Beyond the Congress
Induction Therapy

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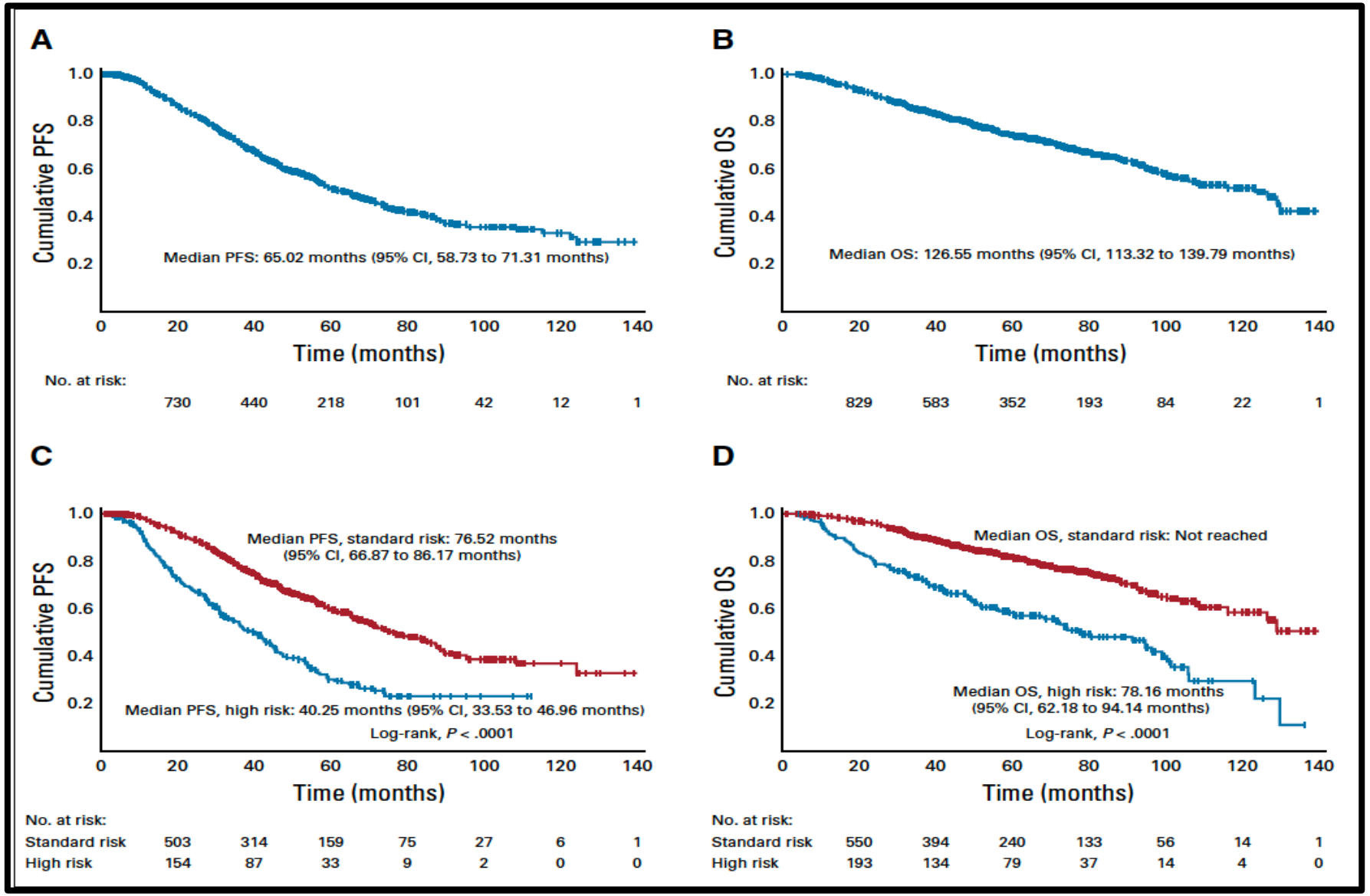
Emory University School of Medicine

Outcomes from RVD 1000 series



Joseph et al, JCO 2020

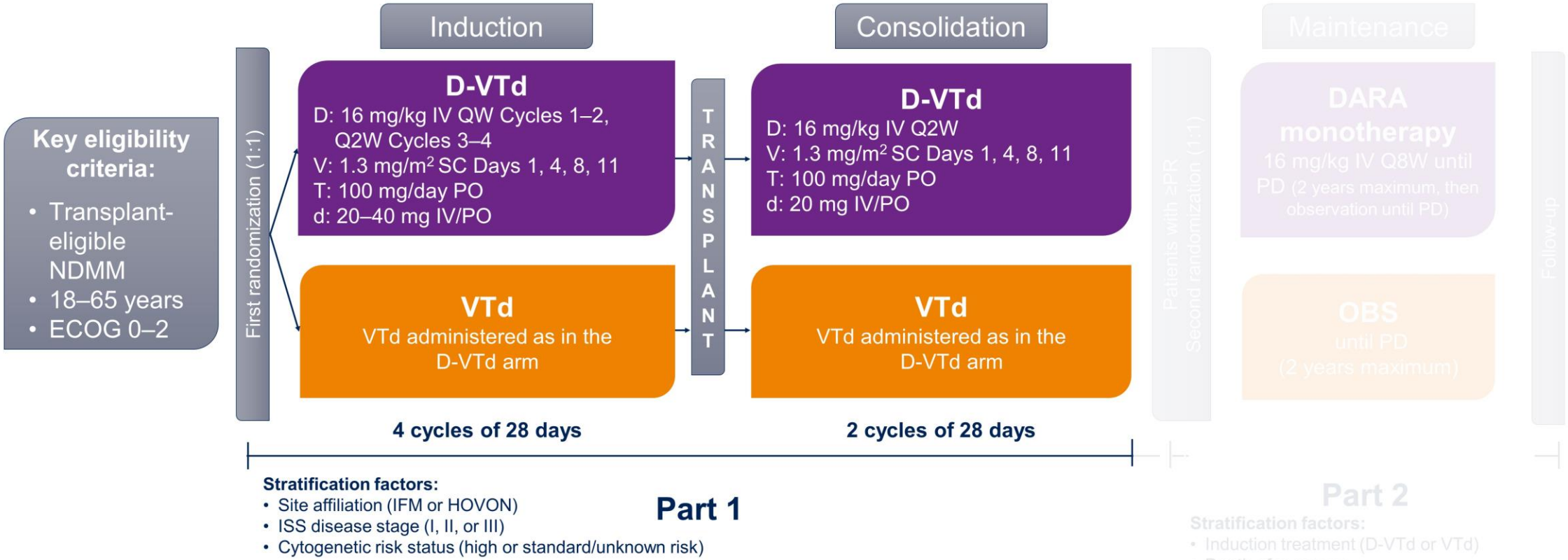
Induction Principles

- Goals are to induce a rapid and deep response
- Do above without significant toxicity

- Current standard of care is IMID+PI+Dex
- Rapidly expanding towards IMID+PI+ Dex+ CD38 Moab

CASSIOPEIA Part 1 Study Design

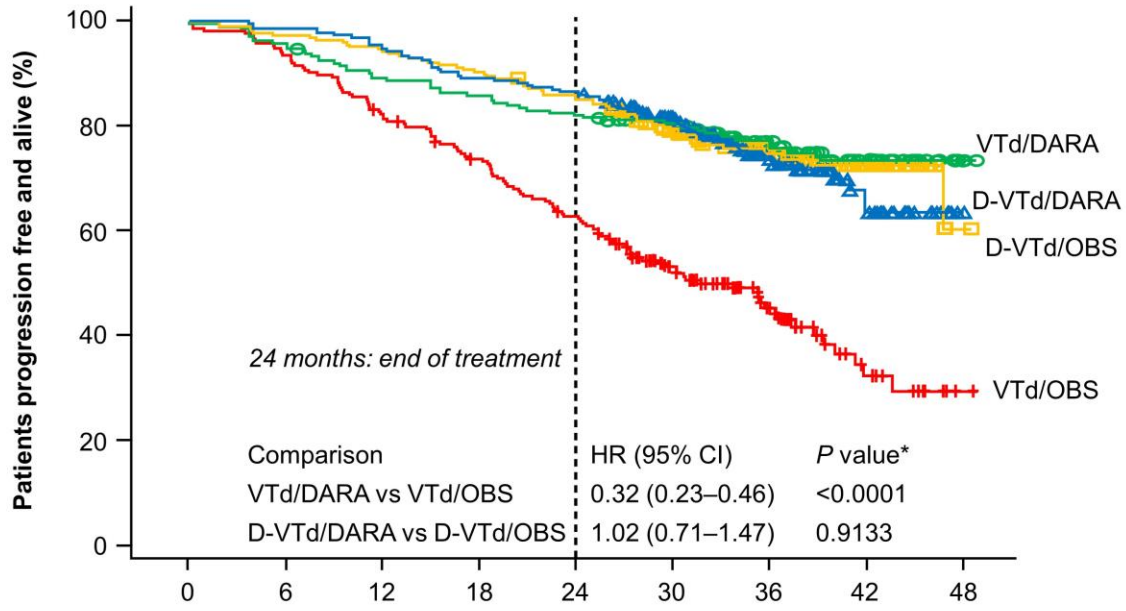
- Part 1 compared D-VTd vs VTd as induction/consolidation



D-VTd, daratumumab, bortezomib, thalidomide, and dexamethasone; ECOG, Eastern Cooperative Oncology Group; IFM, Intergroupe Francophone du Myélome; ISS, International Staging System; HOVON, the Dutch-Belgian Cooperative Trial Group for Hematology-Oncology; IV, intravenous; NDMM, newly diagnosed multiple myeloma; PO, oral; Q2W, every 2 weeks; QW, every week; SC, subcutaneous; VTd, bortezomib, thalidomide, and dexamethasone.

DARA Significantly Improved PFS vs OBS in Patients Treated With VTd Induction/Consolidation

- A prespecified analysis showed significant interaction between maintenance and induction/consolidation therapy
- A PFS benefit was observed for VTd/DARA vs VTd/OBS
- PFS was not different for D-VTd/DARA vs D-VTd/OBS



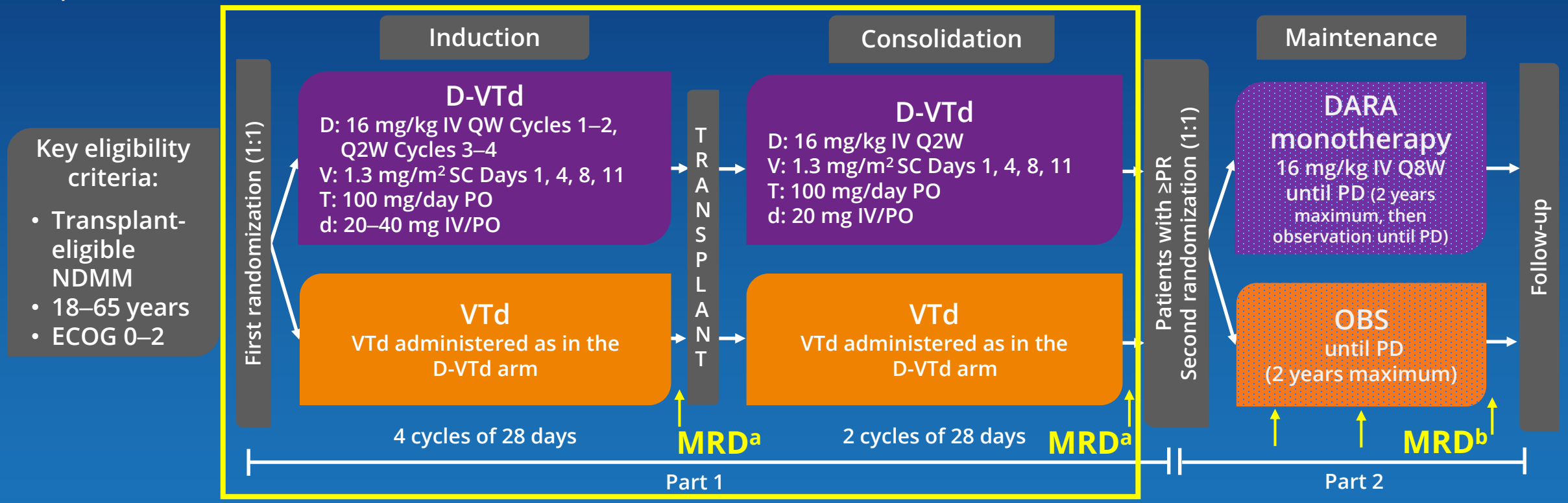
Patients at risk

VTd/OBS	215	201	176	155	131	83	43	15	1
VTd/DARA	213	203	189	182	174	138	79	34	1
D-VTd/OBS	229	223	216	207	195	144	75	38	2
D-VTd/DARA	229	226	217	204	198	145	76	30	0

*Nominal *P* value.
CI, confidence interval; D-VTd, daratumumab, bortezomib, thalidomide, and dexamethasone; DARA, daratumumab; HR, hazard ratio; OBS, observation; PFS, progression-free survival; VTd, bortezomib, thalidomide, and dexamethasone.

CASSIOPEIA: Induction/Consolidation

– Analyses in Part 1 were conducted in the ITT population (N=1085), which included all first-randomization patients

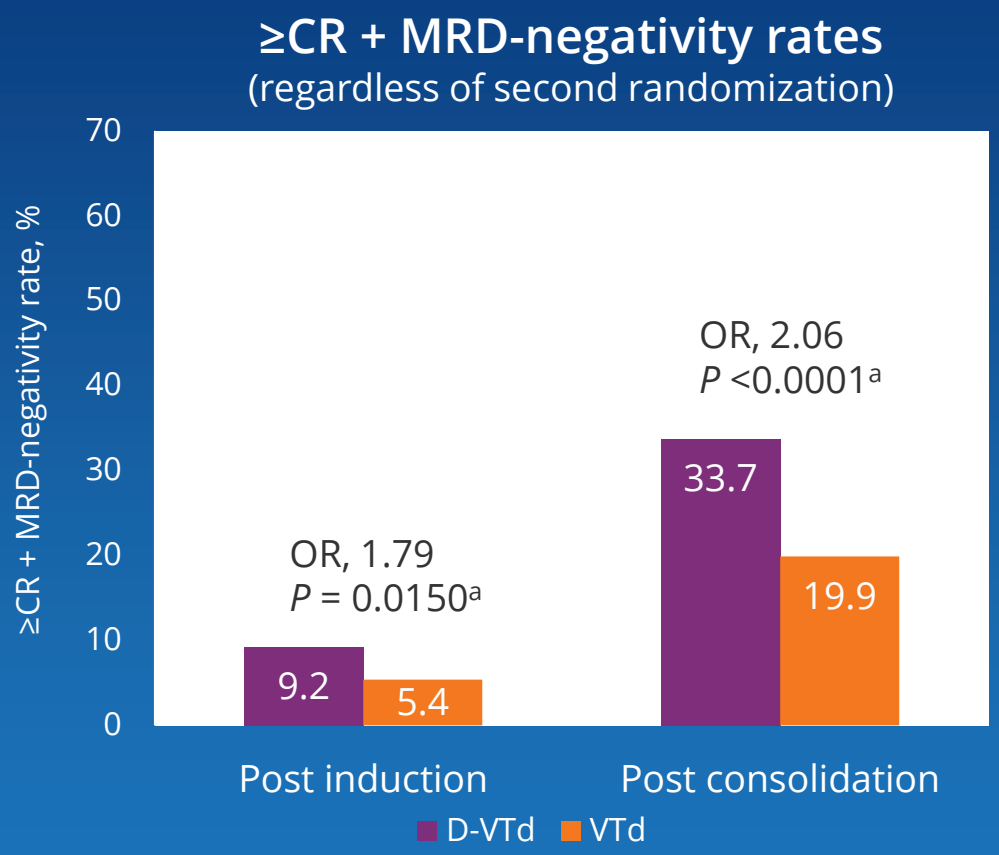


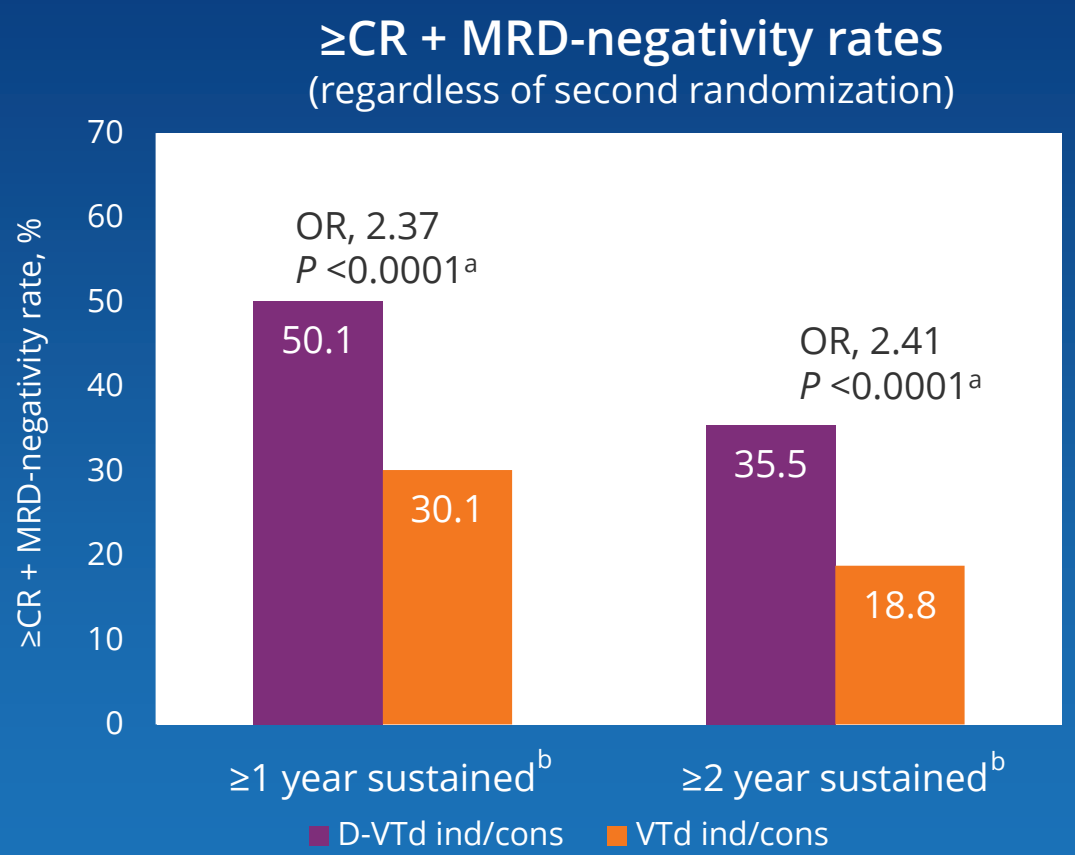
Stratification factors:
- Site affiliation (IFM or HOVON)
- ISS disease stage (I, II, or III)
- Cytogenetic risk status (high or standard/unknown risk)

Stratification factors:
- Induction treatment (D-VTd or VTd)
- Depth of response

≥PR, partial response or better; IV, intravenous; Q8W, every 8 weeks; OBS, observation; ECOG, Eastern Cooperative Oncology Group; QW, every week; Q2W, every 2 weeks; SC, subcutaneous; PO, oral; IFM, Intergroupe Francophone du Myélome; HOVON, the Dutch-Belgian Cooperative Trial Group for Hematology-Oncology; ISS, International Staging System; PD, progressive disease; ≥VGPR, very good partial response or better.
[a]MRD analyses were performed at predefined timepoints for all patients, regardless of response. [b]MRD analyses were performed in patients with ≥VGPR at Weeks 25, 52, and 105.

CASSIOPEIA: D-VTd Improved Rates of ≥CR + MRD Negativity (MFC; 10^{-5}) Versus VTd Following Induction and Consolidation





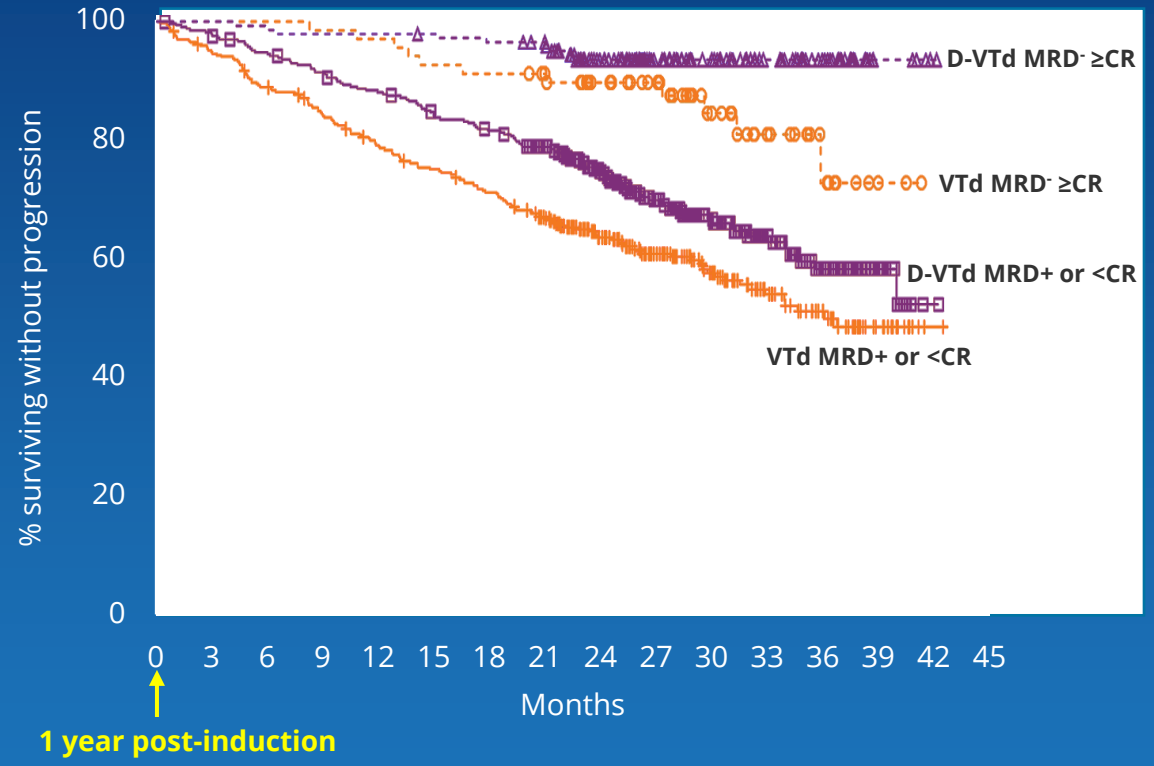
- Post-consolidation MRD-negativity rates among patients who achieved ≥CR were consistent across subgroups, including ISS disease stage and high-risk cytogenetics

MFC, multiparametric flow cytometry.

[a]Cochran-Mantel-Haenszel estimate of the common odds ratio for stratified tables was used. The stratification factors were study site affiliation, ISS disease stage, and cytogenetics. *P* value was calculated based on a stratified Cochran-Mantel-Haenszel chi-squared test.

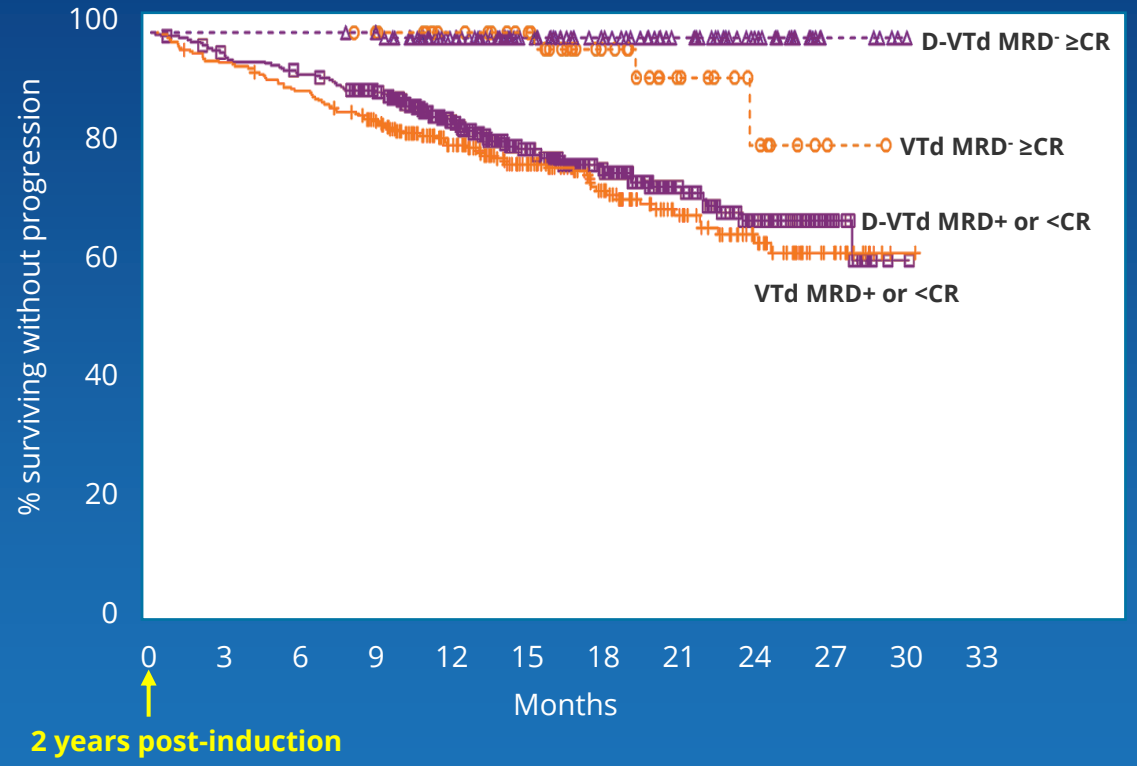
CASSIOPEIA: Landmark PFS Analysis From Post-induction ≥CR + MRD-negativity (MFC; 10^{-5}) Status By Treatment Group

1-year sustained MRD negativity
(regardless of second randomization)



No. at risk																
VTd MRD⁻ ≥CR	380	359	336	315	294	279	264	239	185	137	99	64	43	19	1	0
VTd MRD⁻ ≥CR	70	70	70	69	68	65	64	60	53	45	27	18	9	2	0	0
DVTd MRD⁺ or <CR	337	329	316	305	293	277	269	251	194	148	101	68	42	15	1	0
DVTd MRD⁺ or <CR	147	147	145	144	144	143	141	135	107	79	60	42	26	5	1	0

2-year sustained MRD negativity
(regardless of second randomization)

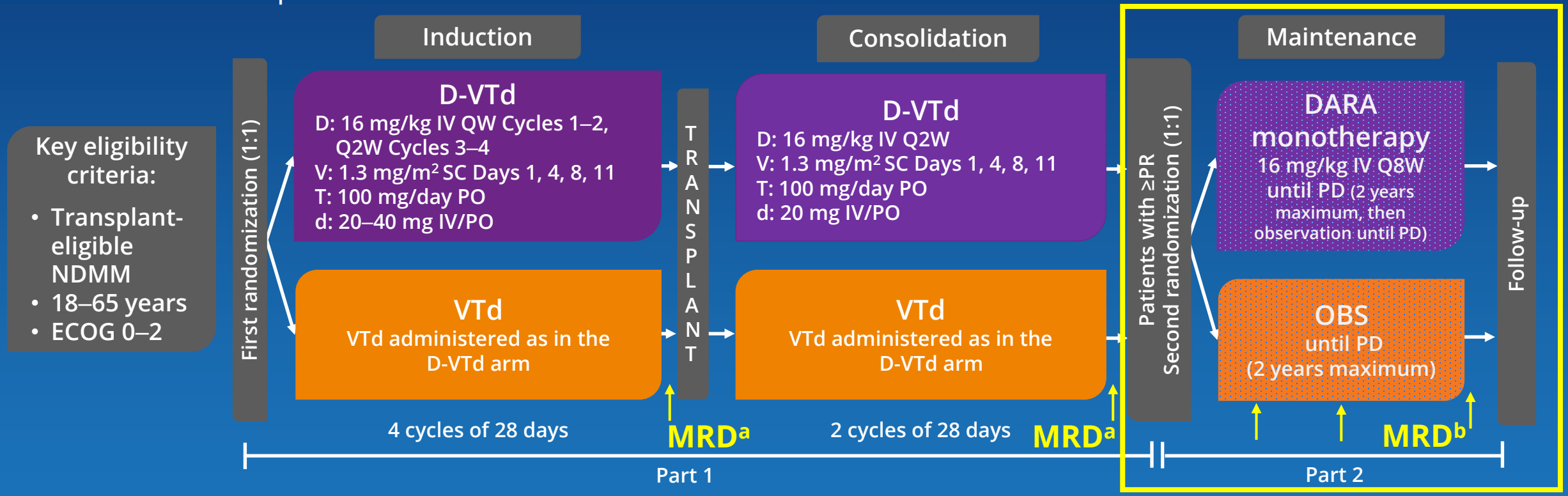


No. at risk												
VTd MRD⁻ ≥CR	311	294	278	252	196	145	104	68	45	20	1	0
VTd MRD⁻ ≥CR	50	50	50	48	42	37	23	14	7	1	0	0
DVTd MRD⁺ or <CR	326	309	299	280	211	159	112	72	46	15	0	0
DVTd MRD⁺ or <CR	111	111	111	108	90	68	51	38	22	5	1	0

MFC, multiparametric flow cytometry.

CASSIOPEIA: Maintenance

– Analyses in Part 2 were conducted in the maintenance ITT population (N=886), which included all re-randomized patients



Stratification factors:
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- ISS disease stage (I, II, or III)
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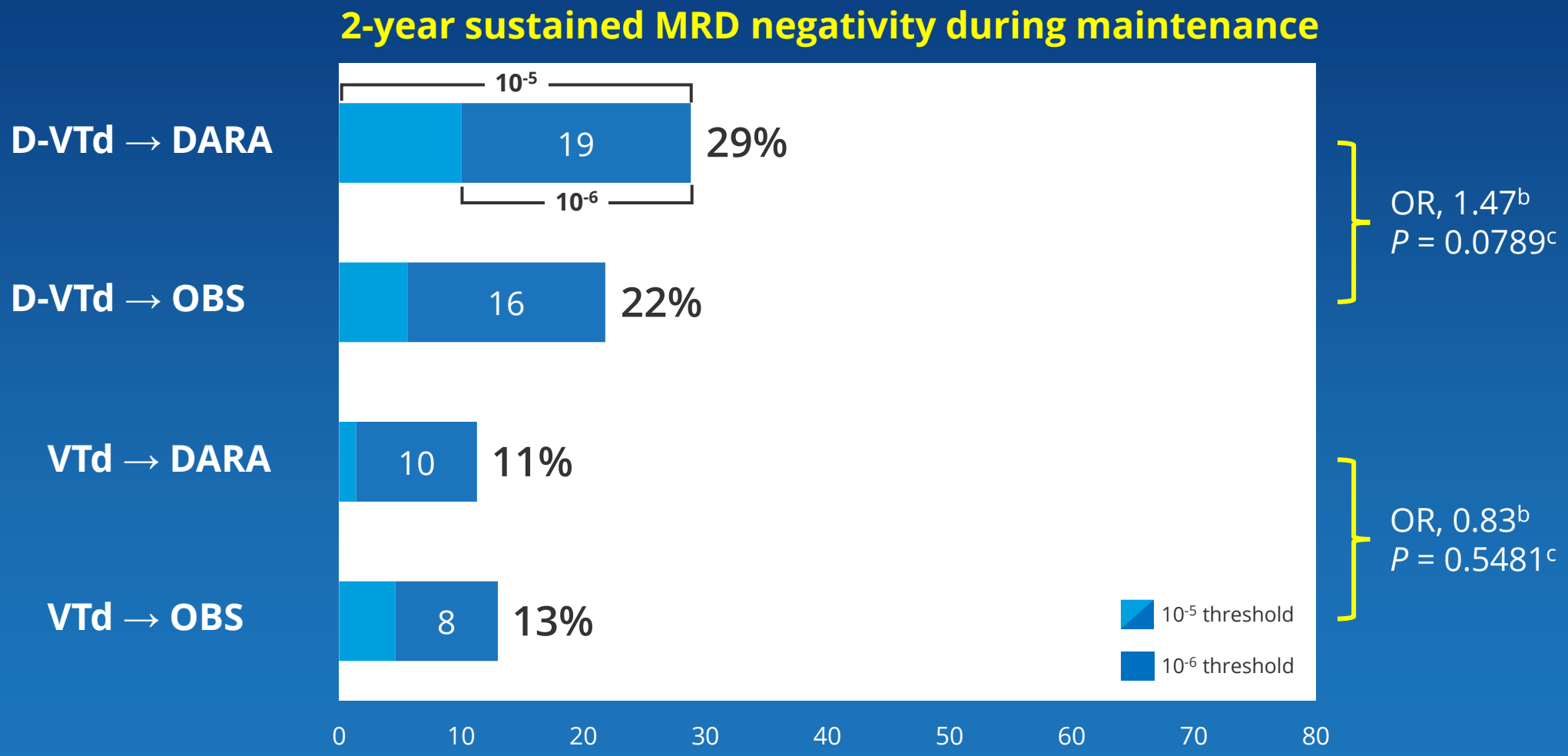
Stratification factors:
- Induction treatment (D-VTd or VTd)
- Depth of response

≥PR, partial response or better; IV, intravenous; Q8W, every 8 weeks; OBS, observation; ECOG, Eastern Cooperative Oncology Group; QW, every week; Q2W, every 2 weeks; SC, subcutaneous; PO, oral; IFM, Intergroupe Francophone du Myélome; HOVON, the Dutch-Belgian Cooperative Trial Group for Hematology-Oncology; ISS, International Staging System; PD, progressive disease; ≥VGPR, very good partial response or better.
[a]MRD analyses were performed at predefined timepoints for all patients, regardless of response. [b]MRD analyses were performed in patients with ≥VGPR at Weeks 25, 52, and 105.

CASSIOPEIA: Rates of 2-year Sustained ≥CR + MRD Negativity at 10^{-5} and 10^{-6} (NGS) at Any Timepoint During Maintenance[a]



[a]Post-consolidation after the second randomization.
[b]Odds ratio for 10^{-5} MRD-negativity rates.
[c]*P* value was calculated based on a stratified Cochran-Mantel-Haenszel chi-squared test.

Daratumumab (DARA) Plus Lenalidomide, Bortezomib, and Dexamethasone (RVd) in Patients (Pts) With Transplant-eligible Newly Diagnosed Multiple Myeloma (NDMM): Updated Analysis of GRIFFIN After 24 Months of Maintenance

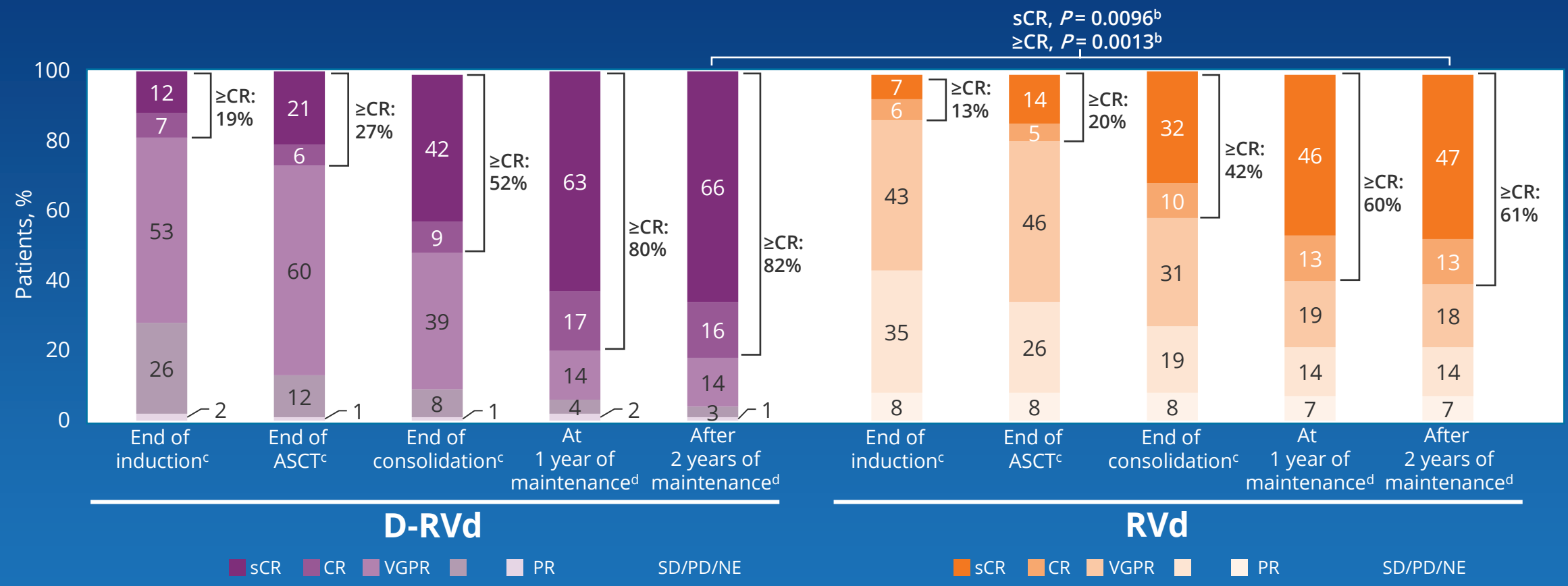
Jacob Laubach,[1,*] Jonathan L. Kaufman,[2] Douglas W. Sborov,[3] Brandi Reeves,[4] Cesar Rodriguez,[5] Ajai Chari,[6] Rebecca Silbermann,[7] Luciano J. Costa,[8] Larry D. Anderson Jr,[9] Nitya Nathwani,[10] Nina Shah,[11] Naresh Bumma,[12] Yvonne A. Efebera,[13] Sarah A. Holstein,[14] Caitlin Costello,[15] Andrzej Jakubowiak,[16] Tanya M. Wildes,[17] Robert Z. Orlowski,[18] Kenneth H. Shain,[19] Andrew J. Cowan,[20] Huiling Pei,[21] Annelore Cortoos,[22] Sharmila Patel,[22] J. Blake Bartlett,[23] Jessica Vermeulen,[24] Thomas S. Lin,[22] Paul G. Richardson,[1] Peter M. Voorhees[25]

[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]Winship Cancer Institute, Emory University, Atlanta, GA, USA; [3]Huntsman Cancer Institute, University of Utah School of Medicine, Salt Lake City, UT, USA; [4]University of North Carolina – Chapel Hill, Chapel Hill, NC, USA; [5]Wake Forest University School of Medicine, Winston-Salem, NC, USA; [6]Tisch Cancer Institute, Mount Sinai School of Medicine, New York, NY, USA; [7]Knight Cancer Institute, Oregon Health & Science University, Portland, OR, USA; [8]University of Alabama at Birmingham, Birmingham, AL, USA; [9]Simmons Comprehensive Cancer Center, UT Southwestern Medical Center, Dallas, TX, USA; [10]Judy and Bernard Briskin Center for Multiple Myeloma Research, City of Hope Comprehensive Cancer Center, Duarte, CA, USA; [11]Department of Medicine, University of California San Francisco, San Francisco, CA, USA; [12]Division of Hematology, The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA; [13]OhioHealth, Columbus, OH, USA; [14]Division of Oncology & Hematology, Department of Internal Medicine, University of Nebraska Medical Center, Omaha, Nebraska, USA; [15]Moores Cancer Center, University of California San Diego, La Jolla, CA, USA; [16]University of Chicago Medical Center, Chicago, IL, USA; [17]Cancer & Aging Research Group, St. Louis, MO, USA; [18]Department of Lymphoma and Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [19]Department of Malignant Hematology, H. Lee Moffitt Cancer Center, Tampa, FL, USA; [20]Division of Medical Oncology, University of Washington, Seattle, WA, USA; [21]Janssen Research & Development, LLC, Titusville, NJ, USA; [22]Janssen Scientific Affairs, LLC, Horsham, PA, USA; [23]Janssen Research & Development, LLC, Raritan, NJ, USA; [24]Janssen Research & Development, LLC, Leiden, The Netherlands; [25]Levine Cancer Institute, Atrium Health, Charlotte, NC, USA.

Presented at the 63rd American Society of Hematology (ASH) Annual Meeting & Exposition; December 11-14, 2021; Atlanta, GA/Virtual

*Presenting author.

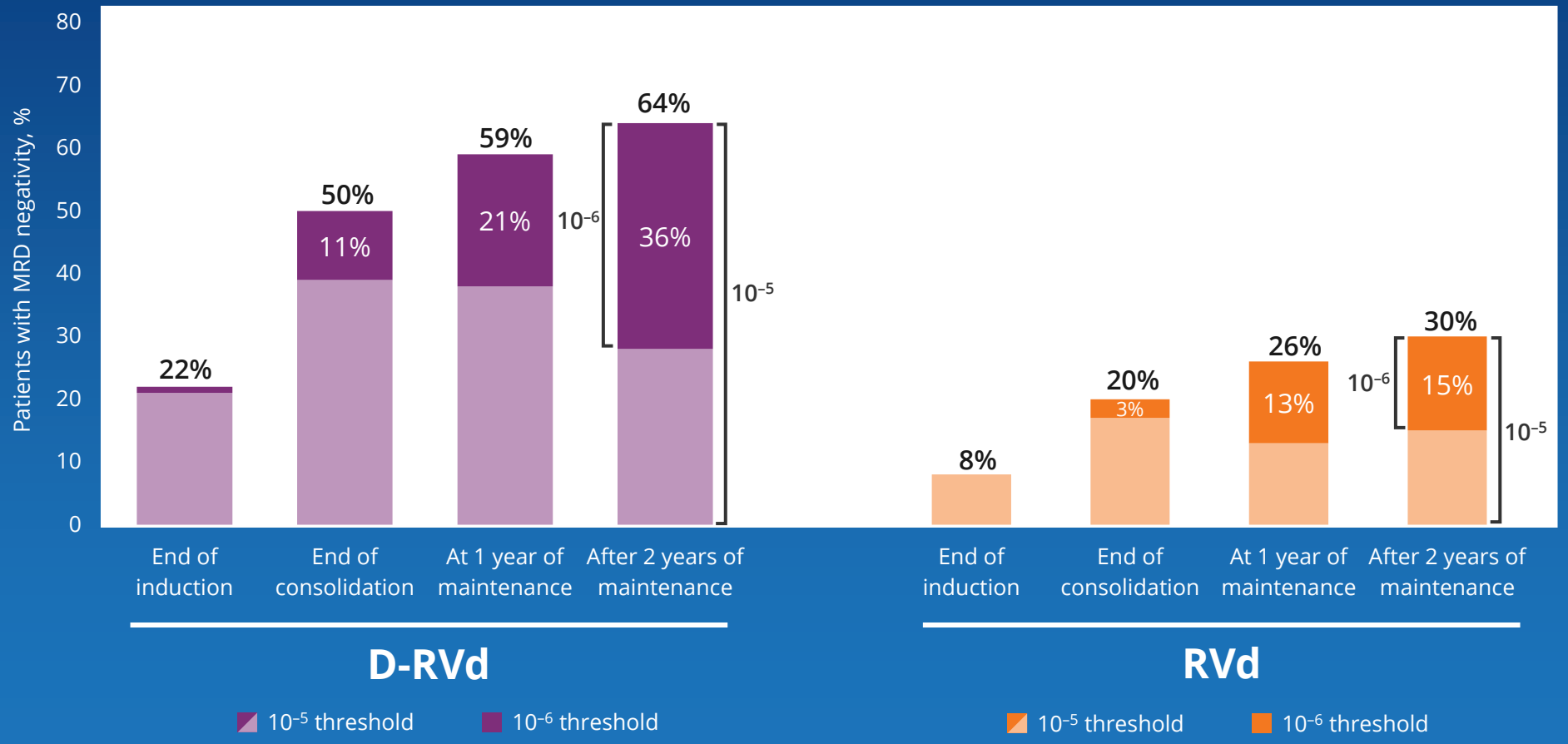
GRIFFIN: Responses Deepened Over Time[a]



- Response rates for sCR and ≥CR were greater for D-RVd versus RVd at all time points, with the deepest responses occurring after 2 years of maintenance therapy

PR, partial response; SD/PD/NE, stable disease/progressive disease/not evaluable. [a]Data are shown for the response-evaluable population. [b]*P* values (2-sided) were calculated using the Cochran–Mantel–Haenszel chi-square test. [c]Response rates are from the primary analysis cutoff (median follow-up: 13.5 mo), and the response-evaluable population included 196 patients (D-RVd, n = 99; RVd, n = 97). [d]Response rates for the maintenance phase have longer follow-up (median: 38.6 mo), and the response-evaluable population included 197 patients (D-RVd, n = 100; RVd, n = 97). Percentages may not add up due to rounding.

GRIFFIN: MRD-negativity[a] Rates Improved Throughout the DR Maintenance Period

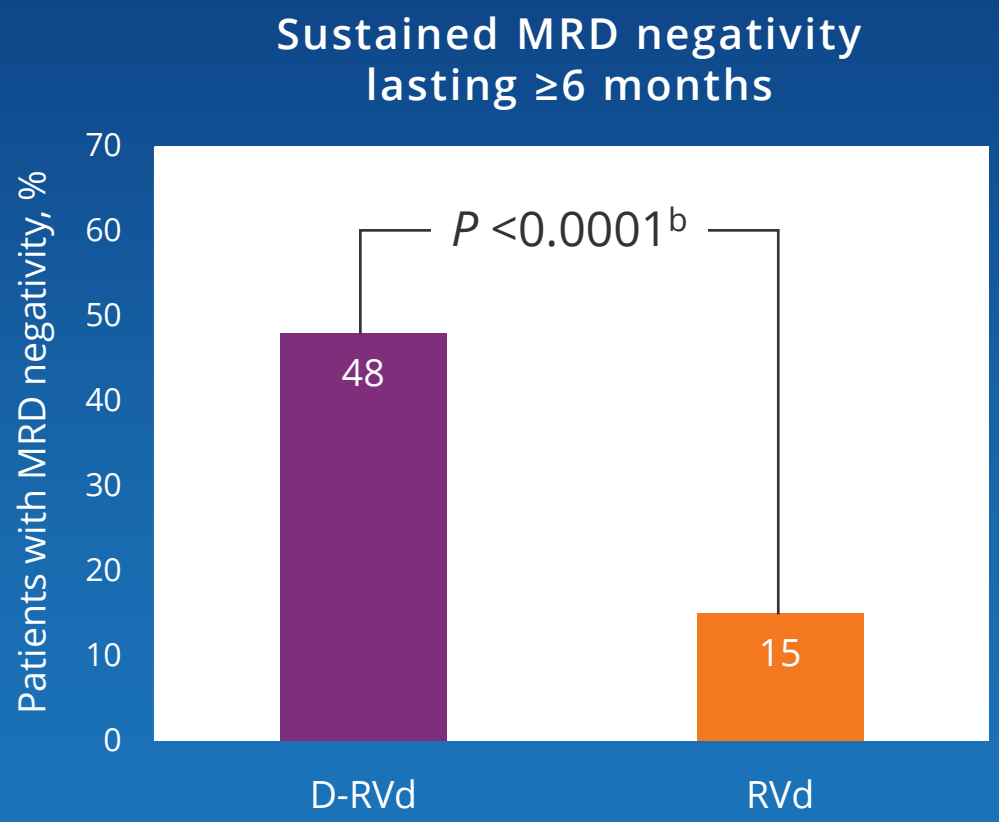


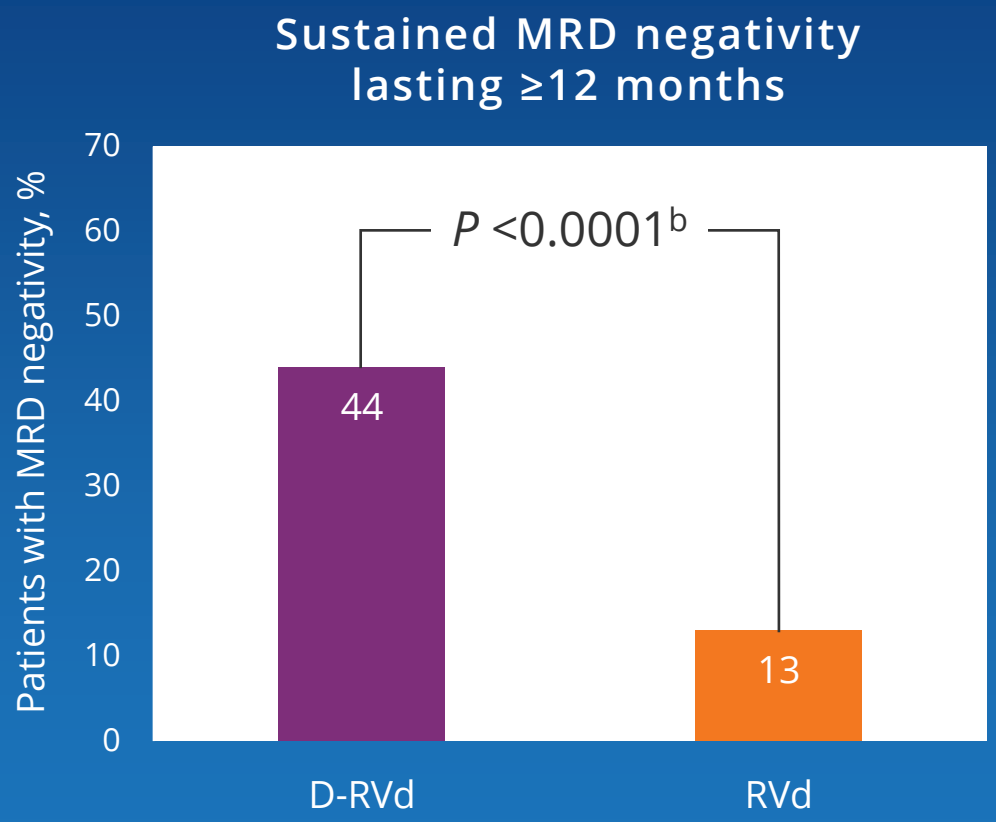
MRD-negative (10^{-5}) conversion rate

- 29% (15/52) of D-RVd patients and 12% (10/82) of RVd patients who were MRD positive at the end of consolidation became MRD negative after 2 years of DR or R maintenance

[a]The threshold of MRD negativity was defined as 1 tumor cell per 10^5 white cells. MRD status is based on the assessment of bone marrow aspirates by NGS in accordance with International Myeloma Working Group criteria. Bone marrow aspirates were assessed at baseline, at first evidence of suspected CR or sCR (including patients with VGPR or better and suspected DARA interference), at the end of induction and consolidation, and after 1 and 2 years of maintenance, regardless of response. Median follow-up was 38.6 months, and MRD-negativity rates are among the ITT population (D-RVd, n = 104; RVd, n = 103).

GRIFFIN: D-RVd Improved Rates of Durable MRD Negativity[a] (10^{-5}) Lasting ≥6 Months or ≥12 Months Versus RVd

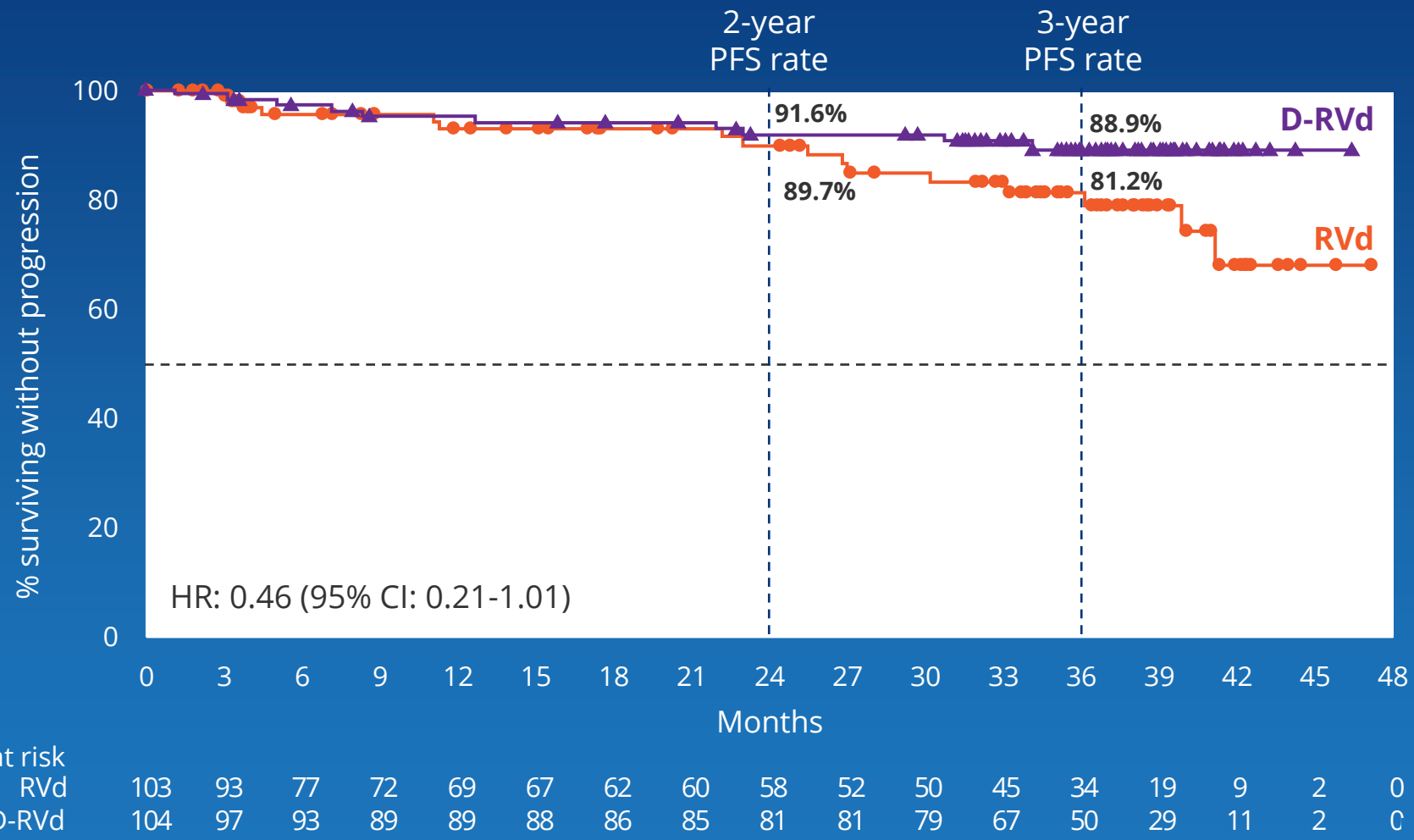




[a]The threshold of MRD negativity was defined as 1 tumor cell per 10^5 white cells. MRD status is based on the assessment of bone marrow aspirates by NGS in accordance with International Myeloma Working Group criteria. Median follow-up was 38.6 months, and MRD-negativity rates are among the ITT population (D-RVd, n = 104; RVd, n = 103). Bone marrow aspirates were assessed at baseline, at first evidence of suspected CR or sCR (including patients with VGPR or better and suspected DARA interference), at the end of induction and consolidation, and after 1 and 2 years of maintenance, regardless of response. [b]*P* values were calculated using the Fisher's exact test.

GRIFFIN: PFS in the ITT Population

- Median follow-up: 38.6 months
- Median PFS was not reached in either group
- There is a positive trend toward improved PFS for D-RVd/DR versus RVd/R
- The separation of the PFS curves begins beyond 1 year of maintenance and suggests a benefit of prolonged DR therapy



HR, hazard ratio.

UNIVERSITÄTS KLINIKUM HEIDELBERG

Addition of Isatuximab to Lenalidomide, Bortezomib and Dexamethasone as Induction Therapy for Newly-Diagnosed, Transplant-Eligible Multiple Myeloma: The Phase III GMMG-HD7 Trial

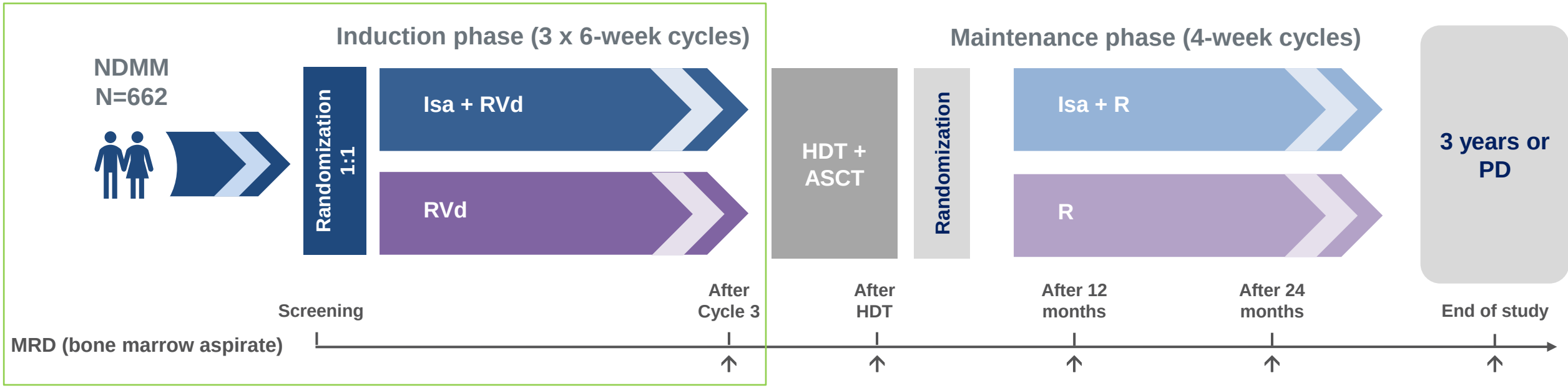
Hartmut Goldschmidt[1,2], Elias K. Mai[1], Eva Nievergall[1], Roland Fenk[3], Uta Bertsch[1,2], Diana Tichy[4], Britta Besemer[5], Jan Dürig[6], Roland Schroers[7], Ivana von Metzler[8], Mathias Hänel[9], Christoph Mann[10], Anne Marie Asemissen[11], Bernhard Heilmeier[12], Stefanie Huhn[1], Katharina Kriegsmann[1], Niels Weinhold[1], Steffen Luntz[13], Tobias A. W. Holderried[14], Karolin Trautmann-Grill[15], Deniz Gezer[16], Maika Klaiber-Hakimi[17], Martin Müller[18], Cyrus Khandanpour[19], Wolfgang Knauf[20], Markus Munder[21], Thomas Geer[22], Hendrik Riesenberg[23], Jörg Thomalla[24], Martin Hoffmann[25], Marc-Steffen Raab[1], Hans J. Salwender[26], Katja C. Weisel[11] for the German-speaking Myeloma Multicenter Group (GMMG)

[1]Department of Internal Medicine V, University Hospital Heidelberg, Heidelberg, Germany; [2]National Center for Tumor Diseases Heidelberg, Heidelberg, Germany; [3]Department of Hematology, Oncology and Clinical Immunology, University Hospital Düsseldorf, Düsseldorf, Germany; [4]Division of Biostatistics, German Cancer Research Center (DKFZ) Heidelberg, Heidelberg, Germany; [5]Department of Internal Medicine II, University Hospital Tübingen, Tübingen, Germany; [6]Department for Hematology and Stem Cell Transplantation, University Hospital Essen, Essen, Germany; [7]Medical Clinic, University Hospital Bochum, Bochum, Germany; [8]Department of Medicine, Hematology/Oncology, University Hospital Frankfurt, Goethe University, Frankfurt am Main, Germany; [9]Department of Internal Medicine III, Clinic Chemnitz, Chemnitz, Germany; [10]Department for Hematology, Oncology and Immunology, University Hospital Gießen and Marburg, Marburg, Germany; [11]Department of Oncology, Hematology and BMT, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [12]Clinic for Oncology and Hematology, Hospital Barmherzige Brueder Regensburg, Regensburg, Germany; [13]Coordination Centre for Clinical Trails (KKS) Heidelberg, Heidelberg, Germany; [14]Department of Oncology, Hematology, Immuno-Oncology and Rheumatology, University Hospital Bonn, Bonn, Germany; [15]Department of Internal Medicine I, University Hospital Dresden, Dresden, Germany; [16]Department of Hematology, Oncology, Hemostaseology, and Stem Cell Transplantation, Faculty of Medicine, RWTH Aachen University, Aachen, Germany; [17]Clinic for Hematology, Oncology and Palliative Care, Marien Hospital Düsseldorf, Düsseldorf, Germany; [18]Clinic for Hematology, Oncology and Immunology, Klinikum Siloah Hannover, Hannover, Germany; [19]Medical Clinic A, University Hospital Münster, Münster, Germany; [20]Center for Hematology and Oncology Bethanien, Frankfurt am Main, Germany; [21]Department of Internal Medicine III, University Hospital Mainz, Mainz, Germany; [22]Department of Internal Medicine III, Diakoneo Clinic Schwäbisch-Hall, Schwäbisch-Hall, Germany; [23]Hematology/Oncology Center, Bielefeld, Germany; [24]Hematology / Oncology Center, Koblenz, Germany; [25]Medical Clinic A, Clinic Ludwigshafen, Ludwigshafen, Germany; [26]Asklepios Tumorzentrum Hamburg, AK Altona and AK St. Georg, Hamburg, Germany

UK HD

ASH 2021; Final Abstract Code: 463

Primary endpoint: MRD negativity at the end of induction phase



Primary endpoint:
- MRD negativity at the end of induction treatment (NGF, sensitivity 10^{-5}) stratified according to R-ISS

Secondary endpoints:
- CR after induction
- Safety

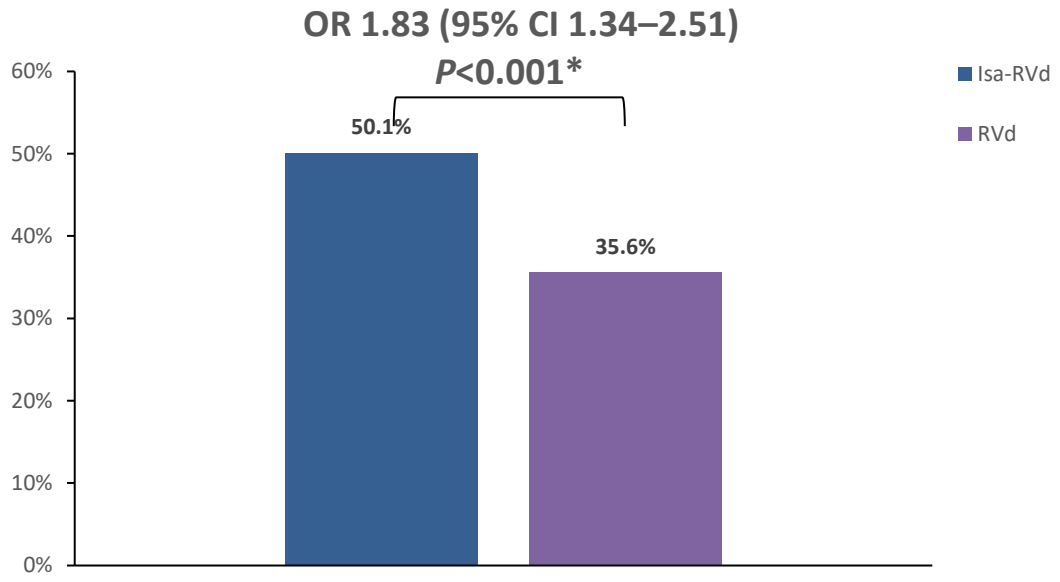
Data cut-off:
- April 2021

ASCT, autologous stem cell transplant; CR, complete response; d, dexamethasone; HDT, high-dose therapy; Isa, isatuximab; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; NGF, next-generation flow; PD, progressive disease; R, lenalidomide; R-ISS, Revised International Staging System; Te, transplant eligible; V, bortezomib

1. ClinicalTrials.gov: NCT03617731

First primary endpoint, end of induction MRD negativity by NGF (10^{-5}), was met in ITT analysis

Patients with MRD negativity at the end of induction therapy

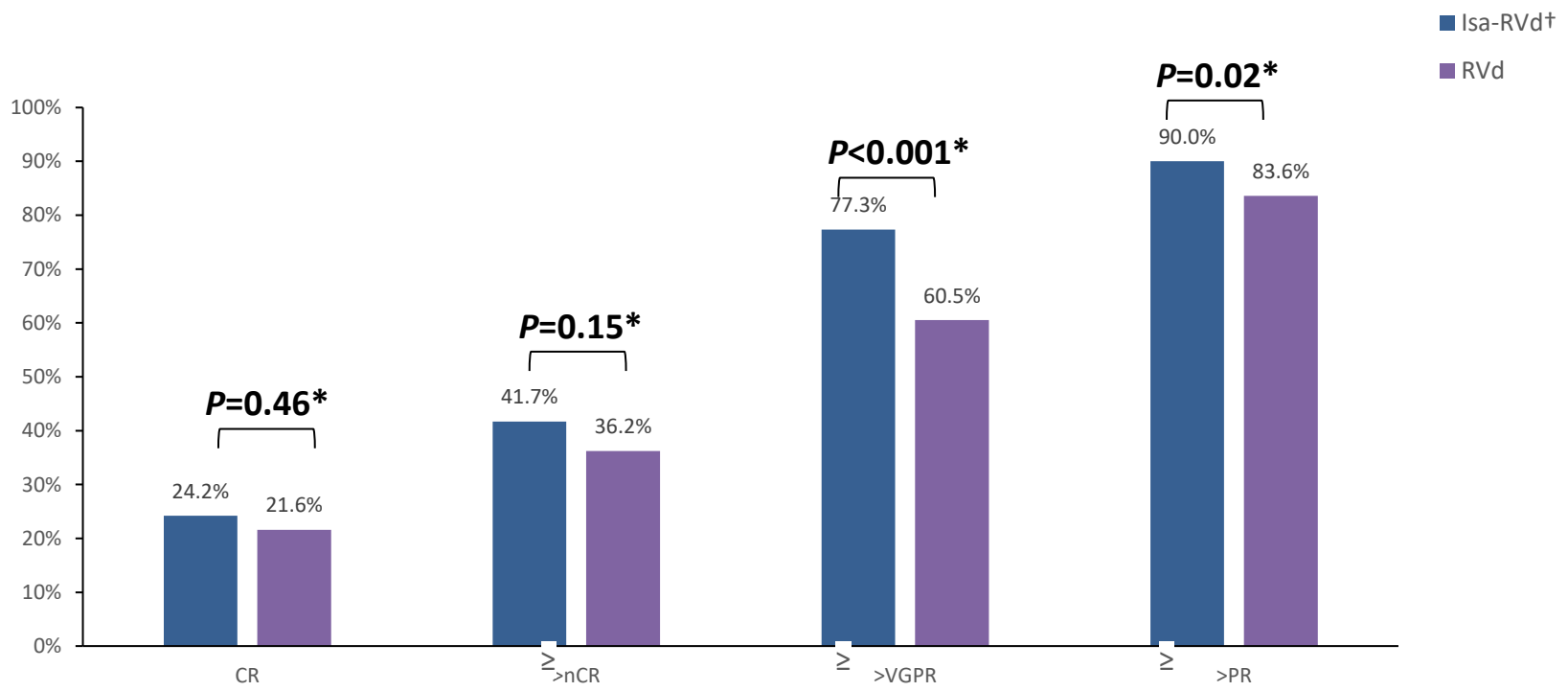


Low number of not assessable/missing† MRD status: Isa-RVd (10.6%) and RVd (15.2%)

Isa-RVd is the first regimen to demonstrate a rapid and statistically significant benefit from treatment by reaching a MRD negativity of 50.1% at the end of induction and to show superiority vs. RVd in a Phase 3 trial

*P value derived from stratified conditional logistic regression analysis
†Missing NGF-MRD values were due to either patients' loss to follow-up during induction therapy or to missing bone marrow samples or technical failures in measurement counted as non-responders, i.e. NGF-MRD positive
CI, confidence interval; d, dexamethasone; Isa, isatuximab; ITT, intent-to-treat; MRD, minimal residual disease; NGF, next-generation flow; OR, odds ratio; R, lenalidomide; V, bortezomib

Response rates after induction therapy



Although the rates of CR after induction therapy did not differ between the Isa-RVd and RVd arms, there was a significant increase in ≥VGPR rates and ORR with Isa-RVd

*P values derived from Fisher's exact test
†Data adjusted per M-protein interference
CR, complete response; d, dexamethasone; Isa, isatuximab; nCR; near-complete response; ORR, overall response rate; PR, partial response; R, lenalidomide; V, bortezomib; VGPR, very good partial response

Addition of Isa to RVd had limited impact on safety profile

AEs CTCAE grade ≥3, n (%)	Isa-RVd (n=330)	RVd (n=328)
Any AE	210 (63.6)	201 (61.3)
Any serious AE (any grade)	115 (34.8)	119 (36.3)
Deaths	4 (1.2)	8 (2.4)
Investigations* (SOC)	79 (23.9)	77 (23.5)
Blood and lymphatic system disorders (SOC)	85 (25.8)	55 (16.8)
Infections and infestations (SOC)	43 (13.0)	34 (10.4)
Nervous system disorders (SOC)	28 (8.5)	33 (10.1)
Gastrointestinal disorders (SOC)	27 (8.2)	31 (9.5)
Metabolism and nutrition disorders (SOC)	12 (3.6)	26 (7.9)

AEs CTCAE grade ≥3, n (%)	Isa-RVd (n=330)	RVd (n=328)
Specific hematologic AE (PT)		
Leukocytopenia/Neutropenia†	87 (26.4)	30 (9.1)
Lymphopenia	48 (14.5)	65 (19.8)
Anemia	13 (3.9)	20 (6.1)
Thrombocytopenia	21 (6.4)	15 (4.6)
Specific non-hematologic AE (PT)		
Peripheral neuropathy	25 (7.6)	22 (6.7)
Thromboembolic events	5 (1.5)	9 (2.7)
Infusion-related reactions‡	4 (1.2)	NA

A comparable number of patients discontinued induction therapy due to AEs in the Isa-RVd arm vs. RVd arm

*SOC considered as "Investigations" as defined by the CTCAE
†Includes five episodes of febrile neutropenia during induction: Isa-VRd (n=3) vs. VRd (n=2)
‡Infusion-related reactions of CTCAE grade 2 or higher in the Isa-RVd arm were n=42 (12.7%)
AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; d, dexamethasone; Isa, isatuximab; NA, not applicable; PT, preferred term; R, lenalidomide; SOC, system organ class; V, bortezomib

Daratumumab, Carfilzomib, Lenalidomide and Dexamethasone (Dara-KRd), Autologous Transplantation and MRD Response-Adapted Consolidation and Treatment Cessation-Final Primary Endpoint Analysis of the MASTER Trial

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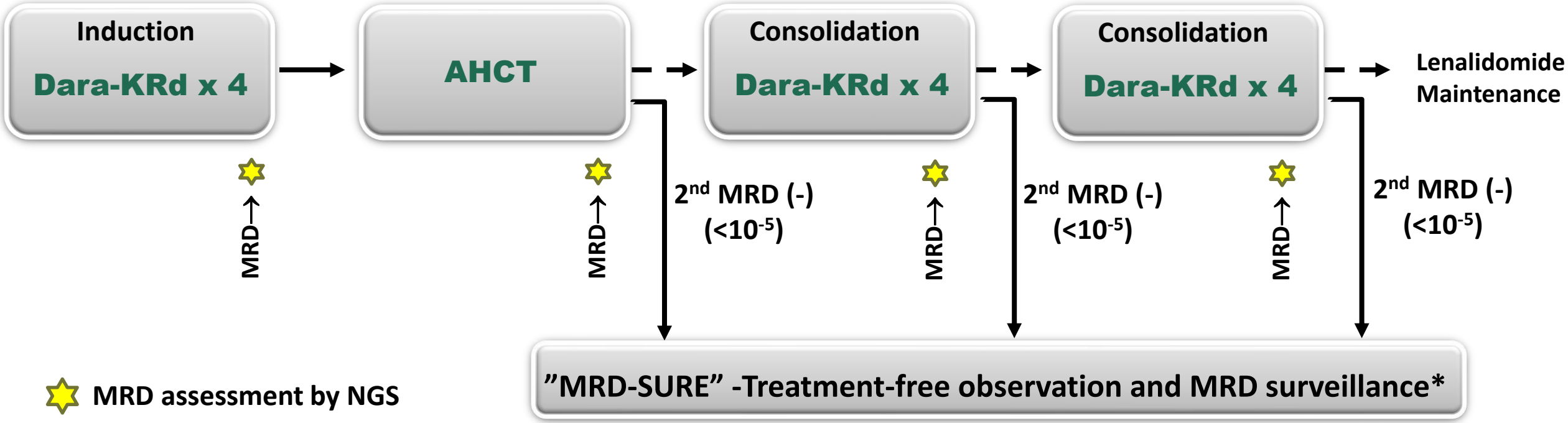
COMMIT- Academic Consortium to Overcome Multiple Myeloma through Innovative Trials

Treatment

Dara-KRd

- Daratumumab 16 mg/m^2 days 1,8,15,22 (days 1,15 C 3-6; day 1 C >6)
- Carfilzomib (20) 56 mg/m^2 Days 1,8,15
- Lenalidomide 25 mg Days 1-21
- Dexamethasone 40mg PO Days 1,8,15,22

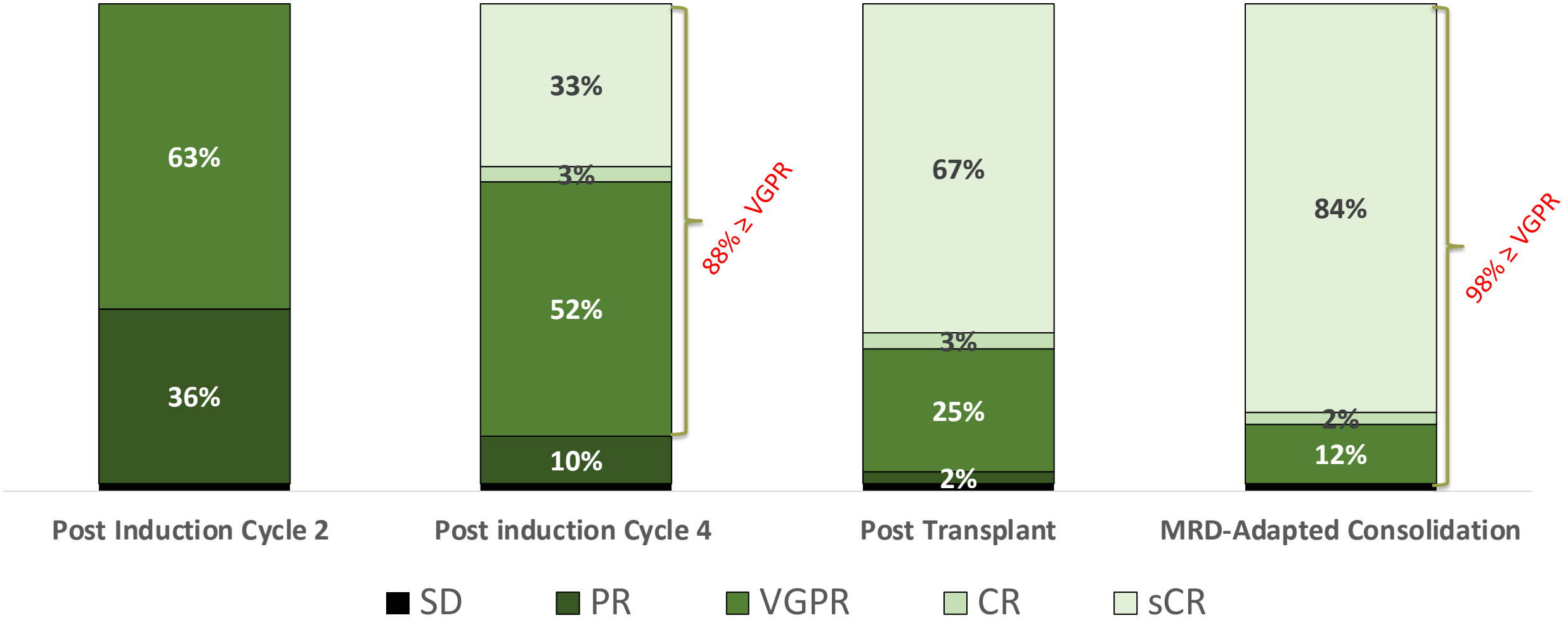
- 123 patients enrolled across 5 sites
- 118 (96%) with MRD trackable by ClonoSEQ®
- Median follow-up of 23.8 months



*24 and 72 weeks after completion of therapy

MASTER trial

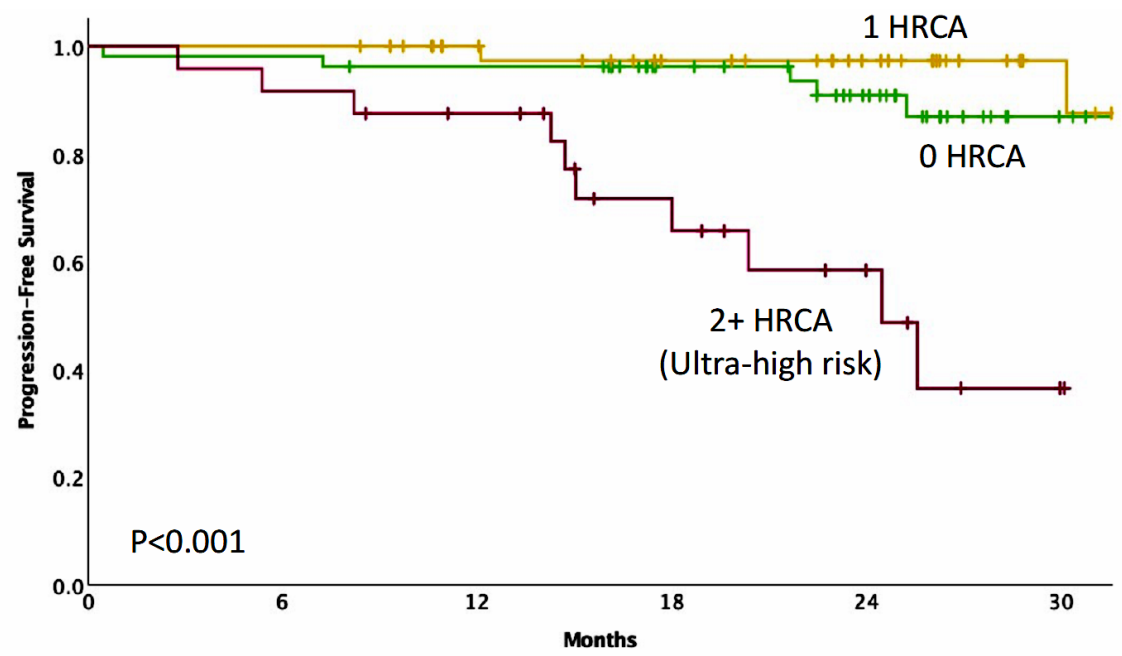
Best IMWG response by phase of therapy (ITT)



N=123

MASTER trial

Progression-Free and Overall Survival

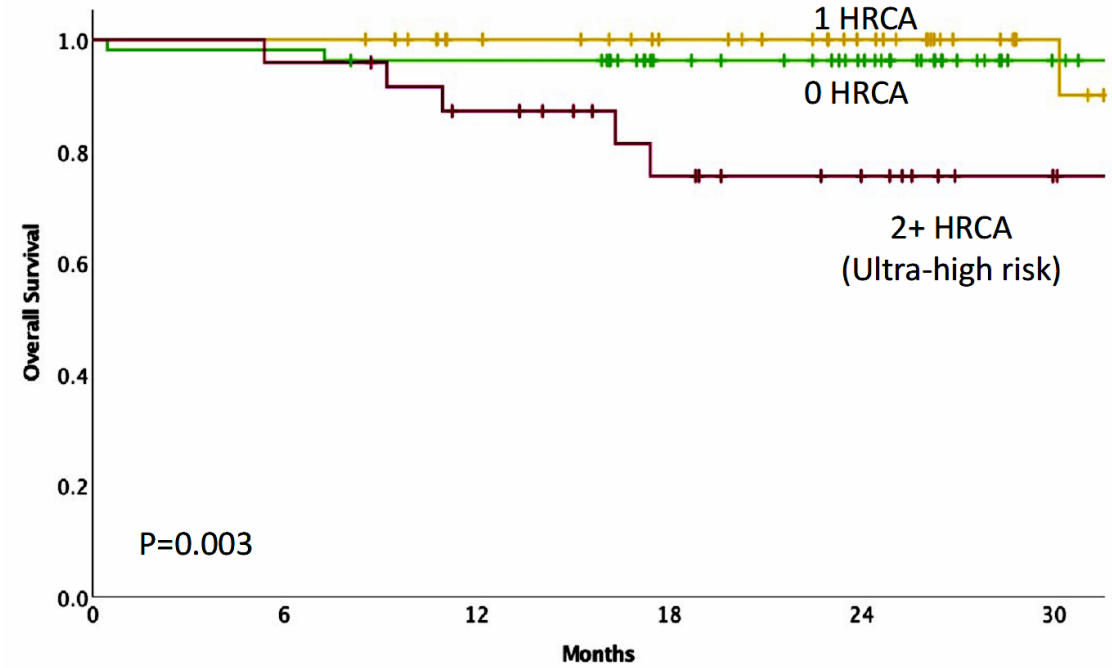


No. at risk:

0 HRCA	50	49	46	36	27	10
1 HRCA	44	44	36	30	23	9
2+ HRCA	24	22	19	12	7	2

2-year PFS

0 HRCA	91%
1 HRCA	97%
2+ HRCA	58%



No. at risk:

0 HRCA	50	49	46	36	29	11
1 HRCA	44	44	36	30	23	9
2+ HRCA	24	23	19	13	9	3

2-year OS

0 HRCA	96%
1 HRCA	100%
2+ HRCA	76%

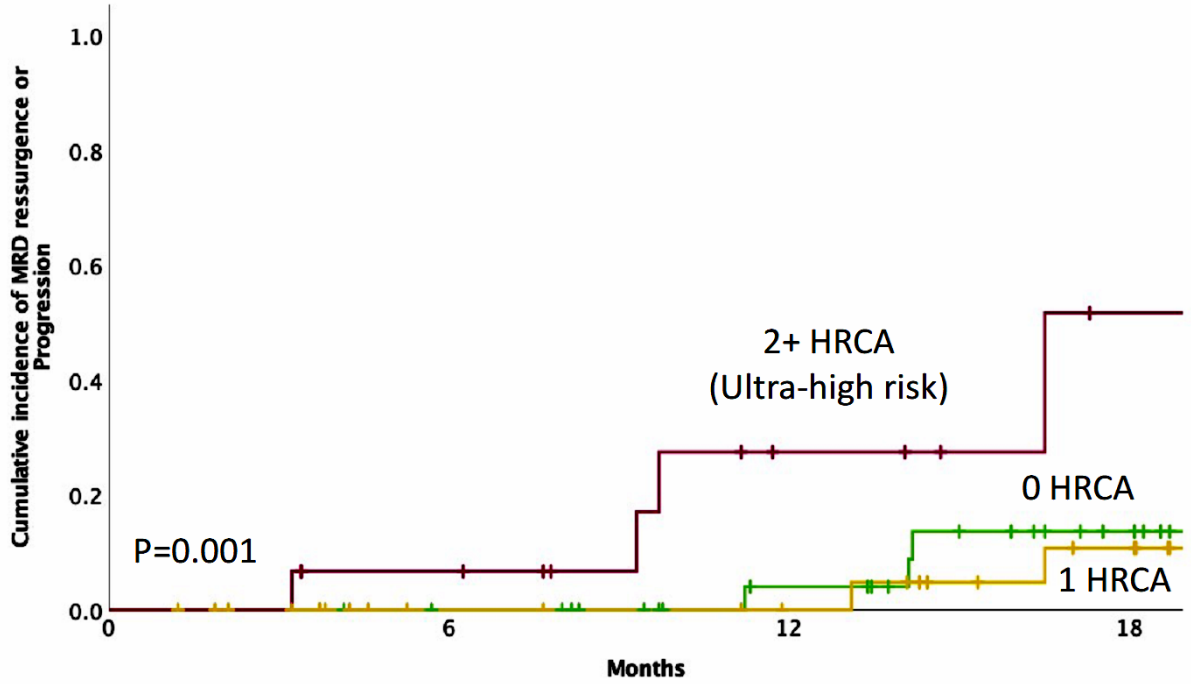
HRCA = gain/amp 1q, t(4;14), t(14;16), t(14;20) or del(17p)

MASTER trial

MRD-SURE

- 84 patients achieved MRD-SURE
  - 0 HRCA – 62%
  - 1 HRCA- 78%
  - 2+ HRCA – 63%
- Median follow up in MRD-SURE: 14.2 mo.
- Risk of MRD resurgence or progression 12 months after treatment cessation
  - 0 HRCA – 4%
  - 1 HRCA- 0%
  - 2+ HRCA – 27%
- **None** of patients entering MRD-SURE died from MM progression

Cumulative incidence of MRD resurgence or progression



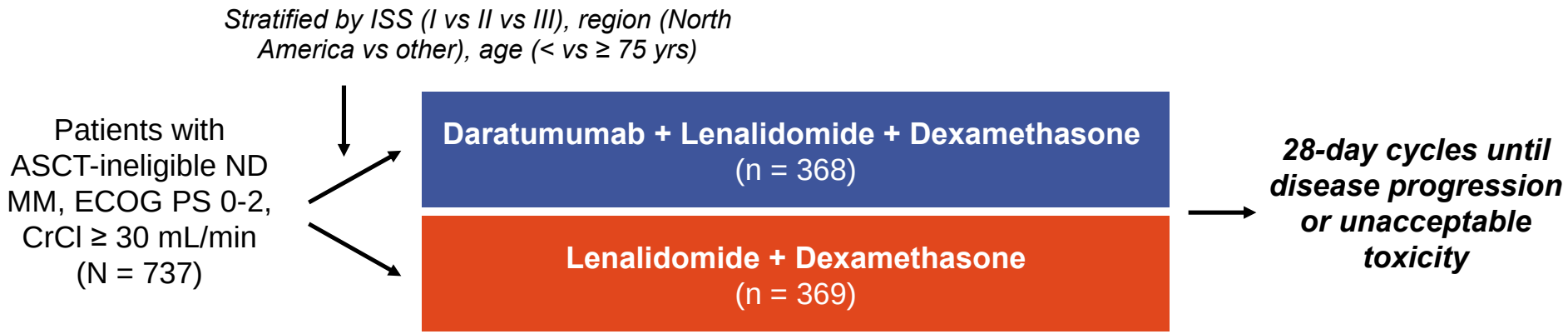
No. at risk:				
0 HRCA	33	31	23	12
1 HRCA	36	24	21	14
2+ HRCA	15	23	5	0

HRCA = gain/amp 1q, t(4;14), t(14;16), t(14;20) or del(17p)

MASTER trial

MAIA: Study Design

- Multicenter, open-label, randomized phase III trial



Dosing: daratumumab, 16 mg/kg IV (QW cycles 1-2, Q2W cycles 3-6, Q4W cycle 7+); lenalidomide, 25 mg QD PO on Days 1-21; dexamethasone 40 mg QW PO or IV.

- Primary endpoint: PFS
- Secondary endpoints: TTP, CR/sCR, MRD by NGS (10^{-5}), PFS2, OS, ORR, safety

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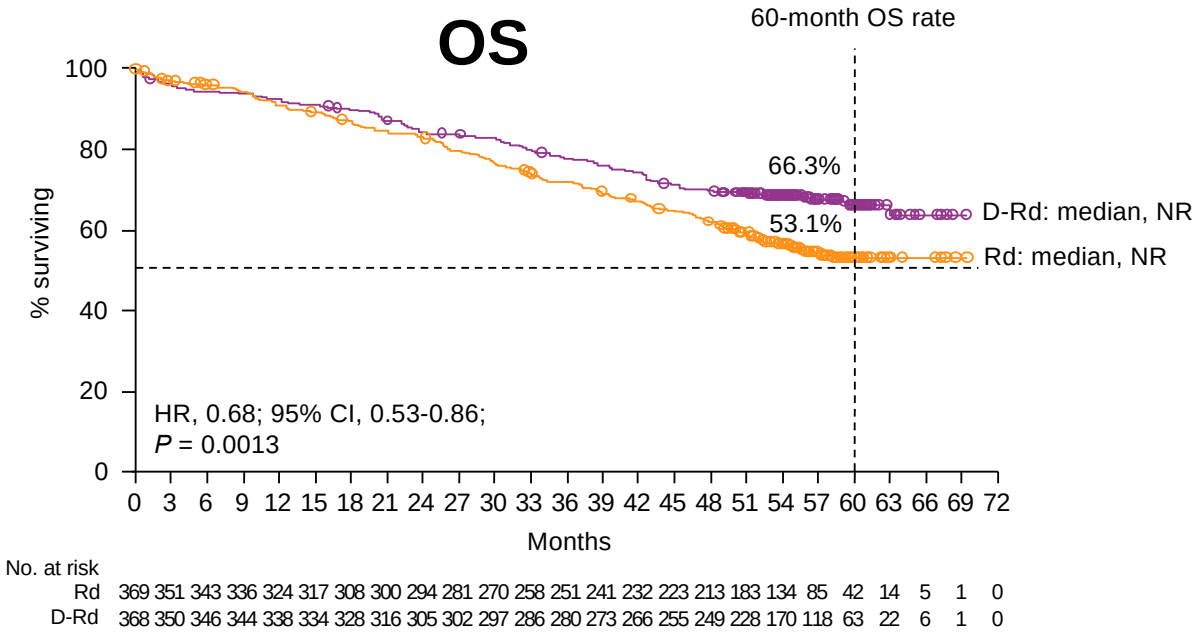
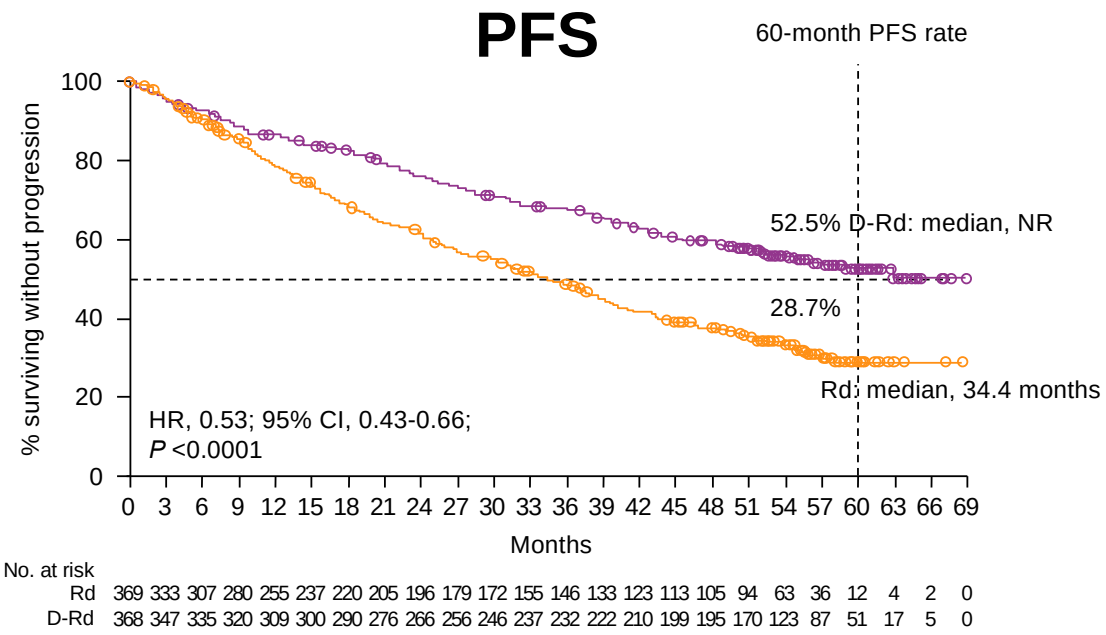
MAIA: OS and PFS with D-Rd and Rd





D-Rd, daratumumab plus lenalidomide and Dexamethasone; Rd, lenalidomide and Dexamethasone; HR, hazard ration; CI, confidence interval; NR, not reached.

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STUDY SCHEME

INDUCTION

9 cycles of 4 weeks

Ixazomib 4 mg	day 1, 8, 15
Daratumumab 16 mg/kg	
cycle 1-2	day 1, 8, 15, 22
cycle 3-6	day 1, 15
cycle 7-9	day 1
Dexamethasone	
cycle 1-2 20 mg	day 1, 8, 15, 22
cycle 3-6 10 mg	day 1, 15
cycle 7-9 10 mg	day 1

MAINTENANCE

8-week cycles (until progression for a maximum of 2 years)

Ixazomib 4 mg	day 1, 8, 15, 29, 36, 43
Daratumumab 16 mg/kg	day 1
Dexamethasone 10 mg	day 1

Antibiotic and -viral prophylaxis: Cotrimoxazole 480 mg/day, Valaciclovir 500 mg twice daily
Vaccinations according to local policy

DEMOGRAPHICS – PATIENT CHARACTERISTICS

	n=65 (%)
Male	35 (54)
Median age (years) [range]	76 [65-80]
≤75 years	28 (43)
76-80 years	37 (57)
WHO performance status (%)	
0	25 (38)
1	28 (43)
2	6 (9)
3	3 (5)
unknown	3 (5)

	n=65 (%)
Activity of Daily Living (ADL)	
≥5	65 (100)
≤4	-
Instrumental ADL (IADL)	
≥6	56 (86)
≤5	9 (14)
Charlson Comorbidity Index (CCI)	
≤1	46 (71)
≥2	19 (29)

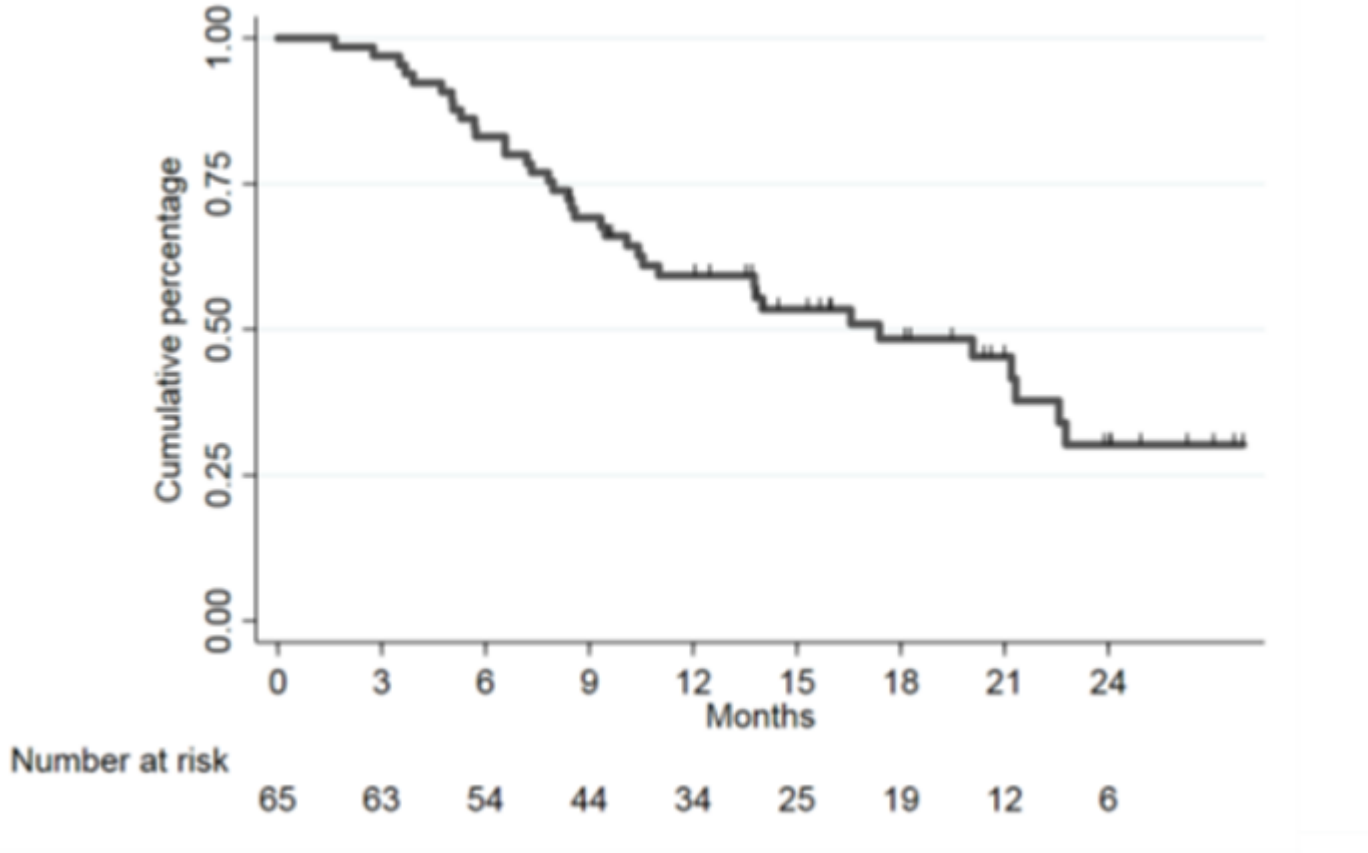
Efficacy

Best response on induction treatment

Response rate (%)	INT-FIT n=65 (%)
ORR	46 (71)
(s)CR	1 (2)
VGPR	23 (35)
PR	22 (34)
MR	11 (17)
SD	7 (11)
Not evaluable	1 (2)

EFFICACY - PROGRESSION FREE SURVIVAL

MEDIAN FOLLOW UP 18.1 MONTHS (RANGE 9.4-27.8)



MEDIAN PFS: 17.4 MONTHS

MEDIAN PFS:

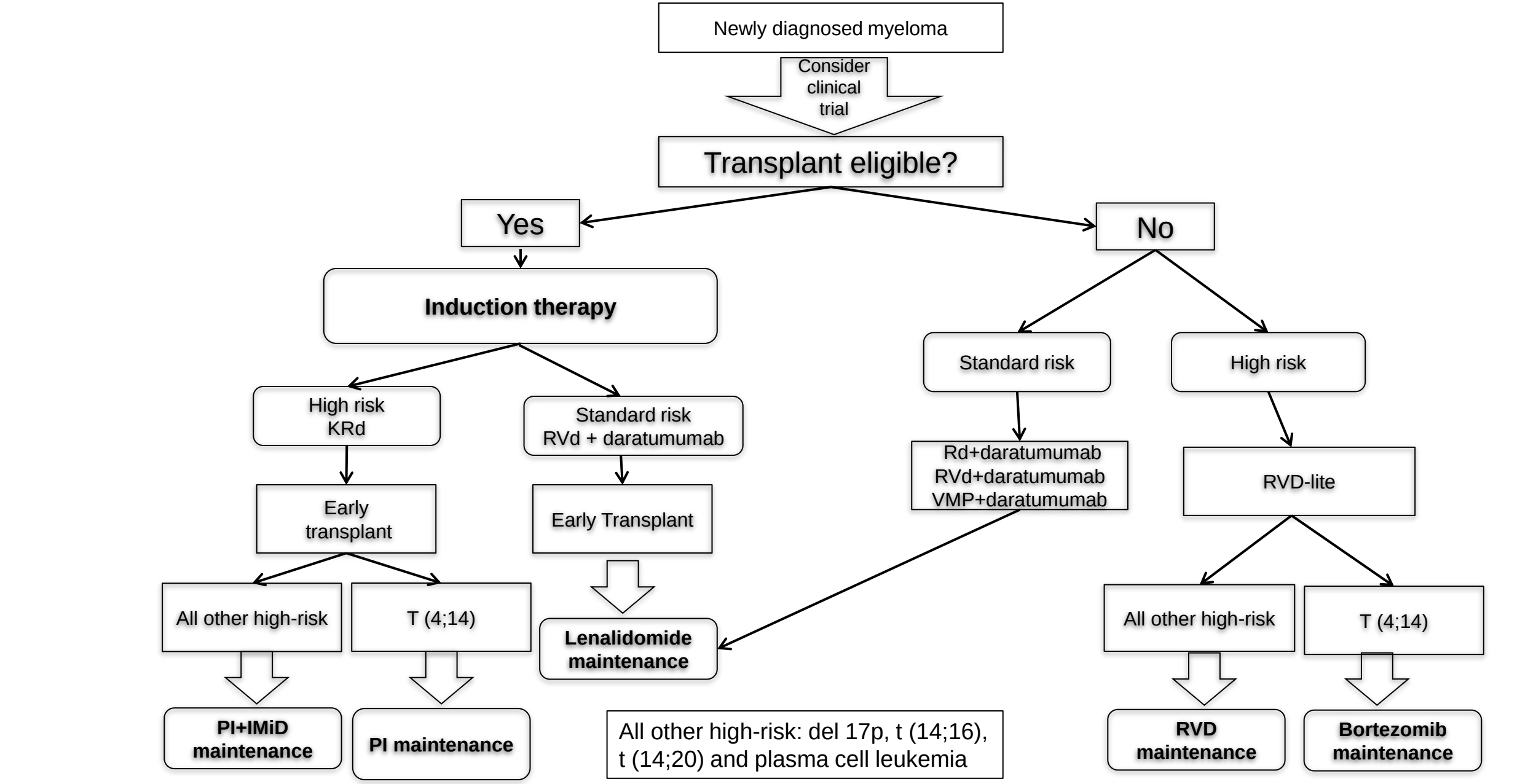
- **AGE: 16.6 MONTHS**
- **CCI/IADL: 18.2 MONTHS**

TOLERABILITY

NON-HEMATOLOGIC TOXICITY

CTCAE grade	**II**	**III**	**IV**
NON-HEMATOLOGIC n (%)	28 (43)	30 (46)	3 (5)
Gastro-intestinal	14 (22)	9 (14)	-
Infections	18 (28)	6 (9)	-
Peripheral neuropathy*	10 (15)	5 (8)	-
Pain	14 (22)	4 (6)	-
Secondary primary malignancy	3 (5)	2 (3)	1 (2)
Cardiac	3 (5)	1 (2)	2 (4)
Infusion related reactions	2 (3)	2 (3)	-

* Grade 1 PNP observed in 12 (18%) patients



Emory Algorithm for newly diagnosed patients

VD: bortezomib/dexamethasone, Rd: lenalidomide/dexamethasone
RVD: bortezomib/lenalidomide/dexamethasone, RVD-lite: modified RVD
VMP: bortezomib/melphalan/prednisone

Conclusions

- CD38 based induction clearly adds value in the induction setting
- Role in the maintenance setting remains unclear given the very long outcomes for standard risk with len alone.
- May be more exciting if addition of a second agent to Len allows one to shorten maintenance duration
- **Do Not** yet use MRD to define duration of maintenance

Patients and Families

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