2017 R&D Update

December 11, 2017
Live in Atlanta and via Webcast 20:00 – 21:45 EST

Genmab

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.

Agenda

20:00	Welcome & Introduction	Dr. Jan van de Winkel, Ph.D., President & CEO, Genmab
20:10	Daratumumab: ALCYONE & EQUULEUS (D-K[R]d) data	Prof. Maria Victoria Mateos, M.D., Ph.D., University Hospital of Salamanca
20:20	Daratumumab: CENTAURUS, PAVO & GRIFFIN data	Dr. Saad Usmani, M.D., FACP, University of North Carolina at Chapel Hill, Levine Cancer Institute
20:30	Daratumumab: POLLUX, CASTOR & EQUULEUS (D-Pom-dex) data	Prof. Philippe Moreau, M.D., University Hospital of Nantes
20:40	CD38 in Solid Tumors	Dr. Kate Sasser, Ph.D., CVP, Clinical Biomarkers, Genmab
20:45	Daratumumab Q&A	All Genmab and daratumumab speakers
21:05	Tisotumab Vedotin	Prof. Ignace Vergote, M.D., Ph.D., Catholic University of Leuven
21:15	Tisotumab Vedotin Q&A	Prof. Ignace Vergote Dr. Judith Klimovsky, M.D., EVP & CDO, Genmab
21:25	2018 and Beyond	Dr. Jan van de Winkel David Eatwell, EVP & CFO, Genmab
21:35	General Q&A	
21:45	Refreshments	

Genmab At-A-Glance

Vision: By 2025, our own product has transformed cancer treatment and we have a pipeline of knock-your-socks off antibodies

DARZALEX®
Arzerra®

2 marketed products generating royalty income

Tisotumab vedotin
HuMax®-AXL-ADC
HexaBody-DR5/DR5
DuoBody-CD3xCD20

4 exciting proprietary clinical programs

DuoBody® Platform
HexaBody® Tech.

2 proprietary next gen. technologies for robust pre-clinical pipeline

Solid financial base

Aim to own at least 50% of product rights
Allows for building capabilities to market own product in future

Key Achievements 2017: Towards our 2025 Vision

Regulatory Achievements

- DARZALEX
  - Approved in Japan
  - Combo with pom + dex approved in US
  - 2nd line combo approved in EU
  - Frontline submitted in US & EU
  - IND for daratumumab in RA
  - Granted Orphan Drug Status by FDA in amyloidosis
- INDs & CTAs for HexaBody-DR5/DR5 & DuoBody CD3xCD20

Clinical Development

- Daratumumab
  - Positive topline ALCYONE data
  - 25 abstracts at ASH
  - Expansion of dev. Including SC & outside MM
- Tisotumab vedotin
  - Data at ESMO & ESGO
  - New potentially reg. trial in cervical cancer
- Study with new DuoBody product, JNJ-64007957

Corporate Development

- Judith Klimovsky joins Genmab as CDO
- Seattle Genetics exercised option to co-develop tisotumab vedotin
- Genmab wins Denmark Bridge Award 2017
- SCRIP award (together w/ Janssen) for Clinical Advance of the Year for CASTOR & POLLUX

Financial Performance

- DARZALEX sales reach USD 1 billion - blockbuster status
- Project DKK 1,090M DARZALEX milestones
- Selective targeted investments in pipeline

Innovative Pipeline: Moving Genmab Forward

Development for Marketed Products

Daratumumab

Target: CD38
Partner: Janssen
- MM, Amyloidosis, NKTCL, MDS, Solid tumors

Ofatumumab

Target: CD20
Partner: Novartis
- FL, RMS

Genmab Proprietary Products: Moving Towards Our Vision

Tisotumab vedotin

Target: TF
Partner: 50:50 with Seattle Genetics
- Cervical cancer, other solid cancers,

HuMax-AXL-ADC

Target: AXL
Genmab Owned
- Solid cancers

DuoBody-CD3xCD20

Target: CD20
Genmab Owned
- B-cell malignancies

HexaBody-DR5/DR5

Target: DR5
Genmab Owned
- Solid cancers

Additional Shots on Goal

Teprotumumab
Target: IGF-1R
Partner: Horizon Pharma
- Graves' orbitopathy

AMG 714
Target: IL-15
Partner: Celimmune
- Celiac Disease

ADCT-301
Target: CD25
Partner: ADCT
- Lymphoma, AML or ALL

JNJ-61186372
Targets: EGFR, cMet
Partner: Janssen
- NSCLC

JNJ-63709178
Targets: CD3, CD123
Partner: Janssen
- AML

JNJ-64007957
Targets: BCMA, CD3
Partner: Janssen
- RRMM

>20 active pre-clinical programs (partnered & Genmab owned)

Strengthening Genmab's Proprietary Pipeline: Tisotumab Vedotin

Phase II Study in Cervical Cancer: Potentially Registrational

Primary endpoint

- ORR

Main secondary endpoints

- Duration of response
- Safety

Key inclusion criteria

- Disease progression on or after platinum containing chemo
- Have received or are ineligible for bevacizumab

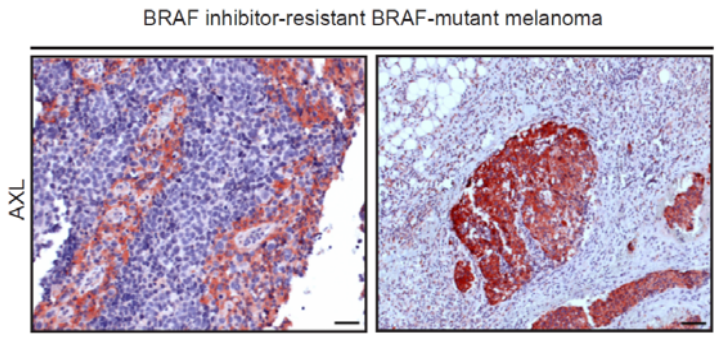
- Single arm
- Multicenter
- Phase II
- Monotherapy
- 100 pts

Strengthening Genmab's Proprietary Pipeline: HuMax-AXL-ADC

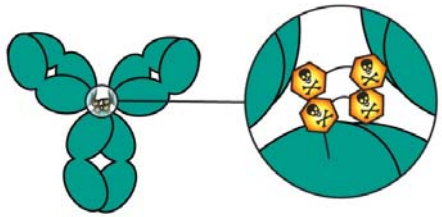
Human ADC
- First-in-class antibody-drug conjugate
- ADC technology from Seattle Genetics
- Genmab owned 100%

AXL as tumor target
- Broadly expressed across (treatment-resistant) solid cancers

First-in-human Phase I/II study ongoing
- Multiple solid tumor indications
- Progress in dose escalation: ongoing in gynecologic cancers (ovarian, cervical, endometrial), thyroid cancer, NSCLC and melanoma
- Expansion cohorts will be initiated in 2018



AXL expression indicated by brown staining



Strengthening Genmab's Proprietary Pipeline: HexaBody-DR5/DR5

DR5 as tumor target

- DR5 (death receptor 5) is a cell surface receptor, mediates programmed cell death
  - Important for natural elimination of cells (apoptosis)
  - Tumor cells specifically sensitive to DR5-mediated apoptosis

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HexaBody-DR5/DR5 (GEN1029)

- Mixture of two non-competing DR5-targeting HexaBody molecules that shows DR5 agonist activity
- Cytotoxicity is dependent on dual epitope targeting and HexaBody-mediated DR5 clustering

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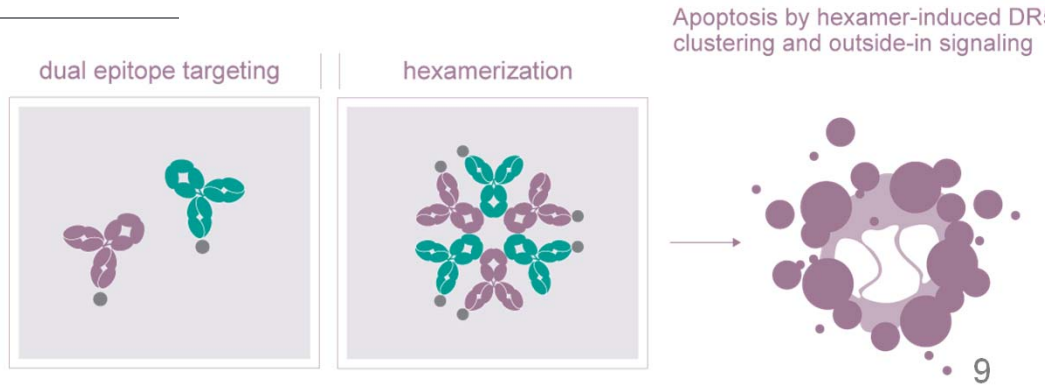
IND and CTAs filed in Q4 2017

- Phase I/II trial initiated in Q1 2018

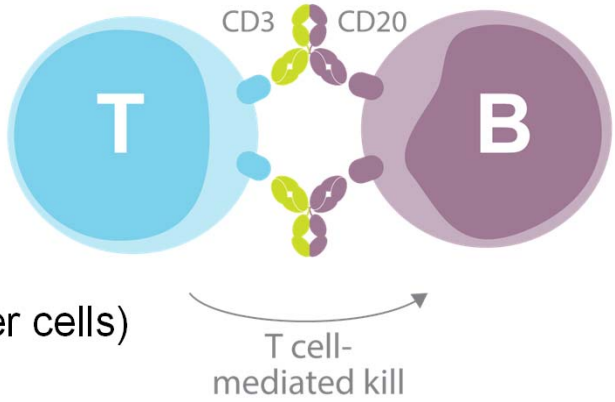


Strengthening Genmab's Proprietary Pipeline: DuoBody-CD3xCD20

Next IND Filing

CD20 as tumor target

- Expression restricted to B cells
- Highest surface expression levels among known B cell malignancy targets
- Broadly expressed on B cell malignancies
- A well established therapeutic target



DuoBody-CD3xCD20

- Effectively bridges $CD20^{+}$ (tumor) cells & T cells (highly potent immune killer cells)
  - Activates T cells to destroy CD20+ tumor cells
- Independent of specificity of the T cells
- Inert Fc region: no general activation of T cells through Fc receptor mediated crosslinking
- Cytotoxicity depends on binding to both CD3 and CD20
- Preclinical data in Cynomolgus monkeys
  - Profound, reversible, dose-dependent depletion of B cells in blood and lymphoid organs
- Optimized formulation to reduce peak cytokine levels

IND and CTA filing Q4 2017

- Phase I/II study initiated in 2018

ALCYONE (MMY3007)

Presented by Prof. Maria Victoria Mateos
University Hospital of Salamanca

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Phase 3 Randomized Study of Daratumumab Plus Bortezomib, Melphalan, and Prednisone (D-VMP) Versus Bortezomib, Melphalan, and Prednisone (VMP) in Newly Diagnosed Multiple Myeloma Patients Ineligible for Transplant (ALCYONE)

Maria Victoria-Mateos,[1] Meletios A. Dimopoulos,[2] Michele Cavo,[3] Kenshi Suzuki,[4] Andrzej Jakubowiak,[5] Stefan Knop,[6] Chantal Doyen,[7] Paulo Lucio,[8] Zsolt Nagy,[9] Polina Kaplan,[10] Ludek Pour,[11] Mark Cook,[12] Sebastian Grosicki,[13] Andre Crepaldi,[14] Anna Marina Liberati,[15] Philip Campbell,[16] Tatiana Shelekhova,[17] Sung-Soo Yoon,[18] Genadi Iosava,[19] Tomoaki Fujisaki,[20] Mamta Garg,[21] Christopher Chiu,[22] Jianping Wang,[23] Robin Carson,[22] Wendy Crist,[22] William Deraedt,[24] Marie Nguyen,[23] Ming Qi,[22] Jesus San-Miguel[25]

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Introduction & Methods

- Outside the US, bortezomib, melphalan & prednisone (VMP) is a standard-of-care for transplant ineligible newly diagnosed multiple myeloma.
- Daratumumab (D) significantly improves PFS & depth of response in combination with standard-of-care in relapsed multiple myeloma
- Treatment-naïve patients may benefit greatly with the addition of daratumumab to standard-of-care regimens
- First Phase 3 study of daratumumab in transplant-ineligible newly diagnosed multiple myeloma patients
- Patients ≥65 years or otherwise ineligible for high-dose chemo. with ASCT randomized 1:1 to VMP ± D
- Primary endpoint was PFS
- Key secondary endpoints: ORR, VGPR, CR, MRD negativity rate, OS & safety

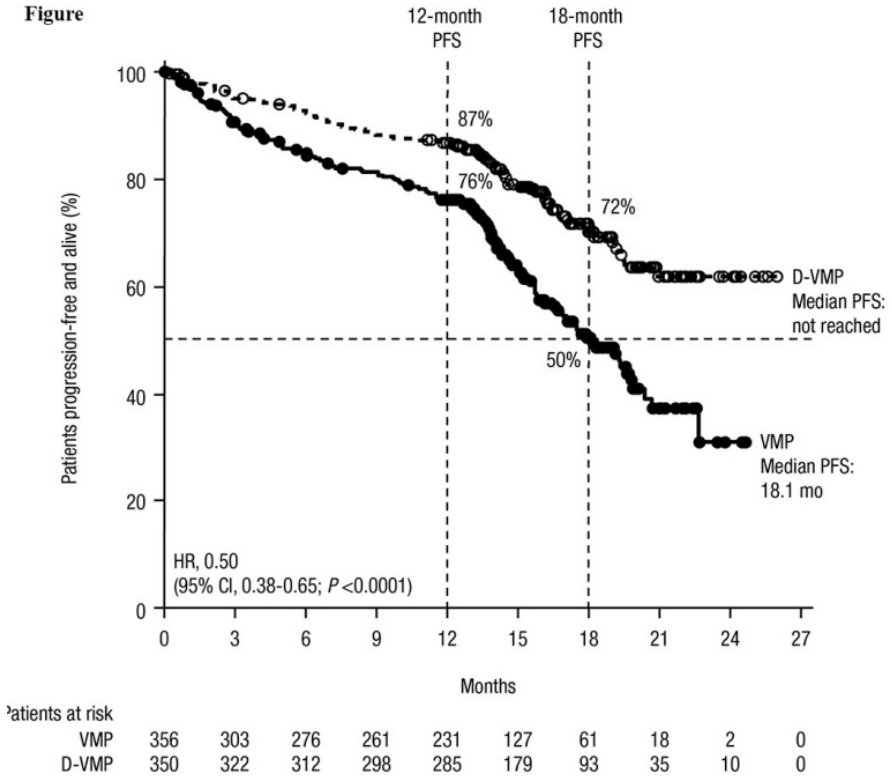
Patient Characteristics

- Total patients
  - 350 D-VMP
  - 356 VMP
- Median age
  - 71 (40 – 93) years
  - 29.9% ≥75 years
- 46.3% male
- 74.9 had ECOG scores ≥1
- ISS stage
  - I: 19.3%
  - II: 42.4%
  - III: 38.4%
- FISH/karyotyping cytogenetic analysis
  - 616 patients evaluable
  - 84.1% standard risk
  - 15.9% high risk

- At time of pre-specified analysis after 231 PFS events
  - Median of 12 (1-24) treatment cycles for D-VMP
  - Median of 9 (1-9) treatment cycles for VMP
  - 80% of patients in D-VMP arm completed 9 treatment cycles of VMP vs 62% of patients in the VMP arm
  - Median cumulative bortezomib doses were 46.9 mg/m^2 for D-VMP
  - Median cumulative bortezomib doses were 42.2 mg/m^2 for VMP

Results

Median follow-up: 16.5 mo.



Overall Responses

Response Category	D-VMP (%)	VMP (%)	Odds Ratio (95% CI)	P value
ORR	90.9	73.9	3.55 (2.30, 5.49)	<0.0001
Stringent CR	18.0	7.0		
CR	24.6	17.4		
VGPR	28.6	25.3		
PR	19.7	24.2		
≥VGPR	71.1	49.7	2.50 (1.83, 3.41)	<0.0001
≥CR	42.6	24.4	2.31 (1.67, 3.20)	<0.0001
MRD negative (10^{-5})	22.3	6.2	4.36 (2.64, 7.21)	<0.0001

Patients treated with D-VMP:
- **50% reduction in risk of progression or death**
- **Median PFS not reached**
- **Treatment benefit consistent across all pre-specified subgroups**

Results: MRD-negativity Rate (10^{-5})

Response Category	D-VMP (%)	VMP (%)	Odds Ratio (95% CI)	P value
MRD negative (10^{-5})	22.3	6.2	4.36 (2.64, 7.21)	<0.0001

Safety

Most common (≥20%) all grade TEAEs

	D-VMP	VMP
Neutropenia	49.7%	52.5%
Thrombocytopenia	48.8%	53.7%
Anemia	28.0%	37.6%
Peripheral sensory neuropathy	28.3%	34.2%
Upper respiratory tract infection	26.3%	13.8%
Diarrhea	23.7%	24.6%
Pyrexia	23.1%	20.9%
Nausea	20.8%	21.5%

Most common (≥10%) grade 3/4 TEAEs

	D-VMP	VMP
Neutropenia	39.9%	38.7%
Thrombocytopenia	34.4%	37.6%
Anemia	15.9%	19.8%
Pneumonia	11.3%	4.0%

No new safety signals

Conclusion

- The combination of daratumumab with VMP in transplant ineligible newly diagnosed multiple myeloma patients doubled the PFS
- More patients achieved deep responses
- Significantly higher ≥CR rate
- Tripling of MRD-negativity rate
- No new safety signals observed
- 3 Phase 3 studies have now demonstrated consistent doubling of PFS & more than threefold increase in MRD-negativity rate when combining daratumumab with standard-of-care regimens

Results support use of a D-VMP in transplant ineligible newly-diagnosed multiple myeloma

EQUULEUS (MMY1001)

Presented by Prof. Maria Victoria Mateos
University Hospital of Salamanca

Genmab

Poster 1869: Daratumumab in Combination with Carfilzomib and Dexamethasone in Patients (Pts) with Relapsed Multiple Myeloma (MMY1001): An Open-label, Phase 1b Study

Sagar Lonial,[1,*] Jesus San-Miguel,[2] Joaquín Martinez-Lopez,[3] Maria-Victoria Mateos,[4] Joan Bladé,[5] Lotfi Benboubker,[6] Albert Oriol,[7] Bertrand Arnulf,[8] Ajai Chari,[9] Luis Pineiro,[10] Kaida Wu,[11] Jianping Wang,[12] Parul Doshi,[11] Jordan M. Schecter,[12] Philippe Moreau[13]

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Poster 1869: Daratumumab in Combination with Carfilzomib and Dexamethasone in Patients (Pts) with Relapsed Multiple Myeloma (MMY1001): An Open-label, Phase 1b Study

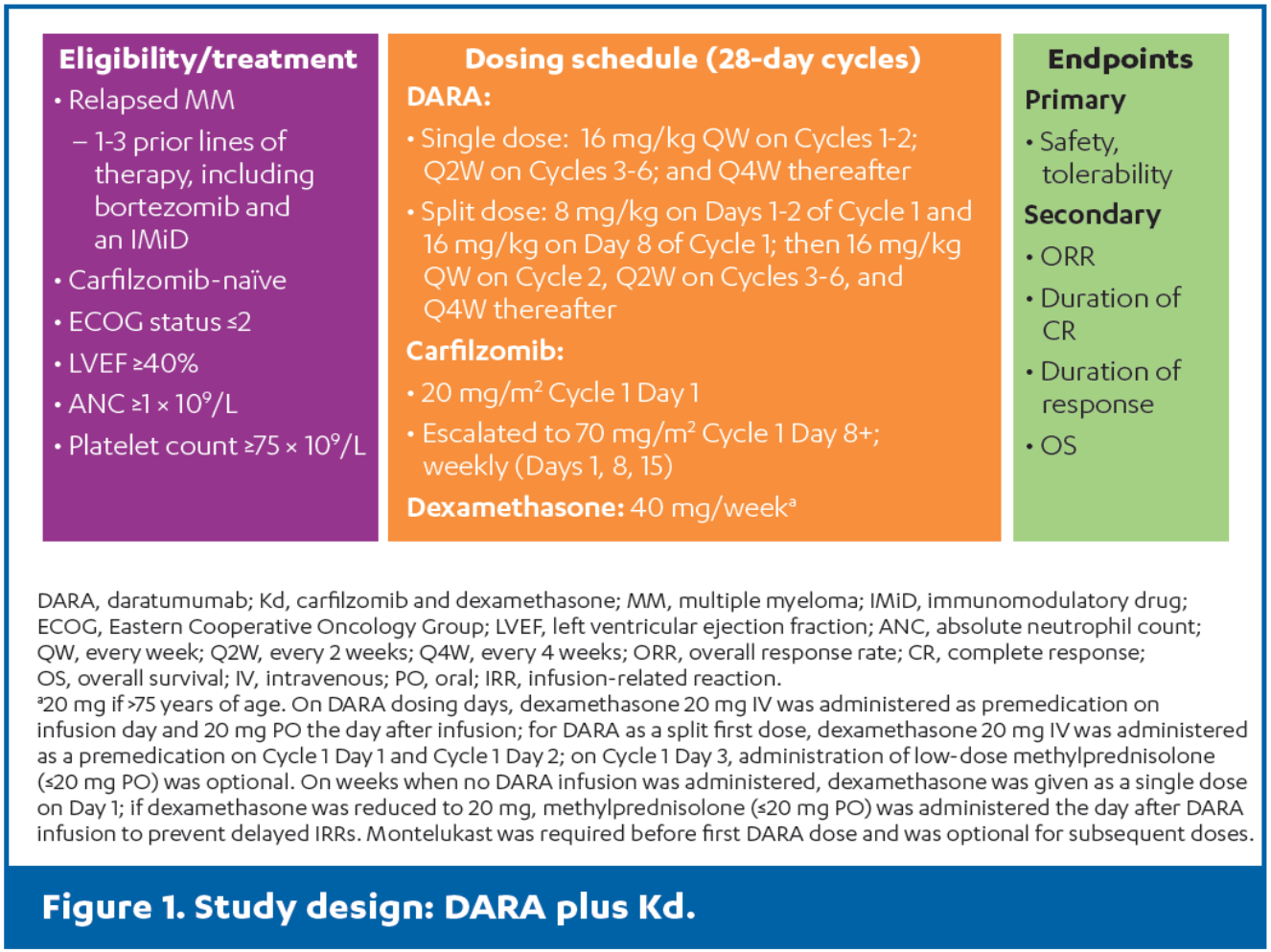


Figure 1. Study design: DARA plus Kd.

Poster 1869: Daratumumab in Combination with Carfilzomib and Dexamethasone in Patients (Pts) with Relapsed Multiple Myeloma (MMY1001): An Open-label, Phase 1b Study

Table 1. Baseline Characteristics and Prior MM Therapies Received

Characteristic	DKd (n = 85)
Age, y	
Median (range)	66 (38-85)
≥75 y, n (%)	8 (9)
ECOG status, n (%)	
0	32 (38)
1	46 (54)
2	7 (8)
Prior lines of therapy, n (%)	
Median (range)	**2 (1-4)**
1	21 (25)
2	39 (46)
3	23 (27)
>3	2 (2)
Prior ASCT, n (%)	62 (73)
Prior PI, n (%)	84 (99)
Bortezomib	84 (99)
Ixazomib	7 (8)
Prior IMiD, n (%)	84 (99)
Lenalidomide	80 (94)
Pomalidomide	13 (15)
Thalidomide	21 (25)
Prior PI + IMiD, n (%)	83 (98)
Prior PI + IMiD + ALKY, n (%)	79 (93)
Refractory to, n (%)	
Lenalidomide	51 (60)
Pomalidomide	11 (13)
PI	27 (32)
PI + IMiD	25 (29)

MM, multiple myeloma; DKd, daratumumab/carfilzomib/dexamethasone; ECOG, Eastern Cooperative Oncology Group; ASCT, autologous stem cell transplantation; PI, proteasome inhibitor; IMiD, immunomodulatory drug; ALKY, alkylator.

Poster 1869: Daratumumab in Combination with Carfilzomib and Dexamethasone in Patients (Pts) with Relapsed Multiple Myeloma (MMY1001): An Open-label, Phase 1b Study

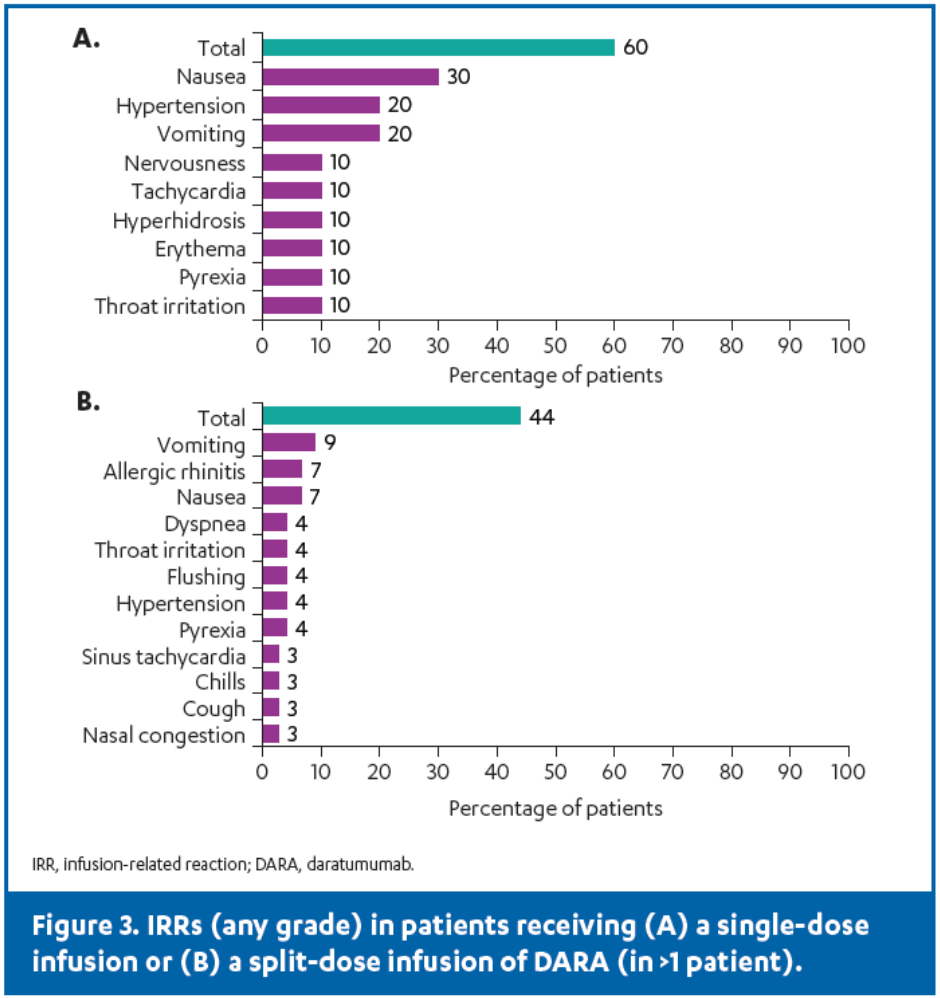
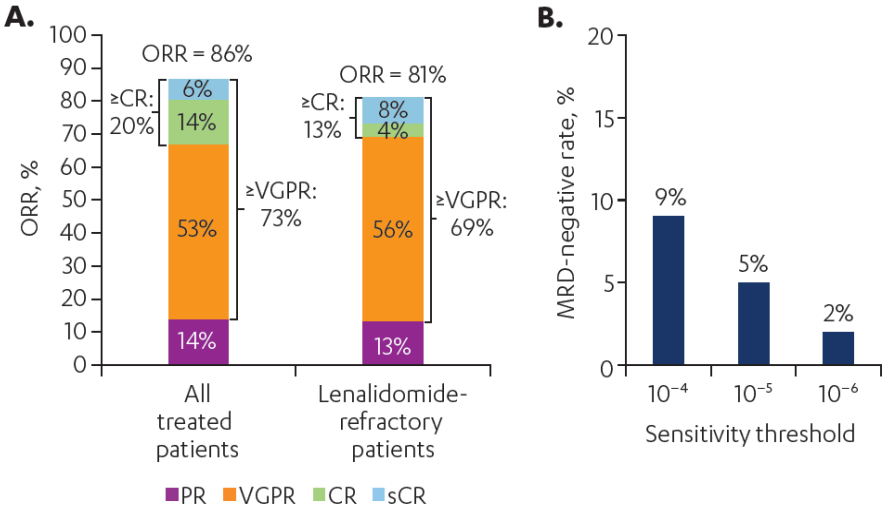


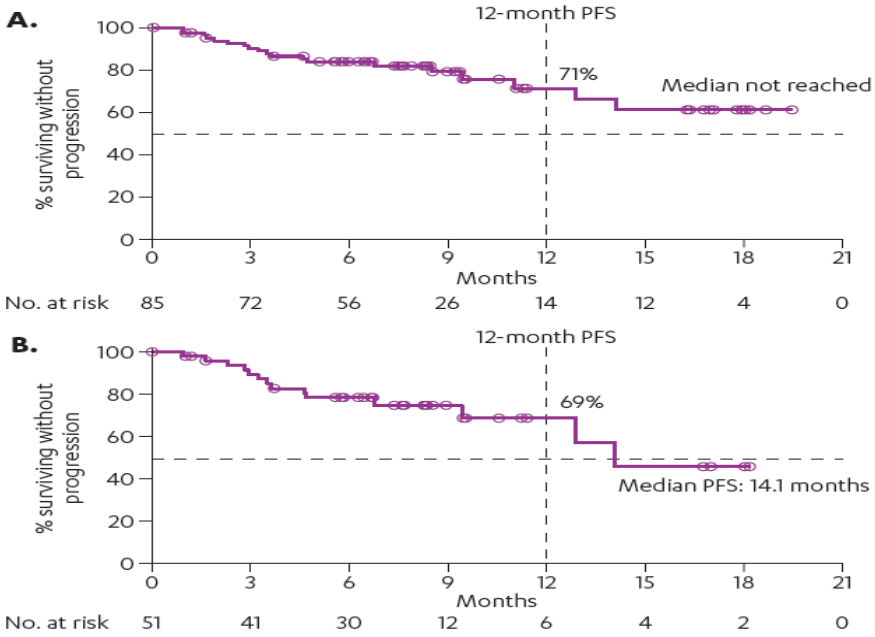
Figure 3. IRRs (any grade) in patients receiving (A) a single-dose infusion or (B) a split-dose infusion of DARA (in >1 patient).

Poster 1869: Daratumumab in Combination with Carfilzomib and Dexamethasone in Patients (Pts) with Relapsed Multiple Myeloma (MMY1001): An Open-label, Phase 1b Study



ORR, overall response rate; MRD, minimal residual disease; CR, complete response; VGPR, very good partial response; PR, partial response; sCR, stringent complete response.
[a]Response-evaluable population.
[b]ORR includes all responses ≥PR.

Figure 4. (A) ORR[a,b] in all treated patients and lenalidomide-refractory patients; (B) MRD-negative rates in all treated patients.



PFS, progression-free survival.

Figure 5. PFS in (A) all treated patients and (B) lenalidomide-refractory patients.

Poster 1869: Daratumumab in Combination with Carfilzomib and Dexamethasone in Patients (Pts) with Relapsed Multiple Myeloma (MMY1001): An Open-label, Phase 1b Study

CONCLUSIONS

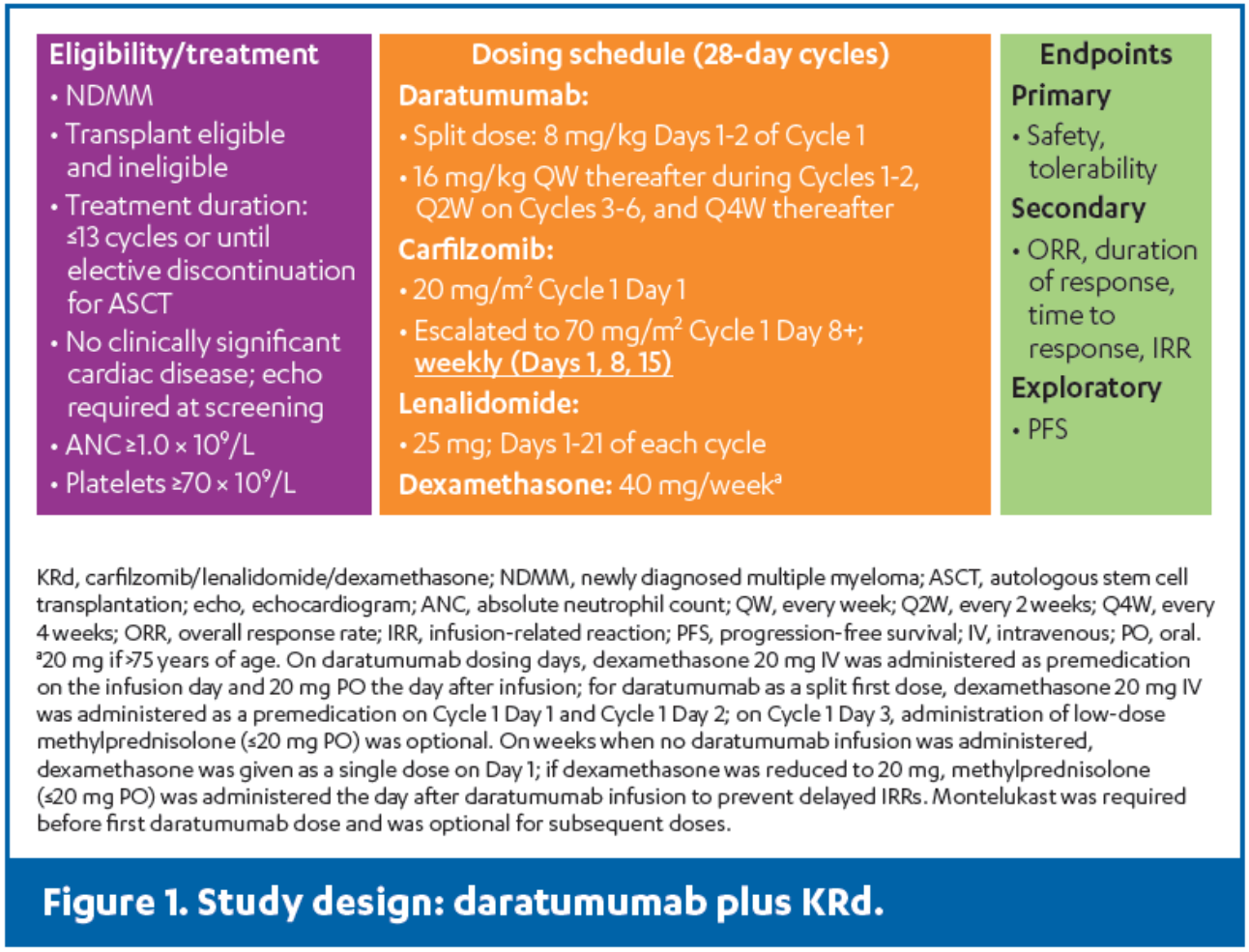
- DARA in combination with Kd (K 70 mg/m^2 weekly) was well tolerated
  - The safety profile is consistent with previous reports of DARA and Kd
- Split first dosing of DARA is feasible and may improve patient convenience
- Despite short follow-up, deep responses were achieved in RRMM patients who were previously treated with standard of care agents
  - With a median follow-up of only 8.5 months, DARA plus Kd was highly effective, with an 86% ORR, including 73% of patients with ≥VGPR and 20% of patients with ≥CR
  - MRD negativity was achieved by 5% of patients at 10^{-5} sensitivity
  - Based on experience with daratumumab plus standard of care regimens,[19,20] we anticipate the responses to continue to deepen with longer follow-up
- Deep responses were maintained in lenalidomide-refractory patients who demonstrated a median PFS of 14.1 months
- Phase 3 randomized studies of DARA in combination with Kd (CANDOR) or pom-dex (APOLLO) for patients with RRMM are ongoing

Poster 3110: Daratumumab (DARA) in Combination with Carfilzomib, Lenalidomide, and Dexamethasone (KRd) in Patients with Newly Diagnosed Multiple Myeloma (MMY1001): Updated Results from an Open-label, Phase 1b Study

Ajai Chari,[1,*] Saad Z. Usmani,[2] Amrita Krishnan,[3] Sagar Lonial,[4] Raymond L. Comenzo,[5] Kaida Wu,[6] Jianping Wang,[7] Parul Doshi,[6] Brendan Weiss,[6] Jordan M. Schecter,[7] Andrzej Jakubowiak[8]

[1]Tisch Cancer Institute, Mount Sinai School of Medicine, New York, NY, USA; [2]Levine Cancer Institute/Carolinas HealthCare System, Charlotte, NC, USA; [3]Judy and Bernard Briskin Myeloma Center, City of Hope, Duarte, CA, USA; [4]Winship Cancer Institute, Emory University, Atlanta, GA, USA; [5]John C. Davis Myeloma and Amyloid Program, Tufts Medical Center, Boston, MA, USA; [6]Janssen Research & Development, LLC, Spring House, PA, USA; [7]Janssen Research & Development, LLC, Raritan, NJ, USA; [8]University of Chicago Medical Center, Chicago, IL, USA.

Poster 3110: Daratumumab (DARA) in Combination with Carfilzomib, Lenalidomide, and Dexamethasone (KRd) in Patients with Newly Diagnosed Multiple Myeloma (MMY1001): Updated Results from an Open-label, Phase 1b Study



KRd, carfilzomib/lenalidomide/dexamethasone; NDMM, newly diagnosed multiple myeloma; ASCT, autologous stem cell transplantation; echo, echocardiogram; ANC, absolute neutrophil count; QW, every week; Q2W, every 2 weeks; Q4W, every 4 weeks; ORR, overall response rate; IRR, infusion-related reaction; PFS, progression-free survival; IV, intravenous; PO, oral. [a]20 mg if >75 years of age. On daratumumab dosing days, dexamethasone 20 mg IV was administered as premedication on the infusion day and 20 mg PO the day after infusion; for daratumumab as a split first dose, dexamethasone 20 mg IV was administered as a premedication on Cycle 1 Day 1 and Cycle 1 Day 2; on Cycle 1 Day 3, administration of low-dose methylprednisolone (≤20 mg PO) was optional. On weeks when no daratumumab infusion was administered, dexamethasone was given as a single dose on Day 1; if dexamethasone was reduced to 20 mg, methylprednisolone (≤20 mg PO) was administered the day after daratumumab infusion to prevent delayed IRRs. Montelukast was required before first daratumumab dose and was optional for subsequent doses.

Figure 1. Study design: daratumumab plus KRd.

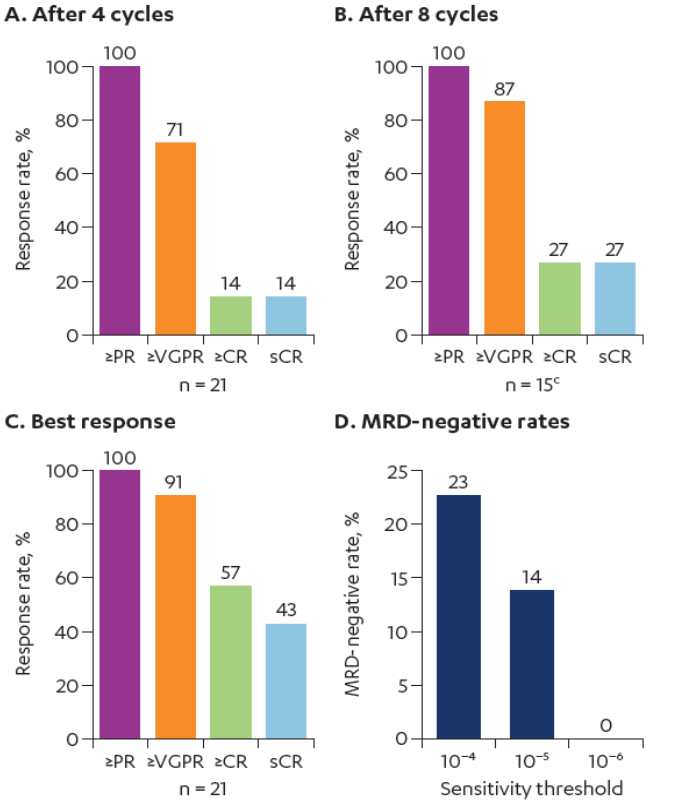
Poster 3110: Daratumumab (DARA) in Combination with Carfilzomib, Lenalidomide, and Dexamethasone (KRd) in Patients with Newly Diagnosed Multiple Myeloma (MMY1001): Updated Results from an Open-label, Phase 1b Study

Table 1. Patient Demographics and Baseline Clinical Characteristics

Characteristic	DARA + KRd (N = 22)
Age, y, n (%)	
Median (range)	59.5 (34-74)
<65	15 (68)
Sex, n (%)	
Male	12 (55)
Female	10 (45)
Race, n (%)	
White	19 (86)
African American	1 (5)
American Indian or Alaska Native	1 (5)
Not reported	1 (5)
ECOG score, n (%)	
0	12 (55)
1	9 (41)
2	1 (5)

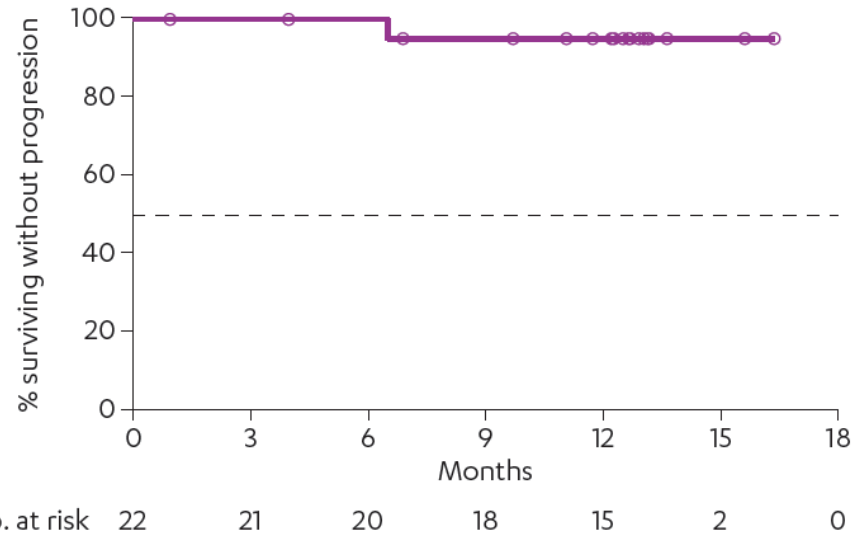
DARA, daratumumab; KRd, carfilzomib/lenalidomide/dexamethasone; ECOG, Eastern Cooperative Oncology Group.

Poster 3110: Daratumumab (DARA) in Combination with Carfilzomib, Lenalidomide, and Dexamethasone (KRd) in Patients with Newly Diagnosed Multiple Myeloma (MMY1001): Updated Results from an Open-label, Phase 1b Study



ORR, overall response rate; MRD, minimal residual disease; PR, partial response; VGPR, very good partial response; CR, complete response; sCR, stringent complete response; ASCT, autologous stem cell transplantation; PD, progressive disease.
[a]Response-evaluable population.
[b]ORR includes all responses ≥PR.
[c]Six patients were excluded: 5 due to ASCT and 1 due to treatment discontinuation (PD in Cycle 7).

Figure 3. (A, B) Response rates by treatment cycle[a]; (C) ORR[a,b]; and (D) MRD-negative rates.



PFS, progression-free survival.

Figure 4. PFS.

Poster 3110: Daratumumab (DARA) in Combination with Carfilzomib, Lenalidomide, and Dexamethasone (KRd) in Patients with Newly Diagnosed Multiple Myeloma (MMY1001): Updated Results from an Open-label, Phase 1b Study

CONCLUSIONS

- Daratumumab in combination with KRd was well tolerated
  - The safety profile is consistent with previous reports of daratumumab and KRd
- Daratumumab plus KRd is highly effective, with a 100% ORR, including 91% of patients with ≥VGPR and 57% of patients with ≥CR
  - Depth of response continued to deepen with longer follow-up
  - MRD-negative rate at 10^{-5} was 14%
- There was no adverse impact on stem cell collection (median $CD34^+$ 10.6×10^6 cells/kg)
  - Daratumumab is feasible as part of induction therapy
  - Deep responses (3 sCRs; 3 VGPRs) were achieved prior to stem cell harvest
  - As responses were not assessed following stem cell transplantation, further deepening of responses induced by daratumumab plus KRd could not be captured in patients electing ASCT
- Ongoing phase 3 studies with daratumumab in novel combinations include:
  - Daratumumab plus bortezomib, melphalan, and prednisone (ALCYONE) and daratumumab plus Rd (MAIA) for patients with transplant-ineligible NDMM
  - Daratumumab plus bortezomib, thalidomide, and dexamethasone (CASSIOPEIA) for patients with transplant-eligible NDMM
  - Daratumumab in combination with Kd (CANDOR) or pomalidomide and dexamethasone (APOLLO) for patients with RRMM

CENTAURUS (SMM2001)

Presented by Dr. Saad Usmani, M.D., FACP,
University of North Carolina at Chapel Hill, Levine Cancer Institute

Genmab

Daratumumab Monotherapy For Patients With Intermediate or High-risk Smoldering Multiple Myeloma (SMM): CENTAURUS, a Randomized, Open-label, Multicenter Phase 2 Study*

Craig C. Hofmeister,[1] Ajai Chari,[2] Yael C. Cohen,[3] Andrew Spencer,[4] Peter Voorhees,[5] Jane Estell,[6] Christopher Venner,[7] Irwindeep Sandhu,[7] Matthew Jenner,[8] Catherine Williams,[9] Michele Cavo,[10] Niels W.C.J. van de Donk,[11] Meral Beksac,[12] Steven Kuppens,[13] Rajesh Bandekar,[14] Tobias Neff,[14] Christoph Heuck,[14] Ming Qi,[14] Hartmut Goldschmidt,[15] C. Ola Landgren[16]

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*ClinicalTrials.gov Identifier: NCT02316106

Background: SMM

- Multiple myeloma evolves from a premalignant asymptomatic precursor stage[1,2]
- No uniform accepted definition of high-risk or intermediate-risk SMM[1]

		% Progressing to Symptomatic MM		
Mayo Clinic[3]	**3 Criteria:**	**1/3 Criteria (Low risk)**	**2/3 Criteria (Intermediate risk)**	**3/3 Criteria (High risk)**
	1. M-protein ≥3 g/dL 2. ≥10% clonal bone marrow plasma cells 3. Free light-chain <0.125 or >8	**25%**	**51%**	**76%**
PETHEMA[4]	**2 Criteria:**	**0/2 Criteria (Low risk)**	**1/2 Criteria (Intermediate risk)**	**2/2 Criteria (High risk)**
	1. ≥95% abnormal plasma cells 2. Low uninvolved serum immunoglobulins	**4%**	**46%**	**72%**

1. Rajkumar SV, et al. *Blood*. 2015;125(20):3069-3075.
2. Landgren O, et al. *Blood*. 2009;1139(22):5412-5417.
3. Dispenzieri A, et al. *Blood*. 2008;111(2):785-789.
4. Pérez-Persona E, et al. *Blood*. 2007;110(7):2586-2592.

SMM, smoldering multiple myeloma; MM, multiple myeloma.

CENTAURUS: Eligibility Criteria

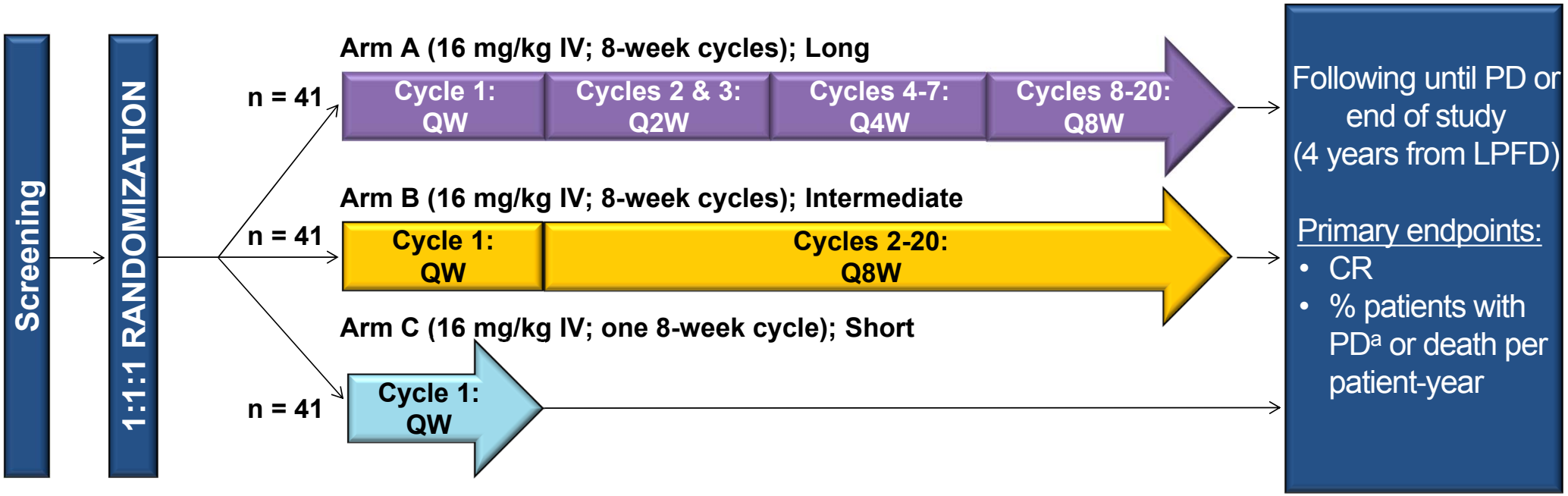
- Key inclusion criteria
  - Diagnosis of SMM <5 years
  - Bone marrow plasma cells ≥10% to <60% and ≥1 of the following:
    - Serum M-protein ≥3 g/dL (IgA ≥2 g/dL)
    - Urine M-protein >500 mg/24 hours
    - Abnormal free light chain ratio (<0.126 or >8) and serum M-protein <3 g/dL but ≥1 g/dL
    - Absolute involved serum free light chain ≥100 mg/L with an abnormal free light chain ratio
      (<0.126 or >8, but not ≤0.01 or ≥100)
- Key exclusion criteria
  - Presence of ≥1 SLiM-CRAB myeloma-defining event[a] (as defined in the 2014 IMWG criteria[1])
  - Clinically relevant organ dysfunction
  - Primary systemic AL amyloidosis

[a]Defined as ≥60% bone marrow plasma cells, free light chain involved/uninvolved ratio ≥100, >1 focal bone lesions on MRI, calcium elevation, renal insufficiency by creatinine clearance, anemia, or bone disease due to lytic bone lesions.

IMWG, International Myeloma Working Group; AL amyloidosis, light-chain amyloidosis.

1. Rajkumar SV, et al. *Lancet Oncol.* 2014;15:e538-e548.

CENTAURUS: Study Design



[a]As defined by 2014 IMWG criteria for SMM.

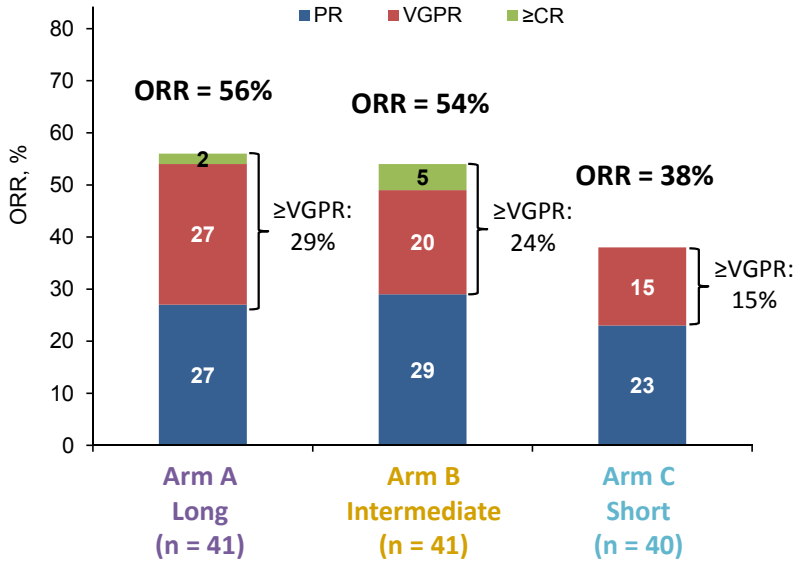
- CR rate: proportion of subjects who achieve CR in each arm
  - First assessed 6 months after last patient randomized
- PD/death rate: ratio of subjects with an event (PD or death) to the total follow-up for all patients
  - Assessed 12 months after last patient randomized
  - **Disease progression to MM assessed according to IMWG guidelines[1]**
- Pre-infusion medication: methylprednisolone 60-100 mg, diphenhydramine 25-50 mg, acetaminophen 650-1,000 mg, montelukast 10 mg (optional)

IV, intravenous; QW, once weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; Q8W, every 8 weeks; PD, progressive disease; LPFD, last patient, first dose; CR, complete response.

1. Rajkumar SV, et al. *Lancet Oncol.* 2014;15:e538-e548.

CENTAURUS: Efficacy

ORR



Co-primary endpoint of CR (>15%) was not met

PD/Death Rate[a]

	Arm A Long (n = 41)	Arm B Intermediate (n = 41)	Arm C Short (n = 41)
P value[b]	<0.0001	<0.0001	0.0213

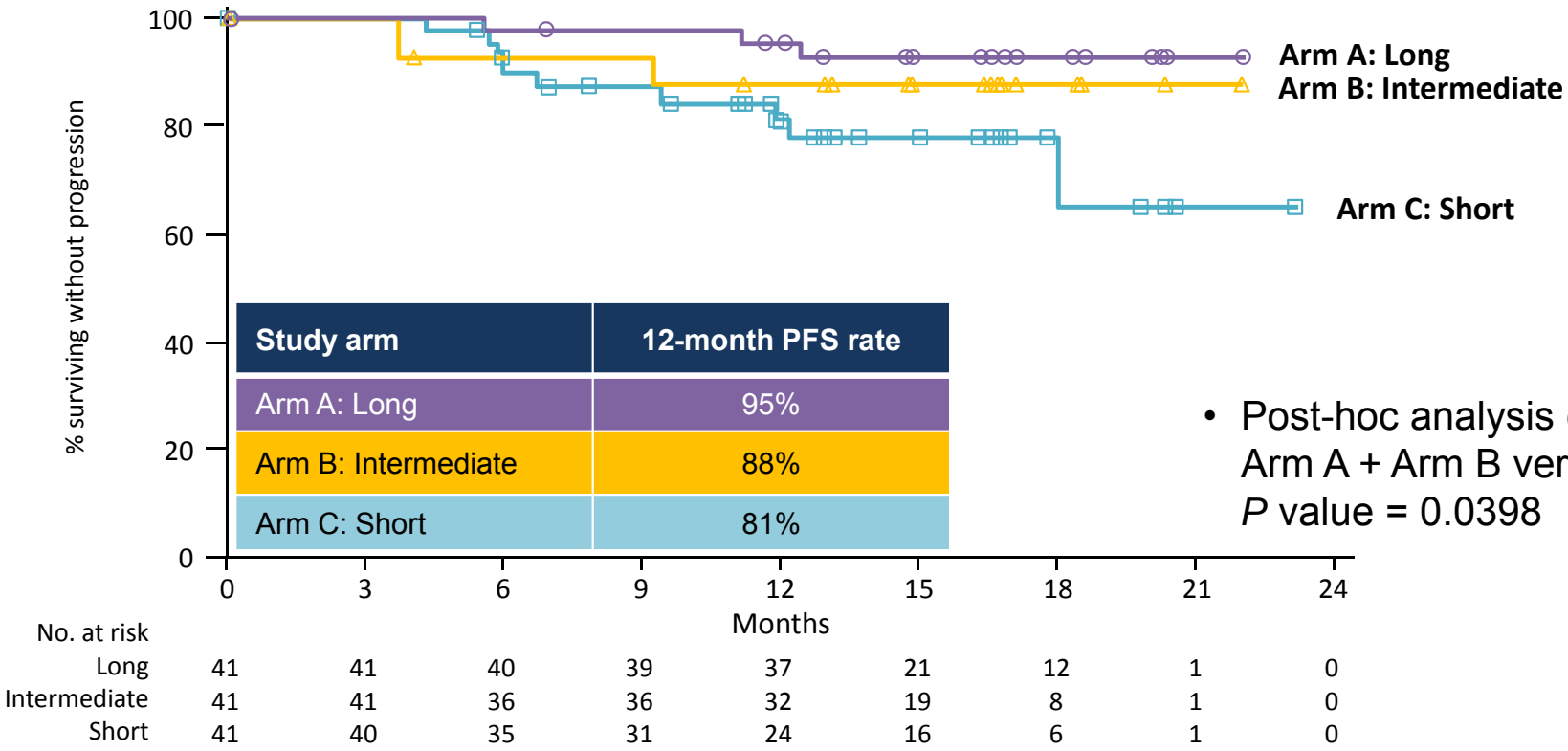
[a]PD/death rate is the ratio of the patients who progressed or died divided by the total PFS for all patients.
[b]*P* value for testing the null hypothesis that the PD/death rate ≥0.346/patient-year (corresponding to median PFS ≥24 months).

Co-primary endpoint of median PFS ≥24 months was met

Single-agent daratumumab shows activity in SMM

ORR, overall response rate; PR, partial response; VGPR, very good partial response; PFS, progression-free survival.

CENTAURUS: PFS (Based on SLiM-CRAB)

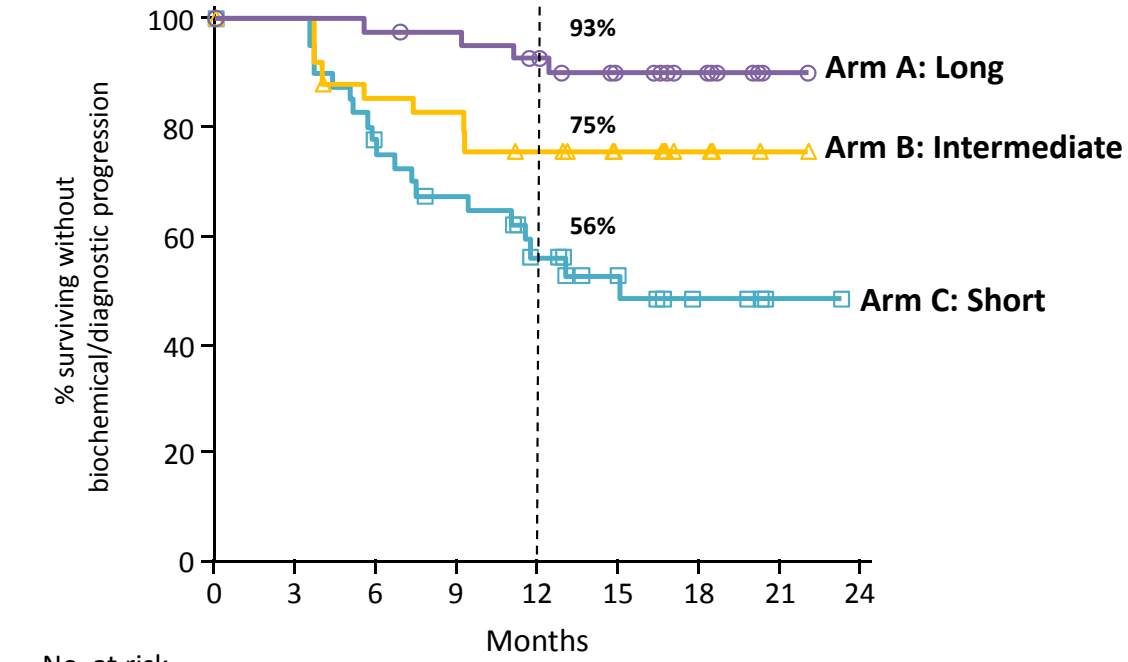


Study arm	12-month PFS rate
Arm A: Long	95%
Arm B: Intermediate	88%
Arm C: Short	81%

- Post-hoc analysis comparing Arm A + Arm B versus Arm C: *P* value = 0.0398

Fewer patients progressed on long and intermediate arms

CENTAURUS: PFS (Biochemical or Diagnostic)



No. at risk									
Long	41	41	40	39	36	21	12	1	0
Intermediate	41	41	34	33	28	16	7	1	0
Short	41	40	30	25	18	13	5	1	0

- Biochemical/diagnostic PFS is defined as the earlier of time to biochemical or diagnostic progression or death
  - Biochemical progression: measurable disease increase from nadir by ≥25% in 2 subsequent assessments per IMWG[1]
  - Diagnostic progression: SLiM-CRAB criteria
- Post-hoc analysis comparing Arm A + Arm B versus Arm C: *P* value = 0.0002

Supports the long dosing schedule for the phase 3 study

1. Rajkumar SV, et al. *Lancet Oncol.* 2014;15:e538-e548.

CENTAURUS: Safety

	Arm A Long (n = 41)	Arm B Intermediate (n = 41)	Arm C Short (n = 40)
Median (range) duration of treatment, months	14.9 (1.0-22.1)	14.8 (1.9-22.1)	1.6 (0-1.9)
Grade 3/4 TEAE, n (%)	15 (37)	4 (10)	6 (15)
Most common (>25%) any-grade TEAE, n (%)			
Fatigue	16 (39)	25 (61)	9 (23)
Cough	14 (34)	13 (32)	11 (28)
Upper respiratory tract infection	11 (27)	11 (27)	4 (10)
Insomnia	11 (27)	13 (32)	5 (13)
Headache	11 (27)	8 (20)	13 (33)
Most common (>1 pt) grade 3/4 TEAE, n (%)			
Hypertension	2 (5)	1 (2)	1 (3)
Hyperglycemia	1 (2)	2 (5)	0 (0)
Serious adverse events, n (%)	10 (24)	1 (2)	4 (10)
Within the first 8 weeks	5 (12)	0 (0)	4 (10)
Discontinued treatment due to TEAE, n (%)	2 (5)	1 (2)	2 (5)
Related to daratumumab	1 (2)[a]	0 (0)	1 (3)[b]
Any-grade IRR rate, n (%)	23 (56)	17 (42)	22 (55)

- Hematologic TEAE rate was <10% across all arms
- Rates of grade 3/4 infection were ≤5% across all arms
- 1 death due to disease progression in Arm C
- 3 SPMs (Arm A: breast cancer, melanoma; Arm B: melanoma)

Findings are consistent with other single-agent daratumumab studies

IRR, infusion-related reaction; TEAE, treatment-emergent adverse event; SPM, secondary primary malignancy.
[a]Thrombocytopenia; [b]Unstable angina.

Conclusions

- Daratumumab has single-agent activity in intermediate- and high-risk SMM
- Daratumumab monotherapy has a favorable safety profile in intermediate- and high-risk SMM
- Efficacy and safety data support Arm A (long) dosing compared to Arm B (intermediate) and Arm C (short)

Findings are the basis for the ongoing AQUILA phase 3 study with single-agent daratumumab in SMM

PAVO (MMY1004)

Presented by Dr. Saad Usmani, M.D., FACP,
University of North Carolina at Chapel Hill, Levine Cancer Institute

Genmab

Subcutaneous Delivery of Daratumumab in Patients with Relapsed or Refractory Multiple Myeloma (RRMM): PAVO, an Open-label, Multicenter, Dose Escalation Phase 1b Study

Ajai Chari,[1] Hareth Nahi,[2] Maria-Victoria Mateos,[3] Henk Lokhorst,[4] Jonathan L. Kaufman,[5] Philippe Moreau,[6] Albert Oriol,[7] Torben Plesner,[8] Lotfi Benboubker,[9] Peter Hellemans,[10] Tara Masterson,[11] Pamela L. Clemens,[11] Kevin Liu,[12] Jesus San-Miguel,[13] Saad Z. Usmani[14]

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ClinicalTrials.gov Identifier: NCT02519452

Background

- DARA 16 mg/kg IV is approved as monotherapy and in combination with Vd, Rd, or Pd in patients with RRMM
- Median duration of the first, second, and subsequent DARA IV infusion was 7.0, 4.3, and 3.5 hours, respectively[1]
- Infusion-related reactions (IRRs) are manageable and occur primarily during the first infusion[2-4]
- Low rates of IRRs with subcutaneous administration of daratumumab have been observed, with short administration time[5]

1. DARZALEX (US PI), Horsham, PA: Janssen Biotech, Inc.; 2017.
2. Usmani SZ, et al. *Blood*. 2016;128(1):37-44.
3. Dimopoulos M, et al. *N Engl J Med*. 2016;375(14):1319-1331.
4. Palumbo A, et al. *N Engl J Med*. 2016;375(8):754-766.
5. Usmani SZ, et al. Presented at: ASH; December 3-6, 2016; San Diego, CA. Abstract 1149.

DARA, daratumumab; IV, intravenous; Vd, bortezomib and dexamethasone; Rd, lenalidomide and dexamethasone; Pd, pomalidomide and dexamethasone; RRMM, relapsed or refractory multiple myeloma.

PAVO Study Design

Phase 1b, open-label, multicenter, dose-finding, proof-of-concept study

Key eligibility criteria
- RRMM with measurable disease
- ≥2 prior lines of treatment
- Not received anti-CD38 therapy

Part 1: mix and deliver

Group 1 (n = 8)
DARA-MD: 1,200 mg
rHuPH20: 30,000 U

→

Group 2[a] (n = 45)
DARA-MD: 1,800 mg
rHuPH20: 45,000 U

Part 2: concentrated co-formulation

Group 3 (n = 25)
DARA SC: 1,800 mg
rHuPH20: 30,000 U

Primary endpoints
- C_{trough} of DARA at Cycle 3/Day1
- Safety

Secondary endpoints
- ORR
- CR
- Duration of response
- Time to response

Infusion/injection time
- DARA-MD 1,200 mg: 20-min via pump (60 mL)
- DARA-MD 1,800 mg: 30-min via pump (90 mL)
- **DARA SC 1,800 mg: 3-5 min manually (15 mL)**

Dosing schedule
- Approved schedule for IV
- 1 Cycle = 28 days

Pre-[b]/post-administration medication
- Acetaminophen
- Diphenhydramine
- Montelukast
- Methylprednisolone[c]

[a]Group 2 comprises 4 distinct cohorts, each treated with DARA 1,800 mg and rHuPH20 45,000 U. C_{trough} on Cycle 3/Day 1 in Group 1 supported dose selection for Group 2. The study evaluation team reviewed safety after Cycle 1 and PK after Cycle 3/Day 1 for each group.
[b]Administered 1 to 3 hours prior to injection. [c]100 mg for the first and second injections; dose may be reduced to 60 mg thereafter; 20 mg for post-administration over 2 days. In the absence of infusion related AEs after the first 3 injections, postinjection corticosteroids should be administered per investigator discretion.

RRMM, relapsed or refractory multiple myeloma; C_{trough}, trough concentration; ORR, overall response rate; CR, complete response.

Baseline Demographics and Clinical Characteristics

	Part 1 (DARA-MD)		Part 2 (DARA SC)
Characteristic	**1,200 mg n = 8**	**1,800 mg n = 45**	**1,800 mg n = 25**
Prior lines of therapy, n (%)			
Median (range)	5 (2-10)	4 (2-11)	3 (2-9)
≤3	3 (38)	16 (36)	16 (64)
>3	5 (63)	29 (64)	9 (36)
Prior ASCT, n (%)	5 (63)	37 (82)	17 (68)
Prior PI, n (%)	8 (100)	45 (100)	25 (100)
Prior bortezomib	8 (100)	43 (96)	24 (96)
Prior IMiD, n (%)	8 (100)	45 (100)	25 (100)
Prior lenalidomide	8 (100)	45 (100)	23 (92)
Refractory to, n (%)			
PI only	0 (0)	1 (2)	3 (12)
IMiD only	1 (13)	7 (16)	2 (8)
Both PI and IMiD	5 (63)	29 (64)	15 (60)
Last line of therapy	7 (88)	36 (80)	19 (76)

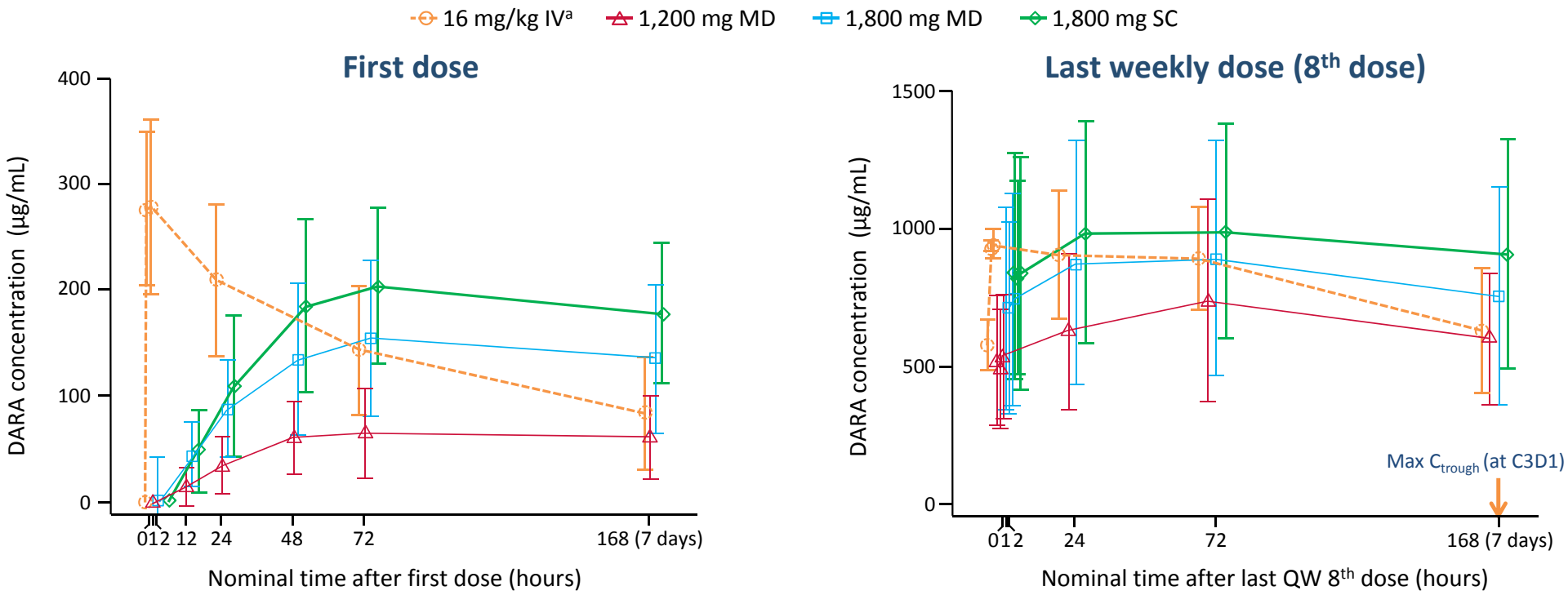
ASCT, autologous stem cell transplantation; PI, proteasome inhibitor; IMiD, immunomodulatory drug.

Patient Disposition

- Clinical cut-off date: Oct 30, 2017

	Part 1: DARA-MD		Part 2: DARA SC
	1,200 mg n = 8	**1,800 mg n = 45**	**1,800 mg n = 25**
Patients treated, n	8	45	25
Patients who discontinued treatment, n (%)	8 (100)	35 (78)	5 (20)
Reason for discontinuation			
Progressive disease	5 (63)	28 (62)	4 (16)
Withdrawal by patient	1 (13)	1 (2)	0 (0)
Physician decision	1 (13)	5 (11)	1 (4)
Death	1 (13)	1 (2)	0 (0)
Median (range) duration of follow up, mo:	**5.2** (1.6-13.9)	**8.3** (1.8-19.5)	**4.6** (2.4-5.5)

Mean (SD) DARA Serum Concentration Profiles



- **SC administration results in slower systemic absorption compared with IV**
- **Maximum C_{trough} is similar or higher following 1800 mg SC compared with 16 mg/kg IV**

[a]From study GEN501.
QW, once weekly.

Summary of Safety Events: DARA SC

	Part 1 (DARA-MD)		Part 2 (DARA SC)
TEAE, n (%)	**1,200 mg n = 8**	**1,800 mg n = 45**	**1,800 mg n = 25**
Drug-related TEAE	5 (63)	31 (69)	12 (48)
Serious drug-related TEAE	1 (13)	3 (7)	0
Grade ≥3 TEAE	5 (63)	22 (49)	10 (40)
All-grade hematologic TEAEs >25%			
Thrombocytopenia	3 (38)	8 (18)	5 (20)
Anemia	2 (25)	15 (33)	3 (12)
Lymphopenia	0	8 (18)	7 (28)
All-grade nonhematologic TEAEs >25%			
Upper respiratory tract infection	3 (38)	11 (24)	2 (8)
Decreased appetite	3 (38)	3 (7)	2 (8)
Insomnia	3 (38)	5 (11)	4 (16)
Pyrexia	2 (25)	12 (27)	4 (16)
Median duration of treatment:	**2.6 months**	**5.4 months**	**4.6 months**

- No TEAE-related treatment discontinuations

TEAE, treatment-emergent adverse event.

Grade 3/4 TEAEs: DARA SC

	DARA-MD		DARA SC
Grade 3/4 TEAE (>1 patient), n (%)	**1,200 mg n = 8**	**1,800 mg n = 45**	**1,800 mg n = 25**
Hematologic			
Anemia	1 (13)	7 (16)	1 (4)
Lymphopenia	0 (0)	5 (11)	4 (16)
Thrombocytopenia	1 (13)	3 (7)	2 (8)
Neutropenia	1 (13)	3 (7)	2 (8)
Nonhematologic			
Fatigue	2 (25)	1 (2)	1 (4)
Hypertension	2 (25)	2 (4)	1 (4)
Hyponatremia	0 (0)	2 (4)	1 (4)
Pneumonia	1 (13)	2 (4)	0
Device related infection	0	2 (4)	0
Respiratory syncytial virus infection	0	2 (4)	0
Median duration of treatment:	**2.6 months**	**5.4 months**	**4.6 months**

AE profile of DARA subcutaneous is consistent with DARA IV

IRRs: DARA SC

- 3/25 (12%) patients in DARA SC reported IRRs, all at first injection (within 6 h)
  - Patient 1: Hypertension (G3), chills (G2), dyspnea (G2)
  - Patient 2: Allergic rhinitis (G1)
  - Patient 3: Sneezing (G1)
- No grade 4 IRRs were reported
- No discontinuations due to IRRs
- No delayed occurrences of IRRs

Low IRR incidence and severity with subcutaneous DARA

IRR, infusion-related reaction.

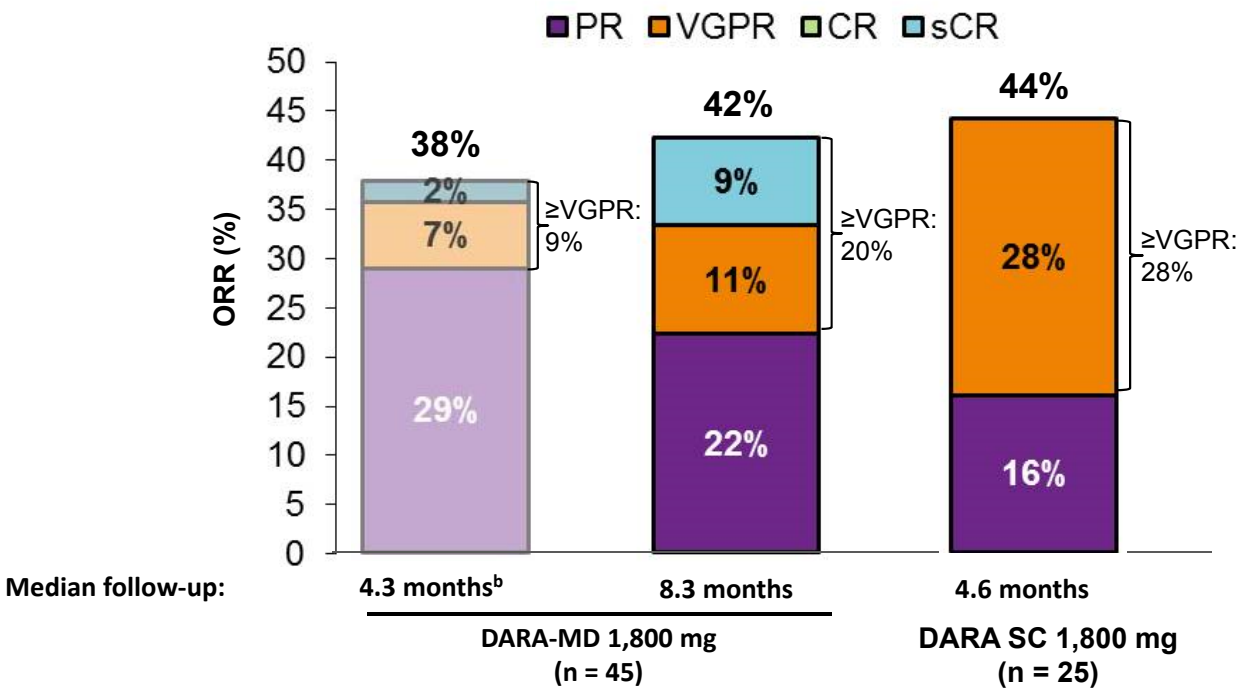
Injection-site Reactions: DARA SC

	Part 2 (DARA SC)
	1,800 mg (15 mL / 3-5 min) n = 25
Injection site TEAEs (investigator reported), n (%)[a]	
Induration	1 (4)
Erythema	1 (4)
Injection-site discoloration	1 (4)
Hematoma	1 (4)
Injection site measurements, n (%)	
Erythema	5 (20)

- **Few injection-site TEAEs with subcutaneous DARA**
- **Measurable erythema was reversible within 1 hour**

[a]All grade 1 in severity.

ORR[a]: 1,800 mg Groups



- **Deepening responses observed in the 1,800-mg DARA-MD group**
- **1,800-mg DARA SC demonstrates similar response rates as 1,800-mg DARA-MD**

[a]Response-evaluable set; [b]Data presented by Usmani SZ, et al. Presented at: ASH; December 3-6, 2016; San Diego, CA. Abstract 1149.

PR, partial response; VGPR, very good partial response; CR, complete response; sCR, stringent complete response.

Conclusions

- DARA co-formulated with recombinant human hyaluronidase (DARA SC) enables dosing in 3 to 5 minutes
- DARA SC 1,800 mg achieves greater maximum C_{trough} compared with standard IV dose at C3D1
- DARA SC was well tolerated
  - Rate of IRRs with DARA SC was 12%; IRRs for DARA IV range between 45%-56% in RRMM[1-6]
- Clinical responses with DARA SC were observed, with rates similar to DARA-IV

These data informed the four ongoing phase 3 studies[a] using DARA SC 1,800 mg

[a]COLUMBA (DARA SC vs IV), AQUILA (smoldering MM, single agent), APOLLO (DARA SC + pom/dex), and ANDROMEDA (amyloidosis, DARA SC + VCd).

1. Usmani S, et al. *Blood.* 2016;128(1):37-44. 2. Plesner T, et al. *Blood.* 2016;128(14):1821-1828. 3. Chari A, et al. Poster presented at: ASH; December 3-6, 2016; San Diego, CA. Abstract 2142. 4. Palumbo A, et al. *N Engl J Med*. 2016;375(8):754-66. 5. Dimopoulos MA, et al. *N Engl J Med*. 2016;375(14):1319-1331. 6. Chari A, et al. *Blood*. 2017; 130(8): 974–981.

GRIFFIN (MMY2004)

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Genmab

Poster 1879: Interim Safety Analysis of a Phase 2 Randomized Study of Daratumumab (Dara), Lenalidomide (R), Bortezomib (V), and Dexamethasone (d; Dara-RVd) vs RVd in Patients (Pts) with Newly Diagnosed Multiple Myeloma (MM) Eligible for High-Doses Therapy (HDT) and Autologous Stem Cell Transplantation (ASCT) (GRIFFIN)

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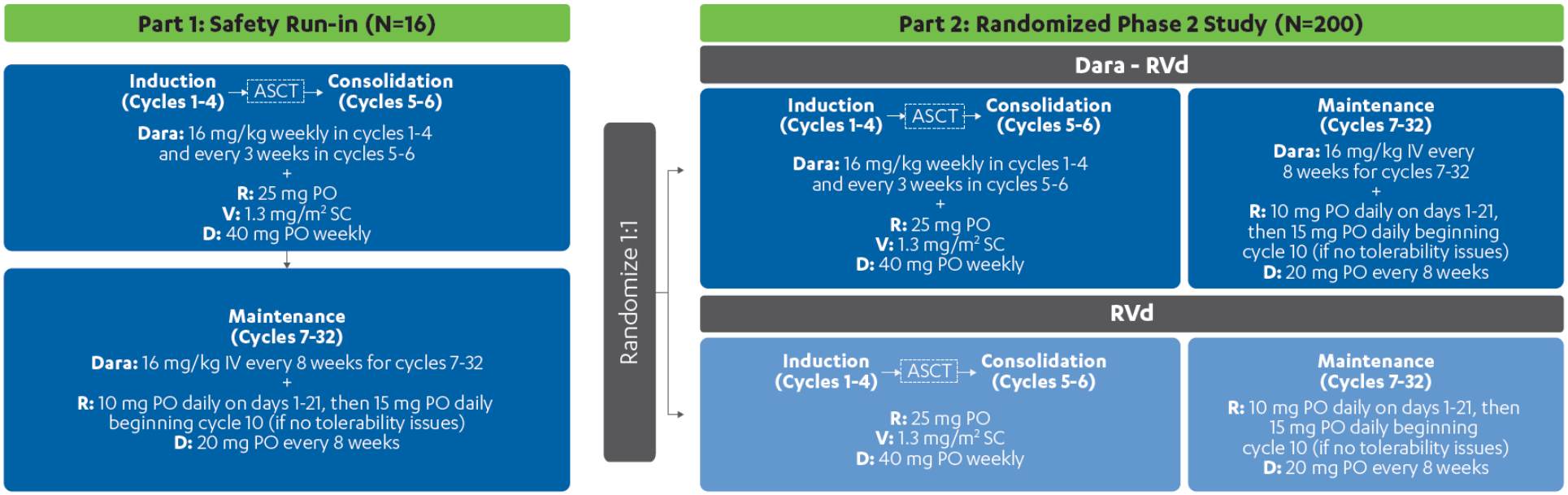
Poster 1879: Interim Safety Analysis of a Phase 2 Randomized Study of Daratumumab (Dara), Lenalidomide (R), Bortezomib (V), and Dexamethasone (d; Dara-RVd) vs RVd in Patients (Pts) with Newly Diagnosed Multiple Myeloma (MM) Eligible for High-Doses Therapy (HDT) and Autologous Stem Cell Transplantation (ASCT) (GRIFFIN)



ASCT, autologous stem cell transplant.
Cycles 1-6 = every 21 days; Cycles 7-32 = every 28 days
Induction and Consolidation:
Lenalidomide given on days 1-14; Bortezomib given on days 1, 4, 8, and 11; Dexamethasone 20 mg given on days 1, 2, 8, 9, 15, and 16.

Figure 1. Study Design for Dara-RVd and RVd Treatment Groups

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Safety Analysis

- Among 16 treated patients, 3 patients experienced adverse events that met sponsor pre-defined DLT criteria during Cycle 1. All DLTs resolved and none of these events were determined by the investigator to require treatment discontinuation.
  - Grade 3 fatigue on Day 15
  - Grade 3 gastroenteritis on Day 21
  - Grade 3 pneumonitis (due to infection) and Grade 3 hypotension on Day 5
- The DRC recommended the study proceed to the randomized phase 2 stage
- 100% of patients experienced at least 1 treatment emergent adverse event (TEAE) (Table 4) and 8 (50%) of patients experienced Grade 3-4 TEAEs (Table 5)
- 3 (19%) patients experienced serious adverse events (SAEs) that included 2 (13%) SAEs (gastroenteritis and pneumonitis) related to daratumumab according to investigator's assessment
- 5 (31%) patients experienced grade ≤2 infusion reactions (Table 6)
- Six (38%) patients experienced infections, including 1 patient with a Grade 3 SAE of gastroenteritis. There were no events of febrile neutropenia.
- Two (12.5%) patients experienced grade 1 peripheral neuropathy
- Six (38%) patients had dose delay due to adverse event
- Dose of the following medications was adjusted due to AE: bortezomib (3 patients), dexamethasone (2 patients), daratumumab and lenalidomide (1 patient each)
- There were no deaths, and no patients discontinued treatment due to TEAEs
- All 16 patients have undergone mobilization as of the clinical cutoff date with a median stem cell yield of 6.05 (range 3.5-10.6) x10^6 CD34+ cells/kg
- All 16 patients in the safety run-in phase continue to be on study treatment

Table 4. Safety Profile of Patients Treated During Cycles 1-4

	N=16
At least 1 treatment emergent adverse event (TEAE), n (%)	16 (100)
Related to daratumumab	14 (88)
Most Common TEAEs (all grades) occurring in ≥20% of patients, n (%)	
Neutropenia	8 (50)
Lymphopenia	7 (44)
Thrombocytopenia	7 (44)
Fatigue	6 (38)
Oedema peripheral	6 (38)
Anemia	5 (31)
Constipation	5 (31)
Leukopenia	4 (25)
Hypoalbuminemia	4 (25)
Hypocalcemia	4 (25)
Insomnia	4 (25)

Table 5. Most Common Grade 3-4 TEAEs in Patients Treated During Cycles 1-4

	N=16
Grade 3-4 TEAEs, n (%)	8 (50)
Related to daratumumab	6 (38)
Grade 3-4 TEAEs occurring in ≥10% of patients, n (%)	
Neutropenia	3 (19)
Thrombocytopenia	3 (19)
Lymphopenia	2 (13)
Leukopenia	2 (13)

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CONCLUSIONS

- **Daratumumab, in combination with RVd, was well tolerated, with clinically manageable side effects consistent with the known toxicities of RVd and the known adverse event profile of daratumumab**
- **No new safety signals were identified with the addition of Dara to RVd during the first 4 cycles of Dara-RVd in 16 safety run-in patients with newly diagnosed MM**
- **All 16 patients in the safety run-in have undergone successful stem cell mobilization**
- **The first 4 cycles of the safety run-in phase were completed, and all 16 patients continue on therapy**
- **Enrollment to the randomized phase 2 study is ongoing, with 106 patients randomized as of 8 November 2017**

POLLUX (MMY3003)

Presented by Prof. Philippe Moreau, M.D.
University Hospital of Nantes

Genmab

Daratumumab, Lenalidomide, and Dexamethasone (DRd) Versus Lenalidomide and Dexamethasone (Rd) in Relapsed or Refractory Multiple Myeloma (RRMM): Updated Efficacy and Safety Analysis of POLLUX*

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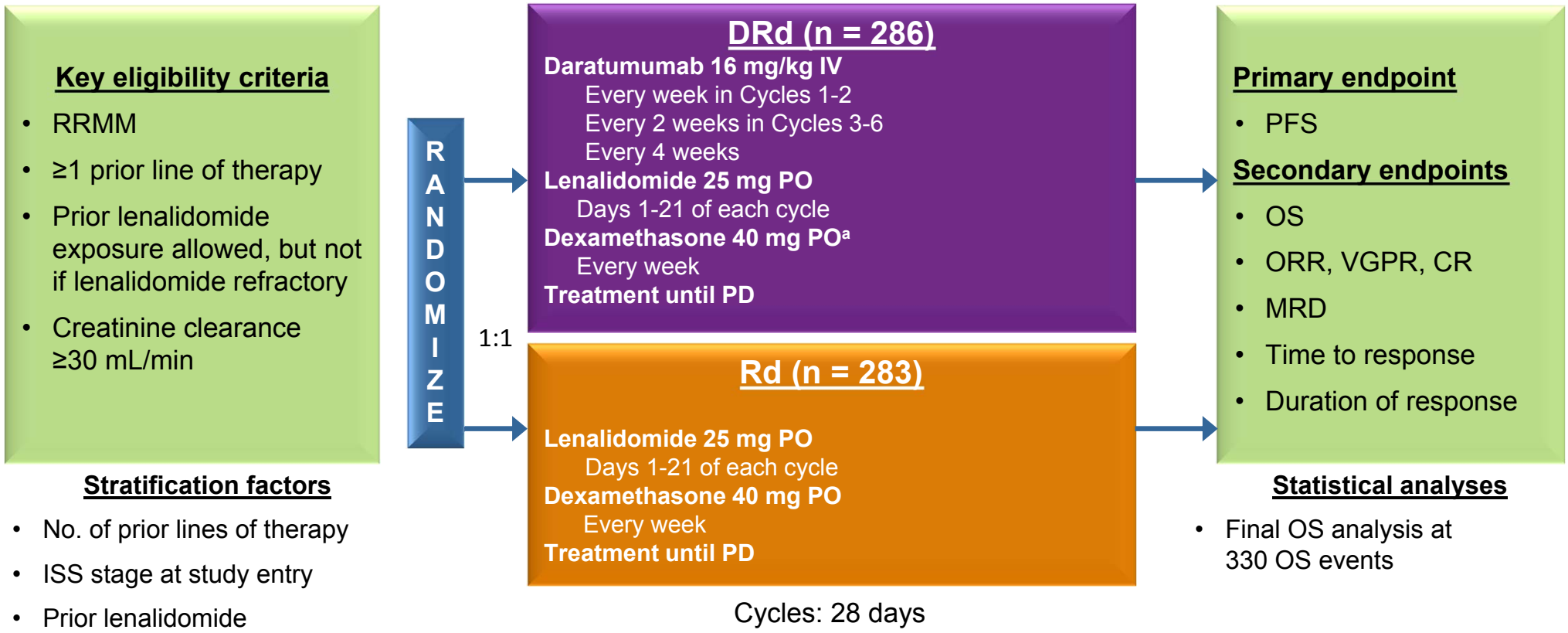
*ClinicalTrials.gov Identifier: NCT02076009

POLLUX Study Design

Open-label, multicenter, randomized (1:1), active-controlled, phase 3 study



ISS, International Staging System; DRd, daratumumab/lenalidomide/dexamethasone; IV, intravenous; PO, oral; PD, progressive disease; Rd, lenalidomide/dexamethasone; PFS, progression-free survival; OS, overall survival; ORR, overall response rate; VGPR, very good partial response; CR, complete response; MRD, minimal residual disease.

[a]On daratumumab dosing days, dexamethasone 20 mg was administered on the day of the infusion and 20 mg was administered the day after the infusion.

Baseline Characteristics (ITT)

Characteristic	DRd (n = 286)	Rd (n = 283)
Age, y Median (range) ≥75, %	 65 (34-89) 10	 65 (42-87) 12
ISS, %[a] I II III	 48 33 20	 50 30 20
Median (range) time from diagnosis, y	3.48 (0.4-27.0)	3.95 (0.4-21.7)
Creatinine clearance (mL/min), % N >30-60 >60	 279 28 71	 281 23 77
Cytogenetic profile, %[b] N Standard risk High risk	 161 83 17	 150 75 25

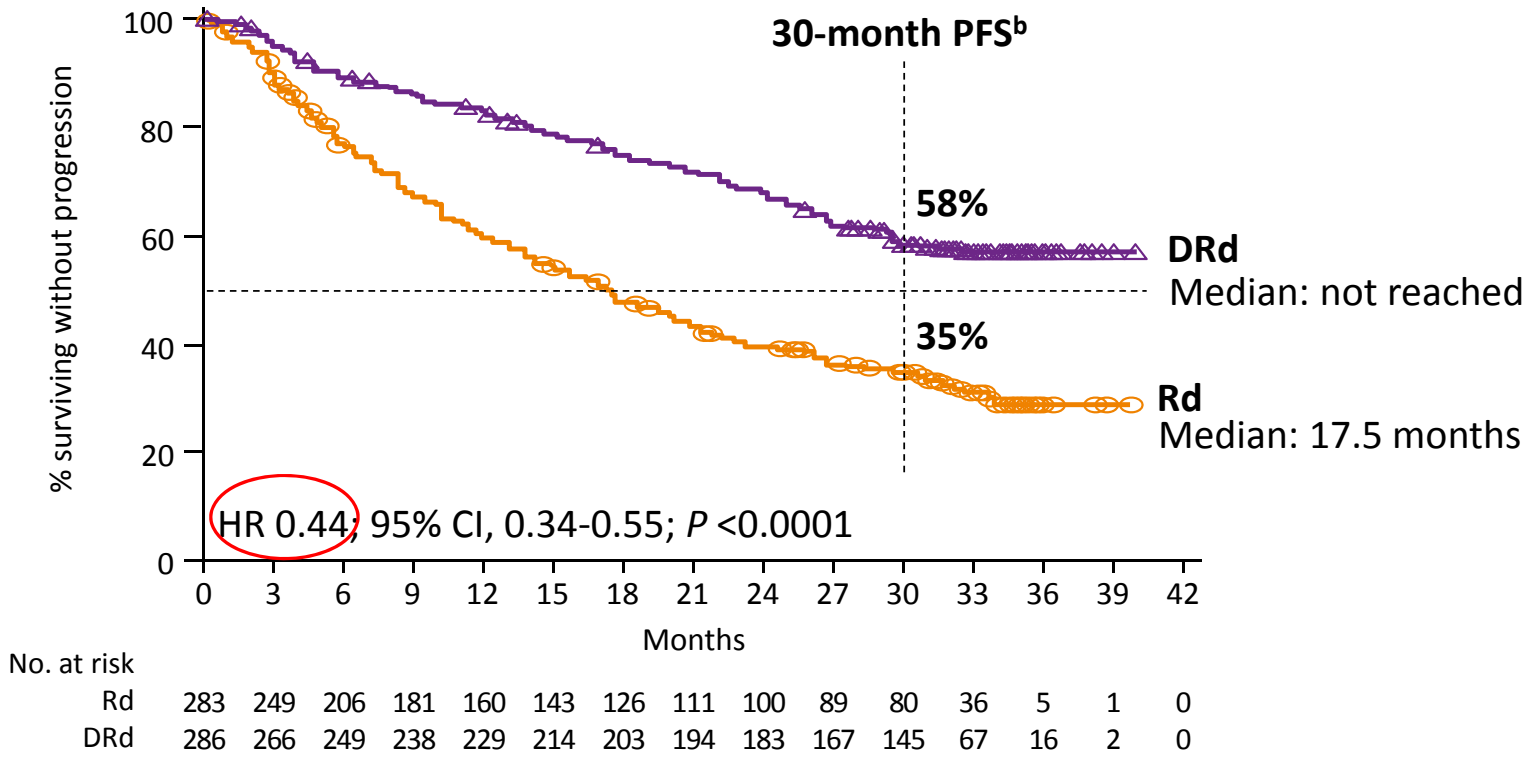
Characteristic	DRd (n = 286)	Rd (n = 283)
Prior lines of therapy, % Median (range) 1 2 3 >3	 1 (1-11) 52 30 13 5	 1 (1-8) 52 28 13 7
Prior ASCT, %	63	64
Prior PI, %	86	86
Prior IMiD, % Prior lenalidomide, %	55 18	55 18
Prior PI + IMiD, %	44	44
Refractory to bortezomib, %	21	21
Refractory to last line of therapy, %	28	27

ITT, intent-to-treat; ASCT, autologous stem cell transplant.

[a]ISS stage was derived based on the combination of serum β2-microglobulin and albumin.
[b]Centralized analysis using next-generation sequencing. Patients with high risk had t(4;14), t(14;16), or del17p abnormalities.

PFS[a]

- Median follow-up: 32.9 months (range, 0 - 40.0 months)

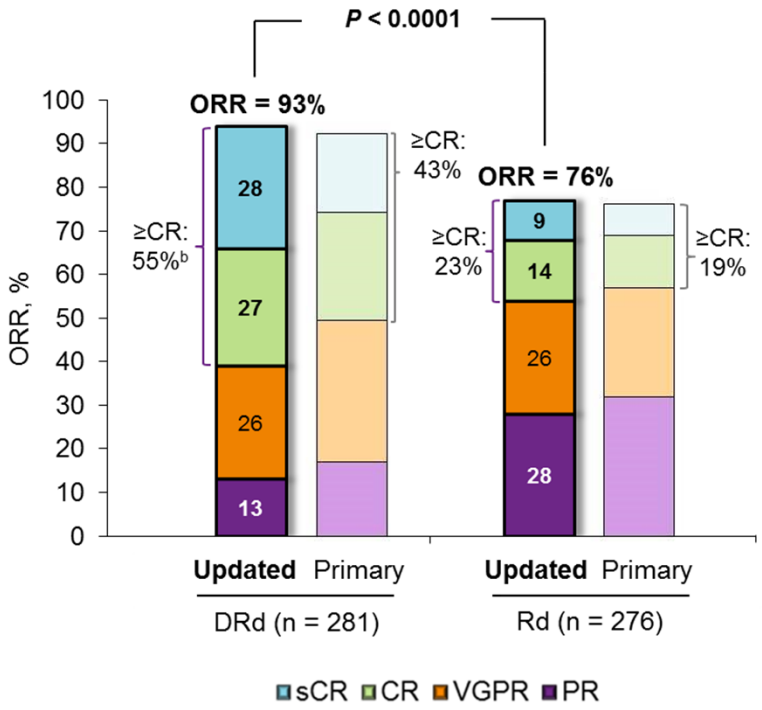


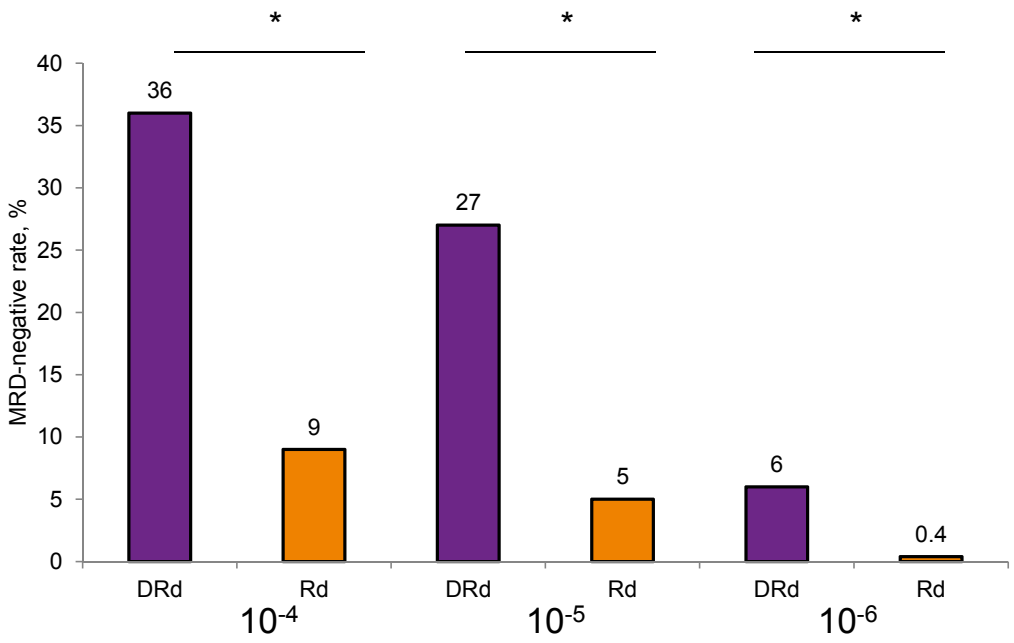
56% reduction in risk of progression/death for DRd versus Rd

HR, hazard ratio; CI, confidence interval.
[a]Exploratory analyses based on clinical cut-off date of October 23, 2017.
[b]Kaplan-Meier estimate.

ORR and MRD-negative Rates[a]

- Median follow-up: 32.9 months (range, 0 - 40.0 months)



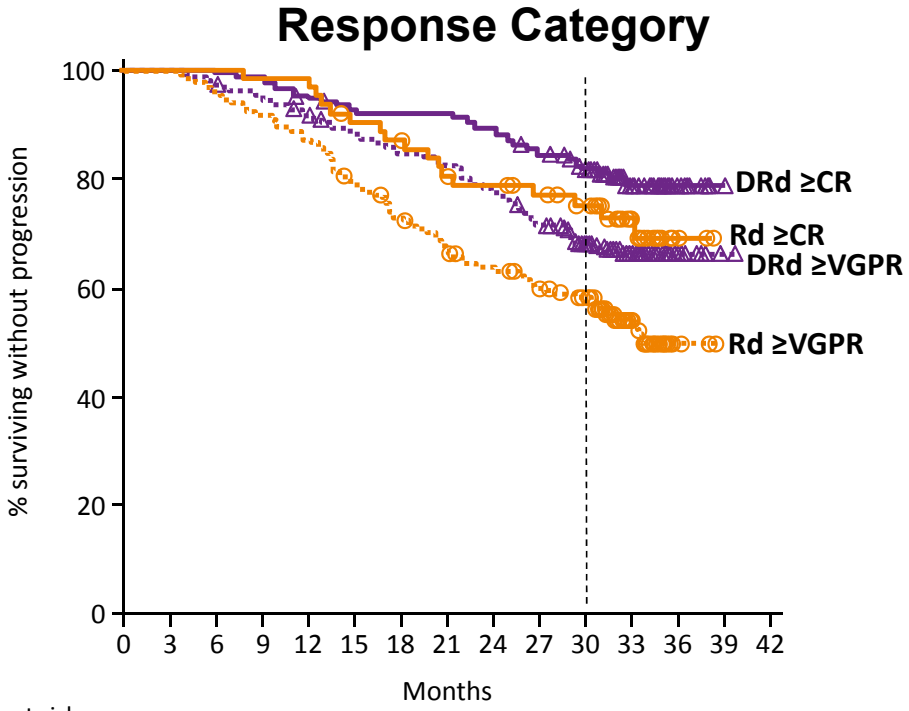


MRD assessed using clonoSEQ® assay V2.0

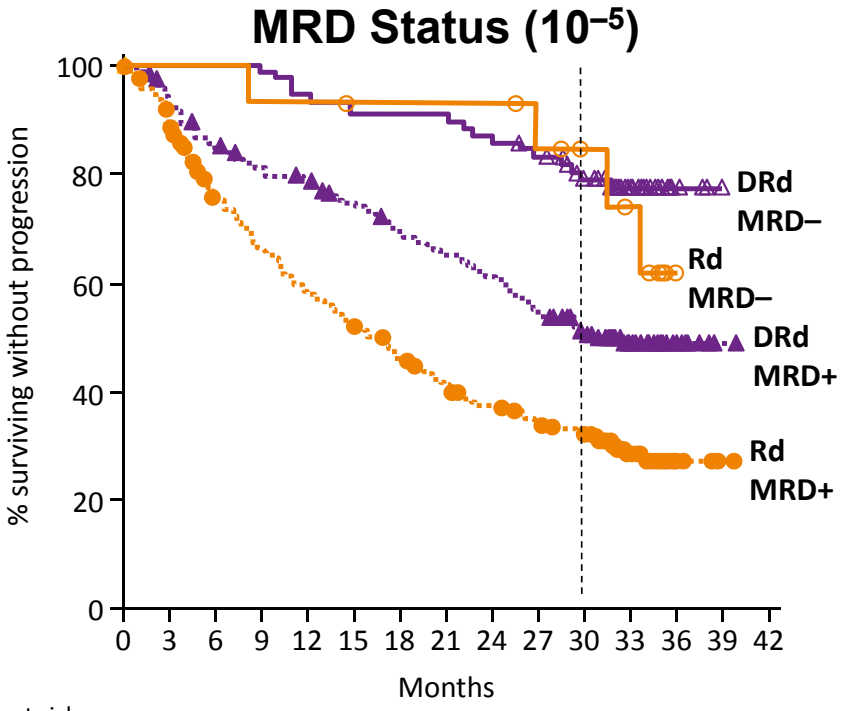
- **Responses continued to deepen in the DRd group**
- **Significantly higher (>3-fold) MRD-negative rates for DRd versus Rd**

sCR, stringent complete response; PR, partial response.
Primary analysis reported in Dimopoulos MA, et al. *N Engl J Med.* 2016;375(14):1319-1331.
[a]Exploratory analyses based on clinical cutoff date of October 23, 2017; [b]*P* <0.0001 for DRd versus Rd.

PFS by Depth of Response



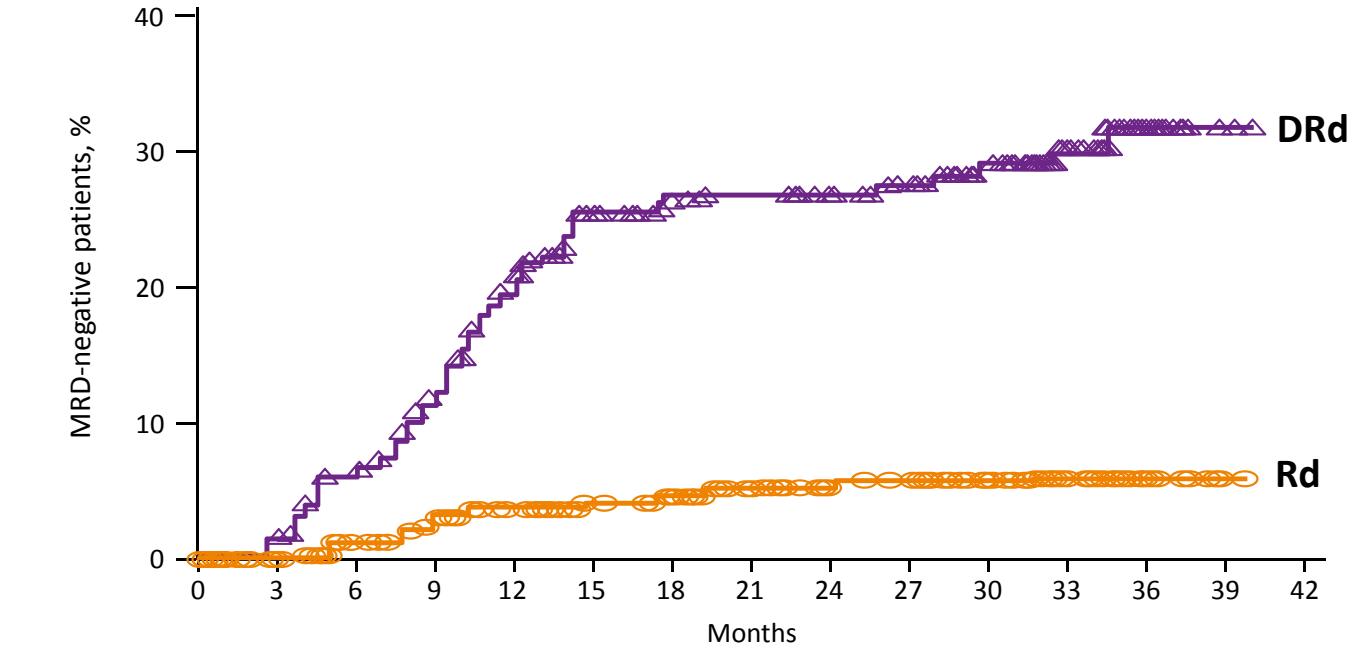
No. at risk															
DRd ≥CR	154	154	154	151	146	141	140	140	136	127	115	53	12	1	0
Rd ≥CR	62	62	62	61	61	56	53	48	46	43	39	22	3	0	0
DRd ≥VGPR	226	226	220	214	206	195	189	183	173	158	137	62	14	2	0
Rd ≥VGPR	134	134	129	123	117	106	96	87	80	73	66	31	4	0	0



No. at risk															
Rd MRD negative	14	14	14	13	13	12	12	12	12	10	8	6	0	0	0
DRd MRD negative	76	76	76	75	72	69	69	69	66	62	54	26	7	1	0
Rd MRD positive	269	235	192	168	147	131	114	99	88	79	72	30	5	1	0
DRd MRD positve	210	190	173	163	157	145	134	125	117	105	91	41	9	1	0

- **Deeper responses were more common on DRd and were associated with longer PFS**
- **MRD negativity was associated with longer PFS**

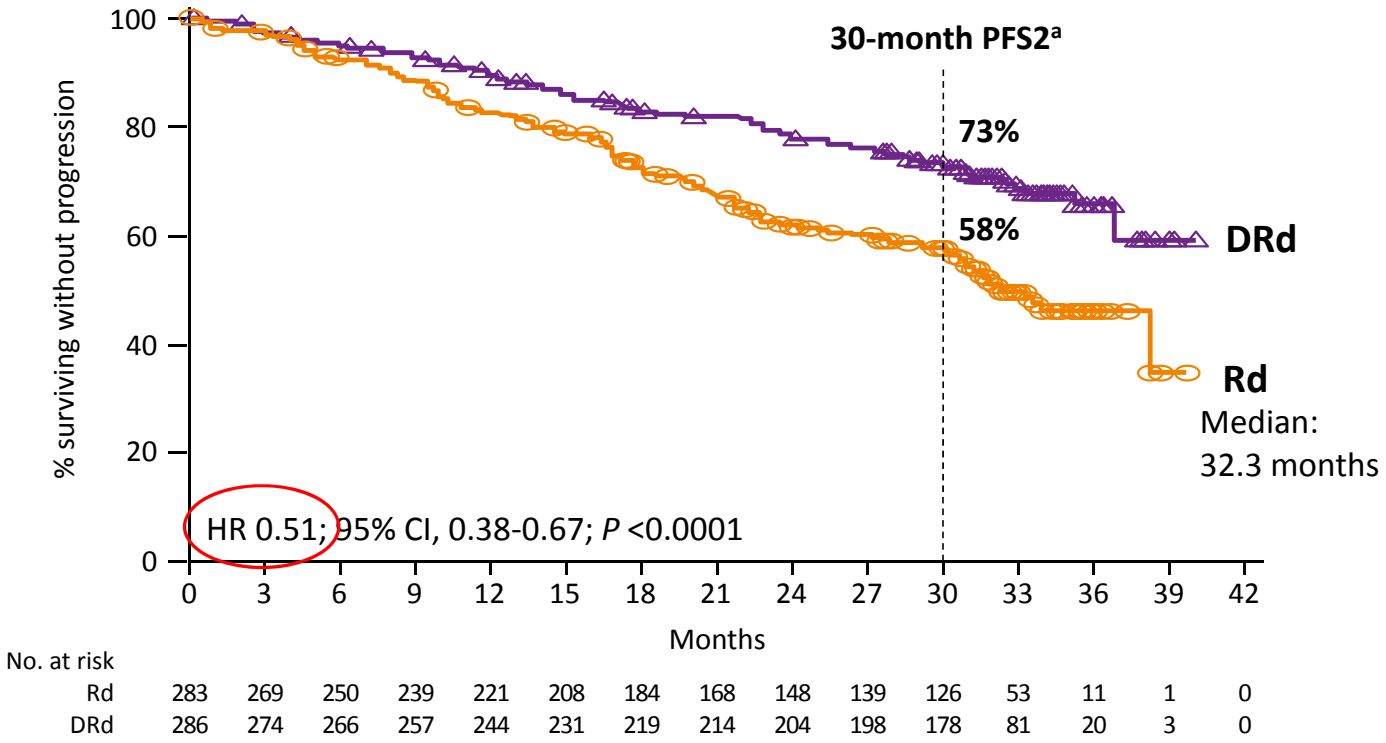
Time to MRD Negativity (10^{-5})



No. at risk															
Rd	283	272	252	242	229	219	209	193	183	181	166	77	22	1	0
DRd	286	273	255	235	208	186	172	167	161	153	139	65	18	2	0

MRD negativity occurs more rapidly with DRd and increases over time

PFS With Subsequent Line of Therapy (PFS2)



DRd does not negatively impact outcomes of subsequent therapy

[a]Kaplan-Meier estimate.

Overview of Safety Profile

	All grades (≥25%)[a]		Grade 3/4 (≥5%)[a]	
TEAE, %	**DRd (n = 283)**	**Rd (n = 281)**	**DRd (n = 283)**	**Rd (n = 281)**
Hematologic				
Neutropenia	62	47	54	41
Febrile neutropenia	6	3	6	3
Anemia	38	41	16	22
Thrombocytopenia	29	31	14	16
Lymphopenia	7	6	6	4
Nonhematologic				
Diarrhea	56	34	7	4
Upper respiratory tract infection	41	27	1	1
Viral upper respiratory tract infection	31	19	0	0
	38	31	6	4
Fatigue	34	15	0.4	0
Cough	31	27	1	0.7
Constipation	29	21	1	1
Muscle spasms	27	18	2	0.7
Nausea	24	16	14	10
Pneumonia	17	11	5	3
Hypokalemia				

- Median duration of treatment: 30.4 months for DRd versus 16.0 months for Rd
- Discontinuations due to TEAEs were similar (13% in both arms)
- Rate of grade 3/4 infections: 39% for DRd versus 26% for Rd
- No differences in rates of SPMs between treatment groups (7% of patients in both groups)
  - Most common SPM in both arms was cutaneous, noninvasive SCC (2% each)

Safety profile remains unchanged with longer follow-up

TEAE, treatment-emergent adverse event; SPM, secondary primary malignancy; SCC, squamous cell carcinoma.
[a]Common TEAEs listed are either ≥25% all grade OR ≥5% grade 3/4.

Conclusions

- DRd continues to significantly improve PFS with longer follow-up
- DRd induces deep and durable responses
- More patients receiving DRd achieved MRD negativity versus Rd
- MRD negativity occurs more rapidly with DRd and increases over time
- DRd does not negatively impact outcomes of subsequent therapy
- Safety profile remains unchanged with longer follow-up

Updated findings continue to support the use of DRd in patients with RRMM

Poster 1883: Daratumumab, Lenalidomide, and Dexamethasone (DRd) Versus Lenalidomide and Dexamethasone (Rd) in Relapsed or Refractory Multiple Myeloma (RRMM) Based on Prior Treatment History, Renal Function, and Cytogenetic Risk: Subgroup Analyses of POLLUX

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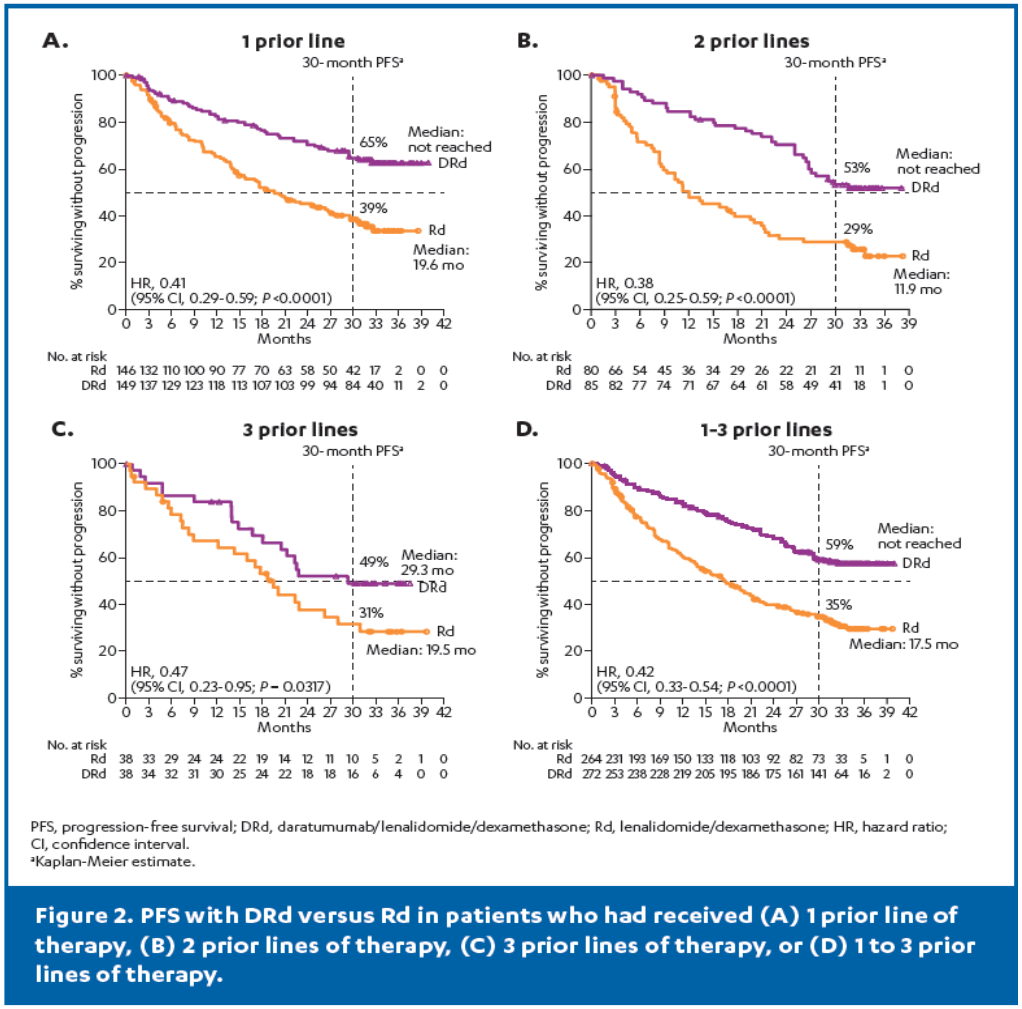

PFS, progression-free survival; DRd, daratumumab/lenalidomide/dexamethasone; Rd, lenalidomide/dexamethasone; HR, hazard ratio; CI, confidence interval.
[a]Kaplan-Meier estimate.

Figure 2. PFS with DRd versus Rd in patients who had received (A) 1 prior line of therapy, (B) 2 prior lines of therapy, (C) 3 prior lines of therapy, or (D) 1 to 3 prior lines of therapy.

Poster 1883: Daratumumab, Lenalidomide, and Dexamethasone (DRd) Versus Lenalidomide and Dexamethasone (Rd) in Relapsed or Refractory Multiple Myeloma (RRMM) Based on Prior Treatment History, Renal Function, and Cytogenetic Risk: Subgroup Analyses of POLLUX

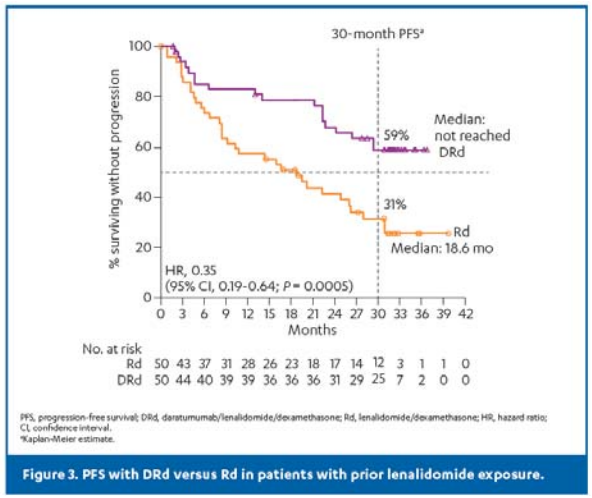

Figure 3. PFS with DRd versus Rd in patients with prior lenalidomide exposure.

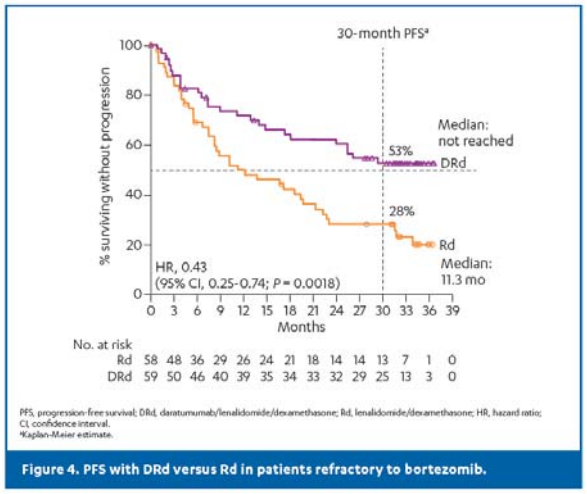

Figure 4. PFS with DRd versus Rd in patients refractory to bortezomib.

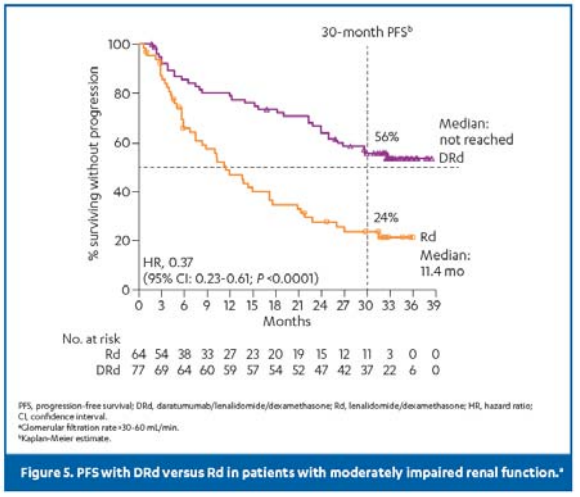

Figure 5. PFS with DRd versus Rd in patients with moderately impaired renal function.[a]

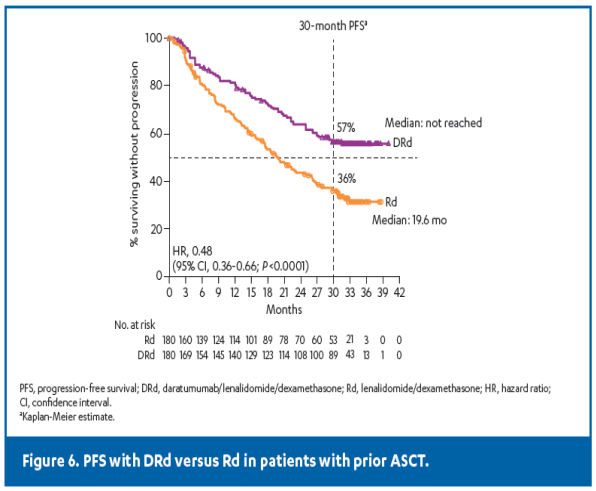

Figure 6. PFS with DRd versus Rd in patients with prior ASCT.

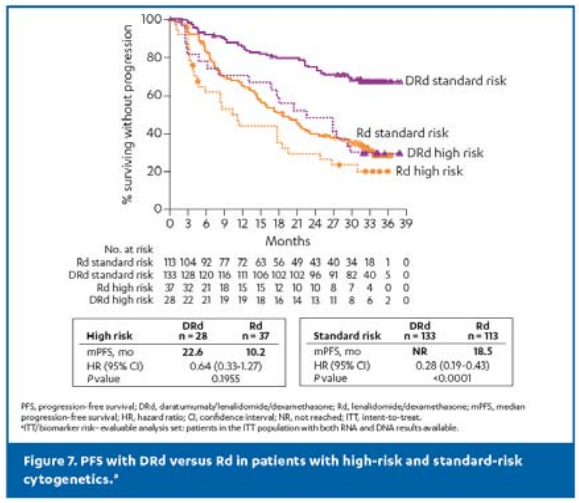

Figure 7. PFS with DRd versus Rd in patients with high-risk and standard-risk cytogenetics.[a]

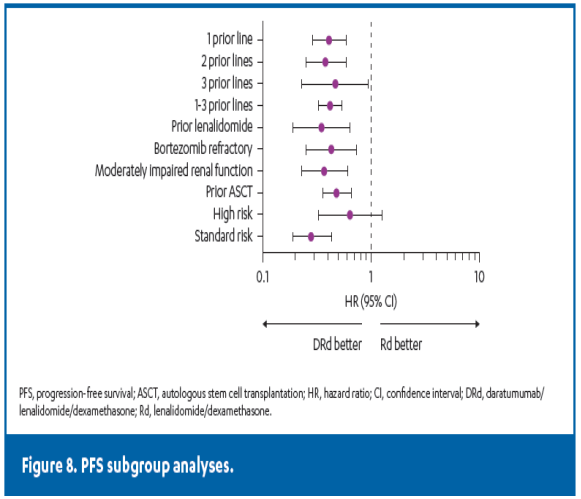

Figure 8. PFS subgroup analyses.

Poster 1883: Daratumumab, Lenalidomide, and Dexamethasone (DRd) Versus Lenalidomide and Dexamethasone (Rd) in Relapsed or Refractory Multiple Myeloma (RRMM) Based on Prior Treatment History, Renal Function, and Cytogenetic Risk: Subgroup Analyses of POLLUX

CONCLUSIONS

- **With a median follow-up of 32.9 months, DRd improved PFS, ORR, sCR, and MRD-negative rates at 10^{-5} versus Rd in patients with RRMM, regardless of prior treatment history, cytogenetic risk, or moderate renal impairment**
- **Results from the POLLUX study suggest that DRd should be considered for patients with RRMM who relapse after lenalidomide-based therapies and for those refractory to bortezomib**

CASTOR (MMY3004)

Presented by Prof. Philippe Moreau, M.D.
University Hospital of Nantes

Genmab

Poster 1852: Daratumumab, Bortezomib and Dexamethasone Versus Bortezomib and Dexamethasone for Relapsed/Refractory Multiple Myeloma (RRMM) Patients: An Update of Overall Survival in CASTOR

Suzanne Lentzsch,[1,*] Hang Quach,[2] Asher Chanan-Khan,[3] Noemi Horvath,[4] Marcelo Capra,[5] Roberto Ovilla,[6] Jae-Cheol Jo,[7] Ho-Jin Shin,[8] Piruntha Thiyagarajah,[9] Himal Amin,[10] Tineke Casneuf,[11] Pieter Sonneveld,[12] Jordan M. Schecter,[10] Vania Hungria[13]

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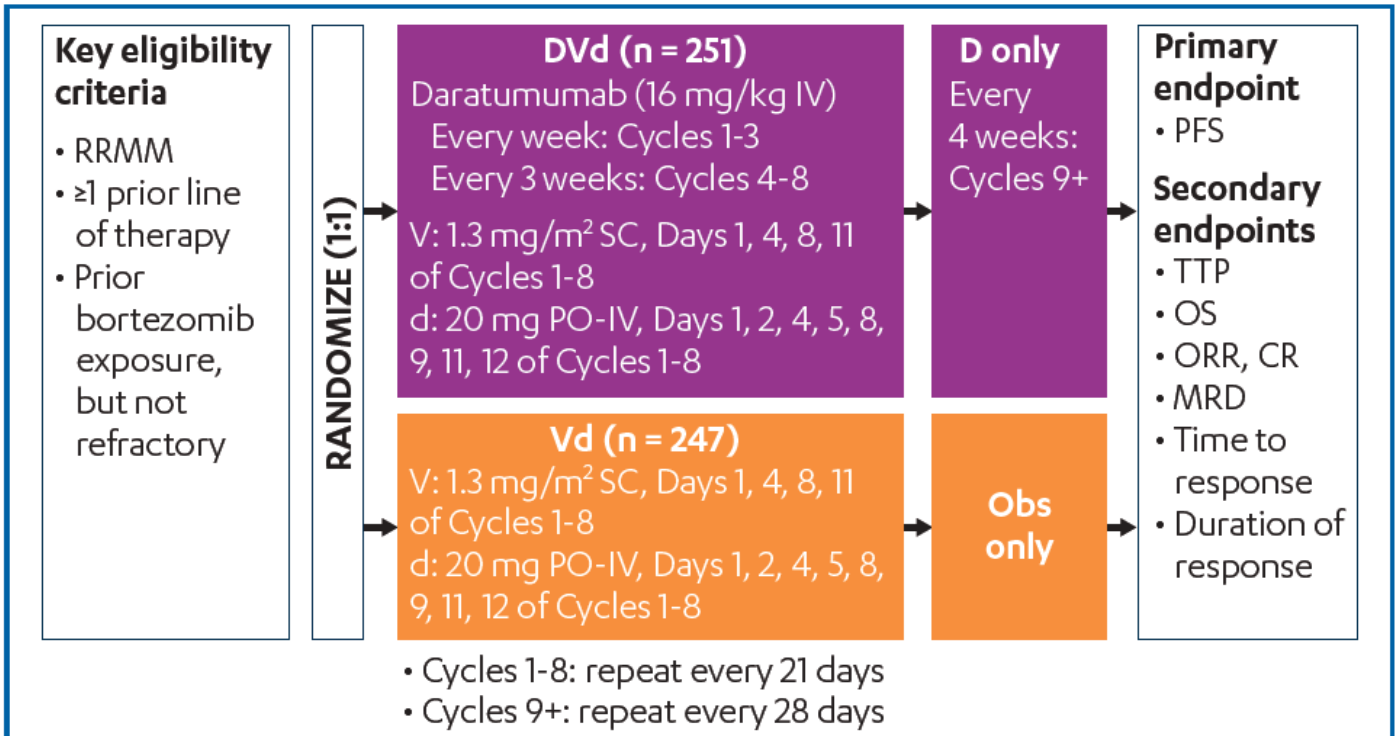
Poster 1852: Daratumumab, Bortezomib and Dexamethasone Versus Bortezomib and Dexamethasone for Relapsed/Refractory Multiple Myeloma (RRMM) Patients: An Update of Overall Survival in CASTOR



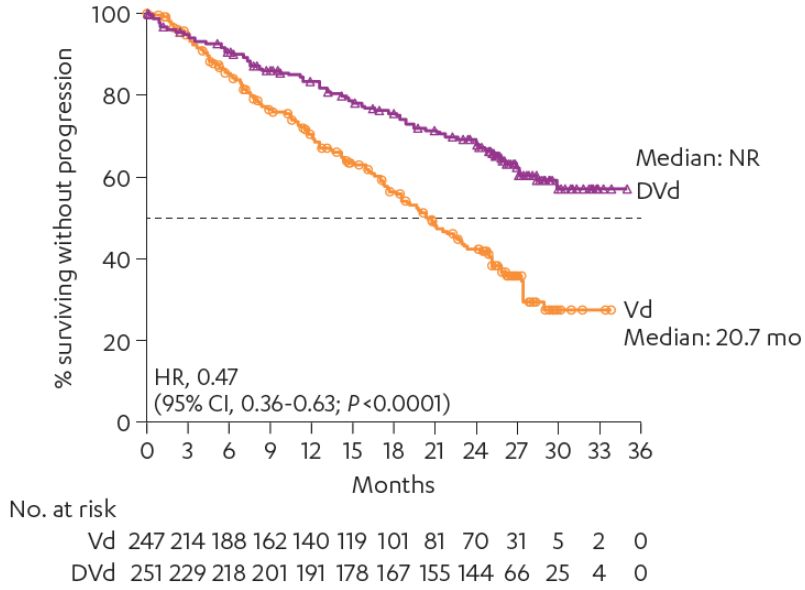
RRMM, relapsed or refractory multiple myeloma; DVd, daratumumab/bortezomib/dexamethasone; IV, intravenous; V, bortezomib; SC, subcutaneous; d, dexamethasone; PO, oral; Vd, bortezomib/dexamethasone; D, daratumumab; Obs, observation; PFS, progression-free survival; TTP, time to disease progression; OS, overall survival; ORR, overall response rate; CR, complete response; MRD, minimal residual disease.

Figure 1. CASTOR study design.

Poster 1852: Daratumumab, Bortezomib, and Dexamethasone Versus Bortezomib and Dexamethasone for Relapsed/Refractory Multiple Myeloma (RRMM) Patients: An Update of Overall Survival in CASTOR

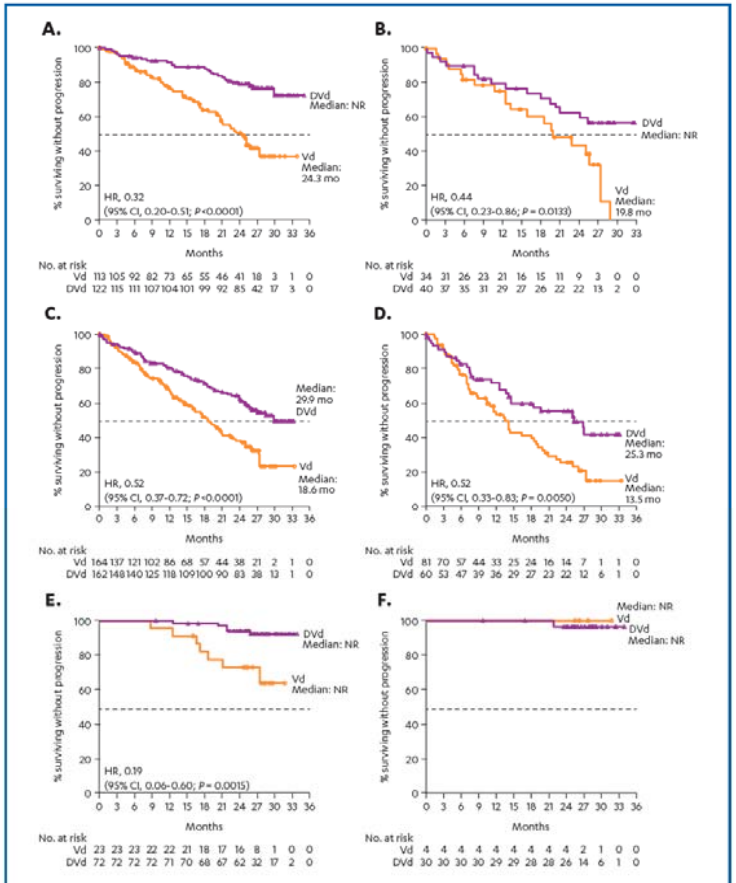
PFS2 in ITT and Subgroup Populations

- In the ITT population, PFS2 was significantly prolonged with DVd compared with Vd (median not reached [NR] vs 20.7 months; HR, 0.47; 95% CI, 0.36-0.63; *P* <0.0001; **Figure 2**)



PFS2, progression-free survival with subsequent line of therapy; ITT, intent-to-treat; DVd, daratumumab/bortezomib/dexamethasone; NR, not reached; Vd, bortezomib/dexamethasone; HR, hazard ratio; CI, confidence interval.

Figure 2. PFS2 in the ITT population.



PFS2, vertical progression-free survival with subsequent line of therapy; CR, complete response; MRD, minimal residual disease; DVd, daratumumab/bortezomib/dexamethasone; NR, not reached; Vd, bortezomib/dexamethasone; HR, hazard ratio; CI, confidence interval.

Figure 3. PFS2 for patients (A) with 1 prior line of therapy; (B) with high cytogenetic risk; (C) previously treated with bortezomib; (D) refractory to lenalidomide; (E) achieving ≥CR; and (F) by MRD negativity at a 10^{-5} sensitivity threshold.

Poster 1852: Daratumumab, Bortezomib, and Dexamethasone Versus Bortezomib and Dexamethasone for Relapsed/Refractory Multiple Myeloma (RRMM) Patients: An Update of Overall Survival in CASTOR

CONCLUSIONS

- **Patients continue to benefit from prior daratumumab treatment, as demonstrated by significant PFS2 benefit in the ITT and subgroup populations**
  - **Patients with deep responses (including MRD negativity at 10^{-5} using clonoSEQ® V2.0) and those with 1 prior line of therapy most benefitted from DVd treatment**
- **Responses were durable among responders receiving maintenance treatment with single-agent daratumumab, and MRD negativity rates continued to accumulate in the DVd arm during this treatment period**
- **These findings highlight the prolonged benefit of adding daratumumab to a standard of care regimen in RRMM**
- **Per study protocol, long-term survival follow-up will continue until 320 deaths have been observed in both arms (ie, when two-thirds of the randomized subjects have died)**
  - **OS data currently remains immature**

Poster 3145: Daratumumab, Bortezomib, and Dexamethasone (DVd) Versus Bortezomib and Dexamethasone (Vd) in Relapsed or Refractory Multiple Myeloma (RRMM): Updated Efficacy and Safety Analysis of CASTOR

Andrew Spencer,[1,*] Vania Hungria,[2] Maria-Victoria Mateos,[3] Ajay K. Nooka,[4] Jane Estell,[5] Wolney Barreto,[6] Paolo Corradini,[7] Chang-Ki Min,[8] Eva Medvedova,[9] Piruntha Thiyagarajah,[10] William Deraedt,[11] Christopher Chiu,[12] Jordan M. Schecter,[13] Katja Weisel[14]

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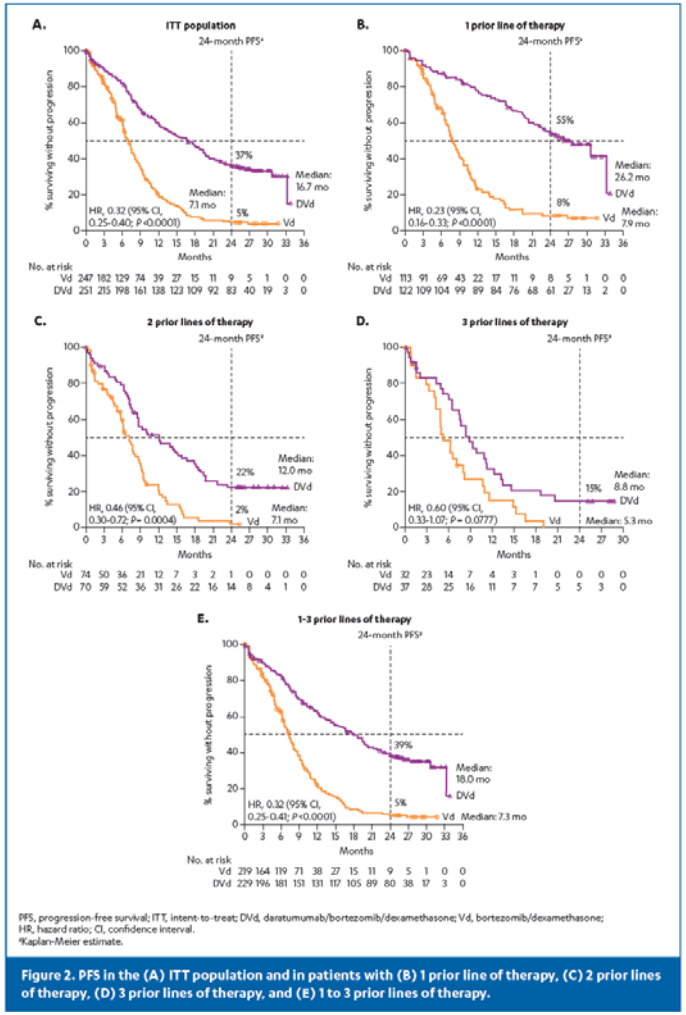
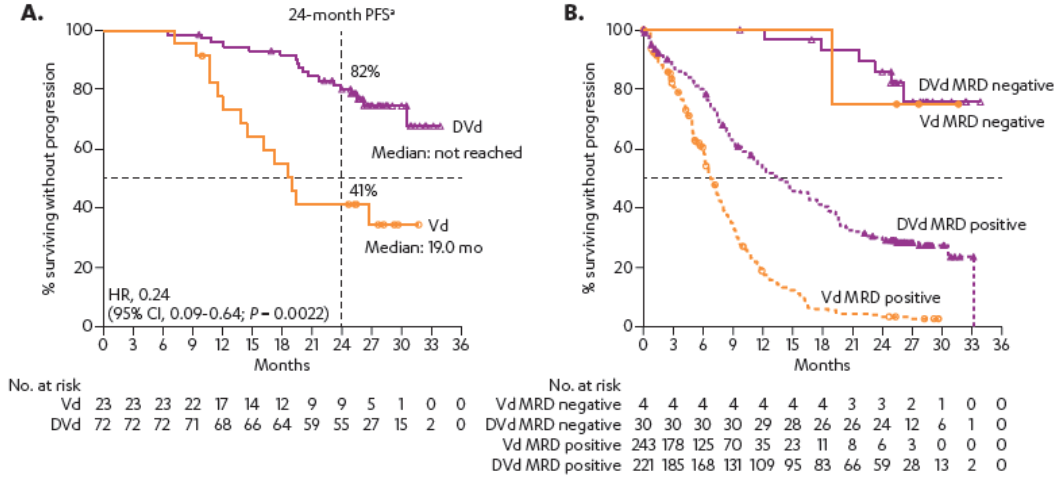
Poster 3145: Daratumumab, Bortezomib, and Dexamethasone (DVd) Versus Bortezomib and Dexamethasone (Vd) in Relapsed or Refractory Multiple Myeloma (RRMM): Updated Efficacy and Safety Analysis of CASTOR



PFS, progression-free survival; ITT, intent-to-treat; DVd, daratumumab/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone; HR, hazard ratio; CI, confidence interval.
²Kaplan-Meier estimate.

Figure 2. PFS in the (A) ITT population and in patients with (B) 1 prior line of therapy, (C) 2 prior lines of therapy, (D) 3 prior lines of therapy, and (E) 1 to 3 prior lines of therapy.



PFS, progression-free survival; CR, complete response; MRD, minimal residual disease; DVd, daratumumab/bortezomib/dexamethasone; Vd, bortezomib/dexamethasone; HR, hazard ratio; CI, confidence interval.
²Kaplan-Meier estimate.

Figure 3. PFS in patients who achieved (A) ≥CR and (B) MRD negativity at 10^{-5}.

Poster 3145: Daratumumab, Bortezomib, and Dexamethasone (DVd) Versus Bortezomib and Dexamethasone (Vd) in Relapsed or Refractory Multiple Myeloma (RRMM): Updated Efficacy and Safety Analysis of CASTOR

CONCLUSIONS

- **Addition of daratumumab to Vd continues to significantly prolong PFS with longer follow-up**
- **DVd improved PFS and ORR regardless of the number of prior lines of therapy**
  - **Patients who received 1 prior line of therapy benefited the most from DVd**
- **Higher MRD-negative rates (6-fold) were observed with DVd at 10^{-5} in the ITT population**
- **Durable responses in the DVd arm translated into longer PFS2 and TTNT**
- **The safety profile of daratumumab remains consistent with previous studies,[7,11] and no new safety signals were reported with longer follow-up**
- **The high rate of deep clinical responses induced by daratumumab supports the use of DVd in relapsed or refractory MM patients and suggests that patients achieve the greatest benefit at first relapse**

EQUULEUS (MMY1001)

Presented by Prof. Philippe Moreau, M.D.
University Hospital of Nantes

Genmab

Poster 1824: Daratumumab in Combination with Pomalidomide and Dexamethasone for Relapsed and/or Refractory Multiple Myeloma (RRMM) Patients with ≥2 Prior Lines of Therapy: Updated Analysis of MMY1001

Thierry Facon,[1,*] Sagar Lonial,[2] Brendan Weiss,[3] Attaya Suvannasankha,[4] Joseph W. Fay,[5] Bertrand Arnulf,[6] Jainulabdeen J. Ifthikharuddin,[7] Carla de Boer,[8] Jianping Wang,[9] Kaida Wu,[3] Ajai Chari,[10] Suzanne Lentzsch,[11] Jordan M. Schecter,[9] Amrita Krishnan[12]

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Poster 1824: Daratumumab in Combination with Pomalidomide and Dexamethasone for Relapsed and/or Refractory Multiple Myeloma (RRMM) Patients with ≥2 Prior Lines of Therapy: Updated Analysis of MMY1001

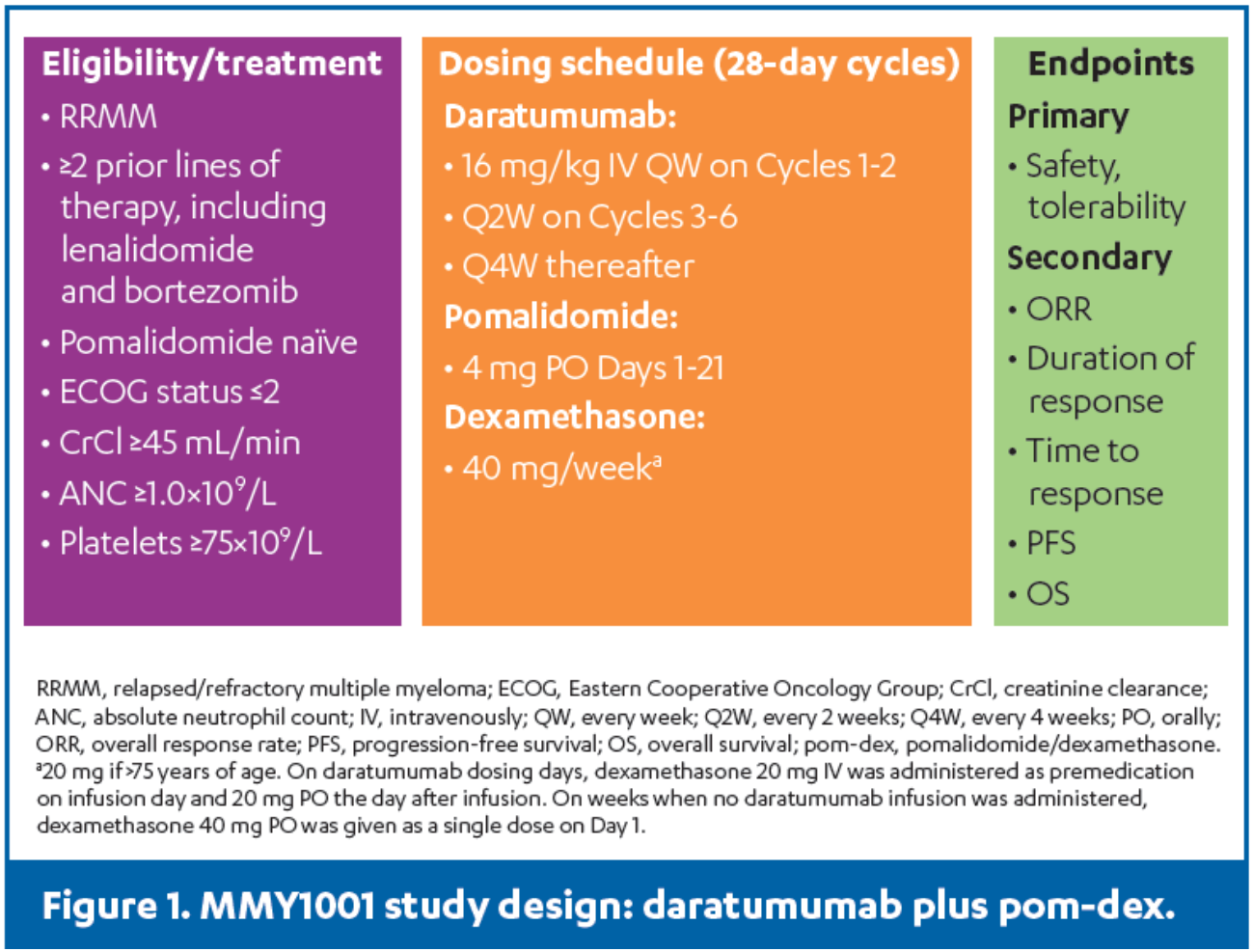
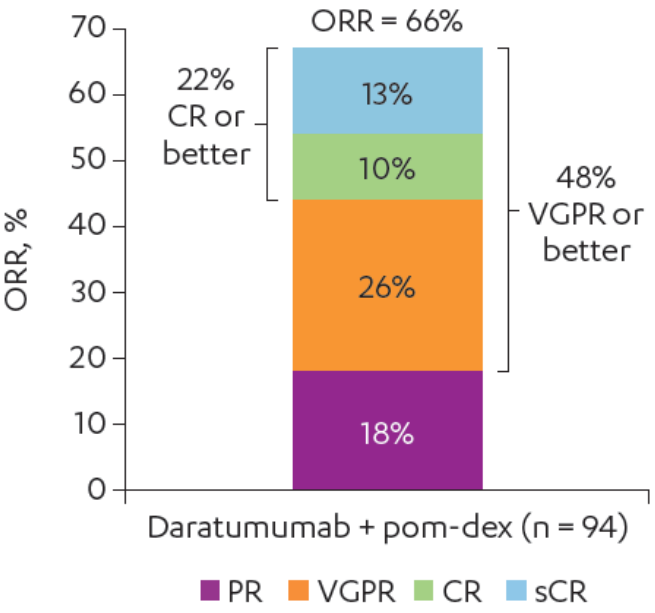


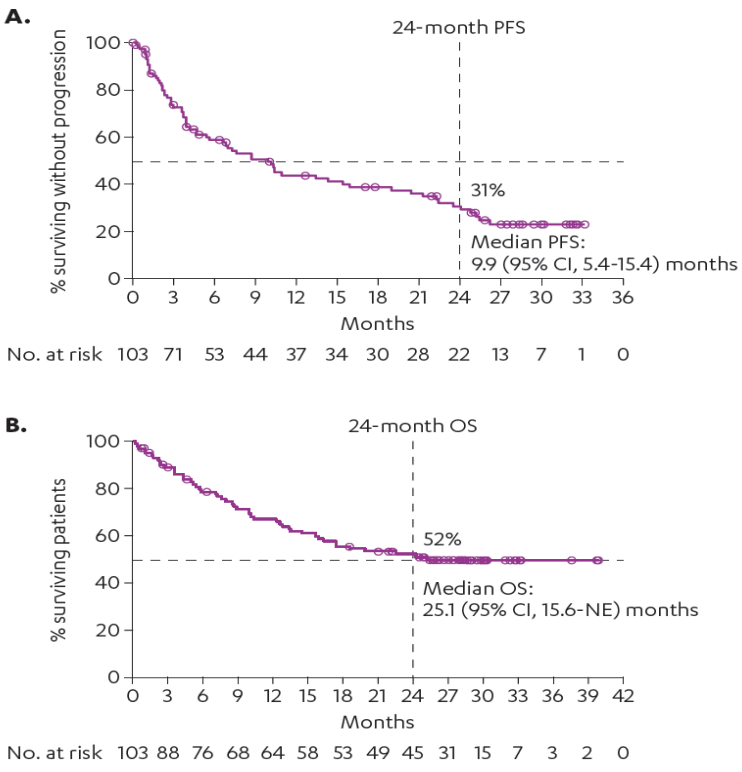
Figure 1. MMY1001 study design: daratumumab plus pom-dex.

Poster 1824: Daratumumab in Combination with Pomalidomide and Dexamethasone for Relapsed and/or Refractory Multiple Myeloma (RRMM) Patients with ≥2 Prior Lines of Therapy: Updated Analysis of MMY1001



ORR, overall response rate; pom-dex, pomalidomide/dexamethasone; PR, partial response; VGPR, very good partial response; CR, complete response; sCR, stringent complete response.

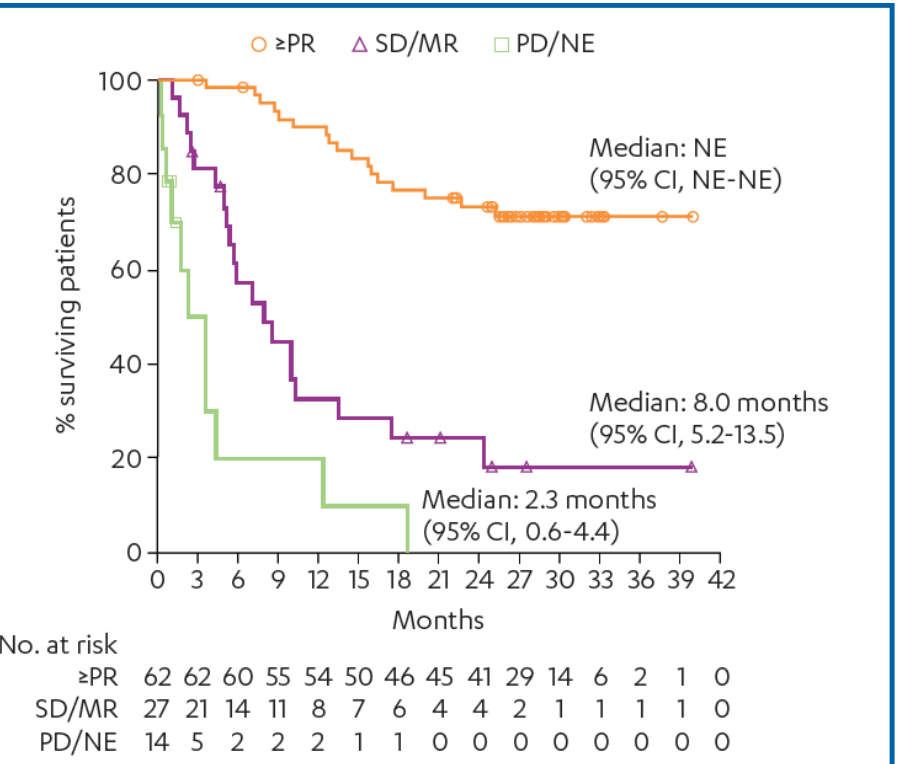
Figure 2. ORR in the response-evaluable population in patients treated with daratumumab plus pom-dex.



PFS, progression-free survival; OS, overall survival; pom-dex, pomalidomide/dexamethasone; CI, confidence interval; NE, not evaluable.

Figure 5. (A) PFS and (B) OS with daratumumab plus pom-dex.

Poster 1824: Daratumumab in Combination with Pomalidomide and Dexamethasone for Relapsed and/or Refractory Multiple Myeloma (RRMM) Patients with ≥2 Prior Lines of Therapy: Updated Analysis of MMY1001



OS, overall survival; pom-dex, pomalidomide/dexamethasone; PR, partial response; SD, stable disease; MR, minimal response; PD, progressive disease; NE, not evaluable; CI, confidence interval.

Figure 6. OS by response category in patients treated with daratumumab plus pom-dex.

Poster 1824: Daratumumab in Combination with Pomalidomide and Dexamethasone for Relapsed and/or Refractory Multiple Myeloma (RRMM) Patients with ≥2 Prior Lines of Therapy: Updated Analysis of MMY1001

CONCLUSIONS

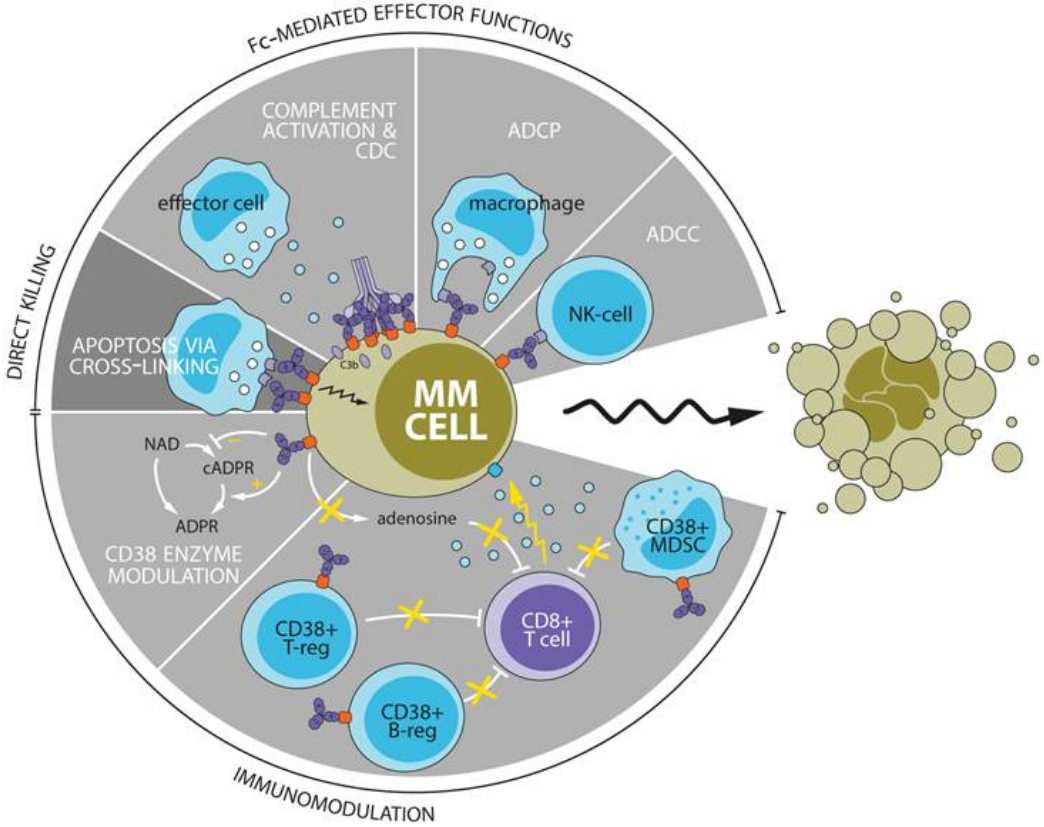
- Adding daratumumab to pom-dex resulted in a safety profile consistent with that of the individual therapies, with the exception of higher rates of neutropenia
- Deep, durable responses were achieved, including MRD negativity, and the regimen was associated with encouraging OS in a heavily pretreated patient population
  - At a median follow-up of 28.1 months, ORR was 66%, including 13% with sCR; rates of VGPR or better and CR or better were 48% and 22%, respectively
  - MRD-negative rate was 7% at 10^{-5}
  - Median PFS was 9.9 months, and the 24-month PFS rate was 31%
  - Median OS was 25.1 months, and the 24-month OS rate was 52%
- Daratumumab plus pom-dex is approved in the United States for use in RRMM patients with ≥2 prior therapies, including lenalidomide and a PI[10]
- A phase 3 study evaluating daratumumab plus pom-dex versus pom-dex alone in RRMM patients is ongoing (APOLLO; NCT03180736)

Daratumumab's Immunomodulatory activities: Potential for solid tumors?

Kate Sasser
CVP, Clinical Biomarkers, Genmab

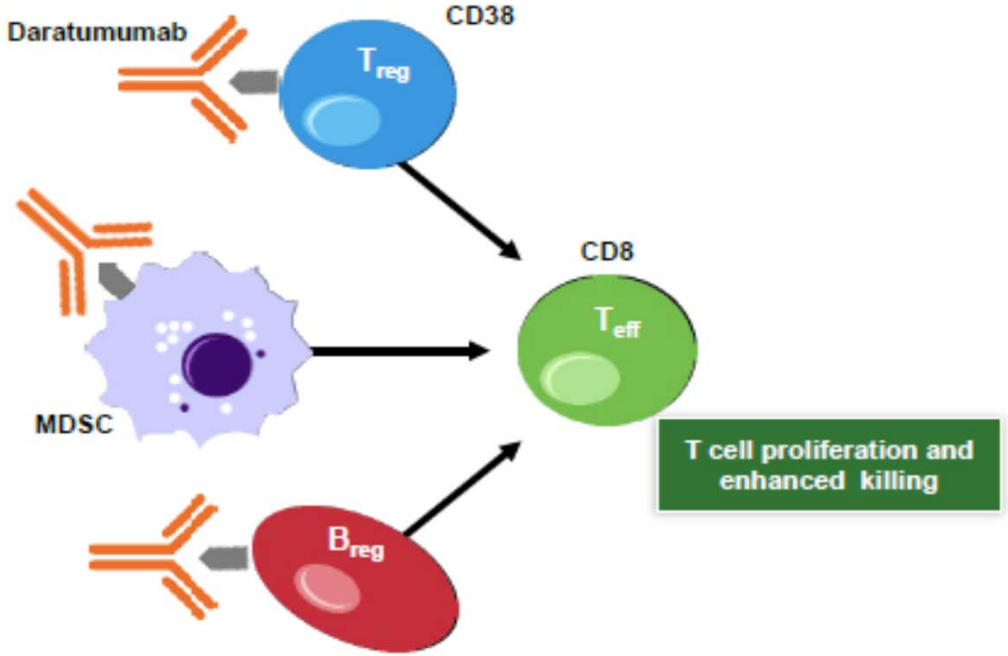
Genmab

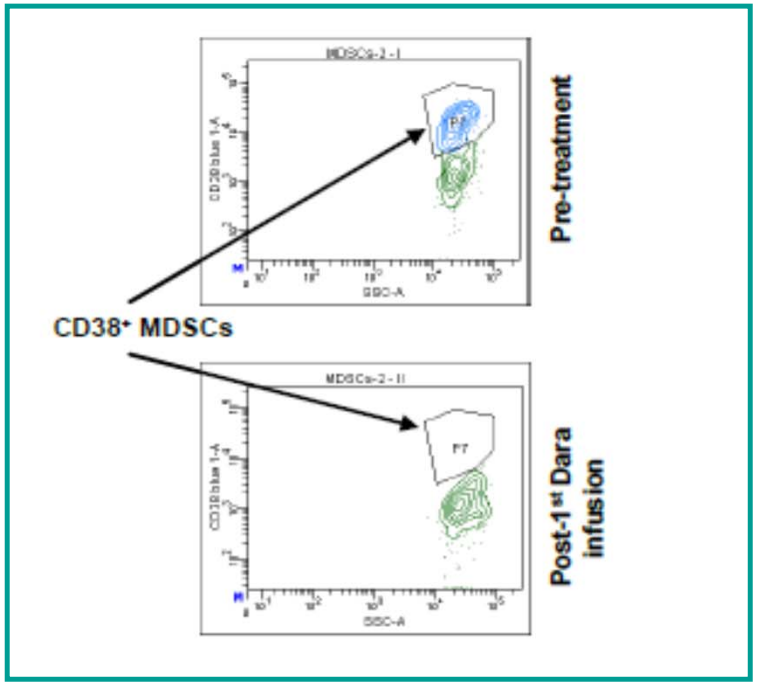
Daratumumab has multiple mechanisms of action (MOA) that lead to tumor cell kill and immune activation



- CDC, ADCC, ADCP, and cross-linking induced apoptosis are all MOA that result in tumor cell killing
- In myeloma patients, daratumumab also induced CD8 T cell expansion and increased clonality, a sign of improved adaptive immunity
- Similarly, $CD38^{+}$ immune suppressive cells (regulatory T cells, regulatory B cells, myeloid derived suppressor cells) were reduced suggesting daratumumab can deplete these cells and improve immune function

Daratumumab decreases regulatory T cells, B cells, and MDSC and increases clonal T cell responses

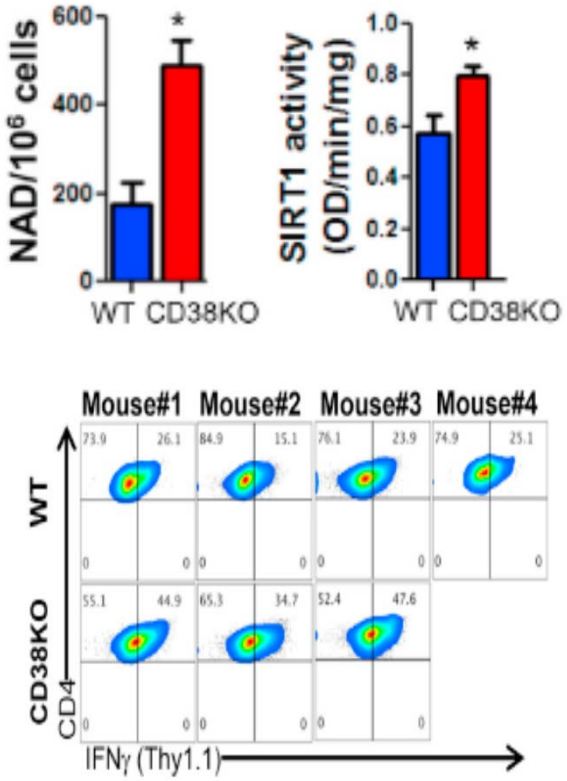


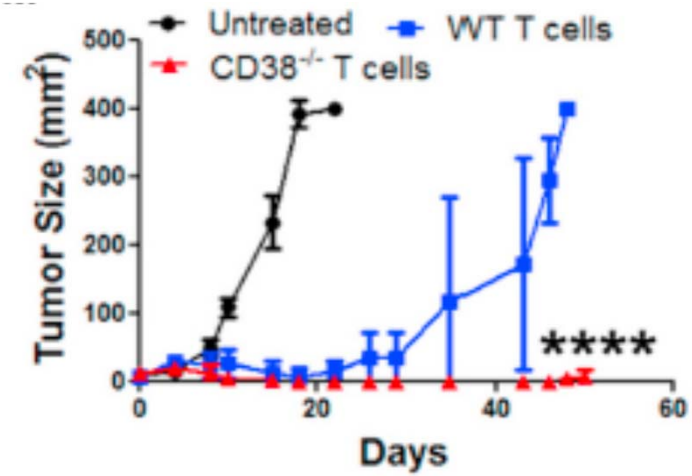


- ❑ Clears immune suppressive cells
- ❑ Allows clonal expansion of CD8+ T cells and improves T cell function

Krejck, et al. Blood. 2016
Chiu et al. ASH. 2016 (T cell clonality abstract #4531)

CD38-NAD+ Axis Regulates Immunotherapeutic T cell response



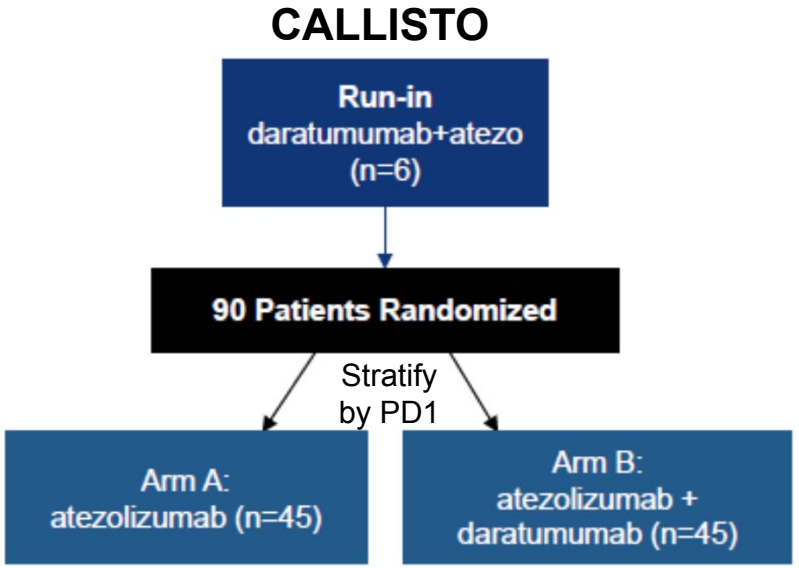


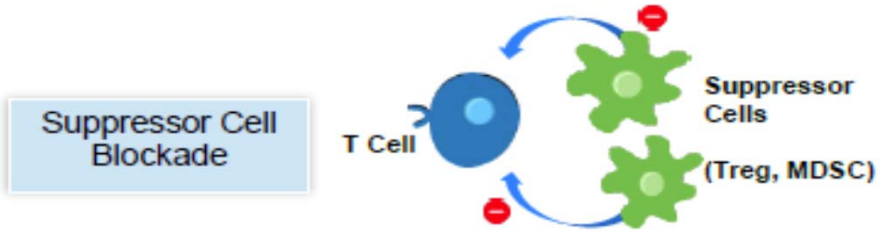
- CD38 knock-out (KO) T cells have more NAD and SIRT1 activity
- CD38 KO T cells have more anti-tumor activity in vivo and produce more IFNγ

Chatterjee, et al. Cell Metabolism. Nov 2017

CD38 may be a therapeutic target in NSCLC

- Daratumumab reduces immune suppression through the elimination of CD38+ Tregs and MDSC
- Expanded CD38+ Tregs and MDSC seen in lung tumor microenvironment
- In NSCLC mouse models, CD38 inhibition alone was able to reduce lung tumor growth, and combinations of CD38 and PDL1 inhibition were synergistic
- Phase 2 trial will test whether daratumumab in combination with atezolizumab can impact immune microenvironment and deliver clinical benefit





Chen, Abstract #79, ASCO-SITC 2017

Kinder, et al. SITC 2017. Abstract#P376

Take home message: Emerging Data indicates CD38 could be a target in other cancers

- **Recent data published or presented in meetings is supportive of CD38 being a target in solid tumors**
  - CD38 is expressed in NSCLC (immune cells and tumor cells)
  - In NSCLC mouse models, CD38 inhibition alone was able to reduce lung tumor growth, and combinations of CD38 and PDL1 inhibition were synergistic
  - Recent immune profiling of renal cell carcinoma determined CD38 to be co-expressed with PD1 in exhausted T cells, and also highly expressed in immune suppressive tumor-associated macrophages
  - CD38-NAD+ pathway was shown to regulate anti-tumor T cell response through T cell metabolic programming and differentiation
  - In CLL, daratumumab Decreases Treg-Mediated Immunosuppression and Potentiates $CD8^+$ T-Cell-Induced Killing of Chronic Lymphocytic Leukemia (CLL) Cells Ex Vivo

- **Current clinical trials testing the safety & efficacy of Daratumumab in combination with PD1 or PDL1 in solid tumors**
  - Janssen trial: Daratumumab in combination with Atezolizumab in NSCLC
  - BMS trials: Daratumumab in combination with Nivolumab in: 1) CRC 2) Pancreas, NSCLC, TNBC 3)Virus-associated tumors.

Chen, Abstract #79, ASCO-SITC 2017
Manna, et al, Abstract #1736. ASH 2017.
Maj, et al. Nature Immunology. Oct 2017
Chatterjee, et al. Cell Metabolism. Nov 2017
Chevrier et al. Cell 169, 736-749

Daratumumab Q&A

Tisotumab Vedotin

Presented by Prof. Ignace Vergote
Catholic University of Leuven

Genmab

A PHASE IIA STUDY OF TISOTUMAB VEDOTIN (HUMAX®-TF-ADC) IN PATIENTS WITH RELAPSED, RECURRENT AND/OR METASTATIC CERVICAL CANCER

Vergote I, Concin N, Dean E, Lassen U, Drew Y, Machiels JP, Nielsen D, Arkenau T, Forster M, Jones R, Slomovitz B, Spicer J, Johnson M, Cornez N, Gennigens C, Fulton B, Basse L, Lisby S, Coleman RL, Hong DS

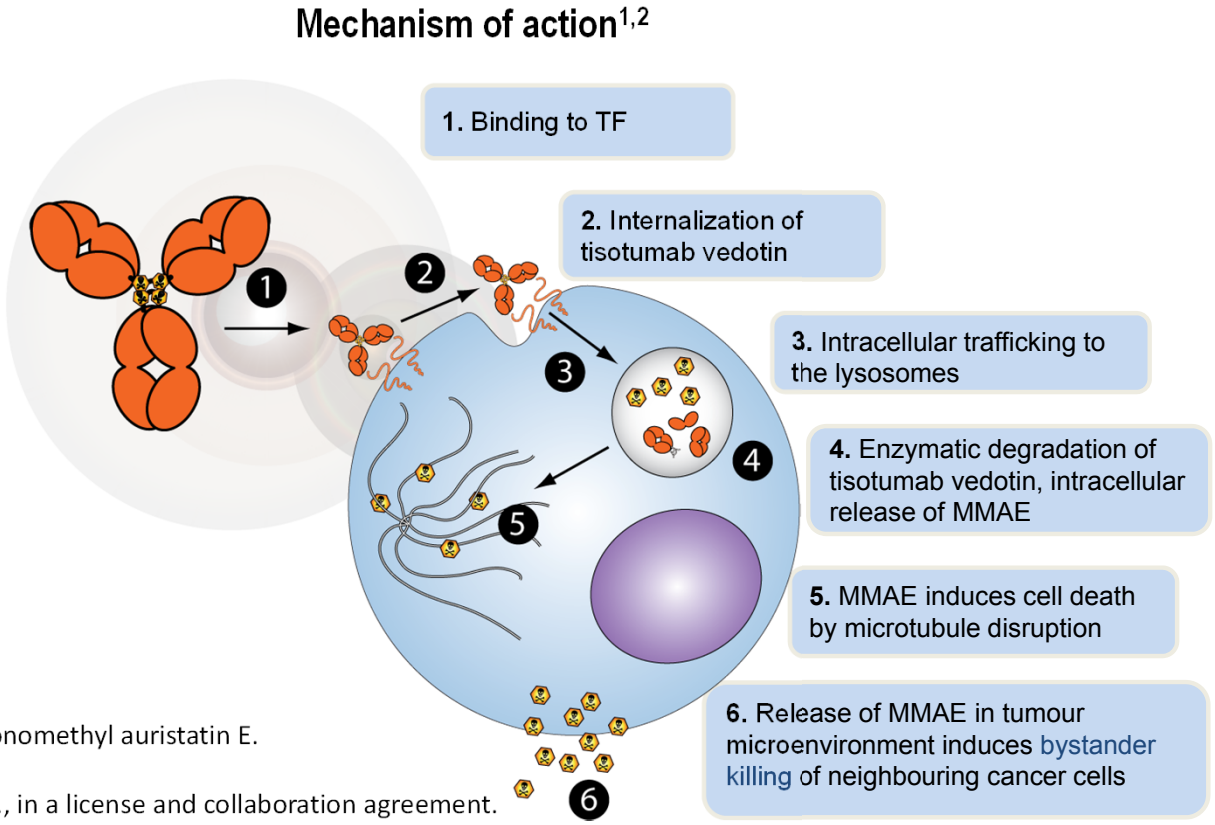
Presented at ESMO 2017, Oral Presentation

Tisotumab Vedotin mechanism of action

Tisotumab vedotin is an Antibody-Drug Conjugate (ADC) composed of a human mAb specific for Tissue Factor (TF), a protease-cleavable linker, and the microtubule disrupting agent MMAE[1,a,b]

•TF is a transmembrane protein that is the main physiological initiator of coagulation and is involved in angiogenesis, cell adhesion, motility, and cell survival[3]

TF is aberrantly expressed in a broad range of solid tumours, including cervical cancer, and is associated with poor prognosis[4,5]



ADC=antibody-drug conjugate; mAb=monoclonal antibody; MMAE=monomethyl auristatin E.

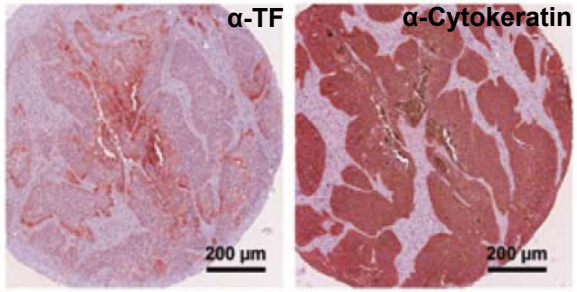
[a]Tissue factor is known as TF, CD142, and thromboplastin.

[b]MMAE-based ADC technology was licensed from Seattle Genetics, Inc., in a license and collaboration agreement.

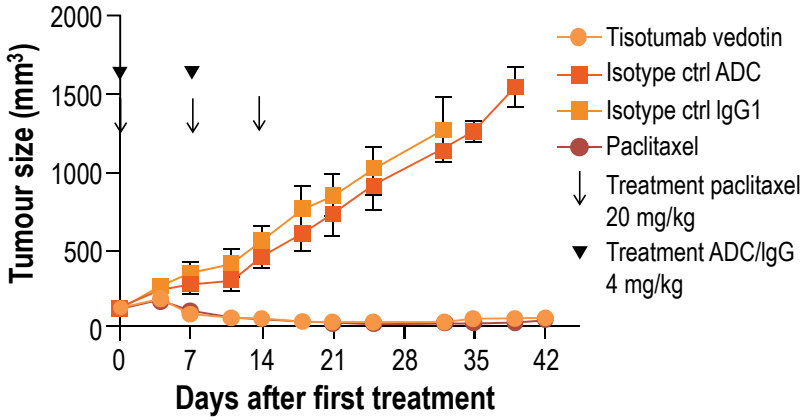
1. Breij EC et al. *Cancer Res.* 2014;74(4):1214-1226. **2.** De Goeij BE et al. *Mol Cancer Ther*. 2015;14(5):1130-1140. **3.** Chu AJ. *Int J Inflam*. 2011;2011. doi: 10.4061/2011/367284.
4. Förster Y et al. *Clin Chim Acta*. 2006;364(1-2):12-21. **5.** Cocco E et al. *BMC Cancer*. 2011;11:263.

Anti-Tumour Activity in a Cervical Squamous Cell Carcinoma PDX Model: Efficacy in a Taxane-Relapsed Setting

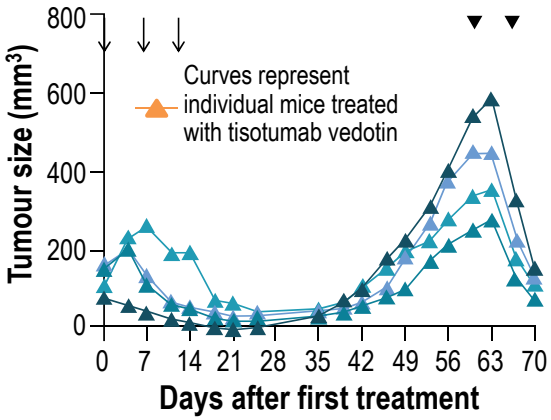
TF expression in a PDX model of cervical squamous cell carcinoma[a]



Primary treatment[b]



Re-treatment after paclitaxel (individual mice)[c]



Despite heterogeneous TF expression, tisotumab vedotin induced robust tumour regression, event after paclitaxel, in cervical cancer PDX models

ADC=antibody-drug conjugate; IgG=immunoglobulin G; PDX=patient-derived xenograft; TF=tissue factor.

[a]A cervical squamous cell carcinoma PDX model was established by subcutaneous implantation of patient tumour fragments into mice. Immunohistochemistry analysis of PDX model using the TF human monoclonal antibody and human cytokeratin, which identifies human tumour cells. [b]Datapoints are the average tumour size per group, with 8 mice per group. [c]Curves and data points represent tumour size in individual mice. Patient-derived cervical squamous cell carcinoma cells were implanted in mice, and when the tumours reached a size of 80-200 mm^3, mice were treated with 20 mg/kg of paclitaxel at the indicated time points. Upon tumour outgrowth following paclitaxel discontinuation, mice were treated with 2 doses of tisotumab vedotin 4 mg/kg at the indicated time points.

Breij EC et al. *Cancer Res.* 2014;74(4):1214-1226.

GEN701 Is the First-In-Human Study of Tisotumab Vedotin

Key inclusion criteria:

- Patients with relapsed, advanced, and/or metastatic cancer who have failed available standard therapy
- Measurable disease

Key exclusion criteria:

- Abnormal coagulation parameters at baseline
- Ongoing major bleeding
- Presence of CTCAE grade ≥2 peripheral neuropathy

Part 1: Dose escalation

- 3+3 dose-escalation design[a]
- Dose range tested: 0.3-2.2 mg/kg IV q3w
- Patients enrolled included those with the following tumour types (N=27):
  - Gynaecologic (ovarian, cervical, and endometrial)
  - Prostate
  - Bladder
  - Oesophageal
  - NSCLC
  - SCCHN[c]

Part 2: Expansion cohort

- **Ongoing expansion cohort**
- **Dose selected: 2.0 mg/kg IV q3w**

Cervical (n=34)[b]
Ovarian (n=36)[b]
Prostate (n=18)
Bladder (n=15)
Oesophageal (n=15)
Endometrial (n=14)
NSCLC (n=15)

- **Primary endpoint:** Safety and tolerability
- **Key secondary endpoints:** Anti-tumour activity

CTCAE=Common Terminology Criteria for Adverse Events; IV=intravenous; NSCLC=non–small cell lung cancer; SCCHN=squamous cell carcinoma of the head and neck.
[a]Subjects were enrolled into cohorts at increasing dose levels of tisotumab vedotin in 21-day treatment cycles. [b]In phase 2, ovarian and cervical cohorts were expanded to approximately 30 patients based on preliminary efficacy observed in the first 14 patients enrolled. [c]The SCCHN cohort was closed by protocol amendment 4 due to an event of pharyngeal tumour haemorrhage with fatal outcome. The event was deemed to be most likely related to the disease itself.
Clinicaltrials.gov. https://clinicaltrials.gov/ct2/show/NCT02001623. Accessed August 7, 2017.

Baseline Patient Characteristics in Cervical Cancer Cohort

	Cervical (N=34)
Age (median, range), y	43 (21-73)
ECOG score, no (%)	
0	7 (21%)
1	26 (76%)
Missing	1 (3%)
Cancer type, no (%)	
Adenocarcinoma	15 (44%)
Adeno-squamous	3 (9%)
Squamous	15 (44%)
Missing/TBD	1 (3%)
Previous lines of systemic treatments, no (%)	
0[a]	3 (9%)
1	13 (38%)
2	11 (32%)
3	4 (12%)
4	3 (9%)

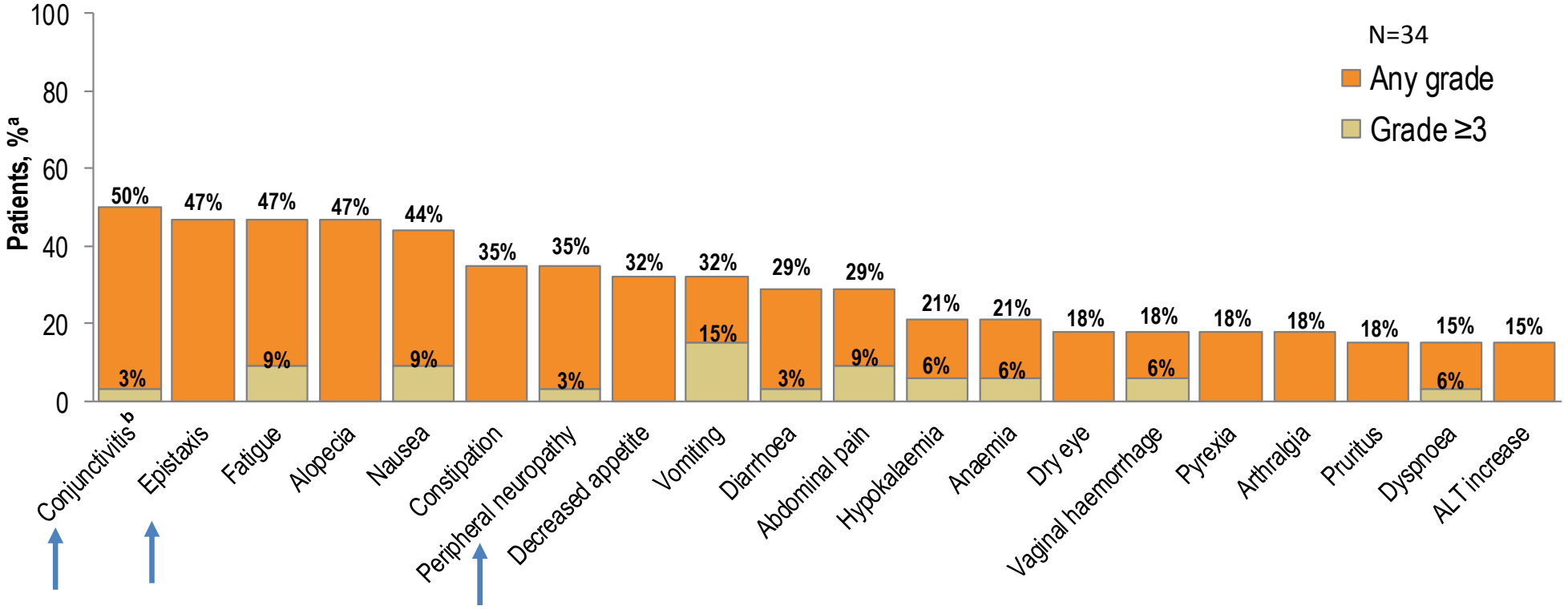
	Cervical (N=34)
Prior treatments, %[b]	
Platinum	91%
Taxane	91%
Bevacizumab[c]	71%
GOG 240 regimen[d]	68%
≥1 platinum doublet	17%
Prior radiotherapy[e]	74%

ECOG=Eastern Cooperative Oncology Group; TBD=to be determined.

[a]Patients progressed on therapy administered for treatment of locally advanced disease. [b]Missing data from 1 patient. [c]Including bevacizumab administered as combination therapy as either platinum/bevacizumab/paclitaxel or topotecan/bevacizumab/paclitaxel. [d]Combination therapy with cisplatin, paclitaxel, and bevacizumab. [e]External beam radiotherapy administered to the cervix or surrounding tissues.

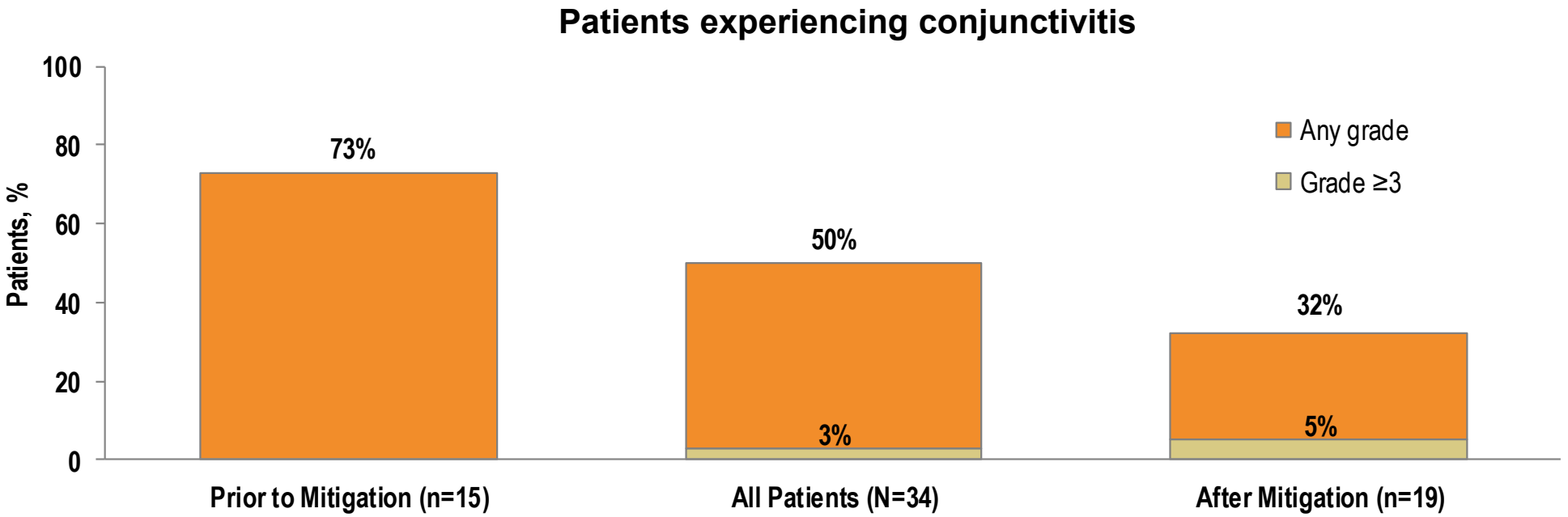
Data cutoff date July 24,2017.

Adverse events (≥15% of patients) in cervical cancer COHORT



ALT=alanine aminotransferase.
[a]Adverse events with events of any grade occurring in ≥15% of patients or of grade ≥3 in 2 or more patients. [b]Grade 2 conjunctivitis was reported in 32% of patients.
Data cutoff date July 24, 2017.

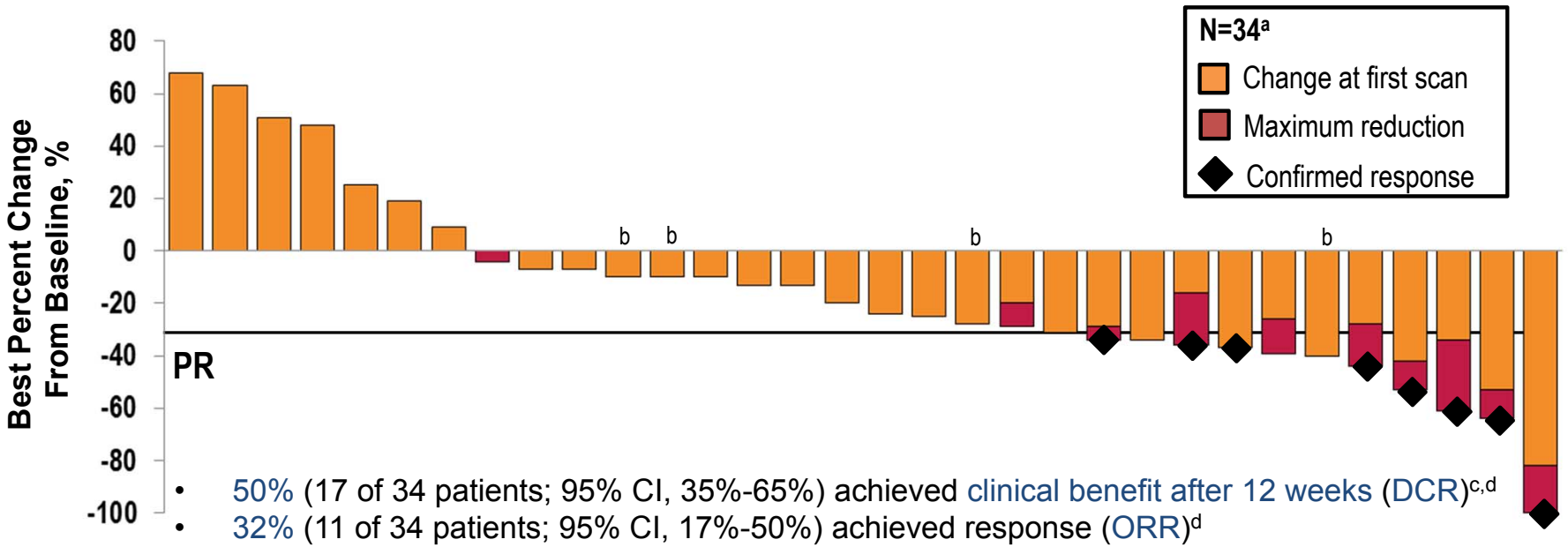
Mitigation Measures substantially reduced conjunctival toxicity in cervical cancer COHORT



- Risk mitigation measures involved a prophylactic steroid, lubricating eye drops, and cooling eye masks worn during treatment infusion, as well as stricter dose adjustment guidance
- Mitigation measures substantially reduced the rates of conjunctival toxicity

Data cutoff date July 24, 2017.

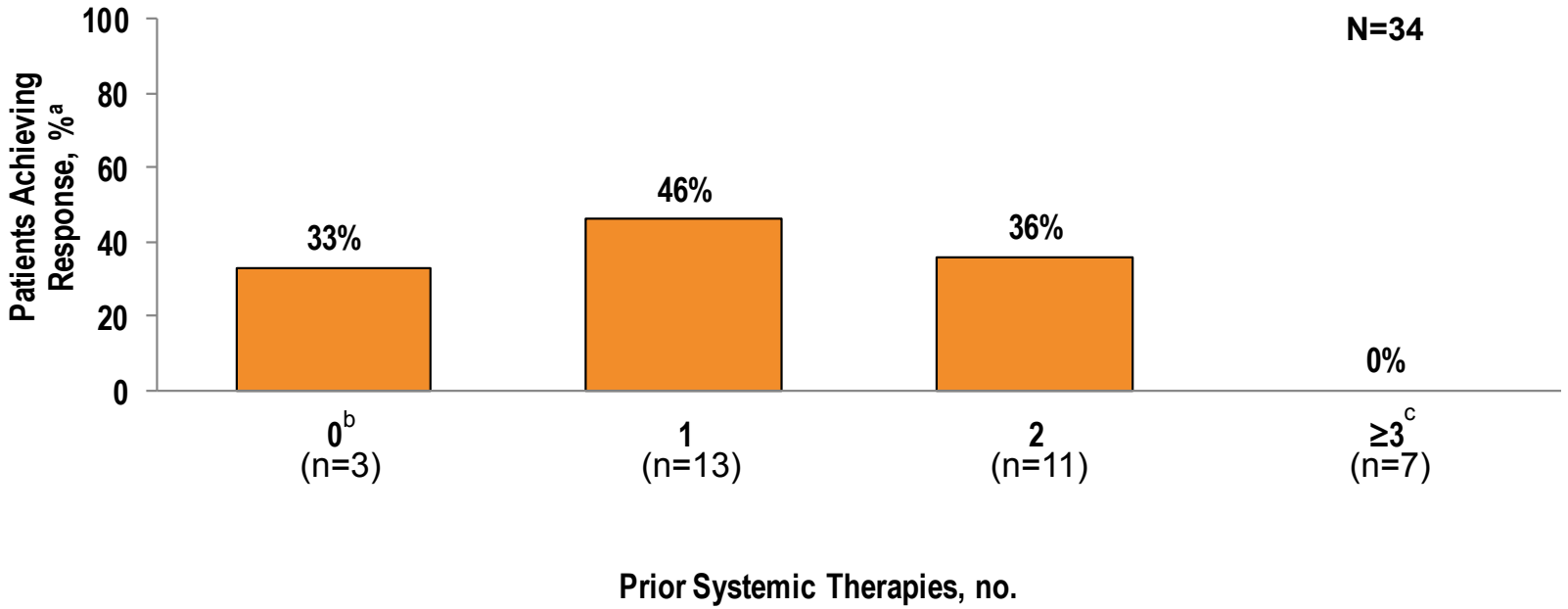
32% of patients with recurrent/Advanced cervical cancer achieved Response with tisotumab vedotin



- 50% (17 of 34 patients; 95% CI, 35%-65%) achieved clinical benefit after 12 weeks (DCR)[c,d]
- 32% (11 of 34 patients; 95% CI, 17%-50%) achieved response (ORR)[d]
  - 8 PR, confirmed
  - 3 PR, unconfirmed[e]

CI=confidence interval; CR=complete response; CT=computed tomography; DCR=disease control rate; ORR=overall response rate; PD=progressive disease; PR=partial response;
RECIST=Response Evaluation Criteria in Solid Tumors; SD=stable disease.
[a]Two patients were withdrawn prior to CT scan, and so are not represented in the graph. [b]PD due to new lesion at same scan. [c]Clinical benefit was defined as the DCR rate, the proportion of patients who achieved a CR, PR, or SD after 12 weeks. [d]Response was as assessed by investigators using standard RECIST 1.1 criteria. [e]One of which is still ongoing. Data cutoff date July 24, 2017.

Responses with Tisotumab vedotin by prior lines in cervical cancer cohort



[a]Including confirmed and unconfirmed responses. [b]Patients were refractory to therapy administered for early stage disease. [c]Patients received either 3 (n=4) or 4 (n=3) prior systemic therapies.
Data cutoff date July 24, 2017.

Current Treatment paradigm in recurrent/advanced cervical cancer

- **First-line standard of care** is paclitaxel-platinum in combination with bevacizumab[1-3]
- Second-line therapies have limited response rates[1]

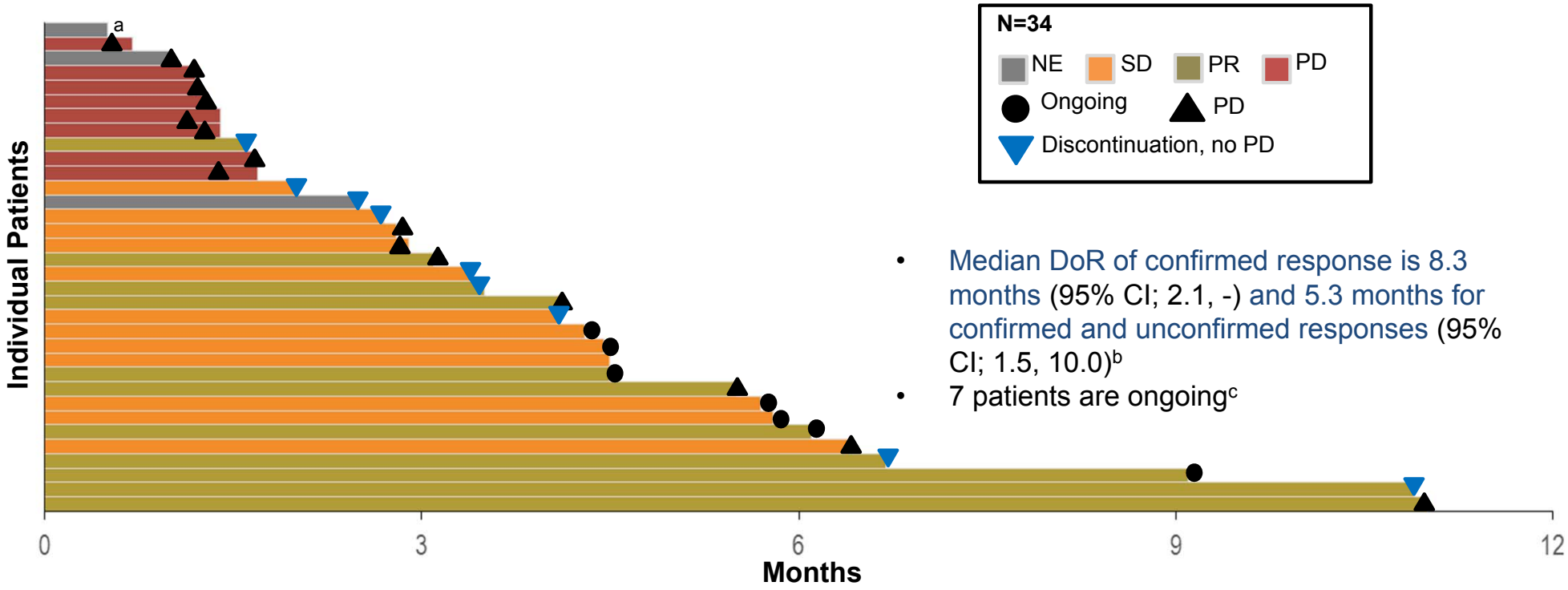
Agent	Overall Response Rate (%)[1]	Agent	Overall Response Rate (%)[1]
Bevacizumab	11%	Pemetrexed	14%-15%
Topotecan	13%-19%	Irinotecan	21%
Vinorelbine	14%	Lapatinib	5%
Gemcitabine	5%	Pazopanib	9%
Albumin-bound paclitaxel[a]	29%	Pegylated liposomal doxorubicin	11%
Docetaxel	9%		

- There is **no standard of care in second-line** cervical cancer, creating an unmet medical need for new treatments[1]

[a]Dose dense regimen.

1. Marth C et al. *Ann Oncol.* 2017;28(suppl 4):iv72-iv83. **2.** Tewari KS et al. *N Engl J Med*. 2014;370(8):734-743. **3.** Koh WJ et al. *J Natl Compr Canc Netw*. 2015;13(4):395-404.

Duration of Response with Tisotumab vedotin in cervical cancer cohort



- Median DoR of confirmed response is 8.3 months (95% CI; 2.1, -) and 5.3 months for confirmed and unconfirmed responses (95% CI; 1.5, 10.0)[b]
- 7 patients are ongoing[c]

DoR=duration of response; NE=not evaluated; PD=progressive disease; PFS=progression-free survival; PR=partial response; SD=stable disease.
[a]Patient withdrawn. [b] 4 responders have progressed as of the data cutoff of July 24, 2017 and 4 have been withdrawn because of other reasons and are thus censored for DoR. [c]Estimated median PFS was 6.4 months.
Data cutoff date July 24, 2017.

Tisotumab vedotin demonstrated robust efficacy and a manageable safety profile in the cervical cancer expansion cohort

- Tisotumab vedotin is an ADC composed of a human mAb specific for TF, a protease cleavable linker, and the microtubule disrupting agent MMAE
- The safety profile of tisotumab vedotin in recurrent cervical cancer was generally consistent with other MMAE-based ADCs
  - Conjunctivitis was the most common TEAE
  - The mitigation measures substantially reduced conjunctival toxicity
- ORR (confirmed + unconfirmed responders) is 32% and median DoR (confirmed responders) is 8.3 months
- The substantial efficacy and the manageable safety warrants further development of tisotumab vedotin in previously treated recurrent/advanced cervical cancer patients

ADC=antibody-drug conjugate; DoR=duration of response; mAb=monoclonal antibody; MMAE=monomethyl auristatin E; ORR=overall response rate; TEAE=treatment-emergent adverse event; TF=tissue factor.
Data cutoff date July 24, 2017.

Tisotumab Vedotin Q&A

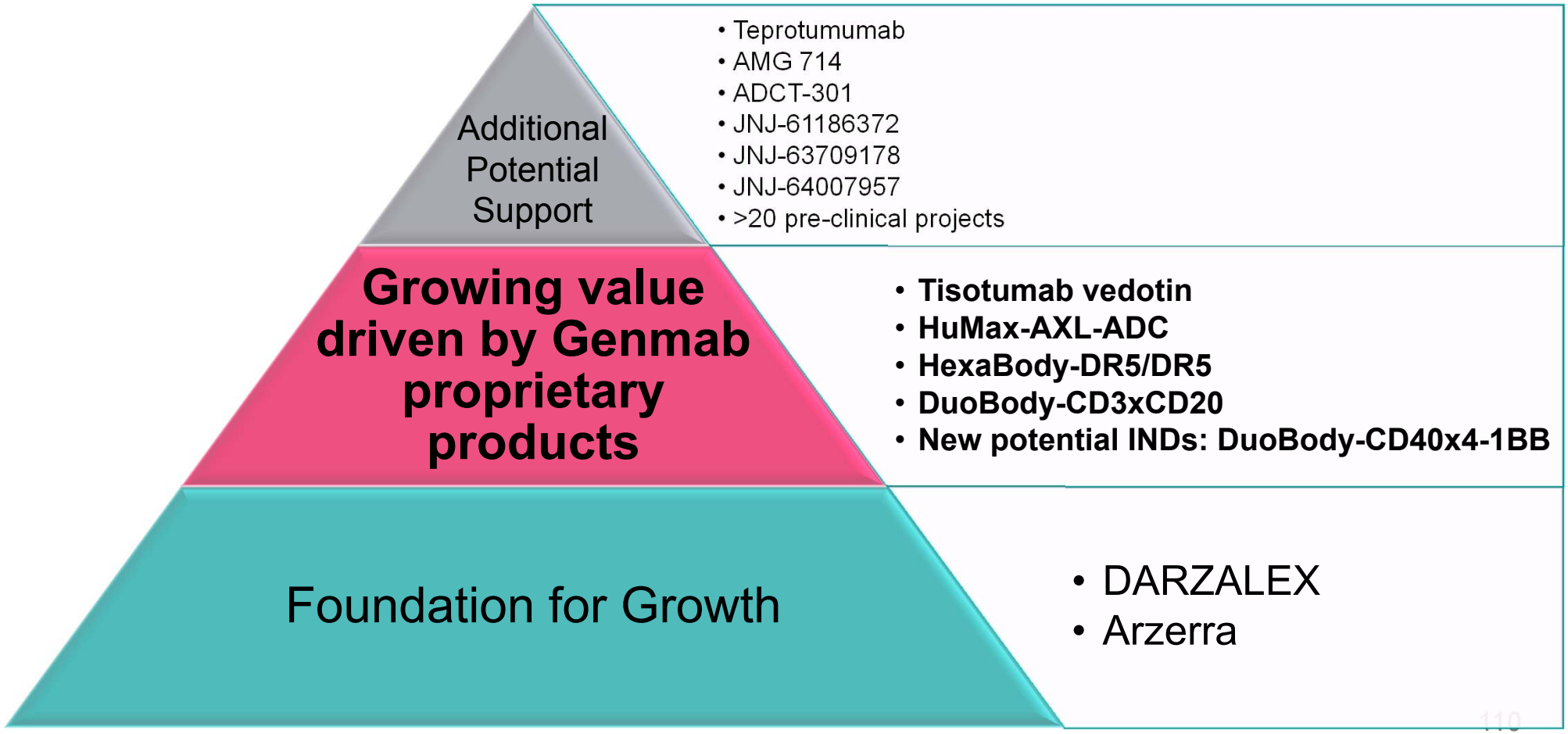
Genmab

2018 & Beyond

Jan van de Winkel
President & CEO

Genmab

Looking Ahead: Building Genmab's Pipeline



DuoBody-CD40x4-1BB

Jan van de Winkel
President & CEO

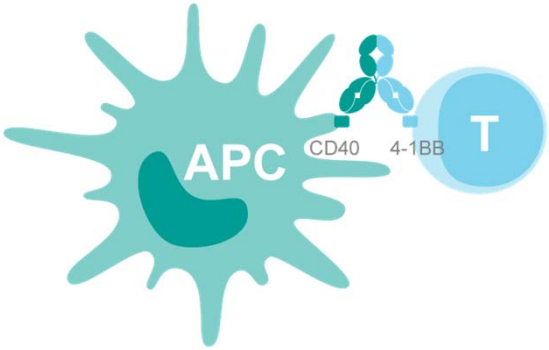
Genmab

DuoBody-CD40x4-1BB

Immunomodulation: targeting two checkpoint activators

Bispecific antibody targeting CD40 and 4-1BB (CD137)

- Trans-activating bispecific targeting two checkpoint activators
- Simultaneously activates antigen-presenting cell (APC) and enhances T cell activation
- Co-engagement of CD40 (APCs) and 4-1BB (T cells) in immune response against tumor
- Conditional activation and expansion of previously activated cytotoxic $CD8^+$ T cells
- Inert Fc backbone



- For treatment of solid cancers
- 2018 IND/CTA candidate
- 50/50 Co-development Genmab and BioNTech

Key 2018 Priorities

Jan van de Winkel
President & CEO

Genmab

2018 Company Goals
Maximizing Differentiated Product Portfolio Value

Priority	✓	Targeted Milestone
Maximize daratumumab progress		» FDA and EMA decision on Phase III ALCYONE multiple myeloma (MM) submission » Start new Phase III MM study » Report early clinical data in solid tumors » Phase III MAIA MM efficacy analysis in frontline » Phase III CASSIOPEIA MM efficacy analysis in frontline
Optimize ofatumumab value		» Complete recruitment Phase III subcutaneous ofatumumab relapsing MS studies
Maximize tisotumab vedotin progress		» Start two Phase II studies cervical cancer (recurrent / metastatic & combination study in frontline) » Start Phase II study in additional solid tumor indications
Strengthen differentiated product pipeline and technology partnership portfolio		» Start HuMax-AXL-ADC expansion phase in ongoing Phase I/II study » Progress HexaBody-DR5/DR5 Phase I/II study » Progress DuoBody-CD3xCD20 Phase I/II study » Accelerate proprietary DuoBody Immuno-Oncology programs towards clinic » Enter new technology or product collaborations
Disciplined financial management and building a commercial footprint		» Execute controlled company growth with selective investments in product & technology pipeline » Continue investing in building commercialization and launch capabilities

Directional Guidance 2018

David Eatwell
EVP & CFO

Genmab

2017 Record Year

	2016 DKK M	2017* DKK M		2016** USD M	2017** USD M
Revenue	1,816	2,340	+29%	288	371
Expenses	(763)	(1,050)	+38%	(121)	(167)
Operating Income	1,053	1,290	+23%	167	204
DARZALEX Royalty	458	1,000	>Double	73	159
Expense Coverage	60%	~100%			
Cash Position	3,922	>4,900	+DKK 1bn	623	778
FTEs	205	~260			

*Guidance midpoint **FX Rate, USD / DKK 6.30

Directional Guidance 2018

Guidance Issued February 21, 2018

Daratumumab Drives Revenue

- Milestones 2017: $171M / Cumulative: $481M
- Lumpy year to year. Lower in 2018

DARZALEX sales continue rapid growth

- US, market share increase
- Long duration builds patient numbers
- RoW continued country RRMM penetration
- Japan launch, full year benefit
- Introduction of FLMM – starts 2018, accelerate in 2019 (DRd)
  - DVMP key for RoW, DRd key for US
- DARZALEX Royalty Funds 100% of expenses

DARZALEX advancing from a blockbuster towards backbone therapy in multiple myeloma

Directional Guidance 2018

Expenses driven by pipeline investments

- 4 proprietary clinical products
- New & larger tisotumab vedotin trials
- 6 pre-clinical products rapidly advancing
- 2018 expense growth 40-50%

Remain profitable & well capitalized

- 2018 6th year of profitability
- Royalty funds 100% of expense investment

Achieving sustainable profitability

- Ability to invest in our own pipeline
- Opportunity to create more value


Q&A
Genmab


Copenhagen · Princeton · Utrecht
Glædelig Jul
og Godt Nytår
Holiday Greetings
Prettige
Feestdagen
Genmab

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