GIORNATE EMATOLOGICHE VICENTINE

X edizione

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Palazzo Bonin Longare - Vicenza

La progressione post-autotrapianto – strategie attuali

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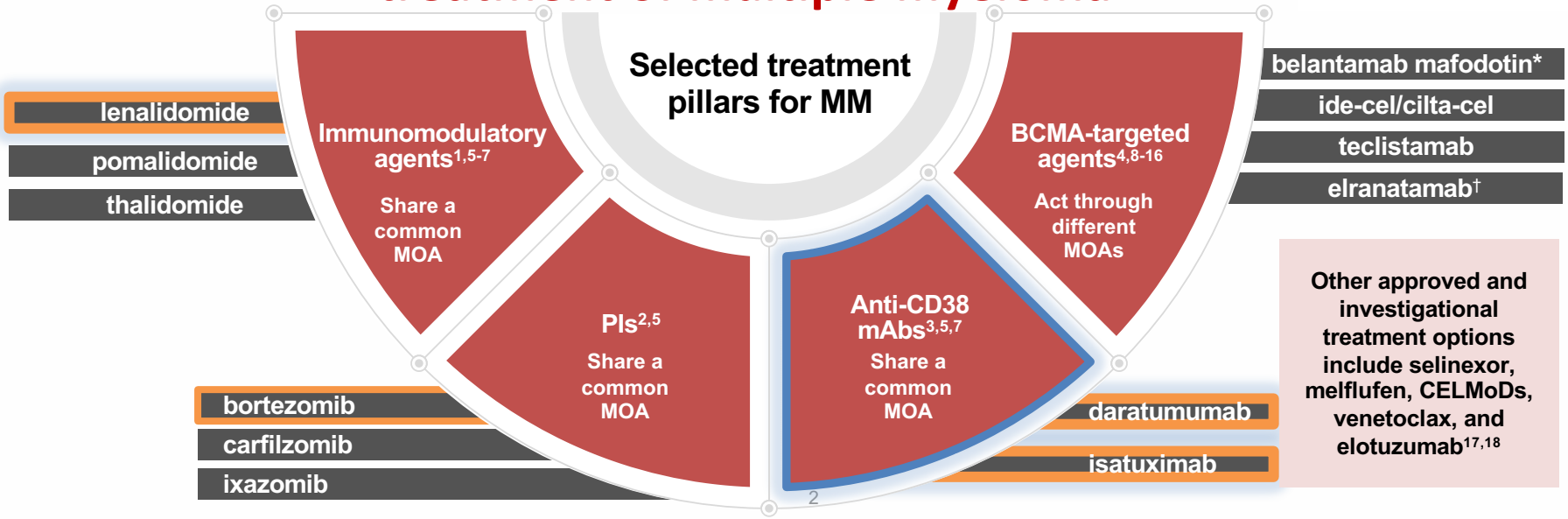
Four treatment pillars are currently key backbones for the treatment of multiple myeloma[1-4]



Anti-CD38 mAbs and lenalidomide are increasingly used in the front-line setting with impressive efficacy, however, patients will relapse at variable intervals after diagnosis[17-20]

***Approved in the European Union only.[8,9] †Approved in the US only.[16]**

BCMA, B-cell maturation antigen; CD, cluster of differentiation; CELMoD, cereblon E3 ligase modulator; cilta-cel, ciltacabtagene autoleucel; ide-cel, idecabtagene vicleucel; mAb, monoclonal antibody; MM, multiple myeloma; MOA, mechanism of action; PI, proteasome inhibitor.

1. HolsteinA, McCarthy PL. *Drugs*. 2017;77(5):505-520. **2.** Nunes AT, Annunziata CM. *Semin Oncol*. Published online April 12, 2018. doi:10.1053/j.seminoncol.2018.01.004 **3.** Gozzetti A et al. *Hum Vaccin Immunother*. 2022;18(5):2052658. doi:10.1080/21645515.2022.2052658 **4.** Shah N et al. *Leukemia*. 2020;34(4):985-1005. **5.** Shah N et al. *Clin Drug Investig*. 2021;41(3):201-210. **6.** Richardson PG et al. *Blood.* 2014;123(12):1826-1832. **7.** Richardson PG et al. *Blood Cancer J.* Published online July 12, 2023. doi:10.21203/rs.3.rs-3117230/v1 **8.** BLENREP. Summary of Product Characteristics. GlaxoSmithKline (Ireland) Limited; 2023. **9.** BLENREP. Dear health care provider letter. GlaxoSmithKline; 2022. **10.** Abecma. Prescribing Information. Bristol Myers Squibb; 2021. **11.** Abecma. Summary of Product Characteristics. Bristol Myers Squibb Pharma EEIG; 2021. **12.** Carvykti. Prescribing Information. Janssen Biotech, Inc.; 2022. **13.** Carvykti. Summary of Product Characteristics. Janssen-Cilag International NV; 2022. **14.** Tecvayli. Prescribing Information. Janssen Biotech, Inc.; 2022. **15.** Tecvayli. Summary of Product Characteristics. Janssen-Cilag International NV; 2022. **16.** Elrexfio. Prescribing Information. Pfizer Inc.; 2023. **17.** Dimopoulos MA et al. *Ann Oncol.* 2021;32(3):309-322. **18.** Bhatt P et al. *Curr Oncol*. 2023;30(2):2322-2347. **19.** Kumar S et al. *Blood Cancer J.* 2022;12(6):98. doi:10.1038/s41408-022-00695-5 **20.** Facon T et al. *N Engl J Med*. 2019;380(22):2104-2115.

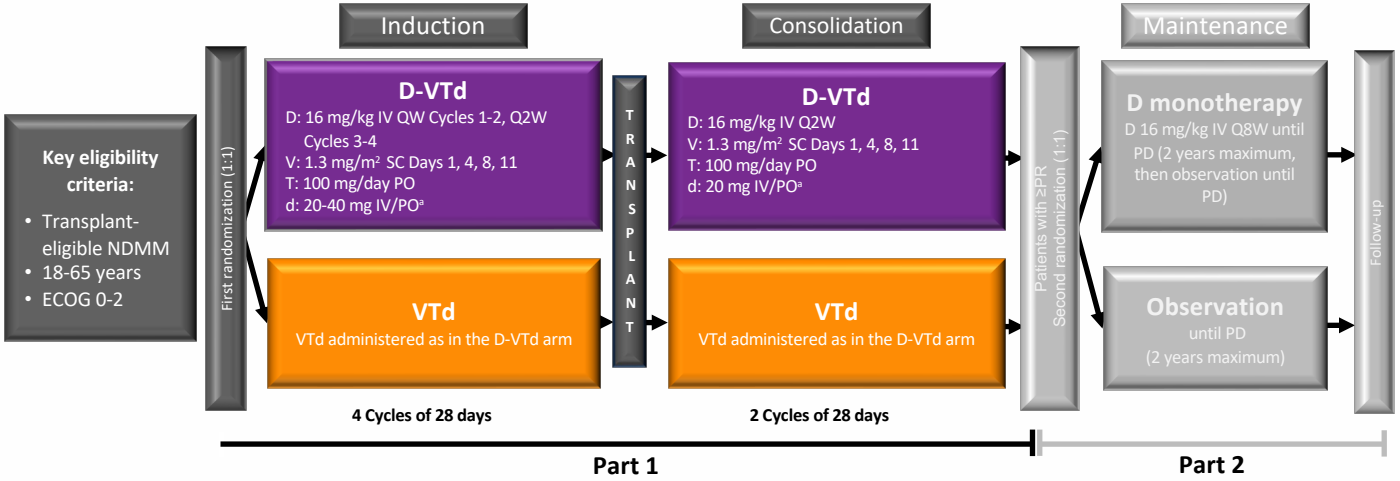
First-line treatment
Transplant eligible multiple myeloma

- ***Global strategy*** ***Induction → ASCT and conditioning → consolidation → maintenance***

- ***2 major changes in first-line treatment***
  - ***incorporation of anti-CD38 MoAb***
  - ***lenalidomide is increasingly be used***

CASSIOPEIA Study Design

Phase 3 study of D-VTd versus VTd in transplant-eligible NDMM (N = 1,085), 111 sites from 9/2015 to 8/2017

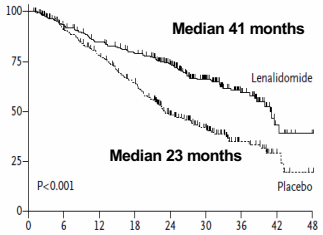


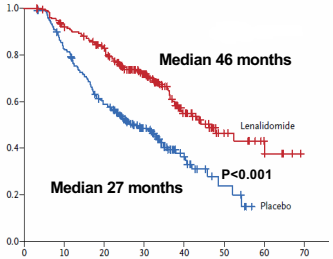
D-VTd, daratumumab/bortezomib/thalidomide/dexamethasone; VTd, bortezomib/thalidomide/dexamethasone; ECOG, Eastern Cooperative Oncology Group; IV, intravenous; QW, weekly; Q2W, every 2 weeks; SC, subcutaneous; PO, oral; PR, partial response; Q8W, every 8 weeks; PD, progressive disease.
[a]Dexamethasone 40 mg on Days 1, 2, 8, 9, 15, 16, 22, 23 of Cycles 1-2 and Days 1 & 2 of Cycles 3-4; 20 mg on Days 8, 9, 15, 16 of Cycles 3-4; 20 mg on Days 1, 2, 8, 9, 15, 16 of Cycles 5-6.

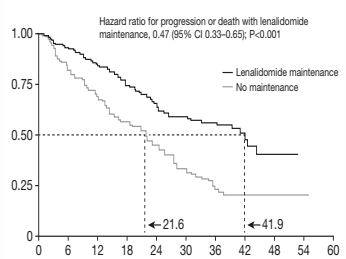
Lenalidomide maintenance

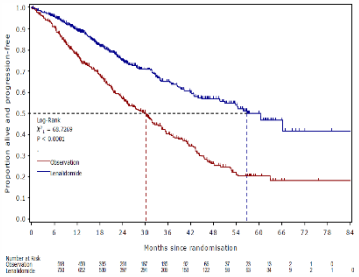
IFM 05-02	CALGB 100104	GIMEMA MM RV 209	Myeloma XI
Median follow-up 45 months	Median follow-up 34 months	Median follow-up 51 months	Median follow-up 31 months

PFS

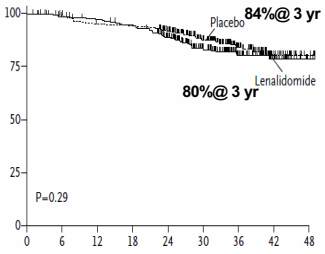


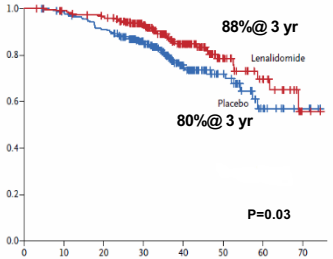


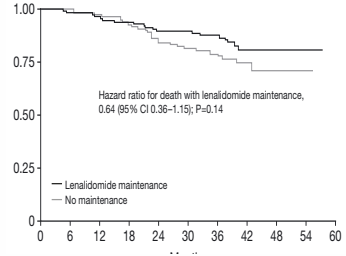


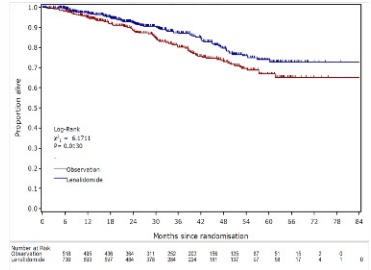


OS









Attal M, et al. NEJM 2012;366:1782

McCarthy PL, et al. NEJM. 2012;366:1770

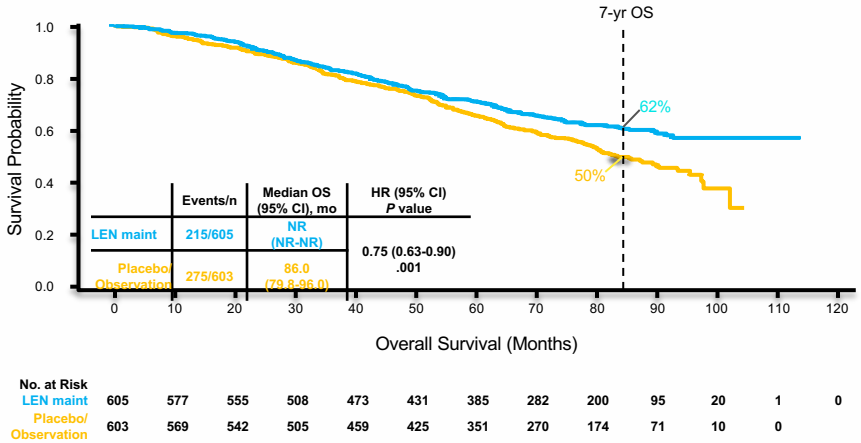
Palumbo A, et al. NEJM 2014;371:10

Jackson G, et al. ASH 2017 (Abs 436)

Meta-analysis of 3 lenalidomide maintenance trials Overall Survival:

Median Follow-Up of 80 Months

There is a 25% reduction in risk of death, representing an estimated 2.4-year increase in median survival[a]



Mc Carthy P et al. IMW Delhi 2017

Multiple myeloma

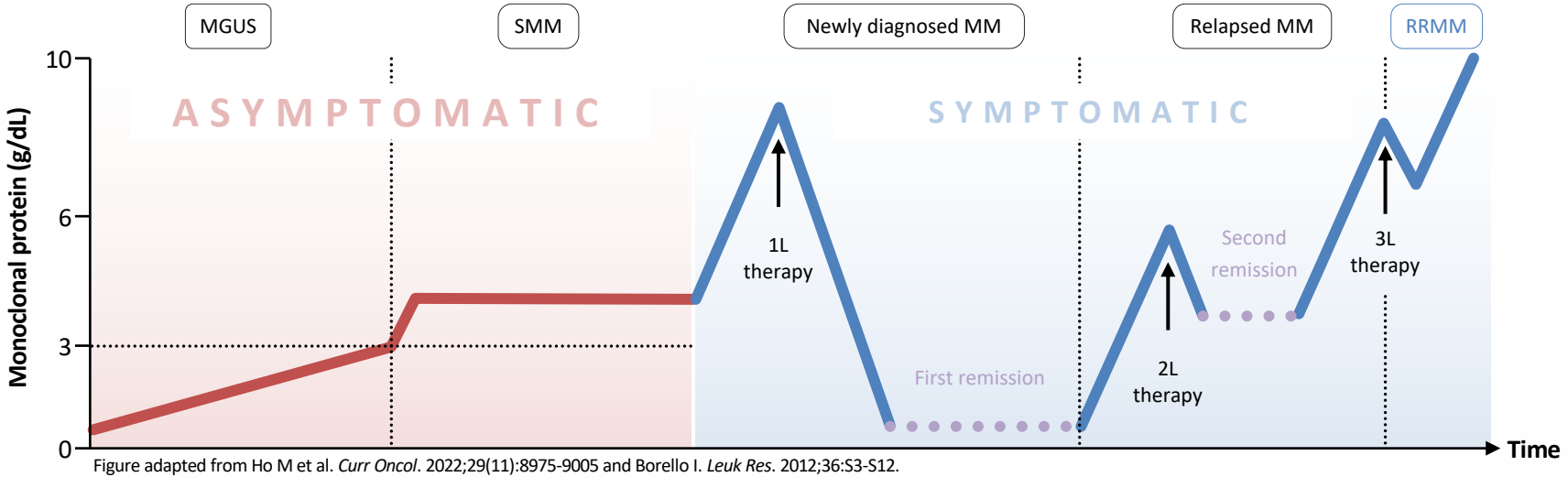


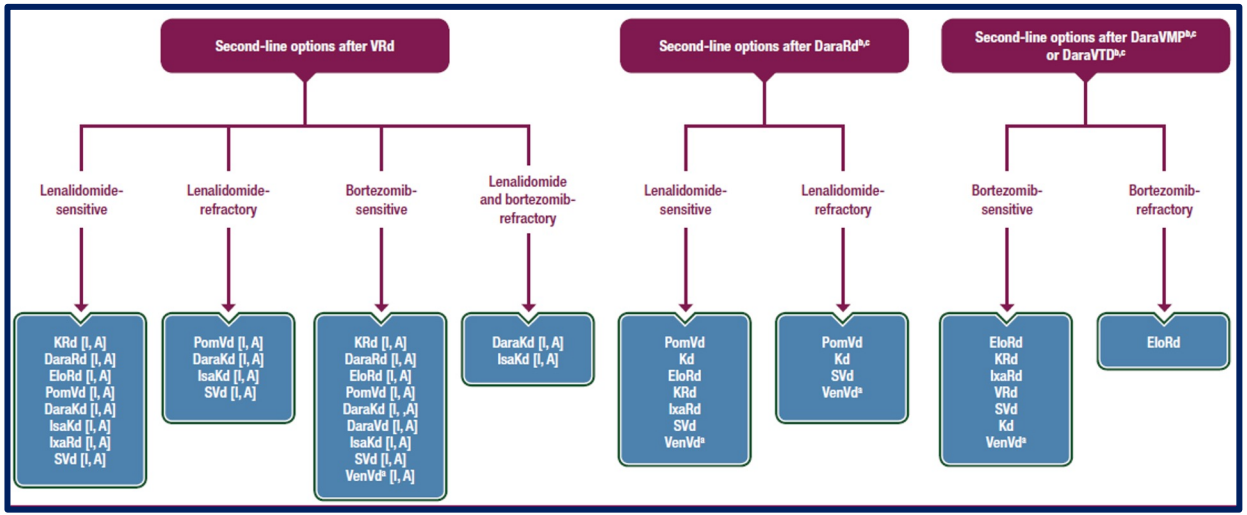
Figure adapted from Ho M et al. *Curr Oncol*. 2022;29(11):8975-9005 and Borello I. *Leuk Res*. 2012;36:S3-S12.

- 1L, first-line; 2L, second-line; 3L, third-line; MGUS, monoclonal gammopathy of undetermined significance; MM, multiple myeloma; RRMM, relapsed/refractory multiple myeloma; SMM, smoldering multiple myeloma.

1. Facon T et al. *N Engl J Med*. 2019;380(22):2104-2115. **2.** Dimopoulos MA et al. *Ann Oncol*. 2021;32(3):309-322. **3.** Dima D et al. *Cancer Manag Res*. 2020;12:7891-7903. **4.** Ho M et al. *Curr Oncol*. 2022;29(11):8975-9005. **5.** Bonello F et al. *Cancers (Basel)*. 2020;12(11):3106. doi:10.3390/cancers12113106 **6.** Borello I. *Leuk Res*. 2012;36:S3-S12.

Treatment options at first relapse: EHA-ESMO guidelines

2017[1]

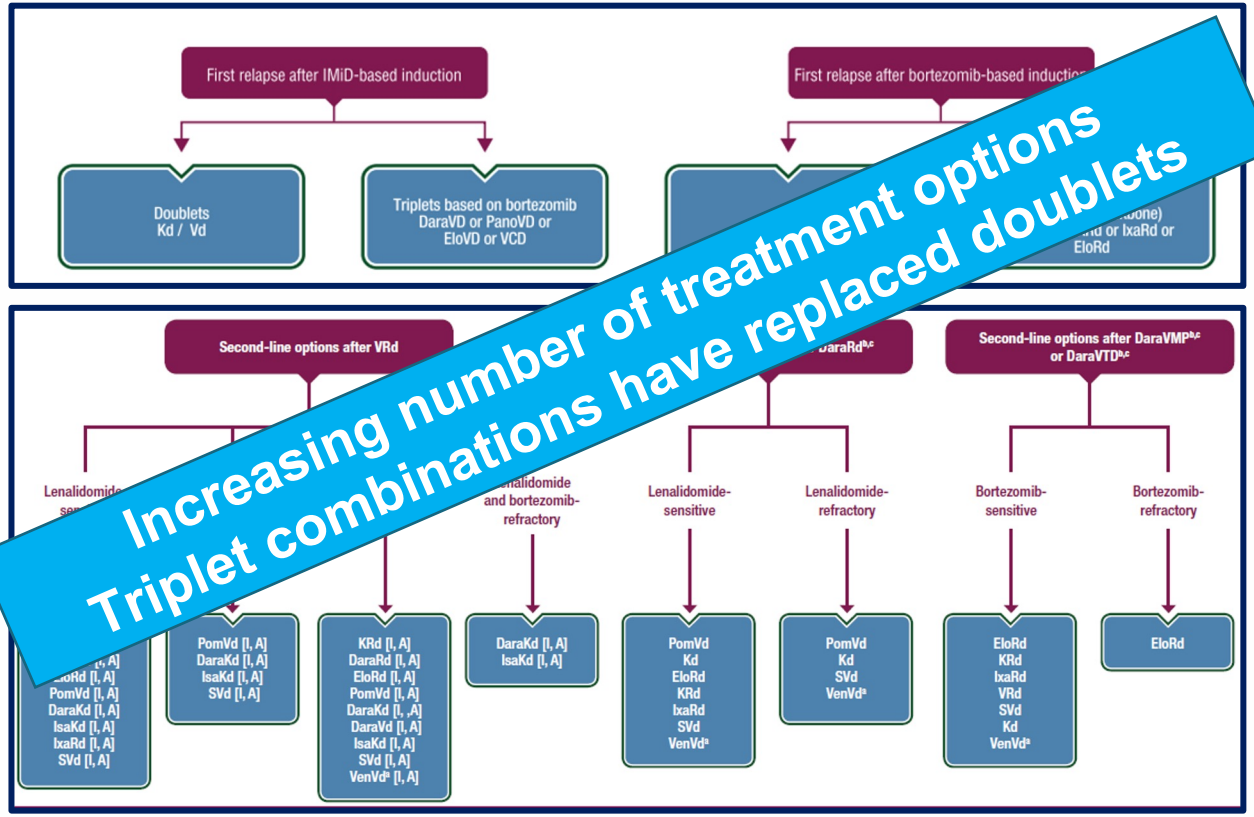


2021[2]

C, cyclophosphamide; d/D, dexamethasone; Dara, daratumumab; Elo, elotuzumab; IMiD, immunomodulatory drug; Isa, isatuximab; Ixa, izaxomib; K, carfilzomib; M, melphalan; P, prednisone; Pano, panobinostat; Pom, pomalidomide; R, lenalidomide; S, selinexor; T, thalidomide; V, bortezomib; Ven venetoclax.

1. Moreau P, et al. Ann Oncol 2017;28:iv52–iv61; 2. Dimopoulos MA, et al. Ann Oncol 2021;32:309–322.

Treatment options at first relapse: EHA-ESMO guidelines



Increasing number of treatment options
Triplet combinations have replaced doublets

2017[1]

2021[2]

C, cyclophosphamide; d/D, dexamethasone; Dara, daratumumab; Elo, elotuzumab; IMiD, immunomodulatory drug; Isa, isatuximab; Ixa, izaxomib; K, carfilzomib; M, melphalan; P, prednisone; Pano, panobinostat; Pom, pomalidomide; R, lenalidomide; S, selinexor; T, thalidomide; V, bortezomib; Ven venetoclax.

1. Moreau P, et al. Ann Oncol 2017;28:iv52–iv61; 2. Dimopoulos MA, et al. Ann Oncol 2021;32:309–322.

Treatment optimisation for patients with relapsed MM[1]

- **Disease-related characteristics**:
  - Biochemical vs symptomatic relapse
  - High-risk vs standard-risk FISH
  - Absence vs presence of extramedullary disease
- **Patient-related factors:**
  - Fit or frail
  - Comorbidities
  - Patient preference
- **Treatment history:**
  - Type of drugs administered
  - Fixed duration treatment or until disease progression
  - Type and reversibility of adverse events

FDA, EMA, AIFA REGULATORY APPROVAL

FISH, fluorescence in situ hybridisation.
1. Adapted from Moreau P, et al. Lancet Oncol 2021;22:e105–118.

First Relapse

- Treatment selection dependent on patient-, tumor-, and treatment-related factors

Availability of drugs:
-Approval status
-Reimbursement

Tumor characteristics:
-High-risk cytogenetic aberrations
-Extramedullary disease
-Rapid increase in tumor load

Patient characteristics:
-Performance / frailty status
-Age
-Comorbidities
-Patient preferences

Treatment:
-Time from prior therapy
-Response to prior therapies

First-line therapy → **First relapse treatment**

Type of first line therapy dictates, in part, what therapy is optimal at second line

- Sequencing of drugs with different modes of action
- Triplet regimens are superior to doublet regimens (response rate and PFS, and in some studies also OS)
- (Dose-adjusted) doublet can be the best option for frail patients
- Reusing a drug can be considered based on prior response and treatment-free interval

Treatment options ('triplets') at first relapse[1]

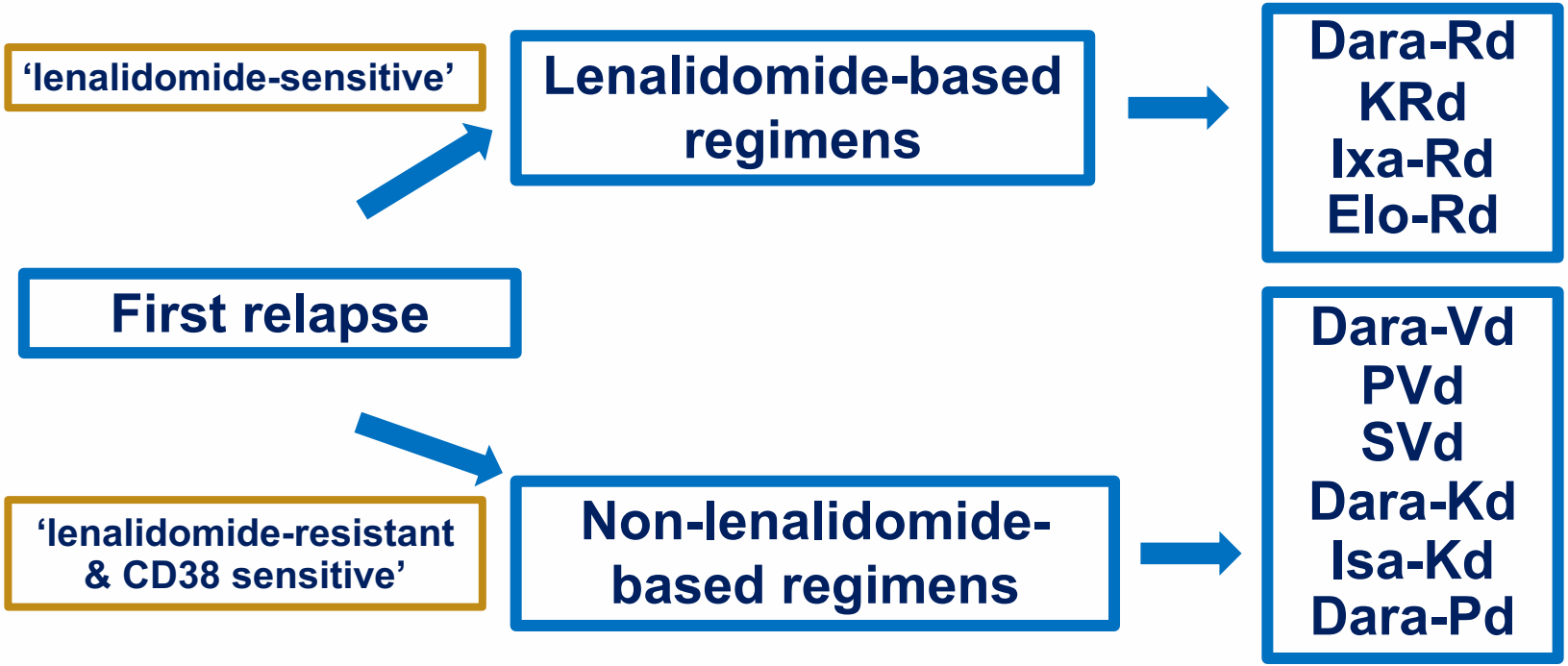
d, dexamethasone; dara, daratumumab; elo, elotuzumab; ixa, ixazomib; K, carfilzomib; R, lenalidomide.
1. Adapted from Moreau P, et al. Lancet Oncol 2021;22:e105–118 and Dimopoulos MA, et al. Ann Oncol 2021;32:309–322.

Lenalidomide-based regimens at first relapse

	mPFS (months)	mOS (months)
Dara-Rd vs Rd (POLLUX)	**53.3** vs 19.6 (HR: 0.42; p<0.0001)[1,2]	**77.8** vs 57.7 (HR: 0.75)[3]
KRd vs Rd (ASPIRE)	**29.6** vs 17.6 (HR: 0.71; p=0.001)[4]	**47.3** vs 35.9 (HR: 0.81)[5]
Ixa-Rd vs Rd (TOURMALINE-MM1)	**20.6** vs 16.6 (HR: 0.88; p=0.41)[6]	**53.6** vs 51.6 (HR: 0.94; p=0.50)*[7]
Elo-Rd vs Rd (ELOQUENT-2)	Not reported (HR: **0.75**)[8]	**48.3** vs 39.6 (HR: 0.82; p=0.04)*[9]

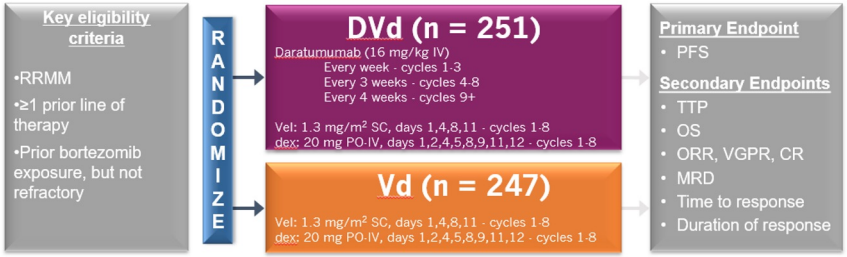
*Results only reported for the global patient population.
d, dexamethasone; dara, daratumumab; elo, elotuzumab; HR, hazard ratio; ixa, ixazomib; K, carfilzomib; (m)OS, (median) overall survival; (m)PFS, (median) progression-free survival; NR, not reached; R, lenalidomide.
1. Bahlis NJ, et al. Leukemia 2020;34:1875–1884; 2. Kaufman JL, et al. Blood 2019;134 (Supplement 1):1866; 3.Dimopoulos MA, et al. J Clin Oncol 2023;41:5190–5199; 4. Dimopoulos MA, et al. Blood Cancer J 2017;7:e554; 5. Siegel DS, et al. J Clin Oncol 2018;36:728–734; 6. Mateos MV, et al. Haematologica 2017;102:1767–1775; 7. Richardson PG, et al. J Clin Oncol 2021;39:2430–2442; 8. Lonial S, et al. N Engl J Med 2015;373:621–631; 9. Dimopoulos MA, et al. Blood Cancer J 2020;10:91.

Treatment options ('triplets') at first relapse[1]



d, dexamethasone; dara, daratumumab; elo, elotuzumab; isa, isatuximab; ixa, ixazomib; K, carfilzomib; P, pomalidomide; R, lenalidomide; S, selinexor; V, bortezomib.
1. Adapted from Moreau P, et al. Lancet Oncol 2021;22:e105–118 and Dimopoulos MA, et al. Ann Oncol 2021;32:309–322.

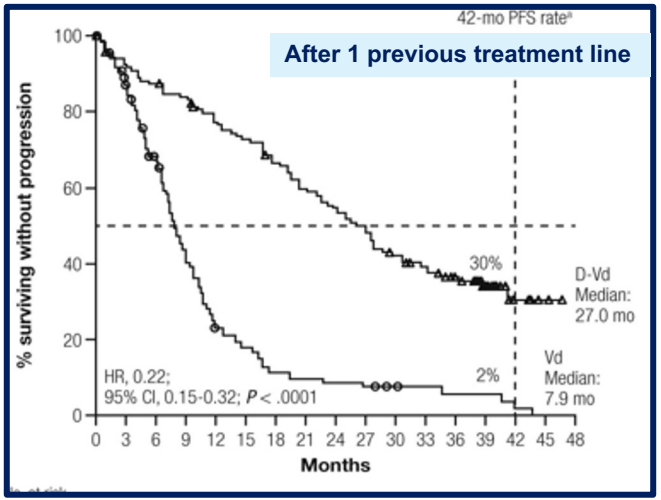
CASTOR: Dara-Vd vs Vd for relapsed MM[1,2]

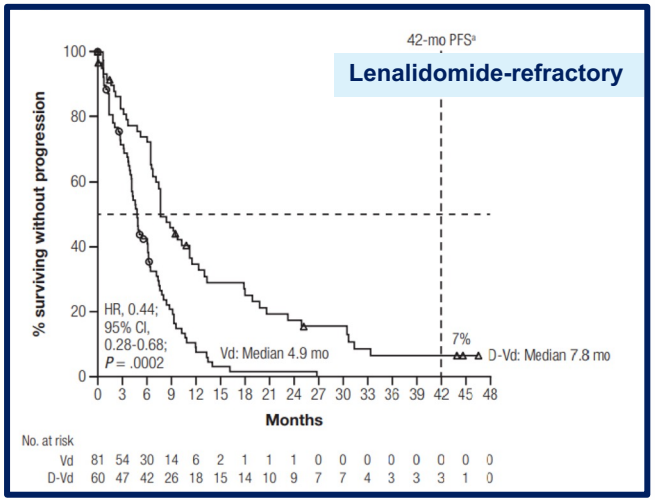


1-3 prior lines (median 2)

24% (Dara-Vd) and **33%** (Vd) len-refractory

PFS 16.7 months vs 7.1 months, HR: 0.31

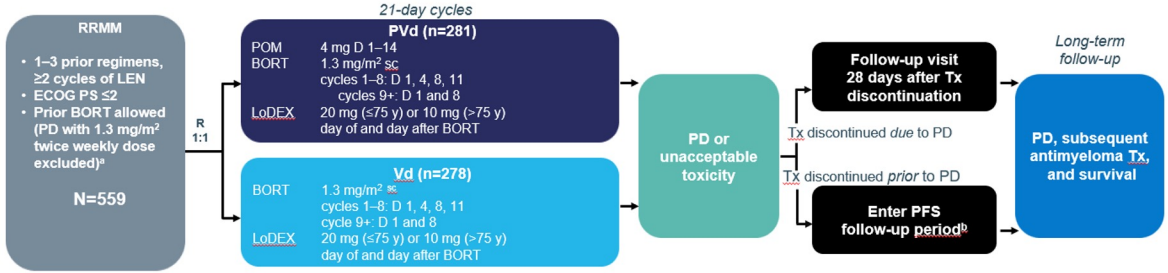




AIFA approved from II line

1. Mateos MV, et al. Clin Lymphoma Myeloma Leuk 2020;20:509–518; 2. Mateos MV, et al. ASH 2018 (Abstract No. 3270 – poster).

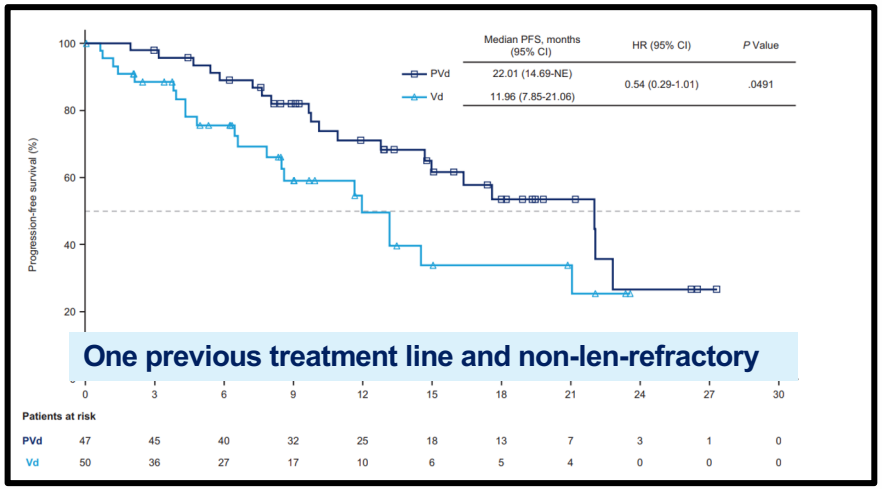
OPTIMISMM: PVd vs Vd for relapsed MM[1,2]

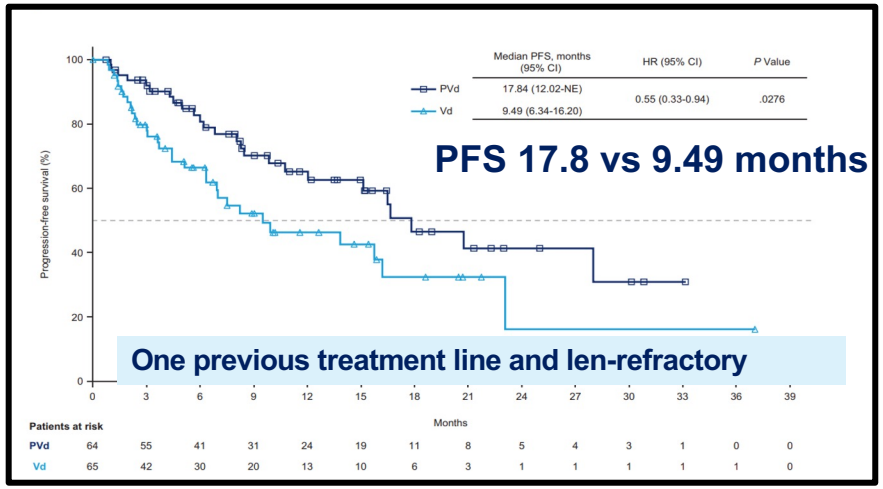


1-3 prior lines (median 2)

71% (PVd) and **69%** (Vd) len-refractory[1]

PFS 11.2 months vs 7 months, HR 0.61





AIFA approved from II line (after lenalidomide)

1. Richardson PG, et al. Lancet Oncol. 2019;20:781–794; 2. Dimopoulos M, et al. Leukemia 2021;35:1722–1731.

BOSTON: SVd vs Vd for relapsed MM[1–3]

Patient Population
- RRMM
- Received 1–3 prior therapies (including bortezomib, carfilzomib, ixazomib, daratumumab, lenalidomide or pomalidomide)

R 1:1

SVd (n=195)
Selinexor QW (100 mg), bortezomib QW (1.3 mg/m²) and dexamethasone BIW (20 mg) in 35-day cycles

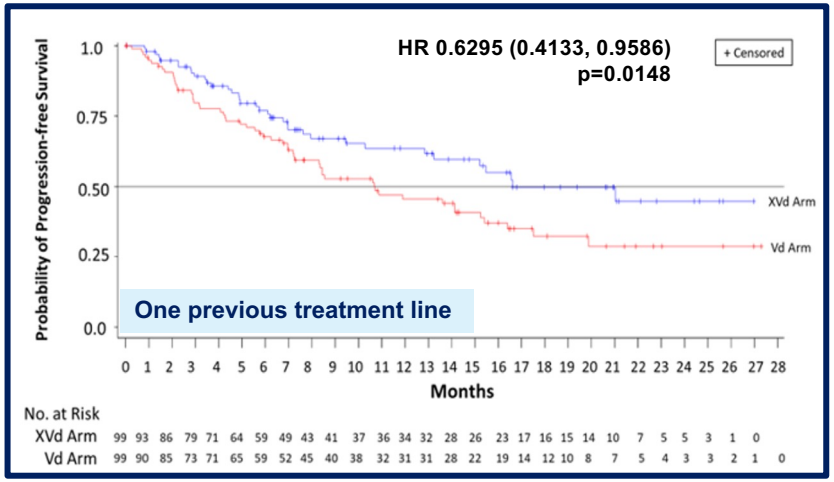
Vd (n=207)
Bortezomib SC (1.3 mg/m² BIW cycles 1–8; QW cycles ≥9) + dexamethasone (20 mg 4x/wk cycles 1–8; then BIW) in 21-day cycles

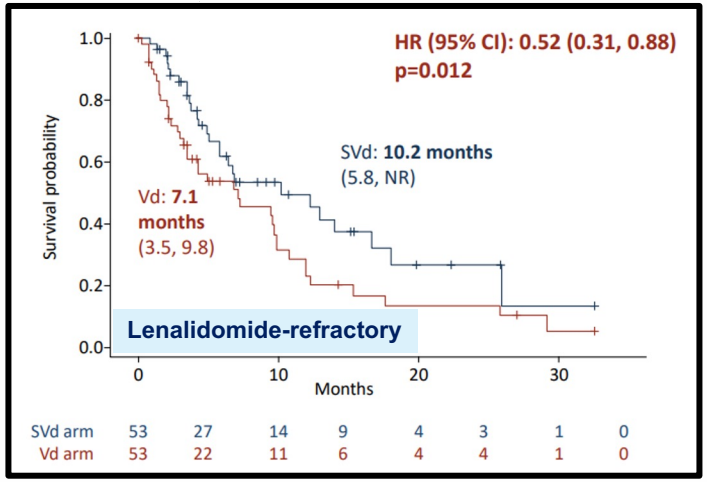
- Crossover allowed from Vd to SVd following confirmation of PD by IRC
- Study treatment continued until PD confirmed by IRC, investigator or patient decision, or unacceptable AEs

Stratification factors:
- Prior PI therapies (yes or no)
- Number of prior anti-MM regimens (1 vs >1)
- R-ISS stage at study entry (III vs I or II)

Primary endpoint: PFS in ITT population

27% len-refractory





FDA/EMA approved from 2L, AIFA awaited

1. Grosicki S, et al. Lancet 2020;396;1563–1573; 2. Mateos MV, et al. EHA 2023 (Abstract No. 886 – poster); 3. Mateos MV, et al. J Hematol Oncol 2021;14:59

ENDEAVOR phase 3 trial: Kd vs Vd

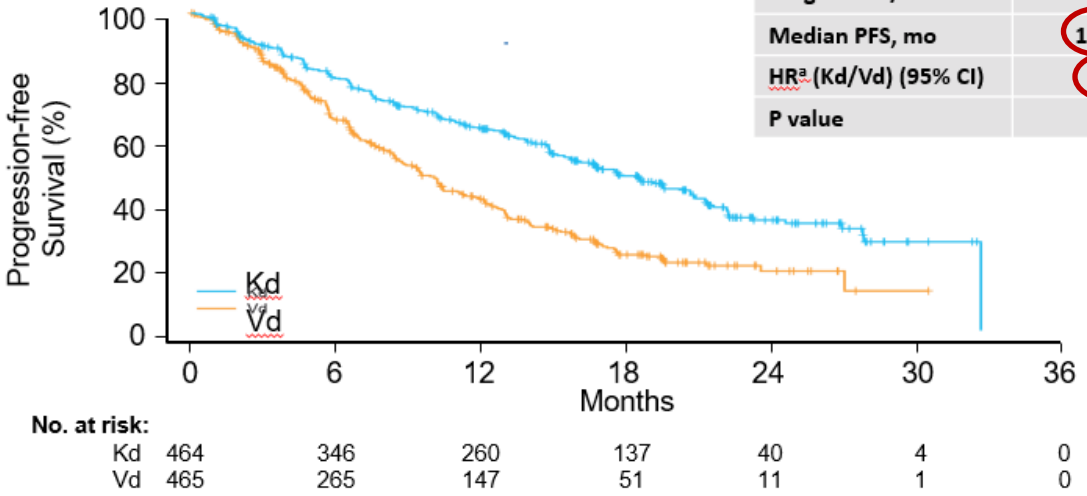
Pts characteristics Kd vs Vd:

- ✓ Median age 65y in both arms
- ✓ ISS II-III 56% in both arms
- ✓ HR cytogenetic: 21% and 24%
- ✓ 1-3 prior line (median 2)
- ✓ lena exposed 38% (refractory 24%)

Median FU 37 months

Kd > Vd in response, PFS and OS

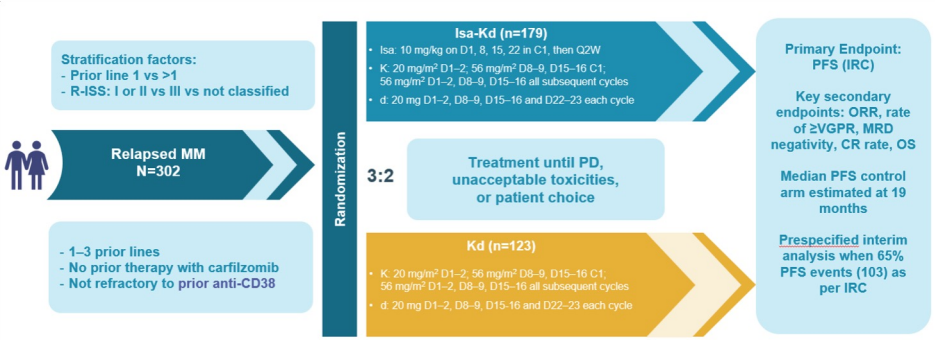
	Kd (N = 464) n (%)	Vd (N = 465) n (%)
Progression/Death	245 (52.8)	298 (64.1)
Median PFS, mo	17.6	9.4
HR[a] (Kd/Vd) (95% CI)	0.53 (0.44 – 0.63)	
P value	<0.0001	



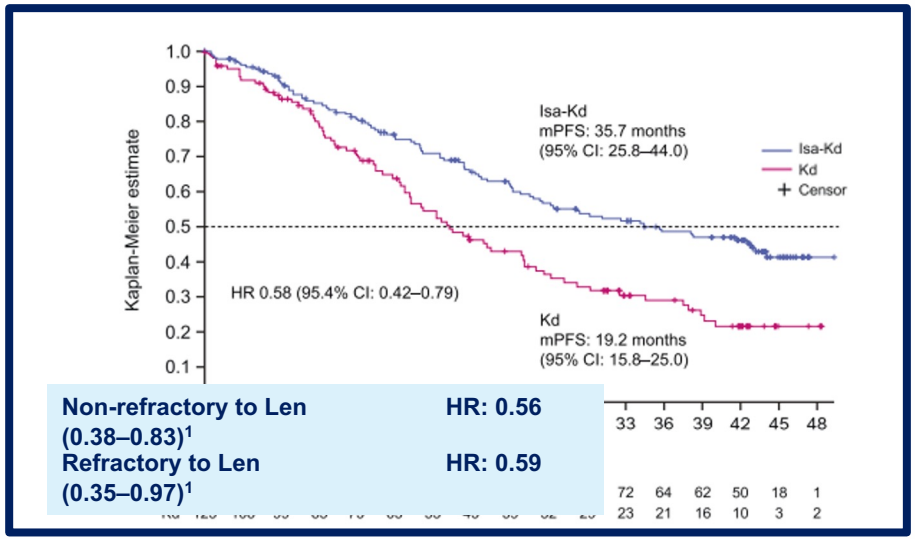
AIFA approved from 2L

Dimopoulos MA et al, Lancet Oncology 2016; Palumbo A et al, N Engl J Med 2016; Spencer at al, Haematologica 2018; Mateos MV et al, Clinical Lymphoma, Myeloma & Leukemia 2019; Moreau P et al. Leukemia 2017; 31(1):115-122; Usmani SZ et al. ASH 2018;132:3288

IKEMA: Isa-Kd vs Kd for relapsed MM[1–4]



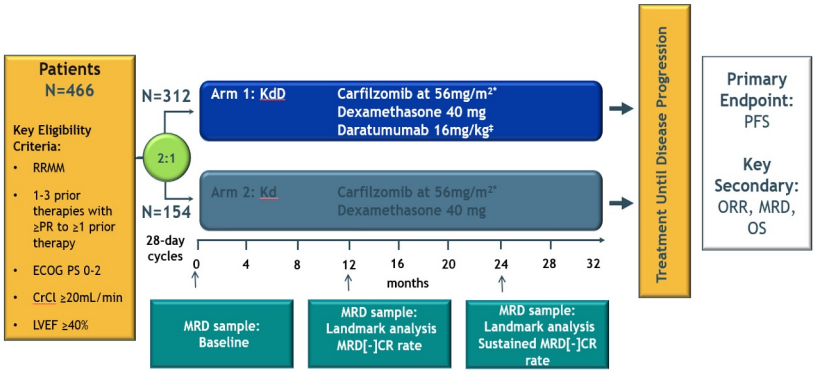
1-3 prior lines
32% (Isa-Kd) and **34%** (Kd) len-refractory[1]
PFS 35.7 vs 19.2 months



AIFA approved from II line to IV line

1. Martin T, et al. Blood Cancer J 2023:13;72; 2. Facon T, et al. EHA 2021 (Abstract No. EP980 – poster); 3. NCT03275285. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT03275285 (last accessed September 2023); 4. Moreau P, et al. Lancet 2021;397:2361–2371.

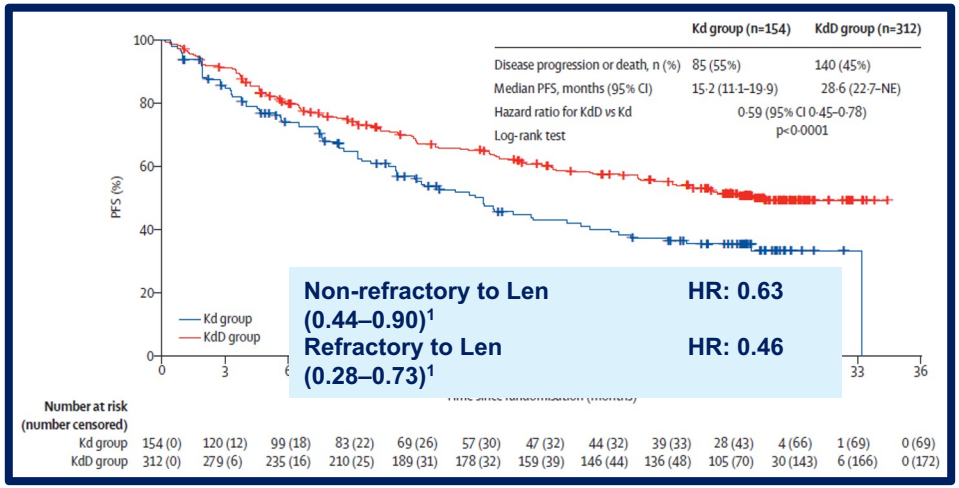
CANDOR: Dara-Kd vs Kd for relapsed MM[1,2]



1-3 prior line

32% (Dara-Kd) and **36%** (Kd) len-refractory[1]

PFS 28.6 vs 15.2

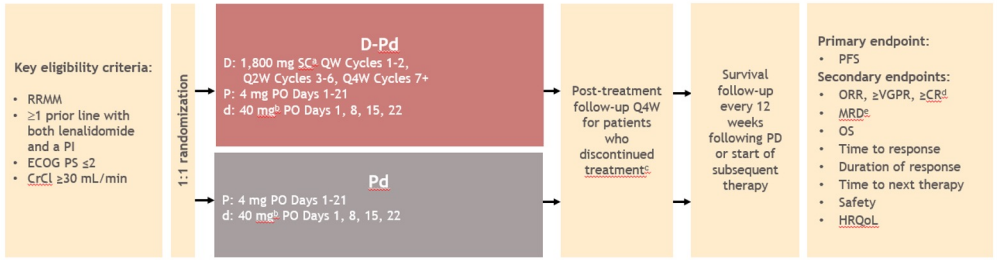


AIFA approved from 2L, but not refund

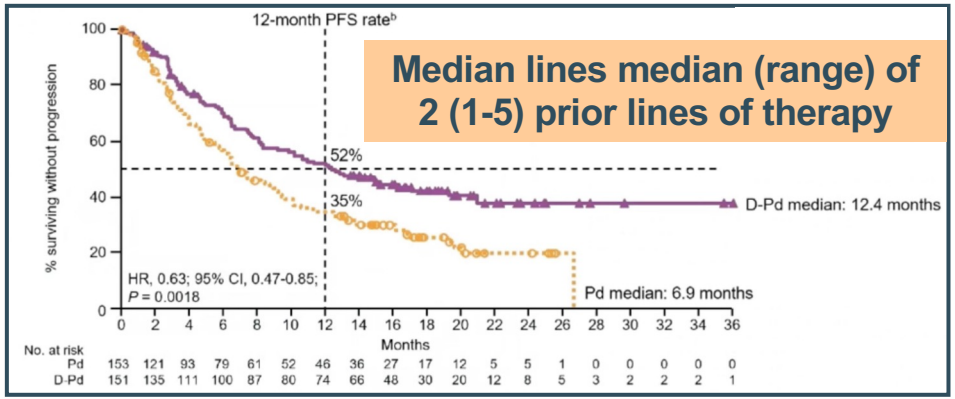
CI, confidence interval; CR, complete response; CrCl, creatinine clearance; d, dexamethasone; D/Dara, daratumumab; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; K, carfilzomib; len, lenalidomide; LVEF, left ventricular ejection fraction; MM, multiple myeloma; MRD, minimal residual disease; NE, non-evaluable; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; RRMM, relapsed/refractory multiple myeloma.

1. Usmani SZ, et al. Lancet Oncol 2022;23:65–76; 2. NCT03158688. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT03158688 (last accessed September 2023).

APOLLO: Dara-Pd for relapsed MM[1–3]



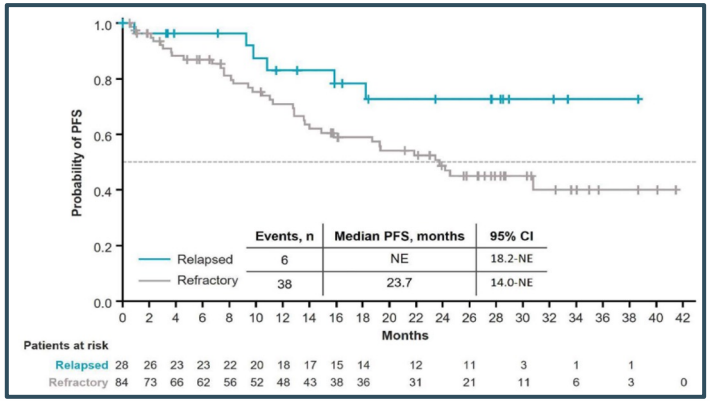
79% (Dara-Pd) and **80%** (Pd) len-refractory[1,2]



Median lines median (range) of 2 (1-5) prior lines of therapy

Phase II MM-014 study, cohort B: non-randomised Dara-Pd[3]

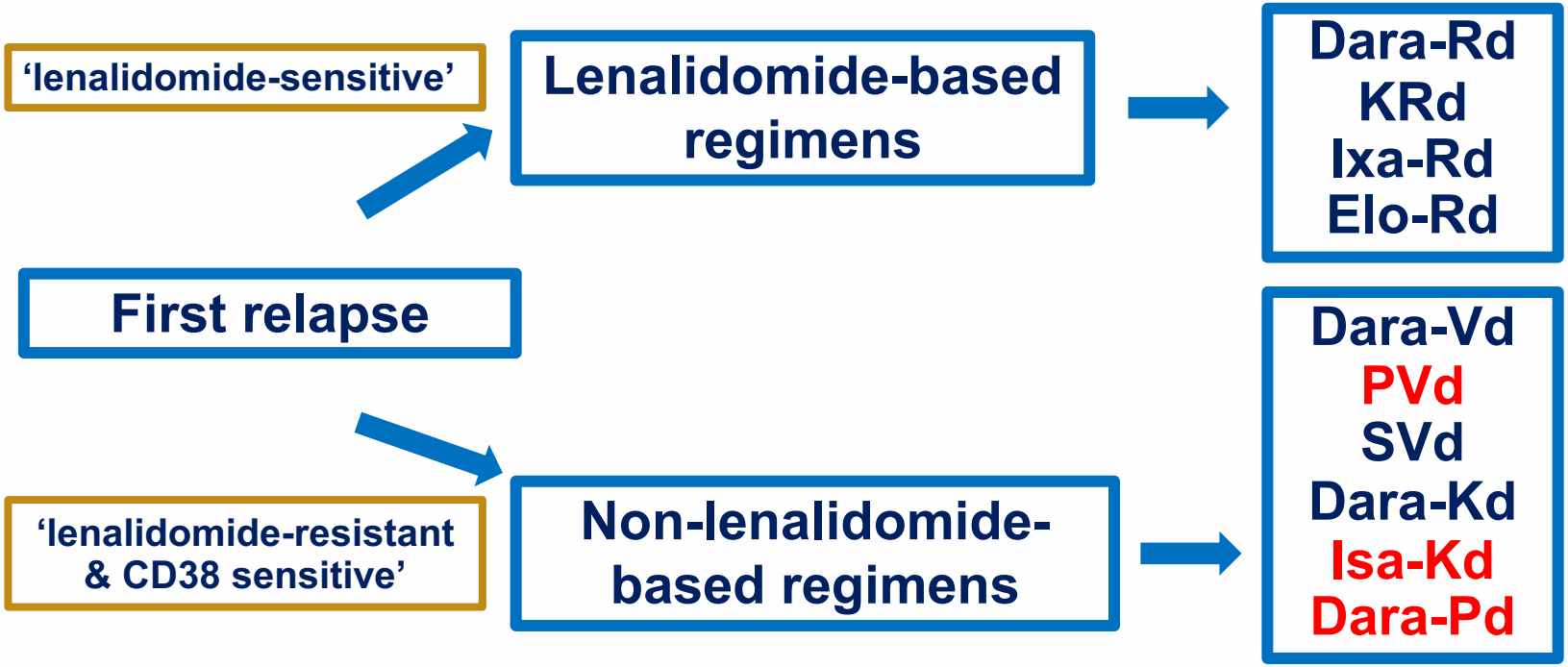
75% len-refractory in ITT population[3]



II line after 1L with PI and LENA and LENA refractory
III line after PI and LENA

1.Dimopoulos MA, et al. Lancet Oncol 2021:22;801–812;
2. Dimopoulos MA, et al. ASH 2020 (Abstract No. 412 – presentation); 3. Bahlis NJ, et al. Leuk Lymphoma 2022:63;1407–1417.

Treatment options ('triplets') at first relapse[1]



d, dexamethasone; dara, daratumumab; elo, elotuzumab; isa, isatuximab; ixa, ixazomib; K, carfilzomib; P, pomalidomide; R, lenalidomide; S, selinexor; V, bortezomib.
1. Adapted from Moreau P, et al. Lancet Oncol 2021;22:e105–118 and Dimopoulos MA, et al. Ann Oncol 2021;32:309–322.

How to further improve the outcome?

- New targets
- Innovative mechanism of action
- Newer combinations

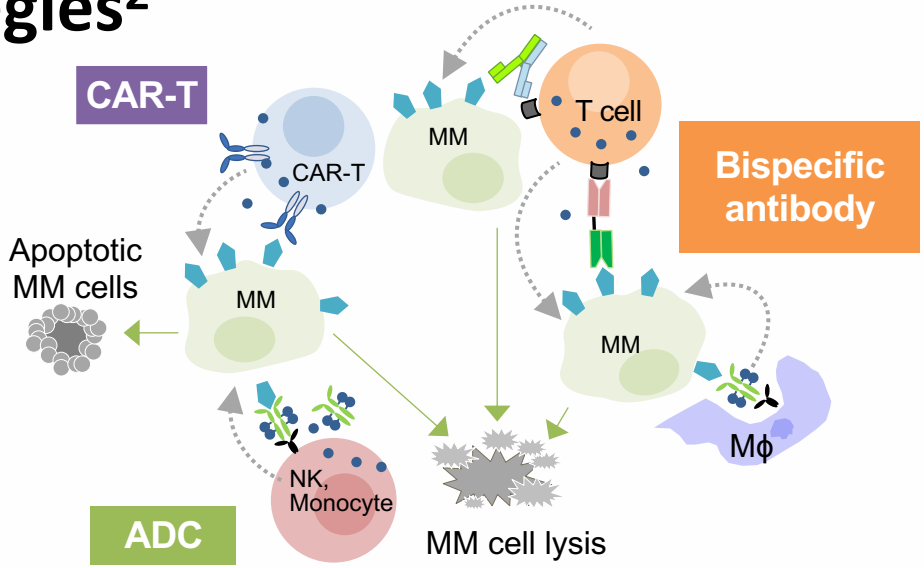
BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; FcRH5, Fc receptor-homolog 5; GPRC5D, G protein–coupled receptor, class C, group 5, member D; MM, multiple myeloma; scFv, single chain variable fragment; SLAMF7, signalling lymphocytic activation molecule family member 7.

1. Rodríguez-Lobato LG, et al. Front Oncol 2020:10;1243; 2. Swan D, et al. Cancers (Basal) 2023:15;1819; 3. Verkleij CPM, et al. Curr Opin Oncol 2020;32:664–71.

BCMA-targeted agents use different modalities to target and kill multiple myeloma cells[1]

- **BCMA-targeted strategies[2]**

ADC	mAbs conjugated to a **toxic payload** that specifically bind BCMA and target myeloma cells[1,3]
CAR-T cell therapy	**Genetically modified T cells** that recognize and kill BCMA-expressing tumor cells[1,4]
Bispecific antibody	Dual-antigen specificity **facilitating cell-to-cell interactions** between T cells and tumor cells[1,5]



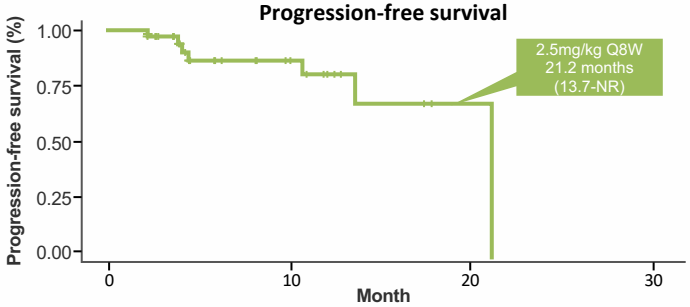
- ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; Mϕ, macrophage; MM, multiple myeloma; NK, natural killer.
- **1.** Shah N et al. *Leukemia.* 2020;34(4):985-1005. **2.** Cho SF et al. *Front Immunol.* 2018;9:1821. doi:10.3389/fimmu.2018.01821 **3.** Montes de Oca R et al. *Mol Cancer Ther.* 2021;20(10):1941-1955. **4.** Wang Q et al. *Cell Immunol.* 2021;363:104342. doi:10.1016/j.cellimm.2021.104342 **5.** Moreau P et al. *N Engl J Med.* 2022;387(6):495-505.

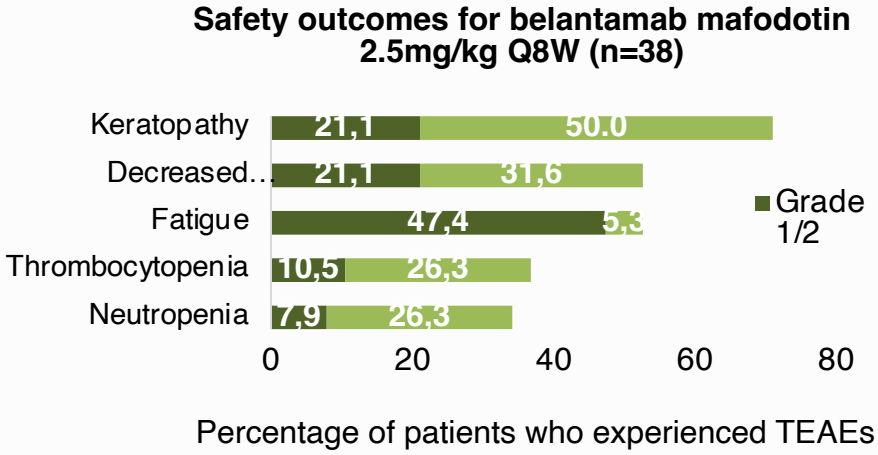
HQ

ALGONQUIN: belaPd demonstrated clinically meaningful combination efficacy in patients with 2L+ RRMM who were CD38- and len-refractory

Part 1 and 2: belantamab mafodotin RP2D in combination with Pd in TCE/TCR RRMM*

Patient characteristics	All cohorts (N=61)
Median age, years (range)	67 (36-85)
Median prior lines of therapy, n (range)	3 (2-5)
Anti-CD38 (dara) exposed/refractory, n (%)	61 (100)/60 (98.4)
Len exposed/refractory, n (%)	61 (100)/60 (98.4)
Efficacy outcomes	**Belantamab mafodotin 2.5mg/kg Q8W (n=38)**
ORR, n (%)	27/33 (82)†
Median follow-up, months (range)	6.2 (0-21.2)





AEs were successfully managed with supportive care and dose modifications, with no treatment discontinuations in the 2.5mg/kg Q8W cohort, suggesting that a **belantamab mafodotin combination regimen could potentially be a good option for all patients, especially those that are elderly and frail**

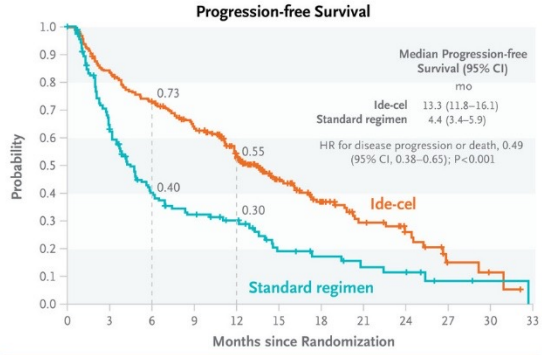
*This analysis reported results for the subgroup of patients exposed to lenalidomide, a PI, and an anti-CD38 agent treated at doses of 1.92mg/kg or 2.5mg/kg belantamab mafodotin in combination with Pd. †ORR calculation out of 33 eligible patients who received a belantamab mafodotin dose of 2.5mg/kg Q8W.

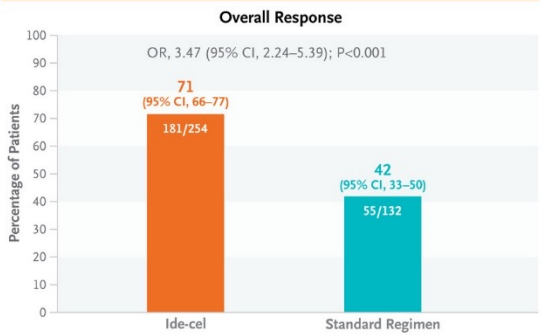
2L, second line; AE, adverse event; belaPd, belantamab mafodotin/pomalidomide/dexamethasone; CD, cluster of differentiation; CI, confidence interval; CR, complete response; len, lenalidomide; mPFS, median progression-free survival; NYR, not yet reached; ORR, overall response rate; Pd, pomalidomide/dexamethasone; PI, proteasome inhibitor; PR, partial response; PRO, patient-reported outcome; Pt, part; Q4W, every four weeks; Q8W, every eight weeks; RP2D, recommended phase II dose; RRMM, relapsed/refractory multiple myeloma; sCR, stringent complete response; TCE, triple-class exposed; TCR, triple-class refractory; TEAE, treatment-emergent adverse event; VGPR, very good partial response.

Trudel S et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 10-13, 2022; New Orleans, LA. Poster 3248.

CAR-T IN EARLY LINES OF THERAPY

KARMMA 3 Ide-cell vs SOC





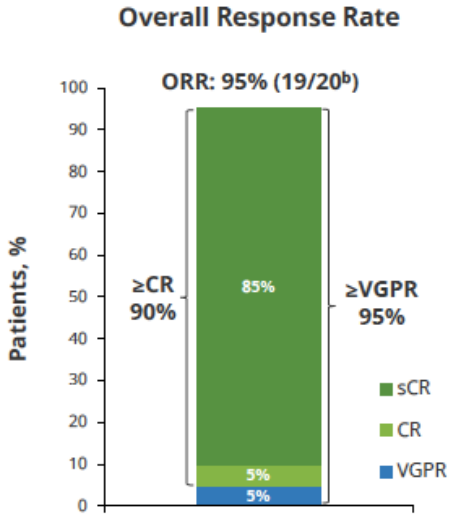
Ide-cell in patients with 2-4 prior lines of therapy

mPFS rate 13.3 months

ORR: 71%

CARTITUDE-2 Cohort A:

Cilta-cel in patients with early relapse (1-3 LOT) and Len-ref (n=20)



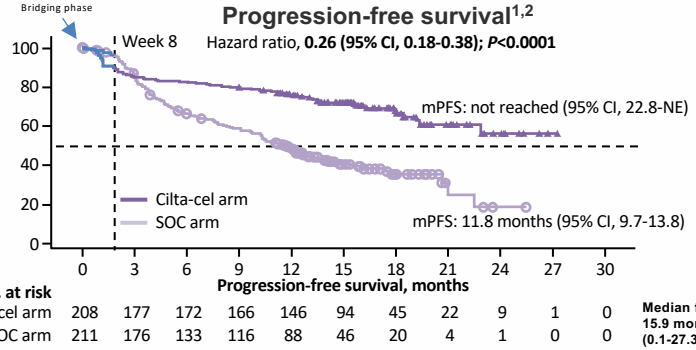
- Median DOR was NR
- **15-month PFS rate was 70%** (95% CI, 45.1–85.3)

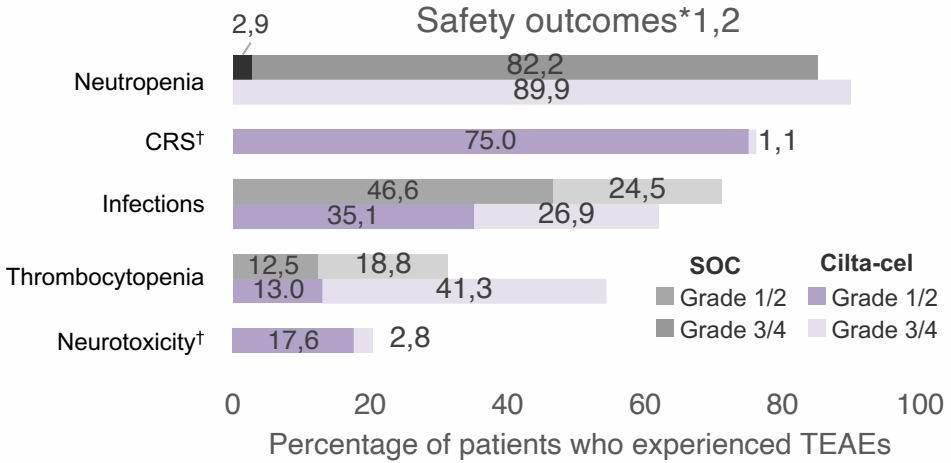
CAR: chimeric antigen receptor; AE: adverse event; LOT: line of therapies; ORR: overall survival; NR: not reached

Rodriguez Otero P et al, NEJM 2023
Cohen AD et al. IMS 2022. Oral presentation.

CARTITUDE-4: cilta-cel vs PVd or DPd in 2L+ RRMM patients, len refractory[1,2]

CARTITUDE-4 (phase III)	Cilta-cel	SOC (PVd or DPd)
ITT population[1,2]	**n=208**	**n=211**
Median age, years (range)	61.5 (27-78)	61.0 (35-80)
ECOG PS ≤1, n (%)	207 (99.5)	210 (99.5)
High-risk cytogenetics, n/N (%)	123/207 (59.4)	132/210 (62.9)
Median prior therapies, n (range)	2 (1-3)	2 (1-3)
Triple-class refractory, n (%)	30 (14.4)	33 (15.6)
ITT population[2]		
mPFS, months	NR	11.8
HR (95% CI)	0.26 (0.18-0.38)	





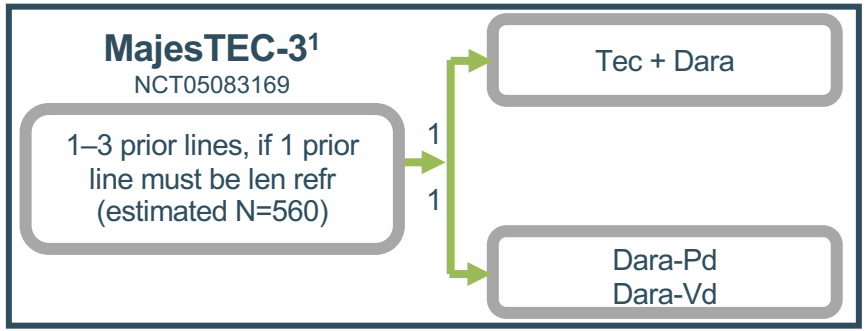
Of the 208 patients in the ITT population, **32 discontinued** treatment before receiving cilta-cel; median time from first apheresis to cilta-cel infusion: **79 days** (range, 45-246)[1,3]

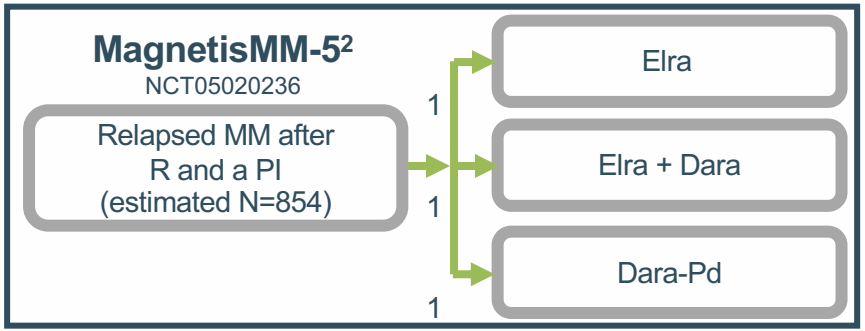
The rate of CRS and infections in this fairly fit and young patient population suggests this regimen **might be difficult** for elderly and immunocompromised patients to tolerate[1,2]

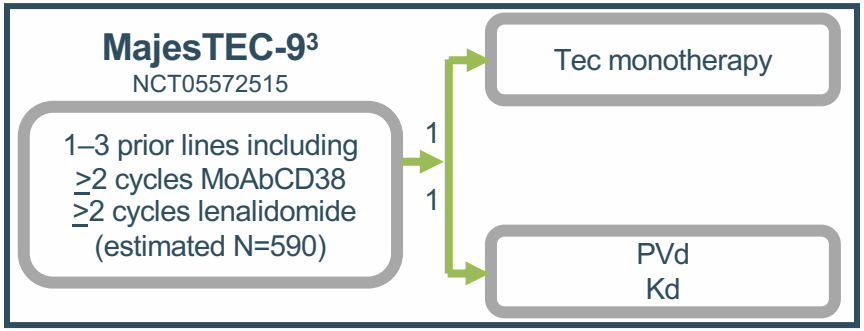
*The safety population had 208 patients in each arm.[1] †In 176 evaluated patients who received cilta-cel in the as-treated population.[1,2] L, second-line; AE, adverse event; cilta-cel, ciltacabtagene autoleucel; CR, complete response; CRS, cytokine release syndrome; DOR, duration of response; DPd, daratumumab/pomalidomide/dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; ITT, intent-to-treat; mPFS, median progression-free survival; NA, not available; NR, not reached; ORR, overall response rate; OS, overall survival; Pd, pomalidomide/dexamethasone; PFS, progression-free survival; PR, partial response; PVd, pomalidomide/bortezomib/dexamethasone; RRMM, relapsed/refractory multiple myeloma; sCR, stringent complete response; SOC, standard of care; VGPR, very good partial response.

1. San-Miguel J et al. *N Engl J Med.* 2023;389(4):335-347. **2.** Dhakal B et al. Presented at: American Society of Clinical Oncology Annual Meeting; June 2-6, 2023; Chicago, IL. Presentation LBA106. **3.** San-Miguel J et al. Supplementary appendix. *N Engl J Med.* 2023;389(4):335-347. doi:10.1056/NEJMoa2303379

Bringing BCMA-targeting bispecific antibodies to earlier lines of relapse



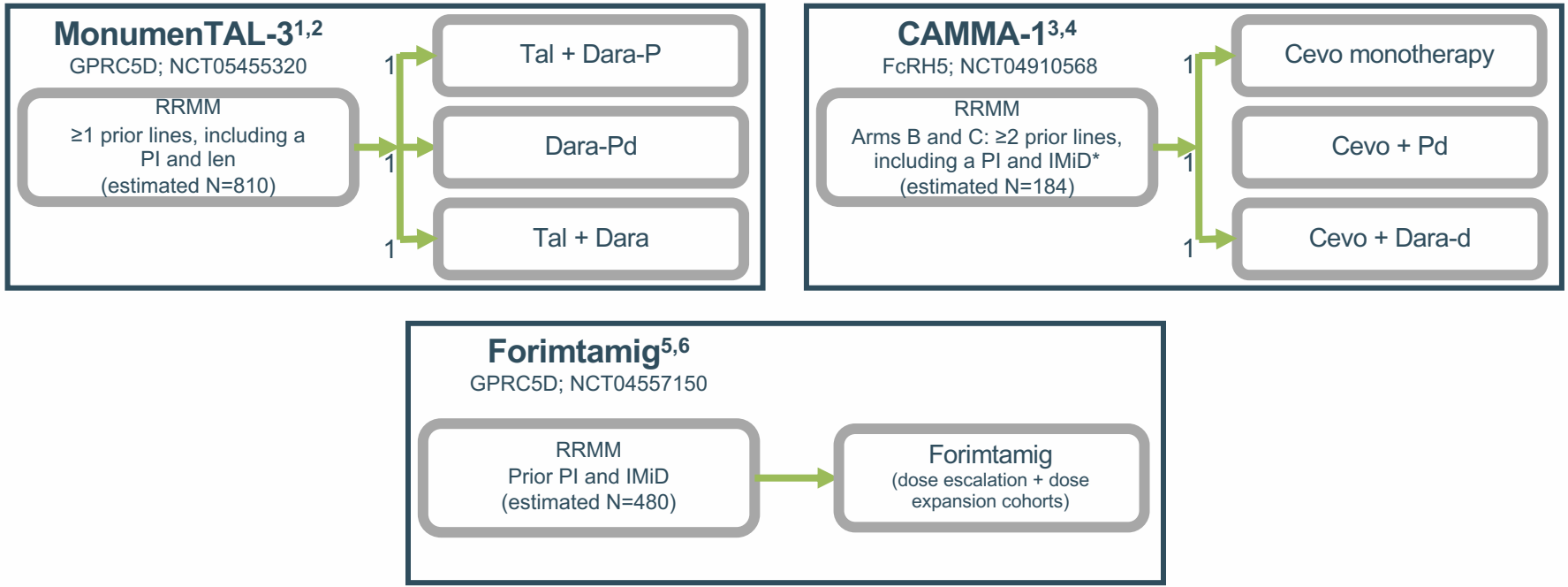




BCMA, B-cell maturation antigen; d, dexamethasone; D/Dara, daratumumab; Elra, elranatamab; K, carfilzomib; MM, multiple myeloma; P, pomalidomide; PI, proteasome inhibitor; R, lenalidomide; Tec, teclistamab; V, bortezomib.

1. NCT05083169. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT05083169 (last accessed September 2023); 2. NCT05020236. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT05020236 (last accessed September 2023); 3. Touzeau C, et al. ASCO 2023 (Abstract No. TPS8067 – presentation).

Other bispecific antibody targets being explored in earlier lines of relapse: GPRC5D and FcRH5



*Arm A inclusion criteria: No established therapy for MM is appropriate and available, or intolerance to established therapies.

Cevo, cevostamab; d, dexamethasone; Dara, daratumumab; FcRH5, Fc receptor-homolog 5; GPRC5D, G protein–coupled receptor, class C, group 5, member D; IMiD; immunomodulatory drug; len; lenalidomide; P, pomalidomide; PI, proteasome inhibitor; RRMM, relapsed/refractory multiple myeloma; Tal, talquetamab.

1. NCT05455320. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT05455320 (last accessed September 2023); 2. Cohen YC, et al. ASH 2022 (Abstract No. 1925 – poster); 3. NCT04910568. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT04910568 (last accessed September 2023); 3. Vij R, et al. HemaSphere 2022;6:1905–1906; 5. NCT04557150. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT04557150 (last accessed September 2023); 6. Carlo-Stella C, et al. ASH 2022 (Abstract No. 161 – presentation).

Conclusions

- The treatment options for relapsed MM have significantly increased over recent years
- Treatment choice should be tailored based on disease and patient characteristics, previous treatment and available options
- Triplet drug combinations are the current standard of care
- However, the majority of patients at first relapse are now lenalidomide-refractory and a growing population will also be progressing on daratumumab, limiting the available treatment options
- Anti-BCMA bispecific antibodies showed great efficacy in heavily pre-treated RRMM patients: ORR and CR rates up to 80% and 40% and durable responses (>12 months).
- Bispecific antibodies are associated with lower rates and grades of CRS and ICANS as compared to CAR T-cells, thus allowing older patients to be treated.
- In the near future, bispecific antibodies are expected to further improve the outcome for patients with relapsed MM
- Based on the results from KarMMa-3 and CARTITUDE-4, BCMA-targeting CAR-T cells are expected to set a new standard in the management of first and later relapse

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