La terapia del mieloma multiplo: un passo avanti

La lenalidomide come "partner" nelle nuove combinazioni

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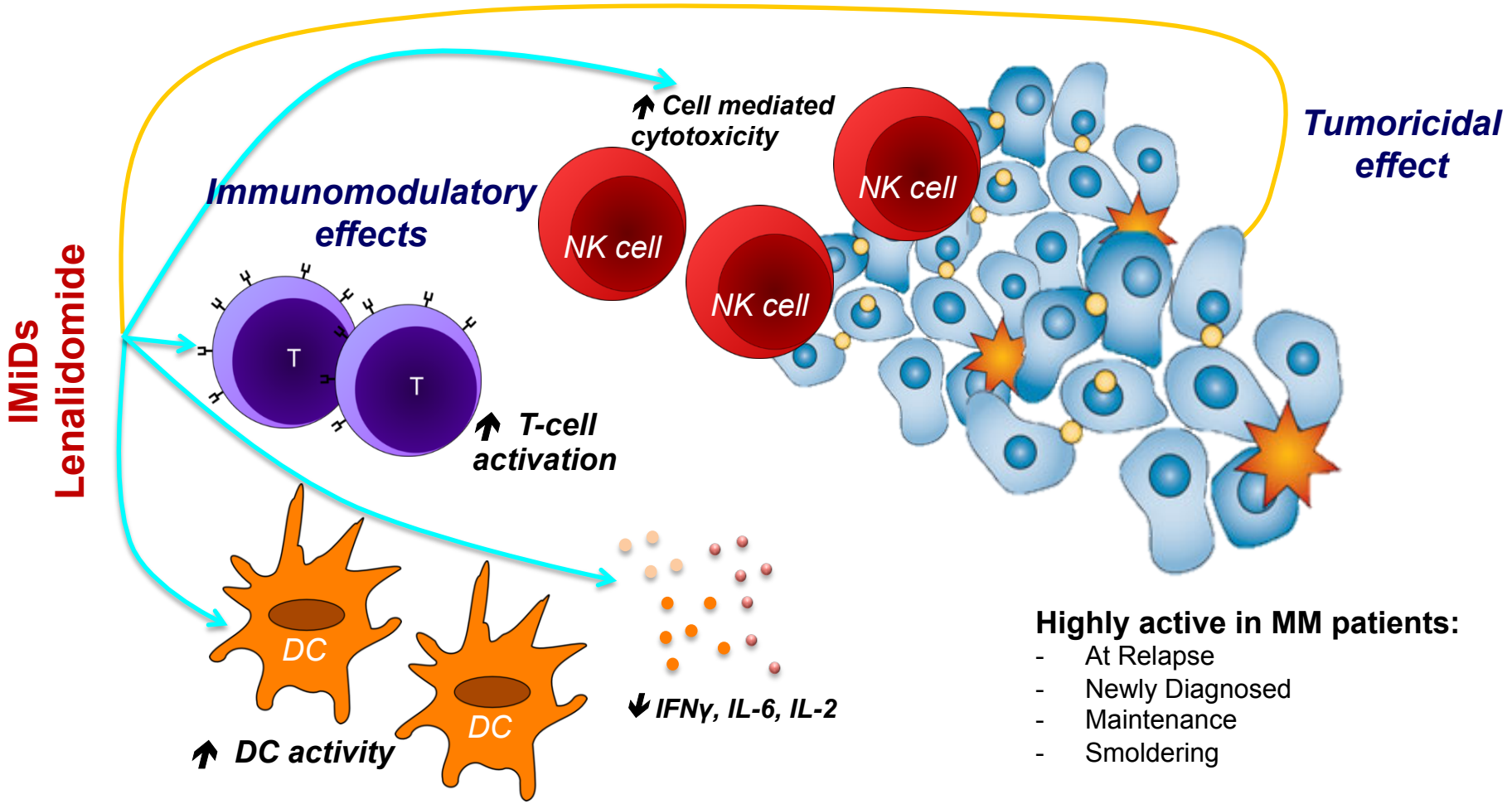
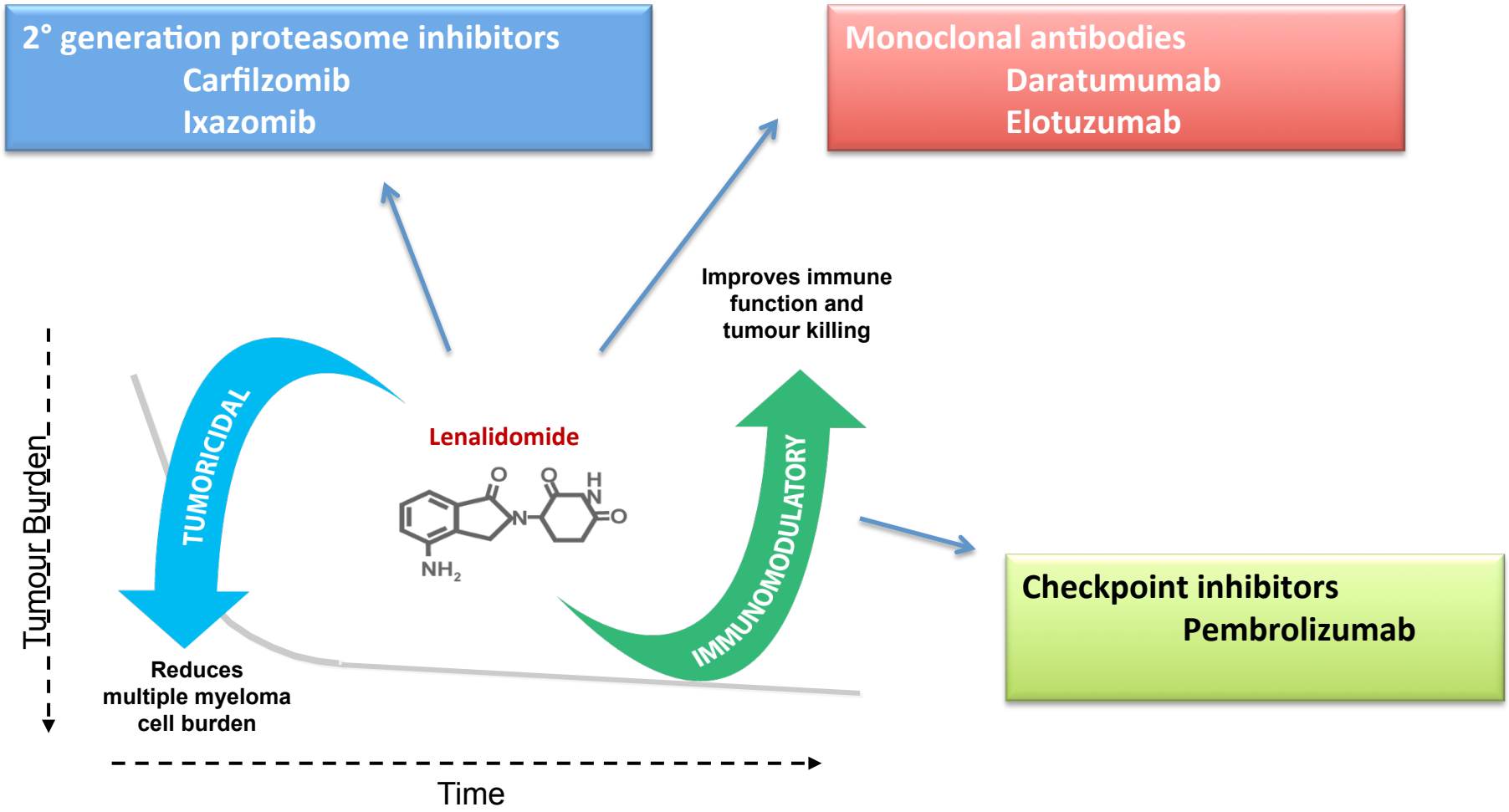
IMiDs: Dual Tumoricidal and Immunomodulatory Mechanism of Action



Highly active in MM patients:

- At Relapse
- Newly Diagnosed
- Maintenance
- Smoldering

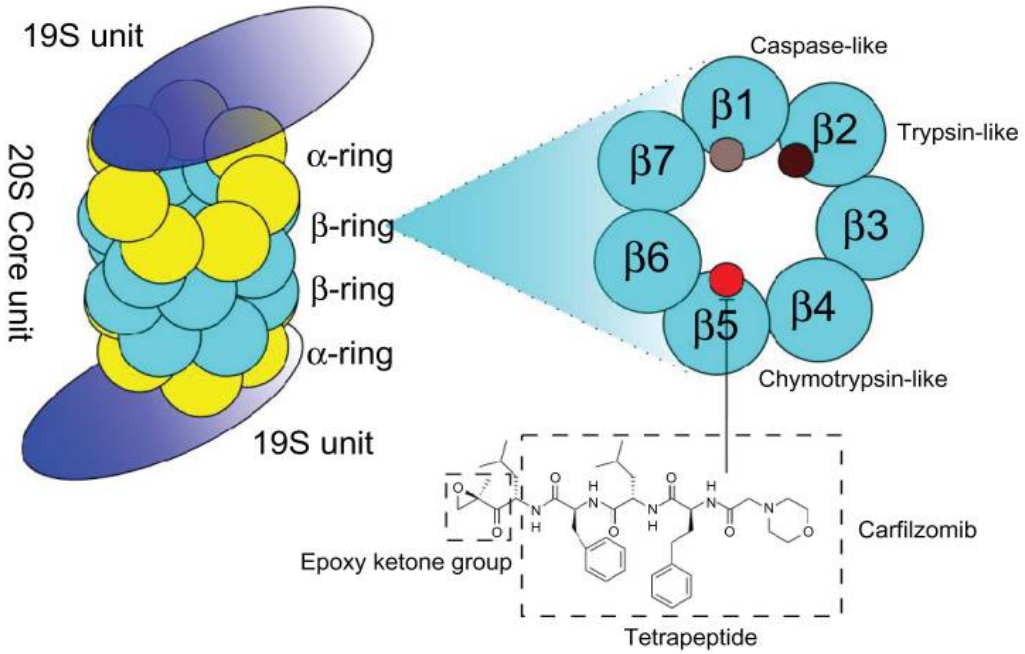
Lenalidomide-based novel combination therapies



These dual effects make lenalidomide an optimal partner for combination

SECOND-GENERATION PROTEASOME INHIBITORS

CARFILZOMIB: MECHANISM OF ACTION



Carfilzomib irreversibly and selectively inhibits the chymotripsin-like activity of the 20S proteasome, necessitating de novo protein synthetis to restore activity.

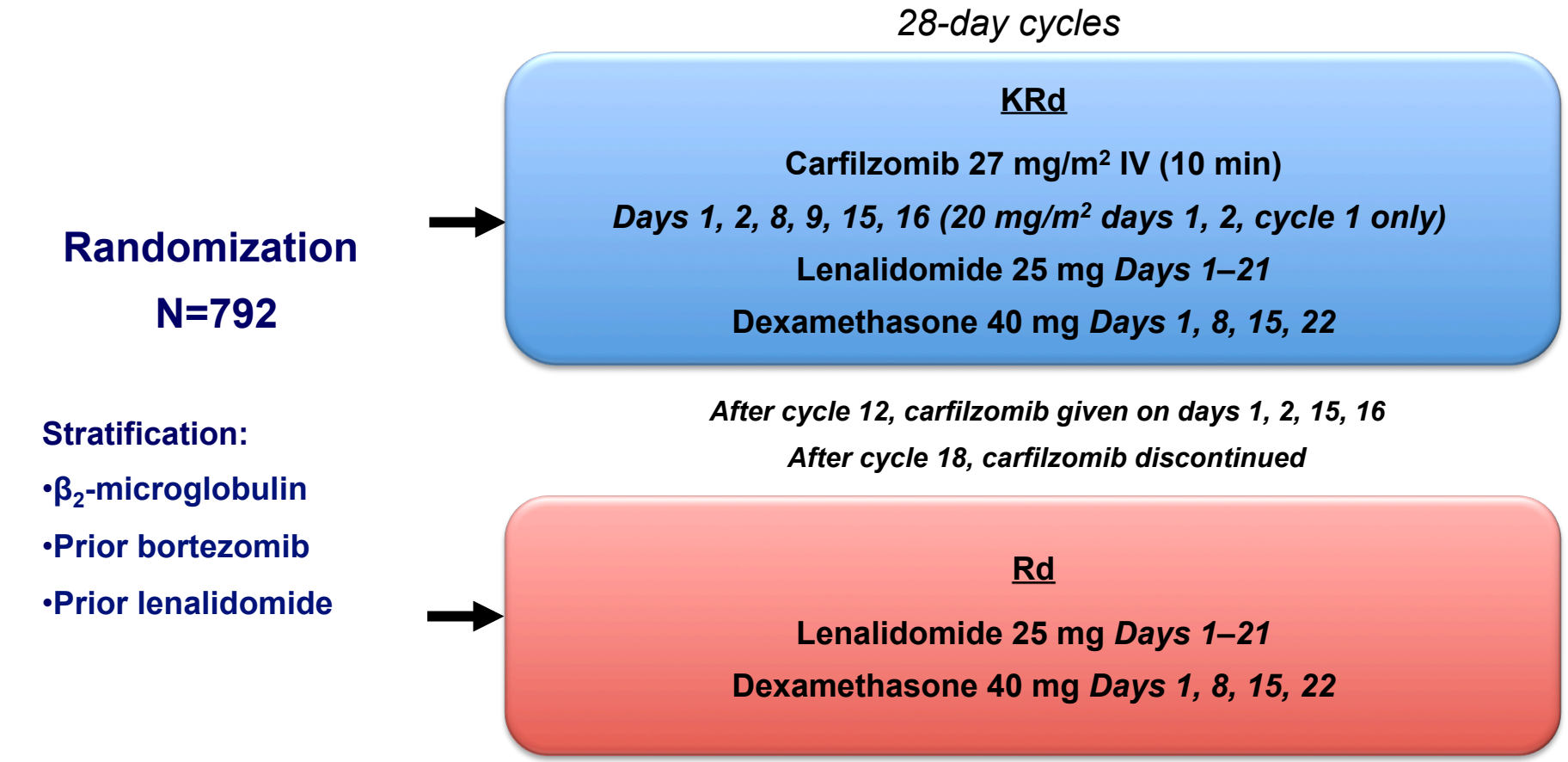
In preclinical studies it demonstrates more potent proteasome inhibition and minimal off-target activity.

Carfilzomib demonstrates significantly less cross-reactivity with nonproteasomal proteases compared to bortezomib, which has been shown to correlate with a lack of neurotoxicity in preclinical study.

Consecutive-day dosing of carfilzomib was well-tolerated and led to prolonged irreversible proteasome inhibition.

ASPIRE: Carfilzomib, Lenalidomide, and Dexamethasone (KRd) vs Lenalidomide and Dexamethasone (Rd)

Carfilzomib is approved by FDA and EMA in combination with lenalidomide-dexamethasone for patients who have received 1–3 prior lines of therapy



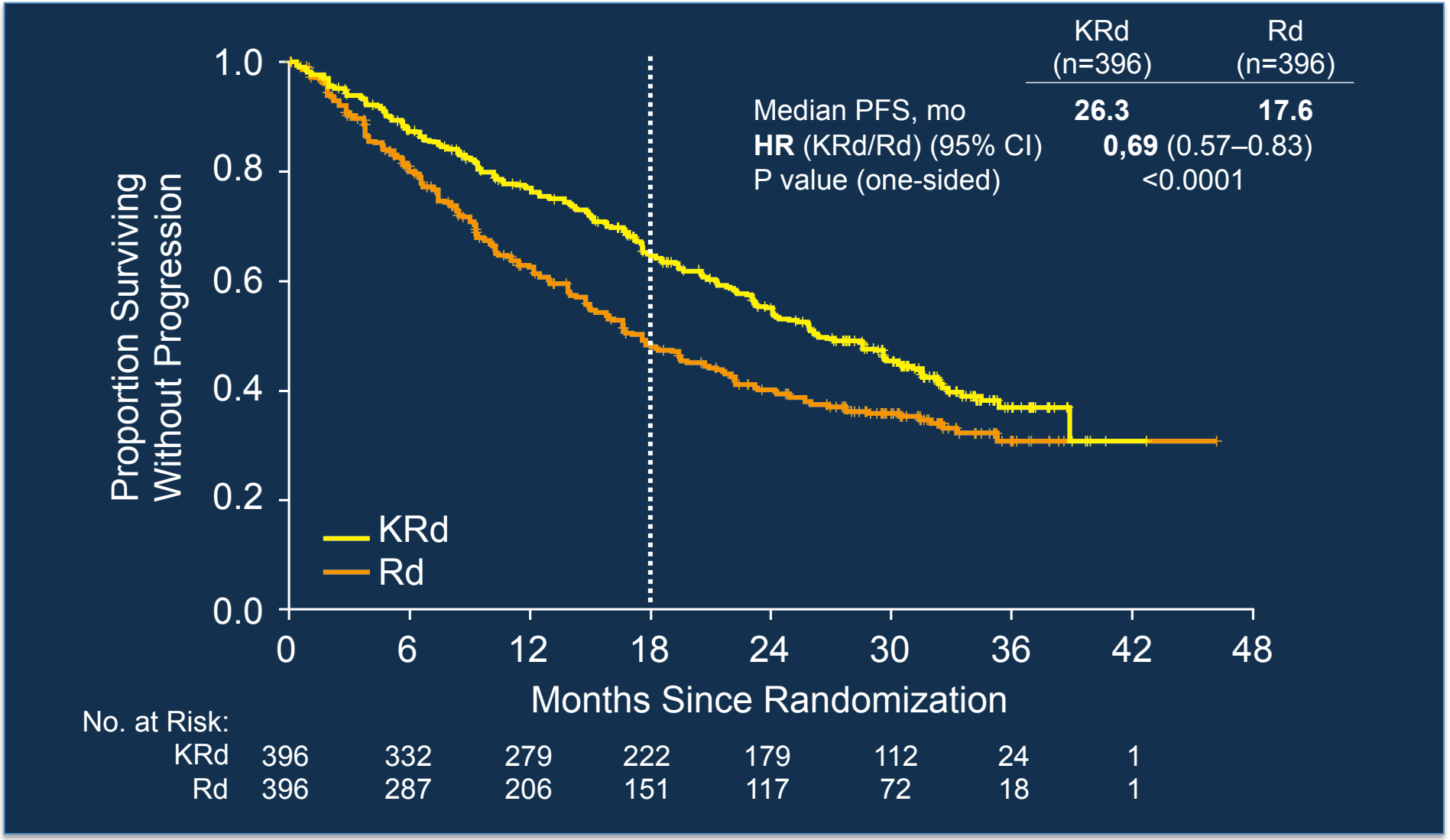
- 1–3 prior treatments, not lena refractory, no PD on bort

(20% lena exposed, 15% bort refractory)

Primary endpoint: PFS

Stewart K et al, NEJM 2015

ASPIRE: Progression-Free Survival
ITT Population (N=792)

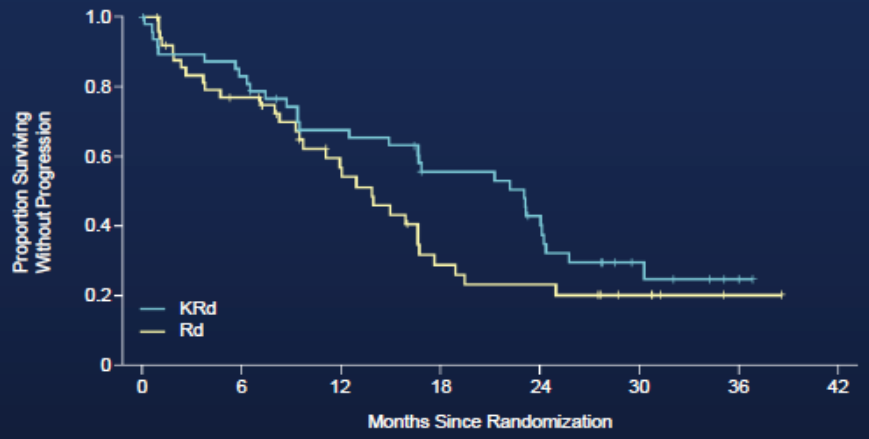


Stewart K et al, NEJM 2015

ASPIRE: KRd vs Rd

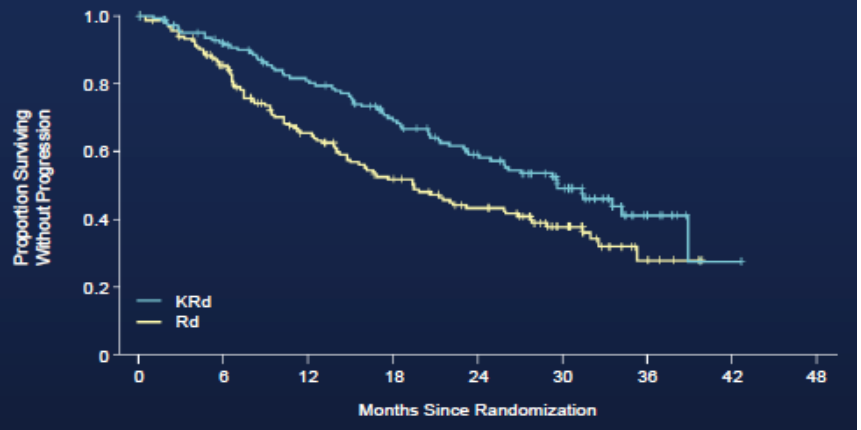
PFS by cytogenetic risk status at baseline

High Risk



	KRd (n=48)	Rd (n=52)
PFS, median months	23.1	13.9
Hazard ratio (95% CI)	0.70 (0.43–1.16)	

Standard Risk

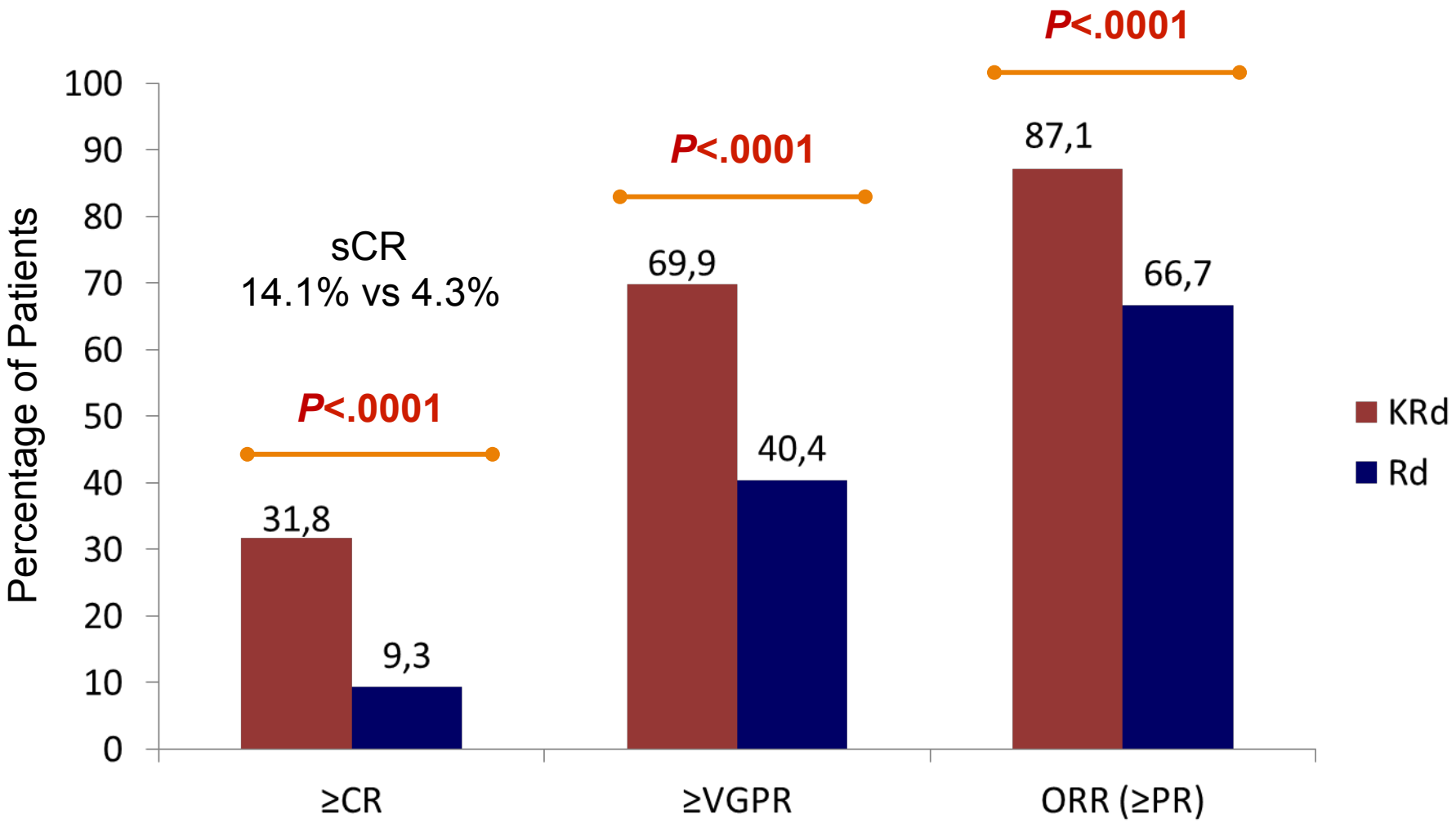


	KRd (n=147)	Rd (n=170)
PFS, median months	29.6	19.5
Hazard ratio (95% CI)	0.66 (0.48–0.90)	

HR: t(4;14), t(14;16), and del(17p)

Avet-Loiseau H et al , Blood 2016

ASPIRE: Response



- **Median duration of response was 28.6 months in the KRd group and 21.2 months in the Rd group**

Stewart K et al, NEJM 2015

ASPIRE: KRd vs Rd

AEs of Interest

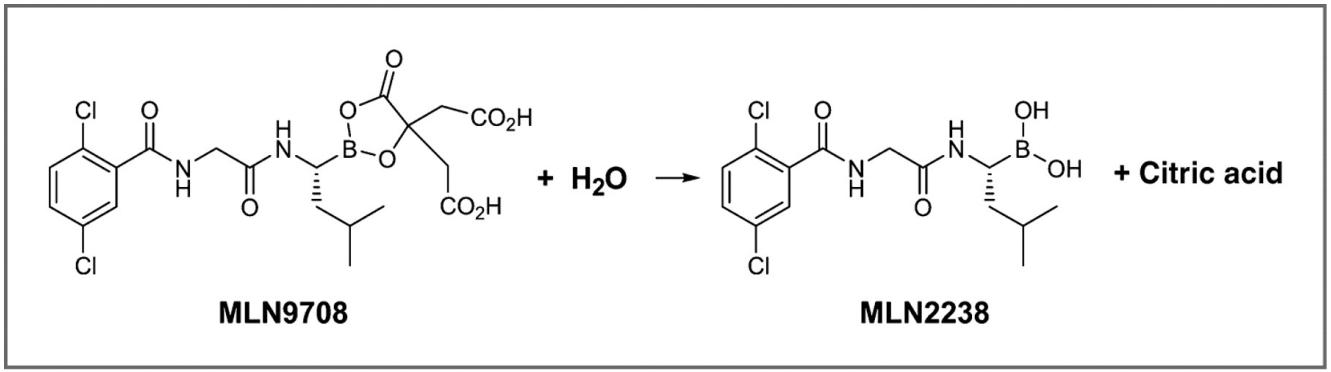
AE, %	KRd (n=392)		Rd (n=389)	
	All Grade	Grade ≥3	All Grade	Grade ≥3
Dyspnea	19.4	2.8	14.9	1.8
Peripheral neuropathy*	17.1	2.6	17.0	3.1
Hypertension	14.3	4.3	6.9	1.8
Acute renal failure*	8.4	3.3	7.2	3.1
Cardiac failure*	6.4	3.8	4.1	1.8
Deep vein thrombosis	6.6	1.8	3.9	1.0
Ischemic heart disease*	5.9	3.3	4.6	2.1
Pulmonary embolism	3.6	3.1	2.3	2.3
Second primary malignancy*	2.8	2.3	3.3	2.8

Stewart K et al, NEJM 2015

SECOND-GENERATION PROTEASOME INHIBITORS

Ixazomib – oral proteasome inhibitor

- Ixazomib is the first oral proteasome inhibitor to be studied in the clinic
  - Ixazomib is a peptide boronic acid proteasome inhibitor that has a distinct chemical structure and pharmacology compared to bortezomib[1,2]
  - Selectively, reversibly and potently inhibits the beta5 site of the 20S proteasome
  - It has a shorter proteasome dissociation half-life compared to bortezomib and it can more readily enter tumor tissues (improved tumor pharmacodynamic response and antitumor activity)
  - Preclinical studies indicated synergy with lenalidomide[3,4]



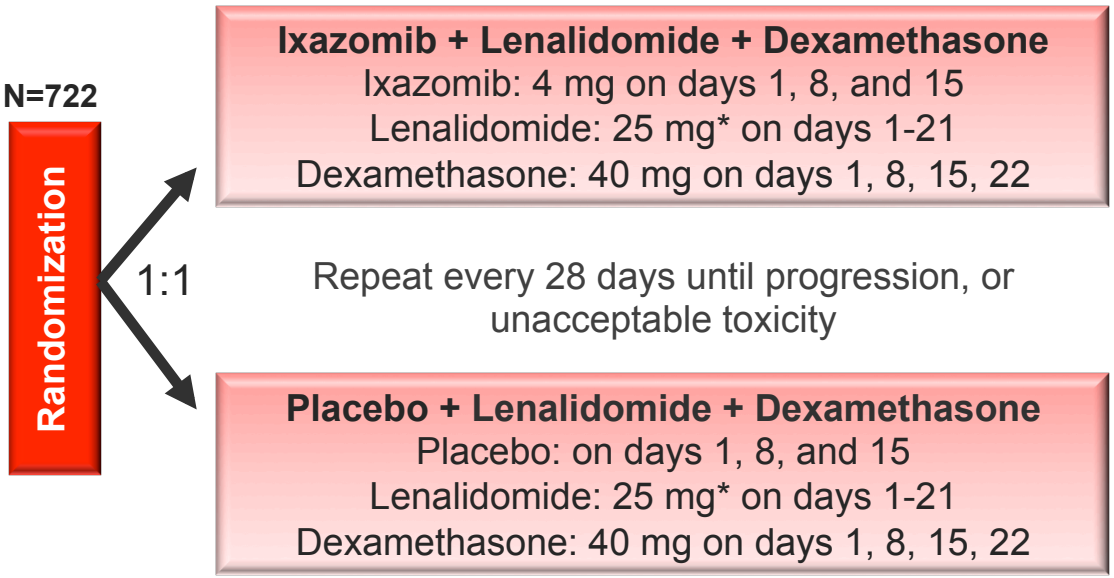
MLN9708 MLN2238

1. Kupperman E, et al. Cancer Res 2010;70:1970–80.
2. Lee EC, et al. Clin Cancer Res 2011; 2011;17:7313–23.
3. Chauhan D, et al. Clin Cancer Res 2011;17:5311–21.
4. Kumar SK, et al., Lancet Oncol. 2014;15:1503–12.

TOURMALINE-MM1: Phase 3 study of weekly oral ixazomib plus lenalidomide-dexamethasone

Ixazomib is approved by FDA and conditionally approved by EMA in combination with lenalidomide-dexamethasone for patients who have received at least 1 prior therapy

Global, double-blind, randomized, placebo-controlled study design



Stratification:
- Prior therapy: 1 vs 2 or 3
- ISS: I or II vs III
- PI exposure: yes vs no

*10 mg for patients with creatinine clearance ≤60 or ≤50 mL/min, depending on local label/practice

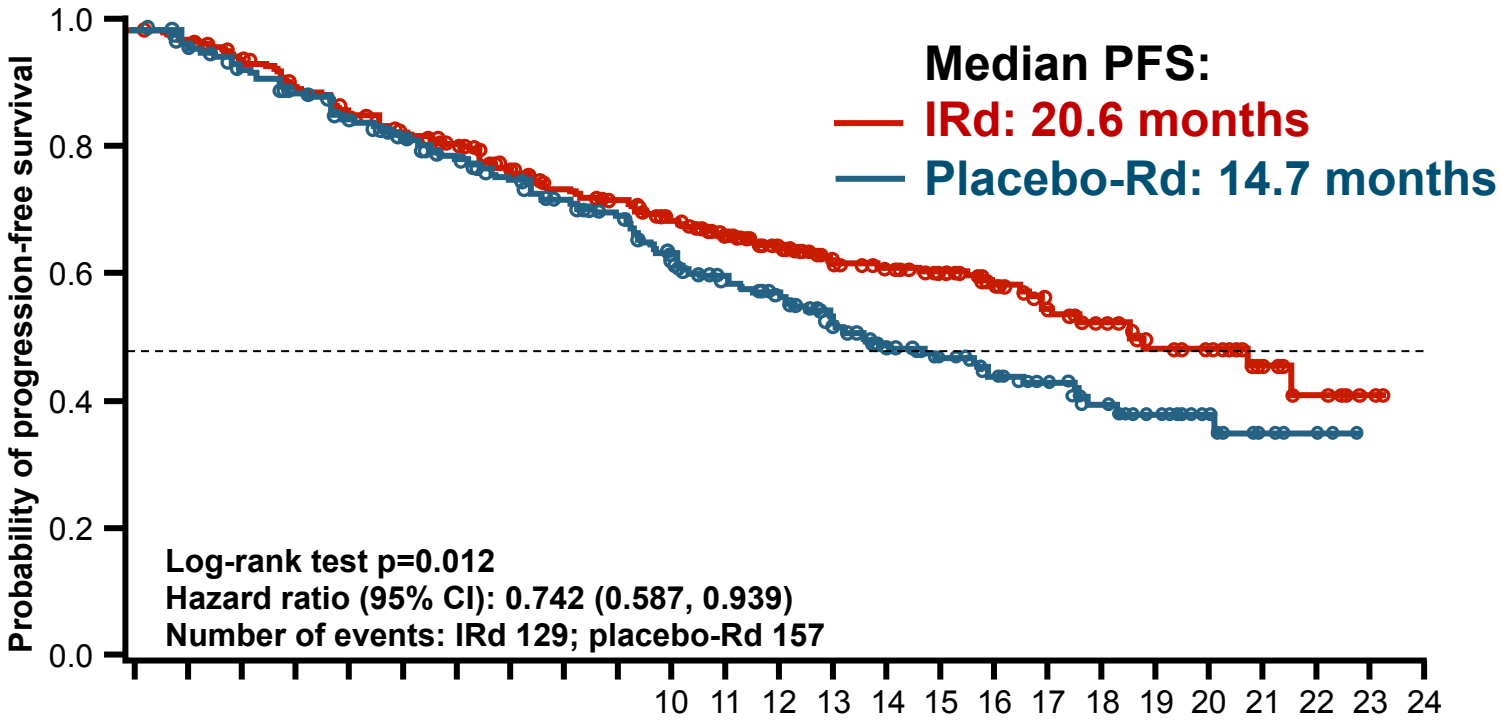
Primary endpoint:
- PFS

Key secondary endpoints:
- OS
- OS in patients with del(17p)

- Received 1–3 prior treatments
- Not refractory to len or bort
- 70% bort exposed, 12% lena exposed

Moreau P et al. NEJM 2016

TOURMALINE-MM1: Final PFS analysis(median fup: 23 mos): A significant, 35% improvement in PFS with IRd vs placebo-Rd



Number of patients at risk:																									
IRd	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-Rd	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

Median follow-up: ~15 months

Moreau P et al. NEJM 2016

TOURMALINE-MM1: Outcomes by cytogenetic risk group

	ORR, %		≥VGPR, %		≥CR, %		Median PFS, months		
	IRd	Placebo-Rd	IRd	Placebo-Rd	IRd	Placebo-Rd	IRd	Placebo-Rd	HR
All patients	78.3*	71.5	48.1*	39	11.7*	6.6	20.6	14.7	0.742*
Standard-risk patients	80	73	51	44	12	7	20.6	15.6	0.640*
All high-risk patients	79*	60	45*	21	12*	2	21.4	9.7	0.543
Patients with del(17p)[†]	72	48	39	15	11*	0	21.4	9.7	0.596
Patients with t(4;14) alone	89	76	53	28	14	4	18.5	12.0	0.645

*$p<0.05$ for comparison between regimens. [†]Alone or in combination with t(4;14 or t(14;16).
Data not included on patients with t(14:16) alone due to small numbers (n=7).

- Median OS could not be estimated
- In the IRd arm, median PFS in high-risk patients was similar to that in the overall patient population and in patients with standard-risk cytogenetics

Moreau P et al, NEJM 2016

TOURMALINE-MM1: Improved response rates, durable responses, and improved time to progression (TTP) with IRd

Response rates	IRd (N=360)	Placebo-Rd (N=362)	p-value
Confirmed ORR (≥PR), %	78.3	71.5	p=0.035
CR+VGPR, %	48.1	39.0	p=0.014
Response categories			
CR, %	11.7	6.6	p=0.019
PR, %	66.7	64.9	–
VGPR, %	36.4	32.3	–
Median time to response, mos	1.1	1.9	–
Median duration of response, mos	20.5	15.0	–
Median TTP, mos	21.4	15.7	HR 0.712 P=0.007

Moreau P et al. NEJM 2016

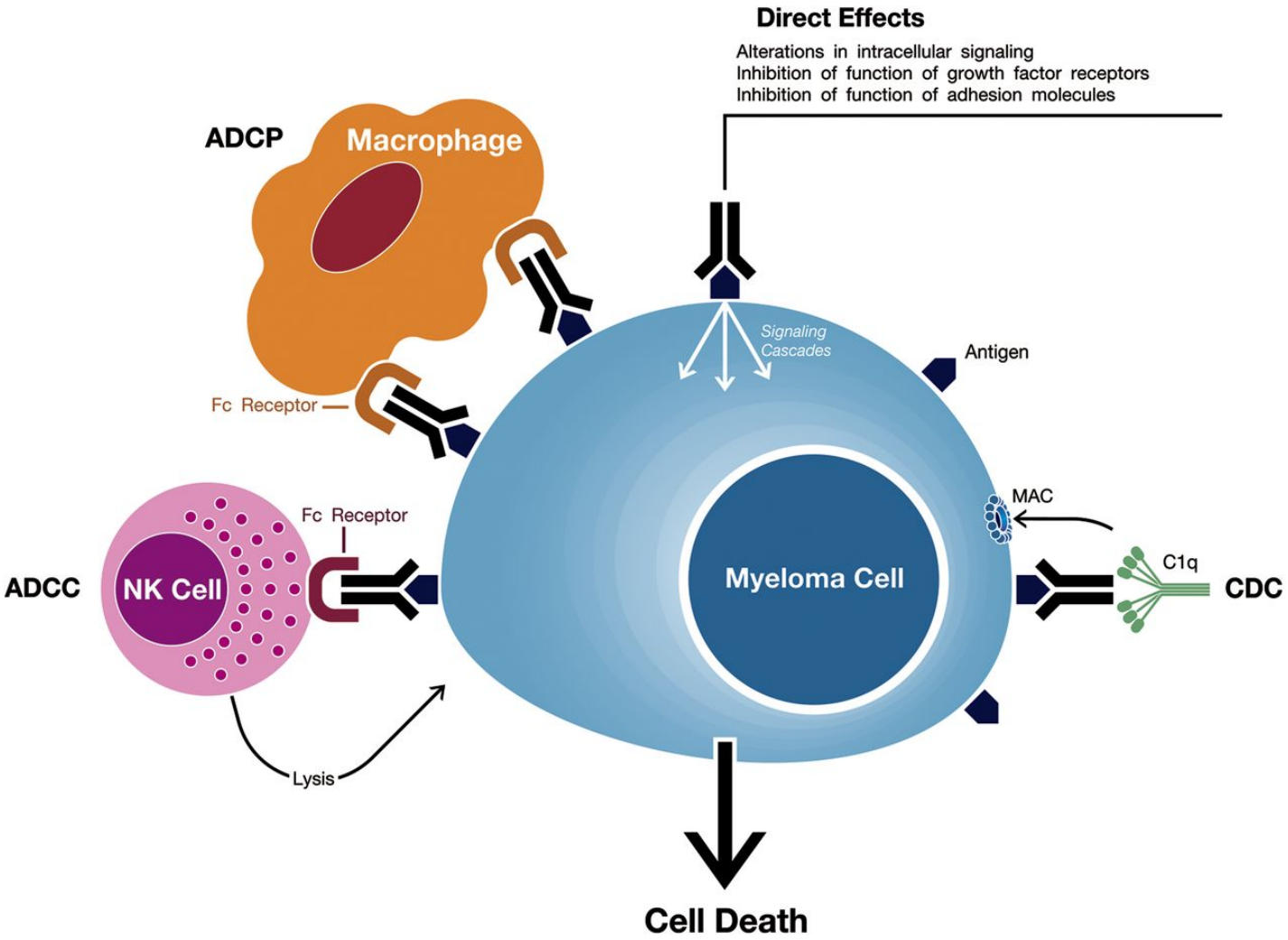
TOURMALINE: AEs after median follow-up of 23 months: increased rates with IRd driven by low-grade events

	IRd (N=361), %			Placebo-Rd (N=359), %		
Preferred terms	**All-grade**	**Grade 3**	**Grade 4**	**All-grade**	**Grade 3**	**Grade 4**
AEs overlapping with lenalidomide						
Diarrhea	45	6	0	39	3	0
Constipation	35	<1	0	26	<1	0
Nausea	29	2	0	22	0	0
Vomiting	23	1	0	12	<1	0
Rash*	36	5	0	23	2	0
Back pain	24	<1	0	17	3	0
Upper respiratory tract infection	23	<1	0	19	0	0
Thrombocytopenia	31	12	7	16	5	4
AEs with proteasome inhibitors						
Peripheral neuropathy*	27	2	0	22	2	0
Peripheral edema	28	1	0	20	1	0
AEs with lenalidomide						
Thromboembolism*	8	2	<1	11	3	<1
Neutropenia*	33	18	5	31	18	6

*Represents multiple MedDRA preferred terms.

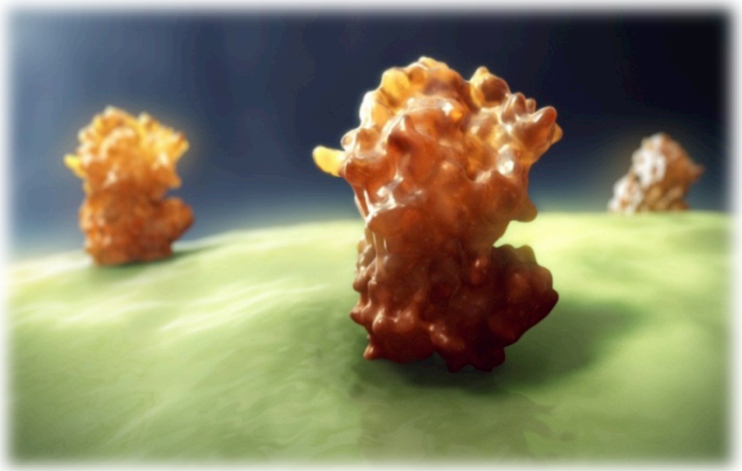
Moreau P et al. NEJM 2016

Mechanisms of action of monoclonal antibodies targeting surface antigens on MM cells



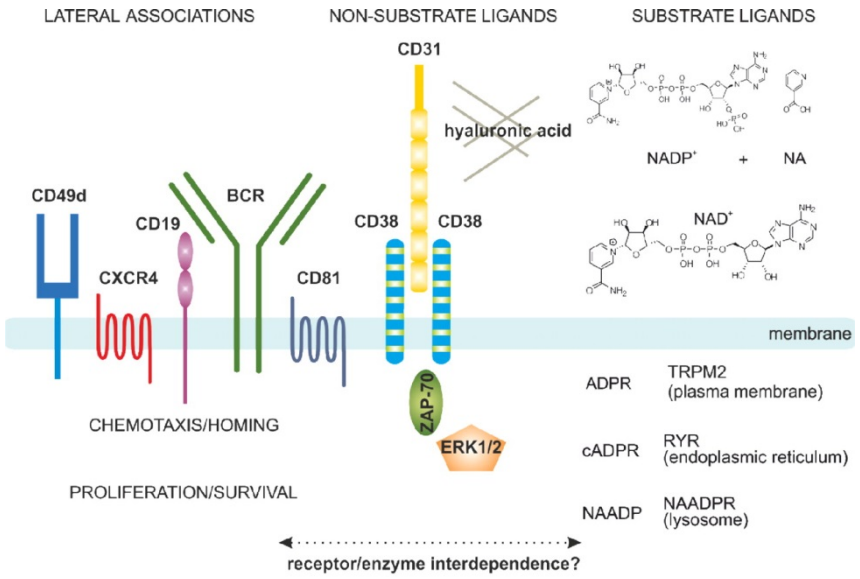
Niels W. C. J. van de Donk et al. Blood 2016;127:681-695

CD38, cell surface receptor and an ectoenzyme, is a rational therapeutic target for treatment of myeloma



- Type II **transmembrane protein** (m.w. ≈45 kDa)
- **Highly and uniformly expressed on myeloma cells**
  - CD38 present on CD4, CD8, NK cells and B lymphocytes at a relatively low level
  - Also some CD38 expression on tissues of non-hematopoietic origin

- CD38 has several intracellular functions
  1. Regulates **signaling, homing and adhesion** in close contact with BCR complex and CXCR4
  2. Regulates **activation and proliferation of human T lymphocytes**
  3. As an ectoenzyme, CD38 interacts with NAD+ and NADP+, which are converted to cADPR, ADPR, and NAADP in **intracellular Ca2+-mobilization**

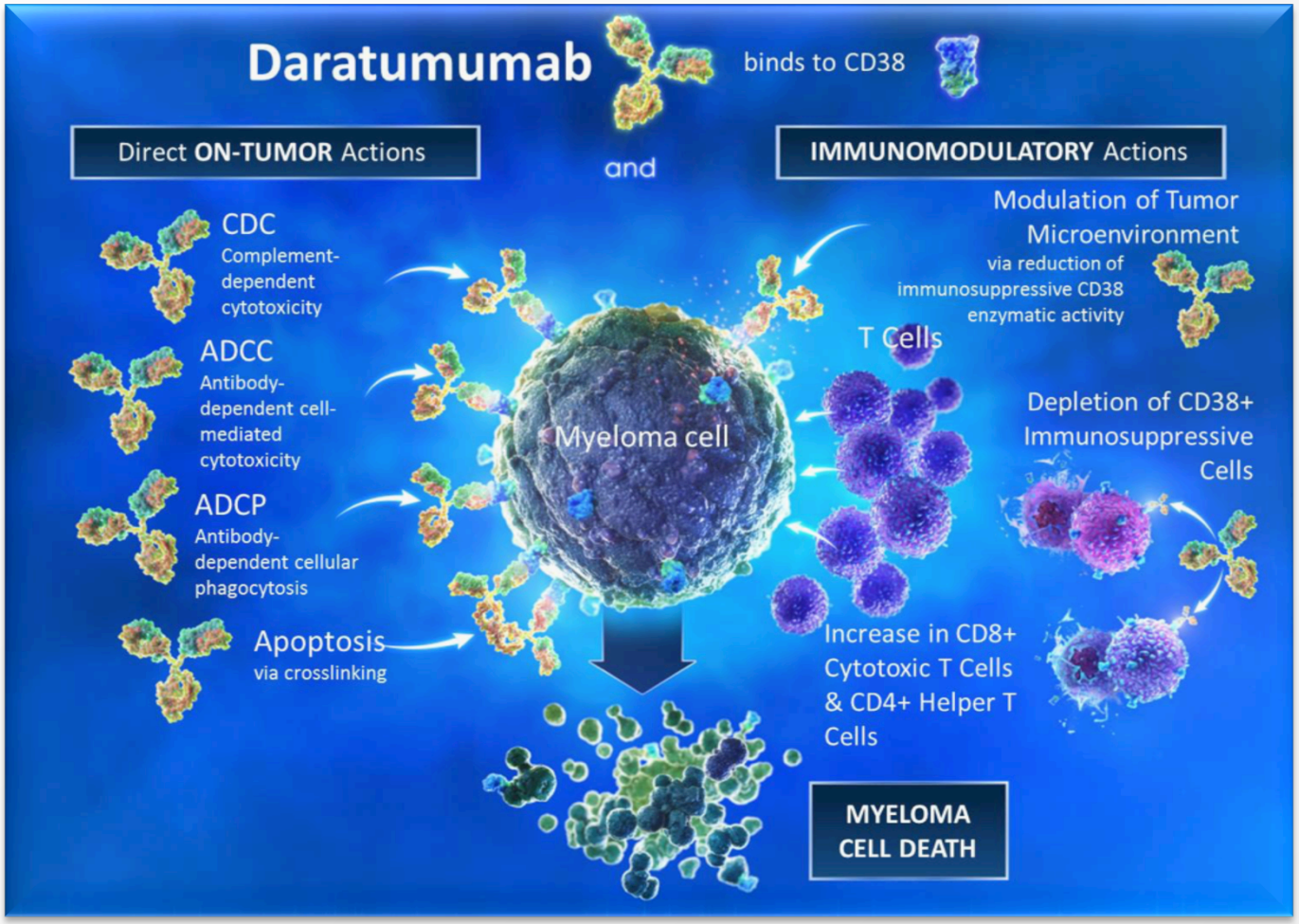


Malavasi F, et al. Blood 2011;118:3470-3478.

Daratumumab: Mechanism of Action

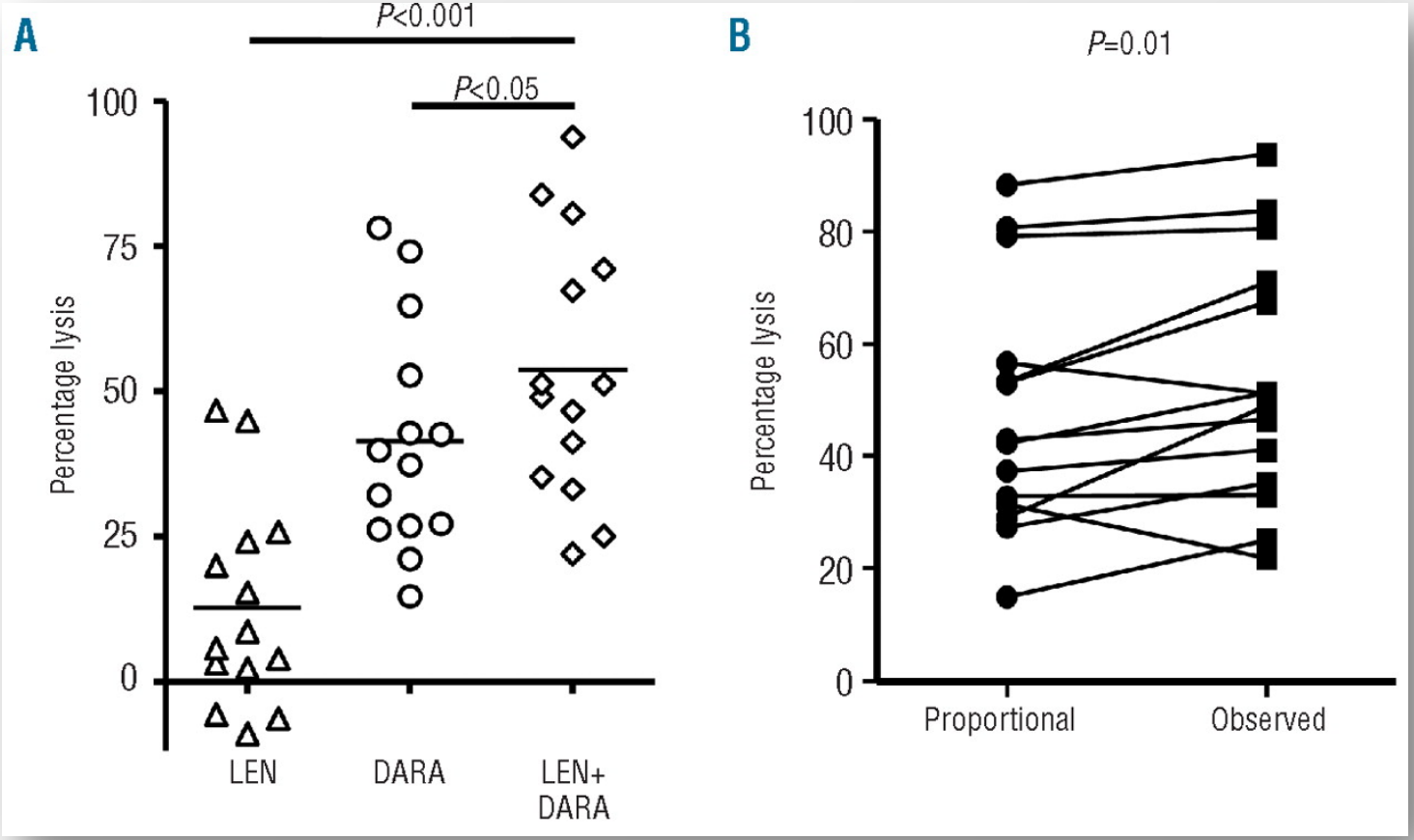
- Human CD38 IgGκ monoclonal antibody
- Direct and indirect anti-myeloma activity[1-5]
- Depletes CD38+ immunosuppressive regulatory cells[5]
- Promotes T-cell expansion and activation[5]

- Daratumumab as a single agent[6,7]
  - Approved by FDA and conditionally approved by EMA in relapsed/refractory multiple myeloma



1. Lammerts van Bueren J, et al. Blood. 2014;124:Abstract 3474
2. Jansen JMH, et al. Blood. 2012;120:Abstract 2974
3. de Weers M, et al. J Immunol. 2011;186:1840-8
4. Overdijk MB, et al. MAbs. 2015;7:311-21Lokhorst HM, et al. *N Engl J Med*. 2015;373:1207-19
5. Lonial S, et al. *Lancet*. 2016;387:1551-60
6. Krejcik J, et al. Blood. 2016. 128(3):384-94

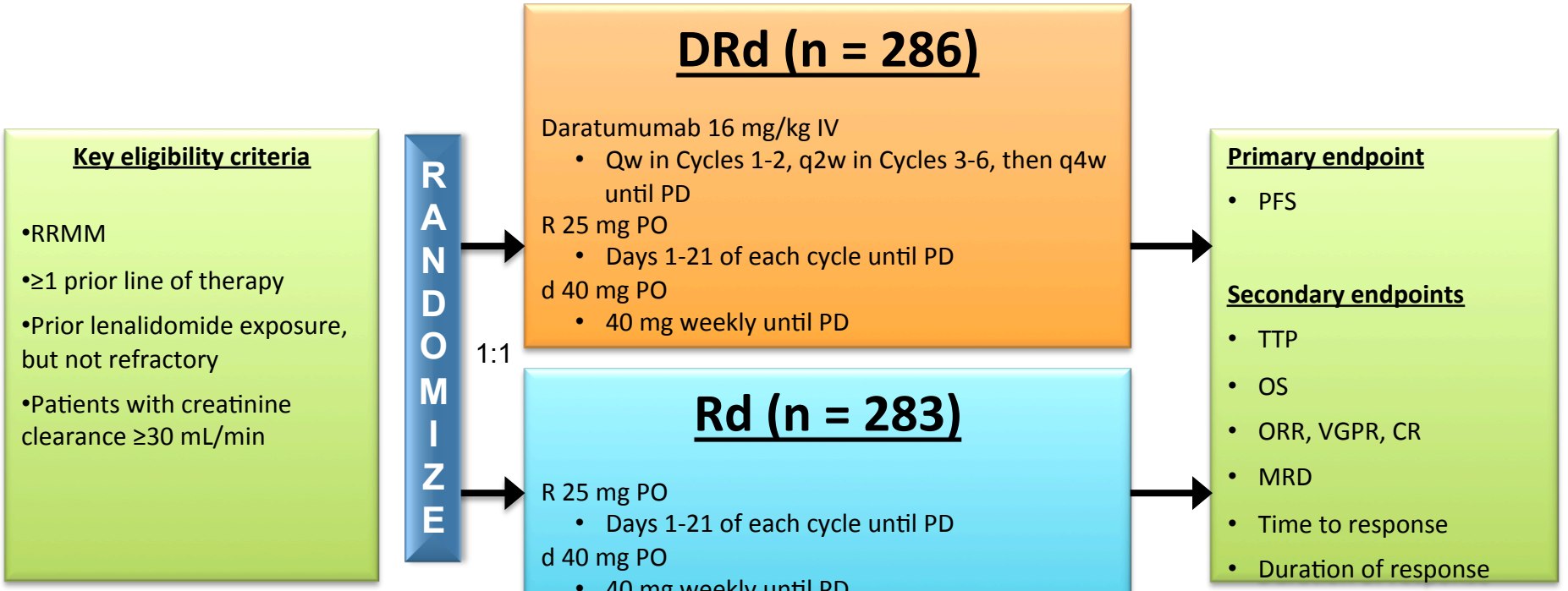
Improvement of DARA-induced ADCC by LEN in BM-MNC of MM patients



Van der Veer et al. Haematologica 2011;96:284-290

POLLUX: Study Design

Multicenter, randomized (1:1), open-label, active-controlled phase 3 study



Stratification factors

- No. prior lines of therapy
- ISS stage at study entry
- Prior lenalidomide

Cycles: 28 days

Statistical analyses

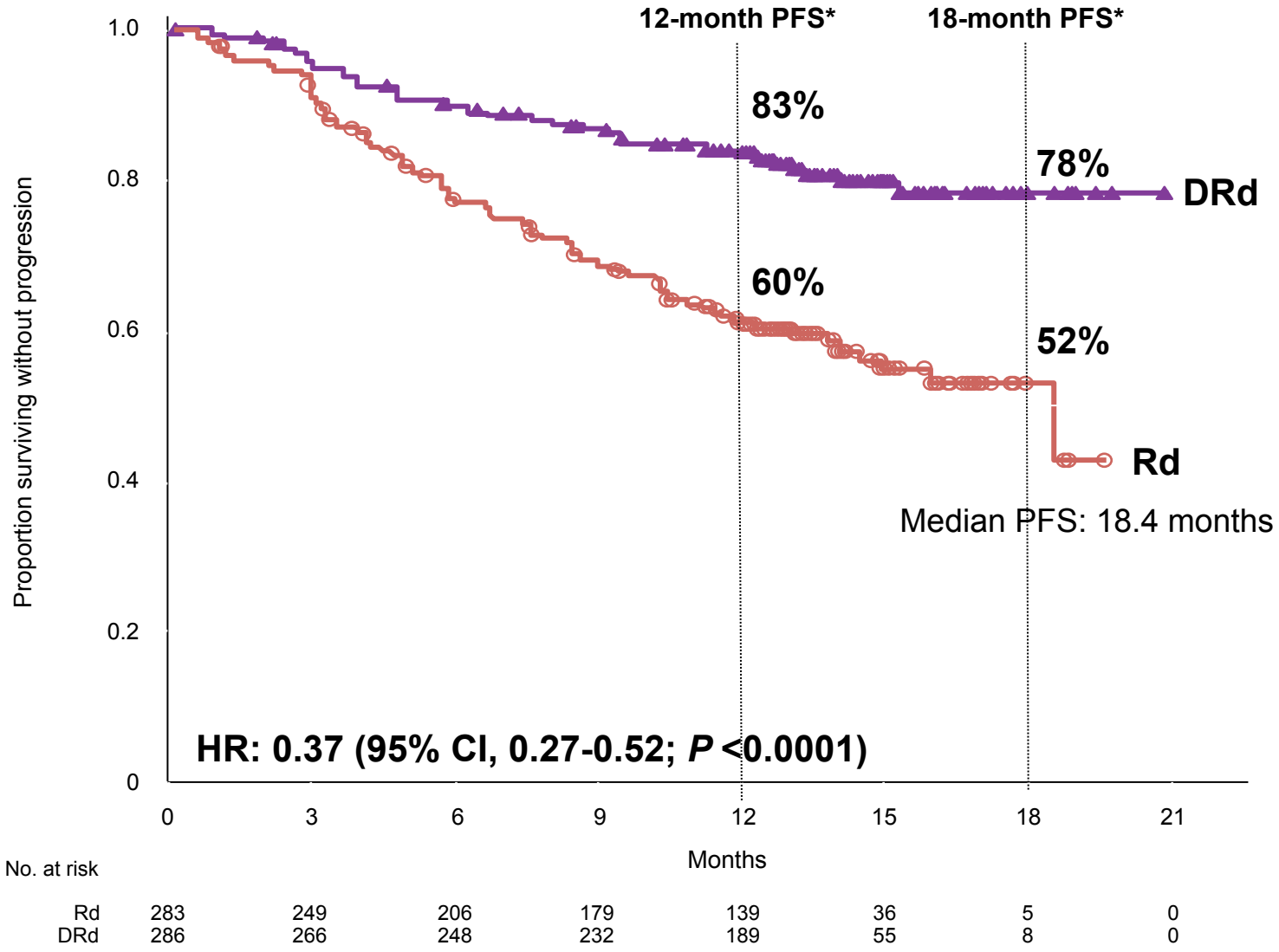
- 295 PFS events: 85% power for 7.7 month PFS improvement
- Interim analysis: ~177 PFS events

Pre-medication for the DRd treatment group consisted of dexamethasone 20 mg[a], paracetamol, and an antihistamine

[a]On daratumumab dosing days, dexamethasone was administered 20 mg premed on Day 1 and 20 mg on Day 2; RRMM, relapsed or refractory multiple myeloma; ISS, international staging system; R, lenalidomide; DRd, daratumumab/lenalidomide/dexamethasone; IV, intravenous; qw, once weekly; q2w, every 2 weeks; q4w, every 4 weeks; PD, progressive disease; PO, oral; d, dexamethasone; Rd, lenalidomide/dexamethasone; TTP, time to progression; MRD, minimal-residual disease.

Dimopoulos MA et al, *N Engl J Med.* 2016;375(14):1319-1331

POLLUX: Progression-free Survival

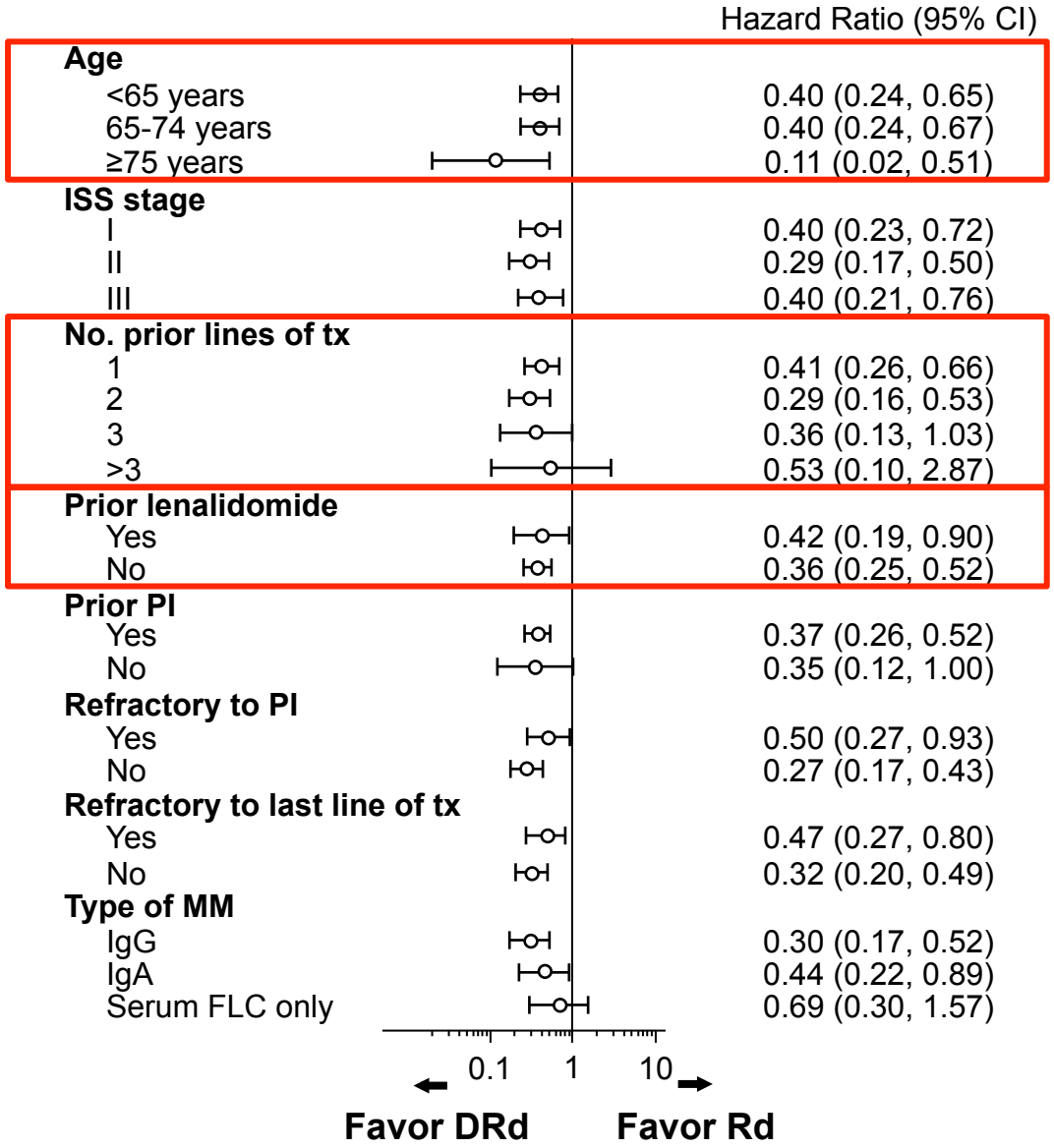


63% reduction in the risk of disease progression or death for DRd vs Rd

*KM estimate; HR, hazard ratio.

Dimopoulos MA et al, *N Engl J Med.* 2016;375(14):1319-1331

POLLUX: PFS, Subgroup Analysis

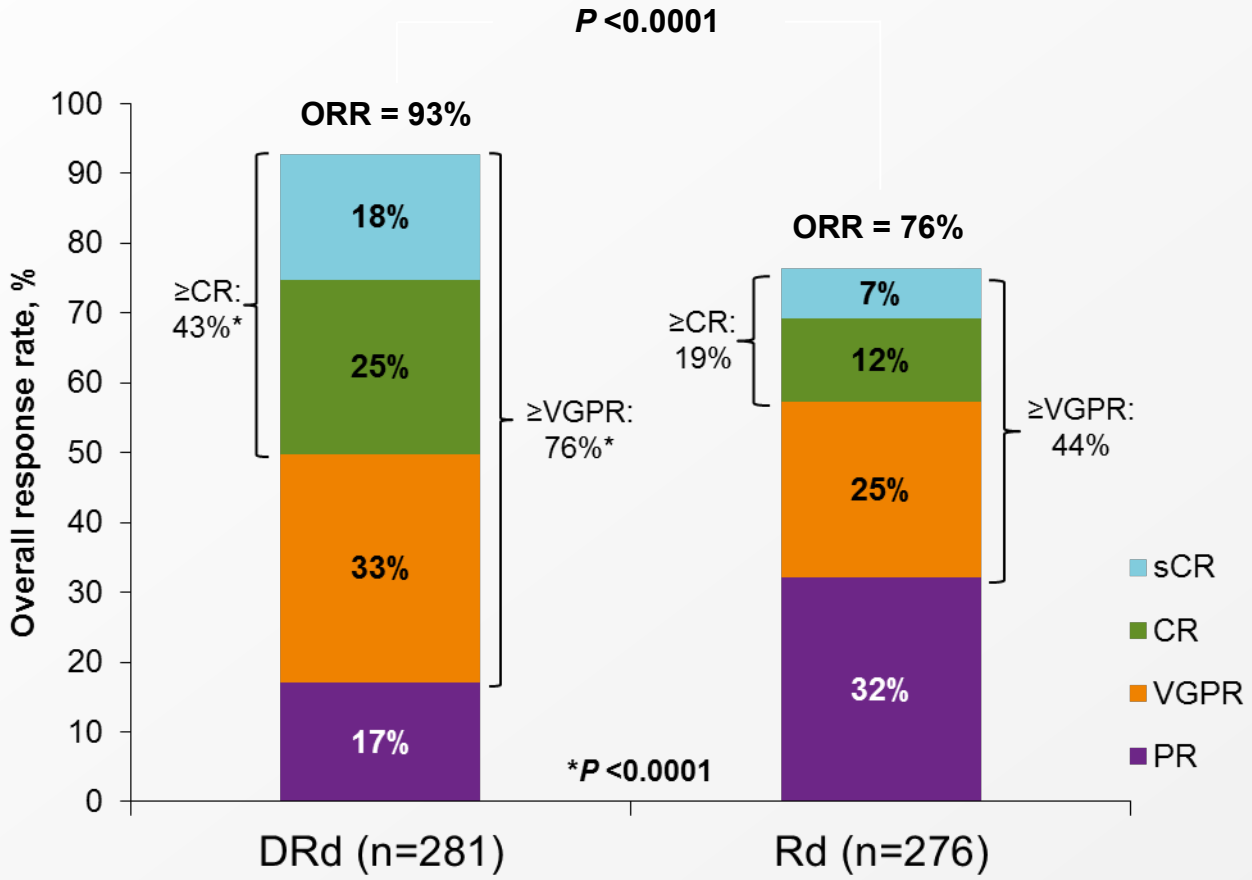


Higher efficacy was observed for DRd versus Rd across all subgroups

Tx, treatment; MM, multiple myeloma; IgG, immunoglobulin G; IgA, immunoglobulin A; FLC, free light chain.

Dimopoulos MA et al, *N Engl J Med.* 2016;375(14):1319-1331

POLLUX: Overall Response Rate[a]

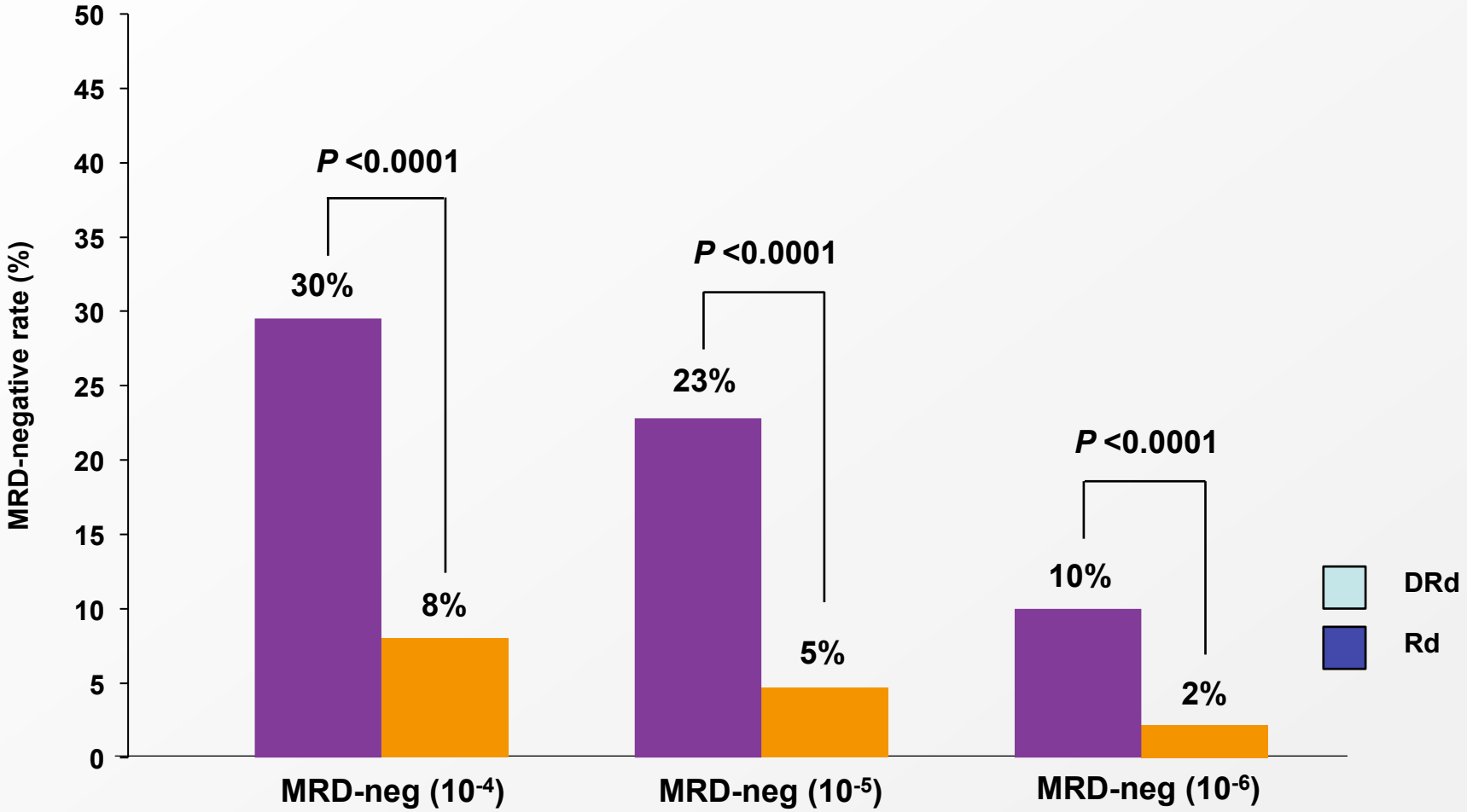


- Median duration of response: Not reached for DRd vs 17.4 months for Rd
- Median time to response: 1.0 month for DRd vs 1.3 months for Rd

[a]When serum interference was suspected, CR was confirmed using the daratumumab interference reflex assay.

Dimopoulos MA et al, *N Engl J Med.* 2016;375(14):1319-1331

POLLUX: MRD-negative Rate



Significantly higher MRD-negative rates for DRd vs Rd

Response-evaluable set. Assessed by next generation sequencing in bone marrow.

Dimopoulos MA et al, *N Engl J Med.* 2016;375(14):1319-1331

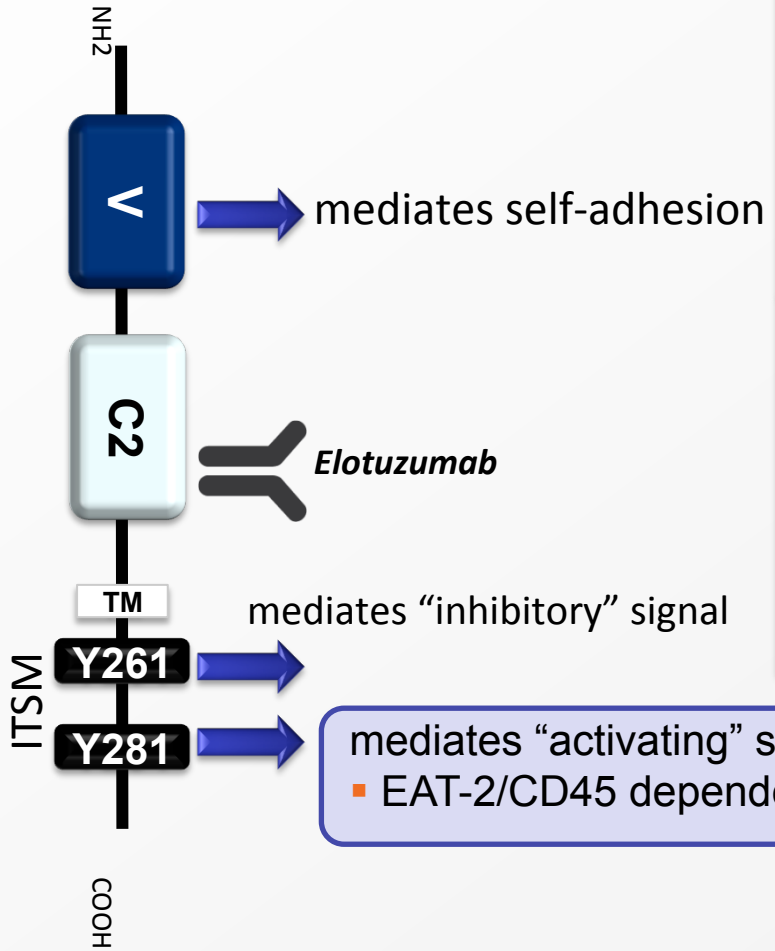
POLLUX: Infusion-related Reactions (IRRs)

IRRs ≥2%	Safety Analysis Set (n = 283)	
	All grades (%)	Grade 3 (%)
Patients with IRRs	48	5
Cough	9	0
Dyspnea	9	0.7
Vomiting	6	0.4
Nausea	5	0
Chills	5	0.4
Bronchospasm	5	0.4
Pruritus	3	0.4
Throat irritation	3	0
Headache	3	0
Nasal congestion	3	0
Wheezing	2	0.7
Laryngeal edema	2	0.4
Rhinorrhea	2	0
Pyrexia	2	0

- No grade 4 or 5 IRRs were reported
- 92% of all IRRs occurred during the first infusion
- 1 patient discontinued daratumumab due to an IRR

Dimopoulos MA et al, *N Engl J Med.* 2016;375(14):1319-1331

Elotuzumab:
A Monoclonal Antibody Targeting SLAMF7



Elotuzumab

- Humanized, IgG1 mab specific for human SLAMF7
  - No cross-reactivity with non-human homologues or other SLAM family members
- Binds to a membrane-proximal motif of SLAMF7
  - Critical for mediating killing of target cells (in vitro)

SLAMF7

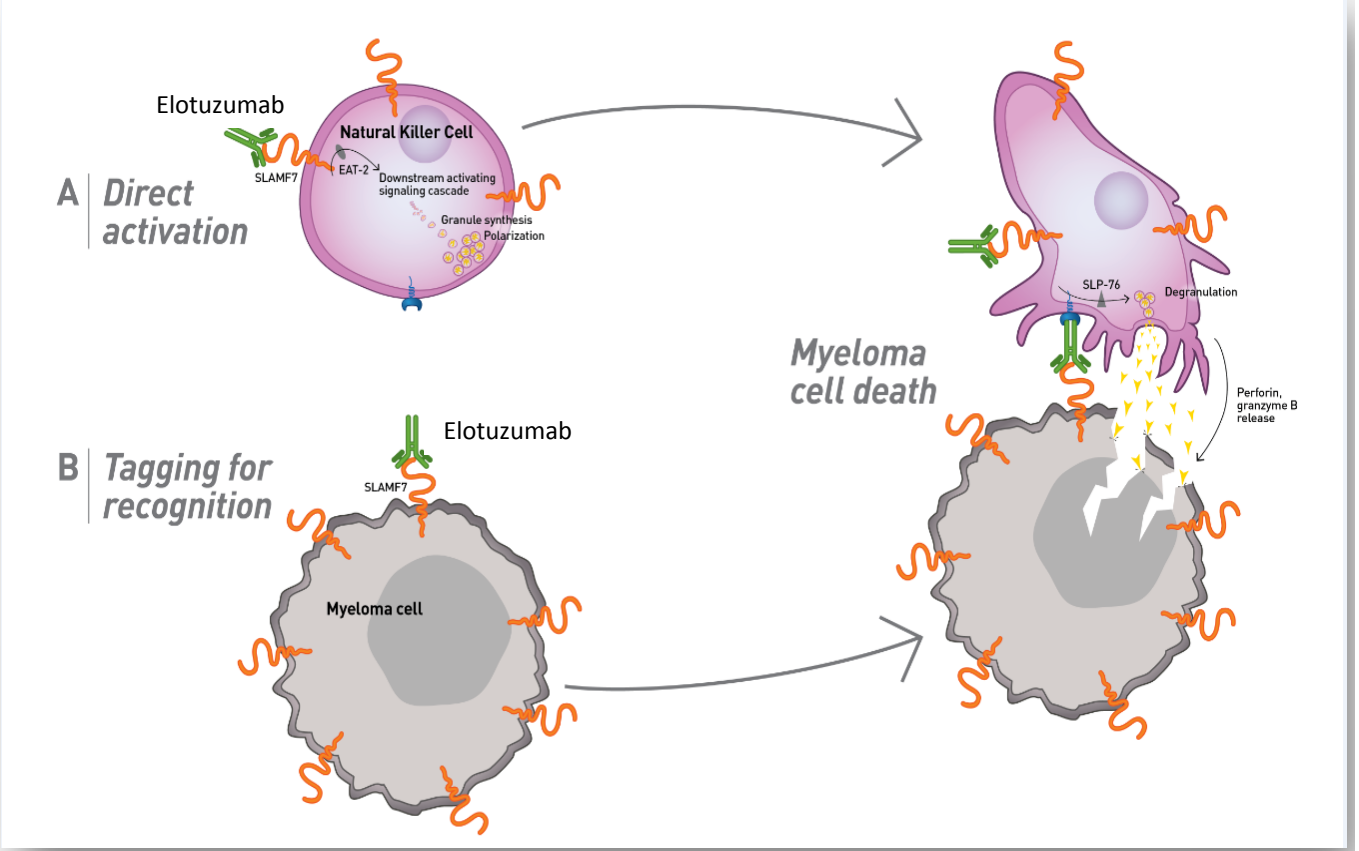
- Expression highest on Plasma Cells
- Varied expression across hematopoietic cells (NK, NK-T, DC, B, TCD8+, PC)
- Not express on non-hematopoietic cells
- SLAMF7 K/O Phenotype: compromised NK function

SLAMF7 = Signalling Lymphocyte Activation Molecule Family 7; ADCC=Antibody-dependent cellular cytotoxicity
ITSM = Intracellular Tyrosine Switch Motif
EAT-2 = Ewing's Sarcoma associated transcript 2

Veillette and Guo, Critical Reviews in Onc and Heme, 2013.
Cruz-Munoz et al, Nature Immunology, 2009.

Elotuzumab works via a dual mechanism of action by both directly activating Natural Killer Cells and through antibody-dependent cell-mediated cytotoxicity (ADCC) to cause targeted Myeloma cell death

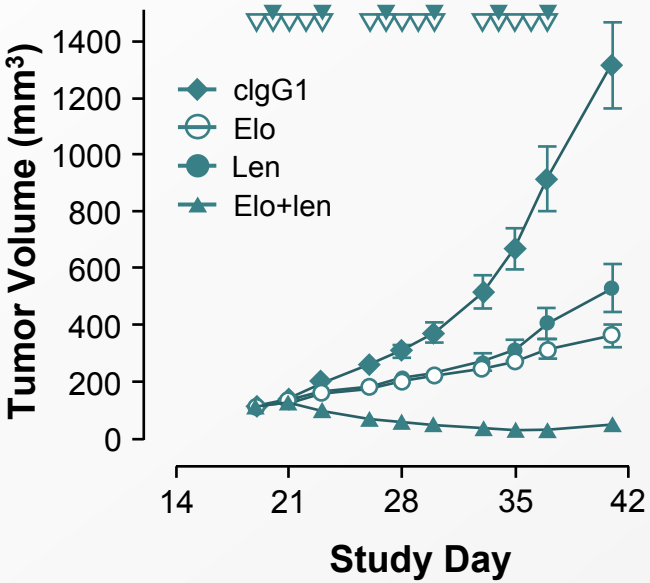
- **A: Direct activation**
  Binding to SLAMF7 directly activates natural killer cells,[2] but not myeloma cells[3]
- **B: Tagging for recognition**
  Elotuzumab activates natural killer cells via CD16, enabling selective killing of myeloma cells via antibody-dependent cellular cytotoxicity (ADCC) with minimal effects on normal tissue[2]



1. Hsi ED et al. Clin Cancer Res 2008;14:2775–84
2. Collins SM et al. Cancer Immunol Immunother 2013;62:1841–9
3. Guo H et al. Mol Cell Biol 2015;35:41–51

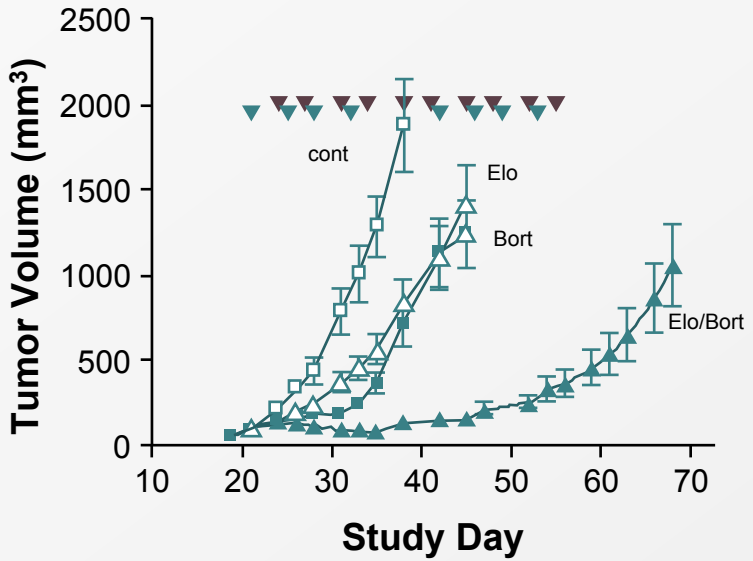
Elotuzumab Exhibits Synergy With Both Lenalidomide and Bortezomib

- No single agent activity
- Lenalidomide and bortezomib enhance the NKC-Mediated anti-myeloma activity of elotuzumab



Elotuzumab/lenalidomide[2]

- Lenalidomide enhances T-cell activation and cytokine production leading to **Natural Killer cell stimulation**
- Lenalidomide also exhibits **direct antimyeloma activity**, which enhances the cells' sensitivity to Natural Killer cell-mediated killing



Elotuzumab/bortezomib[1]

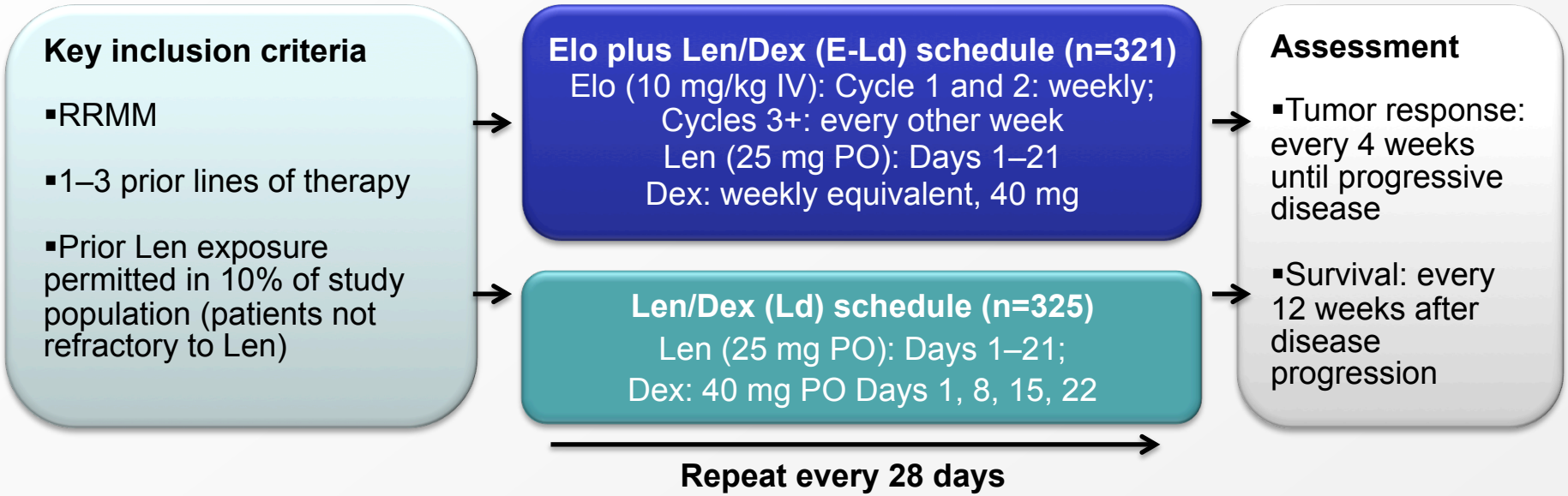
- Bortezomib exhibits direct **antimyeloma activity**, which augments the cells' sensitivity to Natural Killer cell-mediated killing by enhancing activating ligands and reducing inhibitory ligands on myeloma cells

A, B – *in vivo* tumor growth inhibition of OPM2 xenograft in SCID mice.

1. Van Rhee F et al. *Mol CanTher*. 2009;8:2616-2624.
2. Balasa et al. *Cancer Imm and Immunothe*. 2015; 64 (1):61-73.

ELOQUENT-2: Elo-Ld vs Ld in R/R MM

Elotuzumab is approved by FDA and EMA in combination with lenalidomide-dexamethasone for patients who have received at least 1 prior lines of therapy

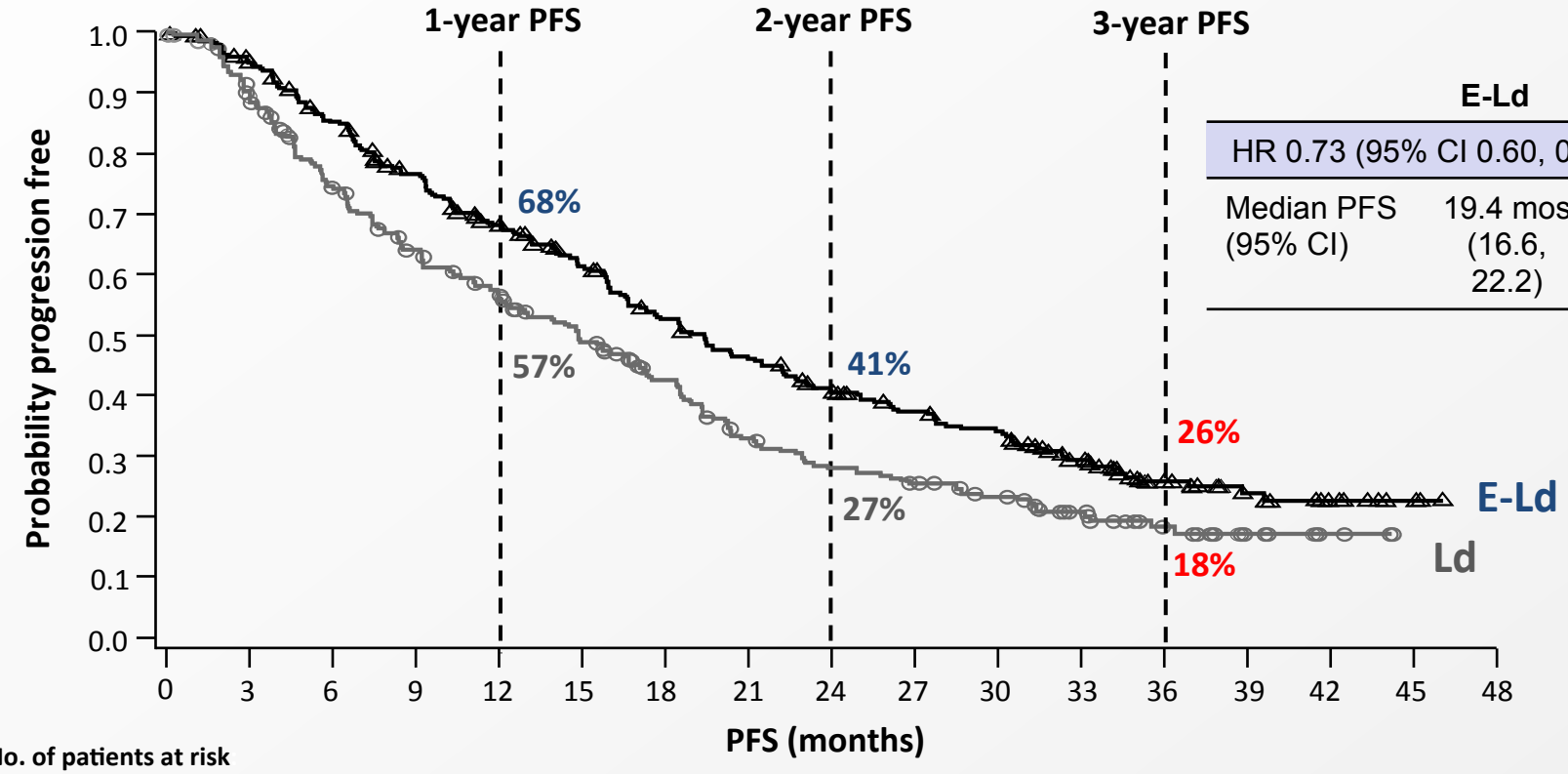


- Open-label, international, randomized, multicenter, **phase 3 trial** (168 global sites)
- **646 pts**
- Median n° treatment cycles Elo Ld: 19 (1-42)
- 83% pts received more than 90% dose intensity

Lonial S et al, NEJM 2015

ELOQUENT-2: Elo-Ld vs Ld in R/R MM

Extended Progression-Free Survival



	E-Ld	Ld
HR 0.73 (95% CI 0.60, 0.89); p=0.0014		
Median PFS (95% CI)	19.4 mos (16.6, 22.2)	14.9 mos (12.1, 17.2)

No. of patients at risk

E-Ld	321	293	259	227	195	171	144	125	107	94	85	59	34	19	8	3	0
Ld	325	266	215	181	157	130	106	80	67	60	51	36	15	7	3	0	0

PFS benefit with E-Ld was maintained over time (vs Ld):

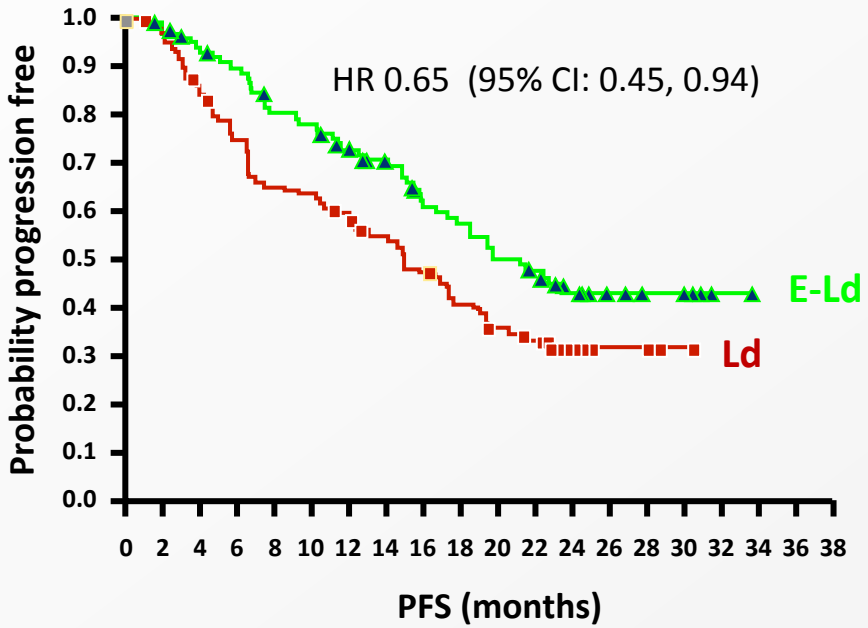
- **Overall 27% reduction in the risk of disease progression or death**
- **Relative improvement in PFS of 44% at 3 years**

Lonial S et al, NEJM 2015
Dimopoulos MA, et al ASH 2015

ELOQUENT-2: EloRd vs Rd

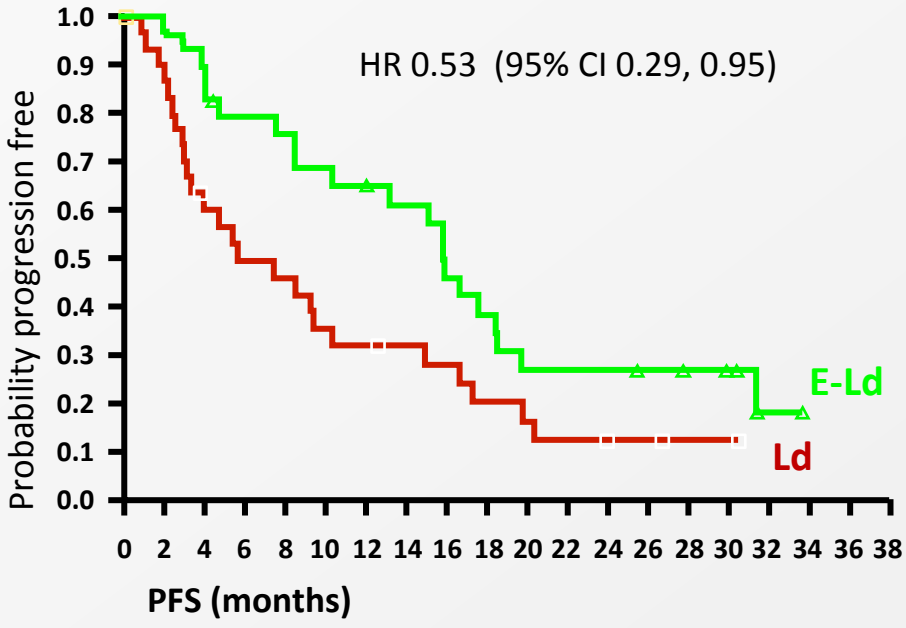
PFS according to del(17p) and t(4;14)

del(17p)+



E-Ld: median (95% CI): 21.19 (16.62, NE)
Ld: median (95% CI): 14.92 (10.61, 18.50)

t(4;14)+



E-Ld: median (95% CI): 15.84 (8.41, 18.46)
Ld: median (95% CI): 5.55 (3.09, 10.25)

Elo-Rd del(17p) negativity: median (95% CI): 18.46 (15.84, 22.77)

Dimopoulos M et al, ASH 2015
Lonial S et al, NEJM 2015

ELOQUENT-2: EloRd vs Rd
INFUSION REACTIONS

Events, n (%)	E-Ld (n=318)		
	Grade 1/2	Grade 3	Grade 4/5
Infusion reaction	29 (9)	4 (1)	0
Pyrexia	10 (3)	0	0
Chills	4 (1)	0	0
Hypertension	3 (1)	1 (<1)	0

- Infusion reactions occurred in 10% of patients
- 70% of infusion reactions occurred with the first dose
- No Grade 4 or 5 infusion reactions
- Elotuzumab infusion was interrupted in 15 (5%) patients due to an infusion reaction (median interruption duration 25 minutes)
- 2 (1%) patients discontinued the study due to an infusion reaction

Lonial S et al, NEJM 2015

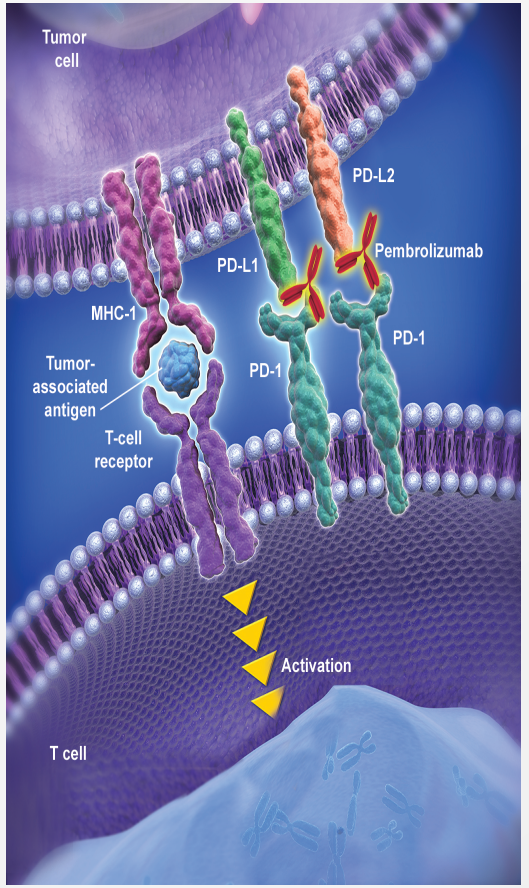
Lenalidomide-based triplet regimens

	ASPIRE KRd vs Rd	TOURMALINE-MM1 IRd vs Rd	POLLUX DRd vs Rd	ELOQUENT-2 ERd vs Rd
PFS HR (95% CI)	0.69 (0.57-0.83)	0.74 (0.59-0.94)	0.37 (0.27-0.52)	0.73 (0.60-0.89)
ORR	87%	78%	93%	79%
≥VGPR	70%	48%	76%	33%
≥CR	32%	14%	43%	4%
Duration of response, mo	28.6	20.5	NE	20.7
OS HR (95% CI)	0.79 (0.63-0.99)	NE	0.64 (0.40-1.01)	0.77 (0.61-0.97)

1. Stewart AK, et al. *N Engl J Med*. 2015;372(2):142-152.
2. Moreau P, et al. *N Engl J Med*. 2016;374(17):1621-1634
3. Dimopoulos MA et al, *N Engl J Med.* 2016;375(14):1319-1331
4. Lonial S, et al. *N Engl J Med*. 2015;373(7):621-631

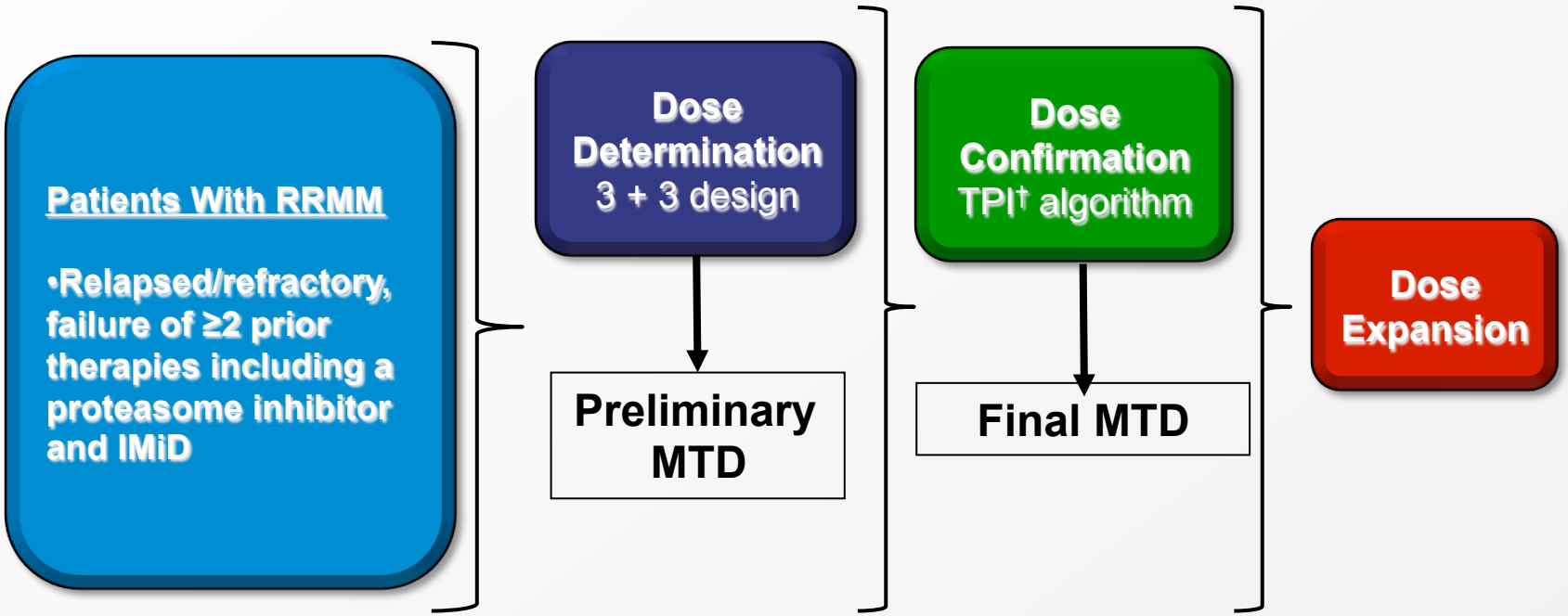
Pembrolizumab
Immuno-oncology

- The PD-1 pathway is often exploited by tumors to evade immune surveillance:[1-3]
  - PD1 is upregulated on activated T-cells
  - *Binding* of the PD-1 receptor to its ligands, PD-L1 and PD-L2 (expressed on the surface of APC & Tumor cells) *inhibits T-cell activation*
- Role of PD-1 inhibitors in multiple myeloma[1-2]
  - PD-1 is increased among T-cells of patients with MRD/RR disease
  - PD-1 blockade prolonged survival mice with 5TGM-1 PD-L1–positive MM cells
- Pembrolizumab blocks interaction between PD-1 and PD-L1/PD-L2[4-6]
  - Robust antitumor activity and manageable safety in multiple cancers
- Rationale for the combination of IMiDs and PD-L1 blockade[7]
  - Lenalidomide reduces PD-L1 and PD-1 expression on MM cells and T and myeloid derived suppressor cells
  - Lenalidomide enhances checkpoint blockade–induced effector cytokine production in MM bone marrow and induced cytotoxicity against MM cells



1. Liu J et al, *Blood*. 2007;110:296-304; 2. Tamura H, et al. *Leukemia*. 2013;27:464-72; 3. Paiva B, et al. *Leukemia*. 2015. 2015;29:2110-3;
4. Keir ME et al. *Annu Rev Immunol*. 2008;26:677-704; 5. Hallett WH et al. *Biol Blood Marrow Transplant*. 2011;17:1133-1145; 6. Homet Moreno B, Ribas A. *Br J Cancer*. 2015;112:1421-1427; 7. Görgün G. et al. *Clin Cancer Res*. 2015;21:4607-18.

KEYNOTE-023: Phase 1 Trial of Pembrolizumab + Lenalidomide and Low-Dose Dexamethasone in RRMM



- Primary end points: Safety and tolerability
- Secondary end points: ORR, DOR, PFS, OS

- **MTD pembro 200 mg iv Q2W + Len 25 mg + Dex**
- **Safety analysis: all patients enrolled in the study (N = 51)**
- **Efficacy analysis: patients who completed 3 cycle of treatment or discontinued for PD (N = 40)**

Mateos MV et al, ASCO 2016

KEYNOTE-023: Treatment-Related Adverse Events

n (%)	All AEs	Grade 3-5
All AEs (N = 51)	48 (94)	33 (65)
AEs in ≥6 Patients		
Neutropenia	19 (37)	17 (33)
Thrombocytopenia	21 (41)	9 (18)
Diarrhea	14 (28)	0
Fatigue	13 (26)	1 (2)
Anemia	11 (22)	6 (12)
Pruritus	6 (12)	0
Hyperglycemia	9 (18)	4 (8)
Muscle spasms	7 (14)	0
Myalgia	8 (16)	0
Blurred vision	7 (14)	0
Dizziness	6 (12)	0
Dyspnea	6 (12)	0

n (%)	Pembro + Len + Dex (N = 51)
Hyperthyroidism Grade 1	1 (2)
Hypothyroidism Grade 1	2 (4)
Thyroiditis Grade 1	1 (2)
Increased transaminases Grade 3	1 (2)
Renal failure Grade 3	1 (2)

Immune-Mediated Adverse Events

Mateos MV et al, ASCO 2016

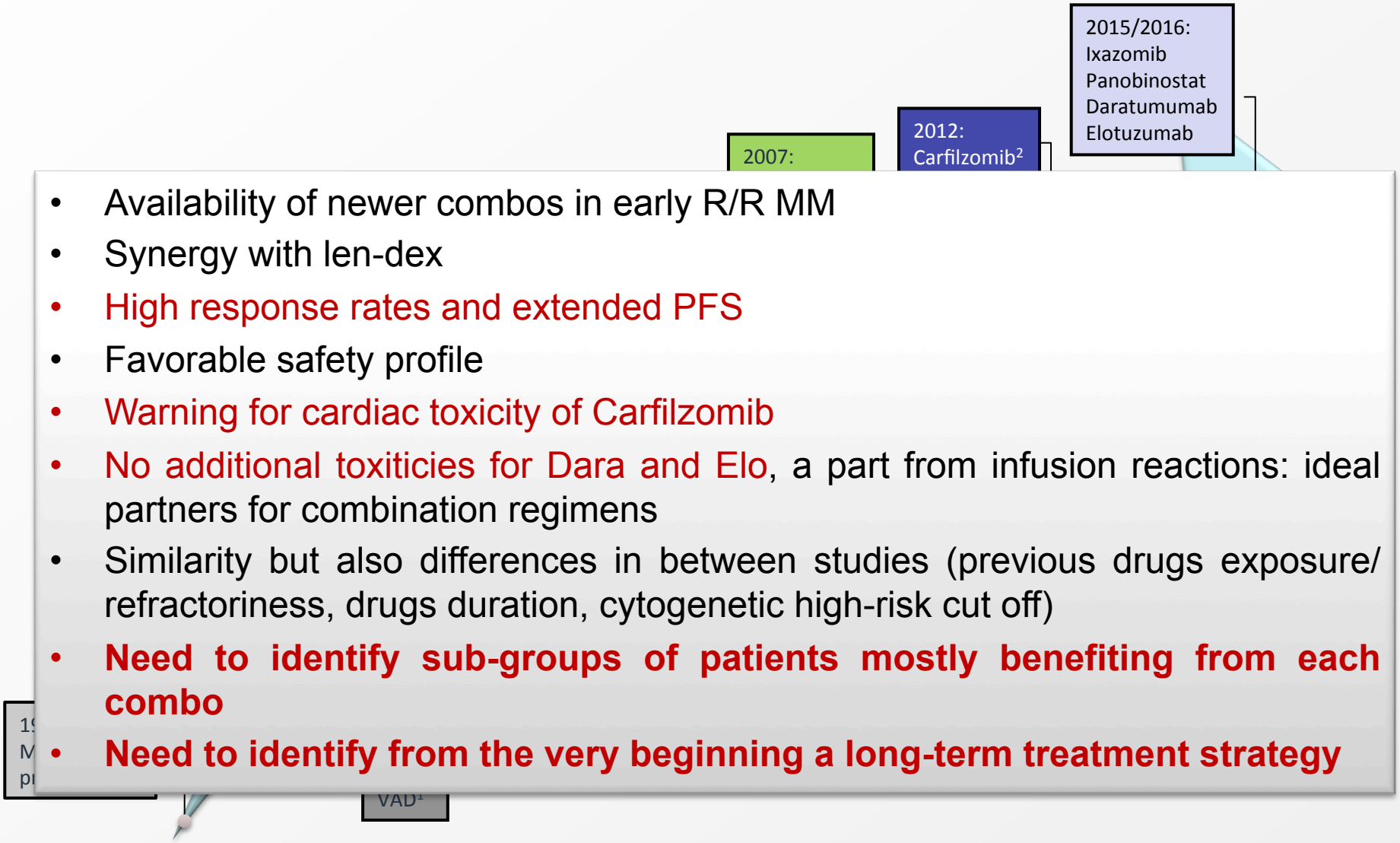
KEYNOTE-023: Antitumor Activity
Central Review (IMWG 2006)

Best Overall Response n (%)	Efficacy Population† (n = 40)	Len-Refractory (n = 29)
Overall response rate	20 (50)	11 (38)
Stringent complete response (sCR)	1 (3)	1 (3)
Very good partial response (VGPR)	5 (13)	3 (10)
Partial response (PR)	14 (35)	7 (24)
Stable disease (SD)	19 (48)	17 (59)
Disease control rate (CR+PR+SD)	39 (98)	28 (97)
Progressive disease (PD)	1 (3)	1 (3)

†11 patients NE by central review
3 discontinued within cycle 1 for reasons other than PD (2 no treatment assessments and 1 SD by investigator)
8 inadequate myeloma data for response assessment (5 PD and 3 SD by investigator)

Mateos MV et al, ASCO 2016

Conclusions and future directions



- Availability of newer combos in early R/R MM
- Synergy with len-dex
- High response rates and extended PFS
- Favorable safety profile
- Warning for cardiac toxicity of Carfilzomib
- No additional toxiticies for Dara and Elo, a part from infusion reactions: ideal partners for combination regimens
- Similarity but also differences in between studies (previous drugs exposure/ refractoriness, drugs duration, cytogenetic high-risk cut off)
- **Need to identify sub-groups of patients mostly benefiting from each combo**
- **Need to identify from the very beginning a long-term treatment strategy**

ABMT=autologous bone marrow transplant; VAD=vincristine/doxorubicin/dexamethasone.

1. Latif T et al. *Exp Hematol Oncol*. 2012;1:27. 2. Kyprolis [prescribing information]. Onyx Pharmaceuticals, Inc; South San Francisco, CA.
3. Pomalyst [prescribing information]. Celgene Corporation; Summit, NJ.