What's New in Multiple Myeloma?

AARON ROSENBERG, MD, MS
ASSISTANT PROFESSOR OF MEDICINE
BONE MARROW TRANSPLANTATION UNIT
DIRECTOR, MULTIPLE MYELOMA AND PLASMA CELL DISEASE CLINIC
UC DAVIS COMPREHENSIVE CANCER CENTER
ASROSENBERG@UCDAVIS.EDU
215-528-9619

Disclosures

- Speakers Bureau (unbranded)
  - Janssen, Millennium-Takeda
- Research
  - Amgen

- Bone Marrow Transplant Attending (probably more important than any of the above!)

Outline

- S0777: Long Term Follow up
- E1A11: VRd vs KRd
- GRIFFIN: Dara-VRd vs VRd
- Extended KRD
- MYRE: CyVD vs VD

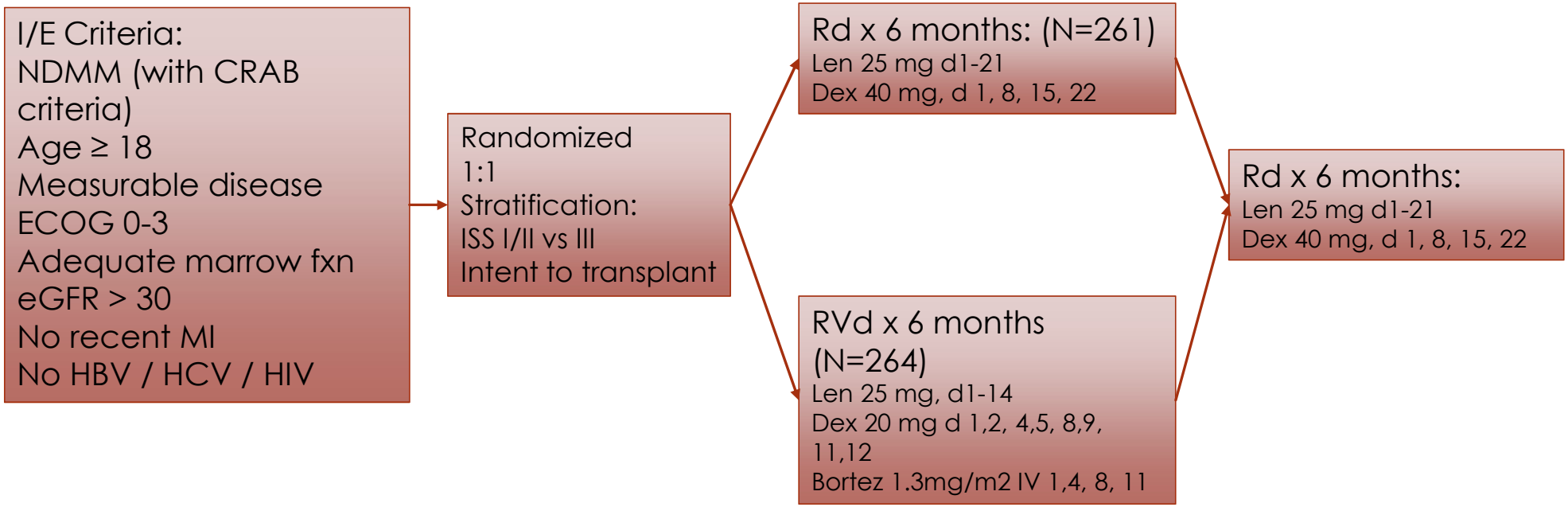
Newly Diagnosed Myeloma

WHAT IS THE CURRENT STANDARD OF CARE IN 2020?

How Should Front Line Therapy be Approached?

- Incurable disease – thus goals of therapy tailored to individual patients
- In modern era of therapy, prolongation of life while minimizing toxicity is achievable
- Minimize treatment related morbidity
  - Patient comorbidity – may need to de-escalate
  - Rapidly progressive renal failure – may need more rapid disease control

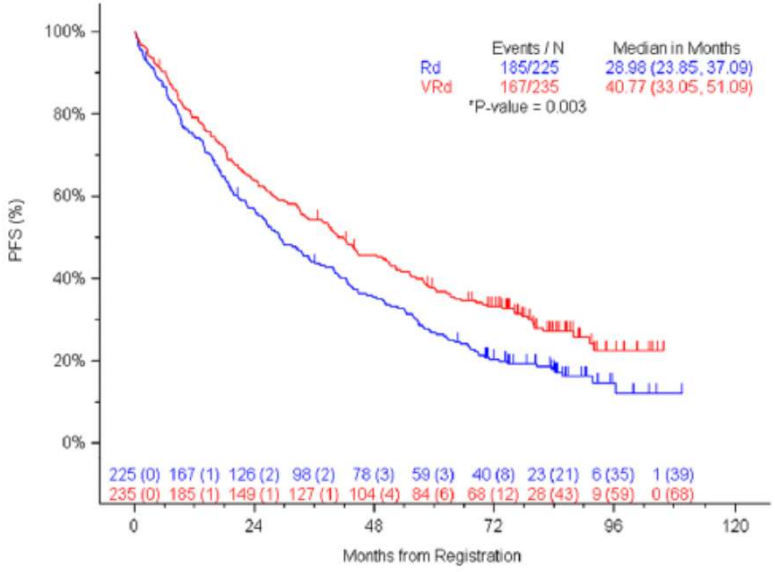
S0777: Trial Schema



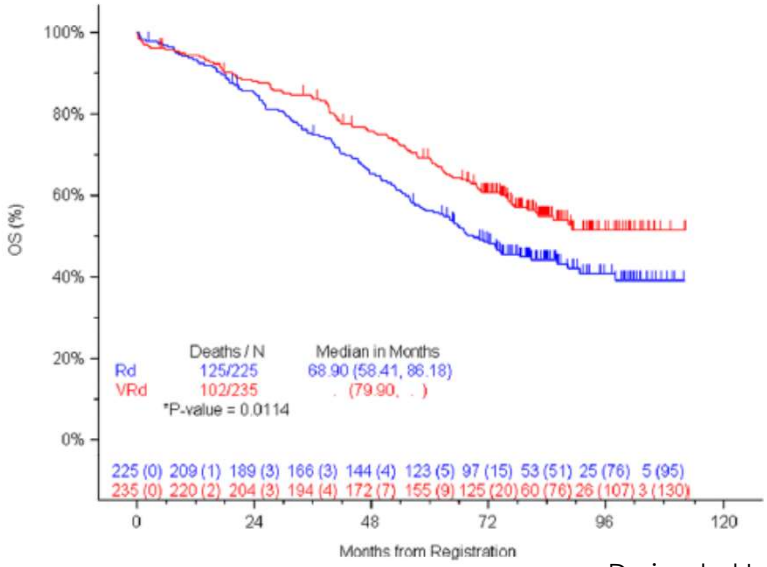
Durie et al Lancet 2017
Durie et al BCJ 2020

S0777: PFS and OS

PFS



OS



Durie et al Lancet 2017
Durie et al Blood Canc Jour 2020

Table 5 Adverse events at least possibly attributable to study drug by category.

Adverse event description	Revlimid/dexamethasone ($N = 222$)					Velcade/Revlimid/dexamethasone ($N = 234$)				
	1	2	3	4	5	1	2	3	4	5
Allergy/immunology	12 (5%)	5 (2%)				10 (4%)	4 (2%)	2 (<1%)		
Auditory/ear	1 (<1%)	16 (7%)				1 (<1%)	8 (3%)			
Blood/bone marrow	22 (10%)	53 (24%)	68 (31%)	39 (18%)		27 (12%)	52 (22%)	70 (30%)	44 (19%)	
Cardiac arrhythmia	5 (2%)	4 (2%)	4 (2%)			10 (4%)	3 (1%)	3 (1%)		
Cardiac general	13 (6%)	9 (4%)	8 (4%)			15 (6%)	17 (7%)	21 (9%)		
Coagulation	1 (<1%)		3 (1%)					5 (2%)		
Constitutional symptoms	61 (27%)	77 (35%)	38 (17%)			60 (26%)	84 (36%)	51 (22%)		
Death					1 (<1%)					2 (<1%)
Dermatology/skin	60 (27%)	23 (10%)	9 (4%)			50 (21%)	41 (18%)	7 (3%)	1 (<1%)	
Endocrine	11 (5%)	8 (4%)				7 (3%)	12 (5%)			
Gastrointestinal	77 (35%)	71 (32%)	19 (9%)			64 (27%)	79 (34%)	51 (22%)	2 (<1%)	1 (<1%)
Hemorrhage/bleeding	13 (6%)	2 (<1%)				9 (4%)	3 (1%)	8 (3%)		
Hepatobiliary/pancreas			2 (<1%)							
Infection	1 (<1%)	31 (14%)	27 (12%)	4 (2%)		1 (<1%)	33 (14%)	34 (15%)	7 (3%)	1 (<1%)
Lymphatics	58 (26%)	19 (9%)	1 (<1%)			73 (31%)	26 (11%)	4 (2%)		
Metabolic/laboratory	56 (25%)	58 (26%)	51 (23%)	13 (6%)		50 (21%)	58 (25%)	57 (24%)	8 (3%)	
Musculoskeletal/soft tissue	25 (11%)	25 (11%)	16 (7%)	1 (<1%)		15 (6%)	31 (13%)	24 (10%)		
Neurology	78 (35%)	44 (20%)	21 (9%)	3 (1%)	1 (<1%)	42 (18%)	70 (30%)	77 (33%)	4 (2%)	
Ocular/visual	21 (9%)	8 (4%)	11 (5%)			39 (17%)	17 (7%)	6 (3%)		
Pain	44 (20%)	29 (13%)	10 (5%)			55 (24%)	43 (18%)	28 (12%)		
Pulmonary/upper respiratory	42 (19%)	27 (12%)	9 (4%)	1 (<1%)		56 (24%)	17 (7%)	15 (6%)	5 (2%)	
Renal/genitourinary	3 (1%)	2 (<1%)	9 (4%)	1 (<1%)		10 (4%)	3 (1%)	6 (3%)		
Secondary malignancy			5 (2%)	1 (<1%)				5 (2%)	2 (<1%)	
Sexual/reproductive function	1 (<1%)	1 (<1%)	1 (<1%)			3 (1%)	1 (<1%)			
Syndromes			2 (<1%)			1 (<1%)	2 (<1%)	4 (2%)		
Vascular		7 (3%)	15 (7%)	6 (3%)		1 (<1%)	9 (4%)	20 (9%)	4 (2%)	

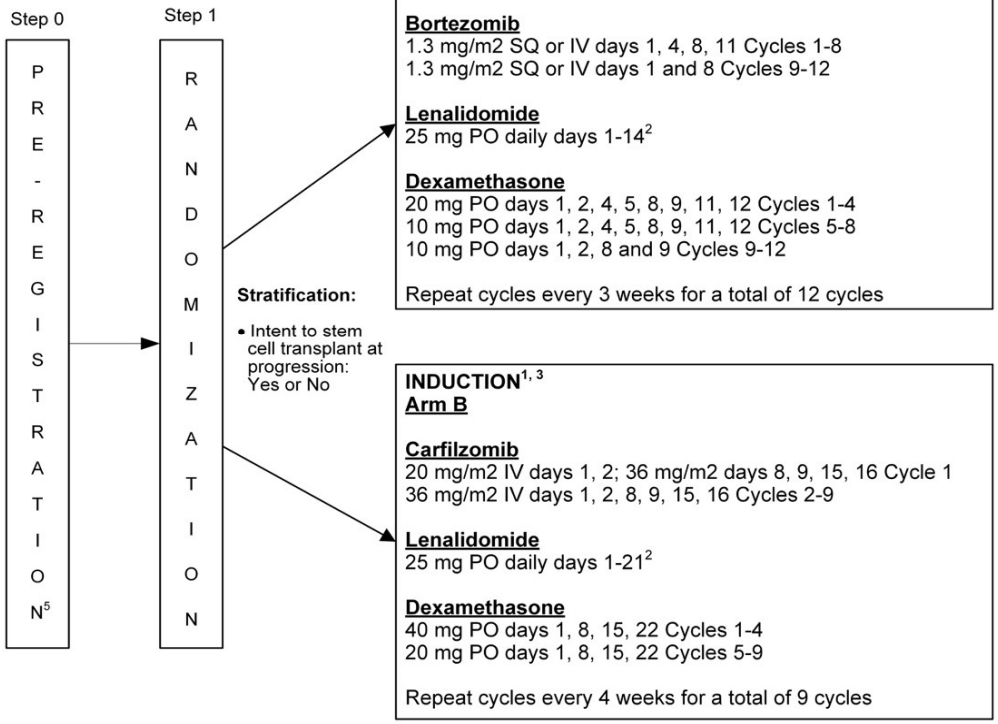
Durie et al Lancet 2017
Durie et al Blood Canc

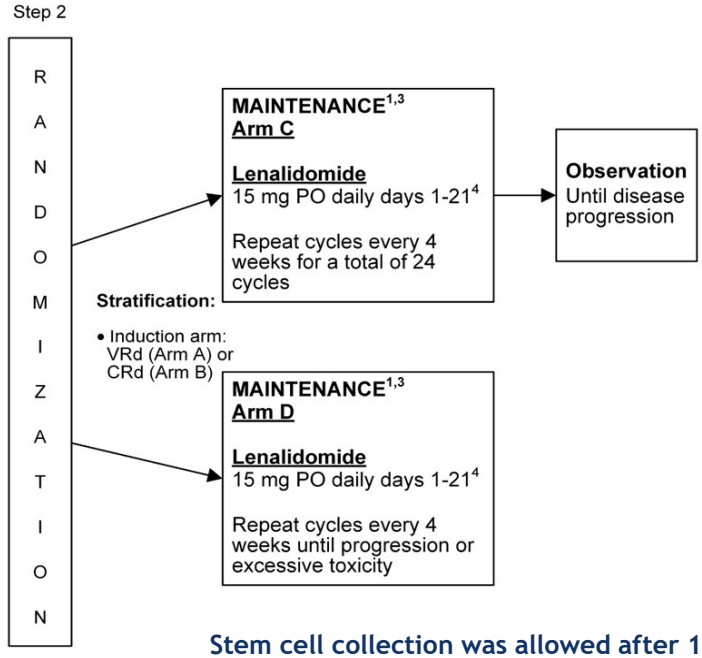
Can we do better than VRd?

Carfilzomib or bortezomib in combination with lenalidomide and dexamethasone for patients with newly diagnosed multiple myeloma without intention for immediate autologous stem-cell transplantation (ENDURANCE): a multicentre, open-label, phase 3, randomised, controlled trial

Shaji K Kumar, Susanna J Jacobus, Adam D Cohen, Matthias Weiss, Natalie Callander, Avina K Singh, Terri L Parker, Alexander Menter, Xuezhong Yang, Benjamin Parsons, Pankaj Kumar, Prashant Kapoor, Aaron Rosenberg, Jeffrey A Zonder, Edward Faber Jr, Sagar Lonial, Kenneth C Anderson, Paul G Richardson, Robert Z Orlowski, Lynne I Waqner, S Vincent Rajkumar

Patient Randomization and Treatment Schedule





Stem cell collection was allowed after 12 weeks of therapy at investigator discretion

Key Eligibility Criteria

- Previously untreated MM with no intent for immediate (upfront) SCT
- **None of the following high-risk features (t(14;20), t(14;16), del17p, LDH > 2 X ULN, no plasma cell leukemia)**
- ECOG performance status 0, 1, or 2 (PS 3 if secondary to pain)
- Adequate hematological parameters and organ function
- Measurable disease in serum, urine, or bone marrow
- No grade ≥2 peripheral neuropathy
- NYHA III or IV heart failure or MI < 6 months were excluded

Baseline Demographics

Variable	Category	VRd (n=542) N (%)	KRd (n=545) N (%)	Total (n=1087) N (%)
Age (y), median (range)		64 (32-88)	65 (35-86)	65 (32-88)
	>/=70 years	167 (30.8)	177 (32.5)	344 (31.6)
	>/=65 years	264 (48.7)	288 (52.8)	552 (50.8)
Gender	Male	315 (58.1)	327 (60.0)	642 (59.1)
Race	White	443 (84.5)	448 (86.3)	891 (85.4)
	Black	68 (13.0)	59 (11.4)	127 (12.2)
	Other	13 (2.5)	12 (2.3)	25 (2.4)
ECOG PS	PS0	212 (39.1)	241 (44.2)	453 (41.7)
	PS1	270 (49.8)	249 (45.7)	519 (47.8)
	PS2-3	60 (11.1)	55 (10.1)	115 (10.5)
ISS Stage	I	144 (30.6)	157 (32.5)	301 (31.6)
	II	203 (43.1)	207 (42.9)	410 (43.0)
	III	124 (26.3)	119 (24.6)	243 (25.5)
Measurable Disease Type	SPEP&UPEP	115 (21.2)	114 (20.9)	229 (21.1)
	SPEP	305 (56.3)	296 (54.3)	601 (55.3)
	UPEP	57 (10.5)	79 (14.5)	136 (12.5)
	FLC	58 (10.7)	51 (9.4)	109 (10.0)
	Bone Marrow	4 (0.7)	4 (0.7)	8 (0.7)
	Not Measurable	3 (0.6)	1 (0.2)	4 (0.4)

Variable	VRd (n=542) median (IQR)	KRd (n=545) median (IQR)	Total (n=1087) median (IQR)
Bone marrow plasma cell (%)	52 (30-75)	50.5 (30-72)	51 (30-75)
Albumin (g/dL)	3.8 (3.4-4.2)	3.8 (3.4-4.2)	3.8 (3.4-4.2)
Beta 2 microglobulin (ug/mL)	3.6 (2.6-5.6)	3.9 (2.8-6)	3.8 (2.6-5.8)
Hemoglobin (g/dL)	11 (9.6-12.4)	11.2 (9.8-12.6)	11.1 (9.7-12.5)
Calcium (mg/dL)	9.3 (8.9-9.8)	9.4 (8.9-9.8)	9.3 (8.9-9.8)
Serum M Spike (g/dL)	3 (1.8-4.2)	2.9 (1.8-4.2)	3 (1.8-4.2)
Urine M Spike (mg/24hr)	297.8 (64.9-1099)	257.1 (49.4-1312.4)	275 (56.4-1157)
Creatinine (mg/dL)	1 (0.8-1.3)	1 (0.8-1.3)	1 (0.8-1.3)
Lactate Dehydrogenase (U/L)	171 (136-222)	166 (135-203)	168 (136-209)

Variable	Category	N (%)	N (%)	N (%)
Cytogenetics	Normal	326 (71.8)	331 (72.3)	657 (72.0)
	Abnormal	128 (28.2)	127 (27.7)	255 (28.0)
	Missing	88	67	175
t(11;14)	Abnormal	87 (20.6)	80 (18.7)	167 (19.7)
t(4;14)	Abnormal	44 (10.4)	36 (8.4)	80 (9.4)

Induction Treatment Status

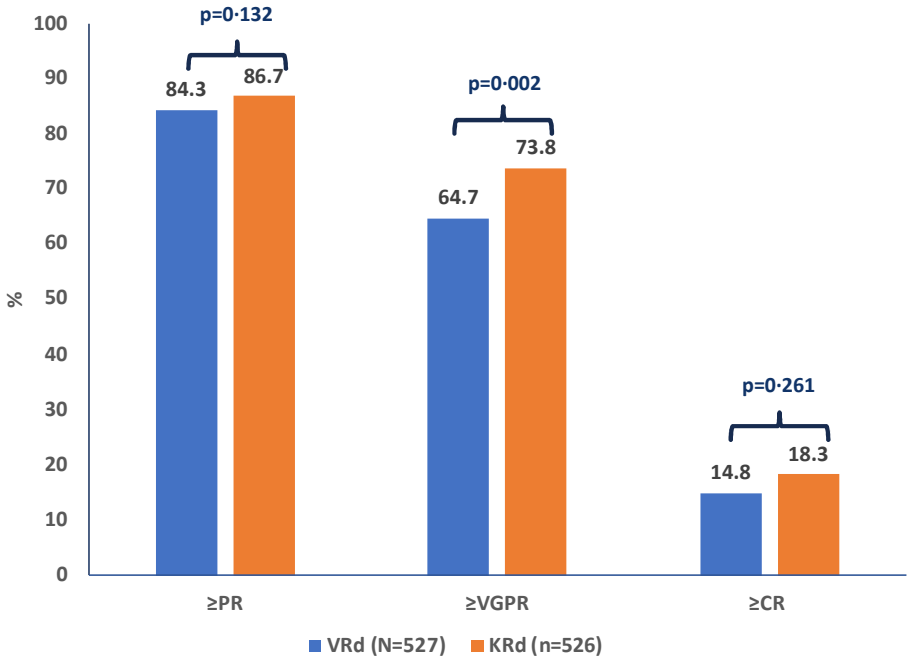
N=1053 starting assigned treatment

	VRd (n=527)	KRd (n=526)	Total (n=1053)
Reason	**N (%)**	**N (%)**	**N (%)**
Treatment Completed	228 (43.3)	324 (61.6)	552 (52.4)
Disease Progression	33 (6.3)	19 (3.6)	52 (4.9)
Adverse Events/ Complications	91 (17.3)	52 (9.9)	143 (13.6)
Death	6 (1.1)	15 (2.9)	21 (2.0)
Patient Withdrawal/ Refusal	39 (7.4)	22 (4.2)	61 (5.8)
Alternative Therapy	93 (17.7)	72 (13.7)	165 (15.7)
Other Complicating Disease	13 (2.5)	5 (1.0)	18 (1.7)
Non-Compliance	7 (1.3)	3 (0.6)	10 (1.0)
MD Decision	8 (1.5)	4 (0.8)	12 (1.1)
Other	9 (1.7)	10 (1.9)	19 (1.8)

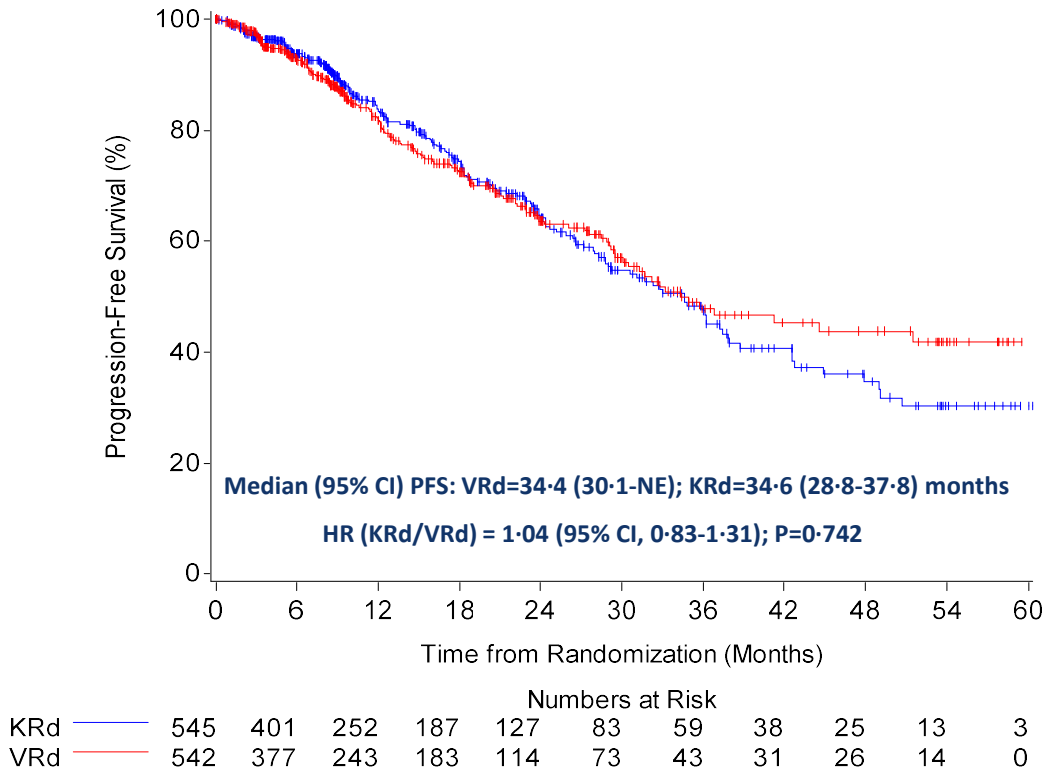
	VRd (n=542)	KRd (n=545)	Total (n=1087)
	N (%)	**N (%)**	**N (%)**
Received SCT	152 (28.0)	146 (26.8)	298 (27.4)
Median (range); months	6.5 (3.5-36.6)	8.9 (3.7-56.9)	
IQR	4.8-10.4	6.0-15.1	

Response To Induction

	VRd (n=527)	KRd (n=526)	Total (n=1053)
Category	N (%)	N (%)	N (%)
Stringent Complete Response	21 (4.0)	31 (5.9)	52 (4.9)
Complete Response	57 (10.8)	65 (12.4)	122 (11.6)
Very Good Partial Response	263 (49.9)	292 (55.5)	555 (52.7)
Partial Response	103 (19.5)	68 (12.9)	171 (16.2)
Stable Disease	40 (7.6)	34 (6.5)	74 (7.0)
Progressive Disease	1 (0.2)	0 (0.0)	1 (0.1)
Unevaluable/Insufficient	42 (8.0)	36 (6.8)	78 (7.4)



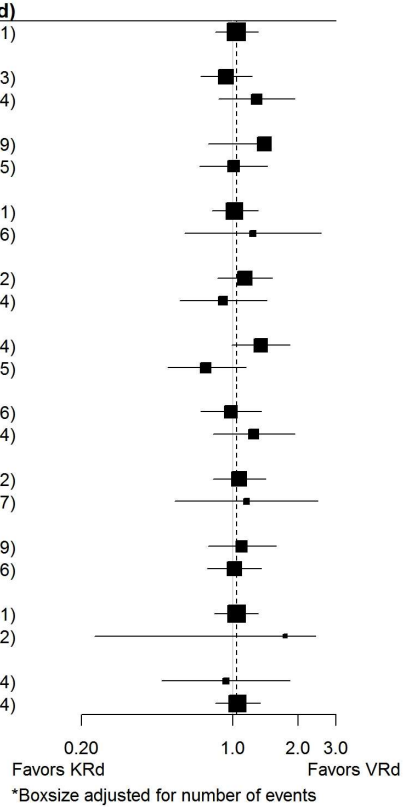
Progression Free Survival from Induction Randomization



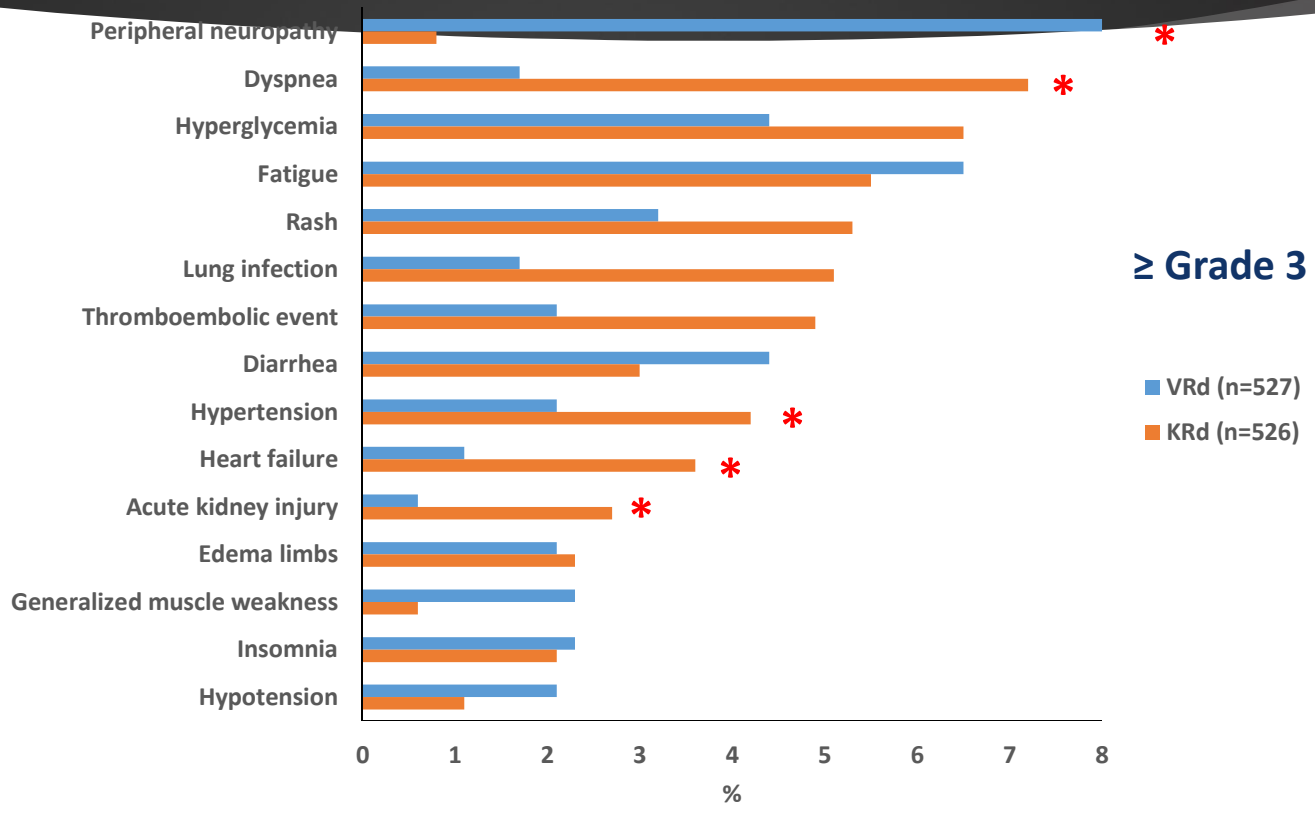
- 2nd interim analysis of PFS (Jan 2020): 298 PFS events (75% of 399 planned)
- Median (95% CI) estimated follow up of 15 (13-18) months
- For patients >/= 70 years, median PFS(95% CI) for VRd = 37 (29-NE) and KRd = 28 (24-36) months
- With censoring at SCT or alternative therapy: Median PFS (95% CI) for VRd = 31 ·7 (28 ·5-44 ·6) and KRd = 32 ·8 (27 ·2-37 ·5) months

Progression Free Survival in Subgroups

Subgroup	N patients/events	Treatment HR (Krd/Vrd)
Overall	1087/298	1.04 (0.83-1.31)
Age		
<70y	743/199	0.93 (0.71-1.23)
>/=70y	344/99	1.29 (0.86-1.94)
Sex		
Male	642/182	1.04 (0.77-1.39)
Female	445/116	1.01 (0.70-1.45)
Race		
White	891/254	1.02 (0.80-1.31)
Non-white	152/31	1.24 (0.60-2.56)
ISS Stage		
I-II	711/186	1.14 (0.85-1.52)
III	243/71	0.90 (0.57-1.44)
Cytogenetics		
Normal	657/166	1.35 (0.99-1.84)
Abnormal	255/93	0.75 (0.50-1.15)
13q Status		
Absent	534/146	0.98 (0.71-1.36)
Present	316/85	1.25 (0.81-1.94)
t(4;14) Status		
Absent	770/203	1.07 (0.81-1.42)
Present	80/28	1.16 (0.54-2.47)
ECOG PS		
0	453/118	1.10 (0.77-1.59)
>0	634/180	1.02 (0.76-1.36)
Creatinine		
<2 mg/dL	1026/283	1.04 (0.82-1.31)
>/=2 mg/dL	61/15	0.75 (0.23-2.42)
Measurable Disease Type		
Light Chain MM	109/35	0.93 (0.47-1.84)
Non-Light Chain MM	978/263	1.05 (0.83-1.34)



Non-hematologic: Treatment-Related AEs (≥2%)

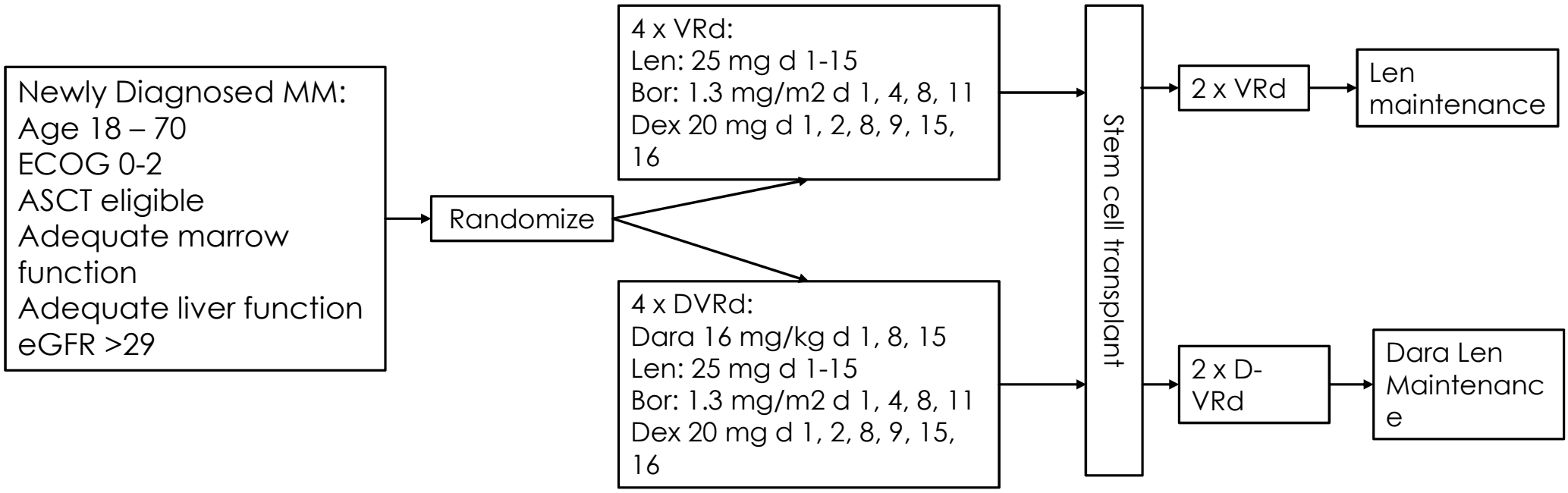


Can we do better than VRd?

Daratumumab, lenalidomide, bortezomib, and dexamethasone for transplant-eligible newly diagnosed multiple myeloma: the GRIFFIN trial

Peter M. Voorhees,[1] Jonathan L. Kaufman,[2] Jacob Laubach,[3] Douglas W. Sborov,[4] Brandi Reeves,[5] Cesar Rodriguez,[6] Ajai Chari,[7] Rebecca Silbermann,[8] Luciano J. Costa,[9] Larry D. Anderson Jr,[10] Nitya Nathwani,[11] Nina Shah,[12] Yvonne A. Efebera,[13] Sarah A. Holstein,[14] Caitlin Costello,[15] Andrzej Jakubowiak,[16] Tanya M. Wildes,[17] Robert Z. Orlowski,[18] Kenneth H. Shain,[19] Andrew J. Cowan,[20] Sean Murphy,[21] Yana Lutska,[21] Huiling Pei,[22] Jon Ukropec,[23] Jessica Vermeulen,[24] Carla de Boer,[24] Daniela Hoehn,[21] Thomas S. Lin,[21] and Paul G. Richardson,[3] for the GRIFFIN Trial Investigators

Design



Voorhees et al Blood

GRIFFIN: Demographics and Toxicity

Table 1. Patient demographic and disease characteristics in the intent-to-treat population at baseline

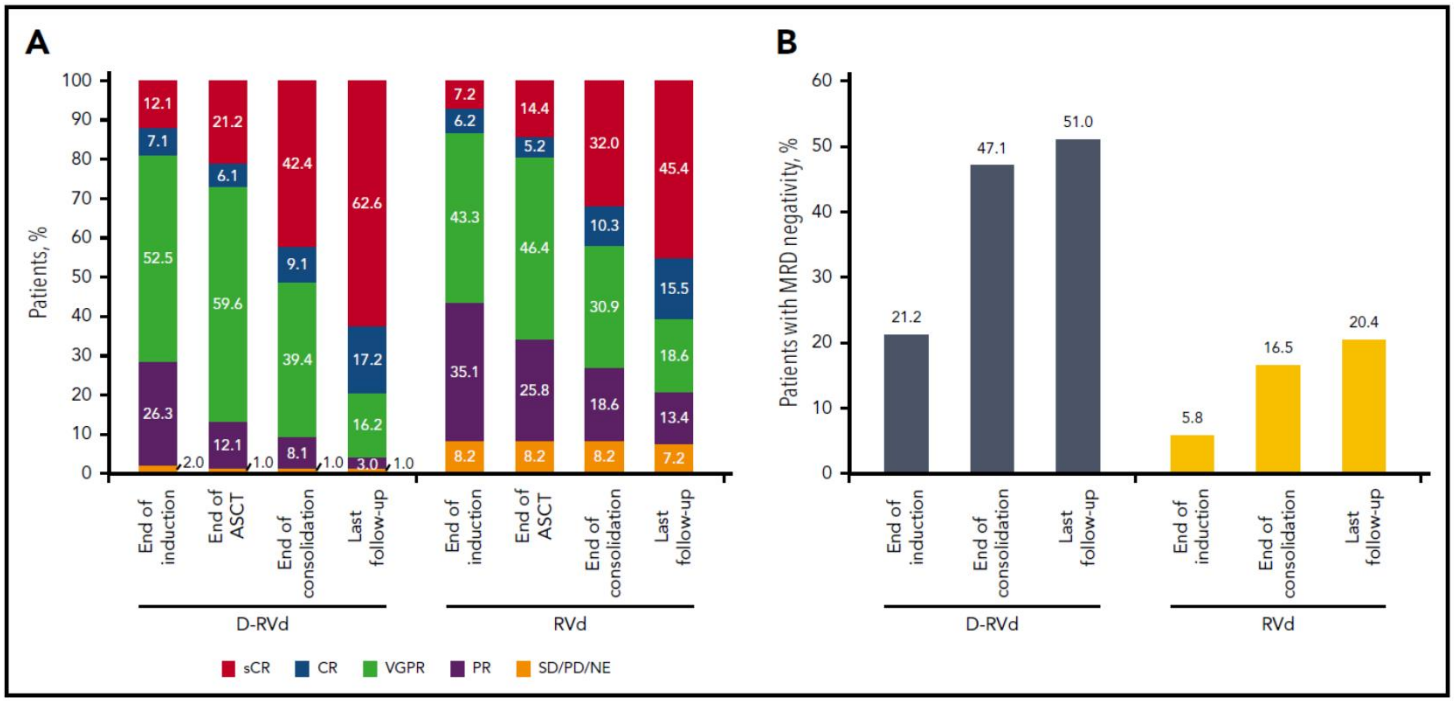
	D-RVd	RVd
Age, y	n = 104	n = 103
Median (range)	59 (29-70)	61 (40-70)
Category, n (%)		
<65	76 (73.1)	75 (72.8)
≥65	28 (26.9)	28 (27.2)
Sex, n (%)	n = 104	n = 103
Male	58 (55.8)	60 (58.3)
Female	46 (44.2)	43 (41.7)
ECOG performance status, n (%)*	n = 101	n = 102
0	39 (38.6)	40 (39.2)
1	51 (50.5)	52 (51.0)
2	11 (10.9)	10 (9.8)
ISS disease stage, n (%)†	n = 104	n = 103
I	49 (47.1)	50 (48.5)
II	40 (38.5)	37 (35.9)
III	14 (13.5)	14 (13.6)
Missing	1 (1.0)	2 (1.9)
Baseline creatinine clearance, mL/min, n (%)	n = 104	n = 103
30-50	9 (8.7)	9 (8.7)
>50	95 (91.3)	94 (91.3)
Cytogenetic risk profile, n (%)‡	n = 98	n = 97
Standard	82 (83.7)	83 (85.6)
High risk	16 (16.3)	14 (14.4)
Time since diagnosis of MM, mo	n = 103	n = 102
Median (range)	0.7 (0-12)	0.9 (0-61)

t(4;14), t(14;16), del(17p)

Adverse event, n (%)	D-RVd, n = 99		RVd, n = 102	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Hematologic				
Neutropenia	57 (57.6)	41 (41.4)	36 (35.3)	22 (21.6)
Thrombocytopenia	43 (43.4)	16 (16.2)	36 (35.3)	9 (8.8)
Leukopenia	36 (36.4)	16 (16.2)	29 (28.4)	7 (6.9)
Anemia	35 (35.4)	9 (9.1)	33 (32.4)	6 (5.9)
Lymphopenia	30 (30.3)	23 (23.2)	28 (27.5)	22 (21.6)
Nonhematologic				
Fatigue	68 (68.7)	6 (6.1)	62 (60.8)	6 (5.9)
Upper respiratory tract infection	62 (62.6)	1 (1.0)	45 (44.1)	2 (2.0)
Peripheral neuropathy*	59 (59.6)	7 (7.1)	74 (72.5)	8 (7.8)
Diarrhea	59 (59.6)	7 (7.1)	51 (50.0)	4 (3.9)
Constipation	51 (51.5)	2 (2.0)	40 (39.2)	1 (1.0)
Cough	50 (50.5)	0	27 (26.5)	0
Nausea	49 (49.5)	2 (2.0)	50 (49.0)	1 (1.0)
Pyrexia	45 (45.5)	2 (2.0)	28 (27.5)	3 (2.9)
Insomnia	42 (42.4)	2 (2.0)	31 (30.4)	1 (1.0)
Back pain	36 (36.4)	1 (1.0)	34 (33.3)	4 (3.9)
Peripheral edema	34 (34.3)	2 (2.0)	35 (34.3)	3 (2.9)
Arthralgia	33 (33.3)	0	33 (32.4)	2 (2.0)
Infusion-related reaction	42 (42.4)	6 (6.1)†	NA	NA

Voorhees et al Blood 2020

GRIFFIN: Responses deepen over time

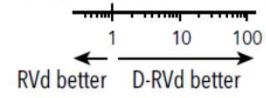


Voorhees et al Blood 2020

D-VRd: Subgroup analysis of sCR rates

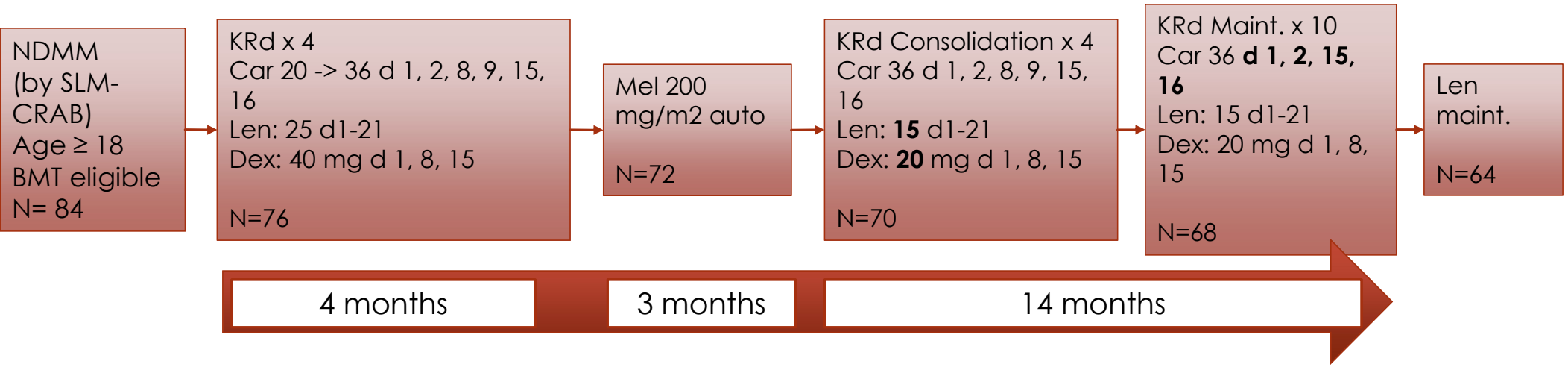
B **Median follow-up, 22.1 months**

Subgroup	RVd minimal residual disease negative, n (%)	D-RVd minimal residual disease negative, n (%)	Odds Ratio (95% CI)
Sex			
Male	10/60 (16.7)	26/58 (44.8)	4.06 (1.73-9.54)
Female	11/43 (25.6)	27/46 (58.7)	4.13 (1.68-10.19)
Age			
<65 yr	16/75 (21.3)	38/76 (50.0)	3.69 (1.81-7.52)
≥65 yr	5/28 (17.9)	15/28 (53.6)	5.31 (1.57-17.97)
ISS disease stage			
I	6/50 (12.0)	25/49 (51.0)	7.64 (2.75-21.19)
II	10/37 (27.0)	20/40 (50.0)	2.70 (1.04-7.01)
III	5/14 (35.7)	8/14 (57.1)	2.40 (0.52-10.99)
Type of multiple myeloma			
IgG	11/52 (21.2)	29/55 (52.7)	4.16 (1.78-9.73)
Non-IgG	10/51 (19.6)	22/46 (47.8)	3.76 (1.53-9.26)
Cytogenetic risk			
High risk	4/14 (28.6)	6/16 (37.5)	1.50 (0.32-6.99)
Standard risk	17/83 (20.5)	45/82 (54.9)	4.72 (2.37-9.40)
ECOG PS score			
0	5/40 (12.5)	21/39 (53.8)	8.17 (2.64-25.25)
1 or 2	16/62 (25.8)	32/62 (51.6)	3.07 (1.44-6.53)



Voorhees et al Blood 2020

Is KRd really dead for NDMM? MMRC Extended KRd trial (The new total therapy?)



Jasielec Blood 2020

MMRC Extended KRd: Demographics and Toxicity

Characteristic	N=76
Age	
Median years (range)	59 (40–76)
≥65 years, n (%)	21 (27.6)
Sex, n (%)	
Male	45 (59.2)
Female	31 (40.8)
ECOG performance status, n (%)	
0–1	65 (85.5)
Unknown	11 (14.5)
ISS Stage, n (%)	
I	31 (40.8)
II	31 (40.8)
III	10 (13.2)
Unknown	4 (5.3)
Cytogenetic risk by FISH*, n (%)	
High	27 (35.5)
Deletion 17p	11 (14.5)
Ultra-high risk†	8 (10.5)
Standard	49 (64.5)
Serum ß$_2$-microglobulin, n (%)	
<3.5 mg/L	45 (59.2)
≥3.5 mg/L, %	24 (31.6
Unknown	7 (9.2)

*Defined per IMWG: t(4;14), del(17p), t(14;16), t(14;20), non-hyperdiploidy and gain(1q).

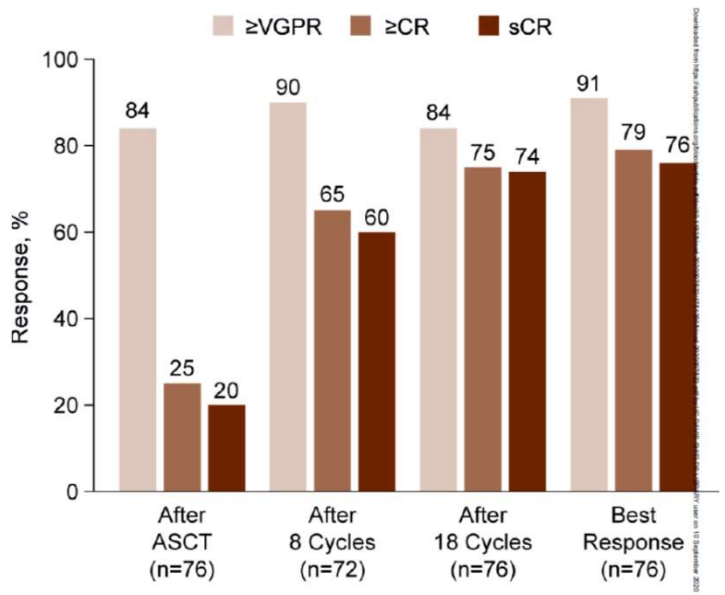
Table 3. Treatment-emergent adverse events during KRd*

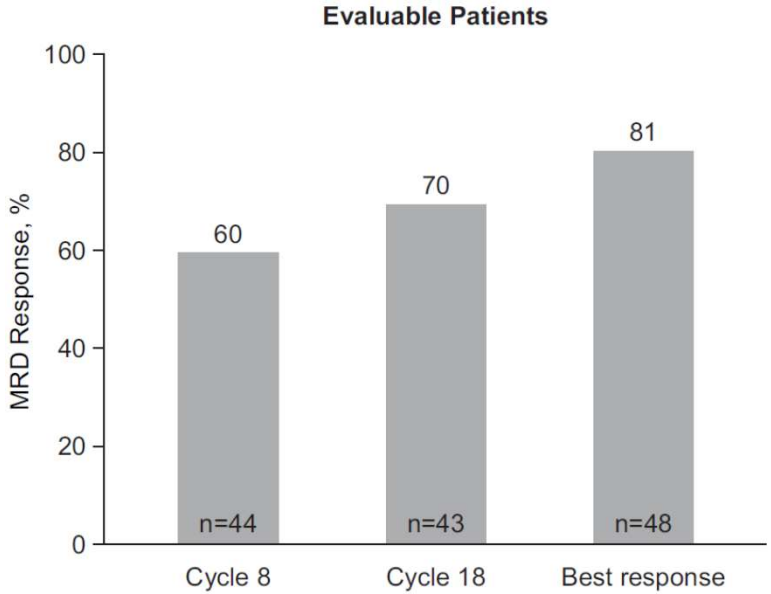
	KRd +ASCT N=76	
	All Grade, n (%)	Grade 3/4, n (%)
Hematologic		
Thrombocytopenia	47 (62)	11 (14)
Anemia	32 (42)	9 (12)
Lymphopenia	32 (42)	24 (32)
Neutropenia	30 (39)	26 (34)
Non-hematologic		
Infection	56 (74)	17 (22)
Fatigue	51 (67)	4 (5)
Diarrhea	39 (51)	7 (9)
Hyperglycemia	33 (43)	6 (8)
Dyspnoea	30 (39)	2 (3)
Peripheral neuropathy	32 (42)	0
Rash	33 (43)	4 (5)
Hypophosphatemia	22 (29)	11 (14)
Hypertension	15 (20)	4 (5)
Thromboembolic events	14 (18)	5 (7)
Cardiac events†	10 (13)	2 (3)

Jasielec Blood

MMRC Extended KRd: Responses improve throughout KRd exposure

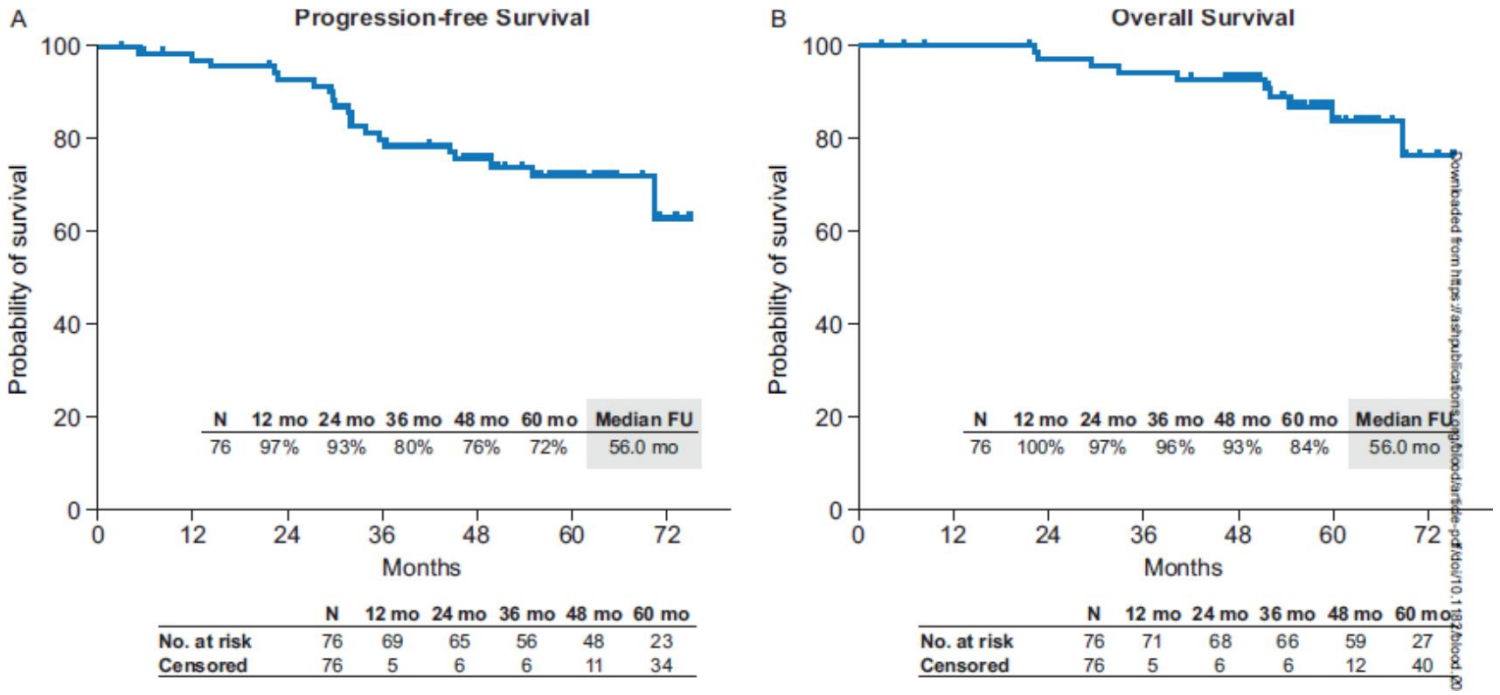
MRD Negativity





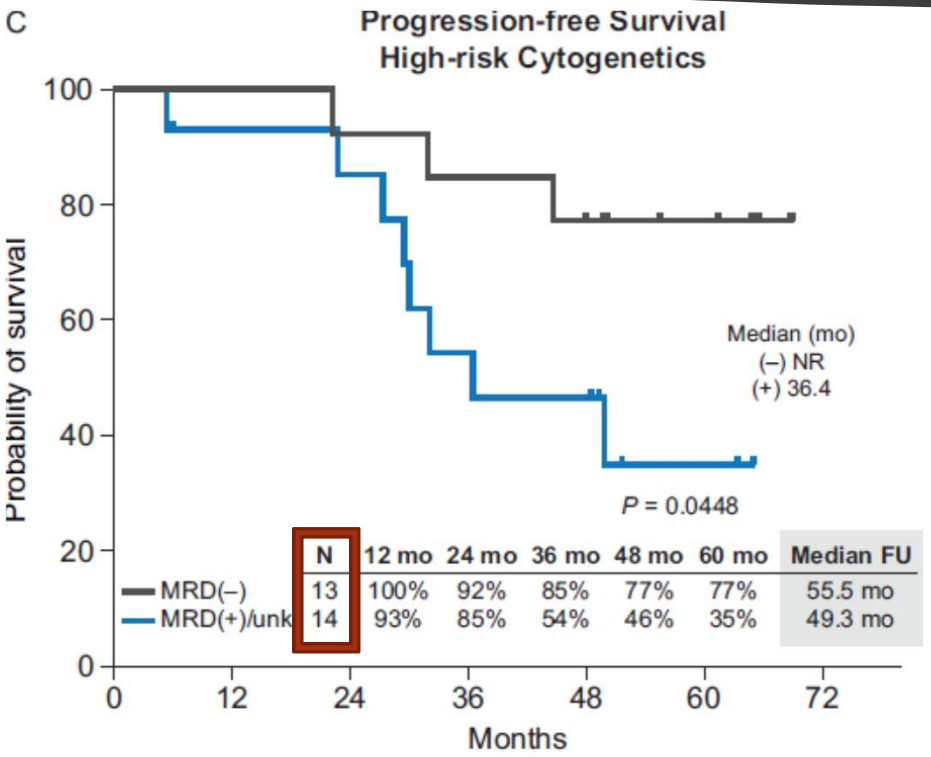
Jasielec Blood

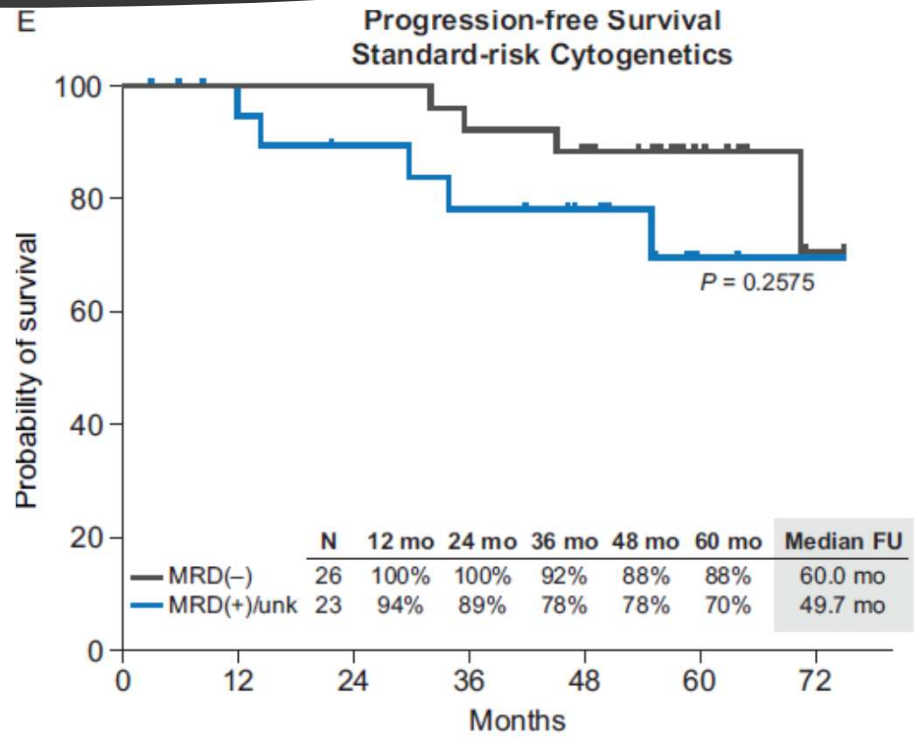
MMRC: Extended KRd PFS and OS



Jasielec Blood 2020

MMRC: Extended KRd: PFS by High Risk and Standard Risk Cytogenetics





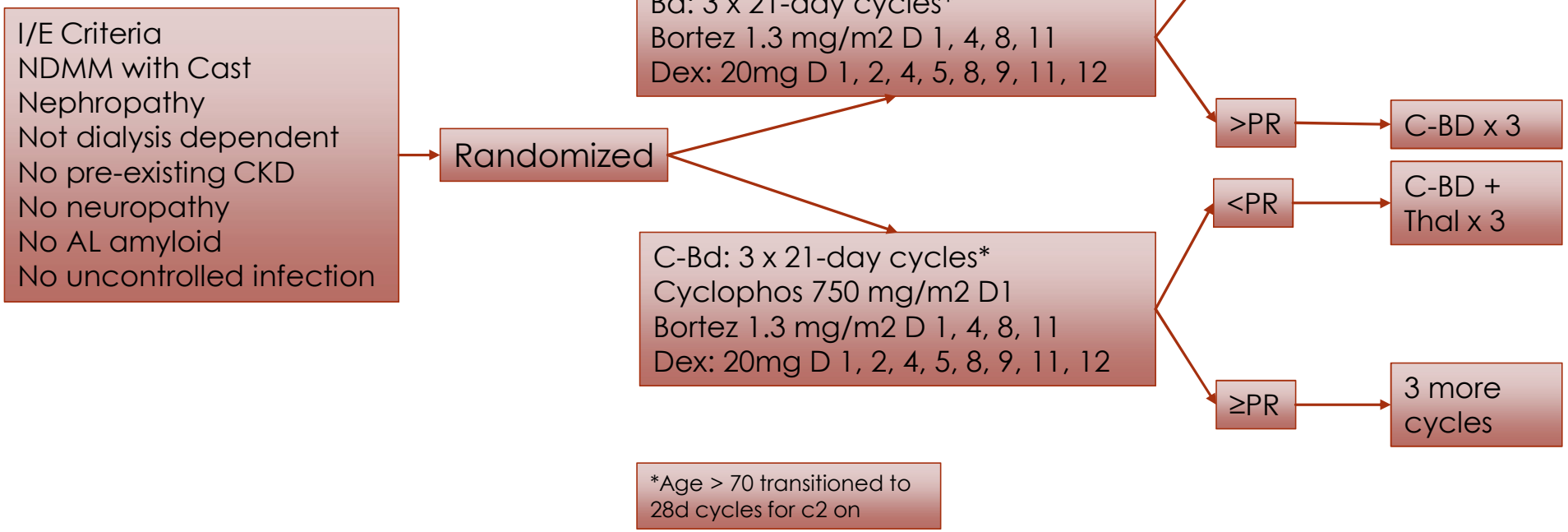
Jasielec Blood 2020

NDMM with Acute Kidney Injury

Randomized Trial Comparing Double Versus Triple Bortezomib-Based Regimen in Patients With Multiple Myeloma and Acute Kidney Injury Due to Cast Nephropathy

Frank Bridoux, MD, PhD[1,2,3]; Bertrand Arnulf, MD, PhD[4]; Lionel Karlin, MD[5]; Nicolas Blin, MD[6]; Nolwenn Rabot, MD[7]; Margaret Macro, MD[8]; Vincent Audard, MD, PhD[9]; Karim Belhadj, MD[10]; Brigitte Pegourie, MD[11]; Pierre Gobert, MD[12]; Emilie Cornec Le Gall, MD, PhD[13]; Bertrand Joly, MD[14]; Alexandre Karras, MD, PhD[15]; Arnaud Jaccard, MD, PhD[2,3,16]; Karine Augeul-Meunier, MD[17]; Salomon Manier, MD, PhD[18]; Bruno Royer, MD[19]; Denis Caillot, MD, PhD[20]; Mourad Tiab, MD[21]; Sébastien Delbes, MD[22]; Felipe Suarez, MD, PhD[23]; Cécile Vigneau, MD, PhD[24]; Sophie Caillard, MD, PhD[25]; Nina Arakelyan-Laboure, MD[26]; Damien Roos-Weil, MD, PhD[27]; Sylvie Chevret, MD, PhD[28]; and Jean Paul Fermand, MD[4]; for the MYRE study group

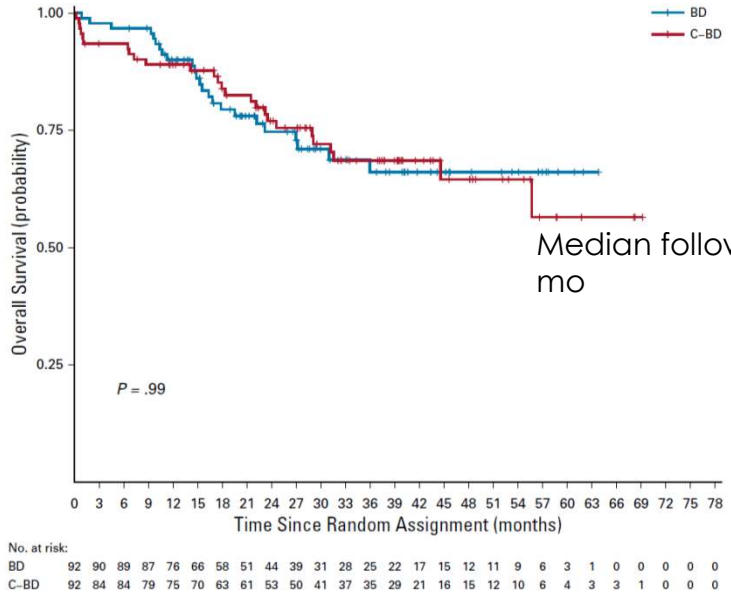
MYRE: Design



Bridoux et al JCO 2020

MYRE: Responses and OS

- Renal response at 3 months
  - BD: 44.6%
  - C-BD: 51.1%
  - Risk ratio 0.87 (0.64 – 1.18)
- Overall Response at 3 months
  - BD: 78.3%
  - C-BD: 77.2%
- ≥VGPR at 6 months
  - BD: 46.8%
  - C-BD51.1%
  - RR 0.88 (0.66 – 1.17)



Median follow up: 27 mo

Bridoux et al JCO

Newly Diagnosed Multiple Myeloma: Summary

- The standard of care of NDMM should be RVd based on S0777 and E1A11: ENDURANCE
  - BUT…. E1A11 excluded t(14;16), t(14;20) and del(17p)
- The CR and MRD- rates with extended KRd in the high risk population are provocative
  - I may still consider this, since these patients were excluded from E1A11
- What about D-RVd?
  - If you're an "early adopter," or if you think MRD- rates are an adequate surrogate, GRIFFIN probably gives you enough push to adopt now
  - While I personally would like to see some data on PFS, we're beginning to incorporate into our treatment plans
  - It will be hard to assess survival outcomes in GRIFFIN because of the difference in post-BMT maintenance
  - Interestingly, D-RVd did not seem to affect outcomes in high-risk populations. More to come with this, I'm sure (along with all the caveats that come with sub-group analyses)
- For NDMM with AKI:
  - Bolus dosing of cyclophosphamide is not effective
  - However, hyper-fractionated cyclophosphamide, or lower dose oral cyclophos may provide improved outcomes by providing more consistent cytotoxic therapy
  - Randomized trials are clearly needed in this population