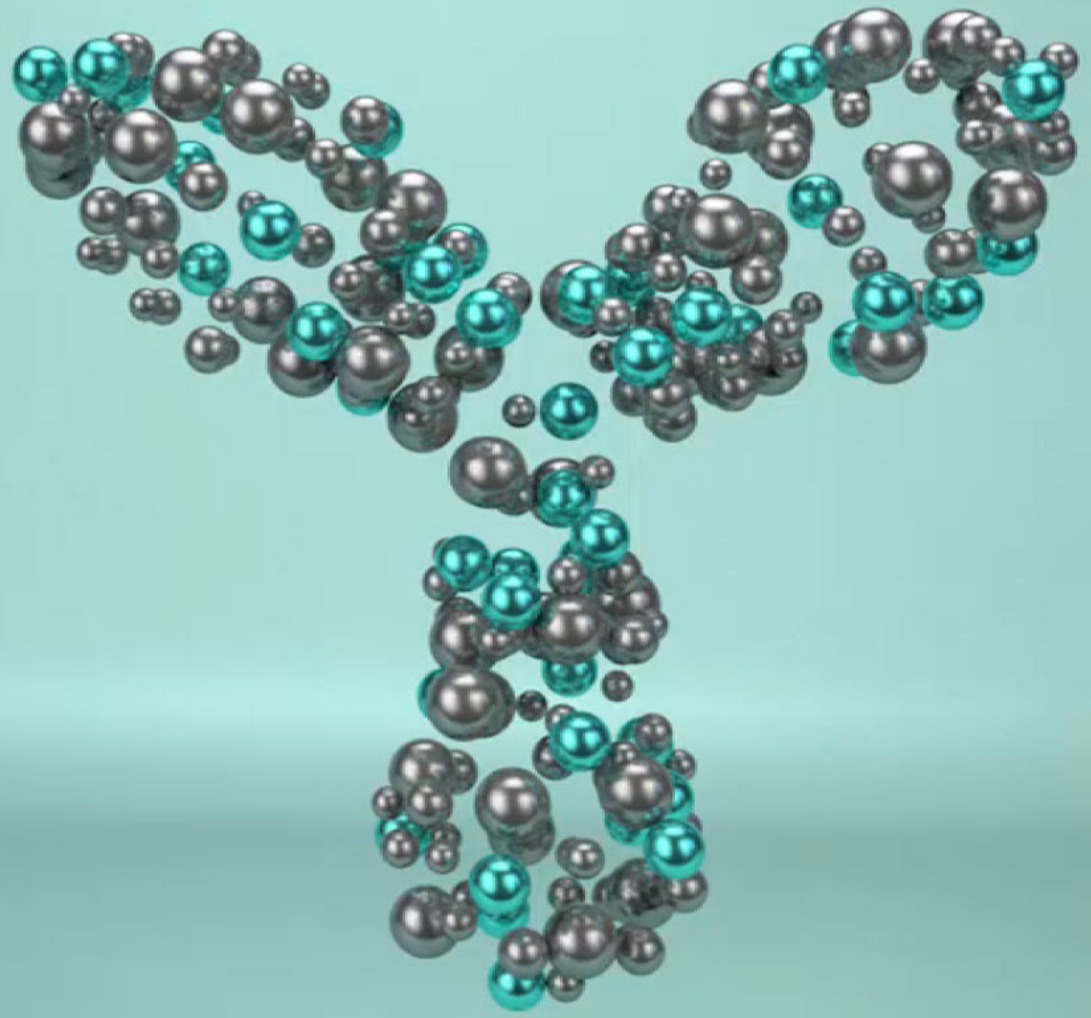
2020 Virtual ASH Data Review



December 8, 2020
Live via Webcast

Forward Looking Statement

This presentation contains forward looking statements. The words “believe”, “expect”, “anticipate”, “intend” and “plan” and similar expressions identify forward looking statements. All statements other than statements of historical facts included in this presentation, including, without limitation, those regarding our financial position, business strategy, plans and objectives of management for future operations (including development plans and objectives relating to our products), are forward looking statements. Such forward looking statements involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by such forward looking statements. Such forward looking statements are based on numerous assumptions regarding our present and future business strategies and the environment in which we will operate in the future. The important factors that could cause our actual results, performance or achievements to differ materially from those in the forward looking statements include, among others, risks associated with product discovery and development, uncertainties related to the outcome of clinical trials, slower than expected rates of patient recruitment, unforeseen safety issues resulting from the administration of our products in patients, uncertainties related to product manufacturing, the lack of market acceptance of our products, our inability to manage growth, the competitive environment in relation to our business area and markets, our inability to attract and retain suitably qualified personnel, the unenforceability or lack of protection of our patents and proprietary rights, our relationships with affiliated entities, changes and developments in technology which may render our products obsolete, and other factors. Further, certain forward looking statements are based upon assumptions of future events which may not prove to be accurate. The forward looking statements in this document speak only as at the date of this presentation. Genmab does not undertake any obligation to update or revise forward looking statements in this presentation nor to confirm such statements to reflect subsequent events or circumstances after the date made or in relation to actual results, unless required by law.

Agenda

12:30 PM	Welcome & Introduction: Transformational 2020	Dr. Jan van de Winkel, President & CEO
12:36 PM	Epcoritamab at ASH	Dr. Martin Hutchings, Department of Hematology, Rigshospitalet, Copenhagen University Hospital
12:46 PM	Daratumumab: ANDROMEDA	Professor Efstathios Kastritis, Department of Clinical Therapeutics, School of Medicine, National and Kapodistrian University of Athens
12:51 PM	Daratumumab: APOLLO, MAIA, GRIFFIN	Dr. Meletios A. Dimopoulos, School of Medicine, National & Kapodistrian University of Athens
1:08 PM	Live Q&A	
1:28 PM	2021 & Beyond: Positioned for Continued Success	Dr. Jan van de Winkel
1:35 PM	Live Q&A	

2020: A Transformational Year in Genmab's 21-Year Journey

Key Corporate Events

- AbbVie partnership
- Opening of cutting-edge labs in Princeton
- Growing internal capabilities to become end-to-end biotech including:
  - Translational Research
  - Data science
  - Medical Affairs

2020: A Transformational Year in Genmab's 21-Year Journey

Pipeline

- 1st epcoritamab[1] Phase 3 clinical trial
- DuoHexBody-CD37[1] (GEN3009) FiH
- DuoBody®-CD3x5T4[1] (GEN1044) IND & FiH
- HexaBody®-CD38[2] (GEN3014) IND

Data

- Epcoritamab: Oral presentation at ASH
- Tisotumab vedotin[3]: innovaTV 204 very favorable results, ESMO late-breaker
- DuoBody-PD-L1x4-1BB (GEN1046)[4]: First clinical data at SITC
- Daratumumab[5] positive data reported
  - CASSIOPEIA part 2
  - ANDROMEDA
  - APOLLO

Regulatory

- First BLA submission for a product candidate created using DuoBody
- US approvals for:
  - Kesimpta®[6]
  - TEPEZZA®[7]
  - DARZALEX *FASPRO*™[5]
- US & EU submissions
  - ANDROMEDA
  - APOLLO

1. 50/50 development with AbbVie Inc.; 2. Developing in an exclusive worldwide license and option agreement with Janssen Biotech, Inc.; 3. 50/50 development with Seagen Inc.; 4. 50/50 development with BioNTech SE; 5. Developed by Janssen Biotech, Inc.; 6. Developed by Novartis; 7. Developed by Horizon Therapeutics

Epcoritamab

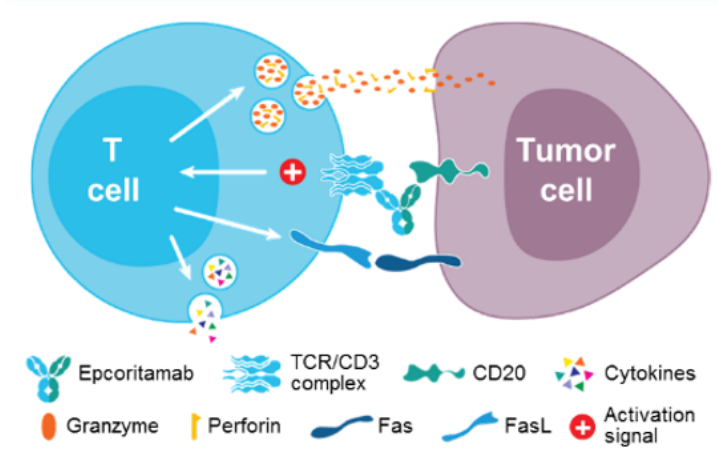
Presented by Dr. Martin Hutchings, Department of Hematology
Rigshospitalet, Copenhagen University Hospital

Subcutaneous Epcoritamab Induces Complete Responses with an Encouraging Safety Profile Across Relapsed/Refractory B-cell Non-hodgkin Lymphoma Subtypes, Including Patients with Prior CAR-T Therapy: Updated Dose-escalation Data

Martin Hutchings, MD, Phd

Background

- A significant proportion of patients with B-NHL relapse or become refractory to chemotherapy and traditional anti-CD20 treatment, facing poor outcomes as treatment options are limited by efficacy and toxicity[1–3]
- Epcoritamab (DuoBody®-CD3×CD20) is a subcutaneously administered bispecific antibody that induces T-cell–mediated killing of CD20-expressing tumors[4,5]
  - **Induces T-cell activation** by binding to CD3 on T cells and CD20 on malignant B cells
  - **Promotes immunological synapse** between bound cells, resulting in apoptosis of B cells
  - **Binds to a distinct epitope on CD20**, different from the epitopes of rituximab and obinutuzumab
  - **Retains activity** in the presence of CD20 mAbs



Epcoritamab is a novel, subcutaneously administered CD3×CD20 bispecific antibody

Epcoritamab Distinguishing Features

Subcutaneous administration

- Rapid, low-volume (1 mL) administration
- More gradual increase and lower peak in plasma cytokine levels compared with intravenous administration[1,2]
- Long plasma half-life[1]
- Favorable safety profile[3]

Potency

- High affinity and preclinical potency[1]
- T-cell–mediated killing occurs even at low CD20 expression levels[1]

Availability

- Off-the-shelf production offers timely treatment and consistency[4]

Dose

- RP2D of 48 mg was determined by clinical findings and informed by a novel PK/PD model that incorporates preclinical, clinical, and biomarker data (ASH 2020 poster 2790)[3,5]

Updated data are presented from the first-in-human trial with longer follow-up

1. Engelberts PJ, et al. EBioMedicine. 2020;52:102625; 2. Chiu C, et al. EHA 2020. EP1330; 3. Hutchings M, et al. ASCO 2020. 8009; 4. Strohl WR, Naso M. Antibodies. 2019;8:41; 5. Li T, et al. ASH 2020. 2790

GCT3013-01: Phase I/II Study Design

Dose escalation*

Expansion part

Flat-dose epcoritamab administered in 28-day cycles until disease progression or unacceptable toxicity

Objectives

Primary

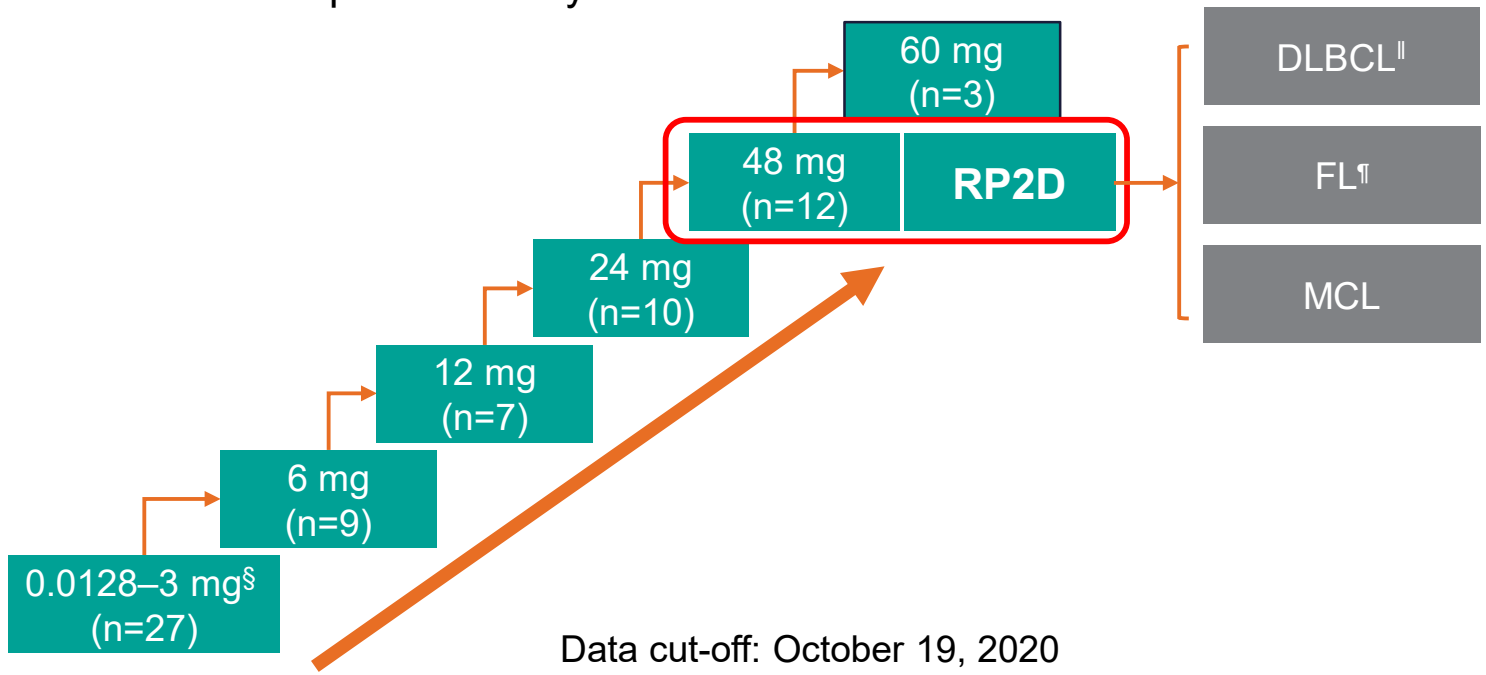
- Maximum tolerated dose (MTD)
- Recommended Phase II dose (RP2D)

Secondary

- Safety/tolerability
- Anti-tumor activity

Inclusion criteria†

- Adults with R/R CD20+ B-NHL
- Prior treatment with anti-CD20 mAbs
- ECOG PS 0–2
- Measurable disease by CT, MRI, or PET/CT scan‡
- Adequate renal, liver, and hematologic function



Data cut-off: October 19, 2020

RP2D determined to be 48 mg. Expansion part is enrolling

*Modified Bayesian optimal interval design consisting of accelerated and standard titration. Accelerated titration includes single-patient cohorts; up to 2 patients may be added (at the currently investigated dose) to obtain additional PK/PD biomarker data. †Patients previously treated with CAR-T cell therapy were allowed (protocol amended after study start). ‡CT or MRI scans: Weeks 6, 12, 18, 24, and every 12 weeks thereafter. PET scans not required in all patients. §Includes the following priming/final dose levels (mg): 0.004/0.0128, 0.0128/0.04, 0.04/0.12, 0.12/0.38, 0.04/0.76, 0.04/0.25/1.5, 0.04/0.5/3. ‖Includes patients with DLBCL or other aggressive histologies. ¶Includes FL or other indolent histologies

Patient Disposition and Exposure

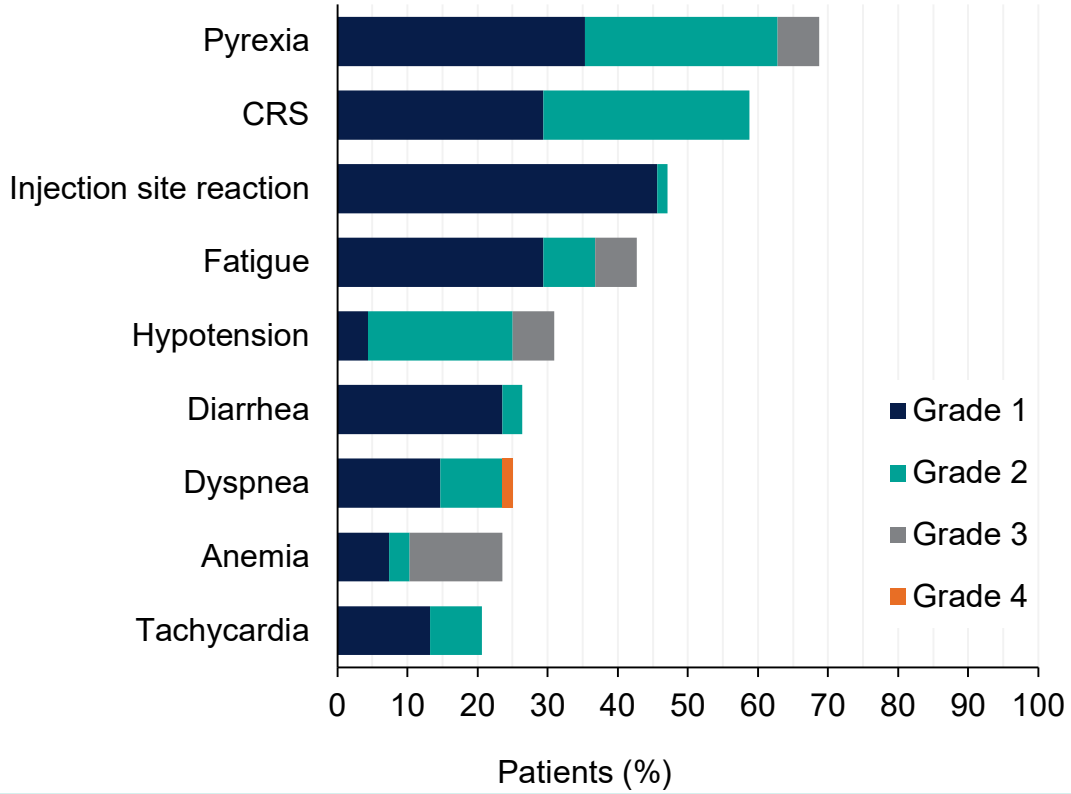
	All histologies (N=68)	DLBCL (n=46)	FL (n=12)
Treatment ongoing, n (%)	17 (25)	11 (24)	5 (42)
Treatment discontinued due to, n (%)			
Disease progression	45 (66)	30 (65)	7 (58)
Adverse events*	1 (2)	1 (2)	–
Initiation of new treatment (SCT)	3 (4)	3 (7)	–
Other†	2 (2)	1 (2)	–
Median duration of exposure, weeks (range)	11 (0–56)	7 (0–52)	26 (13–56)
Median duration of follow-up, months (range)	10 (0–19)	7 (1–19)	12 (4–17)

At a median follow-up of 10 months, treatment is still ongoing in 25% of patients.
There were no discontinuations due to treatment-related adverse events

*Patient had COVID-19. †Other includes death (n=1) and investigator/sponsor chose to discontinue treatment (n=1)

Adverse Events

Treatment-emergent adverse events ≥20%, all histologies



The majority of adverse events were Grade 1–2

Adverse event grading by CTCAE v5.0. Laboratory result grading by CTCAE v4.03

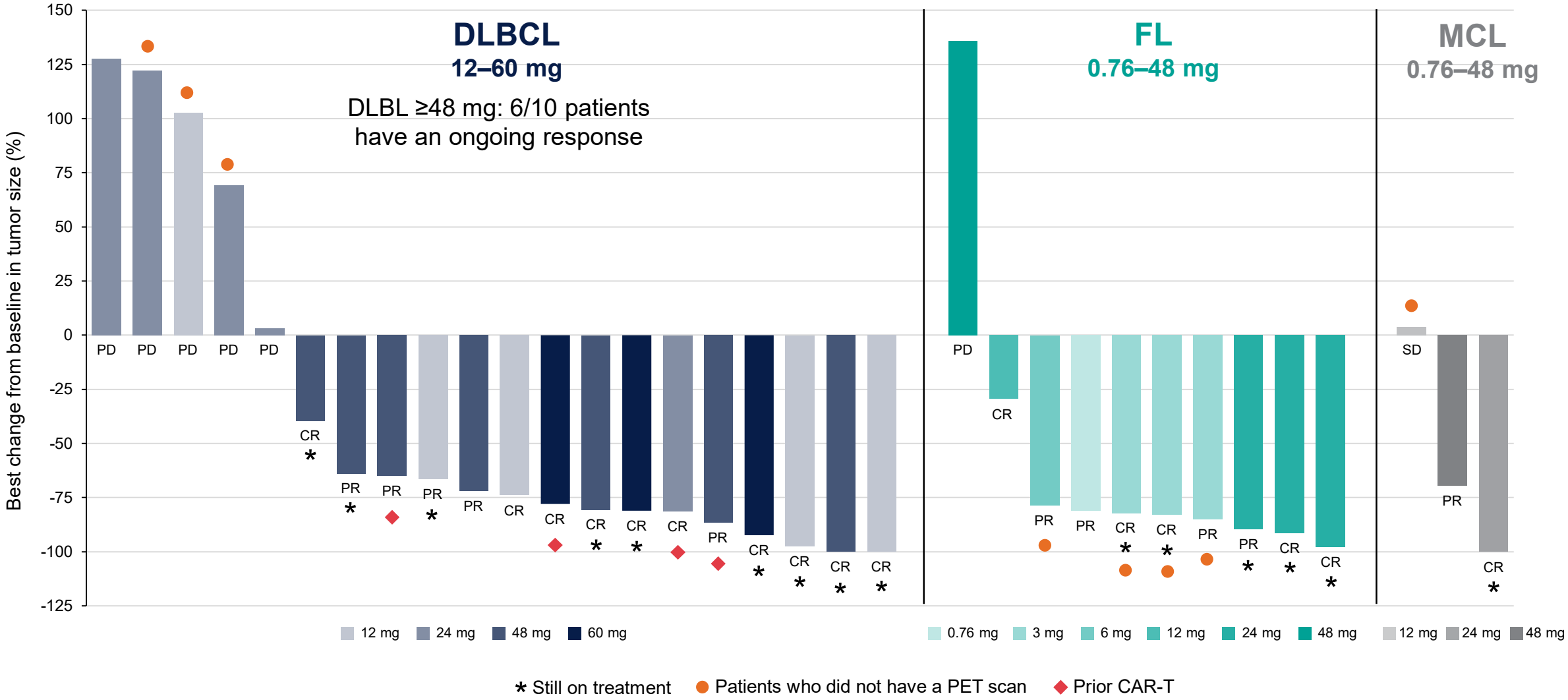
AE of Special Interest - CRS

Adverse events of special interest	All histologies (N=68)
CRS, n (%)	40 (59)
Grade 1	20 (29)
Grade 2	20 (29)
Symptoms of CRS ≥10%, n (%)	
Pyrexia	40 (59)
Hypotension	16 (24)
Hypoxia	12 (18)
Tachycardia	10 (15)
Chills	7 (10)

- Neurological symptoms were transient and manageable with standard therapy; Grade 1 (n=2) and Grade 3 (n=2)

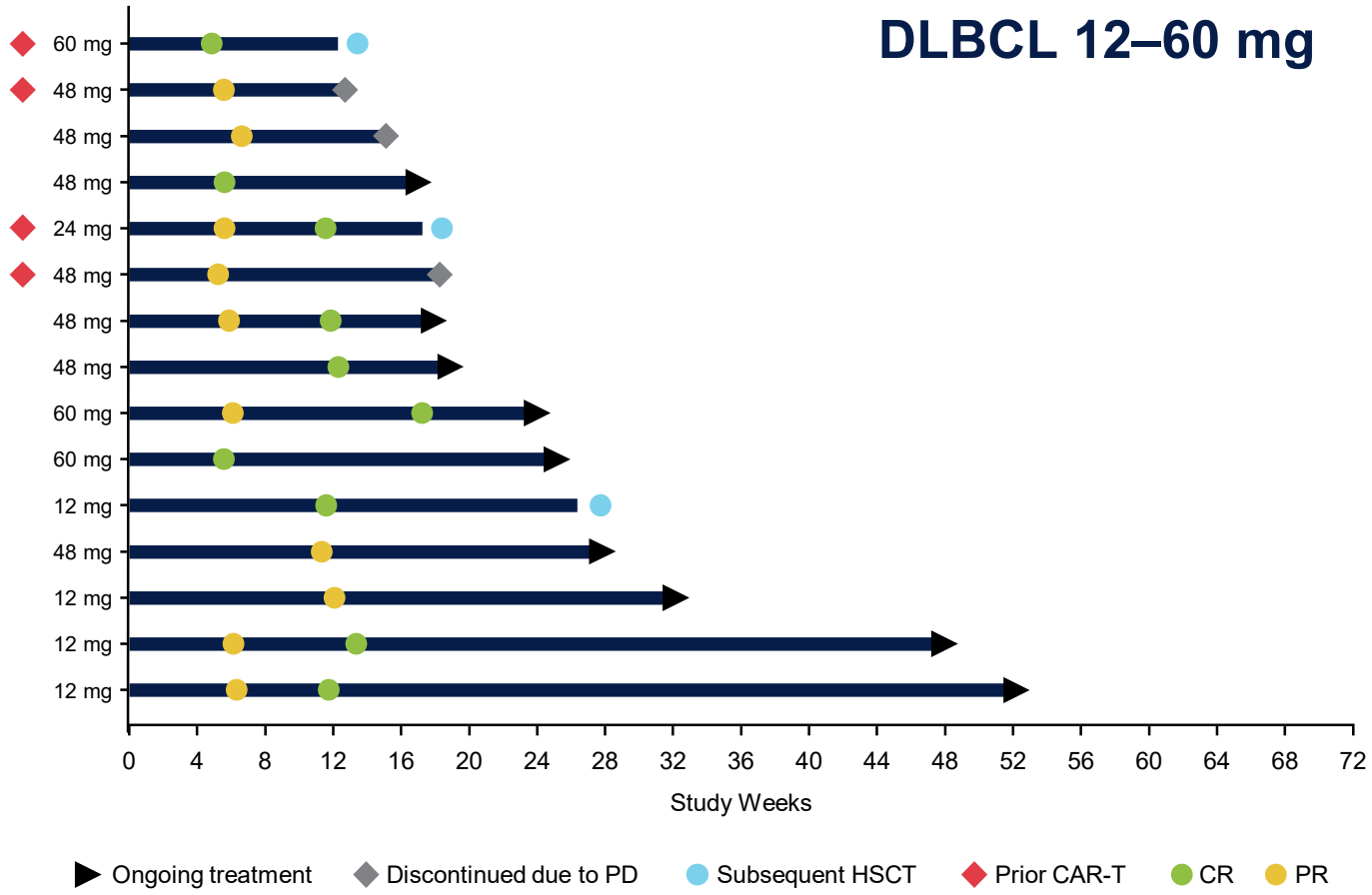
There have been no Grade ≥3 CRS events. Majority of events occurred and resolved in Cycle 1

Best Percent Change from Baseline in Tumor Size



Data shown for modified response-evaluable population. PET scan was not initially required for FL; protocol amendment added PET follow-up of all FDG-avid disease

Anti-tumor Response



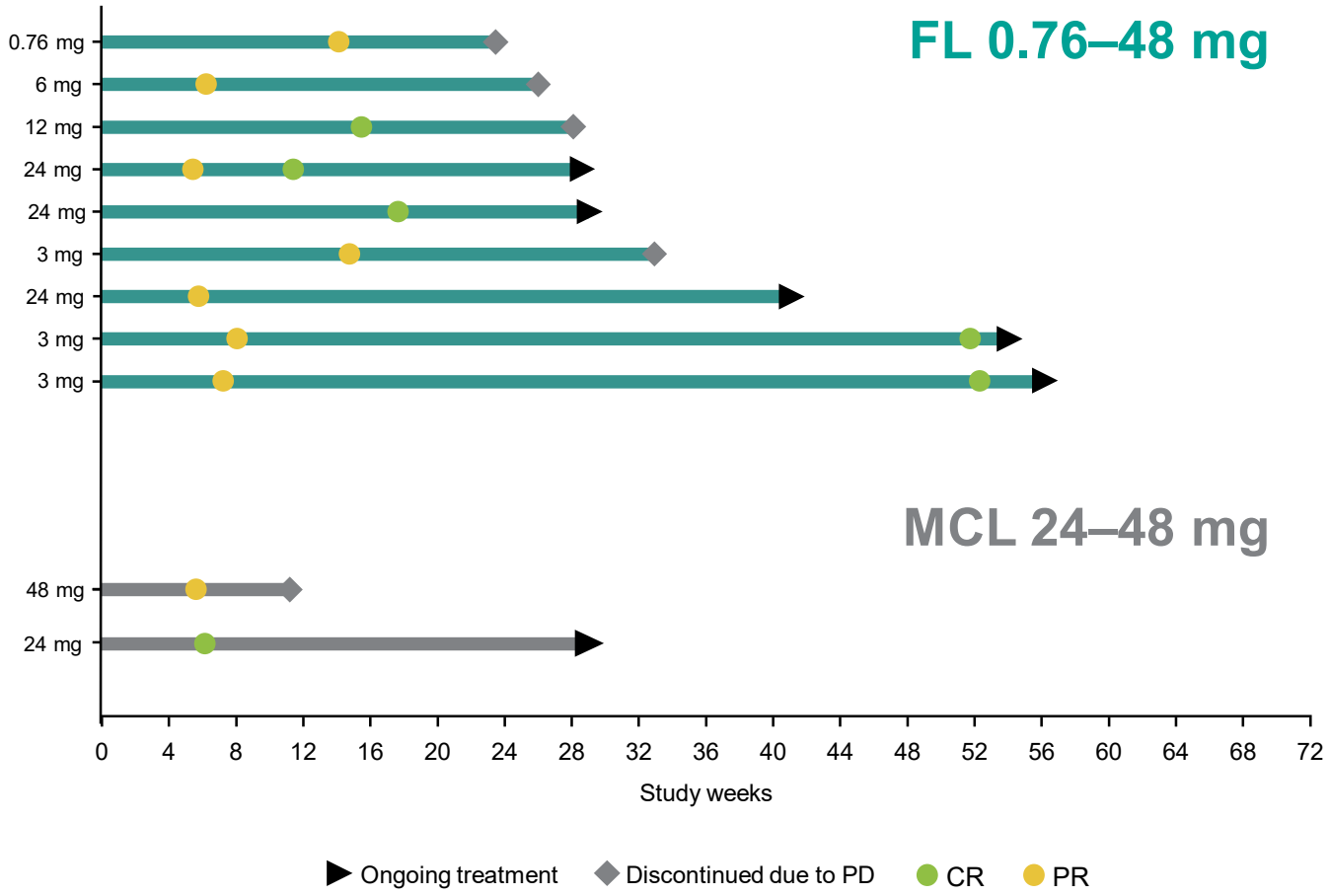
Response*	DLBCL	
	12–60 mg (n=23)	48–60 mg (n=12)
Evaluable patients, n	22	11
ORR, n (%) CR	15 (68) 10 (46)	10 (91) 6 (55)
Median time to response, months (range)	1.4 (1–3)	1.3 (1–3)
Patients still in remission at 6 months, % (95% CI)†	72 (34–90)	N/A

- Responses deepened over time
- 3 patients with DLBCL achieved a CR and received HSCT with curative intent
- All 4 patients with prior CAR-T (1 relapsed, 3 refractory) responded (2 CR, 2 PR)

Epcoritamab induced encouraging clinical response including in prior CAR-T–treated patients

*Response assessments were based on modified response-evaluable population; †Not all patients have reached 6 months of follow-up

Anti-tumor Response



Response*	FL 0.76–48 mg (n=11)	MCL 0.76–48 mg (n=4)
Evaluable pts, n	10	5
ORR, n (%) CR	9 (90) 5 (50)	2 (50) 1 (25)
Median time to response, months (range)	1.9 (1–4)	1.4 (1–1)

- Responses deepened over time

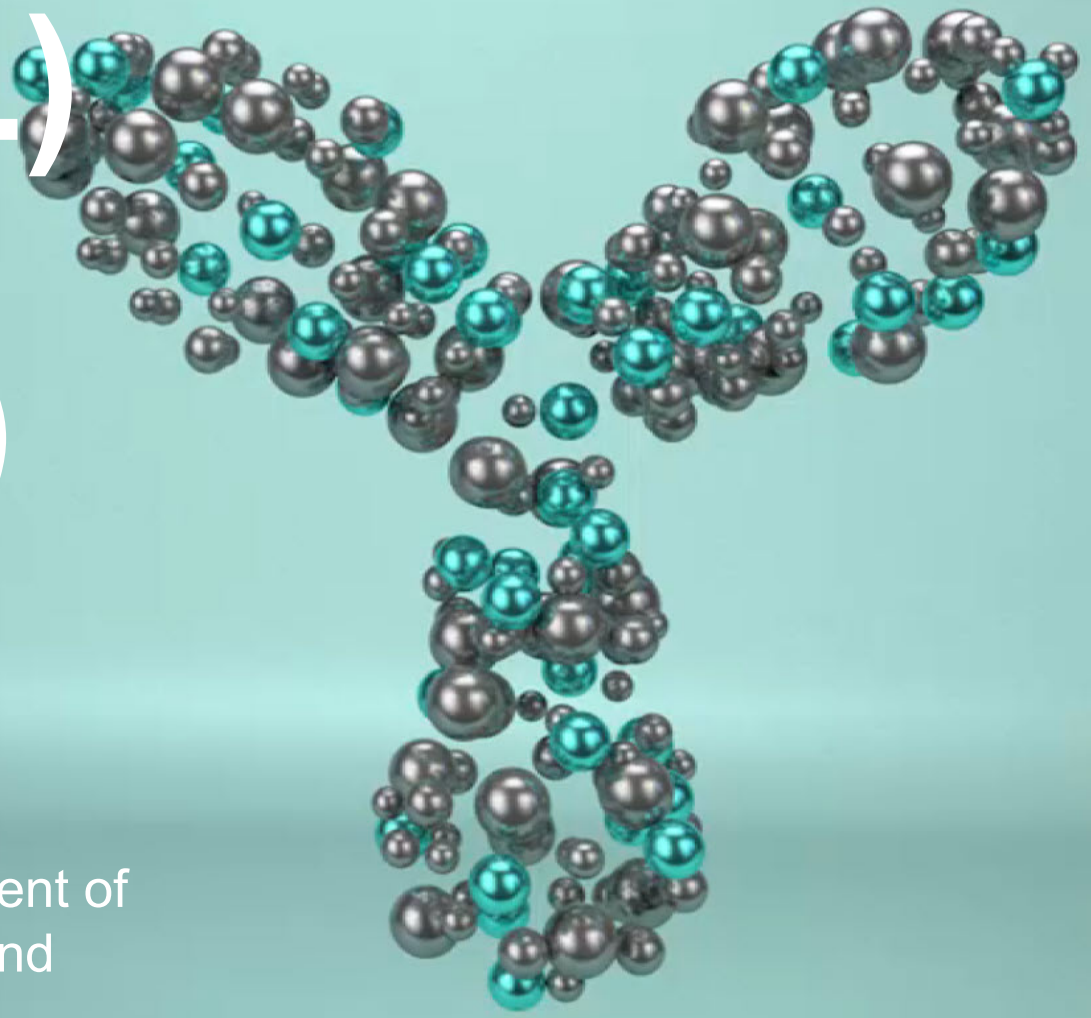
Encouraging responses with patients still on treatment and in remission beyond 12 months

*Response assessments were based on modified response-evaluable population

Summary

- Epcoritamab (DuoBody®-CD3×CD20) is a novel, off-the-shelf therapy that is conveniently subcutaneously administered (low-volume, once-weekly and less frequent thereafter)
  - The RP2D of 48 mg was reached with no dose-limiting toxicities; MTD was not reached
  - Phase II expansion part is ongoing
- Epcoritamab shows a favorable safety profile, supporting the potential for combination therapies and future outpatient administration
  - CRS events were Grade 1 and 2
- Epcoritamab demonstrated substantial single-agent activity in heavily pretreated patients with B-NHL providing deep responses
  - In patients with DLBCL receiving ≥48 mg, responses were achieved in 10 of 11 patients, including CR in 6 patients. All patients receiving ≥12 mg who achieved a CR remain in remission
  - In patients with FL receiving ≥12 mg, ORR was 80%, with 60% CR
  - Encouraging responses, including CR, were observed in 2/4 patients with MCL
- Epcoritamab binds to a distinct epitope, different from that of rituximab and obinutuzumab, and thus has the potential to be the partner of choice in combinations with standard of care therapies that contain rituximab
- Epcoritamab is currently being investigated in several clinical trials across B-cell NHL histologies and in various combinations (NCT03625037, NCT04542824, NCT04623541, NCT04628494)

Daratumumab: Light-chain (AL) Amyloidosis (ANDROMEDA)



Presented by Professor Efstathios Kastritis, Department of Clinical Therapeutics, School of Medicine, National and Kapodistrian University of Athens

POSTER PRESENTATIONS FOR ANDROMEDA

Rapid and Deep Hematologic Responses Are Associated With Improved Major Organ Deterioration Progression-Free Survival in Newly Diagnosed AL Amyloidosis: Results From ANDROMEDA

Outcomes by Cardiac Stage in Newly Diagnosed AL Amyloidosis: Results From ANDROMEDA

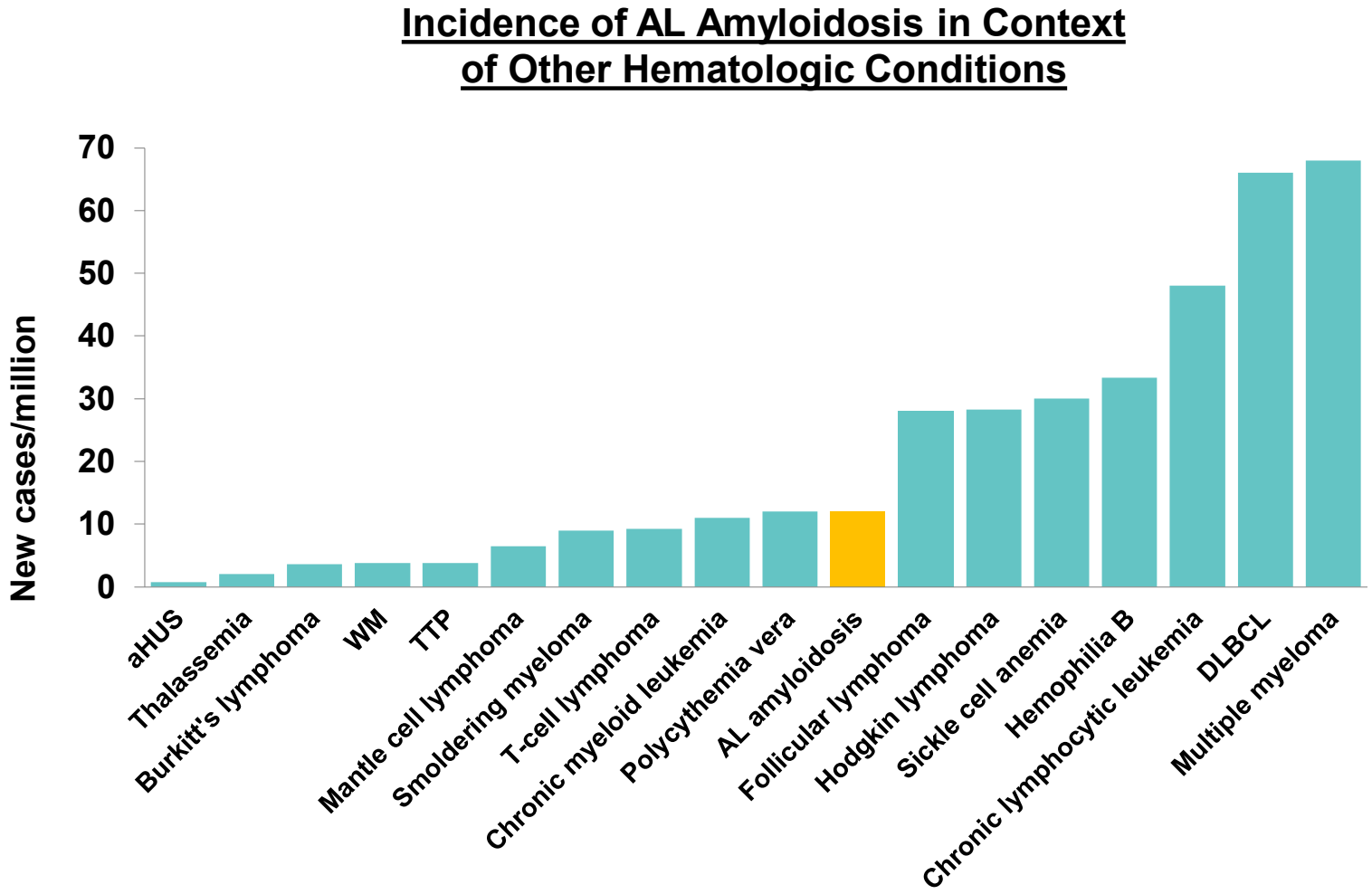
Reduction in Absolute Involved Free Light Chain and Difference Between Involved and Uninvolved Free Light Chain Is Associated With Prolonged Major Organ Deterioration Progression-Free Survival in Patients With Newly Diagnosed AL Amyloidosis Receiving Bortezomib, Cyclophosphamide, and Dexamethasone With or Without Daratumumab: Results From ANDROMEDA

Background

- Systemic AL amyloidosis is a lethal plasma cell disease caused by extracellular deposition of amyloid on organs and tissues (particularly cardiac), leading to progressive organ dysfunction
  - Light chains aggregate into amyloid fibrils resulting in organ damage, progressive disability, and death
  - Extent of cardiac involvement at baseline has a major impact on clinical outcomes2
- Diagnosis of AL amyloidosis is often delayed due to symptoms overlapping with more common diseases, leading to prognosis due to advanced multi-organ involvement
- There are currently no approved therapies for treatment of AL amyloidosis
  - Standard treatment involves the use of approved multiple myeloma therapies such as VCd
- Additional therapies are needed to improve patient outcomes by inducing rapid and deep hematologic responses that lead to improved major organ deterioration (MOD)-PFS and organ function[1]
- ANDROMEDA (NCT03201965) is a randomized, open-label, active-controlled, phase 3 study of DARA-VCd versus VCd alone in patients with newly diagnosed AL amyloidosis
  - Treatment with DARA-VCd resulted in deeper and more rapid hematologic responses with an acceptable safety profile consistent with what has been observed for DARA SC and VCd

Epidemiology of AL Amyloidosis

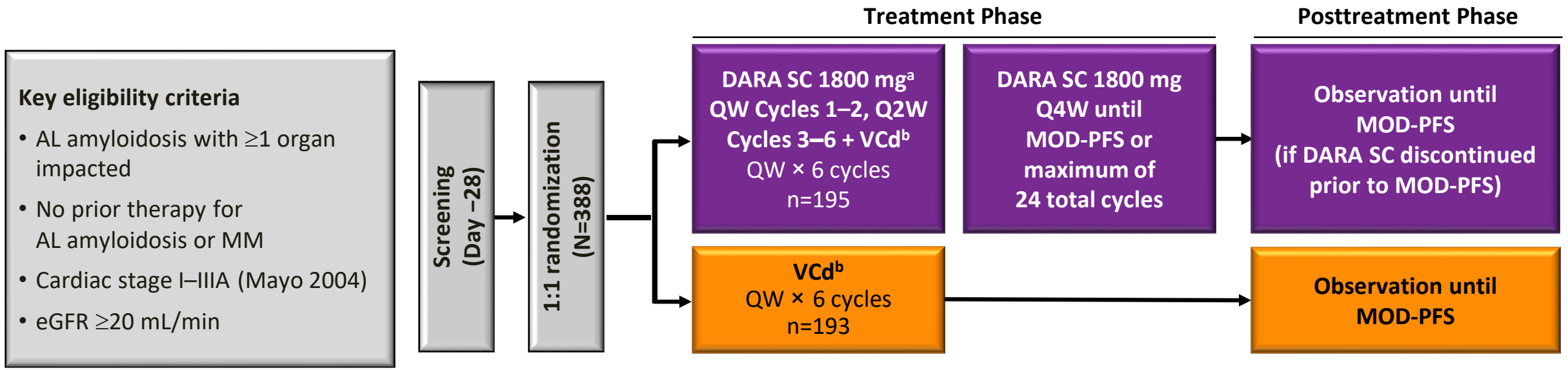
- Incidence ~12 cases/million
- Roughly 1-2 AL per 10 MM cases
- Mean age at diagnosis: 63 years
- 55% of patients are men
- Individuals with pre-existing MGUS have an ~9-fold increased risk of developing AL amyloidosis
- Some patients with myeloma may develop amyloidosis during the course of their disease
- Meets criteria for Orphan Disease status in the US and EU



MGUS, monoclonal gammopathy of undetermined significance; US, United States; EU, European Union; aHUS, atypical hemolytic uremic syndrome; WM, Waldenström´s macroglobulinemia; TTP, thrombotic thrombocytopenic purpura; DLBCL, diffuse large B-cell lymphoma.

Ardissino G, et al. *Eur J Pediatr.* 2016;175(4):465-473. Cela E, et al. *Pediatr Blood Cancer.* 2017;64(7). Smith A, et al. *Br J Cancer.* 2015;112(9):1575-1584. Miller DP, et al. *Epidemiology.* 2004;15(2):208-215. Ravindran A, et al. *Blood Cancer J.* 2016;6(10):e486. Roman E, et al. *Cancer Epidemiol.* 2016;42:186-198. Moulard O, et al. *Eur J Haematol.* 2014;92(4):289-297. Quock TP, et al. *Blood.* 2017;130(suppl 1):5335. Dunn AL. Hemophilia B. In: *Transfusion Med Hemost.* 2009;533-536. Blimark CH, et al. *Haematologica.* 2018;103(3):506-513. National Cancer Institute. www.seer.cancer.gov. Accessed March 8, 2019.

ANDROMEDA Study Design



Stratification criteria
- Cardiac stage (I vs II vs IIIA)
- Transplant typically offered in local country (yes vs no)
- Creatinine clearance (≥60 mL/min vs <60 mL/min)

Primary endpoint: Overall hematologic CR rate

Secondary endpoints: MOD-PFS, organ response rate, time to hematologic response, overall survival, safety

ANDROMEDA is a randomized, open-label, active-controlled, phase 3 study of DARA-VCd versus VCd alone in patients with newly diagnosed AL amyloidosis

AL, amyloid light chain; CR, complete response; DARA, daratumumab; eGFR, estimated glomerular filtration rate; IV, intravenous; MM, multiple myeloma; MOD-PFS, major organ deterioration progression-free survival; PO, oral; Q2W, every 2 weeks; Q4W, every 4 weeks; QW, weekly; SC, subcutaneous; VCd, bortezomib, cyclophosphamide, and dexamethasone.

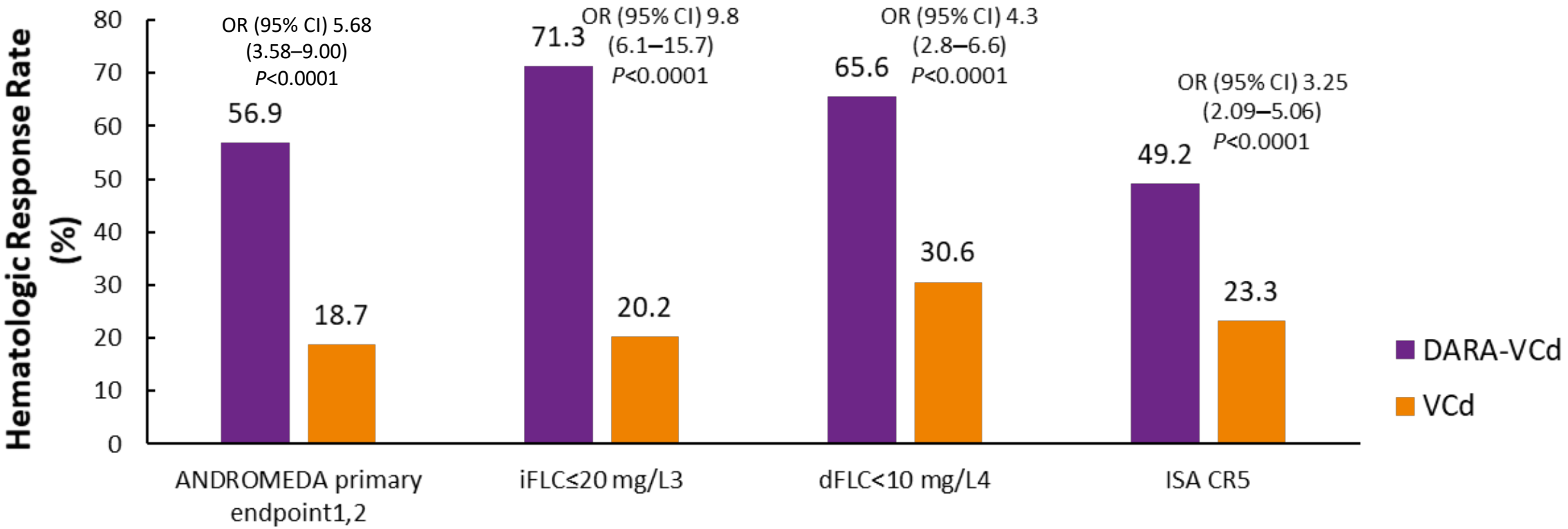
[a]Coformulated with recombinant human hyaluronidase PH20 (rHuPH20; 2000 U/mL; ENHANZE® drug delivery technology, Halozyme, Inc, San Diego, CA, USA).
[b]Dexamethasone 40 mg IV or PO, followed by cyclophosphamide 300 mg/m^2 IV or PO, followed by bortezomib 1.3 mg/m^2 SC on Days 1, 8, 15, and 22 in every 28-day cycle for a maximum of 6 cycles. Patients will receive dexamethasone 20 mg on the day of DARA SC dosing and 20 mg on the day after DARA SC dosing.

ANDROMEDA Primary Results

- The primary endpoint was met, with more patients in the DARA-VCd group achieving hematologic CR at any time during the study compared with the VCd group (53% vs 18%; OR 5.1 [95% CI 3.2–8.2], *P*<0.0001)
- Results were consistent across prespecified subgroups
- Treatment with DARA-VCd prolonged major organ deterioration (MOD)-PFS vs VCd (HR 0.58 [95% CI 0.36–0.93], *P*=0.0211)
- Rates of cardiac and renal response at 6 months were significantly higher with DARA-VCd vs VCd (42% vs 22% and 54% vs 27%, respectively)
- The safety profile of DARA-VCd was consistent with the known profiles of DARA SC and VCd

CI, confidence interval; CR, complete response; DARA, daratumumab; HR, hazard ratio; PFS, progression-free survival; OR, odds ratio; SC, subcutaneous; VCd, bortezomib, cyclophosphamide, and dexamethasone.

Best Hematologic Response Rates at Any Time by Treatment Group



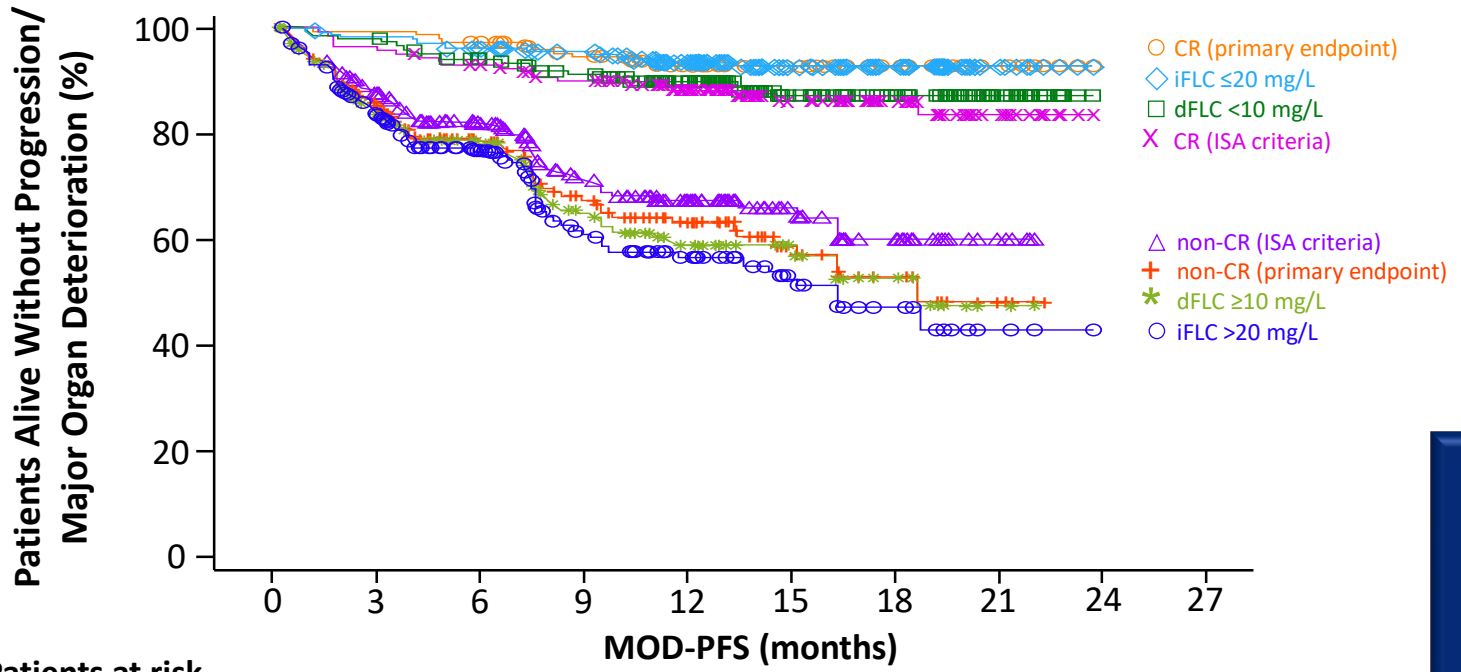
Higher rates of hematologic response were observed with Dara-VCd across all criteria

DARA, daratumumab; dFLC, difference between involved and uninvolved free light chain; FLCr, free light chain ratio; iFLC, involved free light chain; ISA, International Society of Amyloidosis; OR, odds ratio; ULN, upper limit of normal; VCd, bortezomib, cyclophosphamide, and dexamethasone.

Data cutoff: 15Jun20. [a]Defined as negative serum and urine immunofixation and iFLC<ULN regardless of FLCr. [b]Defined as normal FLCr and negative serum and urine immunofixation.

1. Comenzo RL, et al. *Leukemia* 2012;26(11):2317-25. 2. Sidana S, et al. *Leukemia* 2019;34(5):1472-5. 3. Muchtar E, et al. *Leukemia* 2019;33(3):790-4. 4. Manwani R, et al. *Blood* 2019;134(25):2271-80. 5. Palladini G, et al. *J Clin Oncol* 2012;30:4541-9.

MOD-PFS by Hematologic Response



Patients at risk

CR (primary endpoint)	147	146	141	130	107	73	46	21	2	0
non-CR (primary endpoint)	241	173	132	87	61	32	14	5	0	0
CR (ISA criteria)	141	135	128	119	97	68	41	18	2	0
Non-CR (ISA criteria)	247	184	145	98	71	37	19	8	0	0
dFLC <10 mg/L	187	181	169	152	121	76	46	23	2	0
dFLC ≥10 mg/L	201	138	104	65	47	29	14	3	0	0
iFLC ≤20 mg/L	178	174	167	152	121	77	46	22	1	0
iFLC >20 mg/L	210	145	106	65	47	28	14	4	1	0

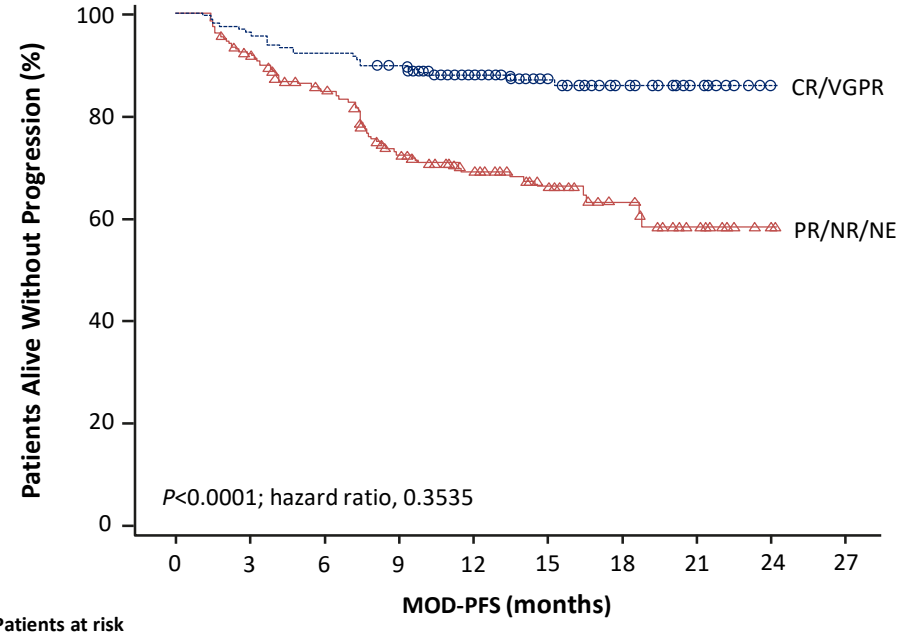
Depth of response as measured by all hematologic response criteria corresponded with MOD-PFS, which was longer in patients who received DARA-VCd

CR, complete response; dFLC, difference between involved and uninvolved free light chain; iFLC, involved free light chain; ISA, International Society of Amyloidosis; MOD-PFS, major organ deterioration–progression-free survival.

Data cutoff: 15Jun20.

MOD-PFS by Hematologic Response at 1 and 3 Months

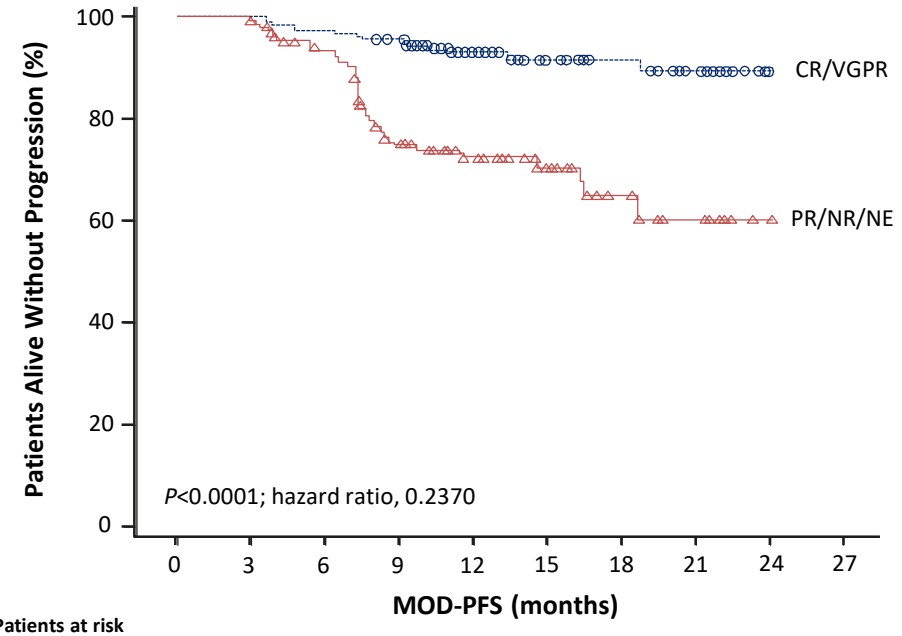
1 Month



Patients at risk

CR/VGPR	169	162	156	150	122	76	41	20	2	0
PR/NR/NE	187	168	145	115	86	55	30	15	2	0

3 Months



Patients at risk

CR/VGPR	184	184	179	174	137	84	51	25	2	0
PR/NR/NE	106	104	91	66	51	36	15	7	1	0

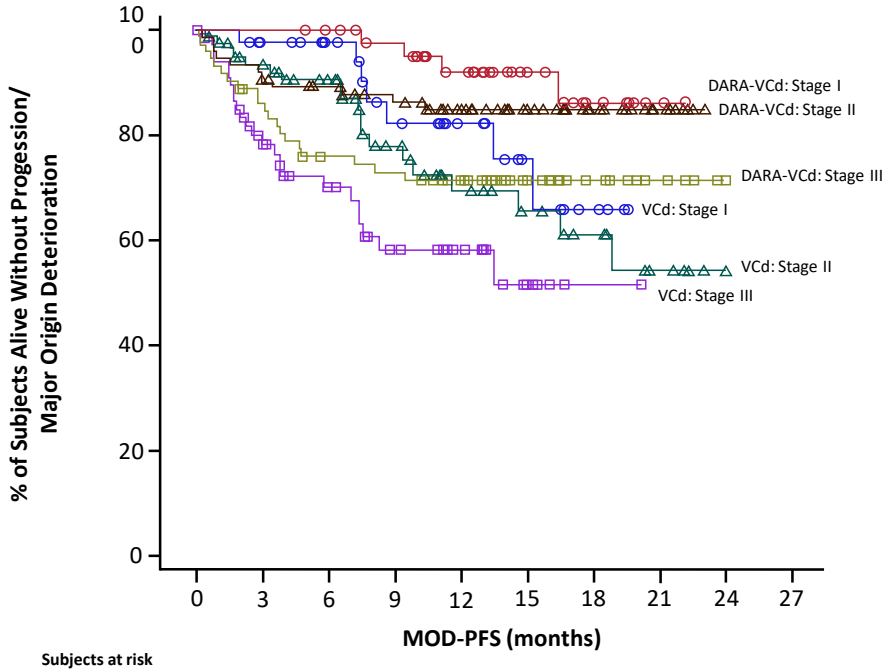
Roughly twice as many patients in the DARA-VCd group achieved CR/VGPR versus the VCd group

CR or VGPR at 1 and 3 months was associated with reduced risk of death or major organ deterioration in a multivariate analysis adjusting for baseline dFLC and cardiac stage

CR, complete response; DARA, daratumumab; dFLC, difference between involved and uninvolved free light chains; MOD-PFS, major organ deterioration progression-free survival; NE, not evaluable; NR, no response; PR, partial response; VCd, bortezomib, cyclophosphamide, and dexamethasone; VGPR, very good partial response.

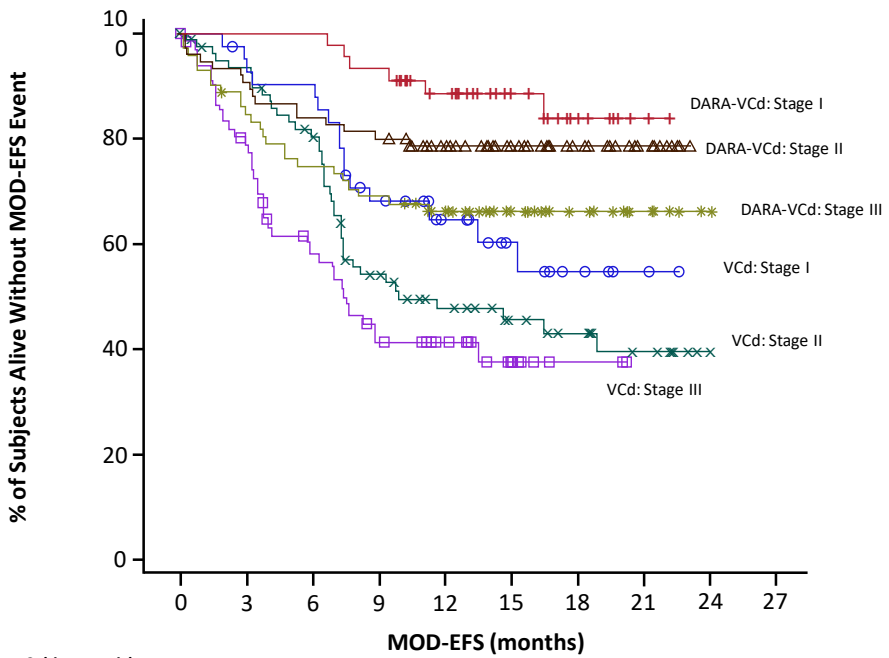
MOD-PFS and MOD-EFS by Baseline Cardiac Stage

MOD-PFS[a]



Subjects at risk										
VCd: Stage I	43	36	29	20	14	8	4	0	0	0
DARA-VCd: Stage I	47	45	43	38	30	18	8	2	0	0
VCd: Stage II	80	68	55	31	22	16	12	6	1	0
DARA-VCd: Stage II	76	67	63	57	46	29	19	9	0	0
VCd: Stage III	70	43	32	22	15	5	1	0	0	0
DARA-VCd: Stage III	72	60	51	49	41	29	16	9	1	0

MOD-EFS[b]



Subjects at risk										
VCd: Stage I	43	39	37	26	17	11	6	2	0	0
DARA-VCd: Stage I	47	45	45	42	34	21	9	2	0	0
VCd: Stage II	80	72	61	37	27	19	15	10	1	0
DARA-VCd: Stage II	76	68	63	60	49	30	19	9	0	0
VCd: Stage III	70	51	35	24	17	7	2	0	0	0
DARA-VCd: Stage III	72	61	53	49	41	29	16	9	1	0

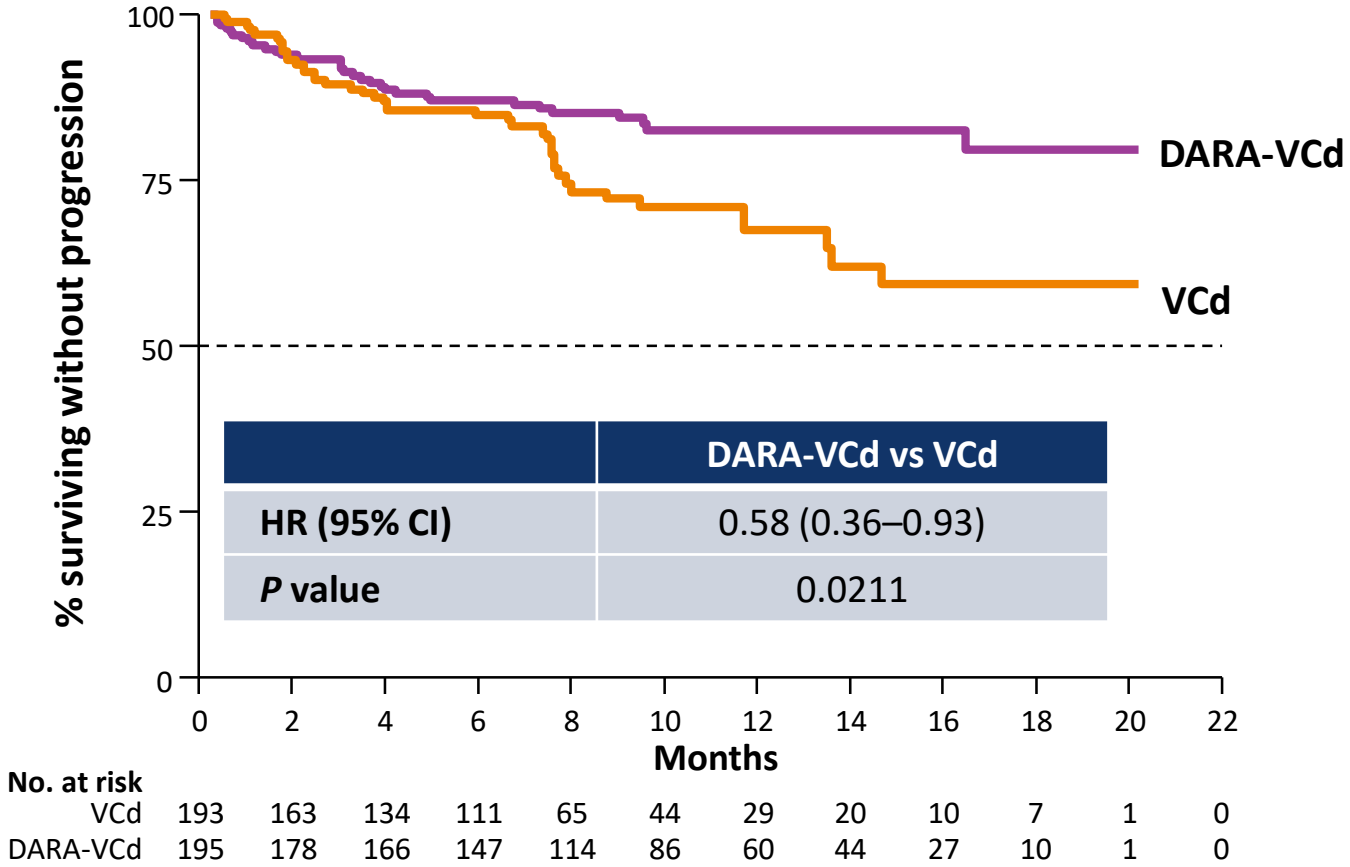
For the overall population, median follow-up was 15.7 months (range, 0.0–24.1)

MOD-PFS and MOD-EFS favored DARA-VCd across baseline cardiac stages

DARA, daratumumab; MOD-EFS, major organ deterioration event-free survival; MOD-PFS, major organ deterioration progression-free survival; VCd, bortezomib, cyclophosphamide, and dexamethasone.

[a]Defined as duration from randomization to either hematologic progression, major organ deterioration (clinical manifestation of cardiac/renal failure), or death (whichever occurs first). [b]Defined as hematologic progressive disease, major organ deterioration, initiation of any subsequent non–cross resistant, anti–plasma cell therapy, or death (whichever comes first).

Major Organ Deterioration (MOD)-PFS by Treatment Group



Treatment with DARA-VCd substantially delayed major organ deterioration, hematologic progression, or death

CI, confidence interval; DARA, daratumumab; HR, hazard ratio; PFS, progression-free survival; VCd, bortezomib, cyclophosphamide, and dexamethasone.

Data cutoff: 15Feb20. [a]At a median follow-up of 11.4 months; after adjusting for dependent censoring due to subsequent therapy.

Rates of 6 Month Cardiac and Renal Response in Patients with Early Hematologic Response

	Cardiac Response Rates at 6 Months, %		Renal Response Rates at 6 Months, %	
Hematologic response	1 month	3 months	1 month	3 months
CR/VGPR	39.6	40.0	48.3	52.0
PR/NR/NE	25.2	34.8	33.9	34.4

Patients who achieved deep, early hematologic response (at 1 and 3 months) had numerically higher rates of cardiac and renal responses at 6 months than patients who did not achieve deep, early responses

CR, complete response; NE, not evaluable; NR, no response; PR, partial response: VGPR, very good partial response.

Conclusions

- Achieving CR or VGPR at 1 and 3 months was associated with:
  - Reduced risk of major organ deterioration and death in patients with newly diagnosed AL amyloidosis
  - Higher rates of organ response
- These data confirm initial therapy that achieves rapid and deep hematologic response is essential to improving outcomes after a median follow-up of 15.7 months in patients with AL amyloidosis
- Hematologic CR and organ response rates were consistently high across cardiac stages in patients treated with DARA-VCd
- MOD-PFS and MOD-EFS were better in the DARA-VCd than in the VCd group across cardiac stages
- Rates of serious AEs were higher in patients with more advanced cardiac stage regardless of treatment
- These results support DARA-VCd as a potential standard of care for patients with newly diagnosed AL amyloidosis irrespective of baseline cardiac stage

AL, amyloid light chain; CR, complete response; DARA, daratumumab; VCd, bortezomib, cyclophosphamide, and dexamethasone; VGPR, very good partial response.

Daratumumab: Multiple Myeloma (APOLLO, MAIA GRIFFIN)

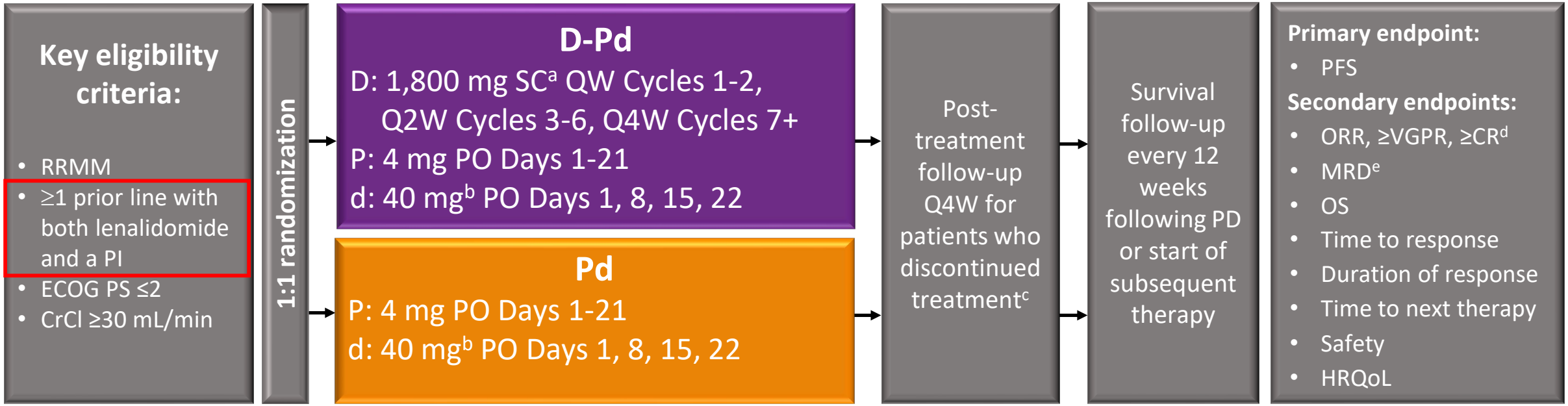
Presented by Dr. Meletios A. Dimopoulos, M.D.,
School of Medicine, National and Kapodistrian University of Athens

APOLLO: Phase 3 Randomized Study of Subcutaneous Daratumumab Plus Pomalidomide and Dexamethasone (D-Pd) vs Pomalidomide and Dexamethasone (Pd) Alone in Patients (Pts) with Relapsed/Refractory Multiple Myeloma (RRMM)*

- DARA is approved as monotherapy and in combination with standard-of-care regimens for RRMM and NDMM[1,2]
- In the phase 1b study of DARA IV plus Pd, D-Pd induced deep responses and was well tolerated in patients with heavily pre-treated RRMM, including those with prior lenalidomide treatment[3]
  - Based on these results, D-Pd is approved in the United States for RRMM patients with ≥2 prior lines of therapy, including lenalidomide and a PI[1]
- The SC formulation of DARA has similar efficacy and safety profiles as DARA IV
  - DARA SC efficacy and pharmacokinetics are noninferior to those of DARA IV[4]
  - DARA SC has significantly lower IRR rates and a shorter administration duration of 5 minutes[4]
  - DARA SC was recently approved in North America, South America, Europe, and Asia

Here we report the primary analysis of the phase 3 APOLLO study of DARA SC plus Pd versus Pd alone in RRMM patients with ≥1 prior line of therapy, including lenalidomide and a PI

Study Design



Stratification factors
- Number of lines of prior therapy (1 vs 2-3 vs ≥4)
- ISS disease stage (I vs II vs III)

Cycle duration: 28 days
Treatment until PD or unacceptable toxicity

EMN, European Myeloma Network; ECOG PS, Eastern Cooperative Oncology Group Performance Status; CrCl, creatinine clearance; QW, every week; Q2W, every 2 weeks; Q4W, every 4 weeks; PO, oral; PD, progressive disease; PFS, progression-free survival; ORR, overall response rate; VGPR, very good partial response; CR, complete response, MRD, minimal residual disease, OS, overall survival; HRQoL, health-related quality of life; ISS, International Staging System; SC, subcutaneous; sCR, stringent complete response. [a]Patients initially were given DARA 16 mg/kg IV; following Protocol Amendment 1, new patients in the D-Pd arm received DARA SC. Patients who had already received DARA IV prior to this amendment may switch to DARA SC on Day 1 of any cycle from Cycle 3+. [b]Patients aged ≥75 years received 20 mg weekly. [c]Follow-up is for patients who discontinued treatment for reasons other than PD, death, lost to follow-up, or withdrawal of consent. [d]Disease assessments were collected every cycle for the first 14 months and every other month thereafter by a central laboratory. [e]MRD was assessed by next-generation sequencing using bone marrow aspirate samples obtained at screening, at the time of suspected CR or sCR, and at 6, 12, 18, 24, and every 12 months after achieving CR or sCR, until disease progression.

Demographic and Baseline Disease Characteristics[a]

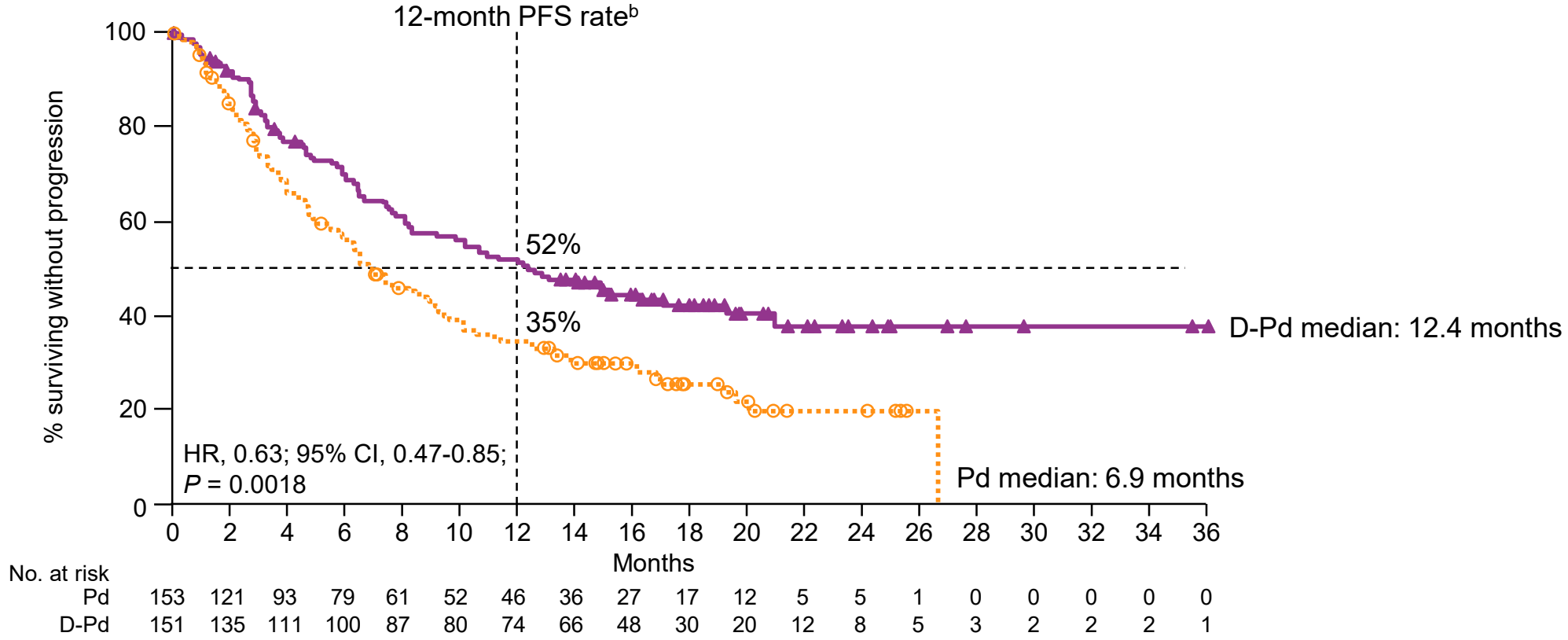
	D-Pd (n = 151)	Pd (n = 153)
Age, years		
Median (range)	67 (42-86)	68 (35-90)
Distribution, n (%)		
<65	63 (42)	60 (39)
65-<75	63 (42)	62 (41)
≥75	25 (17)	31 (20)
ECOG PS score,[b] n (%)		
0	91 (60)	77 (50)
1	54 (36)	57 (37)
2	6 (4)	19 (12)
ISS disease stage,[c] n (%)		
I	68 (45)	69 (45)
II	50 (33)	51 (33)
III	33 (22)	33 (22)
Type of MM,[d] n (%)		
IgG	83 (55)	87 (57)
IgA	34 (23)	30 (20)
Light chain	26 (17)	30 (20)
Cytogenetic profile[e] N	103	108
Standard risk, n (%)	64 (62)	73 (68)
High risk, n (%)	39 (38)	35 (32)

	D-Pd (n = 151)	Pd (n = 153)
Time since MM diagnosis, years Median (range)	4.39 (0.5-20.0)	4.48 (0.6-19.0)
Prior lines of therapy Median (range)	2 (1-5)	2 (1-5)
Distribution, n (%)		
1	16 (11)	18 (12)
2-3	114 (75)	113 (74)
≥4	21 (14)	22 (14)
Prior PI, n (%)	151 (100)	153 (100)
Prior IMiD, n (%)	151 (100)	153 (100)
Prior ASCT	90 (60)	81 (53)
Disease refractory to last line of therapy, n (%)	122 (81)	123 (80)
Disease refractory to, n (%)		
Lenalidomide	120 (79)	122 (80)
PI	71 (47)	75 (49)
PI + lenalidomide	64 (42)	65 (42)

Characteristics were well balanced between treatment arms

MM, multiple myeloma; ASCT, autologous stem-cell transplantation; IMiD, immunomodulatory drug. [a]Intent-to-treat population (N = 304). [b]ECOG PS is scored on a scale from 0 to 5, with 0 indicating no symptoms and higher scores indicating increasing disability. [c]Based on the combination of serum β2-microglobulin and albumin at study entry. [d]Determined by immunofixation. [e]Based on fluorescence in situ hybridization; high risk was defined as del17p, t(4;14), or t (4;16).

PFS at a Median Follow-up of 16.9 Months[a]



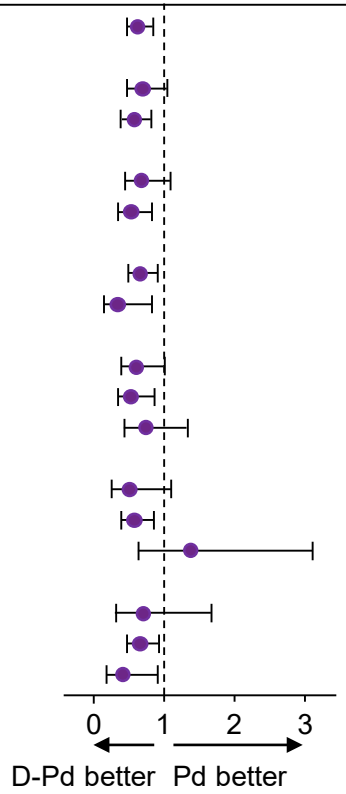
- Median PFS among patients refractory to lenalidomide was 9.9 months for D-Pd and 6.5 months for Pd

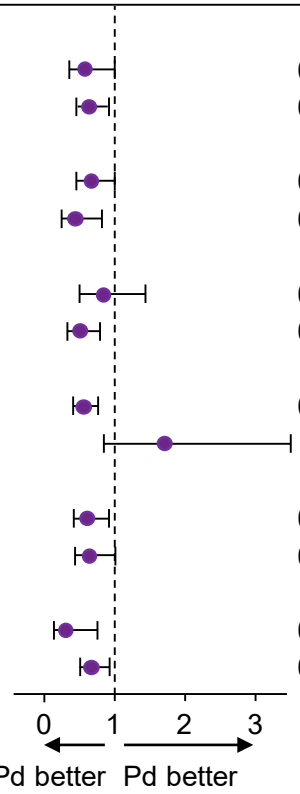
Addition of DARA SC to Pd improved PFS, with a 37% reduction in the risk of progression or death

HR, hazard ratio; CI, confidence interval. [a]Intent-to-treat population. [b]Kaplan–Meier estimate.

PFS in Pre-specified Subgroups

	D-Pd	Pd	HR (95% CI)
	No. of progression events or deaths/total no.		
Overall	84/151	106/153	0.63 (0.47-0.85)
Sex			
Male	46/79	54/82	0.69 (0.47-1.03)
Female	38/72	52/71	0.54 (0.35-0.82)
Age			
<65 years	**36/63**	**41/60**	**0.69 (0.44-1.09)**
≥65 years	**48/88**	**65/93**	**0.55 (0.38-0.81)**
Race			
White	75/135	93/137	0.66 (0.48-0.89)
Non-White	9/16	13/16	0.34 (0.14-0.82)
ISS disease staging[a]			
1	**31/68**	**43/69**	**0.62 (0.39-0.98)**
2	**32/50**	**36/51**	**0.54 (0.33-0.87)**
3	**21/33**	**27/33**	**0.75 (0.42-1.32)**
Revised ISS disease staging[a]			
1	11/26	17/25	0.51 (0.24-1.10)
2	45/74	64/88	0.58 (0.39-0.85)
3	15/19	11/14	1.38 (0.62-3.11)
Number of lines of prior therapy			
1	**9/16**	**12/18**	**0.70 (0.30-1.67)**
2-3	**65/114**	**79/113**	**0.66 (0.48-0.92)**
≥4	**10/21**	**15/22**	**0.40 (0.18-0.90)**
Baseline creatinine clearance			
≤60 ml/min	23/40	36/47	0.59 (0.35-0.99)
>60 ml/min	61/111	70/106	0.64 (0.45-0.90)
Type of multiple myeloma[b]			
IgG	43/76	52/79	0.67 (0.45-1.01)
Non-IgG	20/34	25/32	0.44 (0.24-0.81)
Cytogenetic profile[c]			
High risk	**28/39**	**26/35**	**0.85 (0.49-1.44)**
Standard risk	**30/64**	**50/73**	**0.51 (0.32-0.81)**
Baseline hepatic function			
Normal	69/136	88/127	0.56 (0.41-0.77)
Impaired[d]	15/15	18/26	1.72 (0.84-3.50)
ECOG PS[e]			
0	**49/91**	**53/77**	**0.61 (0.41-0.90)**
≥1	**35/60**	**53/76**	**0.65 (0.42-1.00)**
Refractory to lenalidomide			
No	**8/31**	**17/31**	**0.36 (0.15-0.83)**
Yes	**76/120**	**89/122**	**0.66 (0.49-0.90)**



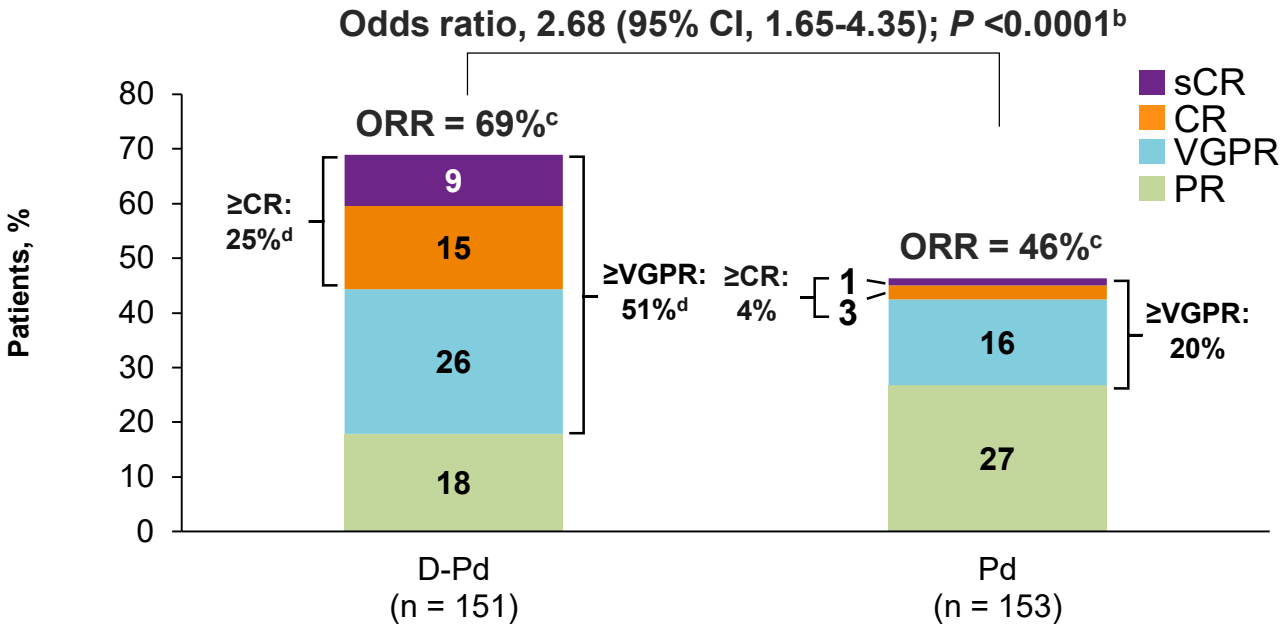


Observed treatment effect was generally consistent across subgroups

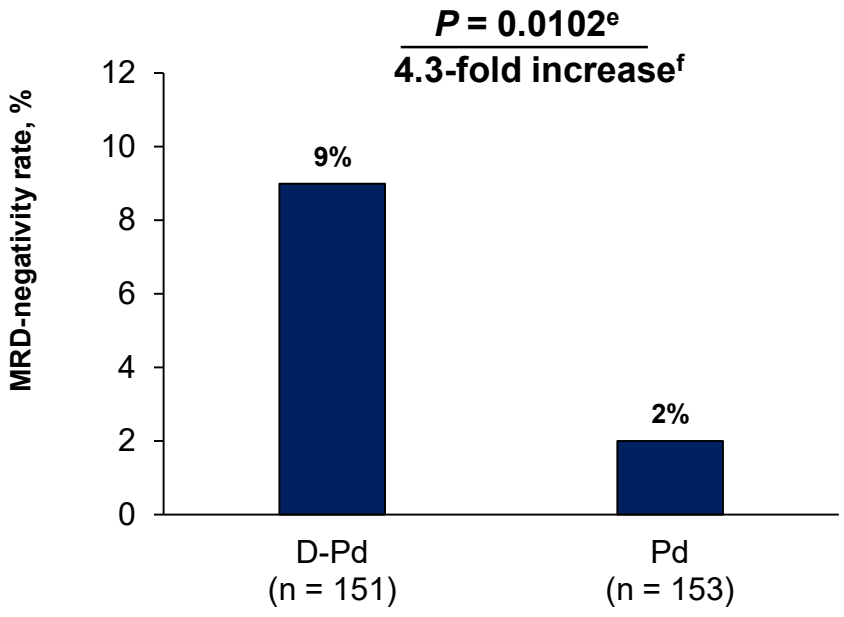
[a]Derived based on the combination of serum β2-microglobulin and albumin levels, with higher stages indicating more advanced disease. [b]Performed on data from patients who had measurable disease in serum. [c]Defined by detection of del17p, t(14;16), and/or t(4;14) on fluorescence in situ hybridization. [d]Includes mild impairment (total bilirubin level ≤ the ULN and aspartate aminotransferase level > the ULN, or total bilirubin level > the ULN and ≤1.5 times the ULN), moderate impairment (total bilirubin level >1.5 times and ≤3 times the ULN), and severe impairment (total bilirubin level >3 times the ULN). [e]Scored on a scale from 0 to 5, with 0 indicating no symptoms and higher scores indicating increasing disability.

Depth of Response[a]

Hematologic response



MRD negativity



ORR, ≥VGPR rate, ≥CR rate, and MRD-negativity rate were significantly higher with D-Pd versus Pd

PR, partial response; IMWG, International Myeloma Working Group; ITT, intent-to-treat. [a]Responses were assessed by computer algorithm in accordance with IMWG recommendations and included patients in the ITT population. [b]*P* value was calculated from the 2-sided Cochran–Mantel–Haenszel chi-square test, stratified for ISS stage (I, II, III) and number of lines of prior therapy (1, 2-3, ≥4). [c]Values may not add to total due to rounding. [d]*P* <0.0001. [e]*P* value (2-sided) was calculated using the Fisher's exact test. [f]Non-rounded values are 8.6% and 2.0%.

Most Common TEAEs[a]

Most common TEAEs, n (%)	D-Pd (n = 149)		Pd (n = 150)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Hematologic				
Neutropenia	105 (70)	101 (68)	80 (53)	76 (51)
Anemia	55 (37)	25 (17)	66 (44)	32 (21)
Thrombocytopenia	48 (32)	26 (17)	50 (33)	27 (18)
Leukopenia	39 (26)	25 (17)	18 (12)	7 (5)
Lymphopenia	22 (15)	18 (12)	12 (8)	5 (3)
Febrile neutropenia	13 (9)	13 (9)	4 (3)	4 (3)
Nonhematologic				
Infections	105 (70)	42 (28)	83 (55)	34 (23)
Upper respiratory tract infection	34 (23)	0	24 (16)	3 (2)
Pneumonia	30 (20)	20 (13)	19 (13)	10 (7)
Lower respiratory tract infection	29 (19)	17 (11)	24 (16)	14 (9)
Fatigue	38 (26)	12 (8)	38 (25)	7 (5)
Asthenia	33 (22)	8 (5)	24 (16)	1 (1)
Diarrhea	33 (22)	8 (5)	21 (14)	1 (1)
Pyrexia	29 (19)	0	21 (14)	0
Hyperglycemia	15 (10)	8 (5)	19 (13)	7 (5)

Safety profile of D-Pd is consistent with the known profiles of DARA SC and Pd

TEAE, treatment-emergent adverse event. [a]All patients who received ≥1 dose of treatment were included in the safety population. TEAEs of any grade that were reported in ≥15% of patients in either group or grade 3/4 TEAEs that were reported in ≥5% of patients in either group are listed (TEAEs were graded according to National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03; terms were coded using MedDRA dictionary version 23.0).

Additional Safety Results

- IRRs were reported in 5% of D-Pd patients; all were grade 1 or 2
- Incidence of local injection-site reactions (DARA SC only) was 2%; all were grade 1
- The most common serious TEAEs[a] were pneumonia (D-Pd, 15%; Pd, 8%) and lower respiratory tract infection (12%; 9%)
- TEAEs leading to treatment discontinuation were similar and low in both groups (D-Pd, 2%; Pd, 3%)
- TEAEs leading to death were similar for both groups (D-Pd, 7%; Pd, 7%)
- Incidence of second primary malignancy was 2% for each group

[a]All patients who received ≥1 dose of treatment were included in the safety population.

Conclusions

- In this first phase 3 study of DARA SC combination therapy in MM, D-Pd significantly reduced the risk of progression or death by 37% versus Pd in RRMM patients with ≥1 prior line of therapy
- D-Pd achieved significantly deeper responses versus Pd alone, including a >6 times higher ≥CR rate (25% vs 4%) and a >4 times higher MRD-negativity rate (9% vs 2%)
- D-Pd achieved longer PFS among patients who were refractory to lenalidomide (9.9 vs 6.5 months)
- D-Pd had a manageable safety profile consistent with the known safety profile of DARA SC and Pd alone; no new safety concerns were observed
- The IRR rate was low and administration duration short, thus increasing convenience for patients and decreasing treatment burden

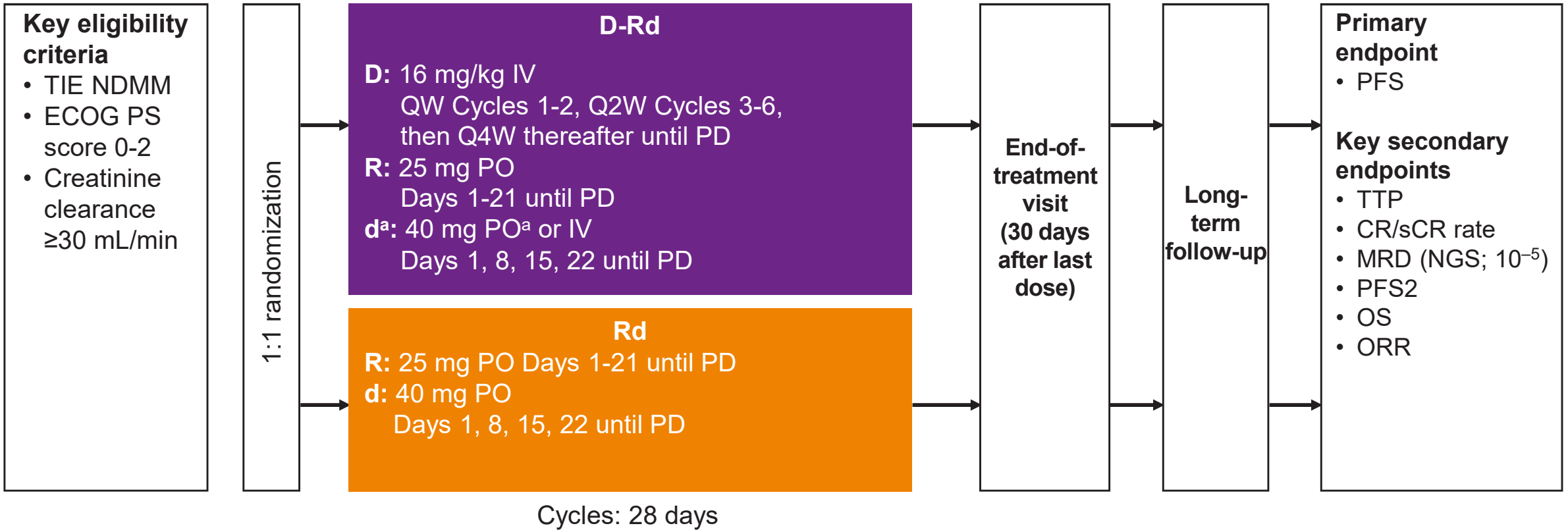
DARA SC plus Pd is an effective and convenient treatment for patients with RRMM who received ≥1 prior therapy, including lenalidomide and a PI

MAIA: Updated Analysis of Daratumumab Plus Lenalidomide and Dexamethasone (D-Rd) versus Lenalidomide and Dexamethasone (Rd) in Patients with Transplant-ineligible Newly Diagnosed Multiple Myeloma (NDMM): the Phase 3 MAIA Study

- DARA is approved as monotherapy in relapsed/refractory multiple myeloma (RRMM) and in combination with standard of care for RRMM and newly diagnosed multiple myeloma (NDMM)[8,9]
- The addition of DARA to standard-of-care regimens in phase 3 studies has consistently improved progression-free survival (PFS) and has led to deep and durable responses, including higher rates of minimal residual disease (MRD) negativity, compared with standard of care[10-14]
- In the primary analysis of the phase 3 MAIA study (median follow-up, 28.0 months), a significant PFS benefit (median, not reached [NR] vs 31.9 months; hazard ratio [HR], 0.56; 95% confidence interval [CI], 0.43-0.73; *P* <0.001) and a >3-fold increase in MRD-negativity rates (10^{-5} sensitivity threshold; 24.2% vs 7.3%; *P* <0.001) were observed with the combination of DARA plus lenalidomide and dexamethasone (D-Rd) versus lenalidomide and dexamethasone (Rd) alone in patients with transplant-ineligible (TIE) NDMM[1]
  - With a longer follow-up (median, 36.4 months), D-Rd maintained a PFS benefit and deeper and more durable responses versus Rd alone[2]

Here, we report updated efficacy and safety findings from MAIA after approximately 4 years of follow-up

MAIA Study Design



TIE, transplant-ineligible; NDMM, newly diagnosed multiple myeloma; ECOG PS, Eastern Cooperative Oncology Group performance status; D-Rd, daratumumab plus lenalidomide/dexamethasone; IV, intravenous; QW, once weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; PD, progressive disease; PO, oral; Rd, lenalidomide/dexamethasone; PFS, progression-free survival; TTP, time to progression; CR, complete response; sCR, stringent complete response; MRD, minimal residual disease; NGS, next-generation sequencing; PFS2, progression-free survival on next subsequent line of therapy; OS, overall survival; ORR, overall response rate; DARA, daratumumab. [a]On days when DARA is administered, dexamethasone will be administered to patients in the D-Rd arm and will serve as the treatment dose of steroid for that day, as well as the required pre-infusion medication.

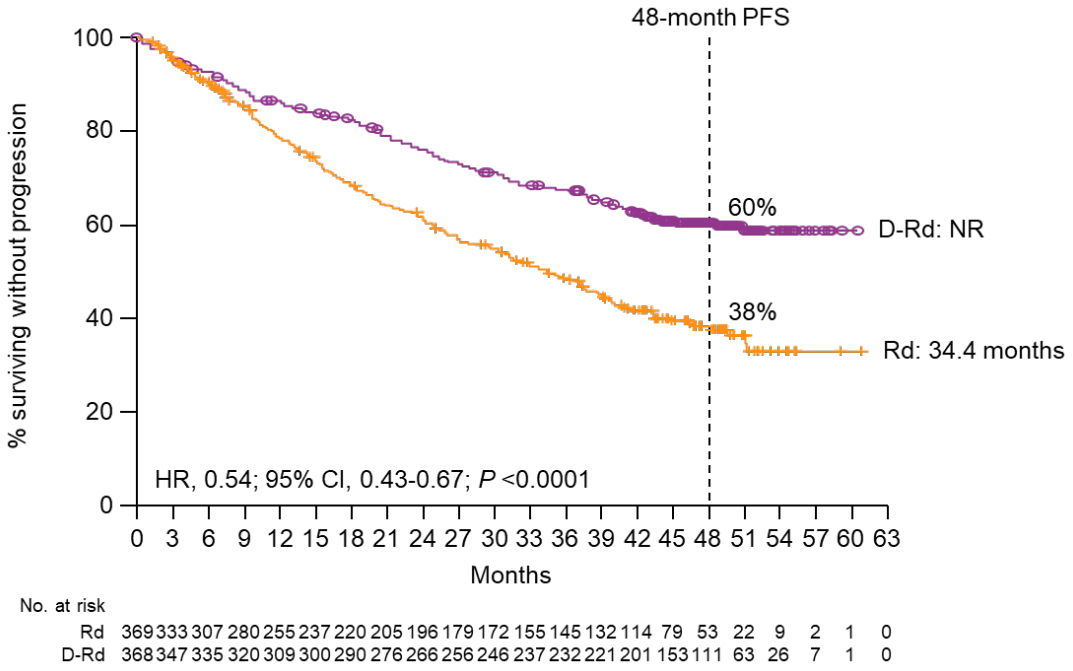
Demographic and Baseline Disease Characteristics

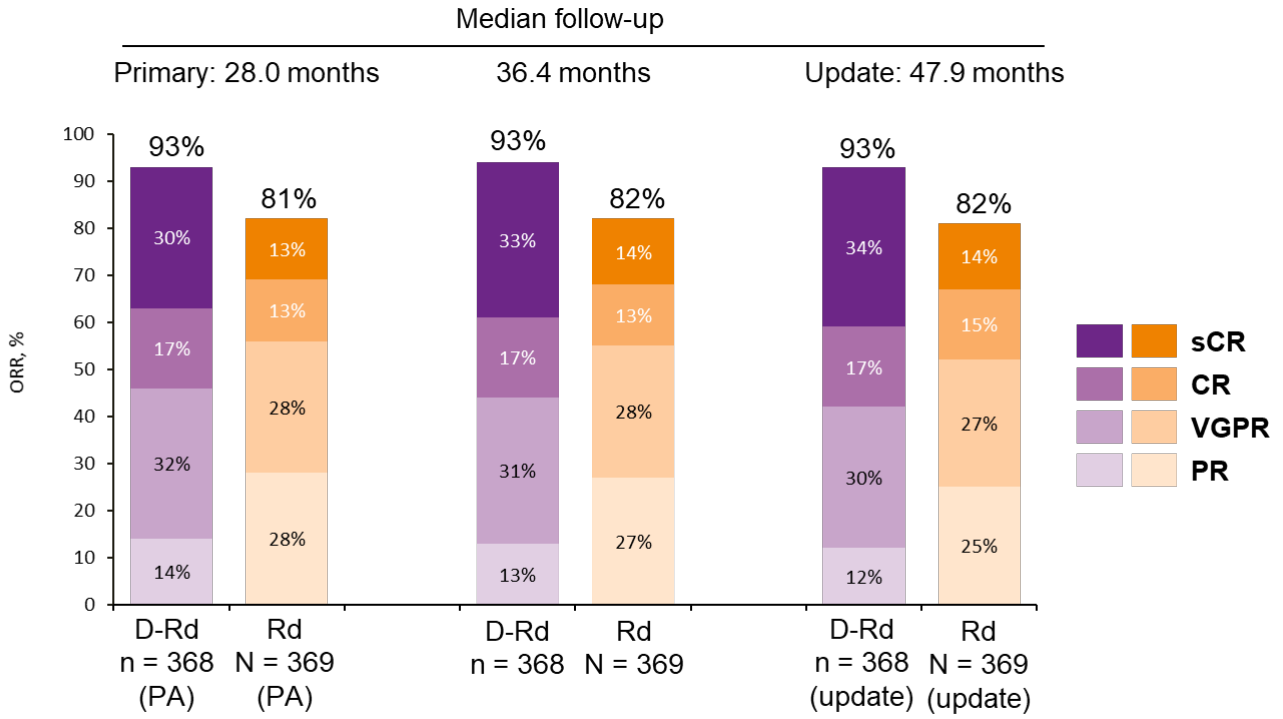
	D-Rd (n = 368)	Rd (n = 369)
Age, years		
Median (range)	73.0 (50-90)	74.0 (45-89)
Distribution, n (%)		
<65	4 (1.1)	4 (1.1)
65-<70	74 (20.1)	73 (19.8)
70-<75	130 (35.3)	131 (35.5)
≥75	160 (43.5)	161 (43.6)
ECOG PS score, n (%)		
0	127 (34.5)	123 (33.3)
1	178 (48.4)	187 (50.7)
2[a]	63 (17.1)	59 (16.0)
ISS stage, n (%)		
I	98 (26.6)	103 (27.9)
II	163 (44.3)	156 (42.3)
III	107 (29.1)	110 (29.8)

	D-Rd (n = 368)	Rd (n = 369)
Type of measurable disease, n (%)		
IgG	225 (61.1)	231 (62.6)
IgA	65 (17.7)	66 (17.9)
Other[b]	9 (2.4)	10 (2.7)
Detected in urine only	40 (10.9)	34 (9.2)
Detected as serum-free light chain only	29 (7.9)	28 (7.6)
Cytogenetic profile, n/total n (%)		
Standard risk	271/319 (85.0)	279/323 (86.4)
High risk	48/319 (15.0)	44/323 (13.6)
Median time since initial diagnosis of MM (range), months	0.95 (0.1-13.3)	0.89 (0-14.5)

D-Rd, daratumumab plus lenalidomide/dexamethasone; Rd, lenalidomide/dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System; MM, multiple myeloma. [a]2 patients had an ECOG PS score >2 (1 patient each with an ECOG PS score of 3 and 4). [b]Includes IgD, IgE, IgM, and biclonal.

Updated Efficacy with D-Rd and Rd in MAIA



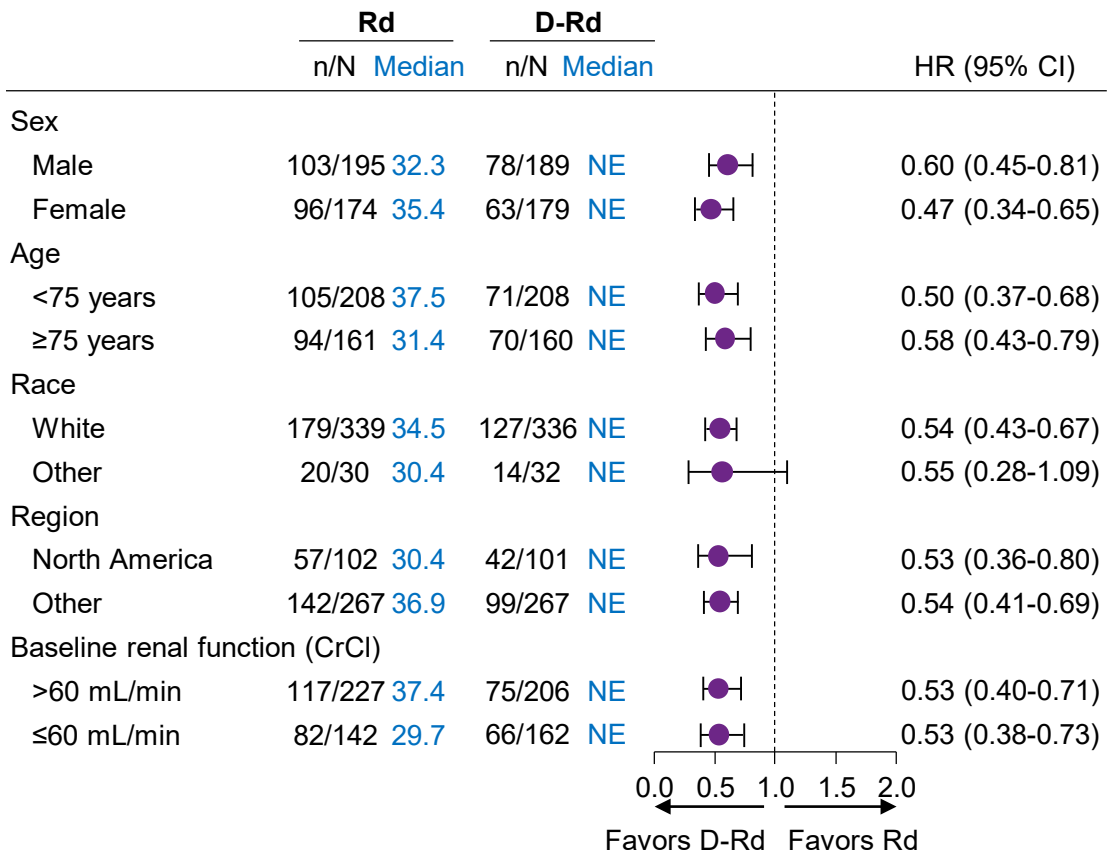


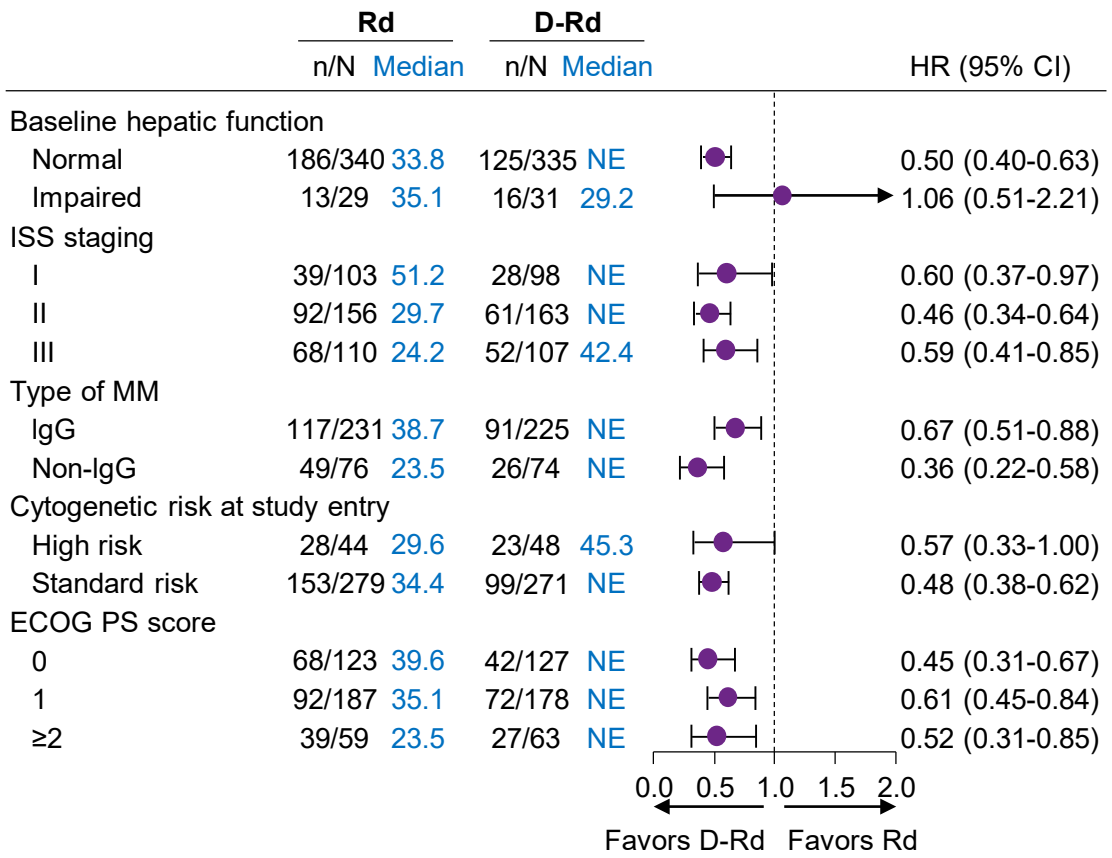
D-Rd demonstrated a significant benefit in PFS, with a 46% reduction in the risk of progression or death

Adding DARA to Rd resulted in deeper responses with higher rates of ≥CR and ≥VGPR, compared with Rd alone

PFS, progression-free survival; D-Rd, daratumumab plus lenalidomide/dexamethasone; Rd, lenalidomide/dexamethasone; NR, not reached; HR, hazard ratio; CI, confidence interval.

Subgroup Analysis of PFS

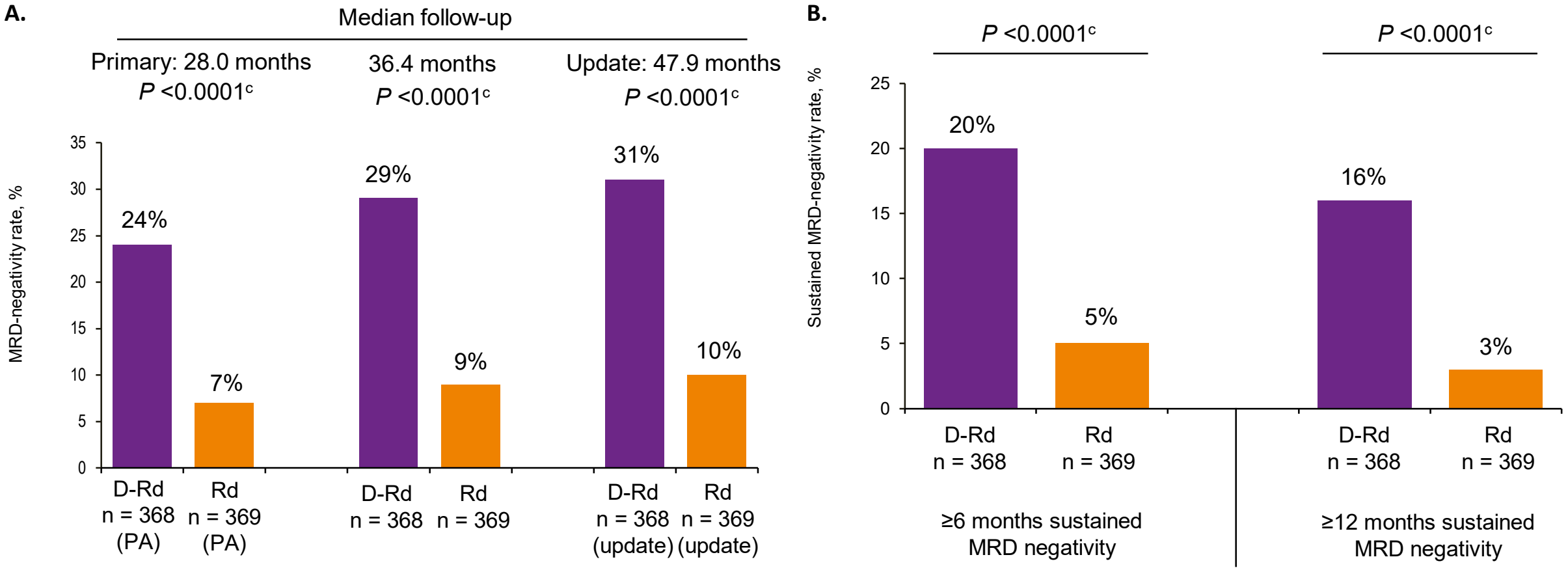




PFS benefit was generally consistent across subgroups, including patients with high cytogenetic risk

PFS, progression-free survival; Rd, lenalidomide/dexamethasone; D-Rd, daratumumab plus lenalidomide/dexamethasone; HR, hazard ratio; CI, confidence interval; NE, not estimable; CrCl, creatinine clearance; ISS, International Staging System; MM, multiple myeloma; ECOG PS, Eastern Cooperative Oncology Group performance status.

(A) MRD-negativity Rate[a] and (B) Sustained MRD Negativity[a] in Patients Treated with D-Rd versus Rd[b]



Significantly higher rates of MRD negativity and sustained MRD negativity were observed with D-Rd versus Rd alone

MRD, minimal residual disease; D-Rd, daratumumab plus lenalidomide/dexamethasone; Rd, lenalidomide/dexamethasone; PA, primary analysis; ITT, intent-to-treat. [a]ITT population. [b]Median follow-up of 47.9 months. [c]*P* value was calculated using Fisher's exact test.

Conclusions

- After a median follow-up of 47.9 months, the addition of DARA to Rd continues to demonstrate a superior PFS benefit and more patients continue to have deeper and more durable responses, including a tripling of the MRD-negativity rate, versus Rd alone in patients with TIE NDMM
  - The estimated 48-month PFS rate was substantially higher for D-Rd than Rd
  - D-Rd showed a PFS benefit and improvement in MRD-negativity rate in patients with high cytogenetic risk
- The longer follow-up also demonstrated a significant benefit in PFS2 favoring D-Rd versus Rd alone
- No new safety concerns were observed with longer follow-up

The results from this study continue to support the use of D-Rd in the first line of treatment for patients with TIE NDMM

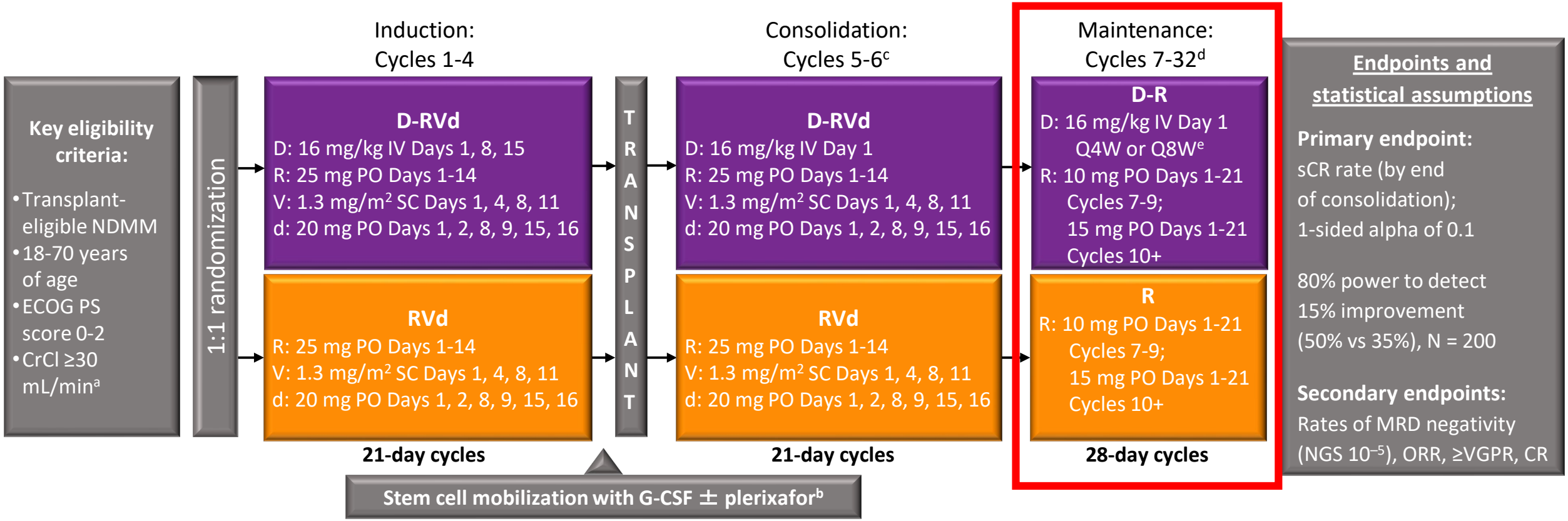
GRIFFIN: Daratumumab (DARA) Plus Lenalidomide, Bortezomib, and Dexamethasone (RVd) in Patients with Transplant-eligible Newly Diagnosed Multiple Myeloma (NDMM): Updated Analysis of GRIFFIN after 12 Months of Maintenance Therapy

- ASCT consolidation is an important standard of care for patients with transplant-eligible NDMM[1-3]
- Maintenance therapy with lenalidomide improves survival and is also standard of care[3-5]
- The phase 2 GRIFFIN study evaluates the efficacy and safety of DARA plus RVd versus RVd for patients with transplant-eligible NDMM
  - In the primary analysis of GRIFFIN (median follow-up, 13.5 months), D-RVd significantly improved rates of sCR by the end of post-transplant consolidation therapy versus RVd (42.4% vs 32.0%; 1-sided $P = 0.0680$), which met the pre-specified 1-sided alpha of 0.1[6]
  - With longer median follow-up (22.1 months), D-RVd versus RVd improved MRD-negativity rates (51.0% vs 20.4%), with estimated 24-month PFS rates of 95.8% versus 89.8%[6]
  - No new safety concerns were observed with D-RVd combination therapy, and there was no clinically significant impact on stem cell mobilization or engraftment[6]

We report updated efficacy and safety from GRIFFIN following 12 months of maintenance therapy

GRIFFIN: Randomized Phase

- Phase 2 study of D-RVd versus RVd in transplant-eligible NDMM, 35 sites in the United States with enrollment between December 2016 and April 2018



ECOG PS, Eastern Cooperative Oncology Group performance status; CrCl, creatinine clearance; IV, intravenous; PO, oral; G-CSF, granulocyte colony-stimulating factor; Q4W, every 4 weeks; Q8W, every 8 weeks; NGS, next-generation sequencing; ORR, overall response rate; VGPR, very good partial response; CR, complete response. [a]Lenalidomide dose adjustments were made for patients with CrCl ≤50 mL/min. [b]Cyclophosphamide-based mobilization was permitted if unsuccessful. [c]Consolidation was initiated 60 to 100 days post transplant. [d]Patients who complete maintenance cycles 7 to 32 may continue single-agent lenalidomide thereafter. [e]Protocol Amendment 2 allowed for the option to dose daratumumab Q4W, based on pharmacokinetic results from study SMM2001 (NCT02316106).

Demographic and Clinical Characteristics (ITT)

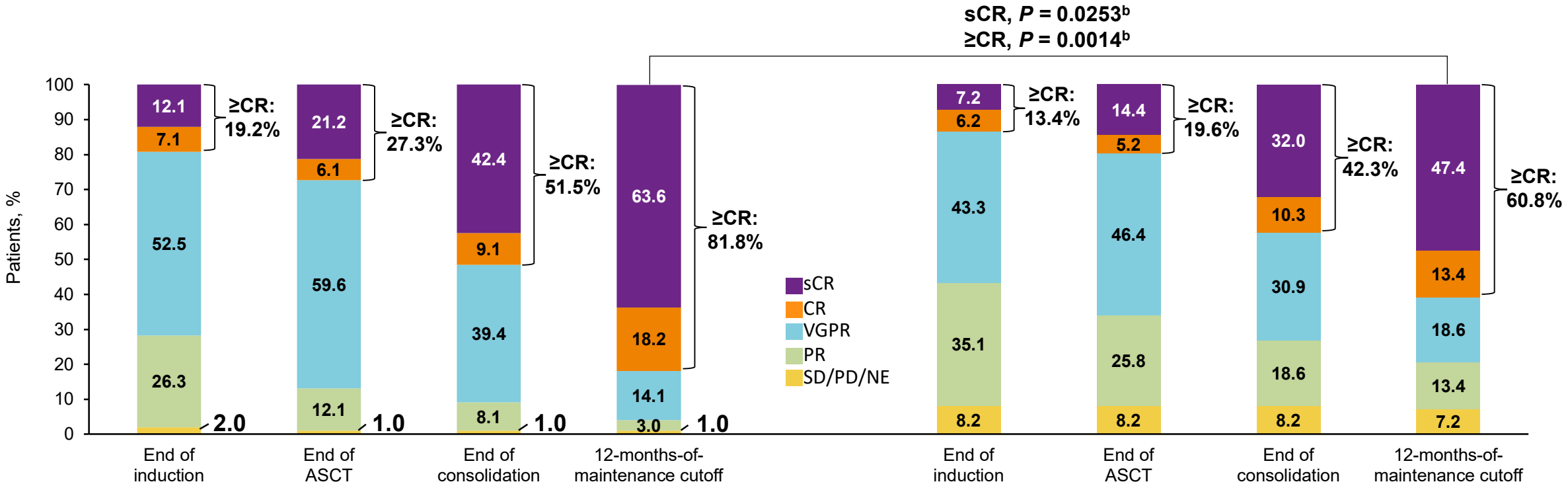
	D-RVd (n = 104)	RVd (n = 103)
Age, years		
Median (range)	59 (29-70)	61 (40-70)
≥65, n (%)	28 (27)	28 (27)
Male, n (%)	58 (56)	60 (58)
ECOG PS score,[a] n (%)	n = 101	n = 102
0	39 (39)	40 (39)
1	51 (50)	52 (51)
2	11 (11)	10 (10)
Baseline CrCl, n (%)		
30-50 mL/min	9 (9)	9 (9)
>50 mL/min	95 (91)	94 (91)

	D-RVd (n = 104)	RVd (n = 103)
ISS disease stage,[b] n (%)		
I	49 (47)	50 (49)
II	40 (38)	37 (36)
III	14 (13)	14 (14)
Missing	1 (1)	2 (2)
Cytogenetic profile,[c] n (%)	n = 98	n = 97
Standard risk	82 (84)	83 (86)
High risk	16 (16)	14 (14)
Time since MM diagnosis, months	n = 103	n = 102
Median	0.7	0.9

Treatment arms were well balanced

ITT, intent-to-treat; ISS, International Staging System; MM, multiple myeloma. [a]ECOG PS is scored on a scale from 0 to 5, with 0 indicating no symptoms and higher scores indicating increasing disability. [b]The ISS disease stage is based on the combination of serum β2-microglobulin and albumin levels. Higher stages indicate more advanced disease. [c]Cytogenetic risk was assessed by fluorescence in situ hybridization (locally tested) among patients with available cytogenetic risk data; high risk was defined as the presence of del(17p), t(4;14), or t(14;16).

Responses Deepened over Time[a]



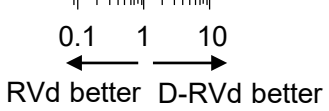
- *Results for end of induction, ASCT, and consolidation are based on a median follow up of 13.5 months at the primary analysis*
- *Median follow up at 12-months-of-maintenance therapy cutoff was 27.4 months*

Response rates and depths were greater for D-RVd at all time points

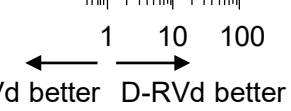
PR, partial response. SD/PD/NE, stable disease/progressive disease/not evaluable. [a]Data are shown for the response-evaluable population. [b]*P* values (2-sided) were calculated using the Cochran–Mantel–Haenszel chi-square test.

Subgroup Analysis of sCR and MRD Negativity[a] by the 12-Months-of-Maintenance Therapy Cutoff

	RVd sCR, n (%)	D-RVd sCR, n (%)	Odds ratio (95% CI)
Sex			
Male	25/55 (45.5)	33/55 (60.0)	1.80 (0.84-3.84)
Female	21/42 (50.0)	30/44 (68.2)	2.14 (0.89-5.15)
Age			
<65 years	35/70 (50.0)	46/72 (63.9)	1.77 (0.90-3.46)
≥65 years	11/27 (40.7)	17/27 (63.0)	2.47 (0.83-7.39)
ISS disease stage			
I	18/48 (37.5)	29/48 (60.4)	2.54 (1.12-5.79)
II	19/35 (54.3)	26/37 (70.3)	1.99 (0.76-5.25)
III	8/13 (61.5)	8/14 (57.1)	0.83 (0.18-3.88)
Type of MM			
IgG	17/51 (33.3)	31/51 (60.8)	3.10 (1.38-6.96)
Non-IgG	29/46 (63.0)	29/45 (64.4)	1.06 (0.45-2.50)
Cytogenetic risk			
High risk	5/13 (38.5)	7/16 (43.8)	1.24 (0.28-5.53)
Standard risk	40/80 (50.0)	55/79 (69.6)	2.29 (1.20-4.39)
ECOG PS score			
0	15/39 (38.5)	22/38 (57.9)	2.20 (0.88-5.47)
1-2	31/58 (53.4)	40/60 (66.7)	1.74 (0.83-3.67)



	RVd MRD negative, n (%)	D-RVd MRD negative, n (%)	Odds ratio (95% CI)
Sex			
Male	14/60 (23.3)	33/58 (56.9)	4.34 (1.96-9.58)
Female	14/43 (32.6)	32/46 (69.6)	4.73 (1.93-11.59)
Age			
<65 years	23/75 (30.7)	46/76 (60.5)	3.47 (1.77-6.79)
≥65 years	5/28 (17.9)	19/28 (67.9)	9.71 (2.78-33.92)
ISS disease stage			
I	10/50 (20.0)	32/49 (65.3)	7.53 (3.03-18.69)
II	13/37 (35.1)	23/40 (57.5)	2.50 (0.99-6.27)
III	5/14 (35.7)	10/14 (71.4)	4.50 (0.91-22.15)
Type of MM			
IgG	13/52 (25.0)	35/55 (63.6)	5.25 (2.28-12.09)
Non-IgG	15/51 (29.4)	28/46 (60.9)	3.73 (1.60-8.69)
Cytogenetic risk			
High risk	4/14 (28.6)	7/16 (43.8)	1.94 (0.42-8.92)
Standard risk	24/83 (28.9)	56/82 (68.3)	5.29 (2.72-10.29)
ECOG PS score			
0	8/40 (20.0)	25/39 (64.1)	7.14 (2.59-19.69)
1-2	20/62 (32.3)	40/62 (64.5)	3.82 (1.81-8.04)

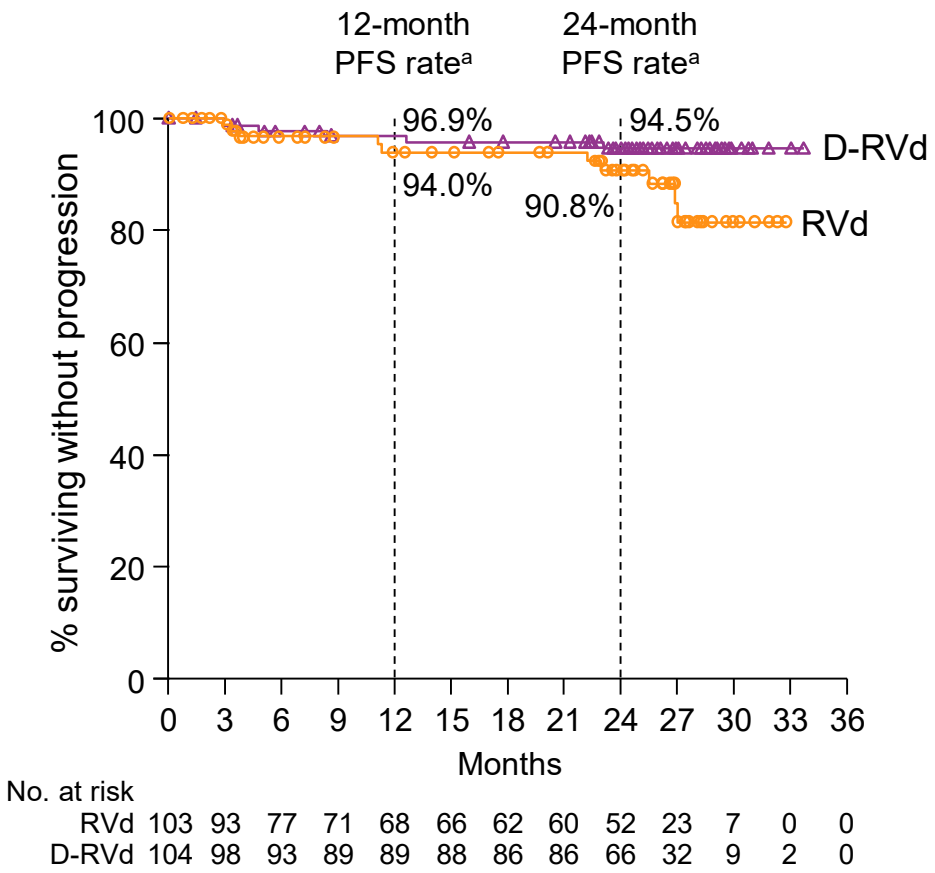


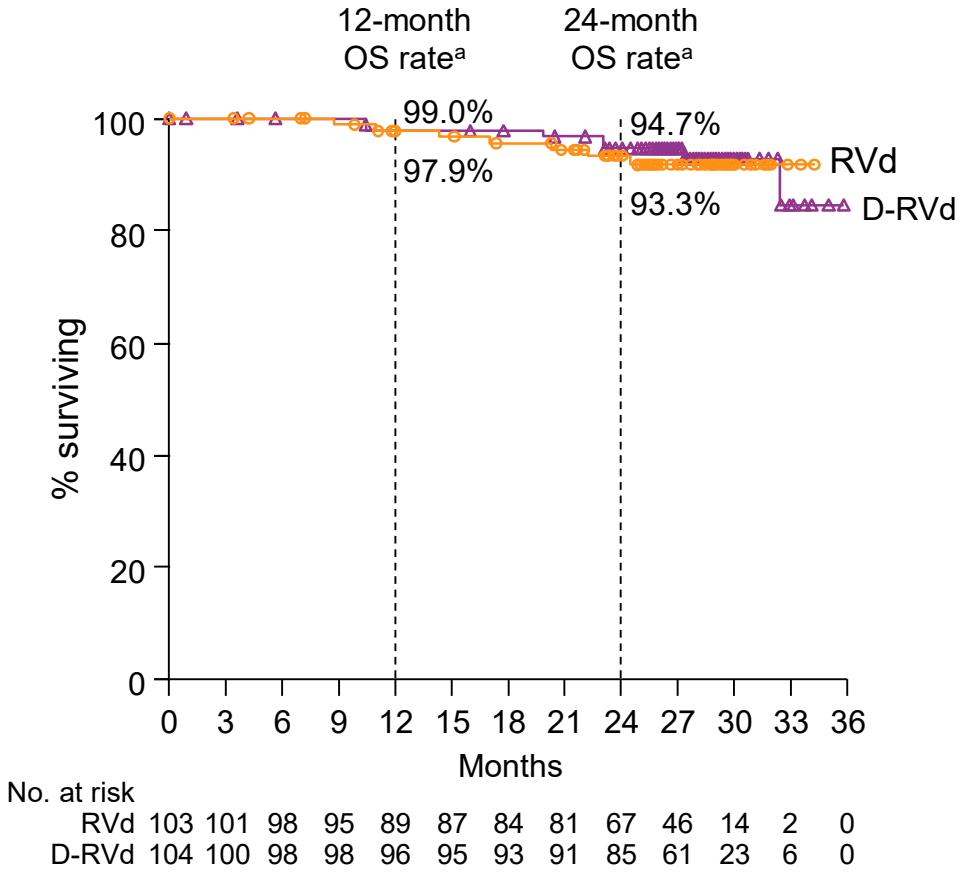
D-RVd improved sCR and MRD-negativity rates across most subgroups

CI, confidence interval. [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 27.4 months.

PFS and OS in the ITT Population

- Median follow-up = 27.4 months





Median PFS and OS were not reached for D-RVd and RVd

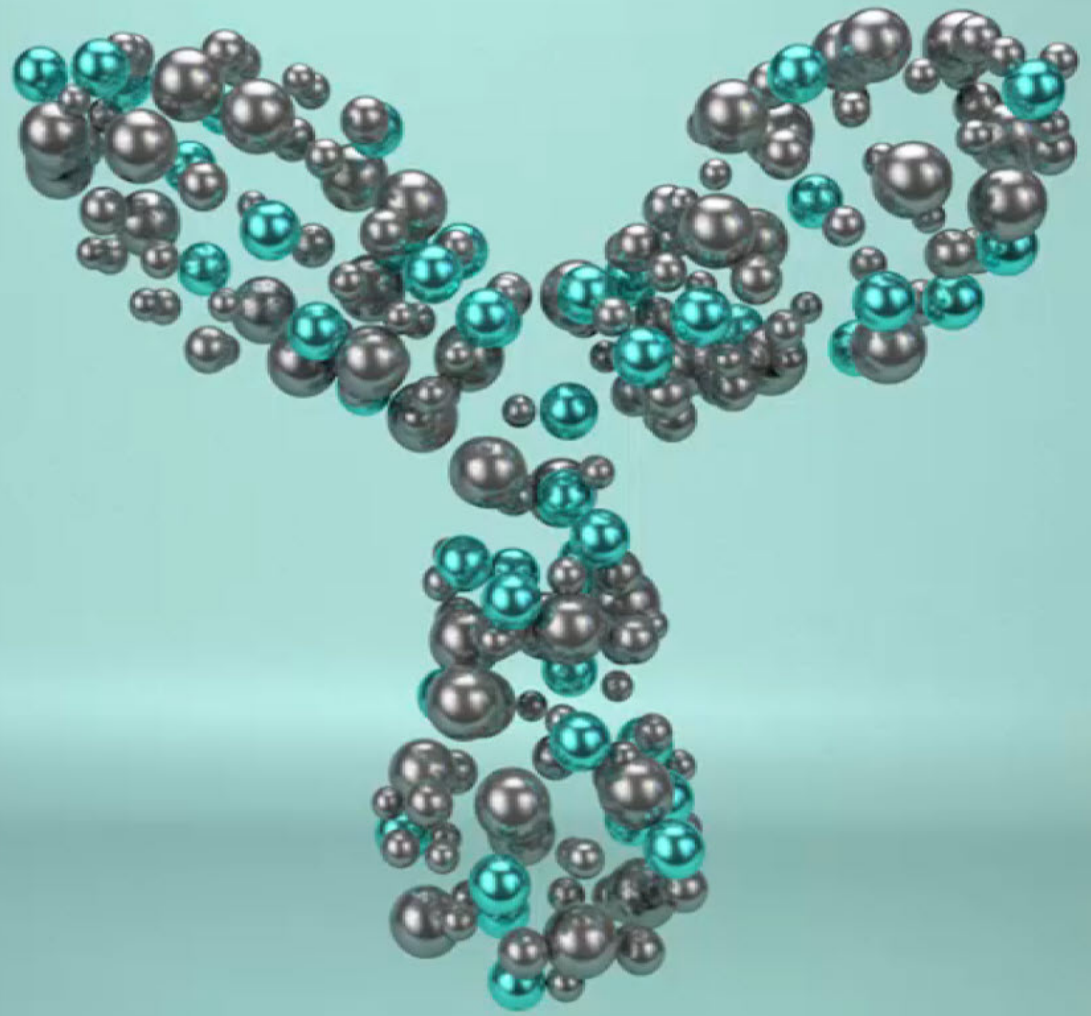
OS, overall survival. [a]Kaplan–Meier estimate.

Conclusions

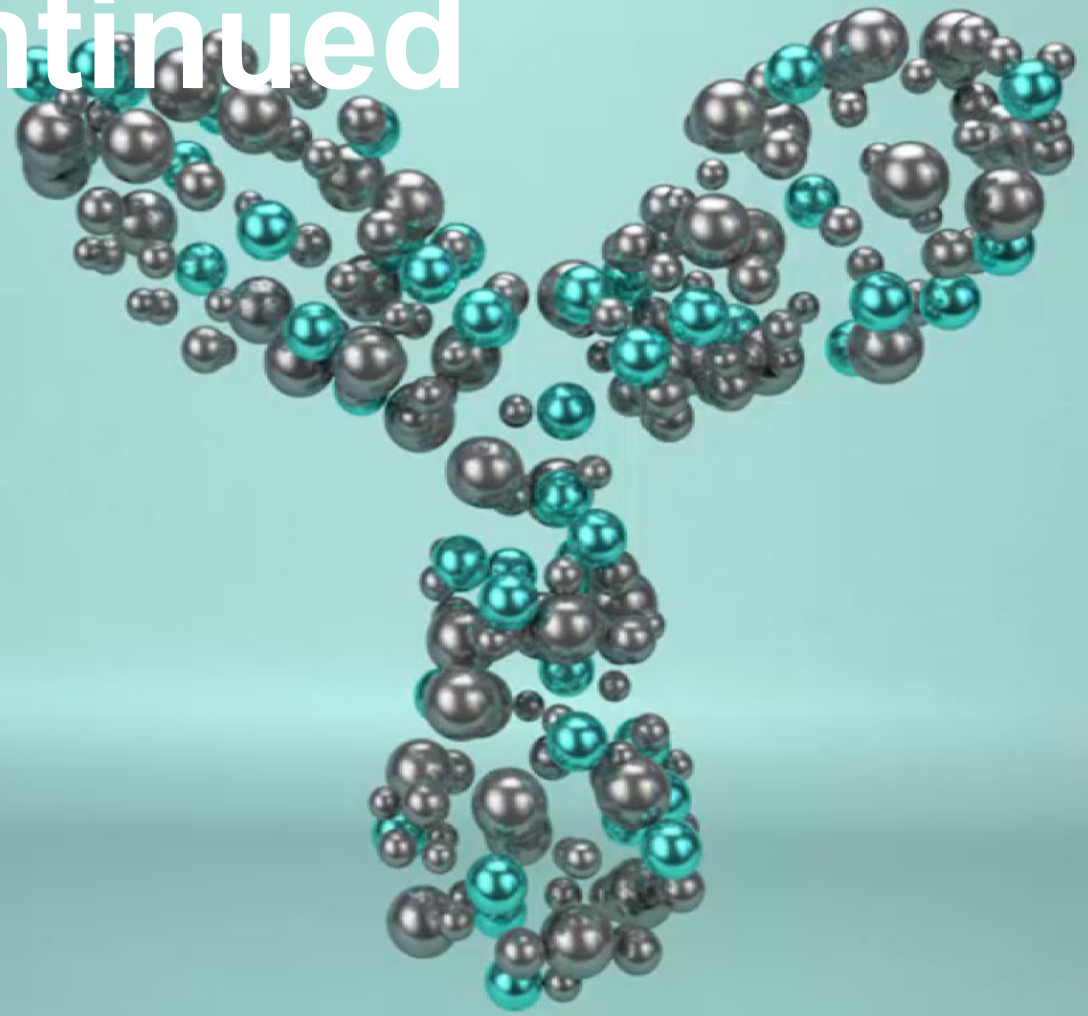
- D-RVd followed by D-R maintenance significantly improved response rates and depth of response versus RVd followed by R maintenance
- D-R maintenance therapy improved depth of response and maintained remissions
  - sCR and MRD-negativity rates improved with maintenance therapy
- The overall safety profile of D-RVd is consistent with previous reports of daratumumab plus standard of care
- Estimated PFS and OS rates at 24 months in the D-RVd group are promising
  - Durability of PFS and OS benefits are suggested by the GRIFFIN safety run-in cohort (>40 months median follow-up; ASH 2020 poster 3243)
- The ongoing phase 3 PERSEUS study is evaluating DARA SC plus RVd in transplant-eligible patients

These results support D-RVd as a potential new standard of care for transplant-eligible NDMM

Q&A



2021 & Beyond: Positioned for Continued Success



Dr. Jan van de Winkel
President & CEO

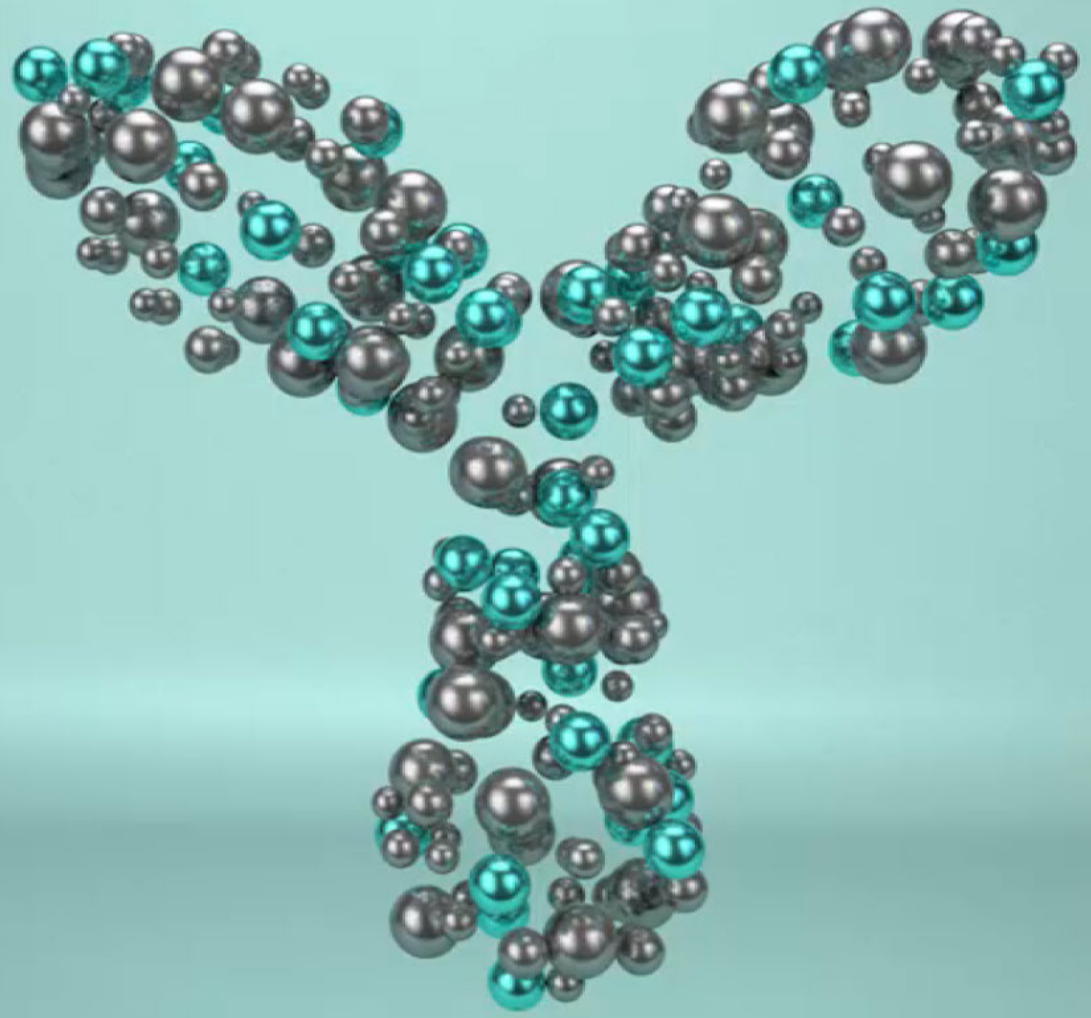
Key 2021 Priorities

Build a Strong Differentiated Product Pipeline & Bring Own Medicines to Market

Priority	✓	Targeted Milestones
Bring our own medicines to patients		» Tisotumab vedotin[1] - U.S. FDA decision on BLA and progress to market » Tisotumab vedotin - JNDA submission in cervical cancer » Epcoritamab[2] - acceleration & maximization of development program by advancing expansion cohorts and initiating additional Phase 3 trials
Build world-class differentiated product pipeline		» DuoBody-PD-L1x4-1BB[3] – expansion cohort data » DuoBody-CD40x4-1BB[3] – dose escalation data » Tisotumab vedotin – data in other tumor indication » Earlier stage products – progress & expand innovative product pipeline
Become leading integrated innovation powerhouse		» Operational commercialization model in US & Japan » Further strengthen solid financial foundation (guidance - Feb 23, 2021)

1. 50:50 dev. w/ Seagen; 2. 50:50 dev w/ AbbVie; 3. 50:50 dev. w/ BioNTech

Q&A



Happy Holidays