Comprehensive Cancer Center
Tübingen-Stuttgart

Post ASH 2023 San Diego

Multiples Myelom

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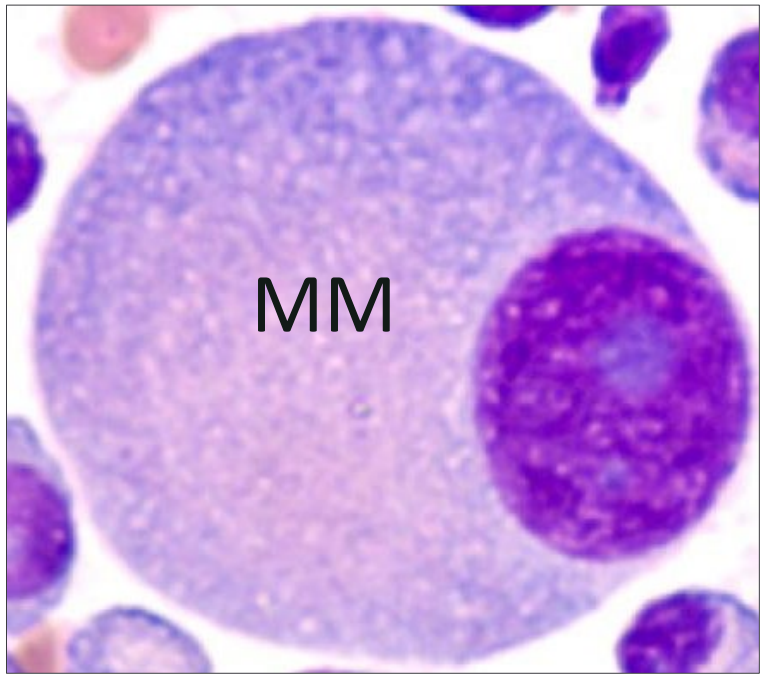
Agenda

1. Smoldering Multiples Myelom – Centaurus, (ImmunoPrism)
2. **Firstline Multiples Myelom: Perseus**
3. Erhaltungstherapie: EMN26 (Iberdomid-Maintenance)
4. RRMM: Cartitude-2, MonumenTAL-1

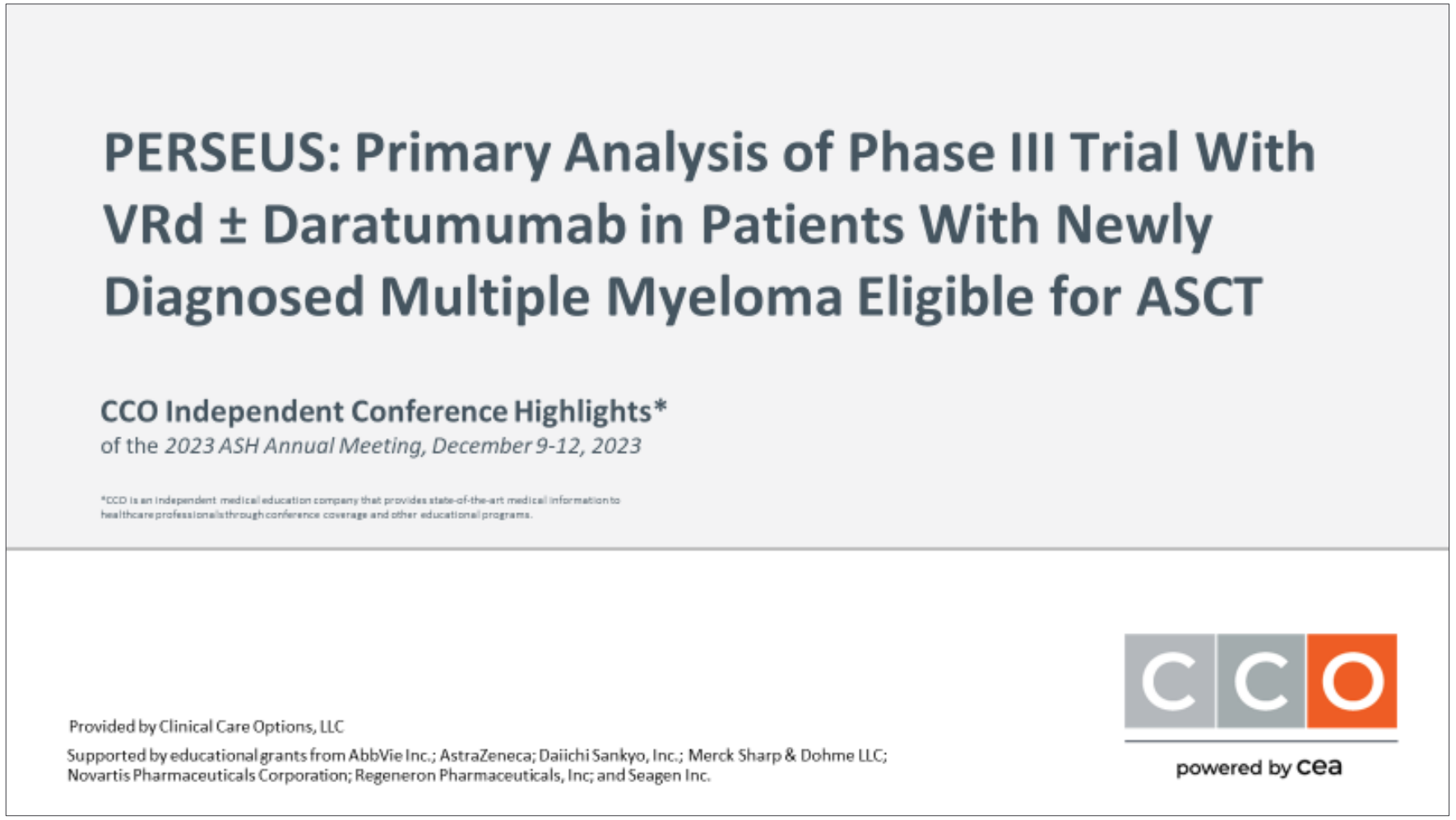
Multiples Myelom (MM) – Firstline (TE)



TE:
DaraVTD/HD-Mel +
ASCT/Lenalidomid-
Erhaltung

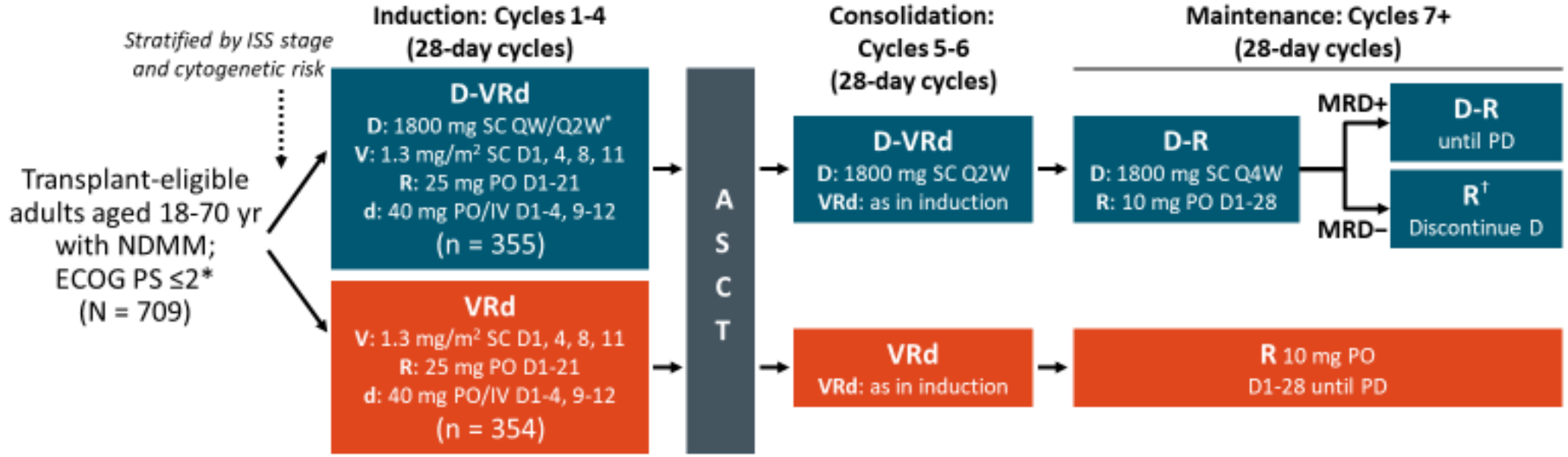
Lenalidomid vs Thalidomid
- weniger Nebenwirkungen/Neurotox
- Höhere Potenz

Multiples Myelom (MM) - Perseus



Multiples Myelom (MM) – Perseus – Study Design

- Multicenter, open-label, randomized phase III trial; current analysis median f/u: 47.5 mo



*QW during cycles 1-2, Q2W during cycles 3-4. †D discontinued after ≥24 mo in patients with ≥CR and 12 mo sustained MRD negativity; D restarted upon confirmed loss of CR without PD or MRD recurrence.

- **Primary endpoint:** PFS
- **Key secondary endpoints:** ≥CR rate, MRD negativity rate, OS

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Multiples Myelom (MM) – Perseus - Patient Characteristics

Baseline Characteristic	D-VRd (n = 355)	VRd (n = 354)
Median age, yr (range)	61.0 (32-70)	59.0 (31-70)
Male, n (%)	211 (59.4)	205 (57.9)
White, n (%)	330 (93.0)	323 (91.2)
ECOG PS, n (%)		
▪ 0	221 (62.3)	230 (65.0)
▪ 1	114 (32.1)	108 (30.5)
▪ 2	19 (5.4)	16 (4.5)
▪ 3	1 (0.3)	0
MM diagnosis, n (%)	(n = 354)	(n = 352)
▪ CRAB criteria only	125 (35.3)	113 (32.1)
▪ Malignancy biomarkers only	52 (14.7)	65 (18.5)
▪ CRAB criteria with malignancy biomarkers	177 (50.0)	174 (49.4)

Baseline Characteristic	D-VRd (n = 355)	VRd (n = 354)
ISS stage, n (%)	(n = 355)	(n = 353)
▪ I	186 (52.4)	178 (50.4)
▪ II	114 (32.1)	125 (35.4)
▪ III	55 (15.5)	50 (14.2)
≥1 extramedullary plasmacytoma, n (%)	15 (4.2)	16 (4.5)
Cytogenetic profile, n (%)		
▪ Standard risk	264 (74.4)	266 (75.1)
▪ Intermediate risk	15 (4.2)	10 (2.8)
▪ High risk	76 (21.4)	78 (22.0)
Median time since diagnosis of MM, mo (range)	1.2 (0-46.5)	1.1 (0.1-184.6)

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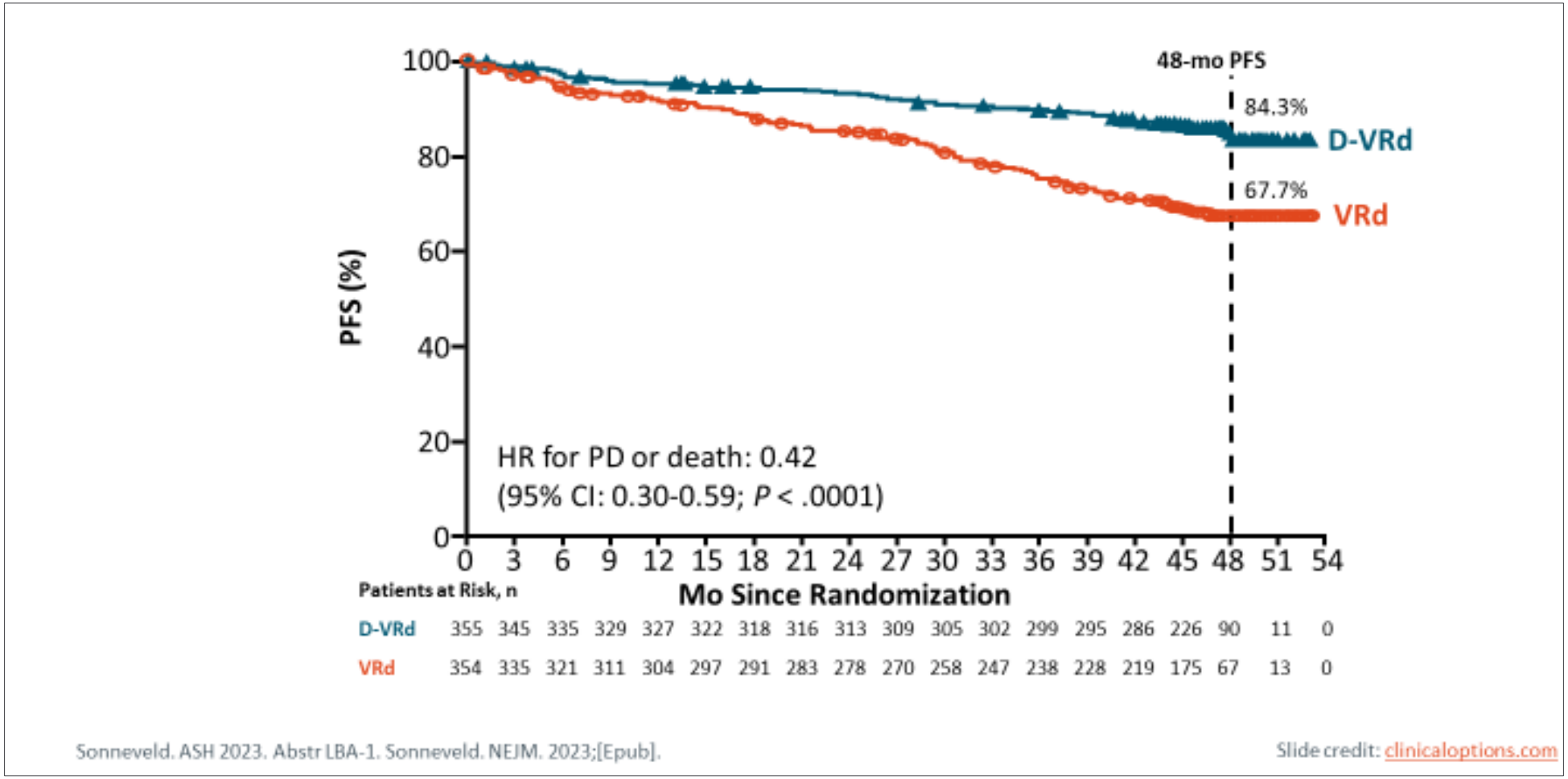
Multiples Myelom (MM) – Perseus - PFS



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Multiples Myelom (MM) – Perseus – CR/MRD

Efficacy Outcome	D-VRd (n = 355)	VRd (n = 354)	OR (95% CI)	*P* Value
≥CR, %	87.9	70.1	3.13 (2.11-4.65)	<.001
▪ sCR	69.3	44.6		
▪ CR	18.6	25.4		
MRD negativity, %				
▪ 10^{-5}	75.2	47.5	3.40 (2.47-4.69)	<.0001
▪ 10^{-6}	65.1	32.2	3.97 (2.90-5.43)	<.0001
Sustained MRD negativity (10^{-5}) ≥12 mo, %	64.8	29.7	4.42 (3.22-6.08)	<.0001

Efficacy Outcome	D-VRd (n = 355)	VRD (n = 354)	Difference Between Arms
MRD negativity (10^{-5}) over time, %			
▪ Post consolidation	57.5	32.5	25.0
▪ Overall	75.2	47.5	27.7
MRD negativity (10^{-6}) over time, %			
▪ Post consolidation	34.4	16.1	18.3
▪ Overall	65.1	32.2	32.9

- Improvements in ≥CR rates with D-VRd vs VRd observed across all subgroups
- 64% of patients in D-VRd arm + D-R maintenance discontinued D after reaching sustained MRD negativity per protocol
- OS data immature
  - Current mortality rate with D-VRd vs VRd: 9.6% vs 12.4% (HR: 0.73)

Sonneveld. ASH 2023. Abstr LBA-1. Sonneveld. NEJM. 2023;[Epub].

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Multiples Myelom (MM) – Perseus - Safety

	TEAEs,* n (%)	D-VRd (n = 351)		VRd (n = 347)	
		Any Gr	Gr 3/4	Any Gr	Gr 3/4
	Any	349 (99.4)	321 (91.5)	344 (99.1)	297 (85.6)
Hematologic	Neutropenia	243 (69.2)	218 (62.1)	204 (58.8)	177 (51.0)
Hematologic	Thrombocytopenia	170 (48.4)	102 (29.1)	119 (34.3)	60 (17.3)
Hematologic	Anemia	78 (22.2)	21 (6.0)	72 (20.7)	22 (6.3)
Hematologic	Febrile neutropenia	34 (9.7)	33 (9.4)	38 (11.0)	35 (10.1)
	Diarrhea	214 (61.0)	37 (10.5)	188 (54.2)	27 (7.8)
	Peripheral sensory neuropathy	188 (53.6)	15 (4.3)	179 (51.6)	14 (4.0)
	Constipation	119 (33.9)	8 (2.3)	118 (34.0)	6 (1.7)
	Pyrexia	111 (31.6)	8 (2.3)	109 (31.4)	9 (2.6)
	Insomnia	95 (27.1)	8 (2.3)	61 (17.6)	6 (1.7)

TEAEs,* n (%)	D-VRd (n = 351)		VRd (n = 347)	
	Any Gr	Gr 3/4	Any Gr	Gr 3/4
Asthenia	94 (26.8)	12 (3.4)	89 (25.6)	9 (2.6)
Cough	85 (24.2)	1 (0.3)	51 (14.7)	0
Fatigue	84 (23.9)	10 (2.8)	92 (26.5)	18 (5.2)
Rash	82 (23.4)	9 (2.6)	94 (27.1)	17 (4.9)
Back pain	80 (22.8)	2 (0.6)	66 (19.0)	1 (0.3)
Peripheral edema	72 (20.5)	4 (1.1)	74 (21.3)	1 (0.3)
Nausea	71 (20.2)	2 (0.6)	66 (19.0)	1 (0.3)
Infections	305 (86.9)	124 (35.3)	266 (76.7)	95 (27.4)
▪ COVID-19	123 (35.0)	12 (3.4)	83 (23.9)	4 (1.2)
▪ URTI	111 (31.6)	2 (0.6)	87 (25.1)	6 (1.7)
▪ Pneumonia	64 (18.2)	37 (10.5)	38 (11.0)	21 (6.1)

*Any grade occurring in ≥25% or grade 3/4 occurring in ≥10%

- Any grade and grade 3/4 IRRs occurred in 6% (n = 21) and 0.9% (n = 3) of patients in the D-VRd arm, respectively
- Secondary malignancies occurred in 10.7% (37) of patients in the D-VRd arm and 7.2% (n = 25) in the VRd arm

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Multiples Myelom (MM) – Perseus - Conclusion

- Primary results from the pivotal phase III PERSEUS trial showed that D-VRd induction → ASCT → D-VRd consolidation → D-R maintenance significantly improved PFS vs VRd induction → ASCT → VRd consolidation → R maintenance in transplant-eligible patients with NDMM
  - 48-mo PFS rate: 84.3% vs 67.7% (HR: 0.42; *P* <.0001)
- D-VRd regimen also significantly deepened response vs VRd regimen
  - ≥CR rate: 87.9% vs 70.1% (*P* <.001)
  - MRD negativity (10^{-5}) rate: 75.2% vs 47.5% (*P* < .001)
  - 64% on D-R maintenance for ≥ 2 yr stopped D after achieving sustained MRD negativity
- Safety profile of D-VRd regimen consistent with safety associated with SC D and VRd
- Investigators conclude that D-VRd induction/consolidation followed by D-R maintenance represents a new standard of care for transplant-eligible patients with NDMM

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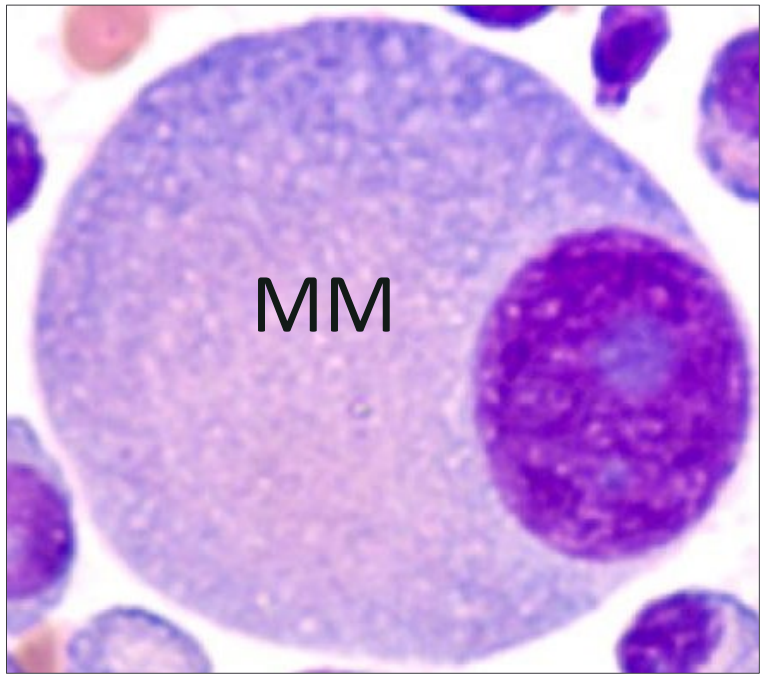
4. RRMM: Cartitude-2, MonumenTAL-1

Multiples Myelom (MM) – Maintenance



Lenalidomid Erhaltung –
bis zum Progress/ MRD
gesteuert(?)

Maintenance – EMN26-Study (Iberdomid)

Iberdomide Maintenance after Autologous Stem Cell Transplantation in Newly Diagnosed MM: First Results of the Phase 2 EMN26 Study

Niels W.C.J. Van De Donk[1], Cyrille Touzeau[2], EvangelosTerpos[3], Aurore Perrot[4], Roberto Mina[5,6], Maaike de Ruijter[1], Elisabetta Antonioli[7], Eirini Katodritou[8],Norbert Pescosta[9], Paulus A.F. Geerts[10], Cécile Sonntag[11], Ruth Wester[12], Angelo Belotti[13], Silvia Mangiacavalli[14],Massimo Offidani[15], Mattia D'Agostino[5,6], Mark van Duin[12], Michele Cavo[16], Sara Aquino[17], Alessandra Lombardo[18], Mark-David Levin[19], Cyrille Hulin[20], Mario Boccadoro[21], Pieter Sonneveld[12] and Francesca Gay[5]

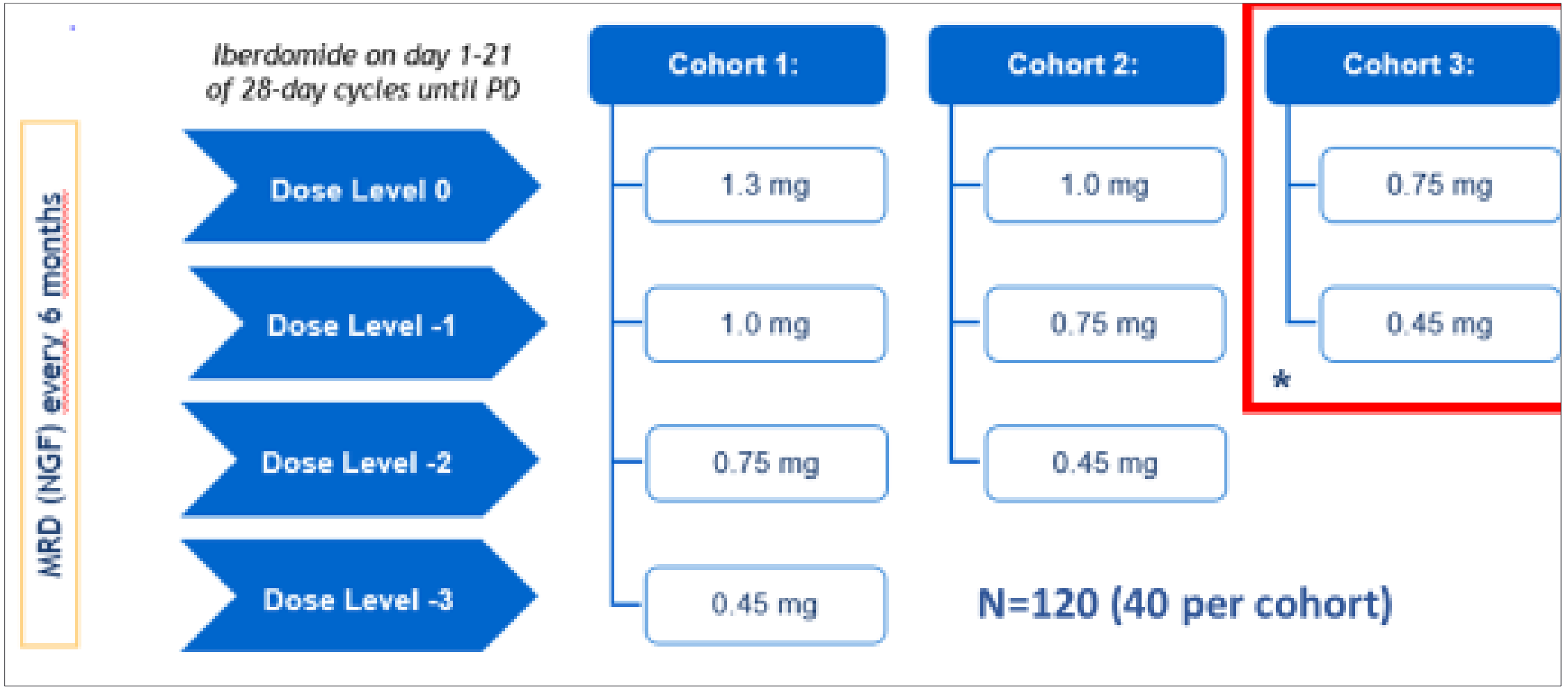
[1]Amsterdam UMC, Vrije Universiteit Amsterdam, Department of Hematology,Cancer Center Amsterdam, Amsterdam, Netherlands; [2]Department of Hematology, University Hospital Hôtel-Dieu, Nantes, France; [3]Department of Clinical Therapeutics, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece; [4]Service d'Hématologie, CHU de Toulouse, Institut Universitaire du Cancer de Toulouse Oncopole, Université de Toulouse, Toulouse, France; [5]Division of Hematology, Department of Molecular Biotechnology and Health Sciences, University of Torino, Torino, Italy; [6]Division of Hematology, Azienda Ospedaliero-Universitaria Città della Salute e della Scienza di Torino, University of Torino, Torino, Italy; [7]HematologyUnit, AOU Careggi, Florence, Italy; [8]Department of Hematology, Theagenion Cancer Hospital, Thessaloniki, Greece; [9]Reparto Ematologia e TMNO, Ospedale Provinciale Bolzano, Bolzano, Italy; [10]Isala Klinieken, Zwolle, Netherlands; [11]University Hospital, Hôpital Hautepierre, Strasbourg, France; [12]Department of Hematology, Erasmus MC Cancer Institute, Rotterdam, Netherlands; [13]Department of Hematology, ASST Spedali Civili di Brescia, Brescia, Italy; [14]Division of Hematology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy; [15]AOU delle Marche, Ancona, Italy; [16]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Seràgnoli Institute of Hematology, and the Department of Medical and Surgical Sciences, Bologna University School of Medicine, Bologna, Italy; [17]Ematologia e Terapie cellulari, IRCCS Ospedale Policlinico San Martino, Genova, Italy; [18]A.O. Santa Maria di Terni - Università degli Studi di Perugia, Terni-Perugia, Italy; [19]Albert Schweitzer hospital,

Maintenance – EMN26-Study (Iberdomid)

- Maintenance with lenalidomide (LEN) is the standard of care after high-dose chemotherapy and autologous stem cell transplantation (ASCT)[1] with improvement of response at 6 months of 26%, and at 12 months of 31%[1,2]
- All patients remain at risk of relapse post ASCT, and between 24-29% of patients discontinue lenalidomide maintenance due to adverse events or poor tolerability; therefore, there is an unmet need for new drugs with improved activity and tolerability in the maintenance setting[1,2,3]

- Iberdomide (IBER) is a novel, potent, oral cereblon (CRBN) E3 ligase modulator (CELMoD™) with greater tumoricidal and immune-modulatory effects compared with IMiDs[1-3]
- Unlike lenalidomide, Iberdomide is administered as a single enantiomer (S isomer), maintained in vivo. This can help to avoid side effects such as sedation and fatigue attributed to the R isomer.
- IBER safety, efficacy, and pharmacodynamic data from the ongoing CC-220-MM-001 trial justify further investigation of this agent in the maintenance setting[4]
- **We present the initial results from the** ongoing EMN26 phase 2 study with IBER maintenance after ASCT in patients with NDMM (NCT04564703)

Maintenance – EMN26-Study- Design



Maintenance – EMN26-Study- Characteristics

Characteristic	IBER 1.3 mg PO (n=40)	IBER 1.0 mg PO (n=40)	IBER 0.75 mg PO (n=40)
Induction type*			
VTD	12 (30)	19 (48)	2 (5)
VRD	13 (33)	7 (18)	3 (8)
D-VTD	12 (30)	13 (33)	33 (83)
D-VRD	3 (8)	1 (3)	2 (5)
Auto-SCT			
Single	34 (85)	30 (75)	36 (90)
Double	6 (15)	10 (25)	4 (10)
Consolidation			
No	35 (88)	36 (90)	22 (55)
Yes	5 (13)	4 (10)	18 (45)
Response at study entry			
sCR	7 (17)	6 (15)	8 (20)
CR	4 (10)	4 (10)	5 (12)
VGPR	26 (65)	25 (62)	22 (55)
PR	3 (7)	5 (12)	5 (12)

Characteristic	IBER 1.3 mg PO (n=40)	IBER 1.0 mg PO (n=40)	IBER 0.75 mg PO (n=40)
MRD status at study entry			
Negative	20 (50)	19 (48)	26 (65)
Positive	15 (38)	19 (48)	10 (25)
Not evaluable	5 (13)	2 (5)	4 (10)
Time from diagnosis to first maintenance dose (months)	10 (9-11)	10 (9-12)	12 (11-14)
Time from last ASCT to first maintenance dose (months)	4 (3-4)	3 (3-4)	4 (3-6)

Data cut-off November 8, 2023. [a]Cytogenetic risk is based on FISH and is defined as ≥1 of the following: del(17p), t(4;14), or t(14;16). *Some patients exchanged one drug for another drug after initiation of induction treatment (most frequently exchange of thalidomide for cyclophosphamide in case of neuropathy)
FISH, fluorescence in situ hybridization; ISS, International Staging System; PO, oral.

Maintenance – EMN26-Study- Safety

AE, n (%)	1.3 mg cohort (n=40)		1.0 mg cohort (n=40)	
	Grade 1/2	Grade 3/4	Grade 1/2	Grade 3/4
Neutropenia	4 (10)	20 (50)	4 (10)	17 (42)
Febrile neutropenia	0	0	0	1 (2)
Thrombocytopenia	6 (15)	0	4 (10)	0
Anemia	2 (5)	0	6 (15)	0
Lymphopenia	3 (8)	1 (2)	2 (5)	1 (2)

Maintenance – EMN26-Study- Safety

AE, n (%)	1.3 mg cohort (n=40)		1.0 mg cohort (n=40)	
	Grade 1/2	Grade 3/4	Grade 1/2	Grade 3/4
Fatigue	7 (18)	6 (15)	7 (18)	4 (10)
Diarrhea	2 (5)	0	8 (20)	0
Constipation	2 (5)	0	2 (5)	0
Peripheral neuropathy	6 (15)	1 (3)	5 (13)	0
Hyper/hypothyroidism	4 (10)	0	9 (23)	0
Rash*	8 (20)	4 (10)	7 (18)	1 (3)
Venous thromboembolism	0	0	0	0
Infections	22 (55)	4 (10)	21 (52)	5 (13)
COVID-19	7 (18)	0	12 (30)	0
Pneumonia	3 (8)	2 (5)*	1 (3)	2 (5)**

*1 of 2 cases is PJP infection

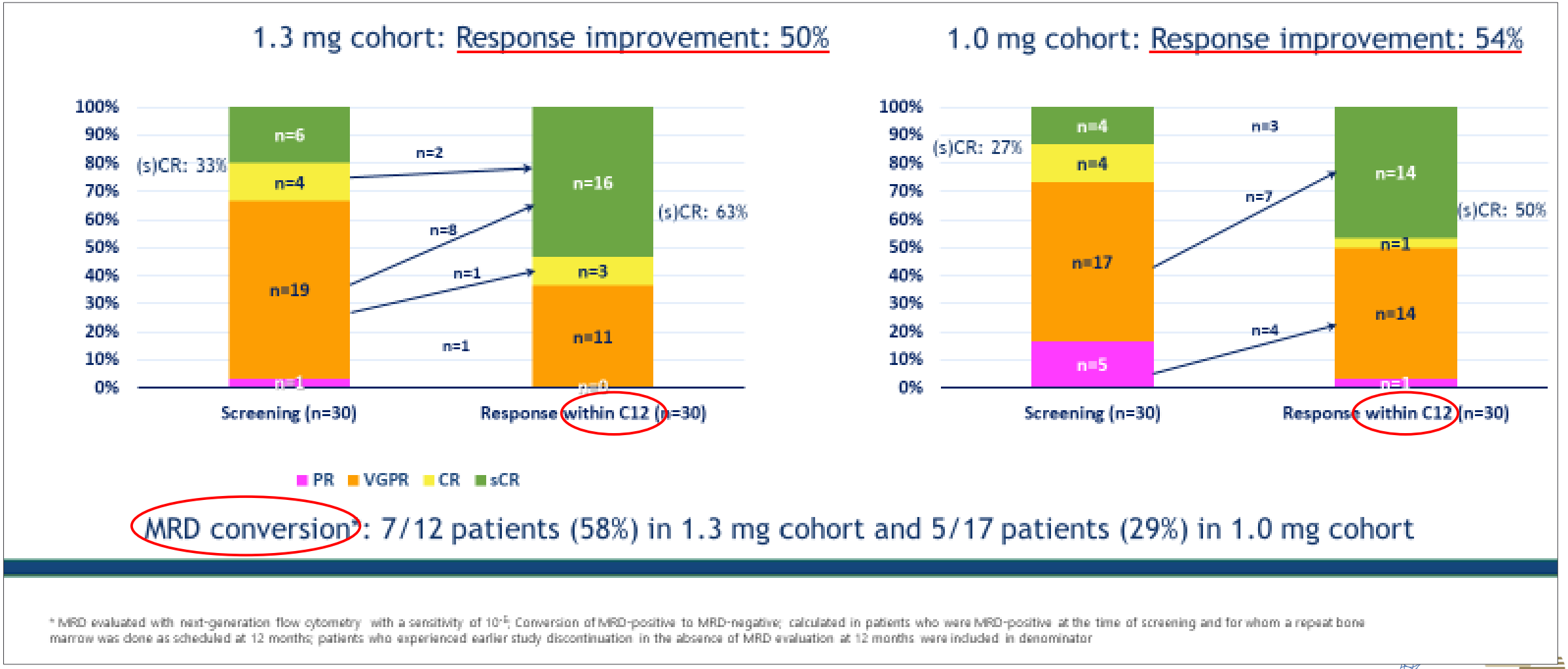
** 1 of 2 cases is PJP infection

The majority of non-hematologic AEs were low grade

No second primary malignancies reported

Rash was transient and occurred mainly during first cycle

Maintenance – EMN26-Study- Response improvement



MRD conversion*: 7/12 patients (58%) in 1.3 mg cohort and 5/17 patients (29%) in 1.0 mg cohort

* MRD evaluated with next-generation flow cytometry with a sensitivity of 10^{-5}; Conversion of MRD-positive to MRD-negative; calculated in patients who were MRD-positive at the time of screening and for whom a repeat bone marrow was done as scheduled at 12 months; patients who experienced earlier study discontinuation in the absence of MRD evaluation at 12 months were included in denominator

Maintenance – EMN26-Study - Conclusion

- Iberdomide maintenance results in an improvement in response over time in patients who received IMiD/PI-based induction +/- anti-CD38 antibody and autologous stem cell transplantation, which compares favorably with lenalidomide maintenance
  - Iberdomide demonstrated at least 50% improvement of response at cycle 12
  - Lenalidomide demonstrated 31% improvement of response at cycle 12 in the EMN02 trial
- Conversion to MRD-negativity during maintenance is an important outcome post-ASCT, and promising data with iberdomide were observed
- Iberdomide showed a manageable safety profile with few grade 3-4 non-hematologic adverse events
- These data support the investigation of iberdomide versus lenalidomide maintenance in the ongoing phase 3 registrational Excaliber maintenance trial

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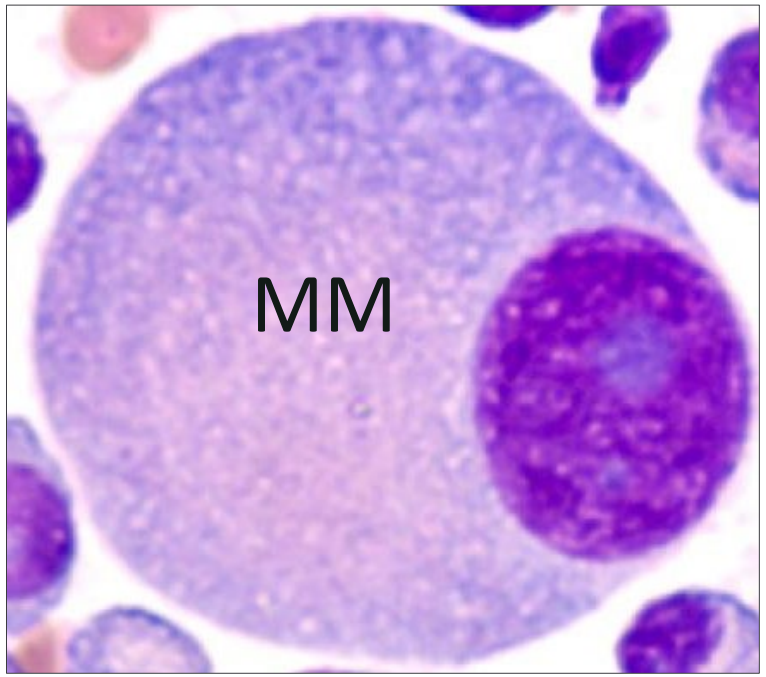
Multiples Myelom (MM) – RRMM („Immuntherapie“)



Bcma-BiTe (ab 4. Linie)
- Teclistamab
- Elranatamab

GPRC5D-BiTe (ab 4. Linie)
- Talquetamab

Bcma-CarT (ab 4. Linie)
- Idecabtagen vicleucel
- *Ciltacabtagen autoleucel*

Cartitude-1 (≥3PL):
med PFS ~3 Jahre
Cartitude-4 (1-3PL):
Med PFS > 3 Jahre(?)

Multiples Myelom (MM) – Cartitude-2

The Phase 2 CARTITUDE-2 Trial: Updated Efficacy and Safety of Ciltacabtagene Autoleucel in Patients With Multiple Myeloma and 1–3 Prior Lines of Therapy (Cohort A) and With Early Relapse After First Line Treatment (Cohort B)

Jens Hillengass[1], Adam D Cohen[2], Mounzer Agha[3], Michel Delforge[4], Tessa Kerre[5], Wilfried Roeloffzen[6], Hermann Einsele[7], Hartmut Goldschmidt[8], Katja Weisel[9], Marc-Steffen Raab[10], Christof Scheid[11], Sébastien Anguille[12], Pieter Sonneveld[13], Sonja Zweegman[14], Jordan M Schecter[15], Kevin C De Braganca[15], Carolyn C Jackson[15,*], Philip Vlummens[16], Helen Varsos[15], Christina Corsale[15], Deepu Madduri[15], Tzu-min Yeh[15], Pankaj Mistry[17], Tito Roccia[18,*], Qingxuan Song[15], Muhammad Akram[19], Octavio Costa Filho[19], Dong Geng[19], Yaël C Cohen[20], Niels WCJ van de Donk[14]

[1]Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; [2]Abramson Cancer Center, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; [3]UPMC Hillman Cancer Center, Pittsburgh, PA, USA; [4]University of Leuven, Leuven, Belgium; [5]Ghent University Hospital, Ghent, Belgium; [6]University Medical Center Groningen, Groningen, Netherlands; [7]Universitätsklinikum Würzburg, Medizinische Klinik und Poliklinik II, Würzburg, Germany; [8]Internal Medicine V, GMMG-Study Group at University Hospital Heidelberg, Heidelberg, Germany; [9]University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [10]University Hospital Heidelberg and Clinical Cooperation Unit Molecular Hematology/Oncology, German Cancer Research Center, Heidelberg, Germany; [11]University of Cologne, Cologne, Germany; [12]Vaccine and Infectious Disease Institute, University of Antwerp, Center for Cell Therapy and Regenerative Medicine, Antwerp University Hospital, Edegem, Belgium; [13]Erasmus MC Cancer Institute, Rotterdam, Netherlands; [14]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, Netherlands; [15]Janssen Research & Development, Raritan, NJ, USA; [16]Janssen Research & Development, Beerse, Belgium; [17]Janssen Research & Development, High Wycombe, UK; [18]Janssen Global Services, Raritan, NJ, USA; [19]Legend Biotech USA Inc., Somerset, NJ, USA; [20]Tel Aviv Sourasky (Ichilov) Medical Center and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
*At the time of the study.

Presented by J Hillengass at the 65th American Society of Hematology (ASH) Annual Meeting; December 9–12, 2023; San Diego, CA, USA

Multiples Myelom (MM) – Cartitude-2 (med. follow up 29 mo)

- In CARTITUDE-1, a single cilta-cel infusion yielded deep and durable responses in heavily pretreated patients with RRMM[1,2]
  - Basis for approval in patients with RRMM with ≥3 and ≥4 prior LOT in Europe and the US, respectively[3,4]
- CARTITUDE-2 is a multicohort study of cilta-cel use in patients as early as after 1 prior LOT[5-7]
  - Cohorts A and B have the potential to yield insight into cilta-cel outcomes in patients in early LOT RRMM, a high unmet need

Cohort A: Len-refractory MM after 1–3 prior LOT, including a PI and IMiD

ORR, 95% (90% ≥CR) as previously reported[5]

Cohort B: 1 prior LOT, including a PI and IMiD, and PD ≤12 months after ASCT or from the start of antimyeloma therapy

ORR, 100% (90% ≥CR) as previously reported[6]

Objective: To report updated efficacy and safety data from CARTITUDE-2 cohorts A and B after a median follow-up of ~29 months

Multiples Myelom (MM) – Cartitude-2

Characteristic	Cohort A (N=20)	Cohort B (N=19)
Age, median (range), y	60 (38–75)	58 (44–67)
Male, n (%)	13 (65.0)	14 (73.7)
Race, n (%)		
White	18 (90.0)	14 (73.7)
Black/African American	2 (10.0)	2 (10.5)
Asian	0	1 (5.3)
Not reported	0	2 (10.5)
Bone marrow plasma cells[a] ≥60%, n (%)	3 (15.0)	4 (21.1)
Extramedullary plasmacytomas, n (%)	3 (15.0)	3 (15.8)
Cytogenetic high risk,[b] n (%)	7 (35.0)[c]	3 (15.8)[d]
del17p	3 (15.0)	3 (15.8)
t(14;16)	5 (25.0)	0
t(4;14)	0	0
1q	0	0

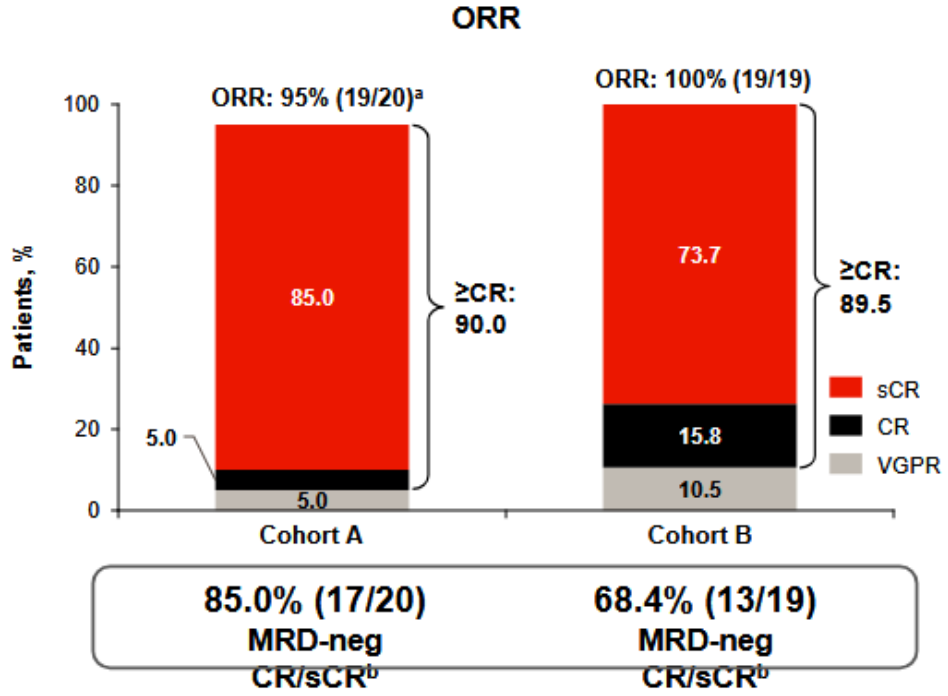
Characteristic	Cohort A (N=20)	Cohort B (N=19)
Years since initial diagnosis to enrollment, median (range)	3.5 (0.7–8.0)	1.15 (0.5–1.9)
Prior LOT, median (range)	2 (1–3)	1 (1–1)
Previous stem cell transplantation,[e] n (%)		
Autologous	17 (85.0)	15 (78.9)
Exposure status, n (%)		
Triple-class[f]	13 (65.0)	4 (21.1)
Penta-drug exposed[g]	4 (20.0)	0
Refractory status, n (%)		
Triple-class[f]	8 (40.0)	3 (15.8)
Penta-drug refractory[g]	1 (5.0)	0
To last line of prior therapy	19 (95.0)	15 (78.9)

- As of April 2023, median follow-up of patients who received cilta-cel infusion was 29.9 months (range, 3.3[h]–35.6) in cohort A and 27.9 months (range, 5.2[h]–32.1) in cohort B

[a]Maximum value from bone marrow biopsy and bone marrow aspirate is selected if both results are available. [b]Any of the following 4 cytogenetic features abnormal: del17p, t(14;16), t(4;14), or 1q. [c]1 patient had both del17p and t(14;16); 6 (30.0%) patients had unknown cytogenetics. [d]3 (15.8%) patients had unknown cytogenetics. [e]17 patients in cohort A and 15 patients in cohort B received prior stem cell transplantation and all were autologous. [f]PI, IMiD, and anti-CD38 antibody. [g]≥2 PIs, ≥2 IMiDs, and 1 anti-CD38 antibody. [h]Includes patients who died. cilta-cel, ciltacabtagene autoleucel; IMiD, immunomodulatory drug; LOT, line of therapy;

Multiples Myelom (MM) – Cartitude-2 – Response/MRD

Cilta-cel led to deep and durable responses



Treatment response among responders	Cohort A (N=19)	Cohort B (N=19)
Time (mo) to first response,[c] median (range)	0.99 (0.7–3.3)	0.95 (0.9–9.7)
Time (mo) to best response, median (range)	3.25 (0.9–13.6)	5.1 (0.9–11.8)
Duration of response		
24-mo DOR rate, % (95% CI)	73.3 (47.2–87.9)	70.5 (42.5–86.7)

[a]1 patient had a minimal response. [b]Only MRD assessments (10^{-5} testing threshold) within 3 months of achieving CR/sCR until death/progression/subsequent therapy (exclusive) are considered. [c]≥PR.
cilta-cel, ciltacabtagene autoleucel; CR, complete response; DOR, duration of response; MRD, minimal residual disease; ORR, overall response rate; PR, partial response; sCR, stringent CR; VGPR, very good partial response.

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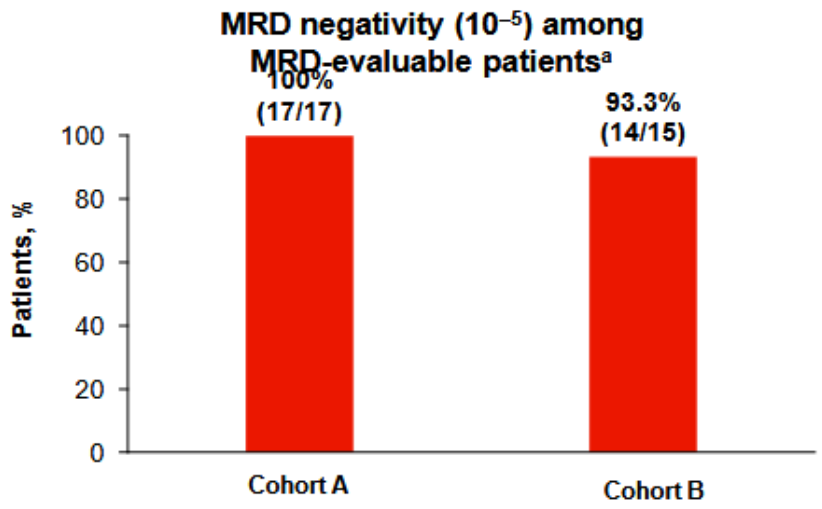
Multiples Myelom (MM) – Cartitude-2 – sustained MRD

Most patients achieved MRD negativity at a threshold of 10^{-5}



Sustained MRD negativity[b]	Cohort A	Cohort B
Patients evaluable for sustained MRD negativity ≥6 mo[c]	**n=11**	**n=13**
Sustained MRD negativity (10^{-5}) ≥6 mo,[d] n (%)	8 (72.7)	10 (76.9)
Patients evaluable for sustained MRD negativity ≥12 mo[e]	**n=14**	**n=13**
Sustained MRD negativity (10^{-5}) ≥12 mo,[f] n (%)	7 (50.0)	8 (61.5)

Per protocol, bone marrow aspirate samples for MRD evaluation were collected at time of suspected CR/sCR; for all dosed patients at months 2, 6, 12, 18, and 24; and yearly thereafter for patients in CR/sCR.

[a]Patients who were MRD evaluable had a clone identified and had at least 1 postbaseline MRD sample that included sufficient cells for evaluation at the 10^{-5} testing threshold (for NGS) or patients who had at least 1 postbaseline sample with the result of either positive or negative (for NGF). [b]Post hoc analysis. [c]Patients who achieved overall MRD negativity and had at least an evaluable MRD sample at the 10^{-5} testing threshold on or after 6 months after their first MRD negativity or progressed, started subsequent therapy, or died due to progressive disease within 6 months after their first MRD negativity. [d]MRD negative confirmed by at least 6 months apart without MRD positive in between. Percentage is calculated with number of patients evaluable for sustained MRD negativity ≥6 months as denominator. [e]Patients who achieved overall MRD negativity and had at least an evaluable MRD sample at the 10^{-5} testing threshold on or after 12 months after their first MRD negativity or progressed, started subsequent therapy, or died due to progressive disease within 12 months after their first MRD negativity. [f]MRD negative confirmed by at least 12 months apart without MRD positive in between. Percentage is calculated with number of patients evaluable for sustained MRD negativity ≥12 months as denominator. CR, complete response; MRD, minimal residual disease; NGF, next-generation flow; NGS, next-generation sequencing; sCR, stringent CR.

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Multiples Myelom (MM) – Cartitude-2 – Conclusion

Cohort A: Len-refractory 1–3 prior LOT RRMM

- 100% of evaluable patients were MRD negative at 10^{-5}
- 85% sCR rate with 73% of responders remaining in response for ≥24 months
- 24-month PFS and OS rates were both 75%
- No new CAR-T–related safety signals were observed

Cohort B: Progressed ≤12 months after 1L therapy

- 93% of evaluable patients were MRD negative at 10^{-5}
- 74% sCR rate with 71% of responders remaining in response for ≥24 months
- 24-month PFS and OS rates were 73% and 84%, respectively
- No new CAR-T–related safety signals were observed

- A similar patient population to CARTITUDE-2 Cohort A was evaluated in the phase 3 CARTITUDE-4 trial[1]

Longer-term results from CARTITUDE-2 cohorts A and B showed deep and durable responses in patients with MM, including in a len-refractory population as early as after first relapse, and in a functionally high-risk population who progressed on frontline therapy within 12 months

1L, first line; CAR, chimeric antigen receptor; len, lenalidomide; LOT, line of therapy; MM, multiple myeloma; MRD, minimal residual disease; OS, overall survival; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma; sCR, stringent complete response.

1. San-Miguel J, et al. *New Engl J Med* 2023;389:335-47.

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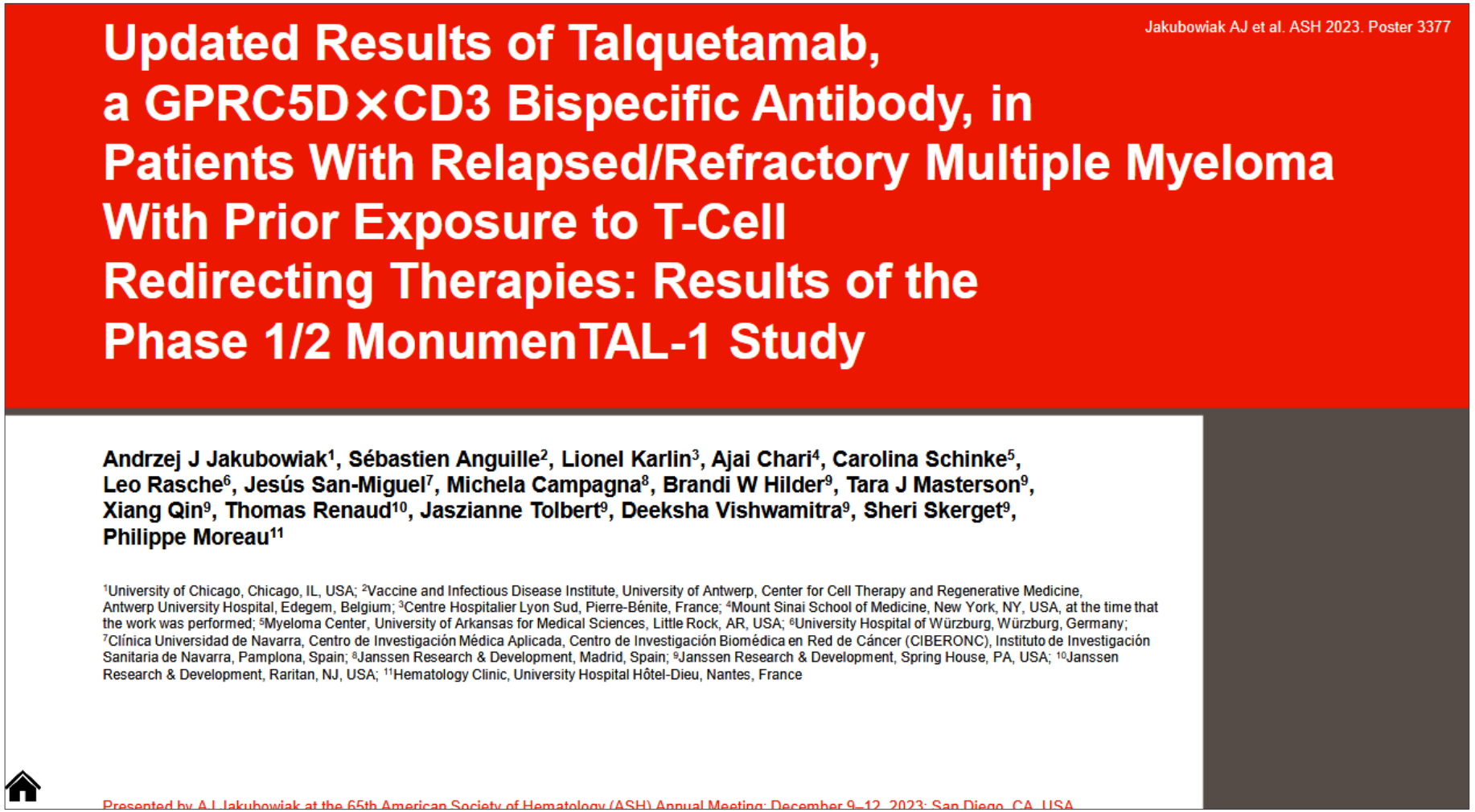
Multiples Myelom (MM) – MonumenTAL-1



Jakubowiak AJ et al. ASH 2023. Poster 3377

Updated Results of Talquetamab, a GPRC5D×CD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma With Prior Exposure to T-Cell Redirecting Therapies: Results of the Phase 1/2 MonumenTAL-1 Study

Andrzej J Jakubowiak[1], Sébastien Anguille[2], Lionel Karlin[3], Ajai Chari[4], Carolina Schinke[5], Leo Rasche[6], Jesús San-Miguel[7], Michela Campagna[8], Brandi W Hilder[9], Tara J Masterson[9], Xiang Qin[9], Thomas Renaud[10], Jaszianne Tolbert[9], Deeksha Vishwamitra[9], Sheri Skerget[9], Philippe Moreau[11]

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Presented by A.J. Jakubowiak at the 65th American Society of Hematology (ASH) Annual Meeting; December 9–12, 2023; San Diego, CA, USA

Multiples Myelom (MM) – MonumenTAL-1 - Talquetamab

- Talquetamab is the first and only GPRC5D BsAb approved for RRMM[1-3]
- Talquetamab demonstrated deep and durable responses in RRMM in MonumenTAL-1[4]
  - ORR of >71% in 288 patients naive to TCR
  - ORR of 65% in 51 patients with prior TCR (ie, CAR-T and BsAbs)
- Novel TCR therapies are important new treatment options for RRMM, and there is a growing unmet need for patients who relapse following these therapies[5-7]

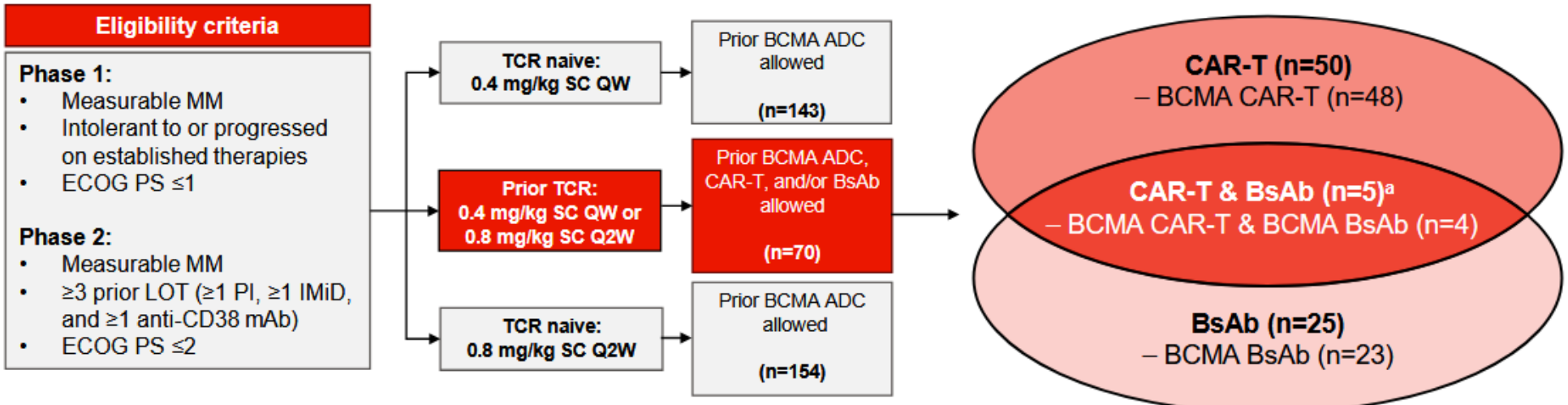
We present updated MonumenTAL-1 results in patients with prior TCR, including an additional 19 patients enrolled since the prior analysis

BsAb, bispecific antibody; CAR, chimeric antigen receptor; GPRC5D, G protein–coupled receptor family C group 5 member D; ORR, overall response rate; RRMM, relapsed/refractory multiple myeloma; TCR, T-cell redirection therapy.

1. Verkleij CPM, et al. *Blood Adv* 2021;5:2196-215. 2. TALVEY (talquetamab-tgvs). Prescribing information. Horsham, PA: Janssen Biotech, Inc.; 2023. 3. TALVEY. Summary of product characteristics. Leiden, Netherlands: Janssen Biologics B.V.; 2023. 4. Schinke CD, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual. Poster 8036. 5. Granger K, et al. *J Oncol Pharm Pract* 2023;29:722-6. 6. Zhang X, et al. *Front Immunol* 2023;14:1101495. 7. ELREXFIO™ (elranatamab-bcmm). Prescribing information. New York, NY: Pfizer Inc.; 2023.

Presented by AJ Jakubowiak at the 65th American Society of Hematology (ASH) Annual Meeting; December 9–12, 2023; San Diego, CA, USA

Multiples Myelom (MM) – MonumenTAL-1 – Study Design



MonumenTAL-1 ClinicalTrials.gov identifiers: NCT03399799/NCT04634552.
[a]Among the overall prior TCR group (N=70), 5 patients treated with both prior CAR-T and BsAb were also counted in each of the respective overall CAR-T (n=50) and BsAb (n=25) groups.
ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; BsAb, bispecific antibody; CAR, chimeric antigen receptor; CD, cluster of differentiation; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; LOT, line of therapy; mAb, monoclonal antibody; MM, multiple myeloma; PI, proteasome inhibitor; Q2W, every other week; QW, weekly; SC, subcutaneous; TCR, T-cell redirection therapy.

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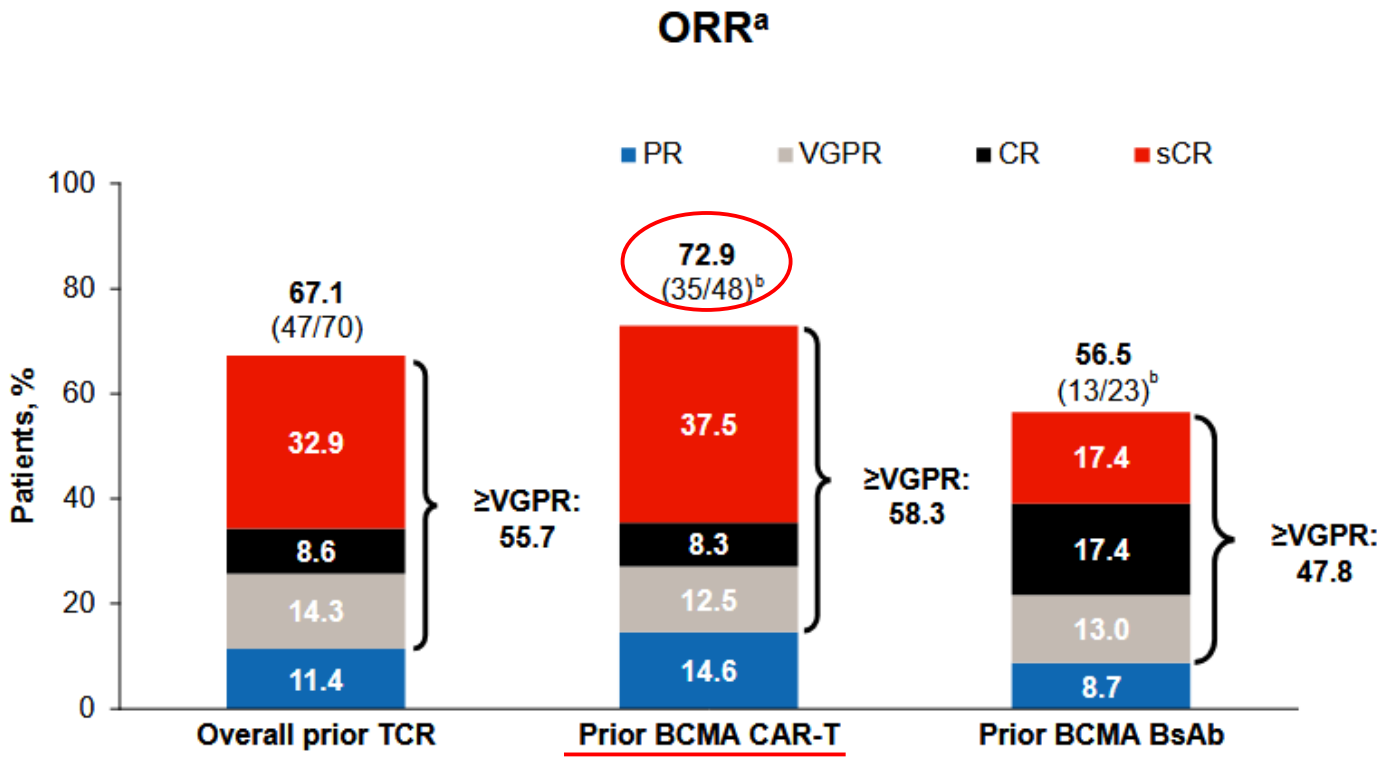
Multiples Myelom (MM) – MonumenTAL-1 - ORR



Data cut-off date: October 11, 2023.
[a]Due to rounding, individual response rates may not sum to the ORR. [b]4 patients received both BCMA CAR-T and BCMA BsAb.
BCMA, B-cell maturation antigen; BsAb, bispecific antibody; CAR, chimeric antigen receptor; CR, complete response; ORR, overall response rate; PR, partial response; sCR, stringent complete response; TCR, T-cell redirection therapy; VGPR, very good partial response.

Multiples Myelom (MM) – MonumenTAL-1 – PFS/Safety

Outcome	Overall prior TCR (N=70)	Prior BCMA CAR-T (n=48[a])	Prior BCMA BsAb (n=23[a])
mFU,[b] mo	18.4	18.4	16.3
12-mo PFS rate, % (95% CI)	44.1 (32.1–55.4)	50.0 (34.9–63.4)	30.4 (13.5–49.3)
12-mo DOR rate, % (95% CI)	55.2 (39.3–68.5)	54.7 (36.0–70.0)	43.3 (16.3–67.9)

- Patients with prior TCR had a higher overall infection rate and slightly higher proportion of severe infections vs TCR-naïve patients, consistent with previously reported results
- Patients with prior CAR-T had similar rates of infections, cytopenias, cytokine release syndrome, and GPRC5D-related AEs (dysgeusia; skin-, nail-, and rash-related AEs) as patients with prior BsAb

Multiples Myelom (MM) – MonumenTAL-1 – Time between Tx

Time from last dose of prior BCMA TCR to first dose of talquetamab		ORR, % (n/N)	12-mo DOR rate, % (95% CI)
BCMA CAR-T	<9 mo	93.8 (15/16)	57.1 (27.5–78.5)
	≥9 mo	62.5 (20/32)	53.0 (28.6–72.4)
BCMA BsAb	<9 mo	50.0 (8/16)	50.0 (15.2–77.5)
	≥9 mo	71.4 (5/7)	26.7 (1.0–68.6)

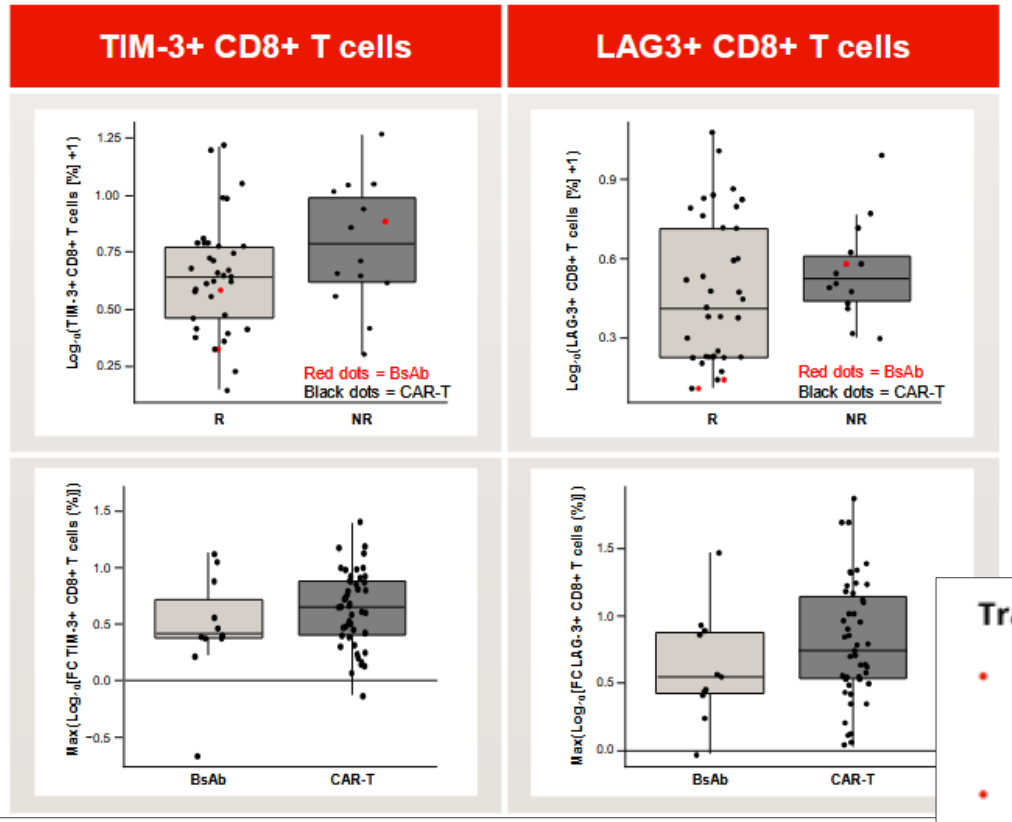
- Although numbers were small at each interval, ORR trended higher in patients with <9 mo between last dose of prior BCMA CAR-T and talquetamab; in contrast, ORR trended higher in patients with ≥9 mo between last dose of prior BCMA BsAb and talquetamab

- ORR was comparable in patients who received CAR-T prior to last therapy vs as last therapy before talquetamab (71.4% vs 75.9%); ORR trended higher in patients who received BsAb prior to last therapy vs as last therapy before talquetamab (66.7% vs 28.6%)

Multiples Myelom (MM) – MonumenTAL-1 – Pharmacodynamic

CD8+ T-cell profile in responders (R) vs nonresponders (NR) receiving prior TCR at baseline

CD8+ T-cell profile in patients receiving prior CAR-T vs BsAb following talquetamab



Translational data

- At baseline, the pharmacodynamic profile in patients with prior TCR had a more exhausted immune phenotype vs TCR-naive patients (see **Poster 1933**)
- Among patients with prior TCR, nonresponders to talquetamab had a more exhausted immune phenotype vs responders, indicated by lower T-cell counts (see **Poster 1933**) and higher counts of TIM-3– and LAG-3–expressing CD8+ T cells at baseline (**Figure 4A**)
- Following talquetamab, patients with prior CAR-T had greater T-cell activation vs patients with prior BsAb, indicated by higher max fold induction of TIM-3– and LAG-3–expressing CD8+ T cells in the first cycle (**Figure 4B**)

Multiples Myelom (MM) – MonumenTAL-1 – Conclusion

- Talquetamab is a versatile treatment that provides robust responses in patients with RRMM and prior exposure to TCR (predominantly targeting BCMA)
  - ORR of 73% and 12-month PFS and DOR rates of ≥50% in patients exposed to prior BCMA CAR-T
  - ORR of 57% and 12-month PFS and DOR rates of 30–43% in patients exposed to prior BCMA BsAb
- Safety profile was similar in patients with prior CAR-T or BsAb
- Although prior TCR patients have a less favorable immune phenotype at baseline vs TCR-naive patients, high response rates are observed, particularly with prior CAR-T, which was associated with greater T-cell activation in the first cycle
- These results may offer insight into strategies for optimizing sequencing of TCRs that target independent MM antigens

Assessment of talquetamab in patients with prior TCR, including a large population of patients with prior BCMA BsAb exposure (n=23), showed continued efficacy in this population

und am Ende....

Vielen Dank für Ihre Aufmerksamkeit

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Agenda

1. Smoldering Multiples Myelom – Centaurus, (ImmunoPrism)
2. Firstline Multiples Myelom: Perseus
3. Erhaltungstherapie: EMN26 (Iberdomid-Maintenance)
4. RRMM: Cartitude-2, MonumenTAL-1

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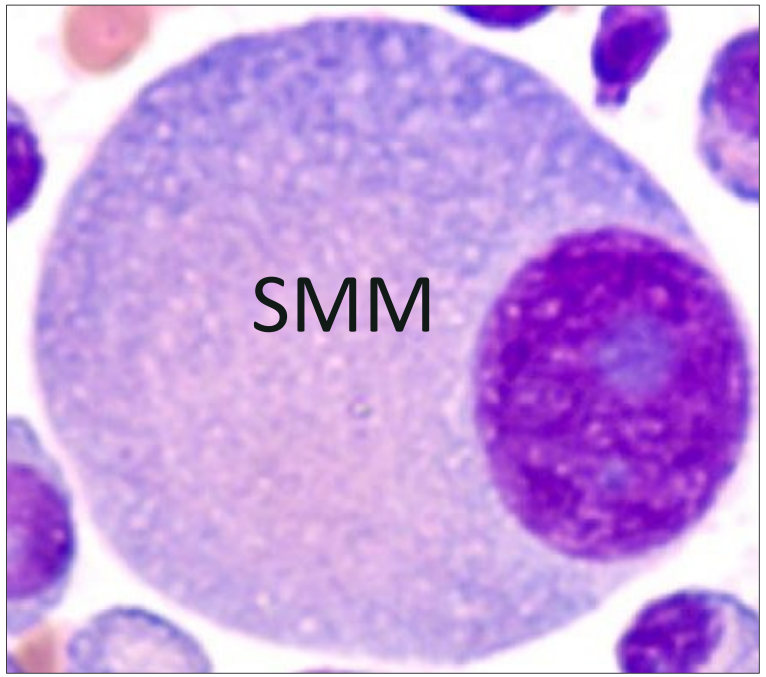
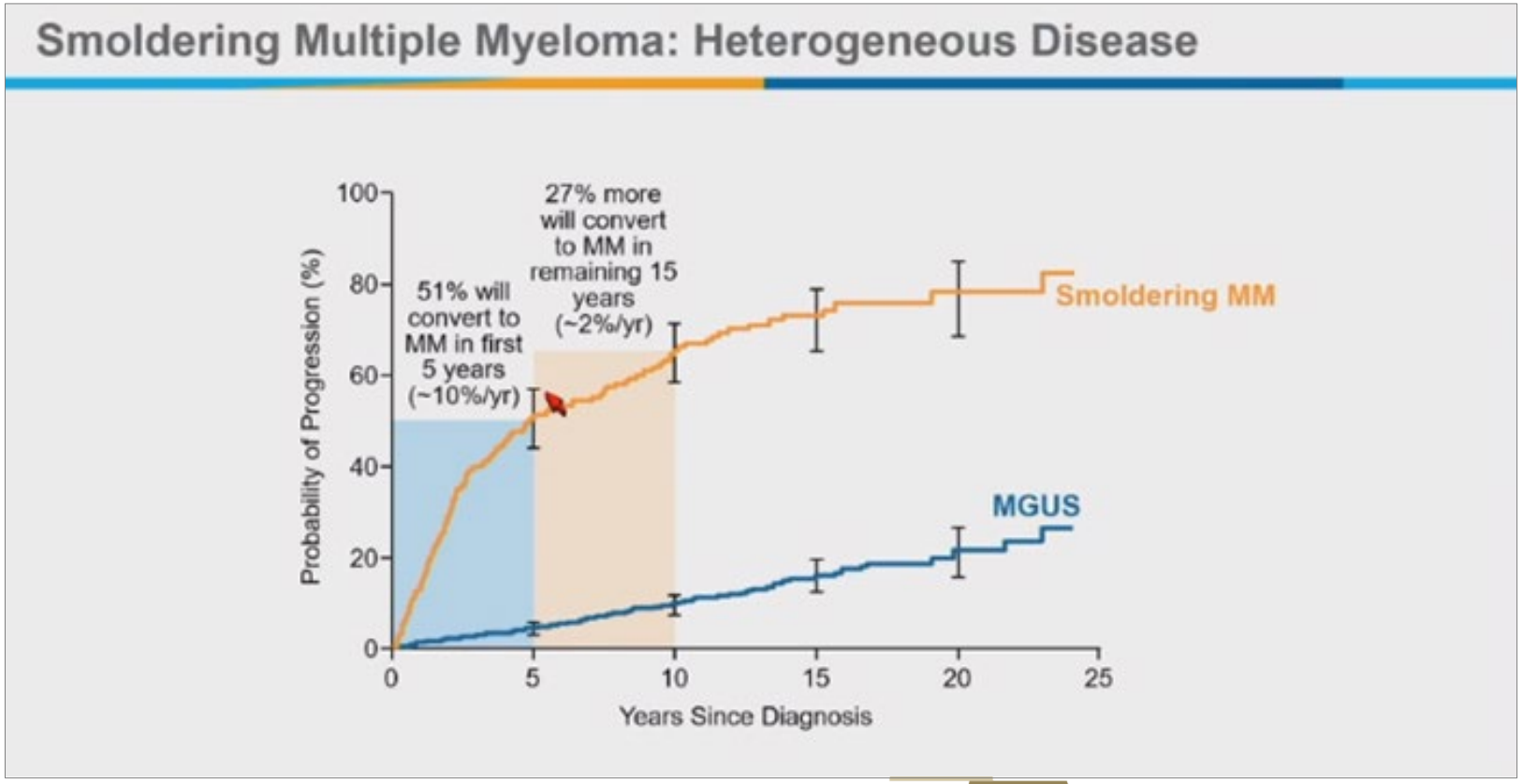
Smoldering Multiples Myelom (SMM)





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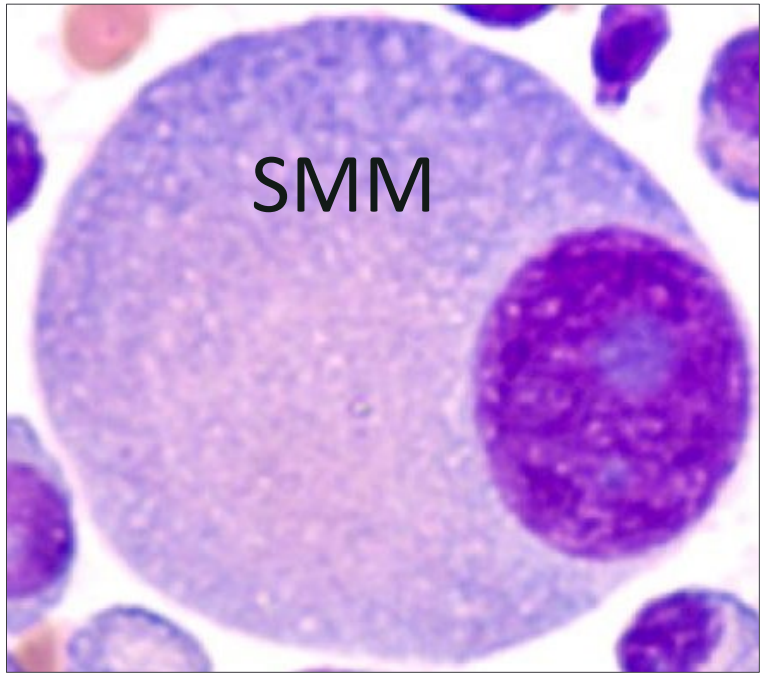
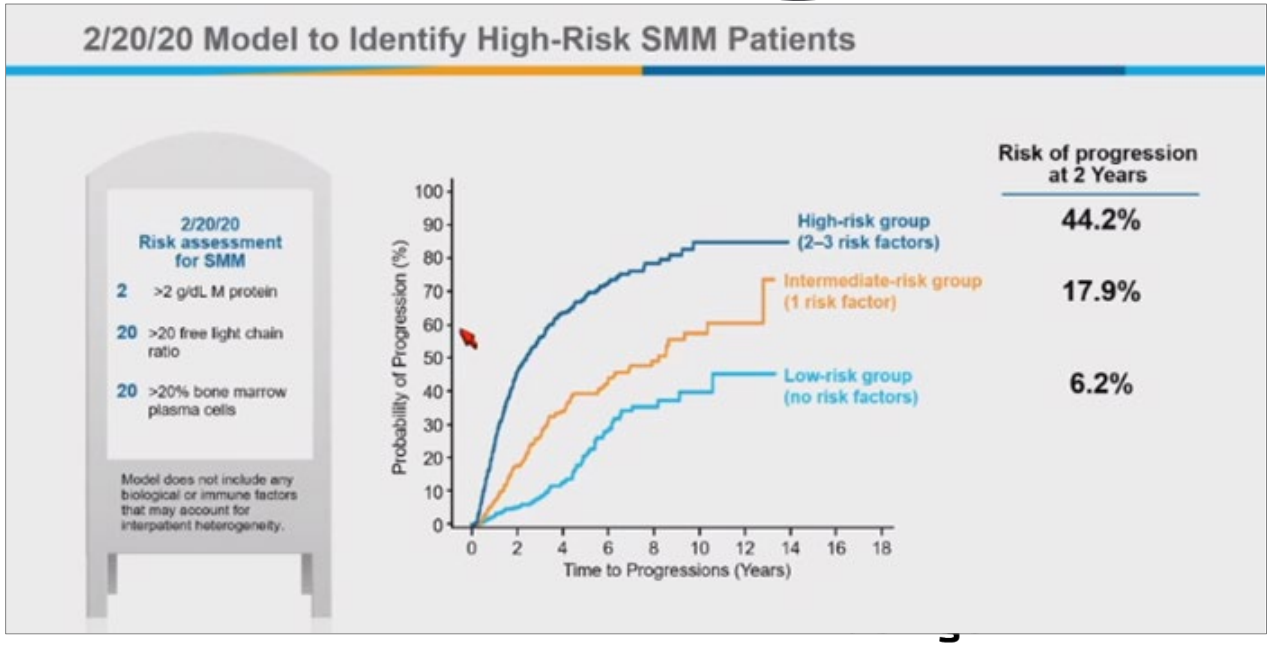
Smoldering Multiples Myelom (SMM)

Zahlreiche Studien/
Kombinationstherapien/
Zytostatika/kurativer Ansatz?/
Toxizität/SPM?

Keine etablierte
Therapie/Zulassung

Risiko-Einteilung
2/20/20 Modell





SMM- Centaurus - Follow up of 85,2 mo (~ 7 Jahre)

Efficacy and Safety of Daratumumab (DARA) Monotherapy in Patients with Intermediate-risk or High-risk Smoldering Multiple Myeloma (SMM): Final Analysis of the Phase 2 CENTAURUS Study

Ola Landgren,[1] Ajai Chari,[2] Yael C. Cohen,[3] Andrew Spencer,[4] Peter Voorhees,[5] Irwindeep Sandhu,[6] Matthew W. Jenner,[7] Dean Smith,[8] Michele Cavo,[9] Niels W.C.J. van de Donk,[10] Meral Beksac,[11] Philippe Moreau,[12] Hartmut Goldschmidt,[13] Linlin Sha,[14] Liang Li,[14] Els Rousseau,[15] Robyn Dennis,[16] Robin Carson,[17] Craig C. Hofmeister[18]

[1]Division of Myeloma, Department of Medicine, Sylvester Comprehensive Cancer Center at University of Miami, Miami, FL, USA; [2]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [3]Department of Hematology, Tel-Aviv Sourasky (Ichilov) Medical Center, and Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel; [4]Malignant Haematology and Stem Cell Transplantation Service, Alfred Health-Monash University, Melbourne, Australia; [5]Levine Cancer Institute, Atrium Health Wake Forest University School of Medicine, Charlotte, NC, USA; [6]Department of Oncology, Cross Cancer Institute, University of Alberta, Edmonton, AB, Canada; [7]University Hospital Southampton, Southampton, UK; [8]Department of Clinical Haematology, Nottingham University Hospitals, Nottinghamshire, UK; [9]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Istituto di Ematologia "Seràgnoli", Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale, Università di Bologna, Bologna, Italy; [10]Department of Hematology, Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands; [11]Ankara University, Ankara, Turkey; [12]Hematology Department, University Hospital Hôtel-Dieu, Nantes, France; [13]GMMG-Study Group at University Hospital Heidelberg, Internal Medicine V, Heidelberg, Germany; [14]Janssen Research & Development, LLC, Shanghai, China; [15]Janssen Research & Development, Beerse, Belgium; [16]Janssen Research & Development, LLC, Raritan, NJ, USA; [17]Janssen Research & Development, LLC, Spring House, PA, USA; [18]Department of Hematology & Medical Oncology, Winship Cancer Institute of Emory University, Atlanta, GA, USA

Presented by O Landgren at the 65th American Society of Hematology (ASH) Annual Meeting; December 9-12, 2023; San Diego, CA, USA

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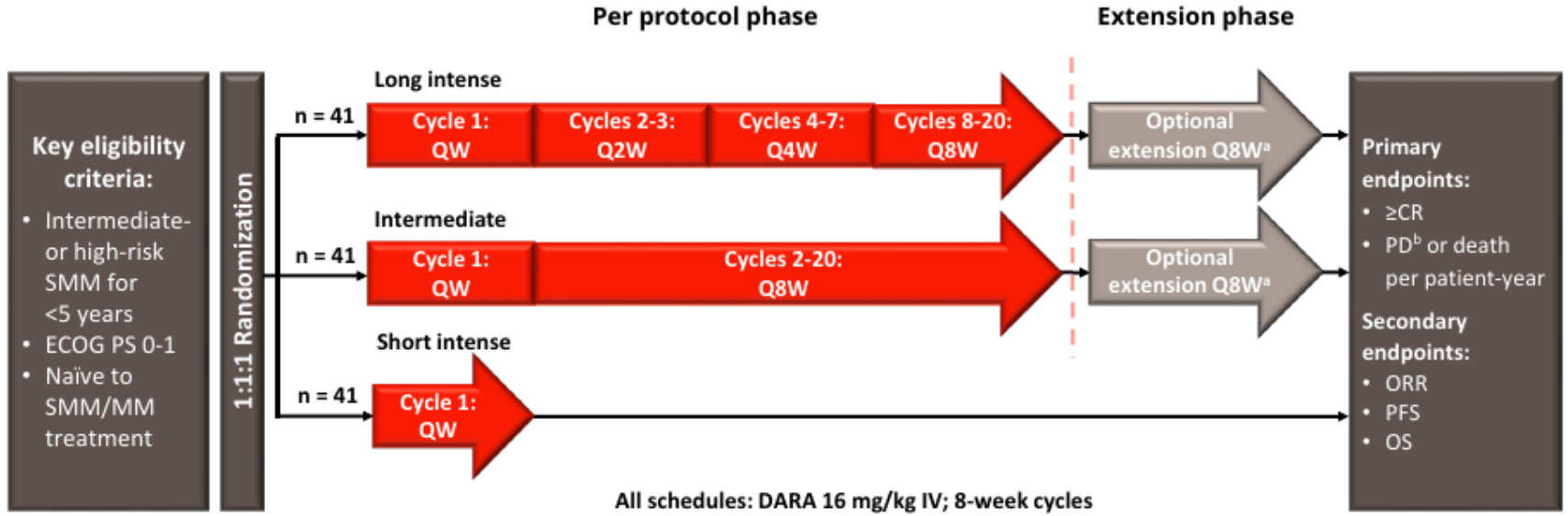
SMM- Centaurus – Study Design



[a]For patients in the Long intense and Intermediate arms, there was an option to extend treatment with DARA IV Q8W after the
no grade ≥3 treatment-related toxicity, and at least stable disease had been achieved.
[b]SLiM CRAB criteria were used for the assessment of disease progression to multiple myeloma. Disease evaluations were perfo
until PD. Skeletal survey or low-dose computed tomography (CT) and magnetic resonance imaging (MRI) every 12 months.
SMM, smoldering myeloma; ECOG PS, Eastern Cooperative Oncology Group performance status; MM, multiple myeloma; QW, w
CR, complete response; PD, progressive disease; ORR, overall response rate; PFS, progression-free survival; OS, overall survival.

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Key study design amendments:

- Optional extension[d] to a maximum of 7 years following the last patient's first dose to permit continued study treatment and collect long-term safety and efficacy data
- Flexibility to switch from DARA IV to DARA SC[d] during the extension phase to limit patients' time at study centers due to the COVID-19 pandemic, and disease evaluations were performed per local standard of care

[a]Completed 20 cycles of treatment (Long intense and Intermediate arms) or completed 1 cycle of treatment (Short intense arm).
[b]Median (range) number of cycles completed at the time of clinical cutoff.
[c]For patients in the Long intense and Intermediate arms, there was an option to extend treatment with DARA IV once every 8 weeks after the end of Cycle 20 per investigator discretion if there was a positive benefit/risk ratio, no grade ≥3 treatment-related toxicity, and at least stable disease had been achieved.
[d]As per investigator discretion.

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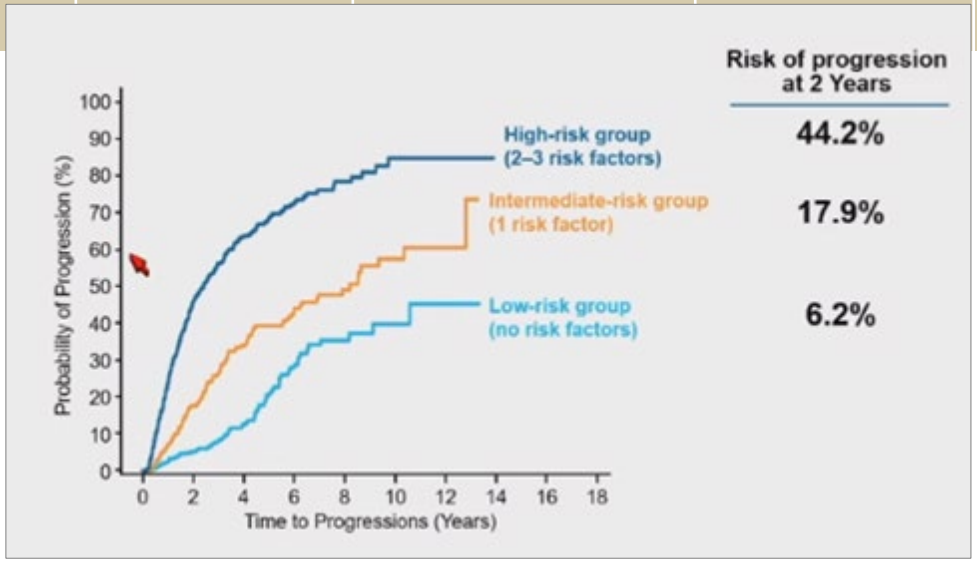
SMM- Centaurus

	ORR	mDoR	CR/sCR-Rate	mPFS	OS (84 mo)	TtNT
Long intense	58,5 %	nr	4,9 %	nr	81,3 %	nr
Intermediate intense	53,7 %	83,4 mo	9,8 %	84,4 mo	89,5 %	nr
Short intense	37,5 %	72,7 mo	0	74,1 mo	88,1 %	76,3 mo



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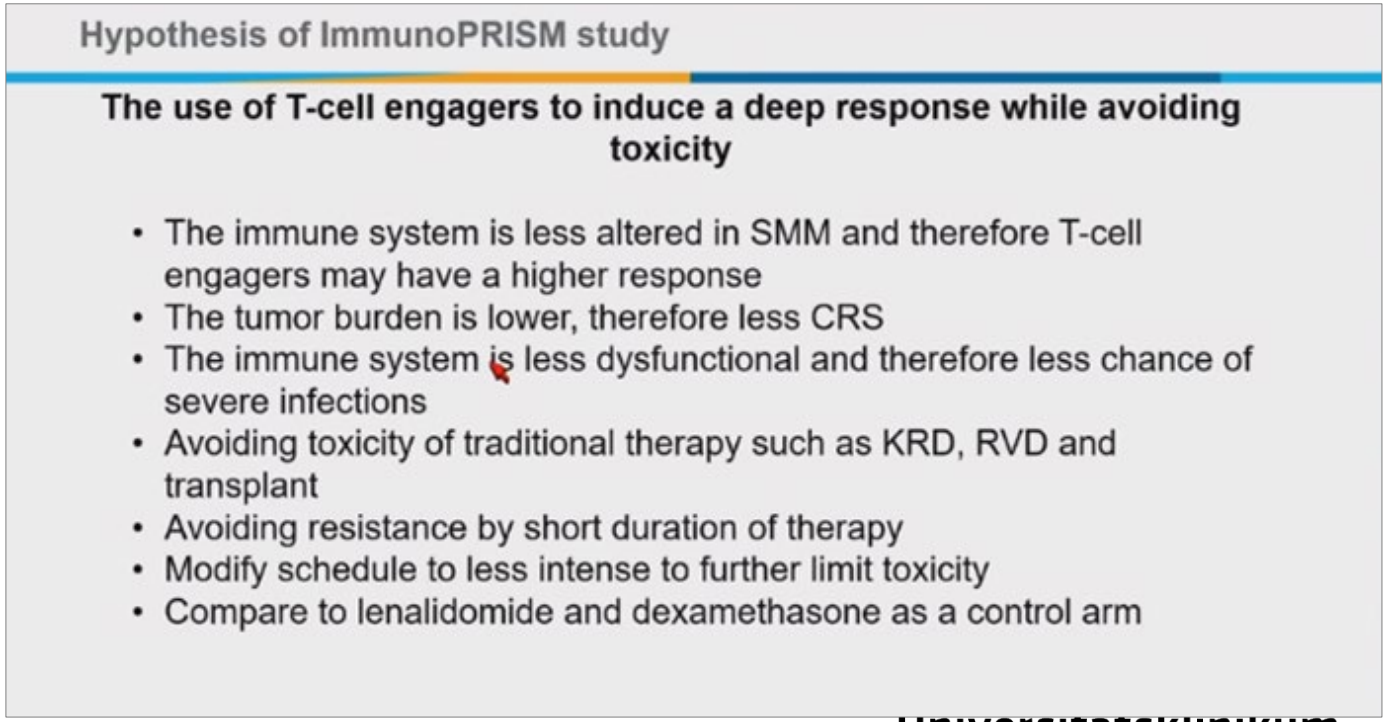
SMM- Centaurus – Conclusion

- **Final analysis of CENTAURUS continued to demonstrate the clinical activity of DARA monotherapy in patients with intermediate-risk or high-risk SMM**
- **With a median follow-up of ~7 years, DARA was well tolerated with no new safety concerns**
- **Approximately 44% of patients in the Long intense and Intermediate arms completed 20 cycles of treatment and continued DARA monotherapy on the optional extension phase,[a] with a median duration of additional treatment of 46.0 months (~4 years)**
- **The Long intense arm had a trend for the longest PFS and time to next treatment and supports the ongoing phase 3 AQUILA study and future SMM studies**

SMM- Immuno-Prism



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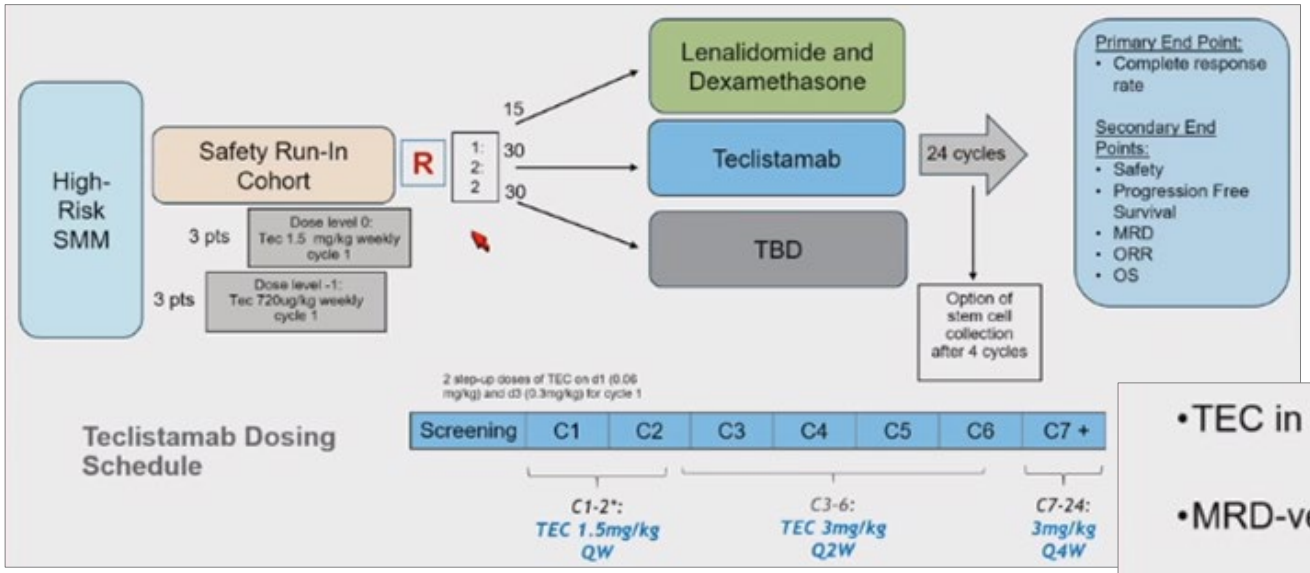
SMM- Immuno-Prism – Study Design



- TEC in HR-SMM demonstrates significant activity with 100% ORR
- MRD-ve (10^6) disease seen in 100% of evaluable patients to date
- Safety profile appears improved compared to RRMM, with fewer grade 3 infections
- Study is enrolling and additional arms to be added
- Longer follow-up is necessary to determine durability of MRD-negative responses

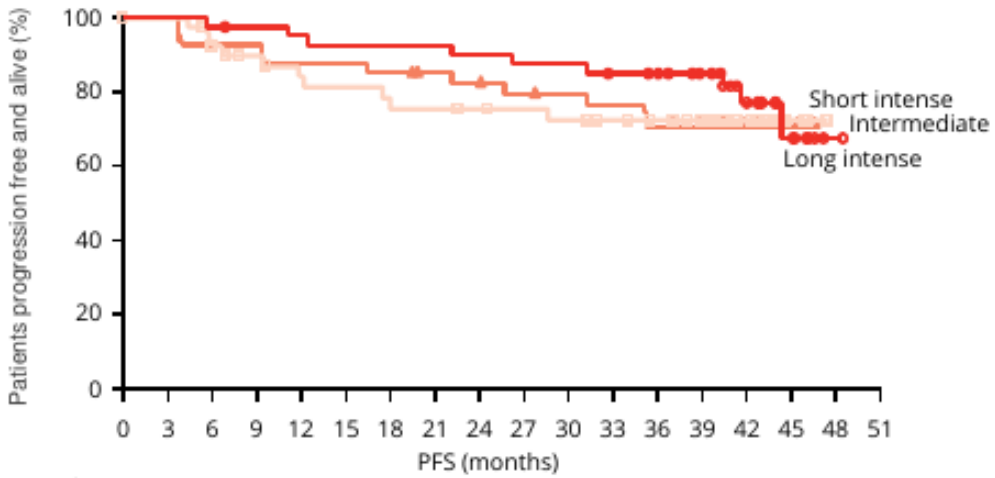
Proof of concept study which demonstrates significantly higher efficacy with early use of immunotherapy

Tübingen

SMM- Centaurus – PFS

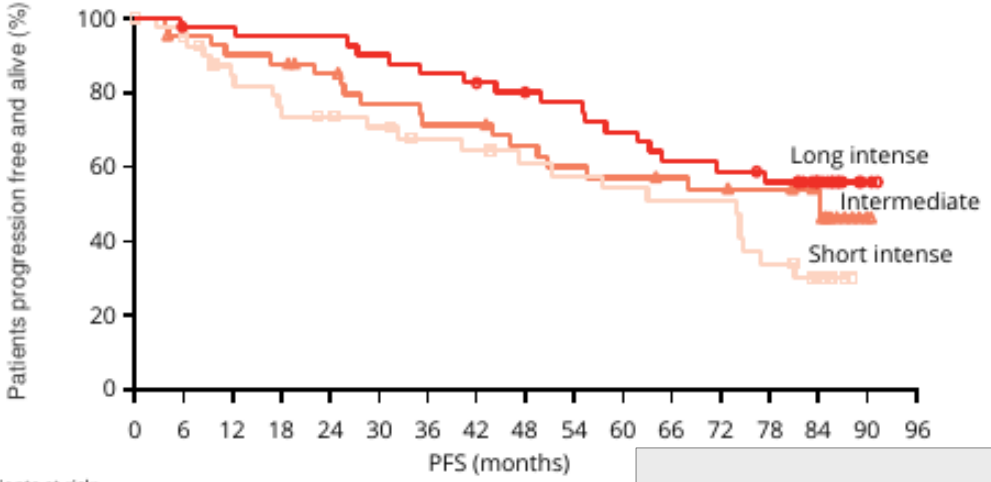
Median PFS including the extension phase was not reached in the Long intense arm, 84.4 months in the Intermediate arm, and 74.1 months in the Short intense arm

PFS per protocol phase[a]



Patients at risk:																		
Long intense	41	41	40	39	38	37	37	37	36	35	35	33	32	28	17	7	1	0
Intermediate	41	41	36	36	34	34	33	31	30	28	27	26	24	17	9	3	0	0
Short intense	41	40	35	32	29	28	27	26	25	24	23	21	19	15	10	3	0	0

PFS including extension phase[b]



Patients at risk:																														
Long intense	41	41	39	39	39	38	38	38	38	37	36	35	34	34	33	31	31	29	29	27	26									
Intermediate	41	41	38	38	36	36	35	33	32	29	28	28	26	26	26	24	23	21	21	20	20									
Short intense	41	39	37	34	31	30	28	27	26	25	24	22	21	21	20	19	18	18	17	17	16									

[a]PFS by central laboratory assessment.
[b]PFS by investigator assessment, as central laboratory assessments were not performed during the optional extension phase.
PFS was defined as the time from the date of randomization to the date of initial documented progressive disease according to the CRAB criteria, myeloma-defining events, or date of death, whichever oc
PFS, progression-free survival.

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