2024:

È già ora di abbandonare la **chemioterapia** nella **malattia recidivata/refrattaria?**

Napoli, Hotel Paradiso • 29–30 aprile 2024

Caratteristiche clinico/biologiche della malattia R/R. L'importanza della I linea effettuata

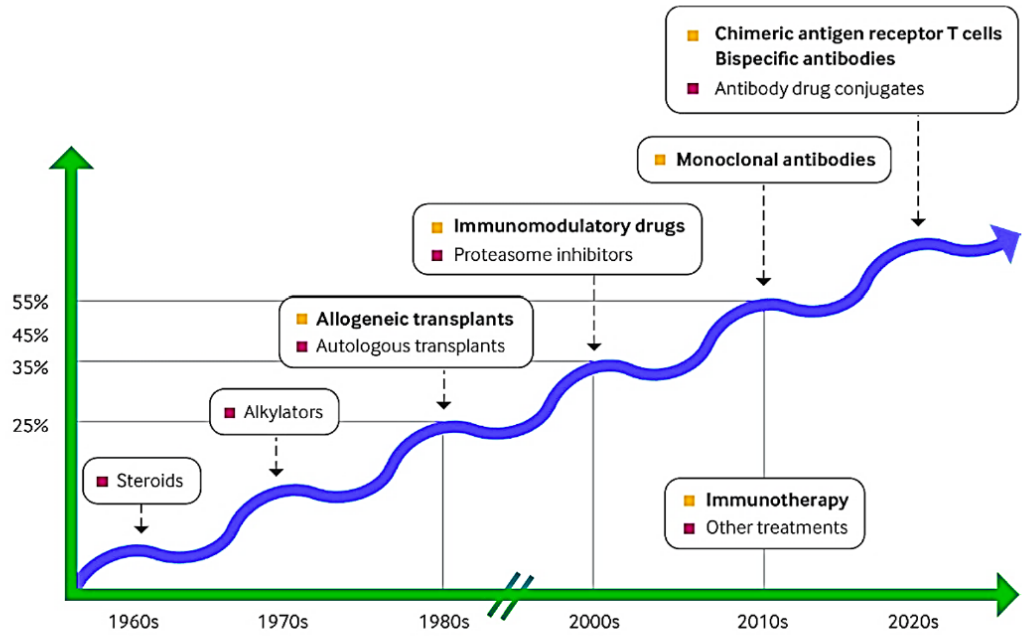
Dott. Ferdinando Frigeri

Disclosures of Ferdinando Frigeri

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
CELGENE					X	X	
JANSSEN-CILAG					X	X	
BMS					X	X	
GSK					X	X	
ABBVIE					X	X	
RECORDATI - EUSAPHARMA					X	X	
NOVARTIS					X	X	
ASTRAZENECA					X	X	
SOBI					X	X	
INCYTE					X	X	
GILEAD					X	X	
ELI LILLY					X		
TEVA - GENTILI					X	X	

Treatment Overview

Relative Survival at 5 Years (%), Based on Year of Diagnosis



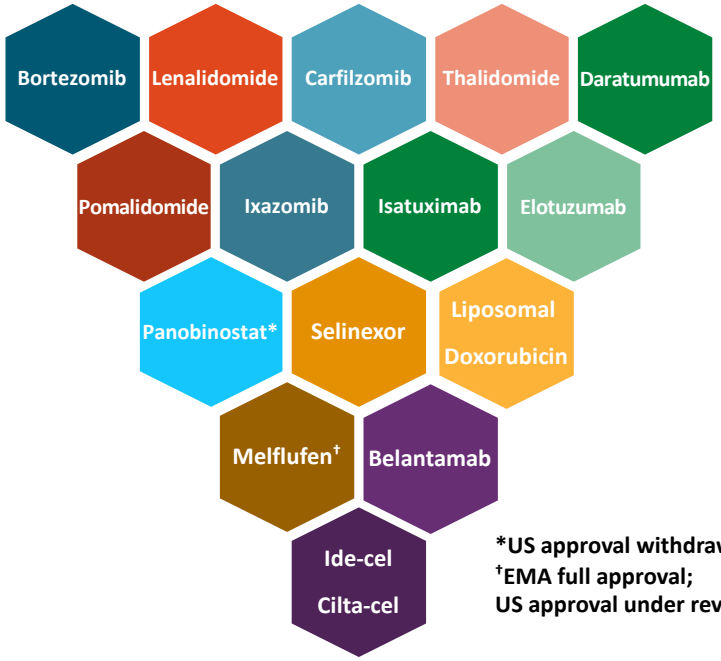
Timeline of drug discovery and year of multiple myeloma diagnosis (by decade)

- New treatments have been emerging to cover the complexity of the disease
- Significant improvement in OS

Mateos MV, personal communication. Image reproduced from Shah UA, et al. *BMJ*. 2020;370:m3176. Moreau P, et al. *Ann Oncol*. 2017;28(Suppl 4):iv52-61.

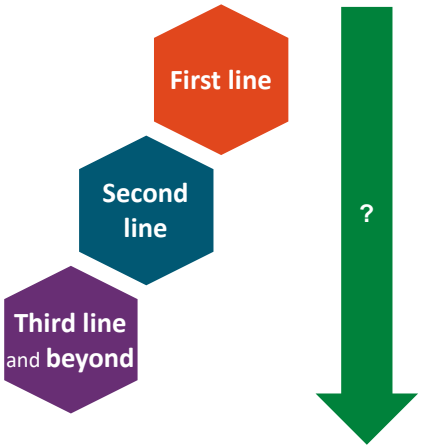
Multiple Novel Agents Now Available to Treat Newly Diagnosed and Relapsed/Refractory Myeloma in 2022

Previously up to 16 but now 14 approved novel agents in MM—with more coming



*US approval withdrawn.
†EMA full approval;
US approval under review.

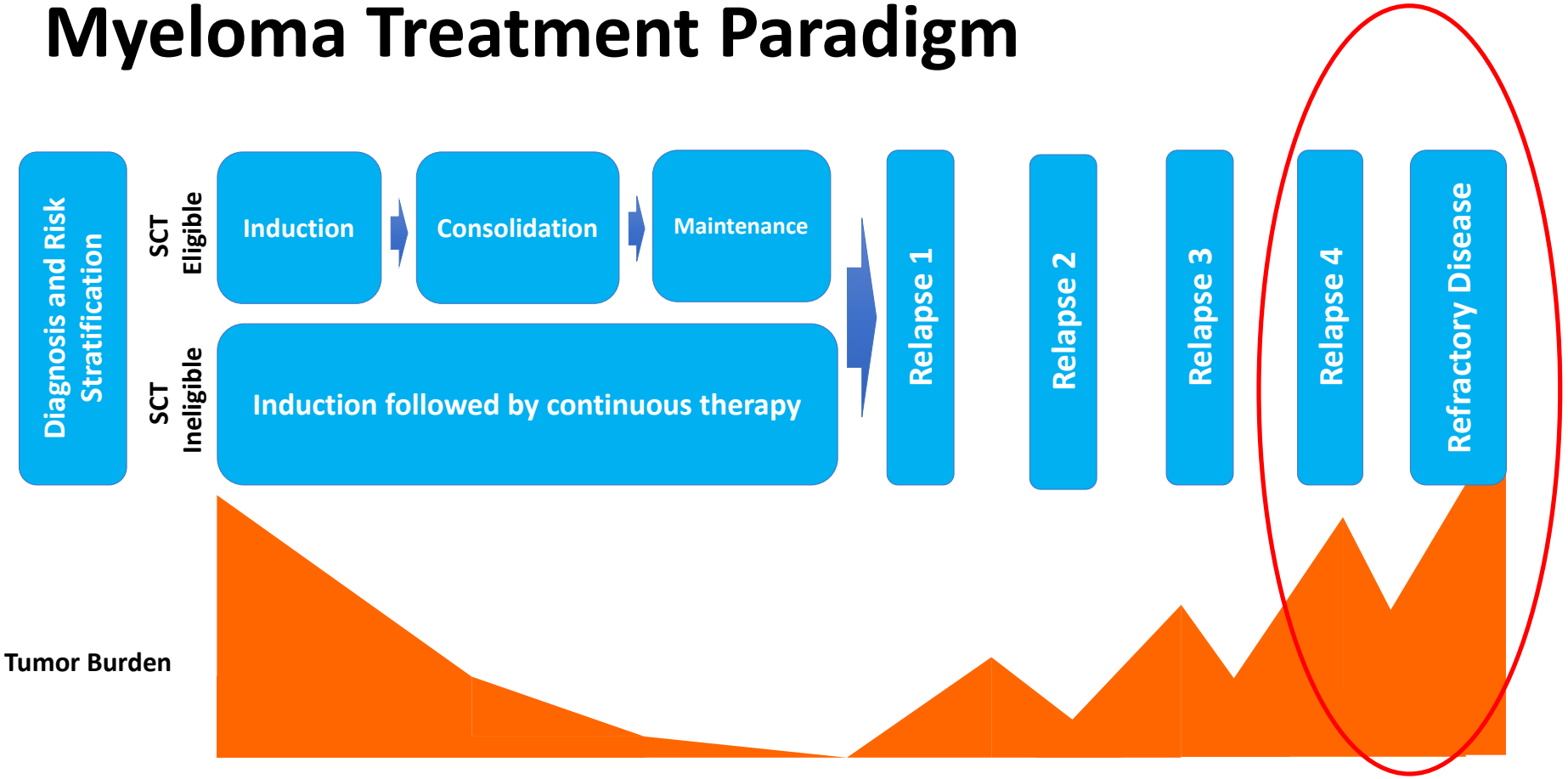
How do we sequence and strategize therapies to ensure the best outcomes for our patients?



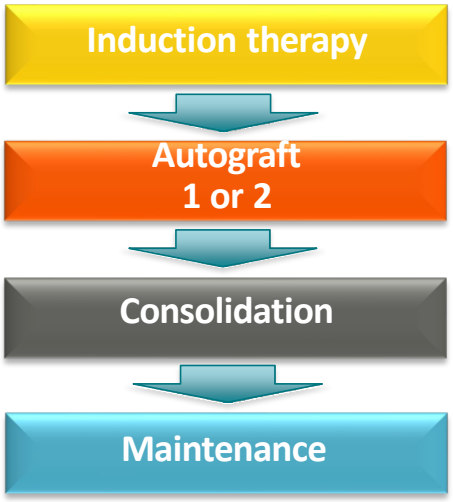
Adapted from Laubach. Leukemia. 2016;30:1005. Moreau. Lancet Oncol. 2021;22:e105.

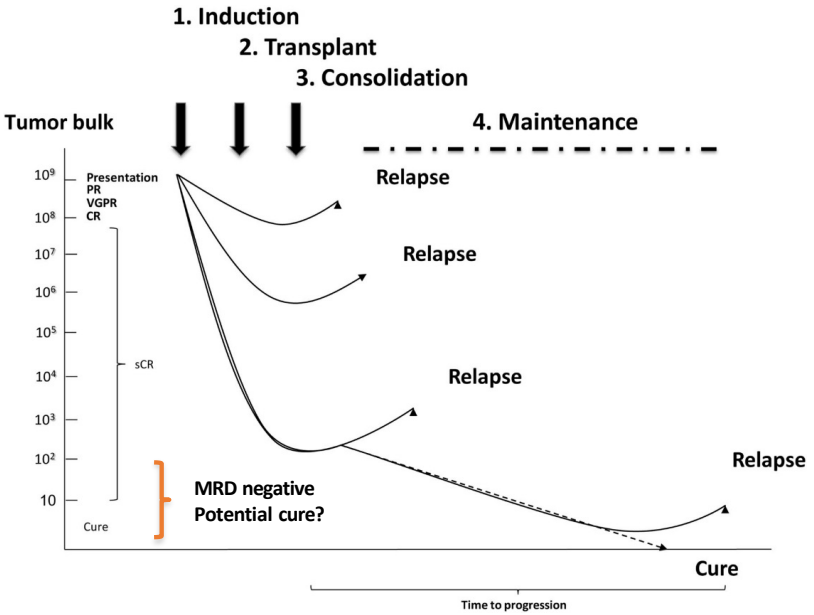
Slide credit: clinicaloptions.com

Myeloma Treatment Paradigm



Treatment paradigm for autotransplant-eligible patients

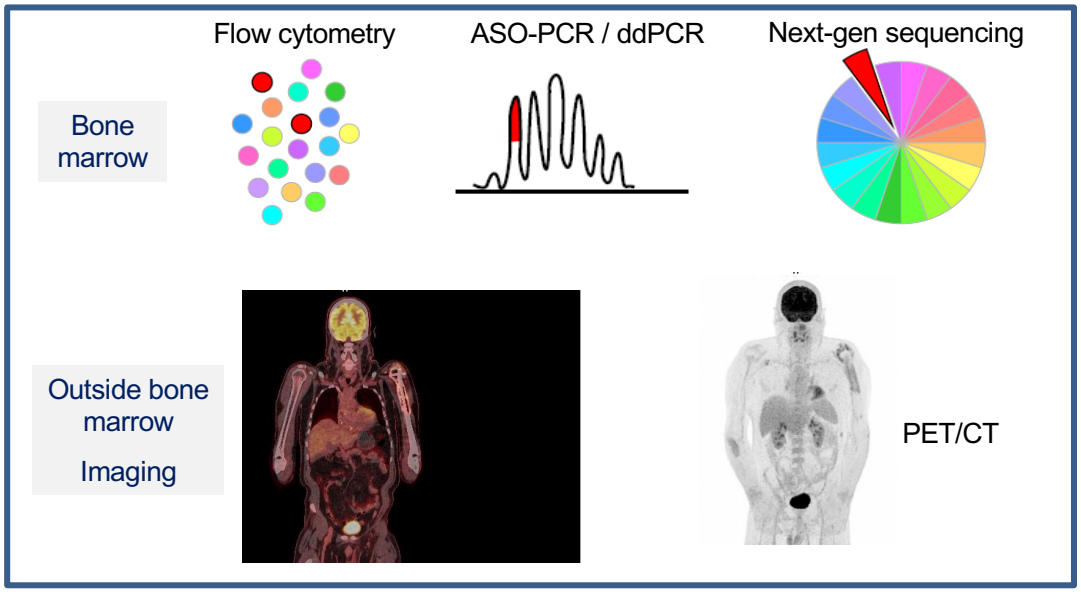




- maximize the speed and depth of tumour burden reduction
- quickly reverse disease-related complications
- prolong disease control

Cavo M, et al. Blood 2011;117(23):6063-73
Cavo M, et al. Blood 2012;120(1):9-19
Morgan GJ, et al. Blood. 2013;122(8):1332-4
Kumar S, et al. Lancet Oncology 2016;17:e328-46

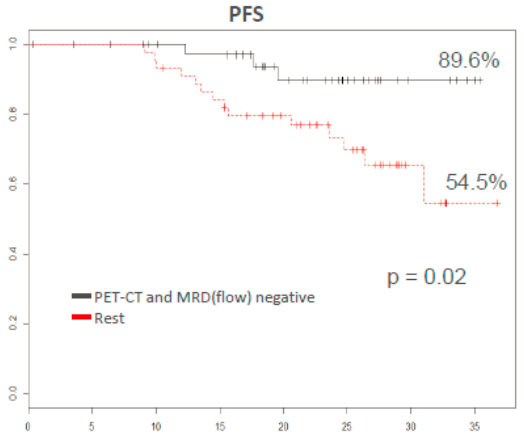
MRD



- 86 subjects with paired PET-CT and MRD(flow) data

	PET-CT pos	PET-CT neg
MRD pos	11	20
MRD neg	14	41

Fisher exact test: p = 0.33
McNemmar test: p = 0.39



Improved outcome for double negative subjects

Adapted from Moreau et al. Blood 2015;126: abstract 395

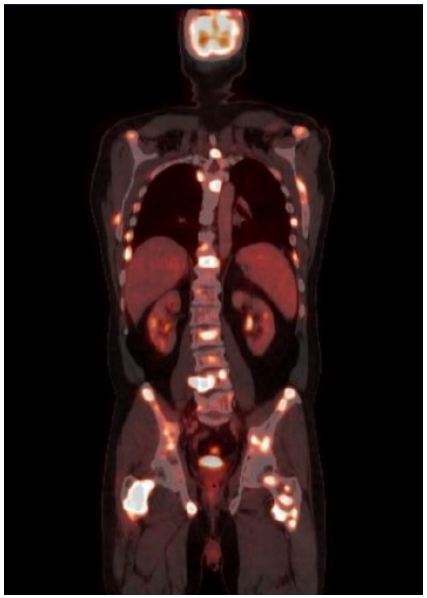
PET/CT imaging used as a confirmatory test in patients who are MRD negative by MFC or NGS[1]

^{18}F-FDG PET allows for ability to determine tumor metabolic activity assessment[2]

Low-dose CT typically done for localization along with ^{18}F-FDG PET is a sensitive screen for MM-associated bone disease[2]

Detects extramedullary disease with involvement of soft tissue or major organs in up to 10% of patients[2]

PET/CT Image of a Patient with Multiple Myeloma



Advantages[3]:

- Potentially powerful tool that complements MRD evaluation by NGF or NGS by detecting pockets of residual cells missed by sampling

Disadvantages[3]:

- Lack of standardization
  - High variability between sites
  - False negatives and false positives
- Only applicable in ~75% of patients
- Limited availability
- High costs
- Further clinical trial evaluation is needed

18F-FDG, 18-fluorine-fluoro-deoxyglucose; PET, positron-emission tomography; CT, computed tomography; MFC, multiparameter flow cytometry.
Image adapted from http://www.myelomapennstate.net/Contents/10a-BoneDis-PET.htm. Accessed 17 April 2018.
1. Yanamandra U, Kumar SK. *Leuk Lymphoma*. 2017;11:1-13. 2. Kumar S, et al. *Lancet Oncol*. 2016;17:e328-e346. 3. Cavo M, et al. *Lancet Oncol*. 2017;18(4):e206-e217.

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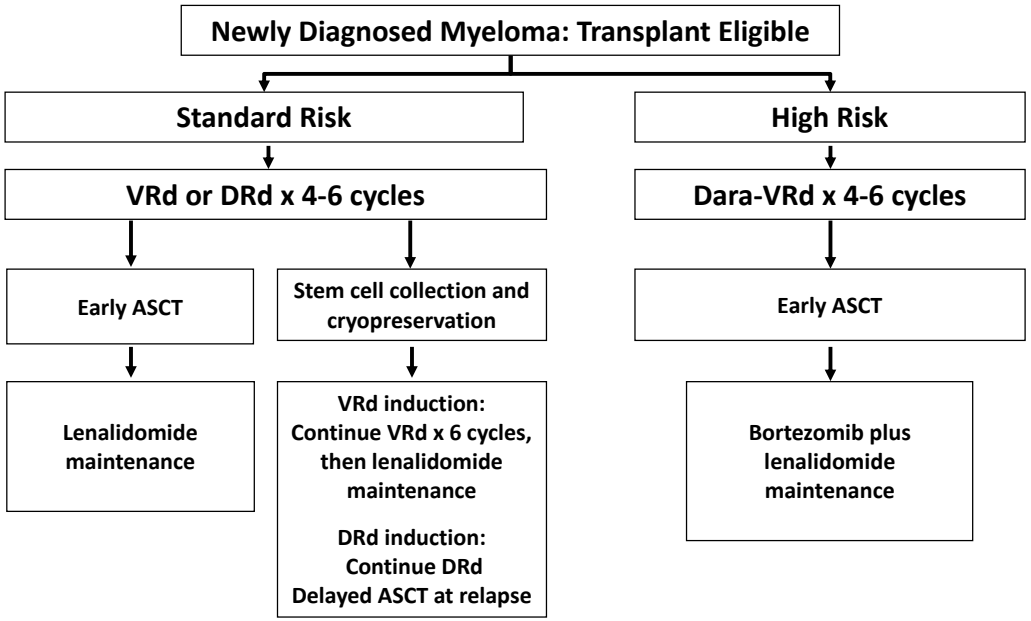
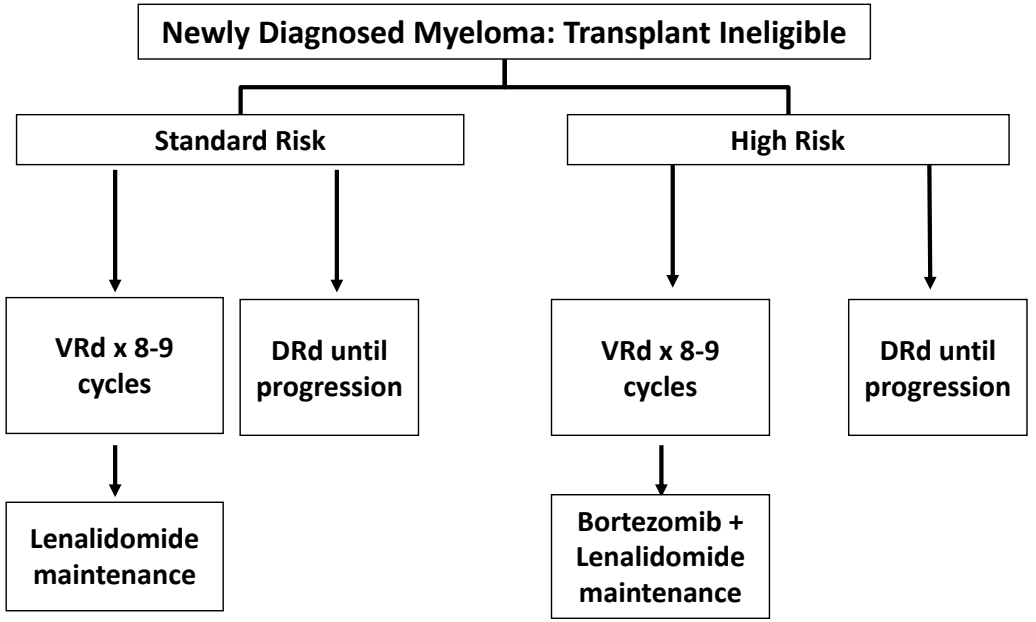
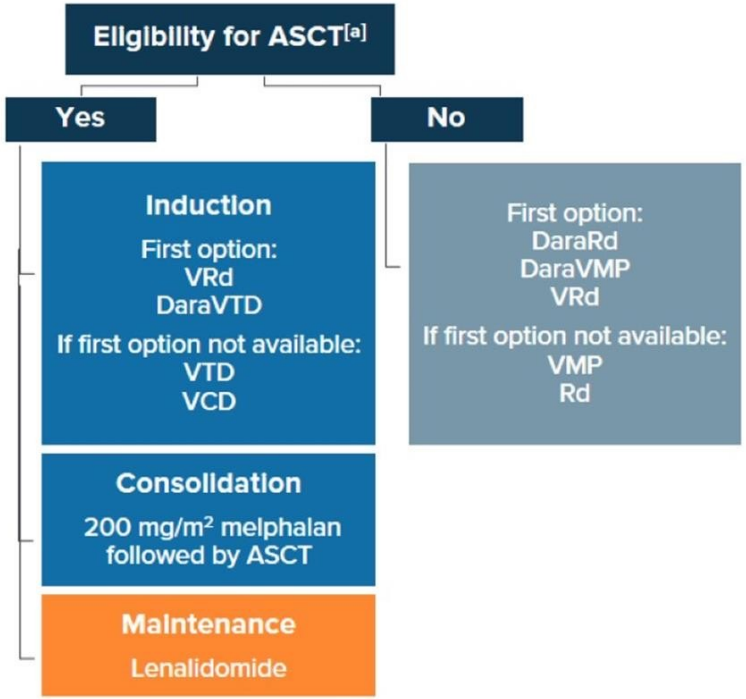




Rajkumar SV, Am J Hematol 2022

EHA-ESMO Guidelines for NDMM Management, 2021

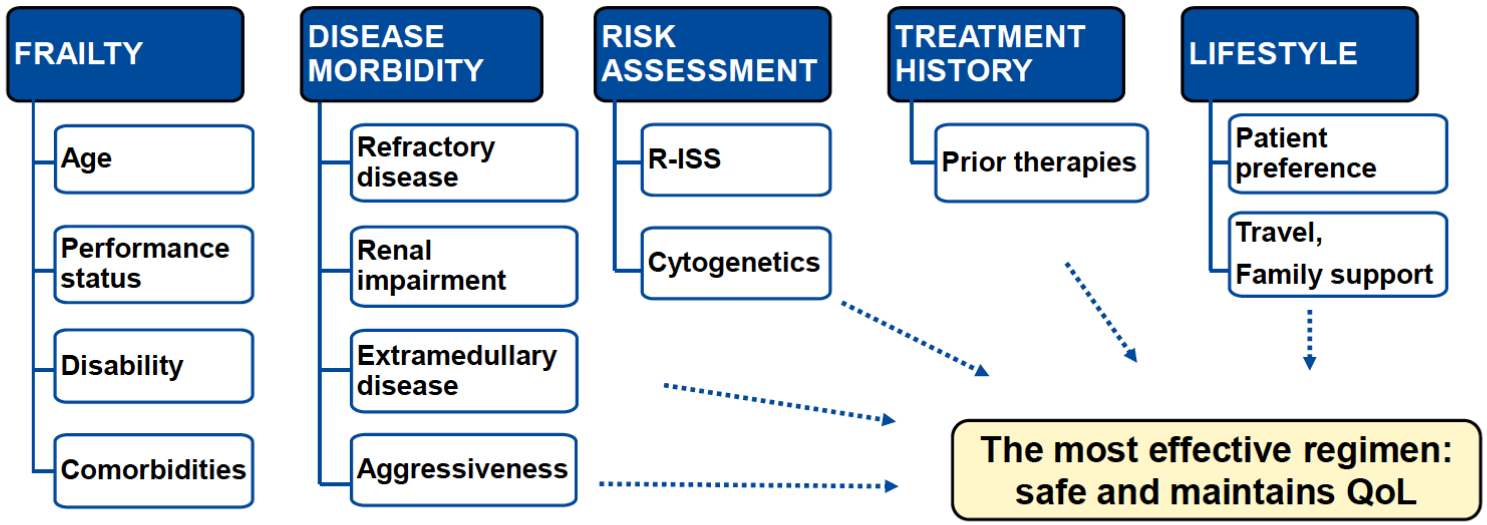


ASCT, autologous stem cell transplantation; Dara, daratumumab; NDMM, newly diagnosed MM; Rd, lenalidomide plus low-dose dexamethasone; VCD, bortezomib, cyclophosphamide, and dexamethasone; VMP, bortezomib, melphalan, and prednisone; VRd, lenalidomide plus low-dose dexamethasone plus bortezomib; VTD, bortezomib, thalidomide, and dexamethasone.
Dimopoulos MA, et al. Ann Oncol. 2021;32:309-322.

Most patients will receive lenalidomide as part of first-line therapy and progress while on it

Dimopolous MA et al, Annals of Oncology 2021

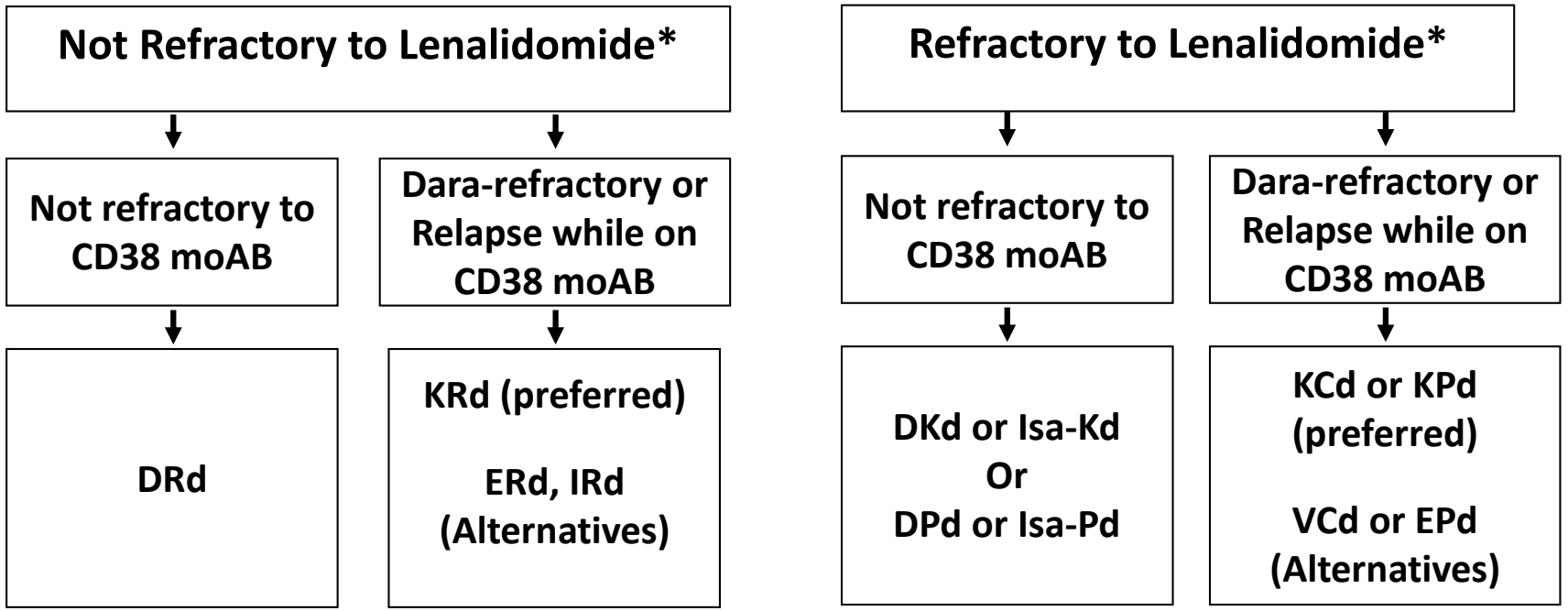
Disease and Patient Factors Influence Treatment Choices in Relapsed/Refractory Myeloma



QoL, quality of life.

Chen X, et al. *Clin Interv Aging*. 2014;9:433-441. Chng WJ, et al. *Leukemia*. 2016;30(5):1071-1078. Chung T-H, et al. *PLoS One*. 2013;20:e66361. Clegg A, et al. *Lancet*. 2013;381(9868:752-762. Faiman BM, et al. *Clin J Oncol Nurs*. 2011;15(suppl):66-76. Greipp PR, et al. *J Clin Oncol*. 2005;23(15):3412-3420. Handforth C, et al. *Ann Oncol*. 2015;26(6):1091-1101. Jhaveri M, et al. *Haematologica*. 2016;101(suppl 1):E1312. Merz M, et al. *Haematologica*. 2016;101(suppl 1):P650. Miceli TS, et al. *Clin J Oncol Nurs*. 2011;15(suppl):9-23. Palumbo A, et al. *Blood*. 2015;125(13):2068-2074. Ramsenthaler C, et al. *BMC Cancer*. 2016;16:427. Sonneveld P, et al. *Leukemia*. 2013;27(10):1959-1969. Tatarczuch M, et al. *Haematologica*. 2017;102(suppl 2):E1457. Williams LA, et al. *J Clin Oncol*. 2016;34:e18127.

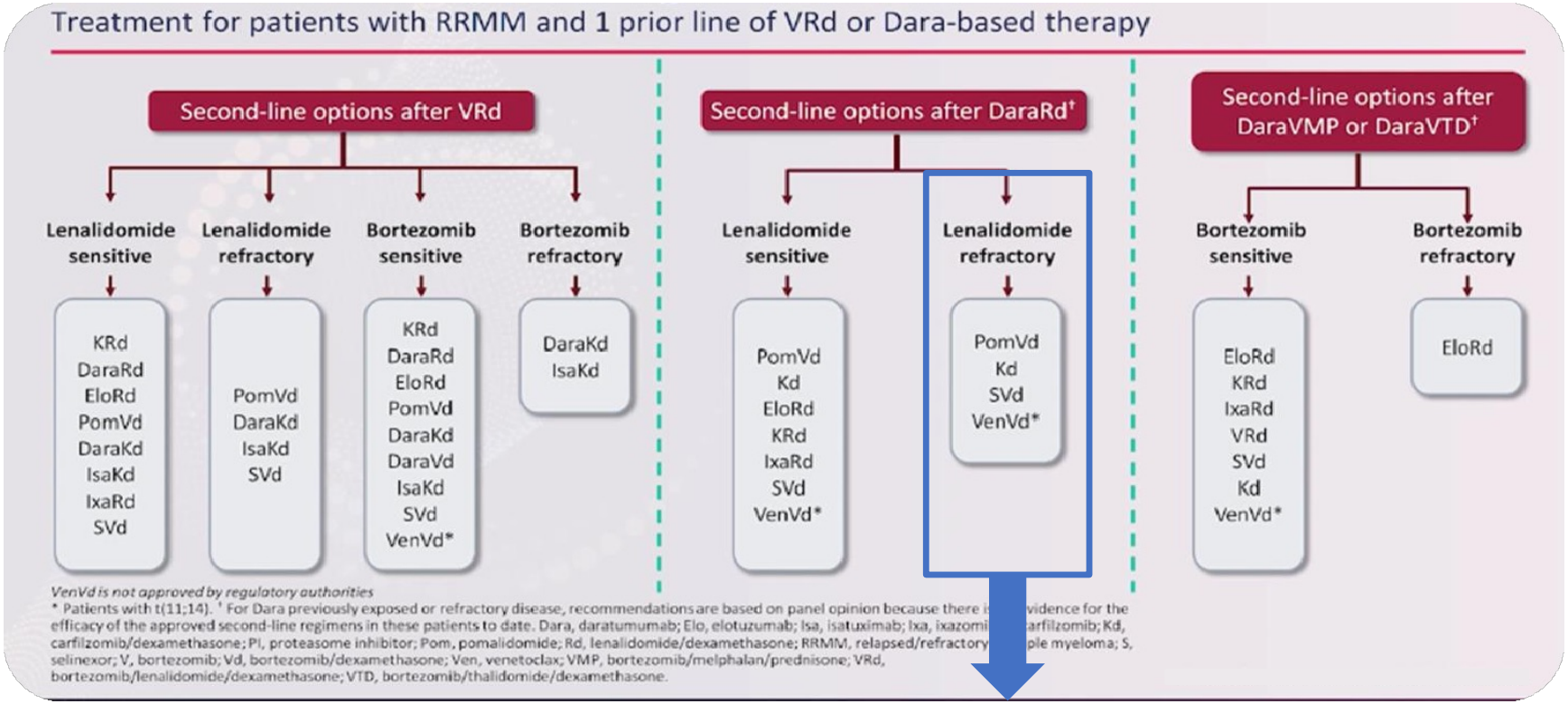
First Relapse



*Consider salvage ASCT in patients eligible for ASCT who have not had transplant before;
Consider 2nd auto SCT if eligible and had >36 months response duration with maintenance to first ASCT

Rajkumar SV, Am J Hematol 2022

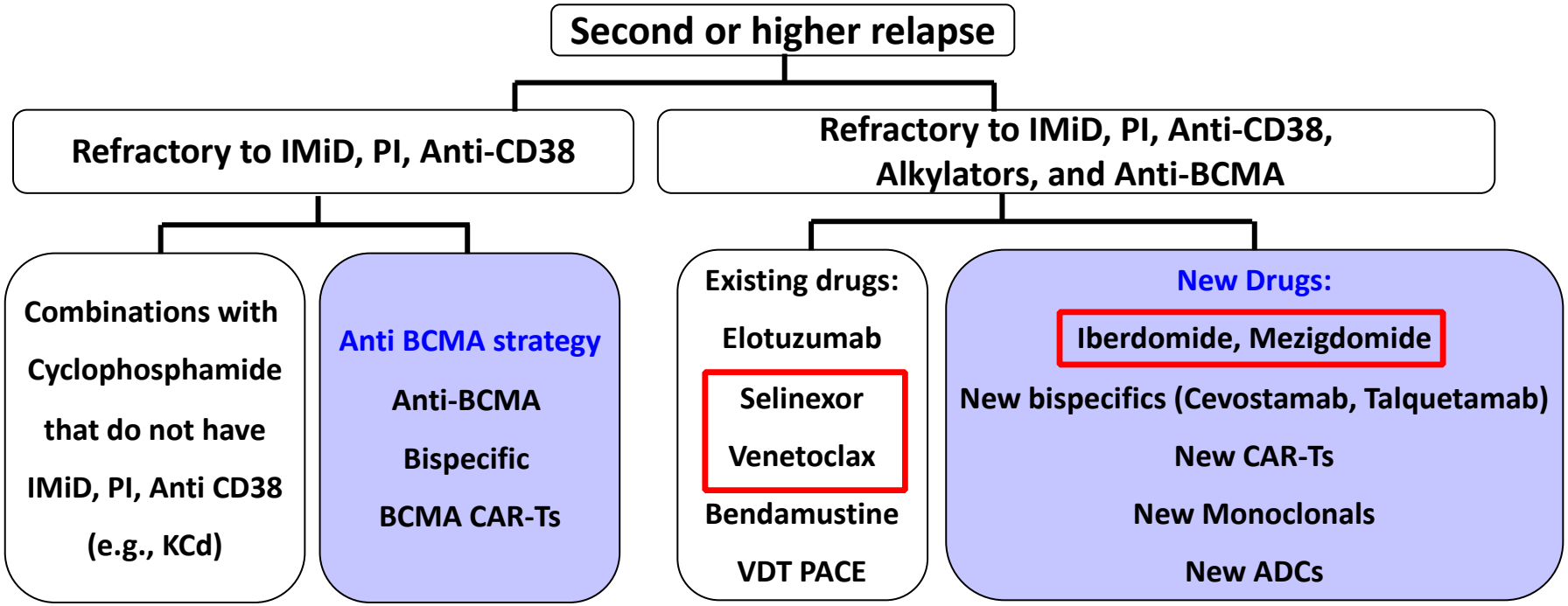
EHA-ESMO clinical practice guidelines 2021: first relapse



2L Treatments for Lena refractory

Dimopolous MA et al, Annals of Oncology 2021

Myeloma: Second or higher relapse



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What Is Refractoriness to Therapy?

- Refractory MM is defined as disease that is:
  - ✓ Non-responsive while on primary or salvage therapy
  - ✓ OR progresses within 60 days of last therapy
- Non-responsive disease is defined as failure to achieve minimal response or progressive disease on therapy
- Can be primary refractory or relapsed/refractory

Definition of Lenalidomide-Refractory MM

Lenalidomide refractory is not well defined, with some issues

Biochemical relapse from 10 mg maintenance vs 25 mg

Relapse after 4 mo of maintenance vs 4 y

Biochemical relapse after 4 y of Rd vs symptomatic relapse after 6 mo of Rd

Moreau P, et al. Blood Cancer J. 2019;9:38.

Definition of Lenalidomide-Refractory MM and re-treatment

Lenalidomide maintenance

Salvage therapy listed in 2 of 3 studies of meta-analysis: no data on Lena dose increase ± Dex

Myeloma XI trial: data on salvage therapy are lacking

Insufficient data on full-dose Lena + Dex retreatment after maintenance Lena 10 mg

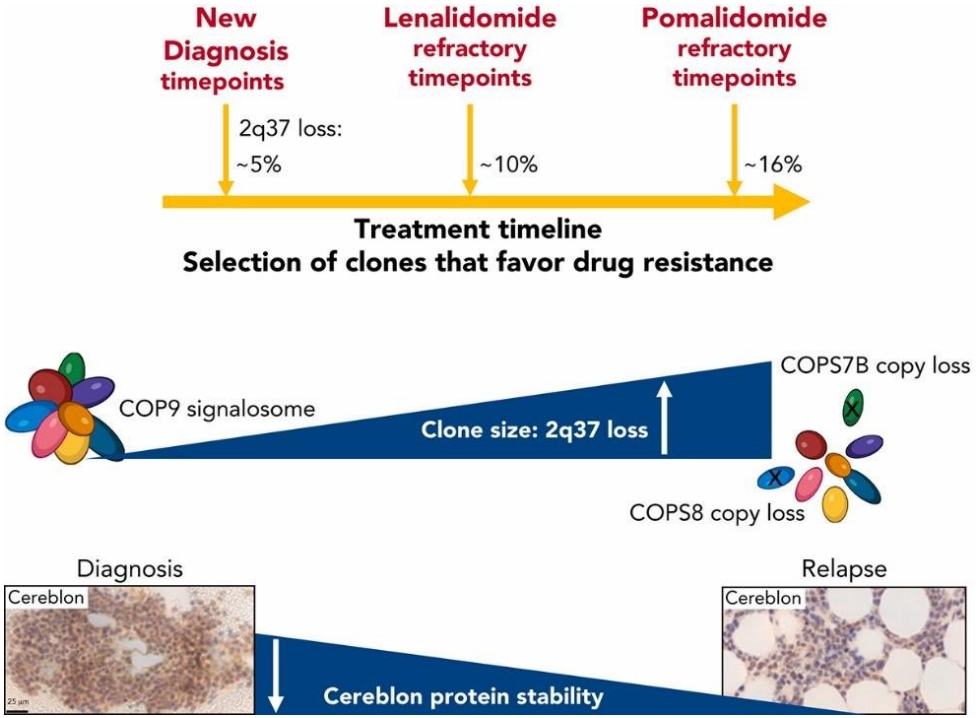
Lenalidomide full-dose

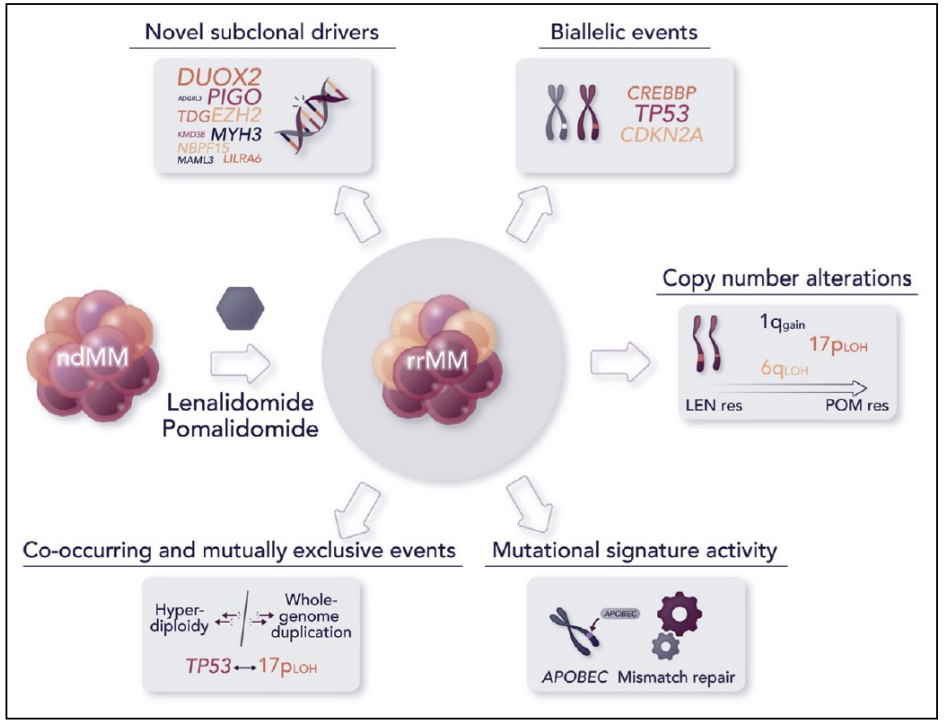
No patients Lena-refractory included in phase III trials containing Lena such as KRd, EloRd, DaraRd, IxaRd

Insufficient data on full-dose Lena retreatment plus other drugs after first relapse

Moreau P et al, Blood Cancer Journal 2019

Loss of COP9 signalosome genes at 2q37 is associated with IMiDs resistance in multiple myeloma





Major findings from the novel study by Ansari-Pour et al include the discovery of novel abnormalities associated with refractoriness to IMiDs and significant changes in the recurrence of high-risk alterations from diagnosis to relapse. Professional illustration by Somersault18:24.

Sarah Gooding et al, Blood 2022

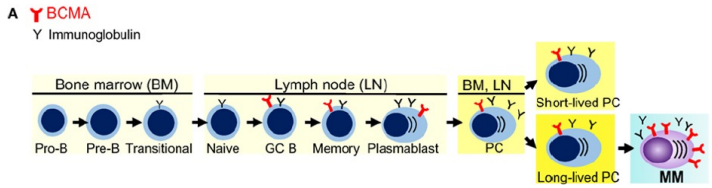
Alessandro Laganà, Blood 2023

Efficacy of 2L Options for R-Refractory Patients - *Phase III Trials*

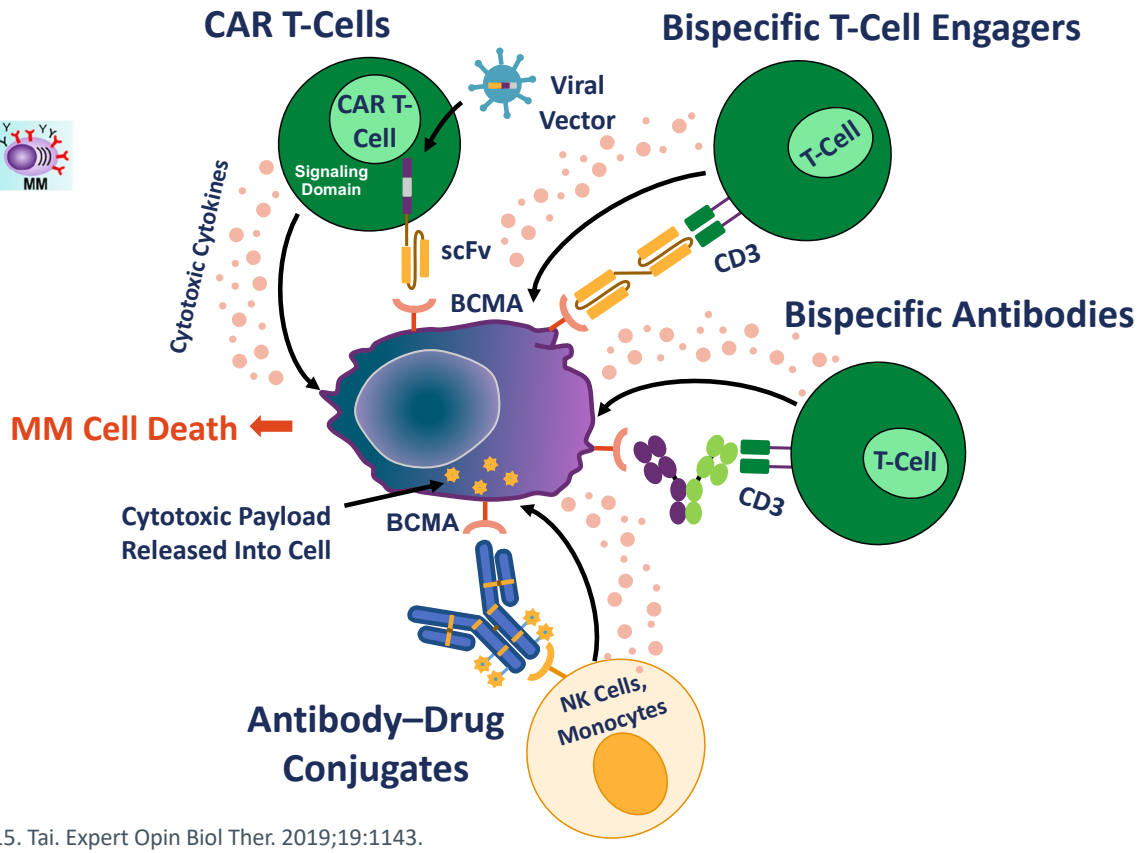
	CASTOR DVd (251)	ENDEAVOR Kd (464)	OPTIMISMM PVd (281)	APOLLO DPd (151)	CANDOR* DKd (312)	IKEMA IsaKd (179)
No of median prior lines	2	2	2	2	2	2
Len-refractory %	**24**	**24**	**71**	**79**	**32**	**32**
≥ CR (%)	**30**	**13**	**16**	**25**	**33**	**44**
NGS MRD neg$^{10\text{-}5}$ ITT (%)	15	NA	NA	9	23	33.5
mPFS ITT **HR**	**17** 0.31	**19** 0.53	**11** 0.61	**12.4** 0.63	**29** 0.59	**35.7** 0.58
mPFS 1PLoT HR	27 0.22	22 0.45	21 0.54	14.1 0.67	NR 0.66	**38.2** 0.72
mPFS Len-refr **HR**	**8** 0.44	**9** 0.36	**9.5** 0.65	**9.9** 0.64	**28** 0.46	**NR** 0.59
mPFS early relapse HR	**15.4** 0.51	**13.9** 0.59	NA	NA	NA	**24.7** 0.66

Anti-CD38 based regimens (DKd not reimbursed)

Immunotherapy Era in Multiple Myeloma



- **Antibody–drug conjugate**
  - Belantamab mafodotin-blmf
- **BCMA-directed CAR T-cell therapy**
  - Idecabtagene vicleucel
  - Ciltacabtagene autoleucel
- **Bispecific antibodies**
- **Naked antibodies**
- **Multiple targets**
  - BCMA
  - GPRC5D
  - FcHR5
  - SLAMF7



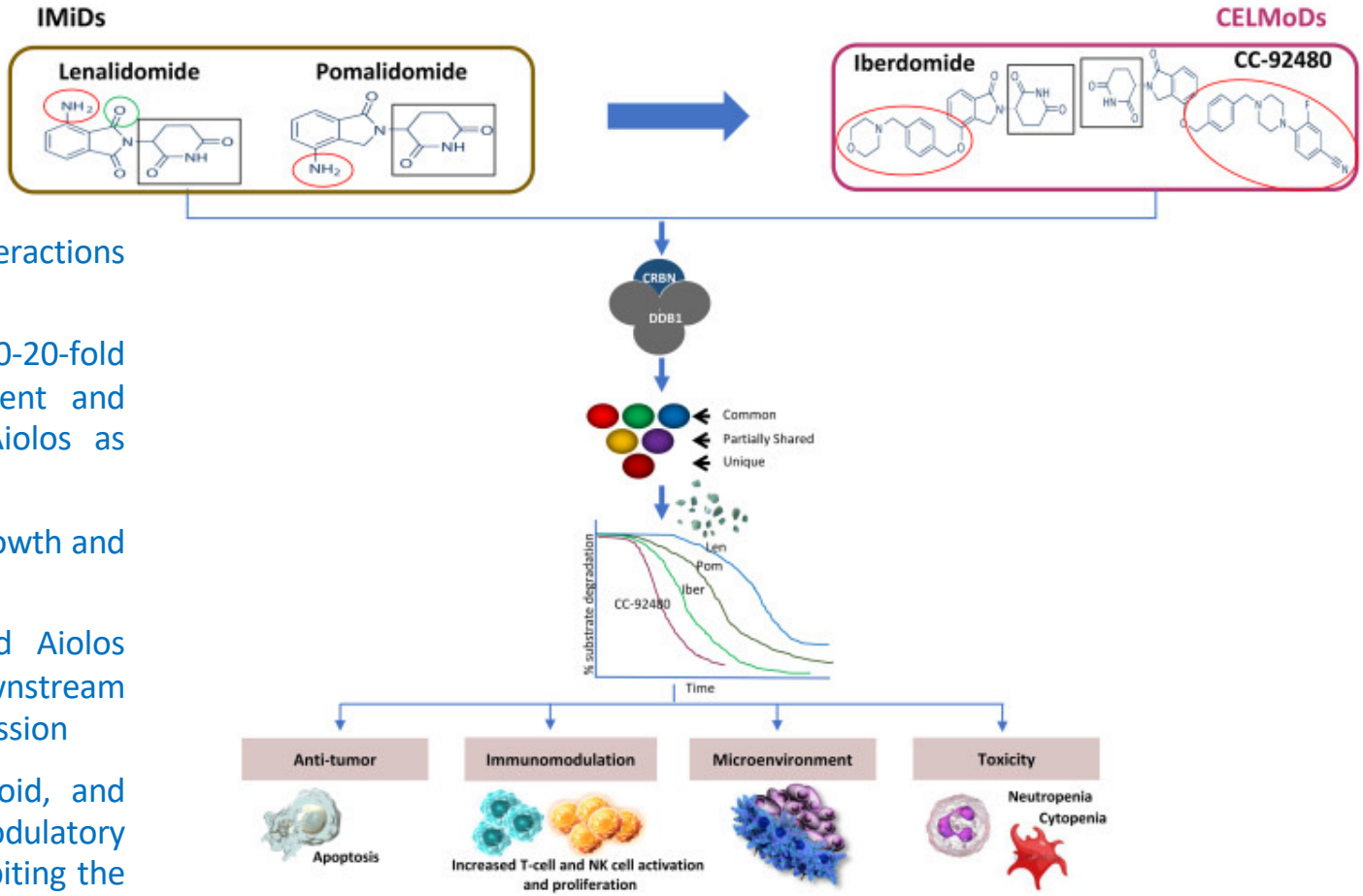
Cho. Front Immunol. 2018;9:1821. Su. J Hematol Oncol. 2021;14:115. Tai. Expert Opin Biol Ther. 2019;19:1143.

New Drugs: CELMoDs

- Cereblon (CRBN) E3 ligase modulators (CELMoDs) are a new class of immunomodulatory drugs (IMIDs) containing an imide group
- CELMoDs are oral medications that have many similarities to other IMIDs (Thalidomide, Lenalidomide, Pomalidomide)
- CELMoDs not only kill myeloma cells directly but also by engaging other immune cells
- Iberdomide and Mezigdomide are being investigated in relapsed/refractory disease and (Iberdomide) as maintenance therapy post SCT in NDMM

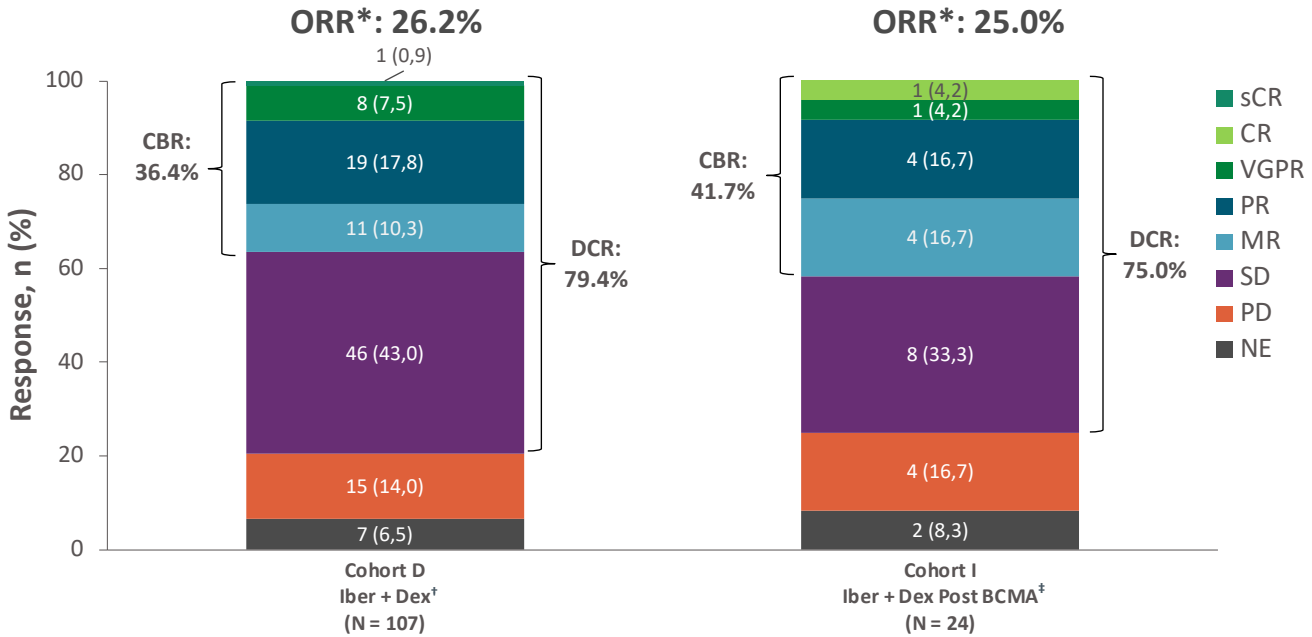
2024: È già ora di abbandonare la **chemioterapia** nella **malattia recidivata/refrattaria?**

- IMIDs and CELMoDs act by physical interactions with the CRBN/DDB1 complex
- IBER and CC-92480 bind CRBN with ~10-20-fold higher affinity and induce more potent and efficient degradation of Ikaros and Aiolos as compared to LEN/POM
- Ikaros and Aiolos are required for the growth and survival of B- and plasma cells
- Pharmacological effects of Ikaros and Aiolos degradation in MM cell lines are the downstream downregulation of IRF4 and c-MYC expression
- CELMoDs act also on lymphoid, myeloid, and stromal cells, leading to immunomodulatory effects by expanding, activating, or inhibiting the functions of these cells



Anjan Thakurta et al, Oncotarget 2021

CC-220-MM-001 Iberdomide + Dexamethasone Dose Expansion: Response

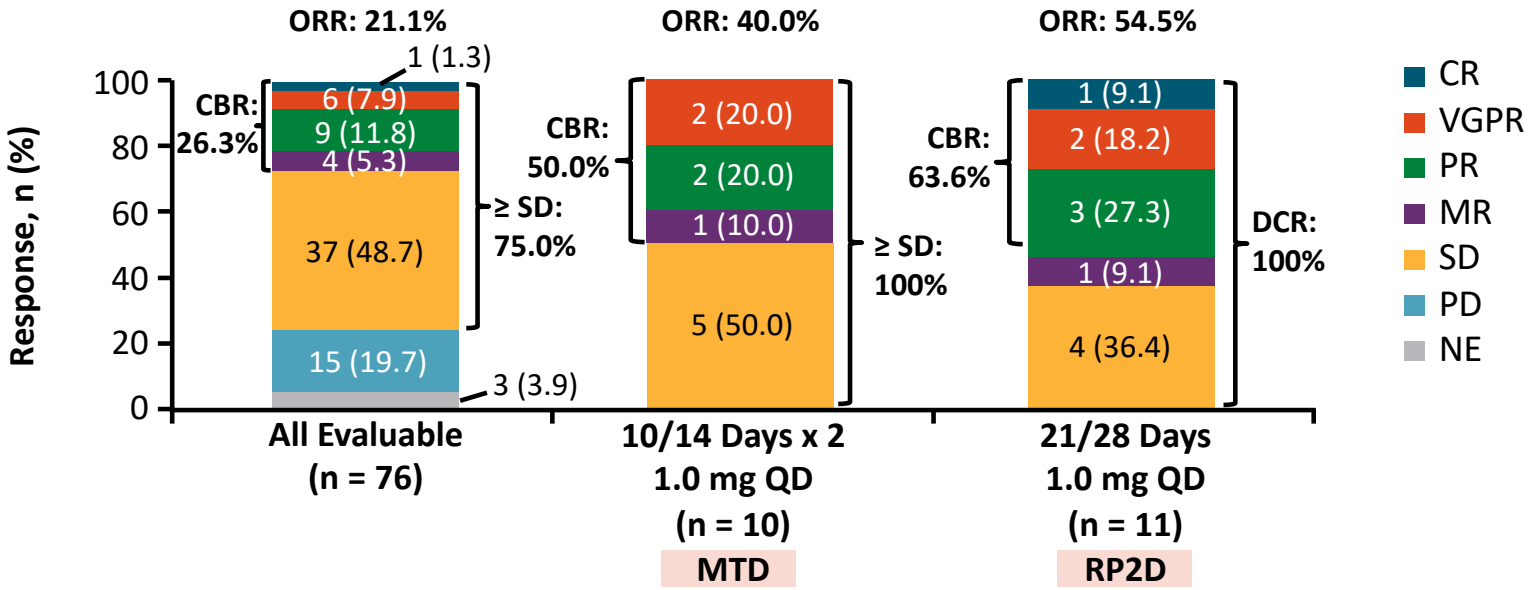


*PR or better. †2 patients in SD and MR discontinued tx due to death caused by COVID-19. ‡Includes all treated patients with post-BL efficacy assessment or patients who discontinued tx before any postbaseline efficacy assessment; 2 patients in cohort 1 with no post-BL efficacy assessments were excluded from analysis.

Lonial. ASH 2021. Abstr 162.

Slide credit: clinicaloptions.com

Mezigdomide + Dexamethasone in Heavily Pretreated R/R MM: Best Response



- 7 of 11 patients at RP2D of 1 mg QD 21/28 days were triple-class refractory (to ≥1 IMiD, 1 PI, and 1 anti-CD38 mAb)
  - Of these patients, 1 had CR, 1 VGPR, 2 PR, and 1 MR

Richardson. ASCO 2020. Abstr 8500.

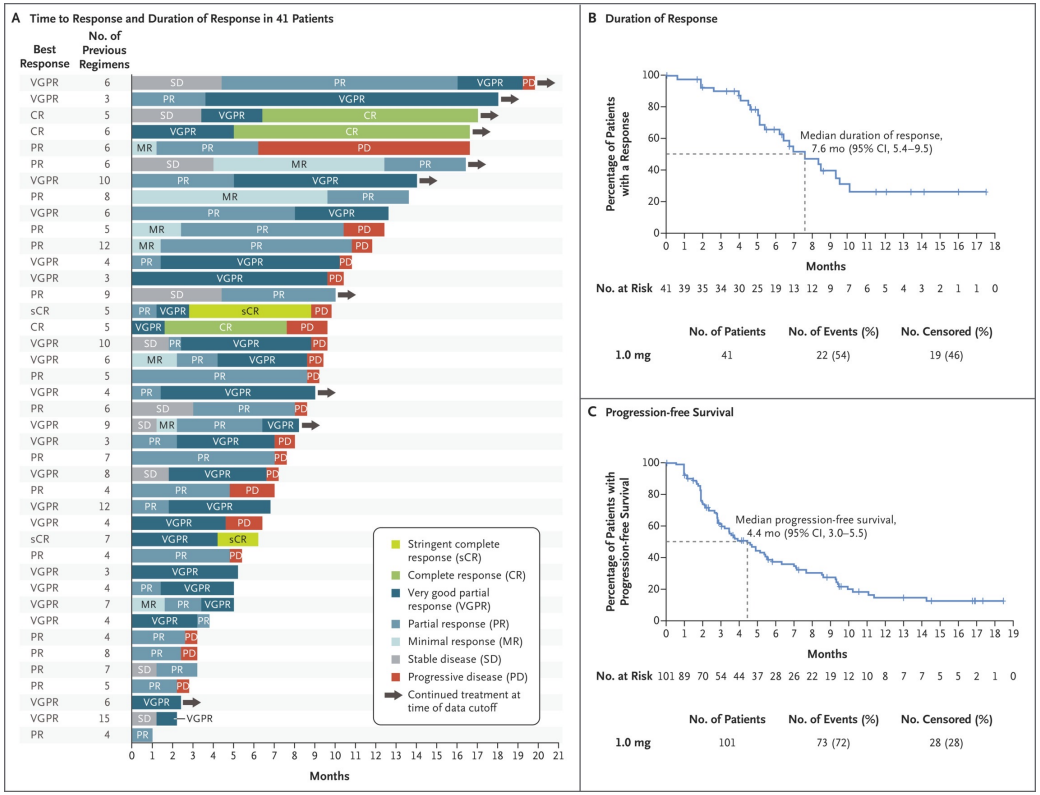
Slide credit: clinicaloptions.com

Mezigdomide + Dexamethasone: Response Dynamics and PFS in the Dose-Expansion Cohort.

Table 3. Summary of Best Overall Response.*

Variable	Dose-Escalation Cohort			Dose-Expansion Cohort		
	All Patients (N=77)	10-Day Schedule, Repeated† (N=10)	21-Day Schedule‡ (N=11)	All Patients (N=101)	Patients with Plasmacytomas§ (N=40)	Patients with Previous Anti-BCMA Therapy (N=30)
	number of patients (percent)					
Overall response¶	19 (25)	4 (40)	6 (55)	41 (41)	12 (30)	15 (50)‖
Stringent complete response	0	0	0	2 (2)	0	0
Complete response	1 (1)	0	1 (9)	3 (3)	2 (5)	1 (3)
Very good partial response	9 (12)	2 (20)	3 (27)	20 (20)	7 (18)	9 (30)
Partial response	9 (12)	2 (20)	2 (18)	16 (16)	3 (8)	5 (17)
Minimal response	4 (5)	1 (10)	1 (9)	6 (6)	0	1 (3)
Stable disease	34 (44)	4 (40)	4 (36)	39 (39)	21 (52)	11 (37)
Progressive disease	17 (22)	1 (10)	0	10 (10)	4 (10)	3 (10)
Response could not be evaluated**	3 (4)	0	0	5 (5)	3 (8)	0

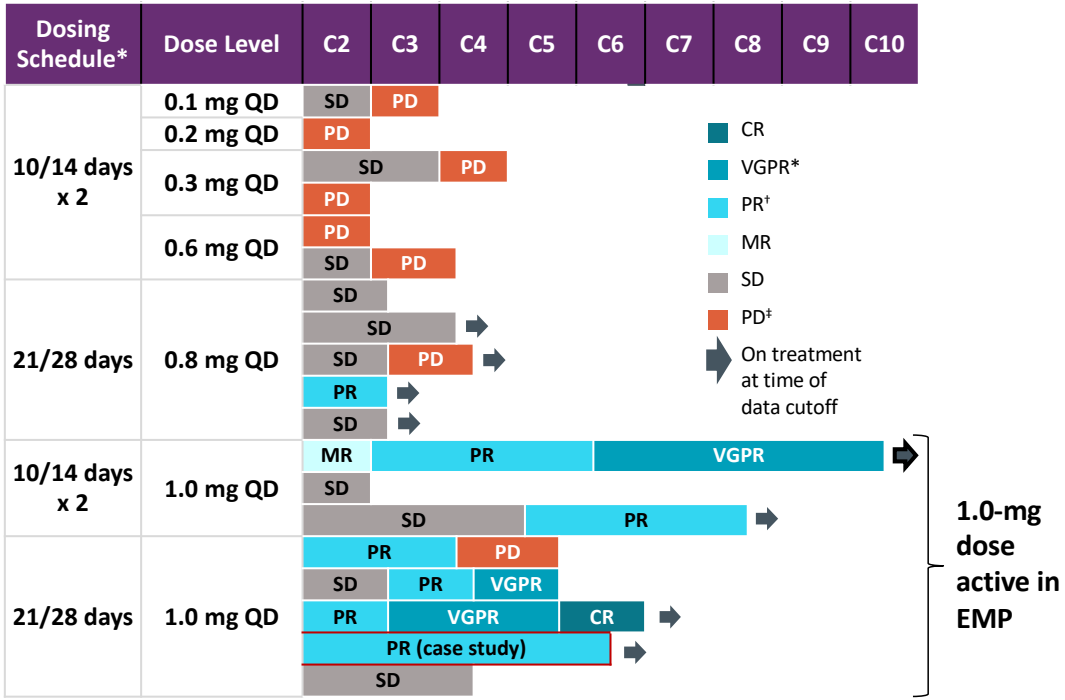
* Response was assessed according to the International Myeloma Working Group (IMWG) Uniform Response Criteria for Multiple Myeloma. Percentages may not total 100 because of rounding.
† The 10-day schedule, repeated, was 10 days of consecutive treatment, followed by 4 days off, and then repeated, in 28-day cycles. Mezigdomide was administered at a maximum tolerated dose of 1.0 mg plus dexamethasone.
‡ The 21-day schedule was 21 days of consecutive treatment, followed by 7 days off, in 28-day cycles. Mezigdomide was administered at the recommended phase 2 dose of 1.0 mg once daily plus dexamethasone.
§ Plasmacytomas included extramedullary soft-tissue only and bone-based plasmacytomas with a measurable soft-tissue component.
¶ An overall response was defined as partial response or better. A stringent complete response was defined as a complete response with a normal serum free light-chain ratio and an absence of clonal plasma cells according to the IMWG response criteria.
‖ Of the 15 patients who had a response and had received previous anti-BCMA therapy, 12 had received antibody–drug conjugates, 2 had received T-cell engagers, and 1 had received CAR T-cell therapy.
** Included are patients whose assessment could not be evaluated for response or who did not have response-assessment data.



Richardson PG et al, N Engl J Med 2023

Responses in Patients With Extramedullary Plasmacytoma

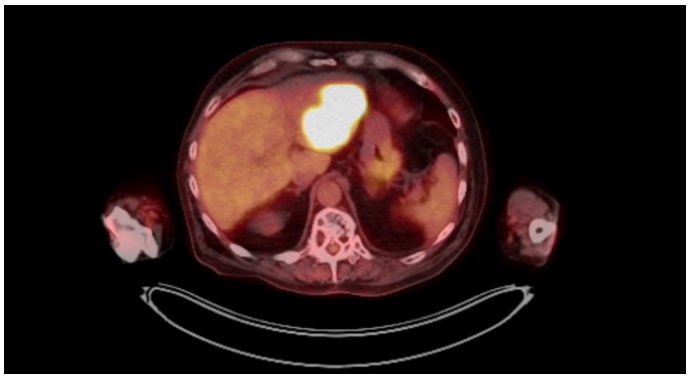
Only patients on continuous schedules are shown



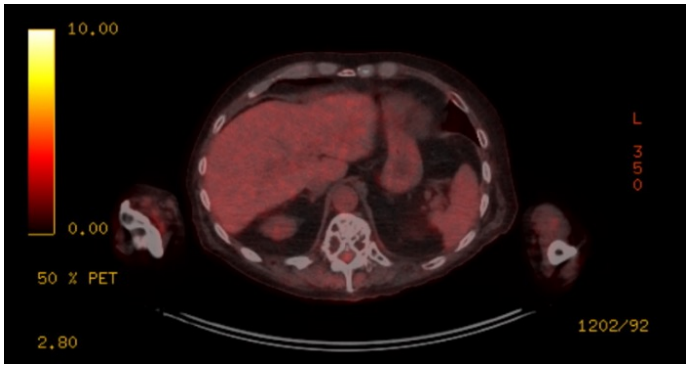
*1 patient in 21/28-day 1.0 mg QD cohort had unconfirmed VGPR as of data cutoff date.
†1 patient in 21/28-day 0.8 mg QD cohort had unconfirmed PR as of data cutoff date.
‡1 patient in 21/28-day 0.8 mg QD cohort had unconfirmed PD as of data cutoff date.

Richardson. ASCO 2020. Abstr 8500.

PET Scan Pretreatment



PET Scan Post-CC-92480 C3D1



Slide credit: clinicaloptions.com

CELMoDs ongoing trials

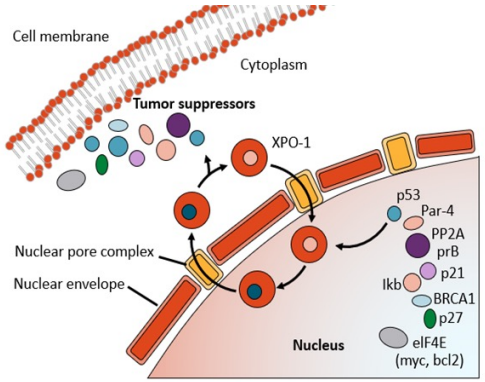
- Excaliber RRMM (1-2 prior lines not including anti-CD38 mAbs) → Iberdomide-Dd vs DVd
- Excaliber Maintenance (NDMM post-SCT) → Iberdomide vs R
- Sucessor 1 (RRMM and 1-3 prior lines with lenalidomide exposure) → Mezigdomide-Vd vs Pom-Vd
- Sucessor 2 (RRMM and 1-3 prior lines with lenalidomide exposure) → Mezigdomide-Vd vs Pom-Vd

Selinexor: the STORM trial

FDA approved in 2020

EMA approved in 2021

SINE: selective inhibitor of nuclear export - XPO1



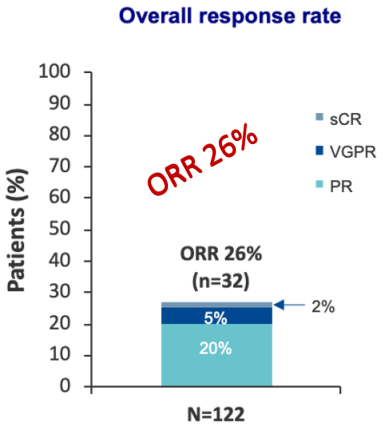
STORM, phase 2b study (N = 122)

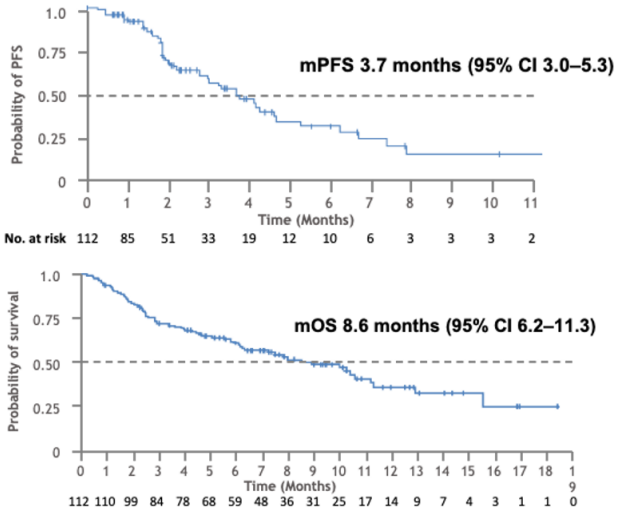
Median prior lines: 7 (3–18)
TCR=100%

All patients were penta-exposed and triple-class refractory

Median duration of treatment: 9.0 weeks (range: 1-60)

SELINEXOR 80 MG, DEX 20 MG – 2X/WK





TEAEs, %	All grade	Grade 3 or 4
Thrombocytopenia	73	59
Fatigue	73	25
Nausea	72	10
Anemia	67	44
Hyponatremia	37	22
Neutropenia	40	21

Chari. NEJM. 2019;381:727.

Data From Phase I/IIb STOMP Trial With Selinexor-Based Triplets

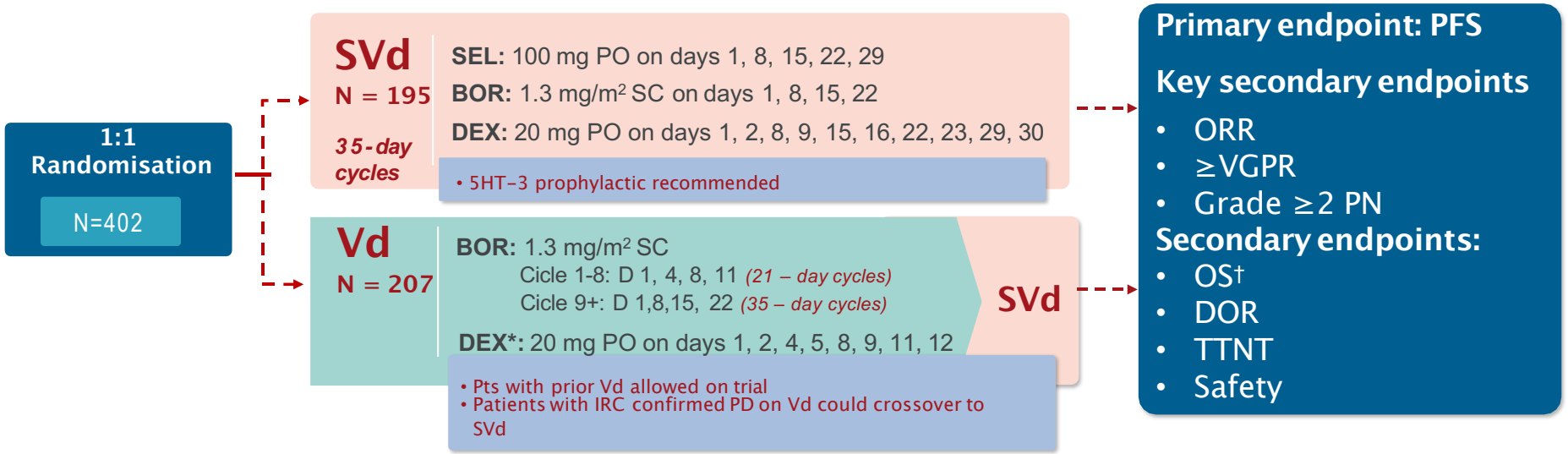
	SVd (N = 40)[1]		SKd (N = 32)[2]		SPd (N = 60)[3]		Dara-Sd (N = 32)[4]	
Patient Population	50% PI refractory, 3 median prior lines of therapy		9% with prior carfilzomib (3% refractory), 44%/22% bort/ixa refractory, 4 median prior regimens		87% Len refractory, 70% Pom naive, 3 median prior regimens		94% Dara naive, 85%/76% PI/IMiD refractory, 3 median prior regimens	
ORR, %	PI sens/ naive: **84**	PI refractory: **43**	All: **78.1**	Triple class refractory: **66.7**	Pom-sens/ naive: **54**	Pom-refractory: **36**	All: 69	Dara-naive: **73**
▪ ≥CR, %	11	5	15.7	0	2.2	0	0	0
▪ VGPR, %	26	19	28.1	50.0	19.6	7.1	34	37
▪ PR, %	47	19	34.4	16.7	32.6	26.8	34	37
Median PFS, mo	17.8	6.1	15.0	23.7	12.3	--	12.5	--

1. Bahlis. Blood. 2019;132:2546. 2. Gasparetto. Br J Cancer. 2022;126:718. 3. Chen. ASH 2020. Abstr 726. 4. Gasparetto. ASCO 2020. Abstr 8510.

BOSTON: Phase 3 trial

Study Design

Phase 3, multicenter, randomised, open-label study [NCT03110562]



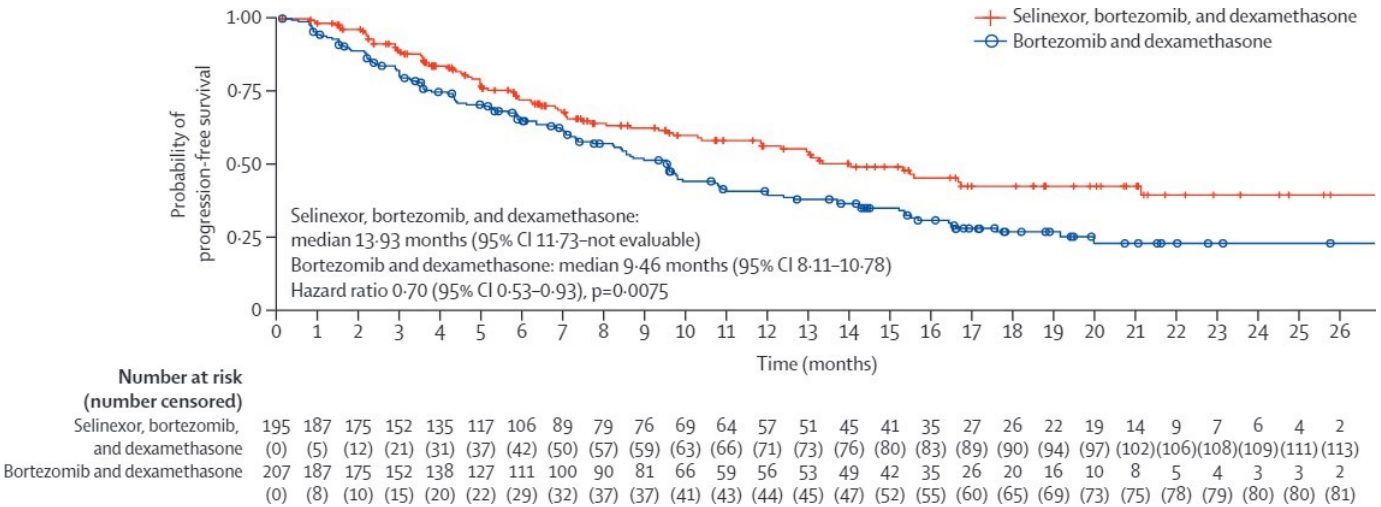
BOR, bortezomib; DEX, dexamethasone; DOR, duration of response; IRC, independent review committee; OS, overall survival; PD, progressive disease; PFS, progression free survival; PN, peripheral neurophathy; PO, taken orally; SC, subcutaneous; SEL, selinexor; SVd, selinexor + bortezomib + dexamethasone; TTNT, time to next treatment; Vd, bortezomib + dexamethasone; VGPR, very good partial response.
*DEX dosing presented is for cycles 1-8; for cycles ≥9 DEX w as given as 20 mg on days 1, 2, 8, 9, 15, 16, 22, 23, 29, and 30 of each 35-day cycle; †OS is not yet reached.

Grosicki S. et al, Lancet. 2020

BOSTON trial: PFS

	SVd arm (n = 195)	Vd arm (n = 207)
Median PFS, months (95% CI)*	13.93 (11.73, NE)	9.46 (8.11, 10.78)
HR=0.70 (95% CI: 0.53, 0.93); one-sided *P* = .0075		

Kaplan-Meier estimates of progression-free survival among patients in the ITT population



Number at risk (number censored)

Selinexor, bortezomib, and dexamethasone	195 (0)	187 (5)	175 (12)	152 (21)	135 (31)	117 (37)	106 (42)	89 (50)	79 (57)	76 (59)	69 (63)	64 (66)	57 (71)	51 (73)	45 (76)	41 (80)	35 (83)	27 (89)	26 (90)	22 (94)	19 (97)	14 (102)	9 (106)	7 (108)	6 (109)	4 (111)	2 (113)
Bortezomib and dexamethasone	207 (0)	187 (8)	175 (10)	152 (15)	138 (20)	127 (22)	111 (29)	100 (32)	90 (37)	81 (37)	66 (41)	59 (43)	56 (44)	53 (45)	49 (47)	42 (52)	35 (55)	26 (60)	20 (65)	16 (69)	10 (73)	8 (75)	5 (78)	4 (79)	3 (80)	3 (80)	2 (81)

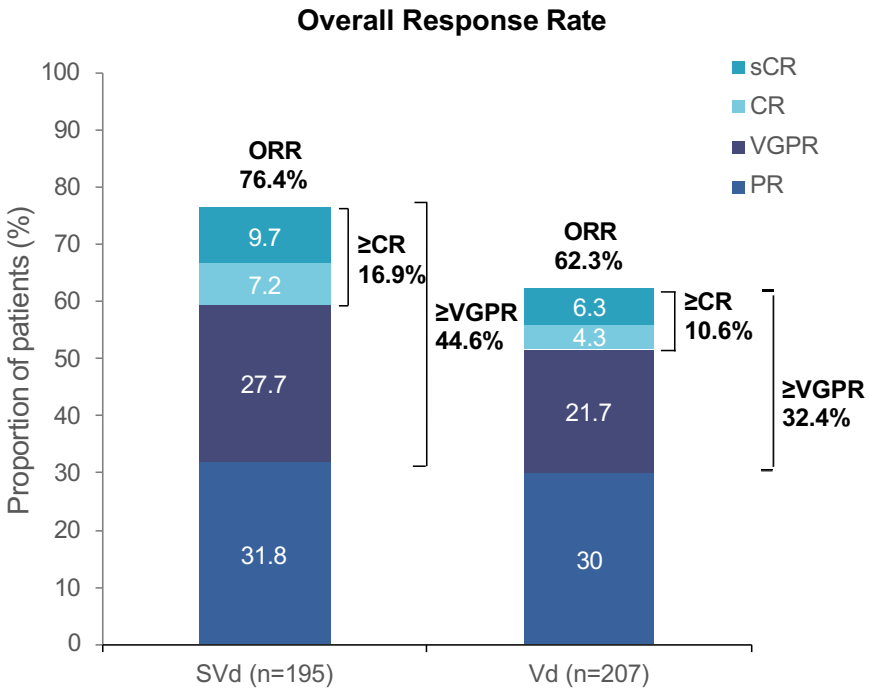
This data represents:

1. An increase of **4.47 months** in median PFS
2. A **30% reduction** in the risk of disease progression

CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; NE, not evaluable; PFS, progression free survival; SVd, selinexor + bortezomib + dexamethasone; Vd, bortezomib + dexamethasone.
*The study was ongoing at the time of publication; the analysis was performed after a median follow-up period of 13.2 months for the SVd arm and 16.5 months for the Vd arm (data cutoff: 18 February 2020).

Grosicki S. et al, Lancet. 2020

BOSTON trial: Treatment response



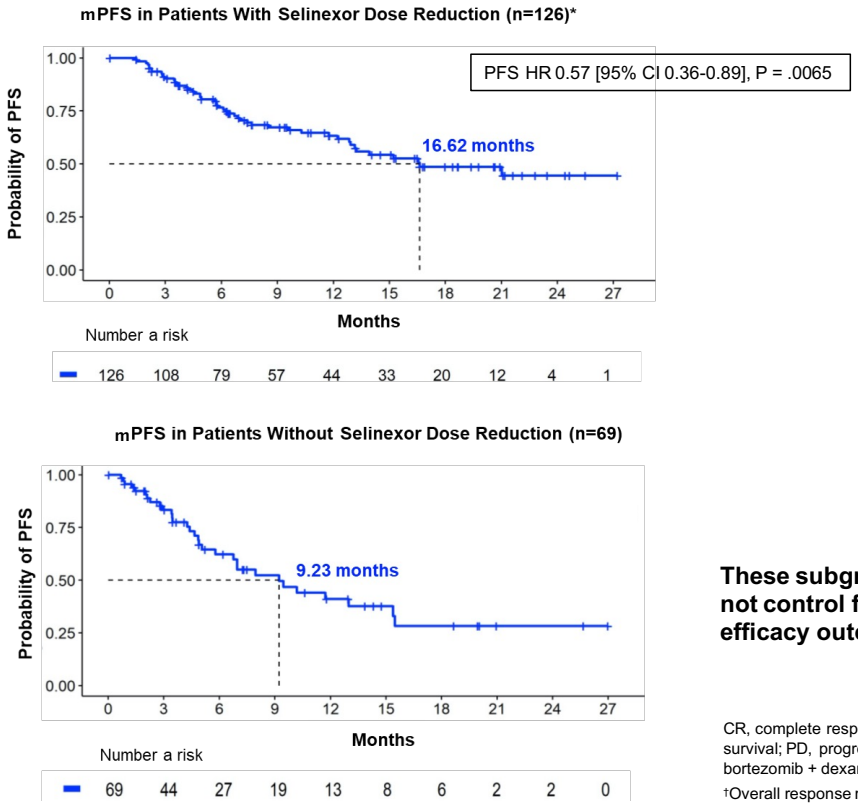
- Key evidence of deep responses:
  - ≥VGPR *P* = .0082*
  - 6% absolute difference in ≥CR
- Clinical benefit was evident in the SVd arm vs the Vd arm:
  - Proportion of patients with progressive disease: 0.5% in the SVd arm vs 5% in the Vd arm

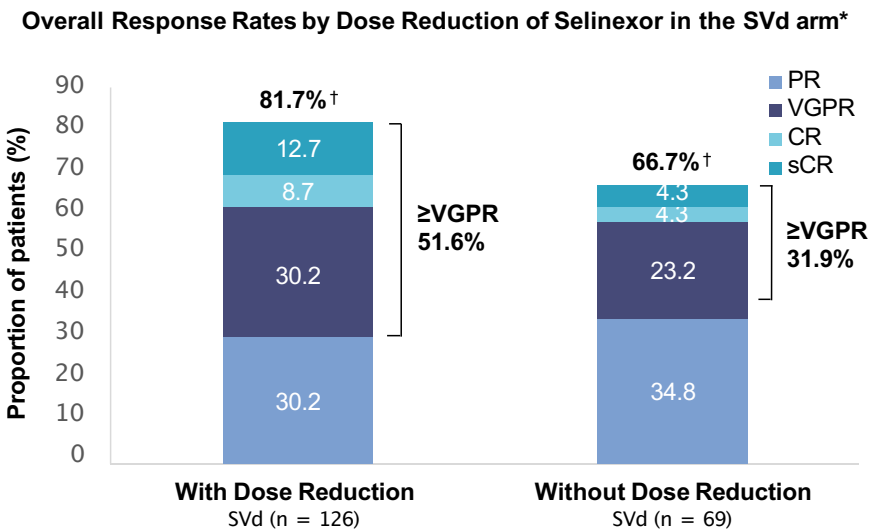
	SVd arm (n = 195)	Vd arm (n = 207)
Median Time to Response, months	1.1	1.4
Median Duration of Response, months	20.3	12.9
Median Time to Next Treatment, months	16.1	10.8

CR, complete response; ORR, overall response rate; PR, partial response; sCR, stringent complete response; SVd, selinexor + bortezomib + dexamethasone; Vd, bortezomib + selinexor; VGPR, very good partial response.
*Statistical analyses using one-sided *P* value.

Grosicki S. et al, Lancet. 2020

BOSTON trial: PFS and OS in Patients with Selinexor Dose Reductions





These subgroup analyses were exploratory in nature, not included in the study objectives and do not control for type 1 error. The analyses were not powered or adjusted for multiplicity to assess efficacy outcomes across these subgroups.

CR, complete response; HR, hazard ratio; IRC, independent review committee; mPFS, median progression free survival; PD, progressive disease PR, partial response; sCR, stringent complete response; SVd, selinexor + bortezomib + dexamethasone; VGPR, very good partial response.

†Overall response rate is the proportion of patients who achieve a partial response or better, before IRC-confirmed PD or initiating a new MM treatment or crossover.

Jagannath S. et al, ASH Meeting 2021, Abstract 3793

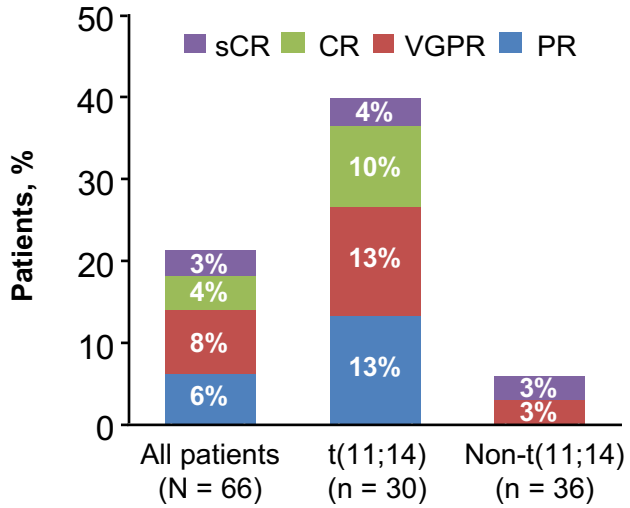
Venetoclax in RRMM: BCL-2 Inhibition

Venetoclax is a selective, orally available small-molecule BCL-2 inhibitor; active in R/R MM[1]

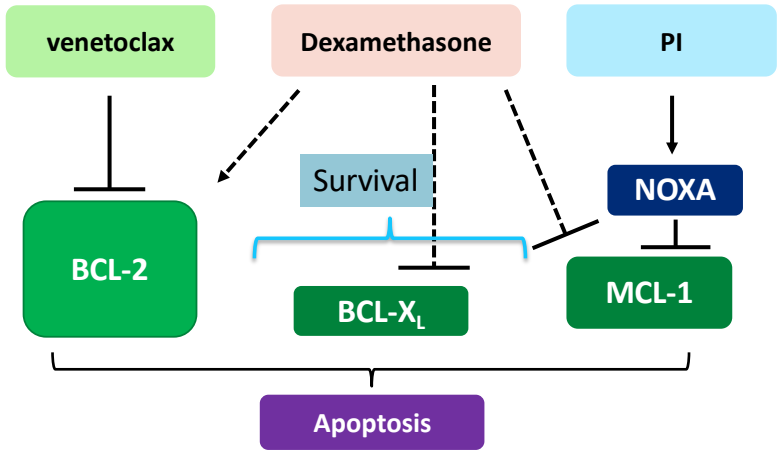
Use in patients with t(11;14)

Venetoclax (daily dose up to 1,200 mg) has an acceptable safety profile in R/R MM, predominantly in patients with t(11;14) abnormality and favorable BCL-2 family profile

Objective Response Rates in All Patients

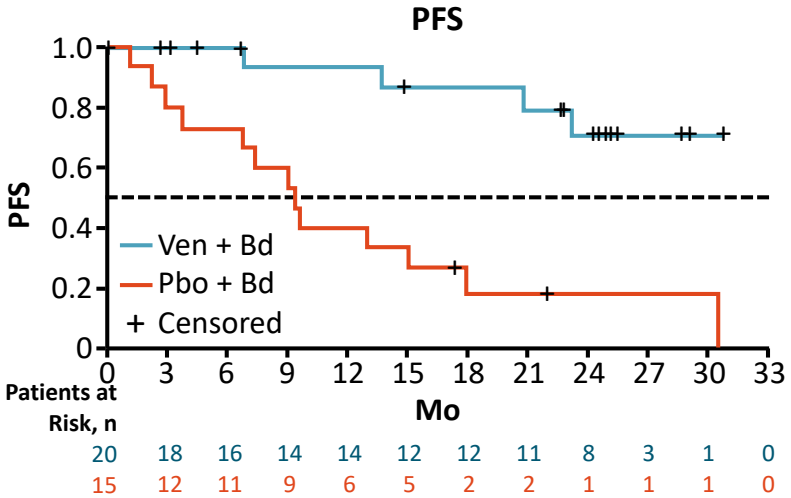


Rationale for Combination Therapy with Venetoclax[2-5]

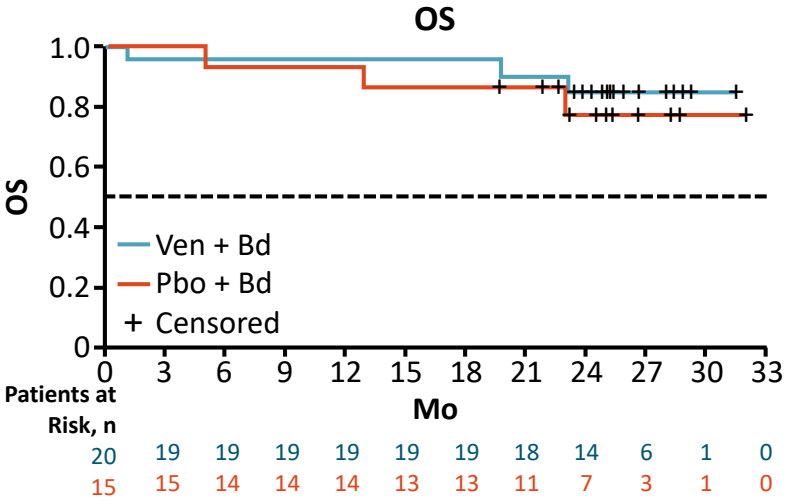


1. Kumar. ASH 2016. Abstr 488. 2. Touzeau. Leukemia. 2018;32:1899. 3. Souers. Nat Med. 2013;19:202.
4. Ponder. Cancer Bio Ther. 2016;17:769. 5. Matulis. Leukemia. 2016;30:1086.

BELLINI: Promise of Venetoclax + Bortez/Dex in t(11;14)-Positive Myeloma



PFS	Ven + Bd	Pb o+ Bd
Median, mo	Not reached	9.3
HR (95% CI)	0.09 (0.02-0.44)	
P value	.003	

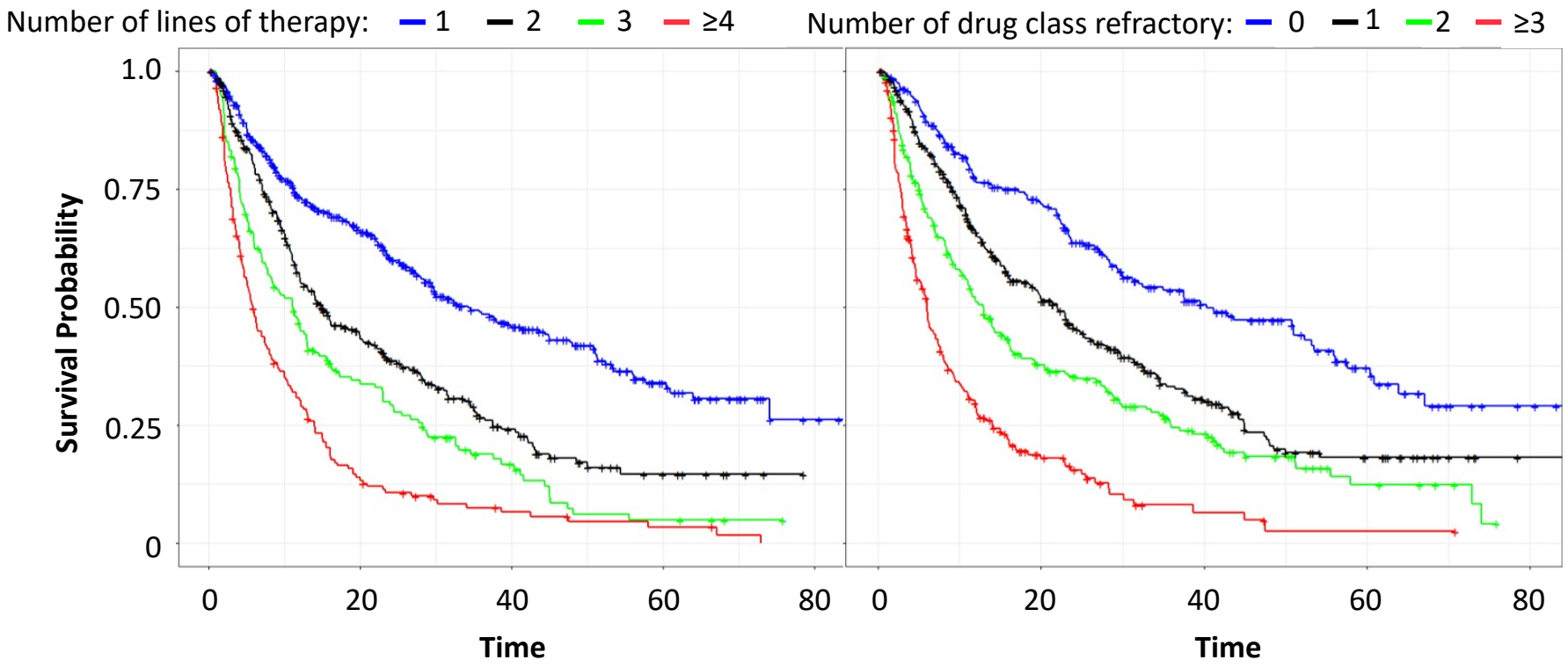


OS	Ven + Bd	Pbo + Bd
Median, mo	Not reached	Not reached
HR (95% CI)	0.68 (0.13-3.48)	
P value	.647	

Harrison. ASH 2019. Abstr 142.

Slide credit: clinicaloptions.com

Lines of Therapy or Drug Class Refractoriness



Goel et al, Unpublished

Take home messages

- Treatment of RR MM is an ever-evolving scenario with a progressive increase of therapeutic options both as single agents and/or drug combinations
- The unmet medical need of lenalidomide-refractory patients is now nearly resolved by new regimens and new drugs
- The use of new classes of drugs within the first-line of therapy makes the therapeutic choice for relapsed MM even more challenging
- It would be desirable to have new drugs with different mechanism of action readily available, without regulatory restriction, to overcome drug resistance

2024: È già ora di abbandonare la **chemioterapia** nella **malattia recidivata/refrattaria?**

Napoli, Hotel Paradiso • 29–30 aprile 2024