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Myeloma Center

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GERMAN-SPEAKING MYELOMA MULTICENTER GROUP

Update zum Multiplen Myelom 2025

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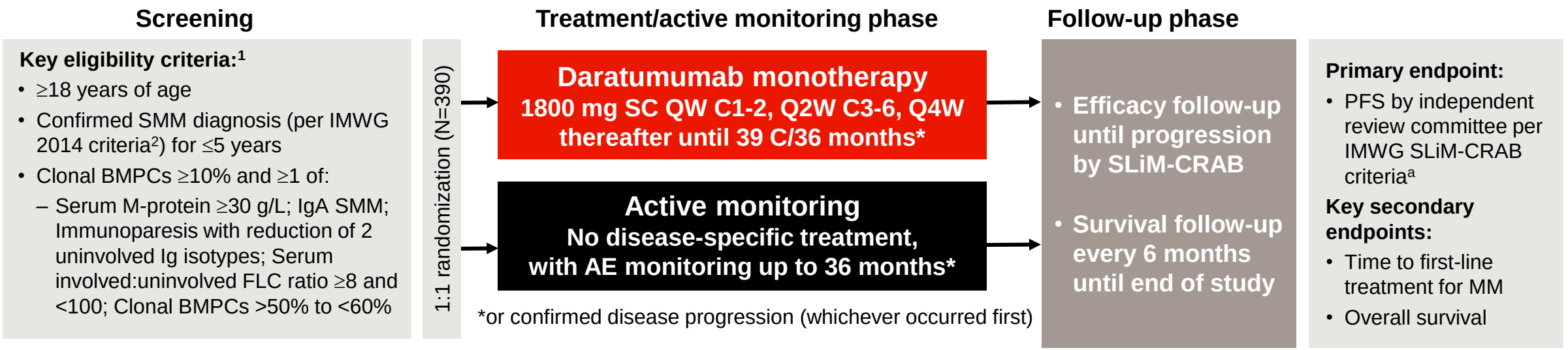
Direktor, Heidelberger Myelomzentrum
Universitätsklinikum Heidelberg

UK HD

1 Smoldering Myeloma

AQUILA: Study Design and Risk Stratification Methods



- For this *post hoc* analysis, outcomes were assessed by:

IMWG 2020 validated risk stratification:
BMPC >20%, M spike >2 g/dL, serum I/U FLC ratio >20
0 factors=low risk; 1 factor=intermediate risk; ≥2 factors=high risk

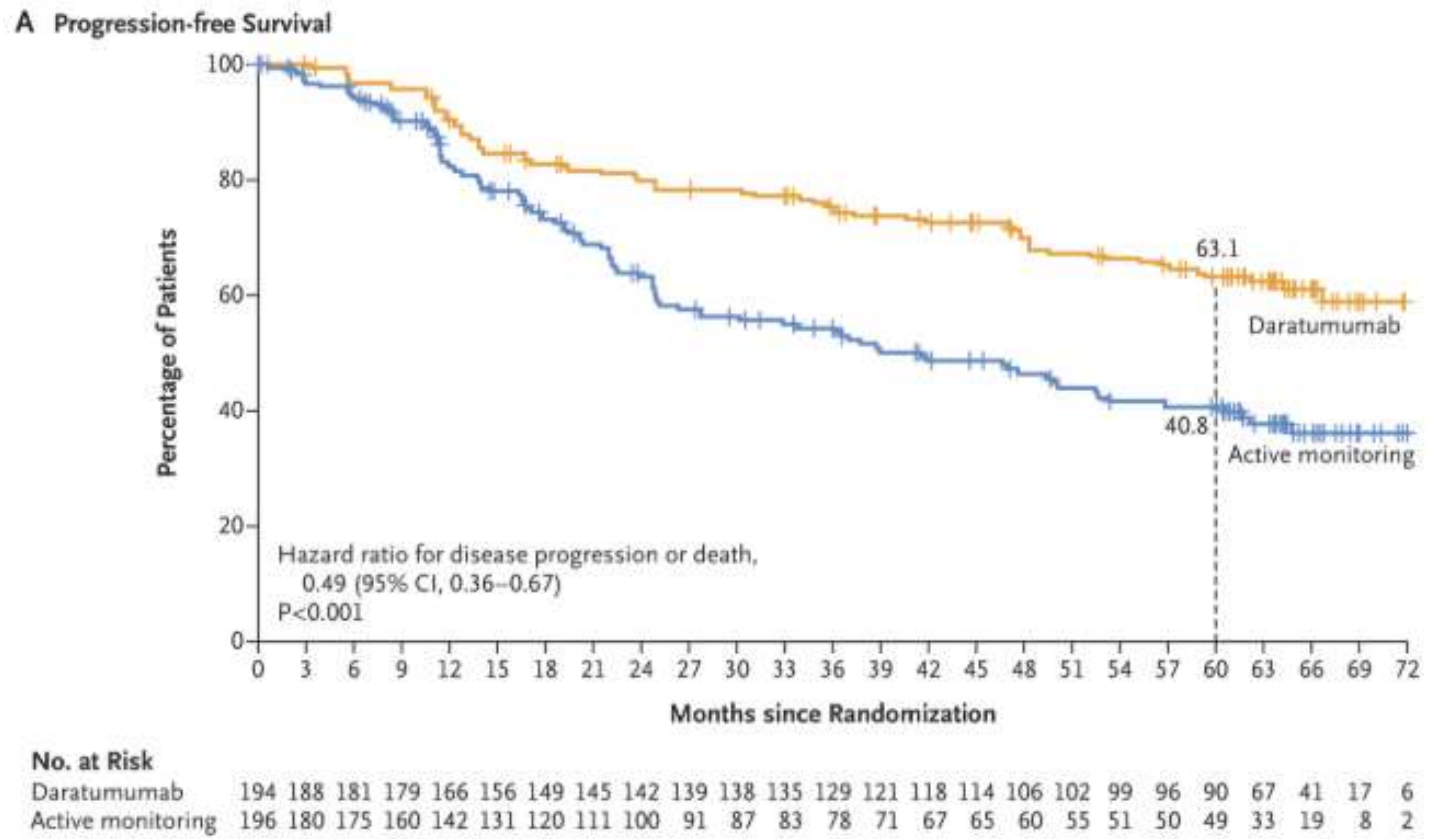
IMWG scoring system:
Points given based on values of serum FLC ratio, M spike g/dL, percentage of BMPCs, and FISH abnormalities
0–4 points=low risk; 5–8 points=low-intermediate risk; 9–12 points=intermediate; >12 points=high risk

Age:
<65 years
65 to <75 years
≥75 years

[a] SLiM-CRAB, ≥60% clonal plasma cells in bone marrow, involved/uninvolved free light chain ratio ≥100 or more with the involved free light chain ≥100 mg/L, magnetic resonance imagine with >1 focal marrow lesion, hypercalcemia, renal insufficiency, anemia, bone lesions. BMPC, bone marrow plasma cell; C, cycle; FLC, free light chain; IMWG, International Myeloma Working Group; M, monoclonal; PFS, progression-free survival; SC, subcutaneous; SMM, smoldering multiple myeloma; QW, once weekly. 1. Dimopoulos MA, et al. *N Engl J Med* 2025;392(18):1777-88. 2. Rajkumar SV, et al. *Lancet Oncol* 2014;15(12):e538-48.

Presented by P Voorhees at the 67th American Society of Hematology (ASH) Annual Meeting; December 6–9, 2025; Orlando, FL, USA

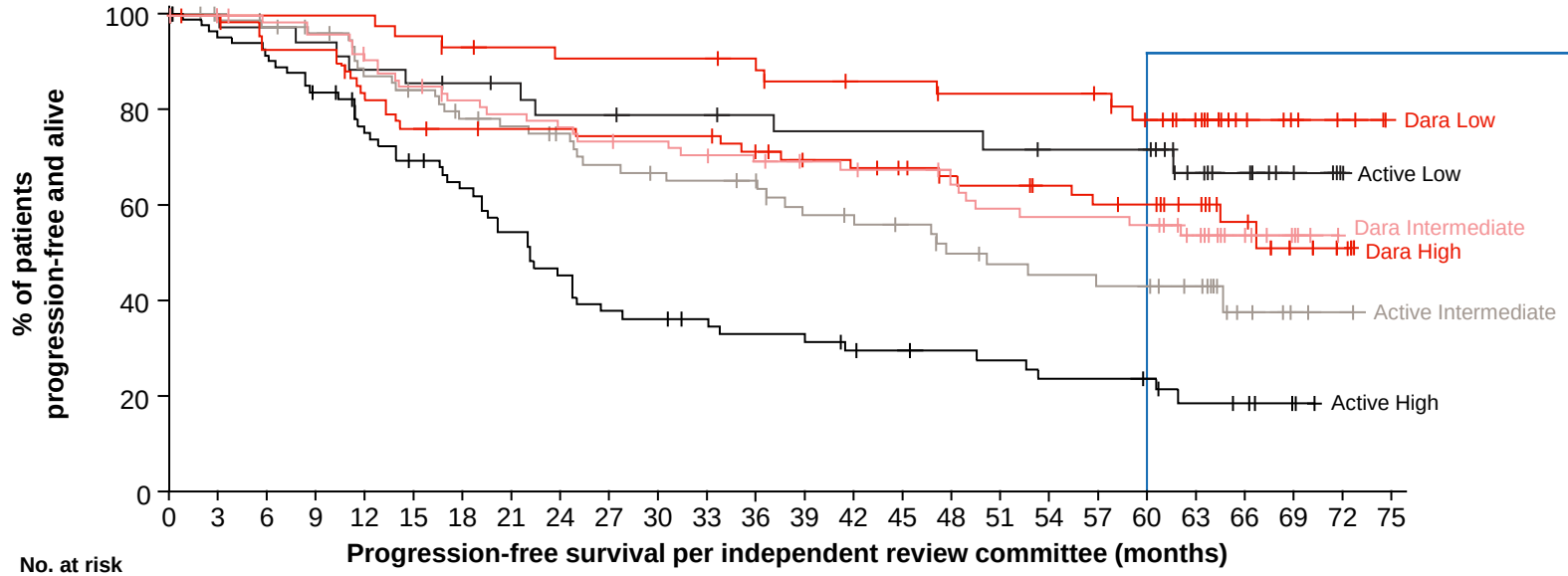
AQUILA: PFS



BMPC, bone marrow plasma cells; FLC, free light chain; IMWG, International Myeloma Working Group; PFS, progression-free survival; SC, subcutaneous; SMM smoldering multiple myeloma.

Presented by P Voorhees at the 67th American Society of Hematology (ASH) Annual Meeting; December 6–9, 2025; Orlando, FL, USA

AQUILA: IMWG 2020 Subgroups: PFS



No. at risk																									
Active: Low	34	33	33	32	30	28	27	26	24	24	23	23	22	21	21	21	21	20	19	19	19	12	9	5	1	0
Active: Intermediate	76	71	69	66	59	56	51	49	46	42	40	39	36	31	29	28	24	21	20	19	19	15	5	2	1	0
Active: High	86	76	73	62	53	47	42	36	30	25	24	21	20	19	17	16	15	14	12	12	11	6	5	1	0	0
Dara: Low	45	45	45	45	45	43	41	40	39	39	39	39	38	35	34	34	32	32	32	31	27	21	10	5	3	0
Dara: Intermediate	77	75	73	71	66	62	58	56	54	52	51	48	47	45	44	42	39	36	35	35	34	23	15	5	0	0
Dara: High	72	68	63	63	55	51	50	49	49	48	48	48	44	41	40	38	35	34	32	30	29	23	16	7	3	0

60-month PFS rates, %:

IMWG 2020 Risk group	Daratumumab	Active monitoring
Low	78.2	71.6
Intermediate	56.2	42.9
High	60.4	23.6

PFS active monitoring vs daratumumab monotherapy, high-risk group:
62.8% vs 37.5% events
HR 0.36 (95% CI: 0.23, 0.58)

Daratumumab monotherapy showed a PFS benefit vs active monitoring across IMWG 2020 risk subgroups, with the largest benefit observed in the high-risk subgroup

IMWG 2020 (aka Mayo 2018 or 20-2-20) risk stratification: BMPC >20%, monoclonal spike >2 g/dL, serum I/U FLC ratio >20.
0 factors=low risk; 1 factor=intermediate risk; ≥2 factors=high risk

BMPC, bone marrow plasma cells; FLC, free light chain; IMWG, International Myeloma Working Group; PFS, progression-free survival; SC, subcutaneous; SMM smoldering multiple myeloma.

Presented by P Voorhees at the 67th American Society of Hematology (ASH) Annual Meeting; December 6–9, 2025; Orlando, FL, USA

2 Erstlinienbehandlungen

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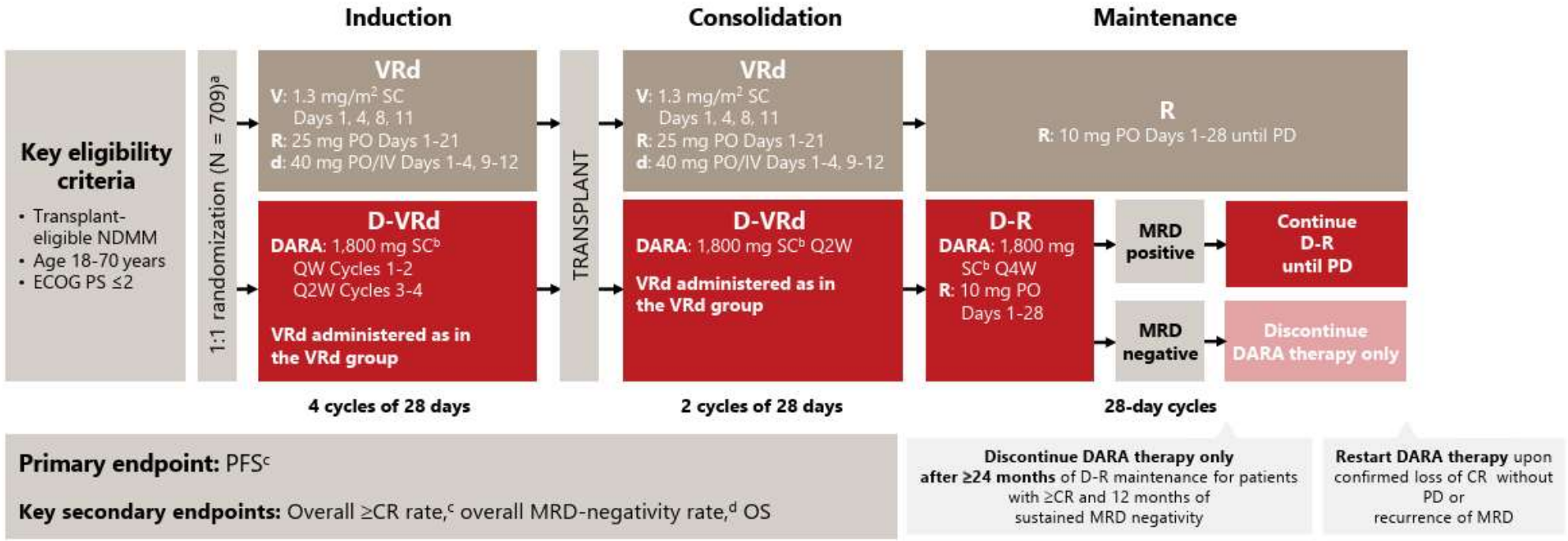
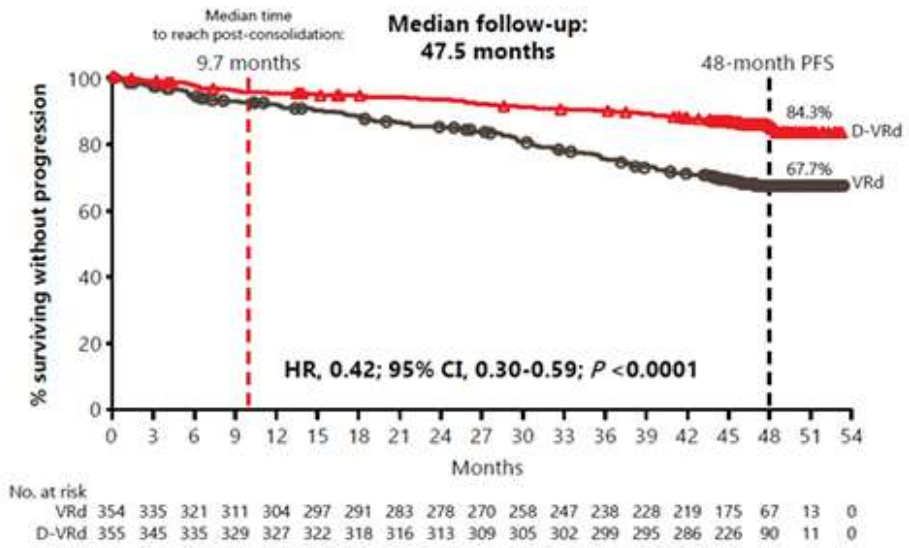
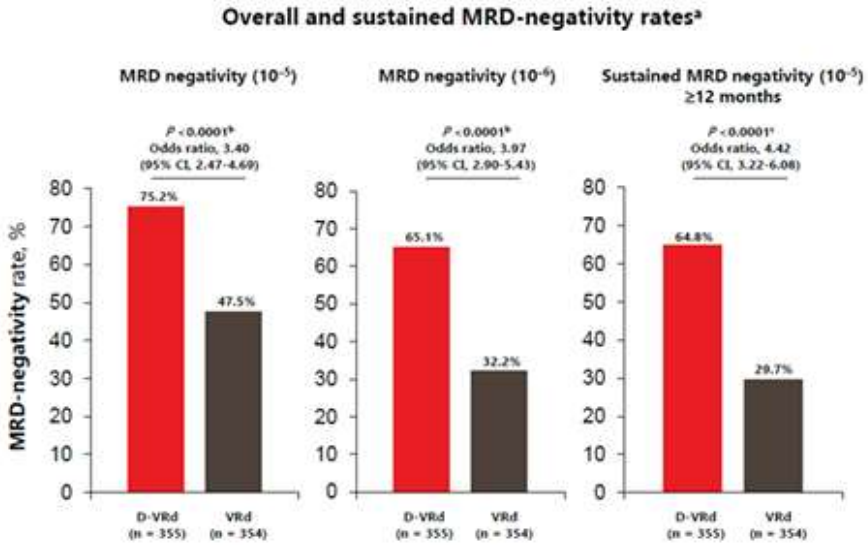
PERSEUS TRIAL – STUDY DESIGN



Sonneveld et al., NEJM, December 2024

PERSEUS TRIAL: D-VRd + D-R Maintenance significantly improved PFS and Depth of Response versus VRd + R





58% reduction in the risk of progression or death in patients receiving D-VRd

Deep and durable MRD negativity achieved with D-VRd

HR, hazard ratio; CI, confidence interval. [a]MRD-negativity rate was defined as the proportion of patients who achieved both MRD negativity and ≥CR. MRD was assessed using bone marrow aspirates and evaluated via NGS (clonoSEQ assay, version 2.0; Adaptive Biotechnologies, Seattle, WA, USA). [b]*P* values were calculated with the use of the stratified Cochran–Mantel–Haenszel chi-square test. [c]*P* value was calculated with the use of Fisher's exact test.

1. Sonneveld P, et al. *N Engl J Med.* 2024;390(4):301-313.

Presented by P Rodriguez-Otero at the American Society of Clinical Oncology (ASCO) Annual Meeting; May 31-June 4, 2024; Chicago, IL, USA

Sonneveld et al., NEJM, December 2024

Isatuximab, Lenalidomide, Bortezomib and Dexamethasone Induction Therapy for Transplant-E Diagnosed Multiple Myeloma: Fina Analysis of Part 1 of an Open-label, Phase 3 Trial (GMMG-HD7)

Zulassung 08/2025

Hartmut Goldschmidt[1,2], Uta Bertsch[1,2], Ema Pozek[3], Axel Benner[3], Roland Fenk[4], Britta Besemer[5], Christine Hanoun[6], Roland Schroers[7], Ivana von Metzler[8], Mathias Hänel[9], Christoph Mann[10], Lisa B. Leypoldt[11], Bernhard Heilmeier[12], Stefanie Huhn[1], Sabine K. Vogel[1], Michael Hundemer[1], Christof Scheid[13], Igor W. Blau[14], Steffen Luntz[15], Tobias A. W. Holderried[16], Karolin Trautmann-Grill[17], Deniz Gezer[18], Maika Klaiber-Hakimi[19], Martin Müller[20], Evgenii Shumilov[21], Wolfgang Knauf[22], Christian S. Michel[23], Thomas Geer[24], Hendrik Riesenberg[25], Christoph Lutz[26], Marc S. Raab[1,2], Martin Hoffmann[27], Katja C. Weisel[11], Hans J. Salwender[28], and Elias K. Mai[1] for the German-speaking Myeloma Multicenter Group (GMMG) HD7 investigators

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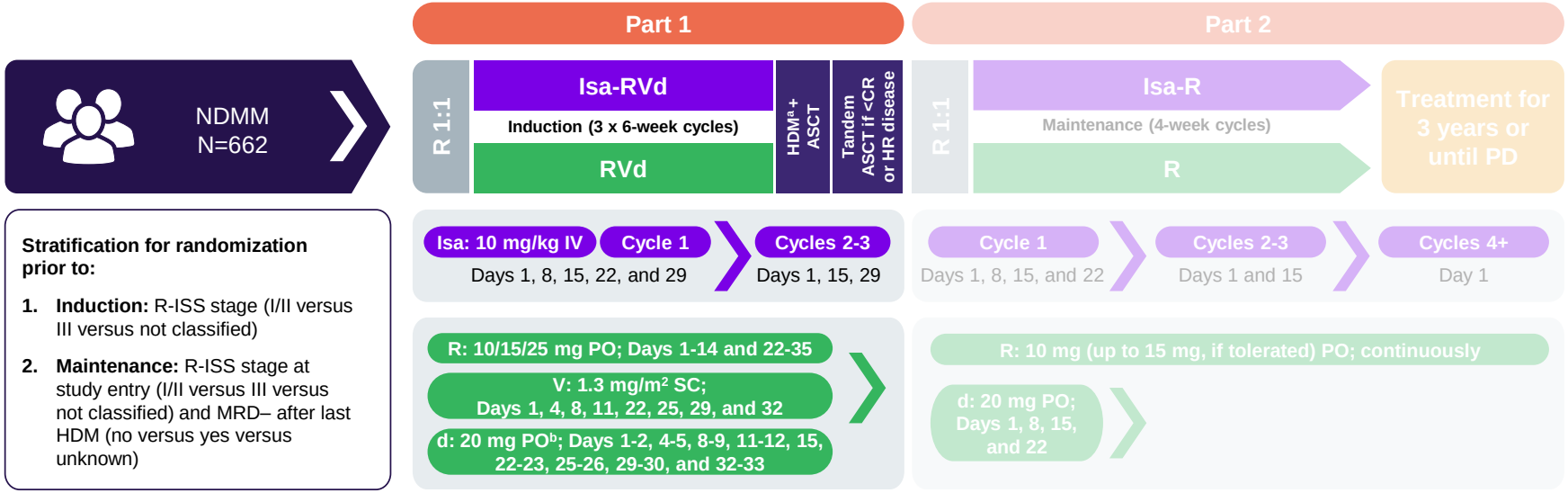
ASH 2024; Final Abstract Code: 769

HD7

Study design – Part 1



Stratification for randomization prior to:

1. **Induction:** R-ISS stage (I/II versus III versus not classified)
2. **Maintenance:** R-ISS stage at study entry (I/II versus III versus not classified) and MRD– after last HDM (no versus yes versus unknown)

Primary end points[c]: Post-induction MRD– (NGF, 10^{-5}); PFS after second randomization

Key secondary end points: PFS (whole study); OS (whole study and from second randomization); post-induction CR; CR and MRD– after HDM and during and after maintenance therapy

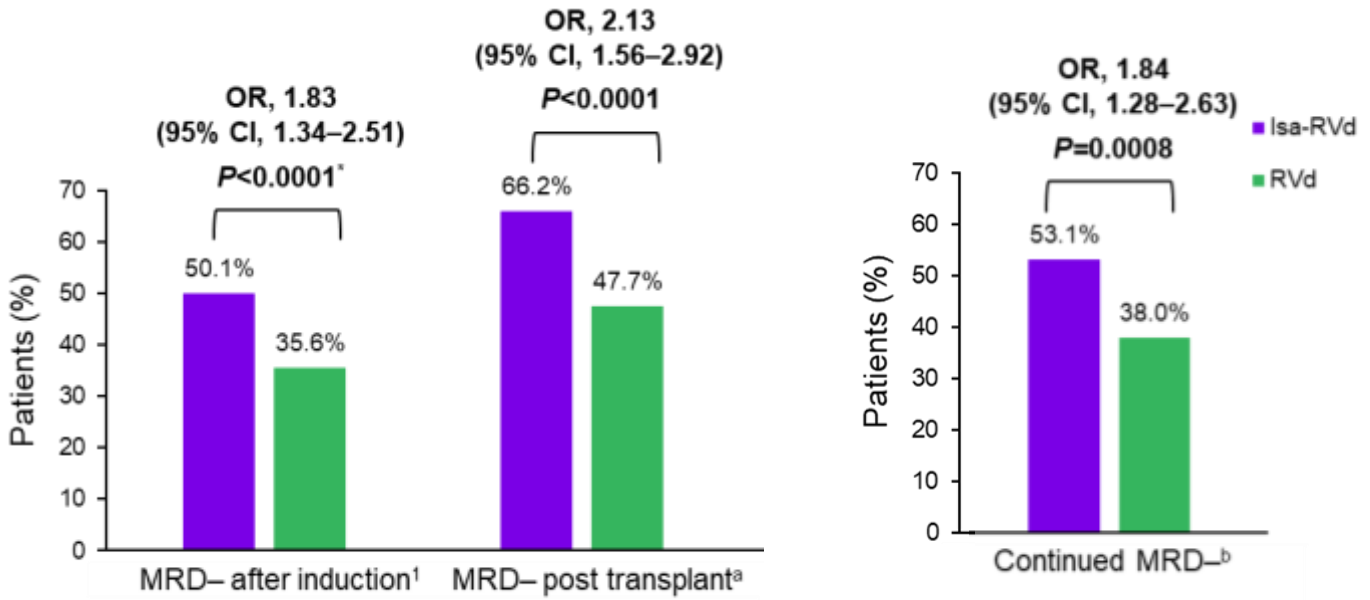
Selected secondary end point: PFS after first randomization

Here, we present the PFS from first randomization comparing Isa-RVd and RVd induction therapies

[a]Melphalan 200 mg/m². [b]On days of isatuximab infusion, dexamethasone will be administered intravenously as part of the premedication.
ASCT, autologous stem cell transplant; CR, complete response; d, dexamethasone; HDM, high-dose melphalan; HR, high-risk; Isa, isatuximab; IV, intravenous; MRD–, minimal residual disease negativity; NDMM, newly diagnosed multiple myeloma; PD, progressive disease; PO, oral; R, lenalidomide; R-ISS, Revised International Staging System; SC, subcutaneous; V, bortezomib.

HD7

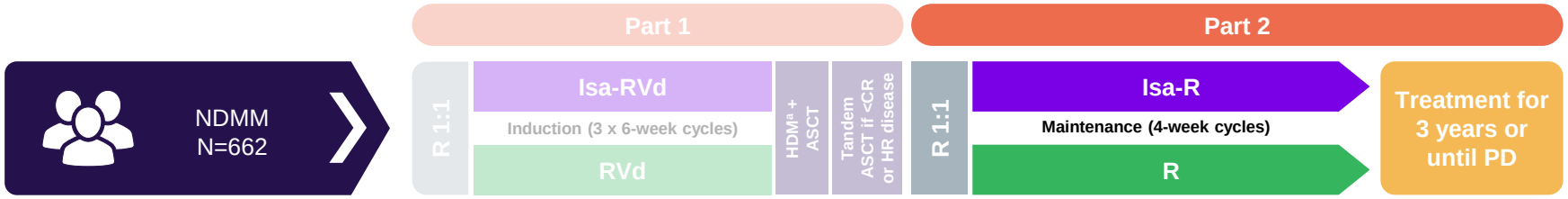
MRD– and continued MRD– rates in the ITT population



Further deepening of MRD response between the end of induction and post transplant was observed with Isa-RVd vs RVd, despite lack of consolidation after transplant

P value derived from stratified conditional logistic regression analysis. [a]Independent of IMWG response status. [b]Continued MRD– defined as MRD– persisting from post induction to post transplant. 1. Goldschmidt H, et al. *Lancet Haematol.* 2022;9:e810-e821.
CI, confidence interval; CR, complete response; d, dexamethasone; Isa, isatuximab; IMWG, International Myeloma Working Group; ITT, intent-to-treat; MRD, minimal residual disease; MRD–, minimal residual disease negativity; OR, odds ratio; R, lenalidomide; V, bortezomib; VGPR, very good partial response.

Future perspectives



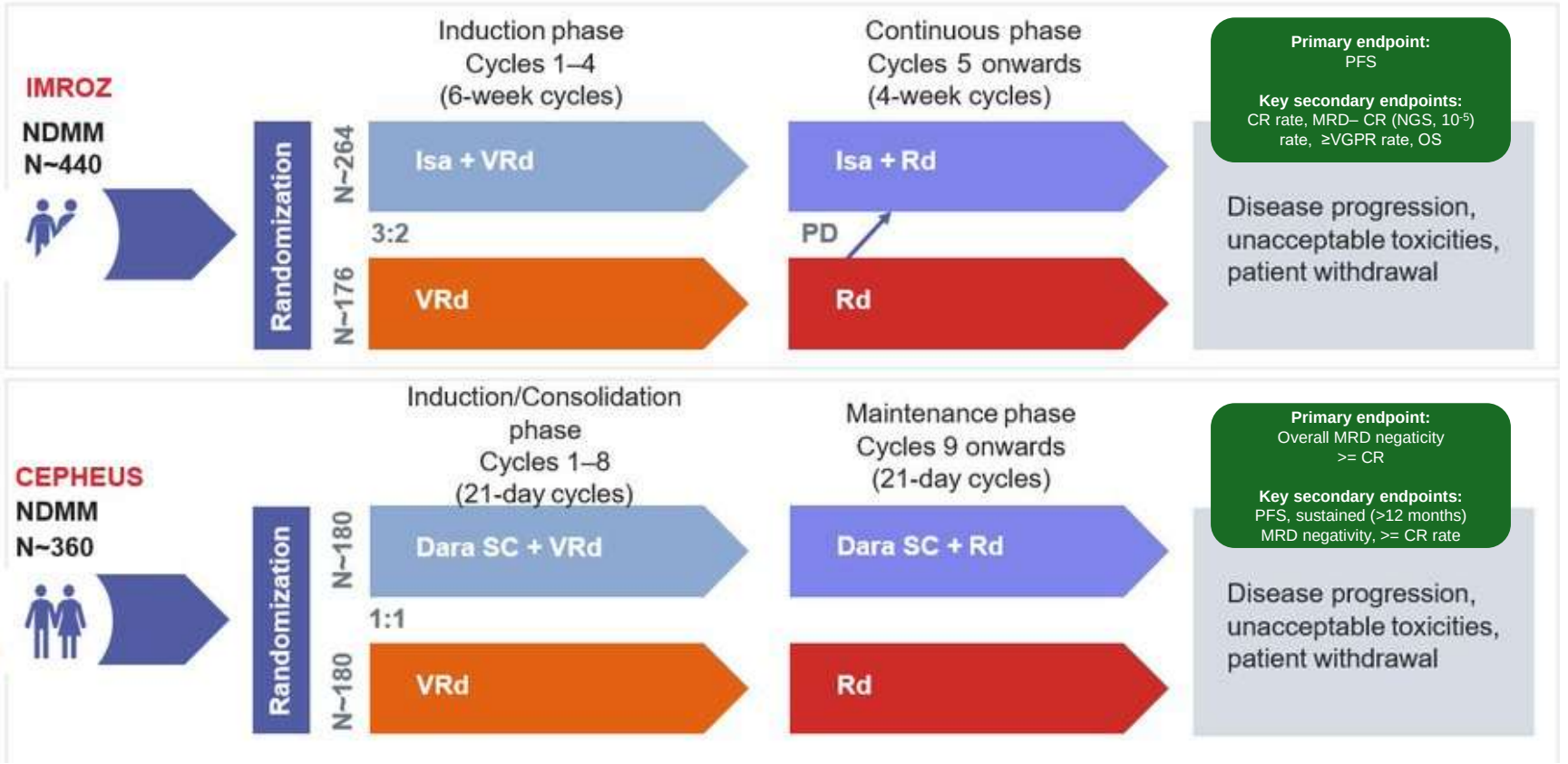
- Follow-up of the GMMG-HD7 trial is ongoing
- The next readout from the GMMG-HD7 trial will be the primary end point for part 2: PFS from second randomization comparing maintenance therapy with Isa-lenalidomide or lenalidomide alone

GMMG-HD7 is the only Phase 3 study with a second randomization before maintenance incorporating SOC lenalidomide, which allows the effects of isatuximab in induction and maintenance to be isolated and evaluated separately

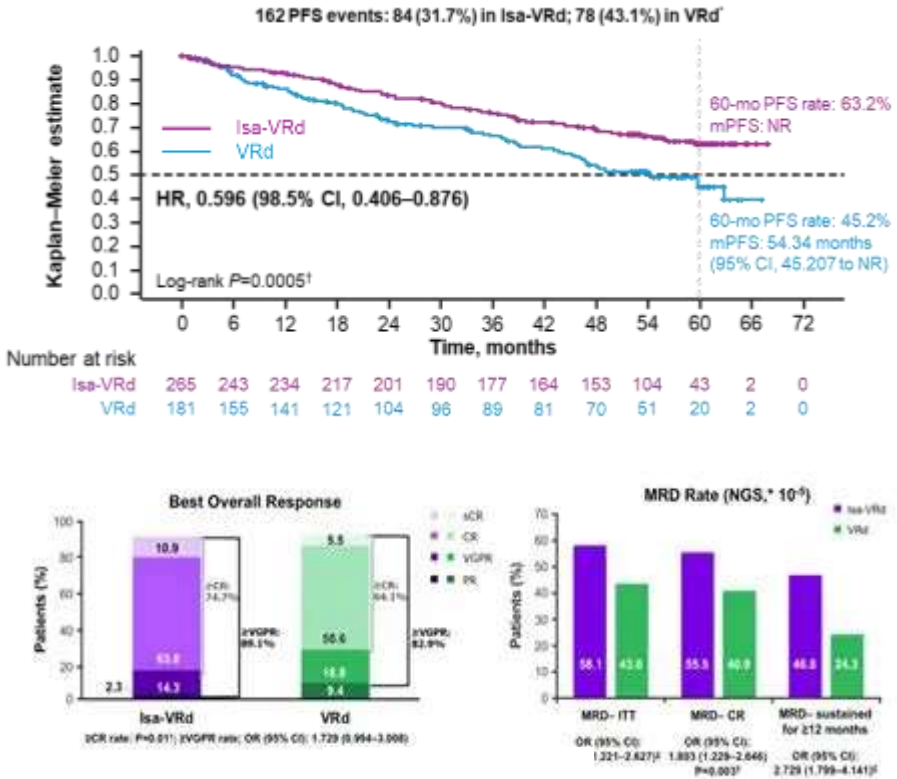
[a]Melphalan 200 mg/m². ASCT, autologous stem cell transplant; CR, complete response; d, dexamethasone; HDM, high-dose melphalan; HR, high-risk; Isa, isatuximab; NDMM, newly diagnosed multiple myeloma; PD, progressive disease; PFS, progression-free survival; R, lenalidomide; SOC, standard of care;
V, bortezomib.

Phase III IMROZ & CEPHEUS: Study Designs

Zulassung 2025

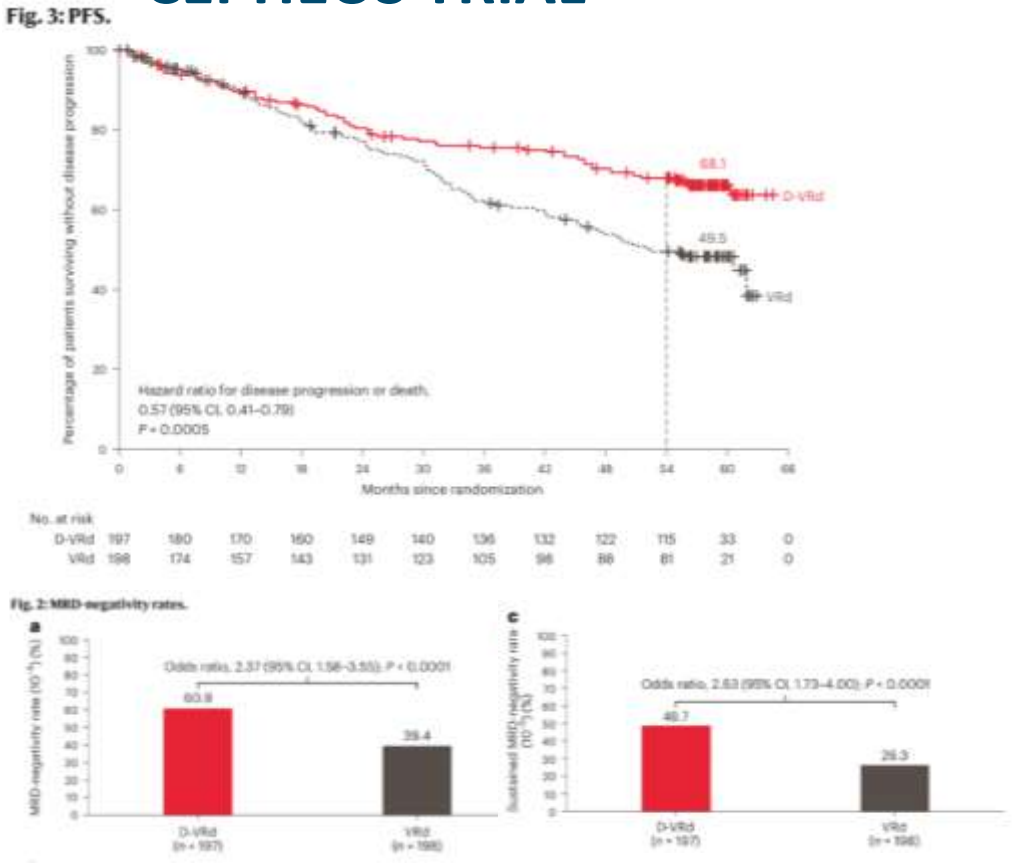


IMROZ TRIAL



Isatuximmab, Bortezomib, Lenalidomide and Dexamethasone for Multiple Myeloma, NEJM, 2024

CEPHEUS TRIAL



Daratumumab plus bortezomib lenalidomide and dexamethasone for transplant-ineligible or transplant-deferred newly diagnosed multiple myeloma: the randomized phase 3 CEPHEUS trial; Nature Medicine, 2025

Was kommt nach 2025?

Auswahl Studien bei NDMM:

- **MIDAS Trial**
  (Erstlinientherapie mit Isa-KRd gesteuert nach MRD)

■ **TE:**

- **MajesTEC5/HD10**
  (5-fach Kombination in Erstlinie: Tec-Dara(V)Rd)
- **CARTITUDE6**
  (Dara-VRd + Ciltacel+ ET vs. SOC)
- **HD8** (Isa s.c. RVd vs. Isa i.v. RVd)

ET nach ABSCT:

-**MajesTEC 4** (Tec-Len vs. Len mono)
-**MAGNETISMM7** (Elranatamab vs. Lenalidomid)
-**HD9** (Iberdomid vs. Iberdomid + Isatuximab s. c.)

■ **NTE:**

- **MajesTEC7** (Tec-DR vs. DRd)
- **DREAMM-9**
  (Belantamab Mafodotin VRd vs. VRd)
- **MAGNETISMM6**
  (Elranatamab-DR vs. DRd)

Fazit Erstlinientherapie:

- Vierfach-Induktion mit einem CD38-Antikörper, IMiD, Proteasominhibitor und Dexamethason ist der Goldstandard für Patienten mit neudiagnostiziertem Multiplen Myelom (NE und NTE)

- Doublette (Daratumumab-Lenalidomid) in Erhaltungstherapie nach Quadruplet Induktionstherapie mit Dara-VRd (analog PERSEUS)

- Etablierung von Carfilzomib-basiertem Quadruplet für HR NDMM (CONCEPT, MIDAS); bisher nicht zugelassen!

- Stellenwert MRD – adaptierter Therapiestrategien? Stellenwert ASCT bei MRD negativen Patienten?

- Outlook: Integration der nächsten Generation an Immuntherapien in die erste Behandlungslinie (bispezifische Antikörper, CAR-T Zellen)

3 Behandlungen bei erneuter Krankheitsaktivität

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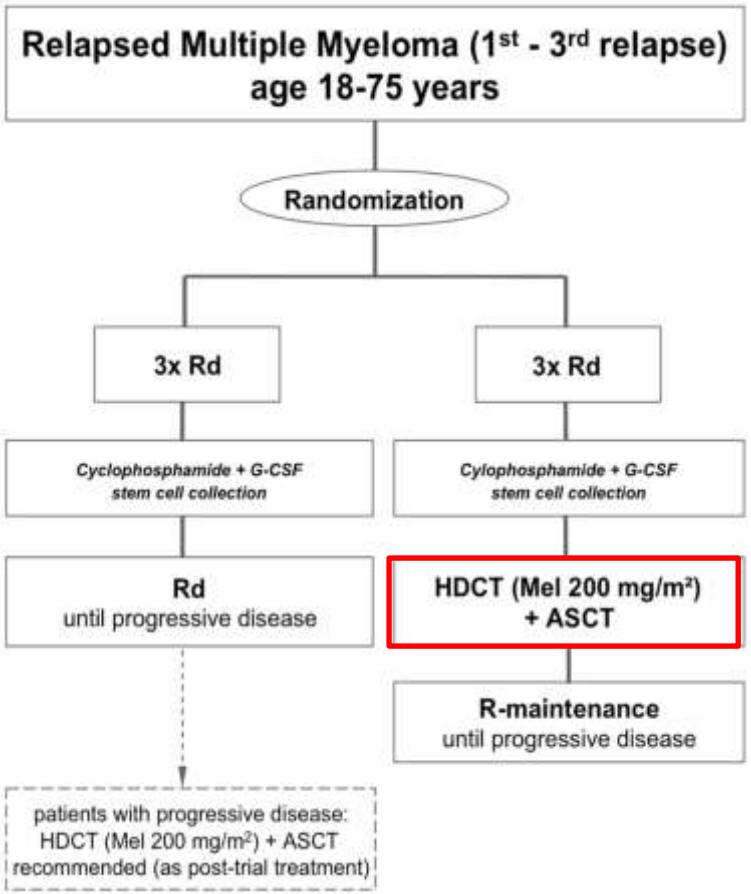
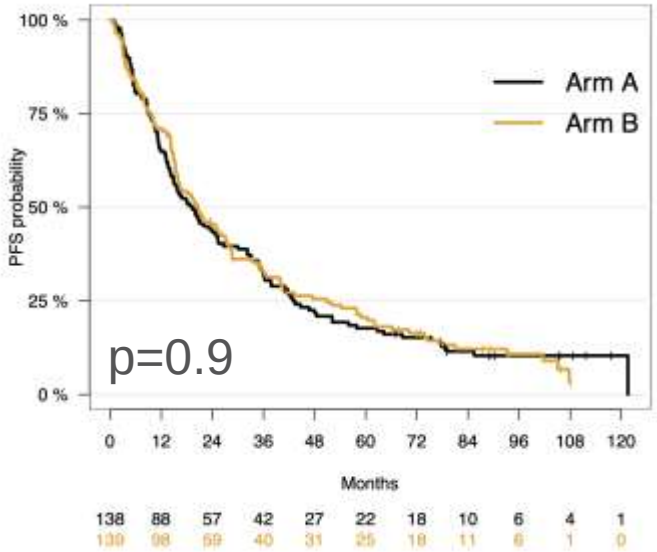
Autologe Rezidivtransplantation?

ReLApsE-Studie Langzeitergebnisse (mFU 8 yrs)



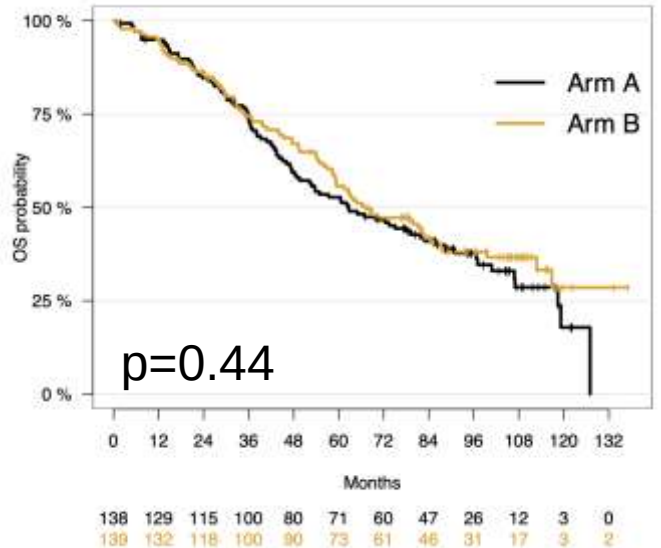
PFS



Median PFS

- Arm A: 19.3 months
- Arm B: 20.5 months
- HR 0.98

OS



Median OS

- Arm A: 62.7 months
- Arm B: 67.1 months
- HR 0.89

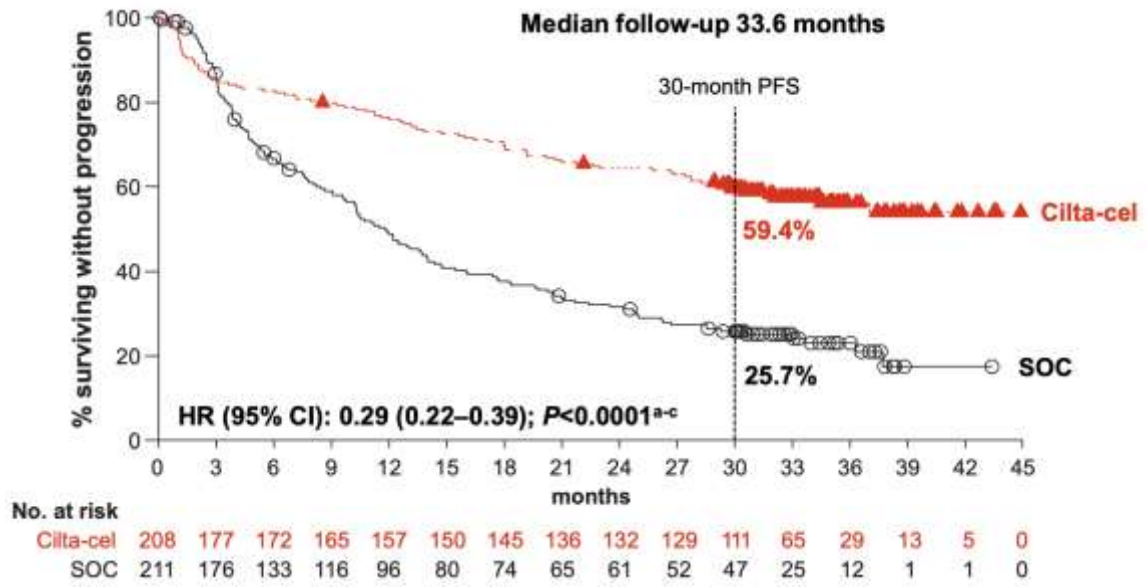
Kein Überlebensvorteil für Rezidiv-TPL nach vorheriger Erstlinien-TPL

Baertsch MA, et al. Blood, 2025

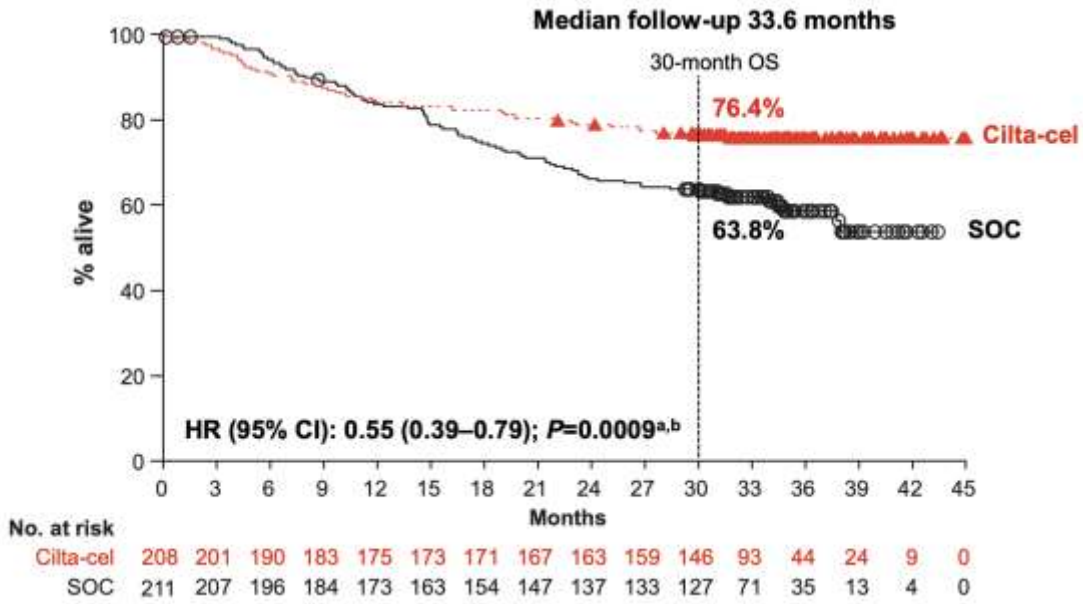
CAR-T-Zell-Therapie ab 2. Linie

Cartitude-4 phase III trial (1-3 Vortherapien) – BCMA-targeted CAR-T cells

PFS



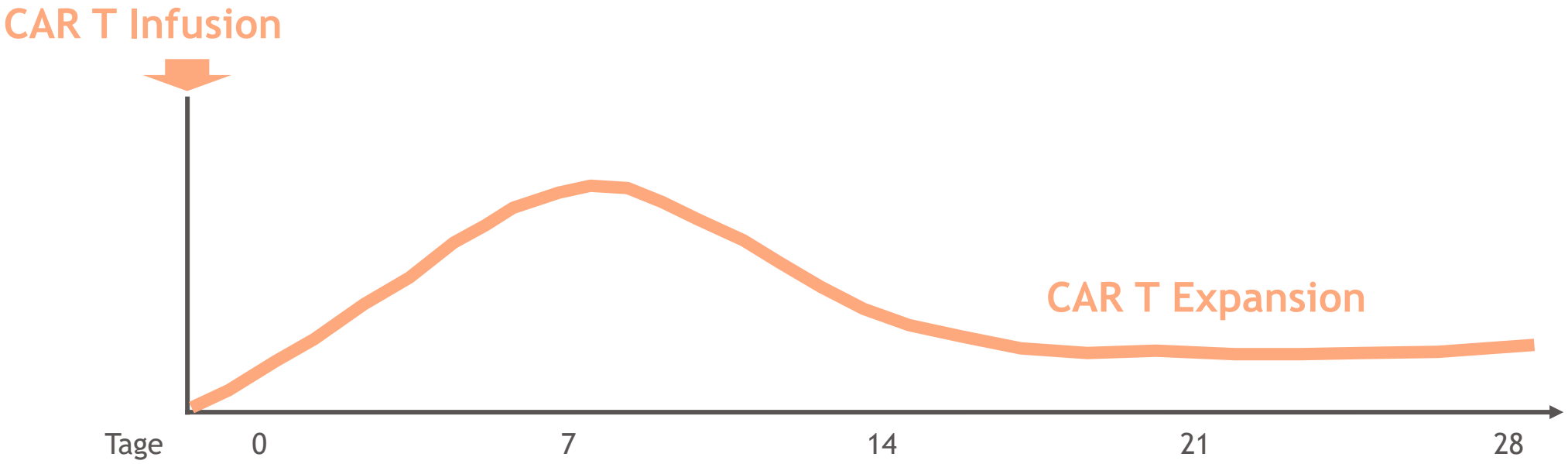
OS



Cilta-cel (Carvykti) als Standard ab der 2. Linie
(Voraussetzungen: CAR-T-Fähigkeit, Lenalidomid-Refrakterität)

San Miguel J et al., NEJM, 2023

Besondere Nebenwirkungen der CAR T Zelltherapie: CRS and ICANS

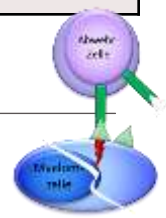


CRS
- Fieber(Beginn wenige Stunden bis 7 Tage nach Infusion) →
- Rigor, Schwäche, Kofschmerzen, Muskelschmerzen →
- Schweelungen, Blutdruckabfall, Sauerstoffmangel

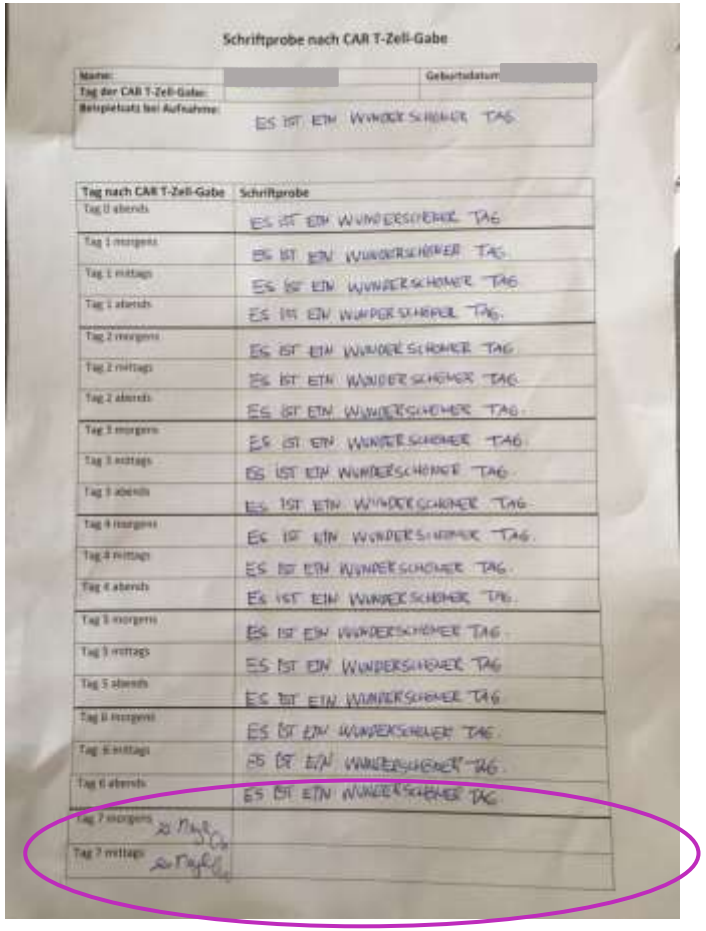
ICANS (meist mit CRS)
- Aufmerksamkeitsdefizit, Sprachstörungen, Zittern, Lethargie, Schreibstörung →
- Aphasie, Krampfanfälle, Gehirnentzündung, Kraftverlust, Kopfschmerzen

Management
IL-6 Hemmung Corticosteroide Supportive care
Corticosteroide Supportive care

ICANS, immune effector cell-associated neurologic syndrome.
Santomasso B, et al. Am Soc Clin Oncol Educ Book. 2019;39:433–44. Siegler EL, et al. Front Immunol. 2020;11:1973.



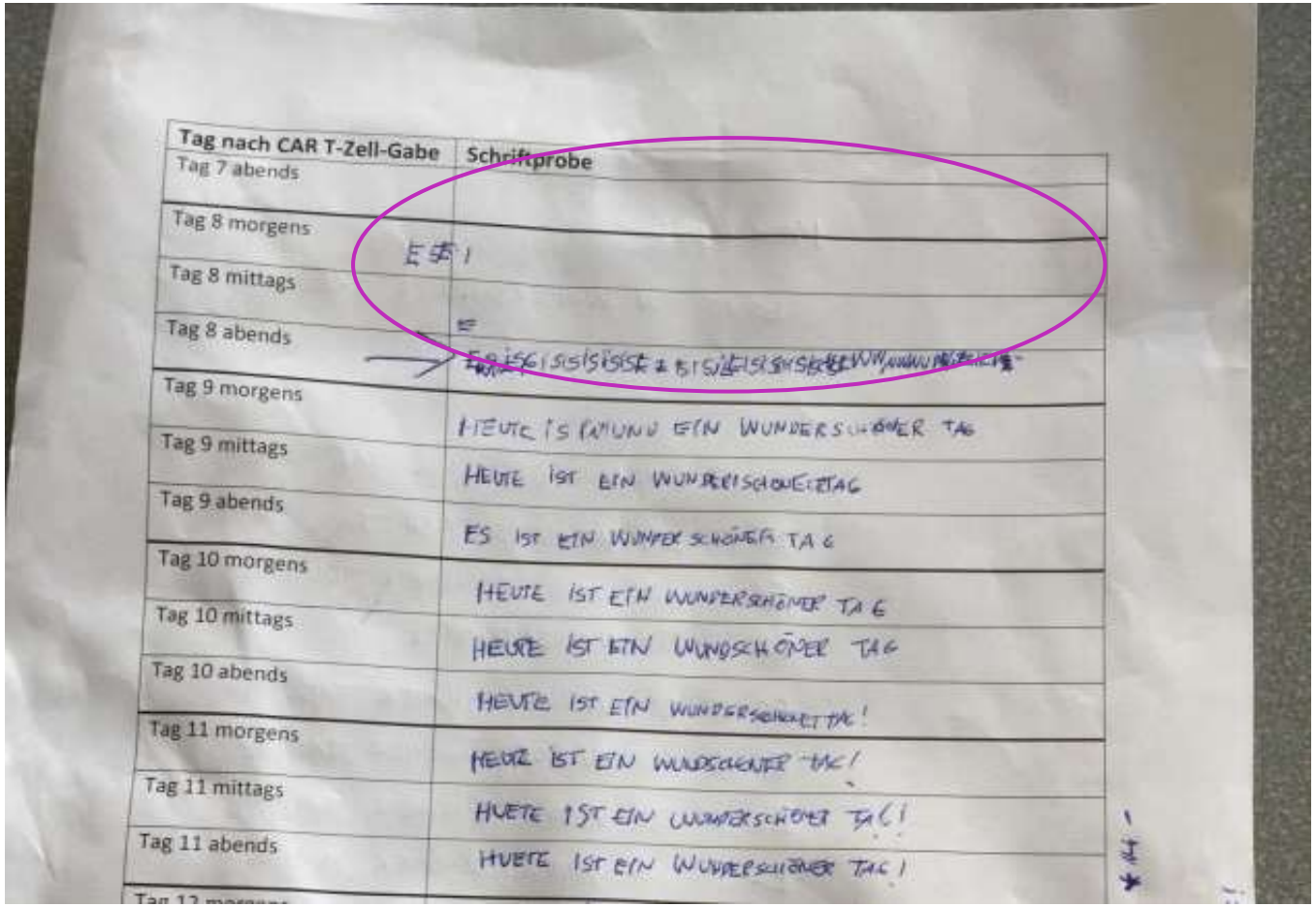
Neurotoxizität



Schriftprobe nach CAR T-Zell-Gabe

Name:		Geburtsdatum:
Tag der CAR T-Zell-Gabe:		
Beispielsatz bei Aufnahme:	ES IST EIN WUNDERSCHÖNER TAG	

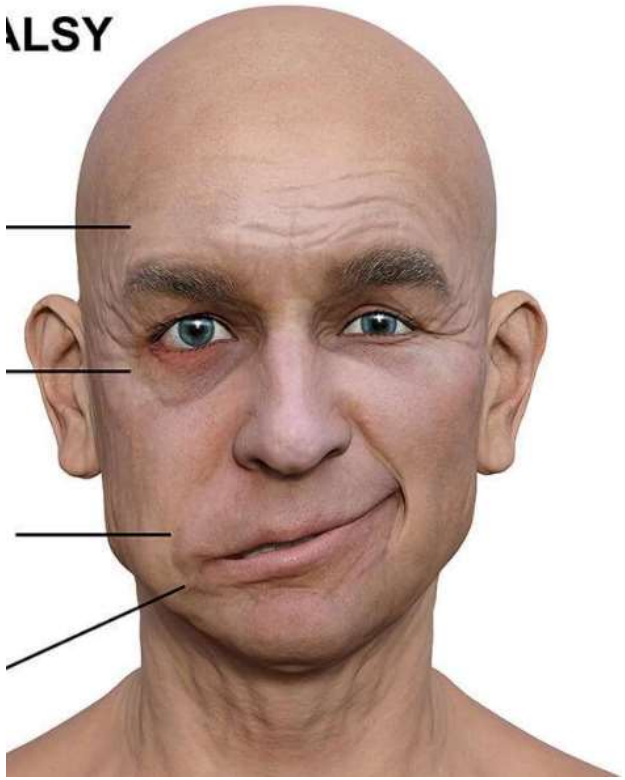
Tag nach CAR T-Zell-Gabe	Schriftprobe
Tag 0 abends	ES IST EIN WUNDERSCHÖNER TAG
Tag 1 morgens	ES IST EIN WUNDERSCHÖNER TAG
Tag 1 mittags	ES IST EIN WUNDERSCHÖNER TAG
Tag 1 abends	ES IST EIN WUNDERSCHÖNER TAG
Tag 2 morgens	ES IST EIN WUNDERSCHÖNER TAG
Tag 2 mittags	ES IST EIN WUNDERSCHÖNER TAG
Tag 2 abends	ES IST EIN WUNDERSCHÖNER TAG
Tag 3 morgens	ES IST EIN WUNDERSCHÖNER TAG
Tag 3 mittags	ES IST EIN WUNDERSCHÖNER TAG
Tag 3 abends	ES IST EIN WUNDERSCHÖNER TAG
Tag 4 morgens	ES IST EIN WUNDERSCHÖNER TAG
Tag 4 mittags	ES IST EIN WUNDERSCHÖNER TAG
Tag 4 abends	ES IST EIN WUNDERSCHÖNER TAG
Tag 5 morgens	ES IST EIN WUNDERSCHÖNER TAG
Tag 5 mittags	ES IST EIN WUNDERSCHÖNER TAG
Tag 5 abends	ES IST EIN WUNDERSCHÖNER TAG
Tag 6 morgens	ES IST EIN WUNDERSCHÖNER TAG
Tag 6 mittags	ES IST EIN WUNDERSCHÖNER TAG
Tag 6 abends	ES IST EIN WUNDERSCHÖNER TAG
Tag 7 morgens	
Tag 7 mittags	



Tag nach CAR T-Zell-Gabe	Schriftprobe
Tag 7 abends	
Tag 8 morgens	ES
Tag 8 mittags	
Tag 8 abends	
Tag 9 morgens	HEUTE IST EIN WUNDERSCHÖNER TAG
Tag 9 mittags	HEUTE IST EIN WUNDERSCHÖNER TAG
Tag 9 abends	ES IST EIN WUNDERSCHÖNER TAG
Tag 10 morgens	HEUTE IST EIN WUNDERSCHÖNER TAG
Tag 10 mittags	HEUTE IST EIN WUNDSCHÖNER TAG
Tag 10 abends	HEUTE IST EIN WUNDERSCHÖNER TAG!
Tag 11 morgens	HEUTE IST EIN WUNDSCHÖNER TAG!
Tag 11 mittags	HUETE IST EIN WUNDERSCHÖNER TAG!
Tag 11 abends	HUETE IST EIN WUNDERSCHÖNER TAG!

Courtesy of L. Schubert.

Neurologische Spätfolgen: Selten aber wichtig zu wissen



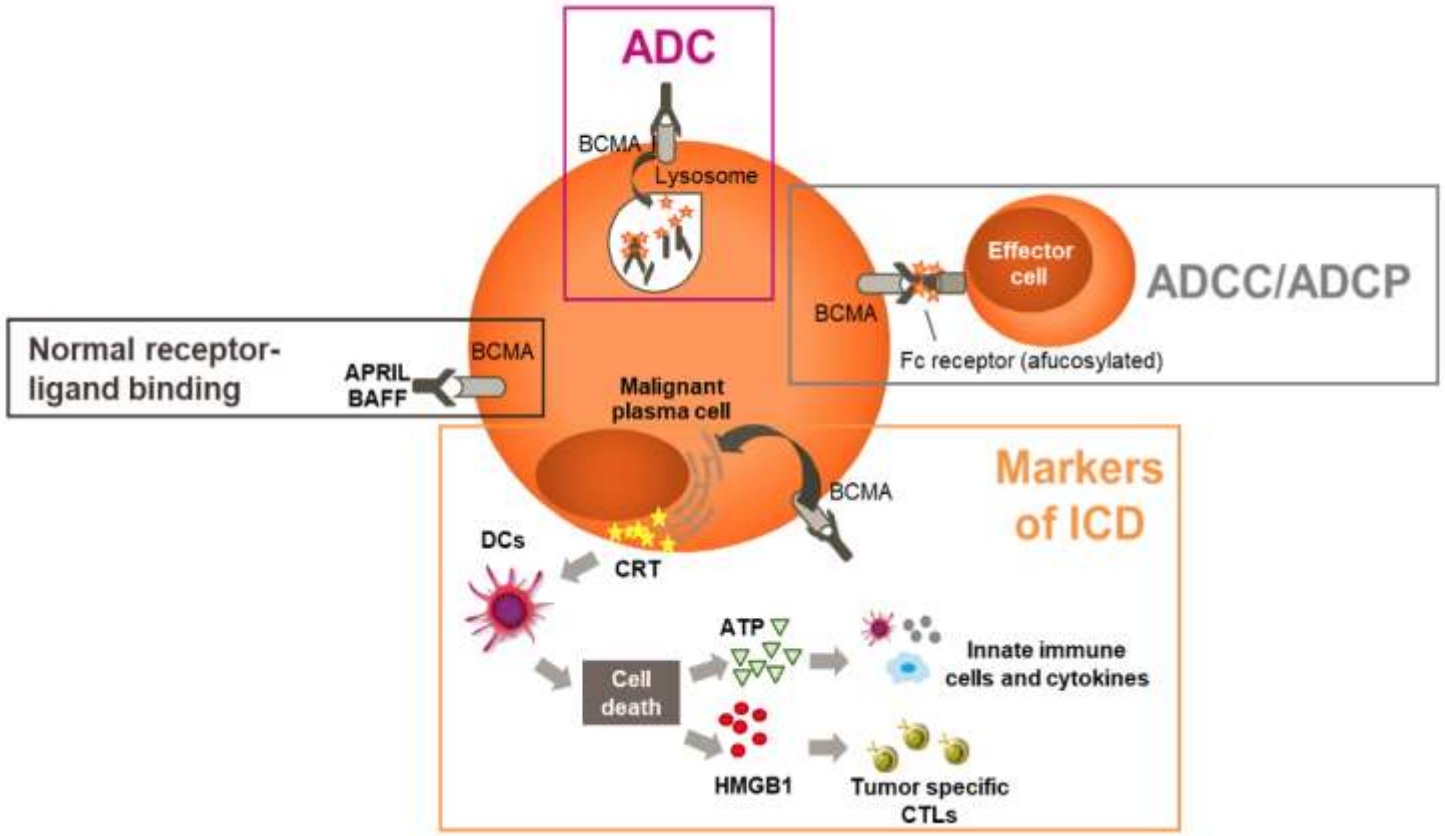
Gesichtsnervenlähmung:
selten, vorübergehend

Parkinson-ähnliches Syndrom
sehr selten, evtl. bleibend

www.bergerhenryent.com; Butler et al., 2017

Belantamab mafodotin

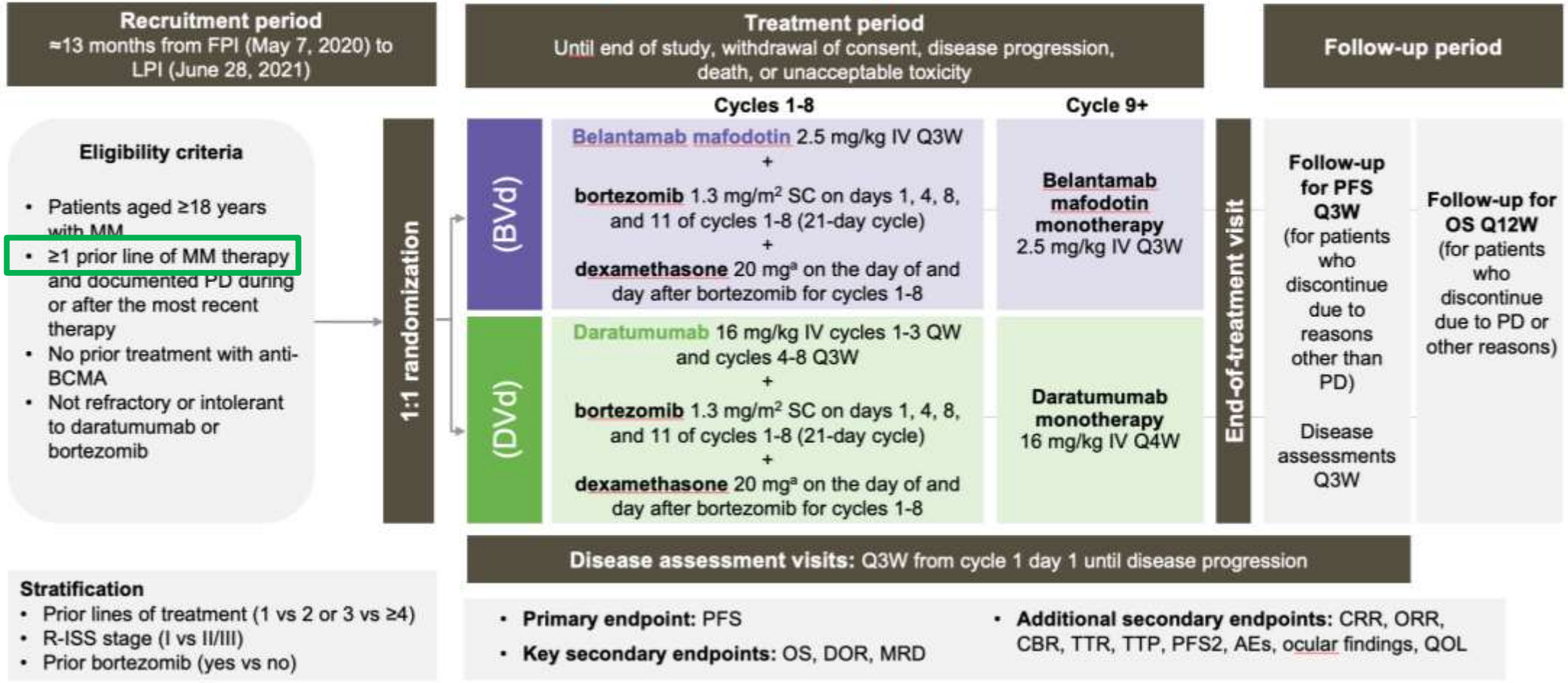
Wirkmechanismen



- Belantamab mafodotin is a humanized, afucosylated, anti-BCMA monoclonal antibody conjugated to the microtubule inhibitor monomethyl auristatin F by a protease-resistant cysteine linker[1-3]
- Belantamab mafodotin induces immune-independent ADC-mediated apoptosis; immune-dependent enhancement of ADCC and ADCP; and release of markers characteristic of ICD, leading to an adaptive immune response[3,4]

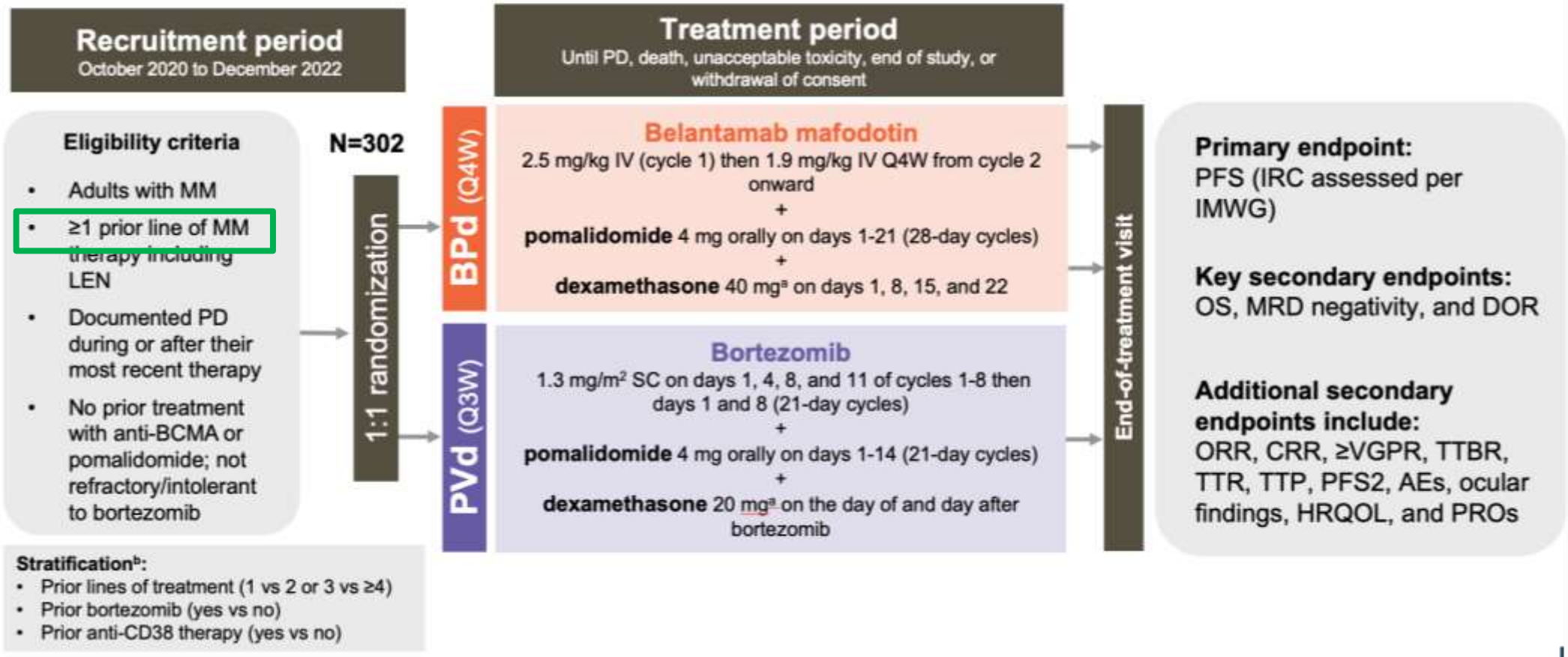
Anti-CD38-refraktär, LEN-refraktär: Belantamab

DREAMM-7 Is a Phase 3 Study Examining a Belantamab Mafodotin–Based Combination in RRMM in 2L+ (NCT04246047)



Anti-CD38-refraktär, LEN-refraktär: Belantamab

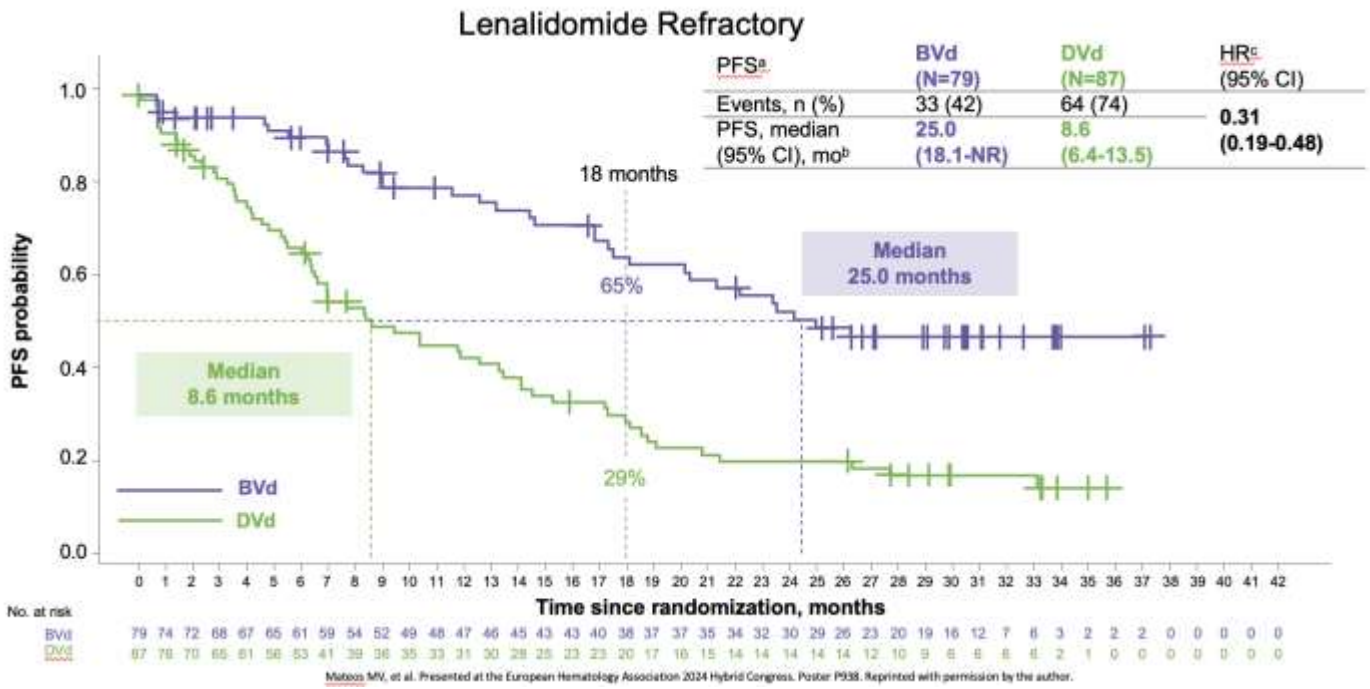
DREAMM-8 is a phase 3 study examining a belantamab mafodotin–based combination in 2L+ RRMM (NCT04484623)[1,2]



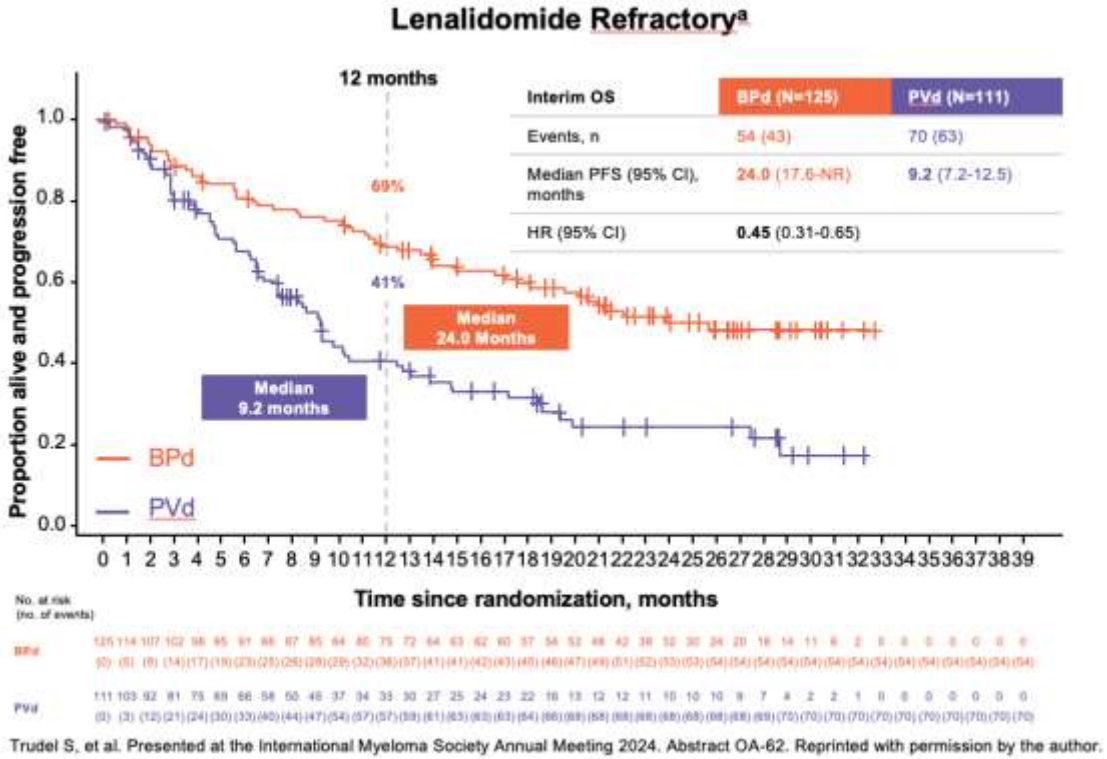
Anti-CD38-refraktär, LEN-refraktär: Belantamab

Subgruppenanalysen LEN-refraktäre Pat.

DREAMM-7 (BVd)



DREAMM-8 (BPd)



Medianes PFS bei LEN-Refrakterität mit BVd/BPd beträgt 2 Jahre (vergleichbar mit Dara-Kd [CANDOR phIII])

Belantamab mafodotin

Okuläre Toxizität: Visusverschlechterung

Changes in BCVA Resolved in Patients With Complete Follow-Up

20/20[1]

20/50[1]

20/200[1]

Reprinted from Shi C, et al. *J Vis.* 2020;20(8):29. Copyright © 2020 The Authors.

BVd[2]	Bilateral worsening of BCVA in patients with normal baseline 20/25 or better	
	(20/50) or worse[a]	(20/200) or worse[a]
Patients, n/N (%)	84/242 (35)	5/242 (2)
Time to onset of first event, median (range), days	79 (16-1320)	105 (47-304)
Time to resolution of first event to baseline, median (range), days[b]	64 (8-908)	87 (22-194)
Time to improvement of first event, median (range), days[c]	22 (6-257)	19 (8-26)
First event resolved, n/N (%)[b]	78/84 (93)	4/5 (80)
First event improved, n/N (%)[c]	81/84 (96)	5/5 (100)
Follow-up ended with event ongoing, n/N (%)	2/84 (2)	0

The rate of discontinuations due to any ocular event was 10%

Zusammenfassung

- **Frühes Rezidiv**
  - Grundsätzlich Therapiewahl nach **Vortherapie, Refrakterität und Patientenfaktoren** (Komorbiditäten, Präferenzen)

  - **Anti-BCMA CAR-T Zellen** entwickeln sich zum **Standard** für geeignete Patienten (Cilta-cel)
    - Fitness, Lenalidomid-Refrakterität

  - Herausforderung der **Lenalidomid- und/oder Anti-CD38-Refrakterität** (nach Erstlinie)
    - **Anti-CD38/Carfilzomib/Dexamethason**
    - **Belantamab** mafodotin/Pomalidomid/Dex bzw. Belantamab mafodotin/Bortezomib/Dex
      - Herausforderung **okuläre Toxizität**: Dosisreduktion, Intervallverlängerung
        - Reversibilität
      - Einfluss auf spätere BCMA-gerichtete Therapien? (bispezifische Antikörper)
    - Weitere Optionen
      - **Selinexor**/Bortezomib/Dexamethason
        - Reduzierte Startdosis und konsequente Antiemeseprophylaxe
      - **Elotuzumab**/Pomalidomid Dexamethason

4 Optionen nach mehrfacher Vortherapie

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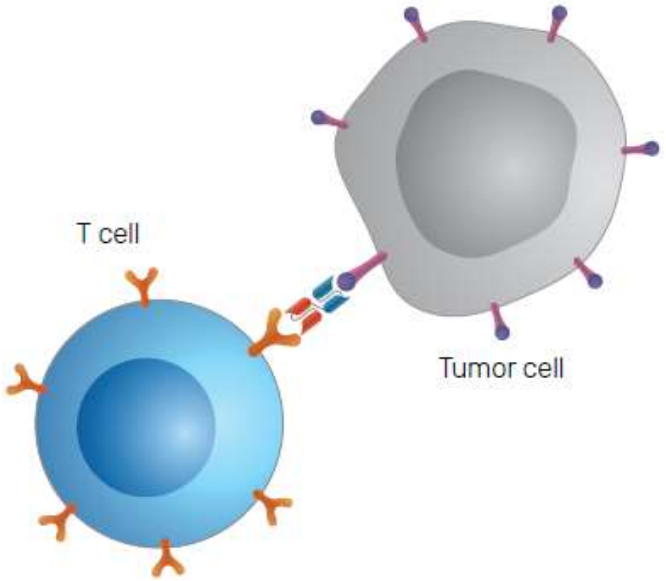
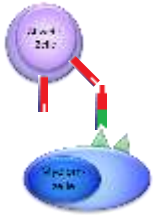
Bispezifische Antikörper

bispezifische AK/BiTE



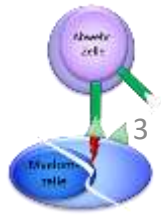
Batlevi CL, et al. Nat Rev Clin Oncol. 2016;13(1):25-40., Marin-Acevedo JA, et al. J Hematol Oncol. 2018;11(1):8., Thomas A, et al. Lancet Oncol. 2016;17(6):e254-e262., Baeuerle PA, et al. Cancer Res. 2009;69(12):4941-4944., Brudno JN, et al. Blood Rev. 2019;34:45-55., Porter DL, et al. N Engl J Med. 2011;365(8):725-733.



Teclistamab, Elranatamab, Linvoseltamab und Talquetamab: zugelassene bispezifische Antikörper

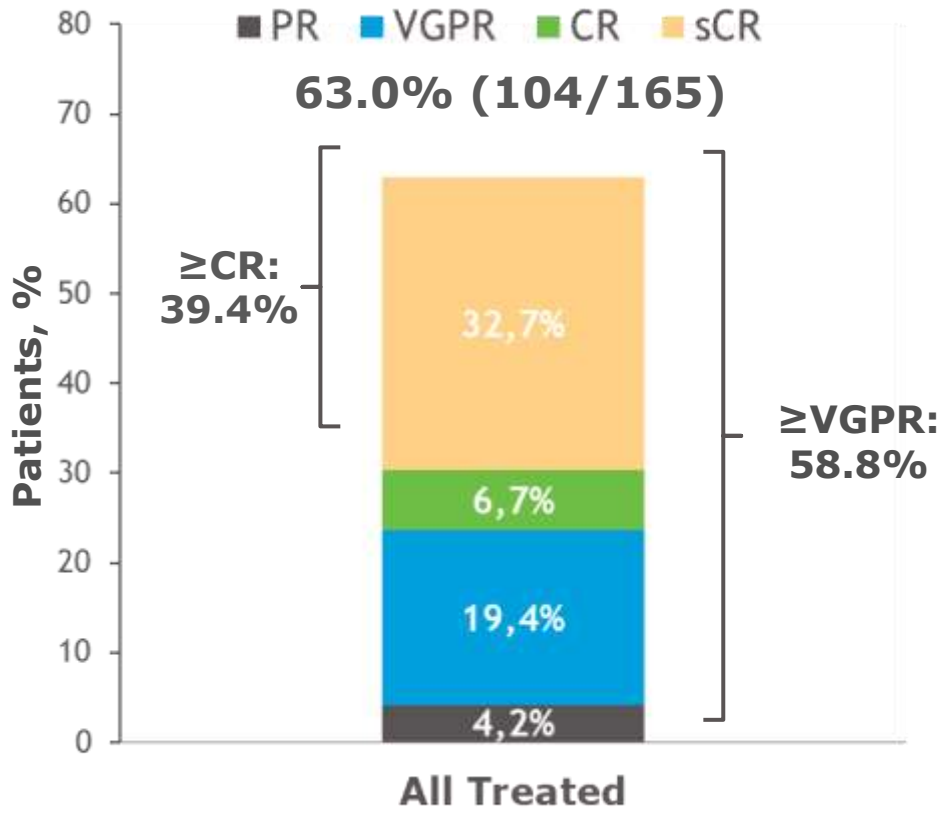
- **EMA Zulassung:**
- Teclistamab, Elranatamab, Linvoseltamab und Talquetamab sind indiziert für die Behandlung des **rezidivierten und refraktären multiplen Myeloms** bei erwachsenen Patienten, die **mindestens drei vorausgegangene Therapien**, einschließlich eines **Immunmodulators**, eines **Proteasominhibitors** und eines **Anti-CD38-Antikörpers**, erhalten und unter der letzten Therapie eine Krankheitsprogression gezeigt haben.

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-idecabtagene-vicleucel-multiple-myeloma



MajesTEC-1: Gesamtansprechen, Beispiel Teclistamab

ORR[a]

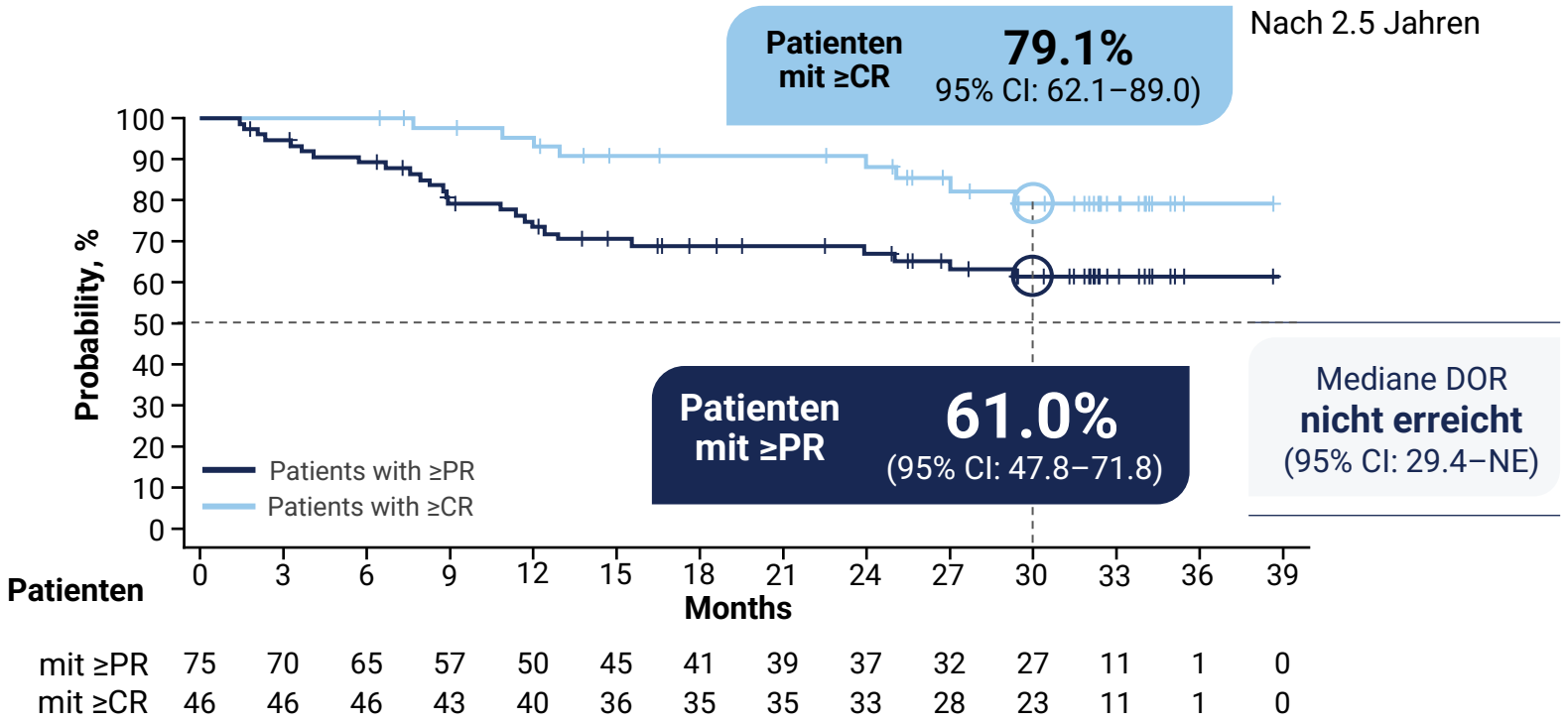


Im Median 5 Vortherapielinien

- 78% Dreifach-refraktär (PI, IMID, CD38)
- Fast 40% mit kompletter Remission
- 46% mit kompletter Remission waren MRD negativ

Dauer des Ansprechens: Beispiel Elranatamab

Dauer des Ansprechens



- Im Laufe der Zeit Vertiefung des Ansprechens
- Dauer des Ansprechens > 30 Monate
- Progressionsfreie Zeit 17 Monate

MajesTEC-3: Phase 3 Study Design

Key inclusion criteria

- RRMM
- 1-3 prior LOTs including a PI and lenalidomide
  - Patients with only 1 prior LOT must have been lenalidomide refractory per IMWG criteria
- ECOG PS score of 0-2

Key exclusion criteria

- Prior BCMA-directed therapy
- Refractory to anti-CD38 mAbs[a]

1:1 randomization N=587

22 Oct 2021 to 29 Sept 2023[b]

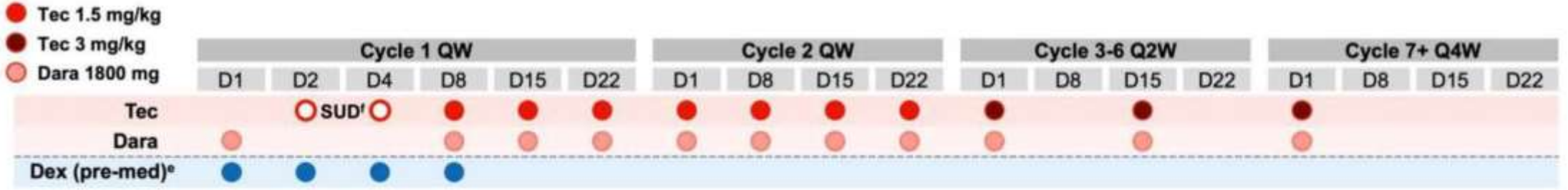
Tec-Dara
N=291
SC dosing following Dara schedule

DPd/DVd
N=296 (91% DPd)
by investigator's choice[c]

Primary endpoint
- PFS per IRC

Key secondary endpoints
- ≥CR[d] and ORR[d]
- MRD negativity (10^{-5})
- OS
- MySIm-Q Total Symptom score

Other secondary endpoints
- Safety
- PK and immunogenicity



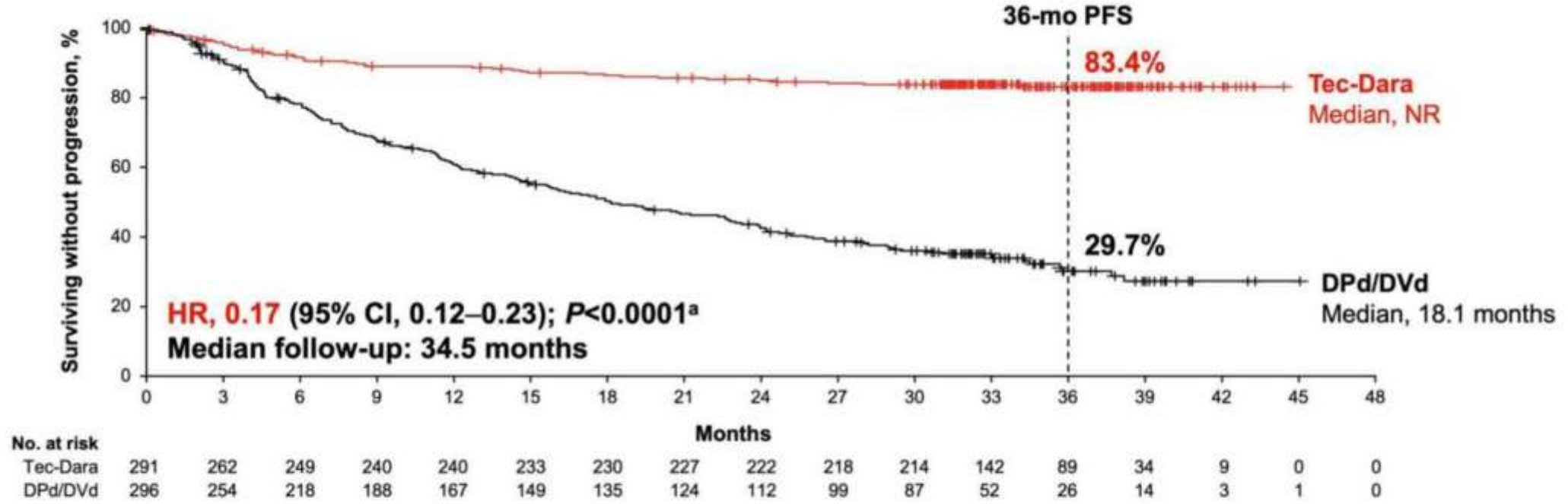
SC dosing aligned with Dara schedule, with monthly dosing after 6 cycles; steroid sparing after Cycle 1 Day 8

[a]Prior exposure to anti-CD38 mAbs was permitted. [b]During the COVID-19 pandemic. [c]DPd/DVd were administered per the approved schedules. [d]Response and disease progression were assessed by a blinded IRC per IMWG criteria. [e]Dexamethasone, acetaminophen, and diphenhydramine pre-medication was required for the first 2 weeks; subsequent dexamethasone was not required thereafter. [f]Patients received SUD of 0.06 mg/kg and 0.3 mg/kg on Days 2 and 4, respectively.

CR, complete response; D, day; Dex, dexamethasone; DPd, daratumumab, pomalidomide, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMWG, International Myeloma Working Group; IRC, independent review committee; MRD, minimal residual disease; MySIm-Q, Multiple Myeloma Symptom and Impact Questionnaire; ORR, overall response rate; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetics; pre-med, pre-medication; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; SC, subcutaneous; SUD, step-up dosing.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

MajesTEC-3: PFS (Primary Endpoint)

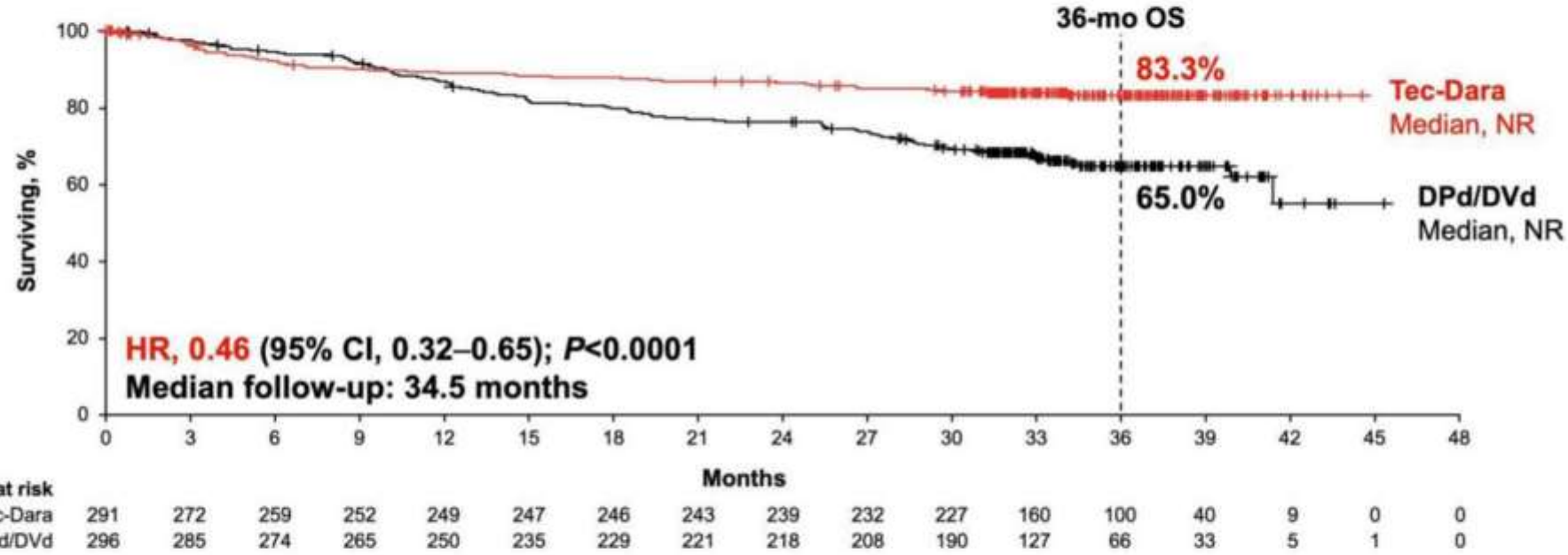


Tec-Dara significantly improved PFS, with a plateauing curve after ~6 months and >90% of patients progression-free at 6 months sustaining such a benefit at 3 years

[a]The *P* value crossed the prespecified stopping boundary for superiority for the first interim analysis (*P*=0.0139).
CI, confidence interval; HR, hazard ratio; NR, not reached.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

MajesTEC-3: OS

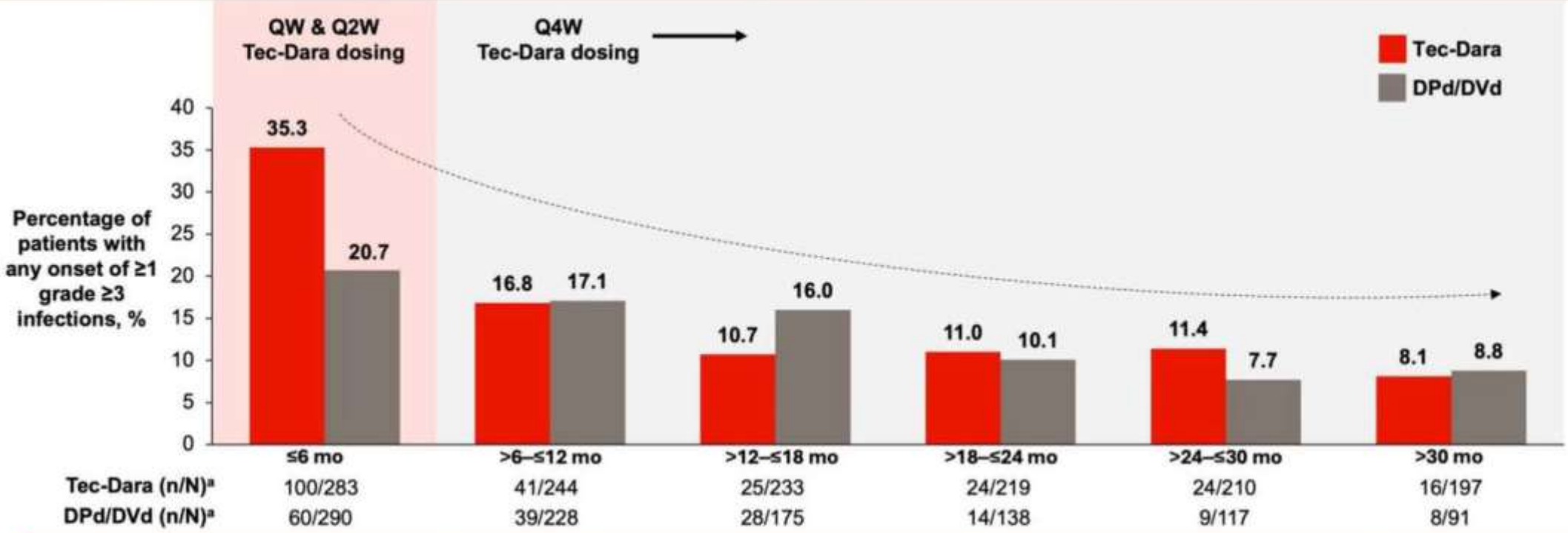


Tec-Dara significantly improved OS versus DPd/DVd, with 83% of patients alive at 3 years

Analysis of RMST demonstrated an OS benefit for Tec-Dara versus DPd/DVd (RMST difference, 2.15 months; *P*=0.0088).
RMST, restricted mean survival time.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

MajesTEC-3: Grade ≥3 Infections Over Time



Any onset grade ≥3 infections were comparable across arms after 6 months and decreased over time

[a]Includes patients who are in the TEAE-reporting period for the specific window. Noting that patients are counted only once in a window for any given event, regardless of the number of times they actually experienced the event within the specific time window.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

Zukunft: Trispezifische Antikörper, z.B. BCMA×GPRC5D×CD3

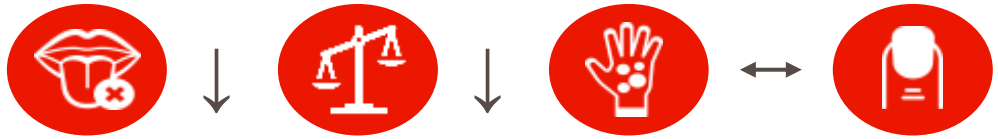
100 mg Q4W SC with 1 step-up dose selected as RP2D

- Dose escalation
- Dose and schedule optimization
- Step-up dose optimization

→ 100 mg Q4W SC (5 mg step-up dose)

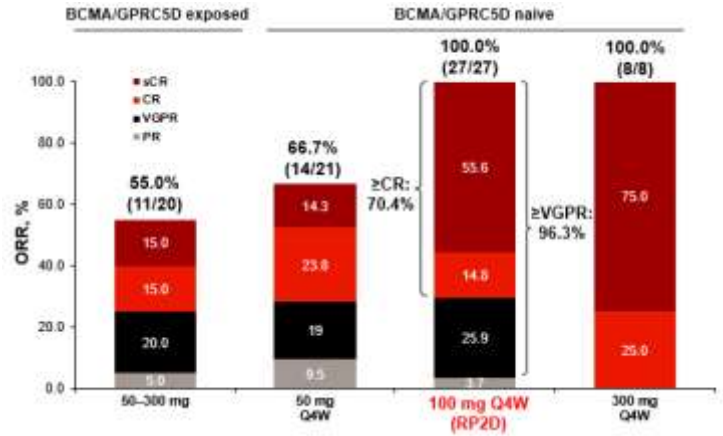
Weniger Nebenwirkungen ?

Taste ↓ Weight decrease ↓ Skin ↔ Nail

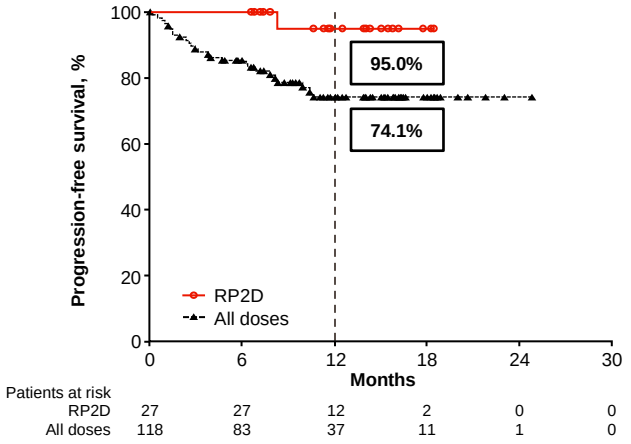


Weniger Geschmacks- und Gewichtsverlust (?)

Sehr häufiges und tiefes Ansprechen



Langes Ansprechen ?



Presented by NWCJ van de Donk at the American Society of Clinical Oncology (ASCO) Annual Meeting; May 30–June 3, 2025; Chicago, IL, USA & Virtual

Zusammenfassung

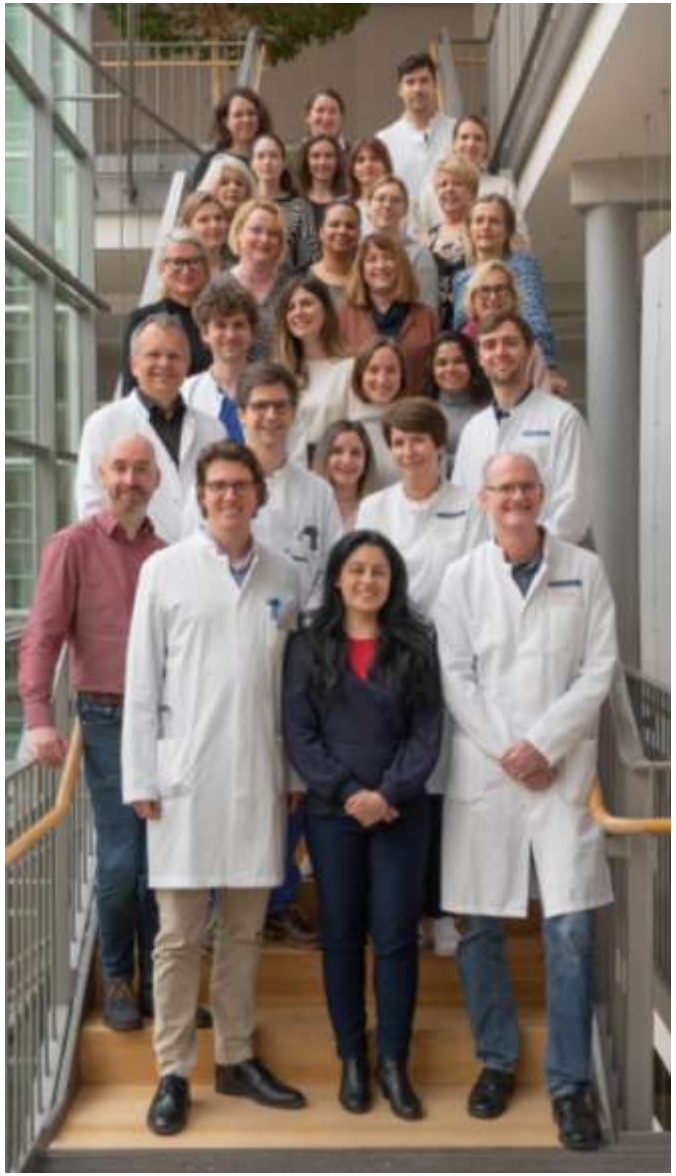
- zur Behandlung des Multiplen Myeloms sind sehr vielversprechende Immuntherapien in der Entwicklung und nun auch zugelassen.
- Sowohl CAR T Zellen als auch bispezifische Antikörper erreichen hohe und andauernde Ansprechraten auch in sehr stark vorbehandelten Patienten.
- Die CAR T Zelltherapie beim Myelom ist ab dem ersten Rezidiv der Erkrankung verfügbar, weitere in der Entwicklung.
- Vier bispezifische Antikörper ebenfalls zugelassen. Ausblick Tri-spezifische Antikörper
- Der beste Zeitpunkt für den Einsatz dieser Therapien im Krankheitsverlauf muss noch herausgefunden werden. CAR T besser vor bispezifischen Antikörpern
- Möglicherweise in Zukunft in vivo CARs (ohne Herstellung, ohne Lymphdepletion)
- Zur erfolgreichen Therapie ist eine vertrauensvolle Zusammenarbeit zwischen Patienten und Ärzten sehr wichtig.

HEIDELBERG UNIVERSITY HOSPITAL

GM MG GERMAN-SPEAKING MYELOMA MULTICENTER GROUP

Heidelberg Myeloma Center

Vielen Dank für Ihre Aufmerksamkeit



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