Neue Behandlungsansätze beim Multiplen Myelom

Dr. Eva Maria Autzinger

09.09.2023

Behandlungsoptionen beim Multiplen Myelom

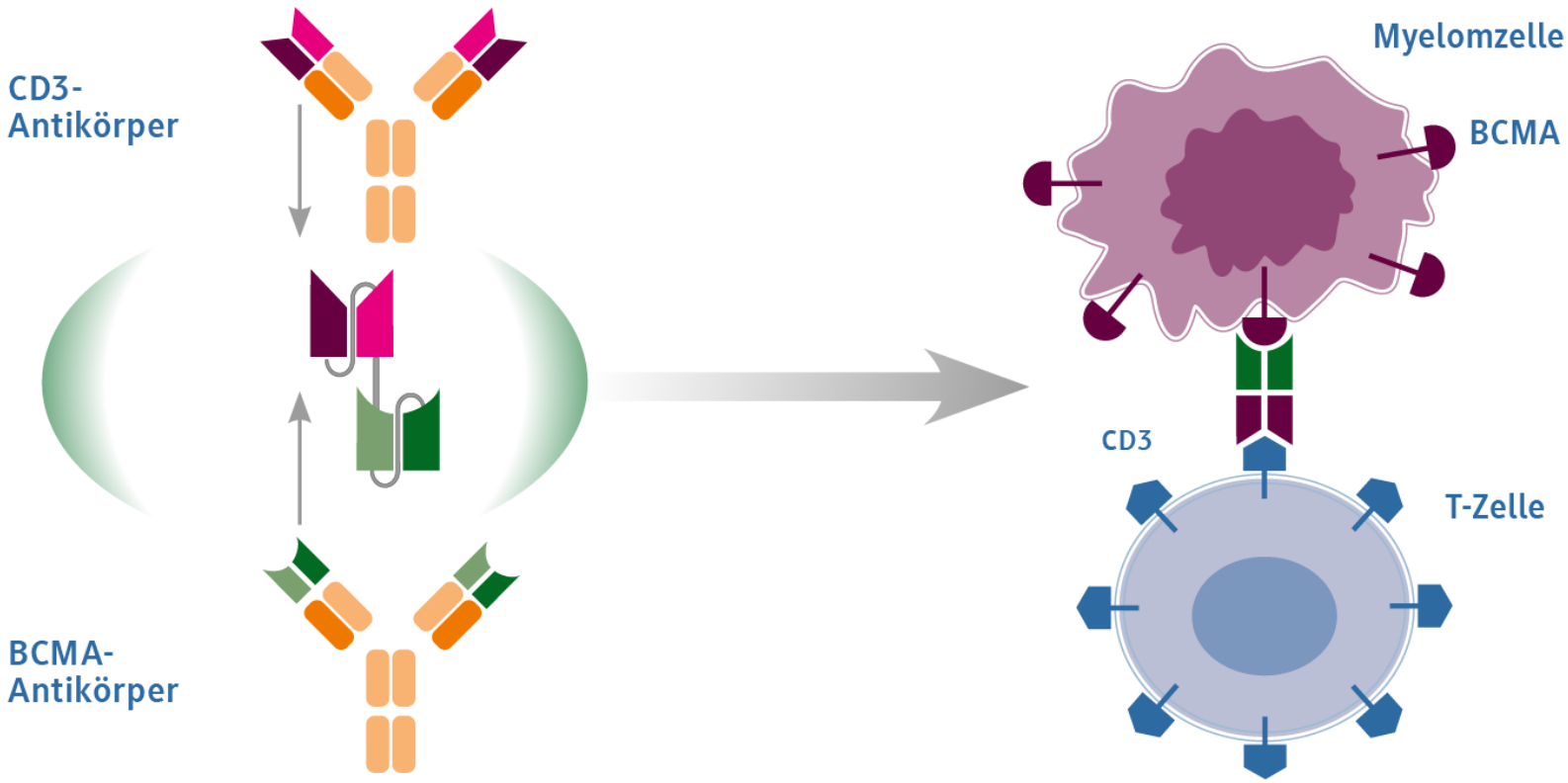
- Dexamethason
- Proteasomenhemmer:
  Bortezomib, Ixazomib, Carfilzomib
- IMiDE:
  (Thalidomid), Lenalidomid, Pomalidomid
- Antikörper:
  Daratumumab, Isatuximab, Elotuzumab
- Weitere Substanzen:
  Belantamab mafodotin, Selinexor, (Venetoclax)
- Zytostatika:
  Cyclophosphamid, Melphalan, Bendamustin, Melflufen


Bispezifische Antikörper
CAR-T-Zelltherapie

Downton Abbey II

Eine Neue Ära

Bispezifische Antikörper



Bispezifische Antikörper

- Teclistamab (Tecvayli®) zeigte in der MajesTEC-1-Studie eine Ansprechrate von 65%.
- Talquetamab (Talvey®) erzielte in der MonumenTAL-1-Studie eine Ansprechrate von über 70%.
- Elranatamab in der MagnetisMM-1-Studie liefert ähnlich gute Daten.
- Linvoseltamab konnte in einer Phase-II-Studie ebenfalls sehr überzeugende Daten zeigen.

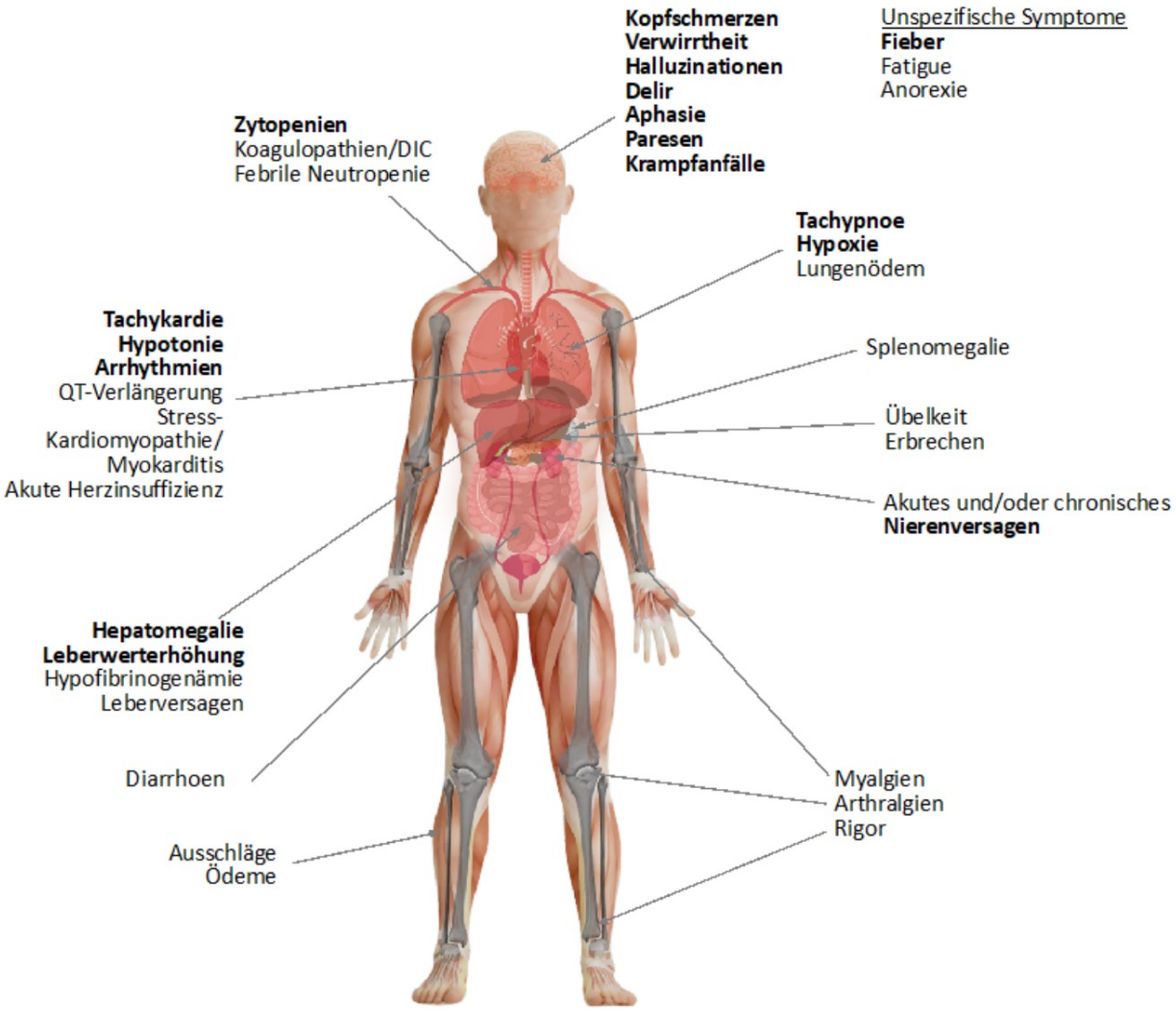
Bispezifische Antikörper

- Therapiedauer:

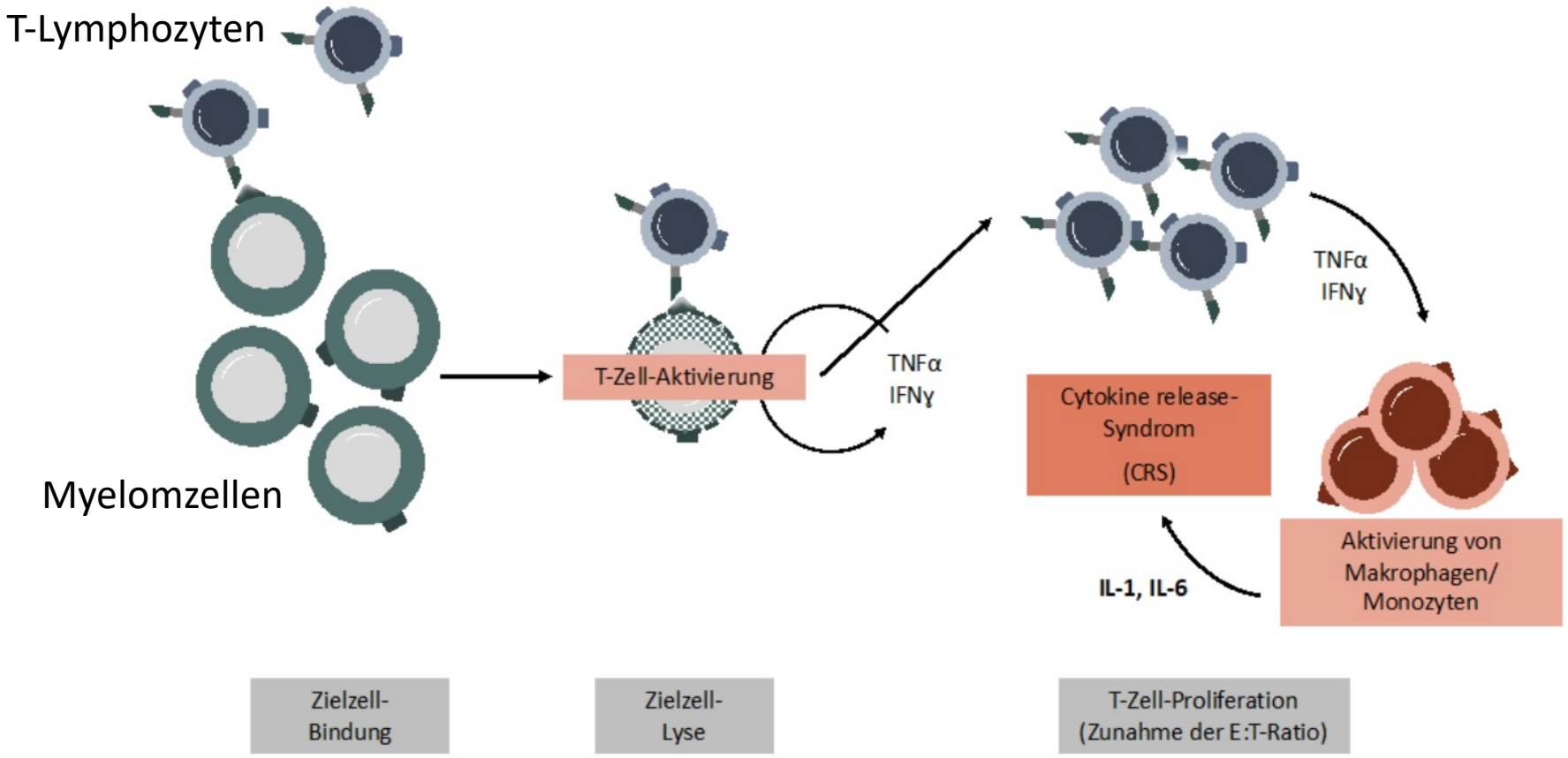
  Die bispezifischen Antikörper werden in regelmäßigen Abständen bis zur Progression oder dem Auftreten nicht-akzeptabler Nebenwirkungen verabreicht.

- In laufenden Studien wird beispielsweise auch die Kombination von 2 bispezifischen Antikörpern oder die Kombination von bispezifischen Antikörpern mit Daratumumab +/- IMiDE untersucht.

Bispezifische Antikörper: Nebenwirkungen



CRS: Zytokine-Freisetzungssyndrom

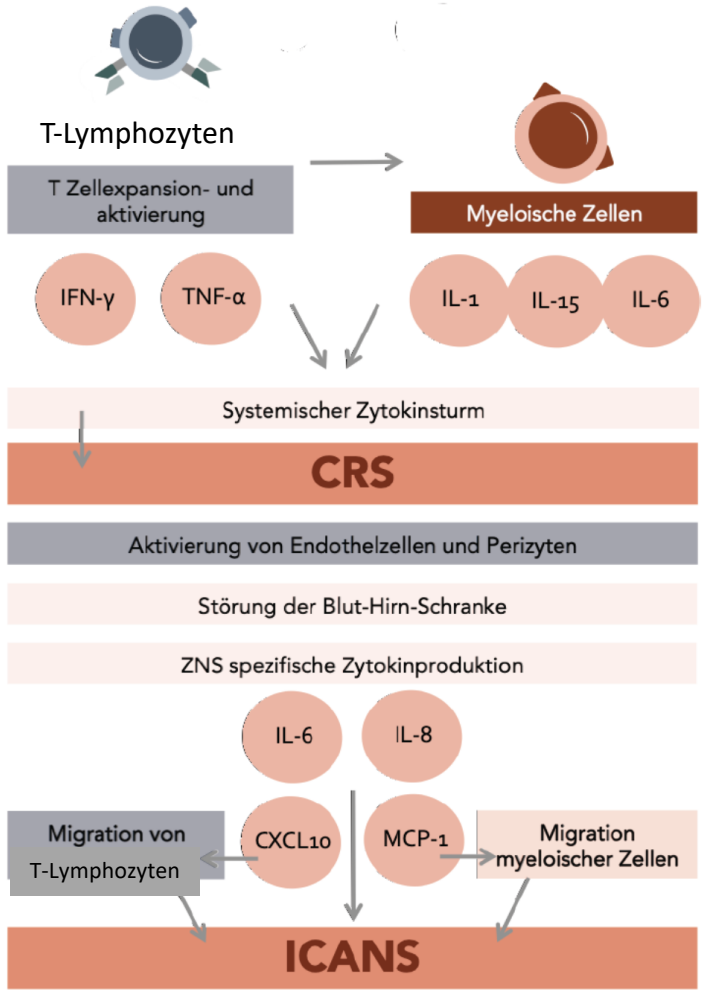


CRS: Zytokine-Freisetzungssyndrom

Vitalzeichen	**CRS Grad 1**	**CRS Grad 2**	**CRS Grad 3**	**CRS Grad 4**
Körpertemperatur (°C)	>38°C**	>38°C**	>38°C**	>38°C**
Hypotonie	Keine	**Ohne** Vasopressor-Bedarf	Mit Bedarf an **einem** Vasopressor ± Vaso-pressin	Mit Bedarf an **mehreren** Vasopressoren (außer Vasopressin)
Hypoxie	Keine	Moderater O_2-Bedarf **(≤6 L/min** über NB)	Hoher O_2-Bedarf **(>6 L/min** über NB, RHM, **ohne PAP**)	Mit **PAP**-Bedarf/ Intubati-ons-notwendigkeit

Legende:
** CRS-assoziierte Organtoxizitäten können nach CTCAE v5.0 klassifiziert werden, beeinflussen das ASTCT CRS-Gra-ding aber nicht.*
*** Nicht erklärbar durch alternative Ursachen (v.a. Infektion)*
Abkürzungen: NB – Nasenbrille; RHM – Rückhaltemaske; PAP – positive airway pressure.

ICANS: Immuneffektorzell-assoziierte Neurotoxizitäts-syndrome



ICANS

	ICANS Grad 1	ICANS Grad 2	ICANS Grad 3	ICANS Grad 4
ICE-Score*	7-9	3-6	0-2	0 (Patient nicht erweckbar; keine Fähigkeit zur Testdurchführung)
Bewusstseins-störung	Spontan erweckbar	Durch Ansprache erweckbar	Durch taktilen Reiz erweckbar	Patient ist nicht erweckbar oder nur durch repetitive taktile Reize. Stupor oder Koma
Epileptischer Anfall	N/A	N/A	Jeder Anfall mit rascher, vollständiger Rückbildung, oder nicht konvulsive Anfälle im EEG die auf Intervention ansprechen	Lebensbedrohlicher Anfall (Dauer >5 min), oder repetitive Anfälle ohne Rückkehr zur Baseline
Motorik	N/A	N/A	N/A	Höhergradiges motorisches Defizit (Hemi- oder Paraparese)
Erhöhter ICP oder zerebrales Ödem	N/A	N/A	Fokales zerebrales Ödem in der zerebralen Bildgebung	Diffuses zerebrales Ödem in der zerebralen Bildgebung; Dekortikations- oder Dezerebrationsstarre, oder Abducensparese oder Papillenödem oder Cushing-Reflex (ICP↑ RR↑, HF↓)

ICE (Immun-Effektorzell-assoziierte Encephalopathie)-Score

Kategorie	Aufgabe	Punkte
Orientieren	Jahr	1
	Monat	1
	Stadt	1
	Krankenhaus	1
Benennen	Gegenstand 1	1
	Gegenstand 2	1
	Gegenstand 3	1
Schreiben	Schreiben eines Standardsatzes	1
Konzentrieren	Rückwärtszählen von 100 auf 10 in 10er-Schritten	1
Befolgen	Durchführen einer Geste (z.B. zwei Finger zeigen, Augen schließen, Zunge herausstrecken)	1
ICE SCORE GESAMT		**10**

Therapie von CRS und ICANS

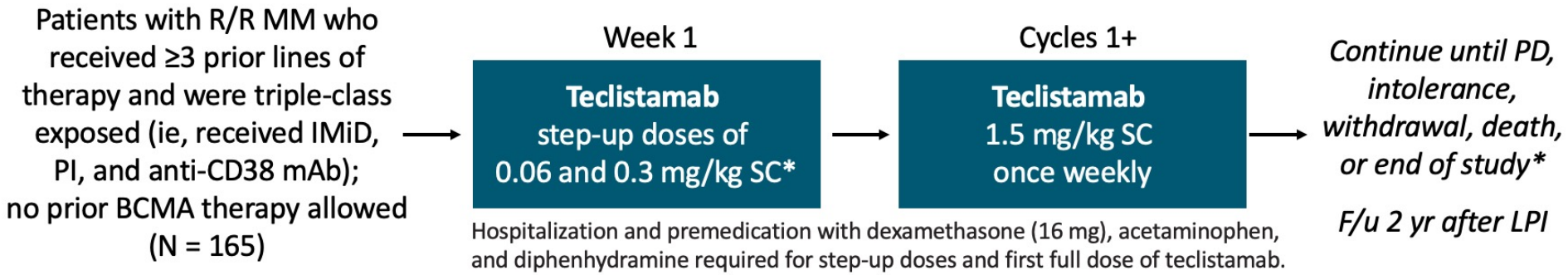
- richtet sich nach dem Schweregrad

- antipyretische Therapie
- Tocilizumab i.v. (IL6-Antikörper)
- Flüssigkeit i.v.
- vasoaktive Medikamente ± Vasopressin i.v.
- Sauerstofftherapie
- Prophylaxe gegen Krampfanfälle (Levetiracetam) i.v.
- Dexamethason/Methylprednisolon i.v.

MajesTEC-1: Teclistamab

Studiendesign

- First-in-human, open-label, dose-escalation/dose-expansion phase I/II trial



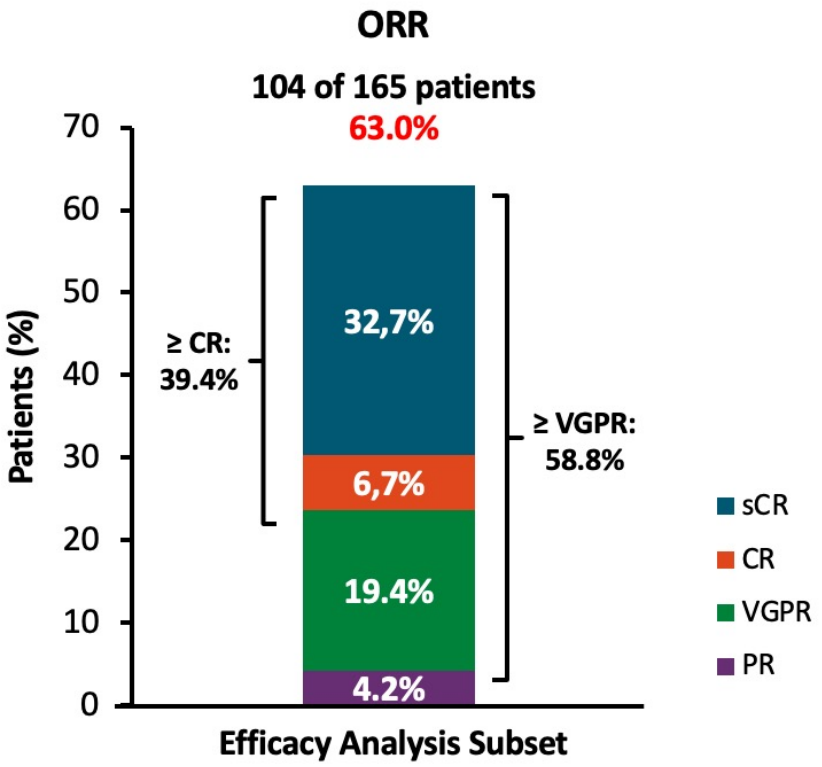
- **Primary endpoint:** ORR
- **Key secondary endpoints:** DoR, ≥VGPR, ≥CR, sCR, TTR, MRD status, PFS, OS, safety, PK, immunogenicity, PROs

*End of study: 2 yr after administration of first dose of teclistamab in last patient enrolled.

Nooka. ASCO 2022. Abstr 8007. Moreau. NEJM. 2022;[Epub].

Slide credit: clinicaloptions.com

MajesTEC-1: Ansprechraten



- Median follow-up: 14.1 mo (range: 0.3-24.4)
- Median treatment duration: 8.5 mo (range: 0.2-24.4)
- Median relative dose intensity: 93.7%

Nooka. ASCO 2022. Abstr 8007. Moreau. NEJM. 2022;[Epub].

- Responses were durable and deepened over time

MRD Event	All Patients (N = 165)
MRD negative (10^{-5}), n/N (%) ▪ All treated ▪ MRD evaluable	 44/165 (26.7) 44/54 (81.5)
MRD negativity with ≥CR, %	46.2

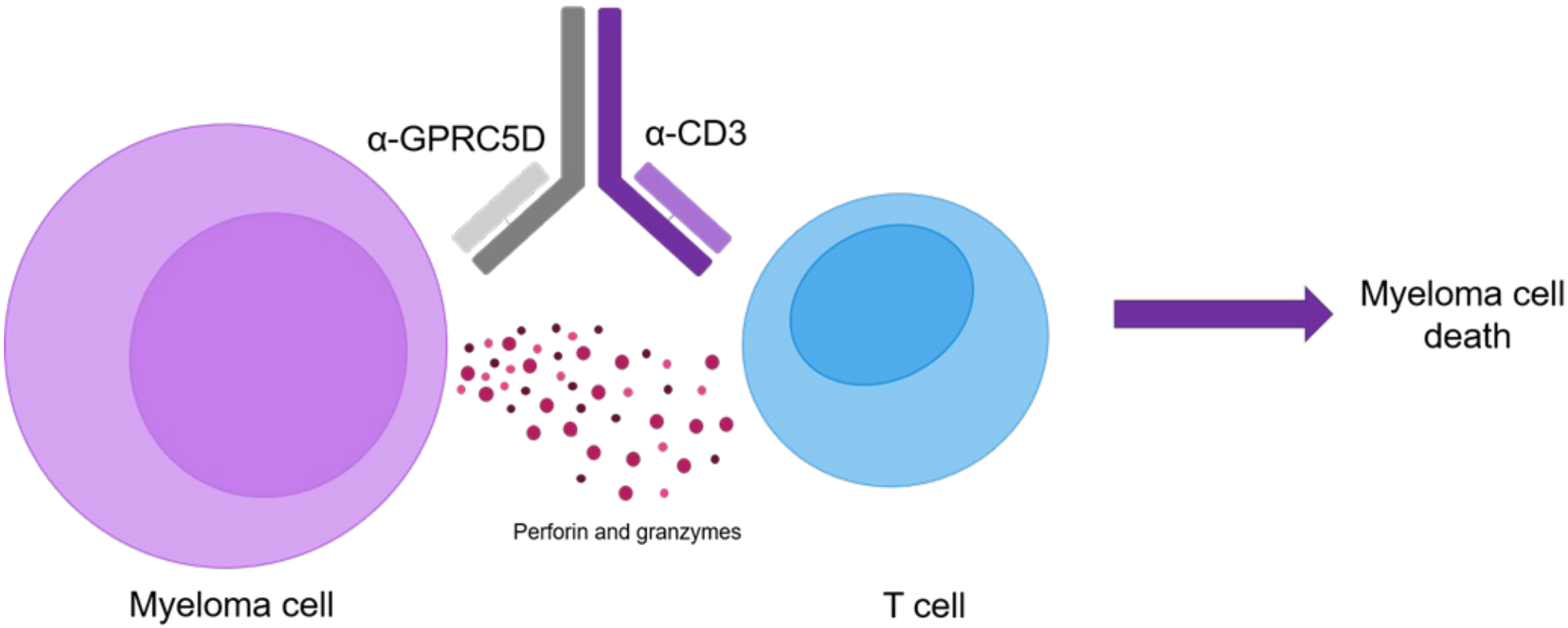
Event	All Patients (N = 165)
Median time to first response, mo (range)*	1.2 (0.2-5.5)
Median time to best response, mo (range)*	3.8 (1.1-16.8)
Median DoR, mo (95% CI)	18.4 (14.9-NE)

*n = 104.

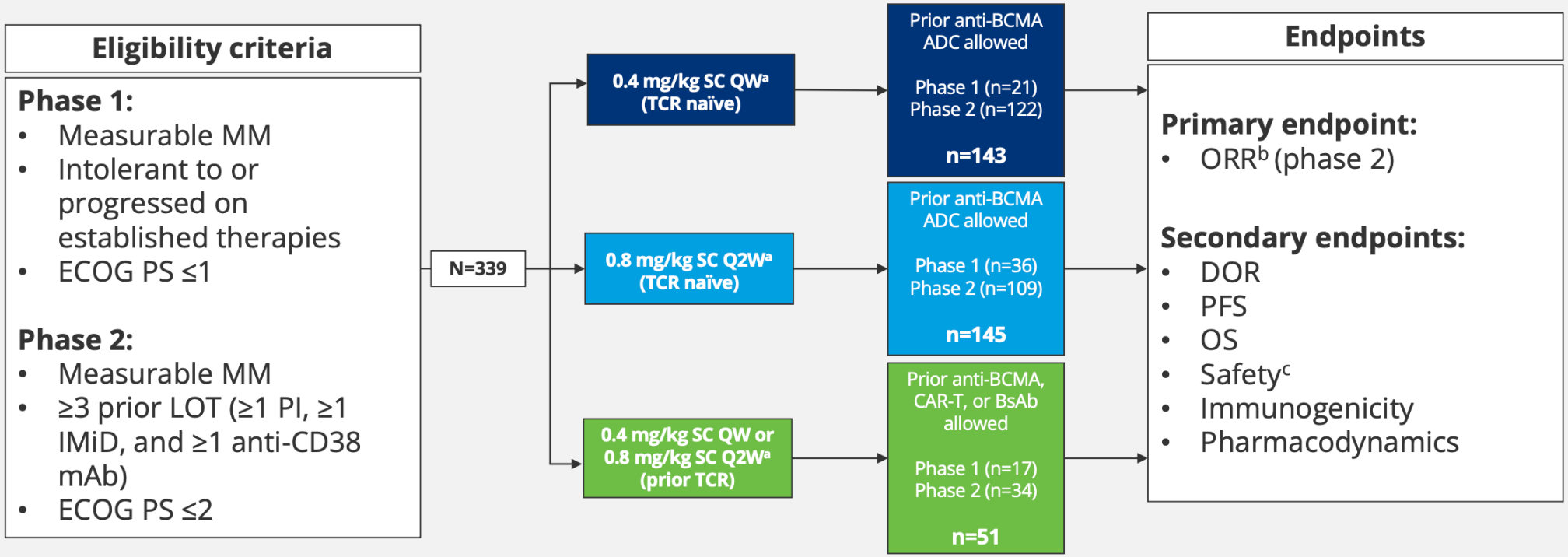
CCO

Slide credit: clinicaloptions.com

Talquetamab



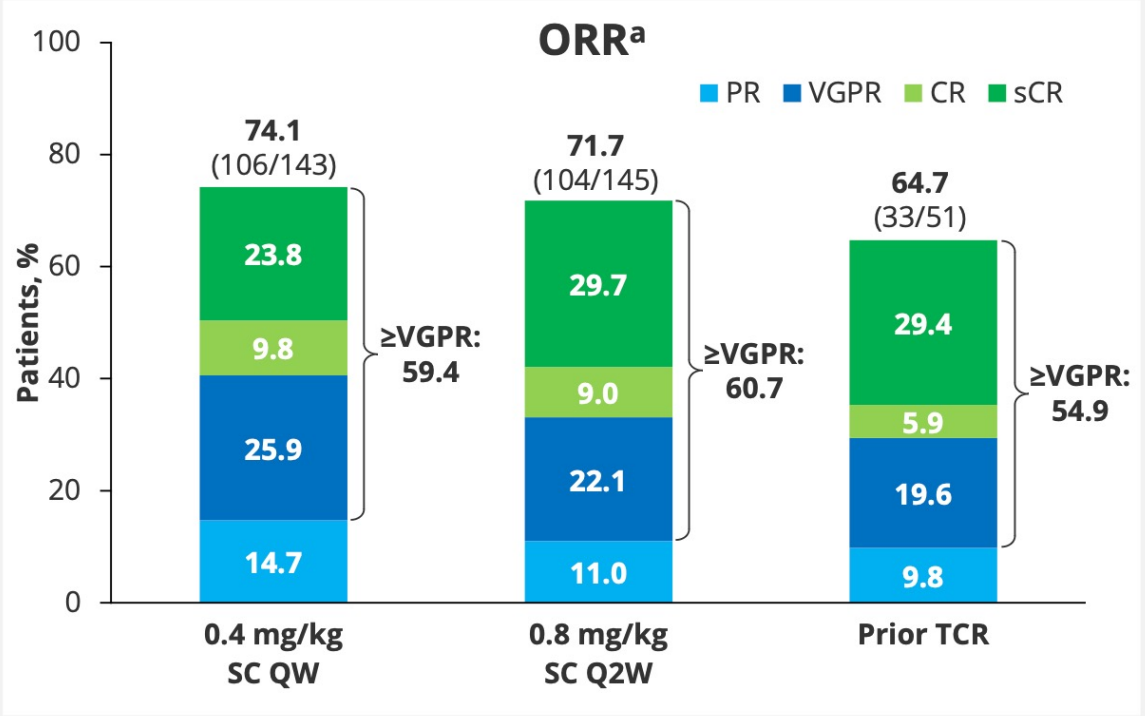
MonumenTAL-1: Studiendesign



[a]With 2–3 step-up doses. [b]Assessed by independent review committee using International Myeloma Working Group criteria. [c]CRS and ICANS were graded by American Society for Transplantation and Cellular Therapy criteria; all other AEs were graded by CTCAE v4.03. ADC, antibody-drug conjugate; AE, adverse event; BCMA, B-cell maturation antigen; BsAb, bispecific antibody; CAR-T, chimeric antigen receptor T-cell; CD38, cluster of differentiation 38; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ICANS, immune effector cell-associated neurotoxicity syndrome; IMiD, immunomodulatory drug; LOT, lines of therapy; mAb, monoclonal antibody; MM, multiple myeloma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; Q2W, every other week; QW, weekly; SC, subcutaneous; TCR, T-cell redirection therapy.

MonumenTAL-1: Ansprechraten

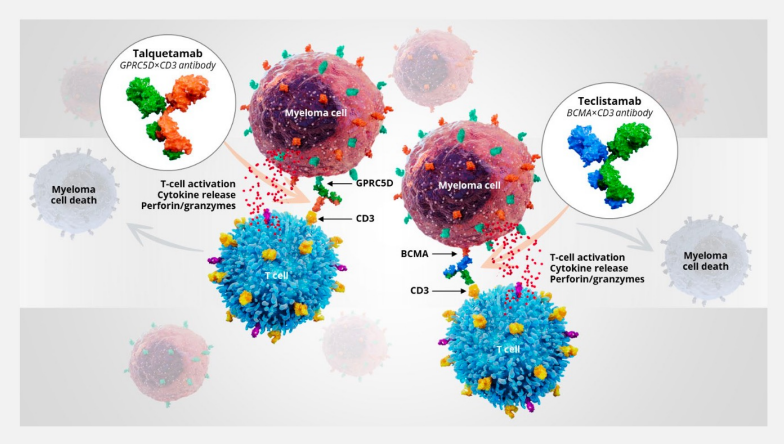
- In the prior TCR cohort, ORR was:
  - 75.0% (n=27/36) with prior CAR-T therapy
  - 44.4% (n=8/18) with prior BsAb
- ORR was consistent across traditionally high-risk subgroups:
  - Cytogenetic risk, ISS stage III disease, ≥4 prior LOT, refractoriness,[b] and prior belantamab
- Patients with EMD had lower ORR:
  - 31–49% with EMD
  - 80–82% without EMD



Data cut-off date: January 17, 2023.
[a]Assessed by independent review committee using International Myeloma Working Group criteria. Due to rounding, individual response rates may not sum to the ORR. [b]Triple-class refractory, penta-drug refractory, and refractory to last line of therapy.
BsAb, bispecific antibody; CAR-T, chimeric antigen receptor T-cell; CR, complete response; EMD, extramedullary disease; ISS, International Staging System; LOT, lines of therapy; ORR, overall response rate; PR, partial response; Q2W, every other week; QW, weekly; SC, subcutaneous; sCR, stringent CR; TCR, T-cell redirection therapy; VGPR, very good partial response.

Teclistamab + Talquetamab

$$T + T = T^2$$



First Results From The RedirecTT-1 Study With Teclistamab + Talquetamab Simultaneously Targeting BCMA and GPRC5D in Patients With Relapsed/Refractory Multiple Myeloma

María-Victoria Mateos[1], Daniel Morillo[2], Moshe Gatt[3], Michael Sebag[4], Kihyun Kim[5], Chang-Ki Min[6], Albert Oriol[7], Enrique M Ocio[8], Sung-Soo Yoon[9], Yaël C Cohen[10], Michael P Chu[11], Paula Rodríguez-Otero[12], Irit Avivi[13], Yue Guo[14], Maria Krevvata[14], Michelle R Peterson[14], Melissa Beelen[14], Jill Vanak[14], Arnob Banerjee[14], Hila Magen[15]

[1]Hospital of Salamanca/IBSAL/CIC/CIBERONC, Salamanca, Spain; [2]Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain; [3]Hadassah Hebrew University Medical Center, Jerusalem, Israel; [4]McGill University and MUHC, Montreal, Quebec, Canada; [5]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [6]Seoul St. Mary's Hospital, Seoul, South Korea; [7]Hospital Germans Trias i Pujol, Badalona, Barcelona, Spain; [8]Marqués de Valdecilla University Hospital, Santander, Spain; [9]Seoul National University College of Medicine, Seoul, South Korea; [10]Tel-Aviv Sourasky (Ichilov) Medical Center, and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel University; [11]Alberta Health Services, Edmonton, Alberta, Canada; [12]Clínica Universidad de Navarra, CIMA, CIBERONC, IDISNA, Pamplona, Spain; [13]Tel Aviv Sourasky Medical Center, Tel Aviv, Israel; [14]Janssen Research & Development, Spring House, PA, USA; [15]Chaim Sheba Medical Center, Ramat-Gan, Sackler Faculty of Medicine, Tel Aviv University, Israel

Presented at the European Hematology Association (EHA) 2023 Hybrid Congress; June 8–11, 2023; Frankfurt, Germany

RedirecTT-1: Studiendesign

Primary objectives

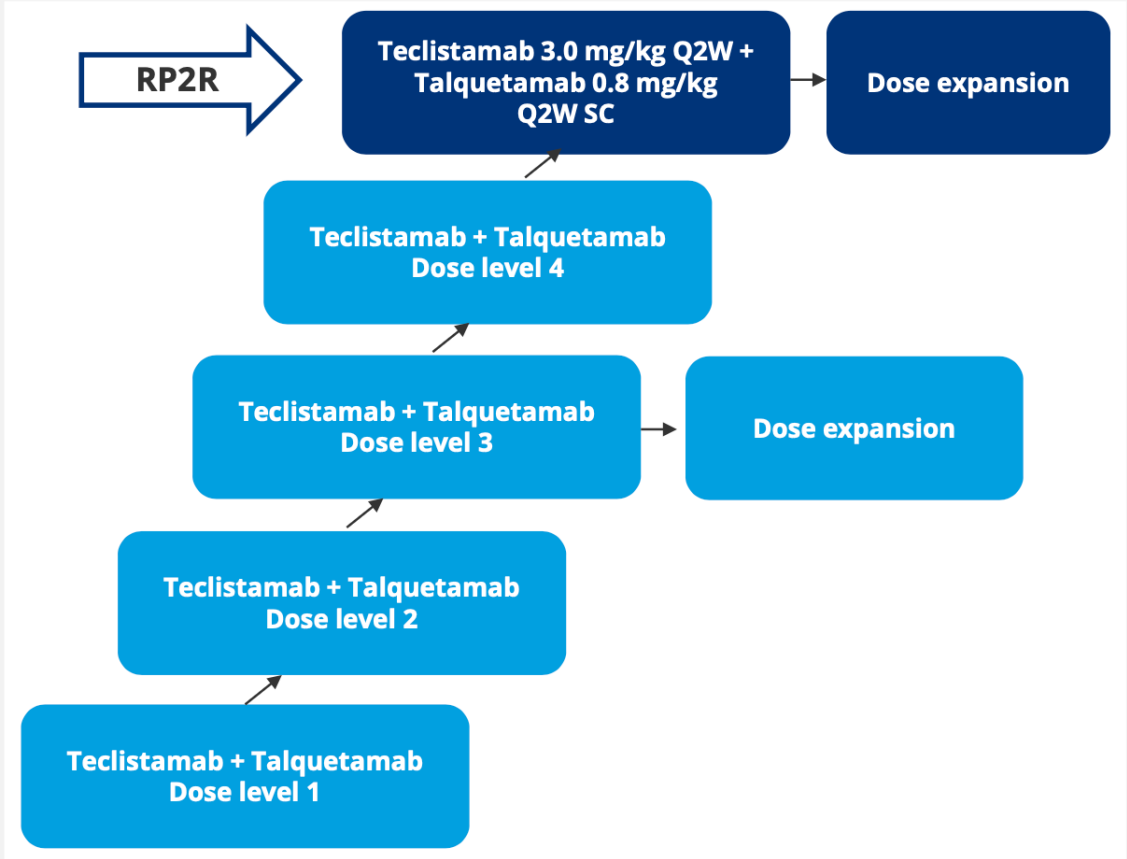
- Evaluate safety
- Identify RP2R(s) and schedule for the combination

Secondary objectives

- Preliminary anticancer activity of each study treatment at RP2R(s) in Part 2, PK, immunogenicity

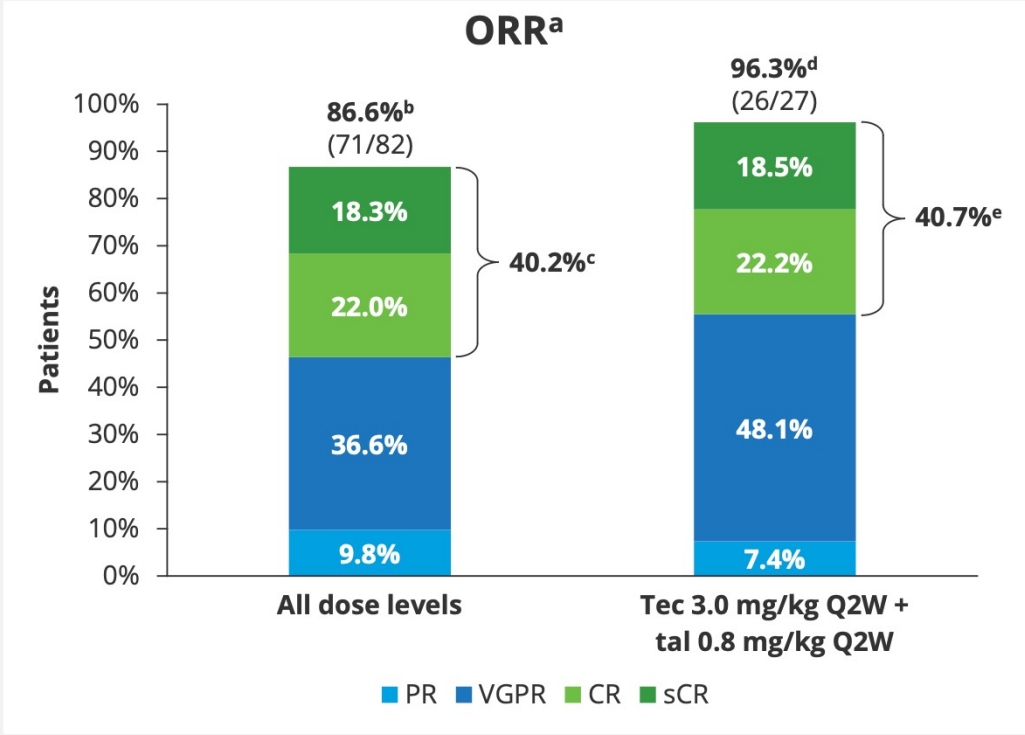
Key eligibility criteria

- Measurable MM
- RR or intolerant to established therapies, including last LOT
- Exposed to a PI, IMiD, and anti-CD38 mAb



IMiD, immunomodulatory drug; LOT, line of therapy; mAb, monoclonal antibody; MM, multiple myeloma; PI, proteasome inhibitor; PK, pharmacokinetics; Q2W, every other week; RP2R, recommended phase 2 regimen; RR, relapsed/refractory; SC, subcutaneous.

RedirecTT-1: Ansprechraten

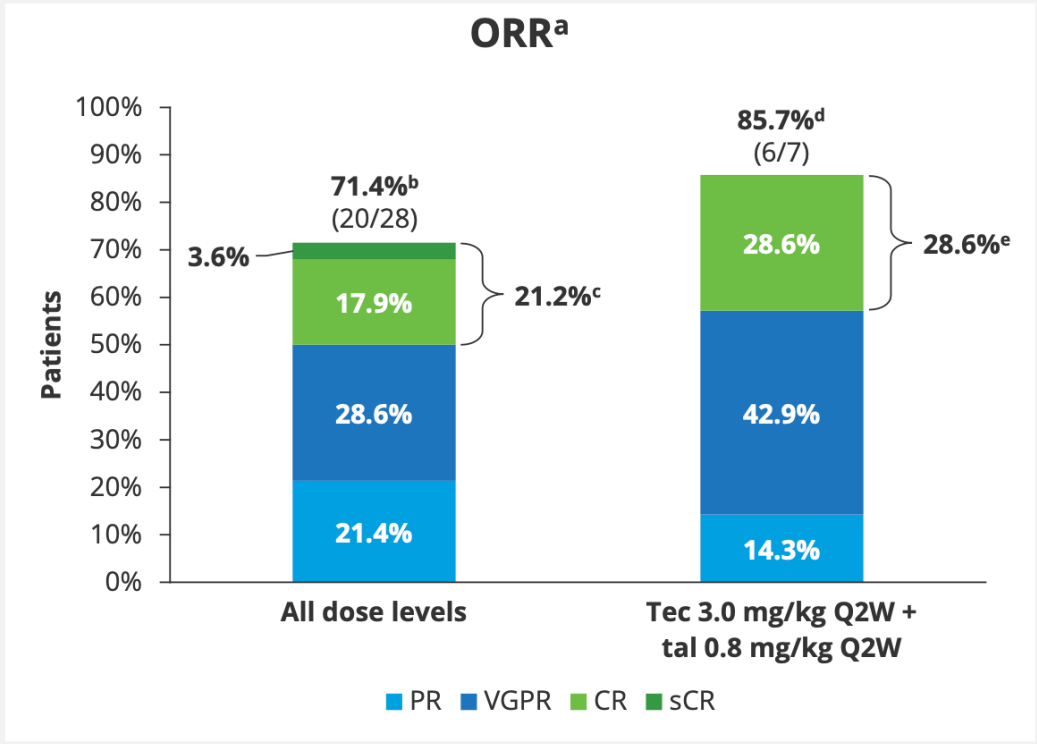


- ORR was high (86.6%) across all dose levels and 96.3% at the RP2R
- At data cut-off, 61% (57/93) of patients remained on treatment

	All dose levels (N=93)	Tec 3.0 mg/kg Q2W + tal 0.8 mg/kg Q2W (n=34)
Median follow-up, months (range)	13.4 (0.3–25.6)	8.1 (0.7–15.0)
Median DOR,[f] months (95% CI)	NE (NE–NE)	NE (NE–NE)
Median time to first response,[f] months (range)	1.97 (0–7.7)	1.48 (0–4.0)
Median time to best response,[f] months (range)	3.98 (1.1–15.7)	3.22 (1.4–10.7)
Median PFS,[g] months (95% CI)	20.9 (13.0–NE)	NE (9.9–NE)
9-month PFS rate[g] (95% CI)	70.1 (58.0–79.4)	77.1 (50.8–90.5)

Data cut-off date, March 16, 2023.
[a]Response was assessed by investigators, based on International Myeloma Working Group criteria; response-evaluable patients have received ≥1 study treatment and have ≥1 postbaseline response evaluation by investigator. [b]95% CI, 77.3–93.1%. [c]95% CI, 29.6–51.7%. [d]95% CI, 81.0–99.9%. [e]95% CI, 22.4–61.2%. [f]Includes patients with confirmed responses. [g]All treated patients. CR, complete response; DOR, duration of response; NE, not estimable; ORR, overall response rate; PFS, progression-free survival; PR, partial response; Q2W, every other week; RP2R, recommended phase 2 regimen; sCR, stringent complete response; VGPR, very good partial response.

RedirecTT-1: Ansprechraten bei extramedullärem Befall



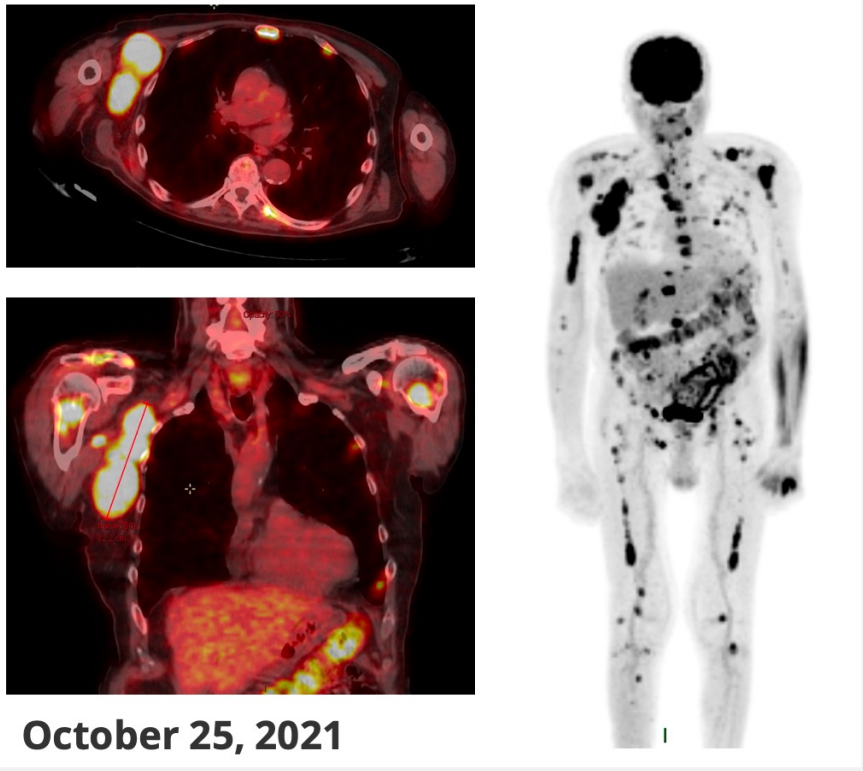
- All were soft tissue plasmacytomas
- At the RP2R (n=11):
  - Median follow-up, 7.2 mo (range 0.7–14.2)
  - 85.7% (6/7 evaluable) ORR
  - 28.6% (2/7 evaluable) ≥CR

	All dose levels (N=35)	Tec 3.0 mg/kg Q2W + tal 0.8 mg/kg Q2W (N=11)
Median DOR,[f] months (95% CI)	12.9 (4.17–NE)	NE (4.17–NE)
Median PFS,[g] months (95% CI)	6.1 (2.5–9.9)	9.9 (2.4–NE)

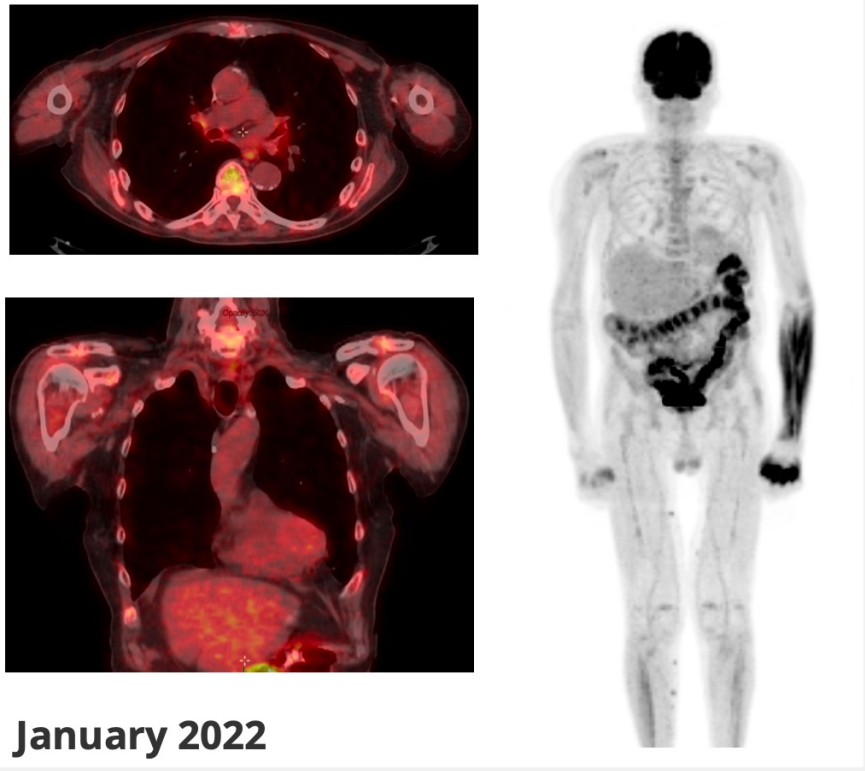
Data cut-off date, March 16, 2023.
[a]Response was assessed by investigators, based on International Myeloma Working Group criteria; response-evaluable patients have received ≥1 study treatment and have ≥1 postbaseline response evaluation by investigator. [b]95% CI, 51.3–86.8%. [c]95% CI, 8.3–41.0%. [d]95% CI, 42.1–99.6%. [e]95% CI, 3.7–71.0%. [f]Includes patients with confirmed responses. [g]All treated patients.
CR, complete response; DOR, duration of response; NE, not estimable; ORR, overall response rate; PFS, progression-free survival; PR, partial response; Q2W, every other week; RP2R, recommended phase 2 regimen; sCR, stringent complete response; VGPR, very good partial response.

RedirecTT-1: Patient mit extramedullärem Befall

- 74-year-old male, penta refractory, 6 prior LOT including ASCT, belantamab mafodotin, and prior RT to humerus



October 25, 2021



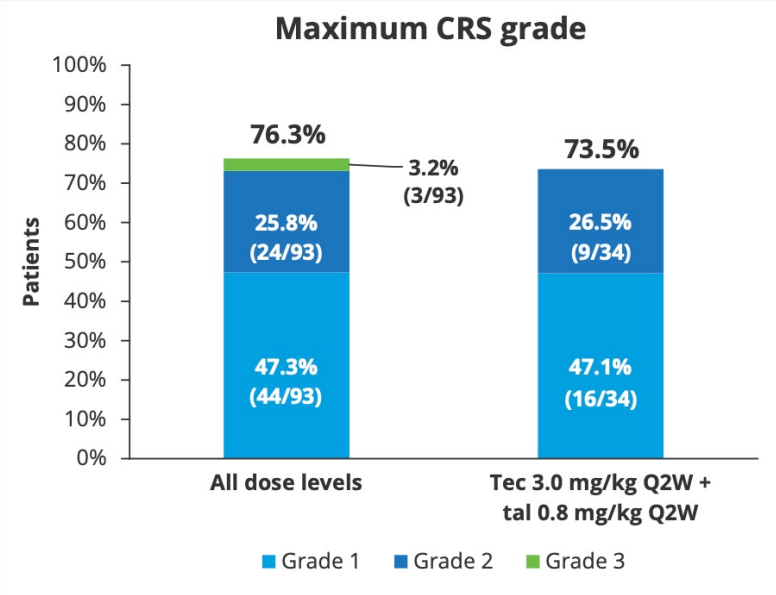
January 2022

ASCT, autologous stem cell transplant; LOT, line of therapy; RT, radiotherapy.

RedirecTT-1: Häufigkeit und Schweregrad von CRS nicht erhöht

	All dose levels (N=93)	Tec 3.0 mg/kg Q2W + tal 0.8 mg/kg Q2W (n=34)
Patients with CRS,[a] n (%)	71 (76.3)	25 (73.5)
Time to onset (days)[b], median (range)	2 (1–5)	2 (1–4)
Duration (days), median (range)	2 (1–8)	2 (1–4)
Patients who received supportive measures,[c] n (%)		
Tocilizumab[d]	25 (26.9)	7 (20.6)
Steroids	4 (4.3)	0
Oxygen	7 (7.5)	0
Vasopressor	1 (1.1)	0

- The majority of CRS events occurred during step-up dosing or cycle 1
- All CRS events resolved



Data cut-off date, March 16, 2023
[a]CRS was graded by ASTCT criteria. [b]Relative to the most recent dose. [c]Patients could receive >1 supportive therapy. [d]Tocilizumab was allowed for all CRS events and was allowed at grade 1 CRS; the protocol did not recommend prophylactic tocilizumab use.
ASTCT, American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome; Q2W, every other week.

TRIMM-2

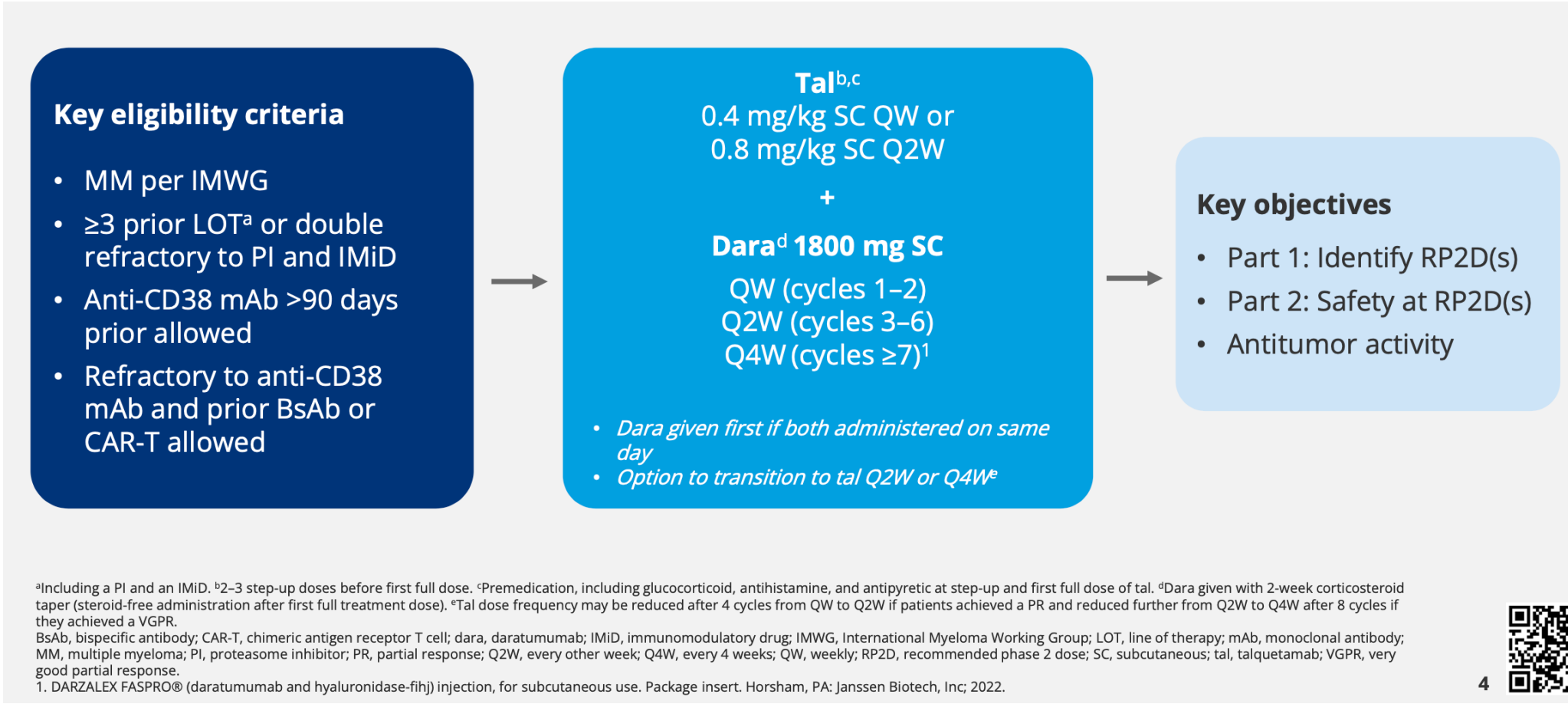
Talquetamab + Daratumumab in Patients With Relapsed/Refractory Multiple Myeloma: Updated TRIMM-2 Results

Nizar Bahlis[1], Katja Weisel[2], María-Victoria Mateos[3], Hartmut Goldschmidt[4], Tom Martin[5], Daniel Morillo[6], Donna Reece[7], Paula Rodríguez-Otero[8], Manisha Bhutani[9], Anita D'Souza[10], Albert Oriol[11], Laura Rosiñol[12], Bhagirathbhai Dholaria[13], Kalpana Bakshi[14], Lijuan Kang[14], Lien Vandenberk[15], M Damiette Smit[16], Ralph Wäsch[17], Niels van de Donk[18], Ajai Chari[19]

[1]Arnie Charbonneau Cancer Institute, University of Calgary, Calgary, AB, Canada; [2]University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [3]University Hospital of Salamanca/IBSAL/CIC/CIBERONC, Salamanca, Spain; [4]Medizinische Klinik V, Universitätsklinikum Heidelberg and Nationales Centrum für Tumorerkrankungen, Heidelberg, Germany; [5]Helen Diller Family Comprehensive Cancer Center, San Francisco Medical Center, University of California, San Francisco, CA, USA; [6]Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain; [7]Princess Margaret Cancer Centre, Toronto, ON, Canada; [8]Clínica Universidad de Navarra, CIMA, CIBERONC, IDISNA, Pamplona, Spain; [9]Levine Cancer Institute/Atrium Health, Charlotte, NC, USA; [10]Medical College of Wisconsin, Milwaukee, WI, USA; [11]Institut Català d'Oncologia and Institut Josep Carreras, Hospital Germans Trias i Pujol, Barcelona, Spain; [12]Hospital Clínic de Barcelona, IDIBAPS, Barcelona, Spain; [13]Vanderbilt University Medical Center, Nashville, TN, USA; [14]Janssen Research & Development, Spring House, PA, USA; [15]Janssen Research & Development, Antwerp, Belgium; [16]Janssen Biologics Europe, Leiden, Netherlands; [17]Freiburg University Medical Center, Freiburg, Germany; [18]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, Netherlands; [19]Mount Sinai School of Medicine, New York, NY, USA.

Presented at the European Hematology Association (EHA) 2023 Hybrid Congress; June 8–11, 2023; Frankfurt, Germany

TRIMM-2: Studiendesign

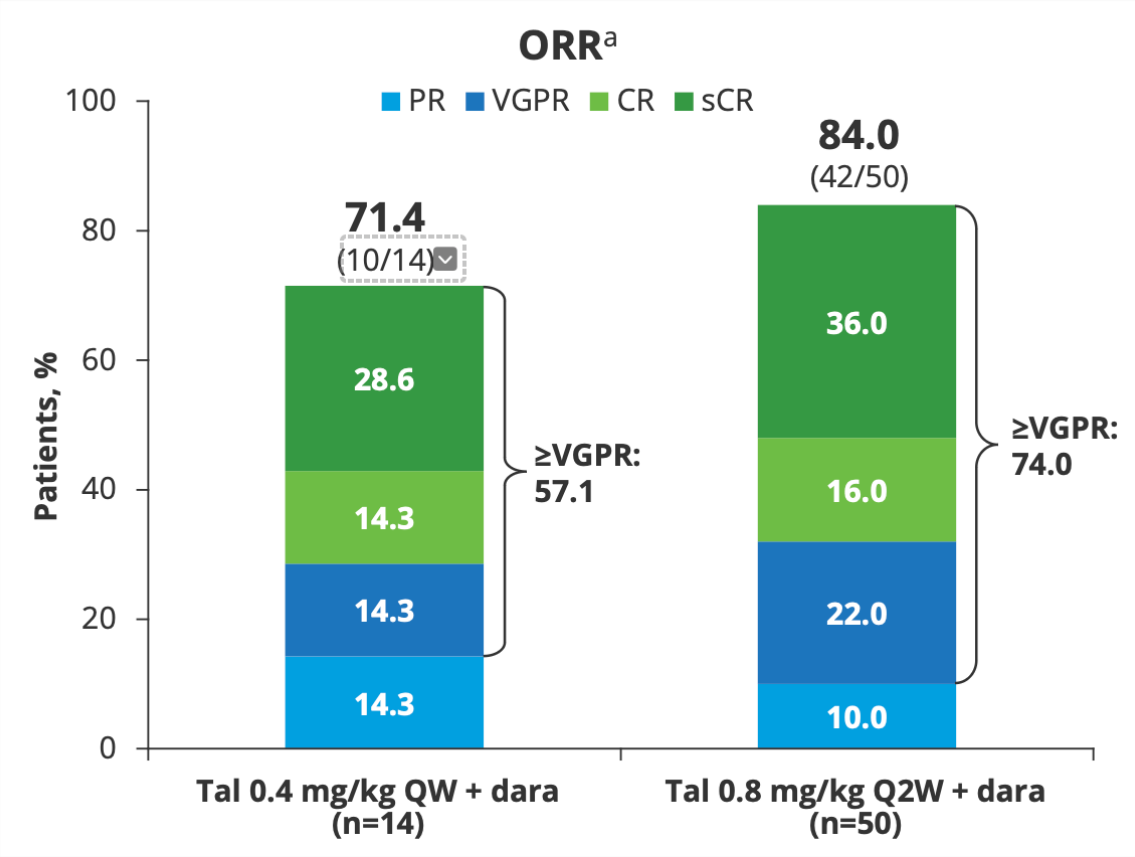


[a]Including a PI and an IMiD. [b]2–3 step-up doses before first full dose. [c]Premedication, including glucocorticoid, antihistamine, and antipyretic at step-up and first full dose of tal. [d]Dara given with 2-week corticosteroid taper (steroid-free administration after first full treatment dose). [e]Tal dose frequency may be reduced after 4 cycles from QW to Q2W if patients achieved a PR and reduced further from Q2W to Q4W after 8 cycles if they achieved a VGPR.

BsAb, bispecific antibody; CAR-T, chimeric antigen receptor T cell; dara, daratumumab; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; LOT, line of therapy; mAb, monoclonal antibody; MM, multiple myeloma; PI, proteasome inhibitor; PR, partial response; Q2W, every other week; Q4W, every 4 weeks; QW, weekly; RP2D, recommended phase 2 dose; SC, subcutaneous; tal, talquetamab; VGPR, very good partial response.

1. DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) injection, for subcutaneous use. Package insert. Horsham, PA: Janssen Biotech, Inc; 2022.

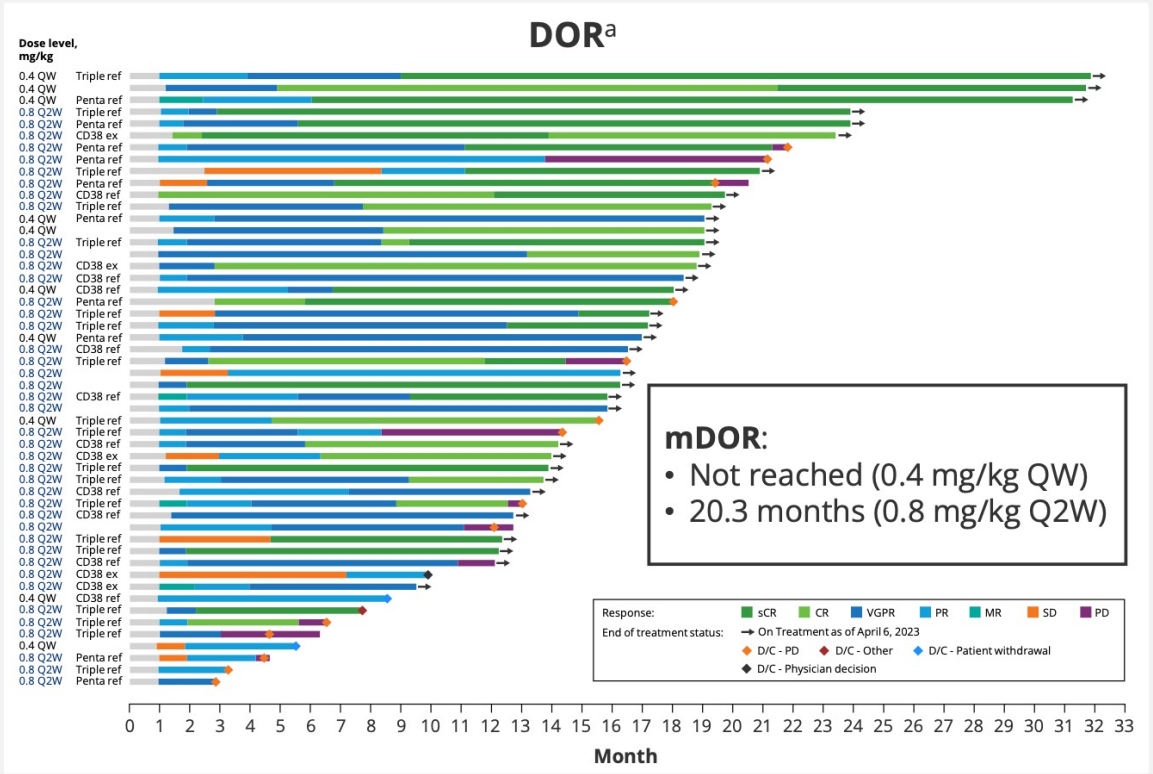
TRIMM-2: Tieferes Ansprechen mit längerem Follow-up



Parameter	Tal 0.4 mg/kg QW + dara (n=14)	Tal 0.8 mg/kg Q2W + dara (n=51)
Median (range) follow-up, mo	16.8 (1.9–31.0)	15.0 (1.0–23.3)
Median (range) time to first response, mo	1.0 (0.9–2.4)	1.0 (0.9–8.3)
ORR in anti-CD38, n (%)		
Naïve	3/3 (100.0)	5/5 (100.0)
Exposed	7/11 (63.6)	37/45 (82.2)
Refractory	7/11 (63.6)	32/40 (80.0)
ORR in T-cell redirection therapy[b] exposed, n (%)	4/6 (66.7)[c]	15/19 (78.9)
CAR-T	1/2 (50.0)	8/9 (88.9)
BsAb	4/5 (80.0)	7/10 (70.0)

Data cut-off: April 6, 2023.
[a]Response was assessed by investigators in response-evaluable patients, based on IMWG criteria. Percentages may not total due to rounding. [b]Prior T-cell redirection therapy includes BCMA and non-BCMA bispecific antibody or CAR-T therapies. [c]One patient received BsAb and CAR-T therapy.
BCMA, B-cell maturation antigen; BsAb, bispecific antibody; CAR-T, chimeric antigen receptor T cell; CR, complete response; dara, daratumumab; IMWG, International Myeloma Working Group; ORR, overall response rate; PR, partial response; Q2W, every other week; QW, weekly; sCR, stringent complete response; tal, talquetamab; VGPR, very good partial response.

TRIMM-2: Ansprechraten waren anhaltend und verbesserten sich im Verlauf



- Proportion of responders who remain in response at 12 months: 80.9% (93.3% with ≥CR)
  - Prior T-cell redirection: 88.4%
  - Patients who switched to less-frequent dosing: 94.1%
- 65.4% of responders remain on therapy
  - 63.6% in anti-CD38 exposed
  - 61.5% in anti-CD38 refractory

Data cut-off: April 6, 2023.
[a]Response was assessed by investigators, based on IMWG criteria. 90.0% of events remain censored in the tal 0.4 mg/kg QW + dara cohort, and 66.7% of events remain censored in the tal 0.8 mg/kg Q2W + dara cohort.
AE, adverse event; CR, complete response; dara, daratumumab; D/C, discontinued; ex, exposed; IMWG, International Myeloma Working Group; mDOR, median duration of response; MR, minimal response; PD, progressive disease; PR, partial response; Q2W, every other week; QW, weekly; ref, refractory; sCR, stringent complete response; SD, stable disease; tal, talquetamab; VGPR, very good partial response.

TRIMM-2: keine zusätzlichen nicht-hämatologische Toxizitäten

Nonhematologic AEs (≥25%), n (%)	Tal 0.4 mg/kg QW + dara (n=14)		Tal 0.8 mg/kg Q2W + dara (n=51)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Oral AEs[a]	12 (85.7)	0 (0)	46 (90.2)	2 (3.9)
Skin AEs[b]	10 (71.4)	2 (14.3)	43 (84.3)	4 (7.8)
CRS	10 (71.4)	0 (0)	41 (80.4)	0 (0)
Nail AEs[c]	8 (57.1)	0 (0)	35 (68.6)	1 (2.0)
Fatigue	11 (78.6)	0 (0)	20 (39.2)	1 (2.0)
Pyrexia	5 (35.7)	0 (0)	19 (37.3)	2 (3.9)
Pruritus	6 (42.9)	0 (0)	16 (31.4)	0 (0)
Decreased appetite	4 (28.6)	1 (7.1)	17 (33.3)	1 (2.0)
Dizziness	6 (42.9)	0 (0)	15 (29.4)	0 (0)
Weight decreased	7 (50.0)	0 (0)	14 (27.5)	0 (0)
Back pain	4 (28.6)	0 (0)	15 (29.4)	1 (2.0)
Diarrhea	5 (35.7)	0 (0)	13 (25.5)	1 (2.0)
Headache	3 (21.4)	0 (0)	15 (29.4)	0 (0)
Arthralgia	5 (35.7)	0 (0)	12 (23.5)	0 (0)

- Skin, nail, and oral AEs were common but mostly low grade
- AEs led to dose reductions of tal in 16.9% and to discontinuation in 1.5% (1 patient, due to toxic skin eruption)
- Rashes managed with topical corticosteroids or short course of oral corticosteroids
- Dysgeusia and dry mouth managed with mouth washes, saliva stimulants, or dose modifications
  - 76.9% had dysgeusia and 6.2% required tal dose reduction

Data cut-off: April 6, 2023. [a]Includes dysgeusia, dry mouth, stomatitis, ageusia, hypogeusia, and taste disorder. [b]Includes skin exfoliation, dry skin, pruritus, rash maculopapular, rash, erythema, and rash erythematous. [c]Includes nail disorder, onychomadesis, nail dystrophy, nail discoloration, nail ridging, onycholysis, nail bed disorder, and onychalgia.
AE, adverse event; CRS, cytokine release syndrome; dara, daratumumab; Q2W, every other week; QW, weekly; tal, talquetamab.

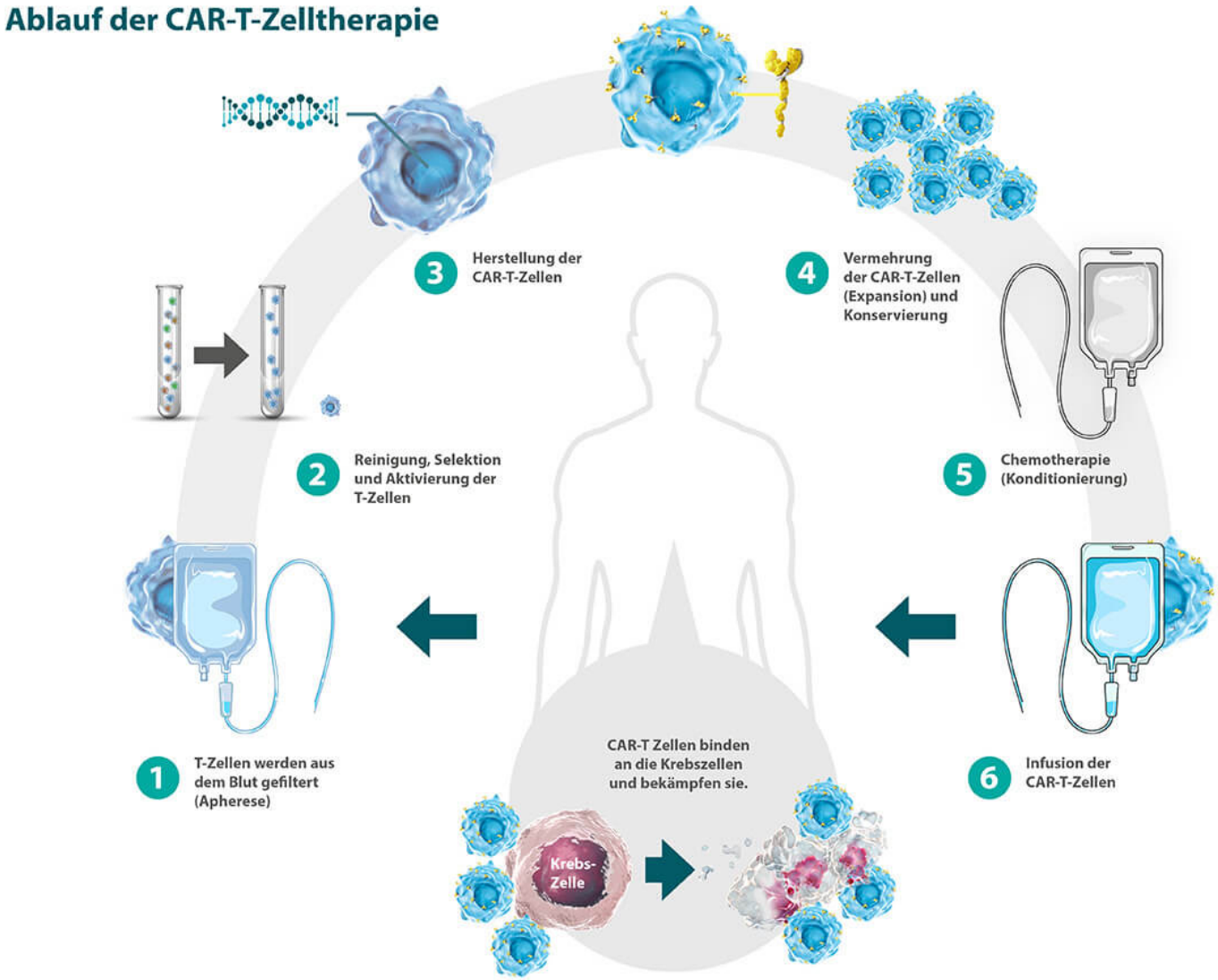
MagnetisMM-3

Title: ELRANATAMAB, A B-CELL MATURATION ANTIGEN (BCMA)-CD3 BISPECIFIC ANTIBODY, FOR PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA: EXTENDED FOLLOW UP AND BIWEEKLY ADMINISTRATION FROM MAGNETISMM-3

- MRD-negativity: 92.0% (n=23/25) of evaluable patients
- Median duration of response (mDOR) has not been reached (95% CI 12.9–NE)

CAR-T-Zell-Therapie

CAR-T-Zell-Therapie



CAR-T-Zell-Therapie

- Derzeit sind die beiden CAR-T-Zell-Produkte Ide-cel und Cilta-cel beim Multiplen Myelom zugelassen, in Österreich aber noch nicht verfügbar.

- Die Zulassung von Ide-cel basiert auf der KarMMa-Studie, die Ansprechrate lag bei 72%.
- Die Daten der CARTITUDE-1-Studie führten zur Zulassung von Cilta-cel, welches eine Ansprechrate von über 90% zeigte.

- Die CAR-T-Zell-Therapie ist eine Therapie, die einmalig verbreicht wird.

- Nebenwirkungen:

  systemische Entzündungsreaktionen (sog. Zytokine-Freisetzungssysteme), neurologische Komplikationen, Infektkomplikationen und Blutbildveränderungen

CARTITUDE-1: Update EHA 2023

Title: CARTITUDE-1 FINAL RESULTS: PHASE 1B/2 STUDY OF CILTACABTAGENE AUTOLEUCEL IN HEAVILY PRETREATED PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA

- mPFS 34.9 Monate (95% CI, 25.2–NE)
- mOS noch nicht erreicht

KarMMa-3: Update EHA 2023

Title: IDECABTAGENE VICLEUCEL (IDE-CEL) VS STANDARD REGIMENS IN PATIENTS WITH TRIPLE-CLASS–EXPOSED (TCE) RELAPSED AND REFRACTORY MULTIPLE MYELOMA (RRMM): A KARMMA-3 ANALYSIS IN HIGH-RISK SUBGROUPS

	High-risk cytogenetics		R-ISS stage III		High tumor burden	
	Ide-cel (n = 107)	Standard regimens (n = 61)	Ide-cel (n = 31)	Standard regimens (n = 14)	Ide-cel (n = 71)	Standard regimens (n = 34)
Median (95% CI) PFS, mo[a]	11.9 (8.0–14.5)	4.2 (2.4–5.7)	5.2 (1.8–7.2)	3.0 (0.8–6.1)	11.0 (7.2–16.2)	4.9 (2.3–10.1)
Unstratified HR (95% CI)[b]	0.608 (0.411–0.899)		0.861 (0.387–1.919)		0.595 (0.367–0.965)	
ORR, n (%)[c]	69 (64.5)	23 (37.7)	14 (45.2)	4 (28.6)	46 (64.8)	18 (52.9)
Unstratified OR (95% CI)[d]	3.00 (1.56–5.76)		2.06 (0.53–8.01)		1.64 (0.71–3.75)	
CRR, n (%)[e]	34 (31.8)	3 (4.9)	5 (16.1)	1 (7.1)	22 (31.0)	3 (8.8)
95% CI	23.0–40.6	0.0–10.3	3.2–29.1	0.0–20.6	20.2–41.7	0.0–18.4

KarMMa-3: Update EHA 2023

Title: IDECABTAGENE VICLEUCEL (IDE-CEL) VS STANDARD REGIMENS IN PATIENTS WITH TRIPLE-CLASS–EXPOSED (TCE) RELAPSED AND REFRACTORY MULTIPLE MYELOMA (RRMM): A KARMMA-3 ANALYSIS IN HIGH-RISK SUBGROUPS

	EMP present		Triple-class refractory	
	Ide-cel (n = 61)	Standard regimens (n = 32)	Ide-cel (n = 71)	Standard regimens (n = 34)
Median (95% CI) PFS, mo[a]	7.2 (4.0–11.8)	2.0 (1.3–3.0)	11.2 (8.7–12.5)	3.5 (2.9–4.7)
Unstratified HR (95% CI)[b]	0.401 (0.248–0.649)		0.458 (0.336–0.624)	
ORR, n (%)[c]	34 (55.7)	6 (18.8)	105 (64.0)	28 (31.5)
Unstratified OR (95% CI)[d]	5.46 (1.96–15.15)		3.88 (2.24–6.72)	
CRR, n (%)[e]	14 (23.0)	1 (3.1)	55 (33.5)	1 (1.1)
95% CI	12.4–33.5	0.0–9.2	26.3-40.8	0.0-3.3

[a]Median and 95% CI are based on Kaplan–Meier approach; [b]Unstratified HR based on univariate Cox proportional hazard model. CI is two-sided; [c]Patients with ≥partial response; [d]Cochran–Mantel–Haenszel test with two-sided Wald CI; [e]Complete response or stringent complete response.
OR, odds ratio; R-ISS, Revised International Staging System.

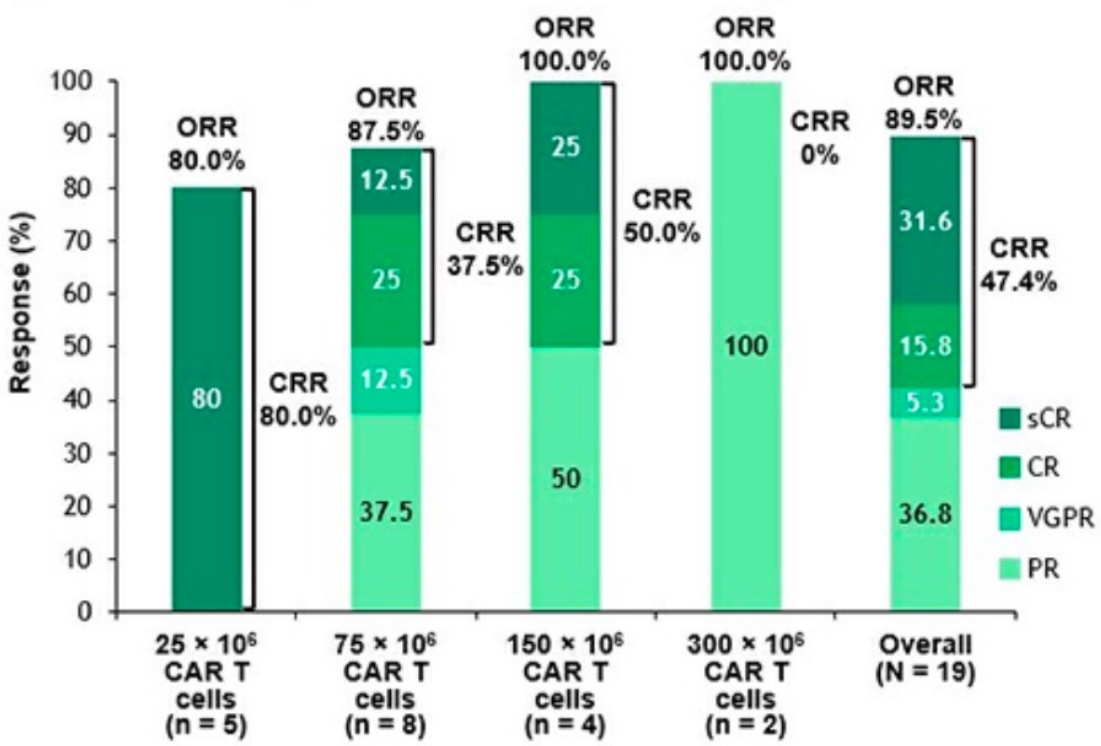
BMS-986393

Title: BMS-986393 (CC-95266), A G PROTEIN–COUPLED RECEPTOR CLASS C GROUP 5 MEMBER D (GPRC5D)–TARGETED CAR T-CELL THERAPY FOR RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM): RESULTS FROM A PHASE 1 STUDY

As of September 7, 2022, 40 pts enrolled and 33 pts received BMS-986393 at doses of 25 (n = 6), 75 (n = 9), 150 (n = 11), 300 (n = 6), and 450 (n = 1) × 10^6 CAR T cells. Among treated pts, 16 (48%) had high-risk cytogenetics (del[17p], t[4;14], and/or t[14;16]) and 15 (45%) had extramedullary plasmacytomas. Eighteen (55%) pts had received prior BCMA-targeted therapies, including BCMA-directed CAR T-cell therapy in 13 (39%) pts. Eight (24%) pts had penta-refractory MM.

Part A includes pts with ≥ 3 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, an anti-CD38 therapy, and autologous stem cell transplant (if eligible). Prior BCMA-directed and CAR T-cell therapies were allowed. After screening and leukapheresis, pts underwent lymphodepletion followed by a single infusion of BMS-986393. Safety and determination of maximum tolerated dose (MTD) and/or recommended phase 2 dose of BMS-986393 were primary objectives.

BMS-986393



[a]Includes all patients who received conforming BMS-986393 cell product, had measurable disease at the last disease assessment prior to BMS-986393 infusion, and had ≥ 1 post-infusion disease-response assessment. The patient in the 450 x 10^6 CAR T-cell group was not included in the set. CAR, chimeric antigen receptor; CR, complete response; CRR, complete response rate; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

Zusammenfassung

- Die bispezifischen Antikörper und die CAR-T-Zelltherapien sind wichtige Meilensteine in der Behandlung des Myeloms. Nebenwirkungen müssen rechtzeitig erkannt und behandelt werden.

- Die Prognose des Multiplen Myeloms wird sich weiterhin deutlich verbessern.

Herzlichen Dank für Ihre Aufmerksamkeit!