Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

ASH 2020 VIRTUAL
5. – 8. Dezember 2020

KML-Experten berichten vom ASH 2020 VIRTUAL

Kompetenznetz Maligne Lymphome

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ASH 2020 VIRTUAL
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Multiples Myelom

Prof. Dr. med. Katja Weisel
II. Medizinische Klinik und Poliklinik | Universitätsklinik Hamburg-Eppendorf

Offenlegung potentieller Interessenskonflikte

LymphomKompetenz KOMPAKT – ASH2020 wird in Kooperation mit fünf unterstützenden Firmen durchgeführt. Diese Firmen haben keinen Einfluss auf die Inhalte dieses Vortrags. Meine weiteren Disclosures betreffen:

Art	Verbundenheit
Anstellungsverhältnis, Führungsposition	
Beratungs-/Gutachtertätigkeit	Amgen, Adaptive, BMS, Celgene, GSK Janssen, Karyopharm, Oncopeptides, Sanofi, Takeda
Besitz von Geschäftsanteilen, Aktien, Fonds	
Patent, Urheberrecht, Verkaufslizenz	
Honorare	Amgen, Adaptive, Abbvie, BMS, Celgene, GSK Janssen, Karyopharm, Roche, Sanofi, Takeda
Finanzierung wissenschaftlicher Untersuchungen	Amgen, Celgene, Sanofi, Janssen (Institution)
Andere (auch immaterielle)	

Multiples Myelom

Erstbehandlung des MM

- Quadruplet bei transplantierbaren Patienten jetzt angekommen- und - der Fels in der Brandung: HD-MEL und autologe PBSCT
- Nicht-transplantierbare Patienten – Unverrückbar MAIA

Rezidivtherapie

Neue Standards:

- APOLLO und CANDOR Studie: Effektive Regime insbesondere nach Lenalidomid

Am Horizont:

- CARs – mit Verve und viel Hoffnung in die Zulassung!

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Erstbehandlung tranplantierbarer Patienten

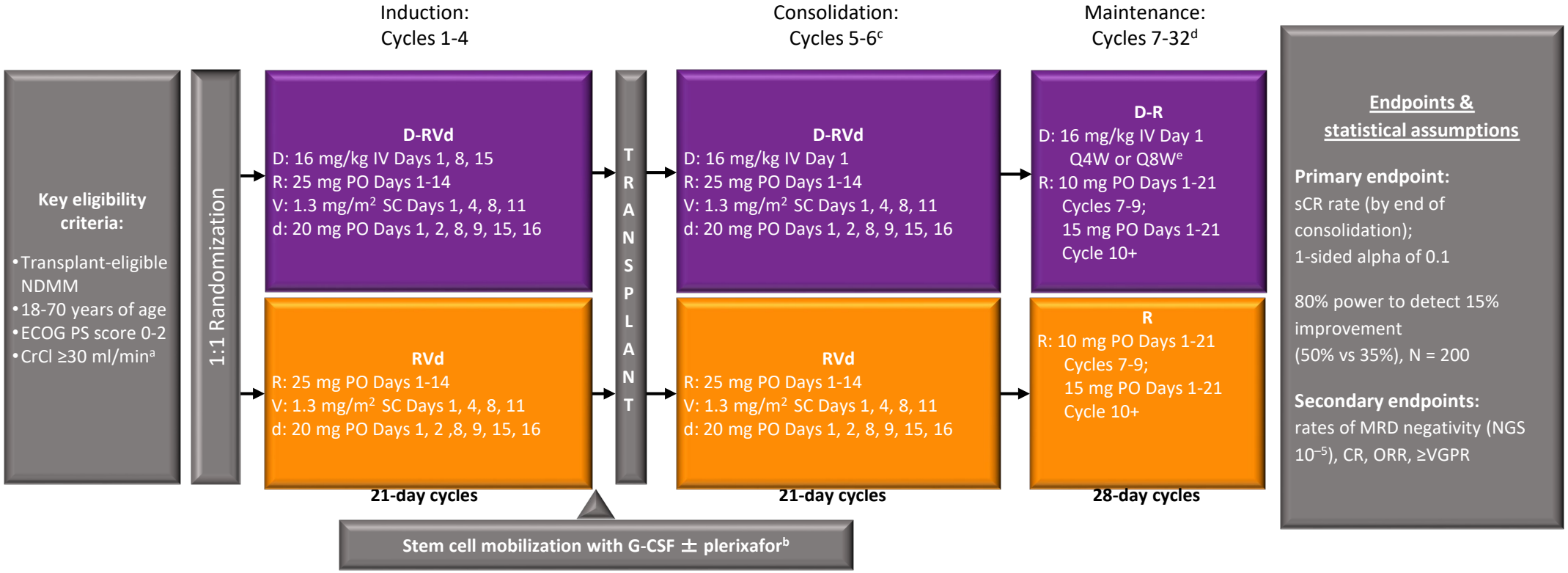
Was bringt die Quadruplettherapie?

Daratumumab (DARA) Plus Lenalidomide, Bortezomib, and Dexamethasone (RVd) in Patients with Transplant-Eligible NDMM: Updated Analysis of Griffin after 12 Months of Maintenance Therapy

J. L. Kaufman *et al*., Atlanta, USA

Abstract 549

- Phase 2 study of D-RVd vs RVd in transplant-eligible NDMM, 35 sites in US with enrollment from 12/2016 and 4/2018



Wirksamkeit und Sicherheit nach 12 Mon. Erhaltungstherapie mit Lenalidomid (R) vs. DARA-R (D-R)

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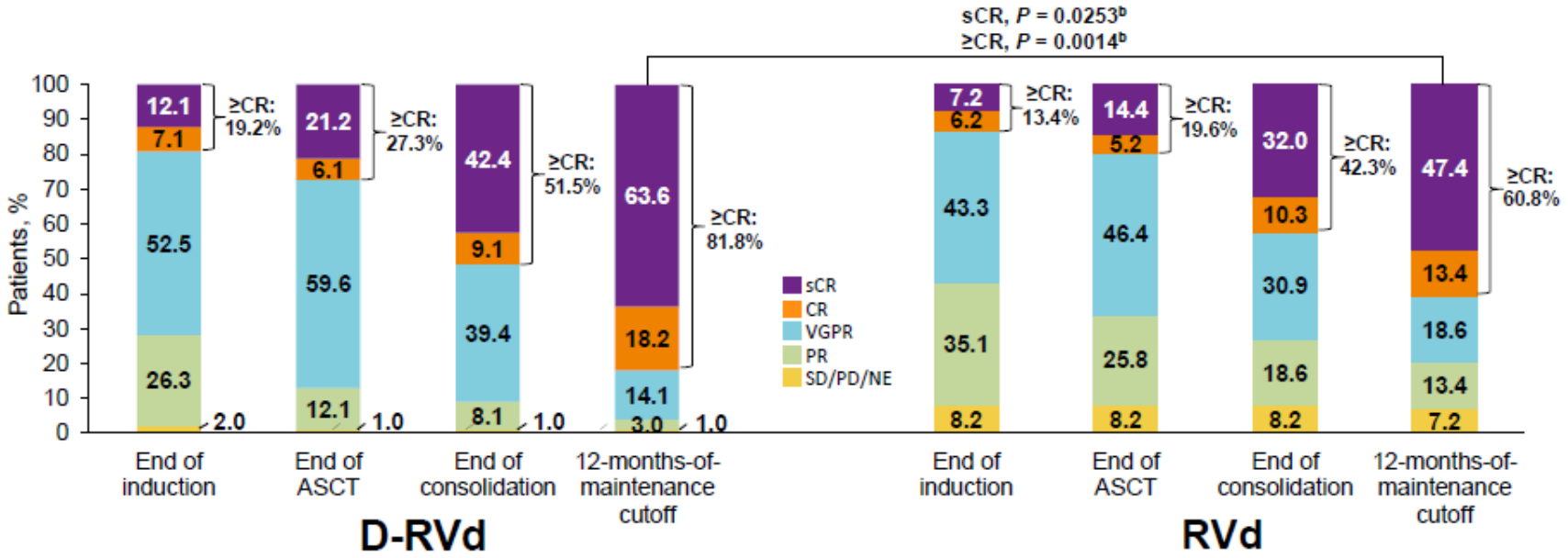
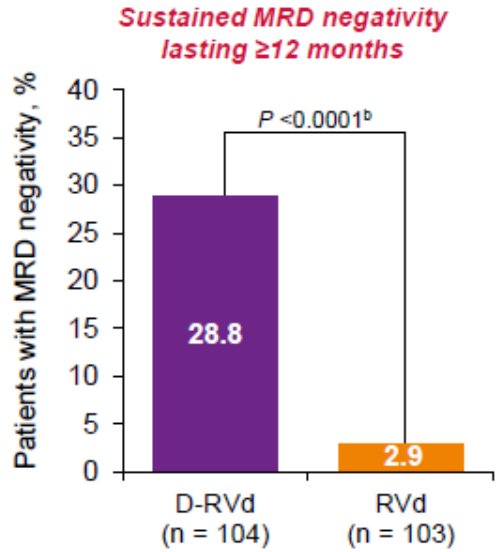




- Nach 26,7 Mon. medianem FU: tiefe, sich verbessernde Ansprechraten mit Dara-RVd vs. RVd
- Erhaltungstherapie erhöht sCR- und MRD-Neg.-Raten mit Dara-Len vs. Len
- Keine neuen Sicherheitsbedenken
- ***Aktuell zugelassene Standardtherapie außerhalb von Studien: Dara-VTd***

Multiples Myelom

Erstbehandlung tranplantierbarer Patienten

Warum bleibt die Hochdosistherapie Goldstandard?

62nd ASH Annual Meeting, December 5-8, 2020
Abstract #141

Survival Analysis of Newly Diagnosed Transplant-Eligible Multiple Myeloma Patients in the Randomized FORTE Trial

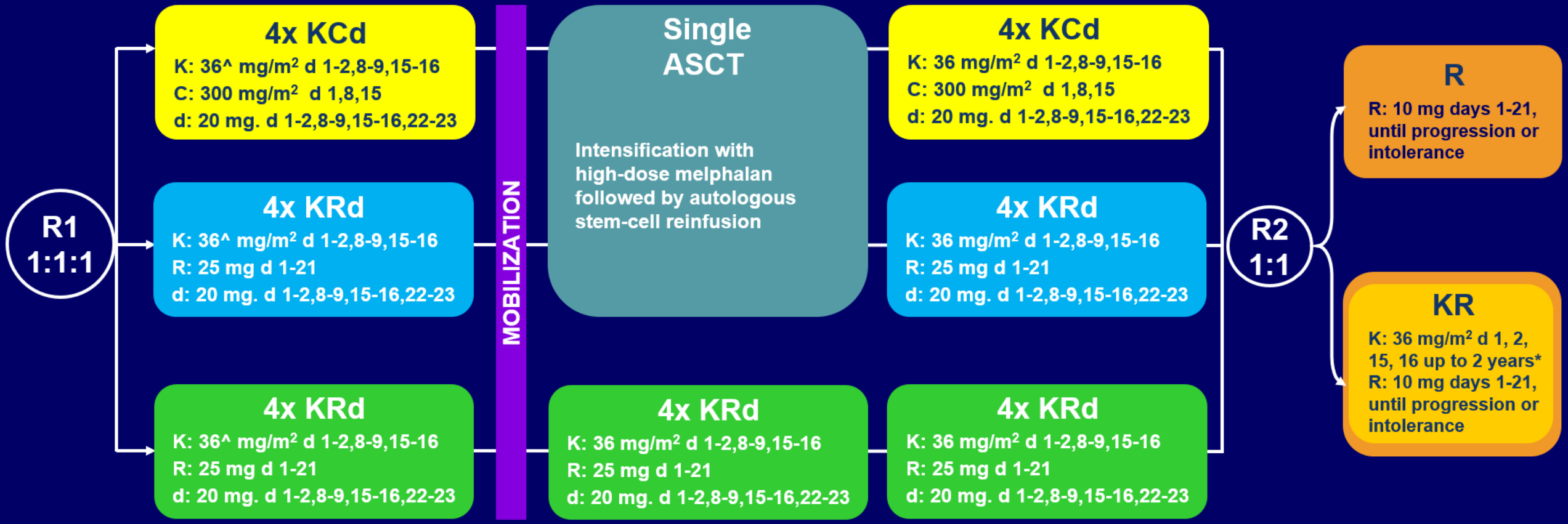
Francesca Gay[1]*, Pellegrino Musto[1], Delia Rota-Scalabrini[1], Monica Galli[1], Angelo Belotti[1], Elena Zamagni[1], Luca Bertamini[1], Renato Zambello[1], Micol Quaresima[1], Giovanni De Sabbata[1], Giuseppe Pietrantuono[1], Mattia D'Agostino[1], Daniela Oddolo[1], Andrea Capra[1], Anna Marina Liberati[1], Salvatore Palmieri[1], Franco Narni[1], Massimo Offidani[1], Michele Cavo[1], Mario Boccadoro.[1]

***Correspondence: fgay@cittadellasalute.to.it**

1. GIMEMA / European Myeloma Network, Italy

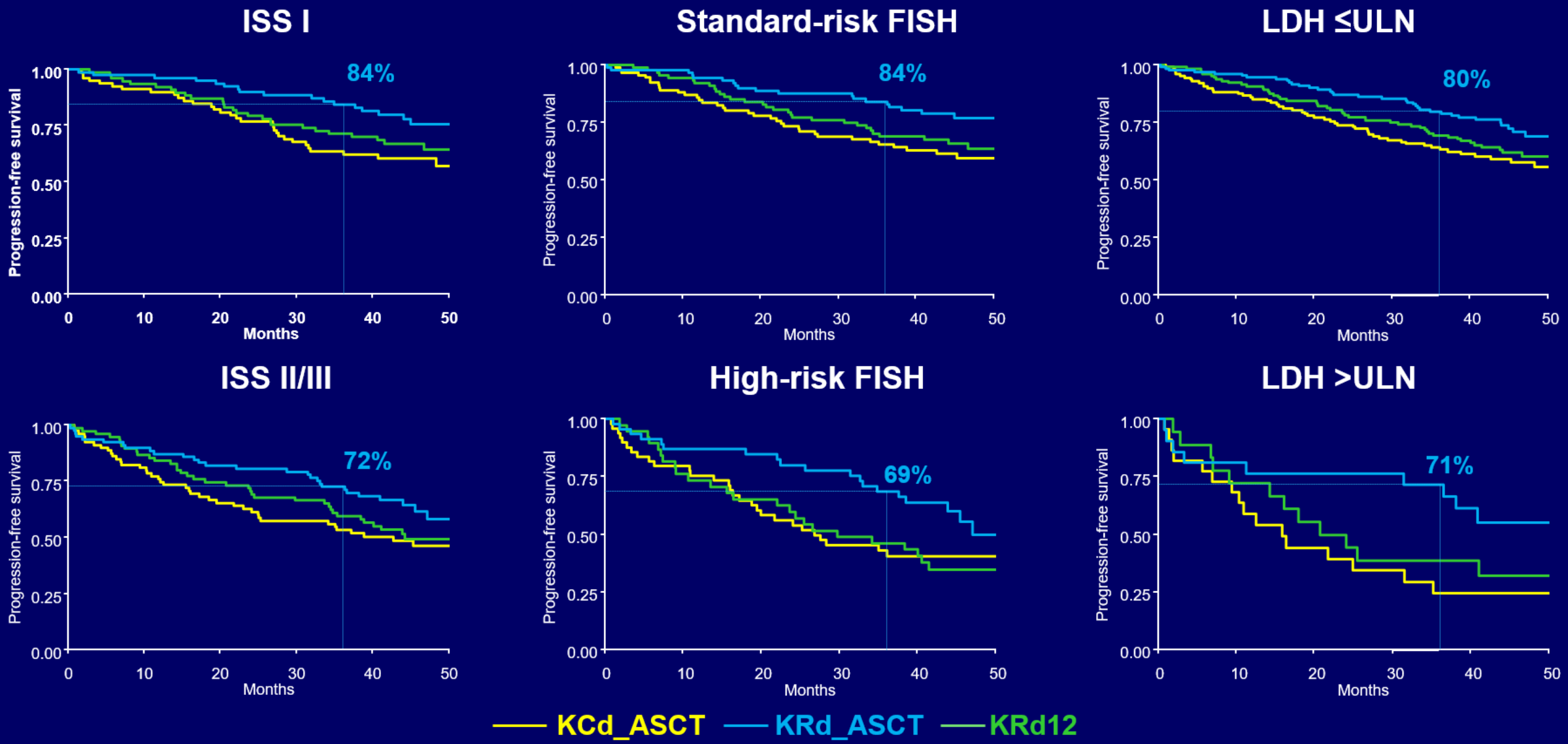
Trial design

474 NDMM patients, transplant-eligible and younger than 65 years



^20 mg/m² on days 1-2, cycle 1 only. *Carfilzomib 70 mg/m² days 1, 15 every 28 days up to 2 years for patients that have started the maintenance treatment from 6 months before the approval of Amendment 5.0 onwards. NDMM, newly diagnosed multiple myeloma, R1, first randomization (induction/consolidation treatment); R2, second randomization (maintenance treatment); IQR, interquartile range K, carfilzomib; C, cyclophosphamide; R, lenalidomide; d, dexamethasone; d, days; ASCT, autologous stem-cell transplantation.

Progression-Free Survival: Random 1 subgroup analyses



PFS, progression-free survival; Random 1, first randomization (induction/consolidation treatment); ASCT, autologous stem-cell trasplantation; K, carfilzomib; R, lenalidomide; C, cyclophosphamide; d, dexamethasone; KCd_ASCT, KCd induction-ASCT-KCd consolidation; KRd_ASCT, KRd induction-ASCT-KRd consolidation; KRd12, 12 cycles of KRd; ISS, International Staging System stage; FISH, fluorescence *in situ* hybridization; LDH, lactate dehydrogenase; ULN, upper limit of normal; 3-year PFS for KRd_ASCT reported in the figures.

Conclusions

- **KRd_ASCT significantly prolonged PFS vs. Krd12 and vs. KCd_ASCT**
  - **3-year PFS → 78%**

- **The benefit of KRd_ASCT was observed in all subgroups of patients:**
  - **KRd_ASCT in ISS I, FISH standard risk, LDH ≤ULN: 3-year PFS 80-84%**
  - **KRd_ASCT in ISS II/III, FISH high-risk, LDH >ULN: 3-year PFS 69-72%**

- **KR significantly prolonged PFS vs. R**
  - **30 months PFS → 81%**

- **The benefit of KR was observed in all subgroups of patients:**
  - **KR in ISS I, FISH standard risk, LDH ≤ULN: 30-months PFS 83-85%**
  - **KR in ISS II/III, FISH high-risk, LDH >ULN: 30-months PFS 60-78%**

- **Maintenance with KR was manageable with no increase in treatment discontinuation due to toxicity**

PFS, progression-free survival; ASCT, autologous stem-cell trasplantation; K, carfilzomib; R, lenalidomide; C, cyclophosphamide; d, dexamethasone; KCd_ASCT, KCd induction-ASCT-KCd consolidation; KRd_ASCT, KRd induction-ASCT-KRd consolidation; KRd12, 12 cycles of KRd; ISS, International Staging System stage; FISH, fluorescence *in situ* hybridization; LDH, lactate dehydrogenase; ULN, upper limit of normal, KR carfilzomib-lenalidomide maintenance; R, lenalidomide maintenance.

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Erstbehandlung nicht-transplantierbarer Patienten

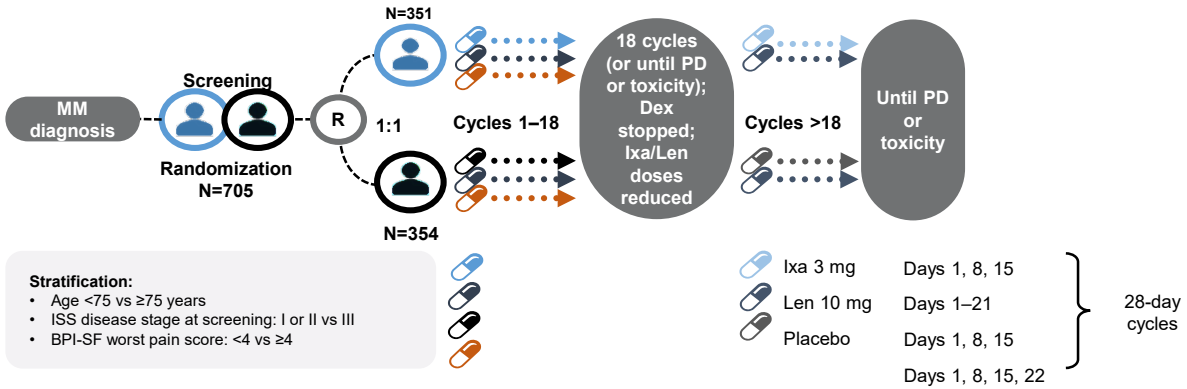
Unverrückbar MAIA?

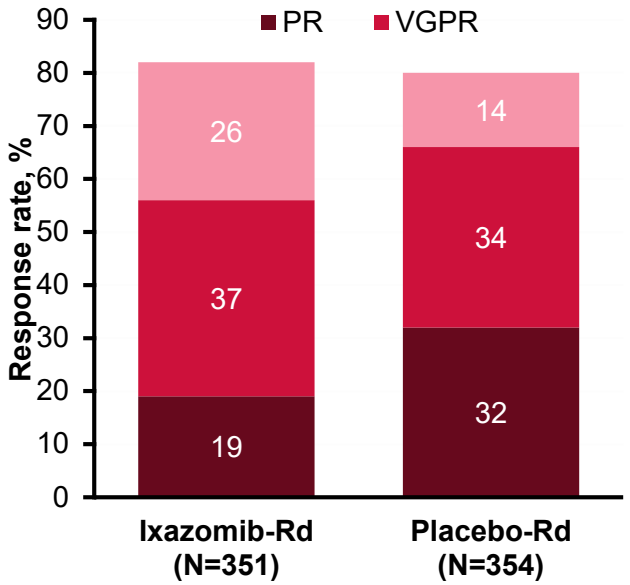
The Phase 3 TOURMALINE-MM2 Trial: Oral Ixazomib, Lenalidomide, and Dexamethasone vs Placebo-Rd for Transplant-Ineligible Patients with Newly Diagnosed Multiple Myeloma

Facon et al., Lille, Frankreich

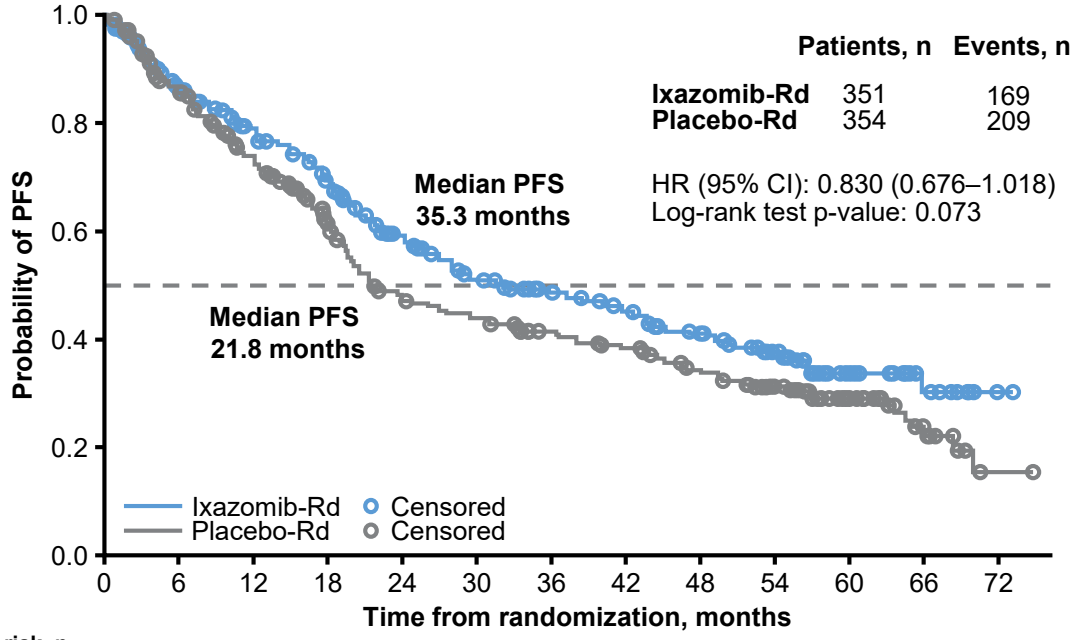
Abstract 551

Multiples Myelom





- Addition of ixazomib to Rd in patients with NDMM led to a clinically meaningful PFS benefit, with a 13.5-month improvement in the median in this elderly, transplant-ineligible patient population.
- Ixazomib-Rd is a feasible treatment option for certain transplant-ineligible patients with NDMM who could benefit from an all-oral triplet combination.



Patients at risk, n

Ixazomib-Rd	351	261	220	187	147	120	107	96	81	64	28	10	1
Placebo-Rd	354	273	225	174	132	121	106	98	82	63	35	16	1

Updated Analysis of Daratumumab Plus Lenalidomide and Dexamethasone (D-Rd) versus Lenalidomide and Dexamethasone (Rd) in Patients with Transplant-ineligible Newly Diagnosed Multiple Myeloma (NDMM): the Phase 3 MAIA Study

Kumar et al., Rochester, USA

Abstract 2276

Multiples Myelom

Rezidivtherapie

Lenalidomid-freie neue Standards: DPd und KdD

Apollo: Phase 3 Randomized Study of Subcutaneous Daratumumab Plus Pomalidomide and Dexamethasone (D-Pd) Versus Pomalidomide and Dexamethasone (Pd) Alone in Patients (Pts) with Relapsed/Refractory Multiple Myeloma (RRMM)

Dimopoulos et al., Athens, Greece

Abstract 412

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Key eligibility criteria:
- RRMM
- ≥1 prior line with both lenalidomide and a PI
- ECOG PS ≤2
- CrCl ≥30 mL/min

1:1 randomization

D-Pd
D: 1,800 mg SC[a] QW Cycles 1-2, Q2W Cycles 3-6, Q4W Cycles 7+
P: 4 mg PO Days 1-21
d: 40 mg[b] PO Days 1, 8, 15, 22

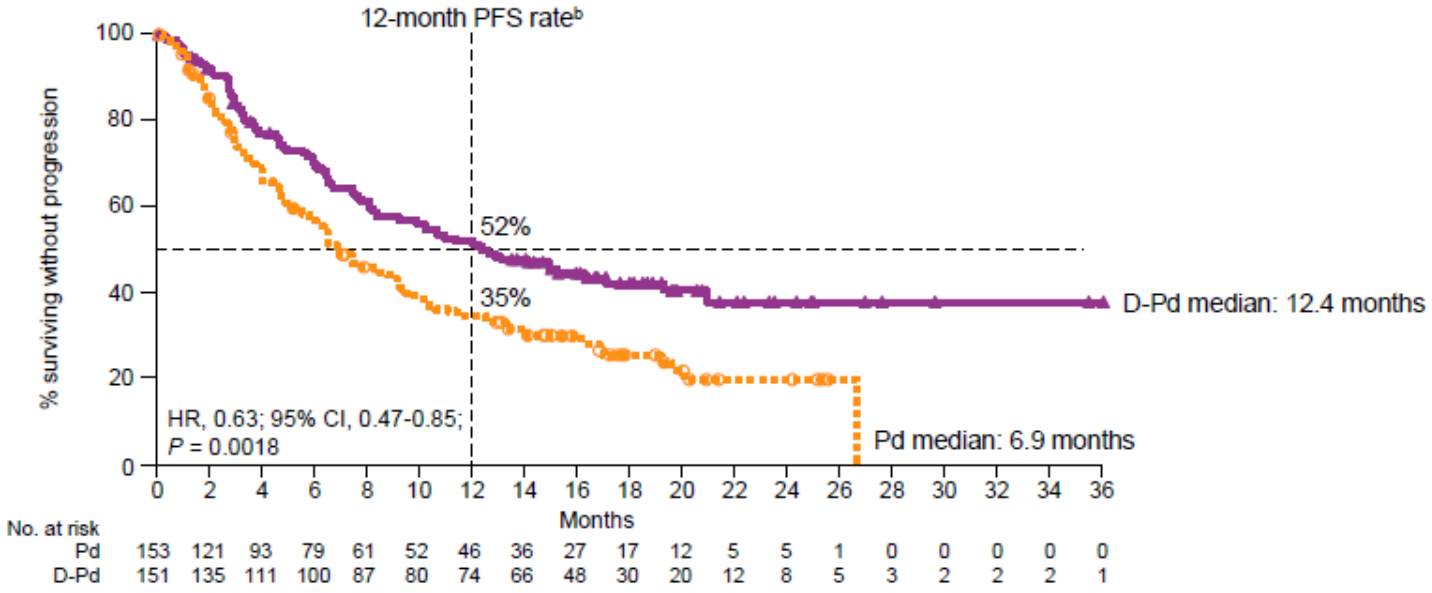
Pd
P: 4 mg PO Days 1-21
d: 40 mg[b] PO Days 1, 8, 15, 22

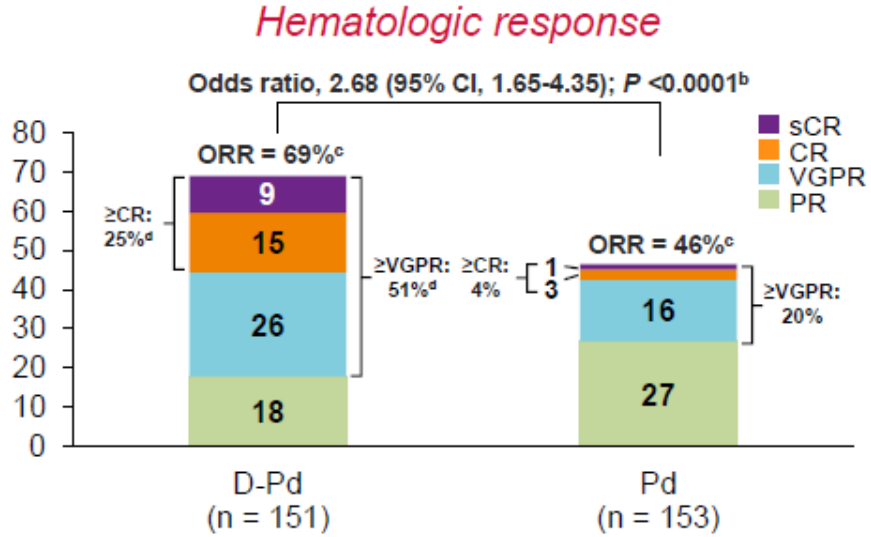
Post-treatment follow-up Q4W for patients who discontinued treatment[c]

Survival follow-up every 12 weeks following PD or start of subsequent therapy

Primary endpoint:
- PFS

Secondary endpoints:
- ORR, ≥VGPR, ≥CR[d]
- MRD[e]
- OS
- Time to response
- Duration of response
- Time to next therapy
- Safety
- HRQoL





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Phase 3: DARA SC und Pd bei RRMM mit ≥ 1 vorherigen Therapielinien

Reduziertes Risiko für Progression oder Tod vs. Pd allein (-37%)

Keine neuen Sicherheitsbedenken

Sehr wenige IRR, kurze Verabreichungsdauer (↑Bequemlichkeit, ↓Behandlungsbelastung)

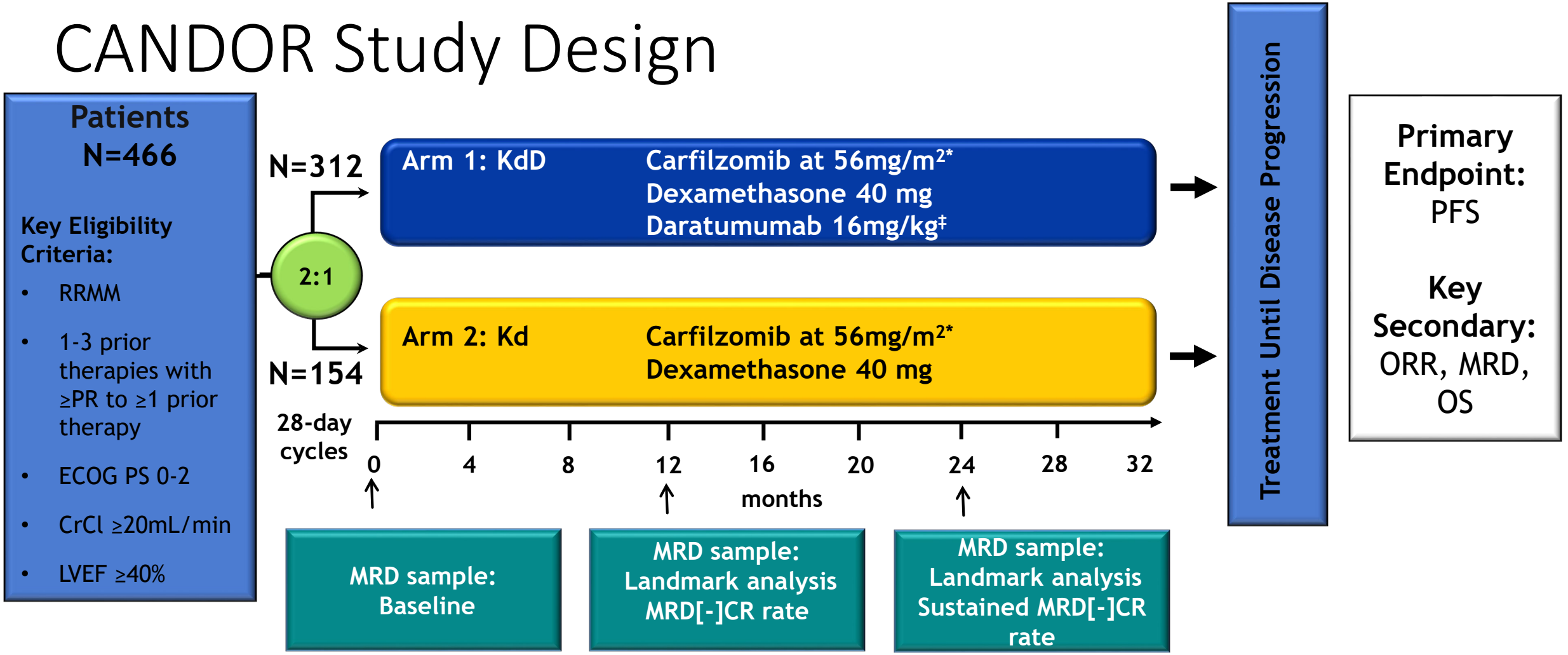
-> EU Zulassung für Dara-Pd wird angestrebt, wichtiges Regime für RRMM-Patienten

Carfilzomib, Dexamethasone, and Daratumumab Versus Carfilzomib and Dexamethasone in Relapsed or Refractory Multiple Myeloma: Updated Efficacy and Safety Results of the Phase 3 Candor Study

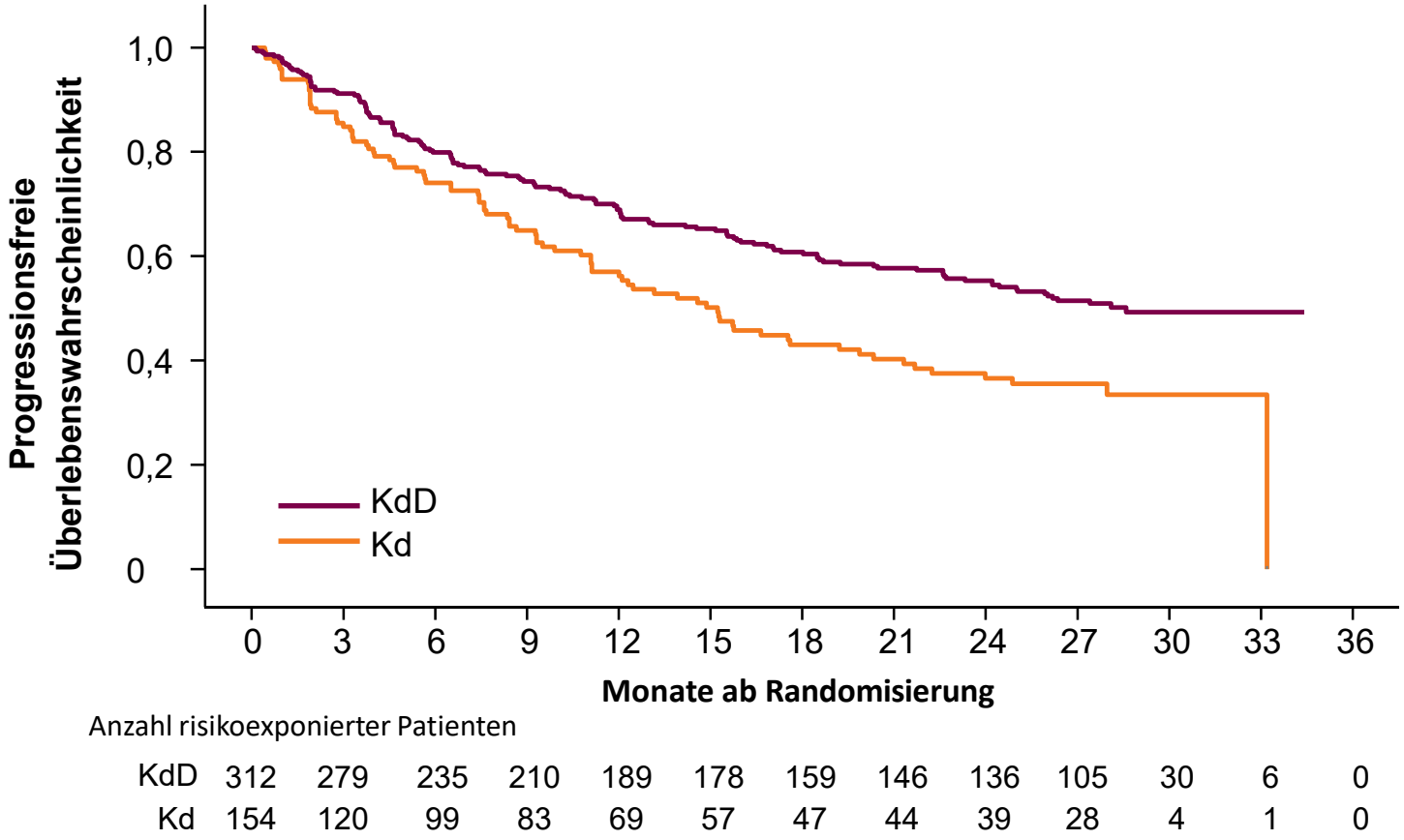
Dimopoulos et al., Athens, Greece

Abstract 2325

CANDOR Study Design



RRMM: KdD vs. Kd **(CANDOR)** – Update Wirksamkeit & Verträglichkeit



Datenschnitt am 15.6.2020
(ca. 36 Monate nach Aufnahme des ersten Patienten)

	KdD (n=312)	Kd (n=154)
Med. Nachbeobachtungszeit, Monate	27,8	27,0
Patienten mit PFS-Ereignissen, n (%)	140 (44,9)	85 (55,2)
Medianes PFS,* Monate	**28,6**	15,2
HR (95 % KI)	**0,59 (0,45–0,78)**	

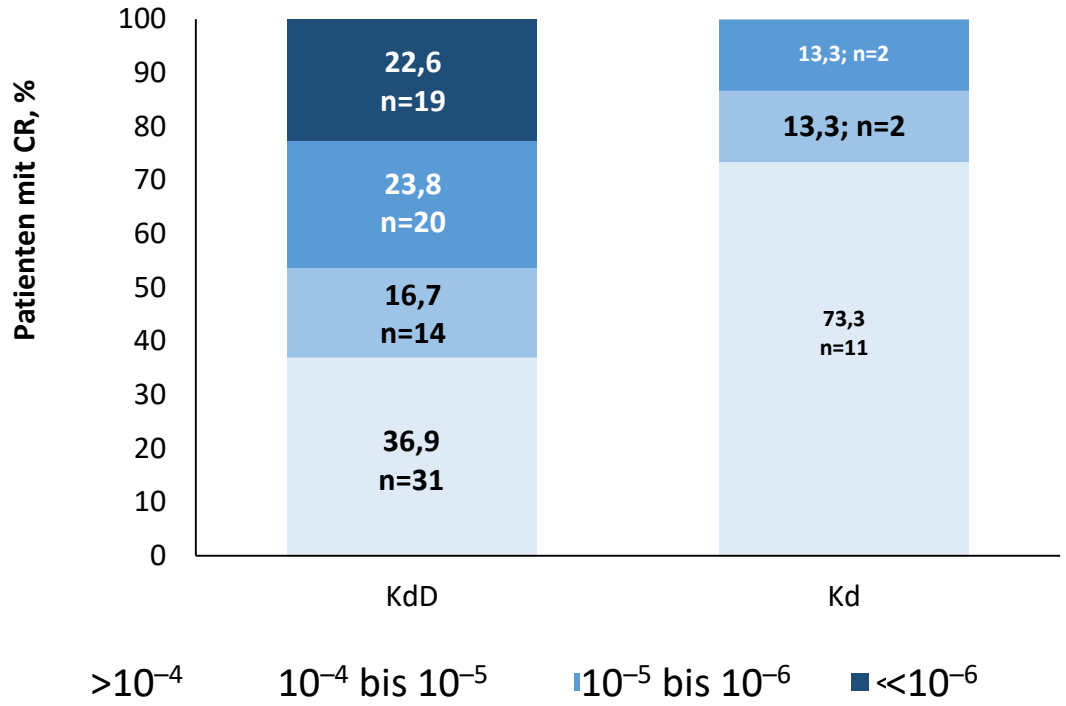
*ORCA (Onyx Response Computer Algorithm)

K = Carfilzomib; d = Dexamethason; D = Daratumumab; RRMM = rezidiviertes/refraktäres multiples Myelom; HR = Hazard Ratio; KI = Konfidenzintervall; PFS = progressionsfreies Überleben.

Dimopoulos MA et al. ASH 2020, Abstract 2325

RRMM: KdD vs. Kd **(CANDOR)** – MRD

MRD-Ansprechen bei Patienten mit CR nach 12 Monaten



- Nach 12 Monaten hatten die Patienten unter Behandlung mit KdD eine höhere CR-Rate (26,9% vs. 9,7%) und ein tieferes Ansprechen bezüglich der MRD^{neg} als Patienten mit Kd.
- Während einer medianen Nachbeobachtungszeit von 6 Monaten kam es bei keinem Patienten mit MRD^{neg} CR zu einer Krankheitsprogression oder einem Todesfall.
- Im KdD-Arm beeinflusst eine Lenalidomid-Vorbehandlung oder –Refraktärität die MRD^{neg} CR-Rate nicht.

CR = komplette Remission; Kd = Carfilzomib + Dexamethason; KdD = Carfilzomib + Dexamethason + Daratumumab; MRD = minimale Resterkrankung; $MRDn^{eg}$ = MRD-negativ; RRMM = rezidiviertes/refraktäres multiples Myelom

Landgren et al. ASH 2020, Abstract 2282

Multiples Myelom

Rezidivtherapie

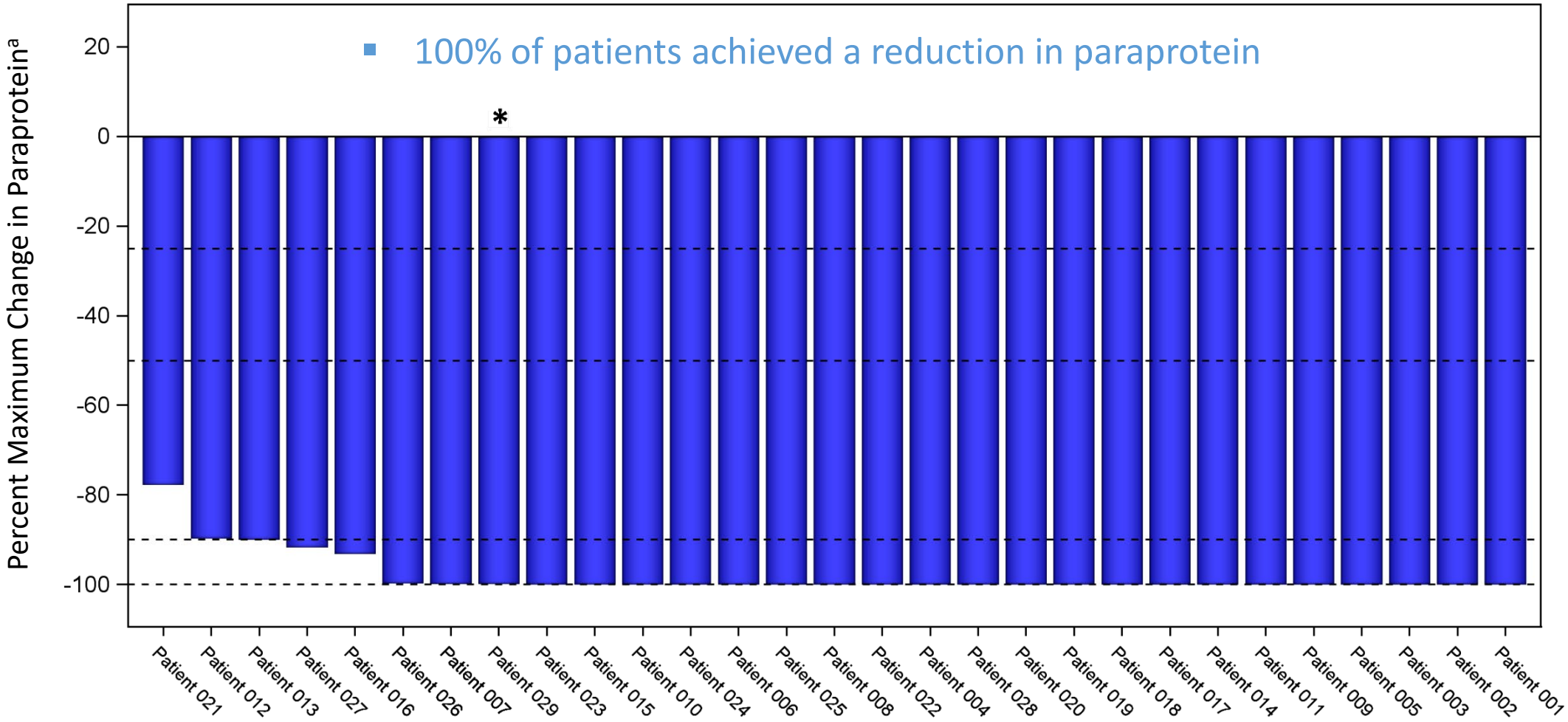
CARs – mit Verve und viel Hoffnung in die Zulassung!

CARTITUDE-1: Phase 1b/2 Study of Ciltacabtagene Autoleucel, a B-Cell Maturation Antigen–Directed Chimeric Antigen Receptor T-Cell Therapy, in Relapsed/Refractory Multiple Myeloma

Madduri et al., New York, USA

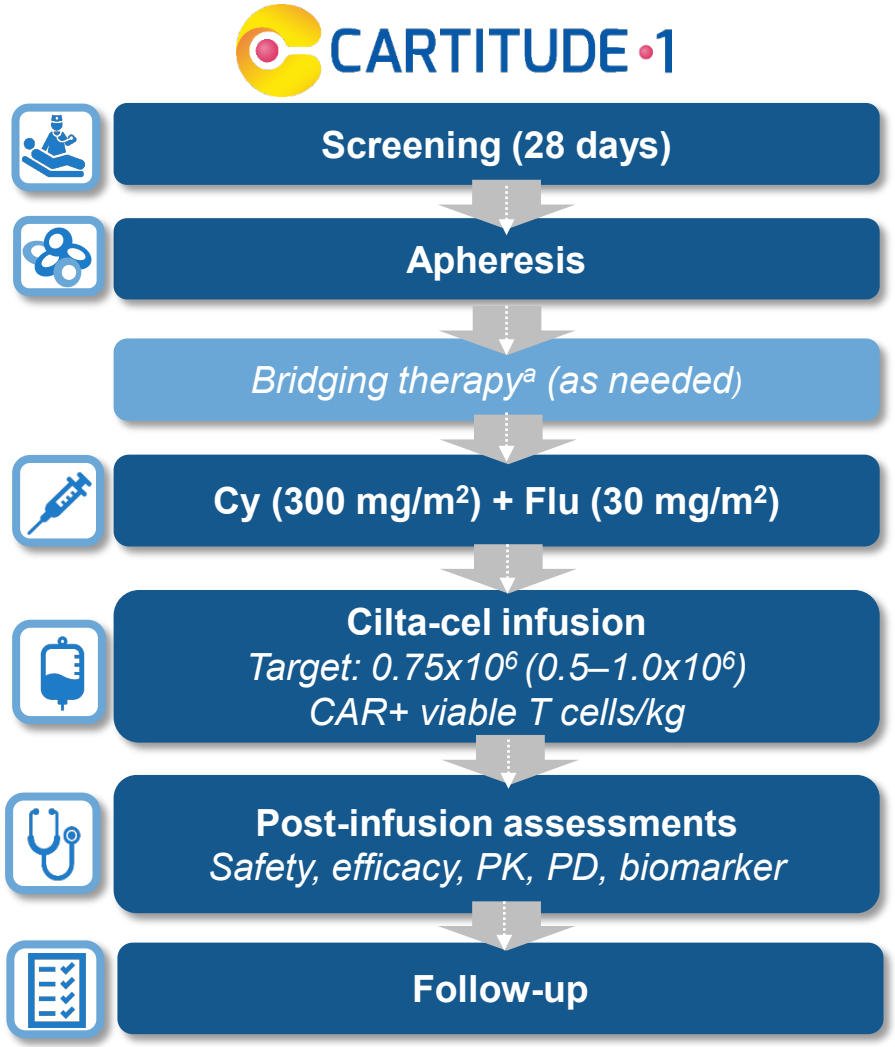
Abstract 177

ASH 2019



[a]Serum M-protein, urine M-protein, or difference between involved and uninvolved free light chain (dFLC).*Bence-Jones proteinuria at baseline, with a transient response during bridging therapy; output represents dFLC value

Multiples Myelom



Characteristic	N=97
Prior lines of therapy, median (range)	6.0 (3–18)
Previous stem-cell transplantation, n (%)	
Autologous	87 (89.7)
Allogenic	8 (8.2)
Triple-class exposed,[c] n (%)	97 (100)
Penta-exposed,[d] n (%)	81 (83.5)
Triple-class refractory[c]	85 (87.6)
Penta-refractory[d]	41 (42.3)
Refractory status, n (%)	
Carfilzomib	63 (64.9)
Pomalidomide	81 (83.5)
Anti-CD38 antibody	96 (99.0)
Refractory to last line of therapy, n (%)	96 (99.0)

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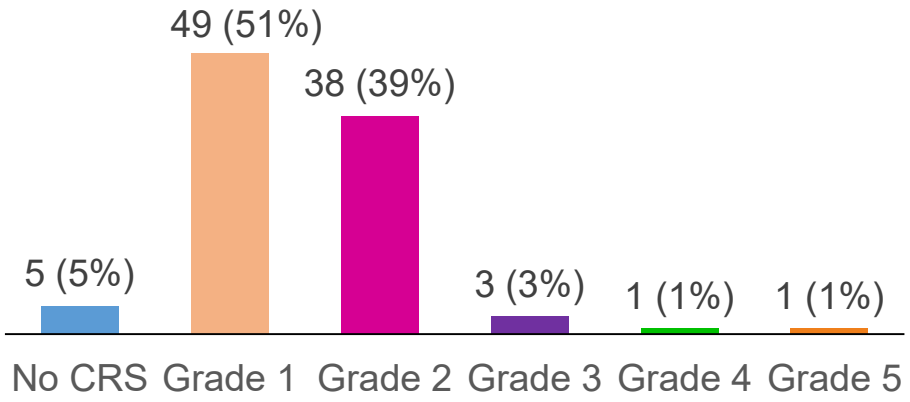
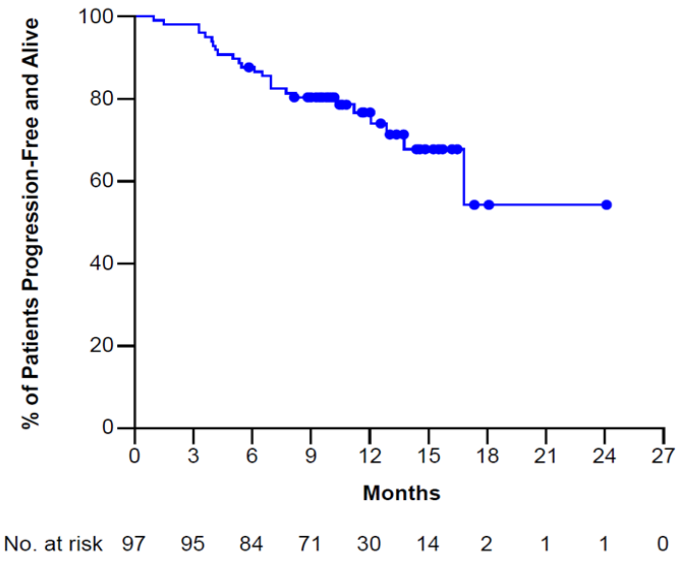
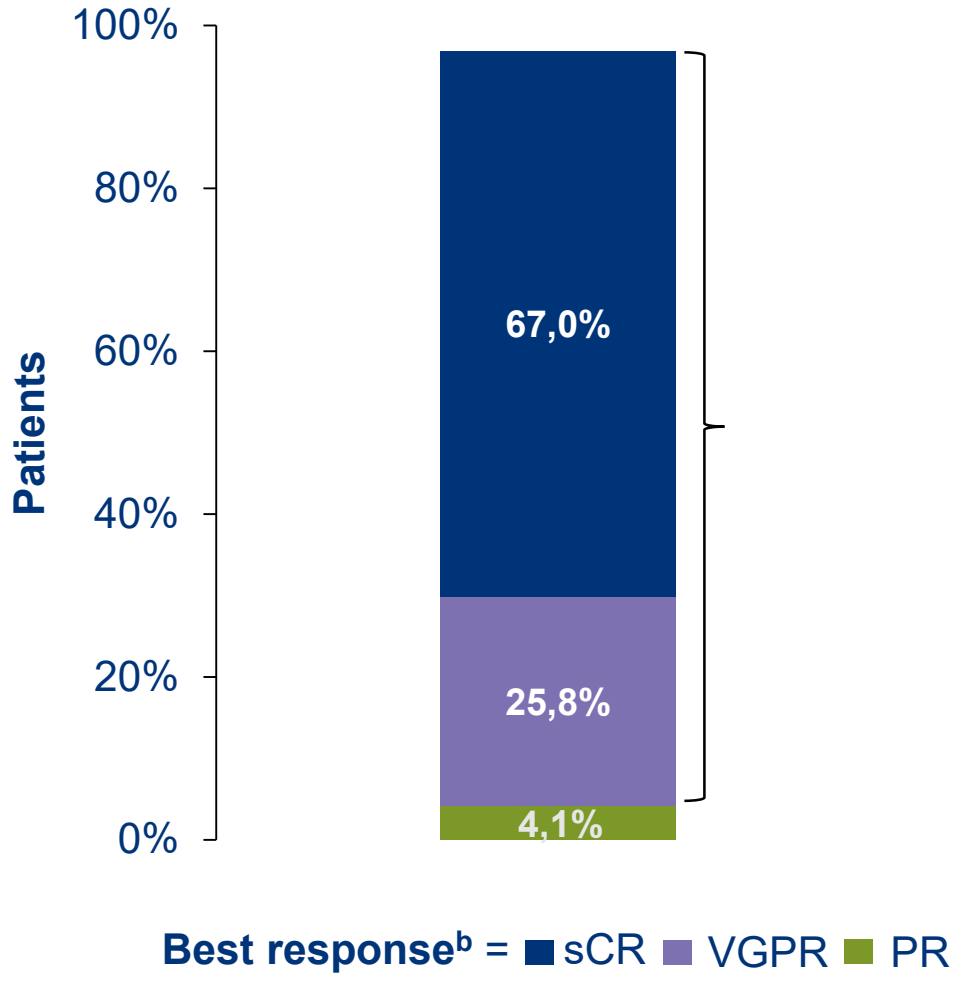
Maximum CRS Grade (N=97)





ORR[a]: 96.9% (94/97)



Idecabtagene vicleucel (ide-cel, bb2121), a BCMA-directed CAR T cell therapy, in patients with relapsed and refractory multiple myeloma: updated results from phase 1 CRB-401 study

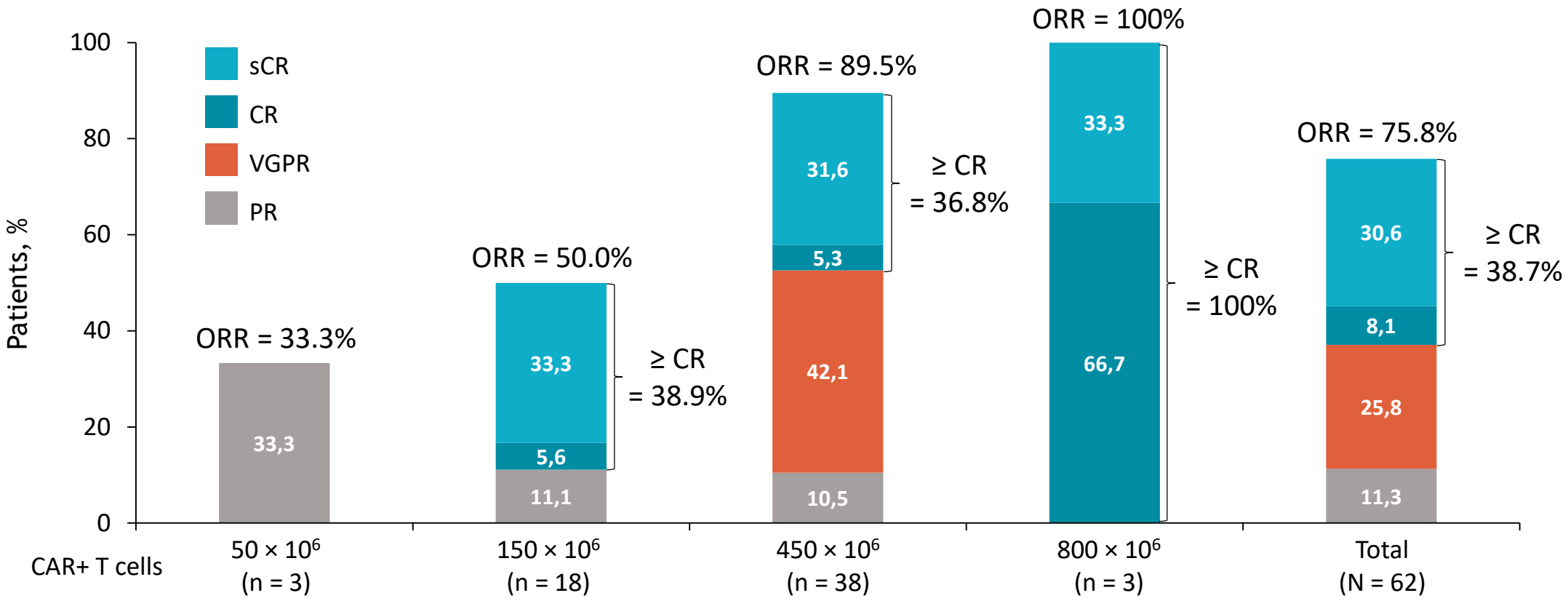
Lin et al., Rochester, USA

Abstract 131

Target dose, × 10^6 CAR+ T cells	50 (n = 3)	150 (n = 18)	**450 (n = 38)**	800 (n = 3)	Total (N = 62)
Age, median (range), y	60 (58-68)	63.5 (44-75)	61 (37-74)	57 (41-67)	61 (37-75)
Male, n (%)	2 (66.7)	13 (72.2)	23 (60.5)	1 (33.3)	39 (62.9)
Time since diagnosis, median (range) y	1.5 (1.4-6.2)	6.2 (1.7-15.2)	5.4 (0.8-35.7)	4.1 (3.9-15.9)	5.5 (0.8-35.7)
ECOG PS 0/1, %[a]	33.3/33.3	27.8/72.2	23.7/73.7	33.3/66.7	25.8/71.0
High-risk cytogenetics, n (%)[b]	0	6 (33.3)	10 (26.3)	1 (33.3)	17 (27.4)
R-ISS III, n (%)	1 (33.3)	2 (11.1)	7 (18.4)	1 (33.3)	11 (17.7)
High tumor burden, n (%)[c]	2 (66.7)	10 (55.6)	14 (36.8)	1 (33.3)	27 (43.5)
Extramedullary disease, n (%)	2 (66.7)	4 (22.2)	16 (42.1)	1 (33.3)	23 (37.1)
Prior regimens, median (range)	4 (3-11)	8 (4-15)	6 (3-18)	6 (5-7)	6 (3-18)
Prior ASCT, n (%)	3 (100)	16 (88.9)	35 (92.1)	3 (100)	57 (91.9)
Prior exposed / refractory, %					
Last prior therapy	100 / 33.3	100 / 61.1	100 / 89.5	100 / 33.3	100 / 75.8
IMiD and PI	100 / 33.3	100 / 83.3	100 / 84.2	100 / 66.7	100 / 80.6
IMiD, PI, and anti-CD38	33.3 / 0	94.4 / 72.2	97.4 / 76.3	100 / 33.3	93.5 / 69.4
Bridging therapy, n (%)	1 (33.3)	9 (50.0)	21 (55.3)	1 (33.3)	32 (51.6)

[a]Two patients (1 each at 50 and 450 × 10^6 target cells) had ECOG PS 2. [b]del17p, t(4;14), and/or t(14;16). [c]≥ 50% CD138-positive cells or percentage of plasma cells in bone marrow biopsy.

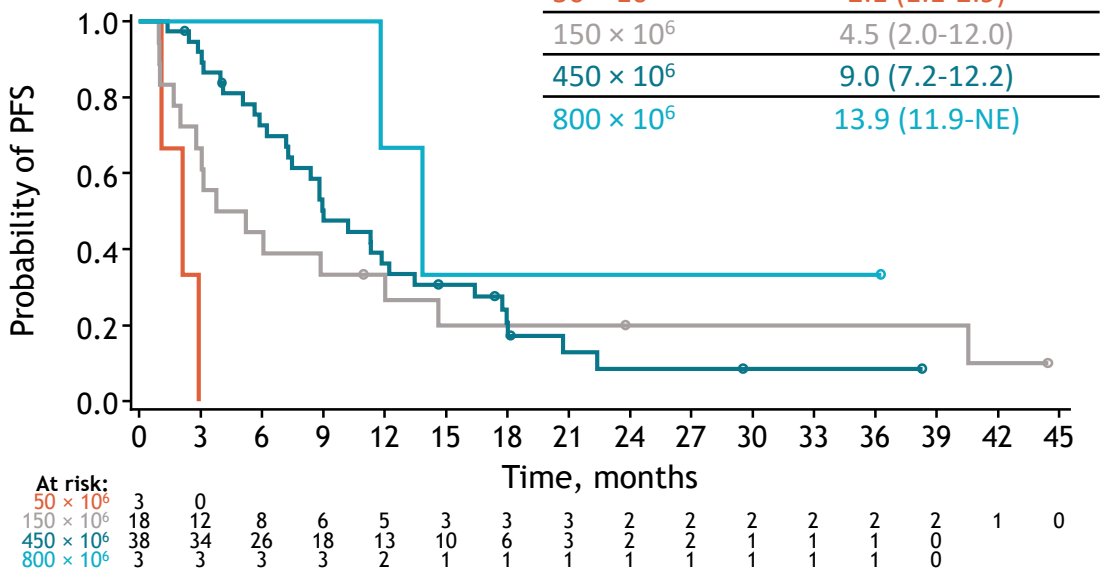
Multiples Myelom



PFS and OS

PFS by target dose

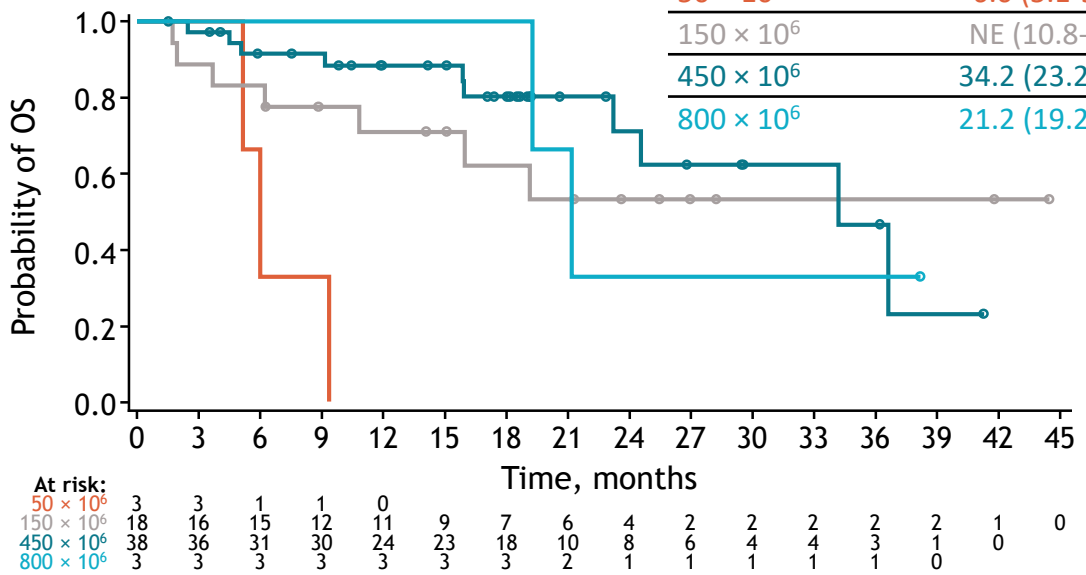
CAR+ T cells	Median (95% CI), months
50 × 10^6	2.1 (1.1-2.9)
150 × 10^6	4.5 (2.0-12.0)
450 × 10^6	9.0 (7.2-12.2)
800 × 10^6	13.9 (11.9-NE)



Median PFS 8.8 months
(95% CI, 5.9-11.9 months) across all treated patients

OS by target dose

CAR+ T cells	Median (95% CI), months
50 × 10^6	6.0 (5.1-9.3)
150 × 10^6	NE (10.8-NE)
450 × 10^6	34.2 (23.2-NE)
800 × 10^6	21.2 (19.2-NE)



Median OS 34.2 months
(95% CI, 19.2-NE months) across all treated patients

Median and 95% CI from Kaplan-Meier estimate. NE, not estimable.

Lin Y, et al. ASH 2020. Abstract 131.

Multiples Myelom

Ide-Cel und Cilta-Cel erzielen bisher unerreichte Ansprechraten und PFS Daten in einer stark vorbehandelten Patientenpopulation

Trotz gleichem Zielantigen ist das Muster des CRS unterschiedlich

Studien in früheren Rezidiven und im randomisierten Vergleich rekrutieren bereits

Die Zulassung beider Konstrukte wird für 2021 erwartet

Die Kurzpräsentationen sind online unter

www.lymphome.de/ash2020

Für den Inhalt verantwortlich:

Prof. Dr. med. Katja Weisel

II. Medizinische Klinik und Poliklinik • Universitätsklinik Hamburg-Eppendorf

Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

ASH 2020 VIRTUAL
5. – 8. Dezember 2020

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