Lymphom Kompetenz KOMPAKT

EHA2020 VIRTUAL
11. – 14. Juni 2020

Kompetenznetz Maligne Lymphome

Vernetzt forschen.
Gut informiert entscheiden.

Prof. Dr. med. Katja Weisel

Multiples Myelom

- Stellvertr. Direktorin der II. Med. Klinik und Poliklinik der Universitätsklinik Hamburg-Eppendorf
- Mitglied der Leitgruppe der German Speaking Myeloma Multicenter Group (GMMG)

Offenlegung potentieller Interessenskonflikte

LymphomKompetenz KOMPAKT **EHA2020** 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, Sanofi, Takeda
Besitz von Geschäftsanteilen, Aktien, Fonds	
Patent, Urheberrecht, Verkaufslizenz	
Honorare	Amgen, Adaptive, Abbvie, BMS, Celgene, GSK Janssen, Karyopharm, Sanofi, Takeda
Finanzierung wissenschaftlicher Untersuchungen	Amgen, Celgene, Sanofi, Janssen (Institution)
Andere (auch immaterielle)	

EHA 2020 – Multiples Myelom

Erstbehandlung des MM

- Quadruplettherapie bei Standard- und Hochrisikopatienten
- Welche Rolle spielt welcher Antikörper?

Rezidivtherapie

Practice-Changing-Results:

- Kombination aus monoklonalem CD38 Antikörper + Carfilzomib und Dexamethason

Am Horizont:

- Neue Ergebnisse von BiTEs und CARs

Erstbehandlung des Multiplen Myeloms

Quadruplettherapie bei Standard- und Hochrisikopatienten: Welche Rolle spielt welcher Antikörper?

p420-2: **Usmani et al.** PRIMARY ANALYSIS OF THE RANDOMIZED PHASE II TRIAL OF BORTEZOMIB, LENALIDOMIDE, DEXAMTHASONE WITH/WITHOUT ELOTUZUMAB FOR NEWLY DIAGNOSED, HIGH RISK MULTIPLE MYELOMA (SWOG-1211)

P420-5: **Weisel et al.** DEPTH OF RESPONSE TO ISATUXIMAB, CARFILZOMIB, LENALIDOMIDE AND DEXAMETHASONE (ISA-KRD) IN FRONT-LINE TREATMENT OF HIGH-RISK MULTIPLE MYELOMA: INTERIM ANALYSIS OF THE GMMG-CONCEPT TRIAL

PRIMARY ANALYSIS OF THE RANDOMIZED PHASE II TRIAL OF BORTEZOMIB, LENALIDOMIDE, DEXAMETHASONE WITH/WITHOUT ELOTUZUMAB FOR NEWLY DIAGNOSED, HIGH RISK MULTIPLE MYELOMA (SWOG-1211)

Saad Z. Usmani[1], Sikander Ailawadhi[2], Rachael Sexton[3], Antje Hoering[3], Brea Lipe[4], Sandi Fredette[5], Jason Valent[6], Matthew Rosenweig[7], Jeffrey A. Zonder[8], Madhav Dhodapkar[9], Natalie Callander[10], Peter M. Voorhees[1], Brian Durie[11], S. Vincent Rajkumar[12], Paul G. Richardson[13], Robert Z. Orlowski[14], for the SWOG1211 Trial Investigators.

1. Levine Cancer Institute/Atrium Health, Charlotte, NC.
2. Mayo Clinic, Jacksonville, FL.
3. Cancer Research And Biostatistics, Seattle, WA.
4. University of Rochester Medical Center, Rochester, NY.
5. SWOG, Portland, Oregon
6. Cleveland Clinic Cancer Institute, Cleveland, OH.
7. City of Hope, Los Angeles, CA.
8. Karmanos Cancer Institute/Wayne State University, Detroit, MI.
9. Emory University Cancer Institute, Atlanta, GA
10. University of Wisconsin Cancer Center, Madison, WI.
11. Cedar-Sinai Medical Center, Los Angeles, CA.
12. Mayo Clinic, Rochester, MN.
13. Dana Farber Cancer Institute, Boston, MA.
14. MD Anderson Cancer Center, Houston, TX.

SWOG 1211 – Key Inclusion Criteria

- Newly diagnosed multiple myeloma

- Subjects had to meet one of the following high risk criteria:
  - ***Poor Risk Score by Gene Expression Profiling***
  - ***One or more of the following cytogenetic/FISH abnormalities:***
    - Translocation (14;20)(q32;q12)
    - Translocation (14;16)(q32.3;q23)
    - Deletion (17p)
    - Chromosome 1q21 amplification
  - ***Primary plasma cell leukemia (PPCL)***
  - ***Elevated serum LDH twice above the institutional ULN***

SWOG 1211 Schema

Randomized Phase II (1:1)

	Induction[1,2] 21-Day Cycle (8 Cycles)	Maintenance 28-Day Cycle
ARM A RVd	Bortezomib 1.3 mg/m2 SC Days 1,4,8,11 Lenalidomide 25 mg PO Days 1-14 Dexamethasone 20 mg PO Days 1,2,4,5,8,9,11,12	Bortezomib 1.0 mg/m2 SC Days 1,8,15 Lenalidomide 15 mg PO Days 1-21 Dexamethasone 12 mg PO Days 1,,8,15
ARM B RVd-Elotuzumab	Bortezomib 1.3 mg/m2 SC Days 1,4,8,11 Lenalidomide 25 mg PO Days 1-14 Dexamethasone 20 mg PO Days 1,2,4,5,8,9,11,12 Elotuzumab 10 mg/kg IV Day 1, 8, 15	Bortezomib 1.0 mg/m2 SC Days 1,8,15 Lenalidomide 15 mg PO Days 1-21 Dexamethasone 12 mg PO Days 1,,8,15 Elotuzumab 10 mg/kg IV Day 1,15

Off-Protocol at Progression/Relapse

PRIMARY ENDPOINT

PFS : 82% power and a one-sided α =0.1 to detect a HR=1.75 between the two treatment arms or an increase in median PFS from 2 years to 3.5 years in the RVd-Elo arm compared to the RVD arm.

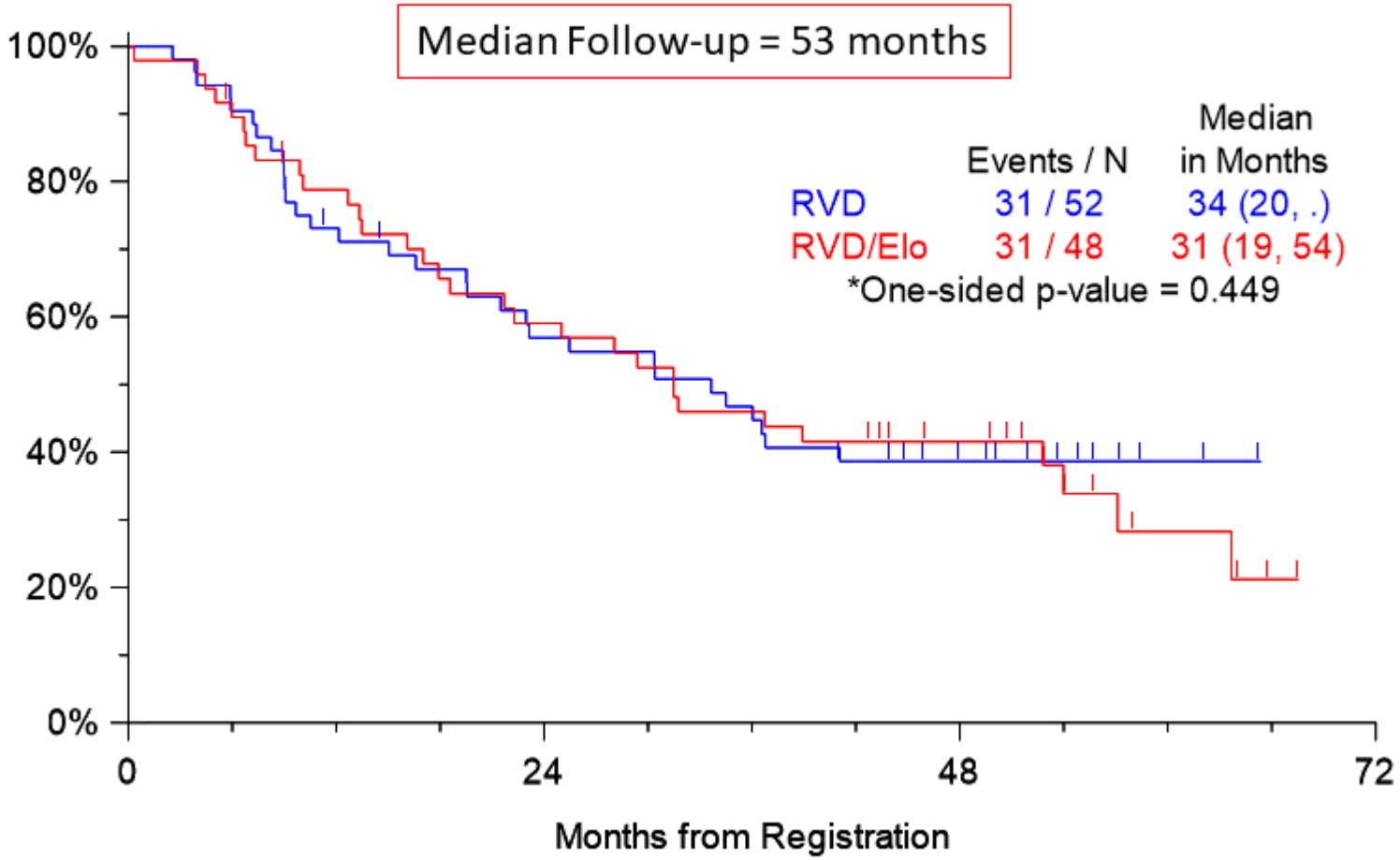
SECONDARY ENDPOINTS

ORR
OS
Safety

1. ONE CYCLE OF PRIOR THERAPY ALLOWED PRIOR TO ENROLLMENT
2. STEM CELL COLLECTION ALLOWED AFTER CYCLE 2 ON PROTOCOL. ASCT ALLOWED OFF-PROTOCOL AT PROGRESSION/RELAPSE

Opened to all National Clinical Trials Network members

SWOG 1211 Phase II– Progression Free Survival



S1211 – Safety Data

- No differences in the safety profile were observed except ≥Grade 3 neutropenia, infections and neuropathy being higher in RVd-Elo arm (≥5% difference).

	RVd (n=52)		RVd-Elo (n=48)	
	Any Grade	≥ Grade 3	Any Grade	≥ Grade 3
HEMATOLOGIC				
Anemia	63%	15%	43%	13%
Leukopenia	45%	8%	44%	10%
Neutropenia	35%	16%	39%	27%
Thrombocytopenia	49%	19%	67%	21%
NON-HEMATOLOGIC				
Infections	23%	8%	32%	17%
Sensory Neuropathy	73%	8%	67%	13%
Motor Neuropathy	10%	2%	22%	8%

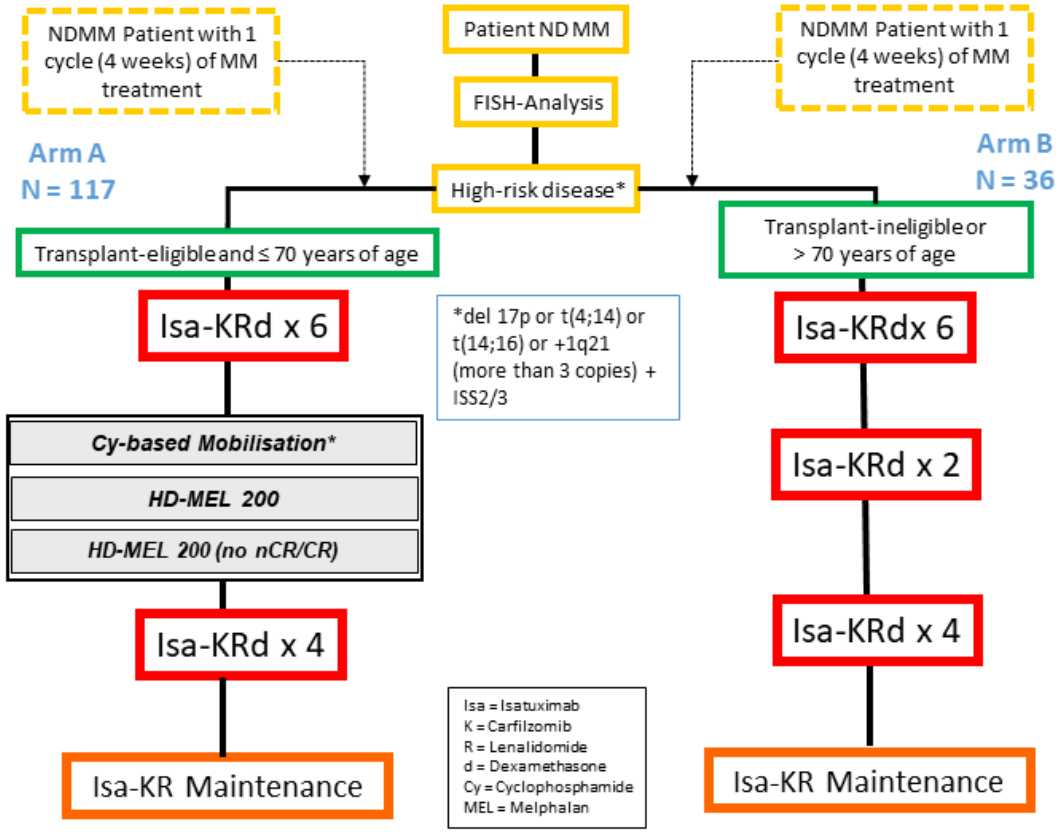
EHA Virtual Convention 2020

Depth of Response to Isatuximab, Carfilzomib, Lenalidomide and Dexamethasone (Isa-KRd) in front-line treatment of high-risk Multiple Myeloma: Interim Analysis of the GMMG-CONCEPT trial

Katja C. Weisel, Anne Marie Asemissen, Britta Besemer, Mathias Haenel, Wolfgang Blau, Martin Goerner, Yon-Dschun Ko, Jan Duerig, Peter Staib, Christoph Mann, Raphael Lutz, Markus Munder, Ullrich Graeven, Rudolf Peceny, Hans Salwender, Manola Zago, Axel Benner, Diana Tichy, Carsten Bokemeyer, Hartmut Goldschmidt

Universitätsklinikum Hamburg-Eppendorf

Study Design – GMMG CONCEPT (NCT03104842)



Isa-KRd Induction
Cycle 1

Isatuximab	10 mg/kg	day 1, 8, 15, 22
Carfilzomib	20 mg/m²	day 1, 2
Carfilzomib	36 mg/m²	day 8, 9, 15, 16
Lenalidomide *	25 mg	day 1-21
Dexamethasone**	40 mg*	day 1, 8, 15, 22
28-day-cycle		

Isa-KRd Induction
Cycle 2-6

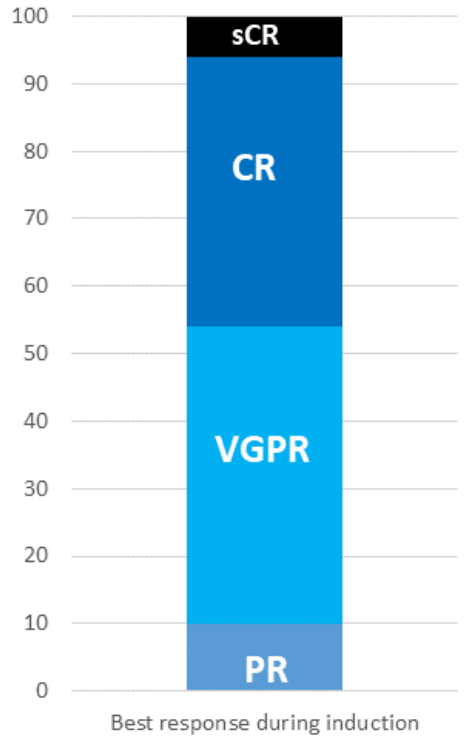
Isatuximab	10 mg/kg	day 1, 15
Carfilzomib	36 mg/m²	day 1, 2, 8, 9, 15, 16
Lenalidomide **	25 mg	day 1-21
Dexamethasone***	40 mg*	day 1, 8, 15, 22
28-day-cycle		

* Cy-based mobilisation was moved in an amendment to the time after 3 induction cycles
**Dose adaption of lenalidomide according to renal function
***20 mg in patients ≥75 years

Katja C. Weisel

Results: Best response to therapy, 6 induction cycles

- All evaluable patients: n = 50
- Overall response rate (ORR, ≥ PR): 100%
- ≥ VGPR : 90%; CR/sCR: 46%
  - Arm A: 41/46 ≥ VGPR
  - Arm B: all (n = 4) VGPR
- Arm A: MRD-assessment in 33 patients during induction
  - 20 patients MRD negative
  - 11 patients MRD positive
  - 2 not assessable



Results of MRD assessments after induction treatment are not reported and available yet

Results: Safety, most common TEAE

Hematologic TEAEs, n = 50	Grade 3 or 4 N (%)
Leukopenia	13 (26%)
Neutropenia	17 (34%)
Lymphopenia	14 (28%)
Anemia	5 (10%)
Thrombocytopenia	7 (14%)

Non-Hematologic TEAEs, n = 50	Any Grade N (%)	Grade 3 or 4 N (%)
Upper respiratory tract Infection	9 (18%)	0
Pyrexia	6 (12%)	0
Rash	8 (16%)	0
Peripheral sensory neuropathy	8 (16%)	1 (2%)
Nasopharyngitis	5 (10%)	0
Hypertension	6 (12%)	6 (12%)
Cardiac failure	2 (4%)	2 (4%)
Infusion reaction	16 (32%)	0

- Low rates of peripheral neuropathy
- No death on study

For hematologic TAE, the following terms were summarized: Leukopenia and white blood cell count decreased, Lymphopenia and lymphocyte count decreased, Neutropenia and neutrophil count decreased, thrombocytopenia and platelet count decreased; AE observed during Cy-mobilization are partially included

EHA 2020 – Multiples Myelom

Erstbehandlung des MM

- Elotuzumab-VRd ist nicht effektiver als VRd in Standard- und Hochrisikopatienten
- E-VRd/VRd gefolgt von HD-MEL und Erhaltung erreicht medianes PFS von > 30 Monaten bei Hochrisikopatienten
- Quadruplet-Therapie mit Isa-KRd erzielt MRD negative Remissionen bei Hochrisikopatienten bereits in der Induktion

Rezidivtherapie des Multiplen Myeloms

Neuer Standard in der Rezidivtherapie

pq205-3 **Moreau et al.** ISATUXIMAB PLUS CARFILZOMIB AND DEXAMETHASONE VS CARFILZOMIB AND DEXAMETHASONE IN RELAPSED/REFRACTORY MULTIPLE MYELOMA (IKEMA): INTERIM ANALYSIS OF A PHASE 3, RANDOMIZED, OPEN-LABEL STUDY

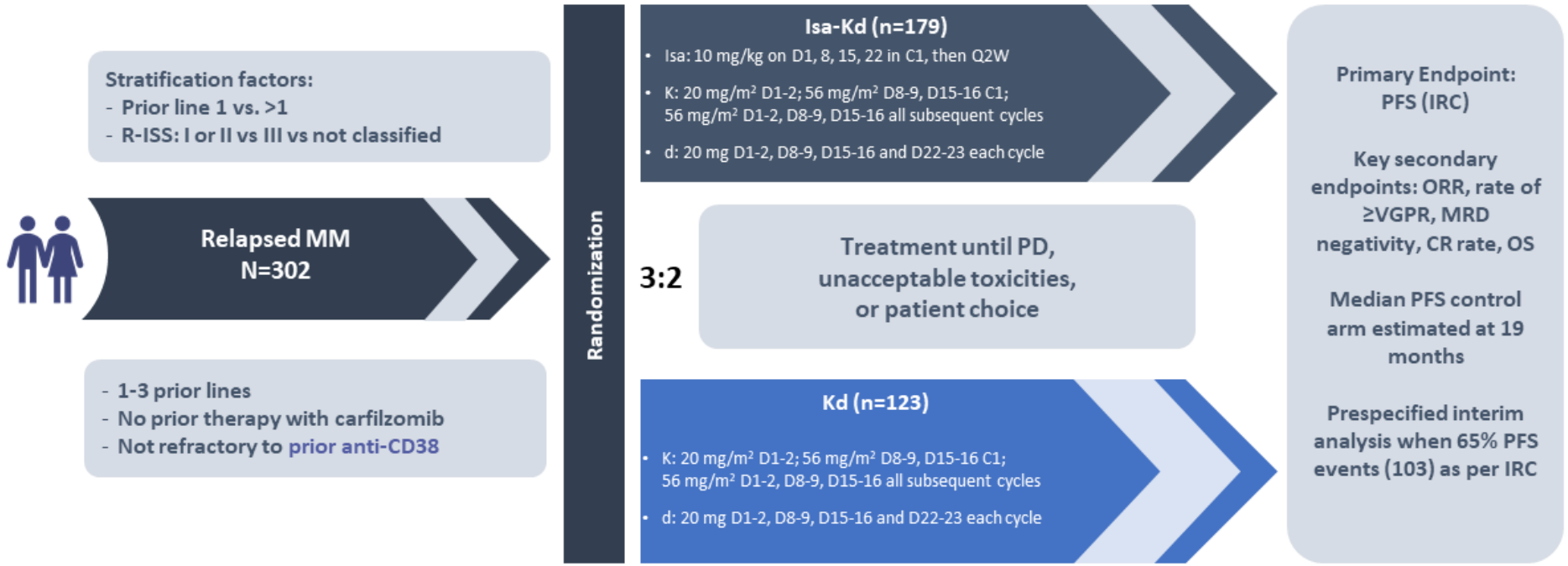
IKEMA Isatuximab Plus Carfilzomib and Dexamethasone vs Carfilzomib and Dexamethasone in Relapsed/Refractory Multiple Myeloma (IKEMA): Interim Analysis of A Phase 3 Randomized, Open-Label Study

Philippe Moreau*,[1], Meletios-Athanasios Dimopoulos[2], Joseph Mikhael[3], Kwee Yong[4], Marcelo Capra[5], Thierry Facon[6], Roman Hajek[7], Ivan Spicka[8], Marie-Laure Risse[9], Gaelle Asset[10], Sandrine Macé[9], Thomas Martin*,[11] on behalf of IKEMA investigators

*Co-primary investigators; [1]Department of Hematology, University Hospital Hôtel-Dieu, Nantes, France; [2]The National and Kapodistrian University of Athens, Athens, Greece; [3]Translational Genomics Research Institute, City of Hope Cancer Center, Phoenix, AZ, USA; [4]Department of Haematology, University College Hospital, London, UK; [5]Hospital Mãe de Deus, Porto Alegre, Rio Grande do Sul; [6]Lille University Hospital, Lille, France; [7]Department of Hemato-Oncology, University Hospital Ostrava, University of Ostrava, Ostrava, Czech Republic; [8]Clinical Department of Hematology, 1st Medical Department, Charles University in Prague; [9]Sanofi R&D, Vitry/Alfortville, France; [10]Sanofi R&D, Chilly-Mazarin, France; [11]Division of Hematology, University of California at San Francisco, San Francisco, CA, USA

EHA 2020; Final Abstract Code: LB2603

IKEMA
Study design: Isa-Kd vs Kd in relapsed multiple myeloma



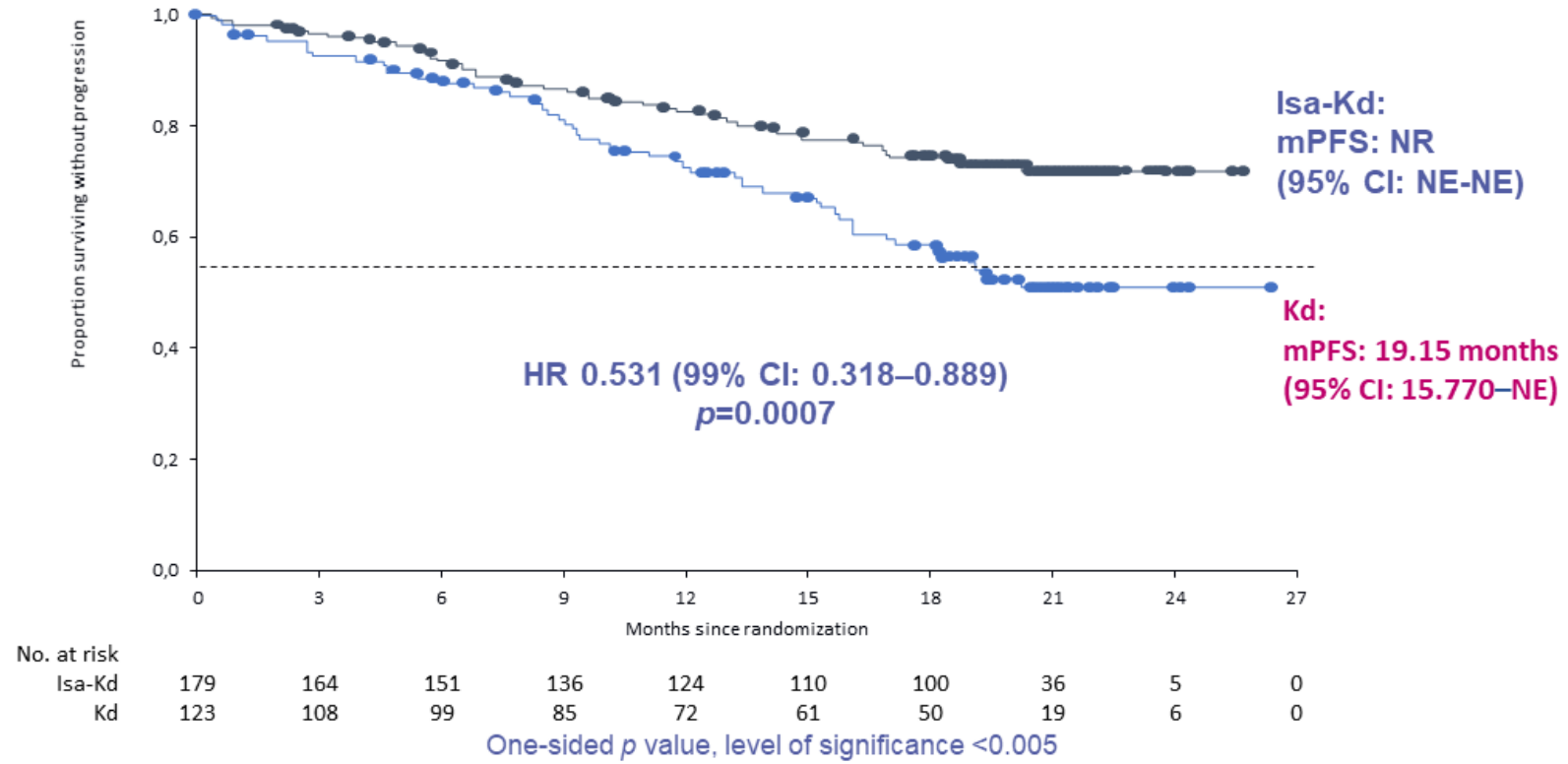
Sample size calculation: ~300 patients and 159 PFS events to detect 41% risk reduction in hazard rate for PFS with 90% power and one-sided 0.025 significance level

Moreau P, et al. Future Oncol 2020;16:4347–58

IKEMA study: NCT03275285
C, cycle; CR, complete response; D, day; d, dexamethasone; IRC, Independent Review Committee; Isa, isatuximab; K, carfilzomib; MM, multiple myeloma; MRD, minimal residual disease; ms, months; ORR, overall response rate; OS, overall survival; PFS, progression free survival; Q2W, once every 2 weeks; R-ISS, revised international staging system; VGPR, very good partial response

IKEMA

Interim PFS analysis – IRC assessment in ITT population (primary endpoint)

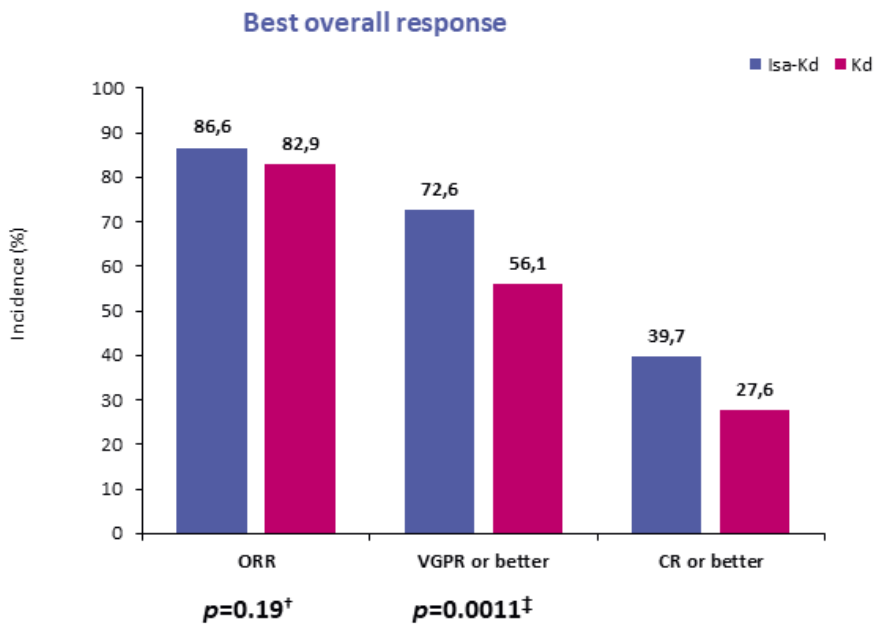


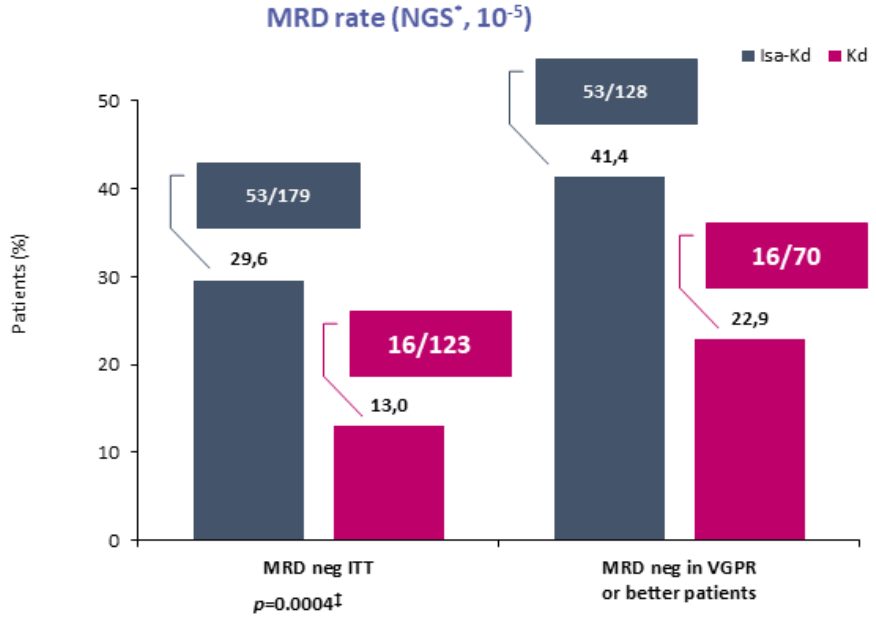
Isa-Kd showed improvement in PFS with 47% reduction of risk of progression or death vs Kd

CI, confidence interval; d, dexamethasone; HR, hazard ratio; IRC, Independent Review Committee; Isa, isatuximab; ITT, intent to treat; K, carfilzomib; m, median; NE, not estimable; NR, not reached; PFS, progression-free survival

IKEMA

Depth of response





Deeper responses were seen with Isa-Kd consistent with striking PFS improvement
MRD negativity rate with Isa-Kd was approximately 30% in ITT population

*Adaptive Biotechnologies NGS, MRD testing performed at time of VGPR or CR
†Stratified Cochran-Mantel_Haenszel test. One sided significant level is 0.025
‡Provided for descriptive purposes only
CR, complete response; d, dexamethasone; Dara, daratumumab; ITT, intent to treat; Isa, isatuximab; K, carfilzomib; MRD, minimal residual disease; neg, negative; NGS, next generation sequencing; ORR, overall response rate; VGPR, very good partial response

IKEMA

Safety summary – continued

Selected TEAEs Preferred term, n (%)	Isa-Kd (n=177)		Kd (n=122)	
	All grades	Grade ≥3	All grades	Grade ≥3
Infusion-related reaction	79 (44.6)	1 (0.6)	4 (3.3)	–
Hypertension	65 (36.7)	36 (20.3)	38 (31.1)	24 (19.7)
Diarrhea	64 (36.2)	5 (2.8)	35 (28.7)	3 (2.5)
Upper respiratory tract infection	64 (36.2)	6 (3.4)	29 (23.8)	2 (1.6)
Fatigue	50 (28.2)	6 (3.4)	23 (18.9)	1 (0.8)
Dyspnea	49 (27.7)	9 (5.1)	26 (21.3)	1 (0.8)
Pneumonia	42 (23.7)	29 (16.4)	24 (19.7)	15 (12.3)
Bronchitis	40 (22.6)	4 (2.3)	15 (12.3)	1 (0.8)
Cardiac failure events				
Cardiac failure, any class*	13 (7.3)	7 (4.0)	8 (6.6)	5 (4.1)
Hematologic laboratory abnormalities				
Anemia	176 (99.4)	39 (22.0)	121 (99.2)	24 (19.7)
Neutropenia	97 (54.8)	34 (19.2)	53 (43.4)	9 (7.4)
Thrombocytopenia	167 (94.4)	53 (29.9)	107 (87.7)	29 (23.8)

Isa-Kd had a manageable safety profile with no new safety signals
IRs mainly occurred during the first infusion and were mostly grade 1 or 2

*Grouping using MedDRA SMQ cardiac failure narrow terms
d, dexamethasone; IR, infusion reaction; Isa, isatuximab; K, carfilzomib; TEAE, treatment-emergent adverse event

EHA 2020 – Multiples Myelom

Rezidivtherapie

Practice-Changing-Results:

- Isa-Kd ist bezüglich Anprechen und PFS der Therapie aus Kd significant überlegen
- Zusammen mit den Daten aus der CANDOR Studie (Dara-Kd vs. Kd) ist zusammenfassend die Kombination aus anti-CD38 Ak und Kd als neuer Standard in der Rezidivtherapie etabliert
- Besonders relevant mit dem zunehmenden Einsatz von Lenalidomid in der ersten Therapielinie

Rezidivtherapie des Multiplen Myeloms

Am Horizont: BiTEs and CARs

p421-5 **San Miguel et al.** IDECABTAGENE VICLEUCEL (IDE-CEL; BB2121), A BCMA-TARGETED CAR T CELL THERAPY, IN PATIENTS WITH RELAPSED AND REFRACTORY MULTIPLE MYELOMA: INITIAL KARMMA RESULTS

p421-1 **Costa et al.** INTERIM RESULTS FROM THE FIRST PHASE 1 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)

p421-2 **Mateos et al.** A PHASE 1 STUDY OF TECLISTAMAB, A HUMANIZED B-CELL MATURATION ANTIGEN (BCMA) X CD3 BISPECIFIC ANTIBODY, FOR THE TREATMENT OF RELAPSED AND/OR REFRACTORY MULTIPLE MYELOMA (RRMM)

EUROPEAN HEMATOLOGY ASSOCIATION

KarMMa™

Idecabtagene vicleucel (ide-cel; bb2121), a BCMA-targeted CAR T cell therapy, in patients with relapsed and refractory multiple myeloma (RRMM): initial KarMMa results

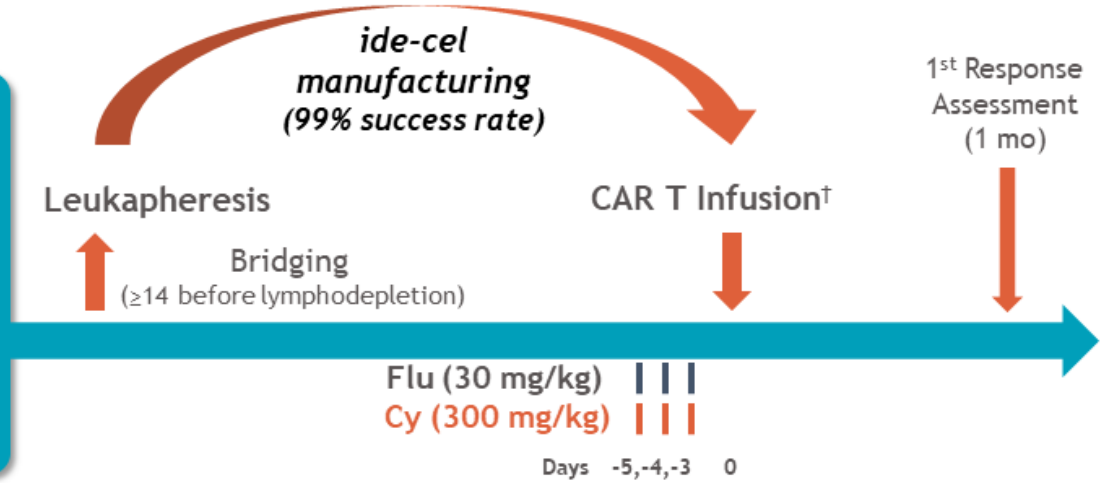
Jesus San-Miguel, MD, PhD[1]; Nina Shah, MD[2]; Albert Oriol, MD[3]; Philippe Moreau, MD[4]; Ibrahim Yakoub-Agha, MD, PhD[5]; Michel Delforge, MD, PhD[6]; Deepu Madduri, MD[7]; Ankit Kansagra, MD[8]; Hermann Einsele, MD, FRCP[9]; Hartmut Goldschmidt, MD, PhD[10]; Katja Weisel, MD[11]; Michele Cavo, MD[12]; Donna Reece, MD[13]; Alessandro Rambaldi, MD[14]; Paula Rodríguez-Otero, MD, PhD[1]; Fabio Petrocca, MD[15]; Jamie N. Connarn, PhD[16]; Julie Wang, PharmD, PhD[16]; Liping Huang, PhD[16]; Timothy B. Campbell, MD, PhD[17]; Kristen Hege, MD[17]; and Nikhil C. Munshi, MD[18] *on behalf of the KarMMa study investigators*

- [1]Clinical Universidad de Navarra, Navarra, Spain; [2]University of California San Francisco, San Francisco, CA, USA; [3]Institut Català d'Oncologia and Josep Carreras Institute, Hospital Germans Trias i Pujol, Badalona, Spain; [4]Centre Hospitalier Universitaire de Nantes, Nantes, France; [5]Univ Lille, Inserm, CHU Lille, INSERM, Infinite, U1286, Lille, France; [6]University Hospital Leuven, Leuven, Belgium; [7]Mount Sinai Hospital, New York, NY, USA; [8]UT Southwestern Medical Center, Dallas, TX, USA; [9]University Hospital Würzburg, Würzburg, Germany; [10]University Hospital Heidelberg, Heidelberg, Germany; [11]University Medical Center of Hamburg-Eppendorf, Hamburg, Germany; [12]Bologna University School of Medicine, Bologna, Italy; [13]Princess Margaret Cancer Centre, Toronto, ON, Canada; [14]Department of Oncology University of Milan and ASST Papa Giovanni XXIII, Bergamo, Italy; [15]Boston University School of Medicine, Boston, MA, USA; [16]Bristol-Myers Squibb, Summit, NJ, USA; [17]Bristol-Myers Squibb, San Francisco, CA, USA; [18]The LeBow Institute for Myeloma Therapeutics and Jerome Lipper Multiple Myeloma Center, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

Presentation Number S209

Phase II Pivotal KarMMa Study

- RRMM
- ≥3 prior regimens with ≥2 consecutive cycles each (or best response of PD)
- Previously exposed to:
  - IMiD agent
  - Proteasome inhibitor
  - Anti-CD38 antibody
- Refractory to last prior therapy per IMWG*



Endpoints

- **Primary**: ORR (null hypothesis ≤50%)
- **Secondary**: CRR (key secondary; null hypothesis ≤10%), Safety, DOR, PFS, OS, PK, MRD‡, QOL, HEOR
- **Exploratory**: Immunogenicity, BCMA expression/loss, cytokines, T cell immunophenotype, GEP in BM

Study Status as of Jan 14, 2020

Screened N=158

Leukapheresed N=140

Treated N=128
(Target Dose CAR+ T cells)

150 × 10^6	n=4
300 × 10^6	n=70
450 × 10^6	n=54

Median Follow-up (mo)

150 × 10^6	18.0
300 × 10^6	15.8
450 × 10^6	12.4
Total	13.3

EudraCT: 2017-002245-29
ClinicalTrials.gov: NCT03361748

CRR, complete response rate; Cy, cyclophosphamide; DOR, duration of response; Flu, fludarabine; GEP in BM, gene expression profile in bone marrow; HEOR, health economics and outcomes research; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PK, pharmacokinetics; QOL, quality of life.
*Defined as documented disease progression during or within 60 d from last dose of prior antimyeloma regimen. †Patients were required to be hospitalized for 14 d post-infusion. Ide-cel retreatment was allowed at disease progression for best response of at least stable disease. ‡By next-generation sequencing.

Munshi et al. Idecabtagene videucel (ide-cel; bb2121), a BCMA-targeted CAR T cell therapy, in patients with relapsed and refractory multiple myeloma (RRMM): Initial KarMMa results. Presentation at American Society of Clinical Oncology (ASCO) meeting, 2020; May 29-31, 2020. Abs. 8503.

Baseline Demographics and Clinical Characteristics

Characteristics		Ide-cel Treated (N=128)
Age, median (range), y		61 (33–78)
Male, %		59
ECOG PS, %	0 1 2	45 53 2
R-ISS Stage,* %	I II III	11 70 16
High-risk cytogenetics [del(17p), t(4;14), t(14;16)],† %		**35**
High tumor burden (≥50% BMPCs), %		**51**
Tumor BCMA expression (≥50% BCMA+),‡ %		**85**
Extramedullary disease, %		**39**

- The majority of patients had high tumor burden and more than one third had extramedullary disease and high-risk cytogenetics
- Tumor BCMA expression identified by IHC in all patients *(≥50% BCMA+ in 85% patients)*

Data cutoff: 14 Jan 2020. BCMA, B-cell maturation antigen; BMPC, bone marrow plasma cells; ECOG PS, Eastern Cooperative Oncology Group performance status; IHC, immunohistochemistry; R-ISS, revised International Staging System.
*R-ISS stage was assessed at enrollment; unknown for 3 patients. †Baseline cytogenetics not evaluable/missing for 17 patients; 45 patients (35%) had 1q amp abnormality. ‡No minimum tumor BCMA expression required for study entry.

Munshi et al. Idecabtagene vicleucel (ide-cel; bb2121), a BCMA-targeted CAR T cell therapy, in patients with relapsed and refractory multiple myeloma (RRMM): Initial KarMMa results. Presentation at American Society of Clinical Oncology (ASCO) meeting, 2020; May 29-31, 2020. Abs. 8503.

Baseline Demographics and Clinical Characteristics

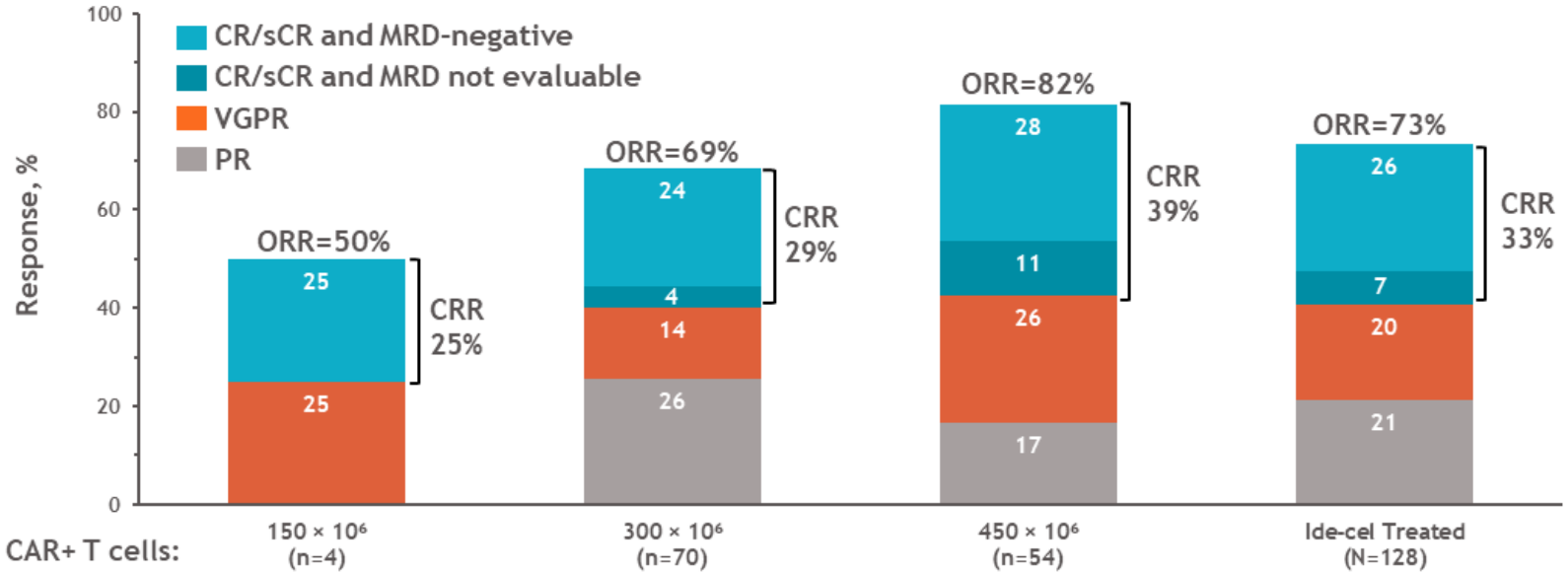
Characteristics		Ide-cel Treated (N=128)
Time since initial diagnosis, median (range), y		6 (1–18)
No. of prior anti-myeloma regimens, median (range)		**6** (3–16)
Prior autologous SCT, %	1 >1	94 34
Any bridging therapies for MM, %		88
Refractory status, %	IMiD agent-refractory PI-refractory Anti-CD38 Ab-refractory Triple-refractory Penta-refractory	98 91 **94** **84** **26**

- Patients were heavily pretreated
- All were refractory to their last line per IMWG criteria
- Most were refractory to all 3 major MM drug classes (IMiD agents, PIs, and anti-CD38 antibodies)
- Most patients (88%) received bridging therapy during CAR T cell manufacturing
  - Only 4% of patients responded (4 PR, 1 VGPR) to bridging therapy

Data cutoff: 14 Jan 2020. Ab, antibody; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; MM, multiple myeloma; PI, proteasome inhibitor; PR, partial response; SCT, stem cell transplant; VGPR, very good PR.

Munshi et al. Idecabtagene videucel (ide-cel; bb2121), a BCMA-targeted CAR T cell therapy, in patients with relapsed and refractory multiple myeloma (RRMM): Initial KarMMa results. Presentation at American Society of Clinical Oncology (ASCO) meeting, 2020; May 29-31, 2020. Abs. 8503.

Best Overall Response



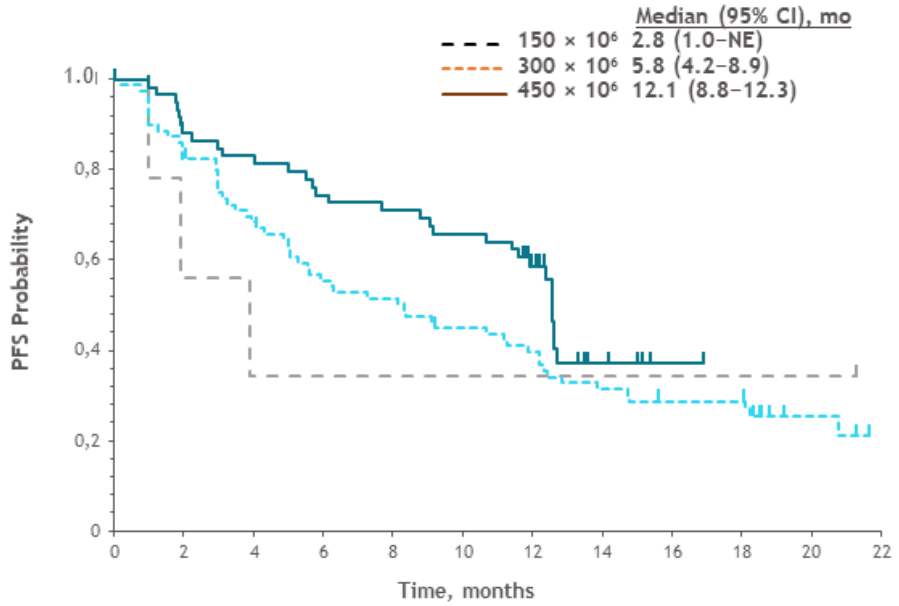
- Primary (ORR >50%) and key secondary (CRR >10%) endpoints were met in the ide-cel treated population
  - *ORR of 73% (95% CI, 65.8–81.1; P<0.0001*) and CRR (CR/sCR) of 33% (95% CI, 24.7–40.9; P<0.0001)*
  - *Both ORR and CRR increased with higher target dose*
- Median time to first response of 1.0 mo (range, 0.5–8.8); median time to CR of 2.8 mo (range, 1.0–11.8)
- Median follow-up of 13.3 mo across target dose levels

Data cutoff: 14 Jan 2020. MRD-negative defined as $<10^{-5}$ nucleated cells by next generation sequencing. Only MRD values within 3 mo of achieving CR/sCR until progression/death (exclusive) were considered. Values may not add up due to rounding.
CR/sCR, complete response/stringent CR; CRR, CR rate; MRD, minimal residual disease; ORR, overall response rate (≥PR); PR, partial response; VGPR, very good PR. **P* value at the primary data cutoff with same ORR and 95% CI.

Munshi et al. Idecabtagene videucel (ide-cel; bb2121), a BCMA-targeted CAR T cell therapy, in patients with relapsed and refractory multiple myeloma (RRMM): Initial KarMMa results. Presentation at American Society of Clinical Oncology (ASCO) meeting, 2020; May 29-31, 2020. Abs. 8503.

Progression-Free Survival By Target Dose and Best Response

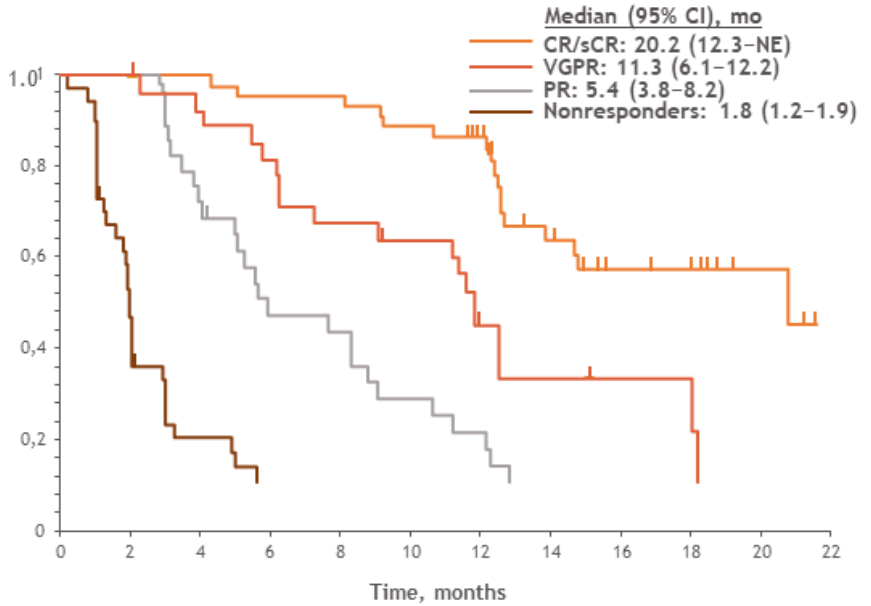
PFS by Target Dose



At risk, N												
150 × 10⁶	4	2	1	1	1	1	1	1	1	1	1	0
300 × 10⁶	70	56	42	33	29	24	17	14	11	7	2	0
450 × 10⁶	54	44	40	36	34	31	17	4	1	0	0	

- PFS increased with higher target dose; median PFS was 12 mo at 450 × 10⁶ CAR+ T cells

PFS by Best Response



CR/sCR	42	42	42	40	39	37	26	16	11	8	4	0
VGPR	25	25	22	20	16	14	8	3	2	0	0	
PR	27	16	10	9	5	1	0	0	0	0	0	
Nonresponders	34	8	83	70	64	56	35	19	13	8	4	0

- PFS increased by depth of response; median PFS was 20 mo in patients with CR/sCR

Data cutoff: 14 Jan 2020. NE, not estimable; PFS, progression-free survival.

Munshi et al. Idecabtagene vicleucel (ide-cel; bb2121), a BCMA-targeted CAR T cell therapy, in patients with relapsed and refractory multiple myeloma (RRMM): Initial KarMMa results. Presentation at American Society of Clinical Oncology (ASCO) meeting, 2020; May 29-31, 2020. Abs. 8503.

28

Most Common Adverse Events

AE,* n (%)	Ide-cel Treated (N=128)	
	Any Grade	Grade ≥3
Hematologic		
Neutropenia	117 (91)	114 (89)
Anemia	89 (70)	77 (60)
Thrombocytopenia	81 (63)	67 (52)
Leukopenia	54 (42)	50 (39)
Lymphopenia	35 (27)	34 (27)
Gastrointestinal		
Diarrhea	45 (35)	2 (2)
Nausea	37 (29)	0
Other		
Hypokalemia	45 (35)	3 (2)
Fatigue	43 (34)	2 (2)
Hypophosphatemia	38 (30)	20 (16)
Hypocalcemia	34 (27)	10 (8)
Pyrexia	32 (25)	3 (2)
Hypomagnesemia	30 (23)	0
Decreased appetite	27 (21)	1 (<1)
Headache	27 (21)	1 (<1)
Hypogammaglobulinemia	27 (21)	1 (<1)
Cough	26 (20)	0
CRS†	107 (84)	7 (5)

- Cytopenias were common; not dose related
- Median time to recovery of grade ≥3 neutropenia and thrombocytopenia was 2 mo (95% CI, 1.9–2.1) and 3 mo (95% CI, 2.1–5.5), respectively
- Delayed recovery (>1 mo) of grade ≥3 neutropenia in 41% of patients and thrombocytopenia in 48%‡
- Infections (including bacterial, viral, fungal) were common (69%); not dose-related
- 5 deaths (4%) within 8 wk of ide-cel infusion
  - 2 following MM progression
  - 3 from AEs (CRS, aspergillus pneumonia, GI hemorrhage)
- 1 additional death from AE (CMV pneumonia) within 6 mo, in the absence of MM progression

rade 5 CRS event was observed. †Includes patients with grade 3/4 cytopenia at 1 mo post-infusion.

Munshi et al. Idecabtagene videucel (ide-cel; bb2121), a BCMA-targeted CA… patients with relapsed and refractory … e myeloma (RRMM): Initial KarMMa results. Presentation at American Society of Clinical Oncology (ASCO) meeting, 2020; May 29-31, 2020. Abs. 8503.

29

EUROPEAN HEMATOLOGY ASSOCIATION

First clinical study of the B-cell maturation antigen 2+1 T cell engager CC-93269 in patients with relapsed/refractory multiple myeloma: interim results of a phase 1 multicenter trial

Luciano J. Costa,[1] Sandy W. Wong,[2] Arancha Bermúdez,[3] Javier de la Rubia,[4] María-Victoria Mateos,[5] Enrique M. Ocio,[3] Paula Rodríguez Otero,[6] Jesús San Miguel,[6] Shaoyi Li,[7] Rafael Sarmiento,[8] Pilar Lardelli,[8] Allison Gaudy,[7] Isaac Boss,[7] Lisa M. Kelly,[7] Michael R. Burgess,[7] Kristen Hege,[7] William I. Bensinger[9]

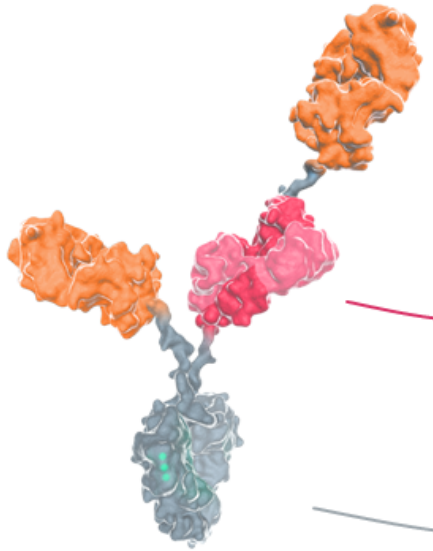
[1]Division of Hematology and Oncology, University of Alabama at Birmingham, Birmingham, AL, USA; [2]Department of Medicine, University of California, San Francisco, CA, USA; [3]Hospital Universitario Marqués de Valdecilla (IDIVAL), Santander, Spain; [4]Hematology Service, University Hospital Doctor Peset, Valencia, Spain; [5]Institute of Cancer Molecular and Cellular Biology, University Hospital of Salamanca, Salamanca, Spain; [6]Department of Hematology, Clínica Universidad de Navarra, CIMA, Pamplona, Spain; [7]Bristol Myers Squibb, Princeton, NJ, USA; [8]Celgene Institute for Translational Research Europe, a Bristol Myers Squibb Company, Sevilla, Spain; [9]Myeloma and Transplant Program, Swedish Cancer Institute, Seattle, WA, USA

Presentation Number S205

• CC-93269-MM-001

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

CC-93269-MM-001 phase 1 trial (NCT03486067): study design

Key eligibility criteria

- RRMM after ≥ 3 prior regimens
- Progressive disease within 60 days of last regimen
- No prior BCMA-directed therapy

Dose schedule

Cycle (all 28-day cycles)

Dose received

C1–3: Days 1, 8, 15, and 22

C4–6: Days 1 and 15

C7 onward: Day 1
Treatment for up to 2 years

All doses administered via IV over 2 hours

Part A: dose escalation

- Stage 1: fixed doses
- Stage 2: step-up in dose on C1D8

Part B: cohort expansion

Endpoints

Primary: safety including DLTs, AEs, NTD, and MTD
Secondary: preliminary efficacy including MRD, PK, ADA, and PD endpoints

ADA, antidrug antibody; AE, adverse event; C, Cycle; D, Day; DLT, dose-limiting toxicity; IV, intravenous; MRD, minimal residual disease; MTD, maximum tolerated dose; NTD, nontolerated dose; PD, pharmacodynamics; RRMM relapsed/refractory multiple myeloma.

32

• CC-93269-MM-001

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

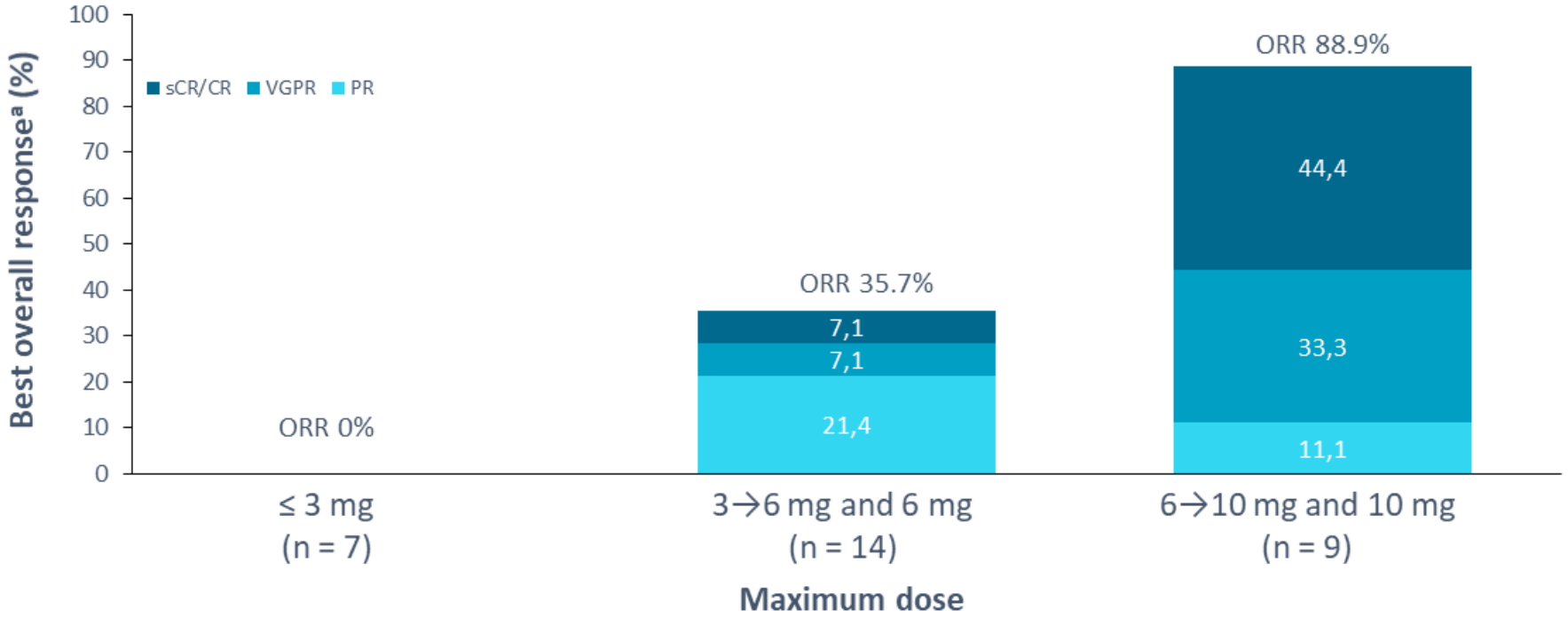
- Deaths (grade 5 TEAEs) were reported in 4 patients during the treatment period:
  - Suspected to be related to CC-93269: cytokine release syndrome (n = 1)
  - Not suspected to be related to CC-93269: sepsis in the setting of advanced prostate cancer, sudden cardiac death, and general health deterioration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

33

• CC-93269-MM-001

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.

A Phase 1 Study of Teclistamab, a Humanized B-Cell Maturation Antigen (BCMA) x CD3 Bispecific Antibody, for the Treatment of Relapsed and/or Refractory Multiple Myeloma (RRMM)

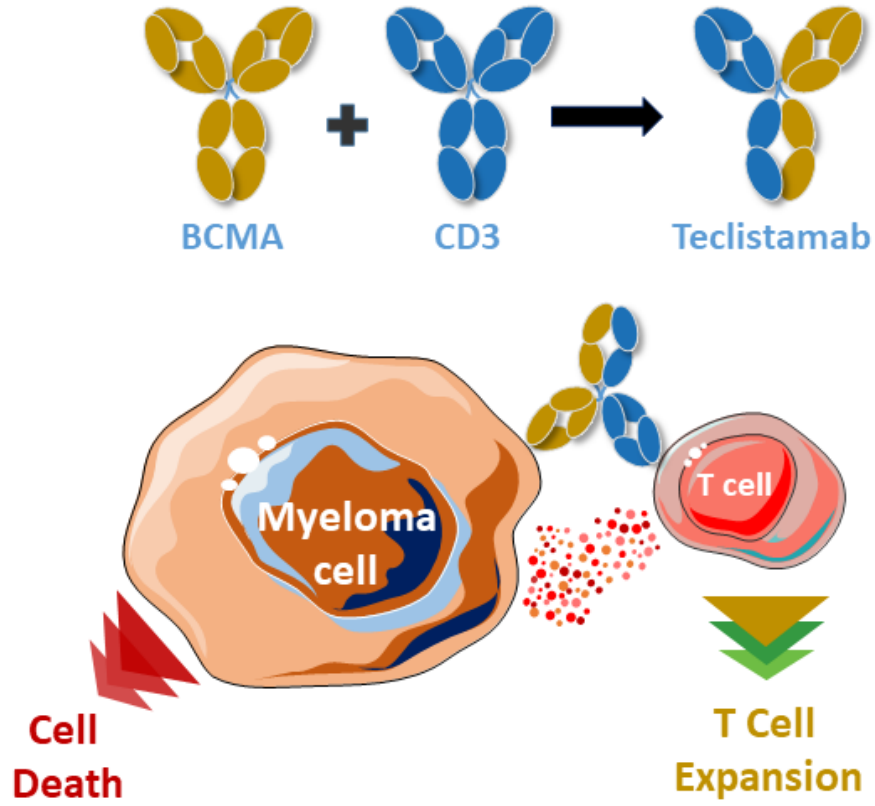
Maria-Victoria Mateos,[1] Saad Z. Usmani,[2] Hareth Nahi,[3] Amrita Y. Krishnan,[4] Jesus F. San-Miguel,[5] Albert Oriol Rocafiguera,[6] Laura Rosinol,[7] Ajai Chari,[8] Homer Adams III,[9] Suzette Girgis,[9] Shun Xin Wang Lin,[9] Tara Stephenson,[9] Kristy Kemmerer,[9] Jennifer Smit,[9] Yusri A. Elsayed,[9] Jeffrey R. Infante,[9] Jenna D. Goldberg,[10] Arnob Banerjee,[9] Alfred L. Garfall,[11] Niels W.C.J. van de Donk[12]

[1]Hospital Clínico Universitario de Salamanca, Salamanca, Spain; [2]Levine Cancer Institute-Atrium Health, Charlotte, NC, USA; [3]Karolinska University Hospital at Huddinge, Stockholm, Sweden; [4]City of Hope, Duarte, CA, USA; [5]Clínica Universidad de Navarra, Navarra, Spain; [6]Institut Català d'Oncologia and Institut Josep Carreras. Hospital Germans Trias i Pujol, Badalona, Barcelona, Spain; [7]Hospital Clinic, Barcelona, Spain; [8]Mount Sinai School of Medicine, New York, NY, USA; [9]Janssen R&D, Spring House, PA, USA; [10]Janssen R&D, Raritan, NJ, USA; [11]Perelman School of Medicine and Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA; [12]Amsterdam University Medical Center, Location VU University Medical Center, Amsterdam, The Netherlands

Previously presented at ASCO 2020 (Abstract #100)

Teclistamab: BCMA x CD3 Bispecific DuoBody® Antibody

- Teclistamab (JNJ-64007957) is a humanized IgG-4 bispecific DuoBody® antibody that binds to BCMA and CD3
- Teclistamab redirects CD3+ T cells to BCMA-expressing myeloma cells to induce cytotoxicity of the targeted cells in preclinical studies[1,2]
- Teclistamab potently kills myeloma cell lines and primary myeloma cells from heavily pretreated patients[2]
- A Phase 1 first-in-human study is underway to evaluate safety and antitumor activity of teclistamab in patients with RRMM (NCT03145181)

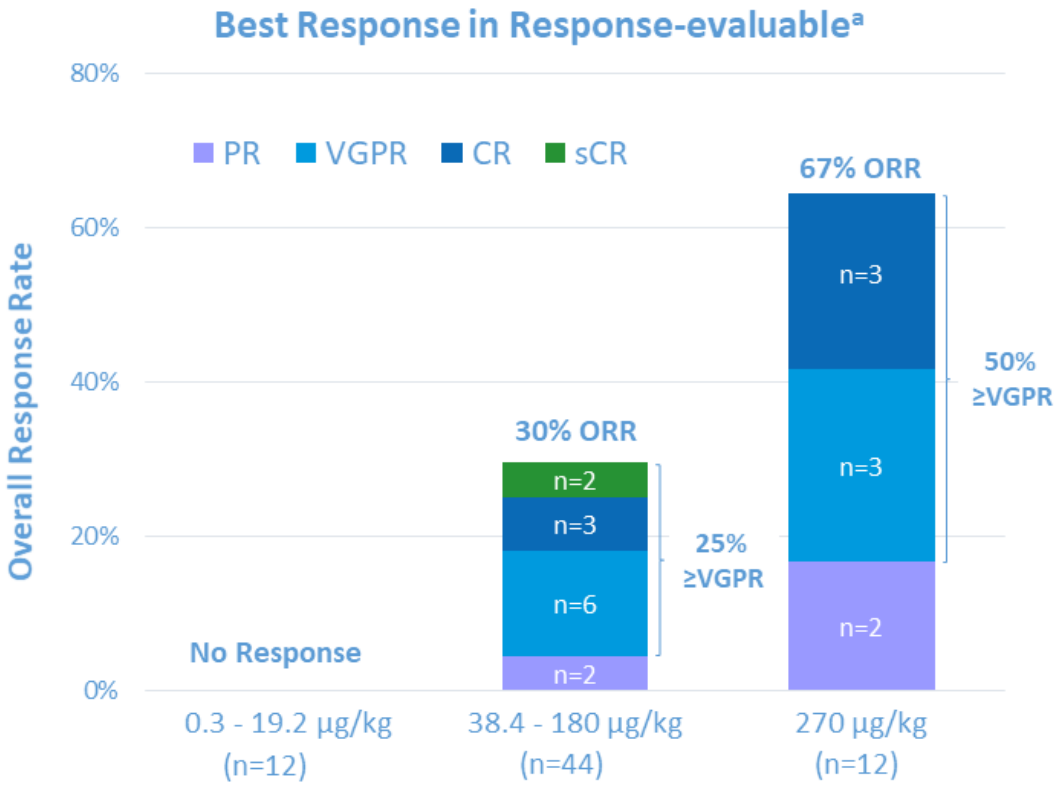


Teclistamab: Demographic and Disease Characteristics

Characteristic	Total (N = 78)
Median age (range), years	62 (24–82)
≥70 years, n (%)	16 (21)
Female, n (%)	41 (53)
ISS stage III, n (%)	21 (27)
≥1 Extramedullary plasmacytomas, n (%)	7 (9)
Bone marrow plasma cells ≥ 60%, n (%)	22 (30)
Median years from diagnosis (range)[a]	7 (1–26)
High-risk cytogenetics, n (%)[b]	19 (31)
Prior transplantation, n (%)	62 (80)

Characteristic	Total (N = 78)
Prior lines of therapy, median (range)	6 (2–14)
Triple-class exposed, n (%)[c]	72 (92)
Penta-drug exposed, n (%)[d]	51 (65)
Refractory status, n (%)	
Carfilzomib	48 (62)
Pomalidomide	56 (72)
Anti-CD38[e]	68 (87)
Triple-class refractory[c]	62 (80)
Penta-drug refractory[d]	32 (41)
Refractory to last line of therapy,[f] n (%)	67 (86)

Teclistamab: Overall Response Rate



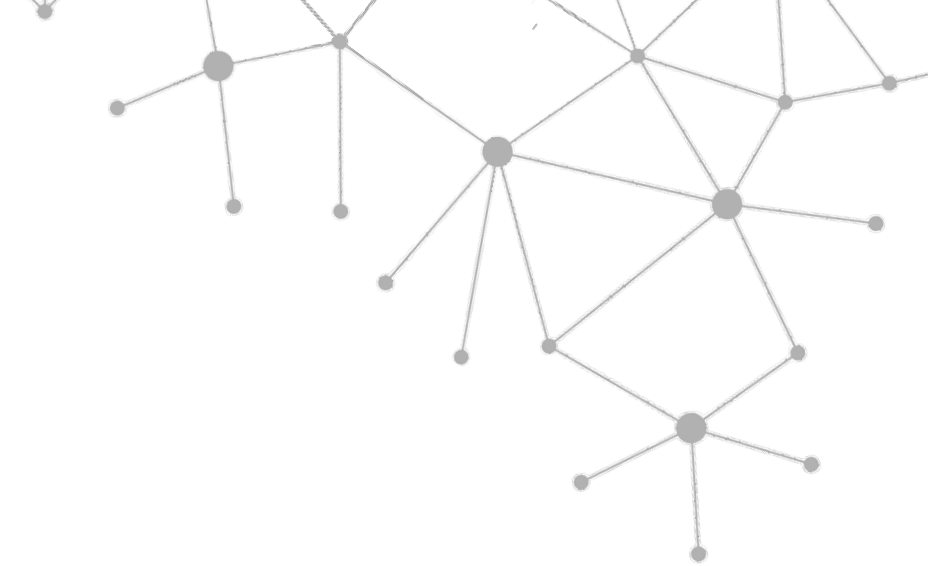
- Efficacy data at 720 µg/kg dose are not mature
- At the 270 µg/kg dose, 7/8 responders were triple-class refractory; 5/8 were penta-drug refractory
- 4/5 evaluable-patients[b] were MRD-negative at 10^{-6}; 2 had MRD-negative CR
- 2/2 evaluable patients maintained MRD-negativity for 5 months (VGPR) and 14 months (CR)

EHA 2020 – Multiples Myelom

Rezidivtherapie

Am Horizont:

- Neue Ergebnisse von BiTEs und CARs
- Ergebnisse der KARMMA Studie zeigen vielversprechende Daten bei refraktären Patienten hinsichtlich Ansprechen und Überleben
- Die neuen Anti-BCMA BiTEs führen zu hohen Ansprechraten bei refraktären Patienten



Die Kurzpräsentationen sind online unter

www.lymphome.de/eha2020

Für den Inhalt verantwortlich:

Prof. Dr. med. Katja Weisel

II. Medizinische Klinik und Poliklinik • Universitätsklinik Hamburg-Eppendorf

Das Informationsprojekt wird von folgenden Firmen unterstützt.

Diese hatten keinen Einfluss auf die Inhalte.

abbvie

AstraZeneca

Bristol Myers Squibb™

Celgene | A Bristol Myers Squibb Company

HEXAL
A Sandoz Brand

janssen
PHARMACEUTICAL COMPANIES OF Johnson&Johnson