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Management of Induction and its impact

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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

Phase 2 KRd Studies in NDMM

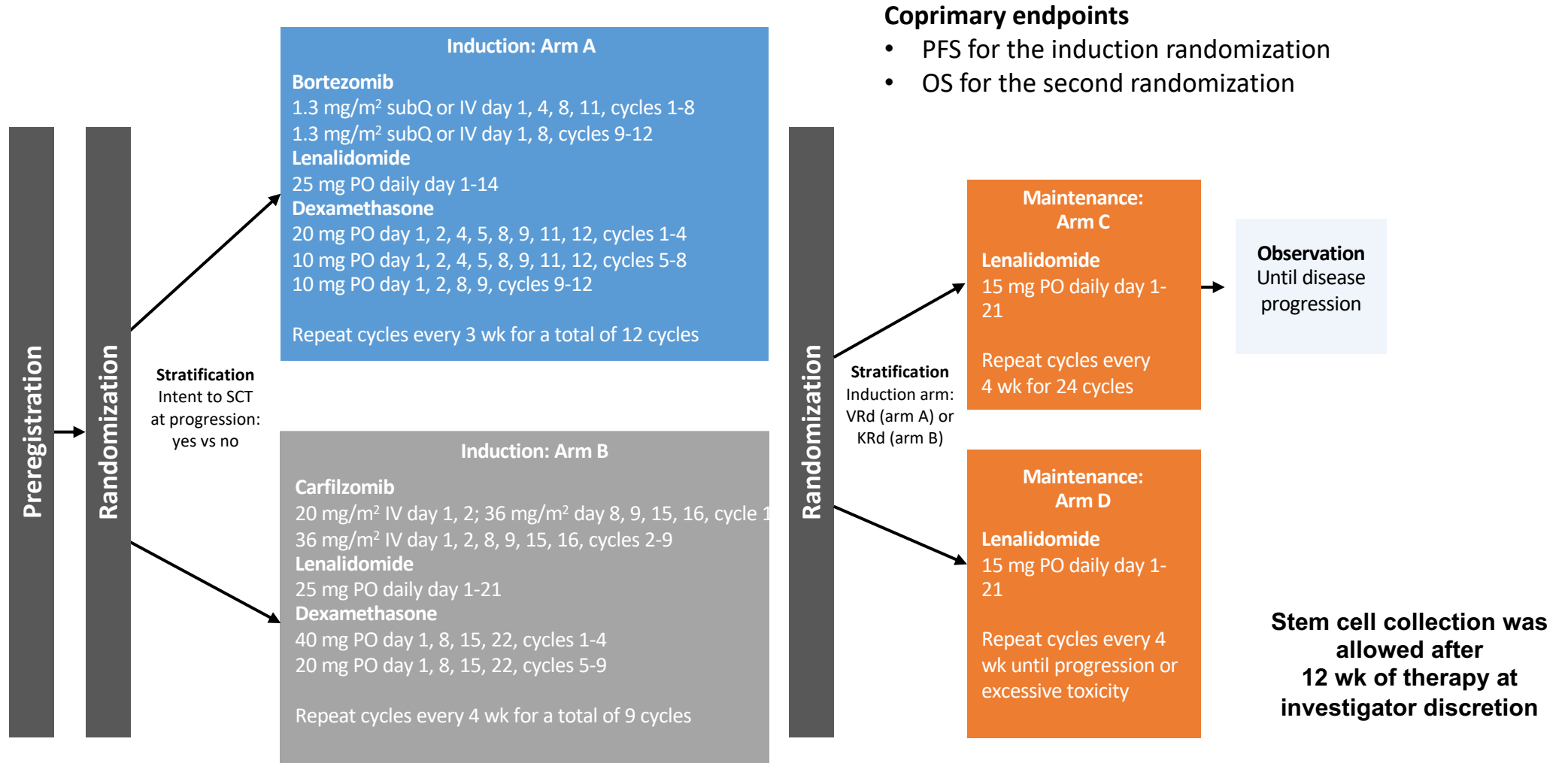
| Trial | Response | Grade 3/4 AEs |
|---|---|---|
| Jakubowiak et al ¹ (N=53) | nCR: 78% sCR: 61% 24-month PFS: 92% | Hypophosphatemia: 25% Hyperglycemia: 23% Anemia: 21% Thrombocytopenia: 17% Neutropenia: 17% |
| Korde et al ² (N=45) | CR/sCR: 56% ≥nCR: 62% ≥VGPR: 89% ≥PR: 98% | Lymphopenia: 76% Anemia: 27% Neutropenia: 33% Thrombocytopenia: 24% |
| Zimmerman et al ³ (N=76) | VGPR: 96% CR: 73% sCR: 69% | Lymphopenia: 28% Neutropenia: 18% Infections: 8% |
| Gay et al ⁴ (N=474); FORTE trial | KRd_ASCT_KRd vs KRd12 ≥VGPR: 89% vs 87% ≥CR: 60% vs 61% sCR: 44% vs 43% | — |

- KRd12, 12 cycles of KRd; nCR, near complete response; PR, partial response.

- 1. Jakubowiak AJ, et al. *Blood*. 2012;120:1801-1809. 2. Korde N, et al. *JAMA Oncol*. 2015;1:746-754. 3. Zimmerman T, et al. ASH 2016 (abstr 675). 4. Gay F, et al. ASH 2020 (abstr 294).

Phase 3 ENDURANCE Study¹

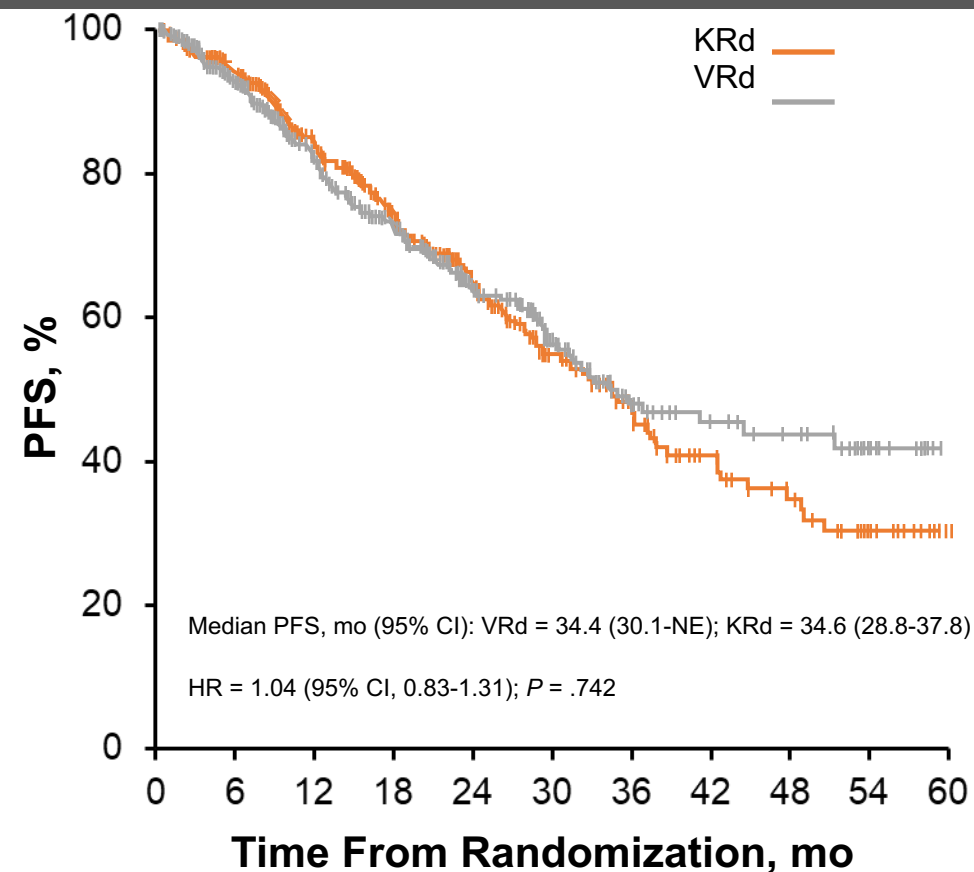
ECOG-ACRIN E1A11



1. Kumar S et al. American Society of Clinical Oncology 2020 Annual Meeting (ASCO 2020). Abstract LBA3.

ENDURANCE: PFS From Induction Randomization¹

- Second interim analysis of PFS (January 2020): 298 PFS events (75% of 399 planned)
- Median (95% CI) estimated follow-up of 15 mo (13-18)
- For patients aged ≥ 70 y, median PFS (95% CI) for VRd = 37 mo (29-NE) and KRd = 28 mo (24-36)
- With censoring at SCT or alternative therapy: median PFS (95% CI) for VRd = 31.7 mo (28.5-44.6) and KRd = 32.8 mo (27.2-37.5)

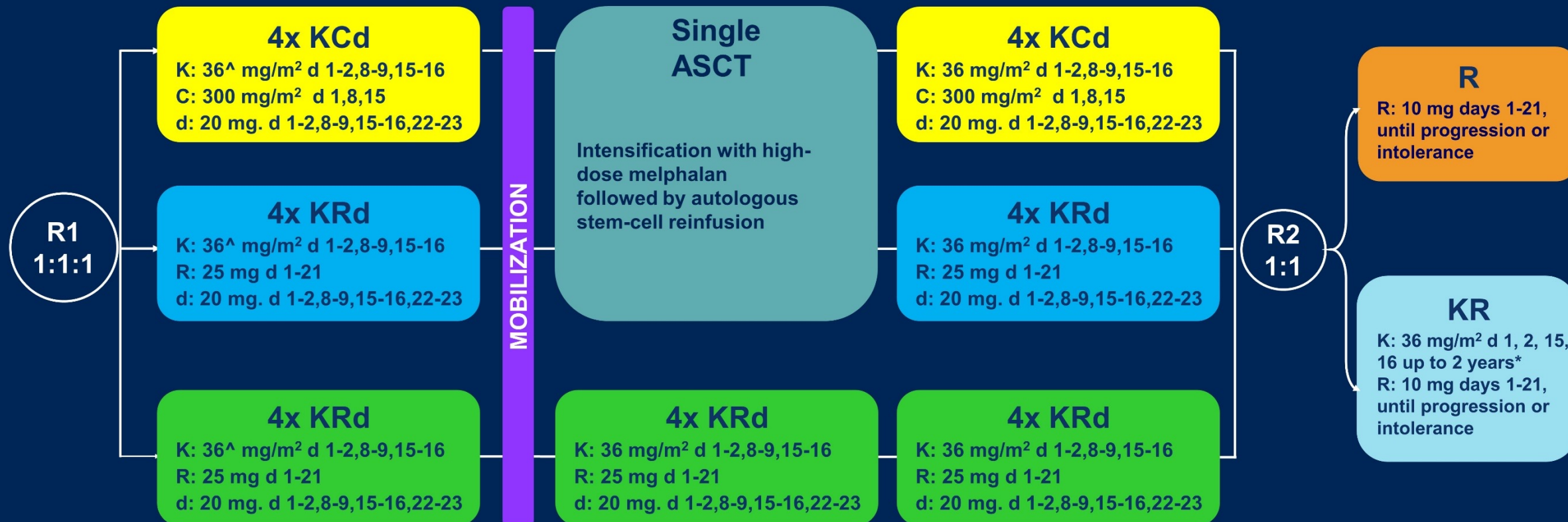


No. at Risk

| | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|----|----|----|----|----|---|
| KRd | 545 | 401 | 252 | 187 | 127 | 83 | 59 | 38 | 25 | 13 | 3 |
| VRd | 542 | 377 | 243 | 183 | 114 | 73 | 43 | 31 | 26 | 14 | 0 |

Trial design

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



[^]20 mg/m² on days 1-2, cycle 1 only. *Carfilzomib 70 mg/m² days 1, 15 every 28 days up to 2 years for patients that have started the maintenance treatment from 6 months before the approval of Amendment 5.0 onwards.

NDMM, newly diagnosed multiple myeloma; R1, first randomization (induction/consolidation treatment); R2, second randomization (maintenance treatment); ASCT, autologous stem-cell transplantation; K, carfilzomib; R, lenalidomide; C, cyclophosphamide; d, dexamethasone; KCd_ASCT, KCd induction-ASCT-KCd consolidation; KRd_ASCT, KRd induction-ASCT-KRd consolidation; KRd12, 12 cycles of KRd.

Presented By: **Francesca Gay**

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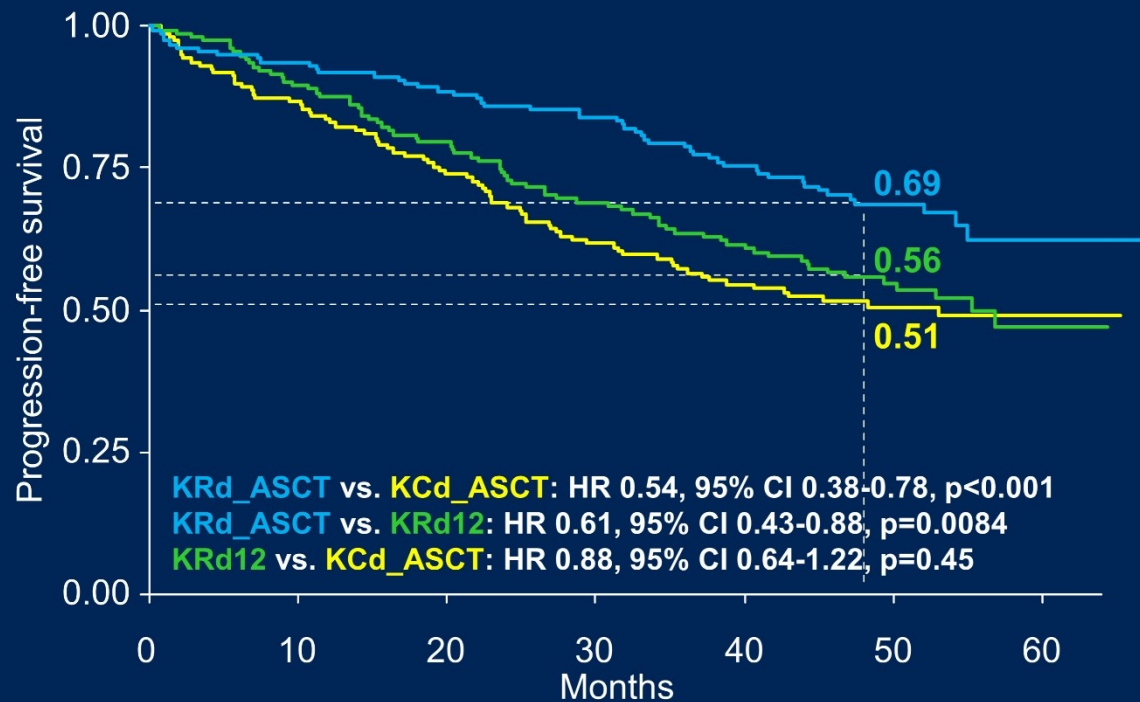
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Progression-free survival

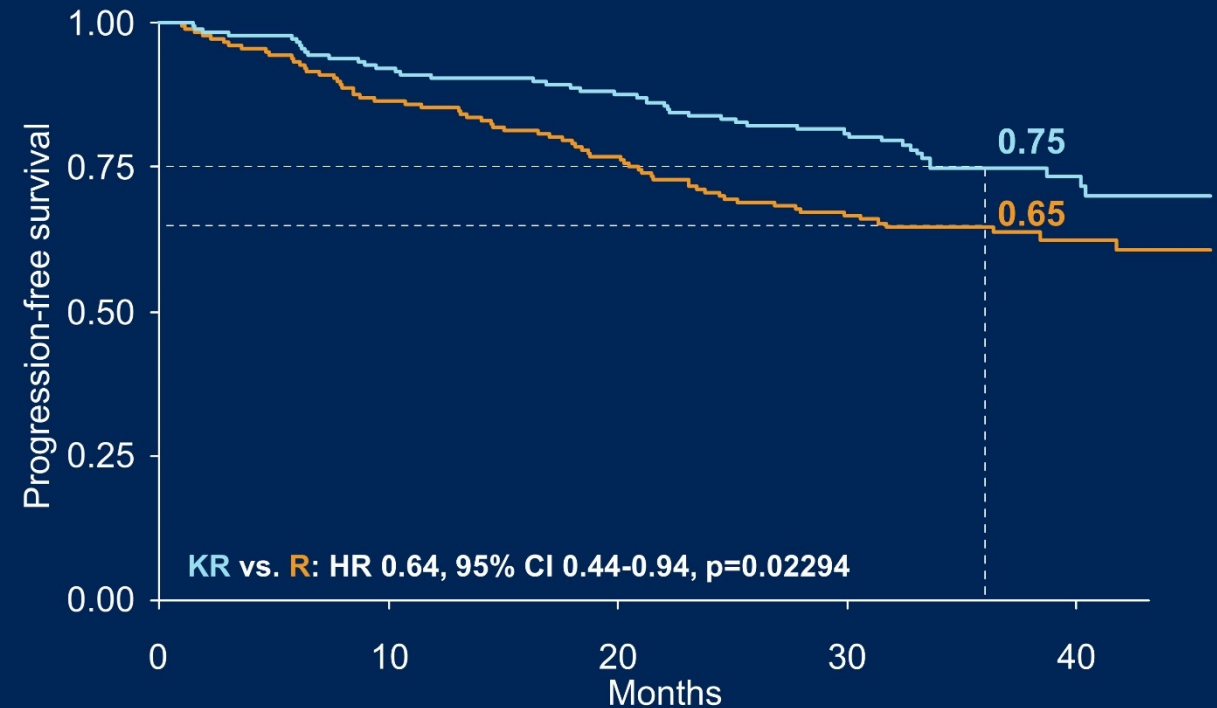
KRd_ASCT vs. KRd12 vs. KCd_ASCT

KR vs. R

Median follow-up from Random 1: 51 months (IQR 46–55)



Median follow-up from Random 2: 37 months (IQR 33–42)



3-year PFS reported in the figure. Random 1, first randomization (induction/consolidation treatment); ASCT, autologous stem-cell transplantation; K, carfilzomib; R, lenalidomide; C, cyclophosphamide; d, dexamethasone; KCd_ASCT, KCd induction-ASCT-KCd consolidation; KRd_ASCT, KRd induction-ASCT-KRd consolidation; KRd12, 12 cycles of KRd; Random 2, second randomization (maintenance treatment); p, p-value; HR, hazard ratio; CI, confidence interval.

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Francesca Gay

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Number at risk
KR vs R: HR 0.64, 95% CI 0.44 - 0.94, p-value=0.02294

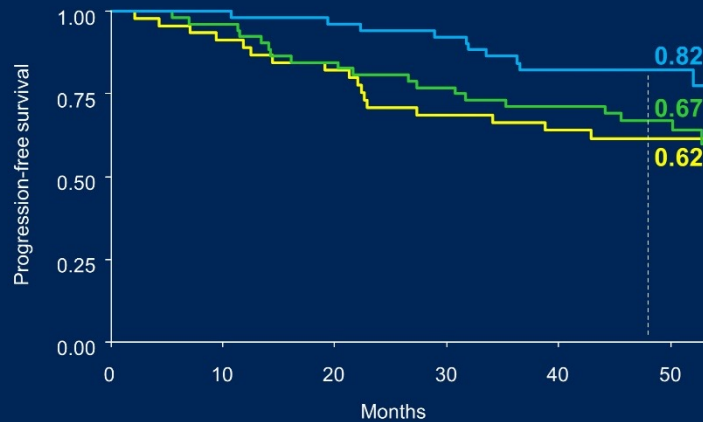
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ANNUAL MEETING

Progression-free survival: Random 1

KRd_ASCT vs. KRd12 vs. KCd_ASCT

Median follow-up from Random 1: 51 months (IQR 46-55)

Standard risk (N=153)

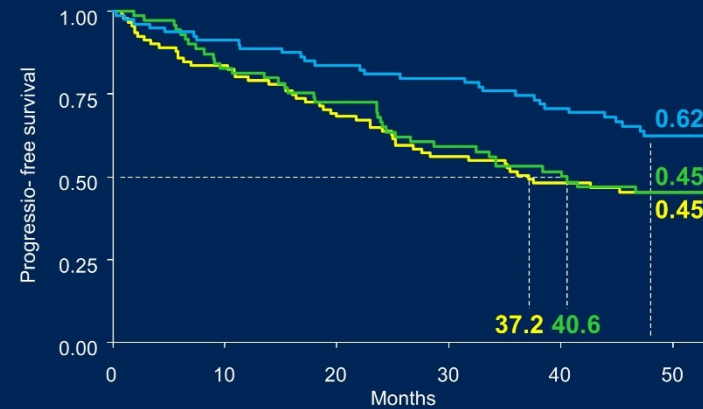


KRd_ASCT vs. KCd_ASCT: HR 0.44, p=0.04

KRd_ASCT vs. KRd12: HR 0.46, p=0.04

KRd12 vs. KCd_ASCT : HR 0.96, p=0.9

High risk (N=243)

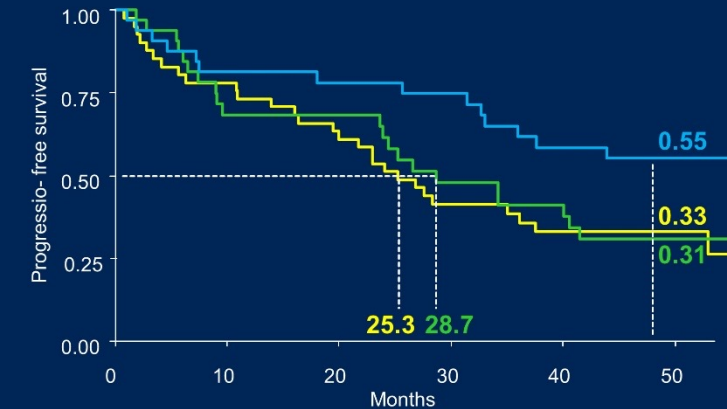


KRd_ASCT vs. KCd_ASCT: HR 0.57, p=0.01

KRd_ASCT vs. KRd12: HR 0.6, p=0.04

KRd12 vs. KCd_ASCT: HR 0.95, p=0.8

Double hit (N=105)



KRd_ASCT vs. KCd_ASCT: HR 0.49, p=0.03

KRd_ASCT vs. KRd12: HR 0.53, p=0.07

KRd12 vs. KCd_ASCT: HR 0.91, p=0.75

Random 1, first randomization (induction/consolidation treatment); ASCT, autologous stem-cell transplantation; K, carfilzomib; R, lenalidomide; C, cyclophosphamide; d, dexamethasone; KCd_ASCT, KCd induction-ASCT-KCd consolidation; KRd_ASCT, KRd induction-ASCT-KRd consolidation; KRd12, 12 cycles of KRd; HR, hazard ratio; CI, confidence interval; p, p-value; iQR, interquartile range.

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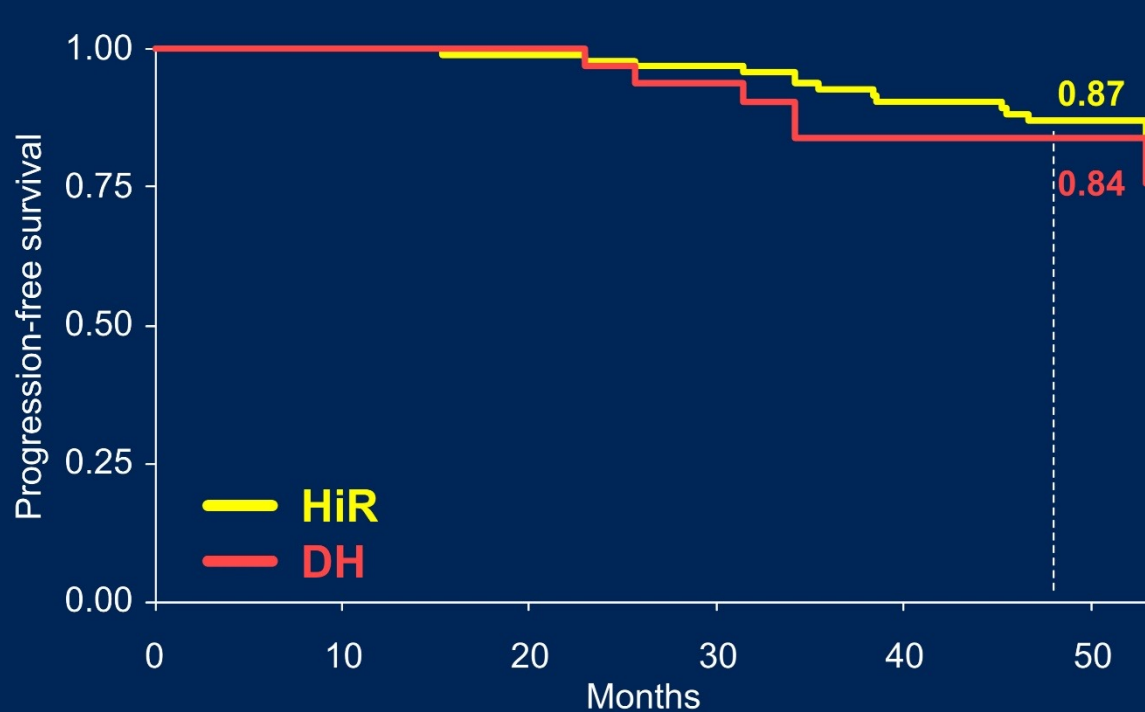
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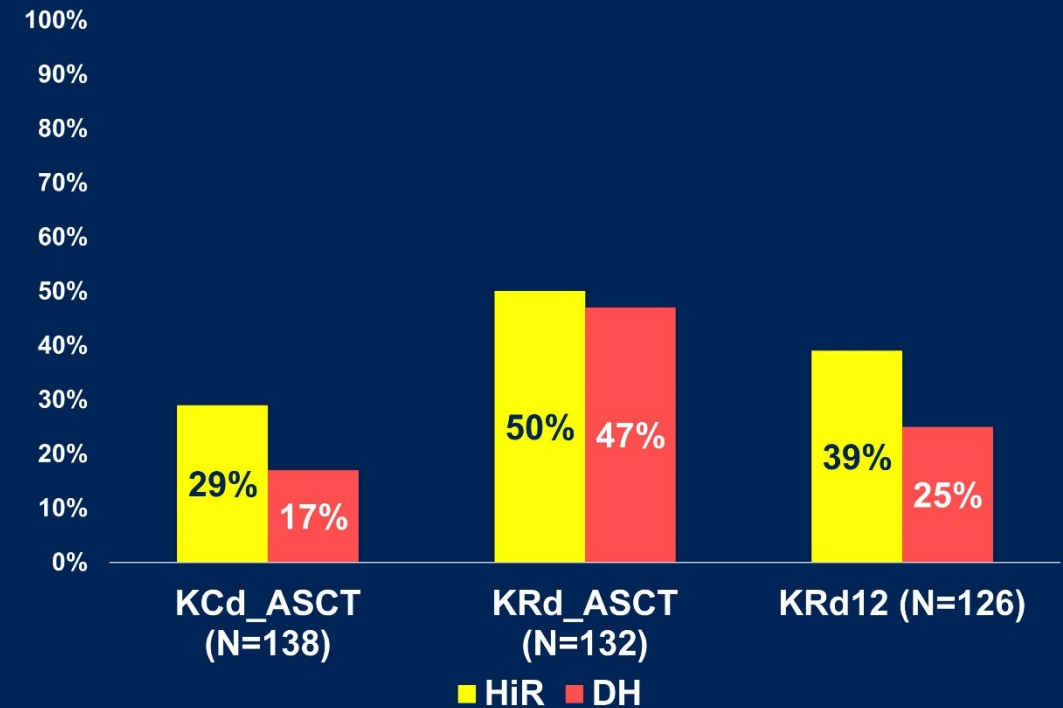
Sustained 1-year MRD negativity in High-risk patients

KRd_ASCT vs. KRd12 vs. KCd_ASCT

**4-year PFS
in 1-year sustained MRD-negative patients**



Sustained 1-year MRD negativity



ASCT, autologous stem-cell transplantation; K, carfilzomib; R, lenalidomide; C, cyclophosphamide; d, dexamethasone; KCd_ASCT, KCd induction-ASCT-KCd consolidation; KRd_ASCT, KRd induction-ASCT-KRd consolidation; KRd12, 12 cycles of KRd; MRD, minimal residual disease; HiR, high risk; DH, double hit; N, number; PFS, progression-free survival.

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IFM 2009 Study design

700 patients randomized stratified on ISS and FISH

Arm A – RVD alone

3 RVD

PBSC collection (cyclophosphamide 3g/m² and GCSF 10 µg/kg/d)

5 RVD

Lenalidomide maintenance 13 cycles (10-15 mg/d)

Arm B - Transplantation

3 RVD

**HD Melphalan 200 mg/m² +
ASCT**

2 RVD

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RVD 21d cycles

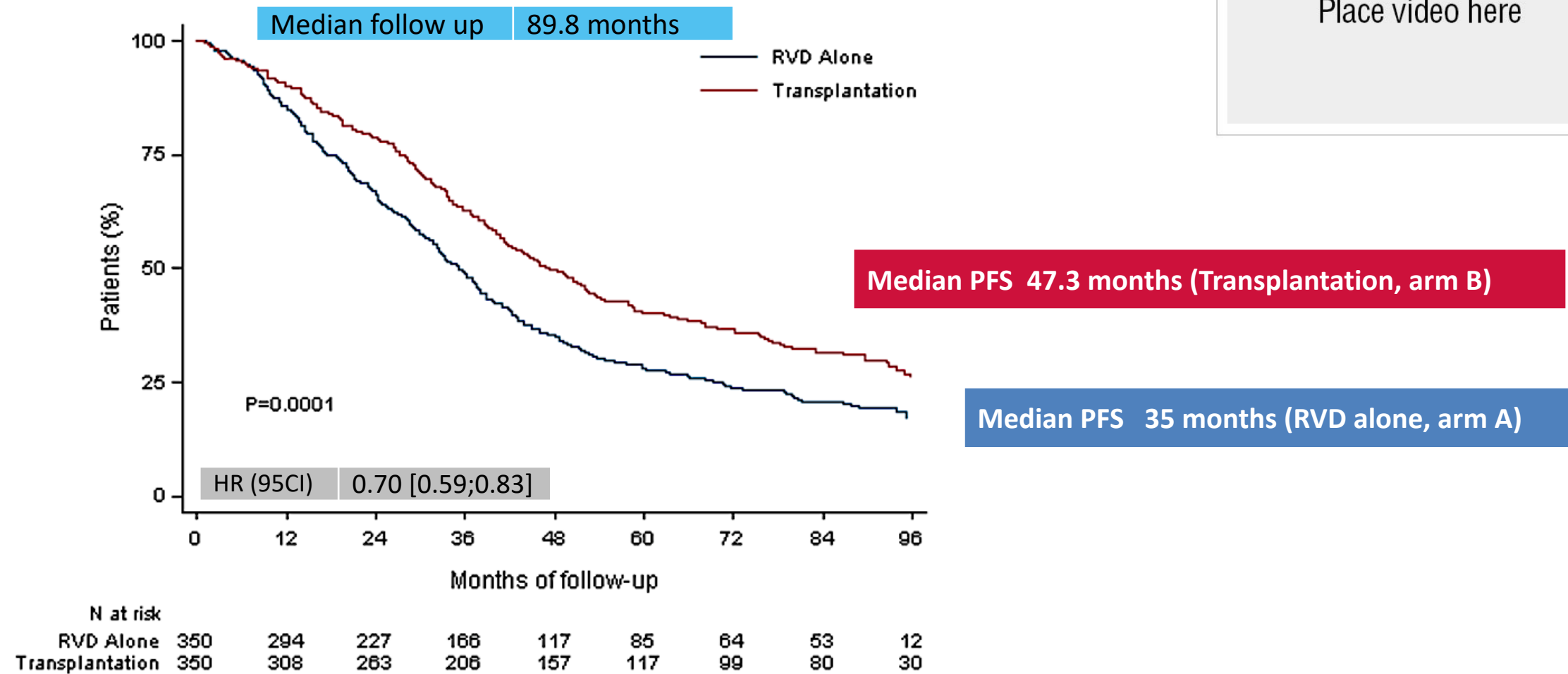
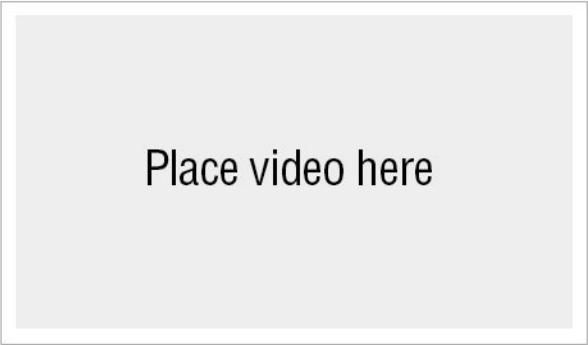
- . Lenalidomide 25 mg/d: D1-D14
- . Bortezomib 1.3 mg/m² D1, D4, D8, D11
- . Dexamethasone 20 mg/d: D1, D2, D4, D5, D8, D9, D11, D12

Primary endpoint = PFS

Secondary endpoints

- . ORR, MRD
- . TTP
- . OS
- . Toxicity

Updated PFS (primary endpoint)

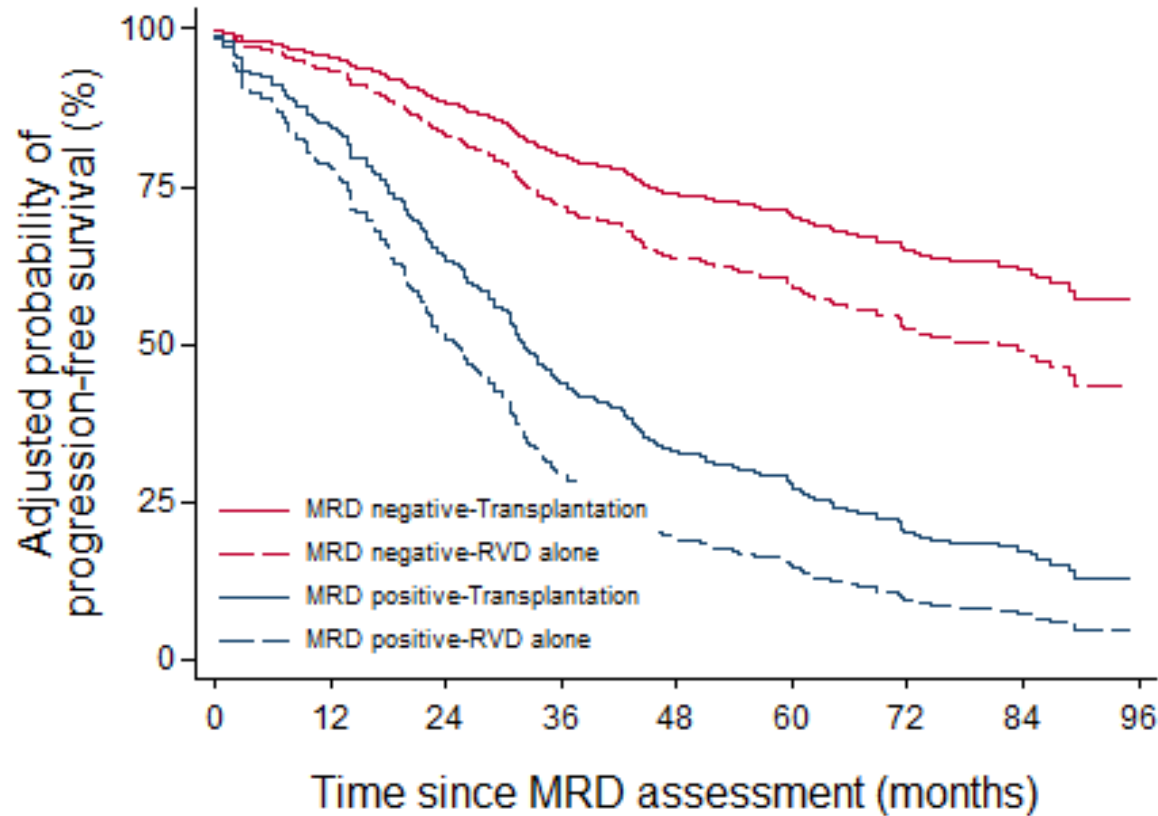


30% reduction in the risk of progression or death in patients receiving transplant

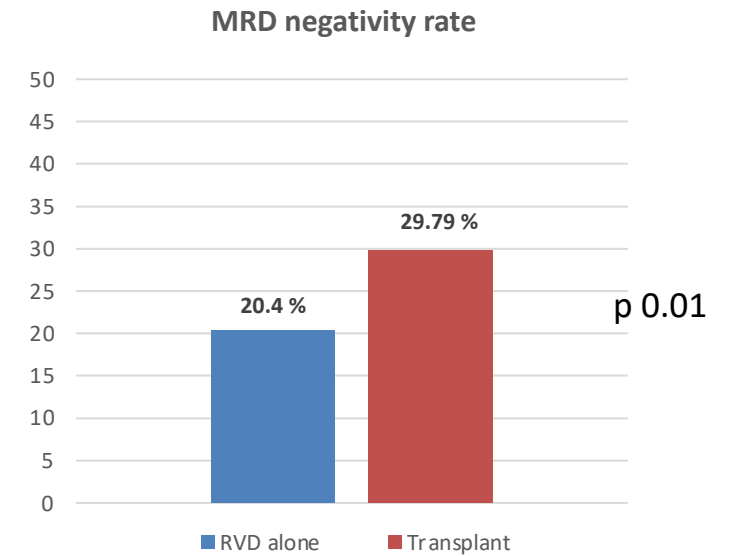


Subgroup analyses

Median follow up 89.8 months



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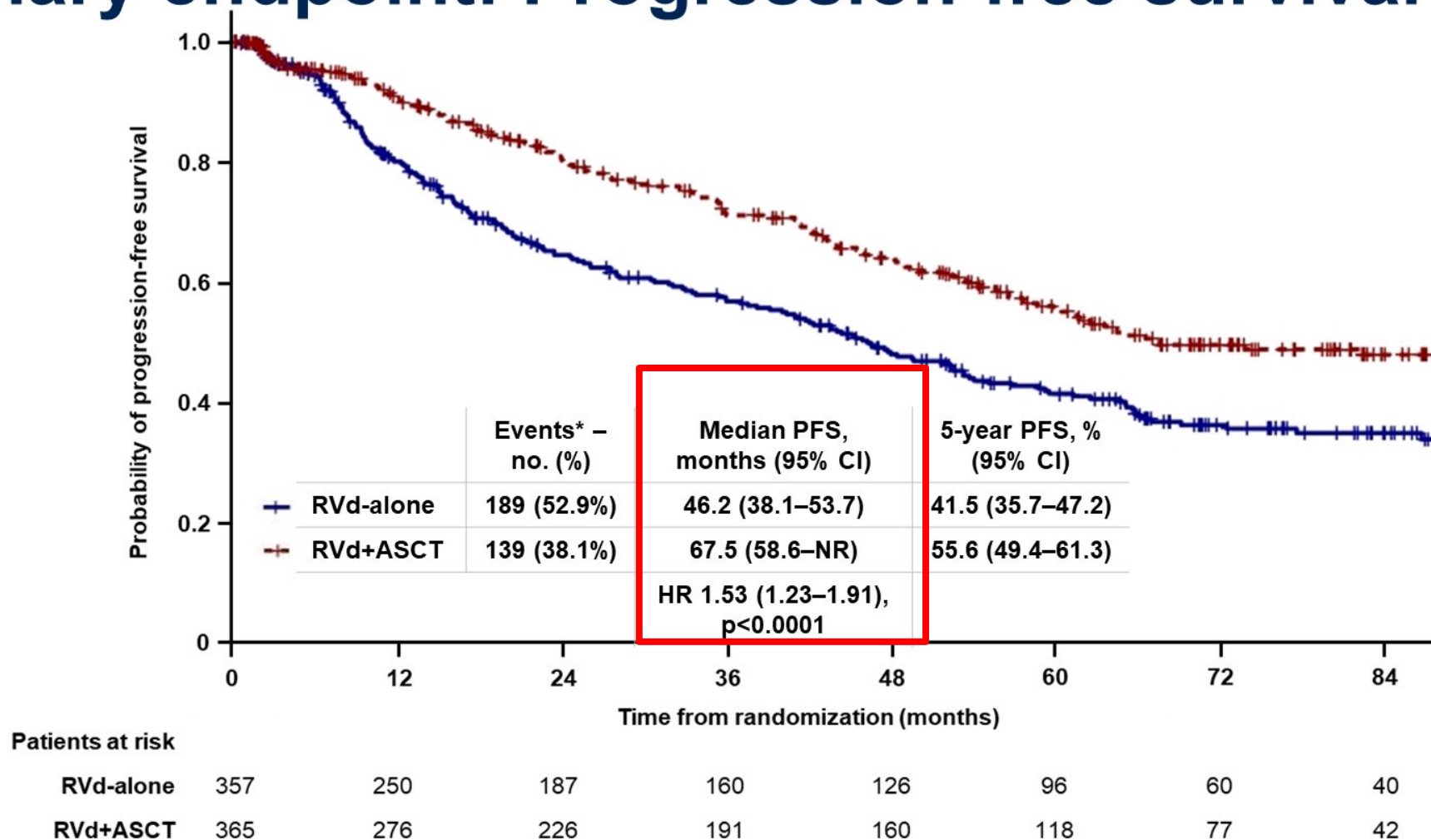
Transplant is superior to VRD alone, even in patients who achieved undetectable MRD at 10^{-6}

RVd ± ASCT and Lenalidomide Maintenance to Progression for NDMM

The Phase 3 DETERMINATION Trial

**Paul G. Richardson, MD, RJ Corman Professor of Medicine, Harvard Medical School
Clinical Program Leader, Director of Clinical Research,
Jerome Lipper Multiple Myeloma Center, Dana-Farber Cancer Institute, Boston, MA**

Primary endpoint: Progression-free survival (PFS)



CI, confidence interval; HR, hazard ratio; Data cutoff: 12/10/21. *PFS events: disease progression or death.

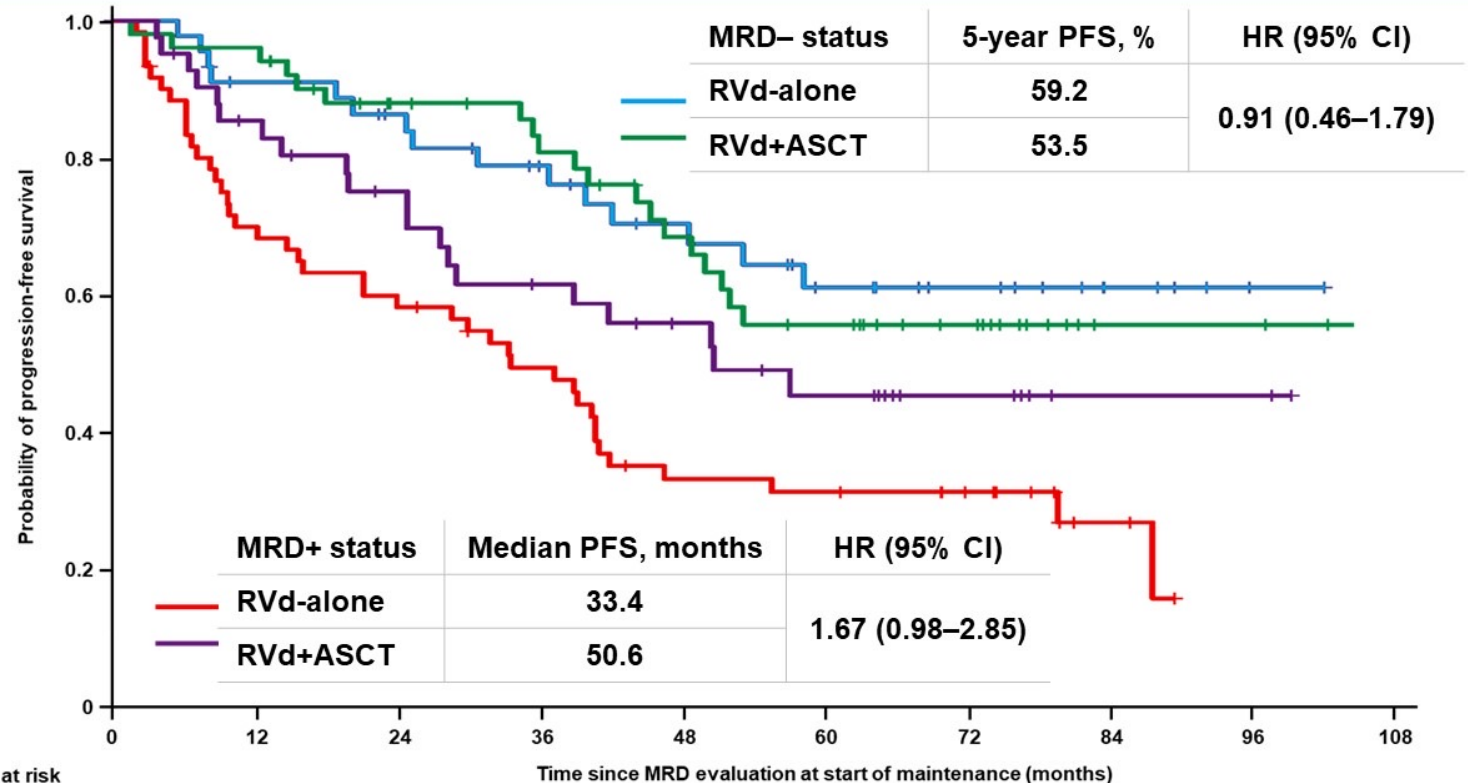
MRD / PFS by MRD status

Preliminary analysis

108 RVd-alone, 90 RVd+ASCT
patients with samples from
start of maintenance

Rate of MRD-negative status
(NGS, 10^{-5}):
39.8% vs 54.4%

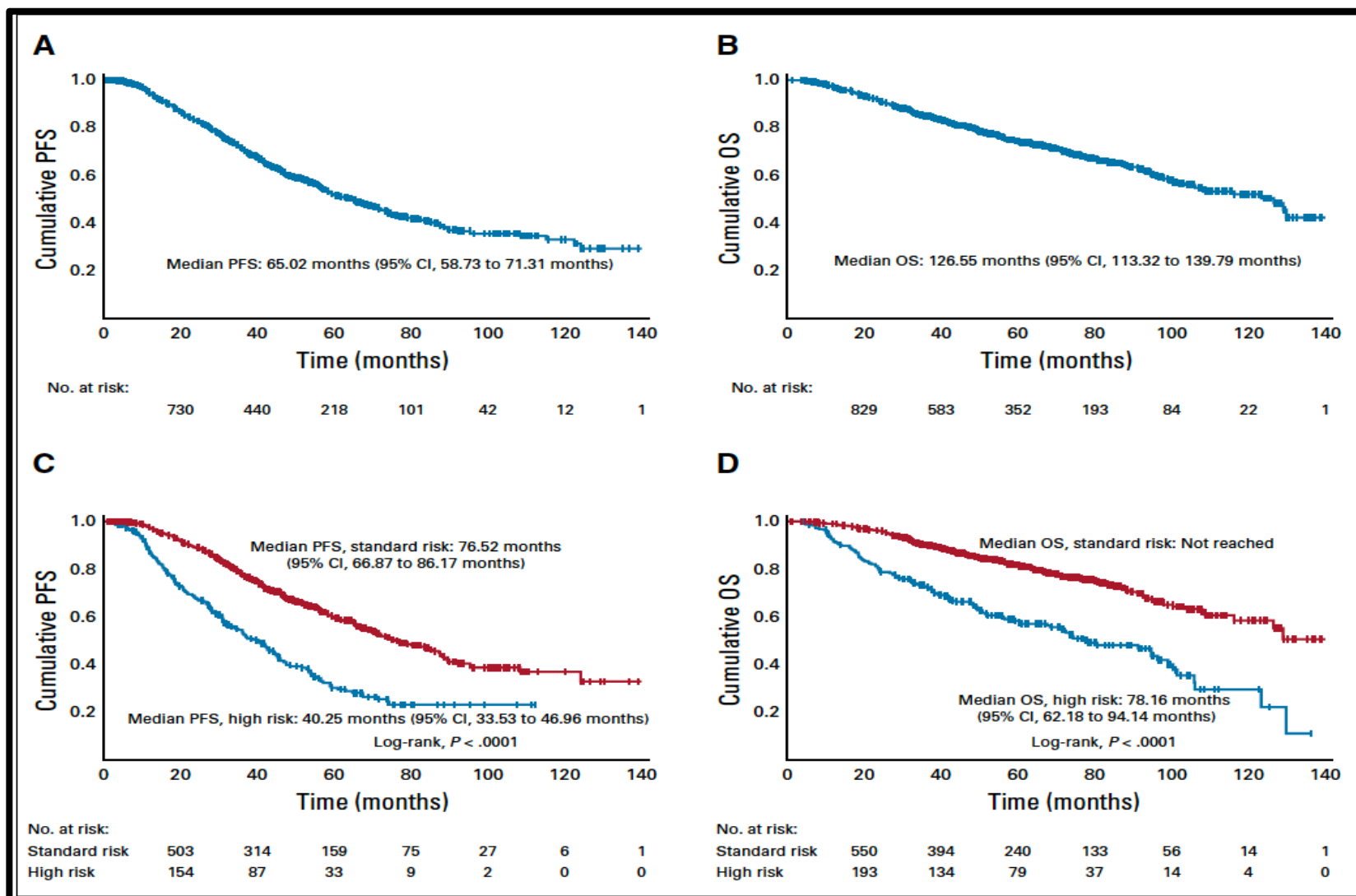
Odds ratio 0.55 (unadjusted
95% CI 0.30–1.01)



Patients at risk

| | 0 | 12 | 24 | 36 | 48 | 60 | 72 | 84 | 96 | 108 |
|-----------------|----|----|----|----|----|----|----|----|----|-----|
| RVd-alone, MRD- | 43 | 37 | 33 | 28 | 22 | 16 | 11 | 5 | 1 | 0 |
| RVd+ASCT, MRD- | 49 | 47 | 37 | 32 | 25 | 19 | 13 | 3 | 3 | 0 |
| RVd-alone, MRD+ | 65 | 39 | 32 | 25 | 15 | 14 | 10 | 3 | 0 | 0 |
| RVd+ASCT, MRD+ | 41 | 32 | 26 | 20 | 15 | 11 | 6 | 2 | 2 | 0 |

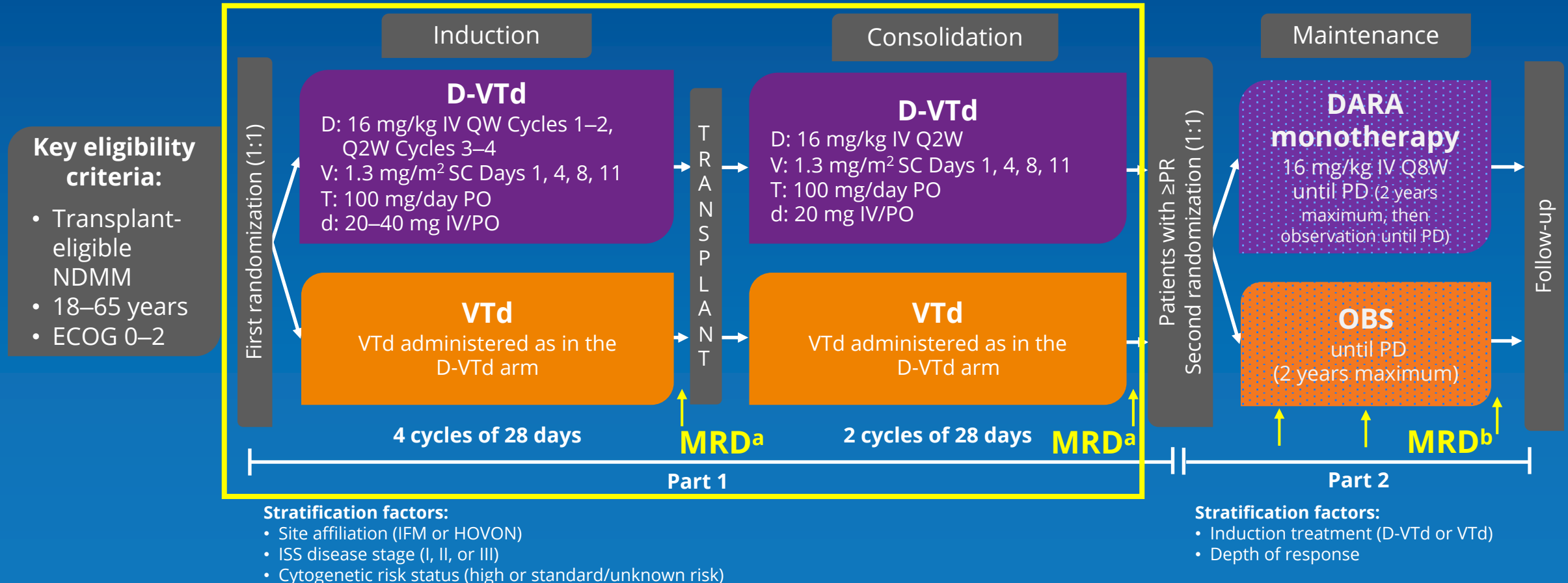
Outcomes From RVD 1000 Series



- RVD, lenalidomide, bortezomib, and dexamethasone combination therapy.
- Joseph NS, et al. J Clin Oncol. 2020;38:1928-1937.

CASSIOPEIA: Induction/Consolidation

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



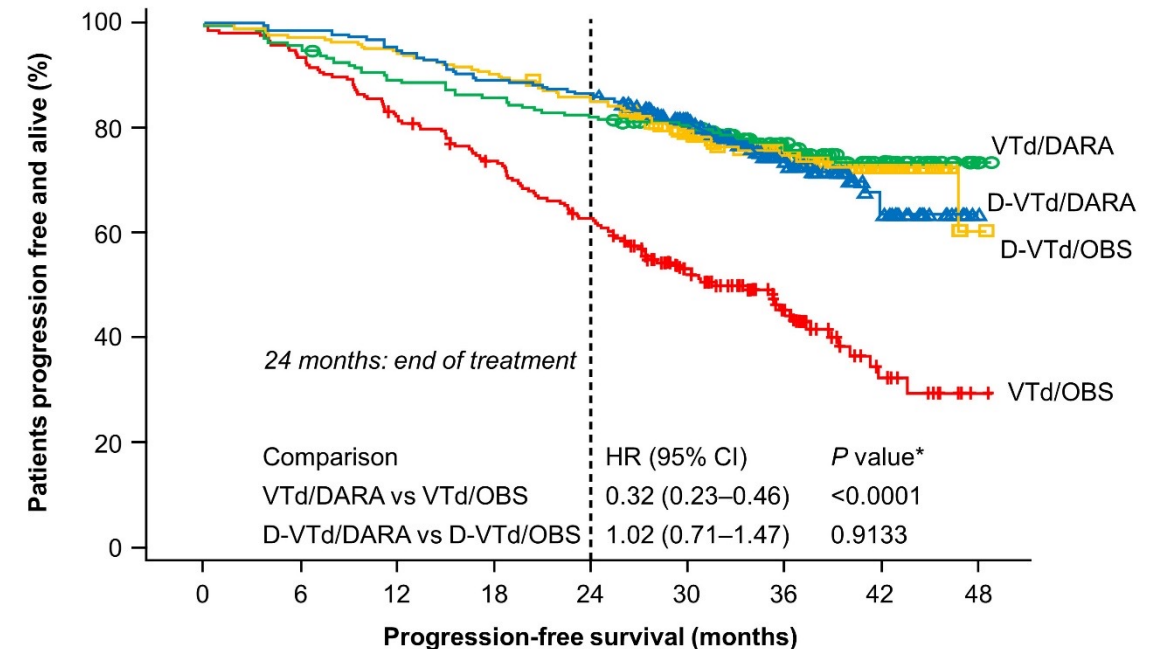
≥PR, partial response or better; IV, intravenous; Q8W, every 8 weeks; OBS, observation; ECOG, Eastern Cooperative Oncology Group; QW, every week; Q2W, every 2 weeks; SC, subcutaneous; PO, oral; IFM, Intergroupe Francophone du Myélome; HOVON, the Dutch-Belgian Cooperative Trial Group for Hematology-Oncology; ISS, International Staging System; PD, progressive disease; ≥VGPR, very good partial response or better.

^aMRD analyses were performed at predefined timepoints for all patients, regardless of response. ^bMRD analyses were performed in patients with ≥VGPR at Weeks 25, 52, and 105.



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

| | 0 | 6 | 12 | 18 | 24 | 30 | 36 | 42 | 48 |
|------------|-----|-----|-----|-----|-----|-----|----|----|----|
| 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 |

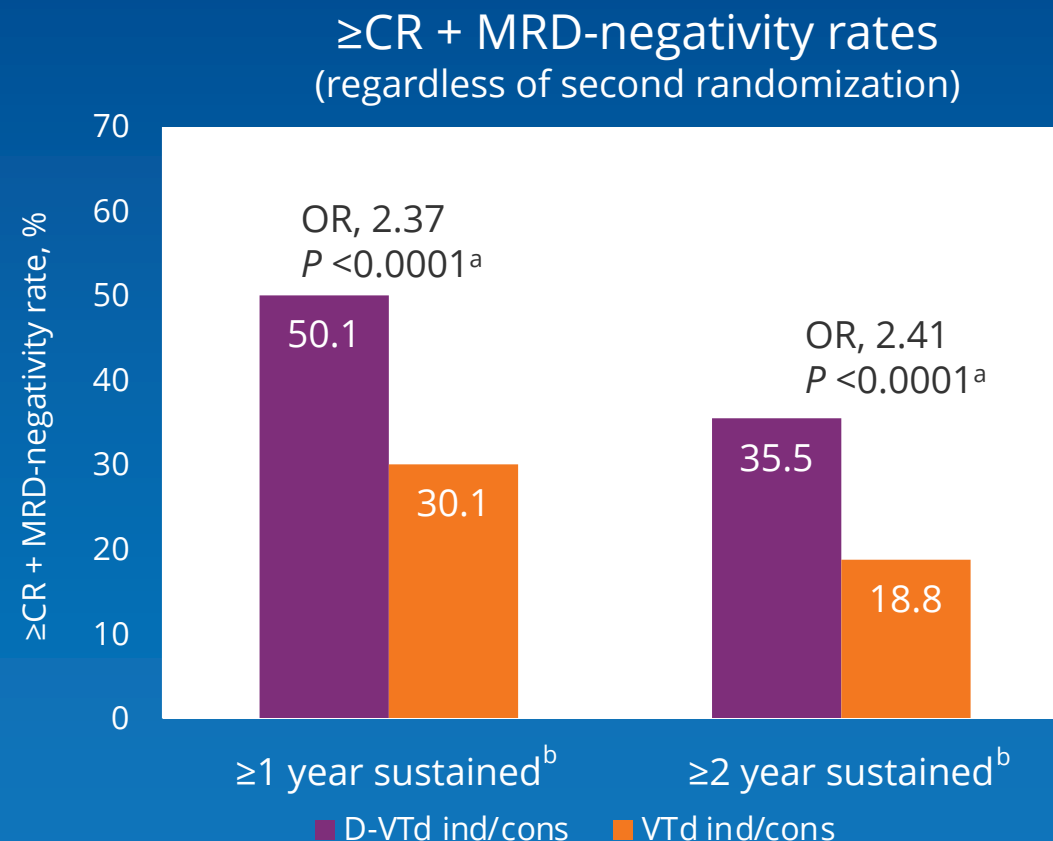
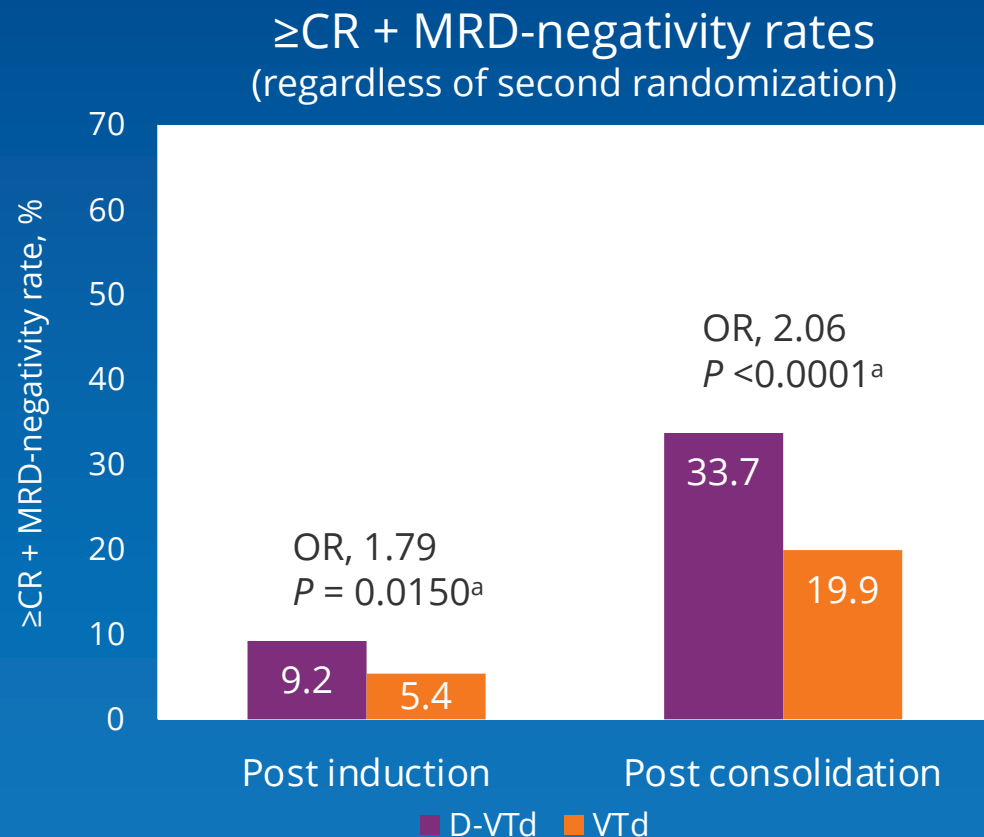
*Nominal P value.
 CI, confidence interval; D-VTd, daratumumab, bortezomib, thalidomide, and dexamethasone; DARA, daratumumab;
 HR, hazard ratio; OBS, observation; PFS, progression-free survival; VTd, bortezomib, thalidomide, and dexamethasone.

Presented By: Philippe Moreau

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



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

MFC, multiparametric flow cytometry.

^aCochran-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.



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. Voorhees²⁵

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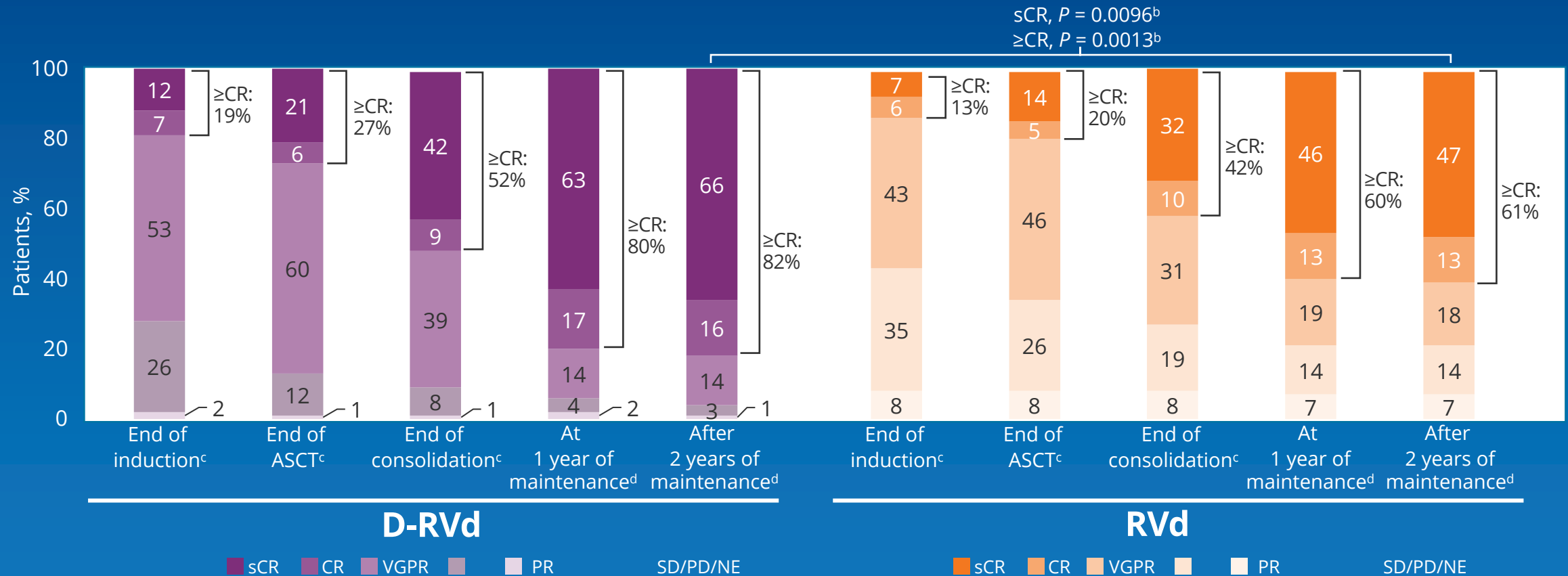
Presented at the 63rd American Society of Hematology (ASH) Annual Meeting & Exposition; December 11-14, 2021; Atlanta, GA/Virtual

*Presenting author.

Additional information can be viewed by scanning the QR code or accessing this link: <https://www.oncologysciencehub.com/ASH2021/Daratumumab/Laubach>. The QR code is intended to provide scientific information for individual reference, and the information should not be altered or reproduced in any way.



GRIFFIN: Responses Deepened Over Time^a

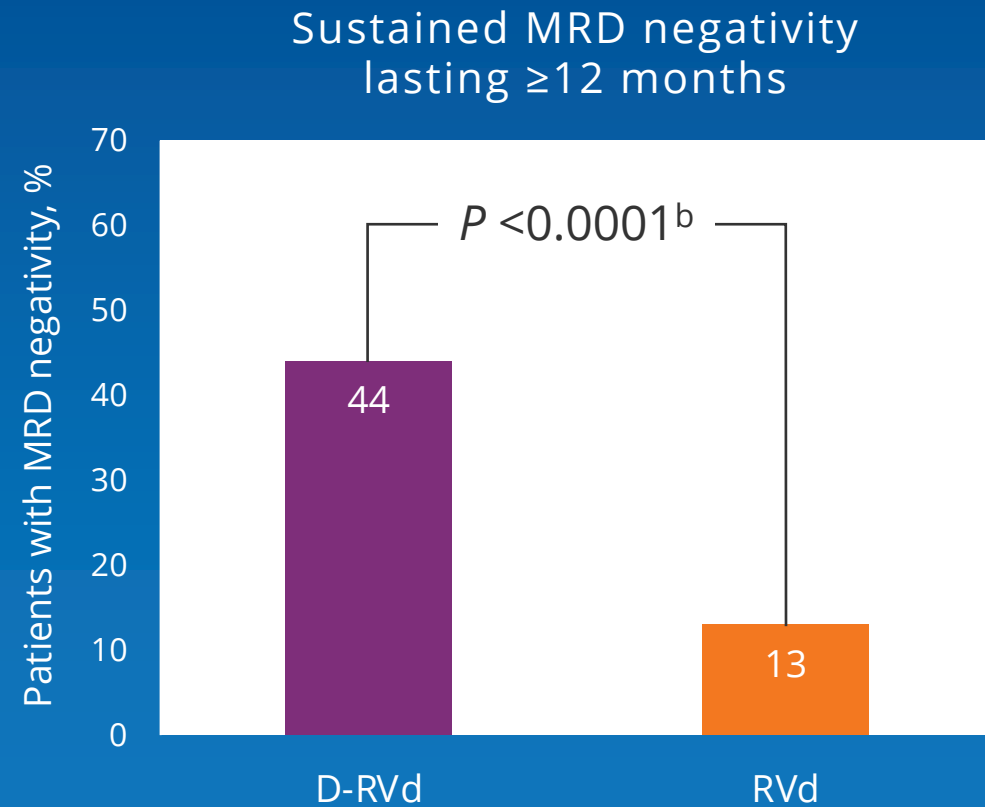
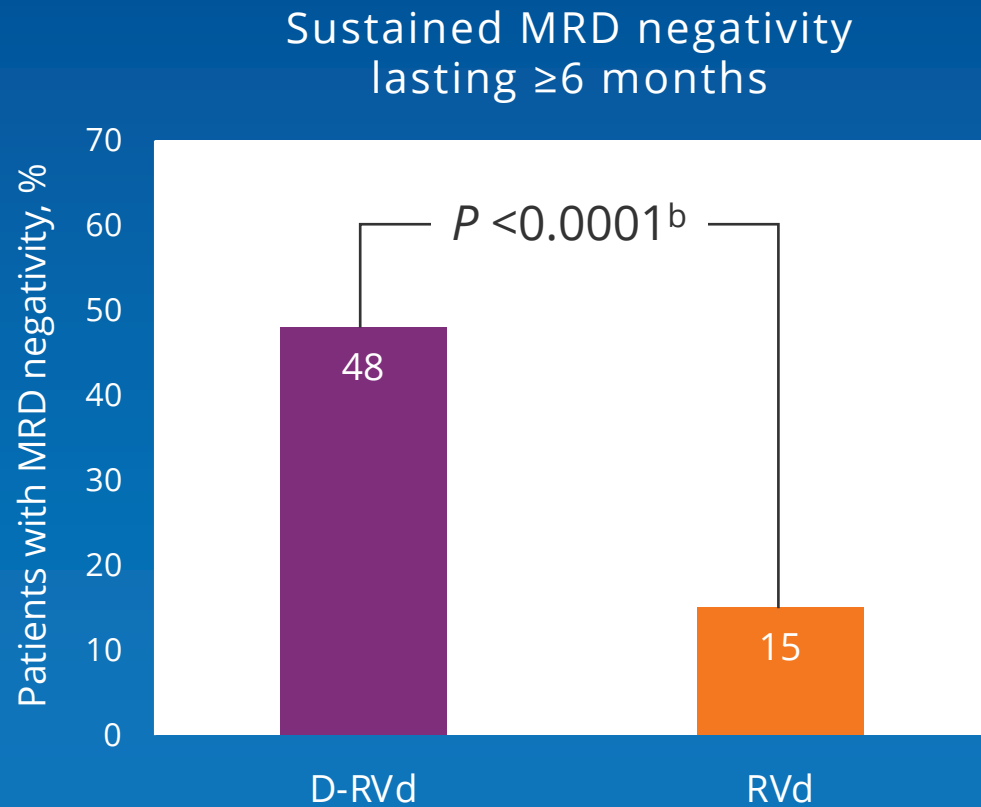


- Response rates for sCR and $\geq CR$ were greater for D-RVd versus RVd at all time points, with the deepest responses occurring after 2 years of maintenance therapy

PR, partial response; SD/PD/NE, stable disease/progressive disease/not evaluable. ^aData are shown for the response-evaluable population. ^bP values (2-sided) were calculated using the Cochran-Mantel-Haenszel chi-square test. ^cResponse 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). ^dResponse 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: D-RVd Improved Rates of Durable MRD Negativity^a (10^{-5}) Lasting ≥ 6 Months or ≥ 12 Months Versus RVd

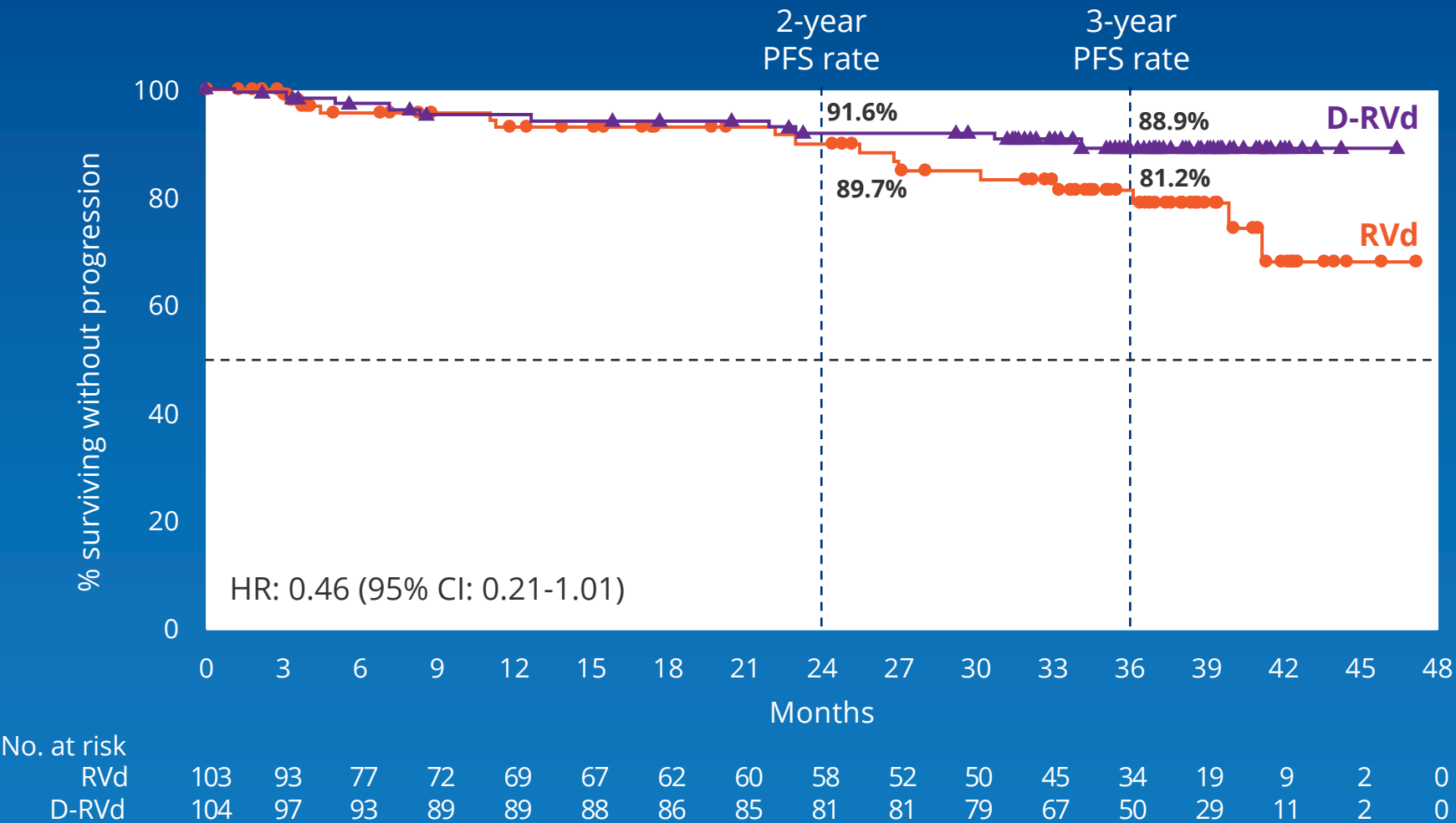


^aThe threshold of MRD negativity was defined as 1 tumor cell per 10^5 white cells. MRD status is based on the assessment of bone marrow aspirates by NGS in accordance with International Myeloma Working Group criteria. Median follow-up was 38.6 months, and MRD-negativity rates are among the ITT population (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.





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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. Mai¹, Eva Nievergall¹, Roland Fenk³, Uta Bertsch^{1,2}, Diana Tichy⁴, Britta Besemer⁵, Jan Dürig⁶, Roland Schroers⁷, Ivana von Metzler⁸, Mathias Hänel⁹, Christoph Mann¹⁰, Anne Marie Asemissen¹¹, Bernhard Heilmeier¹², Stefanie Huhn¹, Katharina Kriegsmann¹, Niels Weinhold¹, Steffen Luntz¹³, Tobias A. W. Holderried¹⁴, Karolin Trautmann-Grill¹⁵, Deniz Gezer¹⁶, Maika Klaiber-Hakimi¹⁷, Martin Müller¹⁸, Cyrus Khandanpour¹⁹, Wolfgang Knauf²⁰, Markus Munder²¹, Thomas Geer²², Hendrik Riesenberger²³, Jörg Thomalla²⁴, Martin Hoffmann²⁵, Marc-Steffen Raab¹, Hans J. Salwender²⁶, Katja C. Weisel¹¹ for the German-speaking Myeloma Multicenter Group (GMMG)

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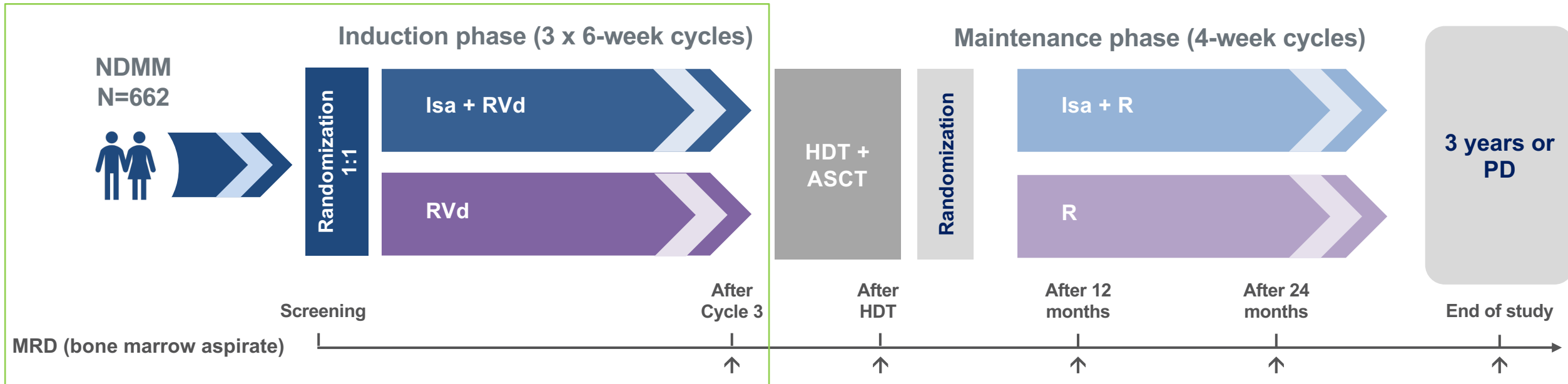
¹¹Department of Oncology, Hematology and BMT, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; ¹²Clinic for Oncology and Hematology, Hospital Barmherzige Brüder Regensburg, Regensburg, Germany; ¹³Coordination Centre for Clinical Trials (KKS) Heidelberg, Heidelberg, Germany; ¹⁴Department of Oncology, Hematology, Immuno-Oncology and Rheumatology, University Hospital Bonn, Bonn, Germany; ¹⁵Department of Internal Medicine I, University Hospital Dresden, Dresden, Germany; ¹⁶Department of Hematology, Oncology, Hemostaseology, and Stem Cell Transplantation, Faculty of Medicine, RWTH Aachen University, Aachen, Germany; ¹⁷Clinic for Hematology, Oncology and Palliative Care, Marien Hospital Düsseldorf, Düsseldorf, Germany; ¹⁸Clinic for Hematology, Oncology and Immunology, Klinikum Siloah Hannover, Hannover, Germany; ¹⁹Medical Clinic A, University Hospital Münster, Münster, Germany; ²⁰Center for Hematology and Oncology Bethanien, Frankfurt am Main, Germany;

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²³Hematology/Oncology Center, Bielefeld, Germany; ²⁴Hematology / Oncology Center, Koblenz, Germany; ²⁵Medical Clinic A, Clinic Ludwigshafen, Ludwigshafen, Germany;

²⁶Asklepios Tumorzentrum Hamburg, AK Altona and AK St. Georg, Hamburg, Germany

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:

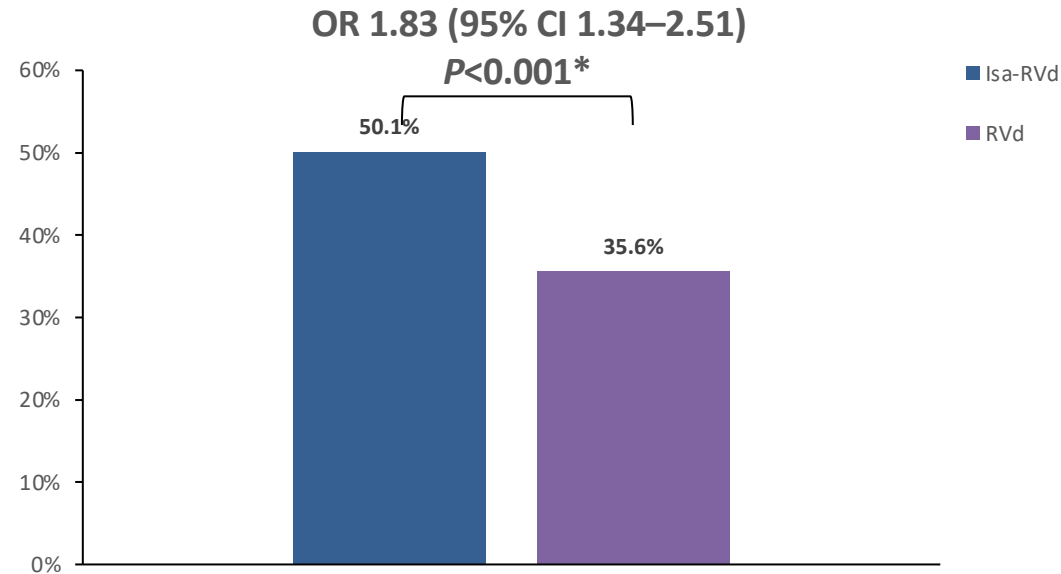
- CR after induction
- Safety

Data cut-off:

- April 2021

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

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

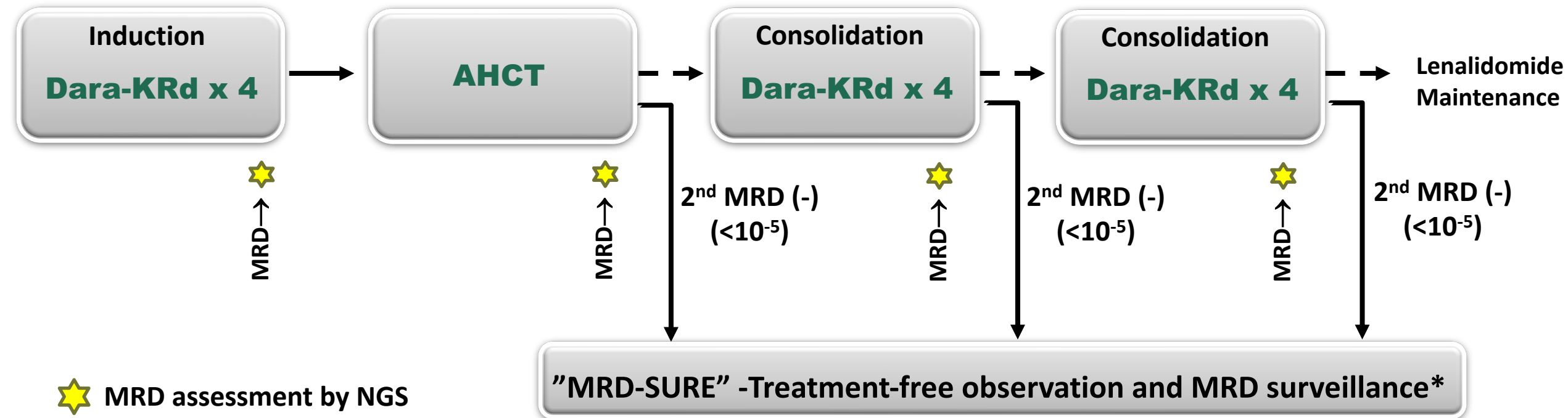
Luciano J. Costa¹, Saurabh Chhabra², Natalie S. Callander, MD³, Eva Medvedova⁴, Bhagirathbhai Dholaria⁵, Rebecca Silbermann⁴, Kelly Godby¹, Binod Dhakal², Susan Bal¹, Smith Giri¹, Anita D'Souza², Timothy Schmidt³, Aric Hall³, Pamela Hardwick¹, Robert F. Cornell⁵, Parameswaran Hari²

1- University of Alabama at Birmingham; 2- Medical College of Wisconsin; 3- University of Wisconsin at Madison;
4- Oregon Health and Science University; 5- Vanderbilt University

Treatment

Dara-KRd

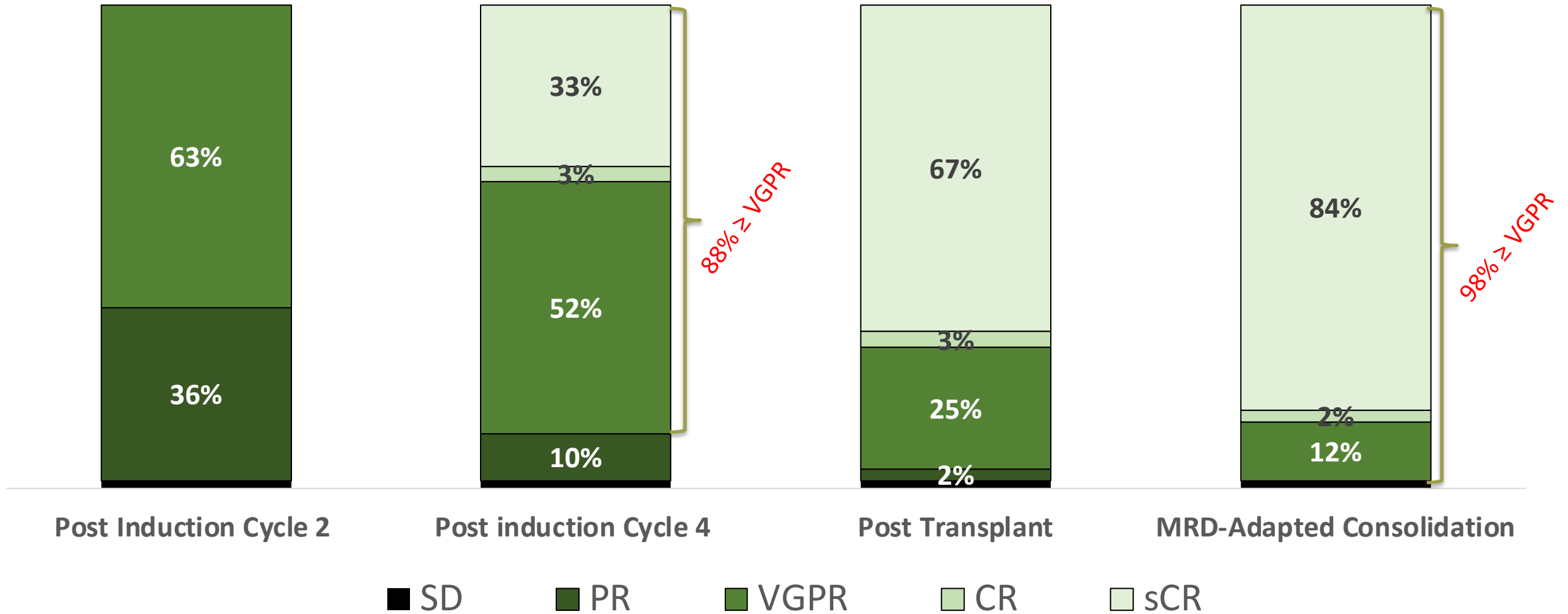
- Daratumumab 16 mg/m² days 1,8,15,22 (days 1,15 C 3-6; day 1 C >6)
- Carfilzomib (20) 56 mg/m² Days 1,8,15
- Lenalidomide 25 mg Days 1-21
- Dexamethasone 40mg PO Days 1,8,15,22



*24 and 72 weeks after completion of therapy

MASTER trial

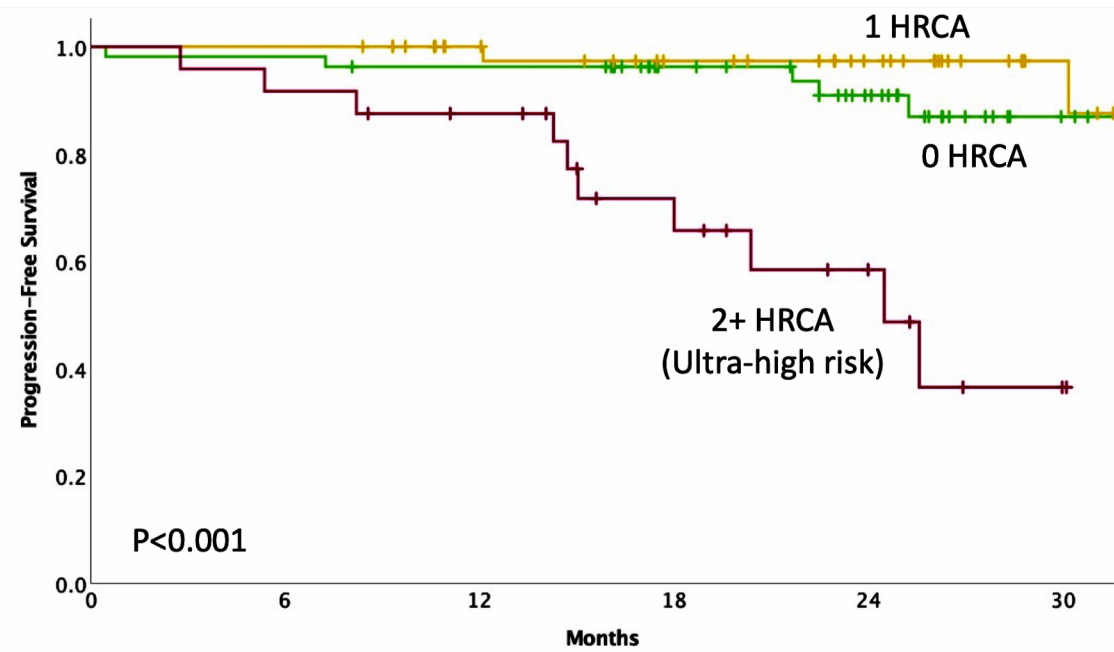
Best IMWG response by phase of therapy (ITT)



N=123

MASTER trial

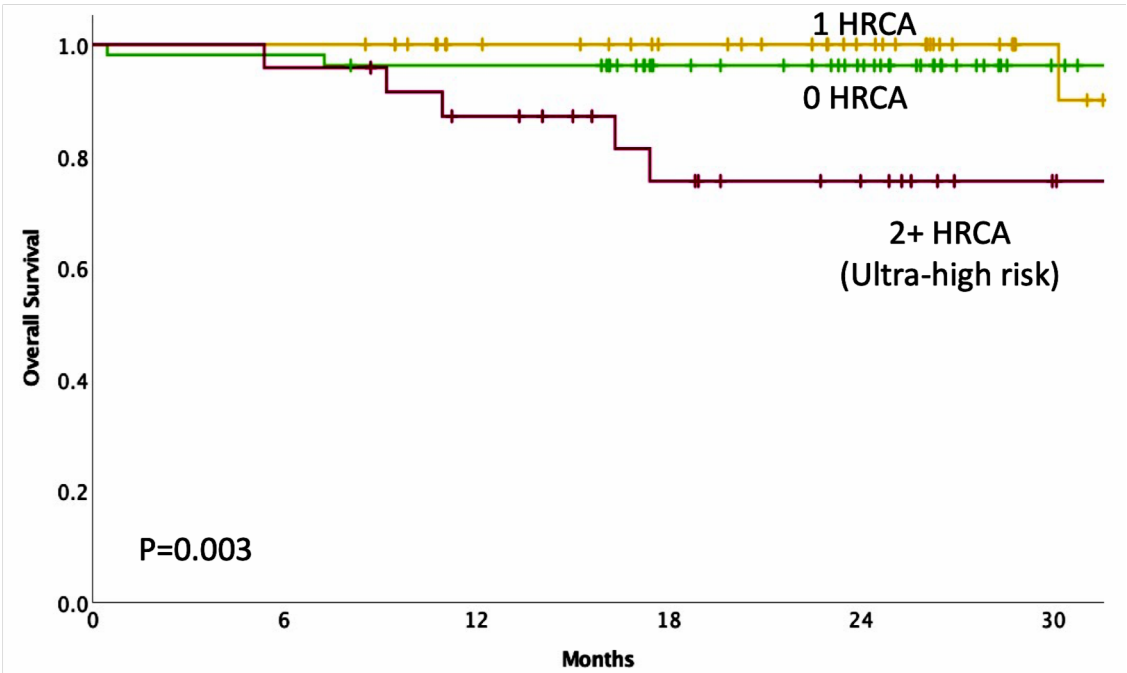
Progression-Free and Overall Survival



| | | | | | | |
|--------------|----|----|----|----|----|----|
| 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% |

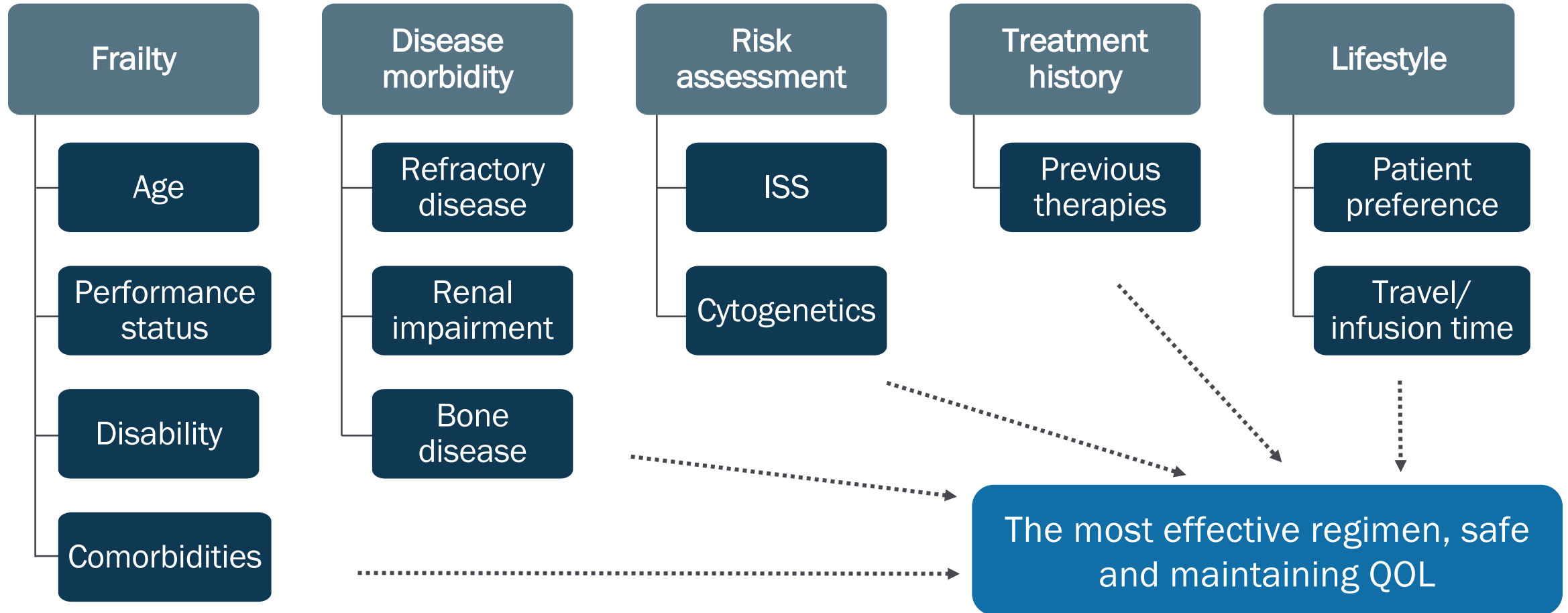
HRCA = gain/amp 1q, t(4;14), t(14;16), t(14;20) or del(17p)



| | | | | | | |
|--------------|----|----|----|----|----|----|
| 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% |

Disease and Patient Factors Influence Treatment Choices in Relapsed/Refractory MM



Questions in relapse

- How long was the first remission
- What is the patient progressing on (Len, Dara, Bz/Car?)
- Resistance/sensitivity drives choice of salvage therapy.
- Ideally if not CD38 resistant, then that becomes the backbone to which you add either an IMiD or PI

Backbones in MM: How to Decide



OR



OR



= CD38 + IMiD *or* CD38 + PI

CD38 monoclonal
antibodies

Immunomodulatory
agents

Proteasome
inhibitors

When choosing a combination in relapsed MM, the true backbone is a CD38 monoclonal antibody among patients who are not CD38-resistant

| Result | dara/len/dex ¹ vs len/dex | dara/car/dex ² vs car/dex | dara/pom/dex ³ vs pom/dex |
|---|---|---|--|
| Prior line of therapy median in months | 1 (1-11, range) 1 (1-8, range) | 2 (1-2, IQR) 2 (1-2, IQR) | 2 (2-3, IQR; 1-5 range) 2 (2-3, IQR; 1-5 range) |
| First relapse (%) | 52.1 51.6 | 46 45 | 11 12 |
| Len non refractory (%) | 100 100 | 68 64 | 21 20 |
| PFS (median in months) | 44.5 (HR 0.44) 17.5 | 28.6 (0.59) 15.2 | 12.4 (HR 0.63) 6.9 |
| PFS, not refractory to len | 44.5 (HR 0.44) 17.5 | 28.6 (HR 0.63) 19.9 | NE (HR 0.36) 10.6 |
| PFS, 1 st relapse | NR (HR 0.42) 19.6 | NE (HR 0.66) 21.3 | 14.1 (HR 0.70) 12.6 |
| 1 st relapse len refractory (%) | 0 0 | 6 4 | ≤ 11 ≤ 12 |

1. Leukemia. 2020 Jul;34(7):1875-1884. doi: 10.1038/s41375-020-0711-6. Epub 2020 Jan 30.

2. Lancet Oncol. 2021 Dec 3:S1470-2045(21)00579-9. doi: 10.1016/S1470-2045(21)00579-9.

3. Lancet Oncol. 2021 Jun;22(6):801-812. doi: 10.1016/S1470-2045(21)00128-5. PMID: 34087126

| Result | dara/len/dex ¹ vs len/dex | isa/car/dex ² vs car/dex | isa/pom/dex ³ vs pom/dex |
|---|---|--|--|
| Prior line of therapy median in months | 1 (1-11, range) 1 (1-8, range) | 2 (1-2, IQR) 2 (1-3, IQR) | 3 (2-4, range) 2 (2-4range) |
| First relapse (%) | 52.1 51.6 | 44 45 | 0 0 |
| Len non refractory (%) | 100 100 | 68 66 | 6 8 |
| PFS (median in months) | 44.5 (HR 0.44) 17.5 | NE (HR 0.53) 19.15 | 11.5 (HR 0.60) 6.5 |
| PFS, not refractory to len | 44.5 (HR 0.44) 17.5 | NC (HR 0.48) NC | 1/10* (HR 0.18) 7/13* |
| PFS, 1 st relapse | NR (HR 0.42) 19.6 | NC (HR 0.59) NC | N/A N/A |
| 1 st relapse len refractory (%) | 0 0 | NR NR | 0 0 |

1. Leukemia. 2020 Jul;34(7):1875-1884. doi: 10.1038/s41375-020-0711-6.

2. Lancet. 2021 Jun 19;397(10292):2361-2371. doi: 10.1016/S0140-6736(21)00592-4.

3. Lancet. 2019 Dec 7;394(10214):2096-2107. doi: 10.1016/S0140-6736(19)32556-5.

DPd in First Relapse: Emory Experience

Figure 1. Median Progression Free Survival in standard risk vs high risk patients treated with DPd at first relapse

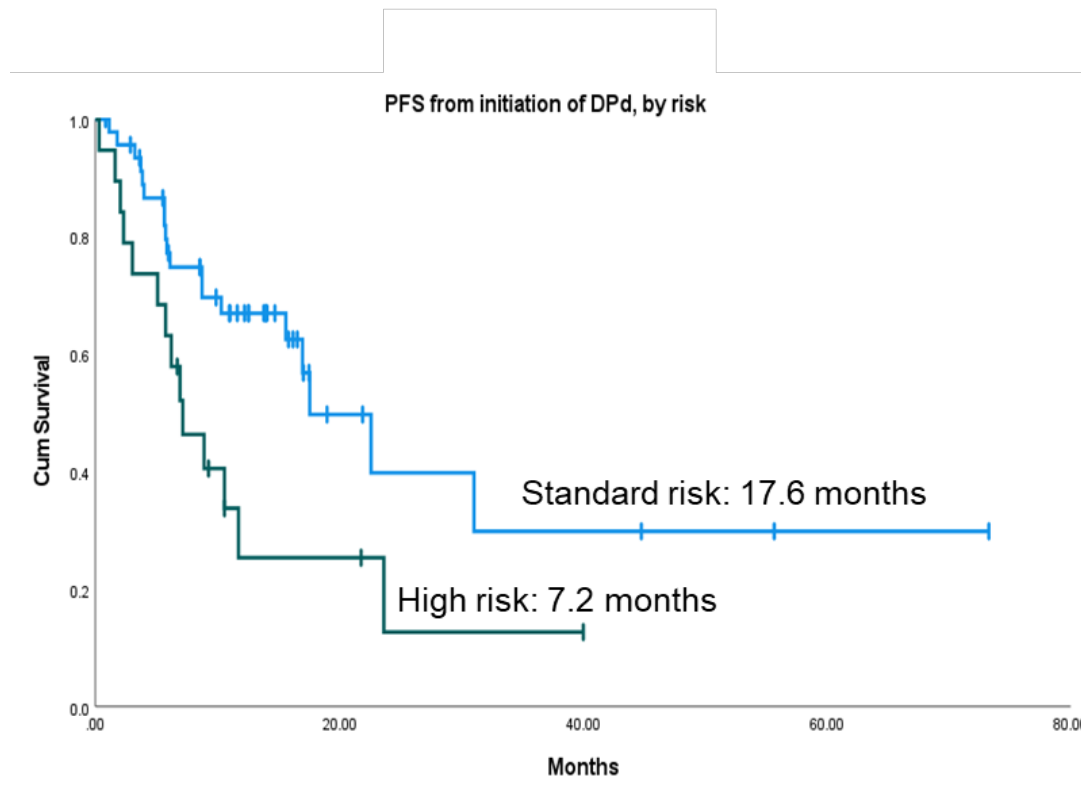
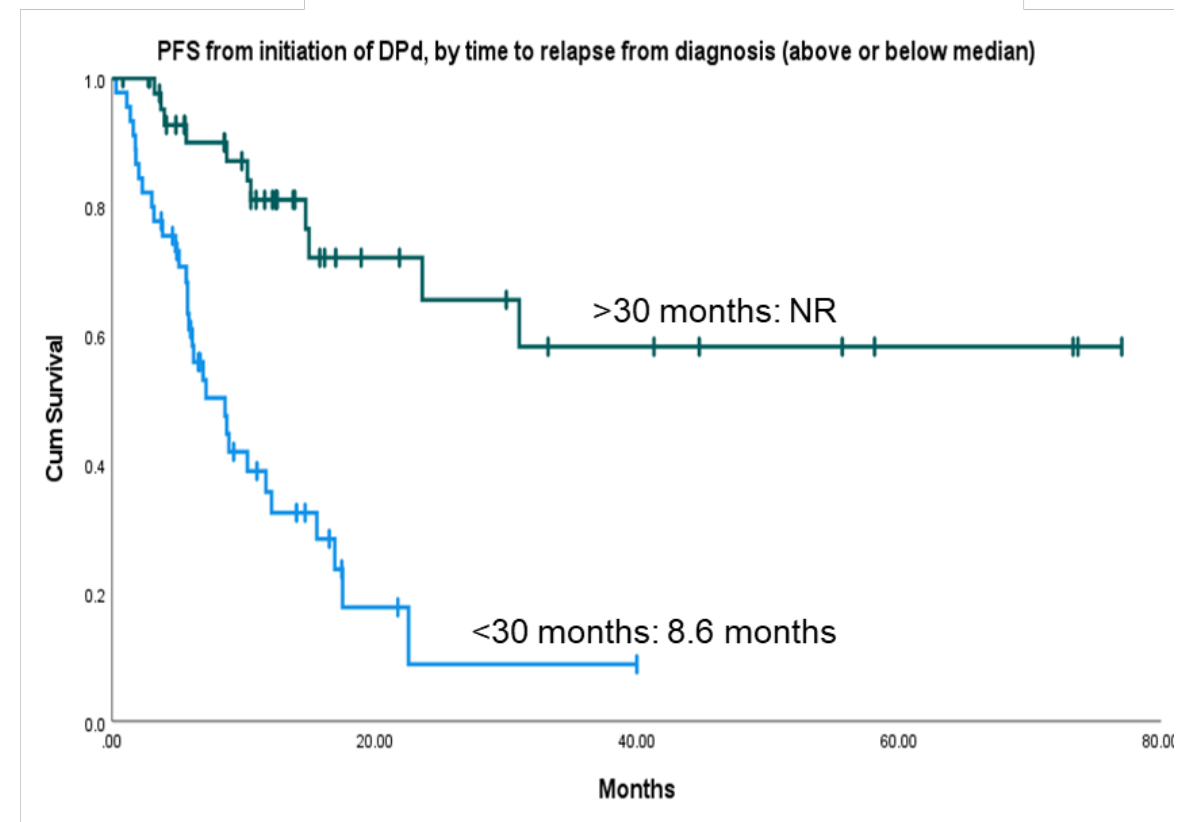


Figure 2. Median Progression Free Survival by time to first relapse from diagnosis (<30 months vs >30 months)



How to Choose

- If CD38 resistant go with IMiD and PI that have not been used
- If CD38 exposed but sensitive IMiD or PI partner based on tolerance and comorbidity
- If CD38 naïve, then consider early relapse approach with longest PFS to date
- Alternatives include Selinexor based combinations or venetoclax t(11;14)
- New targets such as CelMods, and other precision medicine approaches on the way

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Ben Barwick

And the Clinical Research Team

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Patients and Families



Golfers Against Cancer

T.J. Martell Foundation

**And Many Others who
are part of the B-cell Team**

