Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

KML KONGRESSE

Expert:innen berichten zu Lymphomen & Leukämien

Amy Spartwasser, Stock-Fotografie-ID: 1455291856

ASH 2025

ORLANDO | 06.-09. Dezember 2025

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Expert:innen berichten zu Lymphomen & Leukämien

Prof. Dr. med. Katja Weisel
Universitätsklinikum Hamburg Eppendorf

Multiples Myelom (MM)

Offenlegung potentieller Interessenskonflikte

LymphomKompetenz KOMPAKT – ASH2025 wird in Kooperation mit acht unterstützenden Firmen durchgeführt.
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Besitz von Geschäftsanteilen, Aktien oder Fonds	
Patent, Urheberrecht, Verkaufslizenz	
Honorare	Abbvie, Adaptive, Amgen, Bristol Myers Squibb, Celgene, Janssen, GSK, Karyopharm, Novartis, Oncopeptides, Pfizer, Roche Pharma, Takeda, Sanofi
Finanzierung wissenschaftlicher Untersuchungen	Amgen, Celgene, Janssen, Sanofi; GSK, Abbvie (alle an die Institution)
Andere finanzielle Beziehungen	
Immaterielle Interessenkonflikte	

Kapitel 1

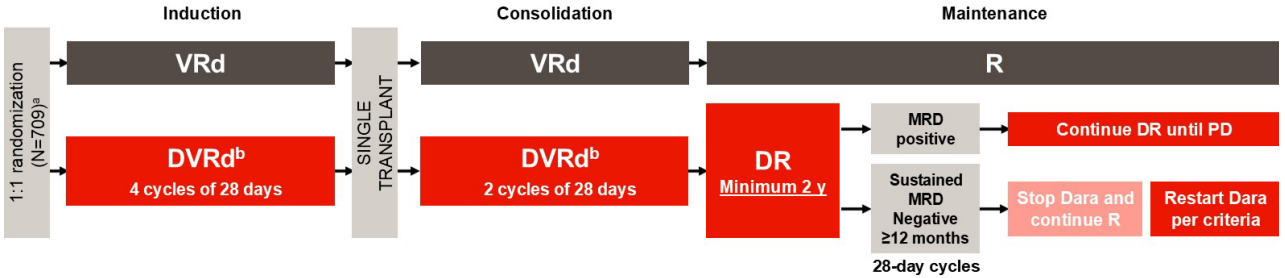
Doppel-Erhaltungstherapie in der ersten Behandlungslinie

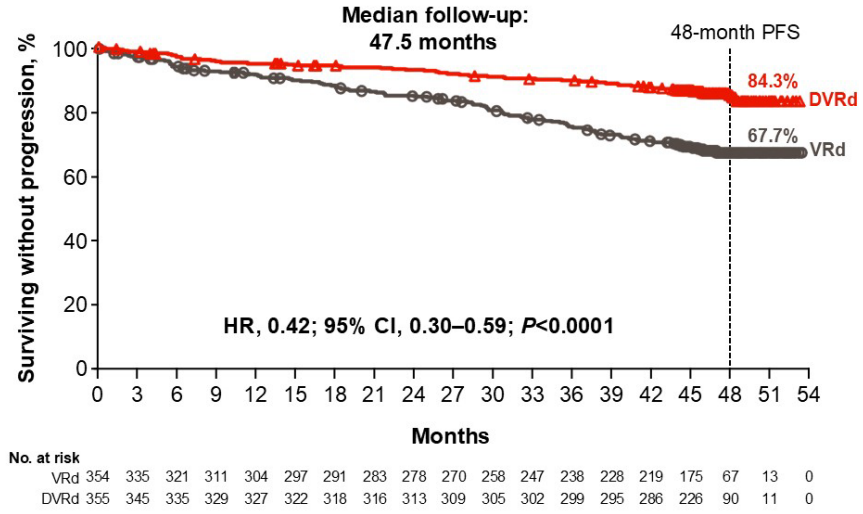
Dara-Len als Kombinationserhaltungstherapie bei TE NDMM

Hintergrund

Die Therapie analog PERSEUS ist Behandlungsstandard beim neu diagnostizierten MM für die Transplantations-geeigneten Patient:innen bis bisher unerreichten Ergebnissen in PFS und OS

PERSEUS impliziert die Doppelerhaltungstherapie für alle Patient:innen





Dara-Len als Kombinationserhaltungstherapie bei TE NDMM

#97: Minimal Residual Disease Dynamics in Post-Transplant Patients With Newly Diagnosed Multiple Myeloma Who Received Daratumumab Plus Lenalidomide Versus Lenalidomide Alone as Maintenance Therapy in the AURIGA Study

Chung et al.

Dara-Len als Kombinationserhaltungstherapie bei TE NDMM

AURIGA: Study Design

- **Objective: to better understand the evolution of MRD status during maintenance and its impact on long-term outcomes**

Key eligibility criteria
- 18-79 years of age
- NDMM with ≥4 cycles of induction therapy and underwent ASCT within 12 months of the start of induction
- ≥VGPR at screening[a]
- MRD[b] positive (10^{-5}) after ASCT
- No prior anti-CD38
- Randomization within 6 months of the ASCT date

Stratification factor
- Cytogenetic risk[c] at diagnosis (standard/unknown vs high risk)

1:1 RANDOMIZATION (N = 200)

Maintenance: up to 36 cycles[d] (28-day cycles)

D-R

DARA: 1,800 mg SC[e] QW Cycles 1-2, Q2W Cycles 3-6, Q4W Cycles 7+
R: 10 mg PO daily Days 1-28
(after Cycle 3, 15 mg PO daily if tolerated)

R

R: 10 mg PO daily Days 1-28
(after Cycle 3, 15 mg PO daily if tolerated)

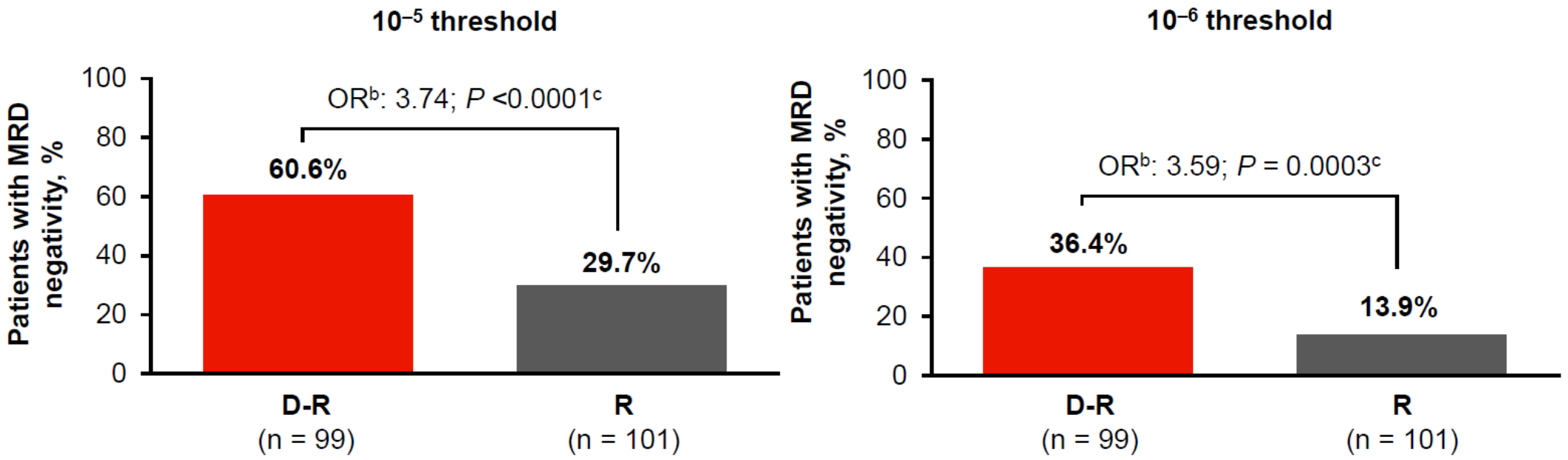
Primary endpoint
- MRD-negative (10^{-5}) conversion rate from baseline to 12 months after maintenance treatment

Secondary endpoints
- Overall MRD-negative conversion rate, sustained MRD-negative rate, PFS, response rate, duration of ≥CR, OS, safety

MRD[b] obtained after 12, 18, 24, and 36 cycles, enabling analysis of *MRD dynamics*

Dara-Len als Kombinationserhaltungstherapie bei TE NDMM

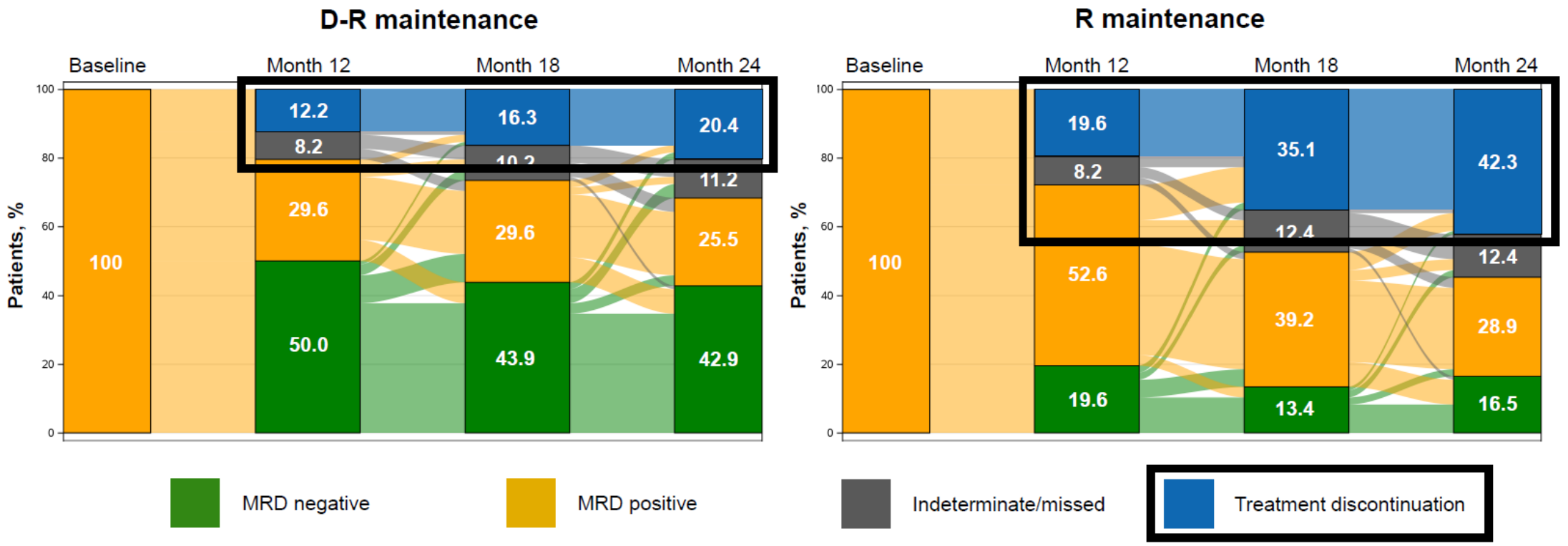
AURIGA: MRD-Negative (10^{-5} and 10^{-6}) Conversion Rates[a]



At a median follow-up of 40.3 months, MRD-negative conversion rates continued to be more than double with D-R at both the 10^{-5} and 10^{-6} thresholds compared with R alone

Dara-Len als Kombinationserhaltungstherapie bei TE NDMM

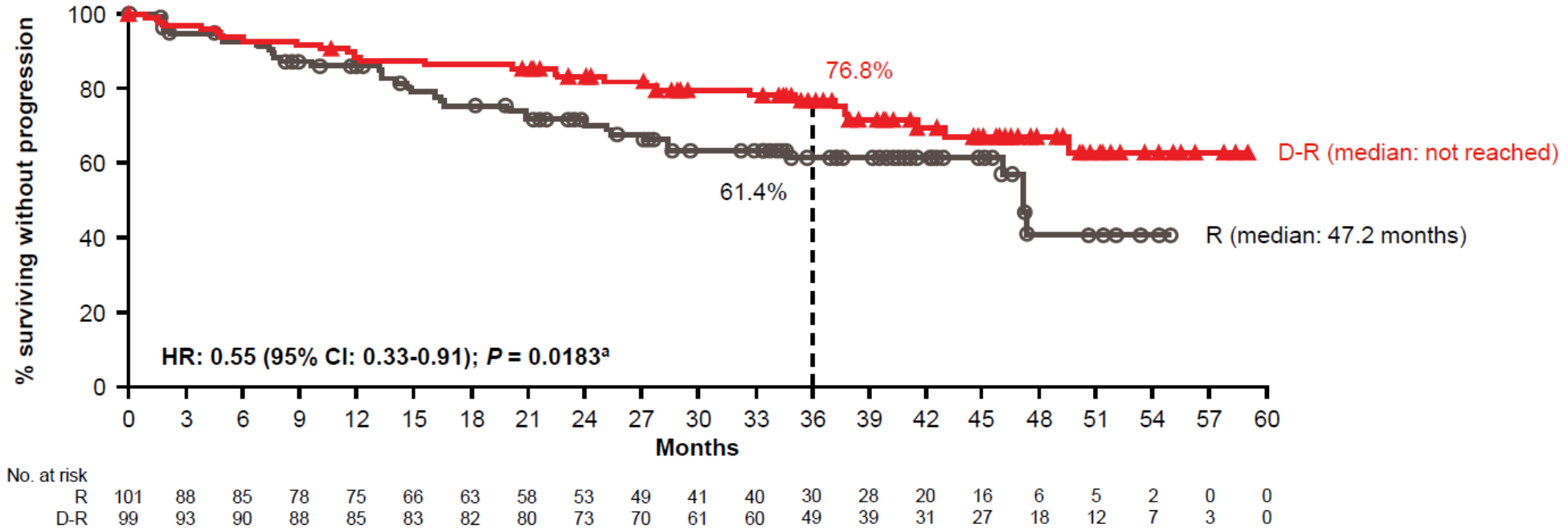
AURIGA: Sankey Plots of MRD (10^{-5}) Status Over Time[a]



D-R maintenance achieved and maintained higher rates of MRD negativity at the 10^{-5} threshold over time versus R alone

AURIGA: PFS by Investigator Assessment

Median follow-up, 40.3 months



PFS favored D-R versus R maintenance, with a 45% reduction in the risk of disease progression or death

Mehr

Dara-Len als Kombinationserhaltungstherapie bei TE NDMM

Zusammenfassung

Die AURIGA Studie bestätigt die wichtige Rolle der Doppelerhaltungstherapie:

- Deutlich höhere Rate an MRD Konversion als imminente Voraussetzung für einen kurativen Behandlungsansatz in der ersten Therapielinie
- Doppelerhaltung führt zu weniger Behandlungsabbrüchen
- Daratumumab kann bei erhaltener MRD Negativität nach 2 Jahren abgesetzt werden

Kapitel 2

Neue Daten zu bispezifischen T-Zell Engagern

TCEs in der Behandlung des rezidivierten und refraktären Myelom

Hintergrund

- Mit der Etablierung der Quadruplet Therapien in der Erstbehandlung steigt der Bedarf an BCMA-gerichteten Therapien ab der 2. Behandlungslinie
- Aktuell ist Cilta cel als BCMA gerichtete CAR-T Zelltherapie ab dem 1. Rezidiv bei Lenalidomid-refraktären Patient:innen zugelassen, die PI exponiert sind und refraktär auf die letzte Behandlungslinie
- Cilta cel hat vs. SOC einen hochsignifikanten Vorteil im PFS und OS gezeigt

ASH 2025: Erste randomisierte Phase III Studie zur Kombinationstherapie des BCMA gerichteten TCE Teclistamab in Kombination mit Daratumumab versus SOC

TCEs in der Behandlung des rezidivierten und refraktären Myelom

	Teclistamab[1-3]	Elranatamab[4-6]	Linvoseltamab[7-8]
Monotherapy Study Data Summary Source	**MajesTEC-1** Phase 1/2	**MagnetisMM-3** Phase 2	**LINKER-MM1** Phase 1/2
Prior Therapy	Prior PI, IMiD, CD38 No prior BCMA	Prior PI, IMiD, CD38 No prior BCMA	Prior PI, IMiD, CD38 Post-CAR T ≥PR
Monotherapy Efficacy	**ORR 63%** **mDOR 18.4 mo** **mPFS 11.4 mo** **mOS 22.2 mo** **(mF/up 30.4 mo)**	**ORR 61%** **24-mo DOR 67%** **mPFS 17.2 mo** **mOS 24.6 mo** **(mF/up 28.4 mo)**	**ORR 71%** **12- mo DOR 81%** **12-mo PFS 70%** **mOS NR** **(mF/up 14.3 mo)**

BCMA=B-cell Maturation Antigen. CAR T=Chimeric Antigen Receptor. GR=Grade. iMiD=Immunomodulatory Drugs. mDOR=Median Duration of Response. mF/up=Median Follow Up. Mo=Months. mOS=Median Overall Survival. mPFS=Median Progression-Free Survival. NE=Not Evaluable. NR=Not Reached. ORR=Overall Response Rate. PI=Proteasome Inhibitors. PR=Partial Response. Q2W=Every 2 Weeks. RRMM=Relapsed/Refractory Multiple Myeloma.

1. Teclistamab-cqyv. EMA SmPC. Janssen-Cilag International NV, Belgium: 2022. Updated 2024. 2. Teclistamab-cqyv. FDA Label. Janssen Biotech, Inc. Horsham, PA 19044: 2022. Updated 2024.
3. Garfall AL, et al. Poster #7540. ASCO Annual Meeting; May 31-June 4, 2024; Chicago, IL. 4. Elrantamab-bcmm. EMA SmPC. Pfizer Europe MA EEIG, Belgium: 2023. Updated 2024.
5. Elrantamab-bcmm. FDA Package Insert. Initial U.S. Approval: 2023. (Updated Aug 2023). 6. Tomasson MH, et al. Hemasphere. 2024 Jul 24;8(7):e136.
7. Linvoseltamab injection, for intravenous use. EMA SmPC. Regeneron Ireland Designated Activity Company (DAC). Dublin, Ireland . May 2025.

Teclistamab-Daratumumab beim rezidivierten/refraktären Multiplen Myelom

LBA-6: Phase 3 Randomized Study of Teclistamab Plus Daratumumab Versus Investigator's Choice of Daratumumab and Dexamethasone With Either Pomalidomide or Bortezomib (DPd/DVd) in Patients With Relapsed Refractory Multiple Myeloma (RRMM): Results of MajesTEC-3

M. Mateos et al.

Teclistamab-Daratumumab beim rezidivierten/refraktären Multiplen Myelom

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

- **Tec-Dara**
- **DPd/DVd per investigator's choice[b]**

Primary endpoint

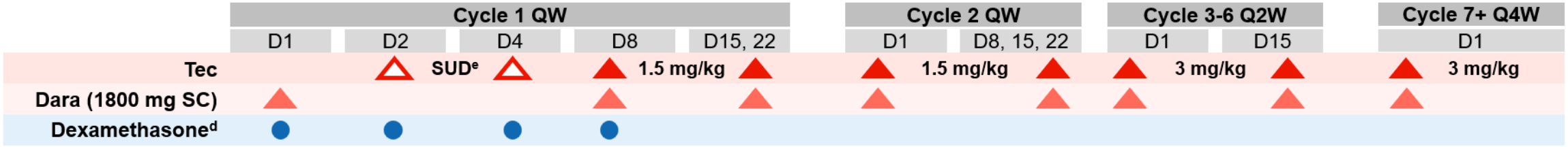
- PFS per IRC

Key secondary endpoints

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

Other secondary endpoints

- Safety
- PK and immunogenicity

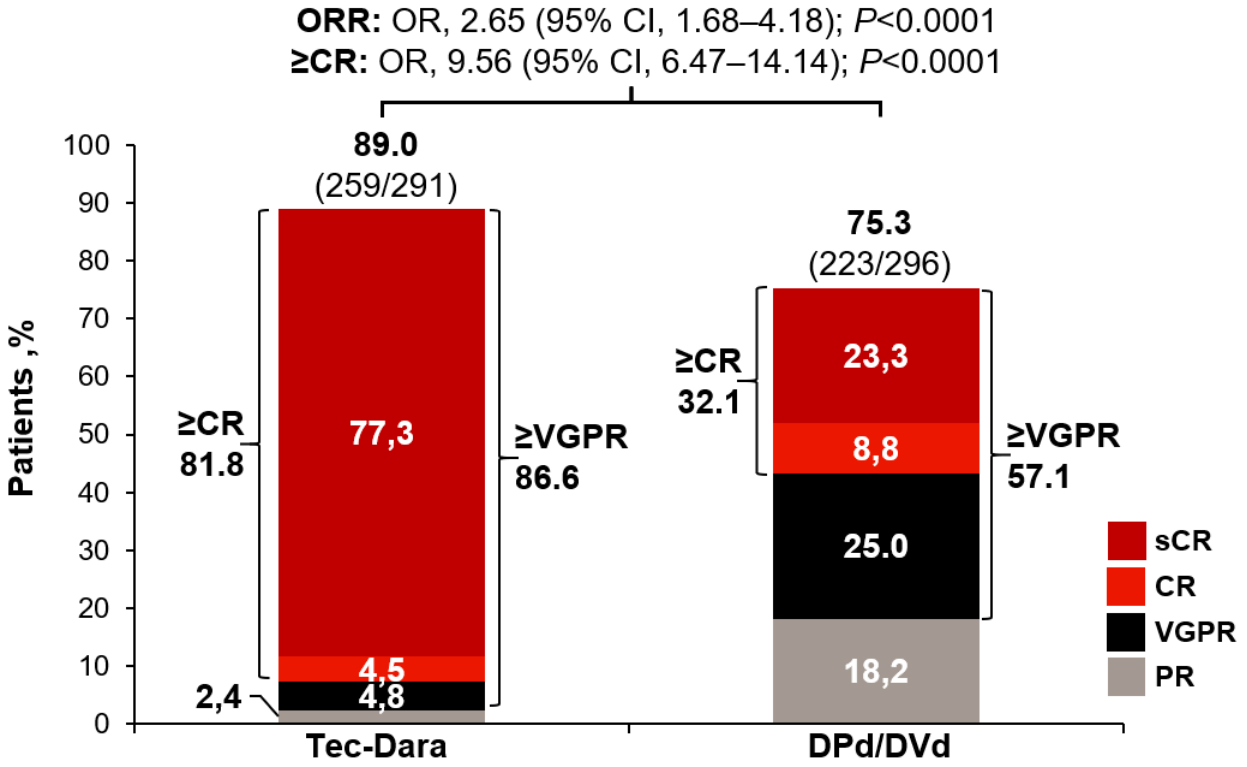


Tec-Dara was dosed using an established Dara SC schedule; steroid free after Cycle 1 Day 8

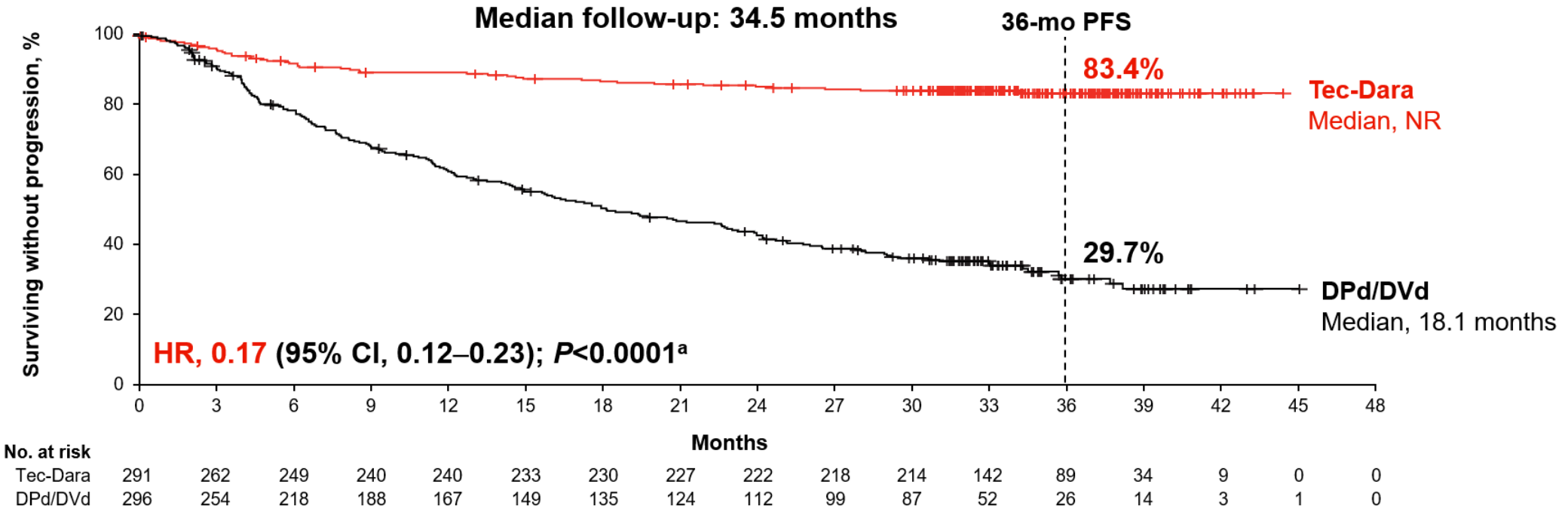
Teclistamab-Daratumumab beim rezidivierten/refraktären Multiplen Myelom

Characteristic	Tec-Dara (n=291)	DPd/DVd (n=296)
Age		
Median (range), years	64 (36–88)	63 (25–84)
≥75 years, n (%)	31 (10.7)	25 (8.4)

Characteristic	Tec-Dara (n=291)	DPd/DVd (n=296)
Prior therapy exposure, n (%)		
PI	290 (99.7)	296 (100)
IMiD	291 (100)	296 (100)
Anti-CD38, n (%)	15 (5.2)	16 (5.4)
Refractory status, n (%)		
To last prior LOT	250 (85.9)	251 (84.8)
Any PI	117 (40.2)	104 (35.1)
Any IMiD	247 (84.9)	253 (85.5)
Lenalidomide	240 (82.5)	251 (84.8)
Double (PI and IMiD)	99 (34.0)	88 (29.7)



MajesTEC-3: PFS (Primary Endpoint)



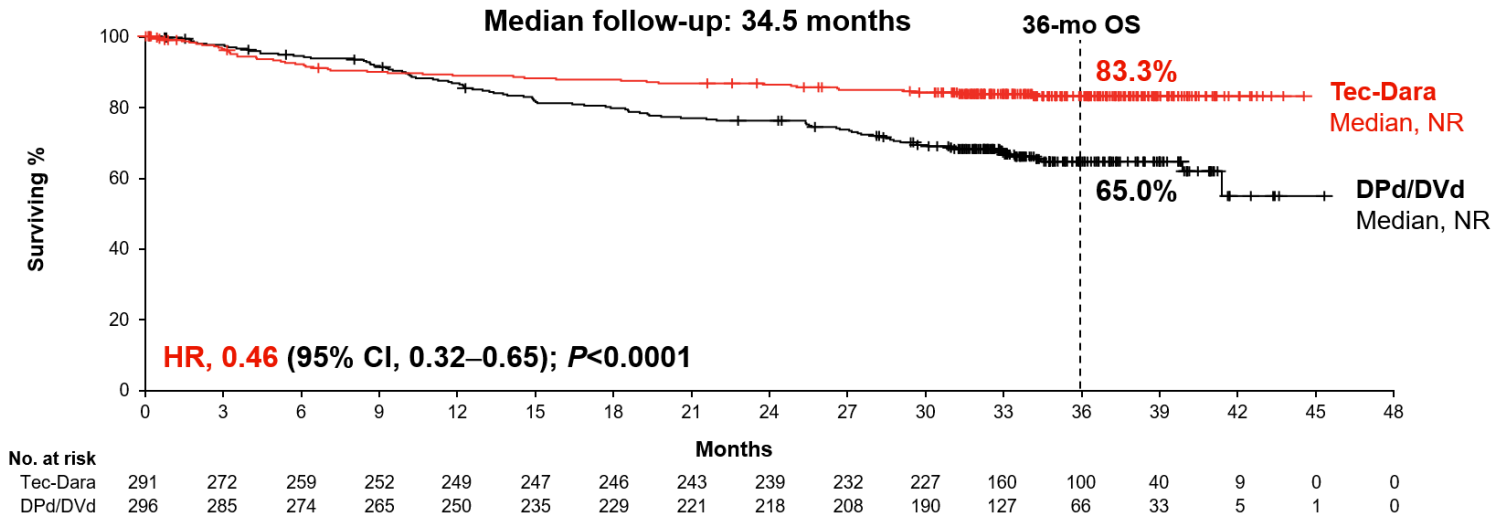
Tec-Dara significantly improved PFS versus DPd/DVd, with 83% of patients alive and progression free at 3 years

Teclistamab-Daratumumab beim rezidivierten/refraktären Multiplen Myelom

OS curves crossed around 10 months

- 29 deaths in each group prior to cross
  - In Tec-Dara, primarily driven by early infectious deaths (n=12)
    - All 12 deaths occurred <6 months
    - 9 patients did not receive any IgRT
  - Remaining 17 Tec-Dara patients died due to AEs (n=6), PD (n=5), or “Other” (n=6)[a]

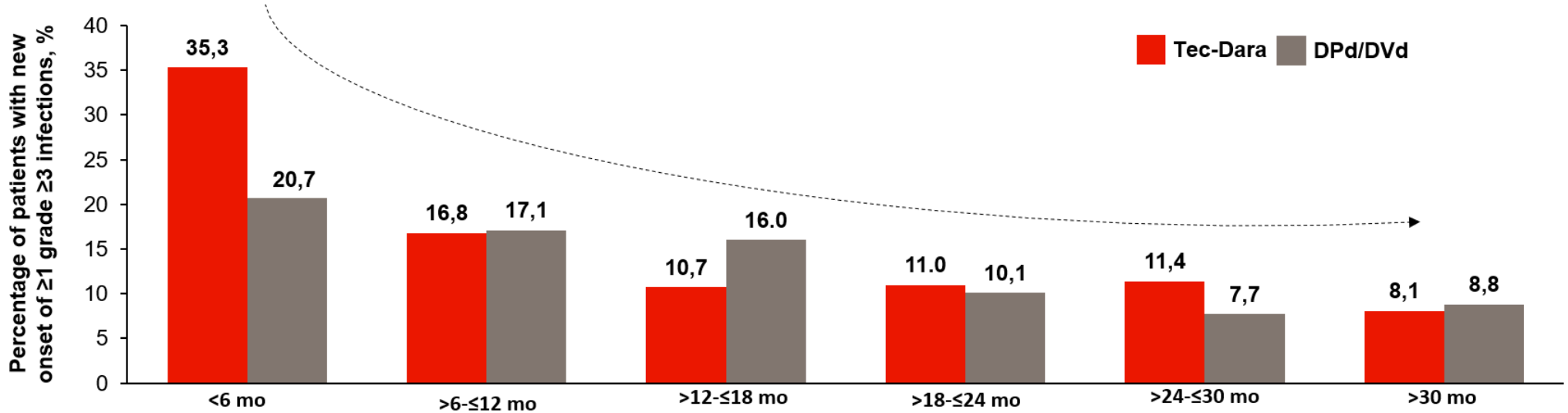
MajesTEC-3: OS



Tec-Dara significantly improved OS versus DPd/DVd, with an emerging plateau from 6 months and 83% patients alive at 3 years

MajesTEC-3: Grade ≥3 Infections Over Time

- New-onset grade ≥3 infections decreased after 6 months of treatment



	<6 mo	>6-≤12 mo	>12-≤18 mo	>18-≤24 mo	>24-≤30 mo	>30 mo
Tec-Dara (n/N)[a]	100/283	41/244	25/233	24/219	24/210	16/197
DPd/DVd (n/N)[a]	60/290	39/228	28/175	14/138	9/117	8/91

Infection rates were comparable across groups from 6 months and substantially decreased over time

Teclistamab-Daratumumab beim rezidivierten/refraktären Multiplen Myelom

Zusammenfassung

Tec-Dara zeigt die beste HR einer Phase III Studie beim RRMM

-> Cilta cel oder Tec-Dara?

- CAR-T Zelltherapie erlaubt eine einmalige Infusion
- Kuratives Signal für die Rezidivtherapie (33% Rezidivfreiheit nach 5 Jahren in CARTITUDE-1)
- Keine T-Zell Erschöpfung und Immunrekonstitution nach CAR-T
- Signifikant weniger Mutationen an BCMA mit CAR-T
- Toxizitätsprofil unterschiedlich: Infektionen (TCE) versus neurologische Toxizität (Cilta cel)

Tec-Tal in der Therapie des extramedullären Myeloms

#698

Efficacy and Safety of Talquetamab + Teclistamab in Patients With Relapsed/Refractory Multiple Myeloma and Extramedullary Disease: Updated Phase 2 Results From the RedirecTT-1 Study With Extended Follow-Up

S. Usmani et al.

Tec-Tal in der Therapie des extramedullären Myeloms

RedirecTT-1 Phase 2 EMD (Tal + Tec): Largest Dedicated Study in Patients With True EMD

Screening

Eligibility criteria

- Triple-class exposed RRMM[a]
- True EMD, defined as ≥1 nonradiated bone-independent soft tissue plasmacytoma ≥2 cm in greatest dimension confirmed by central review of PET-CT scans[b,c]
- Prior CAR-T and non-BCMA/-GPRC5D bispecific antibody therapies were permitted
- Nonsecretory and oligosecretory disease were permitted

Treatment

Tal 0.8 mg/kg Q2W SC[d,e]
+
Tec 3.0 mg/kg Q2W SC[d,e]

Option to switch to monthly dosing after 4 cycles and ≥VGPR, or after 6 cycles (irrespective of response)

Step-up dosing[d] 2–4 days apart (Tal + Tec)
SUD1: 0.01 mg/kg + 0.06 mg/kg
SUD2: 0.06 mg/kg + 0.3 mg/kg
SUD3: 0.4 mg/kg + 1.5 mg/kg

Endpoints

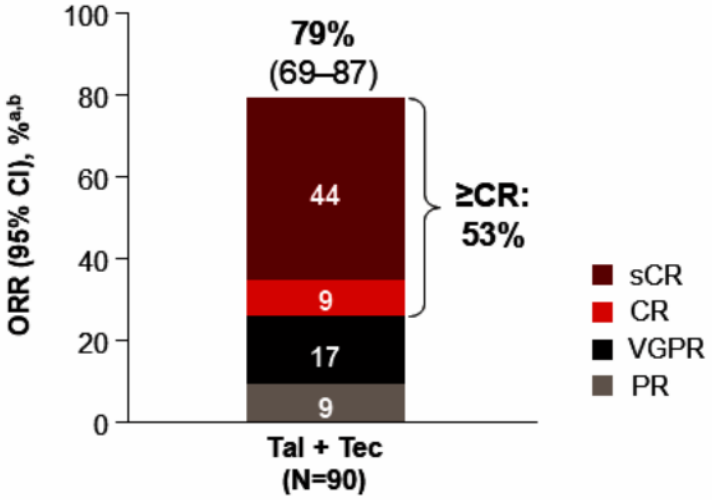
Primary endpoint: ORR[f]

Secondary endpoints:

- DOR[f]
- PFS[f]
- OS
- Safety

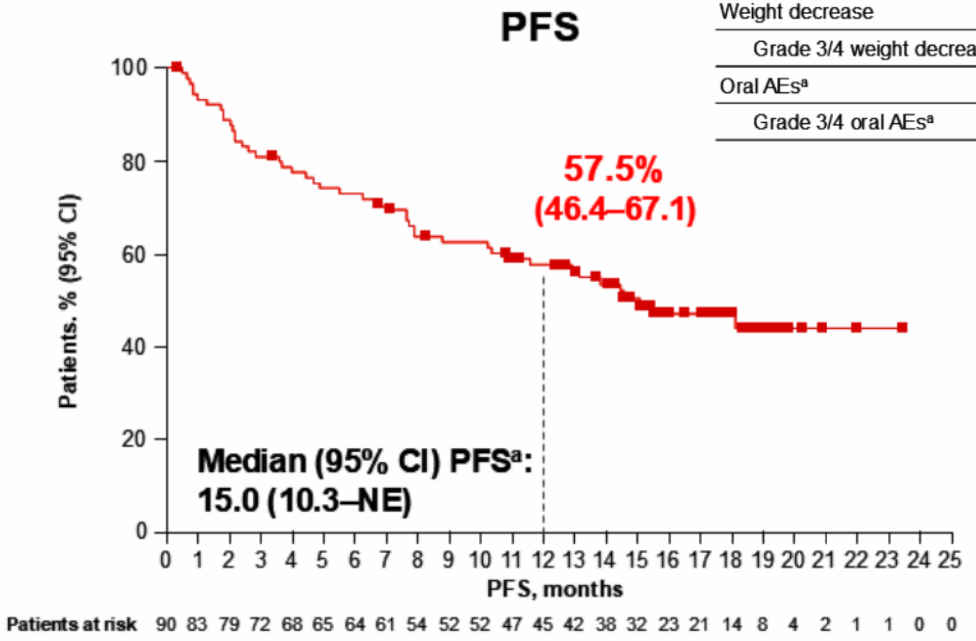
Tec-Tal in der Therapie des extramedullären Myeloms

RedirecTT-1 Phase 2 EMD (Tal + Tec): Deep, Durable Responses at 16.8 Months Median Follow-up



Median (range) time to:

- First response, 2.6 (1.0–5.8) months
- Best response, 5.1 (1.0–16.6) months



Outcome,[f] n (%)	Initial Q2W dosing (N=90)	After adjustment to Q4W dosing (n=56)[g]
Any-grade infections	65 (72.2)	34 (60.7)
Grade ≥3 infections	29 (32.2)	14 (25.0)
Weight decrease	46 (51.1)	15 (26.8)
Grade 3/4 weight decrease	8 (8.9)	5 (8.9)
Oral AEs[a]	77 (85.6)	12 (21.4)
Grade 3/4 oral AEs[a]	3 (3.3)	2 (3.6)

With additional ~4 months of median follow-up, ORR approached 80%; 62% of responders remained in response at 1 year

Weitere wichtige Abstracts zu TCE im Rezidiv

#247: Etentamig Plus Pomalidomide-Dexamethasone Combination Therapy in Relapsed or Refractory Multiple Myeloma: A Phase 1b Dose-Escalation and Safety Expansion Study

P. Vorhees et al.

#100: Safety and Efficacy of Elranatamab in Combination With Iberdomidein Patients With Relapsed or Refractory Multiple Myeloma: Results from the Phase 1b MagnetisMM-30 Trial

A. Suvannasankha et al.

Kapitel 3

Geht noch mehr?

#697

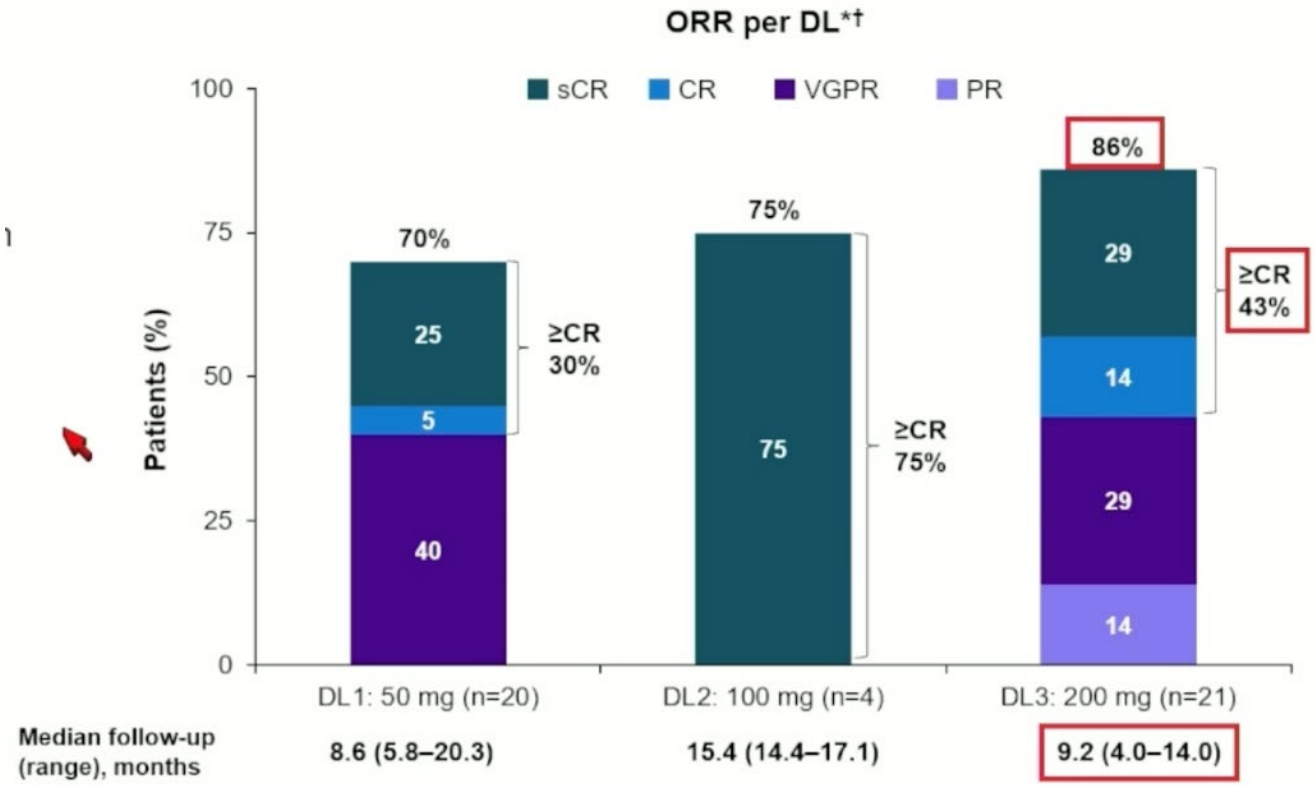
Safety and efficacy of linvoseltamab as a simplified monotherapy first-line regimen in NDMM: Initial results from the window of opportunity Phase 1/2 LINKER-MM4 trial

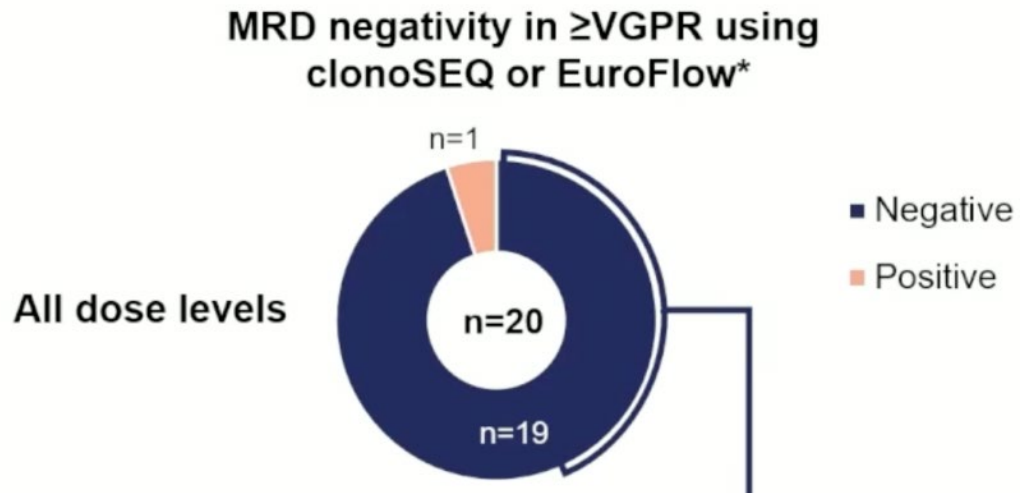
Robert Z. Orlowski[1], Mansi Shah[2], Rajshekhar Chakraborty[3], Pascual Fernández-Abellán[4], Xavier Leleu[5], Albert Oriol[6,7], Henning Schade[8], Don Stevens[9], Laurent Garderet[10], Sarah Larson[11], Lisa Lee[12], Jean-Marie Michot[13], Gareth Morgan[14], Michael Schuster[15], Aurora Breazna[16], Oluwaseun Aina[16], Amishi Dhadwal[16], Jennifer Sims[16], Colby S. Shemesh[16], Anasuya Hazra[16], Daniel J. Lee[16], Glenn S. Kroog[16], Karen Rodriguez Lorenc[16], Steven E. Quatela[16], Christopher Ferreri[17]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Rutgers Cancer Institute, New Brunswick, NJ, USA; [3]Division of Hematology/Oncology, Department of Medicine, Columbia University Irving Medical Center, New York, NY, USA; [4]Hospital General Universitario de Alicante, Alicante, Spain; [5]Centre Hospitalier Universitaire de Poitiers, Poitiers, France; [6]Institut Català d'Oncologia, Badalona, Spain; [7]Institut Josep Carreras, Badalona, Spain; [8]Colorado Blood Cancer Institute, Denver, CO, USA; [9]Norton Cancer Institute, Louisville, KY, USA; [10]Hopital Pitié Salpétrière, Assistance Publique – Hôpitaux de Paris, Sorbonne Université, Paris, France; [11]UCLA Jonsson Comprehensive Cancer Center, Los Angeles, CA, USA; [12]Division of Hematology and Oncology, Department of Medicine, University of California Irvine School of Medicine, Irvine, CA, USA; [13]Département d'Innovation Thérapeutique et d'Essais Précoces, Gustave Roussy, Villejuif, France; [14]New York University Langone Medical Center, New York, NY, USA; [15]Stony Brook University Cancer Center, Stony Brook, NY, USA; [16]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; [17]Atrium Health Levine Cancer Institute, Wake Forest University School of Medicine, Charlotte, NC, USA

ClinicalTrials.gov ID: NCT05828511

#697: Linvoseltamab Monotherapie bei ND TNE Myelom





200 mg dose level: 100% (9/9) of MRD-evaluable patients were negative at 10^{-5} sensitivity

- 100% (8/8) of clonoSEQ evaluable patients were negative at 10^{-6} sensitivity

Teclistamab-Daratumumab beim neu diagnostizierten Multiplen Myelom

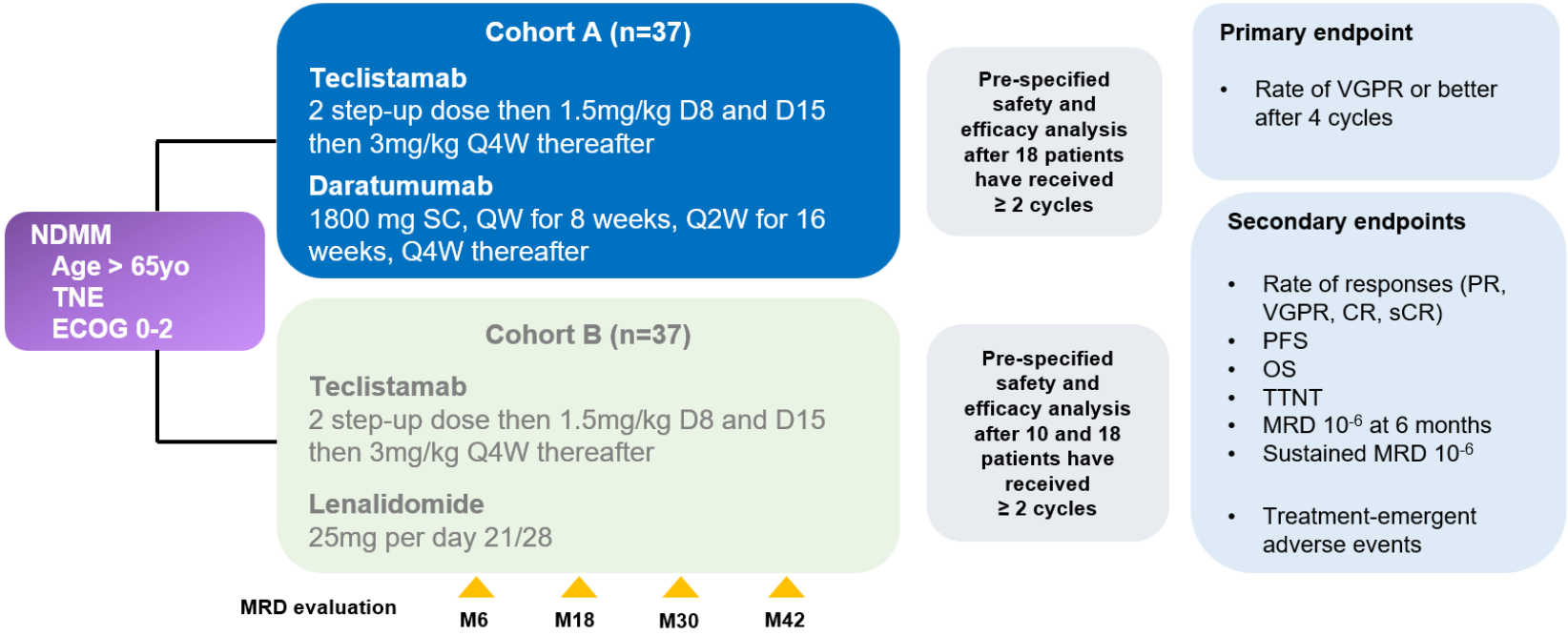
#367: A phase 2 study of teclistamab in combination with daratumumab in elderly patients with newly diagnosed multiple myeloma: the IFM2021-01 TecLille trial, cohort A

S. Manier et al.

Teclistamab-Daratumumab beim neu diagnostizierten Multiplen Myelom

IFM 2021-01 TecLille - Study design

Phase 2 study of Tec-Dara and Tec-Len in TNE NDMM (n = 74)

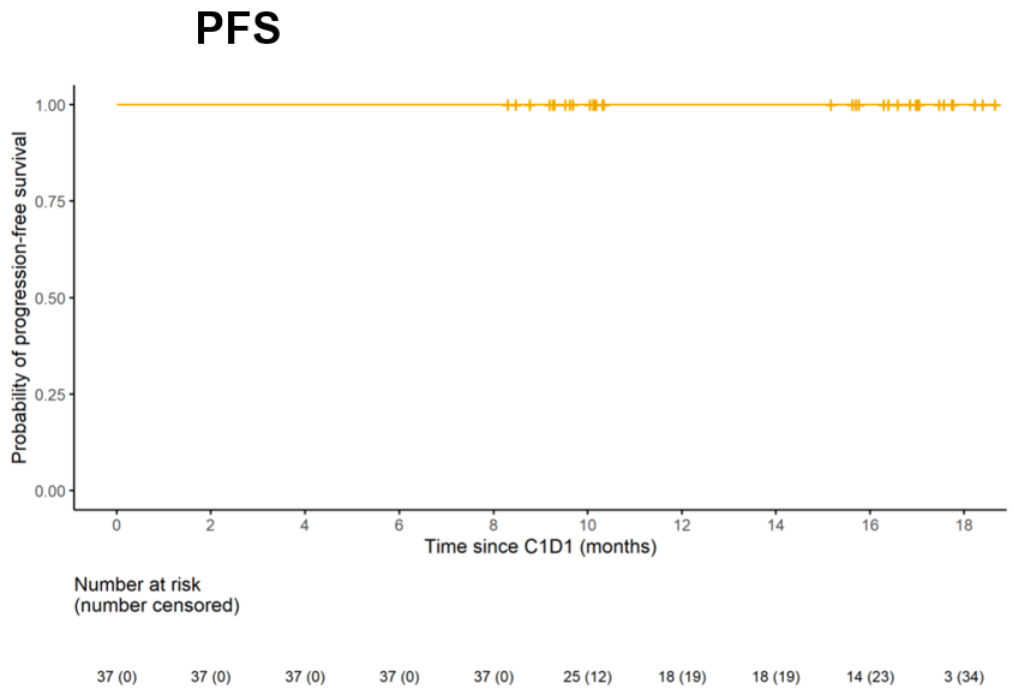


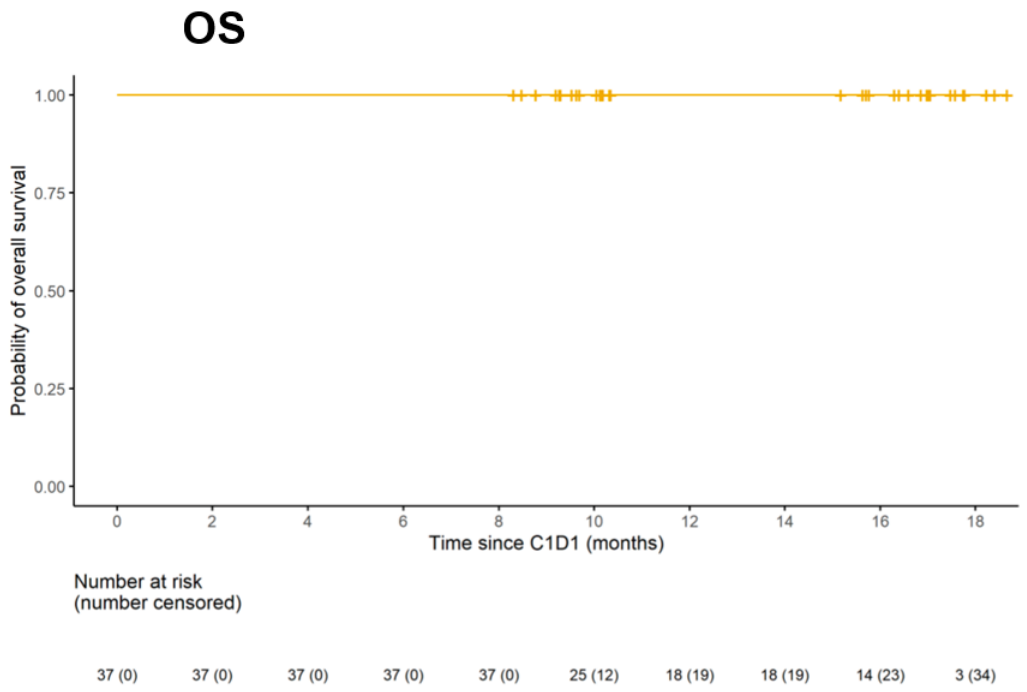
Current amendment:
Teclistamab 3mg/kg Q8W after C13 if CR or better and treatment interruption if 2-years sustained MRD -

NCT05572229

IFM 2021-01 TecLille – cohort A: Tec-Dara
PFS and OS

Median follow up time = 10.3 months





Publication Number: 258

A Dual Targeting BCMA and CD19 FasTCAR-T (GC012F/AZD0120) as First-line Therapy for Newly Diagnosed Multiple Myeloma

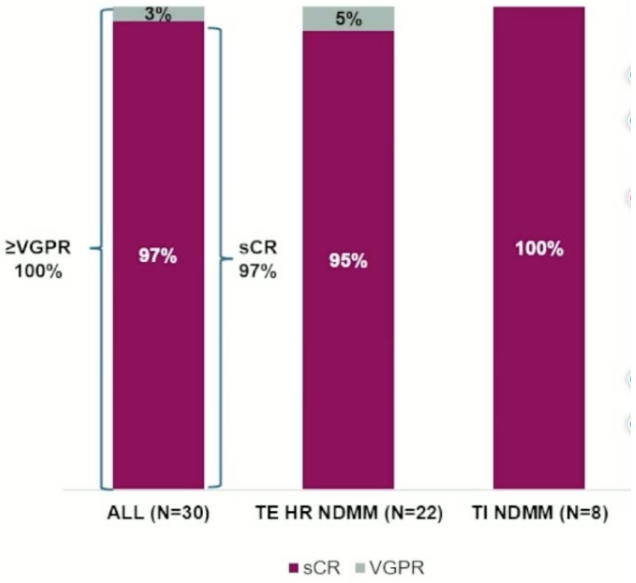
Juan Du,*[1] Wanting Qiang,[1] Jing Lu,[1] Yanchun Jia,[1] Haiyan He,[1] Jin Liu,[1] Pei Guo,[1] Ying Yang,[1] Zhongyuan Feng,[1] Lina Jin,[1] Xiaoqiang Fan,[1] Nina Shah,[2] Qi Zhang,[3] Lianjun Shen,[3] Jia Liu[3]

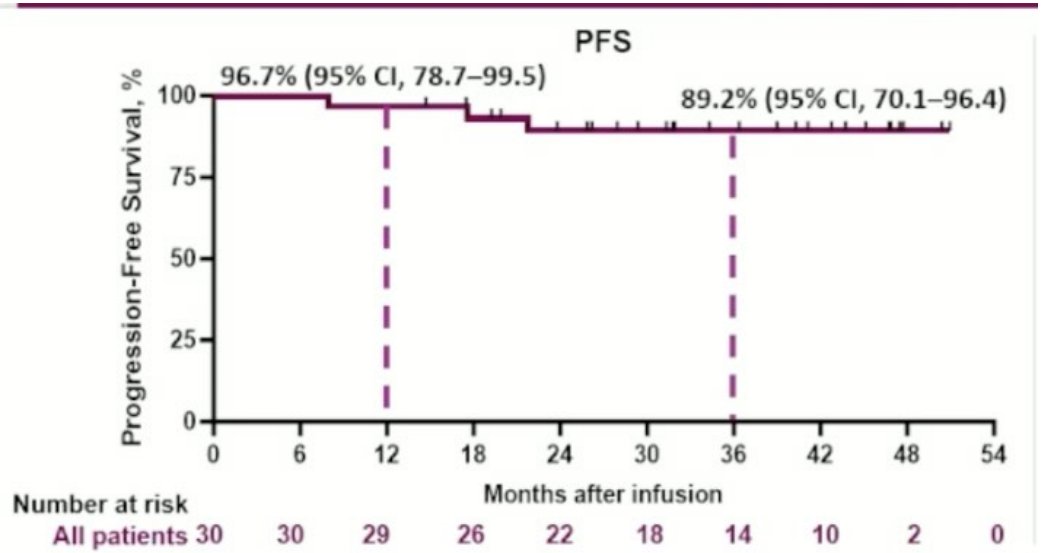
[1]Department of Hematology, Myeloma & Lymphoma Center, Shanghai Changzheng Hospital, Shanghai, China
[2]AstraZeneca, Gaithersburg, MD, USA
[3]Gracell Biotechnologies Ltd., Shanghai, China

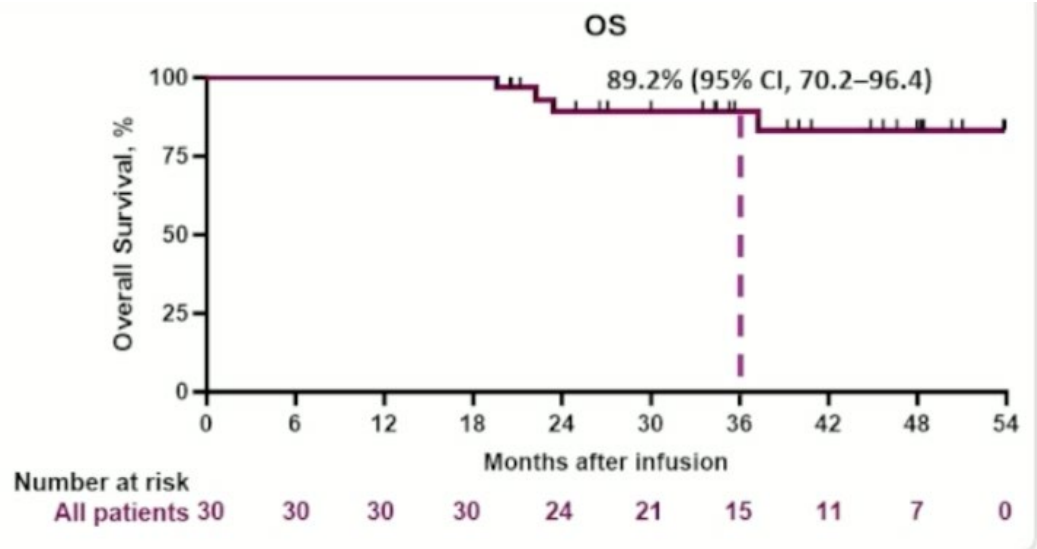
Key eligibility criteria

- Diagnosed with MM per IMWG criteria
- ECOG PS ≤3
- Measurable disease
- **Study 1 (NCT04935580): high risk (HR)* transplant eligible (TE) NDMM (N=22)**
- **Study 2 (NCT05840107): transplant ineligible (TI) NDMM (N=8)**

100% ORR in both cohorts







Zusammenfassung | Take-Home-Messages

- Die Daten zu Daratumumab-Len nach autologer Stammzelltransplantation unterstützen dies als neuen Standard
- Teclistamab-Daratumumab wird eine wichtige Standardtherapie ab dem 1. Rezidiv werden
- Teclistamab-Talquetamab wird eine spezifische Zulassung zur Behandlung des extramedullären Myeloms erhalten, die Zulassung wird in Kürze erwartet
- Erstmals gibt es 2025 in der Myelomtherapie signifikante Kurationssignale in Erstbehandlung und Rezidiv mit den aktuell zugelassenen Therapieoptionen
- Die hervorragenden Daten zu CAR-T und TCE in der ersten Behandlungslinie müssen in Phase III Studien bestätigt werden

Die Kurzpräsentationen sind online unter

www.lymphome.de/ash2025

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