwilt, W Wood, A Bashey, N Raje, M Dhodapkar, B Durie, S Usmani, J Aiello, M Alsina, L Bersagel, Y Biru, B Freidlin, E Gorak, A Hay, A Hoering, S Jacobus, D Jaffe, D Jenkins, E Obote, A Reiman, P Ujhazy, R Wu, S Jagannath, S Lonial, S Lentzsch, W Merritt, N Munshi,
- The NCI/NHLBI: R Little, N DiFronzo, W Merritt, R Wu, H Streicher, L Baizer
- FDA: A Farrell, N Gormley, A Deisseroth
- My wife Jane who puts up with my schedule

Thank you very much.



Q&A SESSION

Multiple Myeloma: Know Your Treatment Options

- **Ask a question by phone:**
  - Press star (*) then the number 1 on your keypad.
- **Ask a question by web:**
  - Click “Ask a question”
  - Type your question
  - Click “Submit”

Due to time constraints, we can only take one question per person. Once you’ve asked your question, the operator will transfer you back into the audience line.

BEATING CANCER IS IN OUR BLOOD.

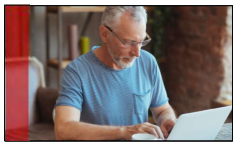
LEUKEMIA & LYMPHOMA SOCIETY®

79

LLS EDUCATION & SUPPORT RESOURCES

- **Information Specialists**

  Master’s level oncology professionals, available to help cancer survivors navigate the best route from diagnosis through treatment, clinical trials and survivorship.
  - **EMAIL:** infocenter@LLS.org
  - **TOLL-FREE PHONE:** 1-800-955-4572
- **Caregiver support:** www.LLS.org/caregiver
- **Free education booklets:** www.LLS.org/booklets
- **Free telephone/web programs:** www.LLS.org/programs
- **Weekly online chats:** www.LLS.org/chat
- **LLS Community:** www.LLS.org/community
- **Information about myeloma:** www.LLS.org/myeloma



BEATING CANCER IS IN OUR BLOOD.

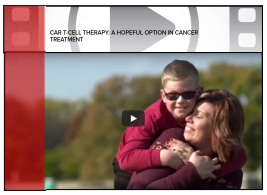
LEUKEMIA & LYMPHOMA SOCIETY®

80

LLS EDUCATION & SUPPORT RESOURCES

- **LLS Patient Podcast, *The Bloodline with LLS***

  Listen in as experts and patients guide listeners in understanding diagnosis, treatment, and resources available to blood cancer patients: **www.thebloodline.org**



- **Education Videos**

  Free education videos about survivorship, treatment, disease updates, and other topics: **www.LLS.org/educationvideos**

- **Patti Robinson Kaufmann First Connection Program**

  Peer-to-peer program that matches newly diagnosed patients and their families: **www.LLS.org/firstconnection**

81

LLS EDUCATION & SUPPORT RESOURCES

- **Free Nutrition Consults**

  Telephone and e-mail consultations with a registered dietitian: **www.LLS.org/nutrition**

- **What to Ask**

  Questions to ask your treatment team: **www.LLS.org/whattoask**

- **Other Support Resources**

  LLS community, blogs, support groups, financial assistance, and more: **www.LLS.org/support**

82


THANK YOU
We have one goal: A world without blood cancers
LEUKEMIA & LYMPHOMA SOCIETY®

83