Myélome Multiple en Rechute, Quand et Comment traiter?

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Service d'Hematologie et Therapie cellulaire
Hôpital de la Mileterie, CHU, Poitiers, France

Ce qu'il se fait de mieux au Monde

- Pourquoi
- Comment
- Est-ce juste une histoire de Voitures?

Pourquoi pas Moi…

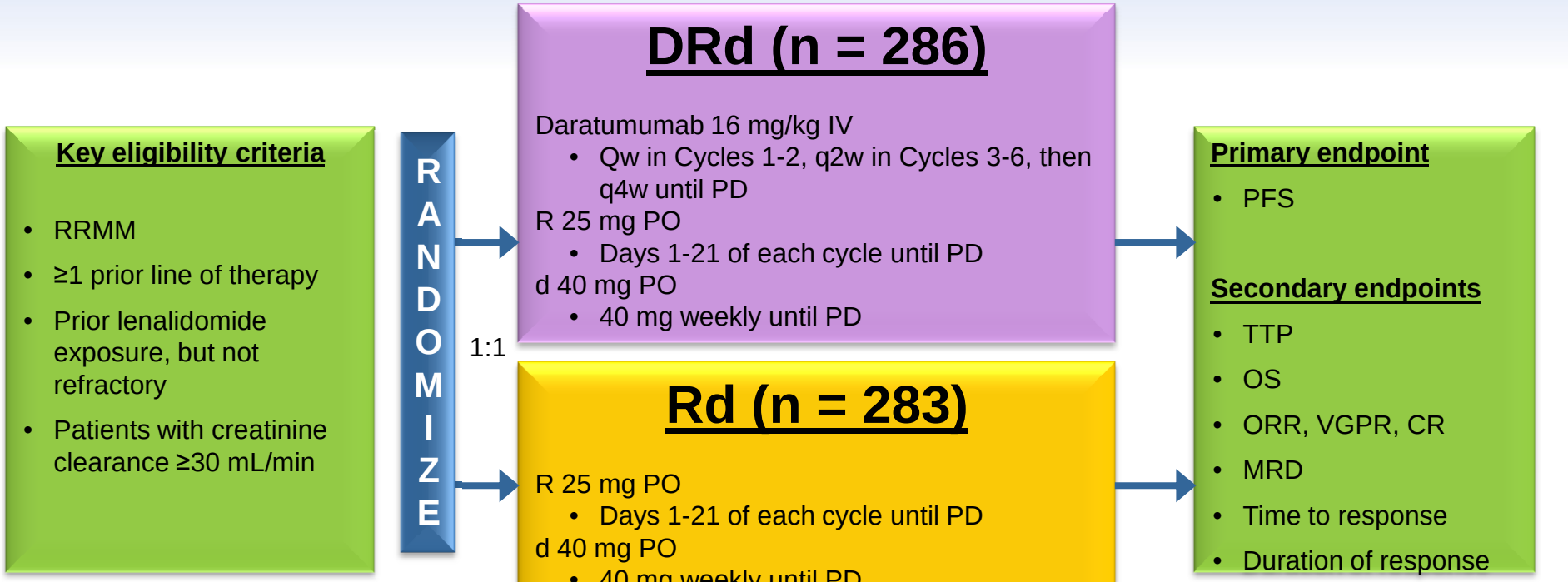
La Bonne Combinaison
Le Choix des Molécules

An Open-label, Randomised, Phase 3 Study of Daratumumab, Lenalidomide, and Dexamethasone (DRd) Versus Lenalidomide and Dexamethasone (Rd) in Relapsed or Refractory Multiple Myeloma (RRMM): POLLUX*

Meletios A. Dimopoulos, Albert Oriol, Hareth Nahi, Jesus San Miguel, Nizar J. Bahlis, Neil Rabin, Robert Z. Orlowski, Mieczyslaw Komarnicki, Kenshi Suzuki, Torben Plesner, Olga S. Samoilova, Sung-Soo Yoon, Dina Ben Yehuda, Paul G. Richardson, Hartmut Goldschmidt, Donna Reece, Nushmia Khokhar, Lisa O'Rourke, Christopher Chiu, Xiang Qin, Mary Guckert, Tahamtan Ahmadi, Philippe Moreau, on behalf of the POLLUX investigators

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

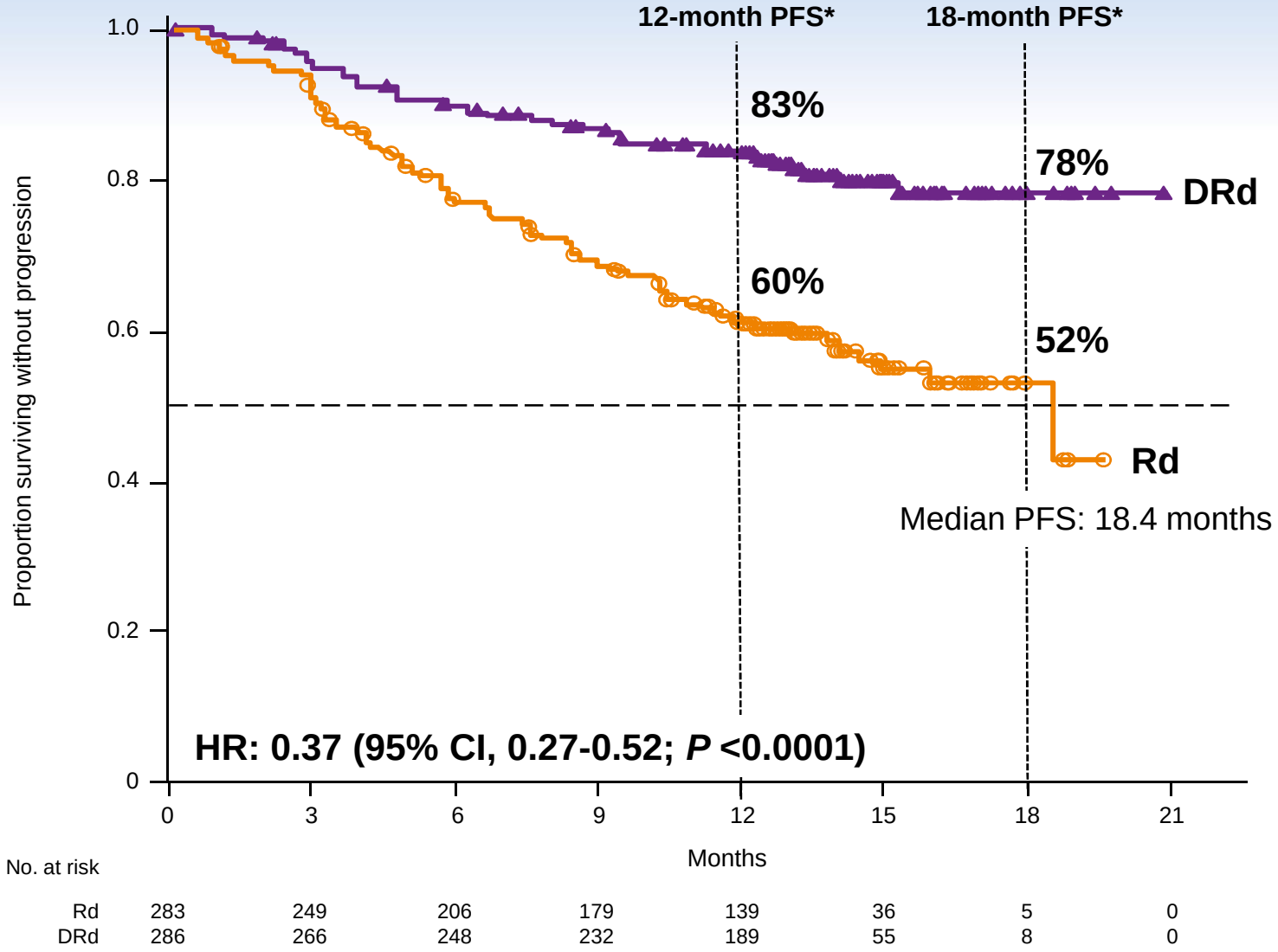
Statistical analyses

- 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.

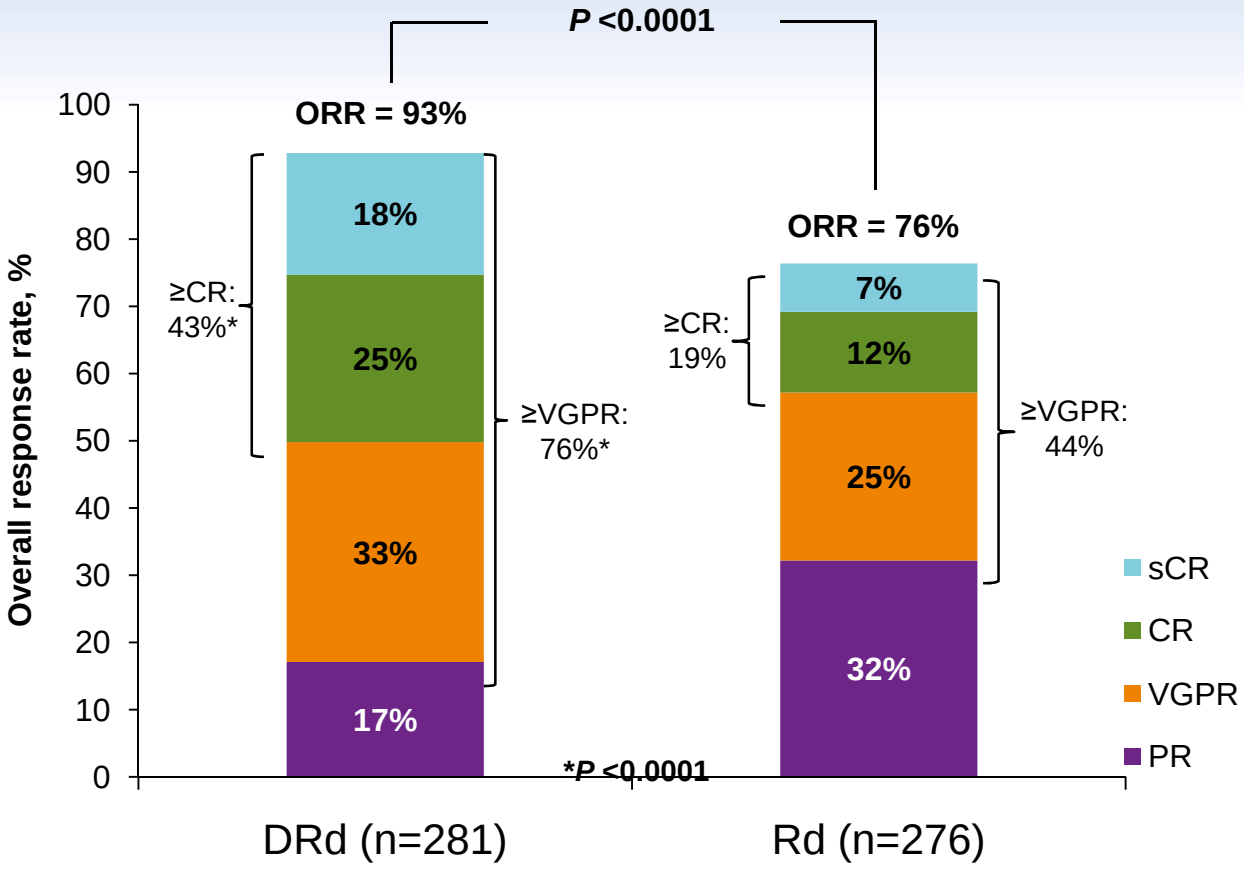
Progression-free Survival



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

*KM estimate; HR, hazard ratio.

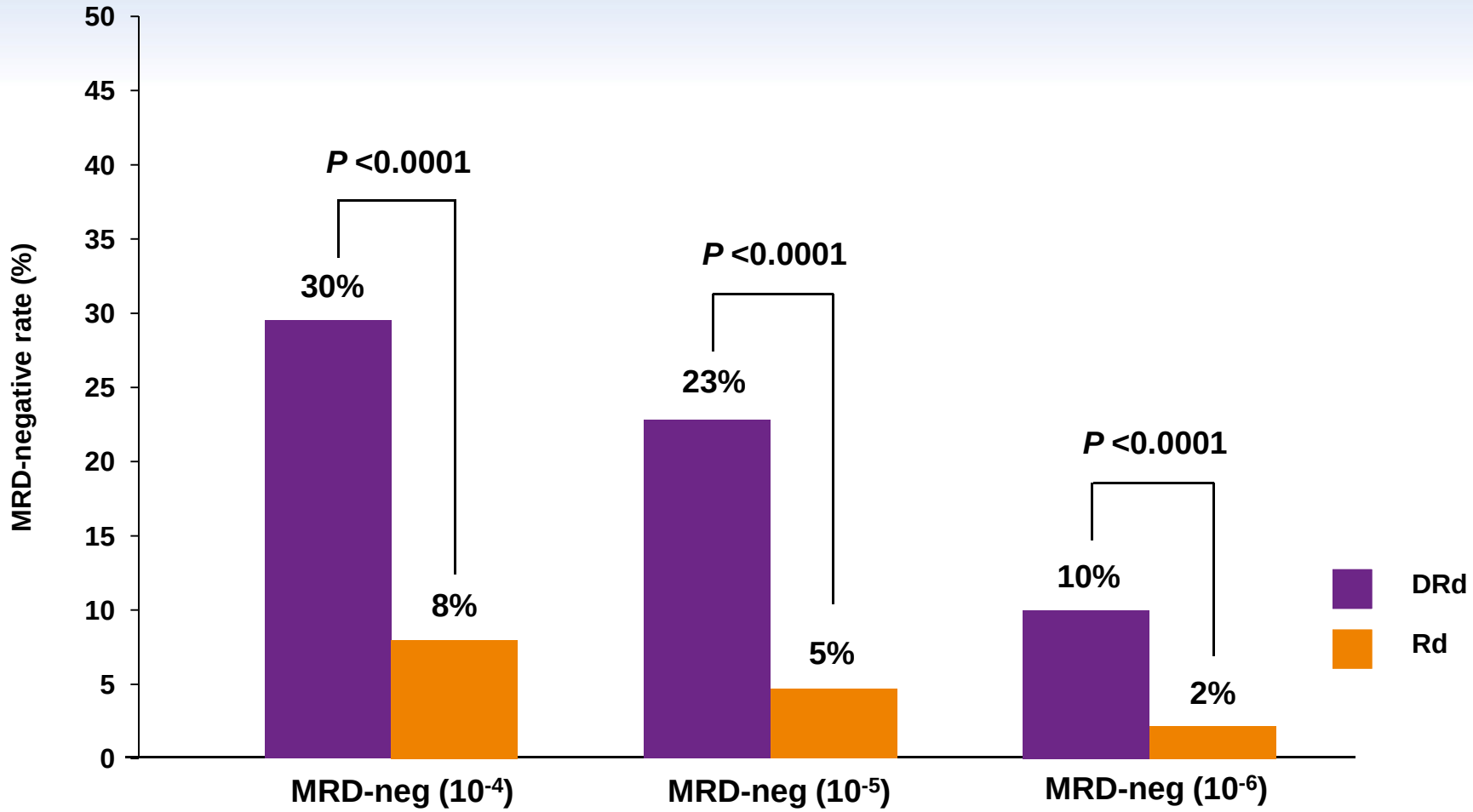
Overall Response Rate[a]



- 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.

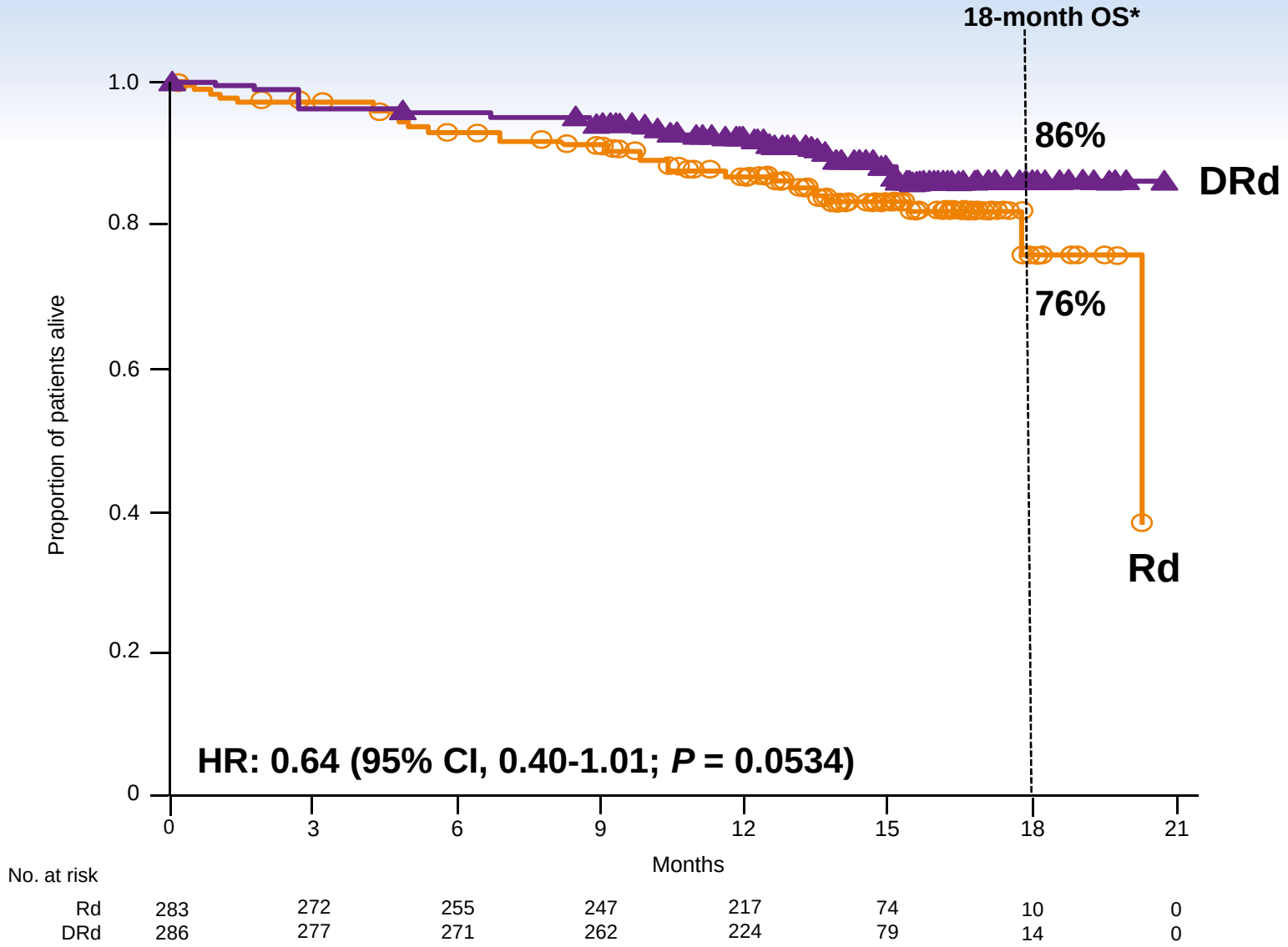
MRD-negative Rate



Significantly higher MRD-negative rates for DRd vs Rd

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

Overall Survival



18-month overall survival: 86% in DRd versus 76% in Rd

*KM estimate.

Phase 3 Randomized Controlled Study of Daratumumab, Bortezomib and Dexamethasone (DVd) vs Bortezomib and Dexamethasone (Vd) in Patients with Relapsed or Refractory Multiple Myeloma (RRMM): CASTOR*

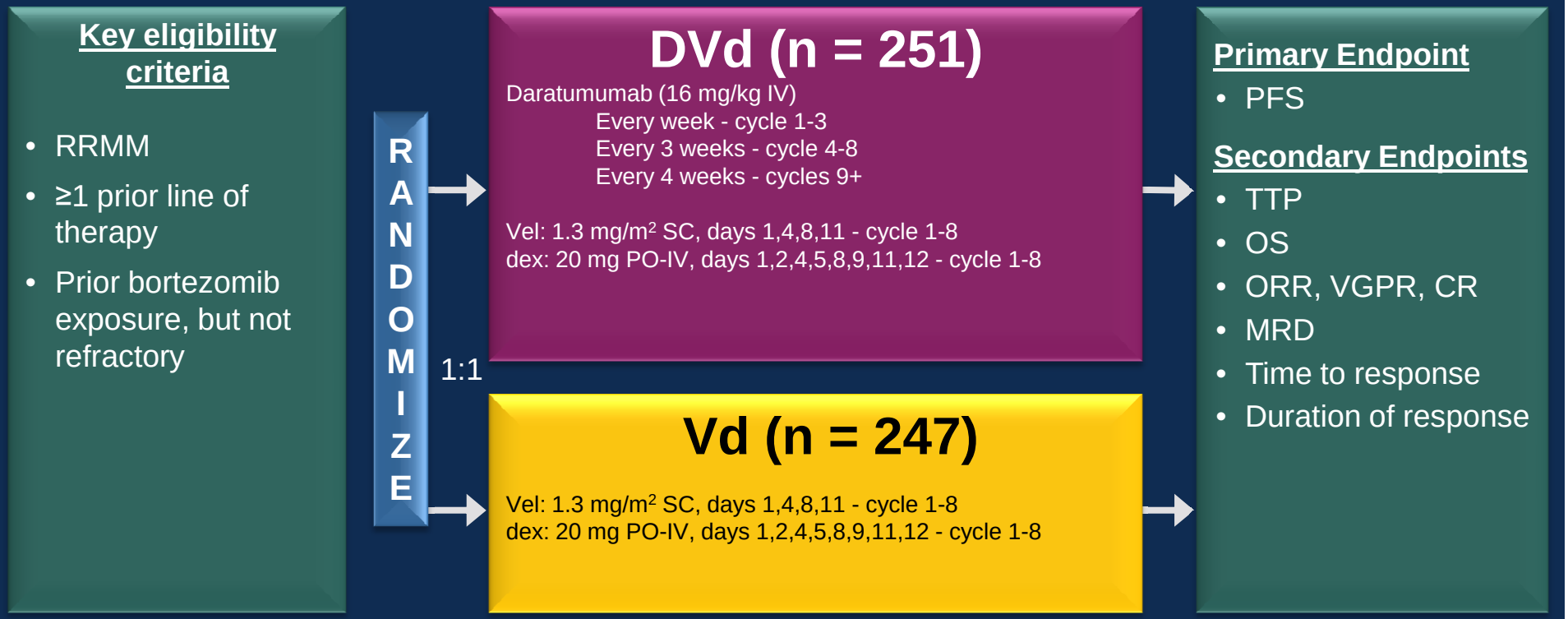
Antonio Palumbo, Asher Chanan-Khan, Katja Weisel, Ajay K. Nooka, Tamas Masszi, Meral Beksac, Ivan Spicka, Vania Hungria, Markus Munder, Maria Victoria Mateos, Tomer Mark, Ming Qi, Jordan Schecter, Himal Amin, Xiang Qin, William Deraedt, Tahamtan Ahmadi, Andrew Spencer, and Pieter Sonneveld on behalf of the CASTOR investigators

PRESENTED AT: ASCO ANNUAL MEETING '16

*NCT02136134

CASTOR: Study Design

Multicenter, randomized, open-label, active-controlled phase 3 study

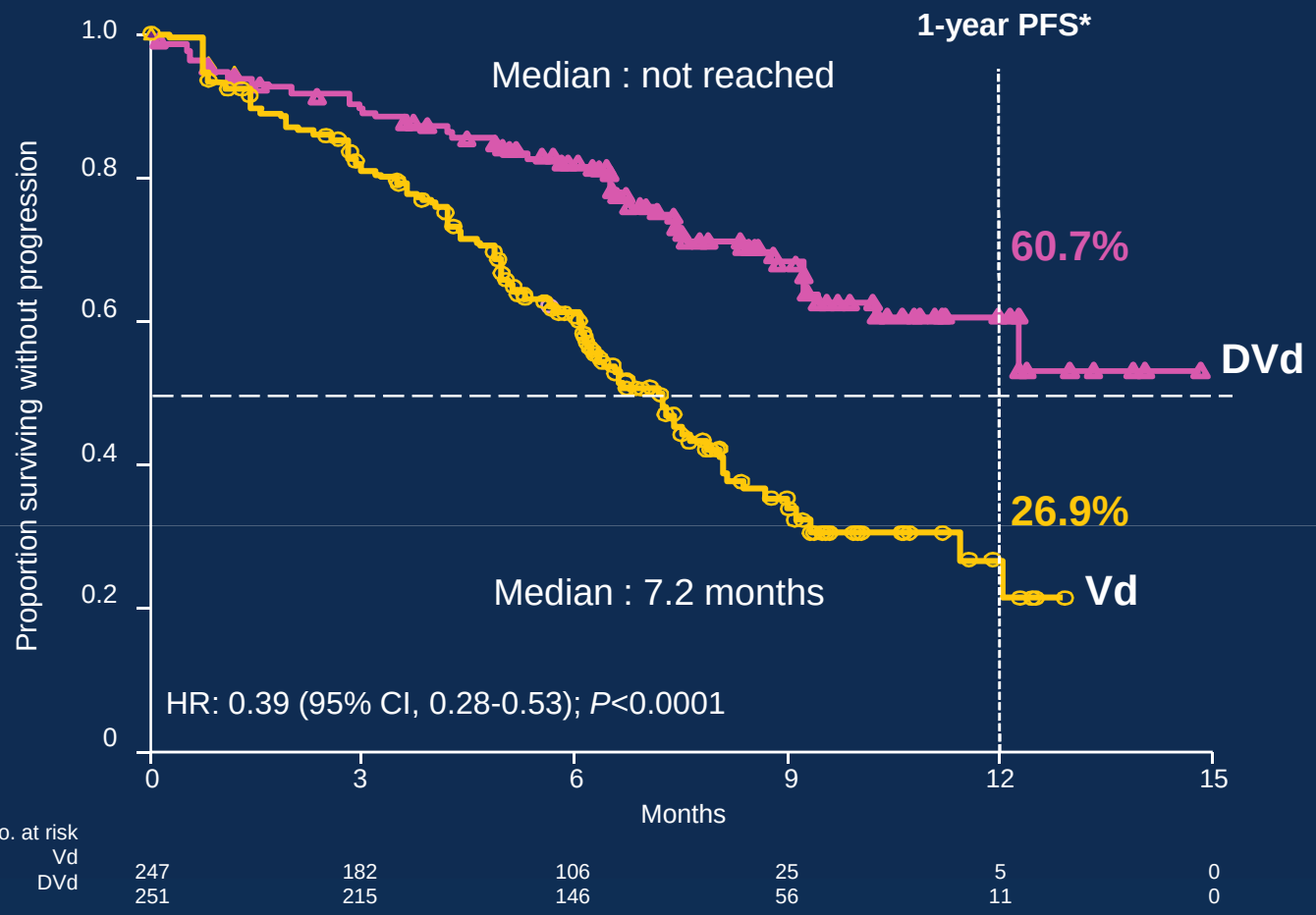


- Cycles 1-8: repeat every 21 days
- Cycles 9+: repeat every 28 days

Daratumumab IV administered in 1000 mL to 500 mL; gradual escalation from 50 mL to 200 mL/min permitted

RRMM, relapsed or refractory multiple myeloma; DVd, daratumumab/bortezomib/dexamethasone; IV, intravenous; Vel, bortezomib; SC, subcutaneous; dex, dexamethasone; PO, oral; Vd, bortezomib/dexamethasone; PFS, progression-free survival; TTP, time to progression; ORR, overall response rate; VGPR, very good partial response; CR, complete response; MRD, minimal residual disease.

Progression-free Survival



61% reduction in the risk of disease progression or death for DVd vs Vd

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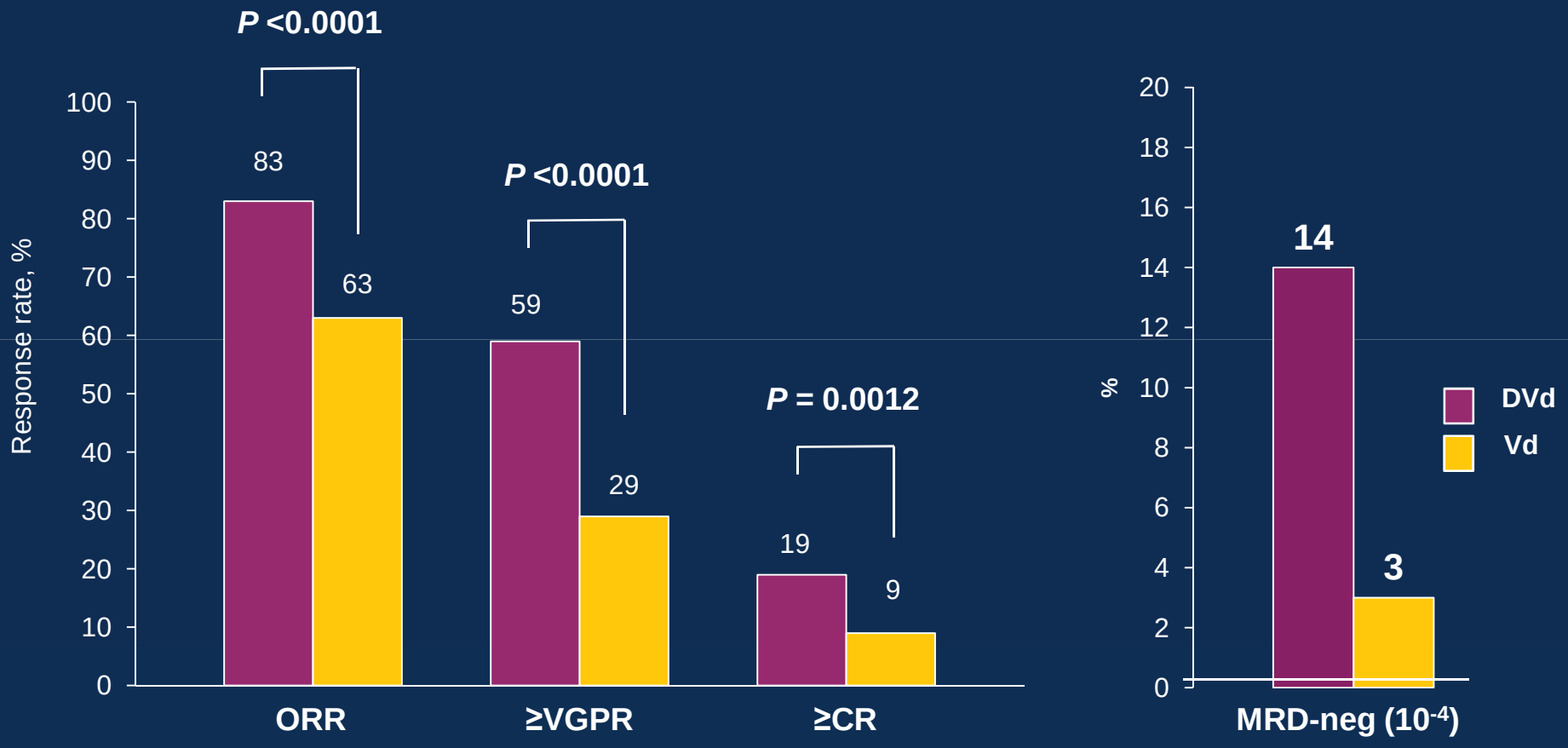
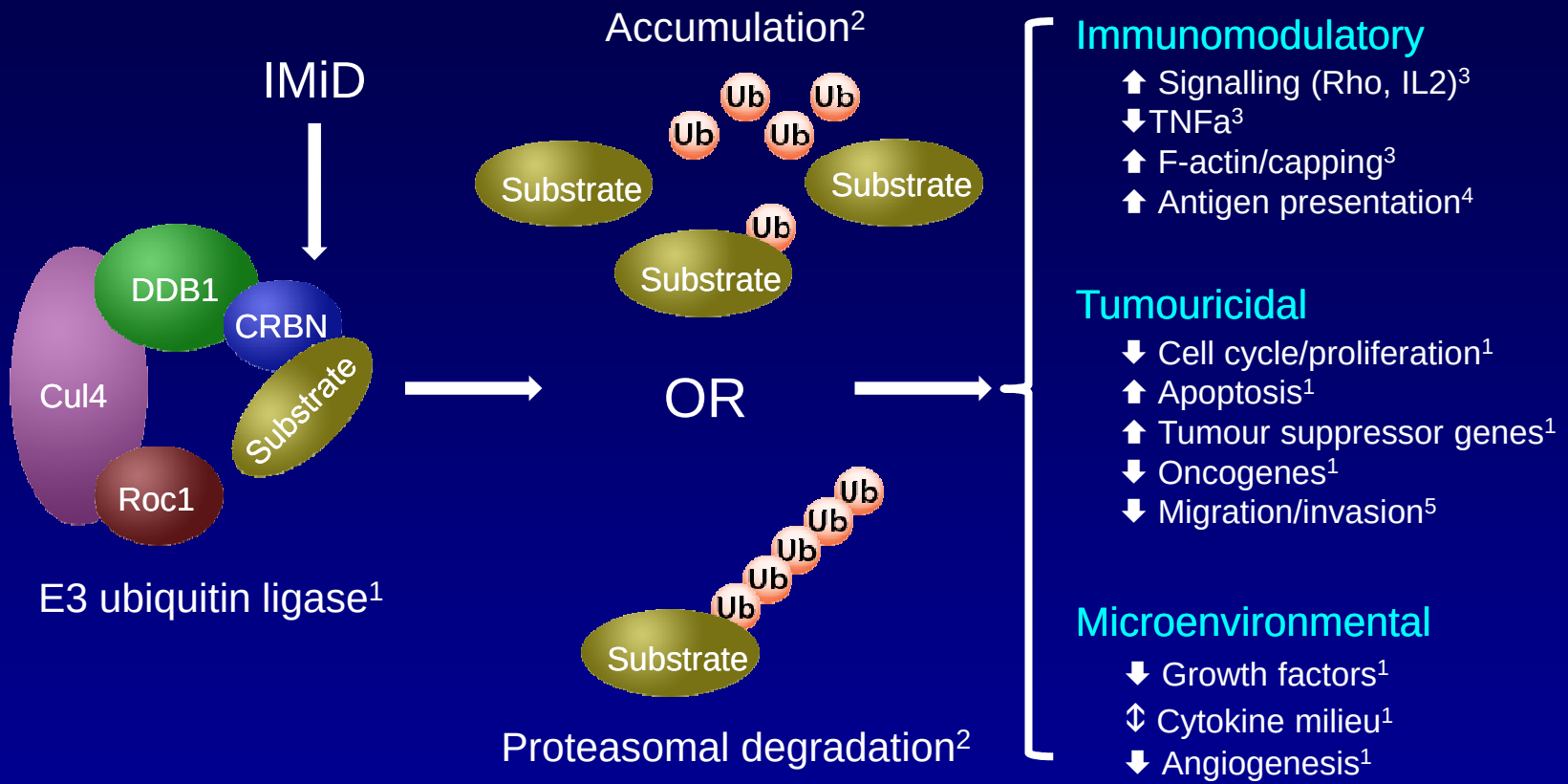


[a]Response-evaluable population.

Pourquoi cette différence?

1. Mécanismes d’action
2. Profil d’Exposition aux molécules dans les lignes antérieures

Lenalidomide mechanism of action: Role of cereblon



- Binding of IMiDs to cereblon is hypothesised to alter the function of the cereblon-containing E3 ubiquitin ligase, leading to alteration of substrate levels in MM cells and pleiotropic anti-cancer activities

CRBN, cereblon; Cul4, cullin 4; DDB1, DNA damage-binding protein 1; IL, interleukin; IMiD, immunomodulatory drug; MM, multiple myeloma; Roc1, regulator of cullins 1; TNF, tumour necrosis factor; Ub, ubiquitin.

1. Lopez-Girona A. *Leukemia* 2012;26:2326-2335.
2. Carter S. *Nat Cell Biol* 2007;9:428-435.
3. Xu Y. *Blood* 2009;114:338-345.
4. Noonan K. *Clin Cancer Res* 2012;18:1426-1434.
5. Chauhan D. *Blood* 2010;115:834-845.

CASTOR: Study Design

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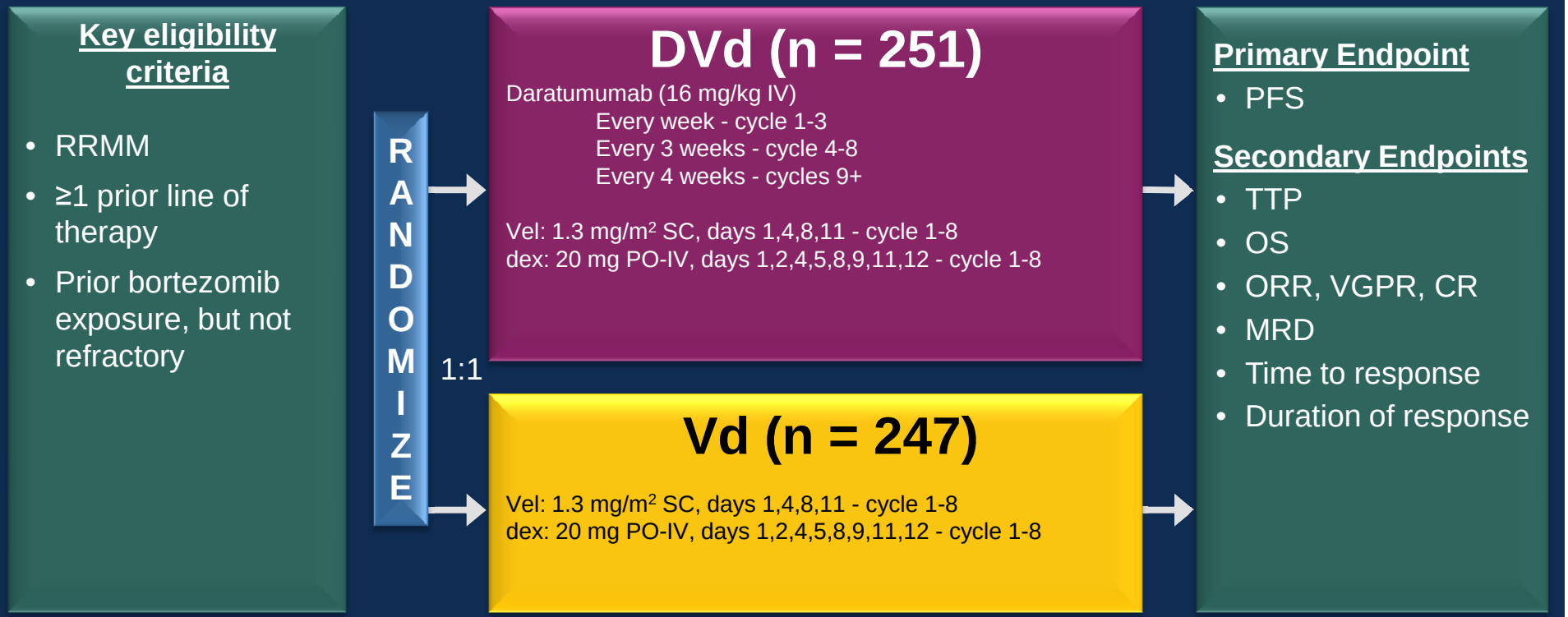

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Baseline Demographics and Clinical Characteristics

Characteristic	DVd (n = 251)	Vd (n = 247)
Age, years		
Median (range)	64 (30-88)	64 (33-85)
≥75, n (%)	23 (9)	35 (14)
ISS staging, n (%)[a]		
I	98 (39)	96 (39)
II	94 (38)	100 (41)
III	59 (24)	51 (21)
Cytogenetic profile, n (%)[b]		
Del17p	28 (16)	21 (12)
t(4;14)	14 (8)	15 (9)
Time from diagnosis, years		
Median (range)	3.87 (0.7-20.7)	3.72 (0.6-18.6)

Characteristic	DVd (n = 251)	Vd (n = 247)
Prior lines of therapy, n (%)		
1	122 (49)	113 (46)
2	70 (28)	74 (30)
3	37 (15)	32 (13)
>3	22 (9)	28 (11)
Prior ASCT, n (%)	156 (62)	149 (60)
Prior PI, n (%)	169 (67)	172 (70)
Prior IMiD, n (%)	179 (71)	198 (80)
Prior PI + IMiD, n (%)	112 (45)	129 (52)
Refractory to IMiD, n (%)	74 (30)	90 (36)
Refractory to last line of therapy, n (%)	76 (30)	85 (34)

POLLUX: Study Design

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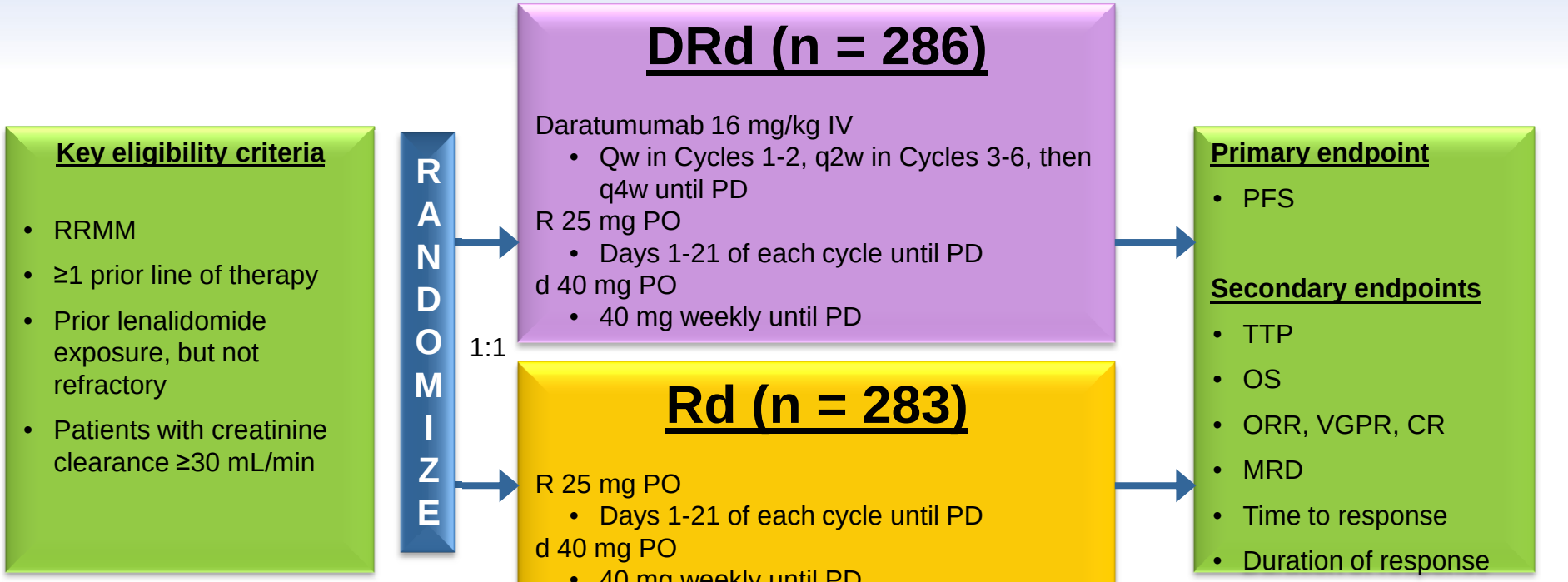

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Baseline Demographics and Clinical Characteristics (cont.)

Characteristic	DRd (n = 286)	Rd (n = 283)
Prior ASCT, %	63	64
Prior PI, %	86	86
Prior IMiD, % Prior lenalidomide, %	55 18	55 18
Prior PI + IMiD, %	44	44
Refractory to PI, %	20	16
Refractory to last line of therapy, %	28	27

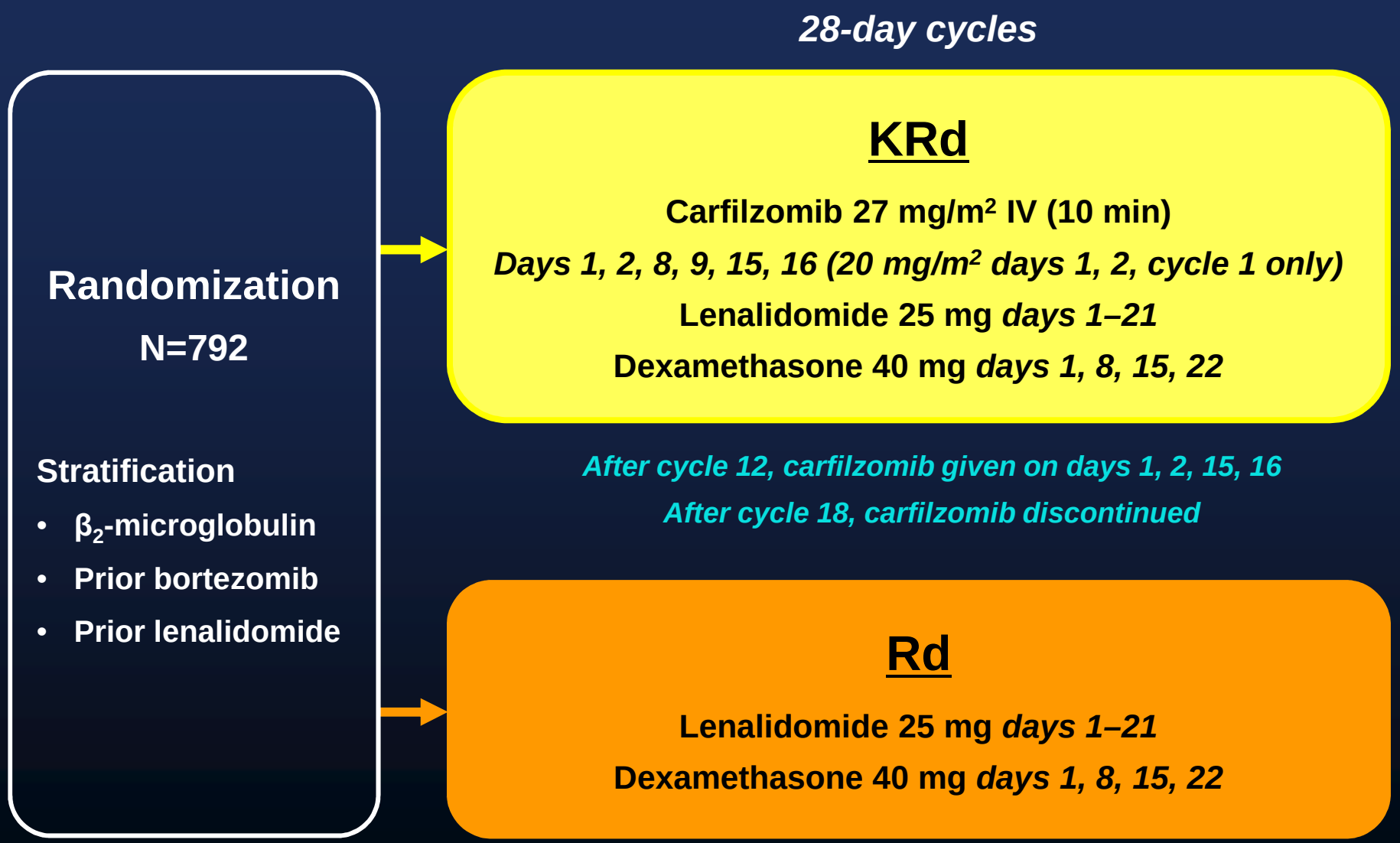
ASCT, autologous stem cell transplant.

Pourquoi pas Moi…

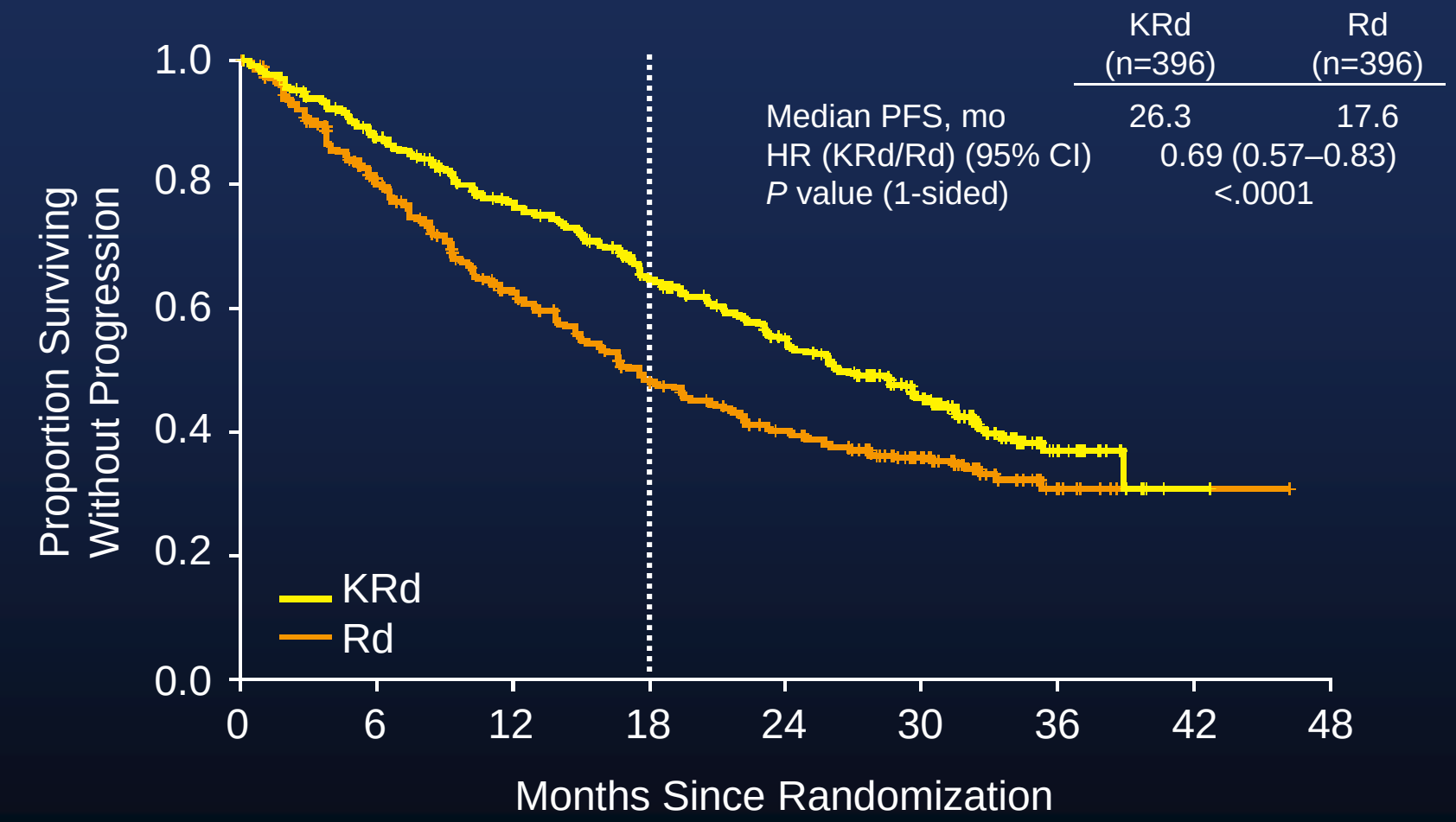
Avec n’importe quelle molécule

Même en Doublet

ASPIRE Study Design

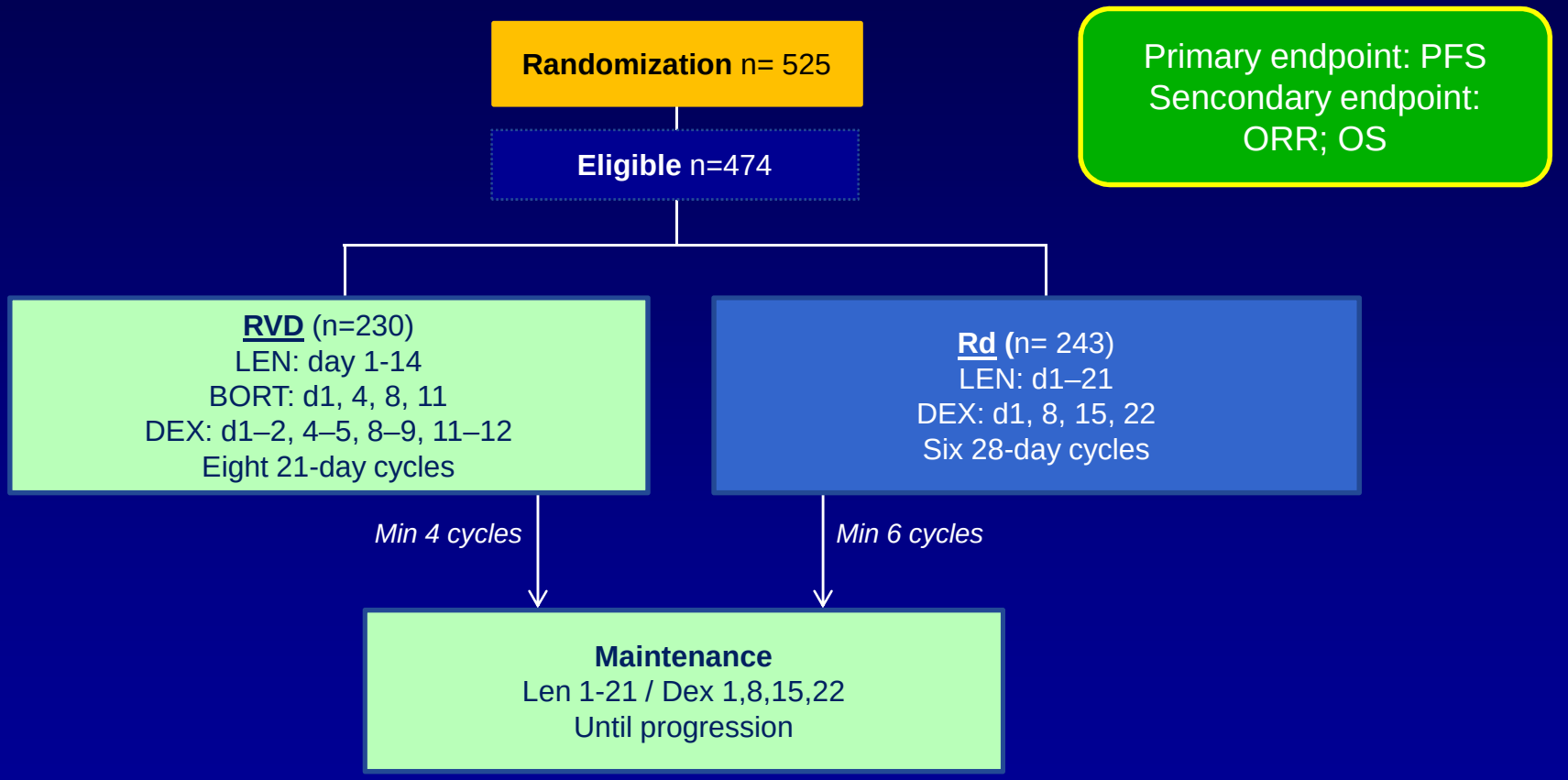


Primary Endpoint: Progression-Free Survival
ITT Population (N=792)



8,7 months difference

RVd vs Rd With Rd Maintenance: SWOG S0777 Study Design[1,2]



BORT, bortezomib; D, day; DEX, dexamethasone; HSV, herpes simplex virus; ISS, International Staging System; LEN, lenalidomide; NDMM, newly diagnosed multiple myeloma; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PO, oral administration; pt, patient; Rd, lenalidomide and low-dose dexamethasone; RVd, bortezomib, lenalidomide, and low-dose dexamethasone; SCT, stem cell transplant.

1. Durie B, et al. Bortezomib, Lenalidomide and Dexamethasone vs Lenalidomide and Dexamethasone in Patients (Pts) With Previously Untreated Multiple Myeloma Without an Intent for Immediate Autologous Stem Cell Transplant (ASCT): Results of the Randomized Phase III Trial SWOG S0777 *ASH 2015, abstract #25. 2.* https://clinicaltrials.gov/ct2/show/NCT00644228

SWOG-S0777:
NDMM without an intent for immediate SCT

	RVd	Rd
PFS median, months	43	30
	HR: 0.712 (0.560–0.906; *P* = 0.0018	
OS, median, months	75	64
	HR = 0.709 (0.516–0.973); *P* = 0.025	
ORR, %	81	71
CR	16	8
VGPR	28	23

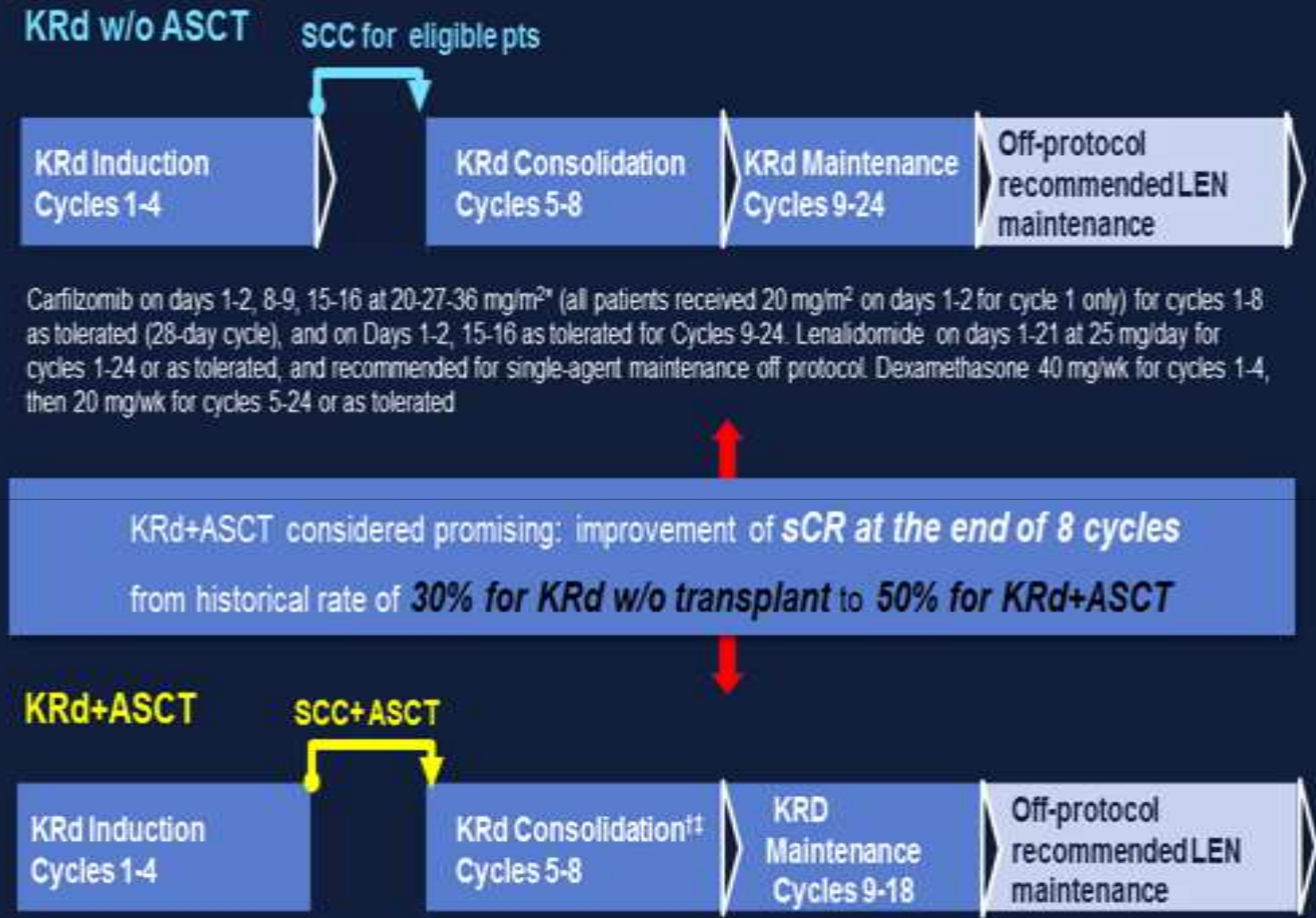
RVd remains superior to Rd for PFS and OS when adjusted for age

1. Durie B, et al. Bortezomib, Lenalidomide and Dexamethasone vs Lenalidomide and Dexamethasone in Patients (Pts) With Previously Untreated Multiple Myeloma Without an Intent for Immediate Autologous Stem Cell Transplant (ASCT): Results of the Randomized Phase III Trial SWOG S0777 *ASH 2015, abstract #25. 2.* https://clinicaltrials.gov/ct2/show/NCT00644228

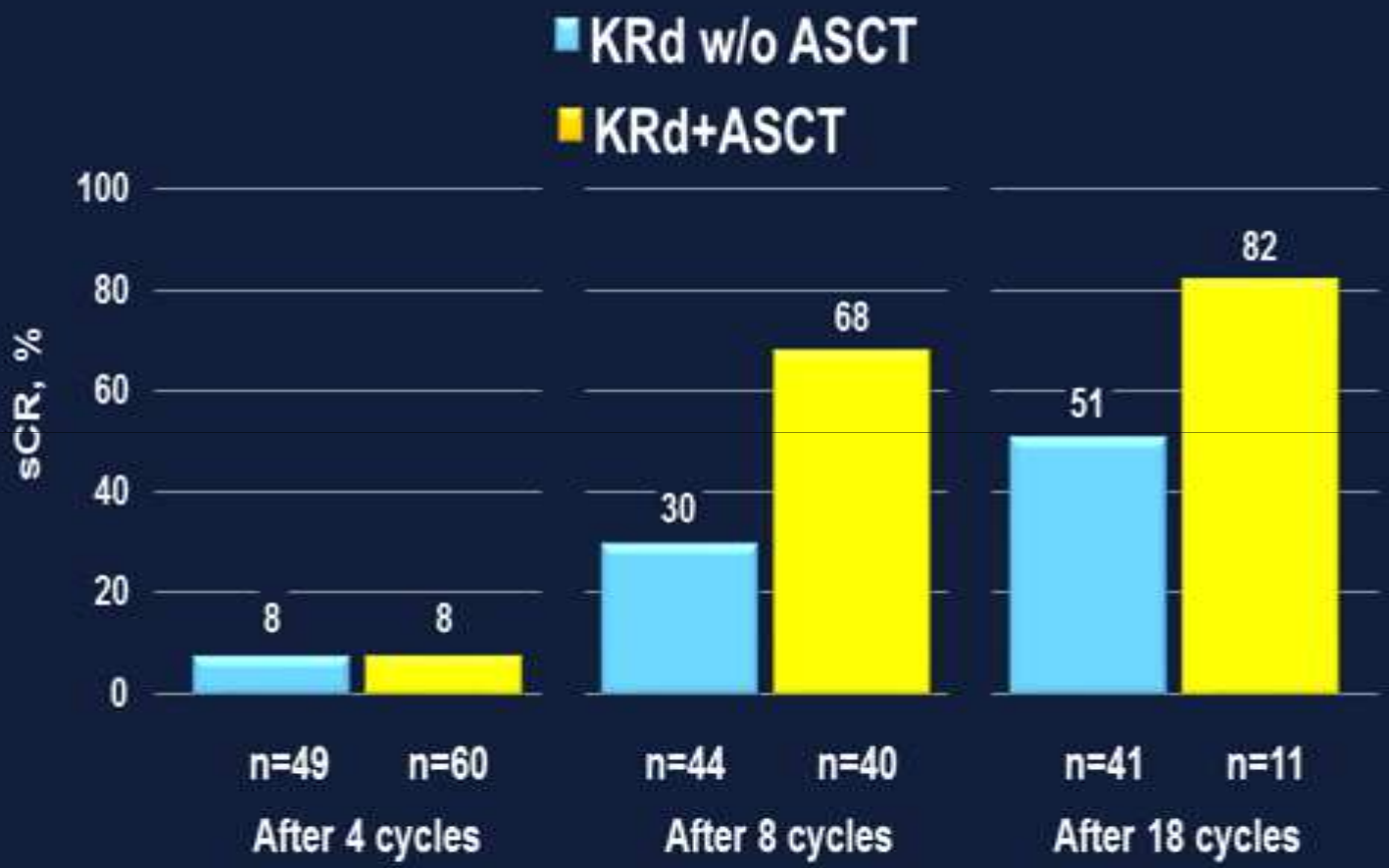
Carfilzomib (CFZ, Kyprolis®), lenalidomide (LEN, Revlimid®), and dexamethasone (DEX) (KRd) combined with autologous stem cell transplant (ASCT) shows improved efficacy compared with KRd without ASCT in newly diagnosed multiple myeloma (NDMM)

Todd M. Zimmerman, Kent Griffith, Jagoda K. Jasielec, Cara A. Rosenbaum, Jesus G. Berdeja, Ravi Vij, Noopur Raje, Donna Reece, David Vesole, Sundar Jagannath, Craig Cole, Jennifer Nam, Leonor Stephens, Shaun Rosebeck, Sandeep Gurbuxani, Dominik Dytfeld, Andrzej J. Jakubowiak

Treatment Schema



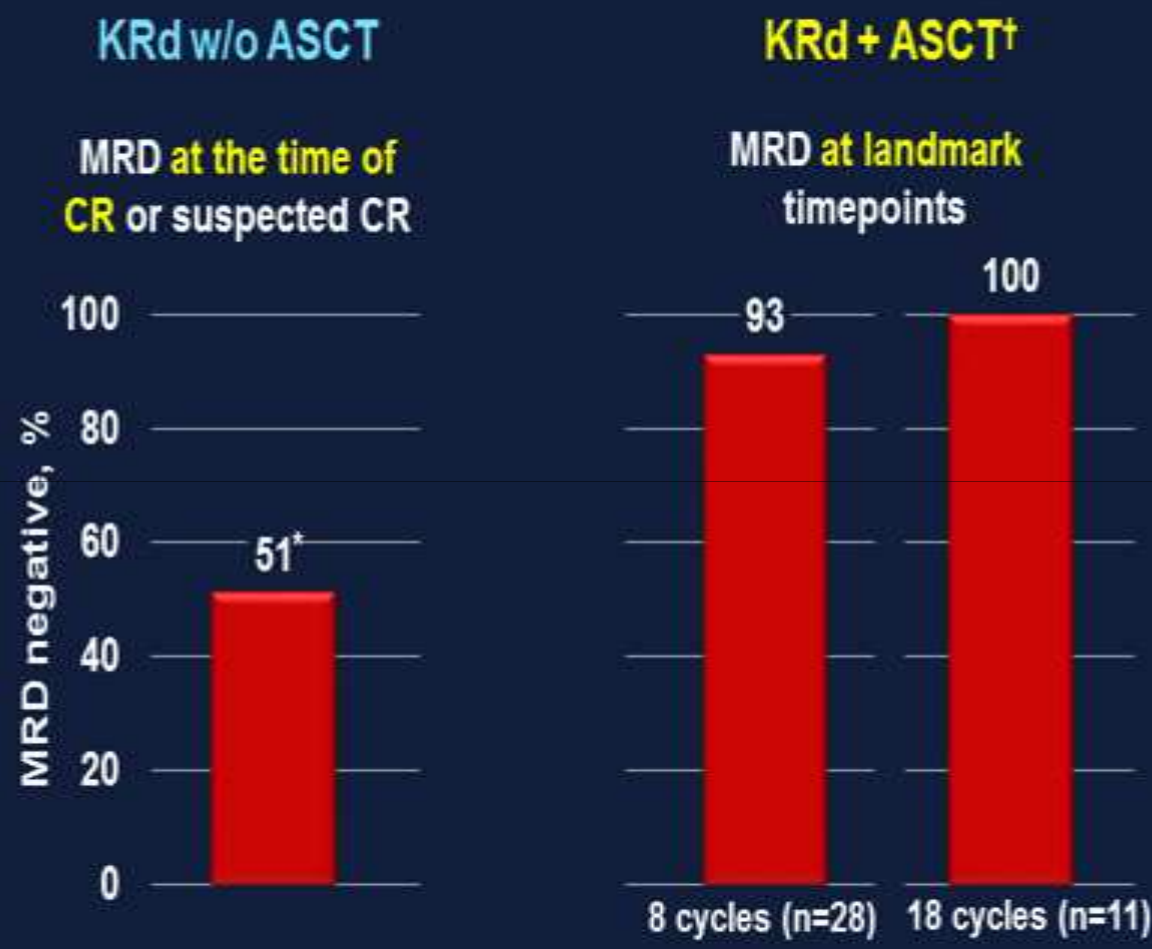
sCR Rates Over the Course Treatment



Studies not designed for comparisons

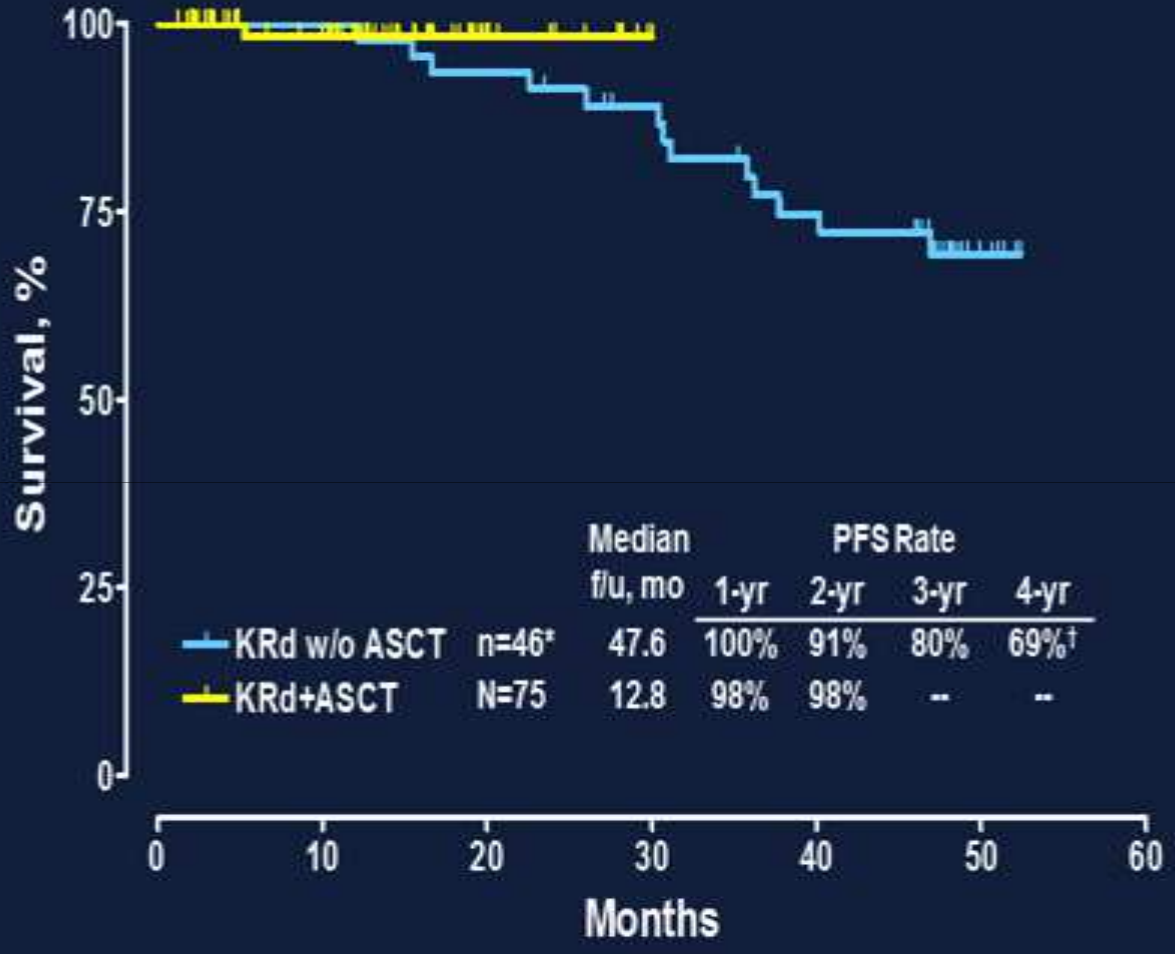
More complete response data for KRd w/o ASCT reported at IMW 2015

MRD Evaluation (10-Color Flow Cytometry)



*Estimated rate based on 23 of 26 evaluated pts assessed for MRD at CR or suspected CR
†Actual rates in subgroup of pts evaluated for MRD at the end of 8 and 18 cycles regardless of level of response; all pts in sCR were MRD negative

Treatment Outcomes – PFS



*Excludes 7 pts who discontinued to pursue ASCT

†Intent-to-treat (N=53), 4-year PFS 64%

Pourquoi pas Moi…

=

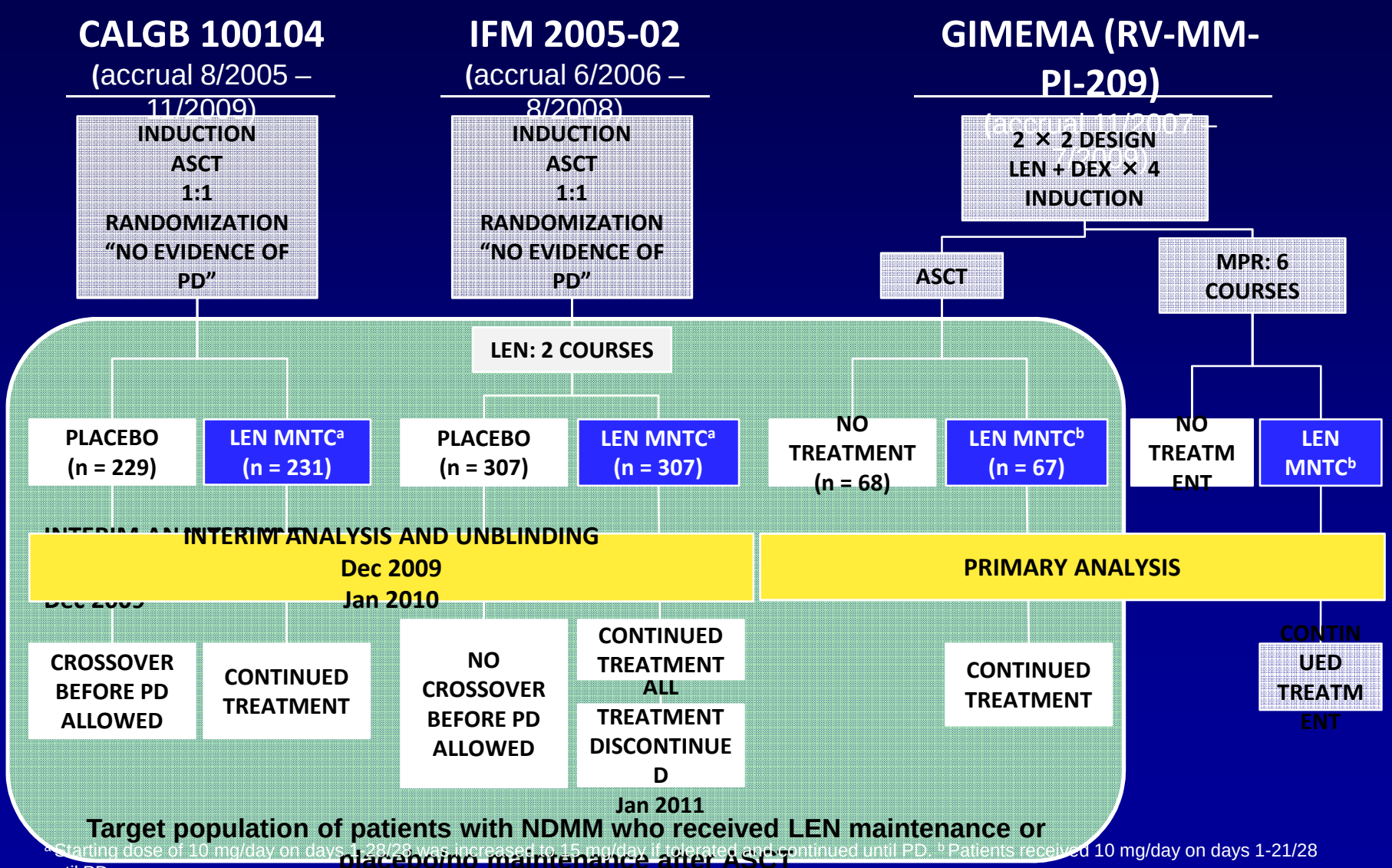
La Bonne Durée de traitement

Lenalidomide Maintenance After High-Dose Melphalan and Autologous Stem Cell Transplant in Multiple Myeloma: A Meta-Analysis of Overall Survival

Michel Attal,[1] Antonio Palumbo,[2] Sarah A. Holstein,[3] Valérie Lauwers-Cances,[1] Maria Teresa Petrucci,[4] Paul Richardson,[5] Cyrille Hulin,[6] Patrizia Tosi,[7] Kenneth C. Anderson,[5] Denis Caillot,[8] Valeria Magarotto,[9] Philippe Moreau,[10] Gerald Marit,[11] Zhinuan Yu,[12] Philip L. McCarthy[13]

[1]Institut Universitaire du Cancer , Toulouse Oncopole, France; [2]The Myeloma Unit, Department of Hematology, University of Turin, Turin, Italy; [3]Roswell Park Cancer Institute, Buffalo, NY; [4]University La Sapienza, Rome, Italy; [5]Dana-Farber Cancer Institute, Boston, MA; [6]Bordeaux Hospital University Center (CHU), Bordeaux, France; [7]Seràgnoli Institute of Hematology and Medical Oncology, Bologna University, Bologna, Italy; [8]Dijon University Hospital Center, Dijon, France; [9]University of Torino, Torino, Italy; [10]University Hospital Hôtel-Dieu, Nantes, France; [11]Centre Hospitalier Universitaire, Bordeaux, France; [12]Celgene Corporation, Summit, NJ; [13]Blood and Marrow Transplant Program, Roswell Park Cancer Institute, Buffalo, NY

Studies Included in Meta-Analysis

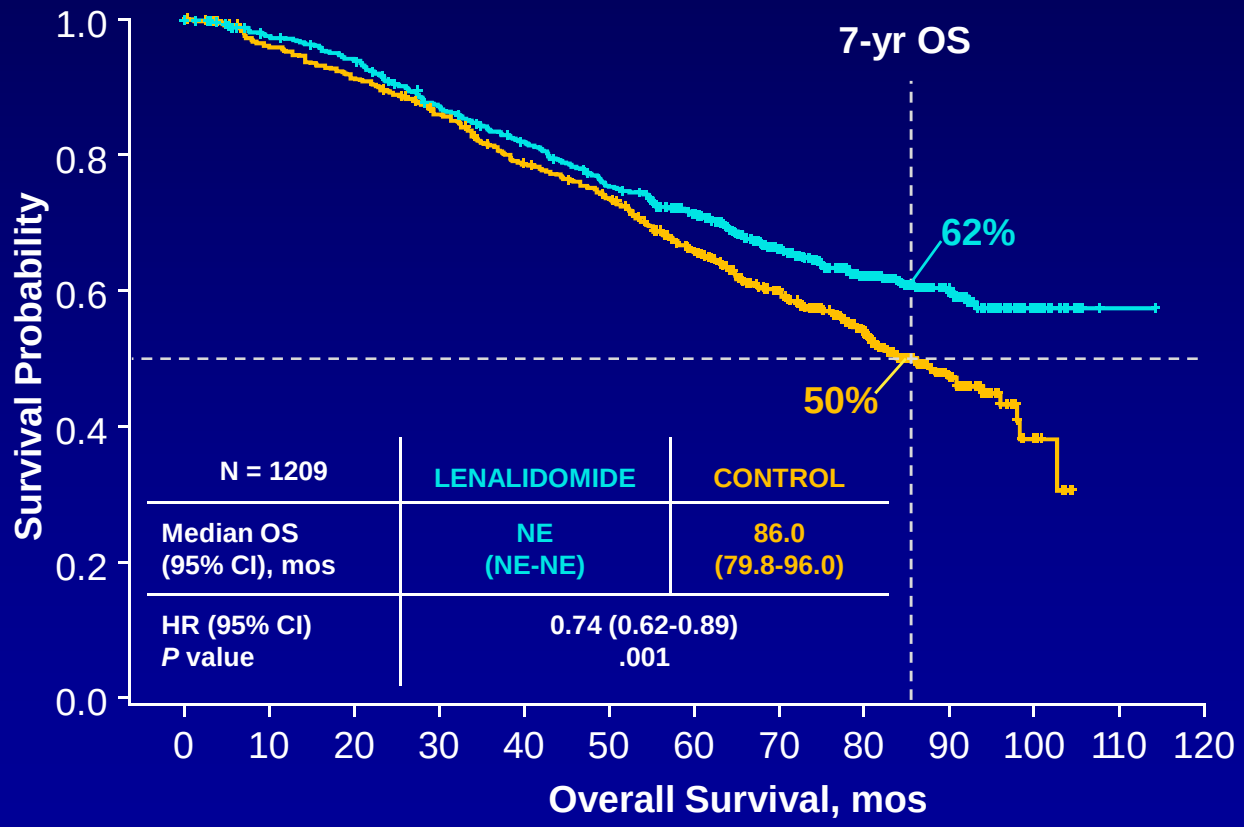


[a] Starting dose of 10 mg/day on days 1-28/28 was increased to 15 mg/day if tolerated and continued until PD. [b] Patients received 10 mg/day on days 1-21/28 until PD.

ASCT, autologous stem cell transplant; LEN, lenalidomide; NDMM, newly diagnosed multiple myeloma; MNTC, maintenance; MPR, melphalan, prednisone, and lenalidomide; PD, progressive disease.

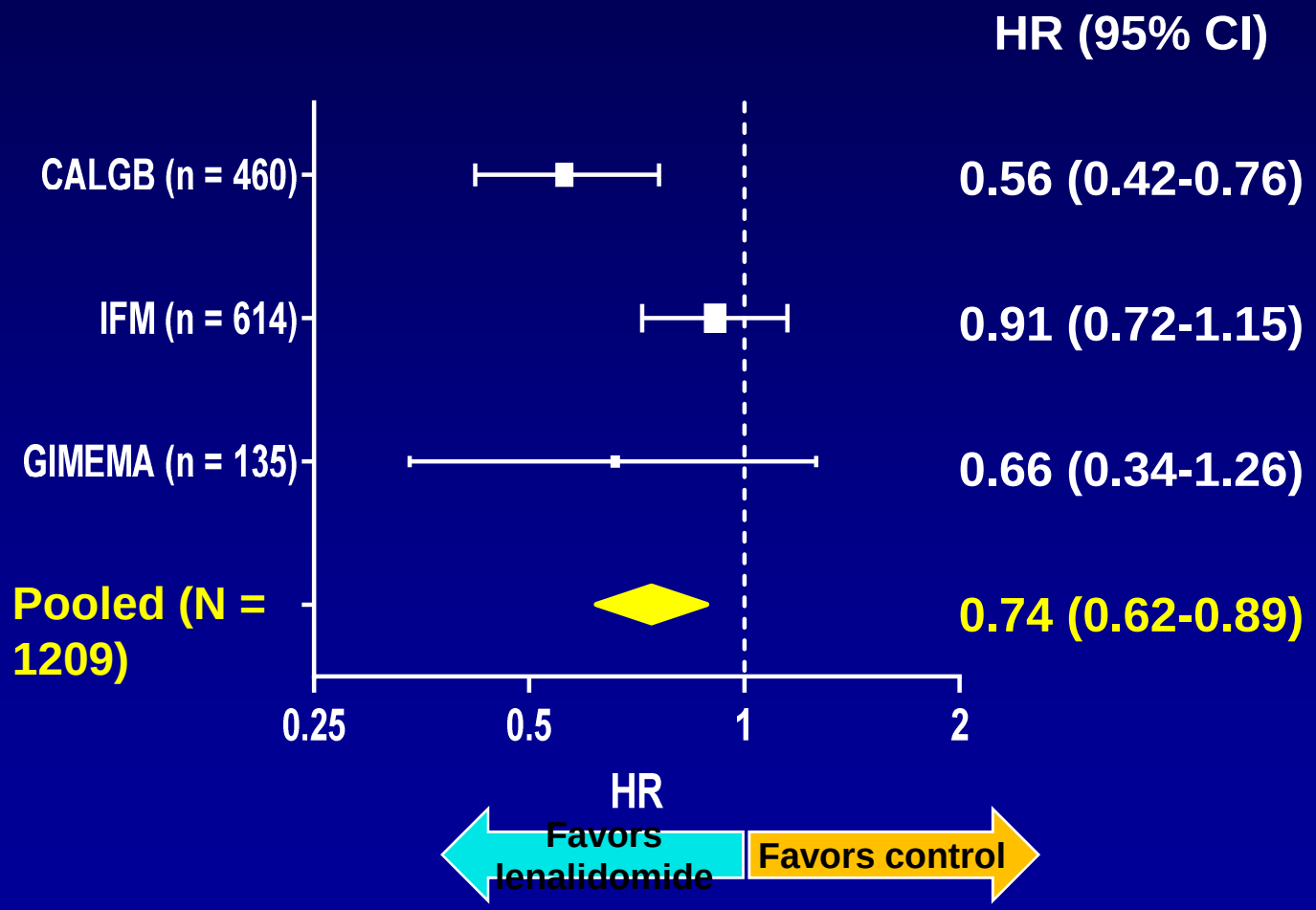
Overall Survival: Median Follow-Up of 80 Months

There is a 26% reduction in risk of death, representing an estimated 2.5-year increase in median survival[a]



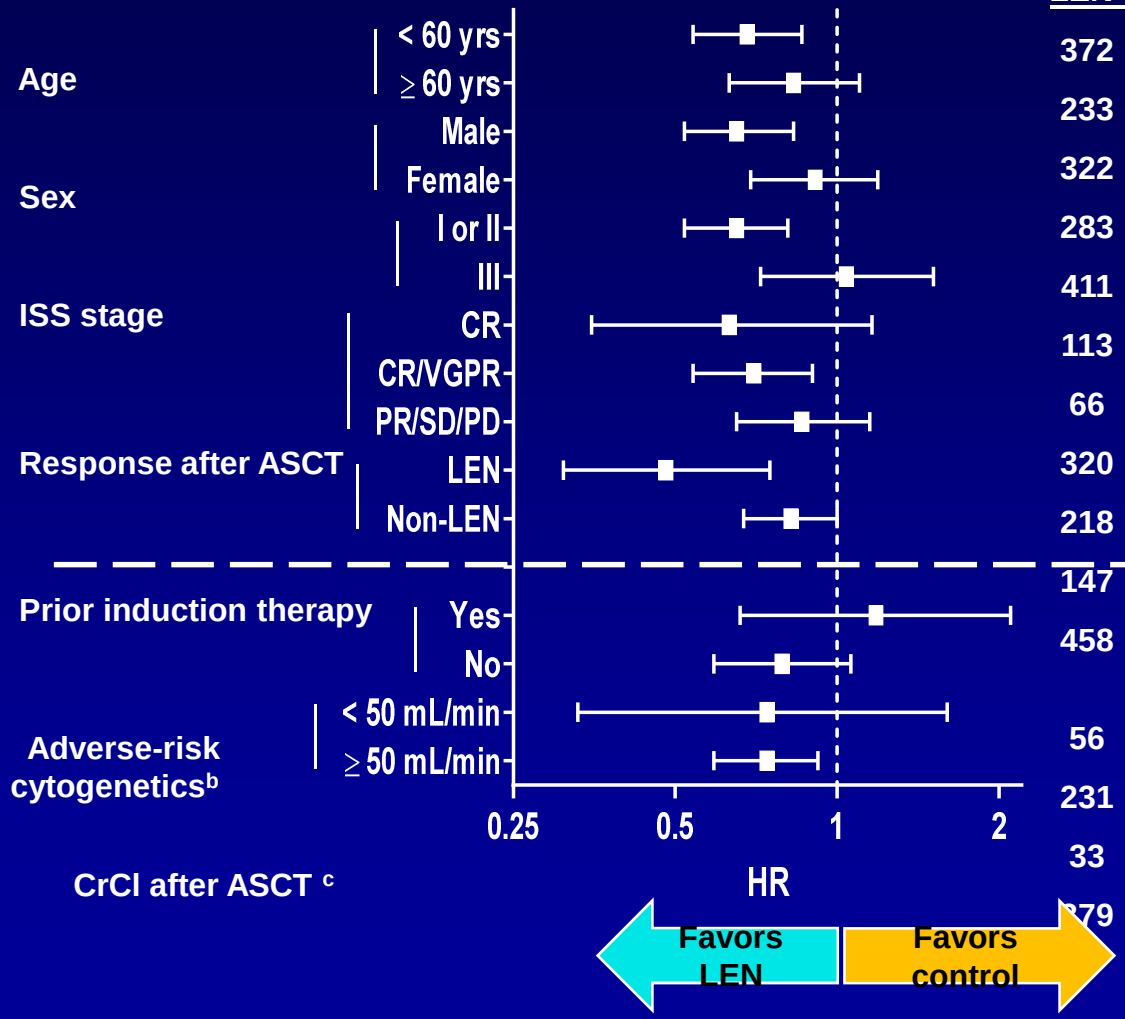
[a] Median for lenalidomide treatment arm was extrapolated to be 116 months based on median of the control arm and HR (median, 86 months; HR = 0.74) .
HR, hazard ratio; NE, not estimable; OS, overall survival.

Overall Survival: Hazard Ratios



The size of the box is related to the size of the individual study. The confidence interval is a function of the overall sample size.
HR, hazard ratio.

Overall Survival: Subgroup Analysis

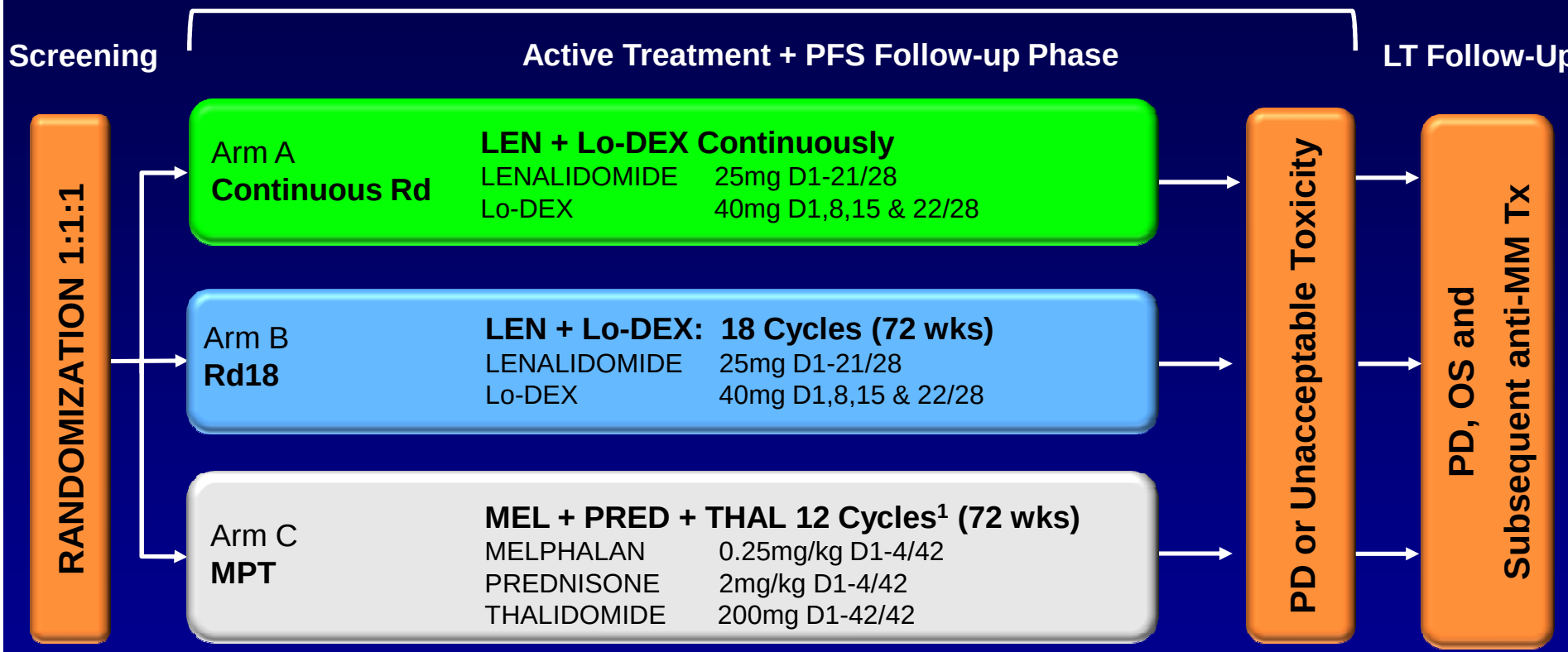


	LEN[a]	CONTROL[a]	HR (95% CI)
Age < 60 yrs	372	375	0.68 (0.54-0.86)
Age ≥ 60 yrs	233	229	0.83 (0.63-1.10)
Sex Male	322	349	0.65 (0.52-0.83)
Sex Female	283	255	0.91 (0.69-1.19)
ISS stage I or II	411	440	0.65 (0.52-0.81)
ISS stage III	113	90	1.04 (0.72-1.51)
Response after ASCT CR	66	80	0.63 (0.35-1.16)
Response after ASCT CR/VGPR	320	339	0.70 (0.54-0.90)
Response after ASCT PR/SD/PD	218	210	0.86 (0.65-1.15)
Prior induction therapy LEN	147	146	0.48 (0.31-0.75)
Prior induction therapy Non-LEN	458	458	0.82 (0.67-1.00)
Adverse-risk cytogenetics[b] < 50 mL/min	56	36	1.18 (0.66-2.10)
Adverse-risk cytogenetics[b] ≥ 50 mL/min	231	243	0.79 (0.59-1.06)
CrCl after ASCT [c] < 50 mL/min	33	25	0.73 (0.33-1.60)
CrCl after ASCT [c] ≥ 50 mL/min	379	404	0.74 (0.59-0.92)

[a] Number of patients. [b] Cytogenetic data were available only for the IFM and GIMEMA studies. [c] CrCl post-ASCT data were available only for the CALGB and IFM studies.

ASCT, autologous stem cell transplant; CR, complete response; CrCl, creatinine clearance; HR, hazard ratio; ISS, International Staging System; LEN, lenalidomide; OS, overall survival; PD, progressive disease; PR, partial response; SD, stable disease; VGPR, very good partial response.

FIRST Trial: Study Design



Pts > 75 yrs: Lo-DEX 20 mg D1, 8, 15 & 22/28; THAL[2] (100 mg D1-42/42); MEL[2] 0.2 mg/kg D1–4

- Stratification: age, country and ISS stage

ISS, International Staging System; LT, long-term; PD, progressive disease; OS, overall survival

[1]Facon T, et al. Lancet 2007;370:1209-18; [2]Hulin C, et al. JCO. 2009;27:3664-70.

Facon T, et al. Continuous Lenalidomide and Low-dose Dexamethasone Demonstrates a Significant PFS and OS Advantage in Transplant Ineligible NDMM Patients – The FIRST Trial: MM-020/IFM 0701. *Plenary presentation at: American Society of Hematology*. 2013; December 7-10; New Orleans, LA.

FIRST Trial - Final Progression-free Survival

Median follow-up of 37 months as of 24 May, 2013

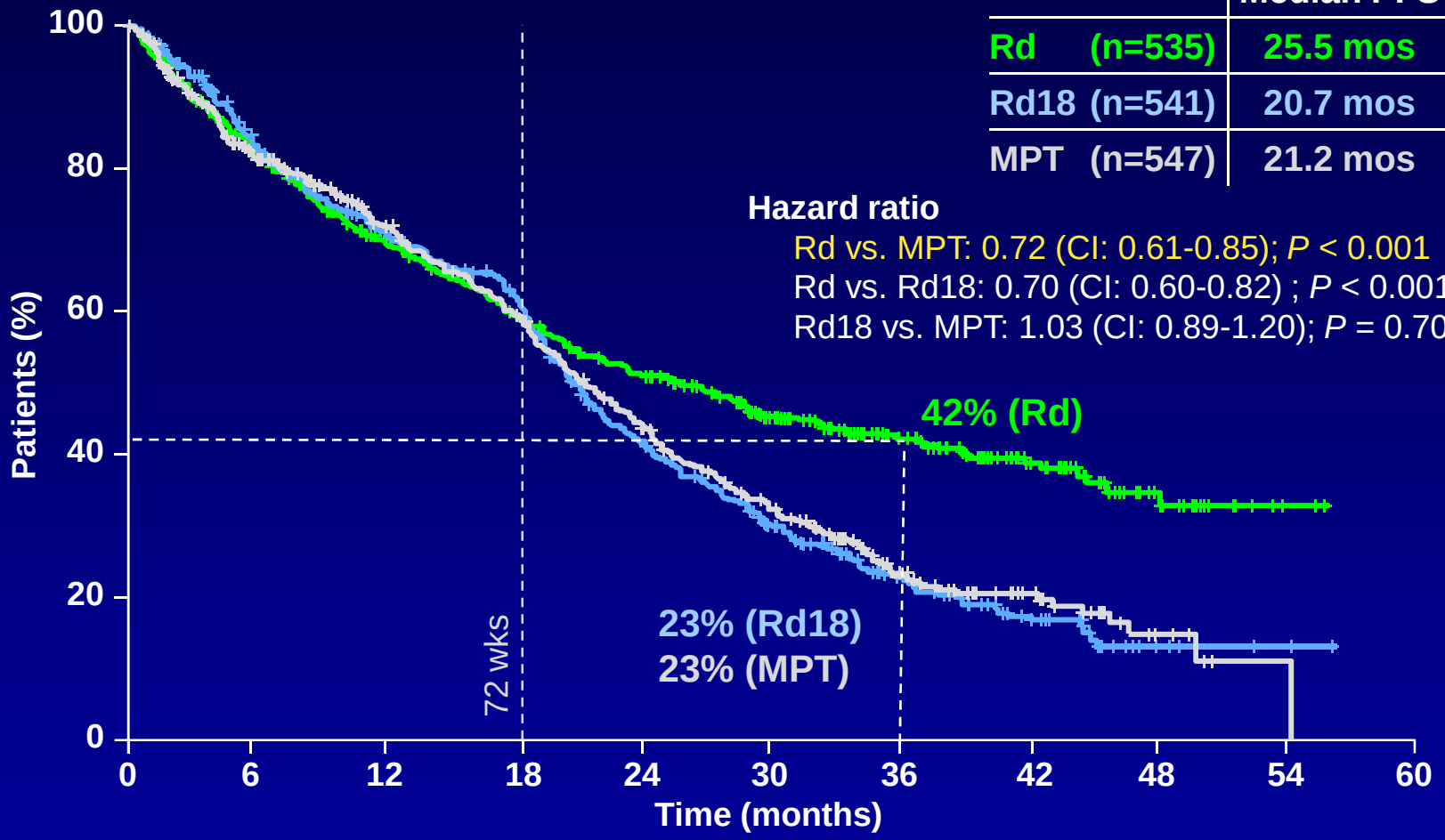
	Median PFS
Rd (n=535)	25.5 mos
Rd18 (n=541)	20.7 mos
MPT (n=547)	21.2 mos

Hazard ratio

Rd vs. MPT: 0.72 (CI: 0.61-0.85); *P* < 0.001

Rd vs. Rd18: 0.70 (CI: 0.60-0.82) ; *P* < 0.001

Rd18 vs. MPT: 1.03 (CI: 0.89-1.20); *P* = 0.70



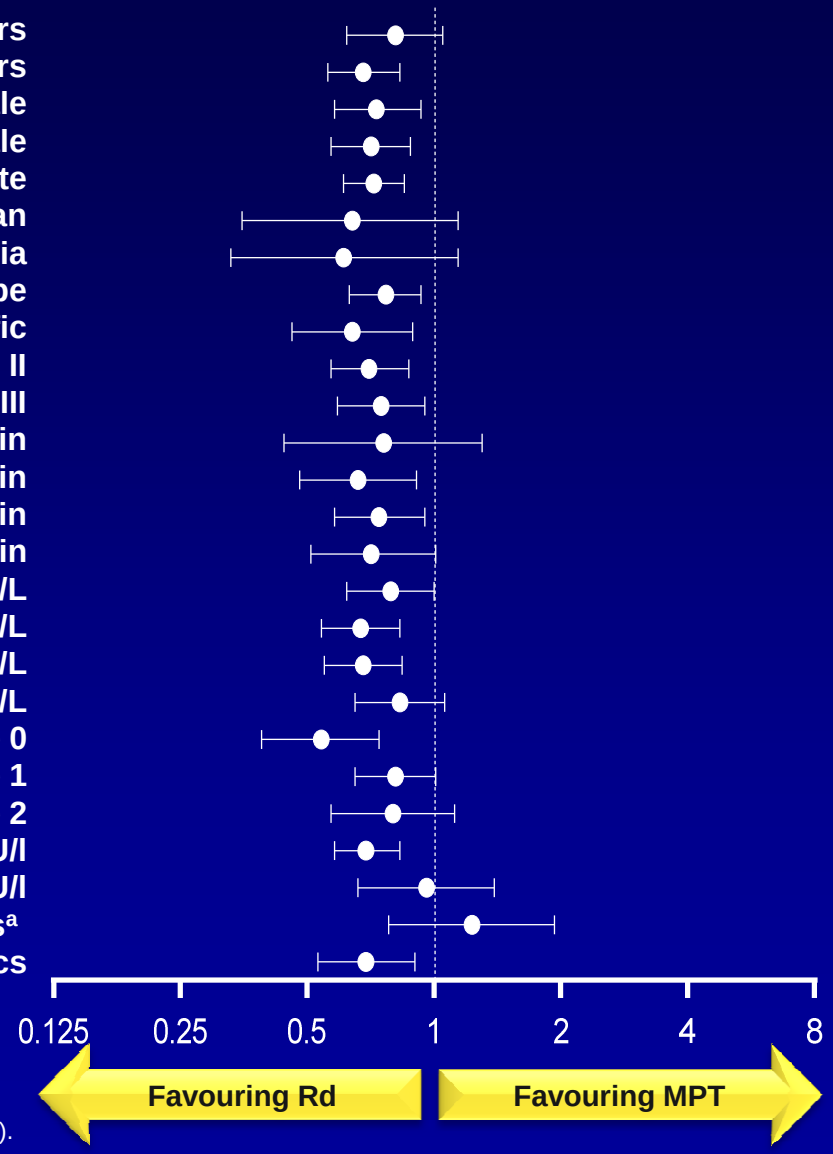
Rd	535	400	319	265	218	168	105	55	19	2	0
Rd18	541	391	319	265	167	108	56	30	7	2	0
MPT	547	380	304	244	170	116	58	28	6	1	0

CI, confidence interval; FIRST, Frontline Investigation of Revlimid and Dexamethasone versus Standard Thalidomide; mos, months; MPT, melphalan, prednisolone, thalidomide; PFS, progression-free survival; Rd, lenalidomide plus low-dose dexamethasone; Rd18, lenalidomide plus low-dose dexamethasone for 18 cycles.

Facon T, et al. *EHA* 2014: Abstract S643;
Benboubker L, et al. *NEJM*. 2014;371:906-17.

FIRST - Consistent PFS Benefit Across Subgroups

Subgroup	Rd	MPT	HR (95% CI)
Age > 75 years	107/186	114/188	0.81 (0.62-1.05)
Age ≤ 75 years	171/349	220/359	0.68 (0.56-0.83)
Sex: female	119/241	153/260	0.73 (0.58-0.93)
Sex: male	159/294	181/287	0.71 (0.57-0.88)
White	244/474	301/491	0.72 (0.61-0.85)
Asian	20/40	26/44	0.64 (0.35-1.14)
Asia	18/36	23/40	0.61 (0.33-1.14)
Europe	197/369	234/374	0.77 (0.63-0.93)
North America and Pacific	63/130	77/133	0.64 (0.46-0.89)
ISS stage: I or II	154/319	191/323	0.70 (0.57-0.87)
ISS stage: III	124/216	143/224	0.75 (0.59-0.95)
CrCl < 30 mL/min	23/45	37/55	0.76 (0.44-1.30)
CrCl 30-50 mL/min	74/126	83/126	0.66 (0.48-0.91)
CrCl 50-80 mL/min	125/241	135/222	0.74 (0.58-0.95)
CrCl ≥ 80 mL/min	56/123	79/144	0.71 (0.51-1.01)
β_2M > 5.5 mg/L	133/224	149/234	0.79 (0.62-1.00)
β_2M ≤ 5.5 mg/L	144/309	184/312	0.67 (0.54-0.83)
Albumin > 35 g/L	162/343	188/324	0.68 (0.55-0.84)
Albumin ≤ 35 g/L	116/192	146/223	0.83 (0.65-1.06)
ECOG PS score 0	63/155	86/156	0.54 (0.39-0.74)
ECOG PS score 1	148/257	172/275	0.81 (0.65-1.01)
ECOG PS score 2	65/119	72/111	0.80 (0.57-1.12)
LDH < 200 U/l	229/448	265/434	0.69 (0.58-0.83)
LDH ≥ 200 U/l	49/86	68/112	0.96 (0.66-1.39)
High-risk cytogenetics[a]	37/43	39/47	1.23 (0.78-1.93)
Non-high-risk cytogenetics	99/205	124/206	0.69 (0.53-0.90)



Median follow-up of 37 months as of 24 May, 2013

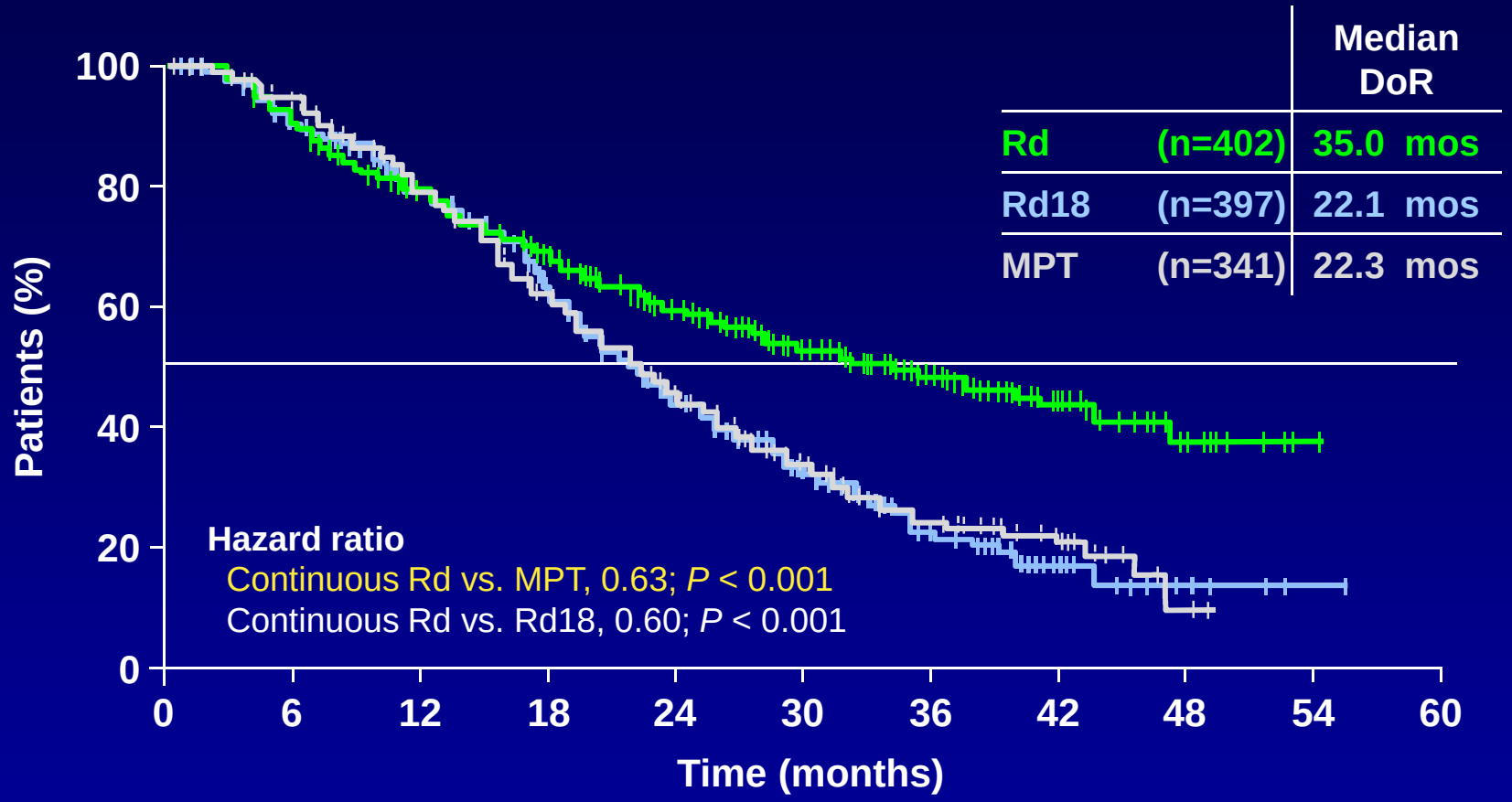
[a]High risk: t(4;14), t(14;16), or del(17p).

β2M, β2 microglobulin; CrCl, creatinine clearance; del, deletion; ECOG PS, Eastern Cooperative Oncology Group Performance Status; FIRST, Frontline Investigation of Revlimid and Dexamethasone versus Standard Thalidomide; LDH, lactate dehydrogenase; MPT, melphalan, prednisolone, thalidomide HR, hazard ratio; ISS, International Staging System; PFS, progression-free survival; Rd, lenalidomide plus low-dose dexamethasone; t, translocation.

Benboubker L, et al. *NEJM*. 2014;371:906-17.

FIRST Trial - Duration of Response

Median follow-up of 37 months as of 24 May, 2013
IRAC assessment of response and progression



No. at Risk											
Rd	402	351	289	241	198	146	84	36	9	1	0
Rd18	397	338	286	214	145	92	40	19	5	1	0
MPT	341	297	239	179	123	75	35	14	2	0	–

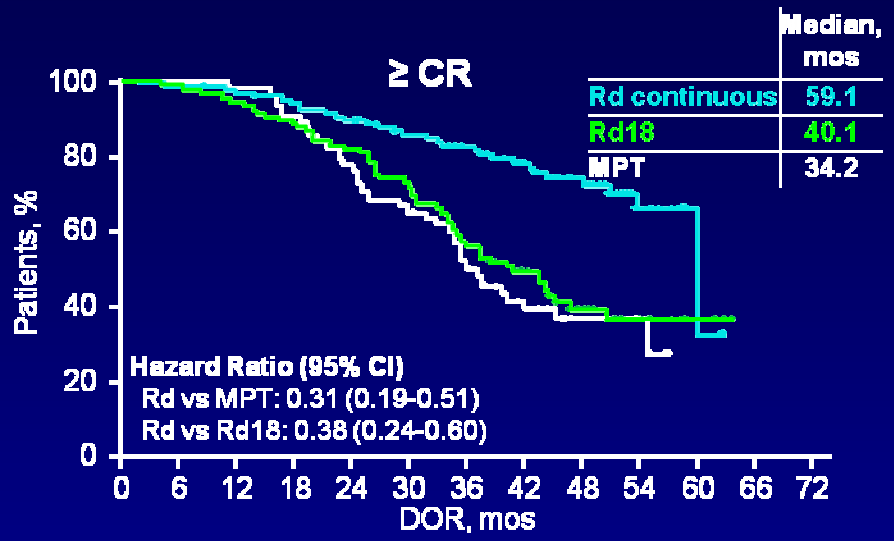
DoR, duration of response; FIRST, Frontline Investigation of Revlimid and Dexamethasone versus Standard Thalidomide; mos, months; MPT, melphalan, prednisone, thalidomide; Rd, lenalidomide plus low-dose dexamethasone; Rd18, lenalidomide plus low-dose dexamethasone for 18 cycles.

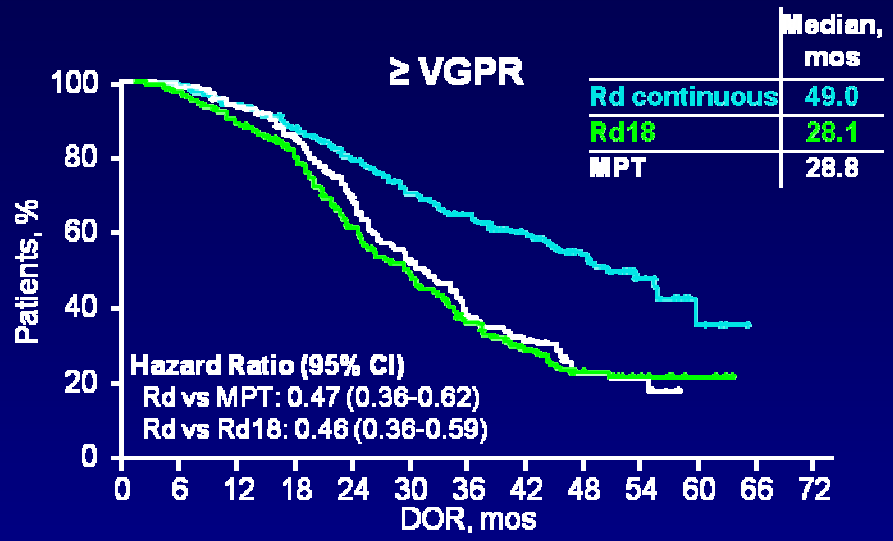
Benboubker L, et al. *NEJM*. 2014;371:906-17.

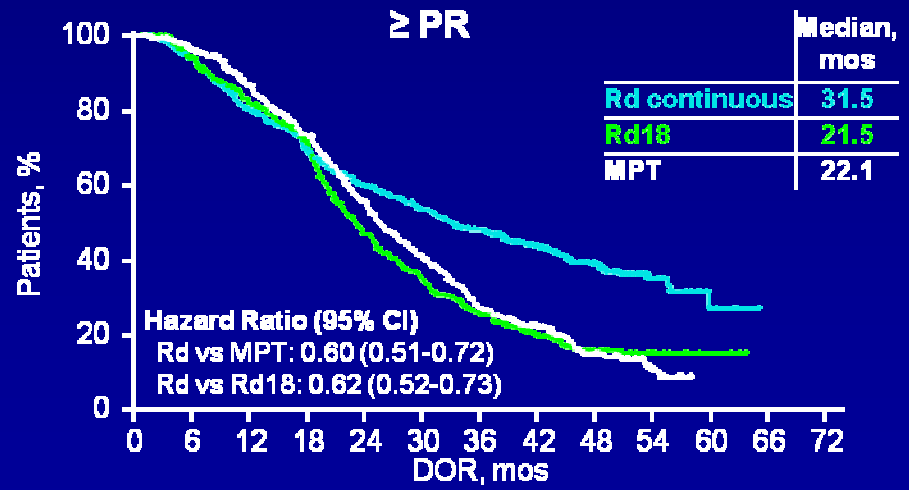
FIRST: Impact of Response

Duration of Response

- Median DOR was prolonged with Rd continuous vs Rd18 or MPT





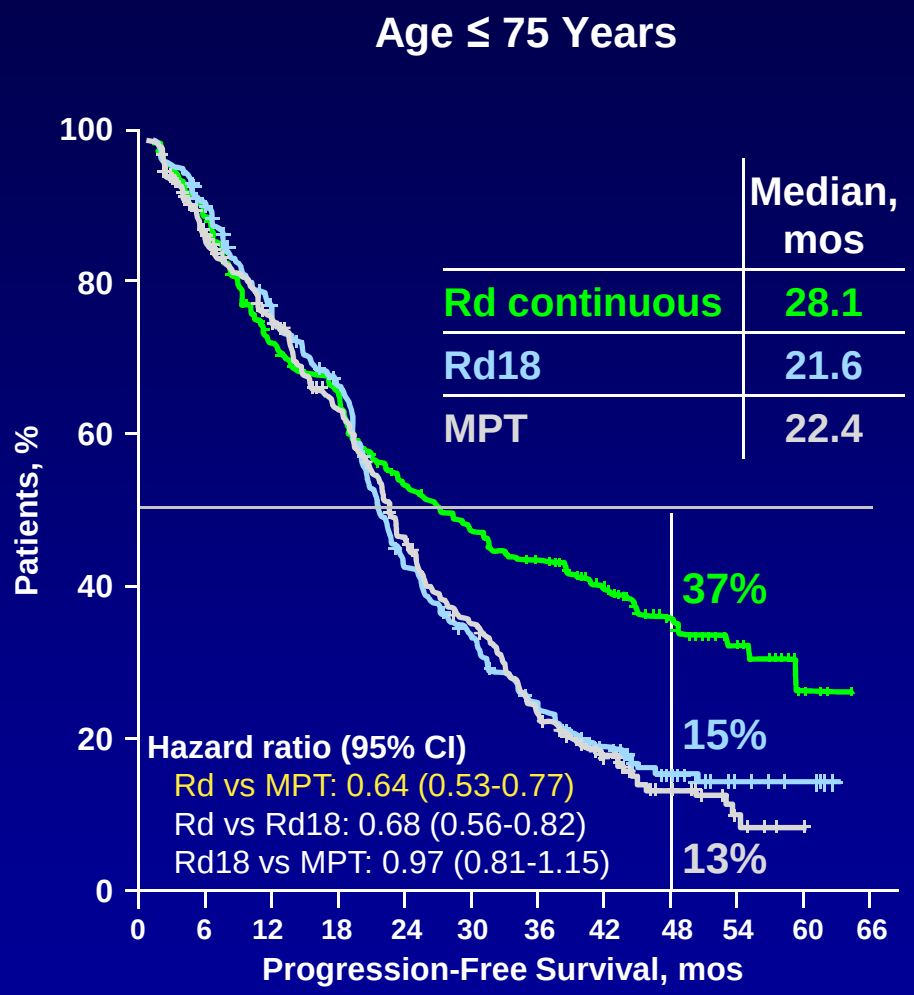


CR, complete response; DOR, duration of response; MPT, melphalan-prednisone-thalidomide; PR, partial response; Rd, lenalidomide and low-dose dexamethasone; Rd18, Rd for 18 cycles; VGPR, very good partial response.

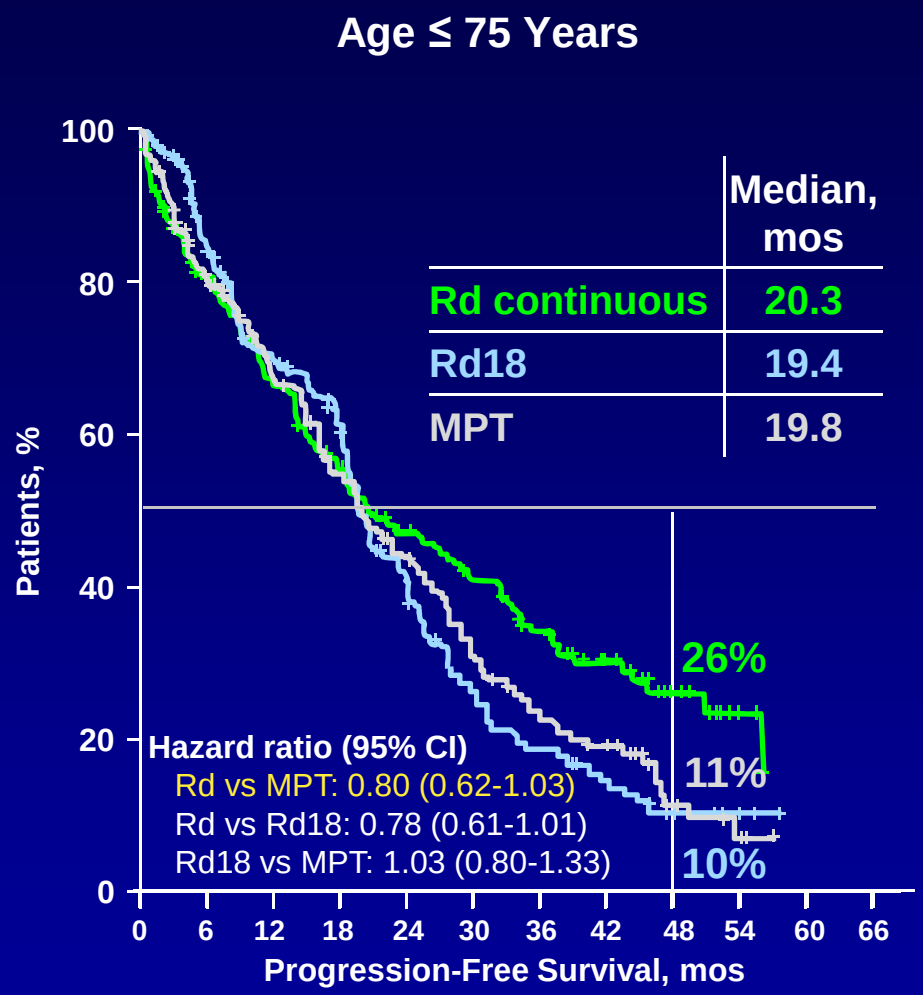
Bahlis N et al. Assessing the Benefit of Continuous Treatment in the FIRST Trial (MM-020): Impact of Response in Patients With Transplant-Ineligible Newly Diagnosed Multiple Myeloma. *EHA 2015, abstract #P277.*

FIRST Trial – Impact of Age: PFS

Median follow-up of 45.5 months as of 03 March, 2014



Rd	349	275	222	188	155	129	117	90	54	22	6	0
Rd18	348	277	231	193	125	94	66	38	20	9	3	0
MPT	359	266	218	177	126	92	61	39	18	9	1	0



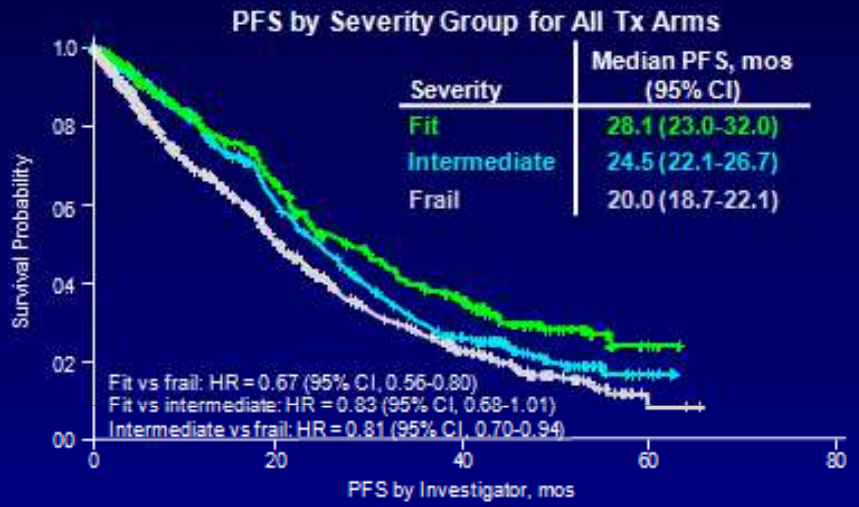
Rd	186	136	108	88	70	57	44	27	12	4	0	
Rd18	193	137	106	83	49	31	23	15	7	4	0	
MPT	188	125	94	72	54	37	26	20	7	3	0	

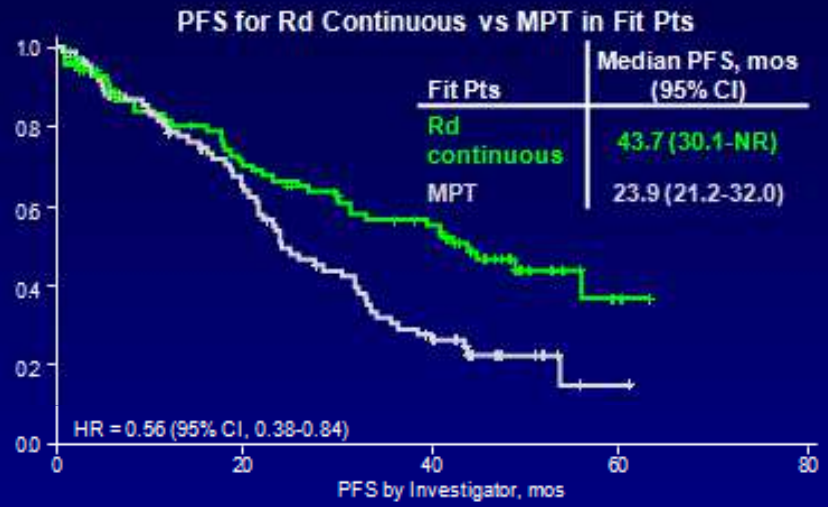
MPT, melphalan, prednisone, thalidomide; Rd, lenalidomide plus low-dose dexamethasone; Rd18, lenalidomide plus low-dose dexamethasone for 18 cycles.

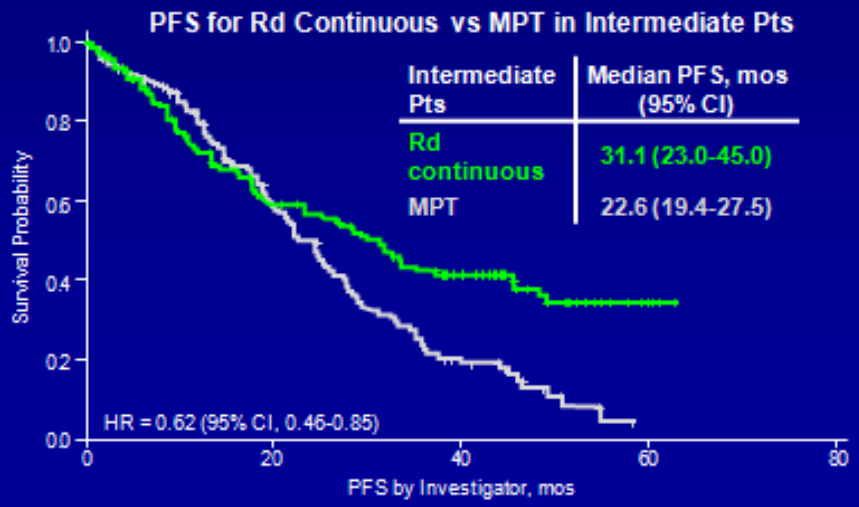
Hulin C, et al. *EHA* 2015: Abstract S429.

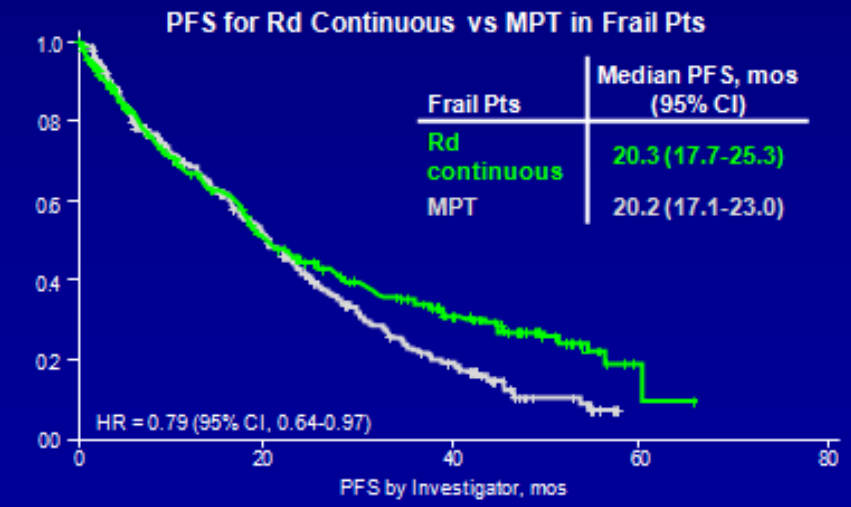
FIRST Trial - Frailty Analysis
PFS by Severity Group

Median follow-up of 45.5 months as of 03 March, 2014







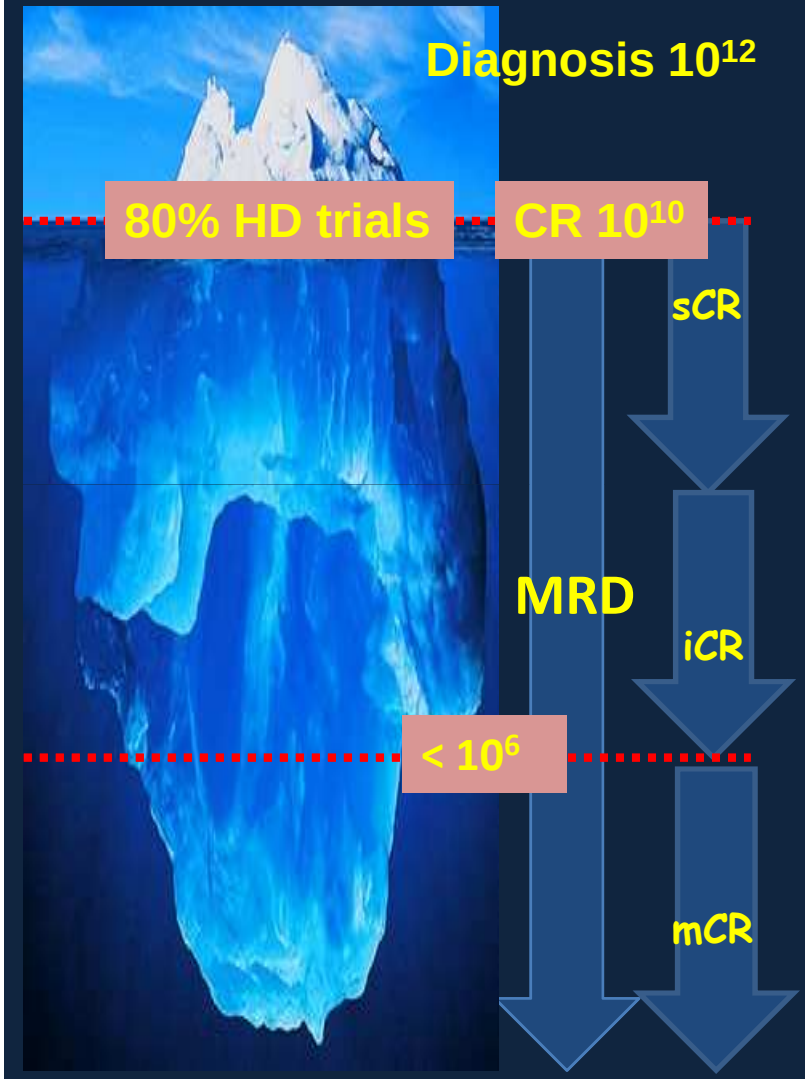


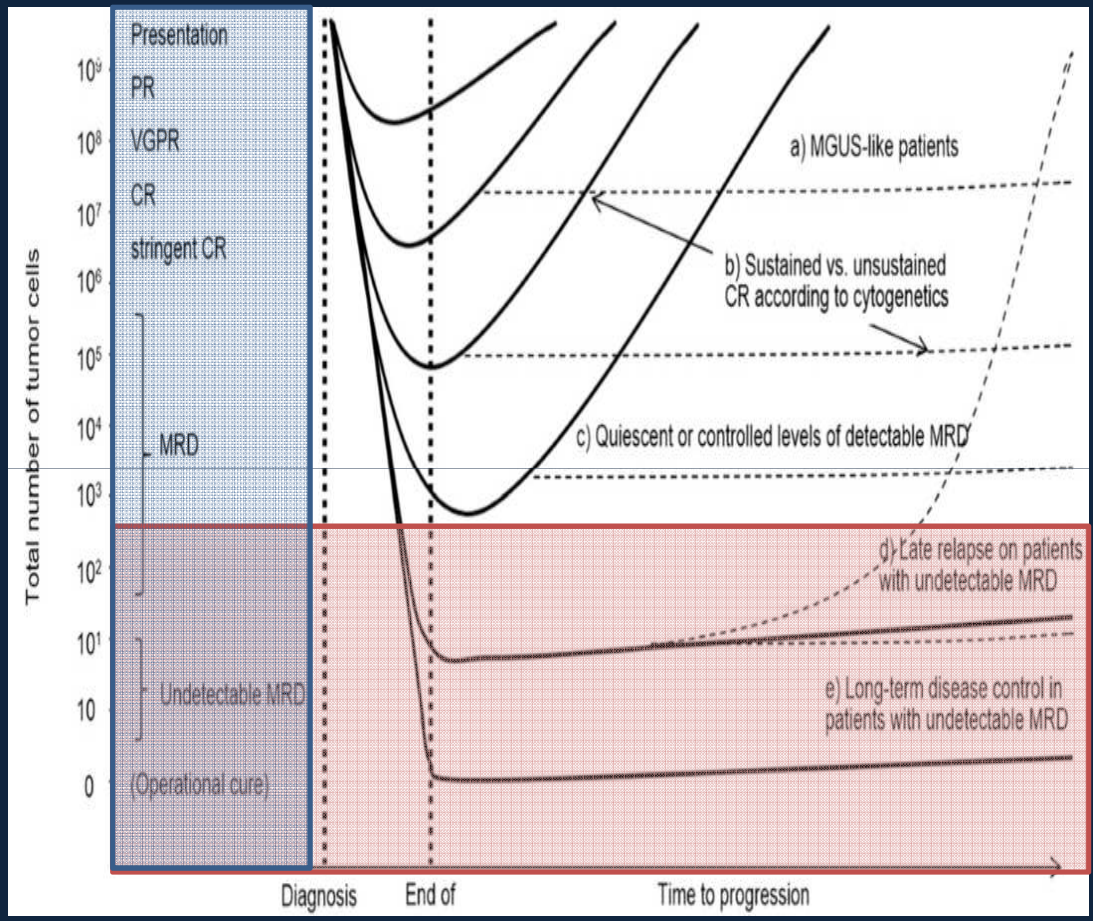
HR, hazard ratio; MPT, melphalan, prednisone, and thalidomide; NR, not reached; PFS, progression-free survival; pt, patient; Rd, lenalidomide and low-dose dexamethasone; Tx, treatment.

Facon T, et al. *ASH* 2015: Abstract 4239.

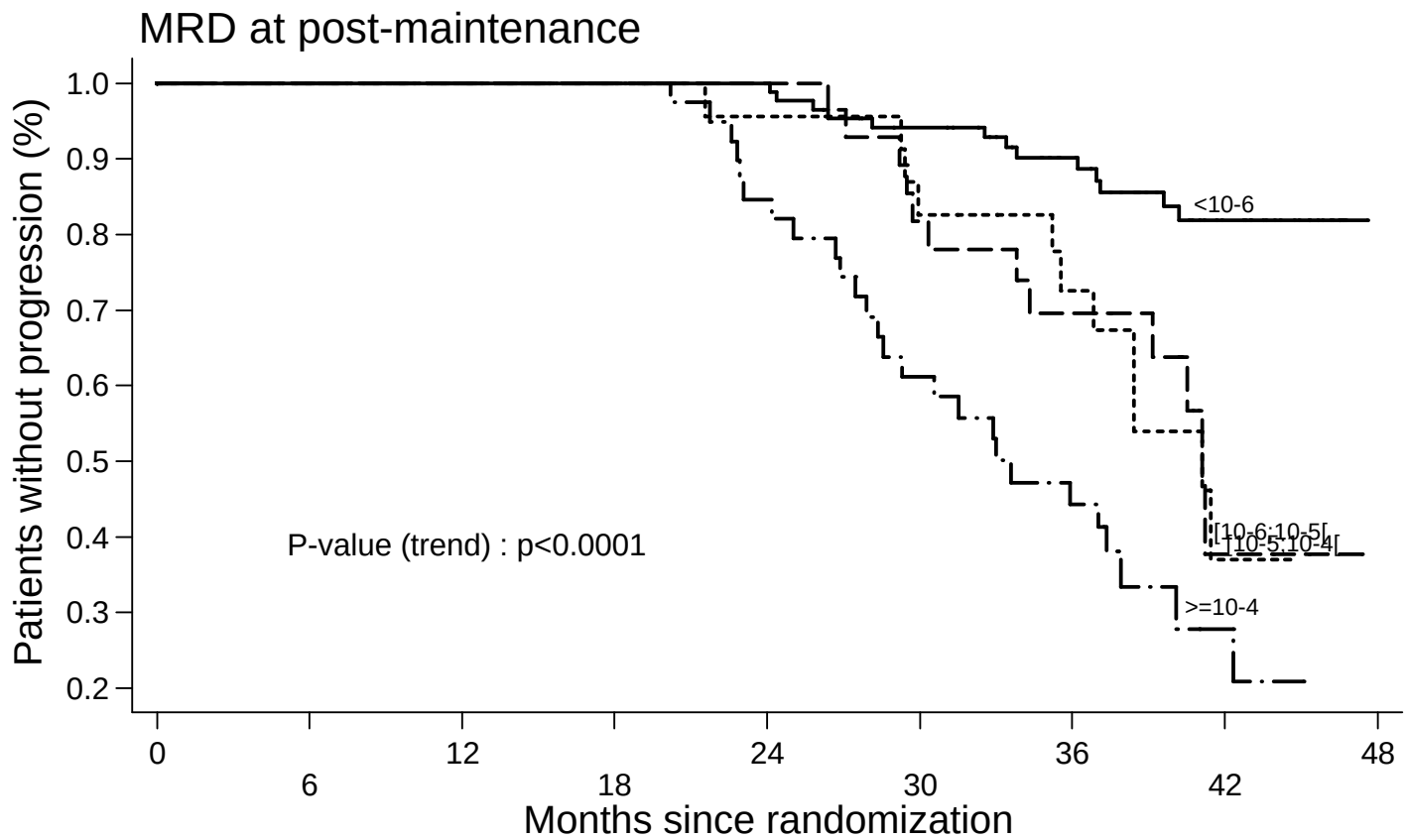
Pourquoi

Depth of response matters





Paiva *et al.*, Blood, 2015

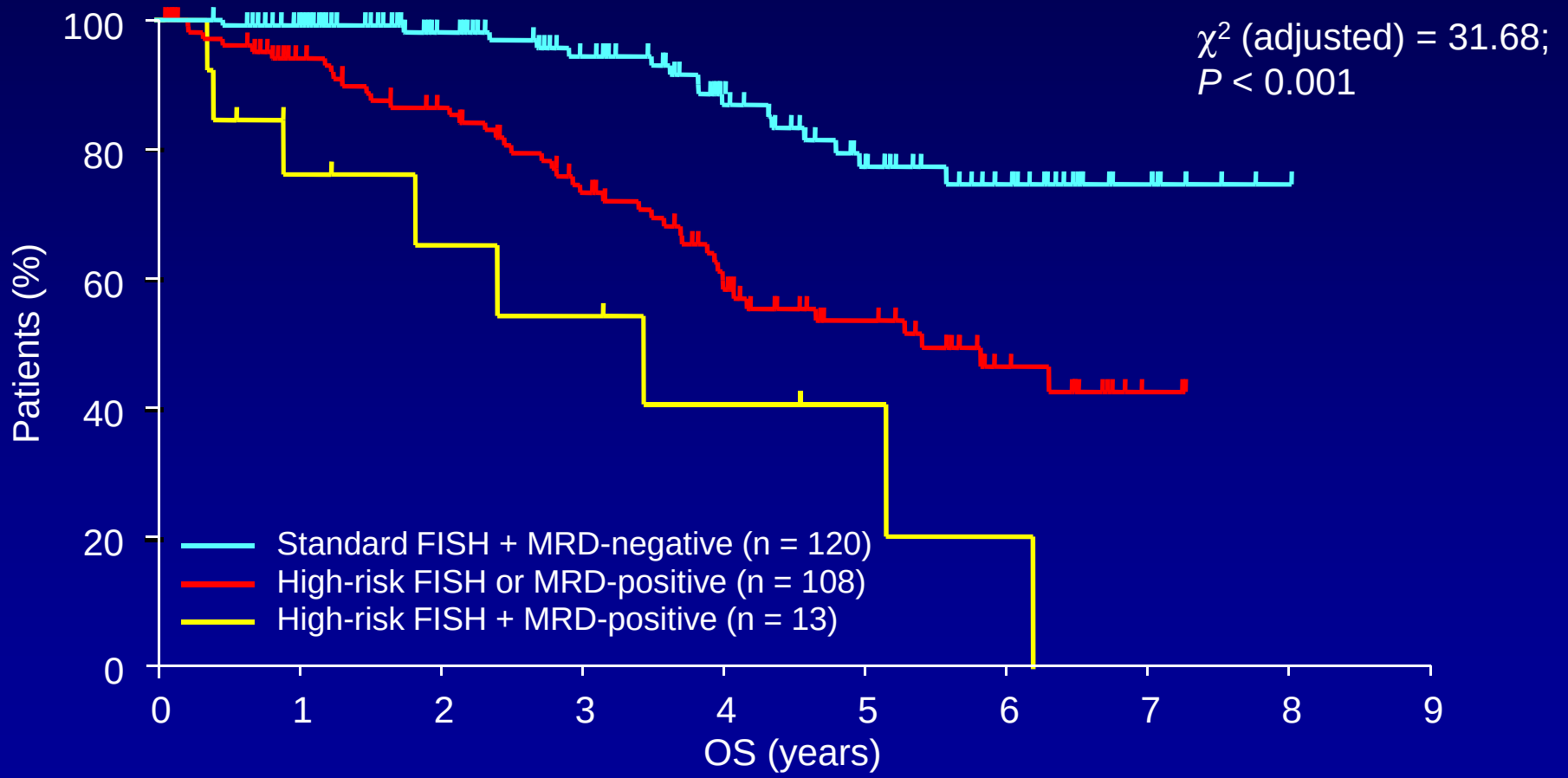


N at risk (events)

$<10^{-6}$	86	(0)	86	(0)	86	(0)	86	(0)	86	(5)	77	(3)	61	(5)	36	(0)	10
$[10^{-6};10^{-5}[$	29	(0)	29	(0)	29	(0)	29	(0)	28	(5)	22	(3)	16	(4)	4	(1)	1
$[10^{-5};10^{-4}[$	23	(0)	23	(0)	23	(0)	23	(1)	22	(3)	19	(2)	14	(5)	3	(0)	2
$[10^{-4};10^{-3}[$	40	(0)	40	(0)	40	(0)	40	(6)	33	(9)	23	(6)	15	(4)	4	(1)	2

High-risk cytogenetics: OS for patients in CR by FISH and MRD status

- Combining UK MRC Myeloma IX[1] with Spanish study[2] data



- Best OS seen in patients with favorable cytogenetics and MRD negativity

CR, complete response; FISH, fluorescent in situ hybridization; MRD, minimal residual disease; OS, overall survival.

1. Rawstron AC, et al. J Clin Oncol. 2013;31:2540-7.
2. Paiva B, et al. Blood. 2012;119:687-91.

Myeloma a Chronic disease for Elderly

Regimens	**Phase 3 trials**
KRd vs Rd	
Ird vs Rd	Tourmaline MM2
ElotuzumabRd vs Rd	Eloquent1
DaratumumabRd vs Rd	MAIA
CRd MRC	MRCXI
Vrd vs Rd	SWOG

Pourquoi pas Moi…

En pratique

H, 69 ans, Diag 2012, R ISS2, VMP mateos x12, VGPR

Fin de L1 en 06/2013. Tolérance OK
R1 clinique. 09/2015

Options

1. Rd
2. Rd puis triplet si pas RC
3. VRd
4. VRd puis KRd si pas RC
5. KRd

Objectif

1. RC
2. Traitement jusque progression
3. Discussion arrêt de traitement seulement si toxicité inacceptable

F, 61 ans, Diag 2010, R ISS2, VTdx4 auto VTDx6, VGPR

Fin de L1 en 06/2013. Tolérance OK
R1 clinique. 09/2015

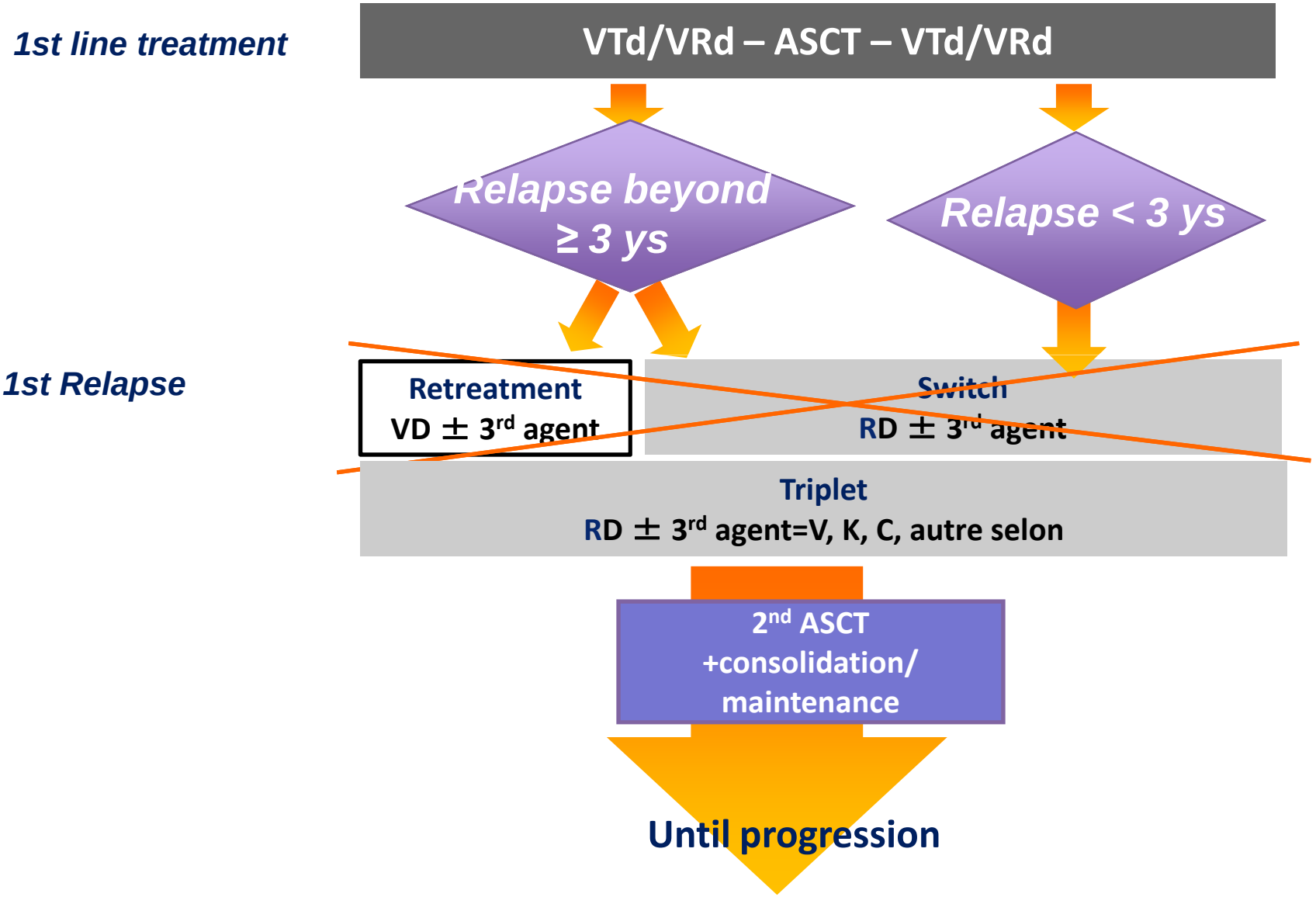
Options

1. Rd
2. Rd puis triplet si pas RC
3. VRd
4. VRd puis KRd si pas RC
5. KRd

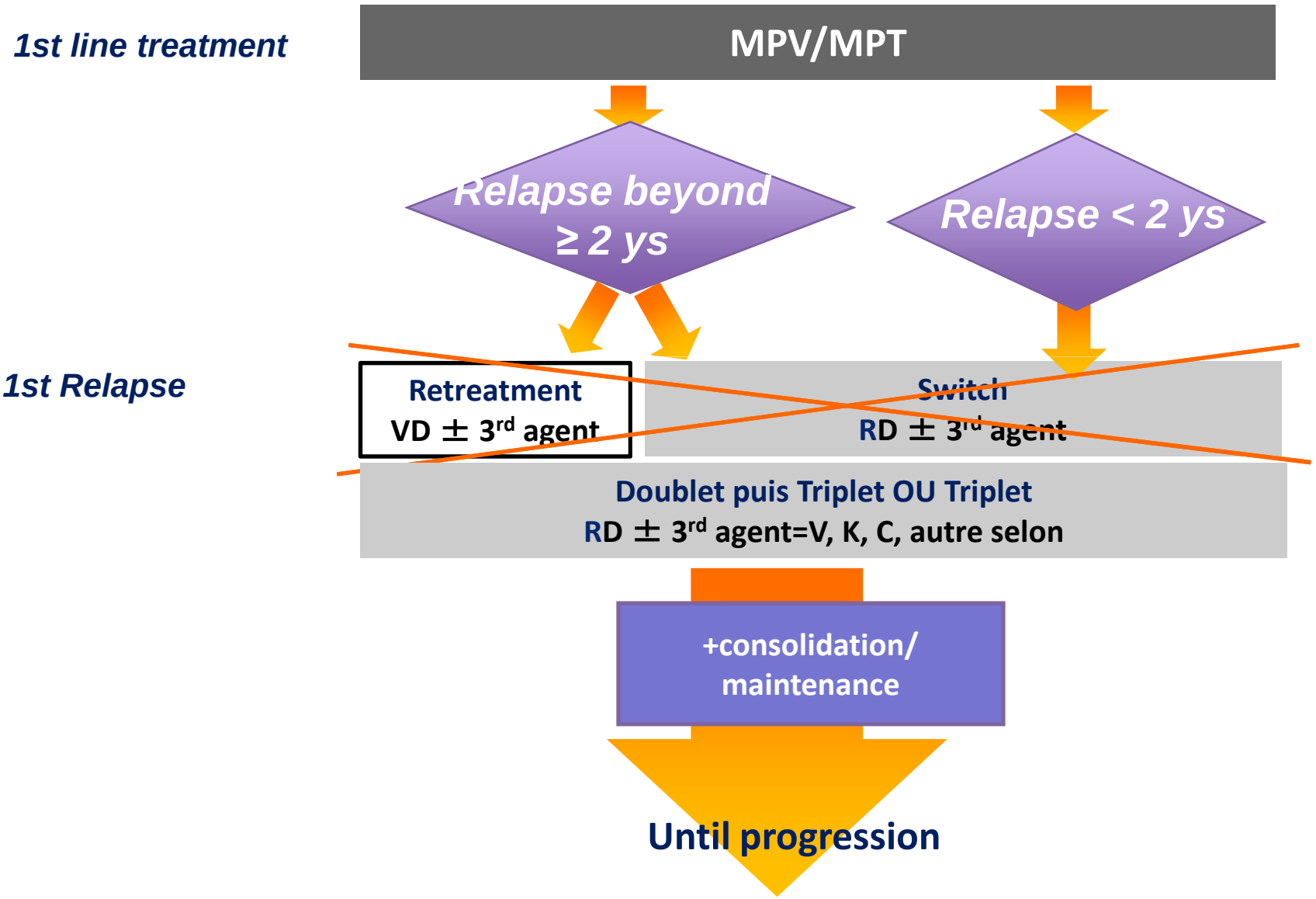
Objectif

1. RC
2. Traitement jusque progression
3. Discussion ASCT MAIS reprise traitement après jusque progression
4. Discussion arrêt de traitement seulement si toxicité inacceptable

Algorythm of First Relapse in Transplant Eligible



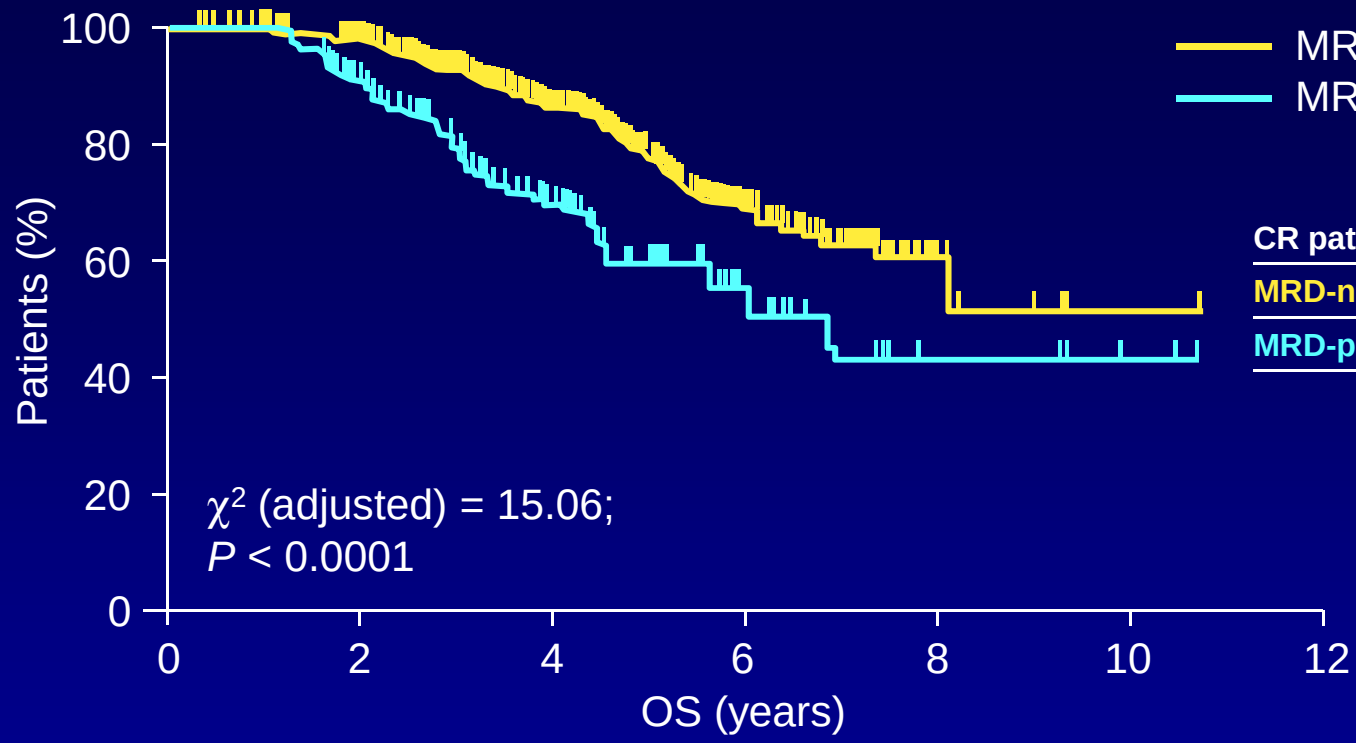
Algorythm of First Relapse in Transplant INEligible



Never give up!

Thank you for your attention

The effect of MRD status on OS (CR patients)



CR patients	Median OS
MRD-negative	NR
MRD-positive	82 months

No. of patients at risk:

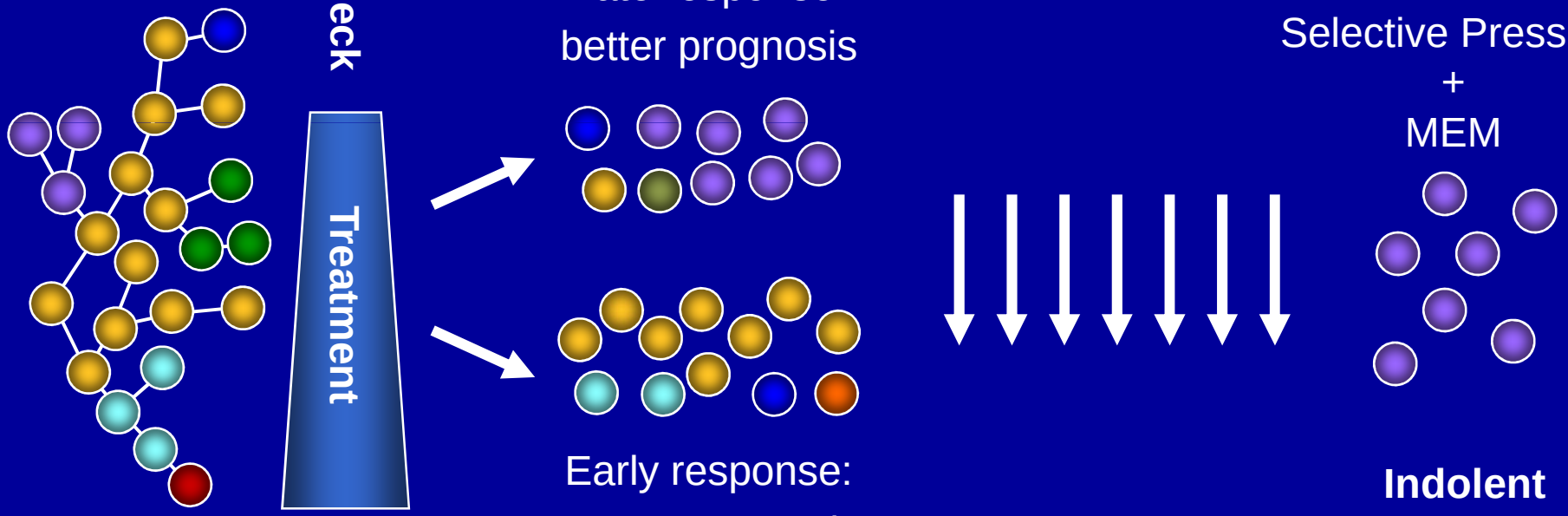
MRD-negative	362	359	331	274	218	138	76	32
MRD-positive134	131	111	81	55	35	20	10	5

Data are adjusted for different proportions of patients being MRD-positive and MRD-negative by study.

- 3-year OS: 93% MRD-negative versus 79% MRD-positive patients
- 5-year OS: 78% MRD-negative versus 60% MRD-positive patients

CR, complete response; MRD, minimal residual disease; NR, not reached; OS, overall survival..

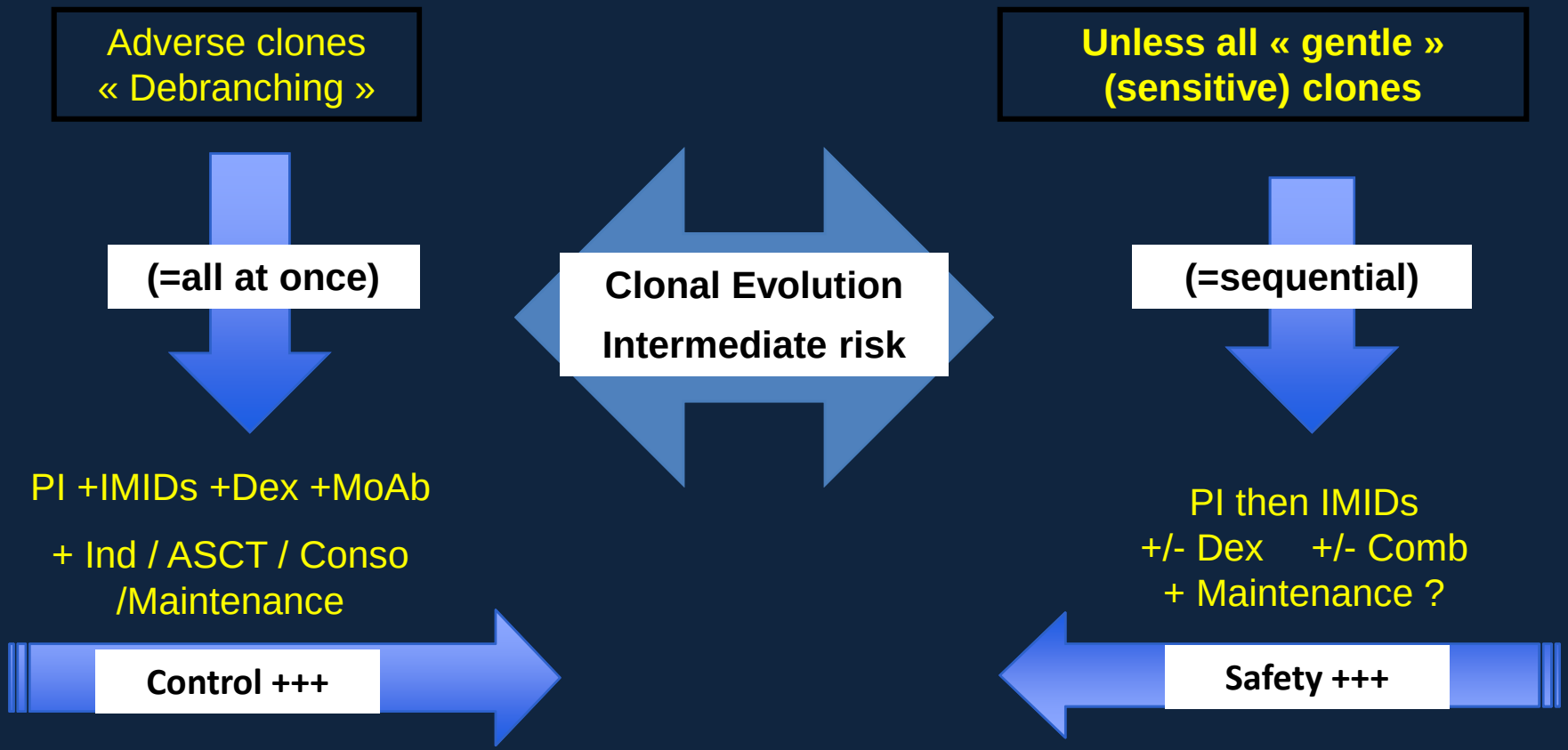
Treatment acts as a selective pressure
Adjust pressure to select for indolent clones



Morgan G, et al. Nat Rev Cancer. 2012;12:335-48.

What should we prioritize in the real life ?

Depending on
– Clones present at diagnosis
– How clones vary with treatment pressure



Morgan G, et al. Nat Rev Cancer. 2012;12:335-48

A simple assumption of how to apply this concept in the real life

*Depth of response corresponds to the amount of remaining clones**

Depth of response corresponds to the potential existence of resistant/adverse sub clones