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HIGHLIGHTS IN MULTIPLE MYELOMA

HOW TO TREAT TRIPLE- OR PENTA-REFRACTORY MULTIPLE MYELOMA?

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CONFLICT OF INTEREST AND FUNDING

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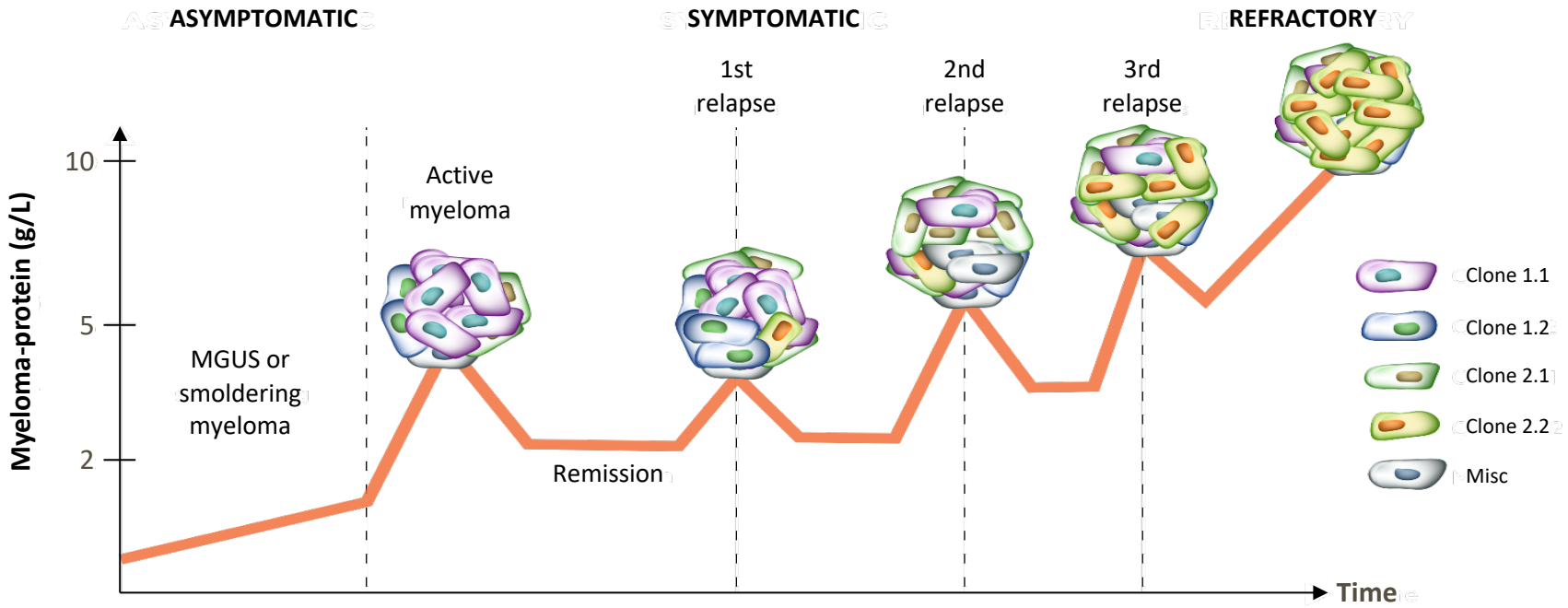
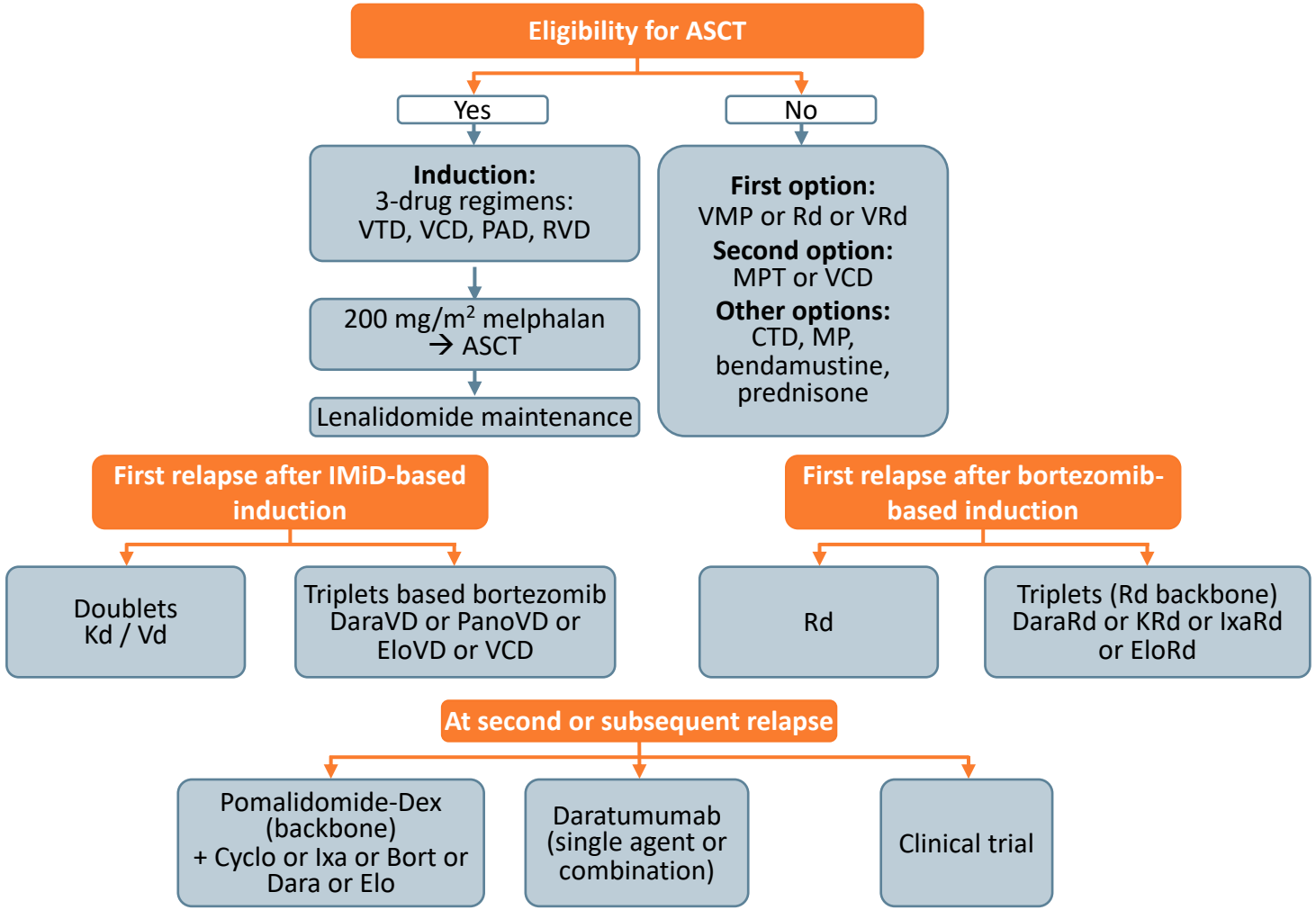
POOR PROGNOSIS AND HIGH RISK OF RELAPSE IN RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM) DESPITE ADVANCES IN TREATMENT

MULTIPLE MYELOMA (MM) DISEASE EVOLUTION



MGUS, monoclonal gammopathy of undetermined significance

SUMMARY OF MANAGEMENT OF MM PATIENTS
ESMO 2017 GUIDELINES



- After 2nd and especially 3rd line of therapy, most MM patients have been exposed to proteasome inhibitors, IMiDs and anti-CD38 monoclonal antibodies

- **Is this population an unmet medical need?**

ASCT, autologous stem cell transplantation; Bort, bortezomib; CTD, cyclophosphamide, thalidomide, dexamethasone; Cyclo, cyclophosphamide; Dara, daratumumab; DaraRd, daratumumab, lenalidomide, dexamethasone; DaraVD, daratumumab, bortezomib, dexamethasone; Dex, dexamethasone; Elo, elotuzumab; EloRd, elotuzumab, lenalidomide, dexamethasone; EloVD, elotuzumab, bortezomib, dexamethasone; ESMO, European Society for Medical Oncology; IMiD, immunomodulatory drug; Ixa, izaxomib; IxaRd, izaxomib, lenalidomide, dexamethasone; Kd, carfilzomib, dexamethasone; KRd, carfilzomib, lenalidomide, dexamethasone; MP, melphalan, prednisone; MM, multiple myeloma; MPT, melphalan, prednisone, thalidomide; PAD, bortezomib, doxorubicin, dexamethasone; PanoVD, panobinostat, bortezomib, dexamethasone; Rd, lenalidomide plus low-dose dexamethasone; RVD, lenalidomide, bortezomib, dexamethasone; VCD, bortezomib, cyclophosphamide, dexamethasone; Vd, bortezomib, dexamethasone; VMP, bortezomib, melphalan, prednisone; VRd, lenalidomide plus low-dose dexamethasone plus bortezomib; VTD, bortezomib, thalidomide, dexamethasone.

Moreau P, et al. Ann Oncol. 2017;28(suppl_4):iv52-iv61

THE MAMMOTH STUDY
Monoclonal Antibodies in MM: Outcomes After THerapy

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PATIENTS FROM 14 US ACADEMIC INSTITUTIONS

Study population

- **Active MM** and **refractory to daratumumab** or **isatuximab**, alone or in combination (index regimen)
- **At least 4 weeks** of CD38 mAB-containing index **regimen treatment**
- **Evidence of PD** while on index regimen or within 60 days of last dose[a]

Excluded: patients with ongoing response to CD38 mAB or discontinued due to reasons other than PD

Retrospective analysis

- **Patient characteristics**
- **Disease characteristics**
- **All therapies administered before and after T_0**
- **Survival status**
- **High-risk cytogenetics**

[a]As defined by International Myeloma Working Group Response Criteria

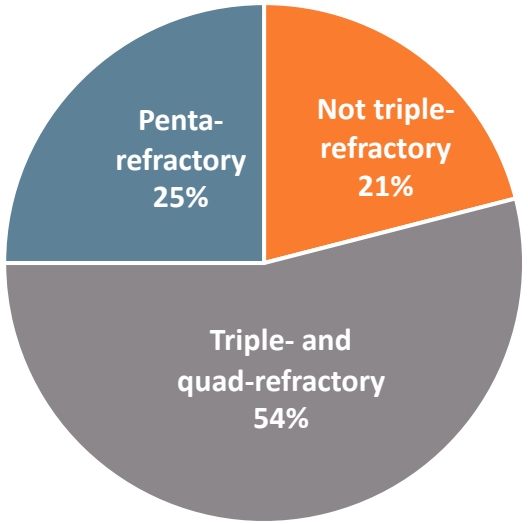
CD38 mAB, CD38-targeted monoclonal antibodies; MM, multiple myeloma; PD, progressive disease; T_0, time at which patients met PD criteria.

Gandhi UH, et al. Leukemia. 2019;33:2266-2275

MEDIAN OVERALL SURVIVAL WAS <1 YEAR IN ALL REFRACTORY STATUS GROUPS

MOST PATIENTS ANALYSED WERE TRIPLE- OR QUAD-REFRACTORY (54%)

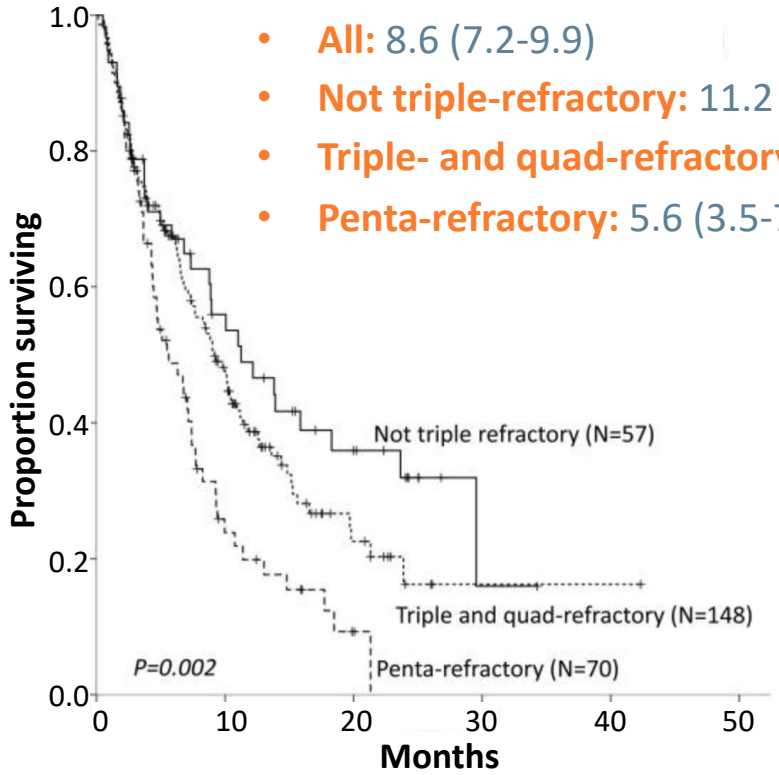
Refractory group status



- **Most patients (93%) were daratumumab-refractory; 7%** were isatuximab-refractory
- **Most patients were refractory to lenalidomide (77%),** pomalidomide **(65%)**, and bortezomib **(68%)**

Median OS, months (95% CI) from T_0

- **All:** 8.6 (7.2-9.9)
- **Not triple-refractory:** 11.2 (5.4-17.1)
- **Triple- and quad-refractory:** 9.2 (7.1-11.2)
- **Penta-refractory:** 5.6 (3.5-7.8)



CI, confidence interval; OS, overall survival; PD, progressive disease; T_0, time at which patients met PD criteria after starting index regimen

Gandhi UH, et al. Leukemia. 2019;33:2266-2275

WHAT HAPPENS AT THIRD LINE AND BEYOND?

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First relapse after PI and/or IMiD-based induction, LEN-refractory

CD38-based

VD-DARA (infrequent use)

- **Kd+dara[a]**
- **Kd+isatuximab[a]**
- **Pom-dex-dara[a]**
- **Pom-cyclo-dex-dara[a]**

Non-CD38-based

- **Pom + Vd[a]**
- Pom + cyclo + dex
- Pom-dex + K
- Pom-dex + belamaf

- **Vd + selinexor[a]**
- Vd + venetoclax[b]
- Kd ± cyclo

2nd and subsequent relapses

- **Pom-dex + isatuximab**
- **Pom-dex + elotuzumab**

- **Selinexor**
- **Melflufen**

- **Belantamab mafodotin**

- **Cell therapy**
- **CAR-T cells**

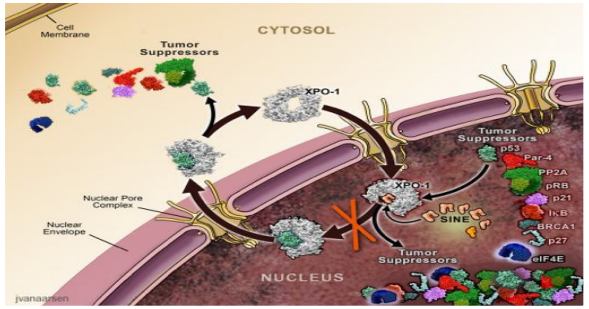
Pom-dex + isa or elo are approved but according to the label, they will move to earlier relapses if available

[a] Based on phase 3 randomised trials. [b] Venetoclax-based combinations for patients with t(11;14) and/or overexpression of bcl-2.
Cyclo, cyclophosphamide; dara, daratumumab; dex, dexamethasone; elo, elotuzumab; IMiD, immunomodulatory drug; isa, isatuximab; K, carfilzomib; Kd, carfilzomib, dexamethasone; LEN, lenalidomide; PI, protease inhibitor; pom, pomalidomide; Vd, bortezomib, dexamethasone
Mateos MV. Personal perspective

SELINEXOR AND MELFLUFEN

XPO1-INHIBITOR SELINEXOR IN RRMM

First-in-class, oral Selective Inhibitor of Nuclear Export (SINE) that inhibits XPO1 and activates tumour suppressor proteins & reduces oncoproteins[1]



- Cancer cells (and MM) overexpress XPO1, causing increased export of tumour suppressors and growth regulatory proteins from the nucleus
- Selinexor inhibits XPO1 mediated nuclear-cytoplasmic transport by transiently binding to the XPO1 cargo binding site
- Accumulation of tumour suppressors in the nucleus amplifies the natural apoptotic function in cancer cells with damaged DNA

STORM study[2]

- 122 patients received **selinexor-dex** after a **median of 7 prior lines of therapy** (68% penta-refractory and 100% three-drug class refractory)
- **ORR 26%,** including two patients in stringent CR
  - Minimal response or better observed in 39%→ sustained across different subgroups
- **Median PFS of 3.7 months and OS of 8.6 months**
- **Safety profile**: thrombocytopenia (58% grade 3-4) and some GI events (nausea and anorexia, grade 3 in 5-10%)

Selinexor-dex is approved by FDA in US and EMA in EU

CR, complete response; dex, dexamethasone; EMA, European Medicines Agency; EXPO1, exportin 1; FDA, Food and Drug Administration; G, grade; GI, gastro-intestinal; MM, multiple myeloma; OS, overall survival; ORR, overall response rate; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma

1. Tai YT, et al. Leukemia. 2014;28:155-165; 2. Chari A, et al. N Engl J Med. 2019;381:727-738

STOMP: SELINEXOR PLUS POM-DEX IN RRMM PATIENTS

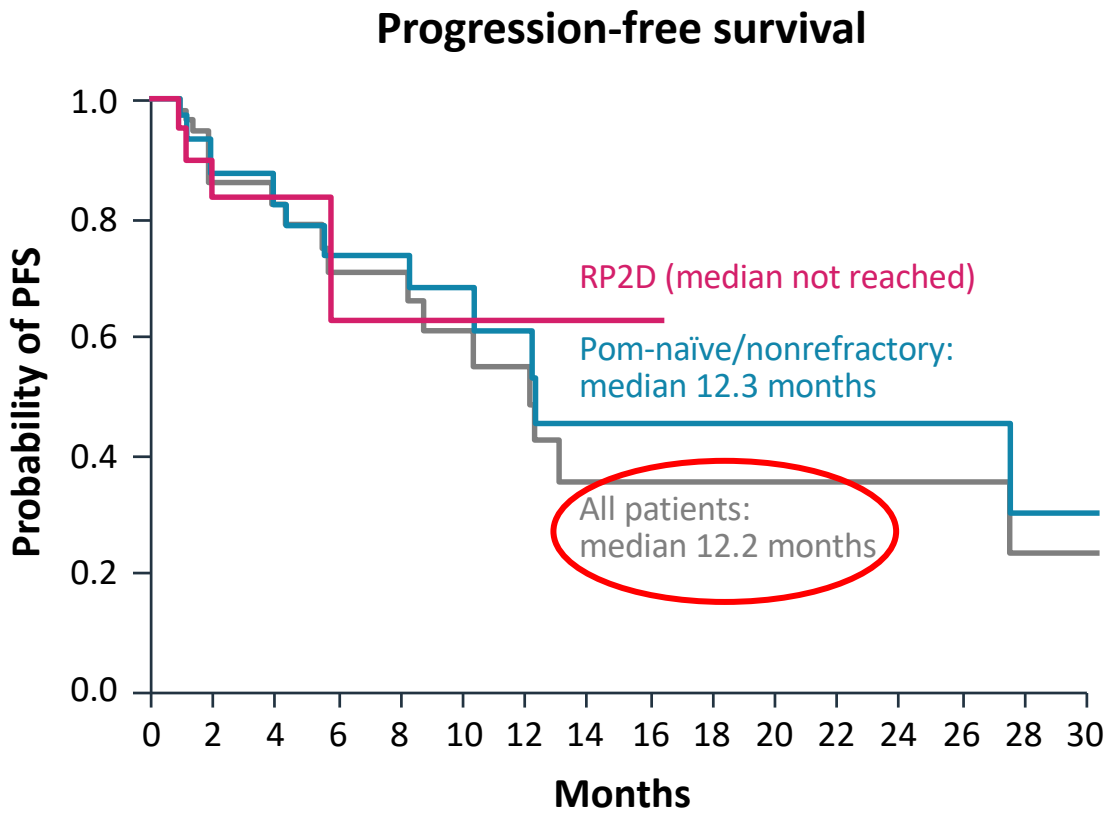
- After the phase 1 part, the **RP2D was selinexor 60 mg qw plus Pom and Dex** at conventional doses in 4-weeks cycles
- 65 patients (20 at the RP2D) were included after a **median of 3 prior lines of therapy,** all len-exposed and 80% len-refractory; 90% bortezomib-exposed; 50% carfilzomib-exposed and 20% dara-exposed and refractory

Clinical response

	N	ORR (%)	CBR (%)
POM naive or nonrefractory	46	25 (54)	33 (72)
POM refractory	14	5 (36)	9 (64)
RP2D: selinexor 60 mg qw + POM 4 mg	20	12 (60)	15 (75)

Safety

n (%)	Any grade	Grade 3/4
Neutropenia	38 (60)	34 (54)
Thrombocytopenia	34 (54)	20 (32)
Nausea	38 (60)	1 (2)
Decreased appetite	28 (44)	1 (2)
Fatigue	32 (51)	6 (10)



CBR, clinical benefit rate; dara, daratumumab; Dex, dexamethasone; len, lenalidomide; ORR, overall response rate; PFS, progression-free survival; Pom, pomalidomide; qw, once weekly; RP2D, recommended phase 2 dose; RRMM, relapsed/refractory multiple myeloma

Chen C, et al. ASH 2020. Abstract #726. Oral presentation

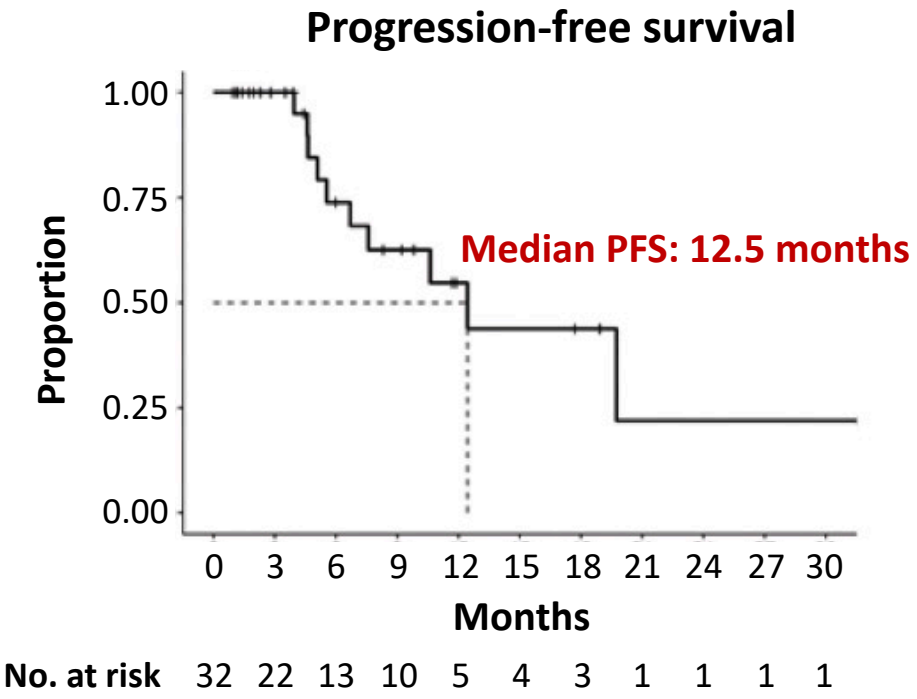
SELINEXOR PLUS DARA-DEX IN RRMM PATIENTS

- After the phase 1 part, the **RP2D was selinexor 100 mg weekly plus Dex and Dara** at conventional doses in 4-weeks cycles
- 34 patients were included after a median of 3 prior lines, 65% len-refractory; 85% PI-refractory; **6% dara-exposed and refractory**

Group	No. of patients	No. of patients (%)			
		ORR	CBR	VGPR	PR
Overall	32	22 (69)	26 (81)	11 (34)	11 (34)
Daratumumab-naïve	30	22 (73)	26 (87)	11 (37)	11 (37)
Lenalidomide-refractory	20	13 (65)	15 (75)	6 (30)	7 (35)
Bortezomib-refractory	19	13 (68)	16 (84)	5 (26)	8 (42)
Pomalidomide-refractory	10	5 (50)	8 (80)	2 (20)	3 (30)
Bortezomib/lenalidomide-refractory	16	11 (69)	13 (81)	4 (25)	7 (44)

Patients with dara-refractory disease did not respond

	Any grade	Grade 3/4
Neutropenia	50%	26.5%
Thrombocytopenia	70.6%	47%
Nausea	70.6%	8.8%
Decreased appetite	35.3%	-
Fatigue	61.8%	17.6%

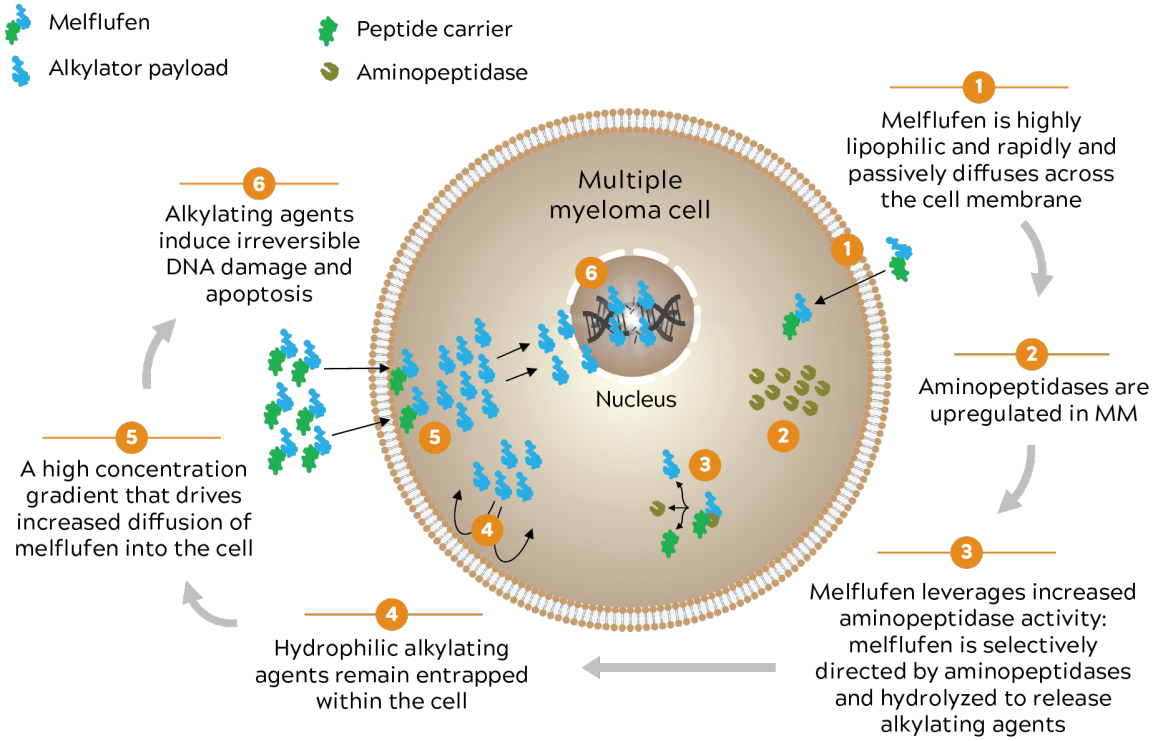


CBR, clinical benefit rate; Dara, daratumumab; Dex, dexamethasone; len, lenalidomide; ORR, overall response rate; PFS, progression-free survival; PI, proteasome inhibitor; PR, partial response; RP2D, recommended phase 2 dose; RRMM, relapsed/refractory multiple myeloma; VGPR, very good partial response

Gasparetto C, et al. eJHaem. 2021;2:56-65

MELFLUFEN IN RRMM

Melphalan flufenamide (melflufen) is an investigational first-in-class peptide-drug conjugate (PDC) **that targets aminopeptidases and rapidly releases alkylating agents into tumour cells.**[1-5]



In the pivotal, phase 2, HORIZON study, **melflufen plus dexamethasone showed clinically meaningful efficacy and a safety profile** characterised primarily by clinically manageable haematologic AEs in patients with heavily pretreated and poor-risk RRMM.[6]

Outcome[6]	Overall Population (N=157)
ORR (95% CI), %	**29 (22-37)**
OS, median (95% CI), months	**11.6 (9.3-15.4)**
PFS, median (95% CI), months	**4.2 (3.4-4.9)**
DOR (≥PR), median (95% CI), months	5.5 (3.9-7.6)

At ASH 2020, Melflufen has demonstrated to maintain the efficacy in:

- **EMD**
- **Patients with HR CA (especially +1q)[7]**
- **Patients exposed and/or refractory to melphalan**

Melflufen is approved by FDA

Mateos MV, et al. ASH 2020 #3237

AE, adverse event; ASH, American Society of Hematology; CI, confidence interval; DOR, duration of response; EMD, extramedullary disease; FDA, Food and Drug Administration; HR CA, high-risk cytogenetic abnormalities; MM, multiple myeloma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; RRMM, relapsed/refractory multiple myeloma

1. Chauhan D, et al. Clin Cancer Res. 2013;19:3019-3031; 2. Ray A, et al. Br J Haematol. 2016;174:397-409; 3. Wickström M, et al. Oncotarget. 2017;8:66641-66655; 4. Wickström M, et al. Invest New Drugs. 2008;26:195-204; 5. Strese S, et al. Biochem Pharmacol. 2013;86:888-895; 6. Richardson PG, et al. EHA 2020. Abstract EP945. Poster presentation; 7. Mateos MV, et al. ASH 2020. Abstract #3237

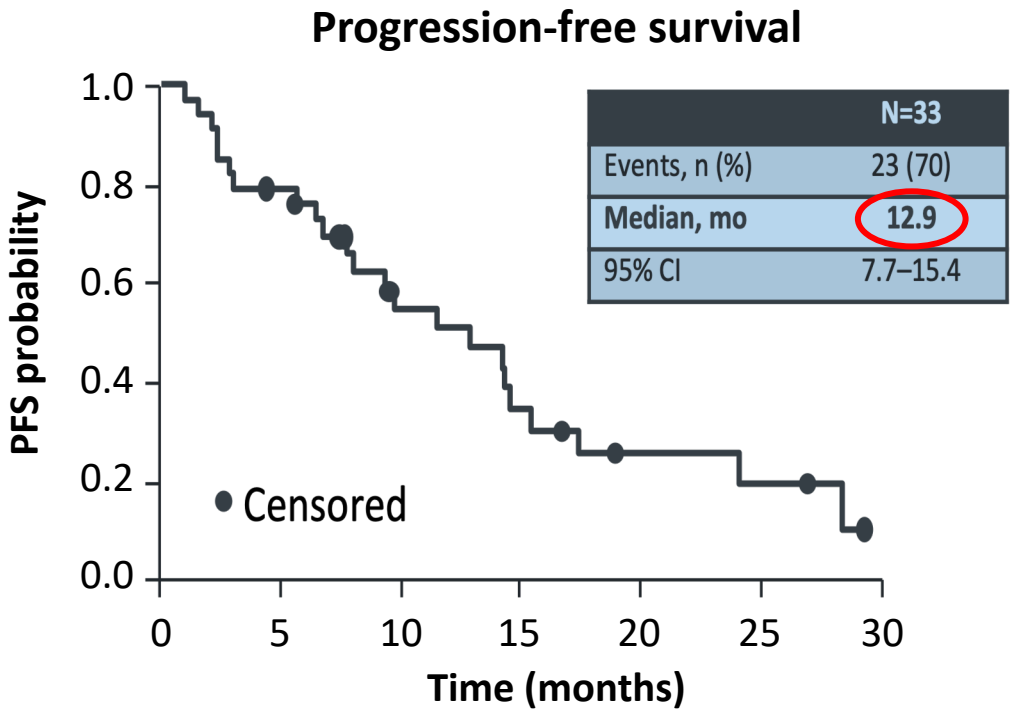
ANCHOR: MELFLUFEN PLUS DEX AND DARA OR BORTEZOMIB

Study design – daratumumab cohort

- 33 patients with median of 2 prior lines of therapy (36% double-refractory; 64% IMiD refractory) received 28-day treatment cycles until PD or unacceptable toxicity
  - **Malflufen (iv):** 40/30/20 mg on Day 1
  - **Daratumumab (iv):** 16 mg/kg on Days 2/1, 8, 15, 22 (cycles 1/2), Days 1 and 15 (cycles 3-6), and Day 1 from cycle 7 onward
  - **Dexamethasone (po):** 40 mg weekly

Subgroup	Best confirmed response (n)							Patients (%)	
	>CR	VGPR	PR	MR	SD	PD	NA	ORR	CBR
Melflufen 30 mg (n=6)	0	4	1	0	0	0	1[a]	83	83
Melflufen 40 mg (n=27)	2	6	11	1	2	1	4[b]	70	74
Total (N=33)	2	10	12	1	2	1	5	73	76

[a] 1 patient had unconfirmed PD in 30 mg group
[b] 4 patients had unconfirmed responses in the 40 mg group (2 PD, 1 SD, 1 PR)



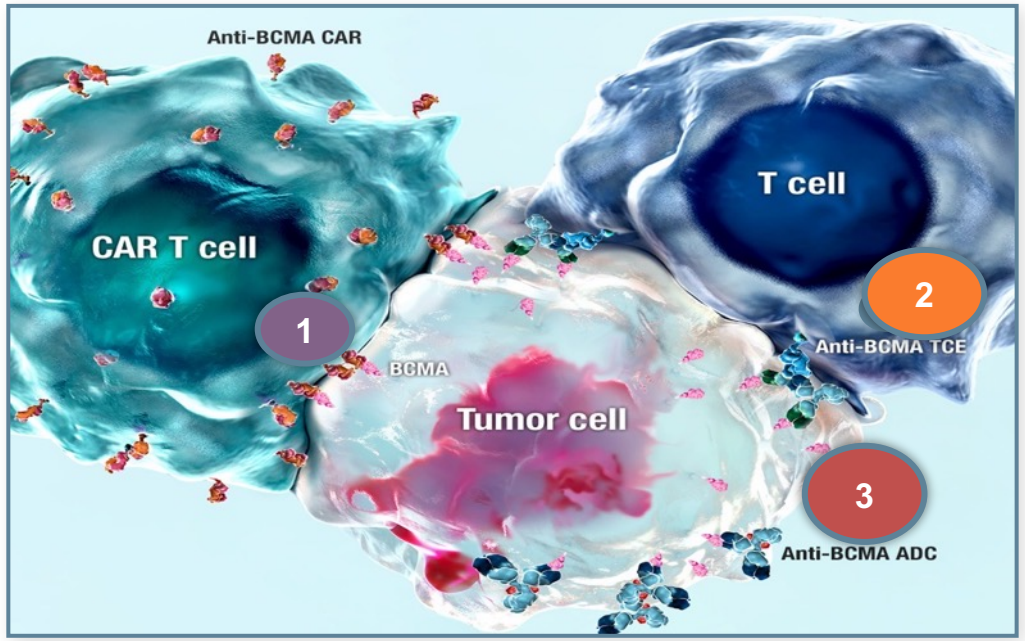
Safety profile:

- Grade ≥3 thrombocytopenia, 73%
- Neutropenia 67%
- Pneumonia 6%
- 2 fatal sepsis

CBR, clinical benefit rate; CI, confidence interval; CR, complete response; DARA, daratumumab; DEX, dexamethasone; IMiD, immunomodulatory drug; iv, intravenous; mo, month; MR, minimal response; NA, not available; ORR, overall response rate; PD, progressive disease; PFS, progression-free survival; po, orally; PR, partial response; SD, stable disease; VGPR, very good partial response

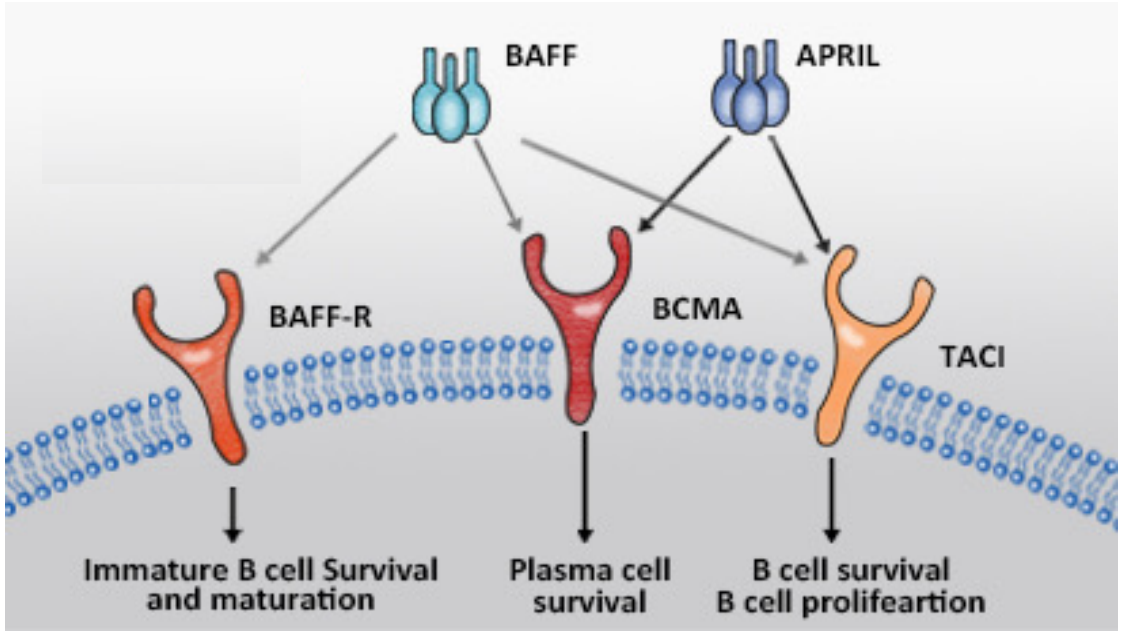
Ocio E, et al. ASH 2020. Abstract #417. Oral presentation.

WHAT ARE THE CELL THERAPY OPTIONS FOR MM?



1 **CAR T-cell therapy (CAR-T)**

2 **T-cell engager antibody (TCE)**



BCMA is extensively studied and is an approved target[1,2]

BCMA expression in PC

In normal physical functions

- Survival of long-lived PCs
- Production of antibodies
- Class switching of immunoglobulin

In MM

- Promotes proliferation and survival of MM cells
- Associated with immunosuppressive BM microenvironment
- Increased sBCMA level is associated with disease progression and poorer outcome

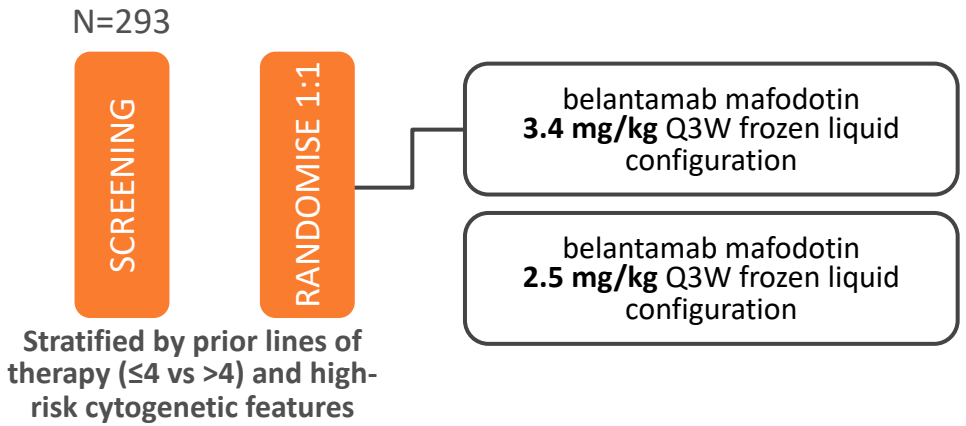
ADC, antibody-drug conjugate; APRIL, a proliferation-inducing ligand; BAFF, B-cell activating factor; BAFF-R, BAFF receptor; (s)BCMA, (serum) B-cell maturation antigen; BM, bone marrow; CAR-T, chimeric antigen receptor T-cell; IMiD, immunomodulatory agent; mAb, monoclonal antibody; MM, multiple myeloma; PC, plasma cell; TACI, transmembrane activator and calcium-modulating cyclophilin ligand interactor; TCE, T-cell engager antibody

1. https://www.ema.europa.eu/en/documents/product-information/blenrep-epar-product-information_en.pdf. Accessed Sept 2020; 2. Yu B, et al. J Hematol Oncol. 2020;13:125

BCMA-ADC

BELANTAMAB MAFODOTIN

Pivotal DREAMM-2 study: single-agent belantamab mafodotin (GSK2857916) in patients with RRMM refractory to PIs, IMiDs, and refractory and/or intolerant to anti-CD38 mABs



	belantamab mafodotin 2.5 mg/kg (N=97)	belantamab mafodotin 3.4 mg/kg (N=99)
ORR:	31% (97.5% CI: 20.8-42.6)	34% (97.5% CI: 23.9-46.0)
mPFS:	2.9 months (95% CI: 2.1-3.7)	4.9 months (95% CI: 2.3-6.2)
CR:	3 (3%)	3 (3%)
mDOR:	11 months	6.2 months
mOS:	13.7 months	14 months

Toxicity profile: Ocular events (keratopathy in >70% of any grade [25% G3-4 in both arms]); thrombocytopenia in 35% and 57% of any grade in 2.5 and 3.4 mg/kg cohorts, respectively

Responders: half of them had a treatment hold for ≥3 cycles and were able to re-start. Most (88%) maintained their response

Belantamab mafodotin (2.5 mg/kg Q3W) has been approved by EMA for the treatment of adult patients with RRMM who have received at least 4 prior therapies including lenalidomide, a PI and anti-CD38 mAB and have demonstrated disease progression on the last therapy

CI, confidence interval; CR, complete response; EMA, European Medicines Agency; G, grade; mDOR, median duration of response; IMiD, immunomodulatory drug; mAB, monoclonal antibody; mOS, median overall survival; mPFS, median progression-free survival; ORR, overall response rate; PI, proteasome inhibitor; Q3W, every 3 weeks; RRMM, relapsed/refractory multiple myeloma

Lonial S, et al. EHA 2020. Abstract EP970. Poster presentation

ALGONQUIN: BELANTAMAB MAFODOTIN + POM-DEX

Study design

PART 1: DLT 3+3

PART 1: RP2D determination phase ≤12 patients/cohort

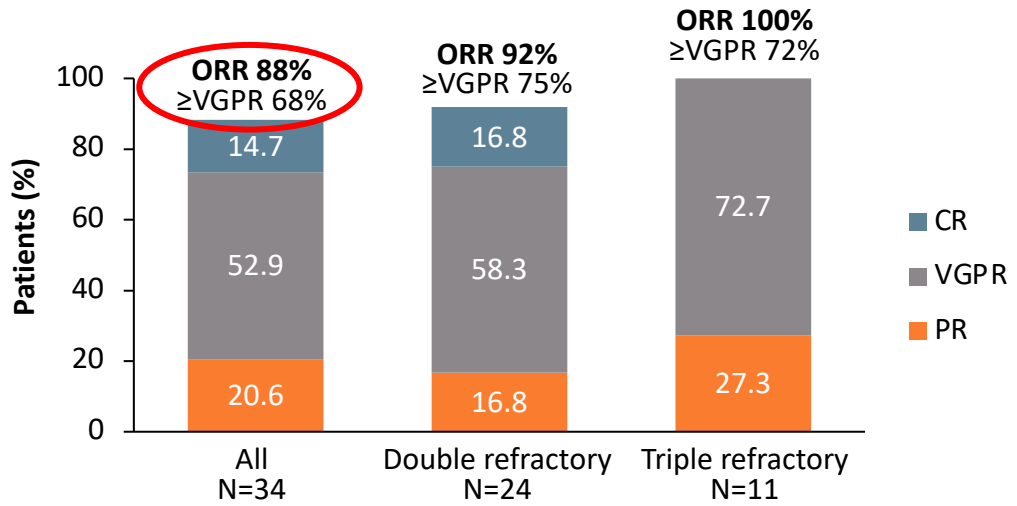
D1 D8 D15 D21 C2D1 C3D1

POM 4 mg po	→				→					
Dex 40 mg po	D	D	D	D	D	D	D	D	D	D
1.92/2.5 mg/kg SINGLE iv	B				B				B	
2.5/3.4 mg/kg SPLIT iv	B	B			B	B			B	B
BELAMAF loading iv	2.5				1.92				1.92	

PART 2

RP2D
N=23 (+12 in PART 1 = 35 evaluable for ORR)

	N=37
Median (range) no. prior lines of therapy	3 (1-15)
Lenalidomide status Exposed Refractory	 37 (100.0) 33 (89.2)
PI status Exposed Refractory	 37 (100.0) 30 (81.1)
DARA status Exposed Refractory	 16 (43.2) 16 (43.2)
Lenalidomide and PI refractory	27 (73.0)
Lenalidomide, PI and DARA refractory	13 (35.1)

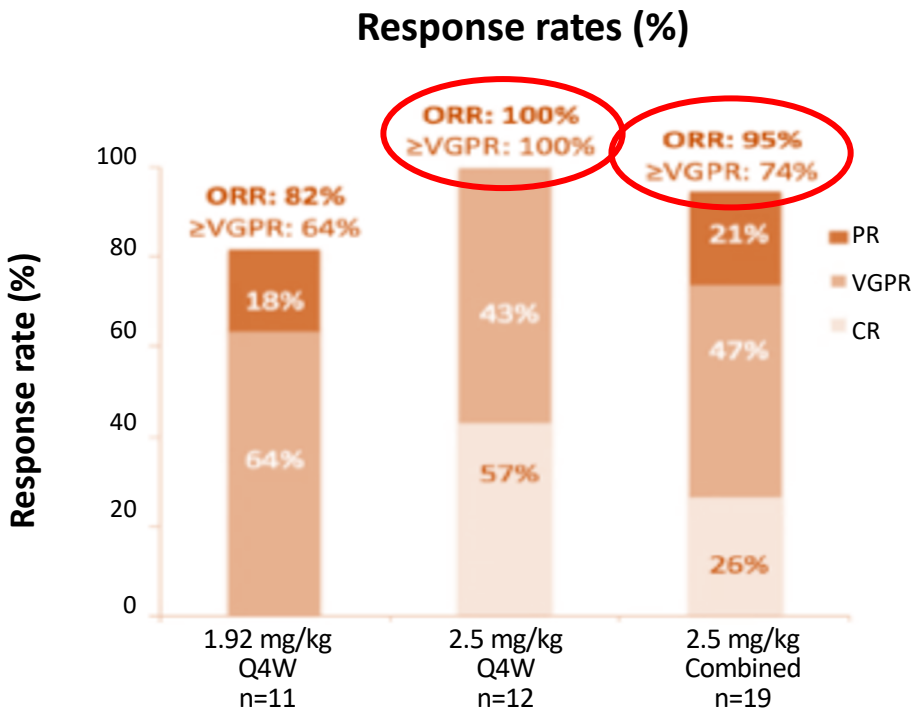


Outcome	All patients	IMiD/PI refractory	IMiD/PI/ DARA refractory
Median PFS, mos (95% CI)	NR (10.8-NR)	NR (10.8-NR)	11.1 (4.9-NR)
Median follow-up, mos (range)	7.8 (1.9-20.3)	7.8 (1.9-18.9)	7.4 (2.1-16.1)

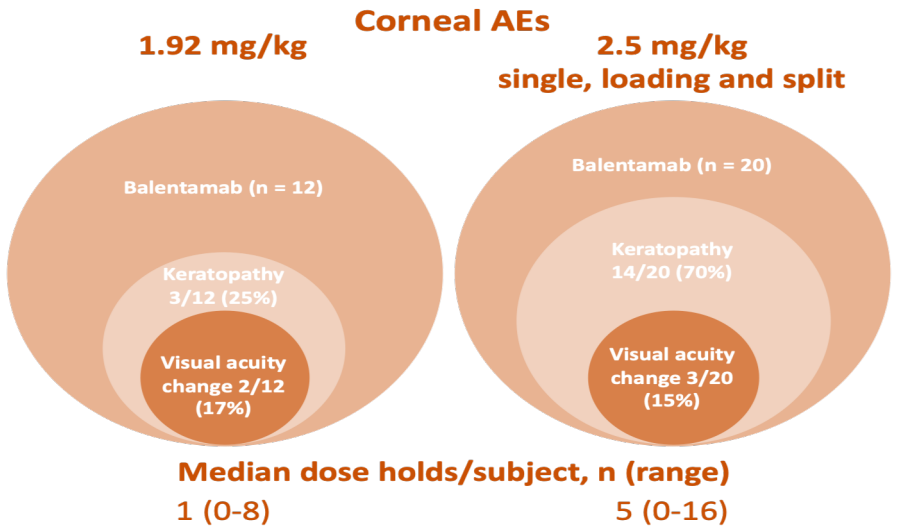
C, cycle; D, day; CI, confidence interval; CR, complete response; DARA, daratumumab; Dex, dexamethasone; DLT, dose limiting toxicity; IMiD, immunomodulatory drug; iv, intravenous; mos, months; NR, not reached; ORR, overall response rate; PFS, progression-free survival; PI, proteasome inhibitor; po, orally; POM, pomalidomide; PR, partial response; RP2D, recommended phase 2 dose; VGPR, very good partial response

Trudel S, et al. ASH 2020. Abstract #725. Oral presentation

ALGONQUIN: BELANTAMAB MAFODOTIN + POM-DEX



TEAE, n (%)	Any grade	Grade ≥3
Keratopathy	28 (75.7)	19 (51.4)
Neutropenia	21 (56.8)	15 (40.5)
Thrombocytopenia	18 (48.6)	12 (32.4)
Decreased visual acuity	17 (45.9)	6 (16.2)
Fatigue	15 (40.5)	4 (10.8)



AE, adverse event; C, cycle; D, day; CR, complete response; Dex, dexamethasone; DLT, dose limiting toxicity; iv, intravenous; ORR, overall response rate; po, orally; POM, pomalidomide; PR, partial response; Q4W, every 4 weeks; RP2D, recommended phase 2 dose; TEAE, treatment-emergent AE; VGPR, very good partial response

Trudel S, et al. ASH 2020. Abstract #725. Oral presentation

BCMA CAR-T

AUTOLOGOUS CAR-T CELL SUMMARY

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	CARTITUDE-1[1] Cilta-cel Phase 1	CRB-401[2] Ide-cel Phase 1	CRB-402[3] Bb21217 Phase 1	LUMMICAR-2[4] CT053 Phase 1b	PRIME[5] BCMA-101 Phase 1/2	GC012F[6] Dual CAR-T BCMA + CD19
Patients	97	62	69	20	55	16
Median prior regimens	6	6	6	5	8	NR
Triple refractory	87.6%	69.4%	64%	85%	60%	NR
CAR-T dose	0.75×10^6 (range $0.5\text{-}1.0 \times 10^6$)	50, 150, 450 and 800×10^6	150, 300 and 450×10^6	$1.5\text{-}1.8/2.5\text{-}3.0 \times 10^8$	$0.75\text{-}15 \times 10^6$	$1.0\text{-}3.0 \times 10^5$
ORR	96.9%	75.8%	68%/84%[a]	94%	67%	93.8%
CR/sCR	67%	38.7%	28%/32%[a]	77%/83%[b]	NR	56.3%
CRS, all grades	94.8%	75.8%	NR	15%/17%[b]	17%	100%
CRS, grade 3/4	4%	6.5%	NR	0%	0%	12.5%
Neurotoxicity, all grades	20.6%	35.5%	NR	15%/17%[b]	3.8%	0%
Neurotoxicity, grade 3/4	10.3%	1.6%	NR	8%/0[c]	3.8%	0%

[a] CAR-Ts made using original manufacturing process/updated manufacturing process
[b] $1.5\text{-}1.8/2.5\text{-}3.0 \times 10^8$ dose

BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T-cell; CRS, cytokine release syndrome; CR/sCR, complete response/stringent CR; NR, not reported; ORR, overall response rate

1. Madduri D, et al. ASH 2020. Abstract #177. Oral presentation; 2. Lin Y, et al. ASH 2020. Abstract #131. Oral presentation; 3. Alsina M, et al. ASH 2020. Abstract #130. Oral presentation; 4. Kumar S, et al. ASH 2020. Abstract #133. Oral presentation; 5. Costello C, et al. ASH 2020. Abstract #134. Oral presentation; 6. Jiang H, et al. ASH 2020. Abstract #178. Oral presentation

BCMA X CD3 ANTIBODIES

BCMA X CD3 BISPECIFIC ANTIBODIES

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Drug	Type and administration	N	Safety	Population	Response	DOR/PFS
Teclistamab[1]	Bi-specific Administered weekly IV/SC (RP2D 1500 µg/kg SC)	40 at RP2D	CRS 70% at RP2D, all G1-2 Neurotoxicity 1% at RP2D (G1) Infections 45% at RP2D (23% G3-4)	Median of 5 prior lines 83% triple refractory 38% penta refractory	At RP2D, ORR: 65% with 40% sCR/CR	Median DOR not reached; 85% alive after median f/u of 7.1 months
AMG 701[2]	BiTe IV Weekly	85	CRS G1-2 55%, G3-4: 9% No ICANs 21% thrombocytopenia	Median of 6 prior lines 62% triple refractory	83% ORR at the top dose level and 50% VGPR	No mature data
REGN5458[3]	Bi-specific IV Weekly, every other week from C4	49	CRS 39%, no G3-4 ICANs 12% Cytopenias 47% and infections 18%	Median of 5 prior lines 100% triple refractory 57% penta refractory	ORR 62.5% at 96 mg (95% in VGPR) Some CR in lower dose levels	Preliminary median DOR: 6 months
TNB-383B[4]	Triple chain anti-BCMA bi-specific IV fixed doses Every 3 weeks	58	CRS 45%, no G3-4 No ICANS Anaemia 21% and ≥G3 infections 14%	Median of 6 prior lines 64% triple refractory 34% penta refractory	80% (13% CR) at dose levels 40-60 mg	No mature data
PF-3135[5]	Bi-specific SC Weekly	18	CRS 61% and no G3-4 No ICANs Cytopenias G3 in 11%	Median of 7 prior lines 100% dara exposed 22% prior BCMA-based therapy	75% at the top two dose levels	No mature data

Key aspects:

- Efficacy, especially durability of response and PFS/OS
- Route of administration: IV vs SC
- Administration schedule: weekly vs every two weeks vs monthly
- Priming dose (yes/no) and number of hospitalisation days requirement

1. Krishnan AY, et al. ASCO 2021. Abstract #8007. Oral presentation; 2. Harrison SJ, et al. ASH 2020. Abstract #181. Oral presentation; 3. Madduri D, et al. ASH 2020. Abstract #291. Oral presentation; 4. Rodriquez C, et al. ASH 2020. Abstract #293. Oral presentation; 5.Lesokhin AM, et al. ASH 2020. Abstract #3206. Poster presentation

BCMA, B-cell maturation antigen; BiTe, bispecific T-cell engager; C, cycle; CRS, cytokine release syndrome; CR/sCR, complete response/stringent CR; dara, daratumumab; DOR, duration of response; f/u, follow up; G, grade; ICAN, immune effector cell associated neurotoxicity syndrome; IV, intravenous; m, month; ORR, overall response rate; PFS, progression-free survival; OS, overall survival; RP2D, recommended phase 2 dose; SC, subcutaneous; VGPR, very good partial response

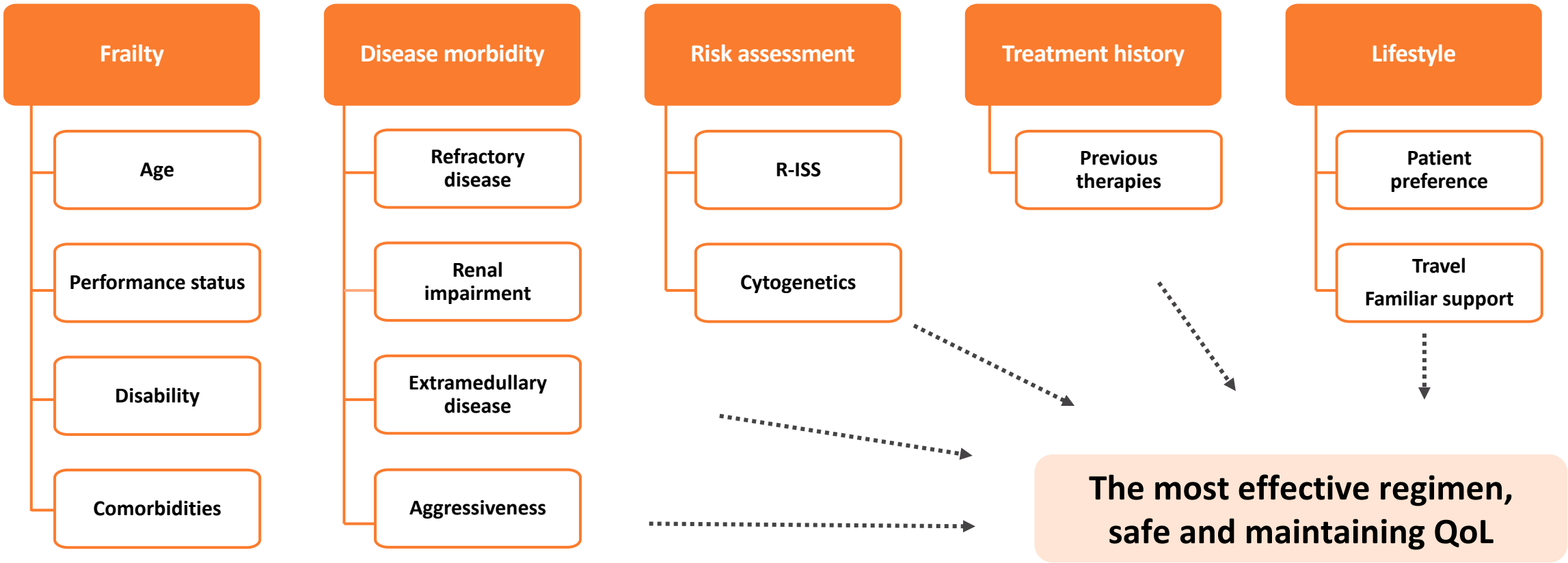
SUMMARY

- **Patients exposed to three or more drug classes are an unmet medical need**
- New molecules are available, such as melflufen and selinexor
- BCMA-targeted therapy is also promising, using antibody-drug conjugates, CAR-T cells or bi-specific monoclonal antibody

Challenging situations:
What is the optimal sequencing?
How to select the optimal BCMA-targeted therapy ?

BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T-cell

PATIENT- AND DISEASE-RELATED FACTORS ARE RELEVANT IN THE SELECTION OF THE RESCUE THERAPY



QoL, quality of life; R-ISS, Revised International Staging System.

Binder M, et al. Haematologica. 2016;101:P665; Chen X, et al. Clin Interv Aging. 2014;9:433-441; Chng WJ, et al. Leukemia. 2016;30:1071-1078; Chung TH, et al. PLoS One. 2013;20:e66361; Clegg A, et al. Lancet. 2013;381:752-762; Faiman BM, et al. Clin J Oncol Nurs. 2011;15:66-76; Greipp PR, et al. J Clin Oncol. 2005;23:3412-420; Handforth C, et al. Ann Oncol. 2015;26:1091-1101; Jhaveri M, et al. Haematologica. 2016;101:E1312; Merz M, et al. Haematologica. 2016;101:P650; Miceli TS, et al. Clin J Oncol Nurs. 2011;15:9-23; Palumbo A, et al. Blood. 2015;125:2068-2074; Ramsenthaler C, et al. BMC Cancer. 2016;16:427; Ramasamy K, et al. Haematologica. 2017;102:E1457; Sonneveld P, et al. Leukemia. 2013;27:1959-1969; Williams LA, et al. J Clin Oncol. 2016;34:e18127

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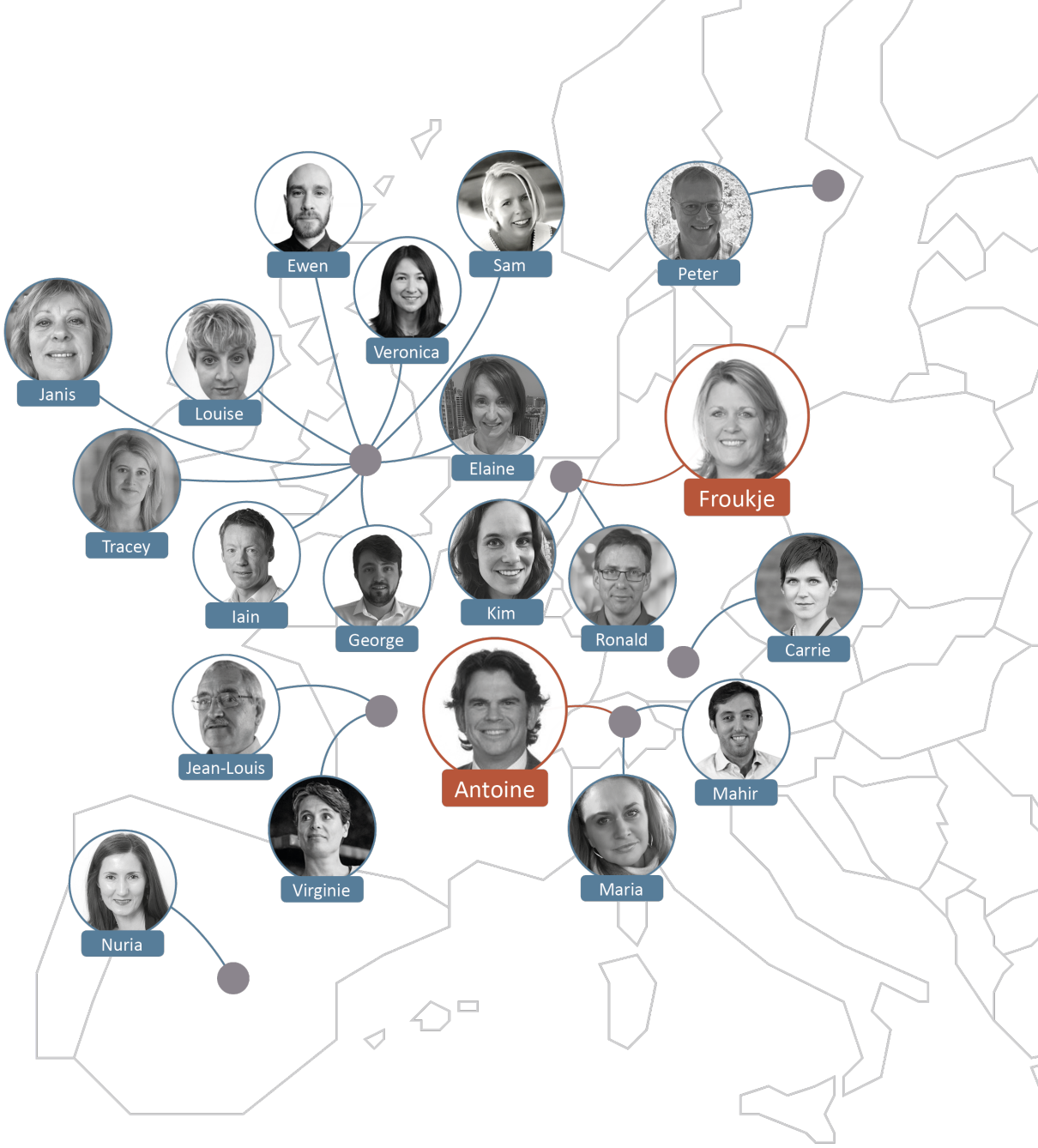

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