Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

KML KONGRESSE

Expert:innen berichten zu Lymphomen & Leukämien

EHA2024 HYBRID

Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

KML KONGRESSE

Expert:innen berichten zu Lymphomen & Leukämien

Prof. Dr. med. Katja Weisel
II. Med. Klinik | Universitätsklinikum Hamburg-Eppendorf

Multiples Myelom (MM)

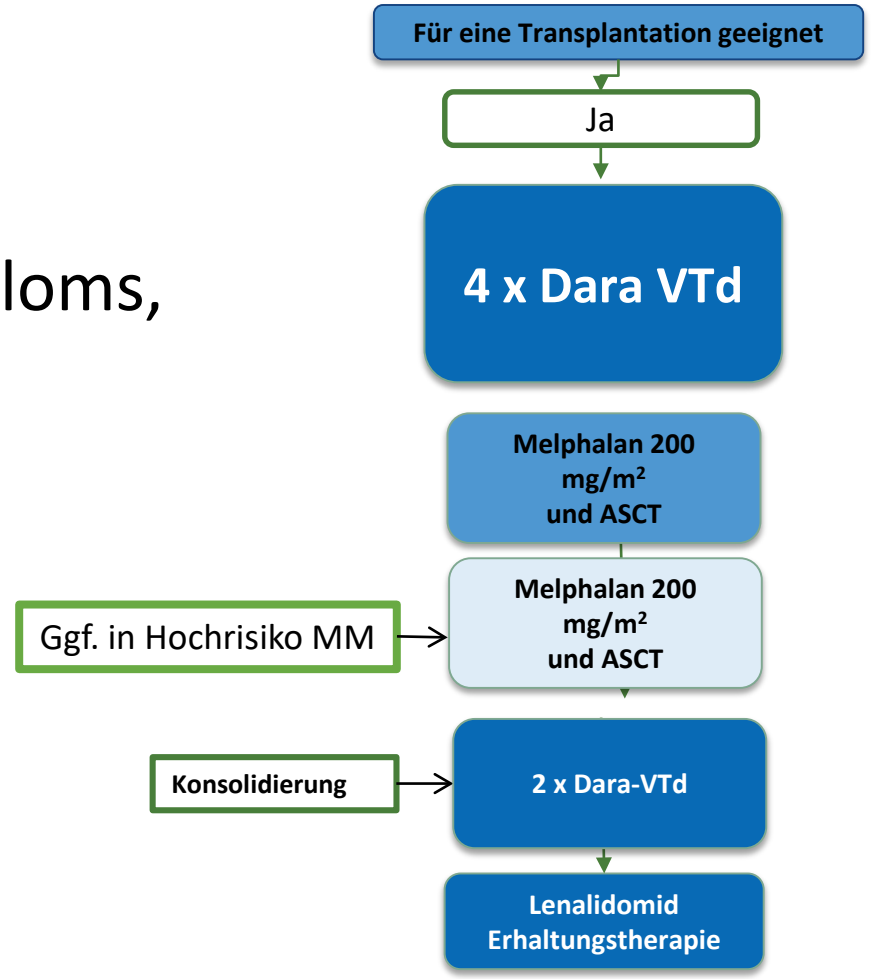
Offenlegung potentieller Interessenskonflikte

LymphomKompetenz KOMPAKT – EHA2024 HYBRID wird in Kooperation mit sieben unterstützenden Firmen durchgeführt.
Meine persönlichen Disclosures betreffen:

Anstellungsverhältnis, Führungsposition	
Beratungs-/ Gutachtertätigkeit	Abbvie, Adaptive, Amgen, Bristol Myers Squibb, Celgene, Janssen, GSK, Karyopharm, Novartis, Oncopeptides, Pfizer, Regeneron, Roche Pharma, Takeda, Sanofi, Stemline
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, Stemline
Finanzierung wissenschaftlicher Untersuchungen	Amgen, Celgene, Janssen, Sanofi; GSK, Abbvie (alle an die Institution)
Andere finanzielle Beziehungen	
Immaterielle Interessenkonflikte	

Kapitel 1

Behandlung des neudiagnostizierten Myeloms, transplantierbare Patienten



Adaptiert von Dimopoulos et al., Ann Oncol 2021

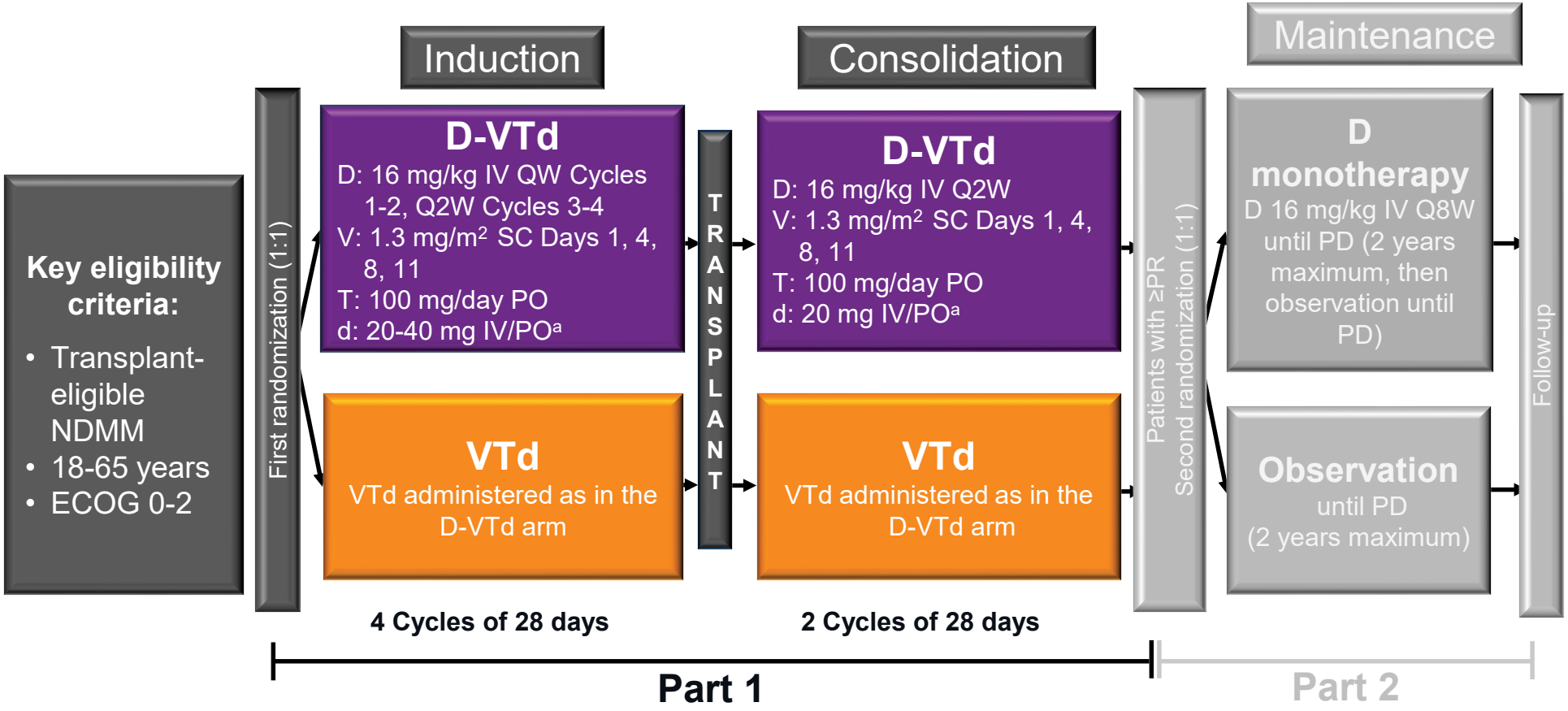
Erstbehandlung NDMM, TE

S204: DARATUMUMAB (DARA) + BORTEZOMIB/THALIDOMIDE/DEXAMETHASONE (D-VTD) FOLLOWED BY DARA MAINTENANCE IN TRANSPLANT-ELIGIBLE (TE) NEWLY DIAGNOSED MULTIPLE MYELOMA (NDMM): >6-YEAR UPDATE OF CASSIOPEIA

Philippe Moreau, Cyrille Hulin, Aurore Perrot, Bertrand Arnulf, Karim Belhadj Merzoug, Lotfi Benboubker, Sonja Zweegman, Hélène Caillon, Denis Caillot, Hervé Avet-Loiseau, Michel Delforge, Thomas Dejoie, Thierry Facon, Cécile Sonntag, Jean Fontan, Mohamad Mohty, Asiong Jie, Lionel Karlin, Frederique Kuhnowski, Jérôme Lambert, Xavier Leleu, Margaret Macro, Frederique Orsini Piocelle, Murielle Roussel, Jean Marc Schiano De Colella, Niels W.C.J. van de Donk, Soraya Wuillème, Annemiek Broijl, Cyrille Touzeau, Mourad Tiab, Jean Pierre Marolleau, Nathalie Meuleman, Marie-Christiane Vekemans, Matthijs Westerman, Saskia K. Klein, Mark-David Levin, Fritz Offner, Martine Escoffre, Jean-Richard Eveillard, Réda Garidi, Winnie Hua, Jianping Wang, Alba Tuozzo, Carla De Boer, Melissa Rowe, Veronique Vanquickelberghe, Robin Carson, Jessica Vermeulen, Jill Corre, Pieter Sonneveld

Erstbehandlung NDMM, TE

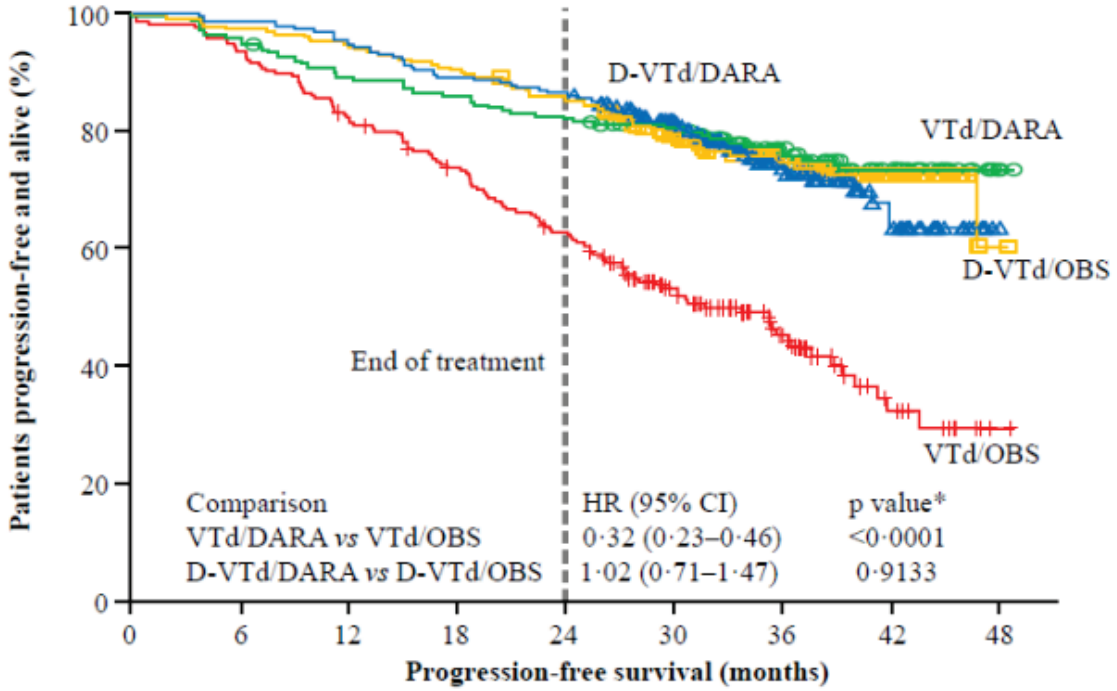
CASSIOPEIA Studie



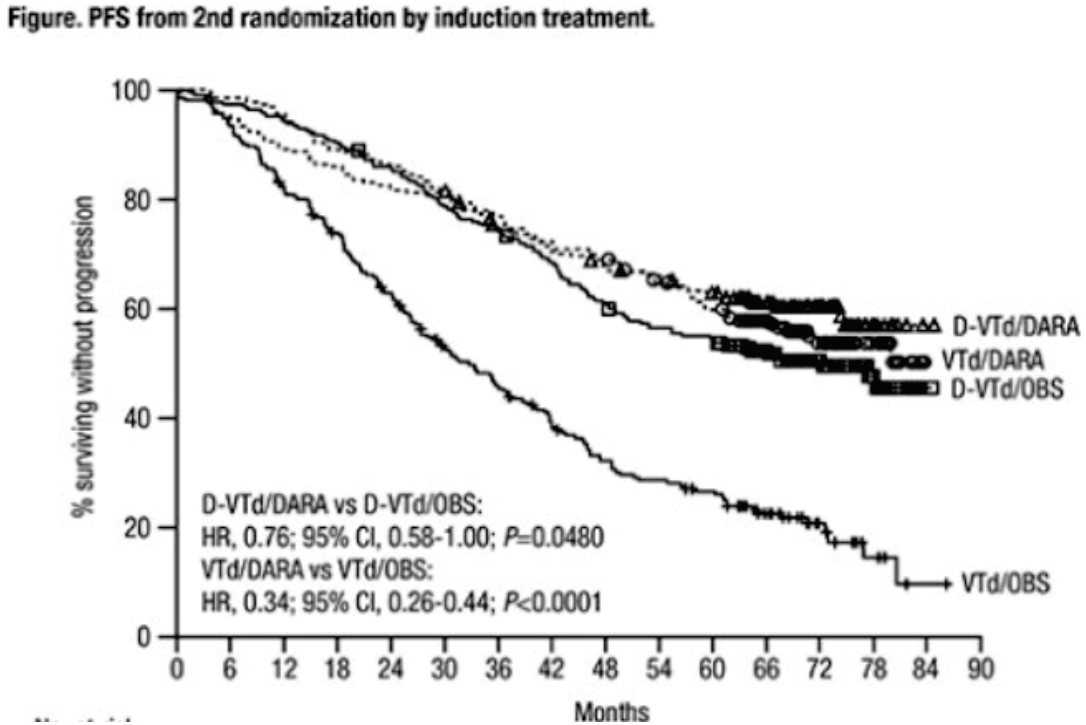
Erstbehandlung NDMM, TE

CASSIOPEIA Studie

Median FU 35.4 months



Median FU 80.1 months



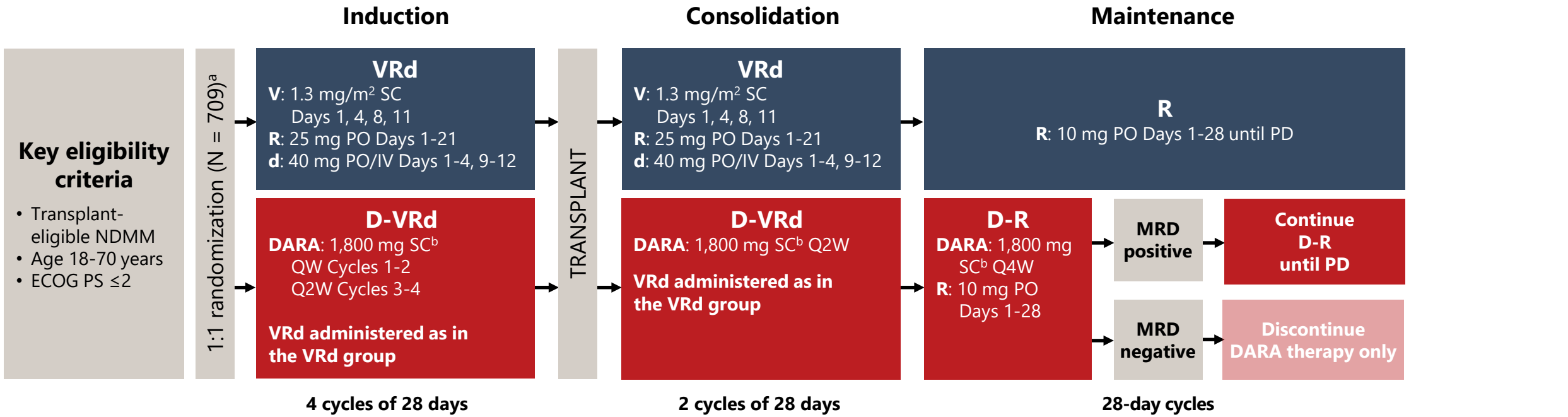
Erstbehandlung NDMM, TE

S201: DARATUMUMAB + BORTEZOMIB/LENALIDOMIDE/DEXAMETHASONE IN TRANSPLANT-ELIGIBLE PATIENTS WITH NEWLY DIAGNOSED MULTIPLE MYELOMA: ANALYSIS OF MINIMAL RESIDUAL DISEASE IN THE PERSEUS TRIAL

Pieter Sonneveld, Philippe Moreau, Meletios A. Dimopoulos, Hang Quach, P. Joy Ho, Meral Beksac, Cyrille Hulin, Elisabetta Antonioli, Xavier Leleu, Silvia Mangiacavalli, Aurore Perrot, Michele Cavo, ANGELO BELOTTI, Annemiek Broijl, Francesca GAY, Roberto Mina, Inger S. Nijhof, Niels W.C.J. van de Donk, Eirini Katodritou, Fredrik Schjesvold, Anna Sureda Balari, Laura Rosiñol, Michel Delforge, Wilfried Roeloffzen, Christoph Driessen, Annette Juul Vangsted, Hermann Einsele, Andrew Spencer, Roman Hájek, Artur Jurczyszyn, Sarah Lonergan, Yanfang Liu, Jianping Wang, Diego Vieyra, Emilie van Brummelen, Veronique Vanquickelberghe, Anna Sitthi-Amorn, Carla De Boer, Robin Carson, Joan Blade, Mario Boccadoro, Paula Rodríguez-Otero

Erstbehandlung NDMM, TE

PERSEUS Studie



Primary endpoint: PFS[c]

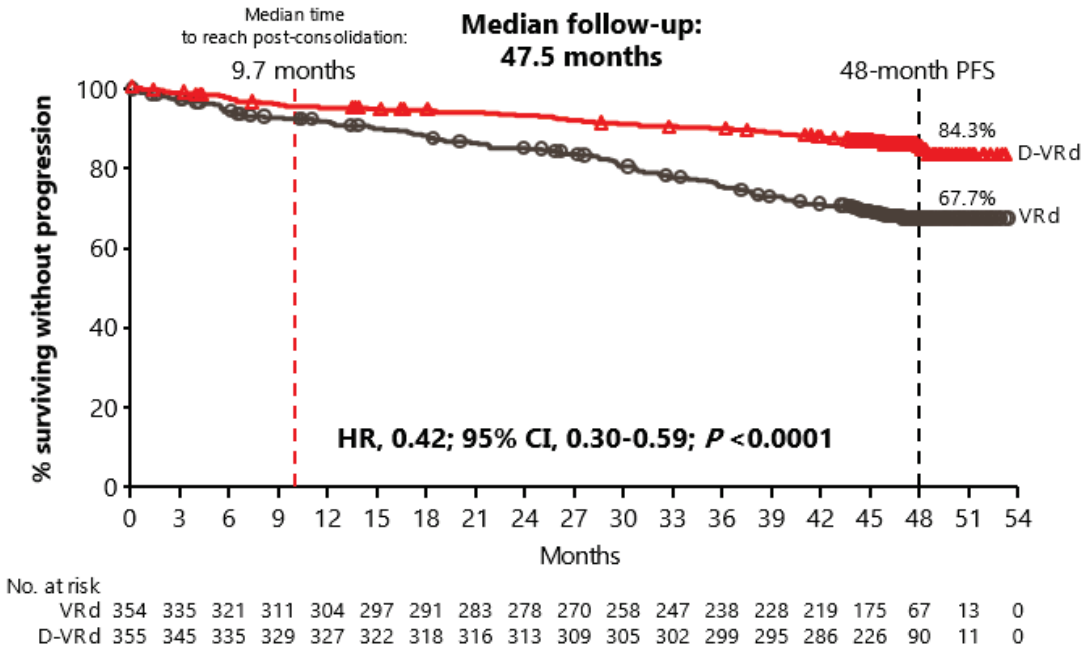
Key secondary endpoints: Overall ≥CR rate,[c] overall MRD-negativity rate,[d] OS

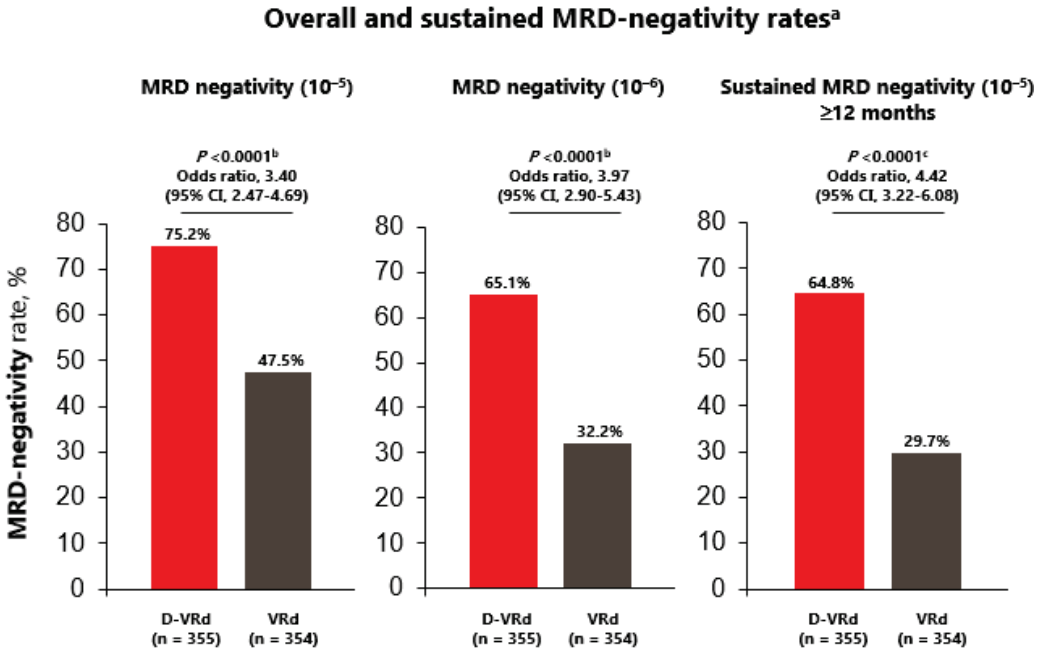
Discontinue DARA therapy only after ≥24 months of D-R maintenance for patients with ≥CR and 12 months of sustained MRD negativity

Restart DARA therapy upon confirmed loss of CR without PD or recurrence of MRD

Erstbehandlung NDMM, TE

PERSEUS Studie





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

Deep and durable MRD negativity achieved with D-VRd

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

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

Erstbehandlung NDMM, TE

PERSEUS Studie

- The potential for a cure in NDMM is predicated on reaching sustained MRD negativity at 10^{-6}

- In the PERSEUS study, for D-VRd + D-R:
  - 47% of patients achieved sustained MRD negativity (10^{-6}) for 12 months versus 19% with VRd + R

- During D-R maintenance:
  - The rate of MRD negativity (10^{-6}) increased by 30% versus 15% with R alone
  - 31% of MRD-positive patients converted to sustained MRD negativity (10^{-6}) versus 10% with R alone
  - 64% of patients stopped DARA after achieving sustained MRD negativity (10^{-5})[1]

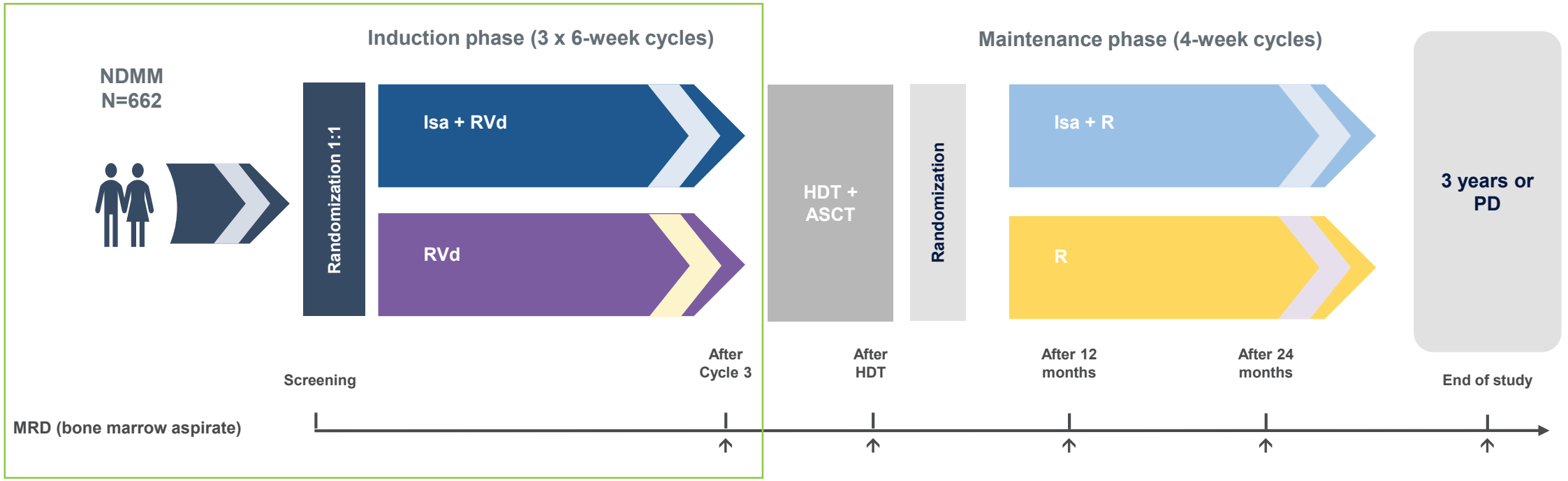
Erstbehandlung NDMM, TE

S202: ISATUXIMAB, LENALIDOMIDE, BORTEZOMIB AND DEXAMETHASONE FOR NEWLY-DIAGNOSED, TRANSPLANT-ELIGIBLE MULTIPLE MYELOMA: POST TRANSPLANTATION INTERIM ANALYSIS OF THE RANDOMIZED PHASE III GMMG-HD7 TRIAL

Marc S. Raab, Elias K Mai, Uta Bertsch, roland fenk, Ema Pozeck, Axel Benner, Britta Besemer, Christine Hanoun, Roland Schroers, Ivana von Metzler, Mathias Hänel, Christoph Mann, Lisa Leypoldt, Bernhard Heilmeier, Sabine Vogel, Stefanie Huhn, Michael Hundemer, Selina Hutzl, Niels Weinhold, Tobias Holderried, Karolin Trautmann-Grill, Deniz Nogueira Gezer, Maika Klaiber, Martin Müller, Evgenii Shumilov, Wolfgang Knauf, Christian Michel, Thomas Geer, Hendrik Riesenberg, Christoph Lutz, Martin Hoffmann, Hans Salwender, Katja Weisel, Hartmut Goldschmidt

Erstbehandlung NDMM, TE

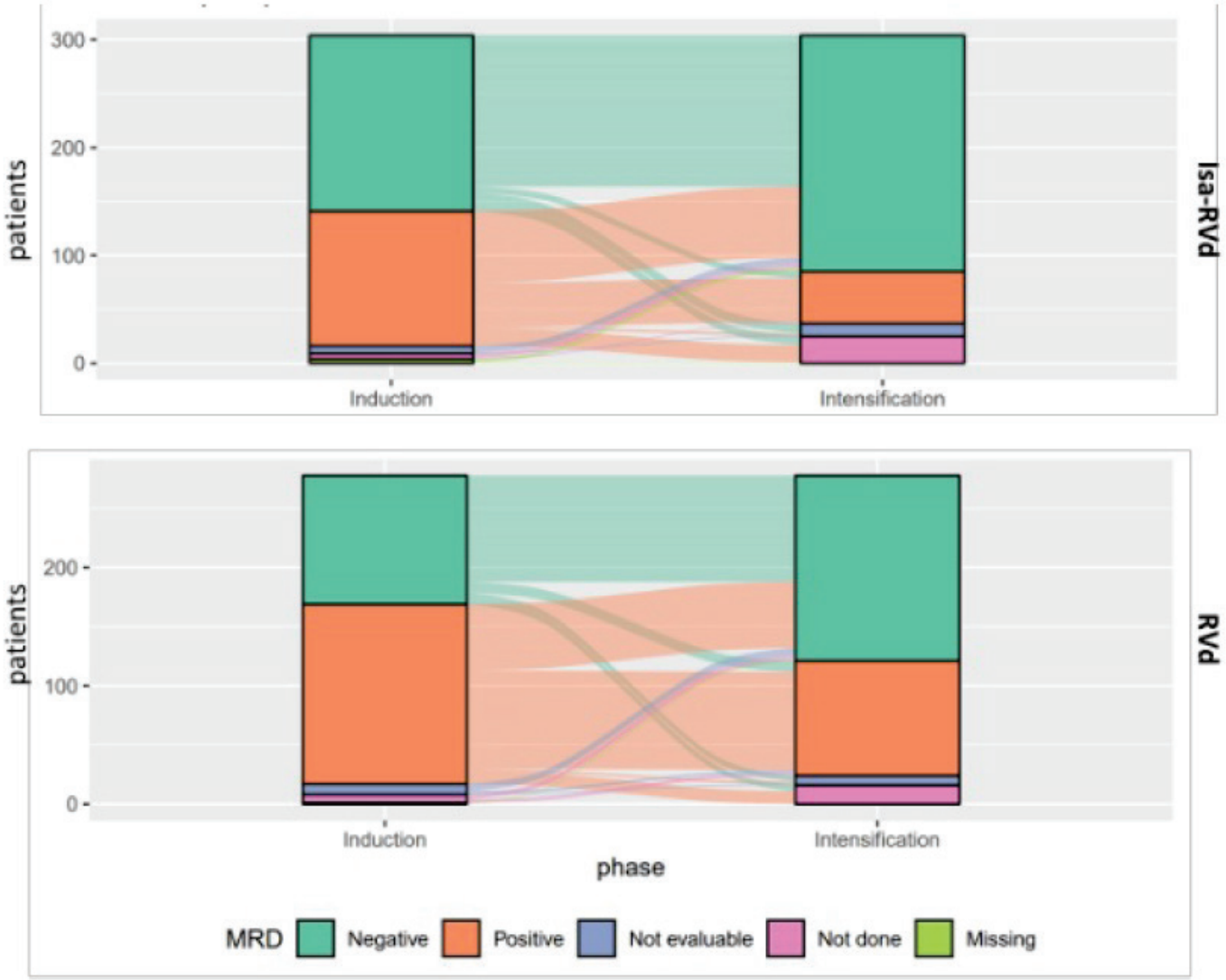
GMMG-HD7 Studie



Erstbehandlung NDMM, TE

GMMG-HD7 Studie

Among pts who per protocol remained on study, the MRD negativity rates at end of intensification were 72.0% after Isa-RVd and 56.5% following RVd



Erstbehandlung NDMM, TE

PERSEUS Studie

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Kapitel 2

Behandlung des neudiagnostizierten Myeloms,
nicht- transplantierbare Patienten

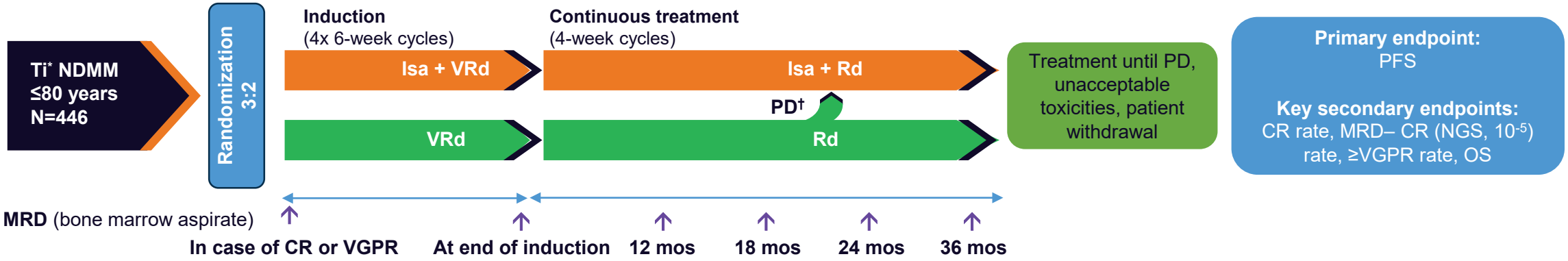
Erstbehandlung NDMM, TNE

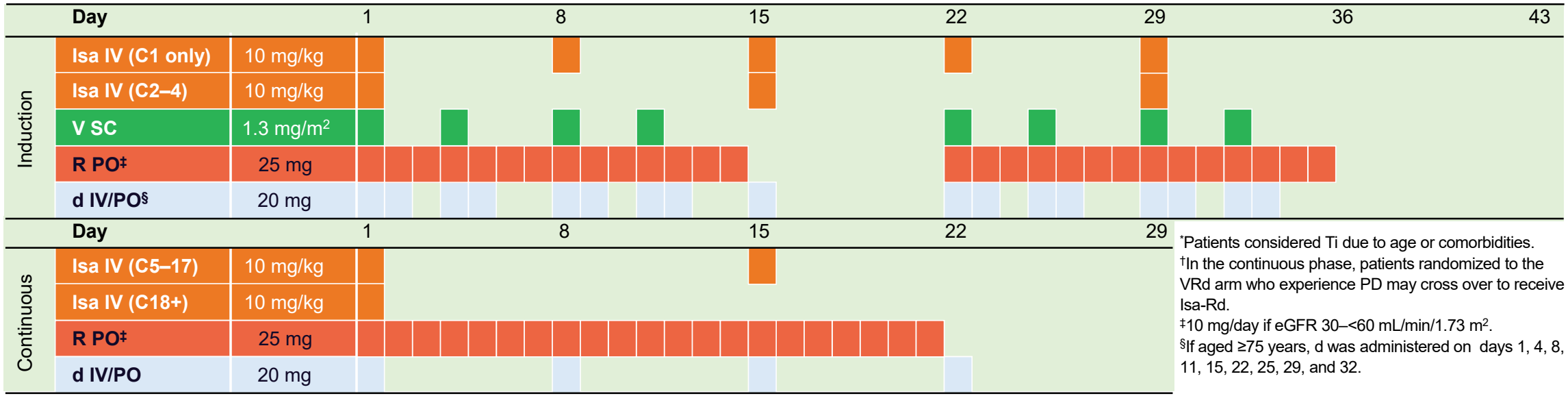
S100: PHASE 3 STUDY RESULTS OF ISATUXIMAB, BORTEZOMIB, LENALIDOMIDE, AND DEXAMETHASONE (ISA-VRD) VERSUS VRD FOR TRANSPLANT-INELIGIBLE PATIENTS WITH NEWLY DIAGNOSED MULTIPLE MYELOMA (IMROZ)

Thierry Facon, Meletios A. Dimopoulos, Xavier Leleu, Meral Beksac, Ludek Pour, Roman Hájek, Zhuogang Liu, Jiri Minarik, Philippe Moreau, Joanna Romejko-Jarosinska, Ivan Špička, Vladimir Vorobyev, Britta Besemer, Tadao Ishida, Wojciech Janowski, Sevgi Kalayoglu-Beşışık, Gurdeep Parmar, Pawel Robak, Michele Cavo, Elena Zamagni, Hartmut Goldschmidt, Thomas Martin, Salomon Manier, Mohamad Mohty, Corina Oprea, Marie-France Brégeault, Sandrine Macé, Rick Zhang, Christelle Berthou, David Bregman, Ercem Kodas, Zandra Klippel, Helgi van de Velde, Robert Z Orlowski

Erstbehandlung, TNE

IMROZ Studie



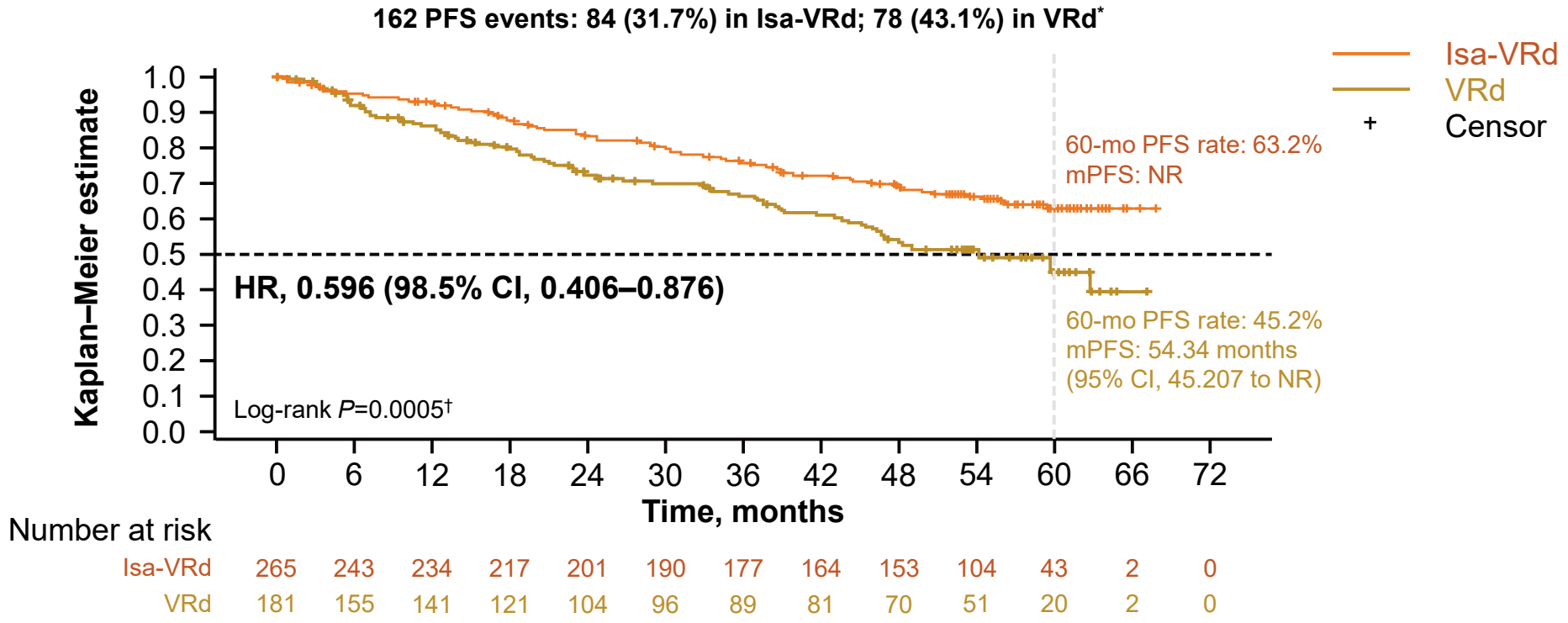


*Patients considered Ti due to age or comorbidities.
†In the continuous phase, patients randomized to the VRd arm who experience PD may cross over to receive Isa-Rd.
‡10 mg/day if eGFR 30–<60 mL/min/1.73 m^2.
§If aged ≥75 years, d was administered on days 1, 4, 8, 11, 15, 22, 25, 29, and 32.

C, cycle; d, dexamethasone; Isa, isatuximab; R, lenalidomide; SC, subcutaneous; V, bortezomib.
Orlowski RZ, et al. ASCO 2018.

Erstbehandlung, TNE

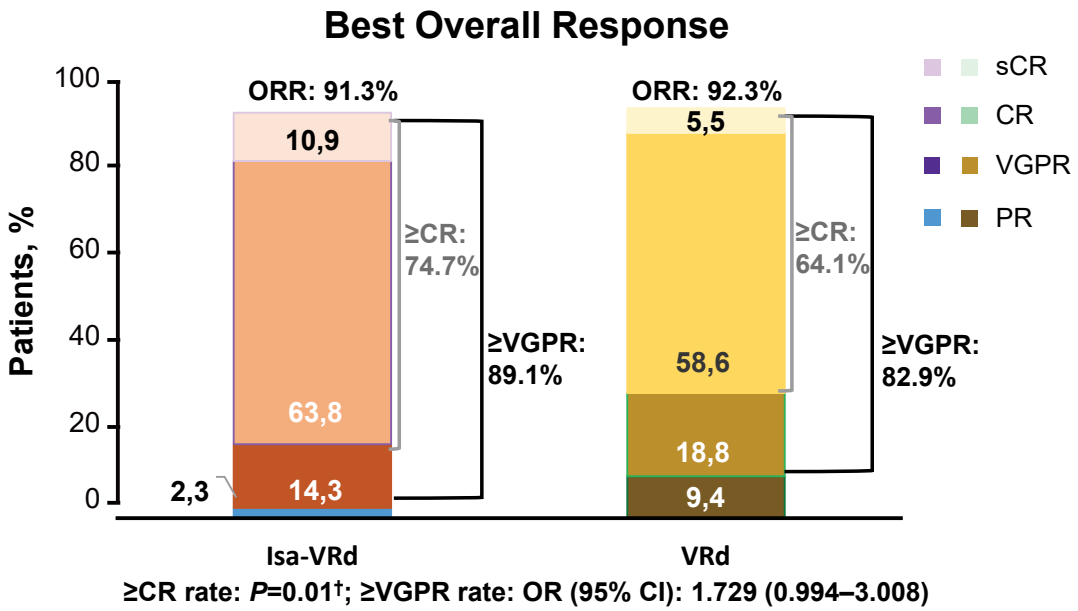
IMROZ Studie

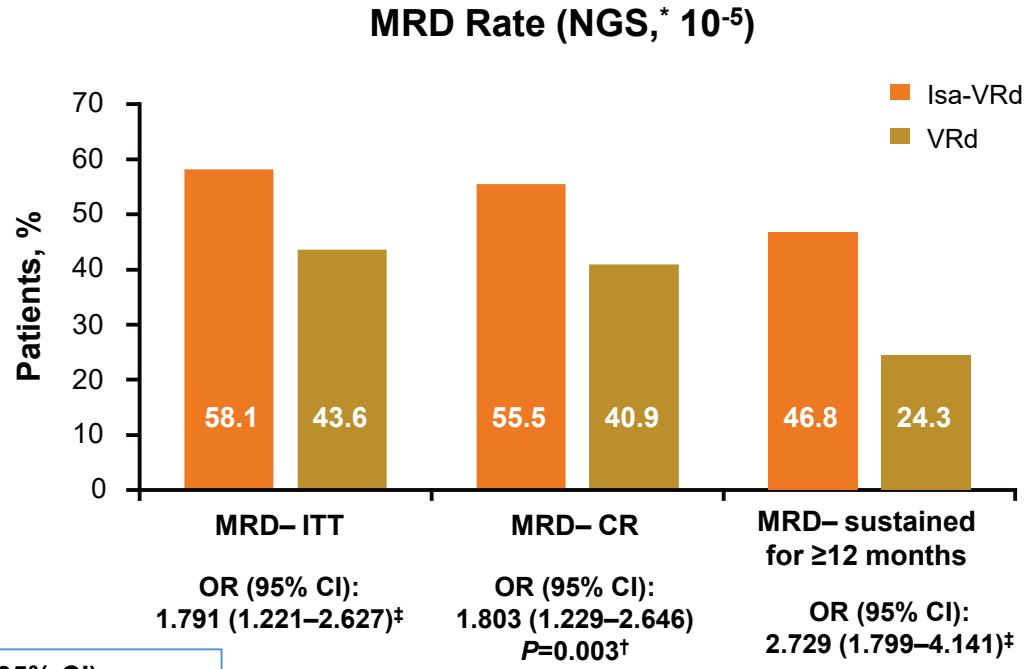


At a median follow-up of 5 years (59.7 months), Isa-VRd followed by Isa-Rd led to a statistically significant reduction in the risk of progression or death by 40.4%

Erstbehandlung, TNE

IMROZ Studie





Time to MRD–, median (95% CI)
Isa-VRd: 14.72 (11.53–24.08) months
VRd: 32.79 (17.51–45.11) months

Isa-VRd followed by Isa-Rd resulted in deep response rates, with a significant improvement in the MRD– CR rate, as well as higher rates of MRD– and sustained MRD– for ≥12 months

Erstbehandlung, TNE

IMROZ Studie

Preferred term, n (%)	Isa-VRd (n=263)		VRd (n=181)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Hematologic laboratory abnormalities				
Neutropenia	230 (87.5)	143 (54.4)	145 (80.1)	67 (37.0)
Nonhematologic adverse events				
Infections	240 (91.3)	118 (44.9)	157 (86.7)	69 (38.1)
Pneumonia	79 (30.0)	53 (20.2)	35 (19.3)	23 (12.7)
Upper respiratory tract infection	90 (34.2)	2 (0.8)	61 (33.7)	2 (1.1)
Diarrhea	144 (54.8)	20 (7.6)	88 (48.6)	15 (8.3)
Peripheral sensory neuropathy	143 (54.4)	19 (7.2)	110 (60.8)	11 (6.1)
Cataract	100 (38.0)	41 (15.6)	46 (25.4)	20 (11.0)
Invasive second primary malignancies				
Solid tumors	22 (8.4)	14 (5.3)	8 (4.4)	6 (3.3)
Hematologic	3 (1.1)	1 (0.4)	2 (1.1)	2 (1.1)

Isa-VRd was well tolerated, and the safety profile remains consistent with the known safety profiles of each agent

Erstbehandlung, TNE

IMROZ Studie

- IMROZ is the first global Phase 3 study of an anti-CD38 mAb in combination with VRd in patients with transplant-ineligible NDMM
- Isa-VRd followed by Isa-Rd led to a statistically significant reduction in the risk of progression or death by 40.4%
- Although OS is still immature, a trend in favor of Isa-VRd was also observed
- Isa-VRd was well tolerated, and the safety profile remains consistent with that of each agent
- **Isa-VRd should be the new SOC in TNE patients with NDMM**

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Isatuximab, Bortezomib, Lenalidomide, and Dexamethasone for Multiple Myeloma

T. Facon, M.-A. Dimopoulos, X.P. Leleu, M. Beksac, L. Pour, R. Hájek, Z. Liu, J. Minarik, P. Moreau, J. Romejko-Jarosinska, I. Spicka, V.I. Vorobyev, B. Besemer, T. Ishida, W. Janowski, S. Kalayoglu-Besisik, G. Parmar, P. Robak, E. Zamagni, H. Goldschmidt, T.G. Martin, S. Manier, M. Mohty, C. Oprea, M.-F. Brégeault, S. Macé, C. Berthou, D. Bregman, Z. Klippel, and R.Z. Orlowski, for the IMROZ Study Group*

Kapitel 3

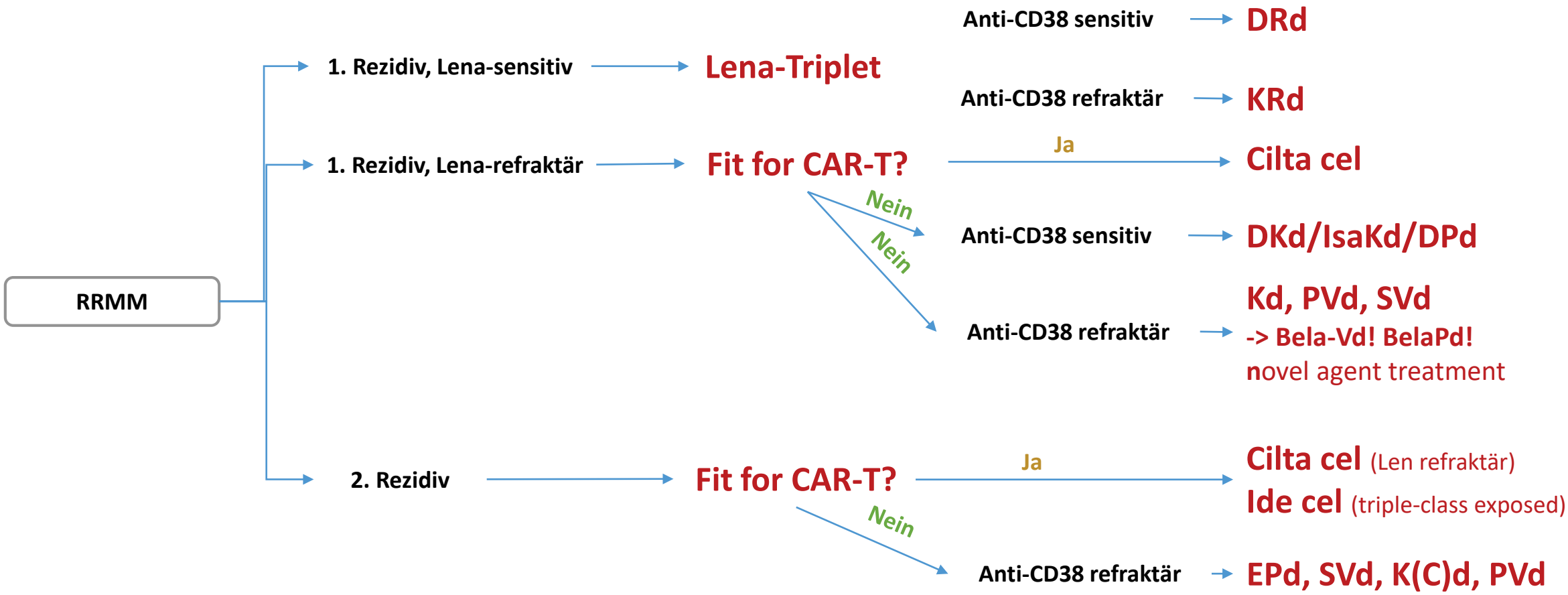
Belantamab mafodotin Kombinationen im Rezidiv

Belantamab mafodotin Kombinationen im Rezidiv

S214: RESULTS FROM DREAMM-7 A RANDOMIZED PHASE 3 STUDY OF BELANTAMAB MAFODOTIN + BORTEZOMIB, AND DEXAMETHASONE VS DARATUMUMAB + BORTEZOMIB, AND DEXAMETHASONE IN RELAPSED/REFRACTORY MULTIPLE MYELOMA

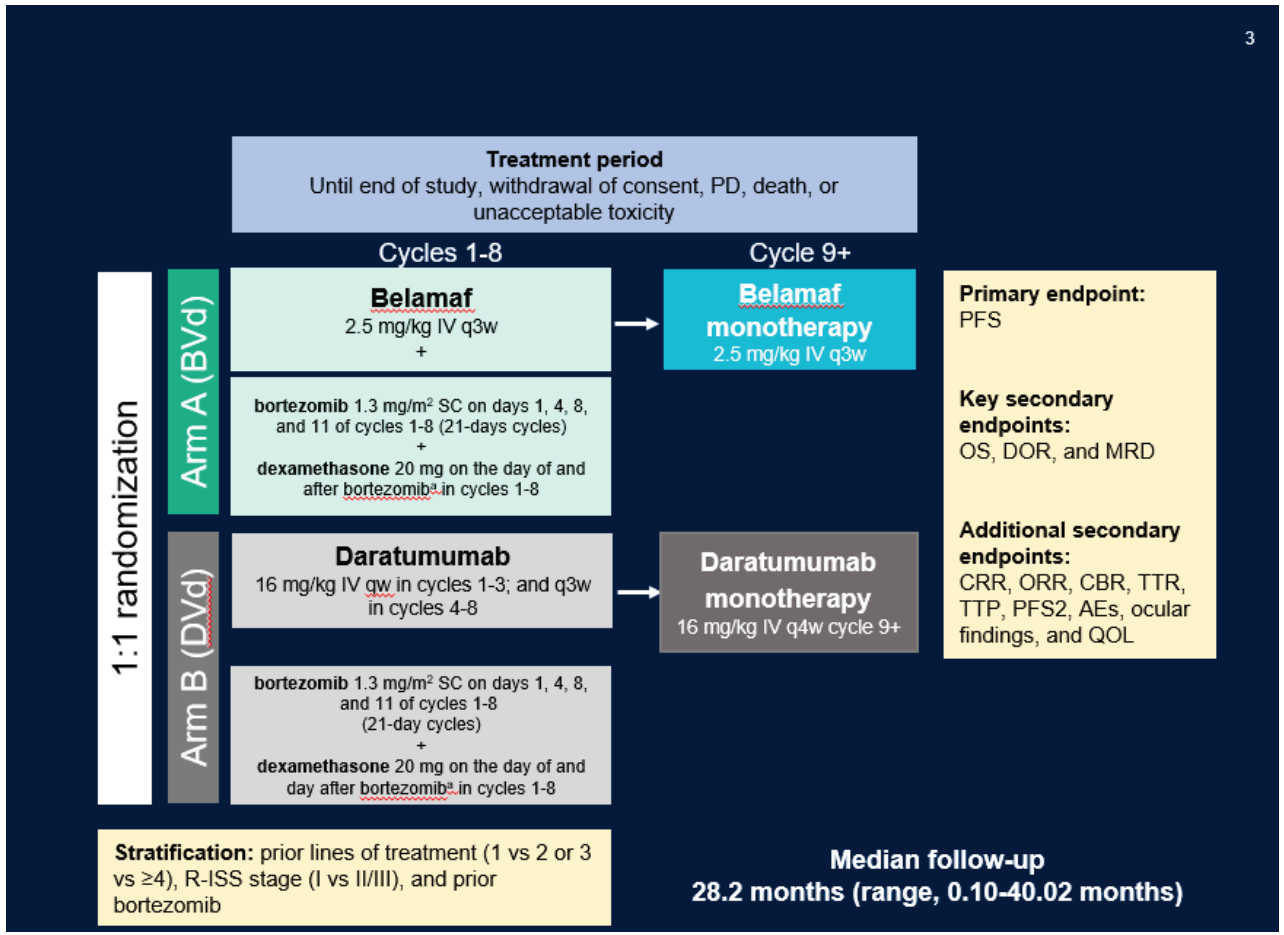
Maria-Victoria Mateos, Pawel Robak, Marek Hus, Zhong-jun Xia, Vera Zherebtsova, Christopher Ward, P. Joy Ho, Ana Carolina Almeida, Roman Hájek, Kihyun Kim, Meletios A. Dimopoulos, Claudio Cerchione, Antonio Riccio, Astrid McKeown, Rachel Rogers, Hena Baig, Lydia Eccersley, Sumita Roy-Ghanta, Joanna Opalinska, Vania Hungria

Therapie des rezidivierten Multiplen Myeloms



Belantamab mafodotin Kombinationen im Rezidiv

DREAMM-7 Studie



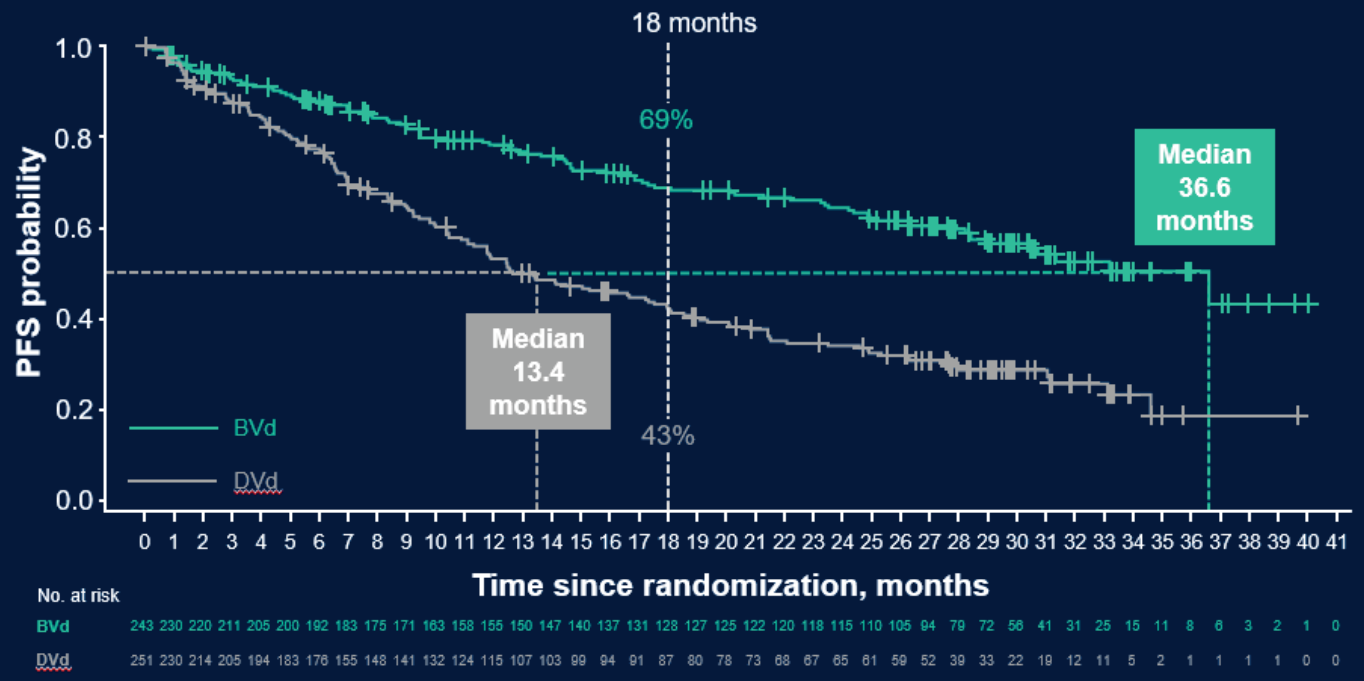
Baseline characteristics	ITT population	
	BVd (N=243)	DVd (N=251)
Age, median (range), years	65.0 (34-86)	64.0 (32-89)
Male, n (%)	128 (53)	144 (57)
ECOG PS ≤1, n/N (%)	232/242 (96)	235/246 (96)
R-ISS stage at screening, n (%)[a] I II III	 102 (42) 130 (53) 9 (4)	 103 (41) 132 (53) 14 (6)
Cytogenetic abnormalities, n (%) High risk[b] Standard risk[c]	 67 (28) 175 (72)	 69 (27) 175 (70)
Prior lines of therapy, n (%) 1 2 or 3 4+	 125 (51) 88 (36) 30 (12)	 125 (50) 99 (39) 27 (11)
Prior proteasome inhibitor, n (%) Prior bortezomib	218 (90) 210 (86)	216 (86) 211 (84)
Prior immunomodulatory drugs, n (%) **Prior lenalidomide** **Refractory to lenalidomide**	**198 (81)** **127 (52)** **79 (33)**	**216 (86)** **130 (52)** **87 (35)**
Prior daratumumab, n (%)	3 (1)	4 (2)

Belantamab mafodotin Kombinationen im Rezidiv

DREAMM-7 Studie

5

DREAMM-7: BVd led to a significant increase in PFS vs DVd



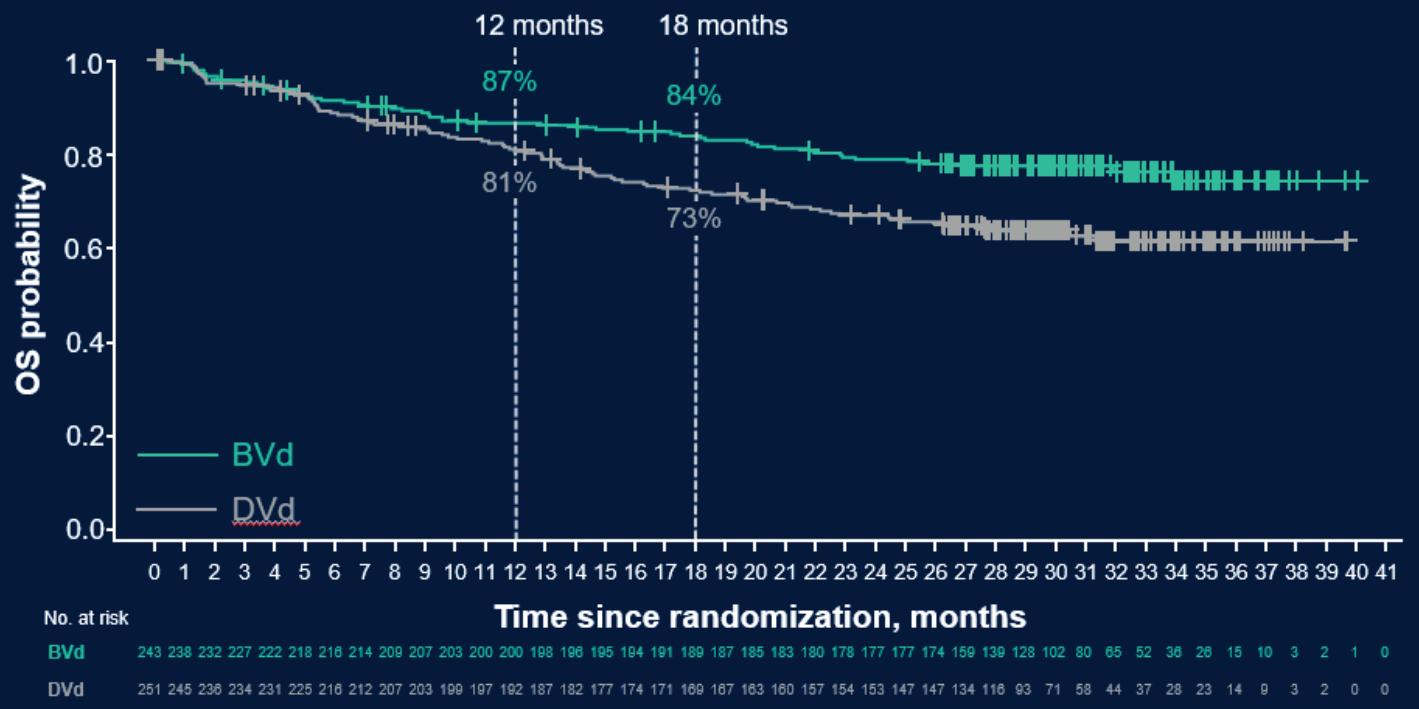
PFS[a]	BVd (N=243)	DVd (N=251)
Events, n (%)	91 (37)	158 (63)
PFS, median (95% CI), months[b]	36.6 (28.4-NR)	13.4 (11.1-17.5)
HR (95% CI)[c]	0.41 (0.31-0.53)	
P value[d]	<.00001	

BVd demonstrated a statistically significant and clinically meaningful PFS benefit, with a median PFS that was 23 months longer than that with DVd

Belantamab mafodotin Kombinationen im Rezidiv

DREAMM-7 Studie

DREAMM-7: early OS trend favoring BVd vs DVd



OS[a]	BVd (N=243)	DVd (N=251)
Events, n (%)	54 (22)	87 (35)
OS, median (95% CI), months[b]	NR	NR
HR (95% CI)[c]	0.57 (0.40-0.80)	
P value[d]	.00049[e]	

OS showed an early, strong, and clinically meaningful trend favoring the BVd arm; additional OS follow-up is ongoing

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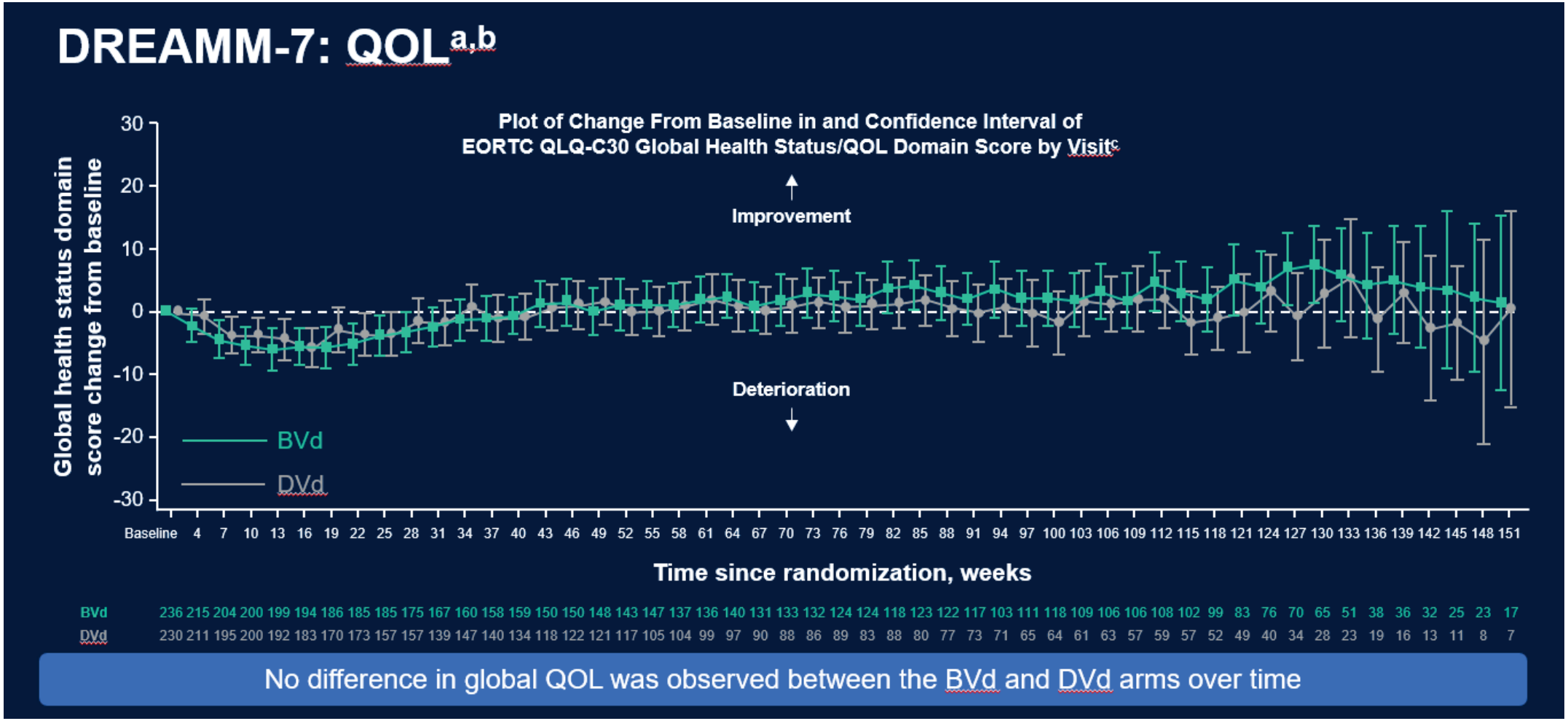
DREAMM-7 Studie



Belantamab mafodotin Kombinationen im Rezidiv

DREAMM-7 Studie

- The DREAMM-7 trial showed a **statistically significant and clinically meaningful PFS benefit** with BVd vs DVd in patients with RRMM at first relapse or later
- A strong and clinically **meaningful OS benefit** favored the BVd arm vs the DVd arm
- BVd was associated with deeper responses and led to doubling of CR rates and MRD negativity rates compared with DVd
- **Ocular adverse events, were generally reversible, manageable with dose modification** without compromising efficacy, and led to low treatment discontinuation rates
- **These results support the potential for BVd to become a therapeutic option for patients with myeloma at or after the first relapse**

See the manuscript now in *New England Journal of Medicine*

The NEW ENGLAND JOURNAL of MEDICINE

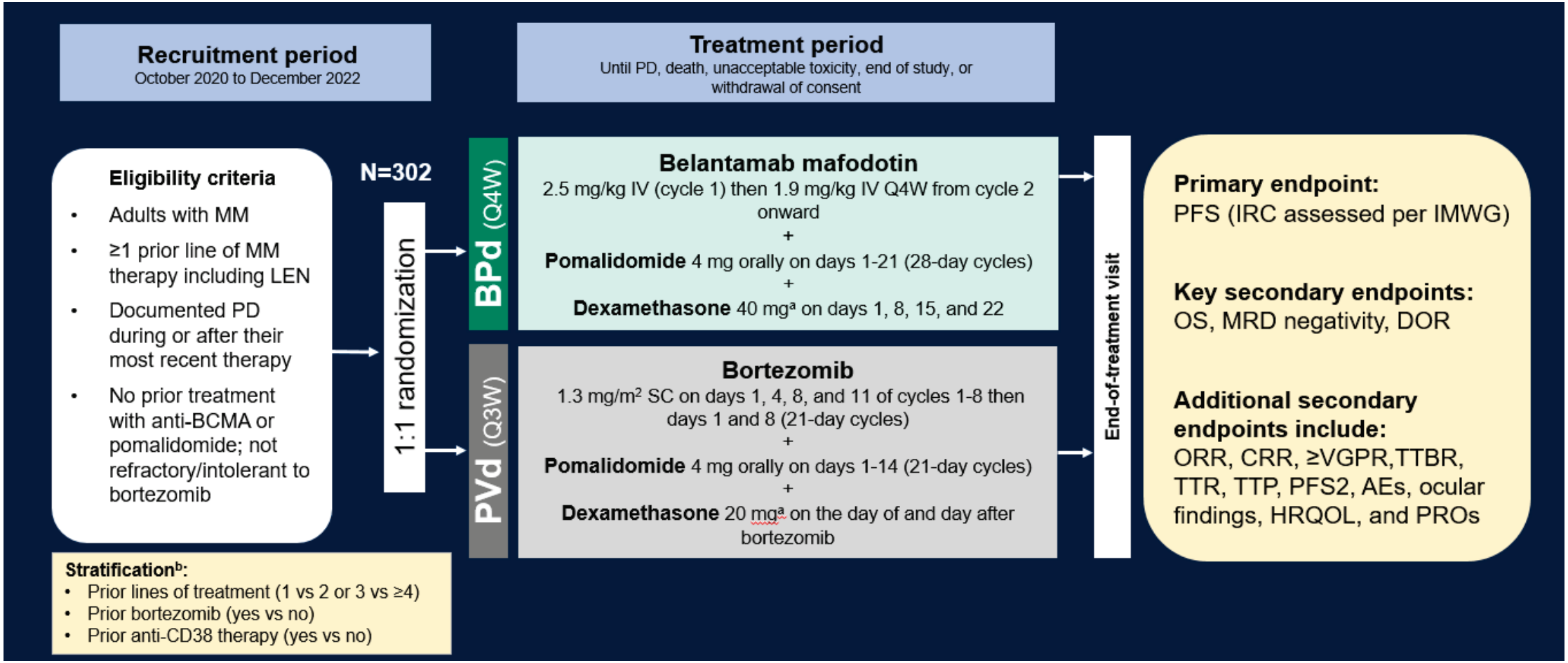
ORIGINAL ARTICLE

Belantamab Mafodotin, Bortezomib, and Dexamethasone for Multiple Myeloma

V. Hungria, P. Robak, M. Hus, V. Zherebtsova, C. Ward, P.J. Ho, A.C. Ribas de Almeida, R. Hajek, K. Kim, S. Grosicki, H. Sia, A. Bryant, M. Pitombeira de Lacerda, G. Aparecida Martinez, A.M. Sureda Balarí, I. Sandhu, C. Cerchione, P. Ganly, M. Dimopoulos, C. Fu, M. Garg, A.-O. Abdallah, A. Oriol, M.E. Gatt, M. Cavo, R. Rifkin, T. Fujisaki, M. Mielnik, N. Pirooz, A. McKeown, S. McNamara, X. Zhou, M. Nichols, E. Lewis, R. Rogers, H. Baig, L. Eccersley, S. Roy-Ghanta, J. Opalinska, and M.-V. Mateos, for the DREAMM-7 Investigators*

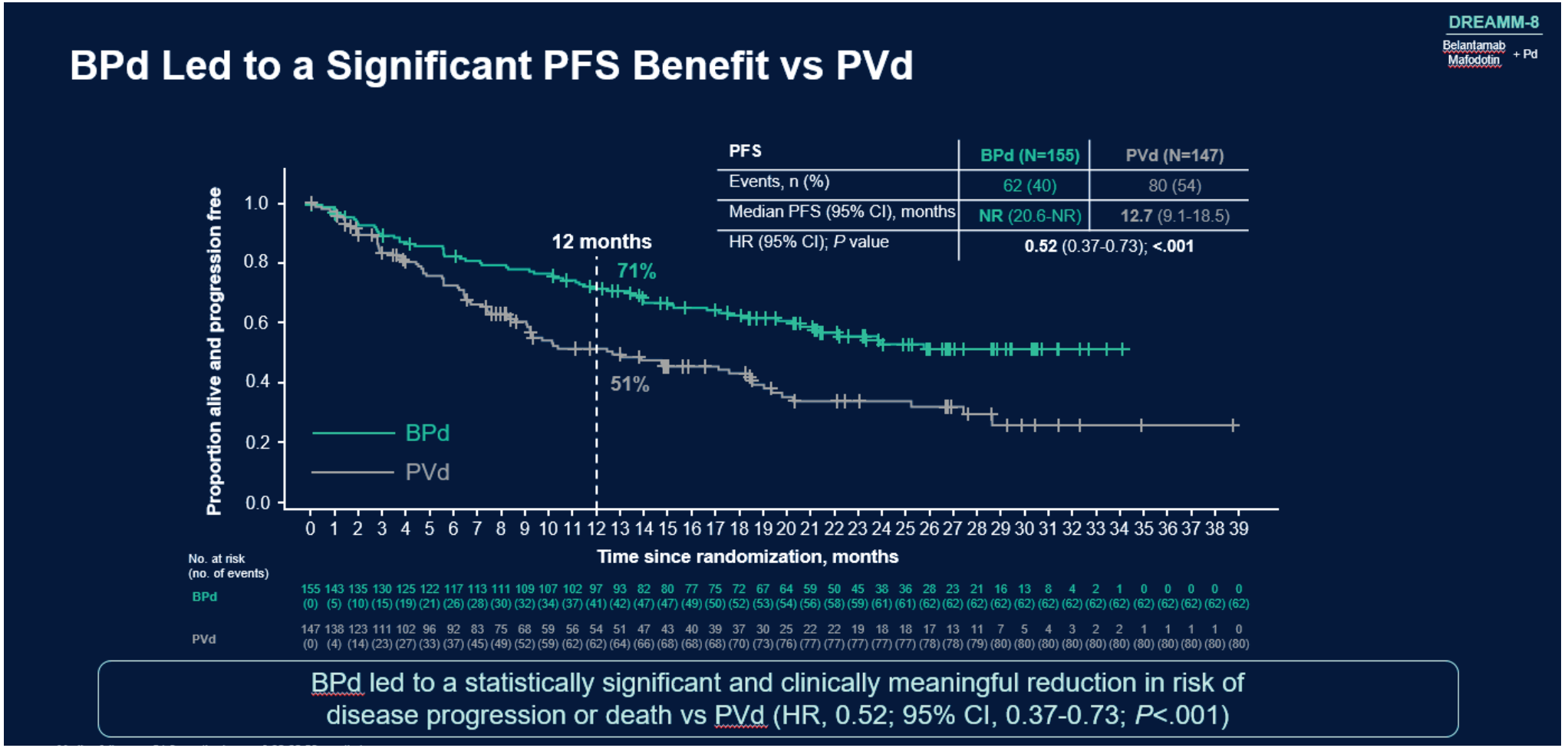
Belantamab mafodotin Kombinationen im Rezidiv

DREAMM-8 Studie



Belantamab mafodotin Kombinationen im Rezidiv

DREAMM-8 Studie



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Belantamab Mafodotin, Pomalidomide, and Dexamethasone in Multiple Myeloma

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- Implementierung von antiCD38 Antikörpern in Induktion, Konsolidierung und Erhaltung ermöglichen hohe Raten an (anhaltenden) MRD-negativen Remissionen
- Dara-VRd Induktion/Konsolidierung und (Dara)-R Erhaltung im Kontext der HD-MEL Therapie werden als zukünftiger europäischer Standard erwartet
- Isa-VRd ist neuer Standard für alle nicht-transplantationsgeeigneten Patienten (bis 80 Jahre)
- Belantamab mafodotin Triplet Kombinationen sind sehr effektiv ab dem 1. Rezidiv mit positiven Überlebensdaten und werden insbesonder für die Post-DRd Patienten ein wichtiger künftiger Behandlungsstandard sein

Die Kurzpräsentationen sind online unter

www.lymphome.de/eha2024

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