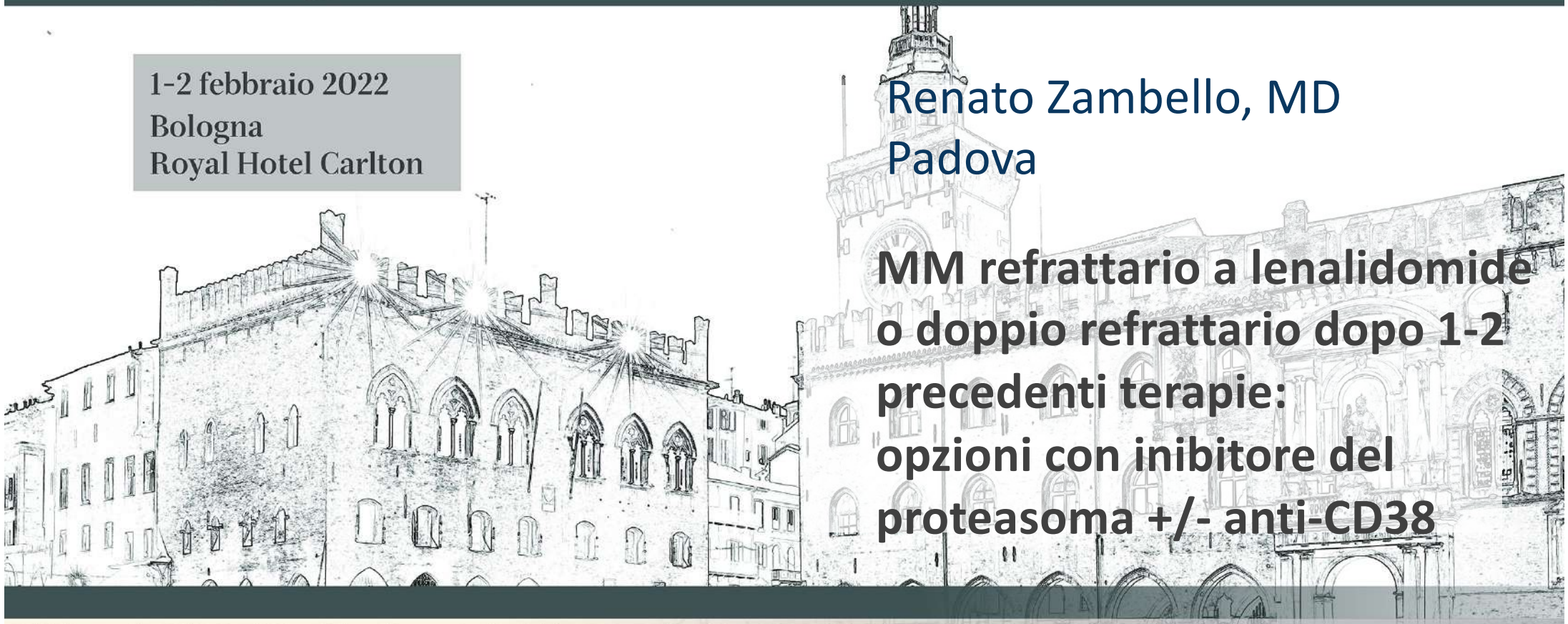
Highlights from IMW 2021

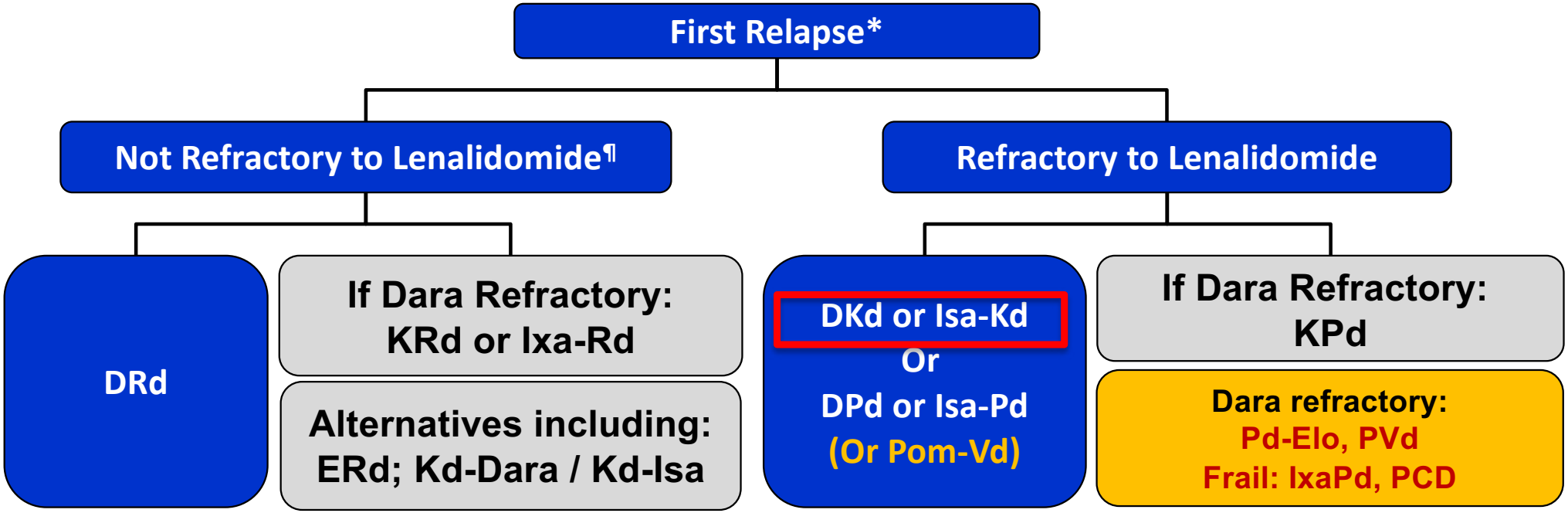
1-2 febbraio 2022
Bologna
Royal Hotel Carlton



Renato Zambello, MD
Padova

MM refrattario a lenalidomide o doppio refrattario dopo 1-2 precedenti terapie: opzioni con inibitore del proteasoma +/- anti-CD38

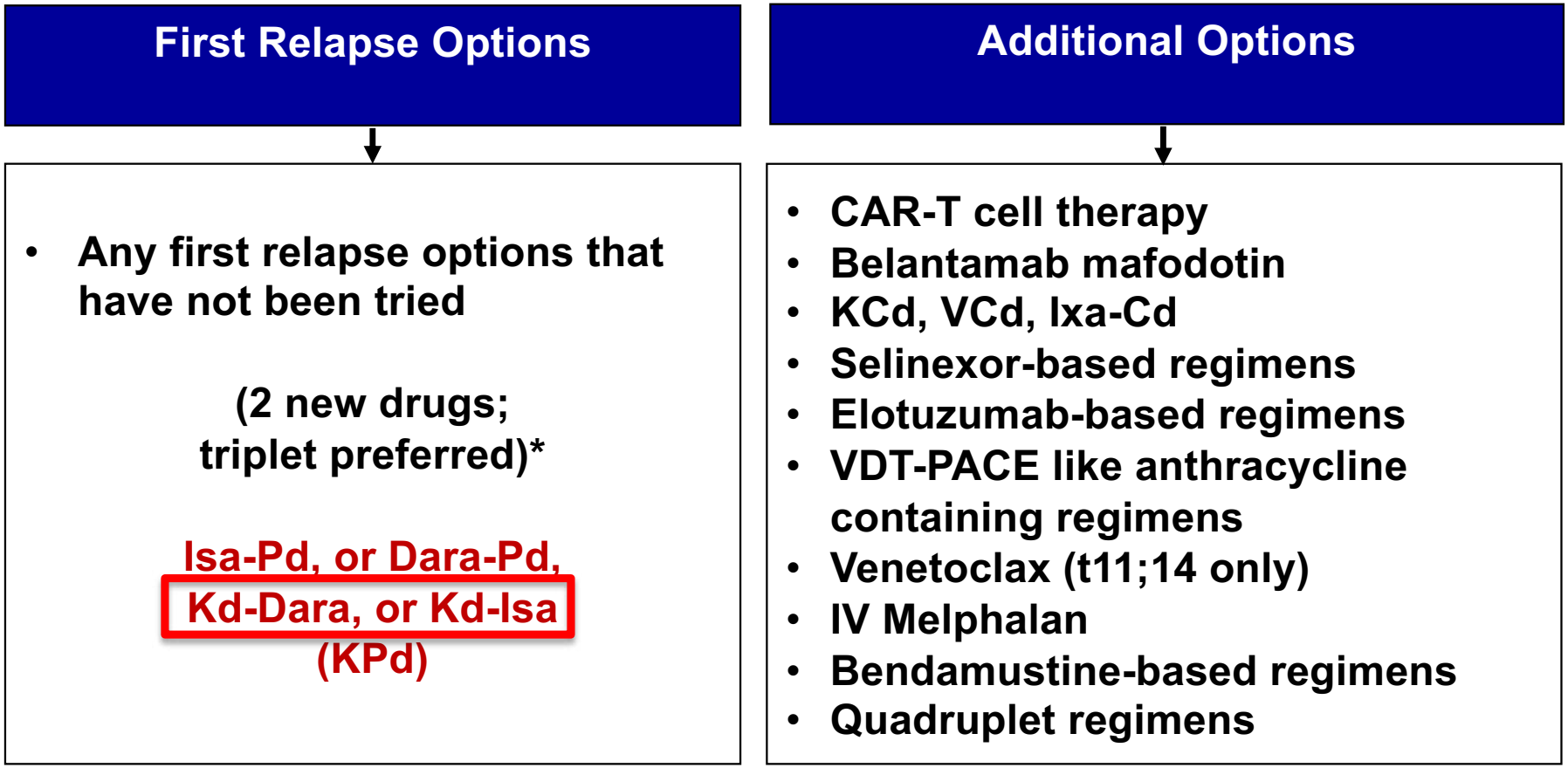
Myeloma: First Relapse



*Consider salvage auto transplant in eligible patients

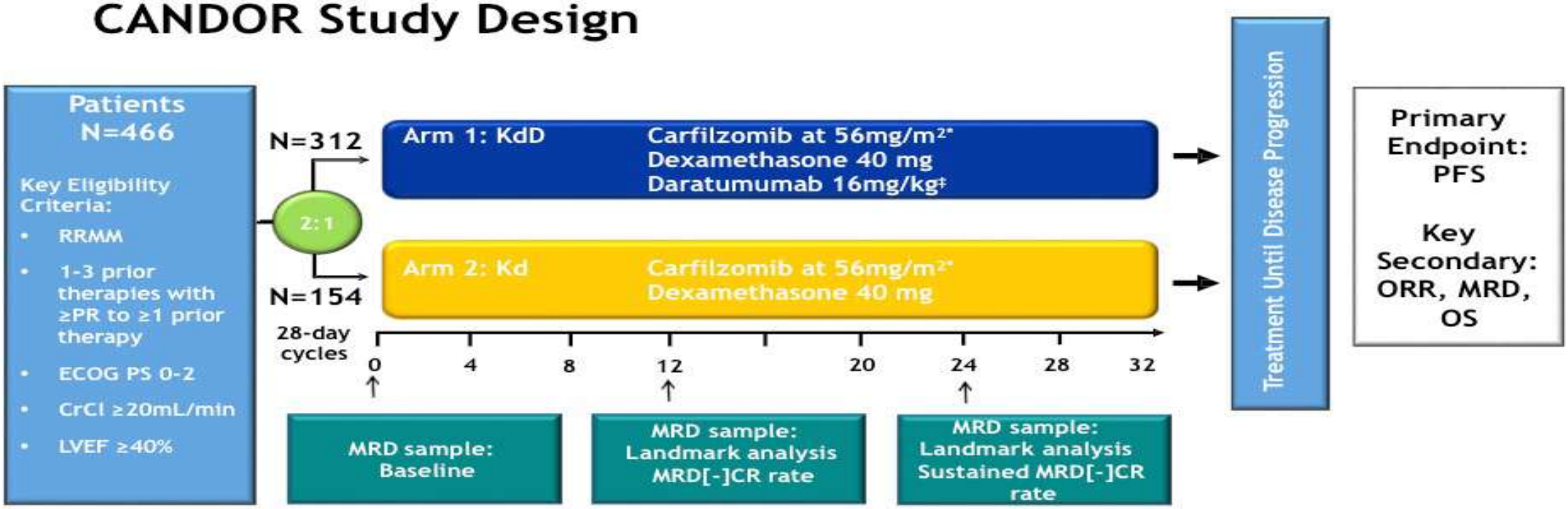
¶Relapse occurring while off all therapy, or while on small doses of single-agent lenalidomide, or on bortezomib maintenance

Myeloma: Second or Higher Relapse



*Consider ixazomib instead of carfilzomib or bortezomib if an all-oral regimen is needed

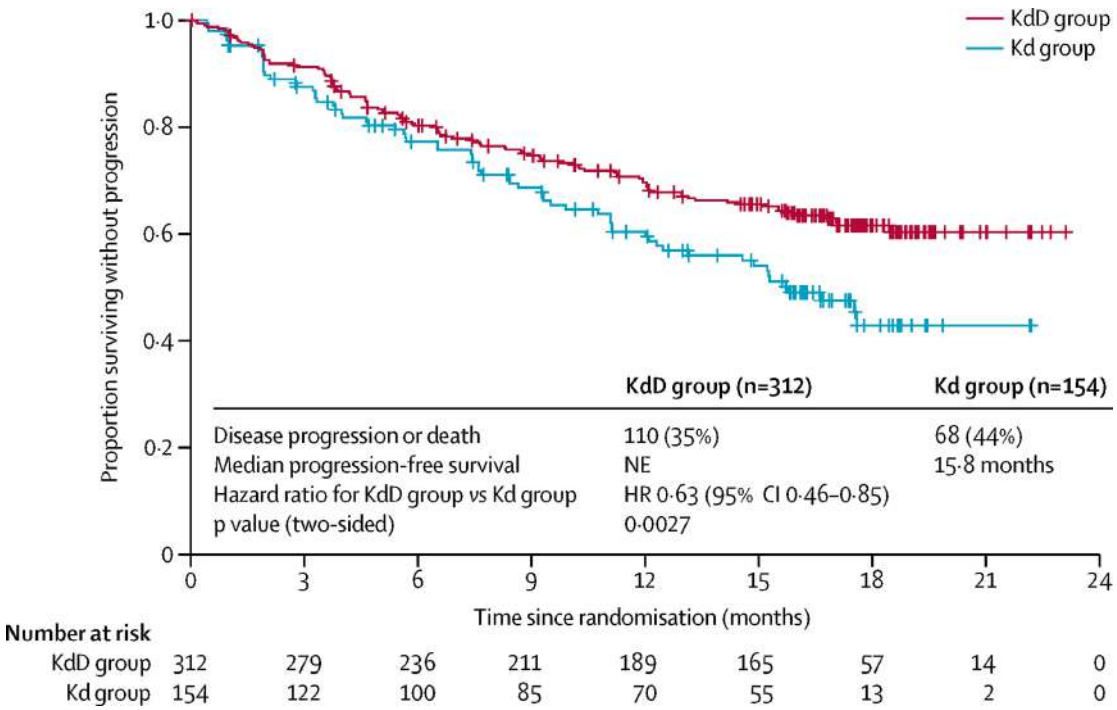
CANDOR Study Design

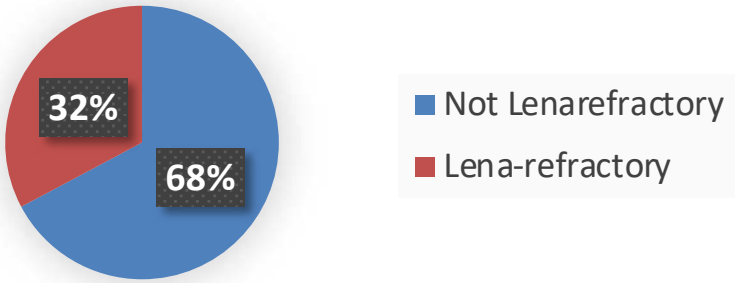


*Carfilzomib at 56 mg/m² administered twice weekly; 20 mg/m² administered on days 1 and 2 of cycle 1 only
‡The first dose of daratumumab is split over two days (8 mg/kg each).
CrCl, creatinine clearance; ECOG PS, Eastern Cooperative Oncology Group Performance Status; LVEF, left ventricular ejection fraction; PD, progressive disease; RRMM, relapsed or refractory multiple myeloma

Dimopulos M et al Lancet 2020; 396: 186–97

CANDOR Trial: DKd versus Kd





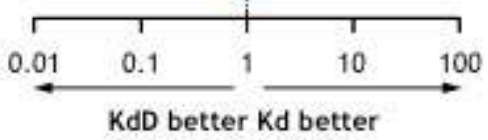
…PFS 28·6 months (95% CI 22·7–not estimable [NE]) in the KdD group and 15·2 months (11·1–19·9) in the Kd group (hazard ratio 0·59 [95% CI 0·45–0·78], log-rank p<0·0001)….

Usmani Lancet Oncol 2022

The Lancet 2020 396186-197DOI: (10.1016/S0140-6736(20)30734-0)

PFS Hazard-Ratios Across Prespecified Subgroups

Subgroup	KdD group (n=312) No. of subjects	Kd group (n=154) No. of subjects	Hazard ratio for KdD group vs. Kd group (95% CI)
Number of prior lines of therapy			
1	133	67	0.70 (0.42-1.17)
≥2	179	87	0.63 (0.44-0.92)
Prior lenalidomide exposure			
No	189	80	0.87 (0.56-1.35)
Yes	123	74	0.52 (0.34-0.80)
Refractory to lenalidomide			
No	213	99	0.85 (0.57-1.27)
Yes	99	55	0.45 (0.28-0.74)
Prior proteasome inhibitor exposure			
No	33	15	0.93 (0.29-3.02)
Yes	279	139	0.64 (0.47-0.88)
Refractory to bortezomib			
No	224	107	0.59 (0.40-0.85)
Yes	88	47	0.83 (0.49-1.41)



P-204

Carfilzomib, Dexamethasone, and Daratumumab (KdD) vs Kd: Subgroup Analysis of the CANDOR Study by Prior Autologous Stem Cell Transplantation, Lenalidomide Exposure, or Lenalidomide-Refractory Disease

Maria-Victoria Mateos, MD, PhD;[1] Saad Z Usmani, MD;[2] Hang Quach, MBBS, FRACP, FRCPA, MD;[3] Meletios Dimopoulos, MD;[4] Rafael Fonseca, MD;[5] Ian McFadden, PhD;[6] Akeem Yusuf, PhD;[6] Monica Khurana, MD;[6] Mihaela Obreja, PhD;[6] Andrew Spencer, MBBS, FRACP, FRCPA, MD[7]

[1]University Hospital Salamanca/ISAI, Salamanca, Spain; [2]Atrium Health, Charlotte, NC, USA; [3]St Vincent's Hospital, Melbourne, Victoria, Australia; [4]National and Kapodistrian University of Athens, School of Medicine, Athens, Greece; [5]Mayo Clinic, Phoenix, AZ, USA; [6]Amgen Inc., Thousand Oaks, CA, USA; [7]Alfred Health-Monash University, Melbourne, Australia

Baseline Characteristic	KdD (N= 312)		Kd (N=154)	
	With Prior ASCT (n = 194)	Without ASCT (n = 118)	With Prior ASCT (n = 75)	Without ASCT (n = 79)
Median age, years (range)	61 (29–76)	70 (37–84)	62 (35–75)	69 (43–83)
≤ 64	124 (63.9)	39 (33.1)	50 (66.7)	27 (34.2)
65–74	65 (33.5)	56 (47.5)	23 (30.7)	32 (40.5)
≥ 75	5 (2.6)	23 (19.5)	2 (2.7)	20 (25.3)
ECOG PS, n (%)				
0 or 1	187 (96.4)	108 (91.5)	73 (97.3)	74 (93.7)
2	6 (3.1)	9 (7.6)	2 (2.7)	5 (6.3)
Missing	1 (0.5)	1 (0.8)	0	0
ISS stage per IXRS at screening, n (%)				
I or II	160 (82.5)	92 (78.0)	64 (85.3)	63 (79.7)
III	34 (17.5)	26 (22.0)	11 (14.7)	16 (20.3)
Number of prior therapies, n (%)				
1	91 (46.9)	53 (44.9)	35 (46.7)	35 (44.3)
≥ 2	103 (53.1)	65 (55.1)	40 (53.3)	44 (55.7)
Prior therapies, n (%)				
Proteasome inhibitor	177 (91.2)	113 (95.8)	68 (90.7)	71 (89.9)
Len	75 (38.7)	48 (40.7)	35 (46.7)	39 (49.4)
Refractory to Len, n (%)	57 (29.4)	42 (35.6)	23 (30.7)	32 (40.5)

- Overall, baseline characteristics were generally similar between treatment arms
- Of 466 patients in the study, 62% in the KdD arm and 49% in the Kd arm had prior ASCT
- Patients without prior ASCT were typically older and more likely to be Len refractory

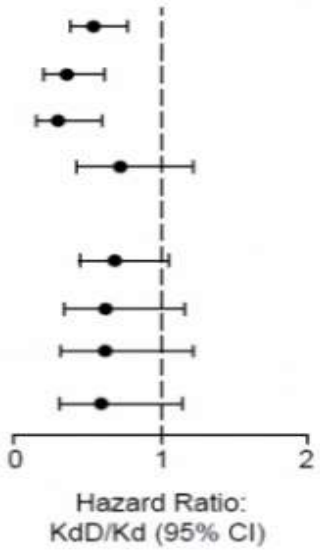
ASCT, autologous stem-cell transplant; ECOG PS, Eastern Cooperative Oncology Group Performance Status; ISS, International Staging System; IXRS, Interactive Voice/Web Response System; Kd, carfilzomib and dexamethasone; KdD, carfilzomib, dexamethasone, and daratumumab; Len, lenalidomide.

Mateos MV P-204

Median PFS by Subgroup

- After a median follow-up of approximately 27 months, PFS consistently favored KdD across all subgroups, consistent with the primary analysis
- Tests for interactions showed no statistically significant differences among subgroups

	KdD (N=312)		Kd (N=154)		
	Events/ Patients	Median PFS, mo	Events/ Patients	Median PFS, mo	Hazard ratio KdD vs Kd (95% CI)
With prior ASCT					
All patients	88/194	28.1	48/75	13.9	0.54 (0.37–0.77)
Prior Len exposure	34/75	25.0	27/35	12.0	0.35 (0.20–0.61)
Len refractory	26/57	25.0	18/23	11.1	0.30 (0.15–0.59)
Len naive	54/119	28.6	21/40	20.3	0.72 (0.42–1.22)
Without ASCT					
All patients	52/118	NE	37/79	15.8	0.68 (0.44–1.05)
Prior Len exposure	23/48	NE	20/39	11.1	0.62 (0.33–1.15)
Len refractory	20/42	NE	17/32	11.1	0.62 (0.31–1.22)
Len naive	29/70	NE	17/40	24.0	0.59 (0.31–1.14)



ASCT, autologous stem-cell transplant; Kd, carfilzomib and dexamethasone; KdD, carfilzomib, dexamethasone, and daratumumab; Len, lenalidomide; NE, not evaluable; PFS, progression-free survival.

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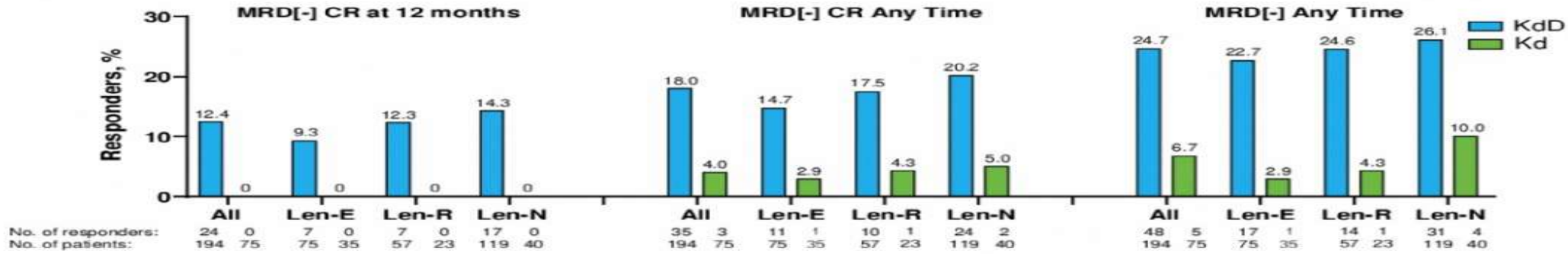
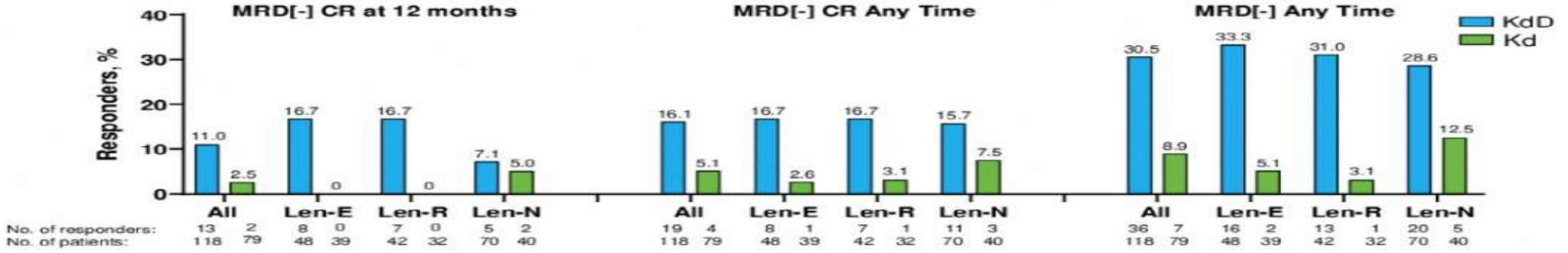
MRD-negative CR Rates by Subgroup

- MRD-negative CR rates consistently favored KdD vs Kd across all subgroups*

With prior ASCT



Without ASCT



*MRD status assessed by next generation sequencing at 12 months (during an 8 to 13 month window) or at any time during the study; MRD-negative disease at the 10^{-5} level.
ASCT, autologous stem-cell transplant; CR, complete response; E, exposed; Kd, carfilzomib and dexamethasone; KdD, carfilzomib, dexamethasone, and daratumumab; Len, lenalidomide; MRD, minimal residual disease; N, naive; R, refractory.

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Grade ≥ 3 Adverse Events by Subgroup

- Grade ≥ 3 adverse events were consistent across Len subgroups

Grade ≥ 3 adverse events	With prior ASCT		Without prior ASCT	
	KdD (n = 192)	Kd (n = 75)	KdD (n = 116)	Kd (n = 78)
Subgroups, n/N (%)				
All patients	172/192 (89.6)	59/75 (78.7)	96/116 (82.8)	57/78 (73.1)
Prior Len exposure	69/74 (93.2)	28/35 (80.0)	39/48 (81.3)	28/39 (71.8)
Len-refractory	51/56 (91.1)	20/23 (87.0)	33/42 (78.6)	22/32 (68.8)
Len naive	103/118 (87.3)	31/40 (77.5)	57/68 (83.8)	29/39 (74.4)
AEs of interest, n (%)				
Acute renal failure	6 (3.1)	5 (6.7)	4 (3.4)	5 (6.4)
Cardiac failure	7 (3.6)	3 (4.0)	5 (4.3)	10 (12.8)
Daratumumab-related infusion reactions	5 (2.6)	0 (0.0)	2 (1.7)	0 (0.0)
Ischemic heart disease	9 (4.7)	2 (2.7)	5 (4.3)	3 (3.8)
Peripheral neuropathy	5 (2.6)	0 (0.0)	1 (0.9)	0 (0.0)
Respiratory tract infections	65 (33.9)	13 (17.3)	39 (33.6)	12 (15.4)
Viral infections	16 (8.3)	3 (4.0)	5 (4.3)	0 (0.0)

AE, adverse event; ASCT, autologous stem-cell transplant; Kd, carfilzomib and dexamethasone; KdD, carfilzomib, dexamethasone, and daratumumab; Len, lenalidomide.

- Rates of treatment-emergent adverse events leading to discontinuation of any study drug:
  - Patients with prior ASCT: 28.6% vs 21.3% for KdD and Kd patients, respectively
  - Patients without prior ASCT: 25.9% vs 28.2% for KdD and Kd patients, respectively
- Median duration of carfilzomib therapy:
  - Patients with prior ASCT: 56 weeks vs 53 weeks for KdD and Kd patients, respectively
  - Patients without prior ASCT: 74 weeks vs 33 weeks for KdD and Kd patients, respectively

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CONCLUSIONS

- These findings are consistent with previous studies and further support the clinical efficacy and safety of KdD among patients with RRMM, with or without prior ASCT
- KdD provides consistent clinical efficacy and safety in the high unmet need group of patients with Len-refractory disease
- The KdD regimen should be considered for RRMM patients beginning at first relapse, including those who are Len-exposed or Len-refractory

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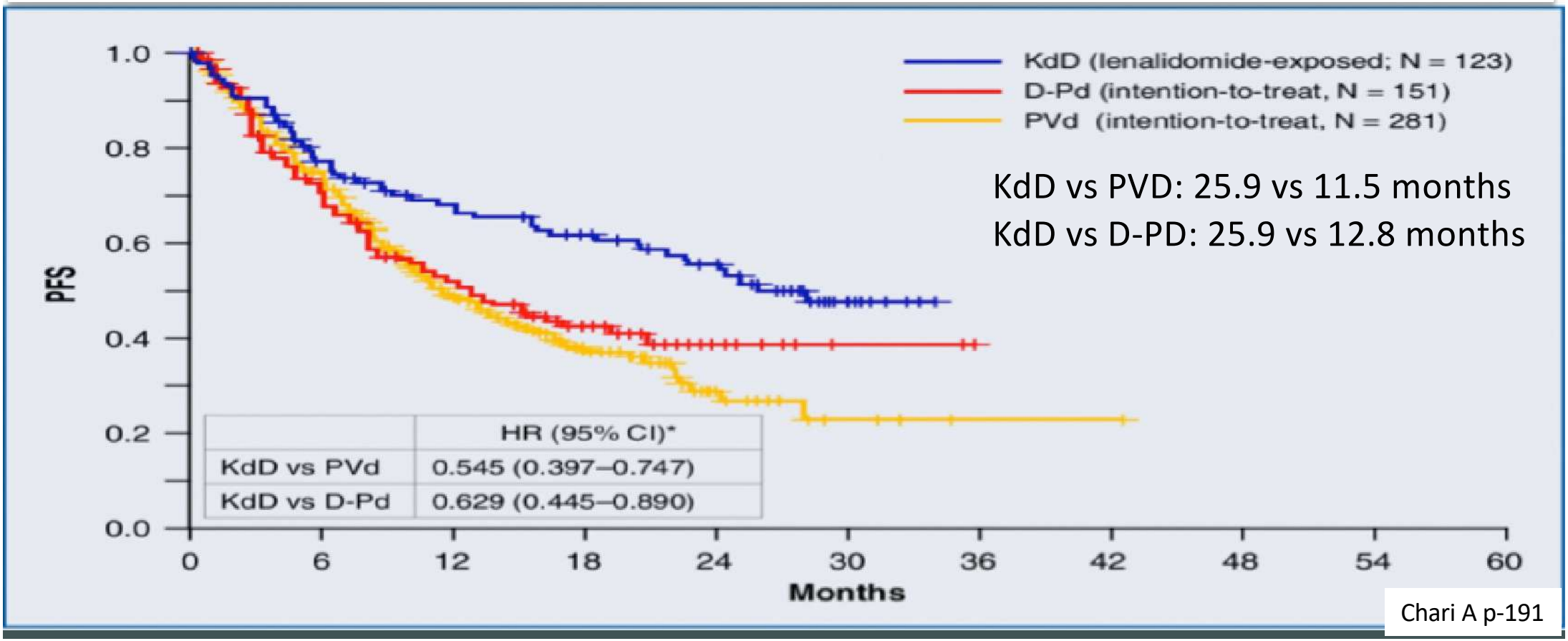
Comparison of Efficacy Outcomes for Carfilzomib Plus Dexamethasone and Daratumumab (KdD) Versus Pomalidomide Plus Bortezomib and Dexamethasone (PVd) and D-Pd in Relapsed or Refractory Multiple Myeloma

Ajai Chari,[1] Meletios A. Dimopoulos,[2] Meral Beksac,[3] Xavier Leleu,[4] Katja Weisel,[5] Joshua Richter,[1] Franziska Dirnberger,[6] Karim Iskander,[6] Akeem Yusuf,[6] Joseph Mikhael[7]

	CANDOR	OPTIMISMM[6]	APOLLO[7]
Data source	CANDOR data (June 2020 data cut)	Richardson et al. Lancet Oncol. 2019	Dimopoulos et al. ASH 2020
Intervention and comparator	KdD (n = 312) vs Kd (n = 154)	PVd (n = 281) vs Vd (n = 278)	D-Pd (n = 151) vs Pd (n = 153)
Comparison of KdD, PVd, and D-Pd populations (lenalidomide-exposed patients)			
Age > 65 years, > 75 years*, %	46.3, 5.7	56.2, 16.4	58.3, 16.6
ISS disease stage: I, II, III, %	50.8, 29.5, 19.7	53.0, 30.2, 16.7	45.0, 33.1, 21.9
≥ 2 prior therapies, %	78.0	60.5	89.4
Lenalidomide exposed, n	123	281	151
Lenalidomide refractory, %	80.5	71.2	79.5
Bortezomib refractory, %	31.7	8.5	Not reported
Comparison of KdD, PVd, and D-Pd outcomes (lenalidomide-exposed patients)			
Median follow-up, months	27.6	15.9	16.9
Median PFS, months	KdD: 25.9 / Kd: 11.1	PVd: 11.2 / Vd: 7.1	D-Pd: 12.4 / Pd: 6.9
Hazard ratio (95%CI)	0.49 (0.33, 0.74)	0.61 (0.49, 0.77)	0.63 (0.47, 0.85)

Naive comparisons for PFS favoured KdD



KdD vs PVD: 25.9 vs 11.5 months
KdD vs D-PD: 25.9 vs 12.8 months

Chari A p-191

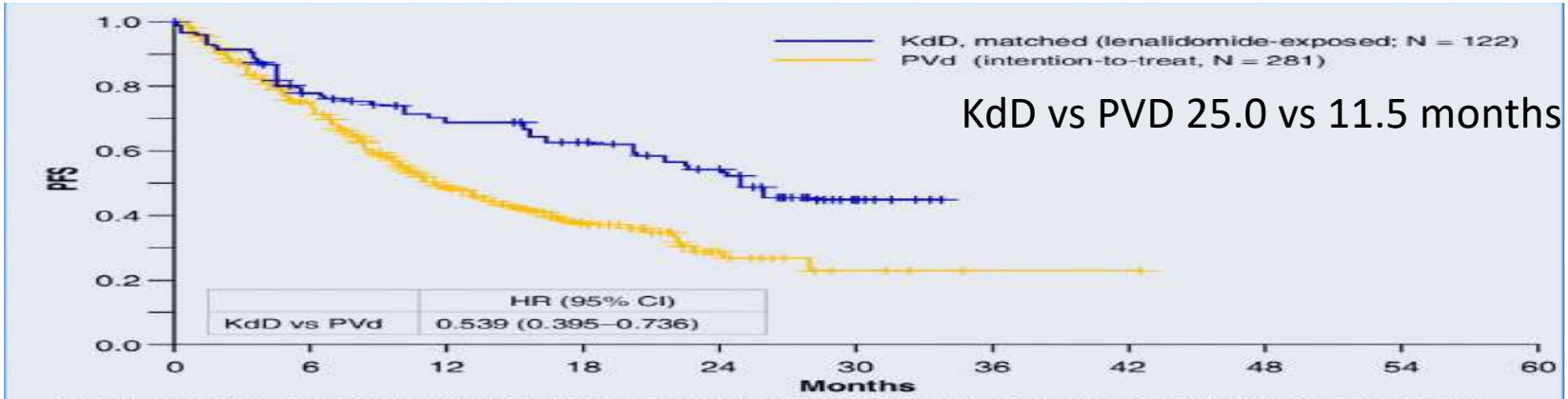
Scenario and Subgroup Analysis among Lenalidomide-Exposed or Refractory patients

- In lenalidomide-exposed patients, scenario analyses indicated MAIC results were robust using different sets of matching variables
- In lenalidomide-refractory patients, the median PFS was 28.1 months for unmatched KdD-treated patients and 9.5 months for PVd-treated patients
  - MAIC was not feasible in this subgroup as baseline characteristics were not reported and sample sizes were small

	Patient population	Description of analysis	Hazard ratio (95% CI)	
			KdD vs D-Pd	KdD vs PVd
Scenario analysis	Len-exposed	Matched: Base case	0.677 (0.474–0.966)	0.539 (0.395–0.736)
	Len-exposed	Matched: included refractoriness to last previous regimen in matching algorithm	0.685 (0.480–0.978)	0.539 (0.395–0.736)
	Len-exposed	Matched: included ECOG status in matching algorithm	0.690 (0.479–0.994)	0.551 (0.404–0.751)
	Len-exposed	Matched: included prior stem-cell transplant in matching algorithm	0.676 (0.473–0.964)	0.527 (0.386–0.721)
Subgroup analysis	Len-refractory	Unmatched	PFS curve not reported	0.468 (0.326–0.671)

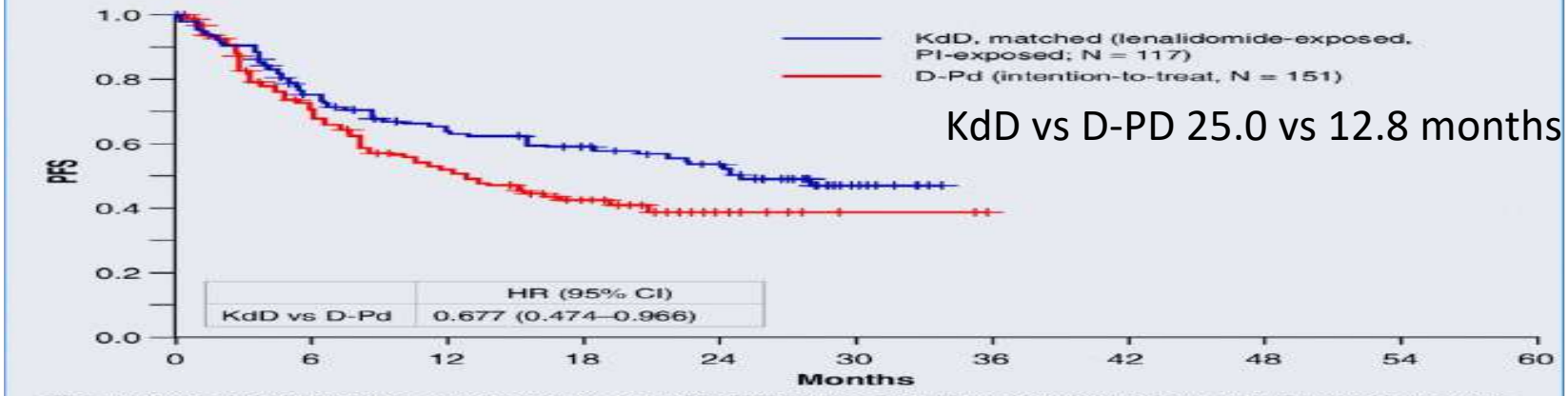
D-Pd, daratumumab, pomalidomide, and dexamethasone; ECOG, Eastern Cooperative Oncology Group; KdD, carfilzomib, dexamethasone, and daratumumab; Len, lenalidomide; PFS, progression-free survival; PVd, pomalidomide, bortezomib, and dexamethasone.

Chari A p-191



KdD vs PVD 25.0 vs 11.5 months

The number of lenalidomide-exposed patients in CANDOR was 123. One patient was excluded due to missing variables used for matching; therefore, the sum of weighted patients was 122. The effective sample size for KdD patients, calculated as the squared sum of weights divided by the sum of squared weights, was 79.



KdD vs D-PD 25.0 vs 12.8 months

The number of lenalidomide-exposed patients in CANDOR was 123. Five patients without prior PI exposure were excluded because APOLLO required patients to have prior PI therapy, 1 other patient was excluded due to missing variables used for matching. Therefore, the sum of weighted patients was 117. The effective sample size for KdD patients, calculated as the squared sum of weights divided by the sum of squared weights, was 108.

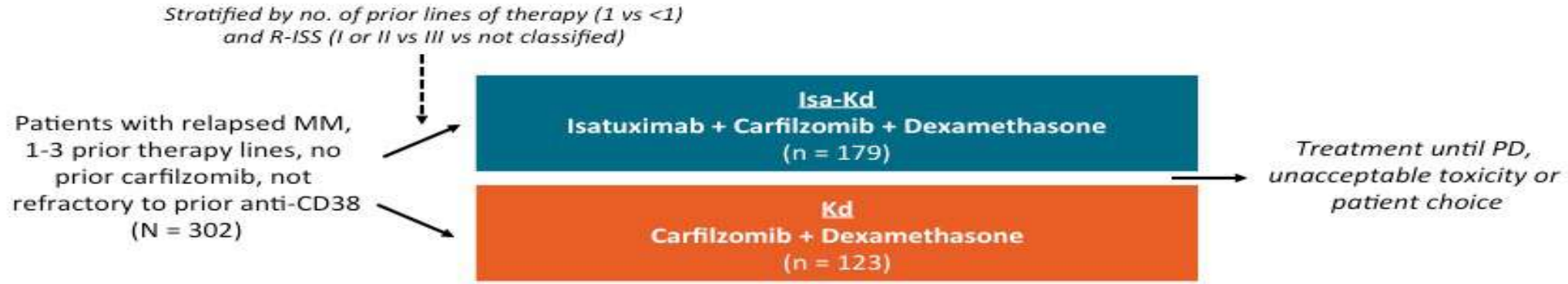
Chari A p-191

CONCLUSIONS

- This analysis shows that in patients with RRMM and previous lenalidomide exposure, KdD extended PFS compared with PVd and D-Pd in both naive and matching-adjusted comparisons
- A comparison of overall survival was not undertaken due to immature data in the studies considered for this analysis
- Results suggest KdD offers clinically meaningful improvements over pomalidomide-based triplet regimens for patients with RRMM previously exposed and/or refractory to lenalidomide

IKEMA: Study Design

- Multicenter, randomized, open-label, active-control phase III trial

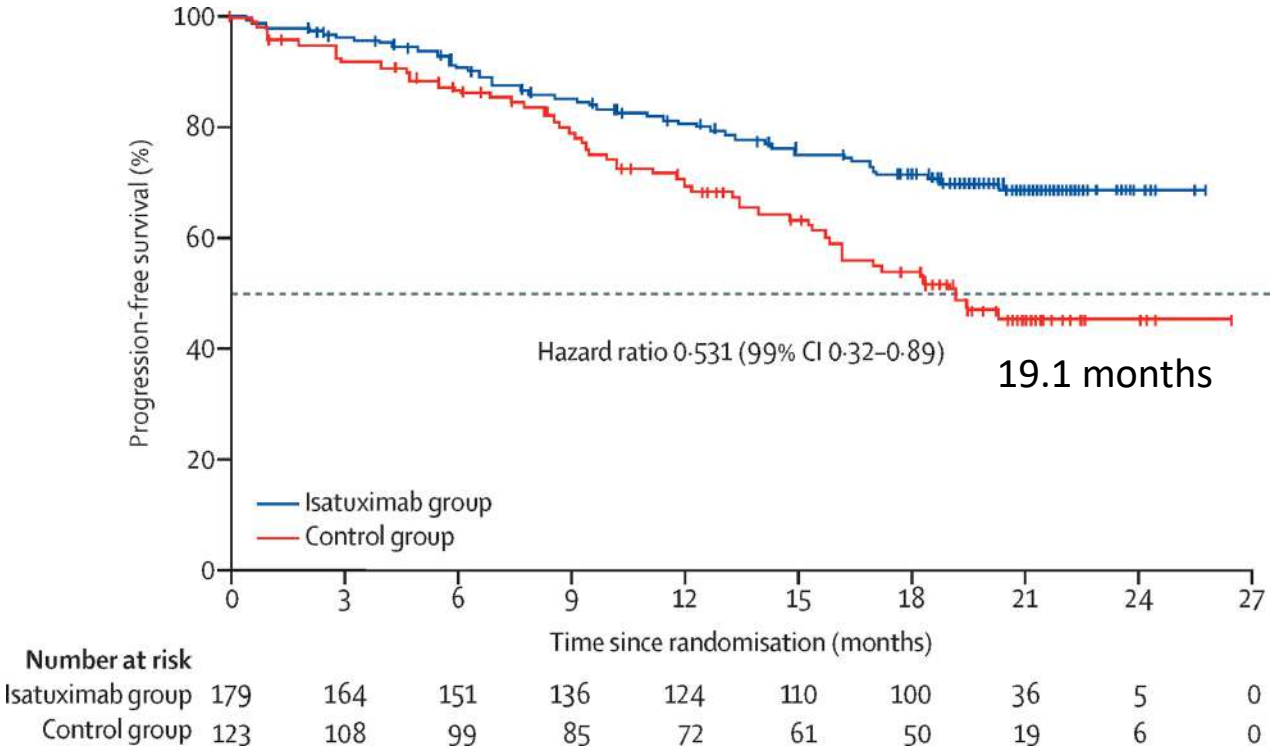


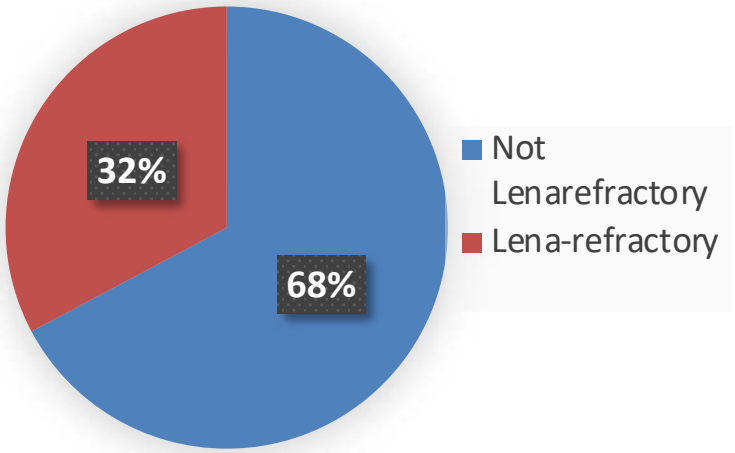
Isatuximab: 10 mg/kg on Days 1, 8, 15, 22 in cycle 1, then Q2W. Carfilzomib: 20 mg/m^2 on Days 1, 2; 56 mg/m^2 on Days 8, 9, Days 15, 16 in cycle 1; 56 mg/m^2 on Days 1, 2, 8, 9, 15, 16 in subsequent cycles. Dexamethasone: 20 mg on Days 1, 2, 8, 9, 15, 16, 22, 23 of each cycle of 28-day cycles.

- Primary endpoint: PFS by IRC
- Key secondary endpoints: ORR, ≥VGPR, MRD negativity, CR, OS, safety

Moreau. Lancet. 2021

IKEMA Trial: Isatuximab-Kd versus Kd





The Lancet 2021 3972361-2371DOI: (10.1016/S0140-6736(21)00592-4)

Highlights from IMW 2021

1-2 Febbraio 2022
Bologna
Royal Hotel Carlton

Isatuximab Plus Carfilzomib and Dexamethasone in Relapsed Multiple Myeloma Patients With High-Risk Cytogenetics: IKEMA Subgroup Analysis

P-217

Ivan Spicka[1], Philippe Moreau[2], Thomas G. Martin[3], Thierry Facon[4], Gracia Martinez[5], Albert Oriol[6], Youngil Koh[7], Andrew Lim[8], Gabor Mikala[9], Laura Rosiñol[10], Münci Yağci[11], Michele Cavo[12], Marie-Laure Risse[13], Gaëlle Asset[14], Sandrine Macé[13], Helgi van de Velde[15], Kwee Yong[16]

[1]1st Department of Medicine – Department of Hematology, First Faculty of Medicine, Charles University and General Hospital, Prague, Czech Republic; [2]University of Nantes, Nantes, France; [3]University of California San Francisco, San Francisco, CA, USA; [4]Department of Hematology, Lille University Hospital, Lille, France; [5]Hospital dos Clínicas de São Paulo, São Paolo, Brazil; [6]Hematology Department, Institut Català d'Oncologia and Josep Carreras Institute, Hospital Germans Trias i Pujol, Barcelona, Spain; [7]Department of Internal Medicine, Seoul National University Hospital, Seoul, Republic of Korea; [8]Austin & Repatriation Medical Center, Heidelberg, Victoria, Australia; [9]Department of Hematology and Stem Cell Transplantation, National Institute for Hematology and Infectious Diseases, South Pest Central Hospital, Budapest, Hungary; [10]Hospital Clínic, IDIBAPS, Barcelona, Spain; [11]Gazi University, Ankara, Turkey; [12]"Seràgnoli" Institute of Hematology, Bologna University School of Medicine, Bologna, Italy; [13]Sanofi R&D, Vitry-sur-Seine, France; [14]Sanofi R&D, Chilly-Mazarin, France; [15]Sanofi, Cambridge, MA, USA; [16]Department of Hematology University College Hospital, London, UK

- High-risk cytogenetics was assessed by central laboratory and patients were classified as high risk if abnormalities were present in ≥1 of the following: del(17p): 50% cut-off; t(4;14) and/or t(14;16): 30% cut-off
- In addition, assessment of gain(1q21) was defined as ≥3 copies: 30% cut-off. Amplification of 1q21 was also evaluated and was defined as ≥4 copies: 30% cut-off
- Median PFS and corresponding CIs were calculated by the Kaplan-Meier method. HR estimates were determined using the stratified Cox proportional hazard model
- Adverse events (AEs) were graded per the National Cancer Information Center Common Terminology Criteria for AEs (NCI-CTCAE) version 4.03

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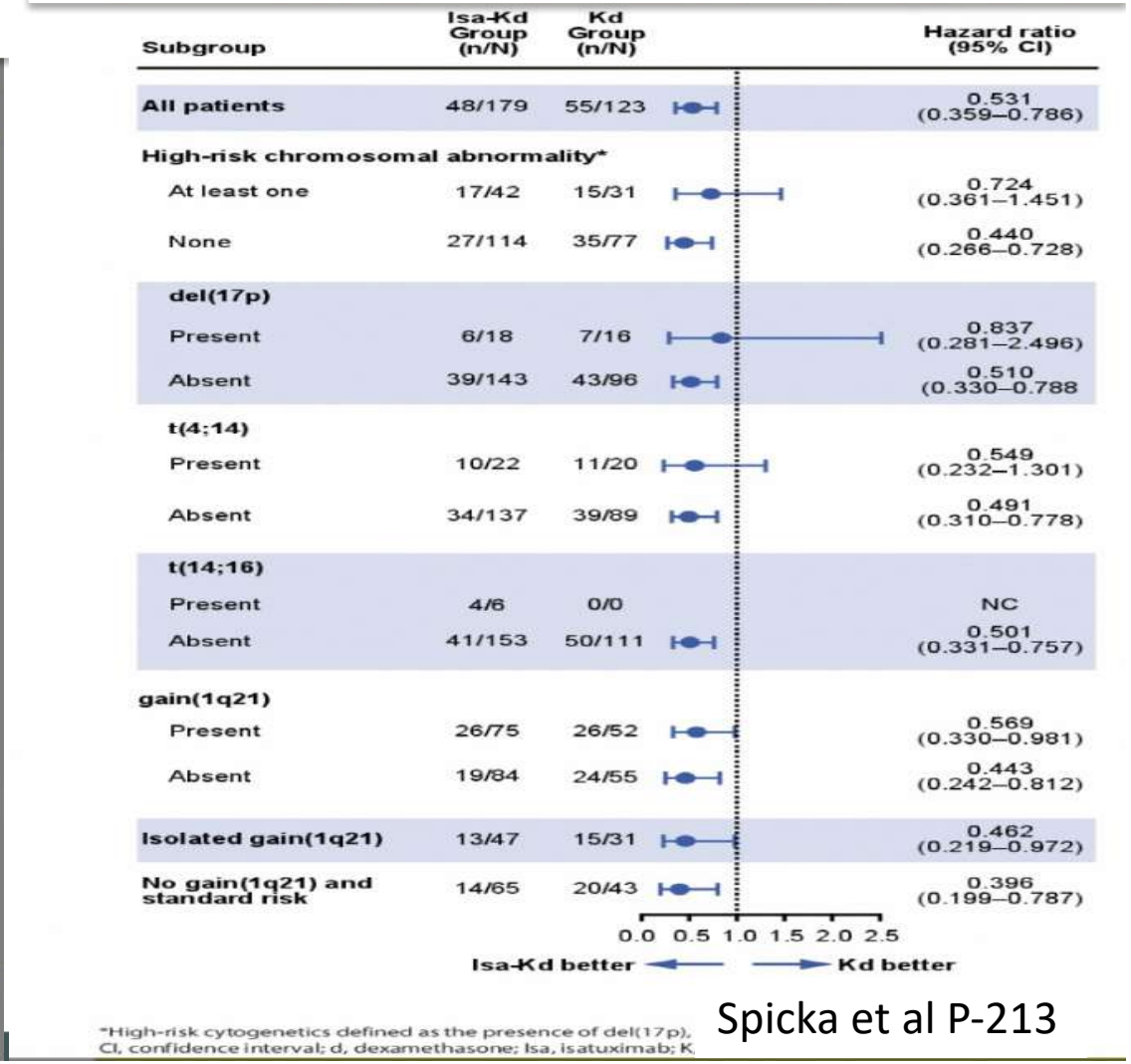
Patients characteristics

Patient characteristic	High risk		Standard risk	
	Isa-Kd (n=42)	Kd (n=31)	Isa-Kd (n=114)	Kd (n=77)
Age in years, median (range)	61.7 (37–83)	62.5 (38–80)	63.5 (38–86)	63.0 (33–90)
<65	23 (54.8)	17 (54.8)	54 (47.4)	41 (53.2)
≥65 to <75	15 (35.7)	10 (32.3)	50 (43.9)	30 (39.0)
≥75	4 (9.5)	4 (12.9)	10 (8.8)	6 (7.8)
ISS stage at study entry, n (%)				
Stage I	20 (47.6)	20 (64.5)	61 (53.5)	41 (53.2)
Stage II	15 (35.7)	6 (19.4)	37 (32.5)	21 (27.3)
Stage III	7 (16.7)	5 (16.1)	16 (14.0)	14 (18.2)
Unknown	0	0	0	1 (1.3)
R-ISS state at study entry, n (%)				
Stage I	0	0	45 (39.5)	33 (42.9)
Stage II	35 (83.3)	26 (83.9)	60 (52.6)	39 (50.6)
Stage III	7 (16.7)	5 (16.1)	8 (7.0)	3 (3.9)
Not classified	0	0	1 (0.9)	2 (2.6)
Cytogenetic risk* at study entry				
del(17p)				
Present	18 (42.9)	16 (51.6)	0	0
Absent	24 (57.1)	15 (48.4)	114 (100)	77 (100)
t(4;14)				
Present	22 (52.4)	20 (64.5)	0	0
Absent	20 (47.6)	10 (32.3)	114 (100)	77 (100)
t(14;16)				
Present	6 (14.3)	0	0	0
Absent	36 (85.7)	31 (100)	114 (100)	77 (100)
gain(1q21)				
Present	25 (59.5)	19 (61.3)	47 (41.2)	31 (40.3)
Absent	17 (40.5)	11 (35.5)	65 (57.0)	43 (55.8)
Unknown/missing	0	1 (3.2)	2 (1.8)	3 (3.9)
Prior lines of therapy, median (range)	1 (1–3)	2 (1–3)	2 (1–4)	2 (1–4)
Patients refractory to treatment				
Refractory to IMiD	16 (38.1)	13 (41.9)	52 (45.6)	37 (48.1)
Refractory to PI	14 (33.3)	12 (38.7)	34 (29.8)	25 (32.5)
Refractory to IMiD and PI	6 (14.3)	5 (16.1)	24 (21.1)	17 (22.1)
Refractory to last regimen	20 (47.6)	18 (58.1)	59 (51.8)	43 (55.8)

*High-risk status was defined as presence of del(17p), t(4;14), or t(14;16) by FISH. Cytogenetics was performed by a central laboratory with cut-off 50% for del(17p), 30% for t(4;14) and t(14;16). The cut-off for gain(1q21) was 30%
d, dexamethasone; IMiD, immunomodulatory drug; Isa, isatuximab; ISS, International Staging System; K, carfilzomib; PI, proteasome inhibitor; R-ISS, Revised International Staging System

Progression free survival across cytogenetic risk groups



*High-risk cytogenetics defined as the presence of del(17p), CI, confidence interval; d, dexamethasone; Isa, isatuximab; K,

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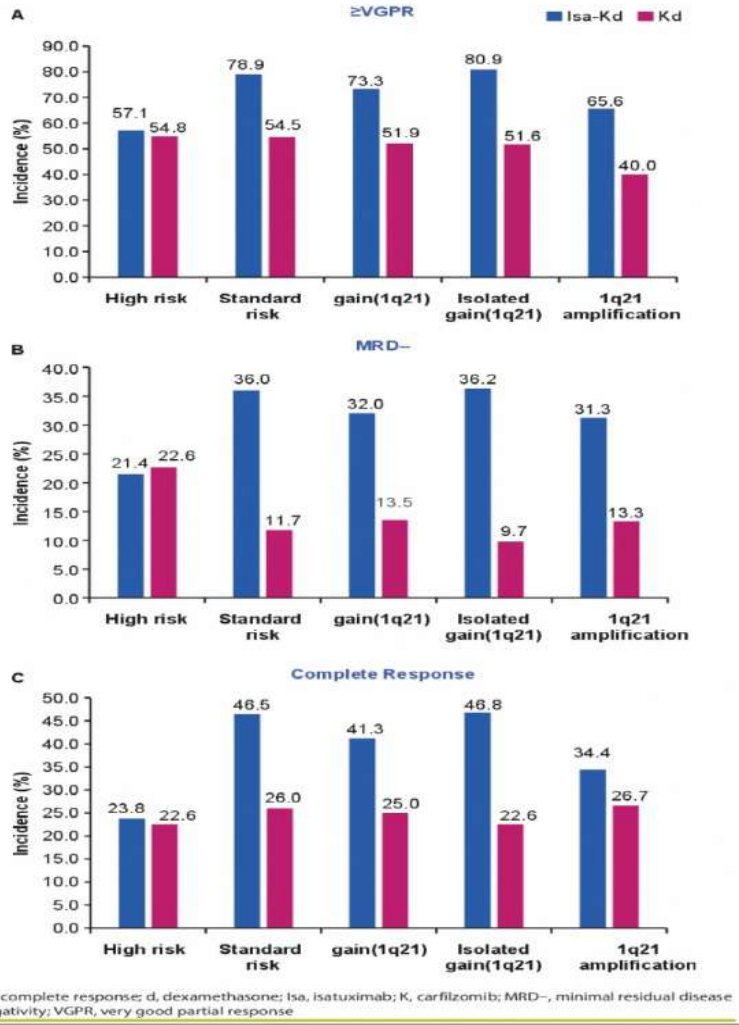
Figure 3. Improved depth of response with Isa-Kd vs Kd in patients with gain(1q21)



CR, complete response; d, dexamethasone; Isa, isatuximab; K, carfilzomib; MRD–, minimal residual disease negativity; VGPR, very good partial response

Safety

- Isa-Kd had a manageable safety profile in all subgroups (**Table 2**)
- Grade ≥3 TEAEs were more common with Isa-Kd vs Kd in patients with high-risk CA and in patients with gain(1q21); however, the incidence of serious TEAEs and TEAEs with fatal outcome during study treatment was similar in both arms for patients with high-risk CA
- Fewer patients treated with Isa-Kd vs Kd experienced TEAEs leading to definitive discontinuation among all cytogenetic risk groups
- Selected TEAEs are shown in **Table 3**

Table 2. Safety summary

	High risk		Standard risk		gain(1q21)	
	Isa-Kd (n=42)	Kd (n=30)	Isa-Kd (n=113)	Kd (n=77)	Isa-Kd (n=73)	Kd (n=51)
Patients with any TEAE	42 (100)	28 (93.3)	108 (95.6)	77 (100)	72 (98.6)	50 (98.0)
Patients with any Grade ≥3 TEAE	36 (85.7)	19 (63.3)	86 (76.1)	59 (76.6)	59 (80.8)	33 (64.7)
Patients with any Grade 5 TEAE*	0	0	5 (4.4)	4 (5.2)	3 (4.1)	1 (2.0)
Patients with any serious TEAE	27 (64.3)	20 (66.7)	65 (57.5)	46 (59.7)	45 (61.6)	28 (54.9)
Patients with any TEAE leading to definitive discontinuation	2 (4.8)	3 (10.0)	11 (9.7)	14 (18.2)	5 (6.8)	6 (11.8)

*TEAE with fatal outcome during the treatment period
d, dexamethasone; Isa, isatuximab; K, carfilzomib; TEAE, treatment-emerg

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Table 3. Selected TEAEs – safety population

	High risk				Standard risk				gain(1q21)			
	Isa-Kd (n=42)		Kd (n=30)		Isa-Kd (n=113)		Kd (n=77)		Isa-Kd (n=73)		Kd (n=51)	
Selected TEAEs by SOC or SMQ or PT, n (%)	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
Infections and infestations (SOC)	35 (83.3)	15 (35.7)	23 (76.7)	8 (26.7)	98 (86.7)	46 (40.7)	67 (87.0)	24 (31.2)	65 (89.0)	30 (41.1)	42 (82.4)	12 (23.5)
Upper respiratory tract infection	16 (38.1)	2 (4.8)	2 (6.7)	1 (3.3)	41 (36.3)	4 (3.5)	23 (29.9)	1 (1.3)	29 (39.7)	3 (4.1)	12 (23.5)	2 (3.9)
Pneumonia	12 (28.6)	7 (16.7)	8 (26.7)	2 (6.7)	25 (22.1)	19 (16.8)	12 (15.6)	11 (14.3)	17 (23.3)	15 (20.5)	9 (17.6)	5 (9.8)
Bronchitis	9 (21.4)	0	6 (20.0)	0	26 (23.0)	4 (3.5)	7 (9.1)	0	15 (20.5)	1 (1.4)	3 (5.9)	0
Others												
Hypertension	13 (31.0)	9 (21.4)	6 (20.0)	2 (6.7)	45 (39.8)	25 (22.1)	31 (40.3)	22 (28.6)	27 (37.0)	16 (21.9)	12 (23.5)	10 (19.6)
Infusion-related reaction	23 (54.8)	1 (2.4)	0	0	44 (38.9)	0	4 (5.2)	0	33 (45.2)	1 (1.4)	2 (3.9)	0

d, dexamethasone; Isa, isatuximab; K, carfilzomib; PT, MedDRA preferred term; SMQ, standardized MedDRA query; SOC, system organ class; TEAE, treatment-emergent adverse event

CONCLUSIONS

- The addition of Isa to Kd improved PFS in patients with high-risk CA [del(17p), t(4;14), and/or t(14;16)] and improved PFS and depth of response in patients with 1q21 gain or amplification, with a manageable safety profile, which was consistent with the benefit observed in the overall IKEMA population
- Isa-Kd is a new treatment option for the difficult-to-treat subgroup of patients with RMM and high-risk cytogenetics

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Highlights from IMW 2021

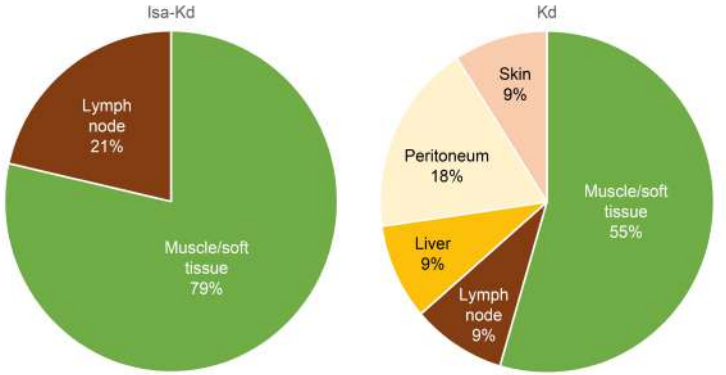
1-2 Febbraio 2022
Bologna
Royal Hotel Carlton

Isatuximab Plus Carfilzomib and Dexamethasone in Patients With Relapsed Multiple Myeloma and Soft-Tissue Plasmacytomas: IKEMA Subgroup Analysis

Patients and treatment exposure

- At study entry, 19 (6.3%) patients had soft-tissue plasmacytomas as per IRC: 12/179 (6.7%) had Isa-Kd and 7/123 (5.7%) had Kd
- The median (range) number of cycles was 10.5 (1–21) in the Isa-Kd arm versus 8.0 (1–20) in the Kd arm
- The overall median (range) duration of exposure was 41.9 (2–87) weeks for Isa-Kd versus 29.9 (4–83) for Kd

Figure 2. Localization of plasmacytomas in each study arm in patients with soft-tissue plasmacytomas



Patients with plasmacytomas at multiple locations were counted separately for each location
d, dexamethasone; Isa, isatuximab; K, carfilzomib

RESULTS

Table 2. Efficacy of Isa-Kd vs Kd in patients with relapsed MM and pre-existing soft-tissue plasmacytomas

Outcome	Isa-Kd (n=12)	Kd (n=7)
Median PFS, months (95% CI)	18.76 (4.435–NC)	NC (0.986–NC)
	HR[a] = 0.574 (0.125–2.640)	
ORR (sCR, CR, VGPR or PR)	6 (50.0)	2 (28.6)
VGPR or better	4 (33.3)	1 (14.3)
MRD negativity rate[b]	4 (33.3)	1 (14.3)
Complete response (sCR or CR)	3 (25.0)	0
MRD negativity[b] and complete response (sCR or CR)	3 (25.0)	0

Data are n (%) unless otherwise specified
[a]Derived using unstratified Cox proportional hazard model with treatment as covariate
[b]For analysis purposes, subjects in the ITT population but without MRD assessment will be considered MRD-positive
CI, confidence interval; CR, complete response; d, dexamethasone; HR, hazard ratio; Isa, isatuximab; ITT, intent-to-treat; K, carfilzomib; MRD, minimal residual disease; ORR, overall response rate; PFS, progression-free survival; PR, partial response; sCR, stringent complete response; VGPR, very good partial response

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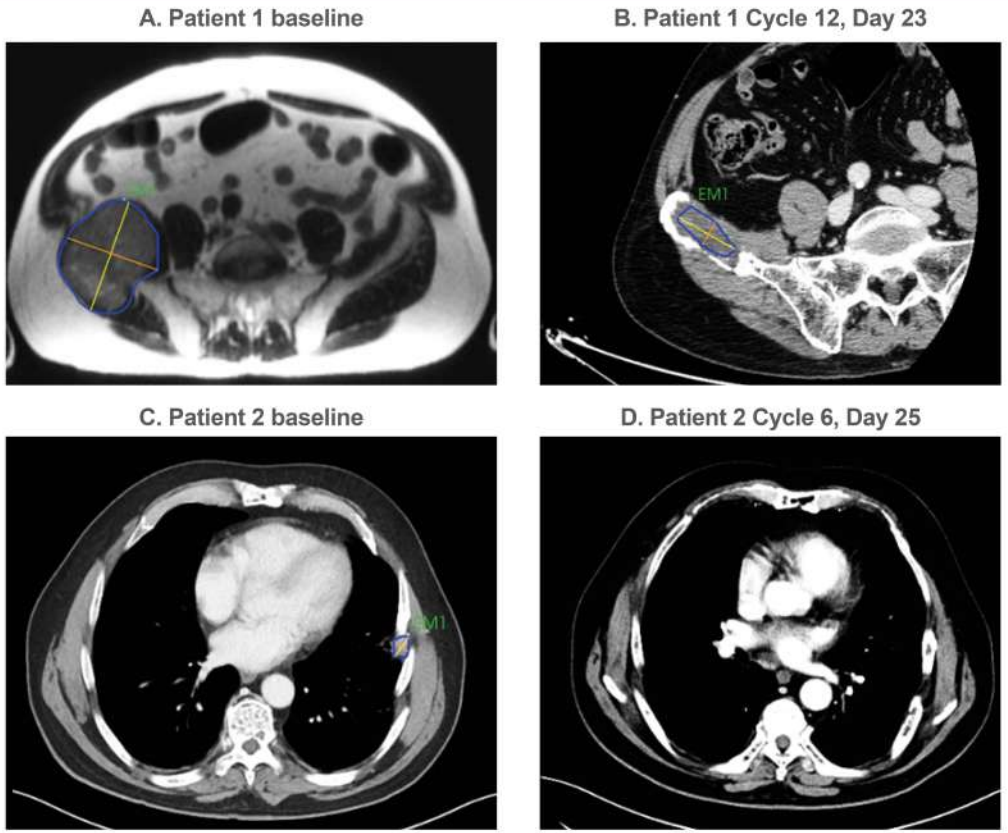
RESULTS

Radiological imaging of Isa-Kd-induced responses: Examples

- Two patients in the Isa-Kd arm presented with a plasmacytoma in the muscle soft-tissue at baseline. Patient 1 had 88% shrinkage in plasmacytoma versus baseline at Cycle 12, Day 23 (**Figure 3A–B**). His best overall response was a partial response. Patient 2 showed no measurable lesion versus baseline at Cycle 6, Day 25 (**Figure 3C–D**) and his best overall response was a complete response

Figure 3. CT scans at baseline and during treatment for two patients receiving Isa-Kd



CT, computed tomography; d, dexamethasone; Isa, isatuximab; K, carfilzomib

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CONCLUSIONS

- In 19 patients with relapsed MM and plasmacytomas, Isa-Kd improved PFS and depth of response compared with Kd alone, with a manageable safety profile, consistent with the benefit observed in the IKEMA study overall population
- In the Isa-Kd arm, the ORR in patients with plasmacytomas was lower than that in the overall IKEMA population; however, MRD negativity rates (33.3% and 29.6%), and CR with MRD negativity rates (25.0% and 20.1%) were similar to those observed in the overall population, respectively

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