IFM - Post IMS 2024
Rechutes - Clinique

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Actualités Ac bispécifiques

RetrosTECtive

TRIMM-2

Redirec-TT1

RetrosTECtive

- Accès précoce français Teclistamab
- N = 303 patients.

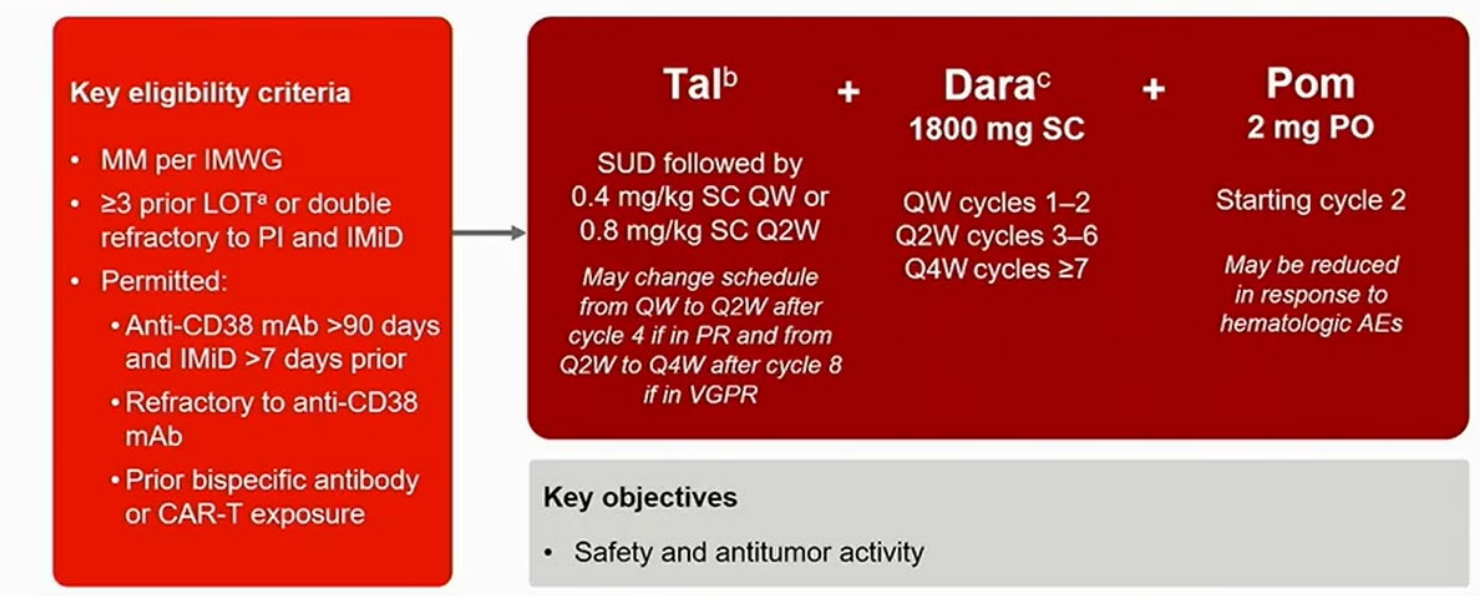
- **Median follow-up: 11.9 months** [95% CI, 9.2- 14.8]
- **ORR rate: 68.8%** including 61.4% VGPR or better
- **Median PFS:**
  - **11.3 months** [95% CI, 8.9 - 14.9] in the overall population
  - **17 months** [95% CI, 16.4 - NA] in the 175 responding patients
- **Median OS: 17 months** [95% CI, 13.8 - NA]

Subgroups (N)	Median PFS	
Age < 75	9.1 months (6.3-13)	p = 0.007
Age 75 or more - 90 (29,7%)	16.4 months (10.7-NR)	
Extra medullary disease – 34 (11,8%)	3.7 months (2-NR)	
No extra medullary disease	11.3 months (8.8-16.2)	p = 0.057
Paramedullar disease – 70 (25,5%)	16.2 months (9.3-NR)	
No paramedullar disease	9.2 months (7.3-13.3)	p = 0.103
Circulating plasmacytosis – 39 (13,8%)	4.7 months (1.7-10.5)	
No circulating plasmacytosis	12.6 months (9.7-16.4)	p = 0.001
del(17p) or TP53 mutation - 54/179 (30.2%)	5.2 months (2.9-9.1)	
No del(17p), no mutation TP53	16.4 months (4.1-NR)	p = 0.009
Ineligibility to MAJESTEC-1 - 86 (28.4%)	3.9 months (2.3-7.9)	
Eligibility to MAJESTEC-1	14.9 months (11.3-NR)	p < 0.001
No previous Auto Transplant	12.5 months (9.7-NR)	
Previous Auto Transplant - 171 (56.4%)	9.1 months (6.3-16.2)	p = 0.357

Perrot et al. IMS 2024

TRIMM-2

- Schéma et population



Caractéristiques	Tal 0,4 mg/kg QW N= 28	Tal 0,8 mg/kg Q2W N= 59
Age	62 (42-75)	64 (33-81)
HR	4 (22,2)	13 (27,7)
EMD		
Triples réfractaires	15 (83,3)	45 (76,3)
Pentaréfractaires	4 (22,2)	20 (33,9)
Exposés CAR T antiBCMA	5 (27,8)	19(32,2)
Exposés Bispé antiBCMA	6 (33,3)	17 (28,8)
Exposés ADC antiBCMA	3 (16,7)	12 (20,3)

Refractory status, n (%)		
Anti-CD38[g]	15 (83.3)	49 (83.1)
Pom	13 (72.2)	45 (76.3)

TRIMM-2

- Toxicités

Most common AEs,[a] n (%)	Tal 0.4 mg/kg QW + dara + pom (n=18)		Tal 0.8 mg/kg Q2W + dara + pom (n=59)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Oral events[b]	18 (100.0)	0 (0)	50 (84.7)	4 (6.8)
CRS	10 (55.6)	0 (0)	47 (79.7)	0 (0)
Nonrash skin events[c]	16 (88.9)	0 (0)	40 (67.8)	0 (0)
Nail events[d]	15 (83.3)	0 (0)	33 (55.9)	0 (0)
Fatigue	11 (61.1)	0 (0)	34 (57.6)	4 (6.8)
Weight decrease ≥10%	12 (66.7)	2 (11.1)	29 (49.2)	10 (16.9)
Pyrexia	7 (38.9)	0 (0)	28 (47.5)	0 (0)
Cough	7 (38.9)	0 (0)	26 (44.1)	2 (3.4)

- Diminution dose Tal
  - 33% cohorte QW et 52% cohorte Q2W
- Arrêt de plus d'une drogue
  - 27,8% cohorte QW et 47,5% cohorte Q2W
- 2 décès toxicité

Most common AEs,[a] n (%)	Tal 0.4 mg/kg QW + dara + pom (n=18)		Tal 0.8 mg/kg Q2W + dara + pom (n=59)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Neutropenia	15 (83.3)	14 (77.8)	47 (79.7)	42 (71.2)
Anemia	9 (50.0)	6 (33.3)	30 (50.8)	22 (37.3)
Thrombocytopenia	6 (33.3)	4 (22.2)	31 (52.5)	20 (33.9)

AEs,[a] n (%)	Tal 0.4 mg/kg QW + dara + pom (n=18)		Tal 0.8 mg/kg Q2W + dara + pom (n=59)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Infections	13 (72.2)	3 (16.7)	46 (78.0)	22 (37.3)

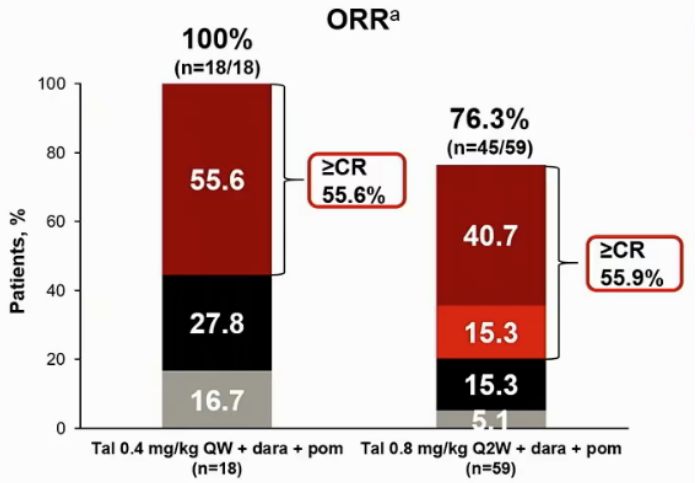
- Of patients with grade 3/4 infections, 84.0% had onset within first 6 months
- Baseline and posttreatment IgG <400 mg/dL observed in 33.8% and 72.7% of patients, respectively
- 53.2% received ≥1 dose of IVIG

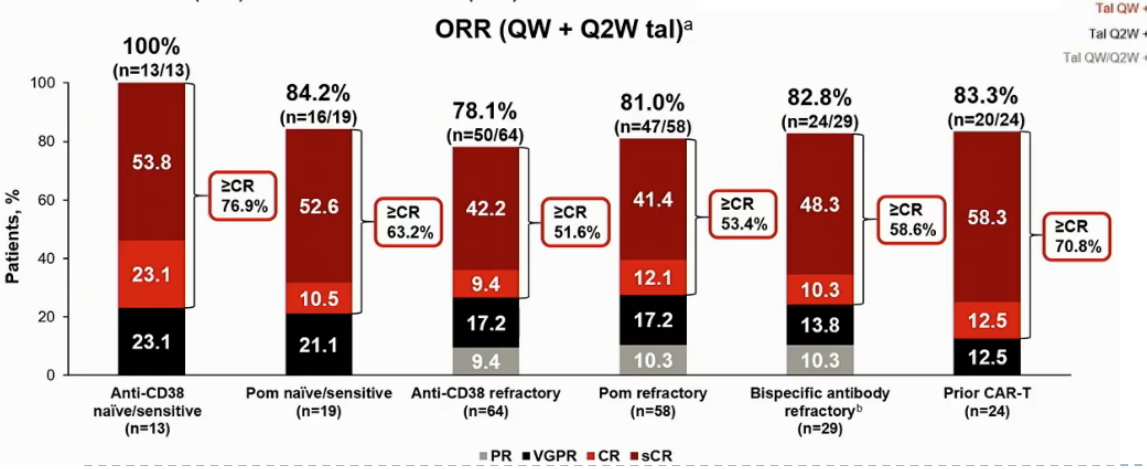
Presented by N Bahlis at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

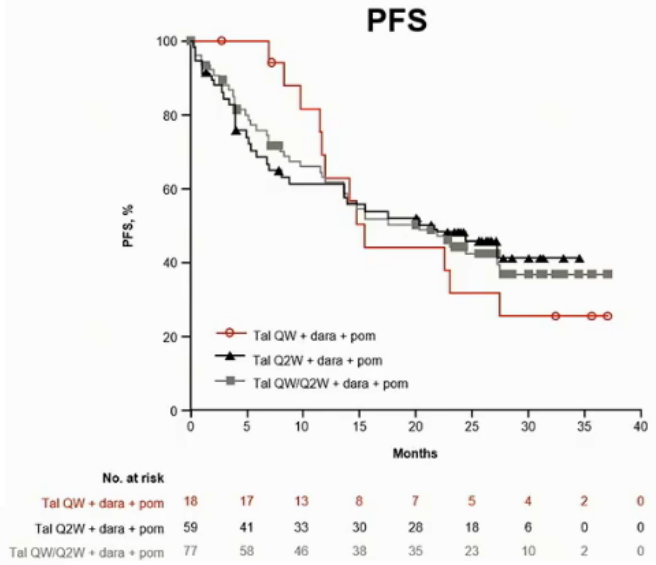
TRIMM-2

- Efficacité

Combined ORR 82% and ≥CR Rate 56%







Parameter	Tal 0.4 mg/kg QW + dara + pom (n=18)	Tal 0.8 mg/kg Q2W + dara + pom (n=59)
Median (range) follow-up, months	15.8 (3.2–37.9)	17.5 (0.2–37.7)
Median PFS, months (95% CI)	15.4 (11.5–27.5)	20.3 (7.9–NE)
12-month PFS, % (95% CI)	62.7 (35.1–81.3)	61.1 (47.1–72.4)

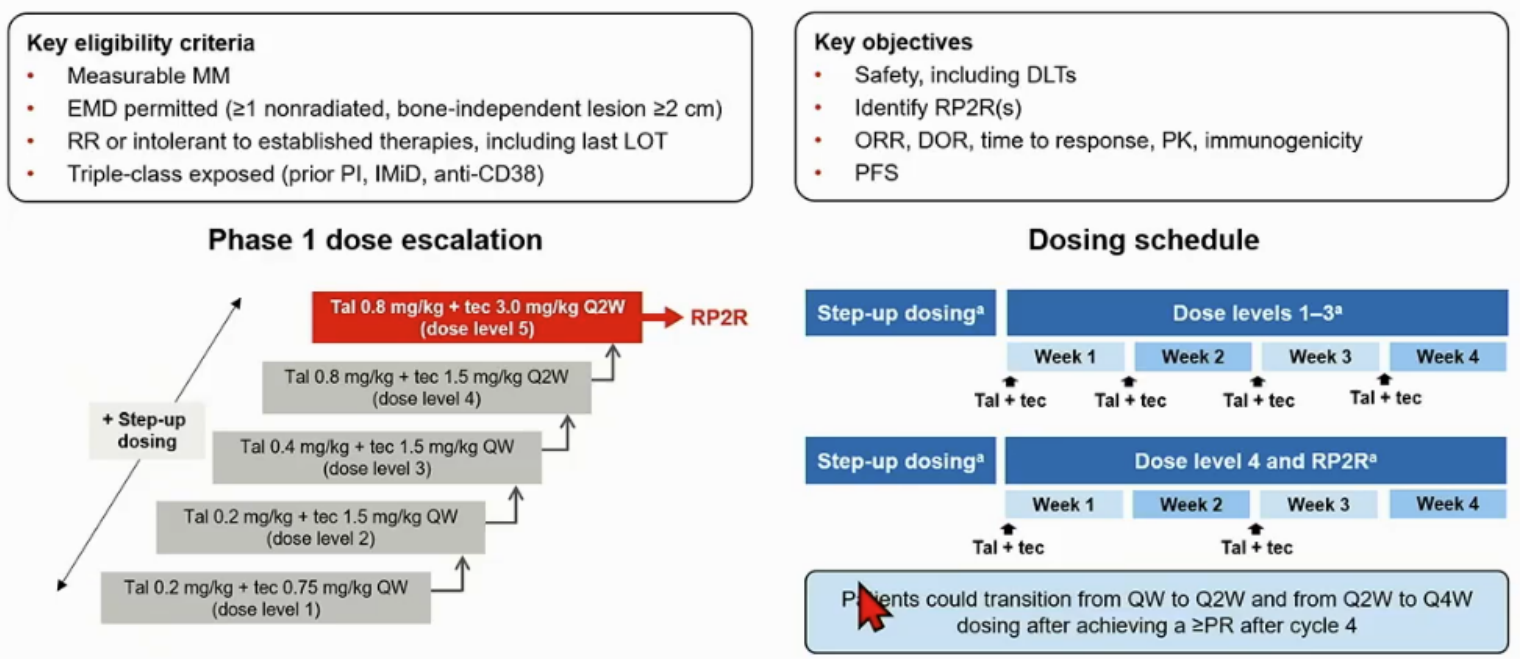
12-month PFS (QW + Q2W tal)

- Anti-CD38 naïve/sensitive (n=13): 84.6%
- Pom naïve/sensitive (n=19): 68.4%
- Anti-CD38 refractory (n=64): 56.9%
- Pom refractory (n=58): 59.4%
- Bispecific antibody refractory (n=29): 69.2%
- Prior CAR-T (n=24): 73.9%

- **Novel triplet combination with Q2W tal warrants further investigation**
  - Phase 3 MonumenTAL-3 trial of tal + dara ± pom vs dara + pom + dex in patients with RRMM and ≥1 prior LOT (NCT05455320)

RedirectTT-1

- Schéma et population



Caractéristiques	Toute dose N= 94	RP2R N= 44
Age	64,5 (39-81)	63 (41-80)
HR	21 (41,2)	8 (42,1)
EMD	34 (36,2)	18 (40,9)
Triples réfractaires	81 (86,2)	37 (84,1)
Pentaréfractaires	31 (33)	13 (29,5)
Exposés CAR T antiBCMA	4 (4,3)	2 (4,5)
Exposés Bispé antiBCMA	7 (7,4)	2 (4,5)
Exposés ADC antiBCMA	18 (19,1)	5 (11,4)

RedirectTT-1

- Toxicités

Most common AEs (≥35% overall),[a] n (%)	RP2R (n=44)		All doses (N=94)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
CRS	33 (75.0)	0 (0)	74 (78.7)	2 (2.1)
Taste changes[b]	22 (50.0)	NA	61 (64.9)	NA
Non-rash skin AEs[c]	25 (56.8)	0 (0)	57 (60.6)	0 (0)
Nail-related AEs[d]	21 (47.7)	0 (0)	49 (52.1)	0 (0)
Pyrexia	14 (31.8)	1 (2.3)	48 (51.1)	2 (2.1)
Diarrhea	21 (47.7)	2 (4.5)	45 (47.9)	3 (3.2)
Cough	13 (29.5)	0 (0)	42 (44.7)	1 (1.1)
Dry mouth	18 (40.9)	0 (0)	40 (42.6)	0 (0)
COVID-19	21 (47.7)	6 (13.6)	38 (40.4)	17 (18.1)
Rash AEs[e]	14 (31.8)	1 (2.3)	37 (39.4)	1 (1.1)
Pneumonia	14 (31.8)	7 (15.9)	34 (36.2)	19 (20.2)

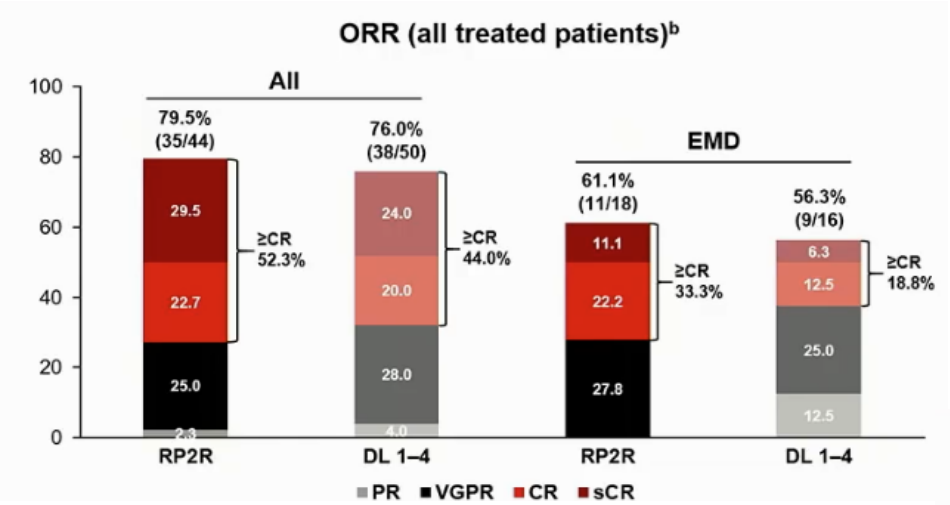
- 3 DLTs: oral herpes (dose level 1), elevated ALT/AST (dose level 3), and thrombocytopenia (RP2R)
- Discontinuations due to AEs:
  - 13.6% (n=6; RP2R), 16.0% (n=15; all doses)
- Grade 5 AEs:
  - 11.4% (n=5; RP2R), 14.9% (n=14; all doses)
  - Most (11/14) due to infections

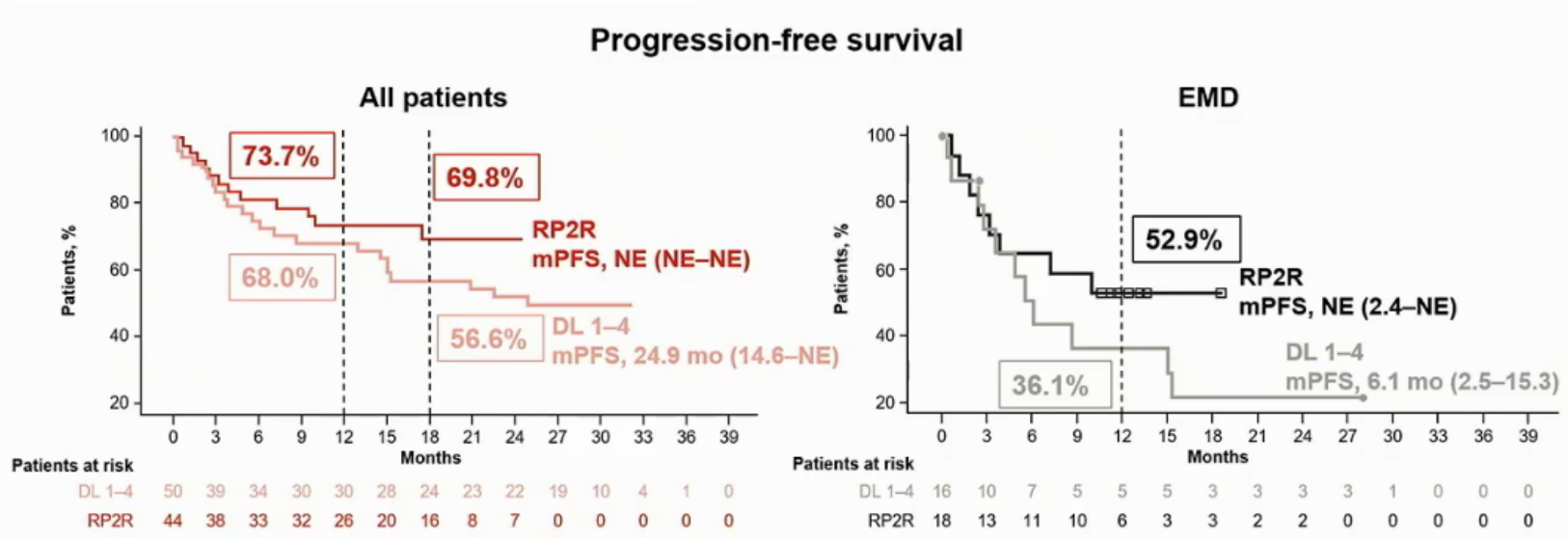
Most common AEs (≥5% overall),[a] n (%)	RP2R (n=44)		All doses (N=94)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Infections	38 (86.4)	21 (47.7)	84 (89.4)	60 (63.8)

- Grade 3/4 infections:
  - 47.7% (RP2R), 63.8% (all doses)
- Grade 5 infections:
  - 6.8% (n=3; RP2R), 11.7% (n=11; all doses)
- Infection prophylaxis given per institutional guidelines
  - 81.9% received antiviral prophylaxis (all doses)
- 56.6% had hypogammaglobulinemia[b]
  - 56.6% received ≥1 dose of IVIG

RedirectTT-1

- Efficacité





Presented by YC Cohen at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

Actualités CAR-T

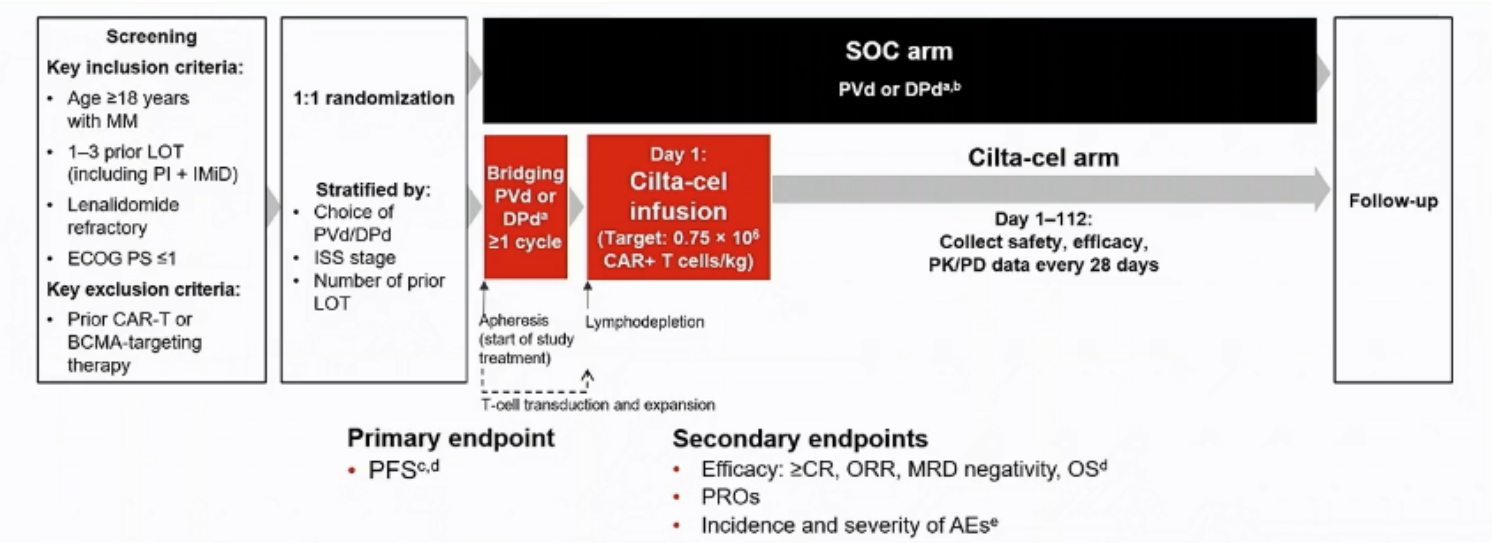
CARTITUDE 4

AnitoCel

BMS-986393

CARTITUDE 4 (suivi 34 mois)

- Schéma et population



Caractéristiques	Cilta-cel N= 208	Ref N= 211
Age	61,5 (27-78)	61 (35-80)
HR	123 (59)	132 (43)
EMD	44 (21)	35 (16)
Triples réfractaires	30 (14,4)	33 (15,6)
Pentaréfractaires		

Prior LOT, median (range)	2 (1–3)	2 (1–3)
1 prior LOT, n (%)	68 (32.7)	68 (32.2)
2 or 3 prior LOT, n (%)	140 (67.3)	143 (67.8)

CARTITUDE 4

- Toxicité

Infections	Cilta-cel (n=208)	SOC (n=208)
Treatment-emergent infections, %		
All grade	63.5	76.4
Grade 3/4	28.4	29.8
Deaths due to TE- and non-TE infections, n	16	19
In first year, n	13	8
In second year, n	2	8

Cause of death	Cilta-cel (n=208)	SOC (n=208)
Deaths, n	**50**	**82**
Due to progressive disease	21	51
Due to TEAE	12	8

- **Both arms had grade 3/4 TEAE around 97%; most frequently cytopenia**

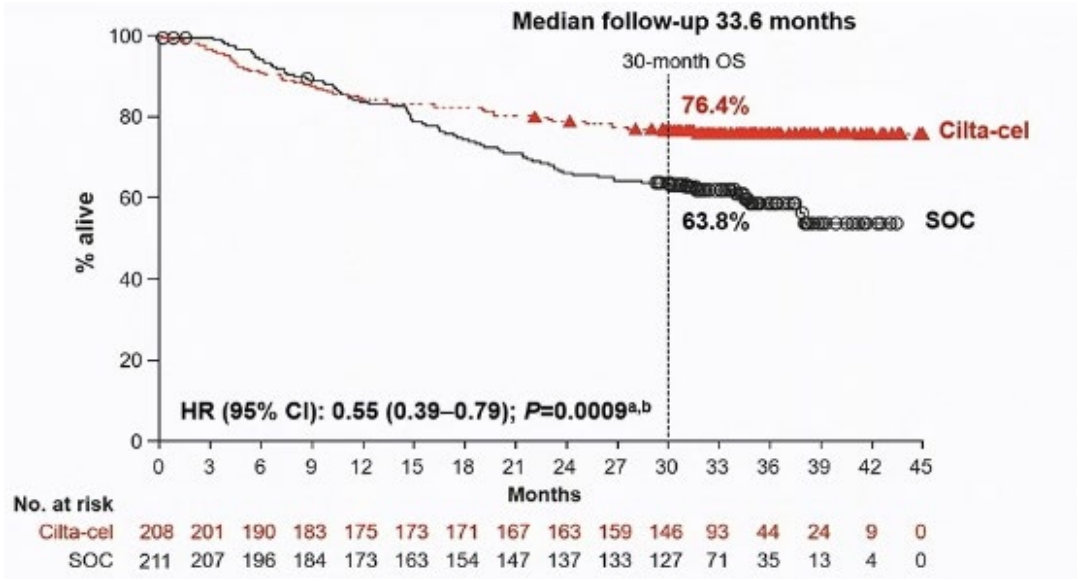
SPM	Cilta-cel (n=208)	SOC (n=208)
SPMs, n (%)	**27 (13.0)**	**24 (11.5)**
Hematologic[a]	7 (3.4)	1 (0.5)
MDS, n	4	0
Progressed to AML, n	2	–
AML, n	1	0
Peripheral T-cell lymphoma, n	2	0
EBV-associated lymphoma, n	0	1
Cutaneous/non-invasive[a]	15 (7.2)	15 (7.2)
Non-cutaneous/invasive[a]	6 (2.9)	8 (3.8)

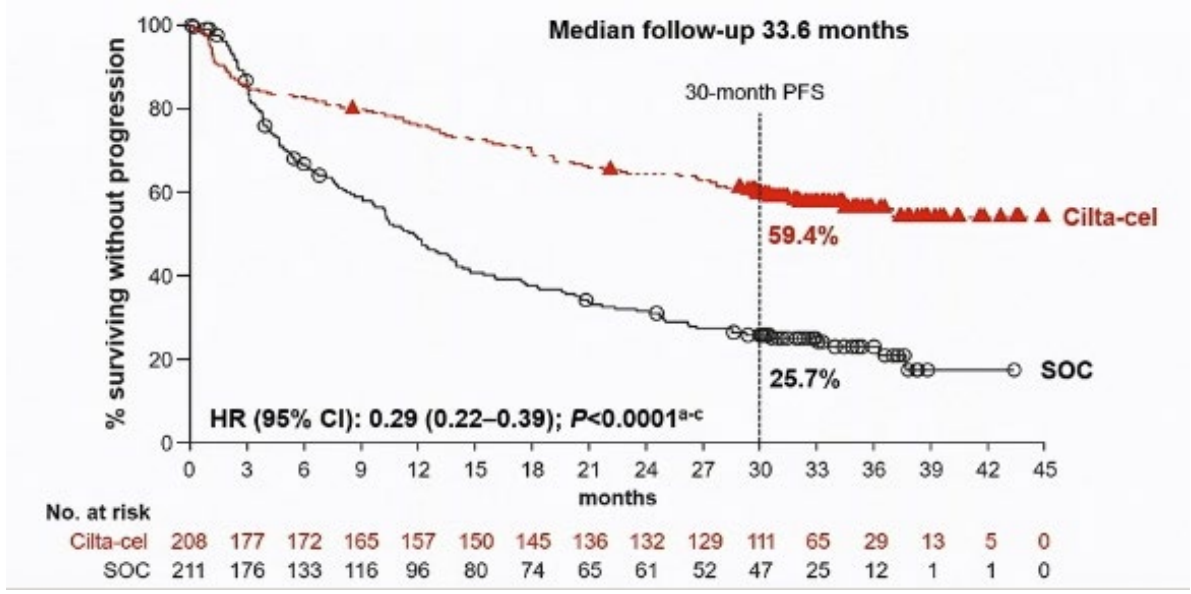
- **No new cases of cranial nerve palsy or MNT in the cilta-cel arm since the previous report[1]**

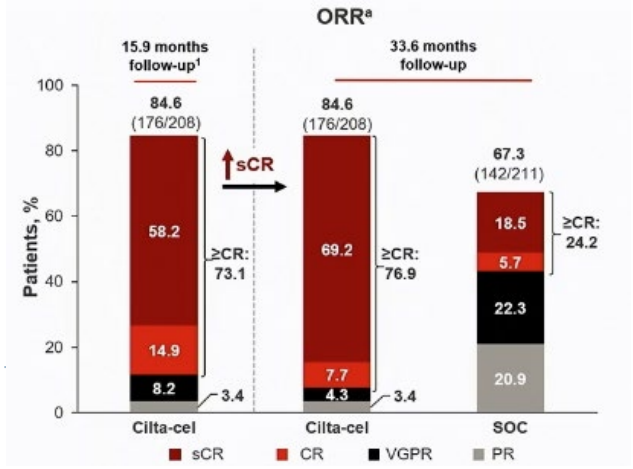
Presented by M-V Mateos at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

CARTITUDE 4

- Efficacité







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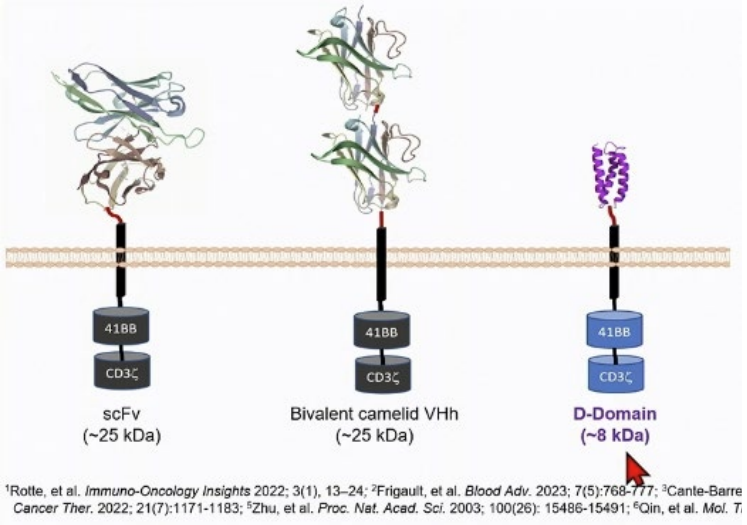
Anito-cel (CART-ddBCMA)



[1]Rotte, et al. *Immuno-Oncology Insights* 2022; 3(1), 13–24; [2]Frigault, et al. *Blood Adv.* 2023; 7(5):768-777; [3]Cante-Barre *Cancer Ther.* 2022; 21(7):1171-1183; [5]Zhu, et al. *Proc. Nat. Acad. Sci.* 2003; 100(26): 15486-15491; [6]Qin, et al. *Mol. T*

Taille

Petite taille : grande quantité de CAR à la surface cellulaire

Stabilité

Repliement rapide, absence de ponts disulfures, centre hydrophobe

Structure

Structure compacte = faible risque de « tonic signaling » : plus efficace

Phase 1 first-in-human trial is in patients with relapsed and/or refractory myeloma

- Prior IMiD, PI, and CD38-targeted therapy
- Received ≥3 prior lines of therapies or triple refractory

2 Dose Levels evaluated, 6 patients in each dose escalation cohort

- DL1 = 100 ± 20% x 10^6 CAR+ cells
- DL2 = 300 ± 20% x 10^6 CAR+ cells

CAR-T-associated AEs Per ASTCT criteria	100 million (n=32)		300 million (n=6)	
Cytokine Release Syndrome (CRS)	**Grade 1/2**	**Grade 3**	**Grade 1/2**	**Grade 3**
	30 (94%)	**0**	**5 (83%)**	**1 (17%)**
Median onset (min-max)*	2 days (1-12 days)		2 days (1-2 days)	
Median duration (min-max)	6 days (1-10 days)		5 days (3-9 days)	
Neurotoxicity (ICANs)	**Grade 1/2**	**Grade 3**	**Grade 1/2**	**Grade 3**
	5 (16%)	**1 (3%)**	**0**	**1 (17%)**
Median onset (min-max)*	4.5 days (3-6 days)		7 days	
Median duration (min-max)	3.5 days (1 - 9 days)		17 days	

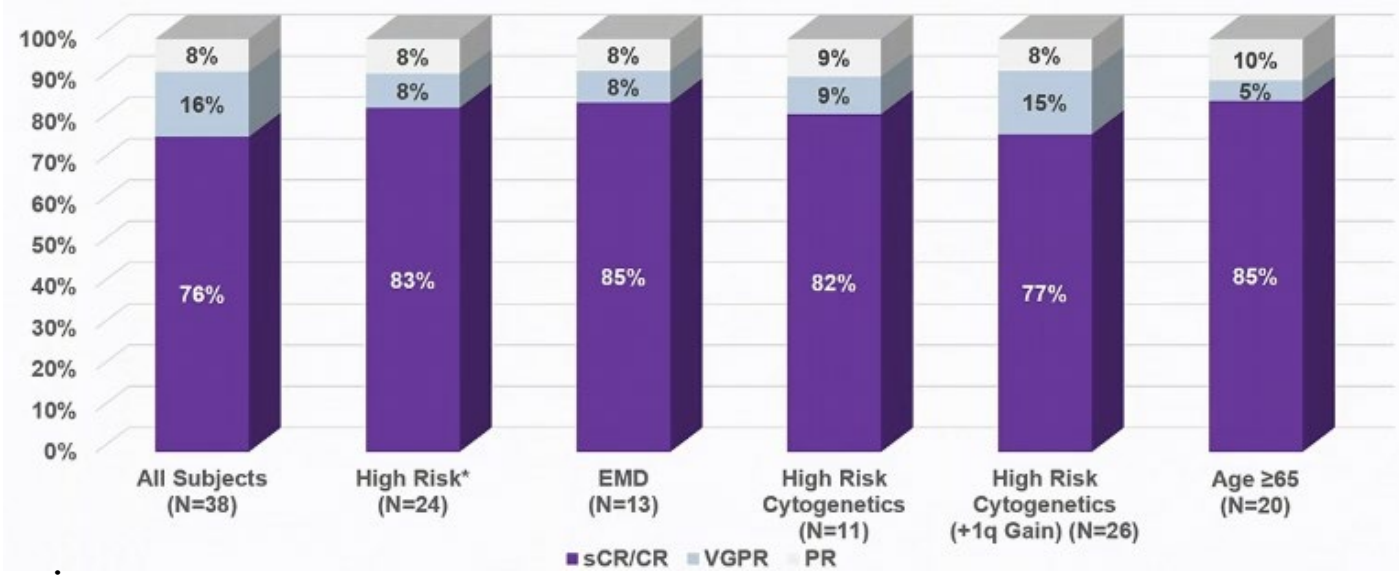
- No delayed neurotoxicities, no Guillain-Barré syndrome, no cranial nerve palsies, and no Parkinsonian-like syndromes in the entire population through the follow-up period
- One Grade 5 AE post study treatment (unrelated cardiac arrest due to non-study drug overdose)
- No change in safety profile as previously presented

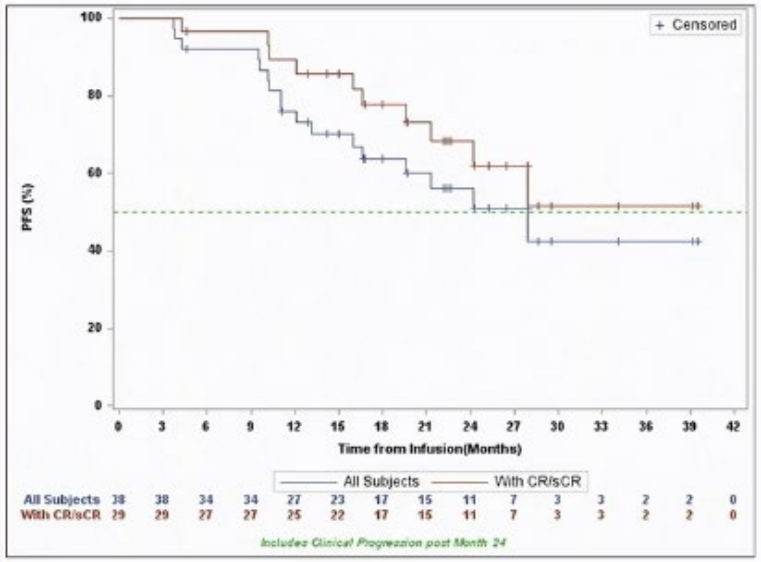
Frigault et al. IMS 24 Abstr OA-30

Anito-cel (CART-ddBCMA)

- Efficacité

Médiane de suivi : 26,5 mois





75% de PFS à 12 mois

- **Median PFS not reached for all patients (n=38)**
- **Median PFS not reached for CR/sCR patients (n=29, 76%)**
- **89% (n=25/28) of evaluable* patients MRD negative at minimum of 10^{-5} sensitivity**

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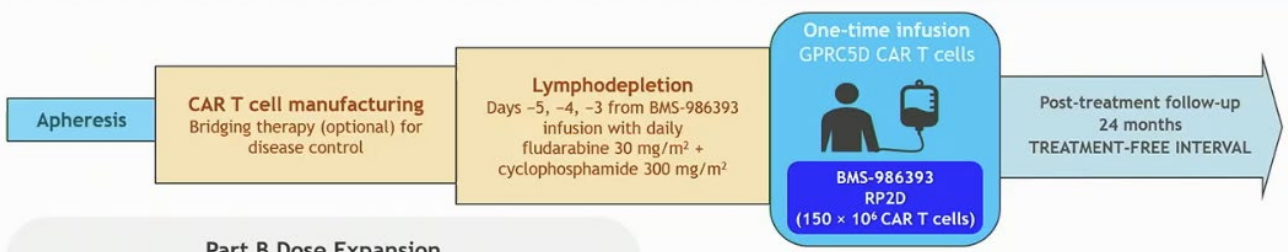
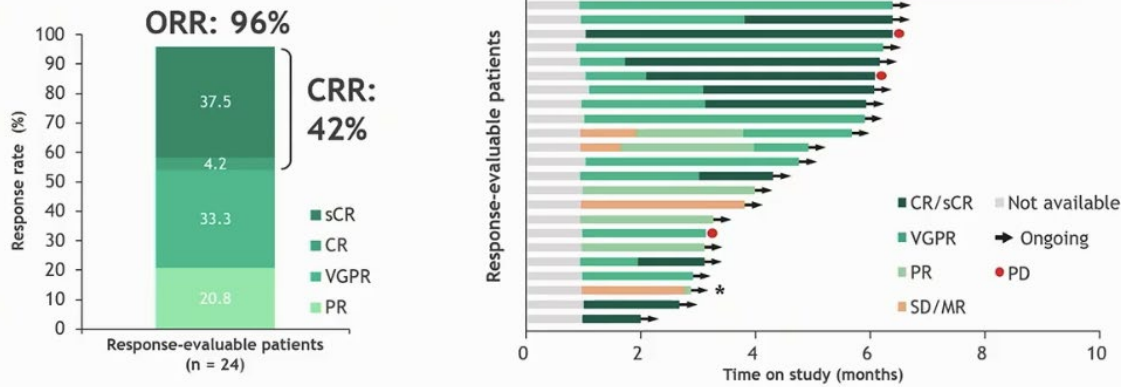
CAR T anti GPRC5D – BMS-986393



Part B Dose Expansion
Cohort C: key eligibility criteria

- RRMM that progressed ≤ 12 months of the most recent regimen per IMWG criteria[a]
- 1-3 prior antimyeloma regimens including a PI and an IMiD, and ASCT[b]
- Prior BCMA-directed therapies allowed, including CAR T cell therapies
- ECOG PS 0-1

- **Primary objective:** safety at the RP2D
- **Secondary objectives:** anti-tumor activity, PK



- 24 patients were evaluable for efficacy; median follow-up was 5.3 months (range 2.0-9.3)
- ORR was 96%; CRR was 42%
- 87% (20/23) of responses were ongoing; 3 patients had experienced disease progression
- Median time to response was 1.0 months (range 0.9-2.9), and median duration of response was not reached

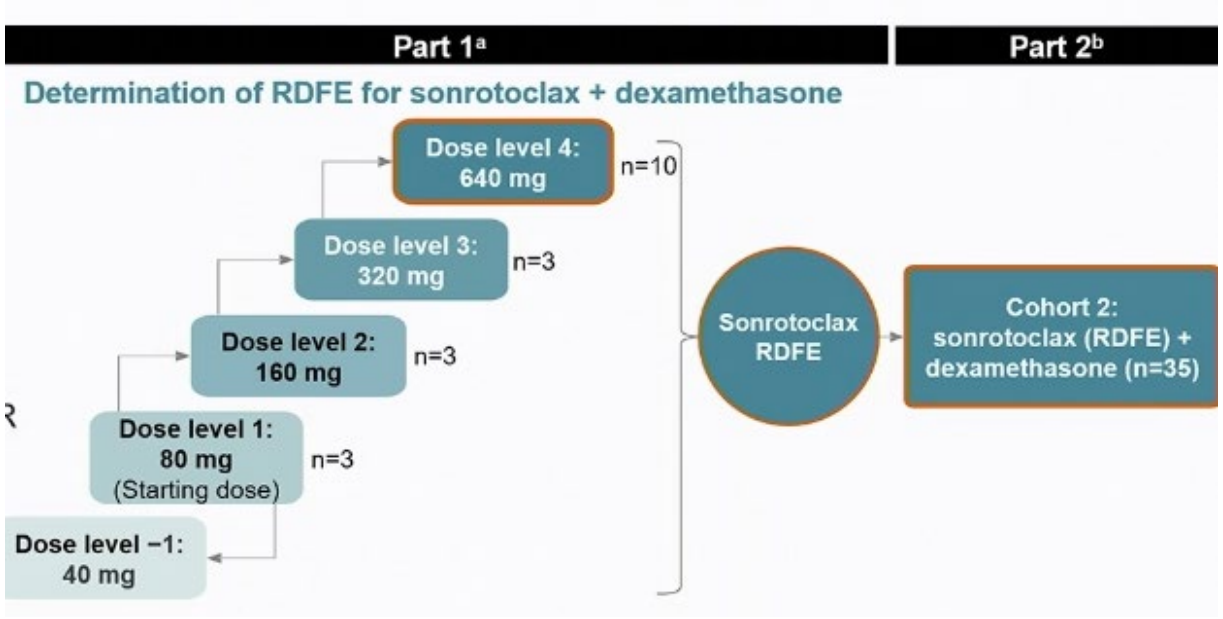
TEAEs, n (%)	All treated patients (N = 31)	
	Any grade	Grade 3/4
Patients with ≥ 1 TEAE	**30 (97)**	**25 (81)**
Hematologic TEAEs[a]		
Neutropenia	22 (71)	21 (68)
Anemia	12 (39)	7 (23)
Thrombocytopenia	16 (52)	7 (23)
Non-hematologic TEAEs[a]		
CRS	25 (81)	0 (0)
Hyperglycemia	11 (35)	1 (3)
Hypocalcemia	11 (35)	0 (0)
Constipation	10 (32)	0 (0)
Infections and infestations	10 (32)	0 (0)
Dysgeusia	9 (29)	0 (0)
Fatigue	8 (26)	0 (0)
Nail disorder	8 (26)	0 (0)
Dry mouth	7 (23)	0 (0)
Nausea	7 (23)	0 (0)

Htut et al. IMS 24

Actualités hors immunothérapie

SONROTOCLAX

- Schéma et population
- Phase1b/2. MM réfractaire ou en rechute t(11,14) +. N=32



Caractéristiques	N= 32
Age	69 (48-80)
HR	9 (28,1)
EMD	
Triples réfractaires	15 (46%)
Pentaréfractaires	
Exposés CAR T antiBCMA	
Exposés Bispé antiBCMA	
Exposés ADC antiBCMA	

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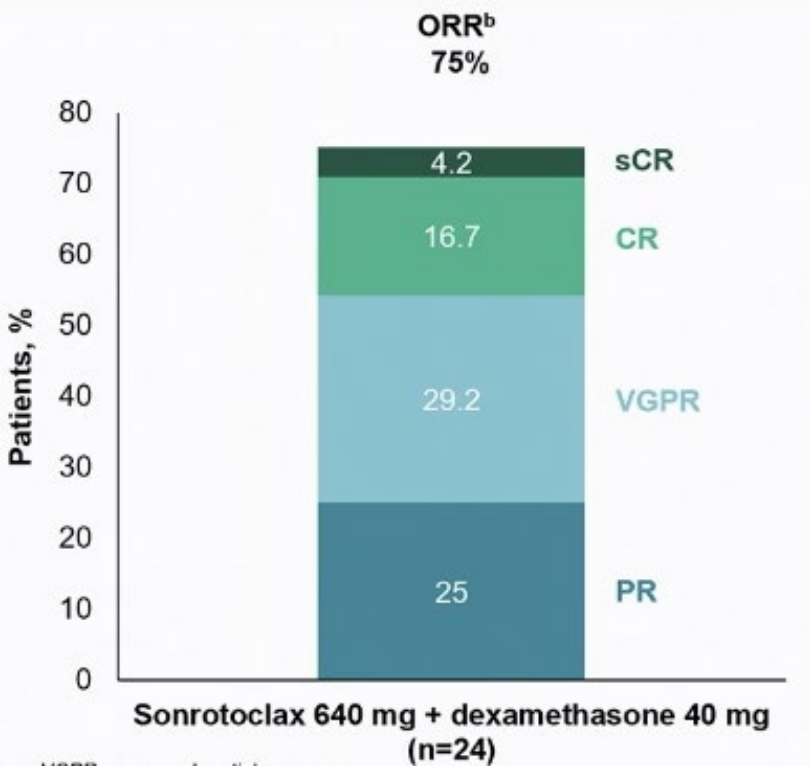
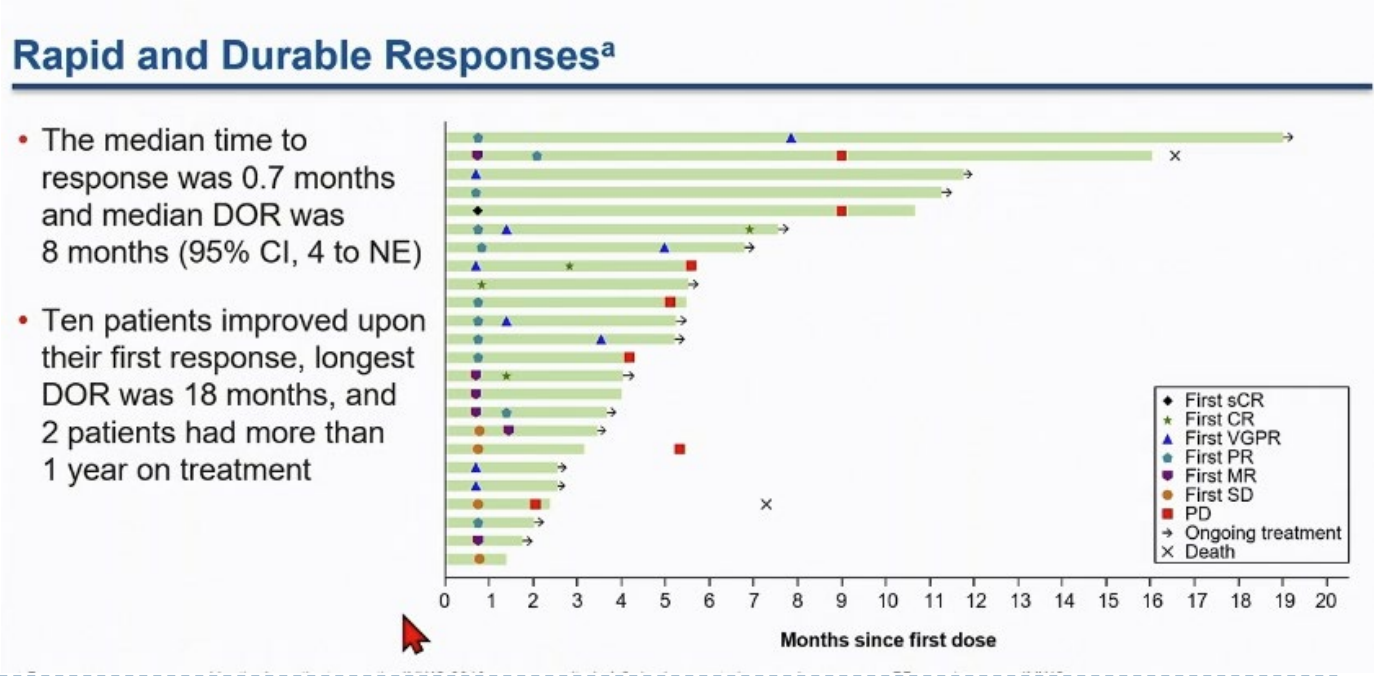
SONROTOCLAX

- Toxicité et Efficacité
- Evaluable chez 24 patients

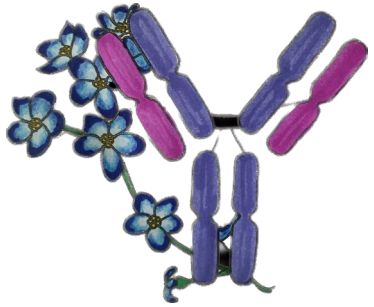


Caractéristiques	N= 32
Tox hématologique	4 (12)
Infections	7 (21,9)
Fatigue	8 (28)
Diarrhées	7 (21,9)
Constipation	5 (15,6))
Nausées	5 (15,6)



Costa et al. IMS 24

Merci!



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