Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

61. ASH Annual Meeting
7. – 10. Dezember 2019

KML-Experten berichten vom ASH 2019 aus Orlando

Prof. Dr. med. Katja Weisel

Multiples Myelom

Oberärztin der II. Medizinischen Klinik und Poliklinik der Universitätsklinik Hamburg-Eppendorf | Mitglied der Leitgruppe der German Speaking Myeloma Multicenter Group (GMMG)

Offenlegung potentieller Interessenskonflikte

LymphomKompetenz KOMPAKT – ASH2019 wird in Kooperation mit vier unterstützenden Firmen durchgeführt. Diese Firmen haben keinen Einfluss auf die Inhalte dieses Vortrags. Meine weiteren Disclosures betreffen:

Anstellungsverhältnis, Führungsposition	keine
Beratungs-/ Gutachtertätigkeit	Amgen, Adaptive Biotech, BMS, Celgene, GSK, Karyopharm, Janssen, Sanofi, Takeda
Besitz von Geschäftsanteilen, Aktien oder Fonds	keine
Patent, Urheberrecht, Verkaufslizenz	keine
Honorare	Amgen, Adaptive Biotech, BMS, Celgene, GSK, Karyopharm, Janssen, Sanofi, Takeda
Finanzierung wissenschaftlicher Untersuchungen	Amgen, Celgene, Sanofi, Janssen
Andere finanzielle Beziehungen	keine
Immaterielle Interessenkonflikte	keine

Kapitel 1

Multiples Myelom

Erstbehandlung | Transplantierbare Patienten

#691

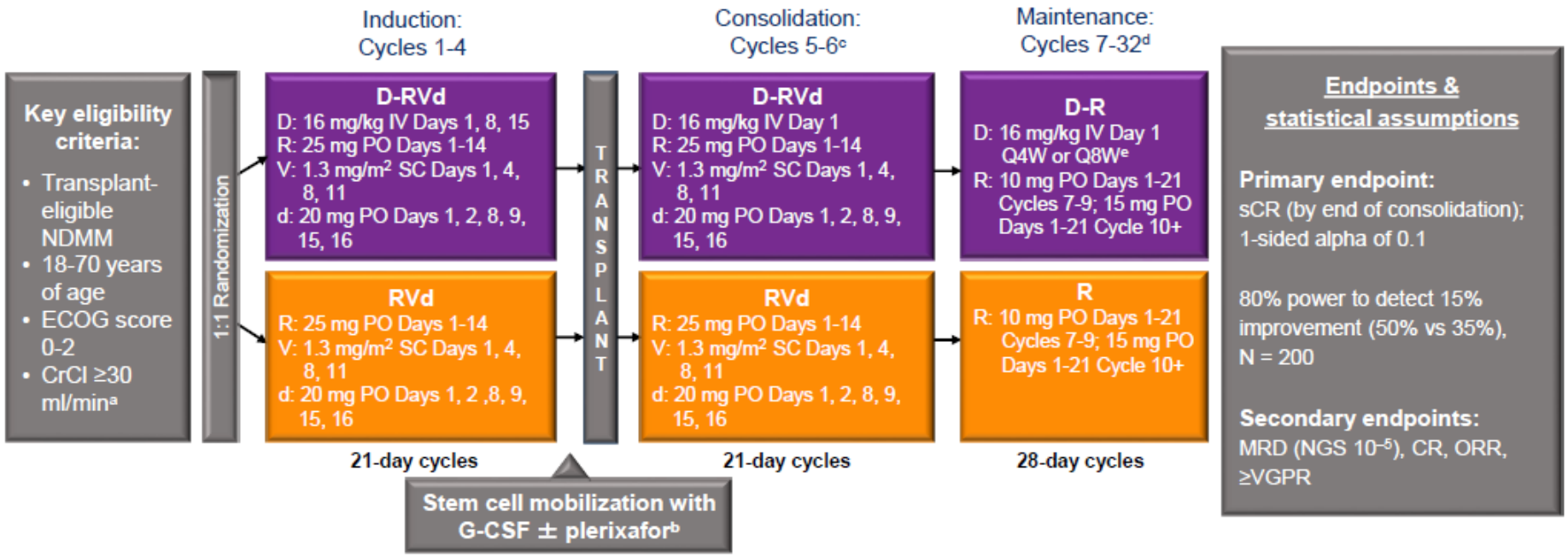
DEPTH OF RESPONSE TO DARATUMUMAB (DARA), LENALIDOMIDE, BORTEZOMIB, AND DEXAMETHASONE (RVD) IMPROVES OVER TIME IN PATIENTS (PTS) WITH TRANSPLANT-ELIGIBLE NEWLY DIAGNOSED MULTIPLE MYELOMA (NDMM): GRIFFIN STUDY UPDATE

Presenter: P. Vorhees, Charlotte, NC, USA

Peter M. Voorhees, Jonathan L. Kaufman, Jacob P. Laubach, Douglas W. Sborov, Brandi Reeves, Cesar Rodriguez, Ajai Chari, Rebecca W. Silbermann, Luciano J. Costa, Larry D. Anderson, Nitya Nathwani, Nina D. Shah, Yvonne A. Efebera, Caitlin L. Costello, Andrzej Jakubowiak, Tanya M Wildes, Robert Z. Orlowski, Kenneth H. Shain, Andrew J. Cowan, Sean Murphy, Yana Lutska, PharmD, Huiling Pei, Jon Ukropec, Jessica Vermeulen, Carla de Boer, Daniela Hoehn, Thomas S. Lin and Paul G. Richardson

GRIFFIN (NCT02874742): Randomized Phase

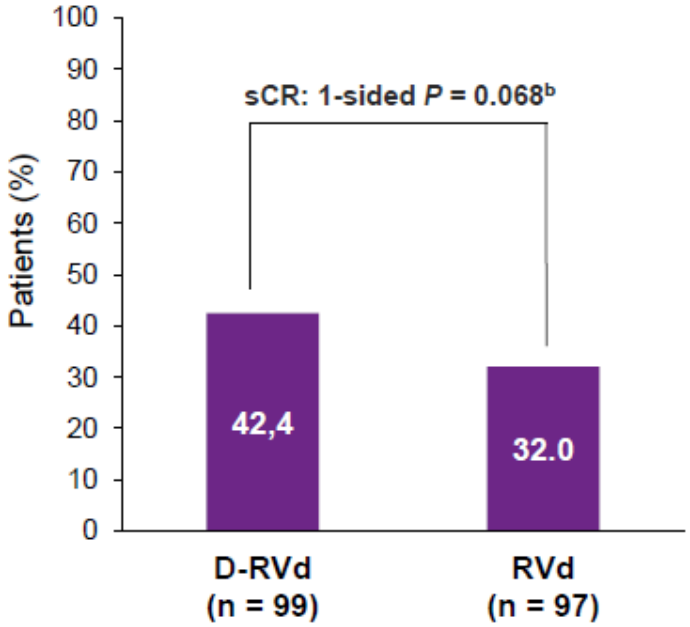
- Phase 2 study of D-RVd vs RVd in transplant-eligible NDMM, 35 sites in US with enrollment from 12/2016 and 4/2018



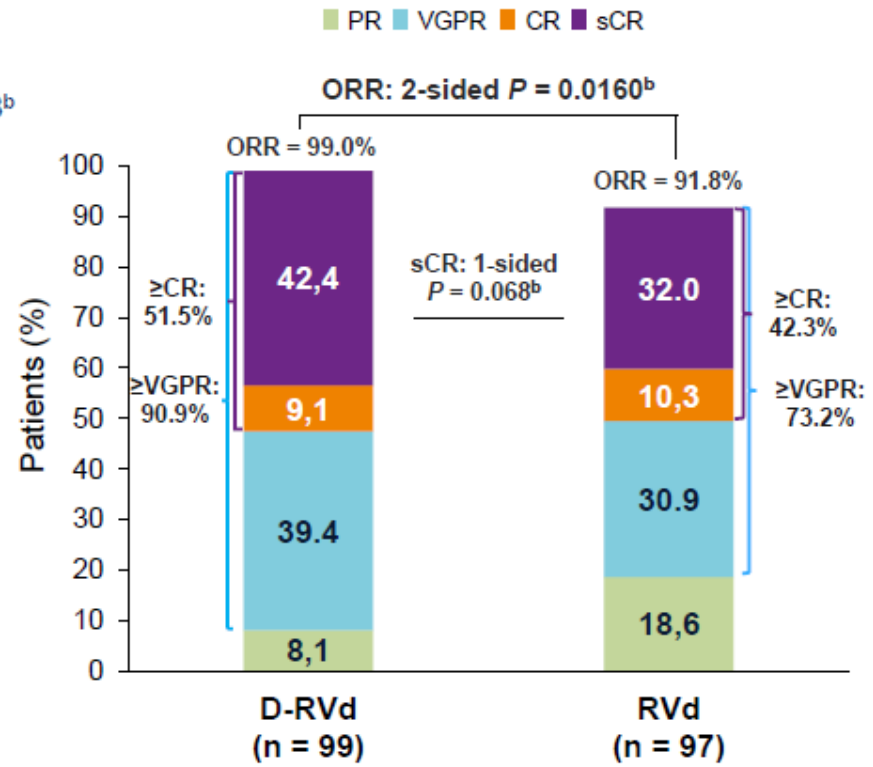
D-RVd, daratumumab-lenalidomide/bortezomib/dexamethasone; RVd, lenalidomide/bortezomib/dexamethasone; NDMM, newly diagnosed multiple myeloma; US, United States; ECOG, Eastern Cooperative Oncology Group; CrCl, creatinine clearance; IV, intravenously; PO, orally; SC, subcutaneously; G-CSF, granulocyte colony-stimulating factor; D-R, daratumumab-lenalidomide; Q4W, every 4 weeks; Q8W, every 8 weeks; sCR, stringent complete response; MRD, minimal residual disease; NGS, next-generation sequencing; CR, complete response; ORR, overall response rate; VGPR, very good partial response.
[a]Lenalidomide dose adjustments were made for patients with CrCl ≤50 mL/min. [b]Cyclophosphamide-based mobilization was permitted if unsuccessful. [c]Consolidation was initiated 60-100 days post transplant. [d]Patients who complete maintenance cycles 7-32 may continue single-agent lenalidomide thereafter. [e]Protocol Amendment 2 allowed for the option to dose daratumumab Q4W, based on pharmacokinetic results from study SMM2001 (NCT02316106).

Primary Endpoint: sCR by the End of Consolidation[a]

- **Primary endpoint met at pre-set 1-sided alpha of 0.1**
  - sCR by end of consolidation
    - 42.4% D-RVd vs 32.0% RVd
    - Odds ratio, 1.57; 95% CI, 0.87-2.82; 1-sided *P* = 0.068[b]



Post-consolidation depth of response[a]



PR, partial response.
[a]Included patients in the response-evaluable population (all randomized patients with a confirmed diagnoses of MM, measurable disease at baseline, received ≥1 dose of study treatment, and had ≥1 post-baseline disease assessment).
[b]*P* values were calculated with the use of the Cochran–Mantel–Haenszel chi-square test. A 1-sided *P* value is reported for sCR; for all other responses, 2-sided *P* values not adjusted for multiplicity are reported.

Post-Consolidation MRD Negativity

MRD-Negative Status (10^{-5}),[a] n (%)	D-RVd	RVd	Odds Ratio (95% CI)	*P* value[b]
In ITT population				
MRD negative regardless of response	46/104 (**44.2**)	15/103 (**14.6**)	4.70 (2.38-9.28)	<0.0001
MRD negative with CR or better	30/104 (**28.8**)	10/103 (**9.7**)	3.73 (1.71-8.16)	0.0007
In patients achieving CR or better	30/51 (**58.8**)	10/41 (**24.4**)	4.65 (1.76-12.28)	0.0014
In patients who received ASCT	45/94 (**47.9**)	14/78 (**17.9**)	4.31 (2.10-8.85)	<0.0001

D-RVd improved MRD-negativity (10^{-5}) rates at the end of consolidation

[a]The threshold of MRD negativity was defined as 1 tumor cell per 10^5 white cells. MRD status is based on assessment of bone marrow aspirates by next-generation sequencing in accordance with International Myeloma Working Group criteria. MRD assessments occurred in patients who had both baseline (with clone identified/calibrated) and post-baseline MRD (with negative, positive, or indeterminate result) samples taken (D-RVd, n = 71; RVd, n = 55). Patients with a missing or inconclusive assessment were considered MRD positive. [b]*P* values were calculated from the Fisher's exact test.

1

#862

WEEKLY CARFILZOMIB, LENALIDOMIDE, DEXAMETHASONE AND DARATUMUMAB (WKRD-D) COMBINATION THERAPY PROVIDES UNPRECEDENTED MRD NEGATIVITY RATES IN NEWLY DIAGNOSED MULTIPLE MYELOMA: A CLINICAL AND CORRELATIVE PHASE 2 STUDY

Presenter: O. Landgren, New York, NY, USA

Ola Landgren, Malin Hultcrantz, Alexander M. Lesokhin, Sham Mailankody, Hani Hassoun, Eric L Smith, Urvi A Shah, Sydney X Lu, Donna Mastey, Meghan Salcedo, Victoria Diab, Kelly Werner, Jenna Rispoli, Allison Sams, Dennis Verducci, Katie Jones, Angela Harrison, Aisara Chansakul, Even H Rustad, Venkata Yellapantula, Francesco Maura, Heather J Landau, Michael Scordo, David J. Chung, Gunjan Shah, Oscar B Lahoud, Katie Thoren, Kazunori Murata, Lakshmi Ramanathan, Maria E Arcila, Caleb Ho, Mikhail Roshal, Ahmet Dogan, Sean M. Devlin, Sergio Giralt and Neha Korde

#860

DARATUMUMAB, CARFILZOMIB, LENALIDOMIDE AND DEXAMETHASONE (DARA-KRD) INDUCTION, AUTOLOGOUS TRANSPLANTATION AND POST-TRANSPLANT, RESPONSE-ADAPTED, MEASURABLE RESIDUAL DISEASE (MRD)-BASED DARA-KRD CONSOLIDATION IN PATIENTS WITH NEWLY DIAGNOSED MULTIPLE MYELOMA (NDMM)

Presenter: L. J. Costa, Birmingham, Vestavia, AL, USA

Luciano J. Costa, Saurabh Chhabra, Kelly N. Godby, Eva Medvedova, Robert F. Cornell, Aric C. Hall, Rebecca W. Silbermann, Racquel Innis-Shelton, Binod Dhakal, Diego DeIdiaquez, Pamela Hardwick, Yelak Biru, James L. Omel, Parameswaran Hari and Natalie Scott Callander

Kapitel 2

Multiples Myelom

Erstbehandlung | Nicht-Transplantierbare Patienten

#3178

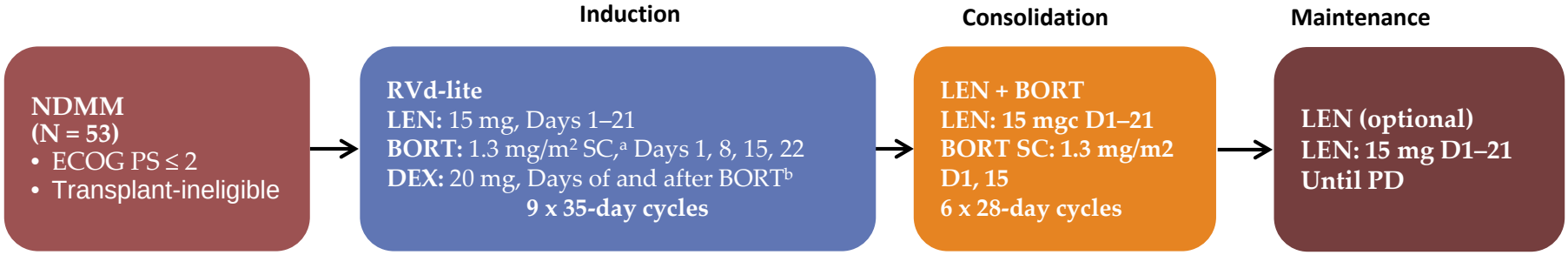
UPDATED RESULTS OF A PHASE 2 STUDY OF MODIFIED LENALIDOMIDE, BORTEZOMIB, AND DEXAMETHASONE (RVD-LITE) IN TRANSPLANT-INELIGIBLE MULTIPLE MYELOMA

Presenter: Elizabeth K. O'Donnell, Boston, MA, USA

Elizabeth K. O'Donnell, Jacob P. Laubach, Andrew J. Yee, Robert Redd, Carol Ann Huff, Frank Basile, Philip M. Wade, Claudia E. Paba-Prada, Irene M. Ghobrial, Robert L. Schlossman, Jill N. Burke, Cynthia C. Harrington, Kathleen J. Lively, Hannah Lyons, Nikhil C Munshi, Kenneth C. Anderson, Paul G. Richardson and Noopur S. Raje

Updated Results of a Phase 2 Study of (RVd-lite) in Transplant-Ineligible NDMM

- Updated analysis (61-month follow-up) of a Phase 2 study of RVd-lite in transplant-ineligible NDMM patients
- **Primary endpoint:** ORR; **Secondary endpoints:** safety, PFS, OS, PK profile of IV and SC BORT



Patient characteristics	(n = 50)
Median age (range), years	72 (65–91)
ISS stage I / II / III, %	38 / 34 / 28

66% of patients received LEN Maintenance

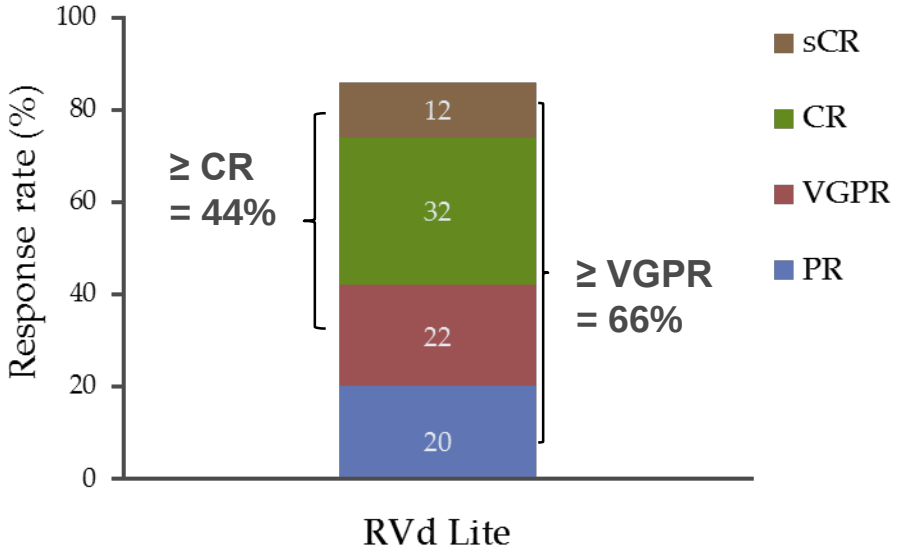
[a] 50 patients received ≥ 1 dose of treatment.

O'Donnell EK, et al. ASH 2019: Abstract 3178. Poster presentation.

RVd Lite (NSCT)

Median follow-up 61 months

- Median PFS 41.9 months (95% CI, 31.2 - ∞)
- 5-year OS 61.3%
- Median OS not reached
- Median TTR 1.1 months
- ORR = 86%



O'Donnell EK, et al. ASH 2019: Abstract 3178. Poster presentation.

RVd Lite (NSCT): Safety and QoL

Treatment-related AEs, %	Any grade	Grade ≥ 3
Haematological		
Neutropenia	not reported	**14**
Non-haematological		
Fatigue	**74**	**58**
Peripheral neuropathy	**64**	**2**
Hypophosphataemia	not reported	**34**
Rash	not reported	**10**

- **QoL:** After treatment, significant improvements compared with baseline were observed in:
  - Physical Functioning ($P = 0.013$)
  - Future Perspective ($P = 0.023$)
  - Disease Symptoms ($P = 0.001$)
- Patients reported fewer symptoms across all symptom domains except diarrhea

O'Donnell EK, et al. ASH 2019: Abstract 3178. Poster presentation.

#859

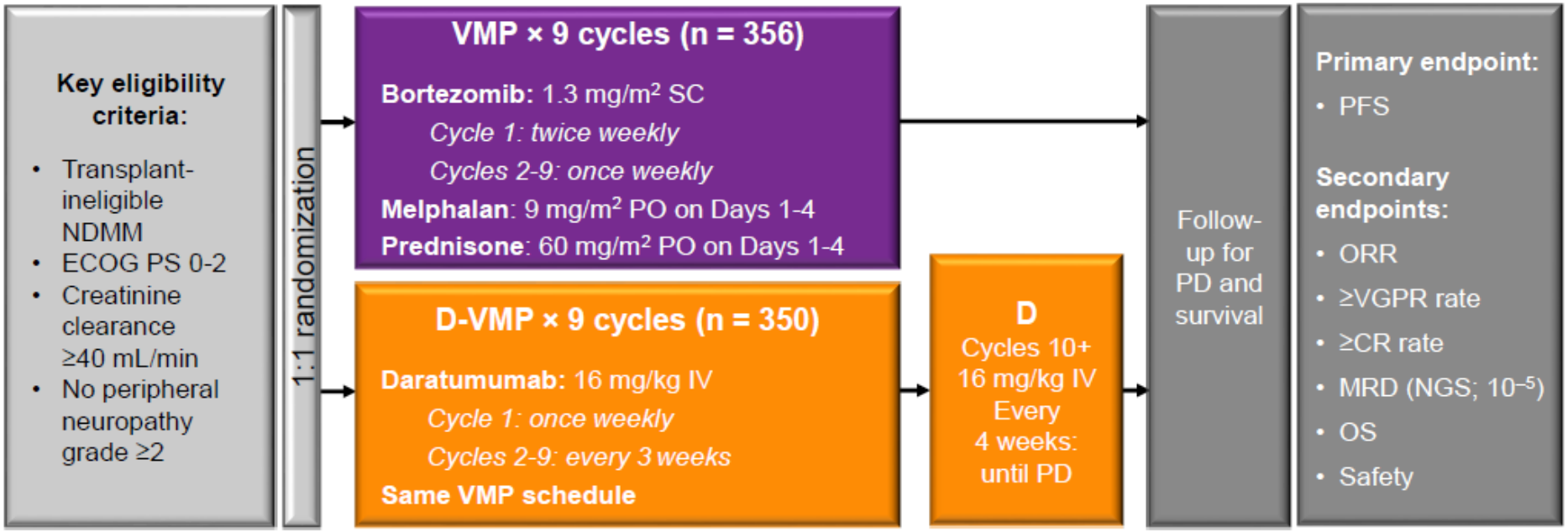
DARATUMUMAB PLUS BORTEZOMIB, MELPHALAN, AND PREDNISONE VERSUS BORTEZOMIB, MELPHALAN, AND PREDNISONE IN PATIENTS WITH TRANSPLANT-INELIGIBLE NEWLY DIAGNOSED MULTIPLE MYELOMA: OVERALL SURVIVAL IN ALCYONE

Presenter: M.-V. Mateos, Salamanca, Spain

Maria-Victoria Mateos, Michele Cavo, Joan Bladé, Meletios A. Dimopoulos, Kenshi Suzuki, Andrzej Jakubowiak, Stefan Knop, Chantal Doyen, Paulo Lucio, Zsolt Nagy, Ludek Pour, Mark Cook, Sebastian Grosicki, Andre H Crepaldi, Anna Marina Liberati, Philip Campbell, Tatiana Shelekhova, Sung-Soo Yoon, Genadi Iosava, Tomoaki Fujisaki, Mamta Garg, Maria Krevvata, Jianping Wang, Anupa Kudva, Jon Ukropec, Susan Wroblewski, Rachel Kobos, and Jesus San-Miguel

ALCYONE Study Design

- Phase 3 study of daratumumab plus VMP versus VMP alone in transplant-ineligible NDMM; N = 706



Stratification factors
- ISS (I vs II vs III)
- Region (EU vs other)
- Age (<75 vs ≥75 years)

- Cycles 1-9: 6-week cycles
- Cycles 10+: 4-week cycles

Statistical analyses
- Prespecified interim analysis for OS (209 events; 63% of planned events)

SC, subcutaneously; PO, orally; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenously; PD, progressive disease; ISS, International Staging System; EU, Europe.

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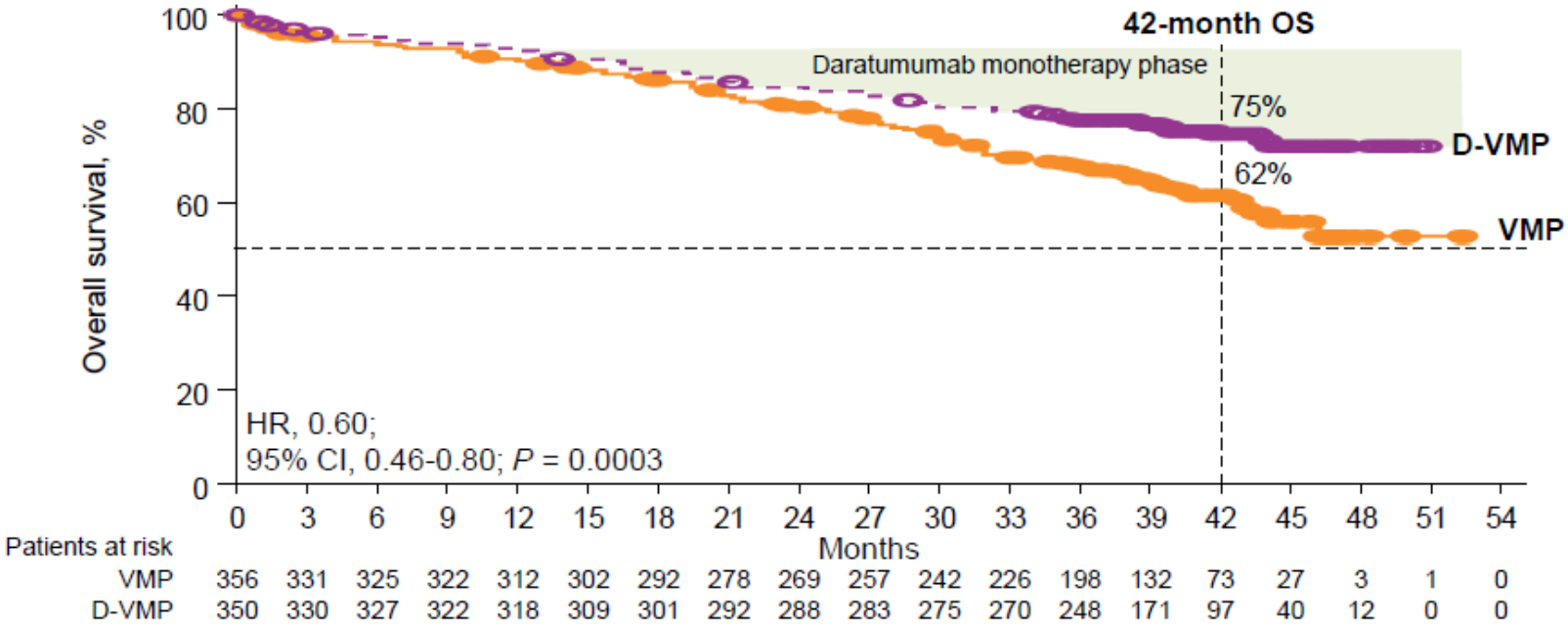
OS[a]

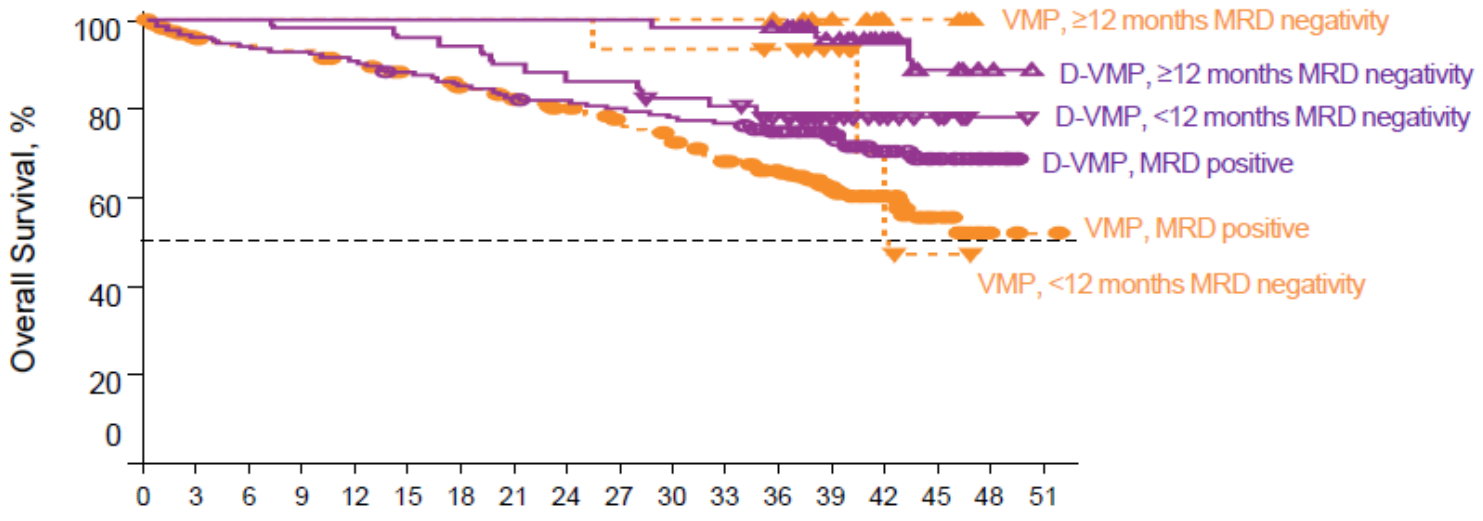
- Median (range) follow-up: 40.1 (0-52.1) months
  - Pre-specified analysis triggered after 209 deaths were observed



40% reduction in the risk of death in patients receiving D-VMP

[a]Kaplan-Meier estimate.

OS by Sustained MRD-negativity Status



Patients at risk																		
D-VMP, <12 months MRD negativity	50	50	50	49	49	48	47	45	43	43	40	39	36	25	12	6	1	0
D-VMP, ≥12 months MRD negativity	49	49	49	49	49	49	49	49	49	49	48	48	46	35	21	9	3	0
D-VMP, MRD positive	251	231	228	224	220	212	205	198	196	191	187	183	166	111	64	25	8	0
VMP, <12 months MRD negativity	15	15	15	15	15	15	15	15	15	14	14	14	13	9	3	1	0	0
VMP, ≥12 months MRD negativity	10	10	10	10	10	10	10	10	10	10	10	10	9	7	3	3	0	0
VMP, MRD positive	331	306	300	297	287	277	267	253	244	233	218	202	176	116	67	23	3	0

Improved OS for patients with sustained MRD-negativity for ≥12 months

#1875

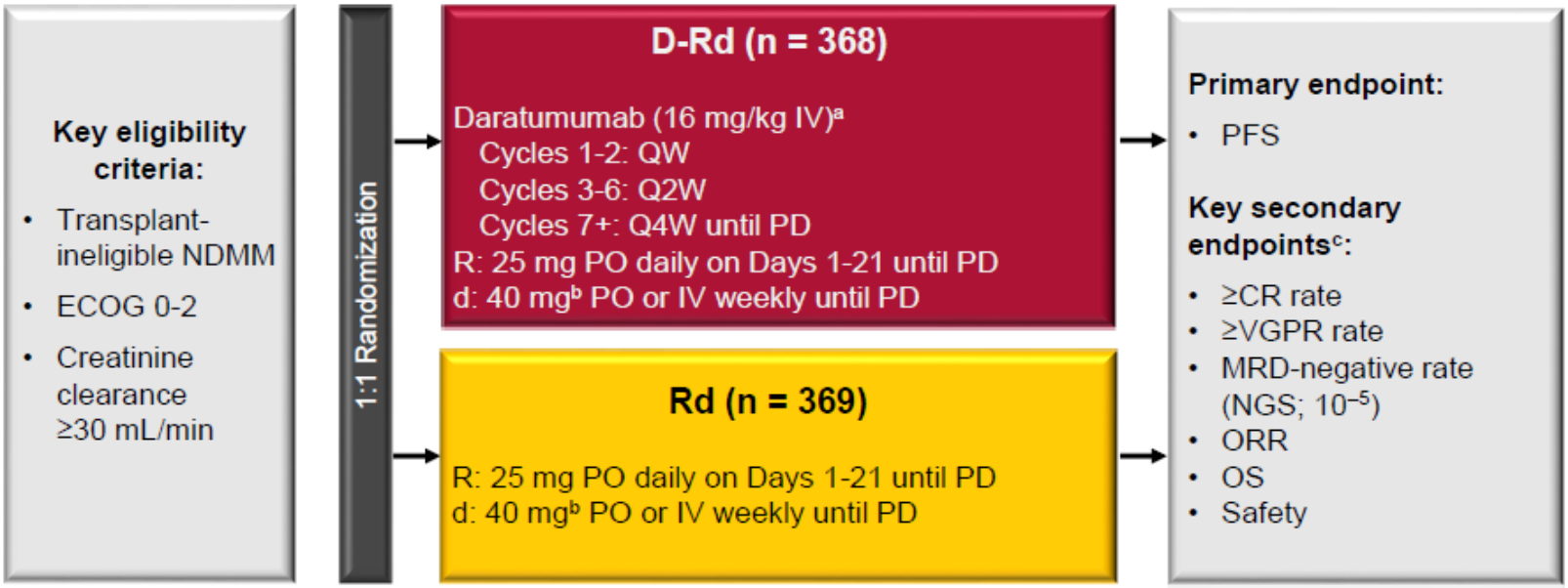
DARATUMUMAB PLUS LENALIDOMIDE AND DEXAMETHASONE (D-RD) VERSUS LENALIDOMIDE AND DEXAMETHASONE (RD) IN PATIENTS WITH NEWLY DIAGNOSED MULTIPLE MYELOMA (NDMM) INELIGIBLE FOR TRANSPLANT: UPDATED ANALYSIS OF MAIA

Presenter: Nizar Bahlis, Calgary, AB, Canada

Nizar Bahlis, Thierry Facon, Saad Z. Usmani, Shaji K. Kumar, Torben Plesner, Robert Z. Orlowski, Cyrille Touzeau, Supratik Basu, Hareth Nahi, Cyrille Hulin, Hang Quach, Hartmut Goldschmidt, Michael E O'Dwyer, Christopher P Venner, Katja C. Weisel, Maria Krevvata, Huiling Pei, Jianping Wang, Rian Van Rampelbergh, Jon Ukropec, Clarissa M. Uhlar, Rachel Kobos and Aurore Perrot

MAIA Study Design

- Phase 3 study of D-Rd vs Rd in transplant-ineligible NDMM (N = 737)



Stratification factors
- ISS (I vs II vs III)
- Region (NA vs other)
- Age (<75 vs ≥75 years)

Cycle: 28 days

[a]On days when daratumumab was administered, dexamethasone was administered to patients in the D-Rd arm and served as the treatment dose of steroid for that day, as well as the required pre-infusion medication.
[b]For patients older than 75 years of age or with BMI <18.5, dexamethasone was administered at a dose of 20 mg weekly.
[c]Efficacy endpoints were sequentially tested in the order shown.

ECOG, Eastern Cooperative Oncology Group; ISS, International Staging System; NA, North America; IV, intravenously; QW, once weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; PD, progressive disease; PO, orally; CR, complete response; VGPR, very good partial response; MRD, minimal residual disease; NGS, next-generation sequencing; ORR, overall response rate; OS, overall survival; BMI, body mass index.

Efficacy: PFS

Median follow-up: 36.4 months

Efficacy

- After a median follow-up of 36.4 months, median PFS was NR with D-Rd versus 33.8 months with Rd (HR, 0.56; 95% CI, 0.44-0.71; *P*<0.0001; **Figure 2**)
  - The estimated 36-month PFS rate was 68% with D-Rd versus 46% with Rd (**Figure 2**)

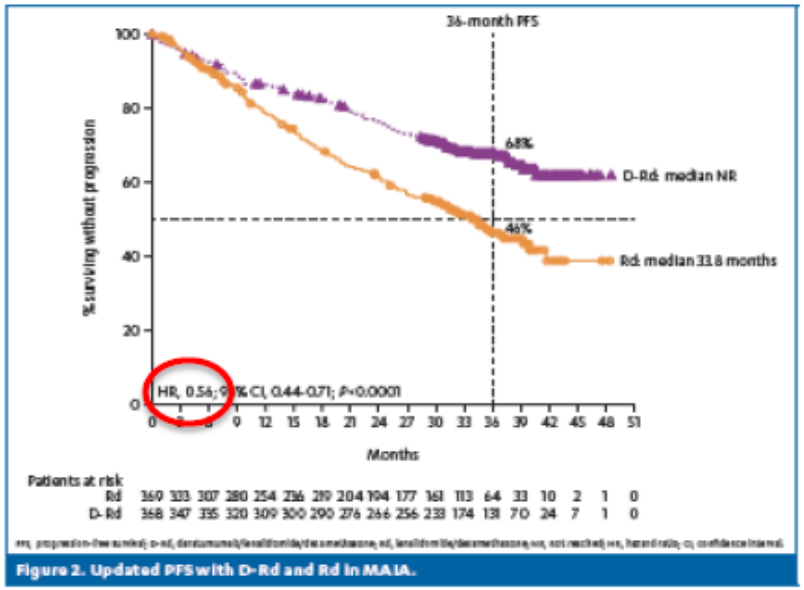


Figure 2. Updated PFS with D-Rd and Rd in MAIA.

44% reduction in the risk of progression or death in patients receiving D-Rd

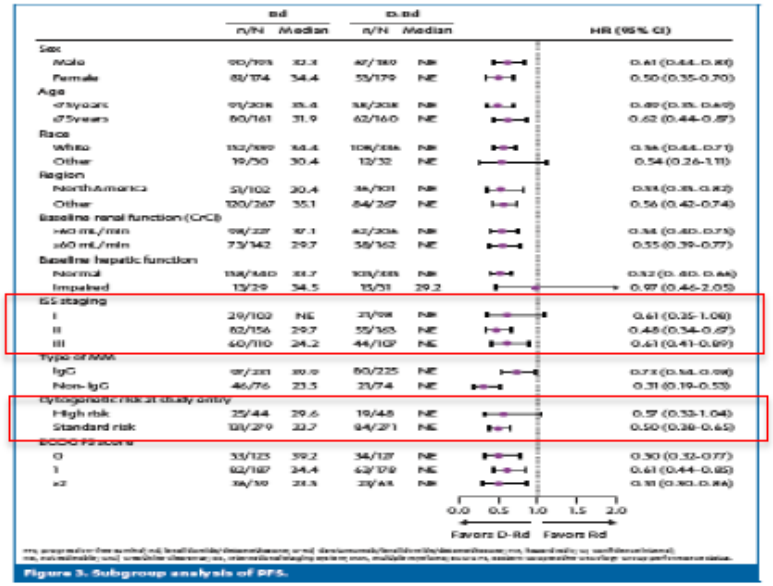


Figure 3. Subgroup analysis of PFS.

CI, confidence interval.
[a]Kaplan-Meier estimate.

Kapitel 3

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1.-3. Rezidiv

#LBA-6

CARFILZOMIB, DEXAMETHASONE, AND DARATUMUMAB VERSUS CARFILZOMIB AND DEXAMETHASONE FOR THE TREATMENT OF PATIENTS WITH RELAPSED OR REFRACTORY MULTIPLE MYELOMA (RRMM): PRIMARY ANALYSIS RESULTS FROM THE RANDOMIZED, OPEN-LABEL, PHASE 3 STUDY CANDOR (NCT03158688)

Presenter: *Saad Z. Usmani*, Charlotte, NC, USA

Saad Z. Usmani, Hang Quach, María-Victoria Mateos, Ola Landgren, Xavier Leleu, David S. Siegel, Katja Weisel, Hui Yang, Zandra K. Klippel, Anita Zahlten-Kumeli and Meletios A. Dimopoulos

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CANDOR Study Design

Patients N = 466

Key eligibility criteria

- RRMM
- 1–3 prior therapies with ≥PR to ≥1 prior therapy
- ECOG PS 0-2
- CrCl of ≥20 mL/in
- LVEF ≥40%

2:1

KdD N = 312

Carfilzomib 20/56 mg/m²*
Days 1, 2, 8, 9, 15, 16; IV; ~30 min infusion

Dexamethasone: 40 mg
Days 1, 8, 15, 22; IV or PO

Daratumumab: 16 mg/kg
Cycles 1–2: days 1,8, 15, 22
Cycles 3–6: every 2 weeks
Cycle 7+: every 4 weeks; IV

Kd N = 154

Carfilzomib: 20/56 mg/m²
Days 1, 2 8, 9, 15, 16; IV

Dexamethasone: 40 mg
Days 1, 8, 15, 22; IV or PO

28-day cycles until PD or unacceptable toxicity

Endpoints

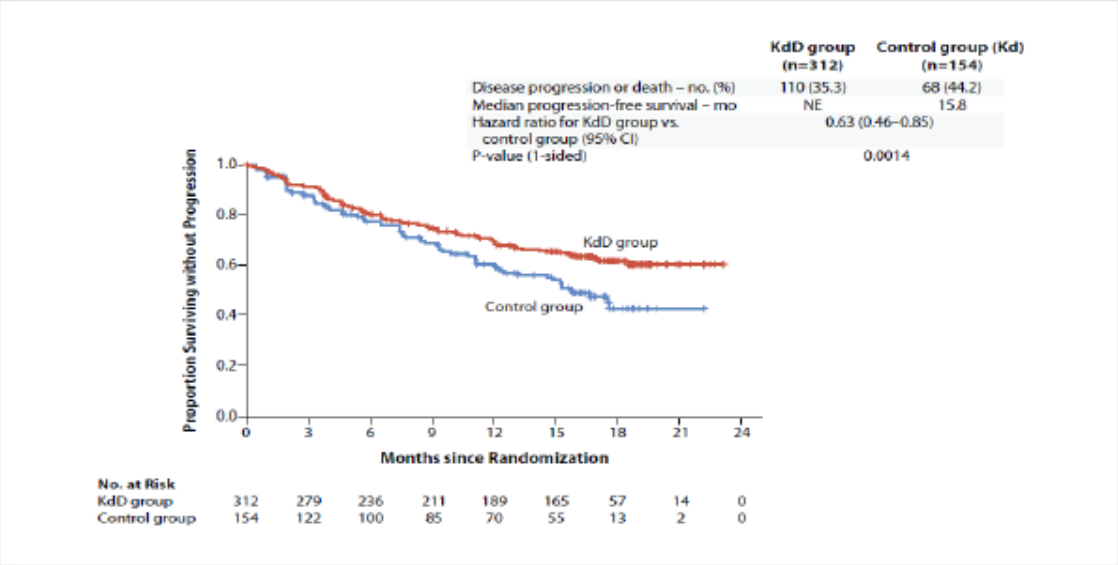
Primary Endpoint: PFS
Secondary Endpoints: ORR, MRD-negative CR Rate at 12 months, overall survival, time to response, and safety

*Carfilzomib 20 mg/m² administered on days 1 and 2 of cycle 1 only, and 56 mg/m² thereafter

Patient and Disease Characteristics at Baseline Were Generally Balanced

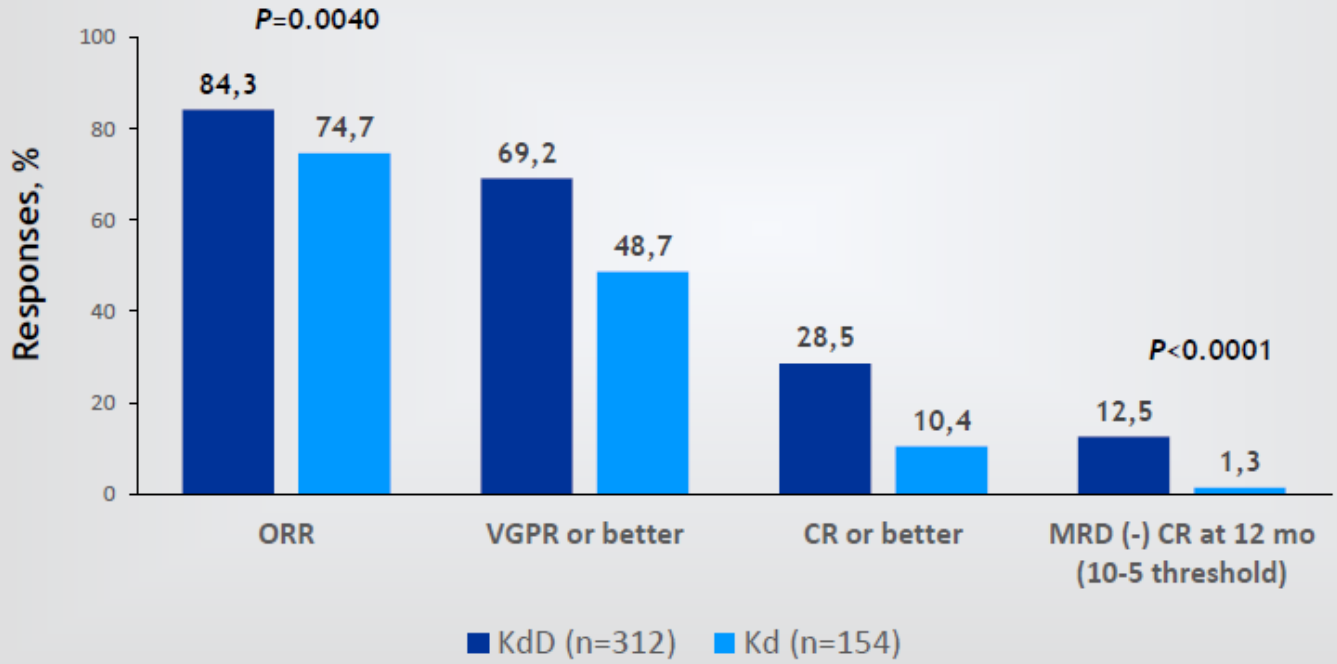
Characteristic	KdD (n=312)	Kd (n=154)
Median age, years (Range)	64 (29-84)	65 (35-84)
ECOG PS, %		
0 or 1	95	96
2	5	5
ISS stage at baseline, %		
I	47	51
II	33	31
III	20	18
Cytogenetic risk category by FISH, %		
High	15	17
Standard	33	34
Unknown	51	49
Number of prior therapies, %		
1	46	46
≥2	54	54
Prior therapies, %		
Bortezomib	92	87
Lenalidomide	39	48
Refractory to prior bortezomib	28	31
Refractory to prior lenalidomide	32	36

Primary Endpoint Met: KdD Significantly Prolonged PFS Compared With Kd



	KdD (n=312)	Kd (n=154)
Median follow-up time, months	16.9	16.3
Progression/Death, n (%)	110 (35%)	68 (44%)
Median PFS, months	NE	15.8
HR (KdD/Kd) (95% CI)	0.63 (0.46-0.85)	
p-value (1-sided)	0.0014	

KdD Improved Response Rates



Median time to first response was 1 month in both treatment arms

Conclusions

- Treatment with KdD resulted in a significant PFS benefit compared with Kd, with a 37% reduction in the risk of progression or death
- Patients treated with KdD achieved deeper responses than patients treated with Kd, with a nearly 10-times higher MRD negative-complete response rate at 12 months versus Kd-treated patients
- The PFS benefit of KdD was maintained across prespecified clinically important subgroups, particularly among lenalidomide-exposed and lenalidomide-refractory patients
  - The estimated PFS of KdD based on the hazard ratio in the lenalidomide-exposed or -refractory subgroups compared favorably with the median PFS range of 7.8 to 11.2 months reported for other triplet lenalidomide-free regimens in lenalidomide-exposed or -refractory populations
- A higher frequency of fatal AEs was observed for KdD that was mostly related to infections; this had no impact on overall survival
- AEs were generally manageable; while 82% of patients in the KdD arm and 74% of patients in the Kd arm experienced grade ≥3 AES, a majority of patients in the KdD arm did not discontinue treatment (64%) or reduce treatment dose (62%) as a result of AEs
- KdD should be considered as a novel, efficacious and tolerable IMiD-free treatment option for RRMM

Kapitel 4

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Refraktäre Patienten

#143

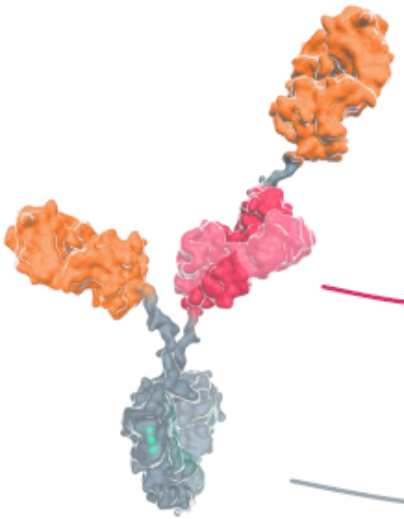
FIRST CLINICAL STUDY OF THE B-CELL MATURATION ANTIGEN (BCMA) 2+1 T CELL ENGAGER (TCE) CC-93269 IN PATIENTS (PTS) WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM): INTERIM RESULTS OF A PHASE 1 MULTICENTER TRIAL

Presenter: L. J. Costa, Birmingham, Vestavia, AL, USA

Luciano J. Costa, Sandy W. Wong, Arancha Bermúdez, Javier de la Rubia, María-Victoria Mateos, Enrique M. Ocio, Paula Rodríguez-Otero, Jesus San-Miguel, Shaoyi , Rafael Sarmiento, Pilar Lardelli, Allison Gaudy, Isaac Boss, Lisa M. Kelly, Michael R. Burgess, Kristen Hege and William I. Bensinger

CC-93269 KEY ENGINEERING CHARACTERISTICS

- CC-93269 is a humanized 2+1 IgG1-based TCE that binds to BCMA on myeloma cells and to CD3ε on T cells, enabling specific and tight BCMA binding[1,2]



Anti-BCMA (bivalent)[1–5]
Bivalent binding to BCMA in a 2+1 format for superior potency, tumor targeting, and retention

Anti-CD3ε (monovalent)[1–5]
Head-to-tail geometry of BCMA- and CD3ε-binding Fab domains using a flexible linker

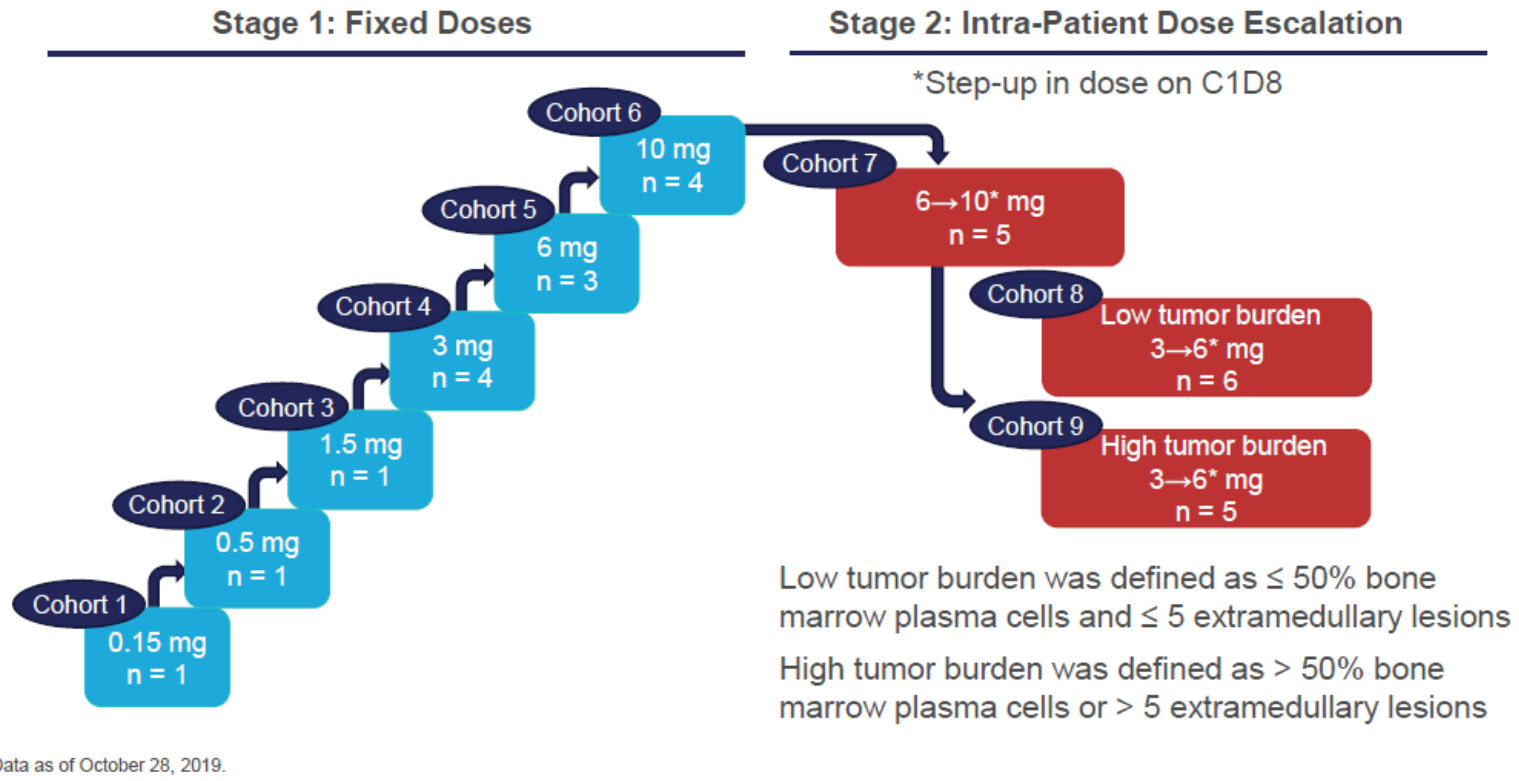
Heterodimeric FcγR-silent Fc[1–6]
No binding to FcγR and C1q to minimize infusion-related reactions and binding to FcRn retained for IgG-like PK

- CC-93269 induces tumor regression in animal models of myeloma and promotes myeloma cell death in primary patient bone marrow aspirates[1,2]

BCMA, B-cell maturation antigen; CD3, cluster of differentiation 3; Fab, antigen-binding fragment; FcγR, Fc gamma receptor, FcRn, neonatal Fc receptor; Ig, immunoglobulin; PK, pharmacokinetics; TCE, T cell engager.

1. Seckinger A, et al. Cancer Cell. 2017;31:396-410. 2. Vu DM, et al. Blood 2015;128;abstract 2998. 3. Klein C, et al. Cancer Res. 2017;77:abstract 3629. 4. Bacac M, et al. Clin Cancer Res. 2016;22:3286-3297. 5. Lehmann S, et al. Clin Cancer Res. 2016;22:4417-4427. 6. Schlothauer T, et al. Prot Eng Des Sel. 2016;29:457-466.

CC-93269-MM-001 PART A: DOSE ESCALATION



Low tumor burden was defined as ≤ 50% bone marrow plasma cells and ≤ 5 extramedullary lesions

High tumor burden was defined as > 50% bone marrow plasma cells or > 5 extramedullary lesions

Data as of October 28, 2019.

BASELINE DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

Characteristics	All Patients (N = 30)
Age, median (range), years	64.0 (42–78)
Male, n (%)	21 (70.0)
Time since initial diagnosis, median (range), years	5.94 (1.4–16.6)
Presence of extramedullary lesions, n (%)	8 (26.7)
Eastern Cooperative Oncology Group performance status, n (%)	
0	8 (26.7)
1	22 (73.3)
Derived International Staging System stage, n (%)	
I	9 (30.0)
II	11 (36.7)
III	9 (30.0)
Unknown	1 (3.3)
High-risk cytogenetics, n (%)[a]	
del(17p) or t(4;14) or t(14;16)	9 (30.0)

Data as of October 28, 2019.
[a] At screening by central laboratory.

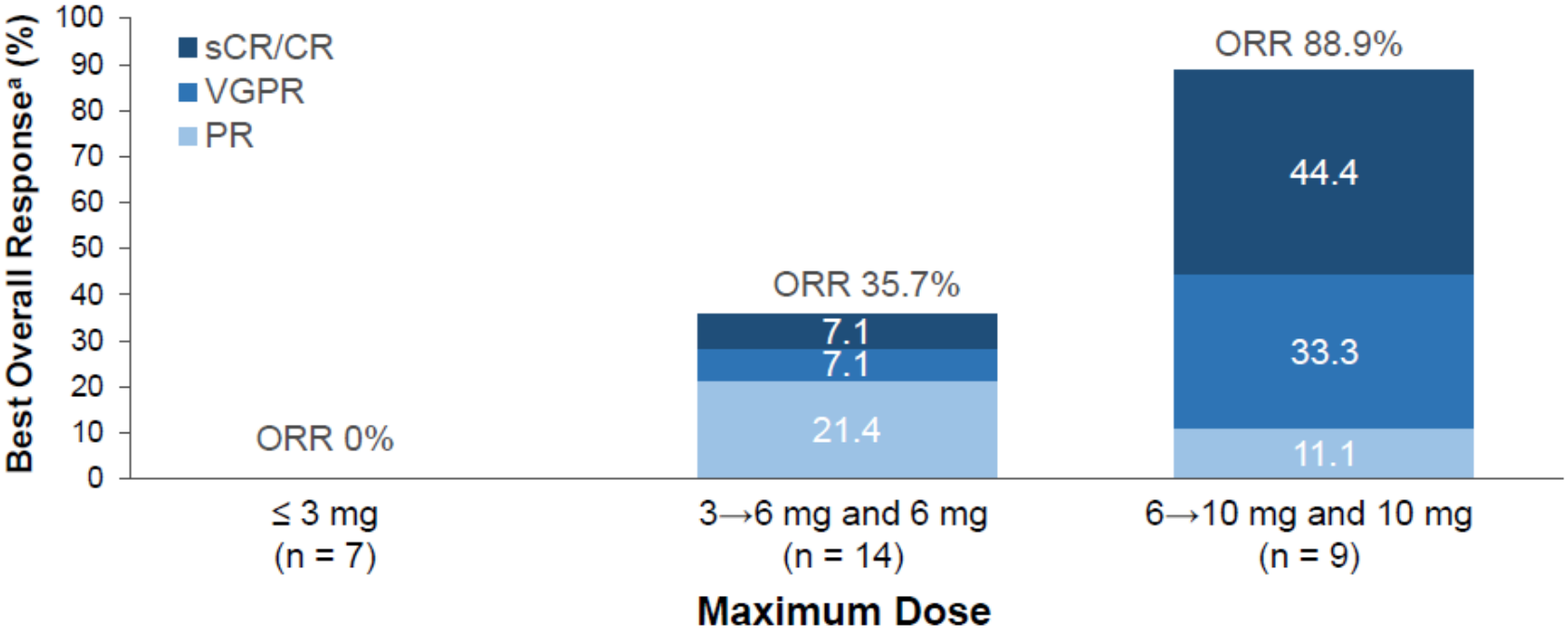
SAFETY SUMMARY

Common (≥ 20% All Grade) TEAEs[a], n (%)	All Patients (N = 30)	
	All Grade	Grade ≥ 3
Patients with ≥ 1 TEAE	29 (96.7)	22 (73.3)
Hematologic TEAEs		
Neutropenia	14 (46.7)	13 (43.3)
Anemia	13 (43.3)	11 (36.7)
Thrombocytopenia	9 (30.0)	5 (16.7)
Nonhematologic TEAEs		
Cytokine release syndrome	23 (76.7)	1 (3.3)
Infections and infestations	17 (56.7)	9 (30.0)
Diarrhea	8 (26.7)	1 (3.3)
Vomiting	8 (26.7)	0
Back pain	7 (23.3)	0
Fatigue	6 (20.0)	0
Infusion-related reaction	6 (20.0)	0
Nausea	6 (20.0)	0

- Deaths (Grade 5 TEAEs) were reported in 4 patients during the treatment period:
  - Suspected to be related to CC-93269: cytokine release syndrome (n = 1)
  - Not suspected to be related to CC-93269: sepsis in the setting of advanced prostate cancer, sudden cardiac death, and general health deterioration due to progressive myeloma (n = 1 each)

Data as of October 28, 2019.
[a] TEAEs include any AEs with onset or worsening between the date of first dose of CC-93269 and 37 days after the date of last dose of study treatment.
TEAE, treatment-emergent adverse event.

CC-93269 PRELIMINARY EFFICACY

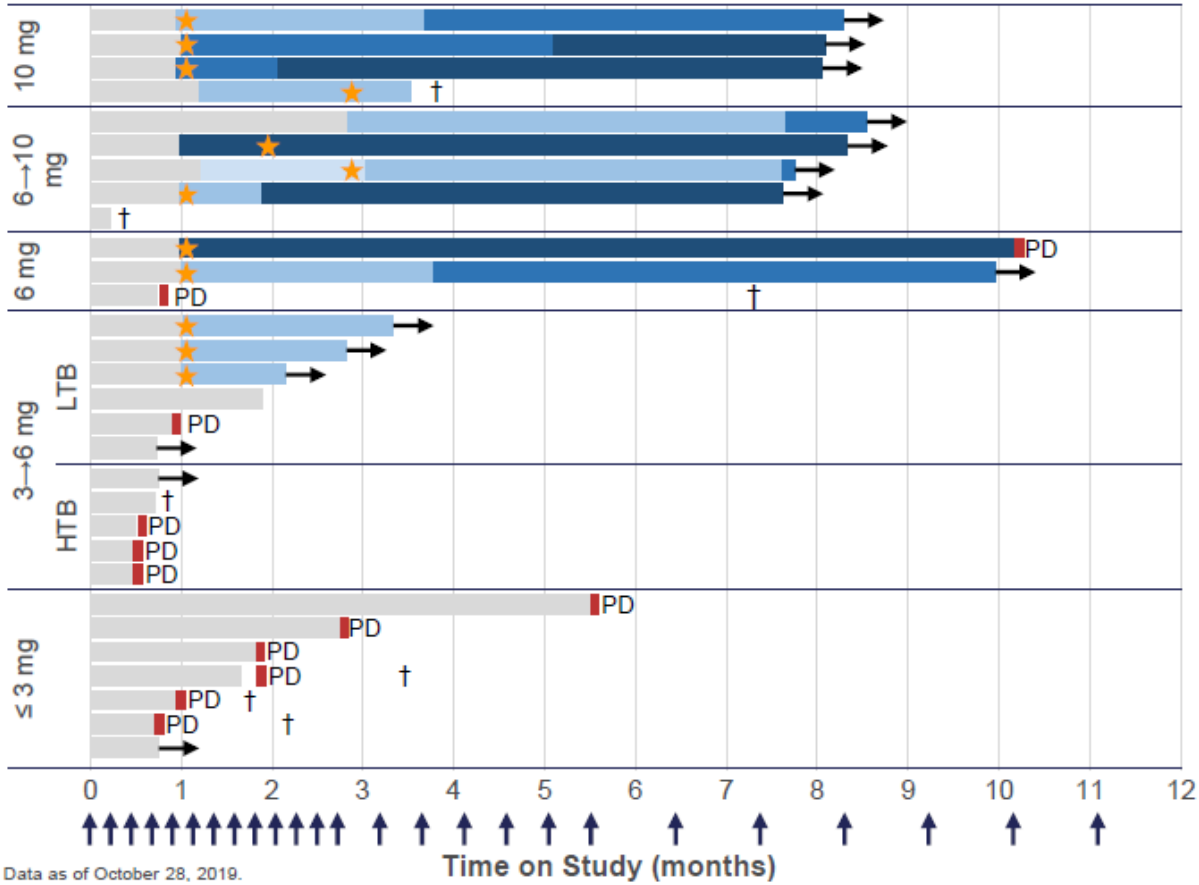


- In all patients (N = 30), the ORR was 43.3% with a sCR/CR of 16.7%
- Among patients receiving 10 mg (n = 9), the ORR was 88.9% with a sCR/CR of 44.4%

Data as of October 28, 2019.
[a] Response as assessed by the investigator.
CR, complete response; ORR, overall response rate (PR or better); PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

Multiples Myelom

RESPONSE OVER TIME



- Median time to first response was 4.1 weeks (range 4.0–13.1)
- 11 of 13 responses are ongoing
- 5 of 30 (16.7%) patients achieved an MRD-negative sCR/CR
  - Of 13 responding patients, 92.3% achieved MRD negativity (≤ $1/10^5$) in the bone marrow on or before C4D1 by Euroflow[a]

sCR/CR	PD
VGPR	† Death
PR	→ Ongoing
MR	↑ CC-93269 dose
SD	★ MRD-negative

Data as of October 28, 2019.

[a] MRD negativity by Euroflow analysis was reported only if a minimum sensitivity of ≤ 1 tumor cell in 10^5 nucleated cells was achieved and in patients who had ≥ 1 baseline and ≥ 1 post-baseline MRD assessment. HTB, high tumor burden (defined as > 50% bone marrow plasma cells or > 5 extramedullary lesions); LTB, low tumor burden (defined as ≤ 50% bone marrow plasma cells and ≤ 5 extramedullary lesions); MR, minimal response.

CONCLUSIONS

- The safety profile of CC-93269 supports further development, and enrollment is ongoing to define the RP2D
  - Most common grade ≥ 3 TEAEs included neutropenia 43.3%, anemia 36.7%, and infections 30.0%
  - CRS events occurred in 76.7% of patients; the majority were grade 1/2
  - No cases of encephalopathy were reported
- Among patients treated with 10 mg, the ORR was 88.9%, including 44.4% sCR/CR
- All patients achieving sCR/CR were MRD-negative
  - 92.3% of responding patients (PR or better) achieved MRD negativity (≤ $1/10^5$) in the bone marrow
- CC-93269 shows promising dose-dependent efficacy, including MRD-negative sCRs, with a convenient administration schedule, in patients with heavily pretreated RRMM

RP2D, recommended phase 2 dose.

Die Kurzpräsentationen sind online unter

www.lymphome.de/ash2019

Für den Inhalt verantwortlich:

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