HEMOCENTRO UNICAMP

O paciente triplo exposto que progride: minhas opções de anticorpos biespecíficos com base em estudos pivotais e dados de vida real

Fernando Pericole

Conflicts of interest – Fernando Pericole

I have the following financial relationships to disclose

Leadership position/advisory role for: Johnson & Johnson

Stockholder in: nothing to disclose

Patents and royalties from: nothing to disclose

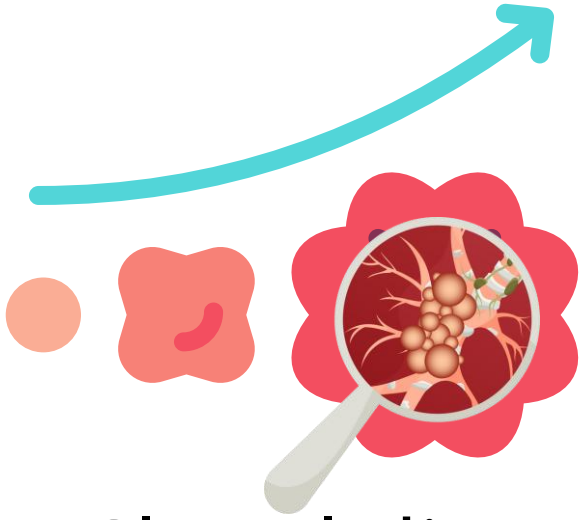
Honoraria (lecture fee) from: Johnson & Johnson, Takeda, Amgen, Abbvie, Astra Zeneca, Beigene

Honorary (manuscript fee) from: Pfizer, Johnson & Johnson

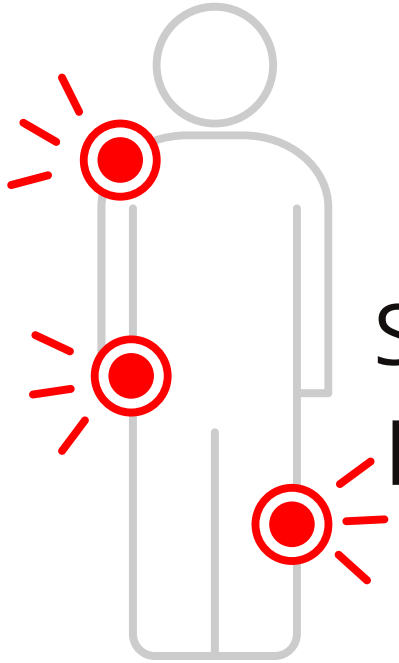
Grant / Research funding from: nothing to disclose

Other remuneration from: nothing to disclose

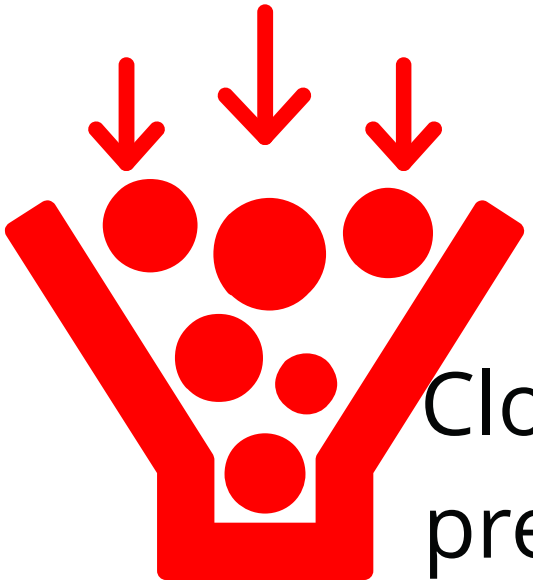
Challenges of relapsed and refractory MM



Clonal diversity



Spatial genetic heterogeneity



Clonal selection by previous therapies

Drug resistance

Slide do autor

REGULAR ARTICLE

blood advances

Outcomes after biochemical or clinical progression in patients with multiple myeloma

Sarah Goldman-Mazur,[1] Alissa Visram,[1,2] Prashant Kapoor,[1] Angela Dispenzieri,[1] Martha Q. Lacy,[1] Morie A. Gertz,[1] Francis K. Buadi,[1] Suzanne R. Hayman,[1] David Dingli,[1] Taxiarchis Kourelis,[1] Wilson Gonsalves,[1] Rahma Warsame,[1] Eli Muchtar,[1] Nelson Leung,[3] Moritz Binder,[1] Amie Fonder,[1] Miriam Hobbs,[1] Yi Lisa Hwa,[1] Robert A. Kyle,[1] S. Vincent Rajkumar,[1] and Shaji K. Kumar[1]

[1]Division of Hematology, Mayo Clinic Rochester, Rochester, MN; [2]Division of Hematology, Ottawa Hospital Research Institute, Ottawa, ON, Canada; and [3]Division of Nephrology, Mayo Clinic Rochester, Rochester, MN

- Retrospective analysis of 1347 MM patients (2001-2018)
- **Biochemical progression:** 60% of cases
- **Clinical progression:** 40% of cases
- **Aggressive relapse:** EMD, plasma cell leukemia or plasmapheresis needed at relapse

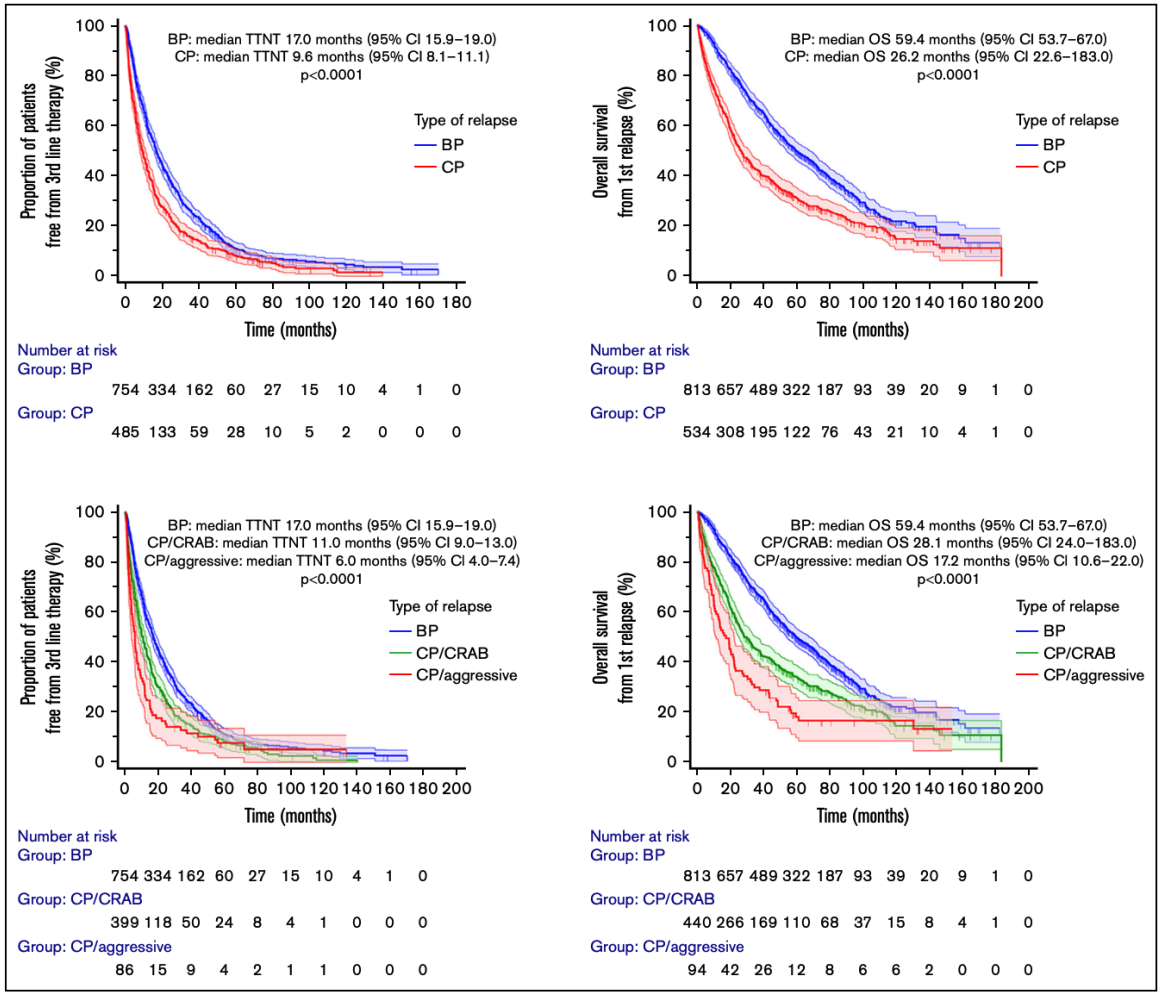


Table 3. Changes in the prevalence of CRAB symptoms at first relapse in patients who experienced a particular CRAB symptom at diagnosis compared with patients without this particular CRAB symptom at diagnosis in the clinical progression group (n = 534)

At baseline \ At first relapse	C: Hypercalcemia	R: Renal insufficiency	A: Anemia	B: New bone disease
C: Hypercalcemia	$P = .004$ **OR, 3.3** 95% CI, 1.4-7.5	NS	NS	NS
R: Renal insufficiency	NS	$P < .001$ **OR, 3.6** 95% CI, 1.9-6.7	NS	NS
A: Anemia	NS	$P = .02$ **OR, 1.9** 95% CI, 1.1-3.5	$P < .001$ **OR, 2.1** 95% CI, 1.4-3.2	$P = .001$ **OR, 0.4** 95% CI, 0.3-0.6
B: Bone disease	NS	$P = .01$ **OR, 0.5** 95% CI, 0.3-0.8	$P < .001$ **OR, 0.4** 95% CI, 0.3-0.6	$P < .001$ **OR, 2.2** 95% CI, 1.5-3.4

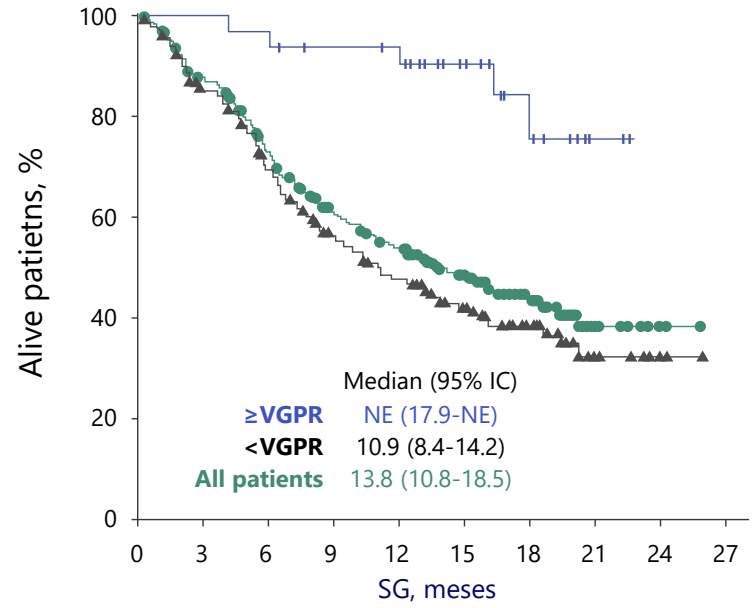
Goldman-Mazur, Sarah, et al. "Outcomes after biochemical or clinical progression in patients with multiple myeloma." *Blood advances* 7.6 (2023): 909-917.

Real life data support that recycled therapies are not good options

LOCOMMOTION[1] (100% triple class exposed)

31,9% ORR

Overall survival



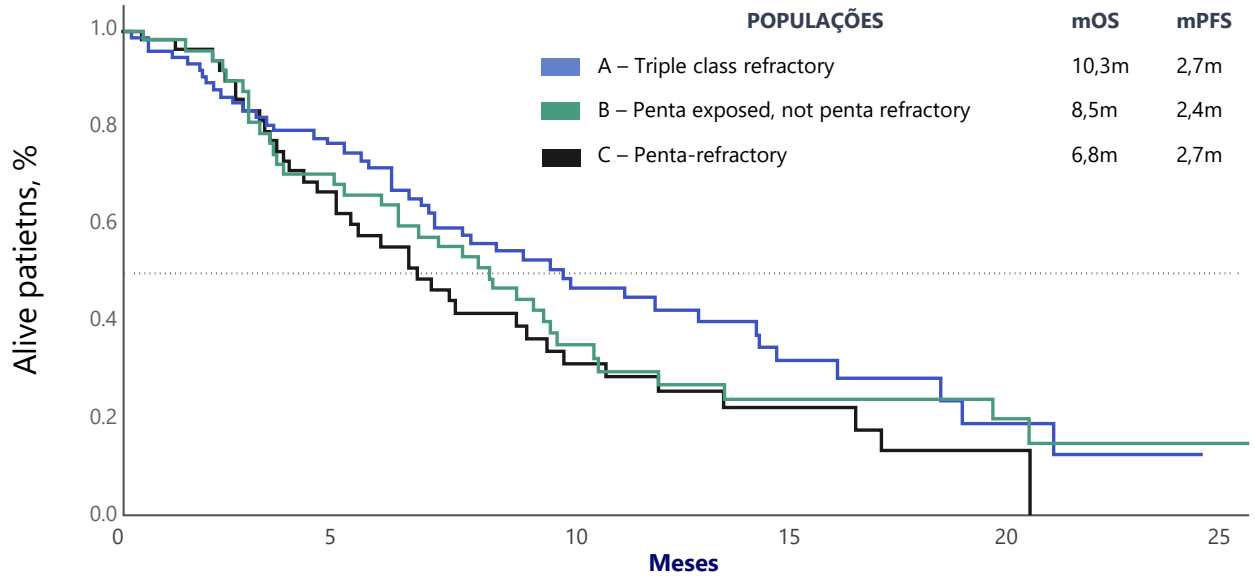
≥VGPR	33	33	32	29	26	17	9	2	0	0
<VGPR	215	179	137	102	85	54	28	8	2	0
All patients	248	212	169	131	111	71	37	10	2	0

Adaptado de Mateos MV, et al. Leukemia, 2022

MAMMOTH[2] (100% triple class refractory)

30% ORR

Overall survival



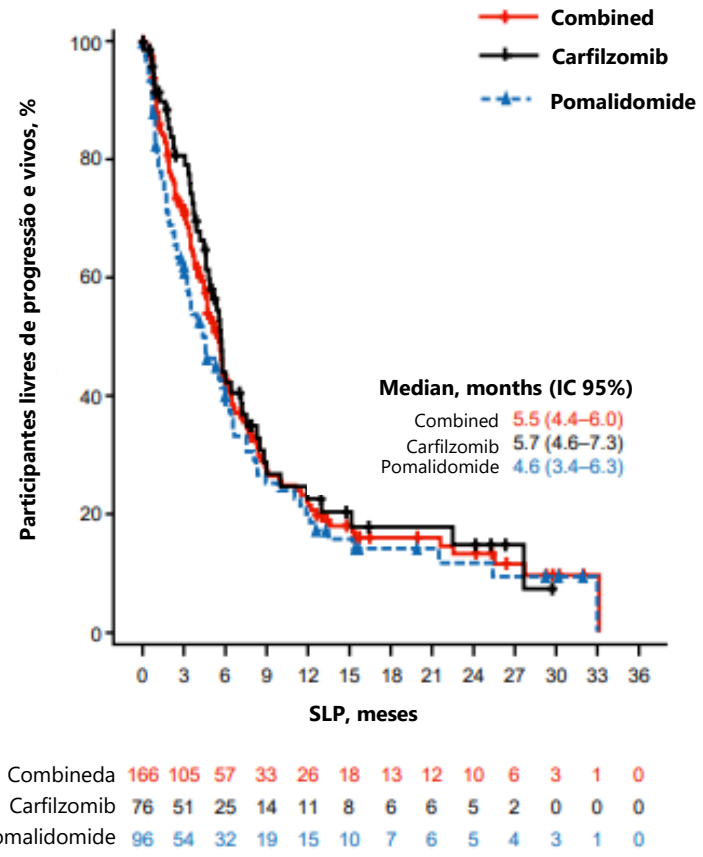
A	75	50	13	4	1	0
B	49	32	8	7	2	1
C	53	29	6	1	0	0

Adaptado de Bal S, et al. Leukemia, 2022

1. Mateos MV, et al. LocoMMotion: a prospective, non-interventional, multinational study of real-life current standards of care in patients with relapsed and/or refractory multiple myeloma. Leukemia. 2022 Mac;36(9):1371-1376;. 2. Bal S, et al. Leukemia. 2022;36:877-80 3. Mikhael J. Treatment Options for Triple-class Refractory Multiple Myeloma. Clin Lymphoma Myeloma Leuk. 2020 Jan;20(1):1-7

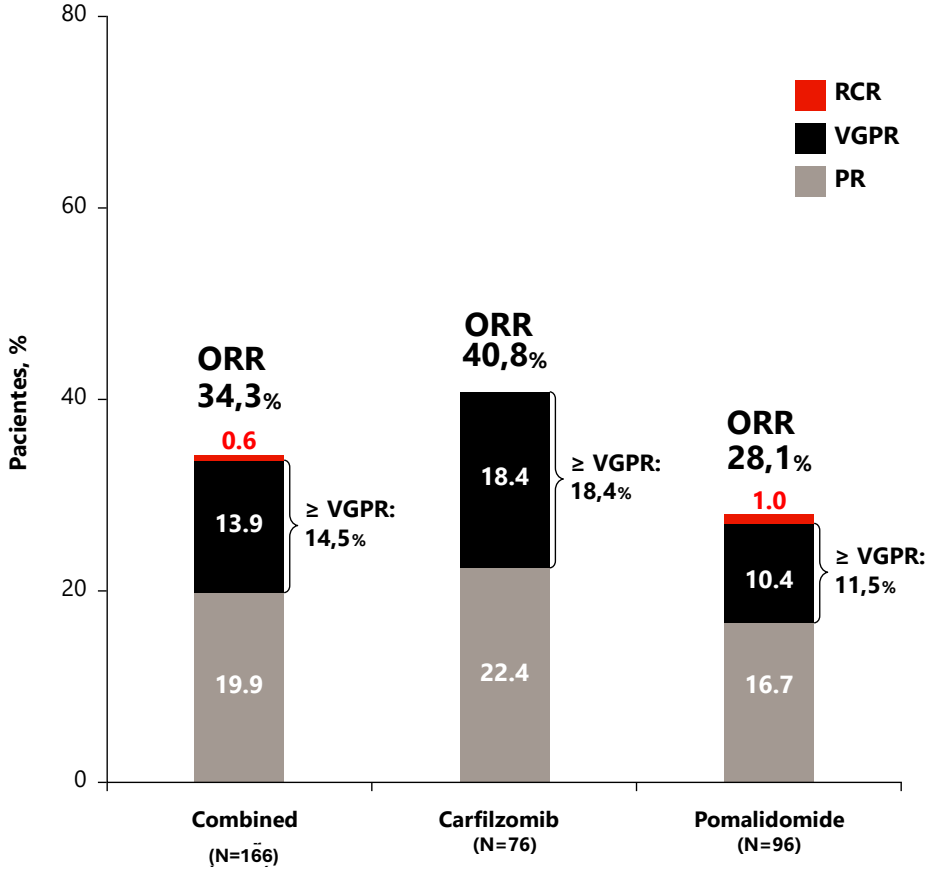
55% of patients of LOCOMMOTION/MOMMENT were treated with **carfilzomib and / or pomalidomide** with poor outcomes (IMS 2024)

PROGRESSION FREE SURVIVAL



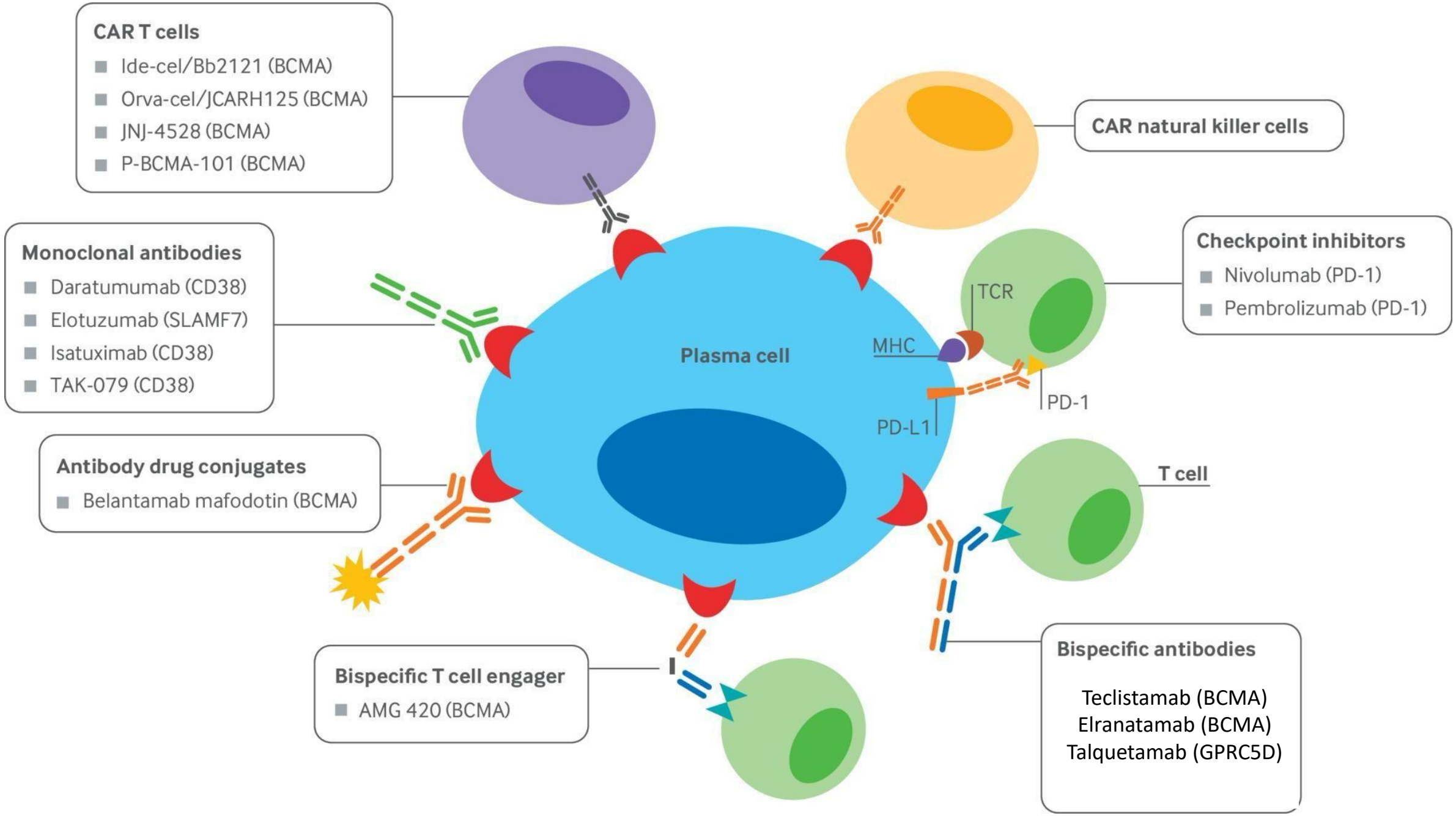
Adaptado de Mateos, et al. IMS, 2024

OVERALL RESPONSE RATE (ORR)

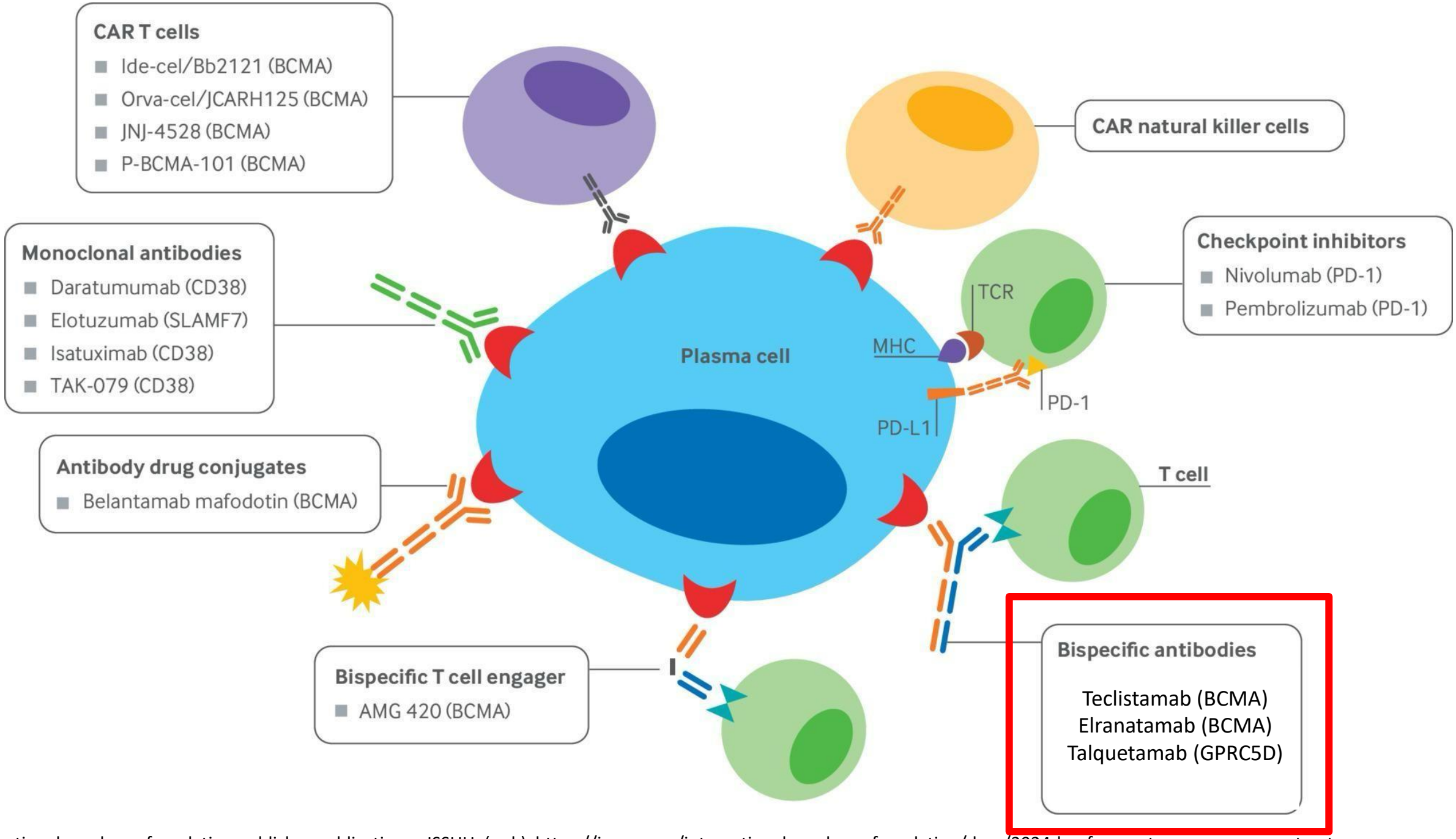


Adaptado de Mateos, et al. IMS, 2024

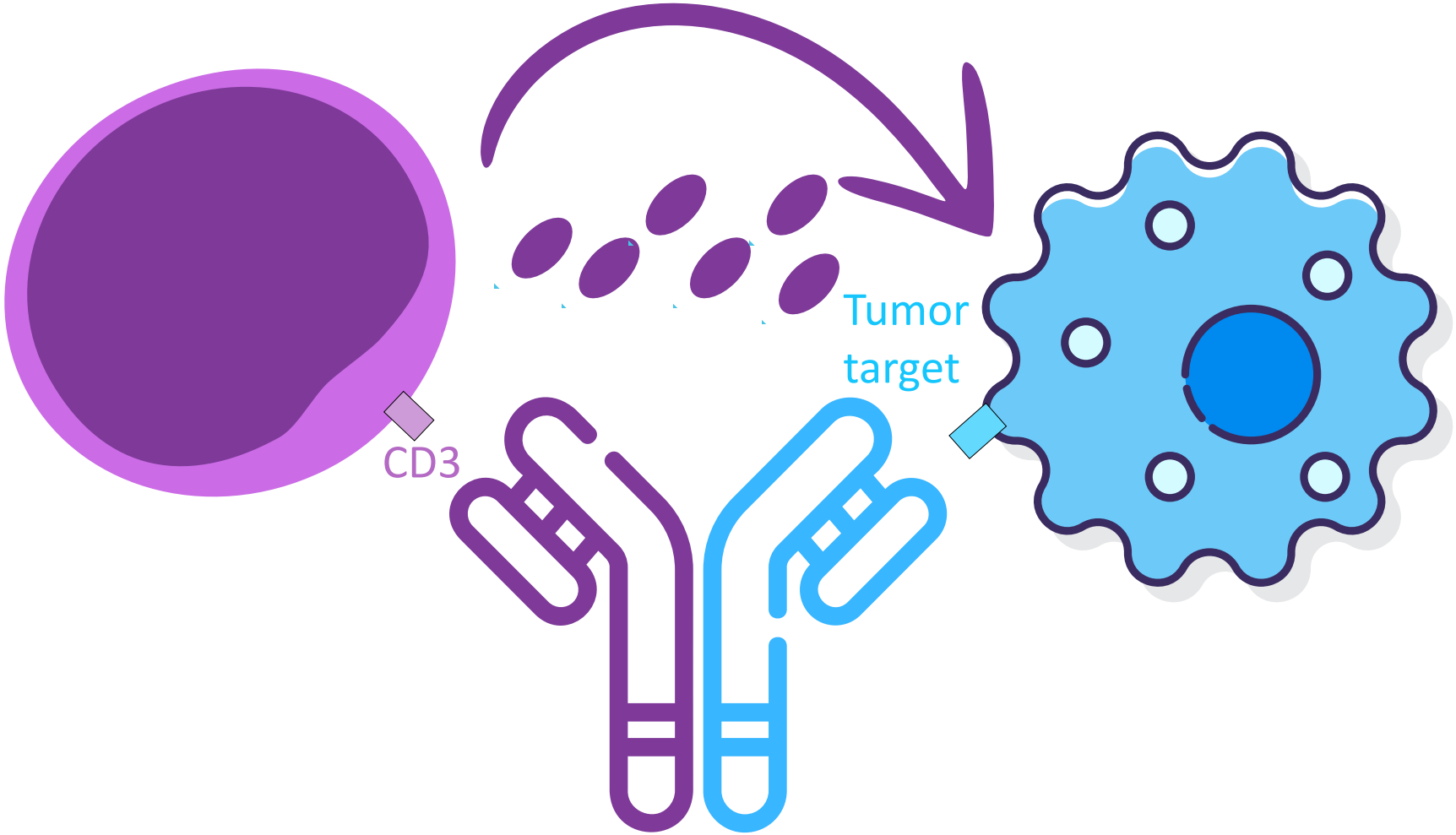
1. Mateos MV, et al. Real-Life Outcomes in Triple-Class Exposed Relapsed/Refractory Multiple Myeloma Treated With Carfilzomib- and/or Pomalidomide-Based Regimens in the LocoMMotion and MoMMent Studies. P-409. IMS 2024



International-myeloma-foundation publisher publications - ISSUU. (n.d.). https://issuu.com/international-myeloma-foundation/docs/2024-la-pfs-symptopm-management.pptx



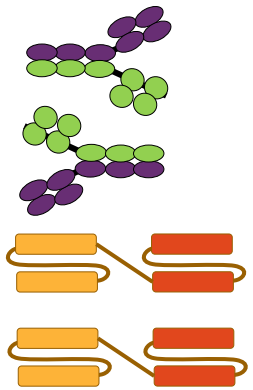
International-myeloma-foundation publisher publications - ISSUU. (n.d.). https://issuu.com/international-myeloma-foundation/docs/2024-la-pfs-symptopm-management.pptx



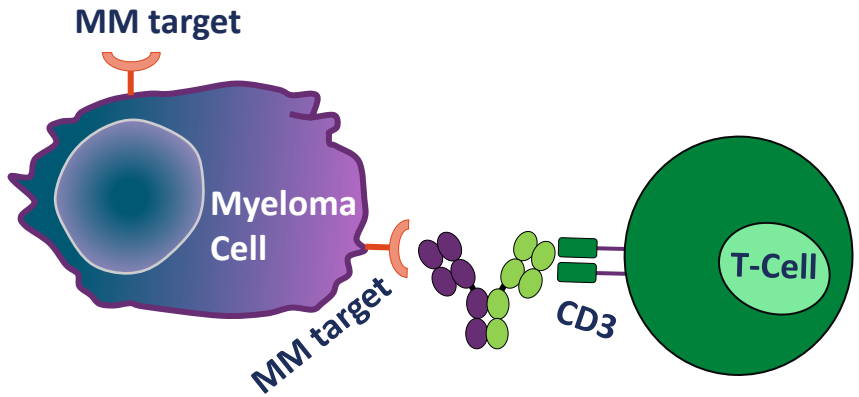
Slide do autor

Biespecific antibodies (BsAb) for R/R MM

- "Off the shelf" immunotherapy
  - Tumor targets: BCMA, GPRC5D, FcRH5
  - Also engages to T cell antigen CD3 (T-cell)
    - Teclistamab*: CD3 x BCMA
    - Elranatamab*: CD3 x BCMA
    - Talquetamab*: CD3 x GPRC5D
    - Cevostamab: CD3 x FcRH5
    - Linvoseltamab: CD3 x BCMA
    - ABBV-383: CD3 x BCMA



- Administration route: SC or IV with step-up dosing



***ANVISA approved for R/R MM with ≥3 previous therapies, including PI, IMiD and anti-CD38 mAb.**

Elranatamab-bcmm PI. Teclistamab-cqyv PI. Talquetamab-tgvs PI. van de Donk. Lancet. 2023;402:142.

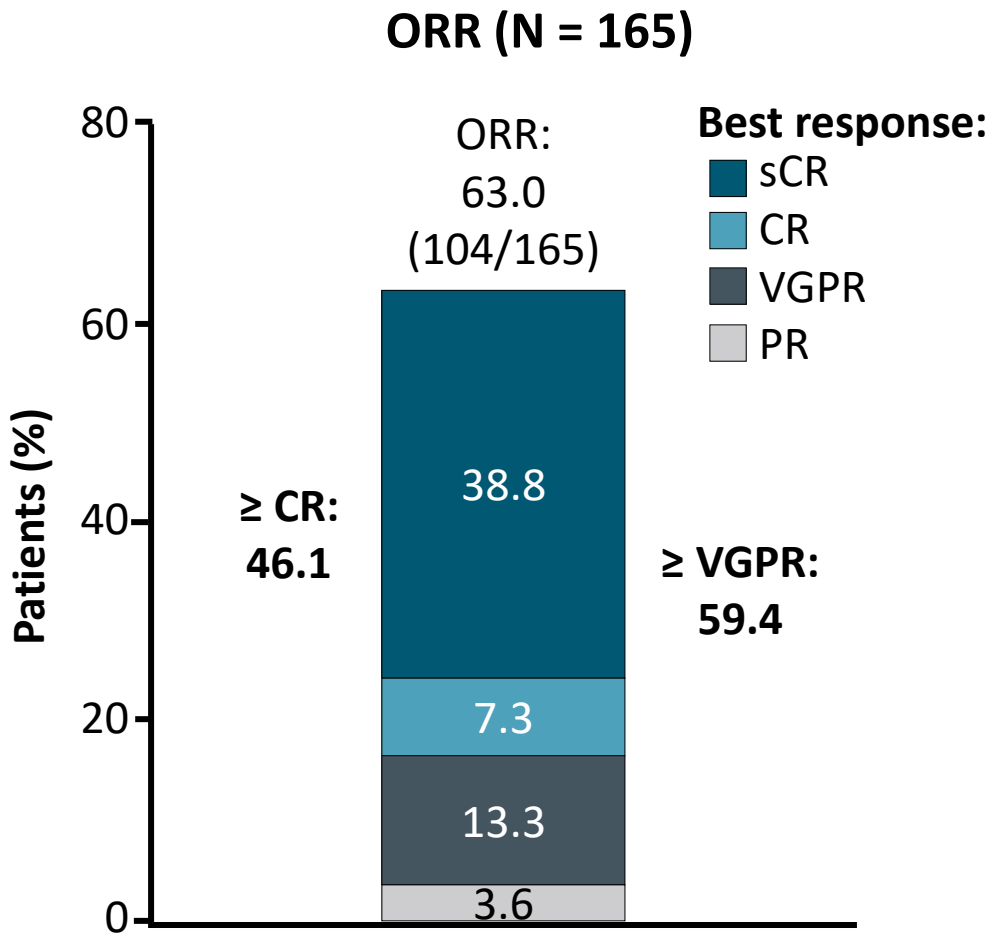
BsAb pivotal studies

Slide do autor

Phase I/II MajesTEC-1: Teclistamab in R/R MM

- R/R MM after ≥3 lines of therapy, including an IMiD, PI, and anti-CD38 mAb
  - 26% high-risk cytogenetics
  - Median 5 prior lines of therapy (range: 2-14)
  - 78% triple-class refractory; 30% penta refractory
  - 90% refractory to last therapy line
- **Teclistamab**: 1.5 mg/kg SC weekly, after step-up

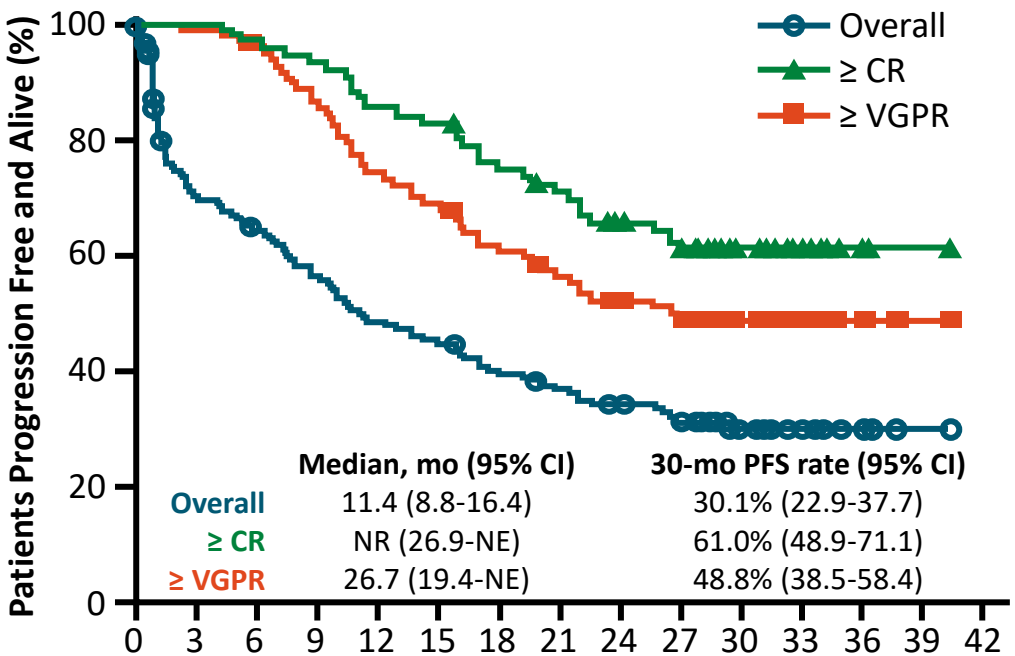
Outcomes, Mo (95% CI)	All Patients (N = 165)
Median DoR	24.0 (17.0-NE)
Median PFS	11.4 (8.8-16.4)
Median OS	22.2 (15.1-29.9)



Moreau. NEJM. 2022;387:495. van de Donk. ASCO 2023. Abstr 8011. Garfall. ASCO 2024. Abstr 7540.

MajesTEC-1: PFS and DoR With Teclistamab in R/R MM

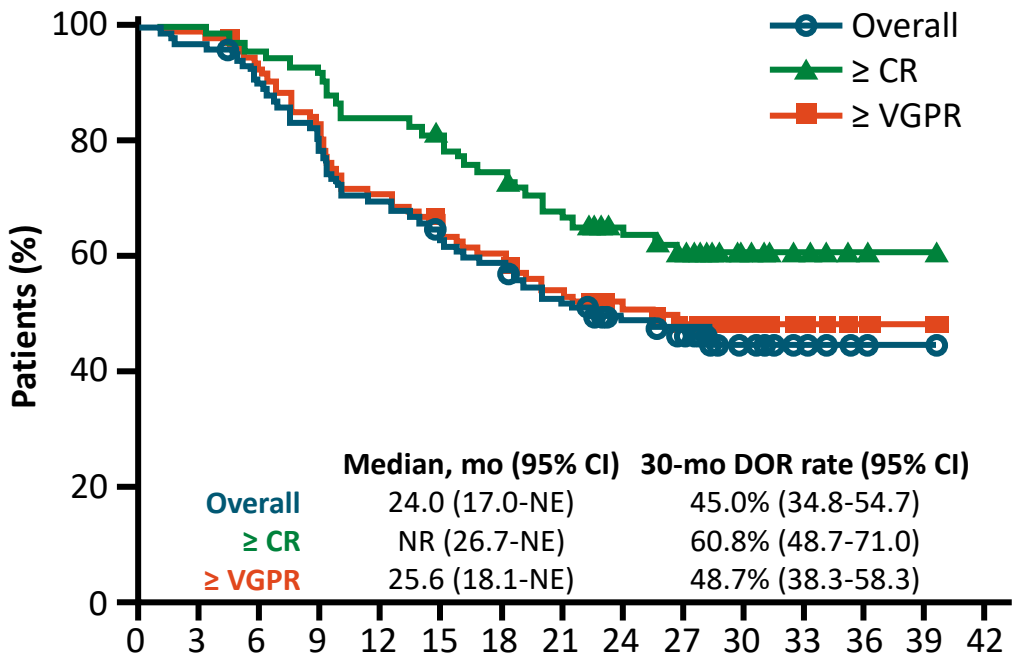
PFS



Patients at Risk, n

Mo	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42
Overall	165	110	99	87	75	70	61	55	49	44	19	10	4	1	0
≥ CR	76	76	74	71	65	63	57	52	46	42	18	9	3	1	0
≥ VGPR	98	97	93	84	72	67	59	53	47	43	19	10	4	1	0

DoR



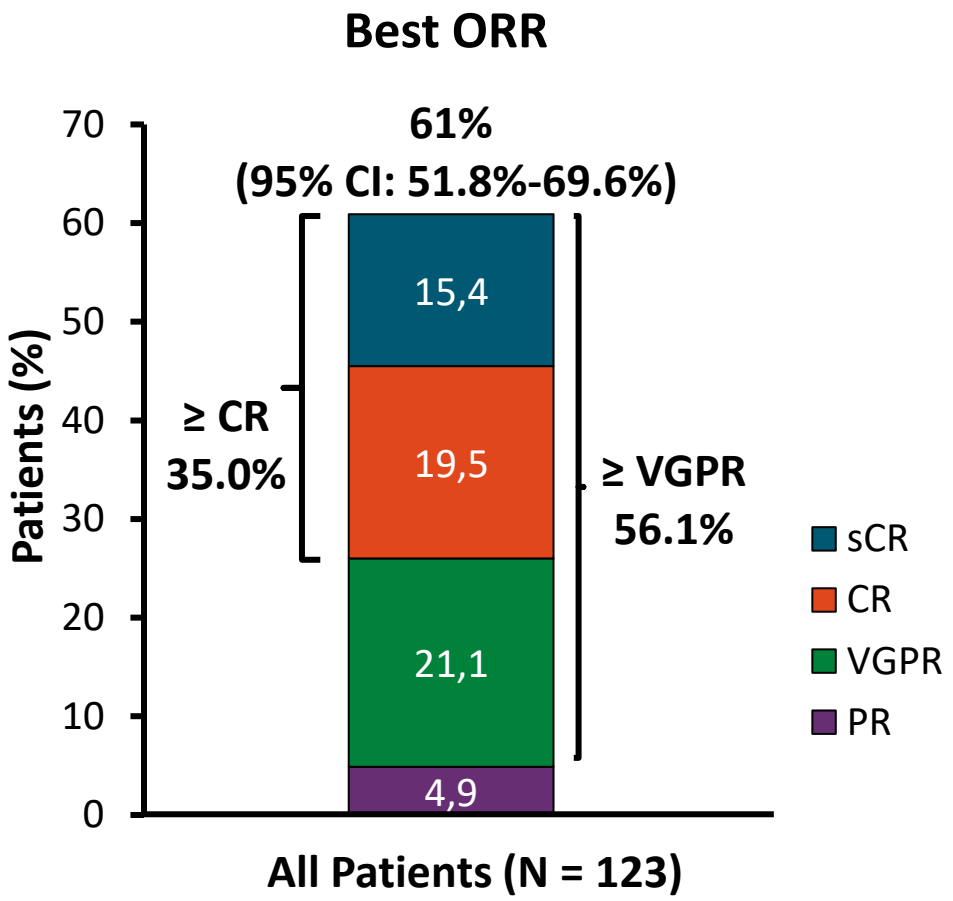
Patients at Risk, n

Mo	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42
Overall	164	101	93	83	72	64	60	53	46	39	16	8	3	1	0
≥ CR	76	76	73	71	64	60	56	50	44	37	15	7	2	1	0
≥ VGPR	98	97	90	80	69	62	58	51	45	38	16	8	3	1	0

Garfall. ASCO 2024. Abstr 7540.

Phase II MagnetisMM-3: Elranatamab for BCMA-Directed Therapy-Naive R/R MM (Cohort A)

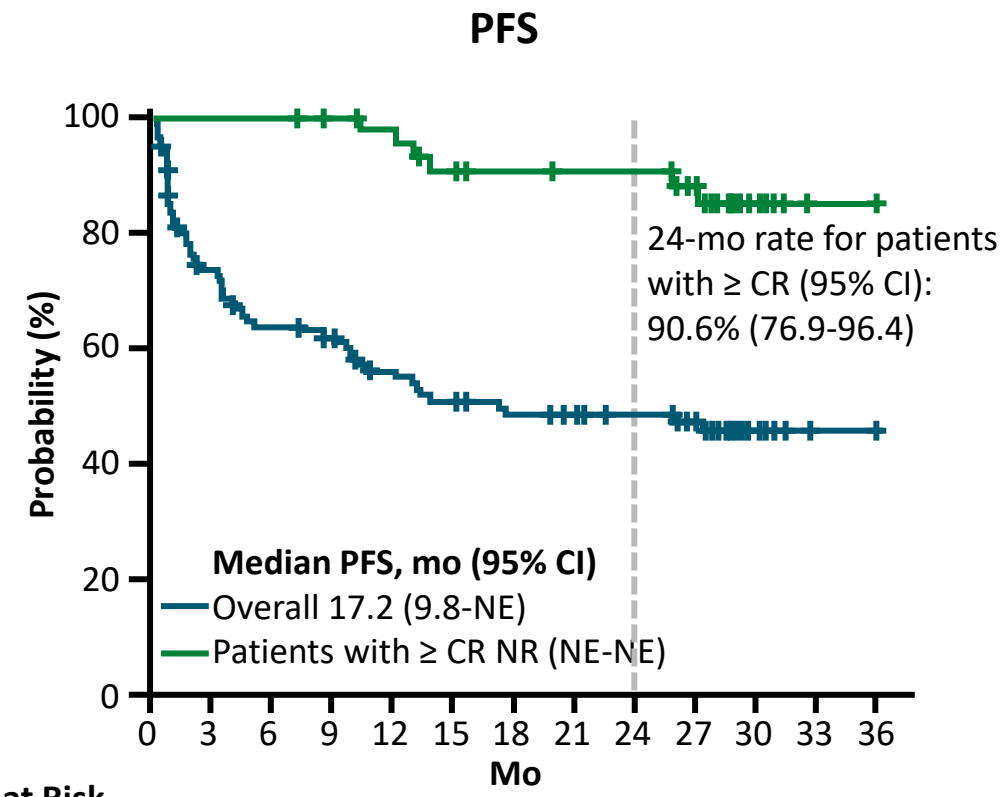
- Patients with MM refractory to ≥1, including an IMiD, PI, and anti-CD38 mAb
  - 97% triple-class refractory
  - Median 5 prior lines of therapy (range: 2-22)
  - 25% with high-risk cytogenetics
  - 32% with extramedullary disease
- **Elranatamab**: 76 mg SC weekly with priming and/or premedication to reduce CRS
  - If weekly dosing given for ≥6 cycles with achievement of ≥ PR for ≥2 mo, then dosing interval changed to every 2 wk
- **Primary endpoint:** ORR
- **Secondary endpoint:** DoR, OS, PFS, safety



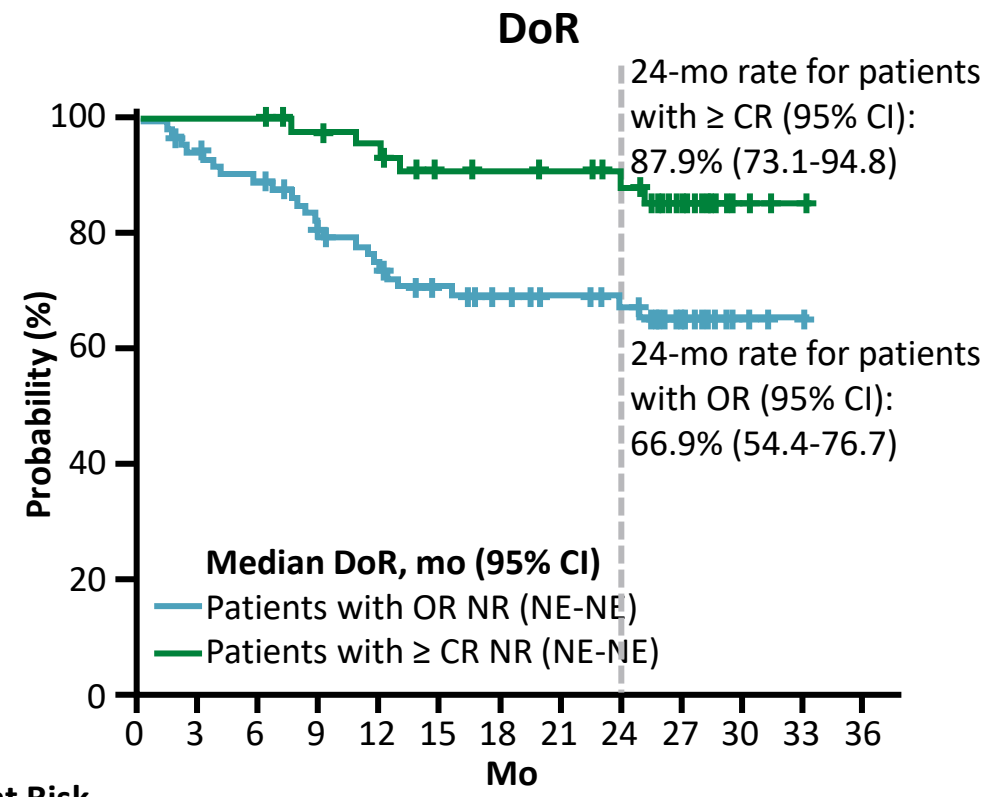
Median follow-up: 14.7 mo

Lesokhin. Nat Med. 2023;29:2259. Mohty. EHA 2024. P932.

MagnetisMM-3: PFS and DoR



No. at Risk													
Overall	123	78	67	63	54	48	44	42	39	32	7	1	0
Patients with ≥ CR	46	46	46	44	42	38	36	35	35	28	7	1	0



No. at Risk													
Patients with OR	75	70	65	57	50	45	41	38	35	18	3	1	0
Patients with ≥ CR	46	46	46	43	40	36	35	34	31	18	3	1	0

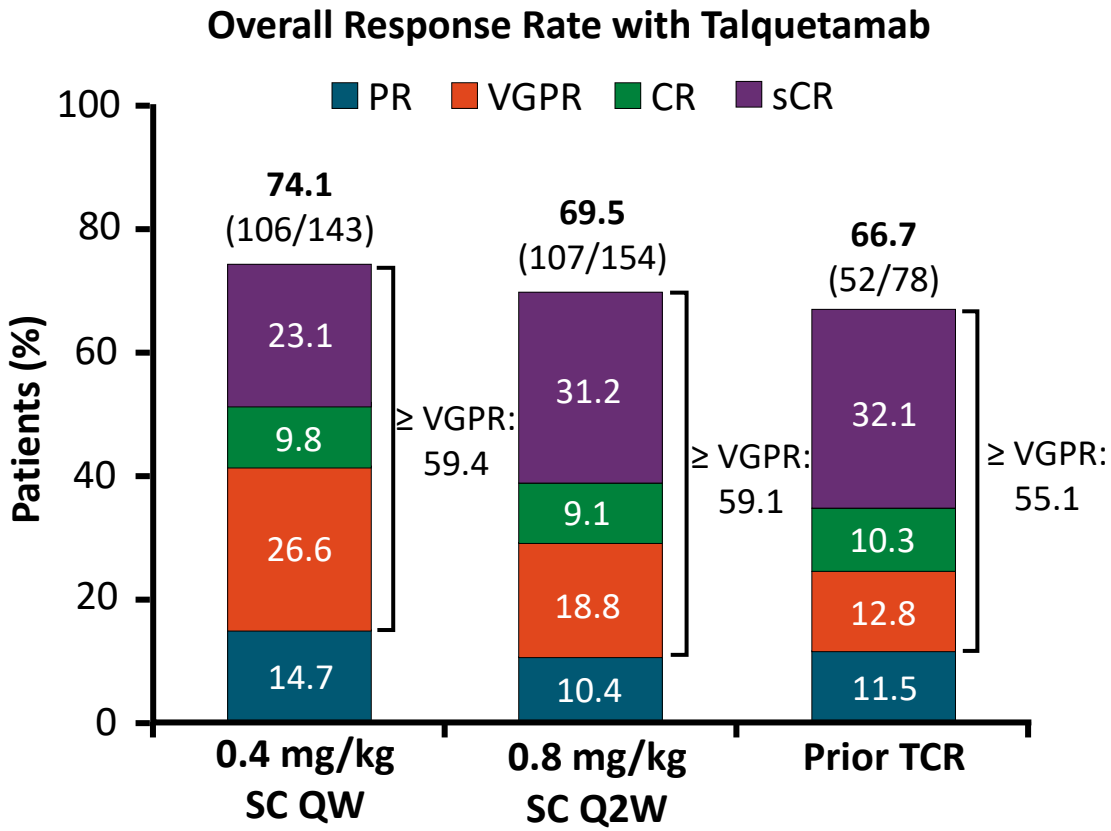
Mohty. EHA 2024. P932.

GPRC5D

talquetamab

Phase II MonumenTAL-1: Talquetamab in R/R MM

- Patients with R/R MM after ≥3 lines of therapy, including an IMiD, PI, anti-CD38 mAb
  - 69%-84% triple-class refractory
  - Median 5-6 prior lines of therapy across all cohorts
  - 27.1% with high-risk cytogenetics; 24.3% with EMD
- **Talquetamab**: 0.4 mg/kg SC QW or 0.8 mg/kg SC Q2W with 2-3 step-up doses and/or premedication to reduce CRS
- **Primary endpoint:** DLTs
- **Key secondary endpoint:** ORR

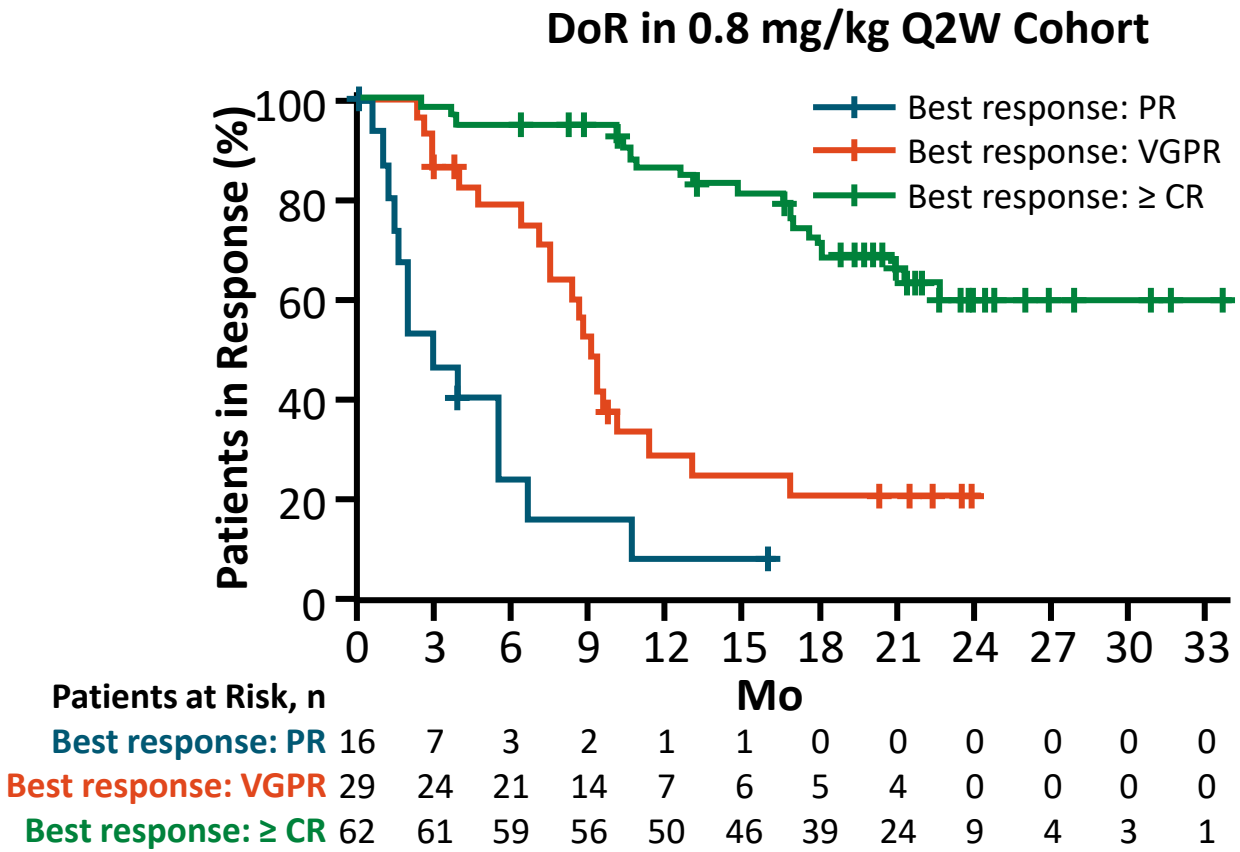


The phase III MonumenTAL-3 (NCT05455320) and MonumenTAL-6 (NCT05455320) trials are actively recruiting.

Chari. NEJM. 2022;387:2232. Schinke. ASCO 2023. Abstr 8036. Rasche. EHA 2024. Abstr P915.

Slide credit: clinicaloptions.com

MonumenTAL-1: DoR and PFS Outcomes



Outcome	0.4 mg/kg QW (n = 143)	0.8 mg/kg Q2W (n = 154)	Prior T-Cell Redirection Tx (n = 78)
Median f/u	29.8	23.4	20.5
Median DoR, mo (95% CI)	9.5 (6.7-13.4)	17.5 (12.5-NE)	N/A
Median PFS, mo (95% CI)	7.5 (5.7-9.4)	11.2 (8.4-14.6)	7.7 (4.1-14.5)
24-Mo OS, %	60.6	67.1	57.3

Rasche. EHA 2024. Abstr P915.

Safety of BsAbs for RRMM

	Teclistamab	Talquetamab	Elranatamab
Target	CD3/BCMA	CD3/GPRC5D	CD3/BCMA
CRS incidence	72%: Gr 1: 50% Gr 2: 21%	76%: Gr 1: 57% Gr 2: 17%	58%: Gr 1: 44% Gr 2: 14%
ICANS incidence	Gr 1/2: 3% Gr 3/4: 0%	Gr 1/2: 3% Gr 3/4: 3%	Gr 1/2: 3% Gr 3/4: 0%
Neutropenia	Gr 3/4: 56%	Gr 3/4: 35%	Gr 3/4: 51%
Infection	Gr 3/4: 35%	Gr 3/4: 17%	Gr 3/4: 31%
Skin/ nail tox	Not reported	62%	Not reported
Oral toxicity	Not reported	80% (dysgeusia: 49%, dry mouth: 34%, dysphagia: 23%, ageusia: 18%)	Not reported

Moreau. NEJM. 2022;387:495. Teclistamab-cqyv PI. van de Donk. ASCO 2023. Abstr 8011. Chari. NEJM. 2022;387:2232. Talquetamab-tgvs PI. Touzeau. EHA 2023. Abstr S191. Elranatamab-bcmm PI. Lesokhin. Nat Med. 2023;29:2259.

Real World Evidence (RWE)

WHY?

- **Fill gaps in clinical trial evidence:** RWE can provide information about how drugs and technologies are used in real-world settings.
- **Improve patient care:** RWE can help identify unmet medical needs and optimize clinical care.
- **Improve public health:** RWE can help identify trends in disease burden and healthcare service utilization.
- **Improve clinical trial design:** RWE can help optimize clinical trial design and feasibility.
- **Improve post-market surveillance:** RWE can help improve surveillance of medical products after they are approved.
  - **Efficacy**
  - **Safety**
  - **Emergent rare adverse events**

CHALLENGE

- Data quality, reproducibility, and accuracy can affect validity
- RWE can be subject to inherent biases

1. Azoulay, Laurent. "Rationale, strengths, and limitations of real-world evidence in oncology: a Canadian review and perspective." *The Oncologist* 27.9 (2022): e731-e738.
2. Naidoo, Poobalan, et al. "Real-world evidence and product development: Opportunities, challenges and risk mitigation." *Wiener Klinische Wochenschrift* 133 (2021): 840-846.

RWE for Teclistamab

Slide do autor

Brazilian Relapsed Refractory Multiple Myeloma Patients Treated with Teclistamab Outside Clinical Trials in an Expanded Access Program

Fernando Vieira Pericole[1], Juliana Souza Lima[2], Erica Marquardt Lammerhirt Ottoni[3], Glaciano Ribeiro[4], Edvan de Queiroz Crusoé[5], Rafael Cunha[6], Abel da Costa Neto[7], Priscilla Cury[8], James Farley Rafael Maciel[9] and Vania Tietsche de Moraes Hungria[8] on behalf of Grupo Brasileiro de Mieloma (GBRAM)

1. Hemocentro Unicamp, Campinas, SP 2. Oncoclínicas Curitiba, PR 3. Hospital Moinhos de Vento, Porto Alegre, RS 4. Universidade Federal de Minas Gerais. (UFMG), Belo Horizonte, MG 5. Oncologia D'Or, Salvador, BA 6. Oncoclínicas Rio de Janeiro, RJ 7. Instituto D'or de Pesquisa e Ensino, São Paulo, SP 8. Clínica São Germano, São Paulo, SP 9. CePCLIN, Natal, RN

EAP Brazil

- 27 patients
- Access before approval: between 2022 e 2023
- Median Follow up time: 12 months

Characteristic	Total (27 pts)
Median age (range)	67 (47-80)
Sex, number (%)	
Male	14 (52%)
Female	13 (48%)
Race, number (%)	
White	24 (89%)
Black	3 (11%)
ECOG performance status score(%)	
0	4 (15%)
1	4 (15%)
2	2 (7%)
Not available	17 (63%)
Diagnostic FISH analysis (%)	
Not performed	67%
Without alterations	7%
1q abnormalities	13%
Others	13%
International Staging System (ISS)	
ISS I	10%
ISS II	38%
ISS III	34%
Not available	18%
Refractory status (%)	
Lenalidomide	85%
Pomalidomide	11%
Carfilzomib	73%
Daratumumab	85%
Triple-class exposed	100%
Triple-class refractory	85%
Median number of previous lines (range)	4 (2-8)
Median time since diagnosis, years (range)	5.3y (1.3-19y)
Median IgG before teclistamab (range)	347 (152-4227)
Median Hb (range)	9.8 (7.3-12.1)
Lymphocyte counts, median (range)	1080 (250-2720)

Pericole, Fernando, et al. "P-278 Brazilian Relapsed Refractory Multiple Myeloma Patients Treated with Teclistamab Outside of Clinical Trials as an Expanded Access Program." *Clinical Lymphoma Myeloma and Leukemia* 24 (2024): S196-S197.

EAP teclistamab Brazil, Safety (N=27)[1]

CRS

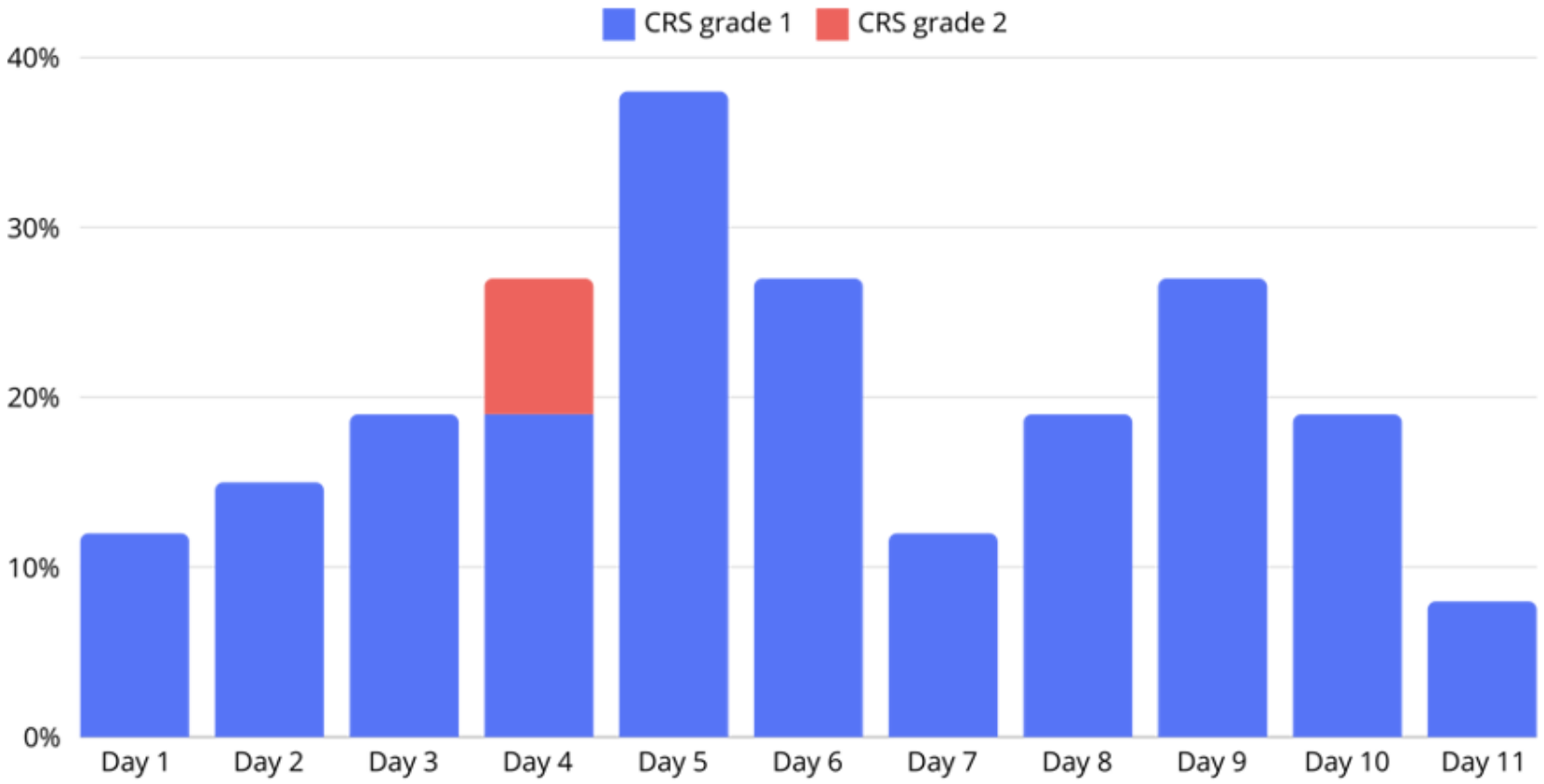
- Total 69%
- 54% grade 1
- 15% grade 2

INFECTIONS

- Total 73%
- Grade 3 or higher: 20%

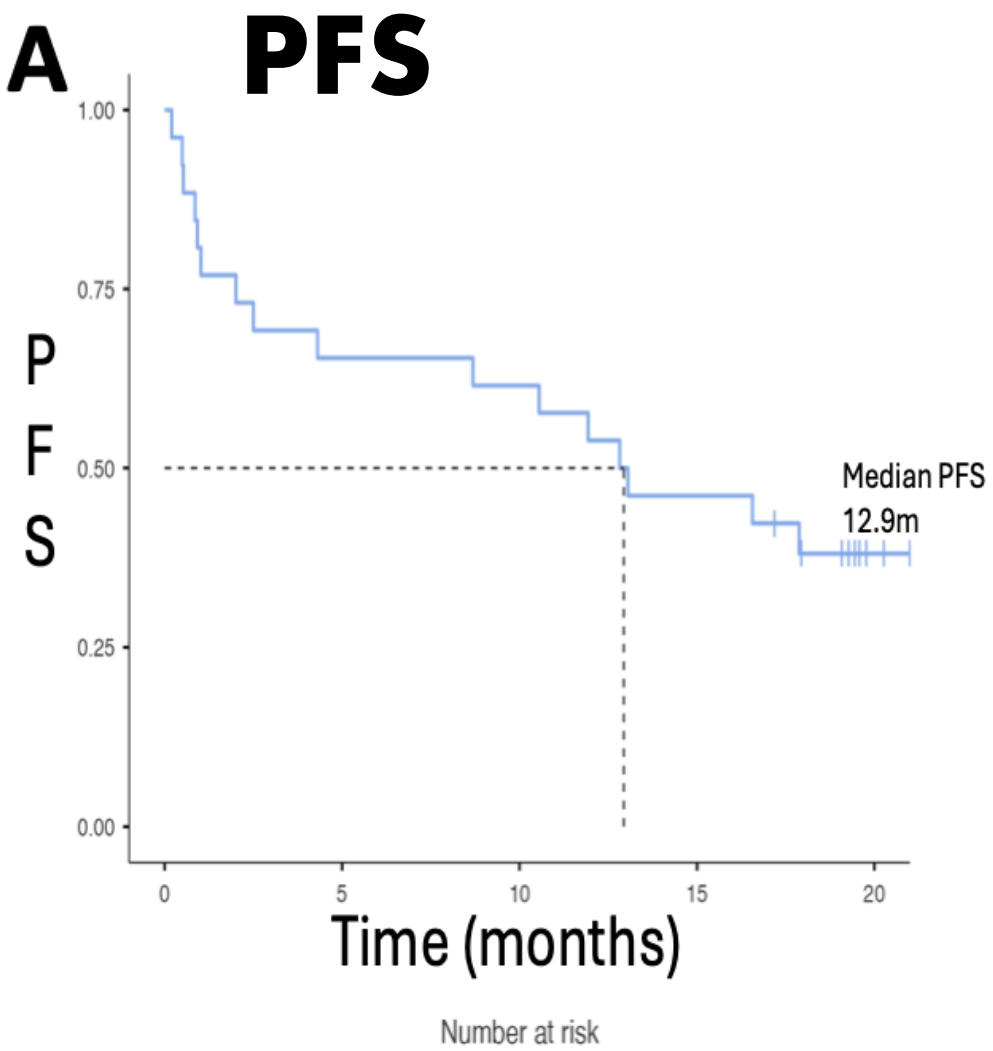
IVIG supplementation

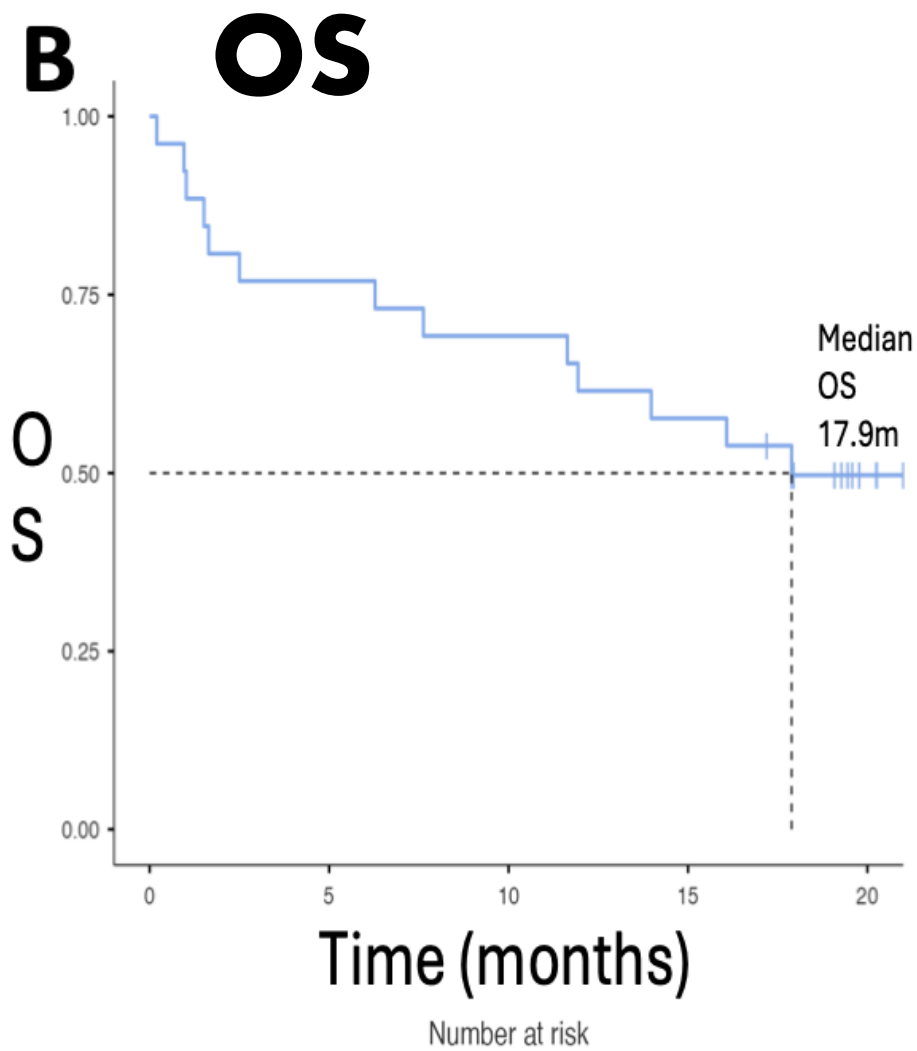
- Total 90%



1. Pericole, Fernando, et al. "P-278 Brazilian Relapsed Refractory Multiple Myeloma Patients Treated with Teclistamab Outside of Clinical Trials as an Expanded Access Program." *Clinical Lymphoma Myeloma and Leukemia* 24 (2024): S196-S197.

EAP teclistamab Brazil, Efficacy (N=27)[1]





Pericole, Fernando, et al. "P-278 Brazilian Relapsed Refractory Multiple Myeloma Patients Treated with Teclistamab Outside of Clinical Trials as an Expanded Access Program." *Clinical Lymphoma Myeloma and Leukemia* 24 (2024): S196-S197.

RetrosTECtive (IFM2024-09)
French RWE study of patients who received teclistamab at 30 centres through the EAP (N=303)[1]

		RetrosTECtive (N=303)[1]	MajesTEC-1 (N=165)[1,2,3]
Baseline characteristics	MajesTEC-1 ineligible, %	28.4	0
	Median follow-up, months	11.9	30.4
	Median prior LOT, n (range)	4 (2–11)	5 (2–14)
	Anti-BCMA exposure, %	13.6	0
	EMD, %	11.8	17.0
Efficacy	ORR, %	68.8	63.0
	mPFS, months	11.3	11.4
	Among responding patients	17 (n=175)	-
	Among patients aged ≥75 years	16.4 (n=90)	-
	Among patients with EMD	3.7 (n=34)	-
	Among MajesTEC-1 ineligible patients	6.6 (n=140)	-
	mOS, months	17	22

EFFICACY	
Median follow-up	**11,9 months**
ORR	**68,8%**
≥VGPR	**61,4%**
mPFS (overall population)	**11,3 months**
mPFS (responding patients)	**17 months**
mOS (overall population)	**17 months**

1. Perrot A, et al. *Haematologica* 2024. doi:10.3324/haematol.2024.286118; 2. Garfall AL, et al. ASCO 2024. Poster 7540; 3. Moreau P, et al. *N Engl J Med* 2022;387:495–505.

Real World Analysis of Teclistamab in 123 patients from Germany (N=123)[1]

TABLE 1. Patient characteristics of real-world patient population

Median age (range) - yr	**67.0 (35.0-87.0)**
Gender: male/female - %	56.9/43.1
Median time since diagnosis - yr (range)	6.5 (0.5-18.7)
Median no. of lines of previous therapy (range)	6 (3-14)
Extramedullary disease - no./total no. (%)	**43/119 (36.1)**
≥60% plasma cells in bone marrow no./total no. (%)	**21/59 (35.6)**
ISS no./total no. (%)	
I	25/92 (27.1)
II	35/92 (38.0)
III	**31/92 (33.7)**
High risk cytogenetic profile no./total no. (%)	**39/107 (36.4)**
Refractory status no./total no. (%)	
triple-class	113/123 (92.6)
penta-drug	74/123 (60.2)
BCMA-pretreatment no./total no. (%)	**45/123 (37.4)**
belantamab mafodotin	23/123 (18.7)
Idecabtagene vicleucel	21/123 (17.1)
Polychemotherapy in last 2 months no./total no. (%)	22/123 (17.9)

FIGURE 1. Response rate and PFS in 123 patients

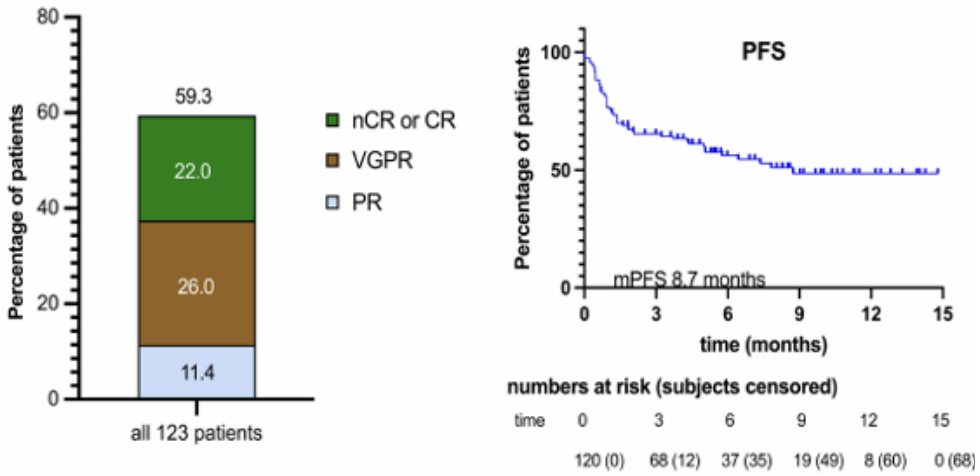


FIGURE 2. PFS in selected subgroups

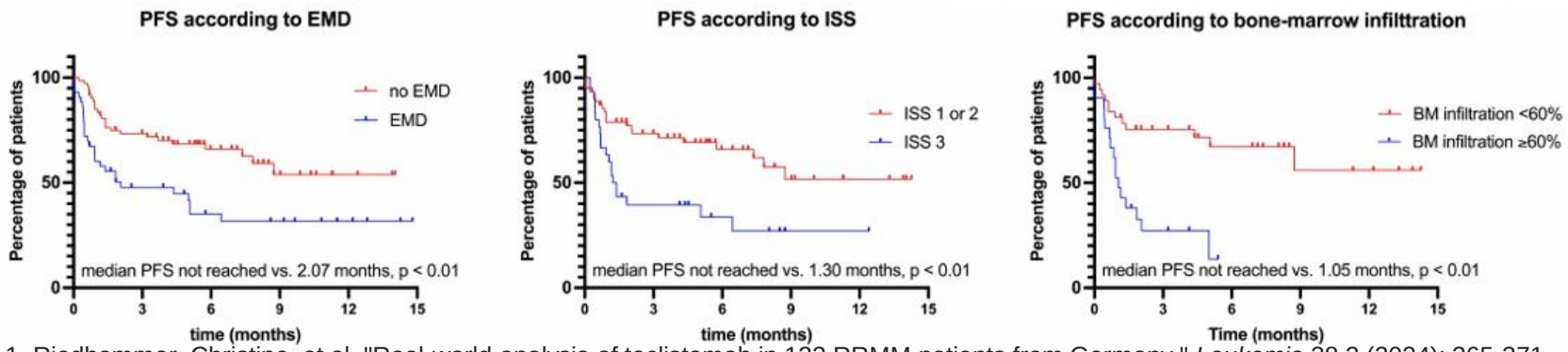
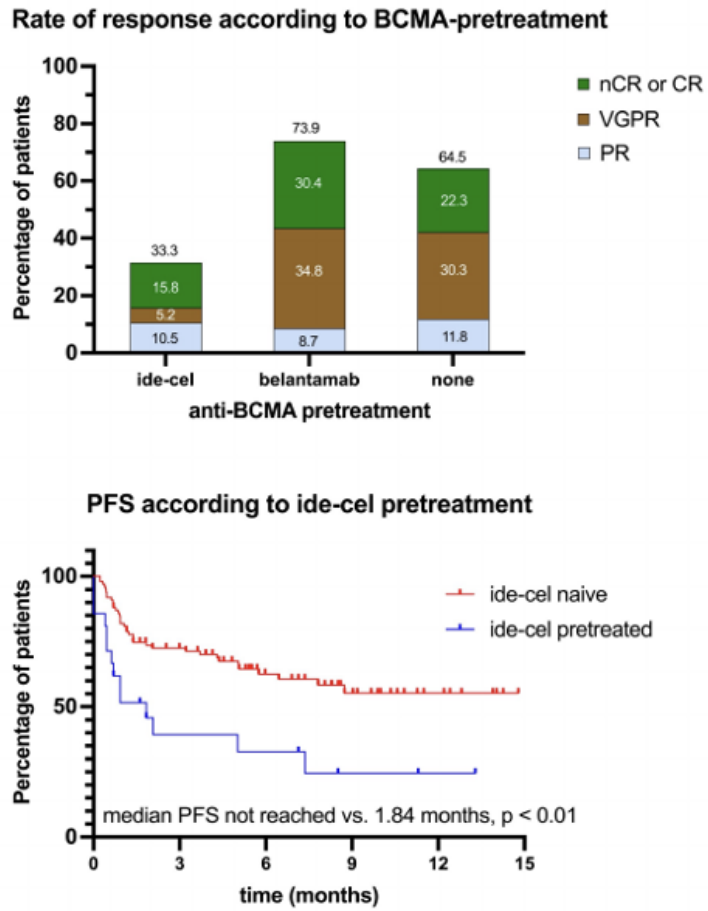


FIGURE 4. Efficacy in BCMA-pretreatment



1. Riedhammer, Christine, et al. "Real-world analysis of teclistamab in 123 RRMM patients from Germany." *Leukemia* 38.2 (2024): 365-371.

Safety and Efficacy of Teclistamab in Patients with Relapsed/ Refractory Multiple Myeloma: A Real-World Experience : USA (N=106)[1]

Characteristic	Value
Male sex	49 (46)
Age, yr, median (range)	66.5 (35-87)
Age >70 yr, n (%)	34 (32)
Race, n (%)	
Non-Hispanic white	72 (68)
Non-Hispanic black	28 (26)
Asian	2 (2)
Hispanic	4 (4)
Time since diagnosis, mo, median (range)	65 (6-240)
IgG subtype, n (%)	58 (55)
R-ISS stage III, n/N (%)	25/80 (31)
ECOG PS, n (%)	
0-1	71 (67)
2-4	35 (33)
High-risk cytogenetics, n/N (%)	56/95 (59)
del(17p)	24 (25)
t(4;14)	7 (7)
t(14;16)	7 (7)
gain/amp 1q	48 (51)
Extramedullary disease, n (%)	45 (42)
Prior LOT (median, range)	6 (4-17)
>4 prior LOT, n (%)	80 (75)
Refractory status, n (%)	
PIs	102 (96)
IMiDs	102 (96)
Anti-CD38 mAbs	106 (100)
Double-refractory	97 (92)
Triple-refractory	97 (92)
Penta-refractory	68 (64)
Prior BCMA-directed therapy, n (%)	56 (53)
Prior SCT, n (%)	
Autologous	61 (58)
Allogeneic	3 (3)
MajesTEC-1 exclusion criteria at teclistamab initiation, n (%)	
Patients meeting exclusion criteria	88 (83)
1 criterion	45 (42)
≥2 criteria	43 (41)
Neutropenia (ANC <1000 cells/μL)	2 (2)
Anemia (hemoglobin <8 g/dL)	27 (25)
Thrombocytopenia (platelets < 75,000 cells/μL)	21 (20)
Any baseline cytopenia	33 (31)
Poor performance status (ECOG PS ≥2)	35 (33)
Renal dysfunction (CrCl < 40 mL/min)	14 (13)
Liver dysfunction	5 (5)
Cardiac dysfunction (LVEF <45%)	4 (4)

Multivariable Models of the Association of Selected Patient Characteristics with ORR, ≥VGPR, and PFS in Teclistamab-Treated Patients

Characteristics	ORR			≥VGPR			PFS		
	Events, n	OR (95% CI)	*P*	Events, n	OR (95% CI)	*P*	Events, n	HR (95% CI)	*P*
Cytogenetics			.50			.43			.12
High risk	35	1.00 (referent)		25	1.00 (referent)		31	1.00 (referent)	
Standard risk	28	1.06 (.89-1.27)		21	1.09 (.89-1.33)		14	.60 (.31-1.15)	
Extramedullary disease			**.001**			.25			**.003**
Yes	21	1.00 (referent)		18	1.00 (referent)		27	1.00 (referent)	
No	49	1.35 (1.13-1.61)		32	1.13 (.92-1.38)		22	.39 (.21-.73)	
ECOG PS			**.002**			**.019**			< **.001**
0-1	53	1.00 (referent)		39	1.00 (referent)		28	1.00 (referent)	
2-4	17	.73 (.6-.89)		11	.76 (.61-.95)		21	4.05 (1.93-8.51)	
Age			.13			.072			**.027**
>70 yr	24	1.00 (referent)		18	1.00 (referent)		14	1.00 (referent)	
≤70 yr	46	.86 (.71-1.05)		32	.81 (.65-1.02)		35	2.33 (1.10-4.94)	
Penta-refractory			.23			.11			.22
Yes	24	1.00 (referent)		34	1.00 (referent)		17	1.00 (referent)	
No	46	.88 (.72-1.08)		16	.83 (.66-1.04)		32	1.55 (.77-3.12)	
Prior BCMA-directed therapy			.59			.74			.83
Yes	37	1.00 (referent)		26	1.00 (referent)		23	1.00 (referent)	
No	33	1.06 (.87-1.28)		24	.96 (.77-1.2)		26	.93 (.48-1.80)	
Prior LOT			**.035**			.11			.11
≤4	21	1.00 (referent)		14	1.00 (referent)		11	1.00 (referent)	
>4	49	.76 (.6-.98)		36	.79 (.6-1.05)		38	2.01 (.84-4.80)	

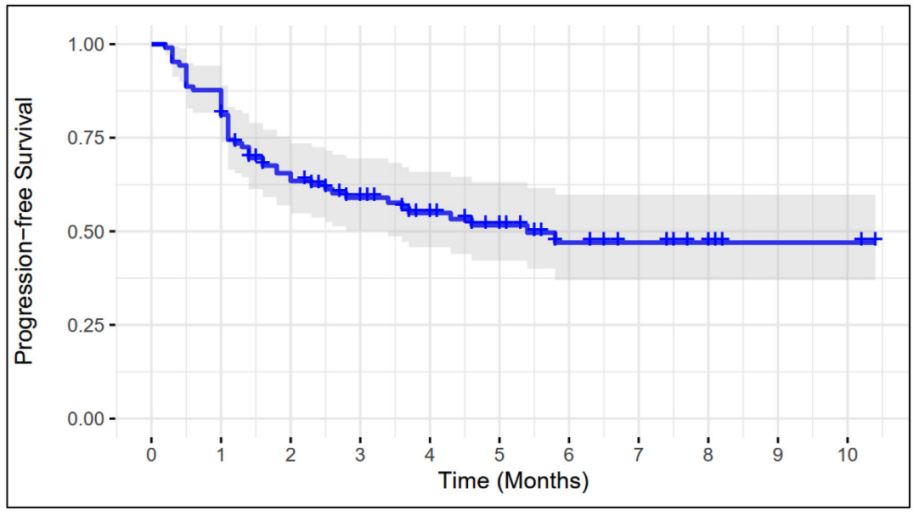
1. Dima, Danai, et al. "Safety and efficacy of teclistamab in patients with relapsed/refractory multiple myeloma: a real-world experience." Transplantation and cellular therapy 30.3 (2024): 308-e1.

Safety and Efficacy of Teclistamab in Patients with Relapsed/ Refractory Multiple Myeloma: A Real-World Experience : USA (N=106)[1]

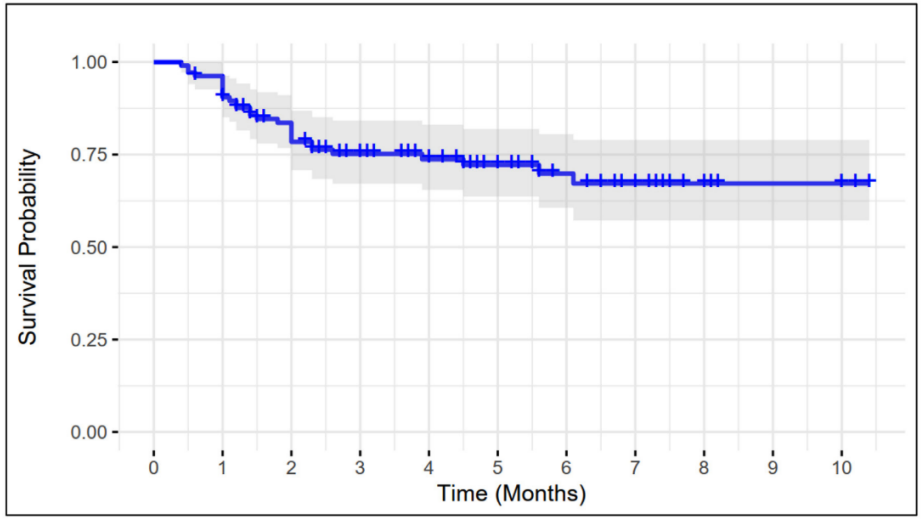
Safety Outcomes: CRS and ICANS

Adverse Event	Value
CRS	
Any grade, n (%)	68 (64)
Grade 1, n (%)	57 (54)
Grade 2, n (%)	10 (9)
Grade 3, n (%)	1 (1)
Grade 4, n (%)	0 (0)
Day of onset, median (range)	3.5 (1-8)
Duration, d, median (range)	1 (1-6)
CRS after second step-up dose, n (%)	41 (39)
Recurrent CRS, n (%)	2 (2)
ICANS	
Any grade, n (%)	15 (14)
Grade 1, n (%)	5 (5)
Grade 2, n (%)	7 (6)
Grade 3, n (%)	2 (2)
Grade 4, n (%)	1 (1)
Day of onset, median (range)	5 (1-10)
Duration, d, median (range)	2 (1-30)
CRS after second step-up dose, n (%)	10 (9)
Recurrent ICANS, n (%)	1 (1)
Management of CRS/ICANS	
Tocilizumab, n (%)	43 (41)
>1 dose of tocilizumab, n (%)	6 (6)
Corticosteroids, n (%)	35 (33)
Both tocilizumab + corticosteroids, n (%)	17 (16)
Hospitalization for step-up dosing, n (%)	106 (100)
Length of stay, d, median (range)	9 (6-37)
Intensive care unit stay, n (%)	7 (7)

A) Progression-Free Survival



B) Overall Survival



Median Follow up: 3.8 months

1. Dima, Danai, et al. "Safety and efficacy of teclistamab in patients with relapsed/refractory multiple myeloma: a real-world experience." Transplantation and cellular therapy 30.3 (2024): 308-e1.

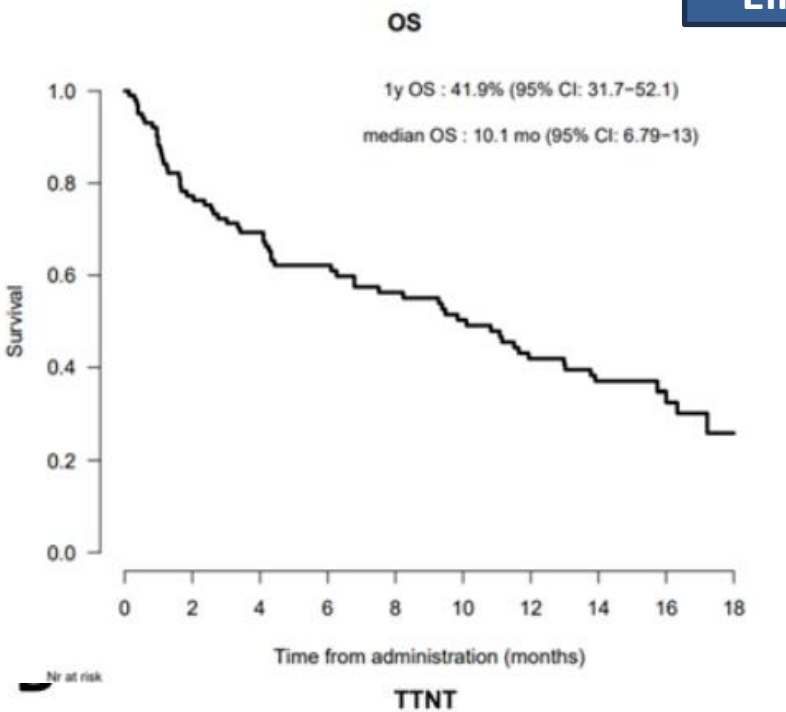
RWE for Elranatamab

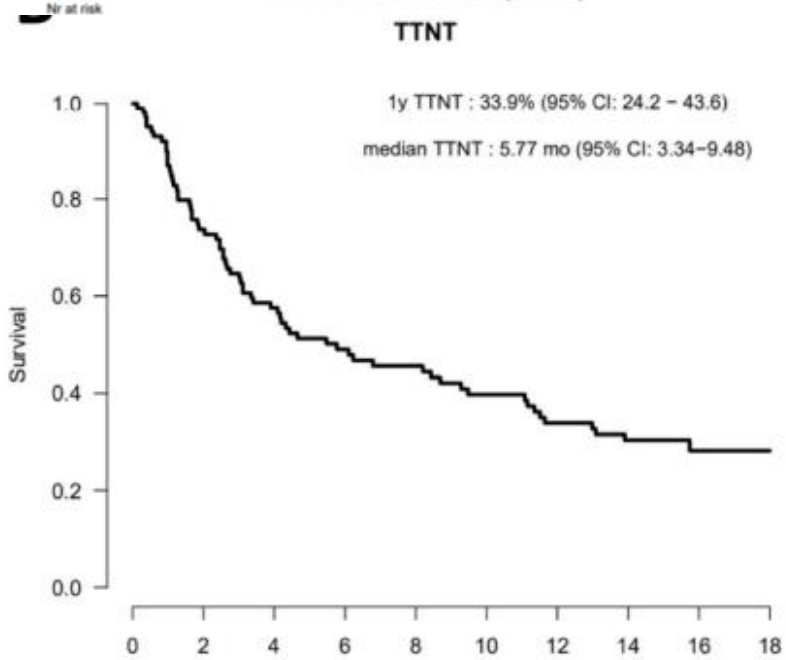
Slide do autor

Elranatamab monotherapy in real-world setting in R/R MM: French compassionate use program (N=101)[1]

Characteristic	Study Population (*N* = 101)
Patient age, years, median (min-max) [IQR]	68 (39–87) [62–75]
Gender	
Male	52 (51%)
Female	49 (49%)
ECOG-PS	
0	16 (18%)
1	41 (47%)
≥ 2	30 (35%)
Missing	14
R-ISS at diagnosis	
1	24 (30%)
2	29 (36.2%)
3	27 (33.8%)
Missing	21
del(17p)	
No	46 (71%)
Yes	19 (29%)
Missing	36
t(4;14)	
No	45 (67%)
Yes	22 (33%)
Missing	34
Extra-medullary disease at elranatamab initiation	
No	57 (65%)
Yes	30 (36%)
Missing	14
Number of previous lines, median (min-max) [IQR]	5 (1–17) [3–6]
Triple-class exposed (at least 1 PI, 1 IMiD, 1 anti-CD38 mAb)	
No	4 (4%)
Yes	97 (96%)
Penta-exposed (at least 2 PI, 2 IMiD, 1 anti-CD38 mAb)	
No	24 (24%)
Yes	77 (76%)
Triple-class refractory (at least 1 PI, 1 IMiD, 1 anti-CD38 mAb)	
No	48 (48%)
Yes	53 (53%)
Penta-refractory (at least 2 PI, 2 IMiD, 1 anti-CD38 mAb)	
No	79 (78%)
Yes	22 (22%)
Previous anti-BCMA	
No	84 (83%)
Yes	17 (17%)

Characteristic	Study Population (*N* = 101)	
Best response		
Minimal response	2 (2%)	
Partial response	10 (10%)	ORR 52%
Very good partial response	23 (23%)	
Complete response	16 (16%)	
Stringent complete response	3 (3%)	
≥ VGPR after one cycle	22 (22%)	
At one year		
Overall survival	42% (95% CI: 31.7–52.1)	
Progression-free survival	34% (95% CI: 24.4–43.7)	
Duration of response	48% (95% CI: 31.1–64.0)	
Time to next treatment	34% (95% CI: 24.2–43.6)	
Progression following elranatamab therapy		
No	53 (53%)	
Yes	48 (47%)	
Subsequent lines of treatment (after 1st progression or elranatamab discontinuation)		
No	71 (74%)	
Yes	25 (26%)	
Missing	5	





1. Malard, Florent, et al. "Elranatamab monotherapy in the real-word setting in relapsed-refractory multiple myeloma: results of the French compassionate use program on behalf of the IFM." *Blood Cancer Journal* 14.1 (2024): 219.

RWE for Talquetamab

Slide do autor

Talquetamab RWE	Costa BA, et al (1)	Janakiram M et al (2)	Grajales-Cruz A, et al (3)
Total patients	28	118	62
Median follow-up (months)	7.7m	NA	NA
Female (%)	61%	NA	55%
Median age	65y	64y	66y
Median LOT (range)	7 (4-14)	6 (NA)	6.6 (4-11)
Triple-class refractory (%)	NA	72%	87%
Penta-refractory (%)	36%	44%	37%
EMD (%)	50%	22%	23%
Previous BCMA therapy (%)	82%	71%	60%
ECOG 0-1 (%)	89%	85%	79%

(1) Costa, Bruno Almeida, et al. "Real-World Safety and Early Efficacy of Talquetamab in Patients with Heavily-Pretreated Relapsed/Refractory Multiple Myeloma." *Blood* 144 (2024): 7026.;
(2) Janakiram, Murali, et al. "Real World Evidence of Outcomes of Patients Treated with Talquetamab in a Heavily Pretreated Population with Multiple Myeloma with High Exposure to Prior BCMA Therapies-a Report from the IMWG Consortium." *Blood* 144 (2024): 3368.
(3) Grajales-Cruz, Ariel E., et al. "Single Center Real World Experience of Talquetamab in Patients with Relapsed and Refractory Multiple Myeloma." *Blood* 144 (2024): 3784.

Talquetamab RWE	Costa BA, et al (1)	Janakiram M et al (2)	Grajales-Cruz A, et al (3)
CRS (%) / Gr ≥ 3 (%)	57% / 4%	67% / 6%	57% / 2%
ICANS (%) / Gr ≥ 3 (%)	14% / 4%	6% / 1%	16% / NA
Infections (%) / Gr ≥ 3 (%)	36% / 18%	34% / NA	31% / NA
Skin / rash AE (%) / Gr ≥ 3 (%)	79% / 4%	62% / 4%	60% / NA
Nail-related AE (%)	43%	20%	60% / NA
Weight-loss (%) / Gr ≥ 3 (%)	68% / 4%	NA	76% / NA
Disgeusia (%)	64%	NA	31%
ORR (%)	62%	64.9%	77%
VGPR or better (%)	46%	43.3%	47%
Median PFS / Median OS	7m / NA	NA	15.5m / Not reached

(1) Costa, Bruno Almeida, et al. "Real-World Safety and Early Efficacy of Talquetamab in Patients with Heavily-Pretreated Relapsed/Refractory Multiple Myeloma." *Blood* 144 (2024): 7026.;
(2) Janakiram, Murali, et al. "Real World Evidence of Outcomes of Patients Treated with Talquetamab in a Heavily Pretreated Population with Multiple Myeloma with High Exposure to Prior BCMA Therapies-a Report from the IMWG Consortium." *Blood* 144 (2024): 3368.
(3) Grajales-Cruz, Ariel F., et al. "Single Center Real World Experience of Talquetamab in Patients with Relapsed and Refractory Multiple Myeloma." *Blood* 144 (2024): 3784.

Conclusions

- BsAb demonstrated encouraging results in pivotal trials compared to recycled therapies.
- Real-world evidence (RWE) suggests the safety and efficacy of BsAb is similar to that observed in pivotal trials so far.
- Larger studies in diverse populations are important to confirm the efficacy and long-term safety suggested by these preliminary results.

Slide do autor

- CLINICAL RESEARCH TEAM
  - Jéssica C. Vianna
  - Lucilia Marques
  - Interns: Camila Francelino, Luisa Rocha
- MEDICAL TEAM
  - Bruno Kosa, MD, PhD
  - Guilherme Brasil, MD
  - Gislaine Borba, MD
  - Samuel Medina, MD
  - Kátia Pagnano, MD, PhD
- GBRAM
  - Vânia Hungria, MD, PhD
  - Edvan Crusoe, MD, PhD
  - Glaciano Ribeiro, MD
  - All the other authors and members of GBRAM

Thank you

Email: pericole@unicamp.br

Phone: 19 35218760