# R&D Update and 2019 ASH Data Review

December 9, 2019
Live in Orlando and via Webcast 20:00 – 21:30 EST

Genmab

# Forward Looking Statement

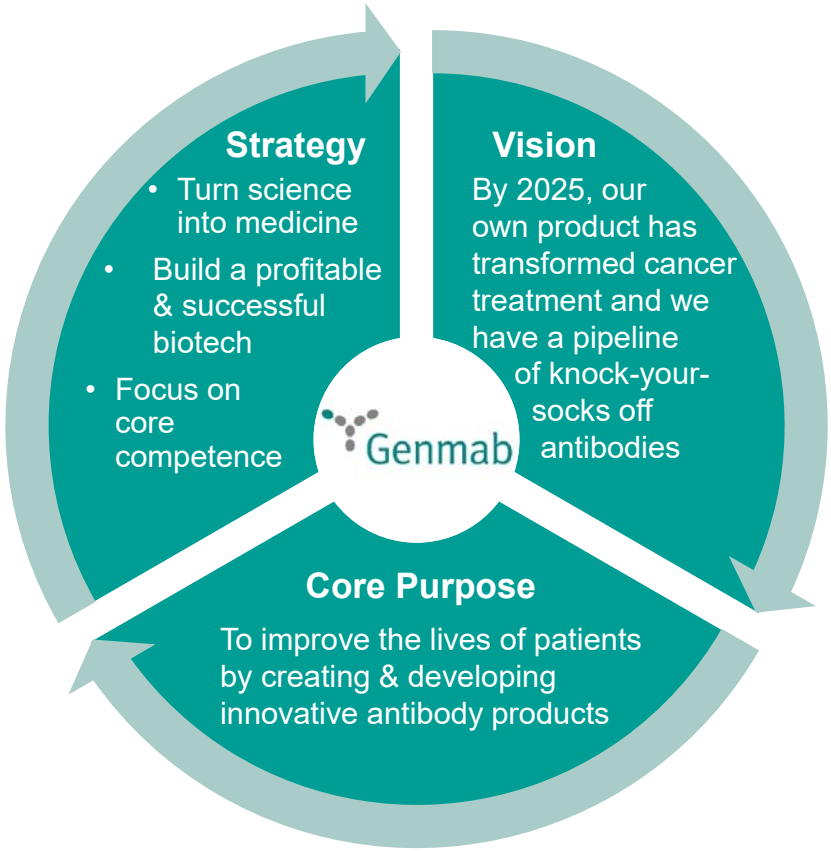
This presentation contains forward looking statements. The words “believe”, “expect”, “anticipate”, “intend” and “plan” and similar expressions identify forward looking statements. All statements other than statements of historical facts included in this presentation, including, without limitation, those 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. 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

| | | |
|---|---|---|
| 20.00 | Welcome & Introduction: Track Record & Growth | Dr. Jan van de Winkel, President & CEO |
| 20.10 | Genmab Preclinical Candidates | Dr. Esther Breij, Sr Director, Translational Research |
| 20.15 | DuoBody-CD3xCD20: Early Data in B-Cell Non-Hodgkin Lymphomas | Dr. Pieternella Lugtenburg, Erasmus University Medical Center Rotterdam |
| 20.25 | Pipeline Q&A | |
| 20:35 | Daratumumab: COLUMBA, GRIFFIN & CANDOR | Dr. Saad Usmani, FACP, University of NC at Chapel Hill, Levine Cancer Institute |
| 20:55 | Daratumumab: ALCYONE, MAIA, POLLUX & CASTOR | Dr. Meletios A. Dimopoulos, National & Kapodistrian University of Athens, School of Medicine |
| 21.10 | Daratumumab Q&A | |
| 21:20 | 2020 & Beyond: Positioned for Success | Dr. Jan van de Winkel |
| 21:25 | General Q&A | |
| 21:30 | Refreshments | |

# Building a Business that Transforms Cancer Treatment

## Our Core Purpose, Strategy & Vision



# Track Record & Growth: 20 Years of Achievement


**6 Years of Profitability & Expanding Top Line**


**Dual-listed in US & DK with 2019 US IPO**


**2 Genmab Created Products on the Market**

**33 Cumulative INDs since 1999**

**18 Genmab Created Products in Ongoing Clinical Trials**

# Track Record & Growth: Differentiated Pipeline

## Foundational Products

- DARZALEX®,[1]
- Arzerra®,[2]
- Ofatumumab[3] [RMS]

## Our Own Clinical Pipeline

- Tisotumab Vedotin[4]
- Enapotamab Vedotin
- HexaBody®-DR5/DR5
- DuoBody®-CD3xCD20
- DuoBody-PD-L1x4-1BB[5]
- DuoBody-CD40x4-1BB[5]
- *2019 IND:* DuoHexaBody®-CD37

## Partner Programs

- 10 product candidates in clinical development w/ partners
- Incl. 6 DuoBody products with Janssen

## Technologies & Pre-Clinical

- DuoBody
- HexaBody
- HexElect®
- DuoHexaBody®
- Rich Pre-Clinical Pipeline

**Solid Financial Base Significant Potential**

**Potential 1st-in-Class/ Best-in-Class**

**Additional Shots on Goal**

**R&D Engine**

[1]In dev. w/ Janssen; [2]with Novartis; [3]In dev. by Novartis; [4]50:50 partnership Seattle Genetics; [5]50:50 partnership BioNTech, GEN1046 & GEN1042 respectively

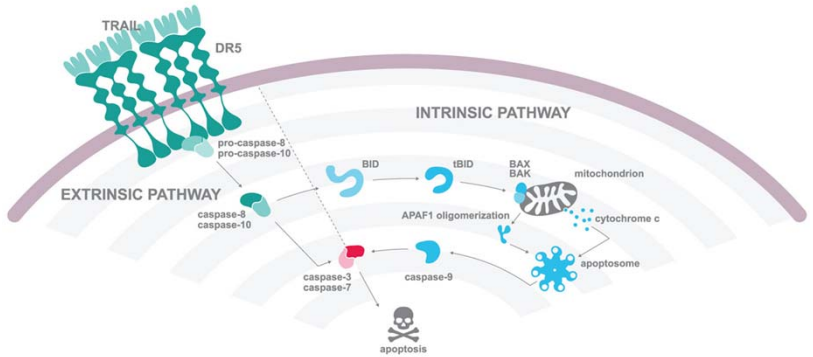
# Track Record & Growth: Genmab's Proprietary* Product Candidates

| Product | Target | Rights | Disease Indications | Most Advanced Development Phase |
|---|---|---|---|---|
| | | | | Pre-Clinical / I / I/II / II / III |
| **Tisotumab vedotin** | TF | 50:50 Genmab / Seattle Genetics | Cervical cancer | I/II |
| | | | Ovarian cancer | I/II |
| | | | Solid tumors | I/II |
| **Enapotamab vedotin (HuMax-AXL-ADC)** | AXL | Genmab | Solid tumors | I |
| **HexaBody-DR5/DR5 (GEN1029)** | DR5 | Genmab | Solid tumors | I |
| **DuoBody-CD3xCD20 (GEN3013)** | CD3, CD20 | Genmab | Hematological malignancies | I |
| **DuoBody-PD-L1x4-1BB (GEN1046)** | PD-L1,4-1BB | 50:50 Genmab / BioNTech | Solid tumors | I |
| **DuoBody-CD40x4-1BB (GEN1042)** | CD40, 4-1BB | 50:50 Genmab / BioNTech | Solid tumors | I |
| **Additional IND in 2019** DuoHexaBody-CD37 (GEN3009) | CD37 | Genmab | Hematological malignancies | Pre-Clinical |

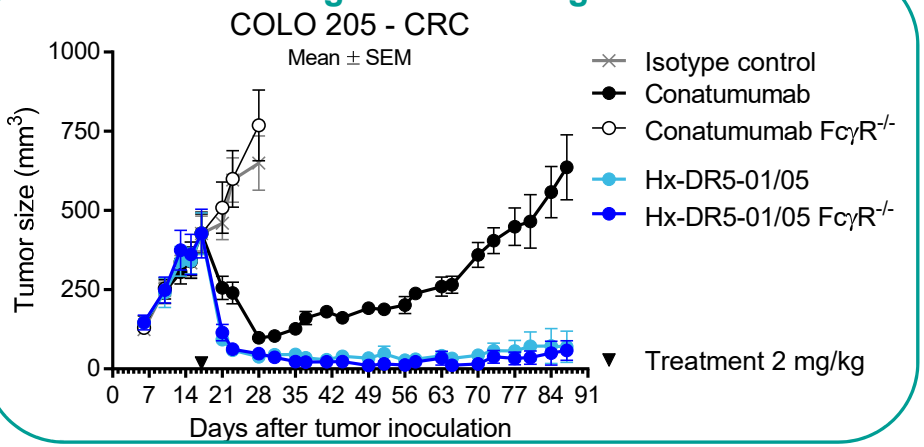
*Certain product candidates in development with partners, as noted.

# Track Record & Growth

## GEN1029 (HexaBody-DR5/DR5) Update: Product Overview




**In vivo xenograft model: Figure 1**




| GEN1029 (HexaBody-DR5/DR5) | |
|---|---|
| **Product description rational** | GEN1029 (HexaBody-DR5/DR5): 1:1 mixture of two non-competing DR5-specific humanized IgG1 antibodies, with a hexamerization-enhancing Fc mutation (HexaBody molecules).<br><br>First HexaBody product in clinical evaluation using clustering potential to improve DR5 targeting.<br><br>Improved antibody-mediated clustering of cell surface receptors, will induce death receptor agonist activity. |
| **Potential indications** | Solid tumors: colorectal, non-small cell lung, triple negative breast, small cell lung, renal clear cell, pancreas and urothelial cancers. |
| **Status** | Phase I First-in-Human dose escalation study [GCT1029-01] ongoing. |
| **Mechanism-of-action** | Anti-tumor activity of HexaBody-DR5/DR5 is independent of FcγR-mediated crosslinking<br><br>In contrast to naked DR5-specific antibody conatumumab (Fig. 1). |

# Track Record & Growth

## GEN1029 (HexaBody-DR5/DR5) Update: GCT1029-01Study Status

**GCT1029-01 trial is a First-in-Human dose escalation study to evaluate safety & recommended phase II dose.**

**Enrollment started in May 2018**

- As of Aug. 2019, 27 patients dosed
- Majority with advanced metastatic colorectal cancer.

**U.S. FDA issued partial clinical hold due to liver toxicity in Aug. 2019, led to temporary recruitment halt**

- Partial clinical hold lifted Oct.18
- After protocol amended with additional provisions to mitigate liver toxicity risk
- Enrollment of patients re-opened

**Next steps**

- Resume enrollment of patients
- Aiming to establish recommended Phase II dose

**High level clinical findings**

- Indication of target-mediated toxicity: transaminase elevation
- Preliminary indication of biological activity:
  - Near complete regression of skin metastasis in CRC patient - stabilization target lesions for almost 1 year
  - 23% tumor shrinkage after single dose in a patient with CRC [discontinued due to AE, LFT elevation]
  - Complete necrosis of primary tumor (biopsy proven) in gastric cancer patient [discontinued due to AE]
  - Partial metabolic response in TNBC patient [+ progressive disease due to new brain lesions]

# Track Record & Growth: Selected Achievements in 2019

## Data

**ASCLEPIOS I&II**
- Ofatumumab[1] in RMS

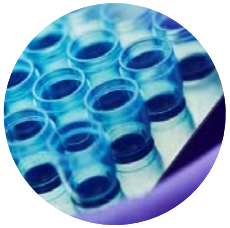
**COLUMBA**
- Subcutaneous daratumumab[2]

**>40 abstracts accepted at ASH**
- GRIFFIN
- CANDOR (Late-Breaking Abstr.)

Teprotumumab[3] Ph III active TED

Enapotamab vedotin at WCLC

**DuoBody-CD3xCD20 (GEN3013) early data at ASH**



## Pipeline

**Tisotumab vedotin[4]**
- Phase I/II innovaTV 206 cervical cancer study in Japan
- Recruitment completed in Ph II innovaTV 204 cervical cancer study

**First pt dosed with DuoBody-PD-L1x4-1BB (GEN1046)[5]**

**First pt dosed with DuoBody-CD40x4-1BB (GEN1042)[5]**

**IND filed for DuoHexaBody-CD37 (GEN3009)**

## Regulatory

**DARZALEX Approvals***
- Split infusion in US & EU
- DRd (MAIA) in US & EU
- DVTd (CASSIOPEIA) in US
- RRMM as mono. in China
- DVMP (ALCYONE) in Japan

**DARZALEX Submissions**
- DVTd (CASSIOPEIA) in EU
- DRd (MAIA) in Japan
- SubQ in US & EU based on COLUMBA & PLEIADES

**Teprotumumab**
- Priority Review received for BLA, active TED

## Corporate & Financial

Conclusion of MorphoSys patent infringement lawsuit

Genmab dual-listed in DK & US

Agreement w/ Janssen for HexaBody-CD38

Agreement w/ BliNK Biomedical

Agreement w/ Tempus

Targeted investment in new capabilities

*See local country prescribing information for precise indications
1. In dev. by Novartis; 2. In dev. w/ Janssen; 3. In dev. w/ Horizon Therapeutics; 4. 50:50 dev. w/ Seattle Genetics; 5. 50:50 dev. w/ BioNTech

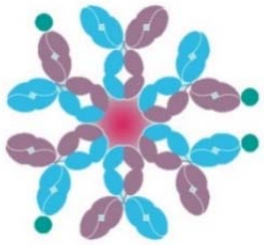
# Genmab Preclinical Candidates

Dr. Esther Breij, Senior Director, Translational Research

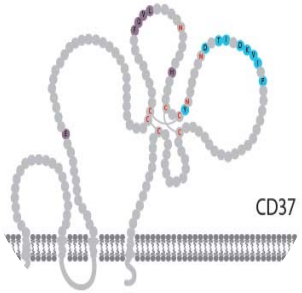
Genmab

# DuoHexaBody-CD37 (GEN3009)

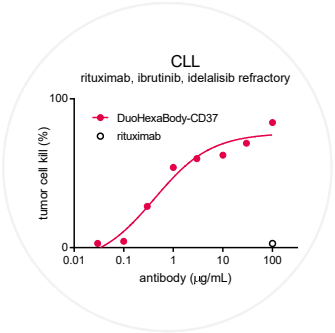
## Next in clinic



Incorporates proprietary DuoBody and HexaBody technologies




Targets two different epitopes on CD37, a target broadly expressed in hematological malignancies




Promising anti-tumor activity in CLL and NHL patient cells *ex vivo*

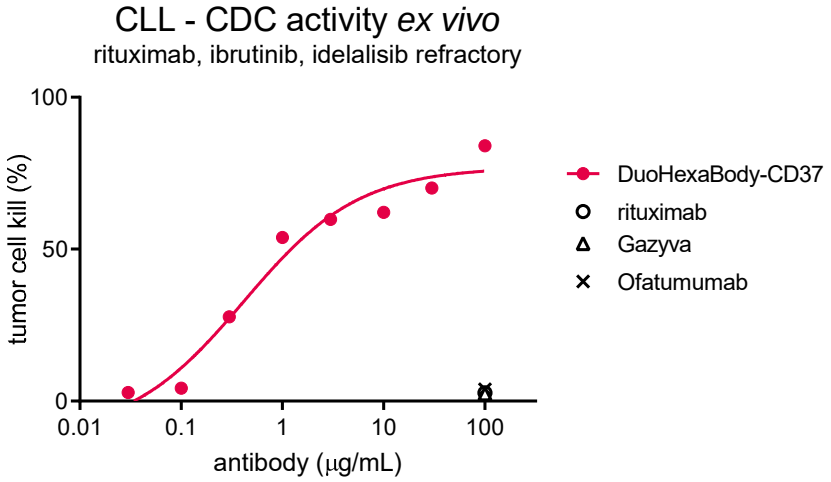
IND Submitted

*Oostindie et al, ASH 2018, Poster 4170; Van der Horst et al, ASH 2018, Poster 4179*

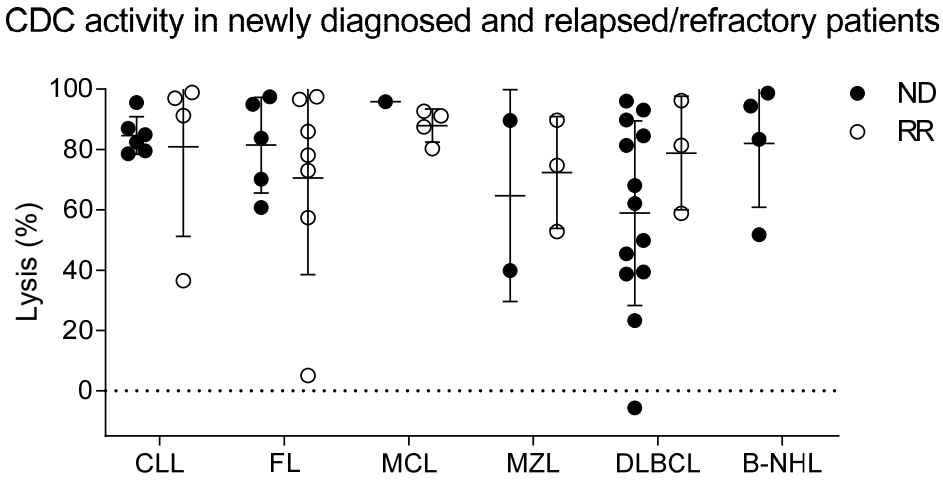
# DuoHexaBody-CD37 (GEN3009)

## Next in clinic

- Excellent preclinical activity in CLL and NHL cells *ex vivo*, irrespective of prior treatment with SoC agents, including CD20 antibodies




*Oostindie et al, ASH 2018, Poster 4170*

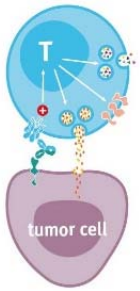



*Van der Horst et al, ASH 2018, Poster 4179*

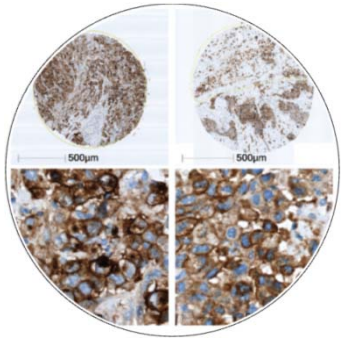
# DuoBody-CD3x5T4 (GEN1044)

## 2020 IND Candidate

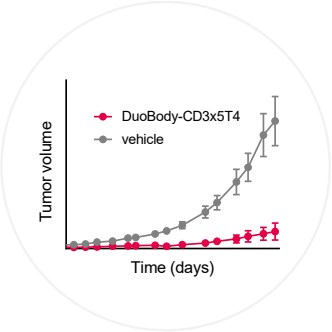
Based on proprietary DuoBody technology




CD3 bispecific, induces T-cell mediated cytotoxicity of 5T4$^{+}$ tumor cells




5T4 is expressed in multiple solid tumors / limited expression in healthy tissue




Potent anti-tumor activity in a diversity of preclinical models

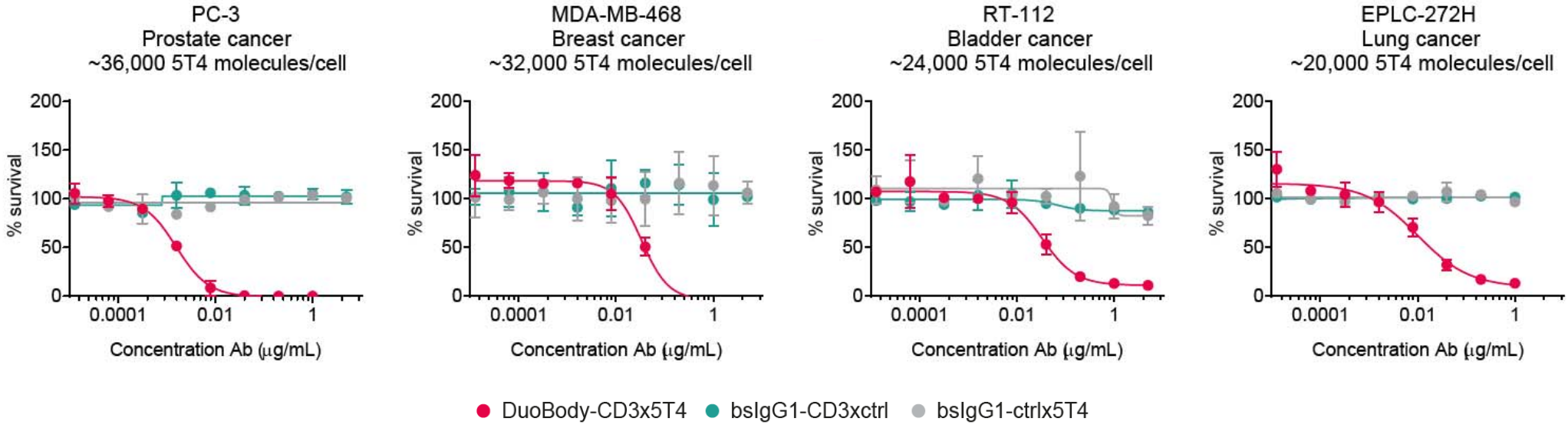
# SITC 2019 Poster 783: DuoBody®-CD3x5T4 shows potent preclinical anti-tumor activity in vitro and in vivo in a range of cancer indications

Kristel Kemper, Ellis Gielen, Laura Smits-de Vries, Sandra Verploegen, Mischa Houtkamp, Saskia M Burm, Edward van den Brink, Rik Rademaker, Dennis Verzijl, Patrick J Engelberts, Bart ECG de Goeij, David Satijn, A Kate Sasser, Esther CW Breij

Genmab, Utrecht, the Netherlands; Copenhagen, Denmark; Princeton, NJ, USA

# DuoBody-CD3x5T4: Preclinical Data

## SITC 2019 Poster 783: Kemper *et al.*



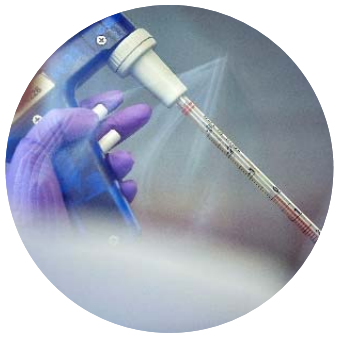

- DuoBody-CD3x5T4 induces T-cell mediated cytotoxicity of cancer cell lines derived from different solid cancers, with a range of 5T4 expression

*Kemper et al, SITC 2019 Poster 783*

# HexaBody-CD38 (GEN3014)

## Expanding the Potential of CD38 Antibodies

Incorporates proprietary HexaBody technology



Highly promising data in preclinical models for MM, lymphoma and leukemia

Could potentially add to and broaden DARZALEX franchise

IND/CTA planned for H2 2020

*Genmab is developing HexaBody-CD38 in an exclusive worldwide license and option agreement with Janssen Biotech, Inc.*

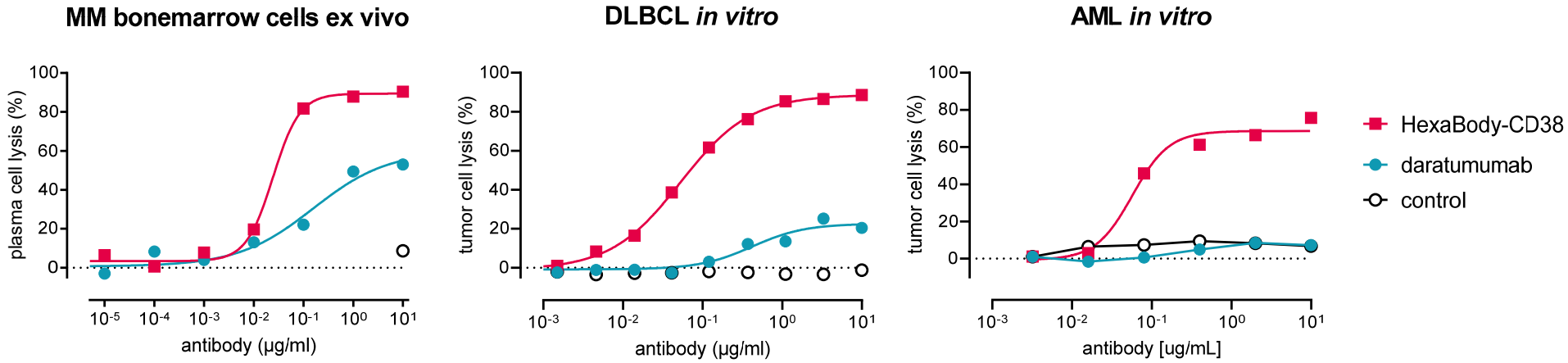
# ASH Poster 3106: HexaBody-CD38, a Novel CD38 Antibody with a Hexamerization Enhancing Mutation, Demonstrates Enhanced Complement-Dependent Cytotoxicity and Shows Potent Anti-Tumor Activity in Preclinical Models of Hematological Malignancies

Bart ECG De Goeij[1], Maarten L Janmaat[1], Grietje Andringa[1], Laurens Kil[1], Berris Van Kessel[1], Kristine A Frerichs[2], Andreas Lingnau[1], Andreas Freidig[1], Tuna Mutis[2], A Kate Sasser[1], Esther CW Breij[1], Niels WCJ Van De Donk[2], Tahamtan Ahmadi[1] and David Satijn[1]

[1]Genmab, Utrecht, Netherlands, Princeton, NJ US
[2]Department of Hematology, Cancer Center Amsterdam, Amsterdam University Medical Center, Vrije Universiteit Amsterdam, The Netherlands

# HexaBody-CD38: Preclinical Data

## ASH 2019 Poster 3106: De Goeij *et al.*




- Superior preclinical activity in MM, DLBCL and AML cells through highly potent CDC
  - Including tumor cells with low expression of CD38 or high expression of complement-regulatory proteins
- More efficient inhibition of cyclase activity compared to daratumumab, possibly leading to more efficient reduction of immune suppression in the tumor microenvironment
- Additional effector mechanisms of HexaBody-CD38 include FcγR-dependent tumor cell kill (ADCC, ADCP and apoptosis)

*De Goeij et al, ASH 2019 Poster 3106*

# DuoBody-CD3xCD20:

# Early Data in B-Cell Non-Hodgkin Lymphomas

Dr. Pieternella Lugtenburg, Erasmus University Medical Center Rotterdam

Genmab

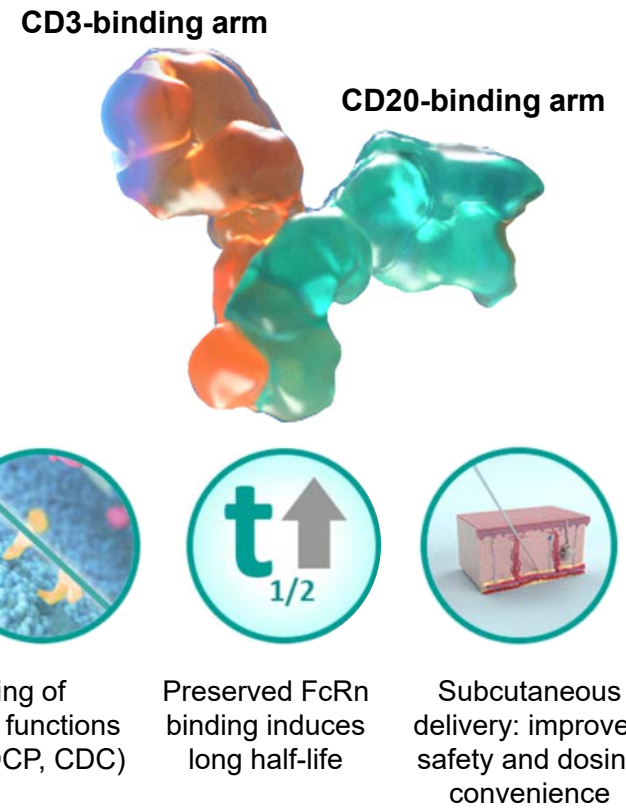
# First-in-Human, Phase 1/2 Trial to Assess the Safety and Clinical Activity of Subcutaneous GEN3013 (DuoBody®-CD3×CD20) in B-Cell Non-Hodgkin Lymphoma

Pieternella Lugtenburg[1,2], Rogier Mous[1,3], Michael Roost Clausen[4], Martine E.D. Chamuleau[1,5], Peter Johnson[6], Kim Linton[7], Simon Rule[8], Roberto S. Oliveri[9], Dena DeMarco[10], Ida H. Hiemstra[11], Guang Chen[10], Ada Azaryan[10], Manish Gupta[10], Tahamtan Ahmadi[10], Martin Hutchings[12]

[1]HOVON Lunenburg Lymphoma Phase I–II Consortium; [2]Erasmus MC Cancer Institute, Rotterdam, Netherlands; [3]Universitair Medisch Centrum Utrecht, Utrecht, Netherlands; [4]Vejle Hospital, Vejle, Denmark; [5]VU University Medical Center, Amsterdam, Netherlands; [6]Cancer Research UK Clinical Centre, Southampton, United Kingdom; [7]Christie Hospital, Manchester, United Kingdom; [8]Plymouth University Medical School, Plymouth, United Kingdom; [9]Genmab, Copenhagen V, Denmark; [10]Genmab, Princeton, NJ; [11]Genmab, Utrecht, Netherlands; [12]Rigshospitalet, Copenhagen, Denmark

# Background: GEN3013 (DuoBody®-CD3×CD20)

- Despite recent advances in the treatment of B-NHL, majority of patients still relapse or become refractory
  - There is an unmet need for novel therapies
  - T-cell redirection therapy has shown promising anti-tumor activity in B-NHL
- GEN3013 is a SC administered, bispecific CD3×CD20 immunotherapy created via Fab-arm exchange using the unique DuoBody® technology platform
  - Retains regular IgG1 antibody structure
  - Long plasma half-life
- Effector function-silenced Fc region ensures:
  - Target-specific T-cell activation
  - No ADCC, ADCP or CDC induction



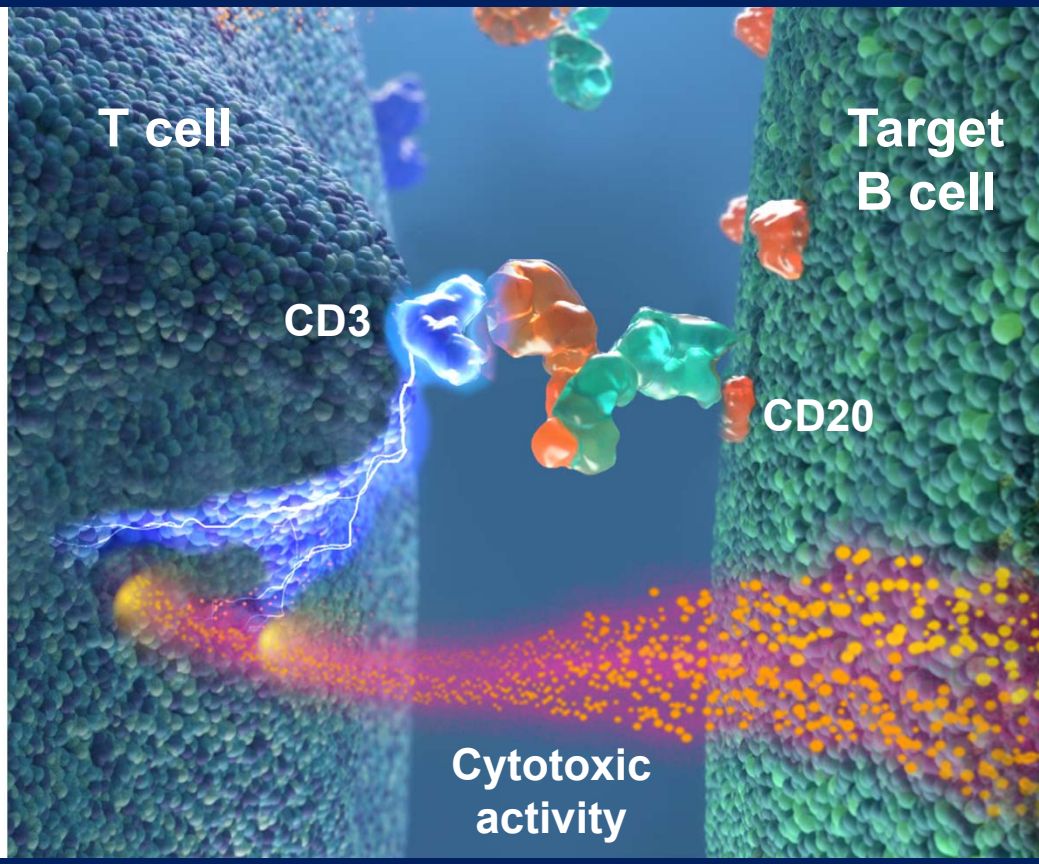

**GEN3013 is a novel subcutaneously administered CD3×CD20 bispecific immunotherapy**

ADCC, antibody-dependent cellular cytotoxicity; ADCP, antibody-dependent cellular phagocytosis; B-NHL, B-cell non-Hodgkin lymphoma; CDC, complement-dependent cytotoxicity.

Chavez et al. Best Prac Res Clin Haematol. 2018;31:135–146; Hiemstra et al. Poster PS1031 presented at EHA 2019; Labrijn et al. PNAS. 2013;110:5145–50; Labrijn et al. Nat Protoc. 2014;9:2450–63; Mohammed et al. J Blood Med. 2019;10:71–84;.

# MOA and Preclinical Data: GEN3013 (DuoBody®-CD3×CD20)

- GEN3013:
  - Promotes T-cell activation and expansion
  - Induces rapid T cell–mediated killing of CD20+ cells, dependent on simultaneous binding of CD3 and CD20
  - Retains activity in presence of CD20 mAbs
- GEN3013 versus three other CD3×CD20 bispecific antibodies showed significantly higher potency at lower doses in vitro*
- SC administration, versus IV, resulted in:**
  - Comparable long-lasting B-cell depletion
    - Potent depletion of CD20-expressing cells from peripheral lymphoid organs
  - Comparable bioavailability
  - Reduced and delayed $C_{max}$ levels
  - Reduced peak cytokine levels in plasma




**Preclinical data with subcutaneous GEN3013 indicate potential for best-in-class therapy**

* Comparator CD3×CD20 bispecific antibodies were produced based on CDR and constant region sequences available from published patent applications and literature: WO2014047231, WO2009018411 (Regeneron); US20170349657 A1, US20140370013 (Xencor); Rodrigues, 1992, US20060034835 A1, US20140242080 A1, US20150166661 (Genentech); ** In cynomolgus monkeys.
Duell et al. Clin Pharmacol Ther. 2019;106:781–791; Hiemstra et al. Poster PS1031 presented at EHA 2019.

# Study Design: Multicenter, Phase 1/2 Trial (NCT03625037)

## Key inclusion criteria

- Adults with relapsed/refractory CD20+ mature B-NHL
- Prior treatment with anti-CD20 mAb
- ECOG PS 0–2
- Measurable disease
- Adequate renal, liver, and hematologic function

## Study objectives

**Primary**

- Maximum tolerated dose (MTD)
- Recommended Phase 2 dose (RP2D)

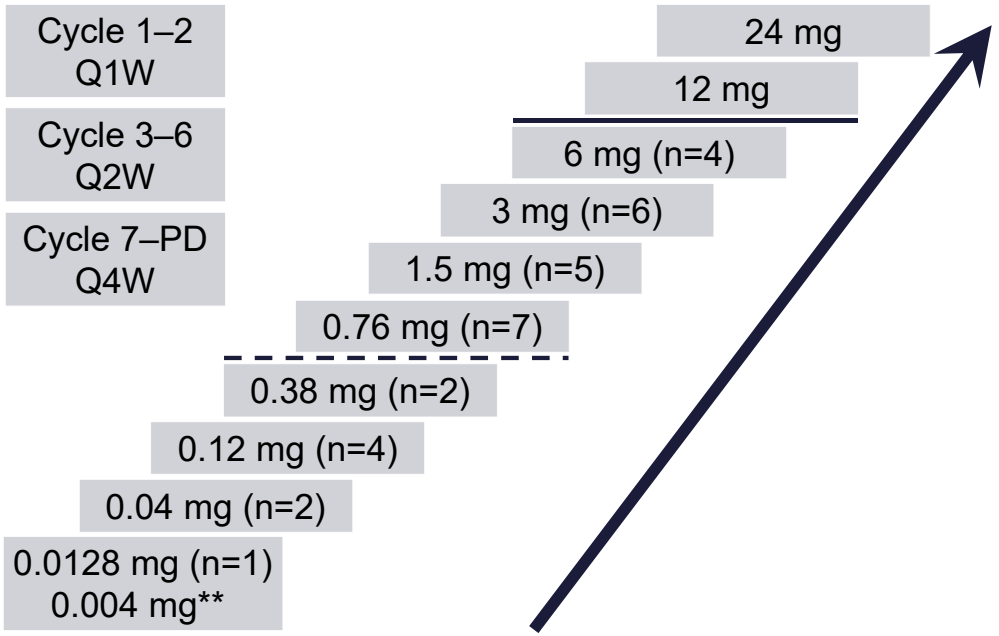
**Secondary**

- Pharmacokinetics/ pharmacodynamics
- Immunogenicity
- Anti-tumor activity

Data cut-offs: 2-DEC-2019 (efficacy), 15-OCT-2019 (safety)
CT or MRI scans: Weeks 8, 16, 24 and every 12 weeks thereafter

## Dose escalation* (ongoing)

GEN3013 subcutaneously administered in 28-day cycles




**Open-label, first-in-human GCT3013-01 study is ongoing; MTD and RP2D not yet determined**

* Modified Bayesian optimal interval design consisting of accelerated and standard titration. Accelerated titration includes single-patient cohorts; up to two patients may be added (at the currently investigated dose) to obtain additional PK/PD biomarker data.
** MABEL. Standard titration contains cohorts of 3 patients. Priming doses/final doses (mg) were as follows: 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, 0.04/0.5/6, 0.04/0.8/12.
Cheson et al. J Clin Oncol 2014;32:3059–67; NCT03625037: https://clinicaltrials.gov/ct2/show/NCT03625037

# Baseline Characteristics: Histology

| | **All patients** (0.004–6 mg) n=31 |
|---|---|
| **Diffuse large B-cell lymphoma (DLBCL)**<br>De novo<br>Transformed | 20 (64.5%)<br>9 (29.0%)<br>11 (35.5%) |
| **Follicular lymphoma (FL)** | 7 (22.6%) |
| **High-grade B-cell lymphoma (HGBCL)** | 2 (6.5%) |
| **Mantle cell lymphoma (blastoid variant)** | 1 (3.2%) |
| **Marginal zone lymphoma** | 1 (3.2%) |

**Majority of patients (74%) had aggressive B-NHL**



Data cut-off: 15-OCT-2019.

# Baseline Characteristics

| | **All patients** (0.004–6 mg) n=31 | **DLBCL/HGBCL** n=22 | **FL** n=7 |
|---|---|---|---|
| **Median age, years (range)** | 65.0 (21–80) | 58.5 (21–80) | 73.0 (35–80) |
| **Male, n (%)** | 23 (74.2%) | 18 (81.8%) | 4 (57.1%) |
| **Median time since diagnosis, months (range)** | 25.0 (6–330) | 17.3 (6–247) | 106.4 (25–330) |
| **Prior lines of therapy, median (range)** | 3.0 (1–18) | 3.0 (1–6) | 5.0 (2–18) |
| **Prior therapies** | | | |
| Anti-CD20 mAb | 31 (100%) | 22 (100%) | 7 (100%) |
| Anthracyclines | 27 (87.1%) | 21 (95.5%) | 5 (71.4%) |
| Alkylating agents | 31 (100%) | 22 (100%) | 7 (100%) |
| Autologous stem cell transplantation* | 5 (16.1%) | 4 (18.2%) | 1 (14.3%) |
| **Refractory to, n (%)** | | | |
| Most recent systemic therapy | 23 (74.2%) | 18 (81.8%) | 3 (42.9%) |
| Most recent anti-CD20 mAb (any line) | 23 (74.2%) | 17 (77.3%) | 4 (57.1%) |
| Most recent anti-CD20 mAb (last line) | 20 (64.5%) | 15 (68.2%) | 3 (42.9%) |
| Alkylating agents | 22 (71.0%) | 17 (77.3%) | 3 (42.9%) |

**Patients were heavily pre-treated; majority of patients were refractory to anti-CD20 therapy**

* Following high-dose chemotherapy.
Data cut-off: 15-OCT-2019.

# Patient Disposition and Exposure

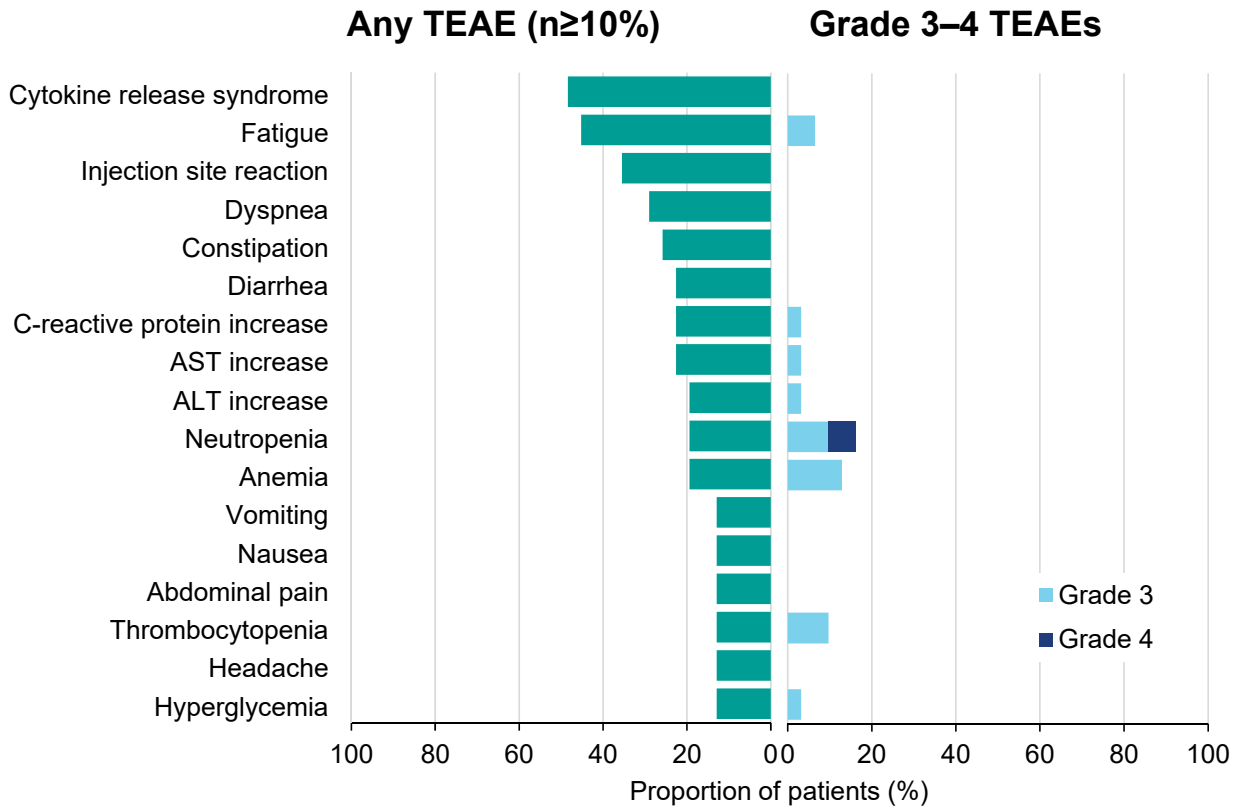
| | **≥0.76 mg** (0.76–6 mg) n=22 | **All doses** (0.004–6 mg) n=31 |
|---|---|---|
| **Median duration of follow-up, weeks (range)** | 7.8 (0–26.1) | 10.9 (0–43.5) |
| **Treatment ongoing, n (%)** | 11 (50.0%) | 11 (35.5%) |
| **Treatment discontinued, n (%)** | | |
| Due to disease progression | 11 (50.0%) | 20 (64.5%) |
| **Number of GEN3013 dose administrations, median (range)** | 5.5 (1–14) | 6.0 (1–16) |
| **Median duration of exposure, days (range)** | 43 (7–127) | 43 (7–171) |

**Treatment is still ongoing in 11 patients; treatment discontinuations were due to disease progression only**



Data cut-off: 15-OCT-2019.

# Treatment-Emergent Adverse Events




| | **≥0.76 mg** (0.76–6 mg) n=22 | **All doses** (0.004–6 mg) n=31 |
|---|---|---|
| Any treatment-emergent AE, n (%) | 22 (100%) | 31 (100%) |
| Serious treatment-emergent AEs, excluding disease progression, n (%) | 9 (41%) | 11 (35%) |
| Grade 3–4 treatment-emergent AEs, n (%) | 14 (63.6%) | 21 (67.7%) |

- No patients experienced febrile neutropenia
- Injection site reactions were Grade 1 only; resolved without intervention in all cases prior to next injection

**The majority of treatment-emergent AEs were Grade 1–2; no DLTs were observed**

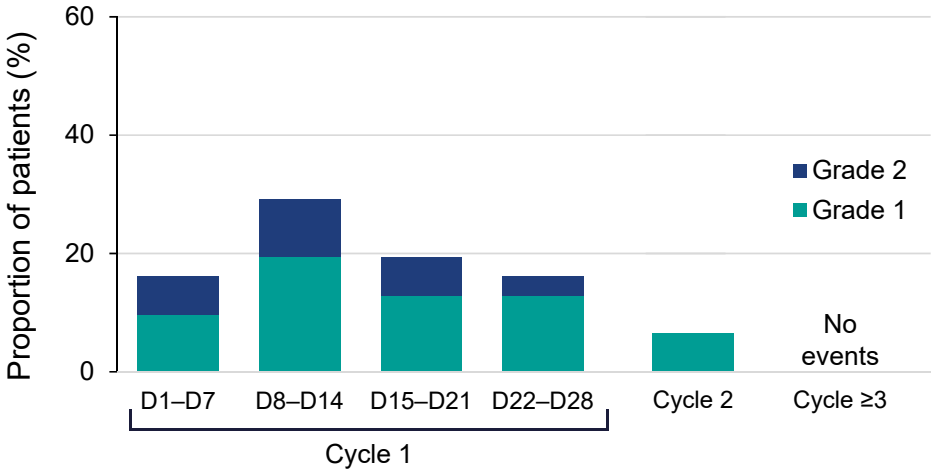


Data cut-off: 15-OCT-2019.

# Treatment-Emergent Adverse Events of Special Interest

| | **≥0.76 mg** (0.76–6 mg) n=22 | **All doses** (0.004–6 mg) n=31 |
|---|---|---|
| **Tumor lysis syndrome** | 0 (0%) | 0 (0%) |
| **Neurological symptoms (change in CARTOX-10 score)** | 0 (0%) | 0 (0%) |
| **Cytokine release syndrome**<br>Grade 1<br>Grade 2<br>Grade ≥3 | 12 (54.5%)<br>8 (36.4%)<br>4 (18.2%)<br>0 (0%) | 15 (48.4%)<br>9 (29.0%)<br>6 (19.4%)<br>0 (0%) |
| **Symptoms of cytokine release syndrome (n≥5%)** | | |
| Pyrexia | 12 | 15 |
| Chills | 2 | 2 |
| Hypotension | 4 | 6 |
| Tachycardia | 3 | 5 |
| Dyspnea | 2 | 2 |
| Hypoxia | 2 | 2 |

- Majority of CRS events occurred in Cycle 1
- 3 patients received treatment with tocilizumab
- Risk of CRS was mitigated with the use of a priming dose and premedication with corticosteroids, antihistamines and antipyretics




**All CRS events were mild or moderate (Grade 1–2); 100% of CRS events resolved; no tumor lysis syndrome or neurological symptoms**



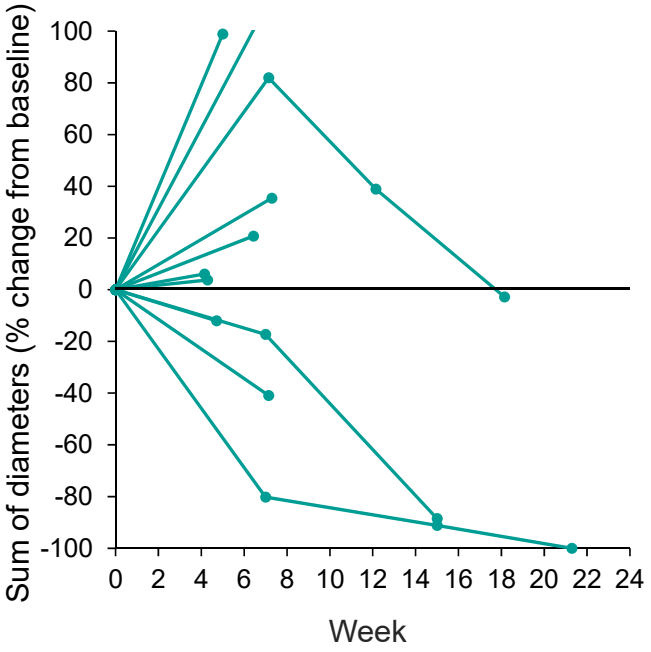
Data cut-off: 15-OCT-2019.

# Efficacy of GEN3013 ≥0.76 mg in R/R B-NHL

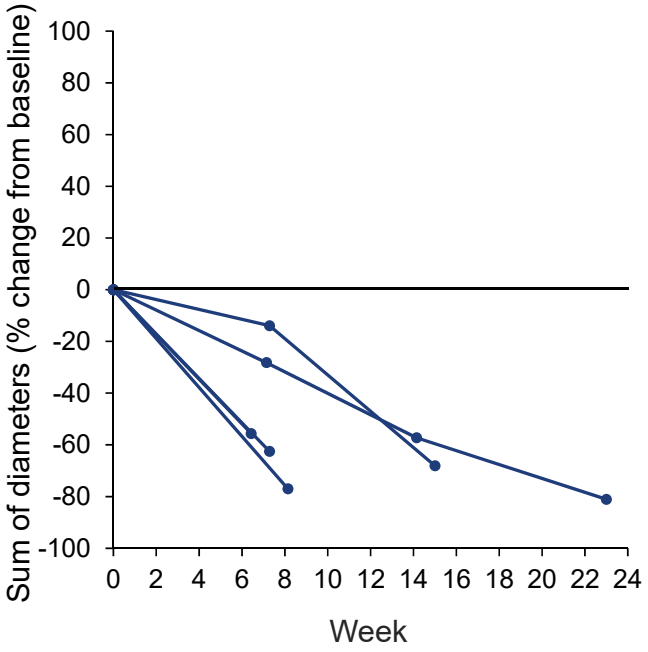
| | ≥0.76 mg |
|---|---|
| **Total patients** | 22 |
| DLBCL/HGBCL | 14 |
| FL | 6 |
| Other B-NHL | 2 |
| **Evaluable patients*** | 19 |
| DLBCL/HGBCL | 13 |
| FL | 5 |
| Other B-NHL | 1 |
| **ORR, n (%)** | 7 (36.8%) |
| CR | 1 (5.3%) |
| PR | 6 (31.6%) |
| SD | 4 (21.1%) |
| PD | 8 (42.1%) |

- One additional patient with DLBCL achieved CR following treatment with GEN3013 0.120 mg

**DLBCL/HGBCL****
2 of 13 evaluable patients achieved a response



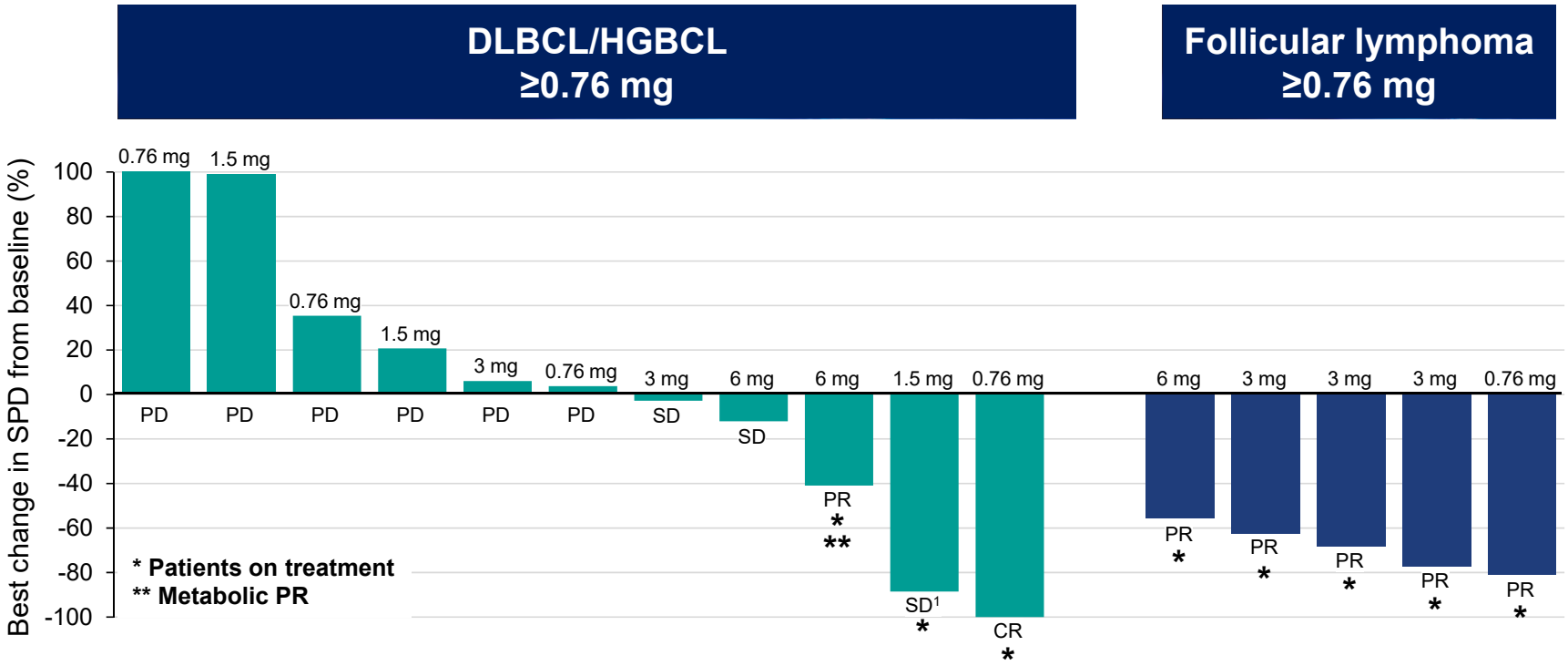

**Follicular lymphoma**
5 of 5 evaluable patients achieved a response




**GEN3013 administered subcutaneously demonstrated anti-tumor activity during dose escalation**

* 3 patients did not have a follow-up; majority of results based on CT scan.
** 2 patients who achieved PD not shown in graph due to not having SPD entry at time of data cut-off.
Data cut-off: 2-DEC-2019.

# Anti-Tumor Activity

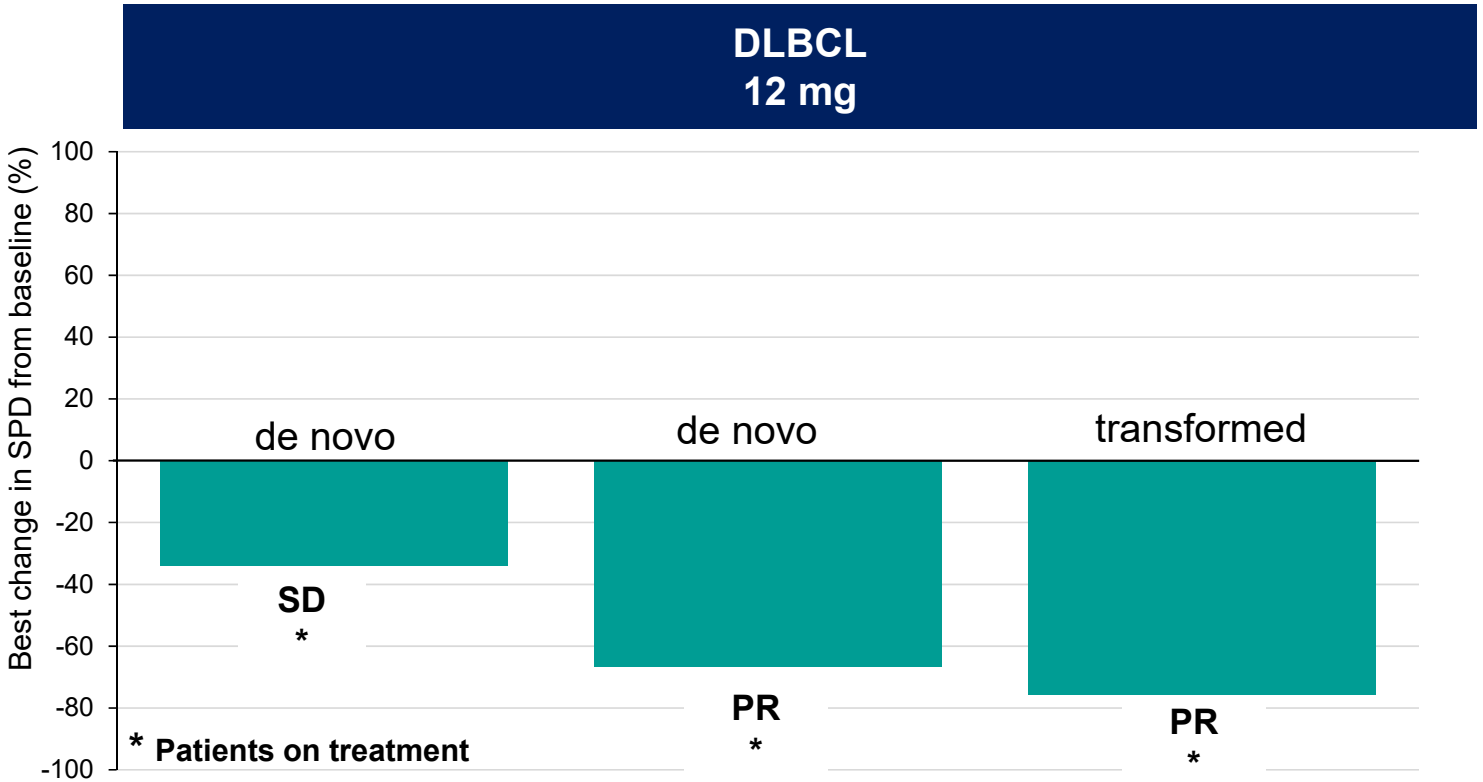



**Highly encouraging clinical activity observed across aggressive and indolent NHL subtypes at low dose levels**

[1] Patient developed new lesions at second responses assessment.
2 patients who achieved PD not shown in DLBCL/HGBCL graph due to not having SPD entry at time of data cut-off. 1 additional patient with DLBCL achieved CR following treatment with GEN3013 0.120 mg.
Data cut-off: 2-DEC-2019.

New Data

# Dose Escalation (12 mg) in 3/3 Evaluable Patients with DLBCL




**Greater DLBCL clinical activity seen with higher doses, consistent with pharmacokinetic modeling**



*

# Summary and Conclusions

- GEN3013 is a SC administered, bispecific CD3×CD20 immunotherapy under development for the treatment of B-NHL
- Preclinical data indicate potential for best-in-class therapy
- The SC administration may offer advantages, such as slow absorption and lower $C_{max}$, reducing the risk of high-grade CRS events, efficient delivery of GEN3013 to lymph nodes, and convenience for patients
- Dose escalation of GEN3013 resulted in no apparent increase in toxicities:
  - Most AEs were mild to moderate, transient, and reversible
  - No DLTs were observed; MTD has not been reached
  - No Grade ≥3 CRS events were observed
  - No tumor lysis syndrome or CRS-related neurological toxicities (based on CARTOX-10) have been observed
- Highly encouraging anti-tumor activity observed across aggressive and indolent NHL subtypes at low dose levels
  - PR or better response seen in 5/5 (100%) patients with FL receiving GEN3013 ≥0.76 mg and 3/5 (60%) patients with DLBCL receiving GEN3013 ≥6 mg
- In conclusion, GEN3013 has shown promising early clinical activity at low doses in a heavily pretreated patient population

**Further dose escalation of subcutaneous GEN3013 is ongoing;***
**new clinical studies will be initiated once RP2D is established**



* NCT03625037: https://clinicaltrials.gov/ct2/show/NCT03625037

# Pipeline Q&A

# Daratumumab Data:

# Phase III COLUMBA Update & Body Weight Subgroup Analysis

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

Genmab

# Poster 1865: Randomized, Open-label, Non-inferiority, Phase 3 Study of Subcutaneous (SC) Versus Intravenous (IV) Daratumumab (DARA) Administration in Patients with Relapsed or Refractory Multiple Myeloma: COLUMBA Update

Saad Z. Usmani,[1,*] Maria-Victoria Mateos,[2] Hareth Nahi,[3] Sebastian Grosicki,[4] Vladimir Vorobyev,[5] Ivan Spicka,[6] Vania Hungria,[7] Sibirina Korenkova,[8] Max Flogegard,[9] Joan Blade,[10] Philippe Moreau,[11] Martin Kaiser,[12] Shinsuke Iida,[13] Jacob Laubach,[14] Tara Masterson,[15] Kristen Lantz,[15] Lisa O'Rourke,[15] Christoph Heuck,[15] Xiang Qin,[16] Dolly A. Parasrampuria,[15] Ming Qi,[15] Nizar Bahlis[17]

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# Poster 1865: Randomized, Open-label, Non-inferiority, Phase 3 Study of Subcutaneous (SC) Versus Intravenous (IV) Daratumumab (DARA) Administration in Patients with Relapsed or Refractory Multiple Myeloma: COLUMBA Update

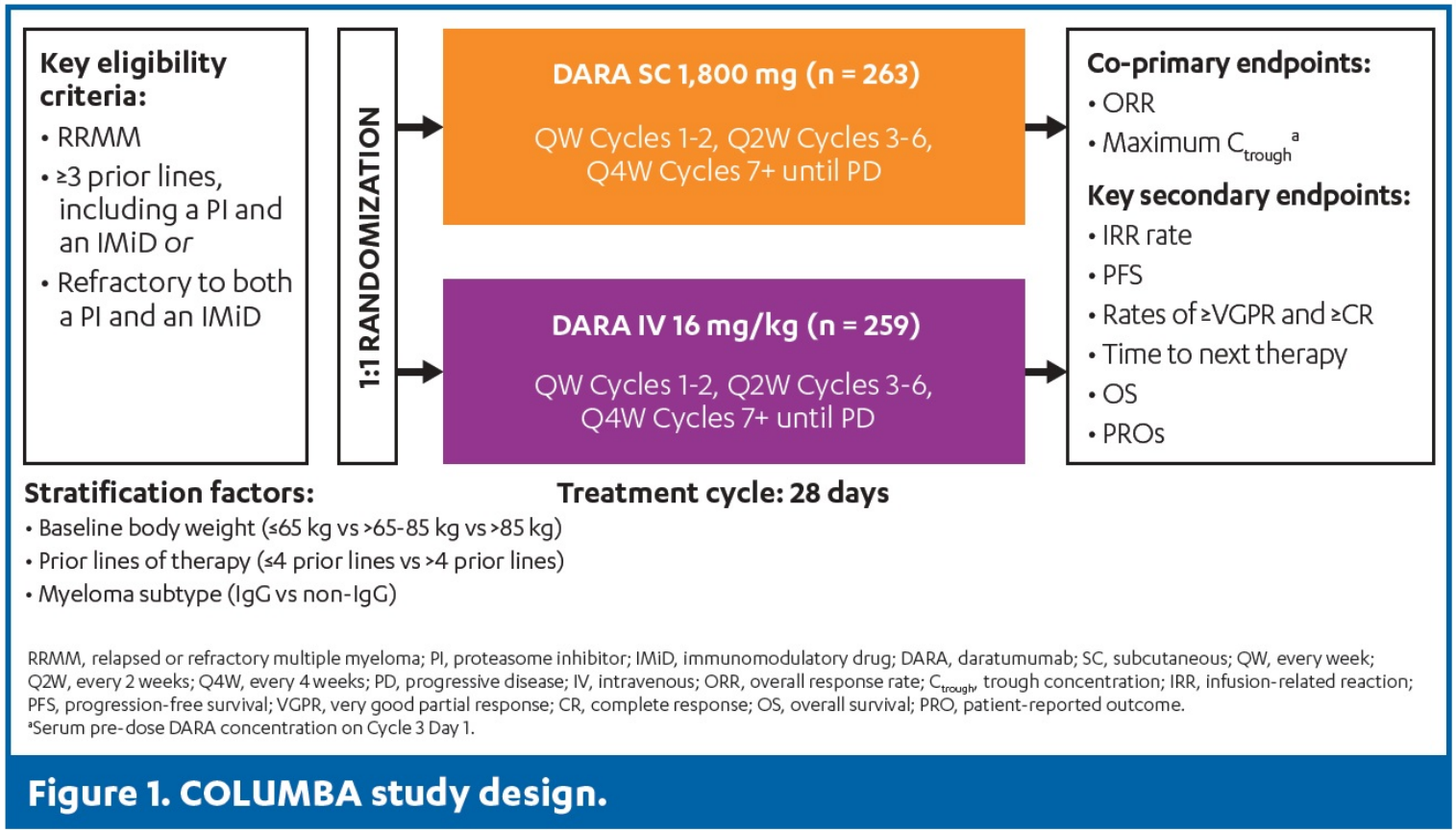



**Figure 1. COLUMBA study design.**



*Usmani et al, ASH 2019 Poster 1865*

# Poster 1865: Randomized, Open-label, Non-inferiority, Phase 3 Study of Subcutaneous (SC) Versus Intravenous (IV) Daratumumab (DARA) Administration in Patients with Relapsed or Refractory Multiple Myeloma: COLUMBA Update

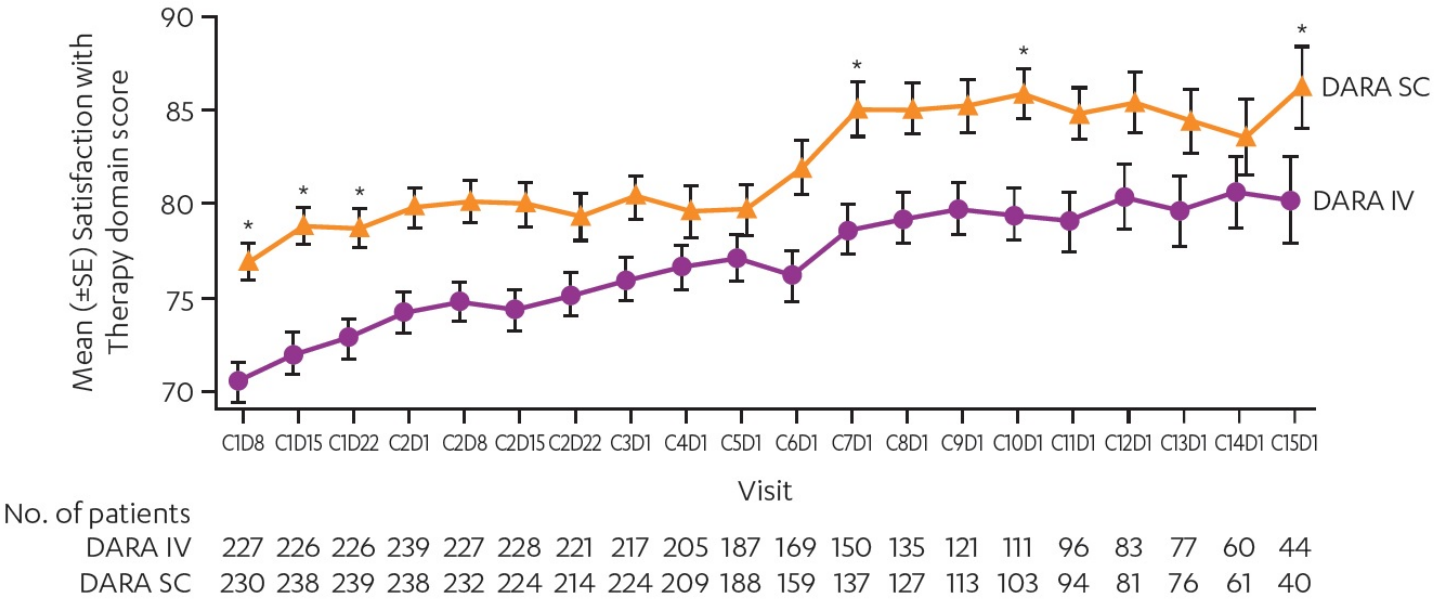
**Table 2. Most Common Any-grade (>10%) and Grade 3/4 (>5%) TEAEs[a]**

| | DARA IV (n = 258) | | DARA SC (n = 260) | |
|---|---|---|---|---|
| TEAE, n (%) | Any grade | Grade 3/4 | Any grade | Grade 3/4 |
| Hematologic | | | | |
| Anemia | 64 (25) | 38 (15) | 71 (27) | 36 (14) |
| Thrombocytopenia | 49 (19) | 35 (14) | 51 (20) | 36 (14) |
| Neutropenia | 35 (14) | 20 (8) | 51 (20) | 34 (13) |
| Lymphopenia | 17 (7) | 16 (6) | 20 (8) | 14 (5) |
| Nonhematologic | | | | |
| Pyrexia | 36 (14) | 2 (1) | 37 (14) | 1 (<1) |
| Back pain | 36 (14) | 7 (3) | 28 (11) | 5 (2) |
| Cough | 35 (14) | 0 (0) | 25 (10) | 2 (1) |
| Diarrhea | 31 (12) | 1 (<1) | 40 (15) | 2 (1) |
| Nausea | 30 (12) | 2 (1) | 24 (9) | 0 (0) |
| Chills | 32 (12) | 2 (1) | 15 (6) | 1 (<1) |
| Upper respiratory tract infection | 29 (11) | 2 (1) | 41 (16) | 0 (0) |
| Fatigue | 29 (11) | 3 (1) | 31 (12) | 2 (1) |
| Dyspnea | 28 (11) | 2 (1) | 14 (5) | 2 (1) |
| Hypertension | 23 (9) | 15 (6) | 15 (6) | 11 (4) |
| Arthralgia | 18 (7) | 0 (0) | 28 (11) | 1 (<1) |

TEAE, treatment-emergent adverse event; DARA, daratumumab; IV, intravenous; SC, subcutaneous.
[a]Safety population, defined as randomized patients who received ≥1 dose of DARA.

*Usmani et al, ASH 2019 Poster 1865*

# Poster 1865: Randomized, Open-label, Non-inferiority, Phase 3 Study of Subcutaneous (SC) Versus Intravenous (IV) Daratumumab (DARA) Administration in Patients with Relapsed or Refractory Multiple Myeloma: COLUMBA Update




CTSQ, Cancer Therapy Satisfaction Questionnaire; SE, standard error; DARA, daratumumab; SC, subcutaneous; IV, intravenous; C, Cycle; D, Day; ITT, intent-to-treat.
[a]ITT population, defined as all randomized patients.
[b]Paper administration. For the modified CTSQ, the Satisfaction with Therapy domain score was calculated on a scale of 0 to 100; a higher score is a more positive indicator.
*Meaningful difference ≥5.9.[21]

**Figure 7. Modified CTSQ.[a,b]**



*Usmani et al, ASH 2019 Poster 1865*

# Poster 1865: Randomized, Open-label, Non-inferiority, Phase 3 Study of Subcutaneous (SC) Versus Intravenous (IV) Daratumumab (DARA) Administration in Patients with Relapsed or Refractory Multiple Myeloma: COLUMBA Update

## CONCLUSIONS

- With longer follow-up, responses with DARA SC monotherapy deepened and remained similar to DARA IV monotherapy
  - PFS and OS were comparable between patients treated with DARA SC and DARA IV
- DARA SC maintained noninferiority to DARA IV in terms of the co-primary endpoints evaluating ORR and PK (maximum $C_{trough}$)
- DARA SC has a similar safety profile compared to DARA IV, with a statistically significant reduction in IRR rates and a low incidence of injection-site reactions
- DARA SC has reduced treatment burden and is associated with a considerably shorter median administration duration (5 minutes)
  - DARA SC patients continue to report higher satisfaction with treatment than DARA IV patients
- These results demonstrate a favorable benefit/risk profile for DARA SC 1,800 mg flat dose

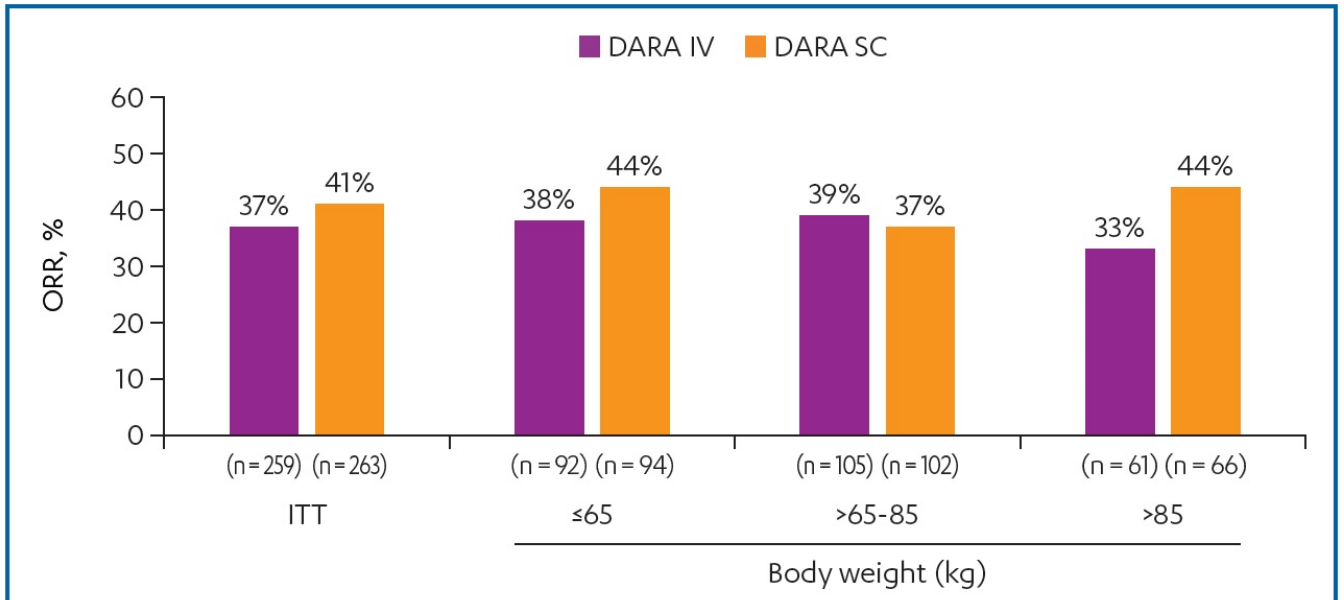
*Usmani et al, ASH 2019 Poster 1865*

# Poster 1906: Randomized, Open-label, Non-inferiority, Phase 3 Study of Subcutaneous (SC) Versus Intravenous (IV) Daratumumab (DARA) Administration in Patients (Pts) with Relapsed or Refractory Multiple Myeloma (RRMM): Body Weight Subgroup Analysis of COLUMBA

Maria-Victoria Mateos,[1,*] Saad Z. Usmani,[2] Sebastian Grosicki,[3] Vladimir Vorobyev,[4] Ivan Spicka,[5] Vania Hungria,[6] Sibirina Korenkova,[7] Nizar Bahlis,[8] Max Flogegard,[9] Joan Blade,[10] Philippe Moreau,[11] Martin Kaiser,[12] Shinsuke Iida,[13] Jacob Laubach,[14] Tara Masterson,[15] Kristen Lantz,[15] Lisa O'Rourke,[15] Xiang Qin,[16] Dolly A. Parasrampuria,[15] Christoph Heuck,[15] Ming Qi,[15] Hareth Nahi[17]

[1]University Hospital of Salamanca/IBSAL, Salamanca, Spain; [2]Levine Cancer Institute/Atrium Health, Charlotte, NC, USA; [3]Department of Hematology and Cancer Prevention, School of Public Health, Silesian Medical University, Katowice, Poland; [4]S. P. Botkin City Clinical Hospital, Moscow, Russian Federation; [5]General Faculty Hospital, Prague, Czech Republic; [6]Santa Casa Medical School, São Paulo, Brazil;[7]Kiev Center for Bone Marrow Transplantation, Kiev, Ukraine; [8]Arnie Charbonneau Cancer Institute, University of Calgary, Calgary, AB, Canada; [9]Department of Internal Medicine, Falun General Hospital, Falun, Sweden; [10]IDIBAPS, Hospital Clinic de Barcelona, Barcelona, Spain; [11]University Hospital of Nantes, Nantes, France; [12]Division of Molecular Pathology, Institute of Cancer Research, Sutton, UK;[13]Department of Hematology and Oncology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan; [14]Department of Hematology and Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; [15]Janssen Research & Development, LLC, Spring House, PA, USA; [16]Janssen Research & Development, LLC, Raritan, NJ, USA;[17]Karolinska Institute, Department of Medicine, Division of Hematology, Karolinska University Hospital at Huddinge, Stockholm, Sweden

# Poster 1906: Randomized, Open-label, Non-inferiority, Phase 3 Study of Subcutaneous (SC) Versus Intravenous (IV) Daratumumab (DARA) Administration in Patients (Pts) with Relapsed or Refractory Multiple Myeloma (RRMM): Body Weight Subgroup Analysis of COLUMBA




ORR, overall response rate; ITT, intent-to-treat; DARA, daratumumab; IV, intravenous; SC, subcutaneous.
[a]ITT population, defined as all randomized patients.

**Figure 2. ORRs in the ITT population[a] and across body weight subgroups.**

ORRs in the DARA SC and DARA IV body weight subgroups were consistent with the ITT population



*Mateos et al, ASH 2019 Poster 1906*

# Poster 1906: Randomized, Open-label, Non-inferiority, Phase 3 Study of Subcutaneous (SC) Versus Intravenous (IV) Daratumumab (DARA) Administration in Patients (Pts) with Relapsed or Refractory Multiple Myeloma (RRMM): Body Weight Subgroup Analysis of COLUMBA

**Table 2. Summary of TEAEs Across Body Weight Subgroups**

| | DARA IV | | | DARA SC | | |
|---|---|---|---|---|---|---|
| | ≤65 kg (n = 92) | >65-85 kg (n = 105) | >85 kg (n = 61) | ≤65 kg (n = 93) | >65-85 kg (n = 102) | >85 kg (n = 65) |
| Any-grade TEAEs, n (%) | 82 (89) | 94 (90) | 54 (89) | 88 (95) | 89 (87) | 51 (79) |
| Infections | 41 (45) | 43 (41) | 33 (54) | 45 (48) | 44 (43) | 30 (46) |
| Patients receiving growth factor, n (%) | 15 (16) | 11 (11) | 3 (5) | 13 (14) | 8 (8) | 6 (9) |
| Grade 3/4 TEAEs, n (%) | 47 (51) | 51 (49) | 28 (46) | 46 (50) | 46 (45) | 26 (40) |
| Most common (≥5%) | | | | | | |
| Anemia | 14 (15) | 15 (14) | 7 (12) | 13 (14) | 14 (14) | 7 (11) |
| Thrombocytopenia | 12 (13) | 14 (13) | 9 (15) | 15 (16) | 15 (15) | 6 (9) |
| Neutropenia | 8 (9) | 9 (9) | 3 (5) | 19 (20) | 10 (10) | 5 (8) |
| Lymphopenia | 6 (7) | 7 (7) | 3 (5) | 8 (9) | 3 (3) | 2 (3) |
| Pneumonia | 5 (5) | 3 (3) | 2 (3) | 4 (4) | 1 (1) | 2 (3) |
| Hypertension | 4 (4) | 6 (6) | 6 (10) | 2 (2) | 3 (3) | 3 (5) |
| Leukopenia | 1 (1) | 0 (0) | 1 (2) | 6 (7) | 1 (1) | 3 (5) |
| Grade 5 TEAEs, n (%) | 6 (7) | 8 (8) | 3 (5) | 6 (7) | 6 (6) | 2 (3) |
| Serious TEAEs, n (%) | 28 (30) | 33 (31) | 15 (25) | 22 (24) | 29 (28) | 17 (26) |
| TEAEs leading to treatment discontinuation, n (%) | 6 (7) | 9 (9) | 6 (10) | 8 (9) | 8 (8) | 2 (3) |
| Any-grade IRRs, n (%) | 27 (29) | 38 (36) | 24 (39) | 13 (14) | 13 (13) | 7 (11) |

TEAE, treatment-emergent adverse event; DARA, daratumumab; IV, intravenous; SC, subcutaneous; IRR, infusion-related reaction.

*Mateos et al, ASH 2019 Poster 1906*

# Poster 1906: Randomized, Open-label, Non-inferiority, Phase 3 Study of Subcutaneous (SC) Versus Intravenous (IV) Daratumumab (DARA) Administration in Patients (Pts) with Relapsed or Refractory Multiple Myeloma (RRMM): Body Weight Subgroup Analysis of COLUMBA

## CONCLUSIONS

- In the primary analysis of COLUMBA, DARA SC was noninferior to DARA IV in terms of the efficacy and PK co-primary endpoints[17]
  - DARA SC had a similar safety profile to DARA IV and was associated with a significant reduction in IRR rates and a considerably shorter administration duration
  - Please see Poster #1865 for an update on efficacy and safety in the overall COLUMBA population after longer follow-up
- In this subgroup analysis, ORRs in all body weight subgroups were consistent with the overall study population for the respective treatment groups, and ORRs were similar across body weight groups for DARA SC versus DARA IV
- DARA SC achieved adequate exposure consistent with DARA IV and was well tolerated across all body weight subgroups
  - The higher concentration of DARA SC in patients ≤65 kg did not have a clinically relevant effect on safety
- Overall, these results suggest that no dose individualization of DARA SC is necessary on the basis of body weight

*Mateos et al, ASH 2019 Poster 1906*

# Daratumumab Data:

# Phase II GRIFFIN Update

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

Genmab

# Depth of Response to Daratumumab (DARA), Lenalidomide, Bortezomib, and Dexamethasone (RVd) Improves Over Time in Patients (pts) With Transplant-eligible Newly Diagnosed Multiple Myeloma (NDMM): GRIFFIN Study Update*

**Peter M. Voorhees,[1]** Jonathan L. Kaufman,[2] Jacob Laubach,[3] Douglas W. Sborov,[4] Brandi Reeves,[5] Cesar Rodriguez,[6] Ajai Chari,[7] Rebecca Silbermann,[8] Luciano J. Costa,[9] Larry D. Anderson, Jr,[10] Nitya Nathwani,[11] Nina Shah,[12] Yvonne A. Efebera,[13] Caitlin Costello,[14] Andrzej Jakubowiak,[15] Tanya M. Wildes,[16] Robert Z. Orlowski,[17] Kenneth H. Shain,[18] Andrew J. Cowan,[19] Sean Murphy,[20] Yana Lutska,[20] Huiling Pei,[21] Jon Ukropec,[22] Jessica Vermeulen,[23] Carla de Boer,[23] Daniela Hoehn,[20] Thomas S. Lin,[20] Paul G. Richardson[3]

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*ClinicalTrials.gov Identifier: NCT02195479.

# Introduction

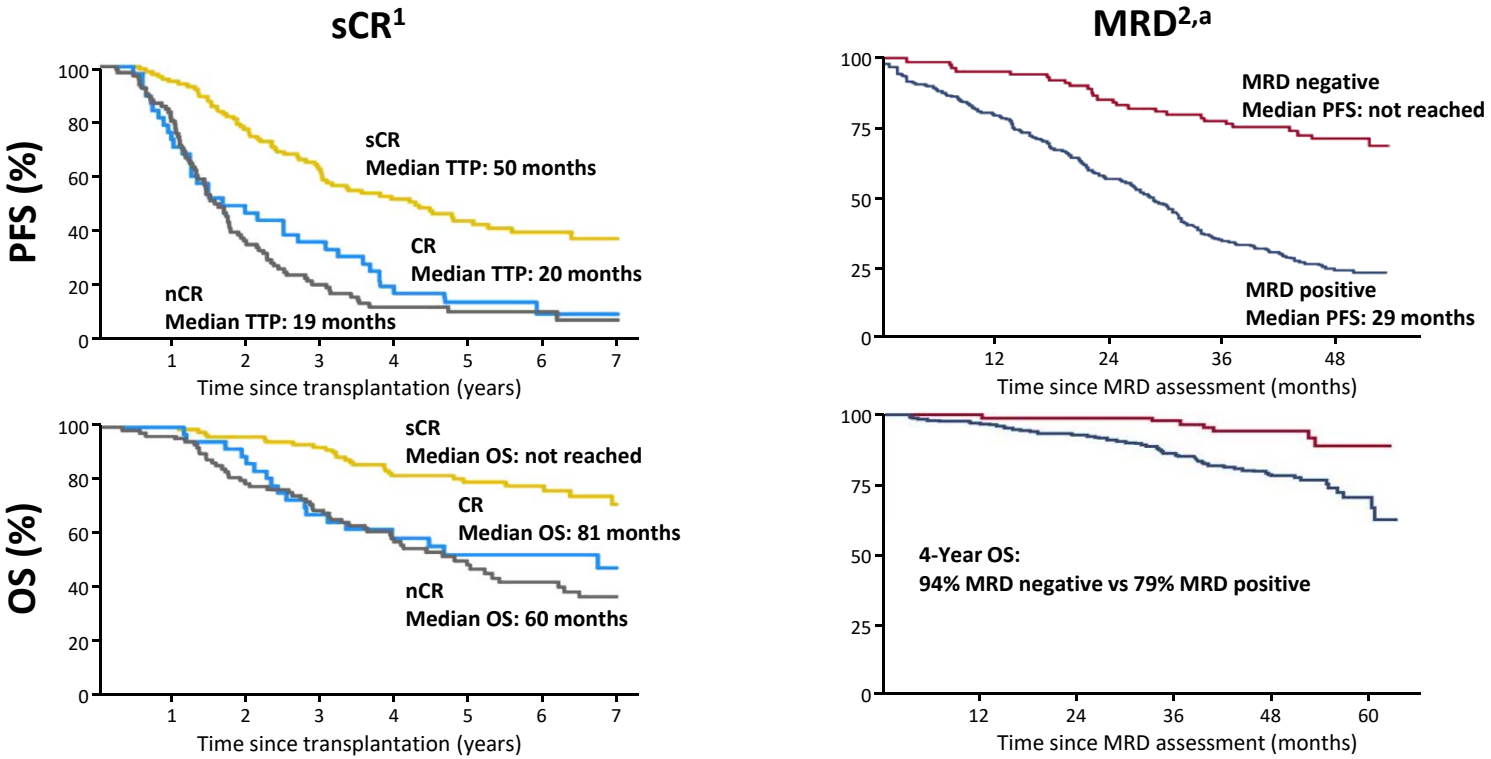
- ASCT consolidation is an important standard of care for transplant-eligible patients with NDMM[1-3]
- Lenalidomide, bortezomib, and dexamethasone (RVd) induction improved responses, PFS, and OS for NDMM patients in the non-transplant setting[4,5] and demonstrated notable clinical activity with frontline ASCT[6,7]
- The addition of DARA to lenalidomide and dexamethasone (Rd) or bortezomib and dexamethasone (Vd)-based therapy in NDMM and RRMM significantly improved depth of response, MRD negativity, and PFS[8-13]
- In the IFM 2009 study, RVd plus early ASCT versus RVd alone improved PFS (median, 50 vs 36 months)[6]
- The GRIFFIN study evaluated the addition of DARA to RVd plus ASCT in transplant-eligible NDMM
  - Part 1: Safety run-in phase (presented at ASH 2018)[14]
    - Toxicity was manageable and all 16 patients underwent successful stem cell collection and transplantation

**We report updated efficacy and safety from GRIFFIN, after a median follow-up of 22.1 months**

ASCT, autologous stem cell transplant; PFS, progression-free survival; OS, overall survival; MRD, minimal residual disease.

1. Engelhardt M, et al. *Haematologica.* 2014;99(2):232-242. 2. Moreau P, et al. *Ann Oncol.* 2017;28(suppl 4):iv52-iv61. 3. NCCN Clinical Practice Guidelines in Oncology. Multiple Myeloma V2.2020. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. 4. Richardson PG, et al. *Blood.* 2010;116(5):679-686. 5. Durie BGM, et al. *Lancet.* 2017;389(10068):519-527. 6. Attal M, et al. *N Engl J Med.* 2017;376(14):1311-1320. 7. Rosinol L, et al. *Blood.* 2019;134(16):1337-1345. 8. Dimopoulos MA, et al. *N Engl J Med.* 2016;375(14):1319-1331. 9. Palumbo MD, et al. *N Engl J Med.* 2016;375(8):754-766. 10. Facon T, et al. *N Engl J Med.* 2019;380(22):2104-2115. 11. Dimopoulos MA, et al. *Haematologica.* 2018;103(12):2088-2096. 12. Spencer A, et al. *Haematologica.* 2018;103(12):2079-2087. 13. Mateos MV, et al. *N Engl J Med.* 2018;378(6):518-528. 14. Voorhees P, et al. Presented at the 60th American Society of Hematology (ASH) Annual Meeting & Exposition; December 1-4, 2018; San Diego, CA.

# sCR and MRD as Surrogate Endpoints for PFS and OS




- Achievement of sCR and MRD negativity after ASCT are associated with better PFS and OS

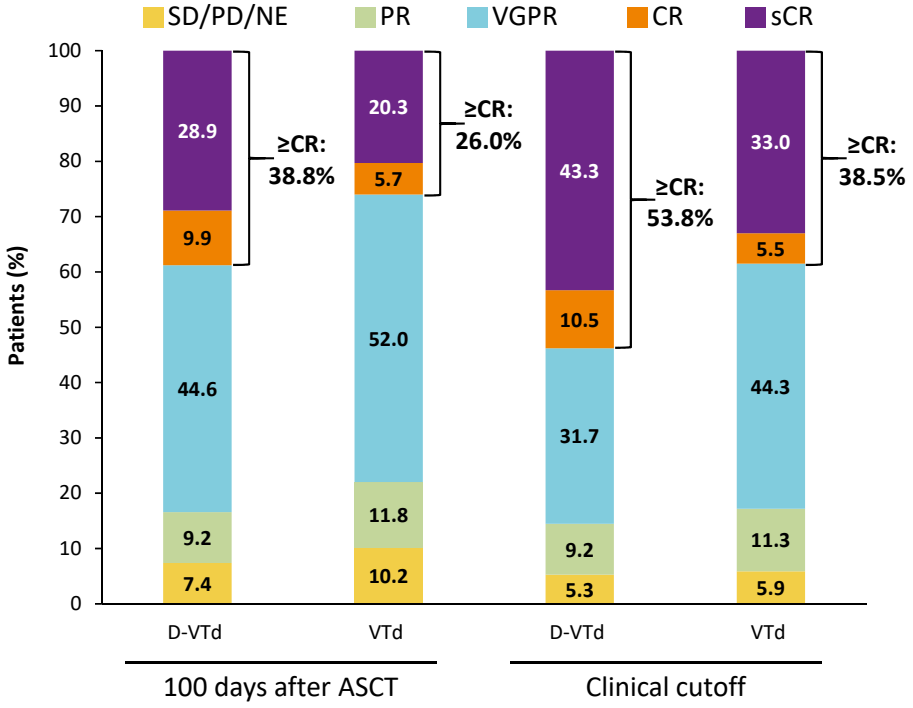
TTP, time to progression; nCR, near complete response.
[a]According to MRD status at the start of maintenance therapy.

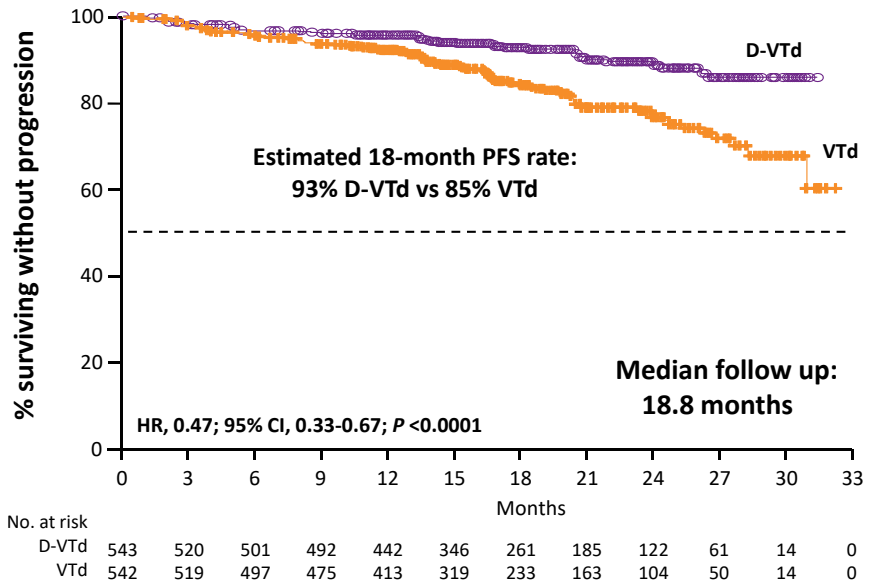


1. Kapoor P, et al. *J Clin Oncol*. 2013;31(36):4529-4535. 2. Perrot A, et al. *Blood.* 2018;132(23):2456-2464.

# Rationale for Adding Daratumumab to PI + IMiD Induction Therapy in Transplant-Eligible Patients

**DARA + VTd (D-VTd) as induction and consolidation in the transplant setting (CASSIOPEIA)[1]**



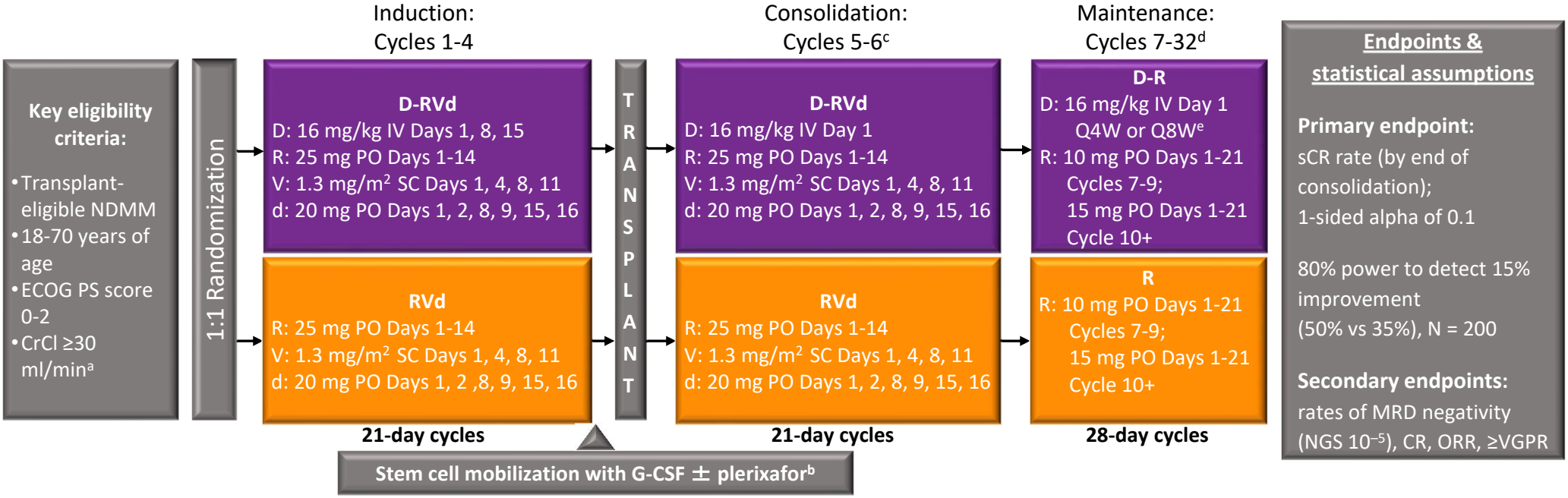

PI, proteasome inhibitor; IMiD, immunomodulatory drug; VTd, bortezomib/thalidomide/dexamethasone; D-VTd, daratumumab plus bortezomib/thalidomide/dexamethasone; HR, hazard ratio; CI, confidence interval; SD/PD/NE, stable disease, progressive disease, or not evaluable; PR, partial response; VGPR, very good partial response; CR, complete response; sCR, stringent complete response.



1. Moreau P, et al. *Lancet*. 2019;394(10192):29-38.

# GRIFFIN: Randomized Phase

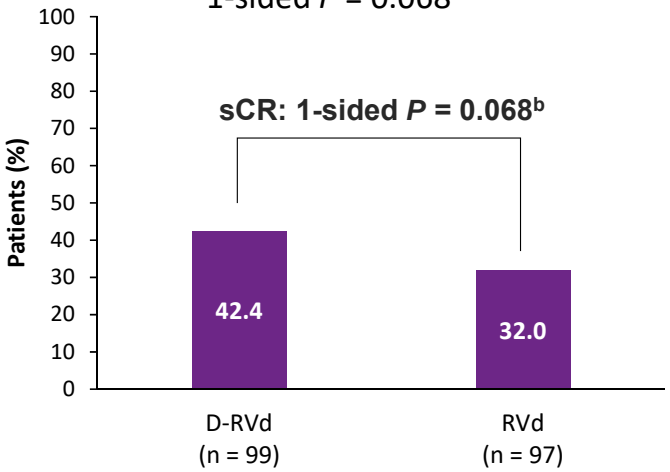
- Phase 2 study of D-RVd vs RVd in transplant-eligible NDMM, 35 sites in US with enrollment from 12/2016 and 4/2018



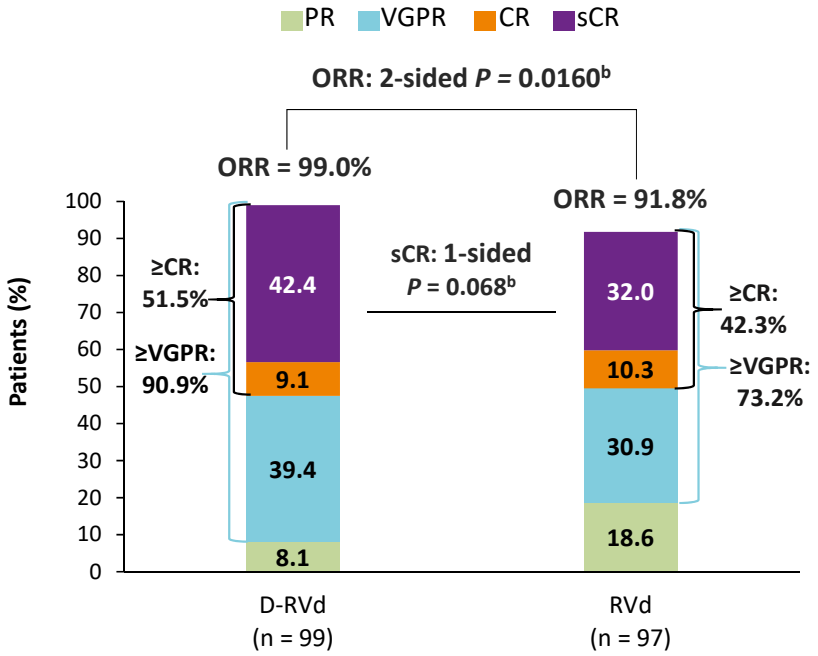

D-RVd, daratumumab plus lenalidomide/bortezomib/dexamethasone; RVd, lenalidomide/bortezomib/dexamethasone; NDMM, newly diagnosed multiple myeloma; US, United States; ECOG PS, Eastern Cooperative Oncology Group performance status; CrCl, creatinine clearance; IV, intravenously; PO, orally; SC, subcutaneously; G-CSF, granulocyte colony-stimulating factor; D-R, daratumumab-lenalidomide; Q4W, every 4 weeks; Q8W, every 8 weeks; NGS, next-generation sequencing; ORR, overall response rate; VGPR, very good partial 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 60-100 days post transplant.
[d]Patients who complete maintenance cycles 7-32 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).

# Primary Endpoint: sCR by the End of Consolidation[a]

- **Primary endpoint met at pre-set 1-sided alpha of 0.1**
  - sCR by end of consolidation
    - 42.4% D-RVd vs 32.0% RVd
    - Odds ratio, 1.57; 95% CI, 0.87-2.82; 1-sided *P* = 0.068[b]

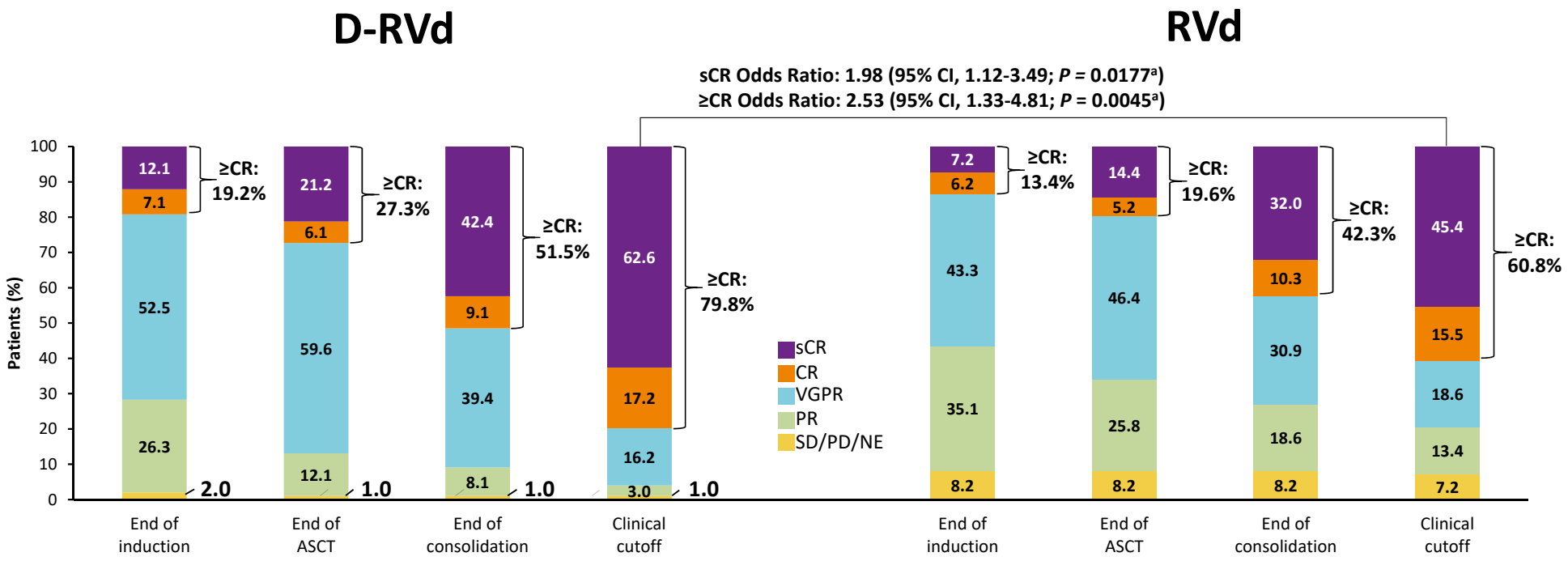



Post-consolidation depth of response[a]




[a]Results from primary analysis cutoff date (median follow-up, 13.5 months). Included patients in response-evaluable population (all randomized patients with confirmed MM diagnoses, measurable disease at baseline, received ≥1 dose of study treatment, and had ≥1 post-baseline disease assessment). [b]*P* values calculated using Cochran–Mantel–Haenszel chi-square test. A 1-sided *P* value is reported for sCR; for all other responses, 2-sided *P* values not adjusted for multiplicity are reported.

# Responses Deepened Over Time

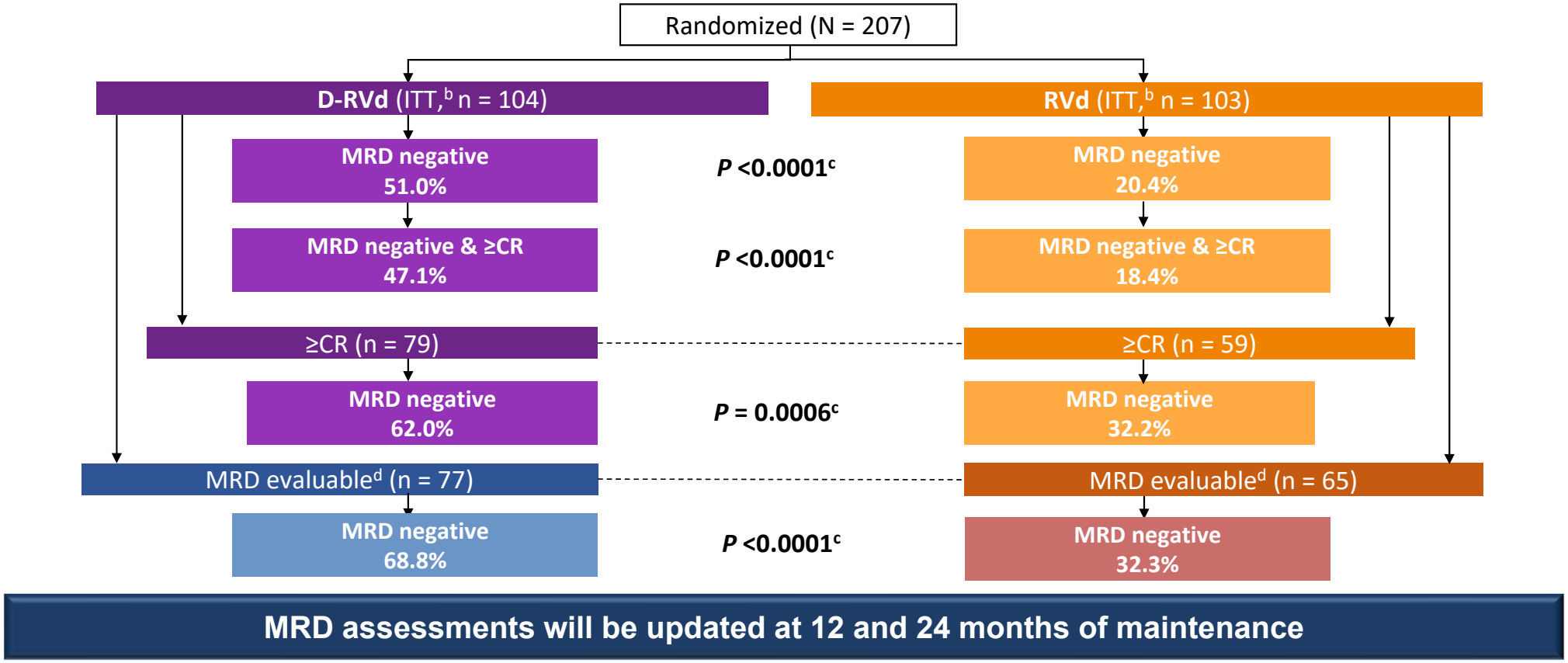



- Median follow up at primary analysis (end of consolidation) was 13.5 months; median follow up at clinical cutoff was 22.1 months

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

[a]*P* values (2-sided) calculated using Cochran–Mantel–Haenszel chi-square test.

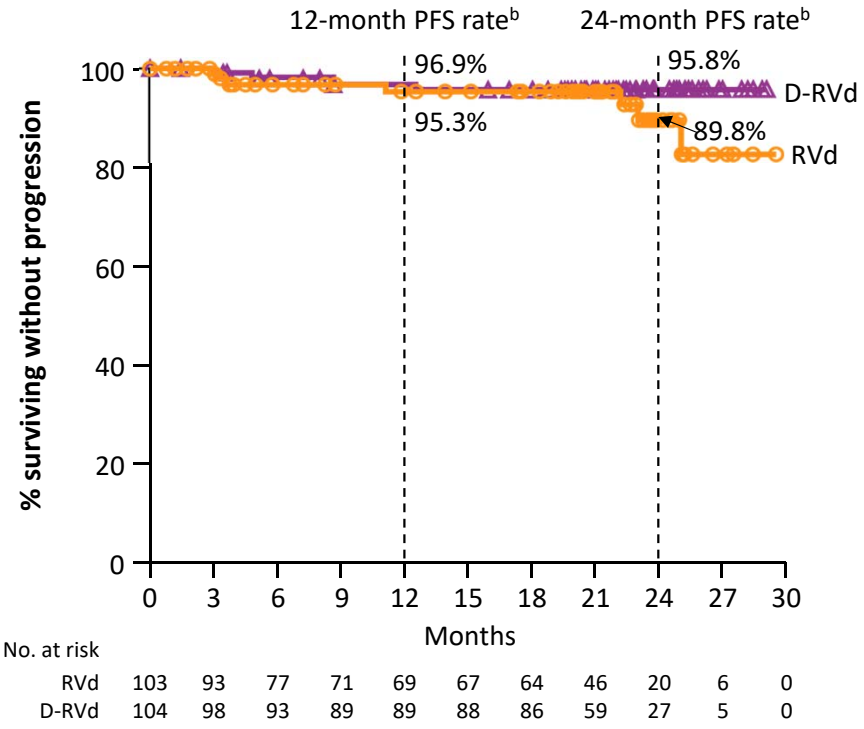
# MRD ($10^{-5}$) Negativity[a] at Clinical Cutoff

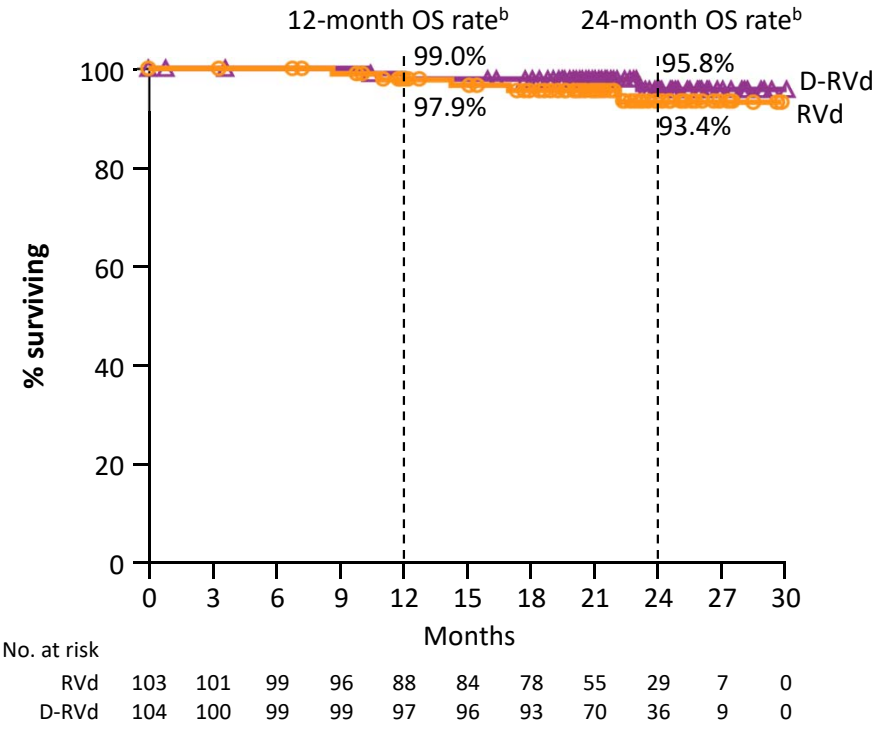



[a]The threshold of MRD negativity was defined as 1 tumor cell per $10^5$ white cells. MRD status is based on assessment of bone marrow aspirates by next-generation sequencing in accordance with International Myeloma Working Group criteria. Median follow-up was 22.1 months. [b]For the ITT population, patients with a missing or inconclusive assessment were considered MRD positive. [c]*P*-values were calculated from the Fisher's exact test. [d]The MRD-evaluable population includes patients who had both baseline (with clone identified/calibrated) and post-baseline MRD (with negative, positive, or indeterminate result) samples taken.

# D-RVd Results in Durable Estimated PFS and OS (>95%) at 2 Years[a]

- Median follow-up = 22.1 months




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

[a]ITT population. [b]Kaplan–Meier estimate.

# Most Common TEAEs[a]

| | D-RVd (n = 99) | | RVd (n = 102) | |
|---|---|---|---|---|
| | Any grade | Grade 3/4 | Any grade | Grade 3/4 |
| **Hematologic, n (%)** | | | | |
| Neutropenia | 57 (58) | 41 (41) | 36 (35) | 22 (22) |
| Thrombocytopenia | 43 (43) | 16 (16) | 36 (35) | 9 (9) |
| Leukopenia | 36 (36) | 16 (16) | 29 (28) | 7 (7) |
| Anemia | 35 (35) | 9 (9) | 33 (32) | 6 (6) |
| Lymphopenia | 30 (30) | 23 (23) | 28 (28) | 22 (22) |
| **Non-hematologic, n (%)** | | | | |
| Fatigue | 68 (69) | 6 (6) | 62 (61) | 6 (6) |
| Upper respiratory tract infection | 62 (63) | 1 (1) | 45 (44) | 2 (2) |
| Peripheral neuropathy[b] | 59 (60) | 7 (7) | 74 (73) | 8 (8) |
| Diarrhea | 59 (60) | 7 (7) | 51 (50) | 4 (4) |
| Constipation | 51 (52) | 2 (2) | 40 (39) | 1 (1) |
| Cough | 50 (51) | 0 | 27 (26) | 0 |
| Nausea | 49 (49) | 2 (2) | 50 (49) | 1 (1) |
| Pyrexia | 45 (45) | 2 (2) | 28 (27) | 3 (3) |
| Insomnia | 42 (42) | 2 (2) | 31 (30) | 1 (1) |
| Back pain | 36 (36) | 1 (1) | 34 (33) | 4 (4) |
| Peripheral edema | 34 (34) | 2 (2) | 35 (34) | 3 (3) |
| Arthralgia | 33 (33) | 0 | 33 (32) | 2 (2) |
| **Infusion-related reaction, n (%)** | 42 (42) | 6 (6)[c] | – | – |

- Any-grade infection rates were higher for D-RVd vs RVd (91% vs 62%), largely due to grade 1/2 upper respiratory tract infections
- Grade 3/4 infection rates were similar (23% vs 22%)
- The rate of any-grade pneumonia was similar for D-RVd and RVd (13% vs 15%)

TEAE, treatment-emergent adverse event.
[a]Any-grade TEAEs are listed that occurred in ≥30% of patients in either group. The safety analysis population included all randomized patients who received ≥1 dose of study treatment; analysis was according to treatment received. [b]Includes patients with neuropathy peripheral and peripheral sensory neuropathy. [c]No grade 4 IRRs were reported.

# Conclusions

- D-RVd significantly improved response rates and depth of response compared with RVd
  - The benefit of DARA continues with longer follow up, as D-RVd shows continued improvement of sCR and MRD-negativity rates beyond post-ASCT consolidation
- The overall safety profile of D-RVd is consistent with previous reports of daratumumab plus standard of care
- Stem cell mobilization was feasible and hematopoietic reconstitution was not impacted with D-RVd
- PFS and OS rates at 24 months in the D-RVd group (≥95%) are promising
- The ongoing phase 3 PERSEUS study is evaluating subcutaneous DARA plus RVd in transplant-eligible patients

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

# Daratumumab Data:

# Phase III CANDOR Data

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

Genmab

# LBA-6: Carfilzomib, Dexamethasone, and Daratumumab Versus Carfilzomib and Dexamethasone for the Treatment of Patients with Relapsed or Refractory Multiple Myeloma (RRMM): Primary Analysis Results from the Randomized, Open-Label, Phase 3 Study CANDOR

Saad Z. Usmani, MD, MBBS[1], Hang Quach, MD[2], María-Victoria Mateos[3], Ola Landgren, MD, PhD[4], Xavier Leleu, MD, PhD5, David S. Siegel[6], Katja Weisel[7]*, Hui Yang[8]*, Zandra K. Klippel, MD[8], Anita Zahlten-Kumeli[8] and Meletios A. Dimopoulos, MD[9]

[1]Atrium Health, Charlotte, NC; [2]St. Vincent's Hospital, Melbourne, Australia; [3]University Hospital Salamanca/IBSAL, Salamanca, Spain [4]Memorial Sloan Kettering Cancer Center, New York, NY; [5]Hopital Claude Huriez, Lille, France; [6]John Theurer Cancer Center at Hackensack University Medical Center, Hackensack, NJ; [7]Department of Oncology, Hematology and Bone Marrow Transplantation with Section of Pneumology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [8] Amgen, Inc., Thousand Oaks, CA; [9]National and Kapodistrian University of Athens, School of Medicine, Athens, Greece

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## Introduction & Methods

- Use of lenalidomide & bortezomib in NDMM pts, along with continuous or maintenance therapy paradigm have improved survival outcomes
- However, many pts progress while on these agents or discontinue them due to toxicity
- There is a need for novel, efficacious & tolerable regimens that can treat MM pts who are exposed or refractory to lenalidomide or bortezomib
- The combination of D-Kd has been shown to be efficacious and safe in RRMM in the phase 1 study MMY1001 (Chari, Blood 2019)
- RRMM pts with measurable disease who had received 1–3 prior lines of therapy, with partial response or better to ≥1 line of therapy were eligible
- Pts were randomized 2:1 to D-Kd or Kd
- Primary endpoint was PFS
- Secondary endpoints: ORR, MRD negative-complete response at 12 months (threshold, 10-5 cells), OS, time to response & safety.



*Usmani et al, ASH 2019 Abstract LBA-6*

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## Patient Characteristics & Dosing

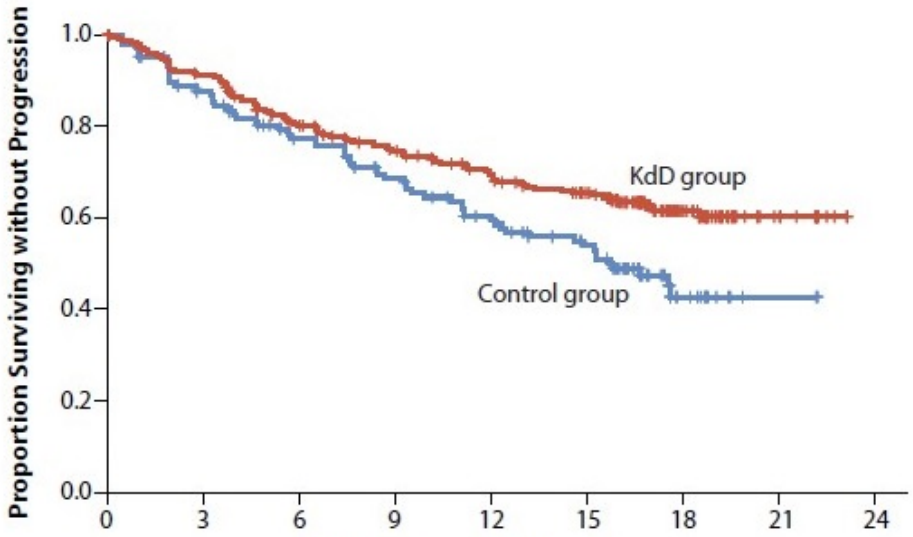
- Total patients
  - 312 D-Kd
  - 154 Kd
- Baseline characteristics balanced between arms
- Median age: 64 years
- Of randomized pts
  - 42.3% received previous lenalidomide-containing regimens
  - 90.3% received bortezomib-containing regimens
- 33% of pts were lenalidomide-refractory

- All pts received K as 30-min IV infusion on days 1, 2, 8, 9, 15 & 16 of each 28-day cycle (20 mg/m2 on days 1 and 2 during cycle 1 and 56 mg/m2 thereafter)
- IV Daratumumab (8 mg/kg) administered on days 1 and 2 of cycle 1 and at 16 mg/kg once weekly for the remaining doses of the first 2 cycles, then every 2 wks for 4 cycles (cycles 3 to 6), and every 4 wks thereafter
- All pts received 40 mg dex oral or IV weekly (20 mg for pts >75 years)



*Usmani et al, ASH 2019 Abstract LBA-6*

# LBA-6: Carfilzomib, Dexamethasone, and Daratumumab Versus Carfilzomib and Dexamethasone for the Treatment of Patients with Relapsed or Refractory Multiple Myeloma (RRMM): Primary Analysis Results from the Randomized, Open-Label, Phase 3 Study CANDOR




| No. at Risk | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| KdD group | 312 | 279 | 236 | 211 | 189 | 165 | 57 | 14 | 0 |
| Control group | 154 | 122 | 100 | 85 | 70 | 55 | 13 | 2 | 0 |

| | D-Kd (n=312) | Kd (n=154) |
|---|---|---|
| **Disease progression or death (%)** | 35.3 | 44.2 |
| **Median PFS (mo)** | NE | 15.8 |
| **Hazard ratio for D-Kd vs Kd (95% CI)** | 0.63 (0.46 -0.85) | |
| **P-value (1-sided)** | 0.0014 | |
| **ORR (%, P=0.0040)** | 84.3 | 74.7% |
| **≥CR (%)** | 28.5 | 10.4 |
| **MRD-neg. CR at 12mo (%, P<0.0001)** | 12.5 | 1.3 |
| **Median treatment duration (wks)** | 70.1 | 40.3 |
| **Median OS** | Not reached at median follow-up of 17mo (HR, 0.75; 95% CI, 0.49–1.13; P=0.08) | |

*Usmani et al, ASH 2019 Abstract LBA-6*

# LBA-6: Carfilzomib, Dexamethasone, and Daratumumab Versus Carfilzomib and Dexamethasone for the Treatment of Patients with Relapsed or Refractory Multiple Myeloma (RRMM): Primary Analysis Results from the Randomized, Open-Label, Phase 3 Study CANDOR

## Safety

- Incidence of grade ≥3 AEs:
  - D-Kd: 82.1%
  - Kd: 73.9%
- Serious Aes:
  - D-Kd: 56.2%
  - Kd: 45.8%
- Rate of treatment discontinuation due to AEs similar in both arms (KdD, 22.4%; Kd, 24.8%)
- Frequency of grade ≥3 cardiac failure:
  - D-Kd: 3.9%
  - Kd: 8.5% (Kd)
  - Rate of cardiac failure event leading to K discontinuation similar in both arms (3.9% and 4.6%)
- 5 deaths were reported as treatment-related:
  - All in D-Kd arm
  - Pneumonia, sepsis, septic shock, acinetobacter infection, and cardio-respiratory arrest [n=1 each]



*Usmani et al, ASH 2019 Abstract LBA-6*

# LBA-6: Carfilzomib, Dexamethasone, and Daratumumab Versus Carfilzomib and Dexamethasone for the Treatment of Patients with Relapsed or Refractory Multiple Myeloma (RRMM): Primary Analysis Results from the Randomized, Open-Label, Phase 3 Study CANDOR

## Conclusions

- D-Kd resulted in a significant PFS benefit over Kd: 37% reduction in the risk of progression or death
- Pts treated with D-Kd achieved deeper responses, with a nearly 10-times higher MRD negative-complete response rate vs Kd-treated pts
- PFS benefit of D-Kd maintained across prespecified clinically important subgroups, particularly among lenalidomide-exposed and -refractory pts
- AEs were generally manageable / incidence of AEs leading to treatment discontinuation was similar in both arms.

- **Overall, D-Kd was associated with favorable benefit-risk profile & represents an efficacious new regimen for RRMM, including for lenalidomide-exposed and/or -refractory pts**



*Usmani et al, ASH 2019 Abstract LBA-6*

# Daratumumab Data:

# Phase III ALCYONE Update

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

Genmab

# Daratumumab Plus Bortezomib, Melphalan, and Prednisone Versus Bortezomib, Melphalan, and Prednisone in Patients With Transplant-ineligible Newly Diagnosed Multiple Myeloma: Overall Survival in ALCYONE*

**Maria-Victoria Mateos,**[1] Michele Cavo,[2] Joan Blade,[3] Meletios Dimopoulos,[4] Kenshi Suzuki,[5] Andrzej Jakubowiak,[6] Stefan Knop,[7] Chantal Doyen,[8] Paulo Lucio,[9] Zsolt Nagy,[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] Maria Krevvata,[22] Jianping Wang,[23] Anupa Kudva,[23] Jon Ukropec,[24] Susan Wroblewski,[22] Rachel Kobos,[23] Jesus San-Miguel[25]

[1]University Hospital of Salamanca/IBSAL, Salamanca, Spain; [2]Seràgnoli Institute of Hematology, Bologna University School of Medicine, Bologna, Italy; [3]Hospital Clínic de Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona, Barcelona, Spain; [4]National and Kapodistrian University of Athens, Athens, Greece; [5]Department of Hematology, Japanese Red Cross Medical Center, Tokyo, Japan; [6]University of Chicago Medical Center, Chicago, IL, USA; [7]Würzburg University Medical Center, Würzburg, Germany; [8]Université catholique de Louvain, CHU UCL Namur, Yvoir, Belgium; [9]Champalimaud Centre for the Unknown, Lisbon, Portugal; [10]Semmelweis Egyetem, Budapest, Hungary; [11]University Hospital Brno, Brno, Czech Republic; [12]University Hospitals Birmingham NHS Trust, Birmingham, United Kingdom; [13]Department of Cancer Prevention, School of Public Health, Silesian Medical University in Katowice, Poland; [14]Clinica de Tratamento E, Cuiaba, Brazil; [15]Azienda Ospedaliera "Santa Maria," Terni, Italy; [16]Andrew Love Cancer Centre, Geelong, Australia; [17]Clinic of Professional Pathology, Saratov, Russia; [18]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, South Korea; [19]LTD "Medinvent" Institute of Health, Tbilisi, Georgia; [20]Matsuyama Red Cross Hospital, Matsuyama, Japan; [21]Leicester Royal Infirmary – Haematology, Leicester, United Kingdom; [22]Janssen Research & Development, LLC, Spring House, PA, USA; [23]Janssen Research & Development, LLC, Raritan, NJ, USA; [24]Janssen Global Medical Affairs, Horsham, PA, USA; [25]Clínica Universidad de Navarra-CIMA, IDISNA, CIBERONC, Pamplona, Spain.

# Background

- Standard of care for transplant-ineligible NDMM patients includes combination therapies such as Rd, VMP, and VRd[1-3]
- In the primary analysis of the phase 3 ALCYONE study, after median 16.5 months follow-up, the addition of daratumumab to VMP (D-VMP) significantly reduced the risk of progression or death by 50% in transplant-ineligible NDMM patients (HR, 0.50; 95% CI, 0.38-0.65)[4]
- After an additional year of follow-up, D-VMP continued to demonstrate efficacy versus VMP5
  - D-VMP continued to demonstrate a significant benefit in PFS, with a 57% reduction in the risk of progression or death at median 27.8 months follow-up (HR, 0.43; 95% CI, 0.35-0.54)
  - Based on the significant benefit in PFS2 with D-VMP versus VMP, longer survival outcomes were projected for D-VMP, although OS was not assessed

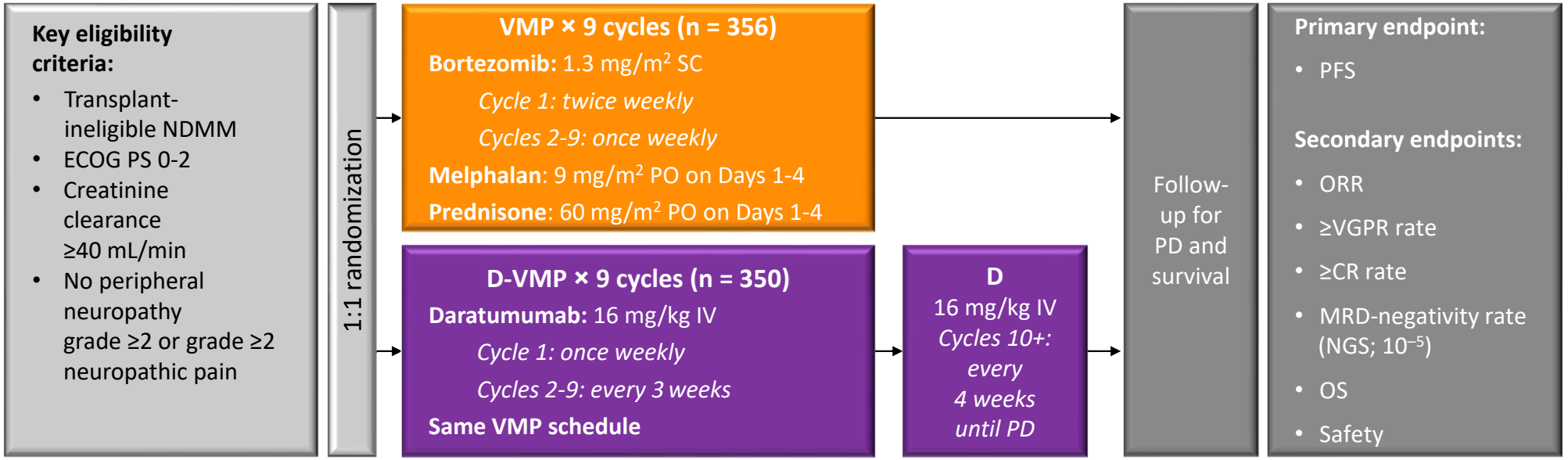
**Here we present updated efficacy and safety from ALCYONE, after >3 years of follow-up**

HR, hazard ratio; CI, confidence interval; PFS, progression-free survival; PFS2, PFS on next subsequent line of therapy; OS, overall survival.

1. Moreau P, et al. *Ann Oncol.* 2017;28:iv52-iv61. 2. Moreau P, et al. *Ann Oncol*. 2013;24 Suppl 6:vi133-vi7. 3. NCCN Clinical Practice Guidelines in Oncology. Multiple Myeloma V2.2020. (https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf.). 4. Mateos MV, et al. *N Engl J Med*. 2018;378(6):518-528. 5. Dimopoulos MA, et al. *Blood.* 2018;132:156.

# ALCYONE Study Design

- Phase 3 study of daratumumab plus VMP versus VMP alone in transplant-ineligible NDMM; N = 706




**Stratification factors**
- ISS disease stage (I vs II vs III)
- Region (EU vs other)
- Age (<75 vs ≥75 y)

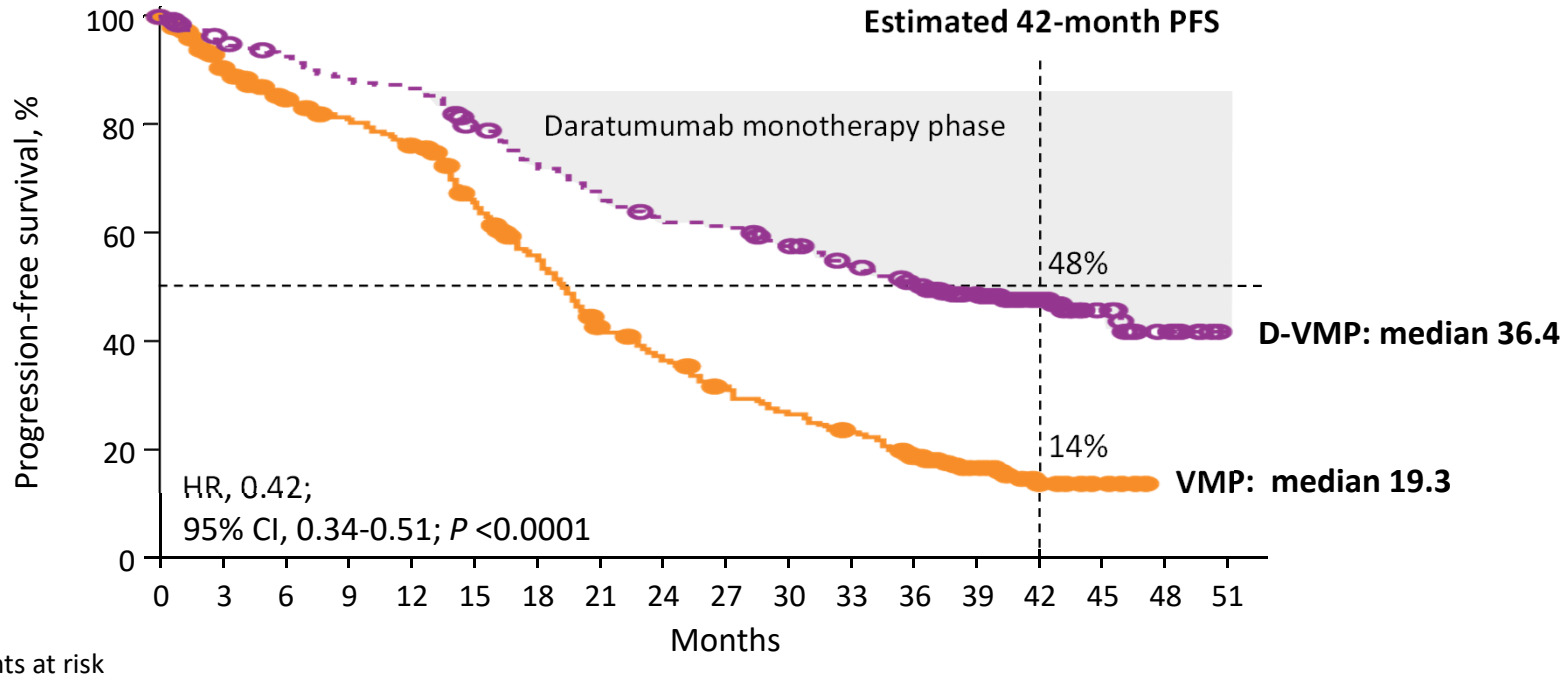
- Cycles 1-9: 6-week cycles
- Cycles 10+: 4-week cycles

**Statistical analyses**
- Prespecified interim analysis for OS (209 events; 63% of planned events)

SC, subcutaneously; PO, orally; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenously; PD, progressive disease; ISS, International Staging System; EU, Europe.

# PFS[a]

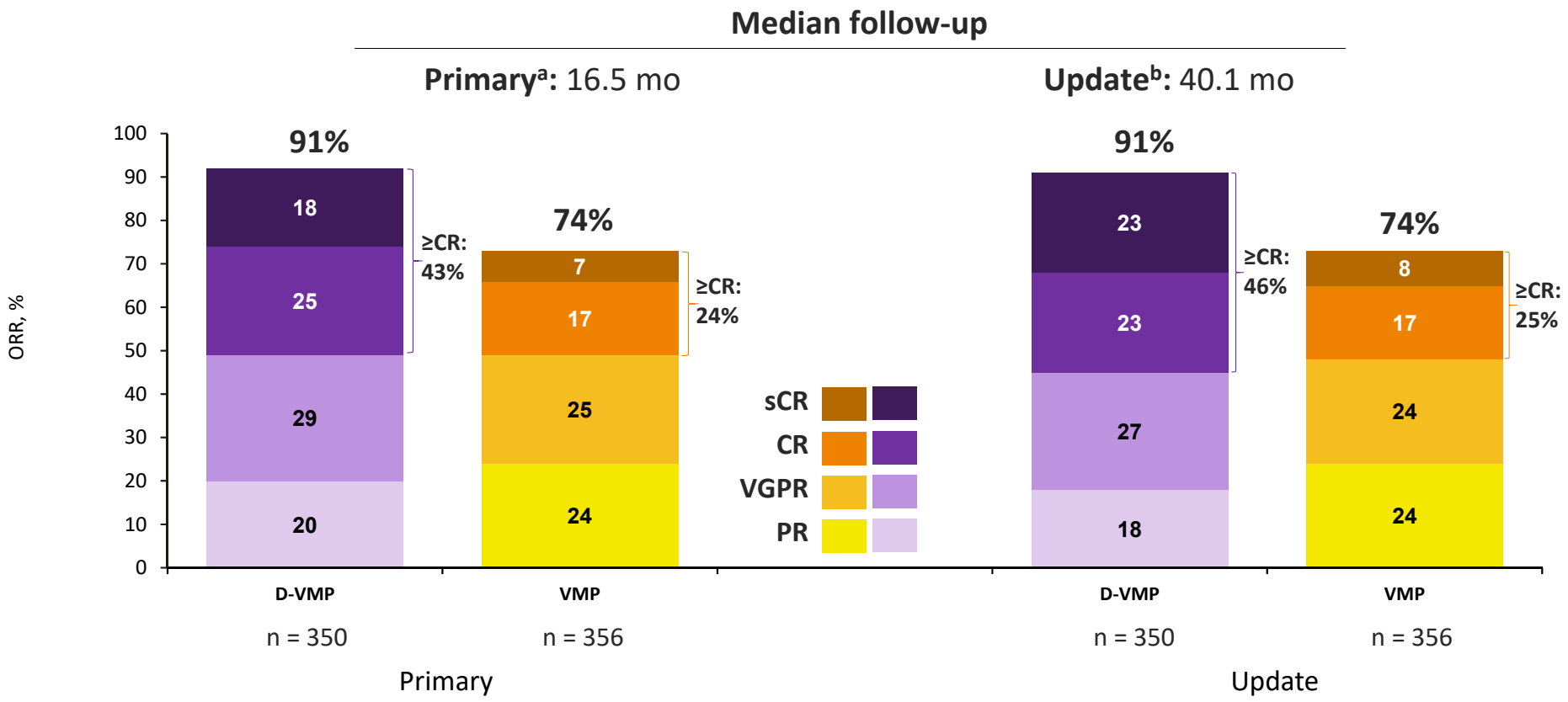
- Median (range) follow-up: 40.1 (0-52.1) months




**D-VMP continued to demonstrate a significant PFS benefit with extended follow up**

[a]Kaplan-Meier estimate.

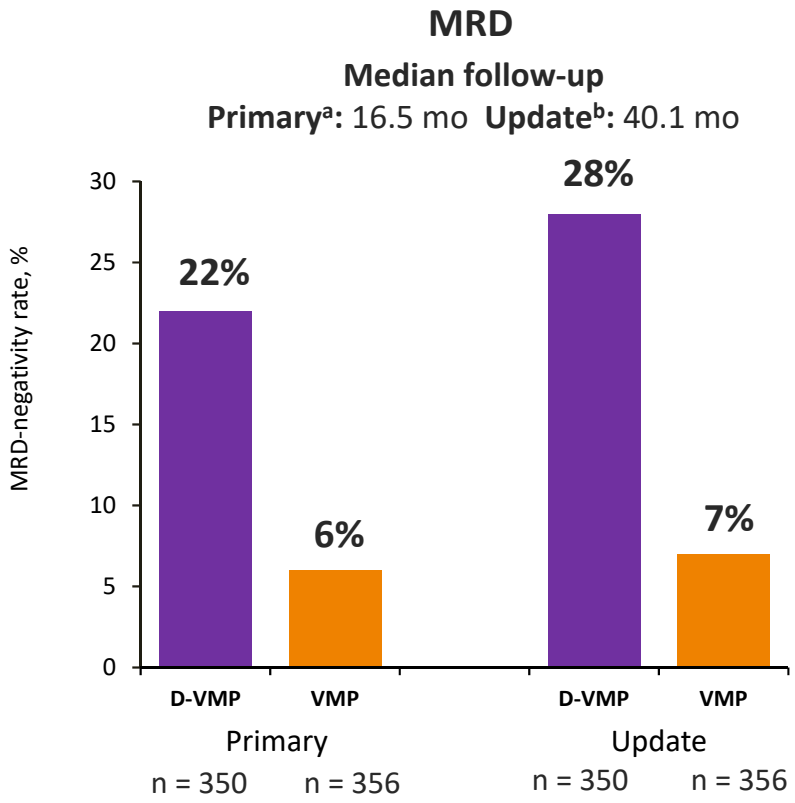
# ORR

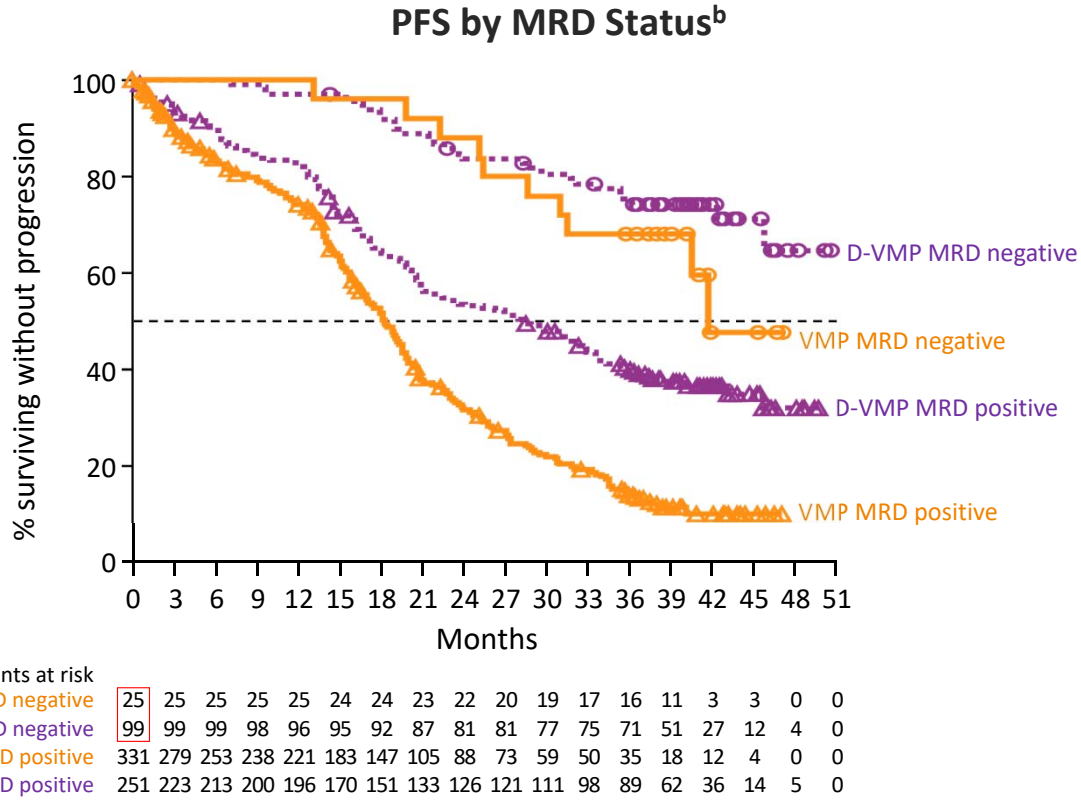



**Significantly higher ORR, ≥VGPR rate, ≥CR rate with D-VMP**

ORR, overall response rate; sCR, stringent complete response; VGPR, very good partial response; PR, partial response.
[a]Respnse-evaluable population. [b]ITT population.

# MRD-negativity Rates and PFS by MRD Status ($10^{-5}$)



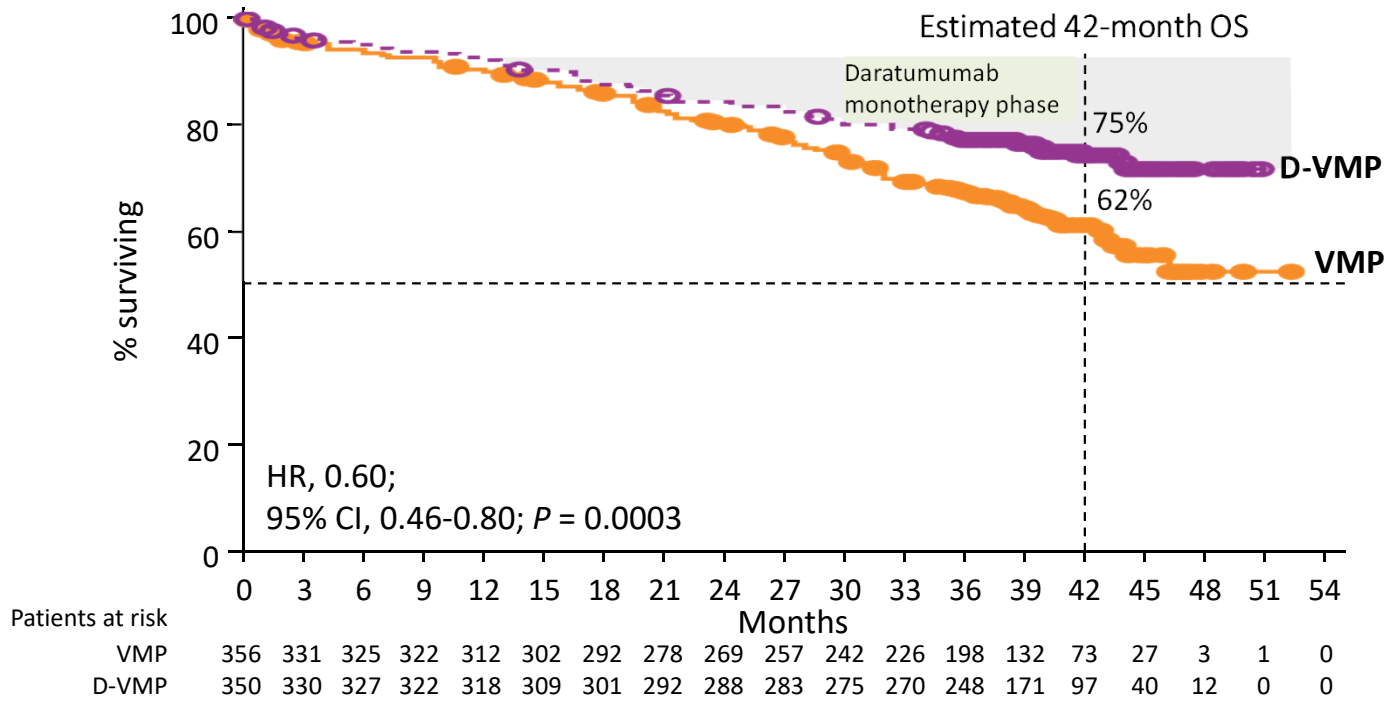




- **Four-fold higher rates of MRD negativity with D-VMP**
- **Improved PFS in patients with MRD negativity**

[a]Response-evaluable population. [b]TT population.

# OS[a]

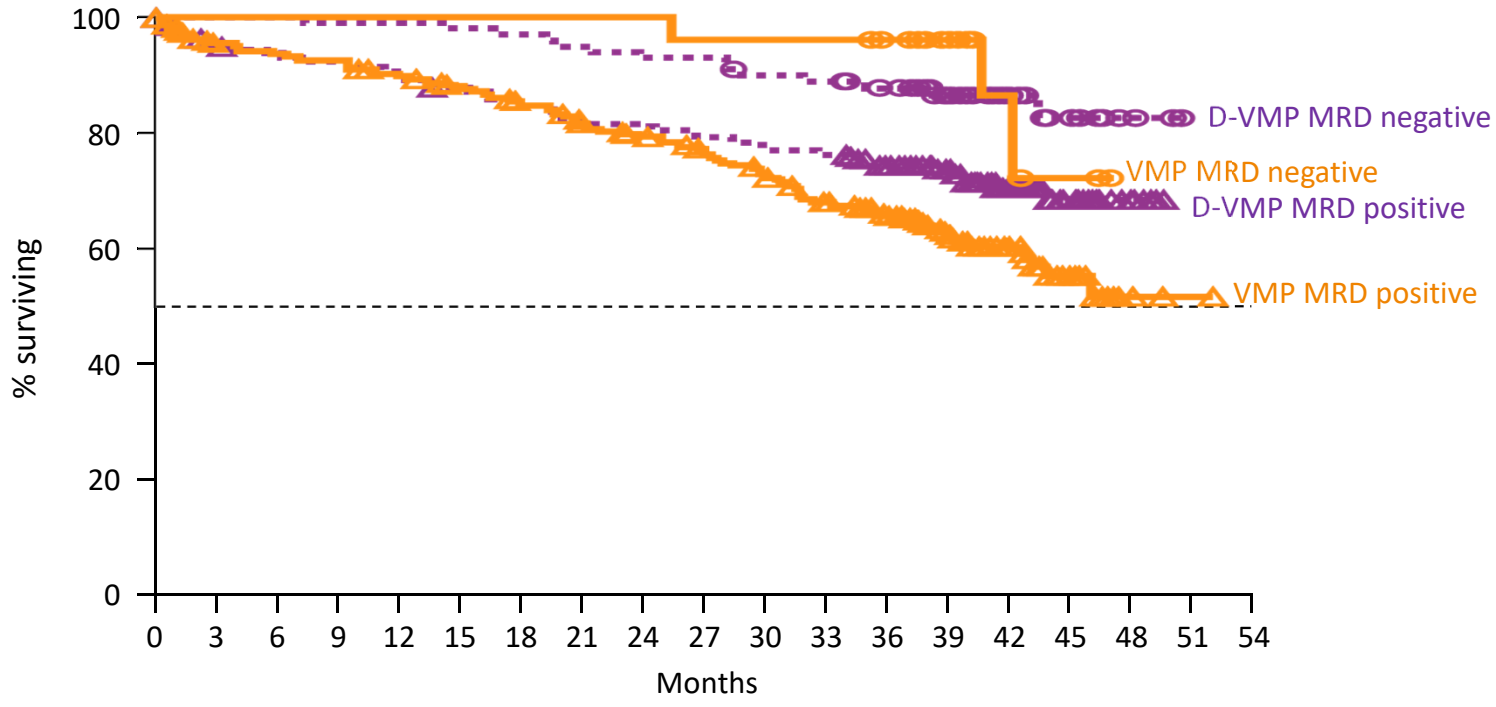
- Median (range) follow-up: 40.1 (0-52.1) months
  - Pre-specified analysis triggered after 209 deaths were observed




**40% reduction in the risk of death in patients receiving D-VMP**

[a]Kaplan-Meier estimate.

# OS by MRD Status ($10^{-5}$)




| Patients at risk | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| VMP MRD negative | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 24 | 24 | 24 | 22 | 16 | 6 | 4 | 0 | 0 | 0 |
| D-VMP MRD negative | 99 | 99 | 99 | 98 | 98 | 97 | 96 | 94 | 92 | 92 | 88 | 87 | 82 | 60 | 33 | 15 | 4 | 0 | 0 |
| VMP MRD positive | 331 | 306 | 300 | 297 | 287 | 277 | 267 | 253 | 244 | 233 | 218 | 202 | 176 | 116 | 67 | 23 | 3 | 1 | 0 |
| D-VMP MRD positive | 251 | 231 | 228 | 224 | 220 | 212 | 205 | 198 | 196 | 191 | 187 | 183 | 166 | 111 | 64 | 25 | 8 | 0 | 0 |

# Conclusions

- D-VMP continued to demonstrate a significant PFS benefit versus VMP alone
- Responses with D-VMP continued to deepen over time from the primary analysis,[1] with improvements in rates of ≥CR and MRD negativity
- Patients with sustained MRD negativity had improved outcomes
  - Significantly more patients with D-VMP remained MRD negative for ≥12 months
- D-VMP significantly prolonged OS in patients with transplant-ineligible NDMM
  - 40% reduction in the risk of death versus VMP alone after median follow-up of 40.1 months
  - Based on PFS2 results, longer survival outcomes are projected with other daratumumab-based regimens in the frontline setting

**This first report of an OS benefit with daratumumab continues to support the use of daratumumab-based regimens for treatment of patients with MM**



1. Mateos MV, et al. *N Engl J Med*. 2018;378(6):518-528.

# Daratumumab Data:

# Phase III MAIA Update

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

Genmab

# Poster 1875: Daratumumab Plus Lenalidomide and Dexamethasone (D-Rd) Versus Lenalidomide and Dexamethasone (Rd) in Patient with Newly Diagnosed Multiple Myeloma (NDMM) Ineligible for Transplant: Updated Analysis of MAIA

Nizar Bahlis,[1,*] Thierry Facon,[2] Saad Z. Usmani,[3] Shaji K. Kumar,[4] Torben Plesner,[5] Robert Z. Orlowski,[6] Cyrille Touzeau,[7] Supratik Basu,[8] Hareth Nahi,[9] Cyrille Hulin,[10] Hang Quach,[11] Hartmut Goldschmidt,[12] Michael O'Dwyer,[13] Christopher P. Venner,1[4] Katja C. Weisel,[15] Maria Krevvata,[16] Huiling Pei,[17] Jianping Wang,[18] Rian Van Rampelbergh,[19] Jon Ukropec,[20] Clarissa M. Uhlar,[16] Rachel Kobos,[18] Aurore Perrot[21]

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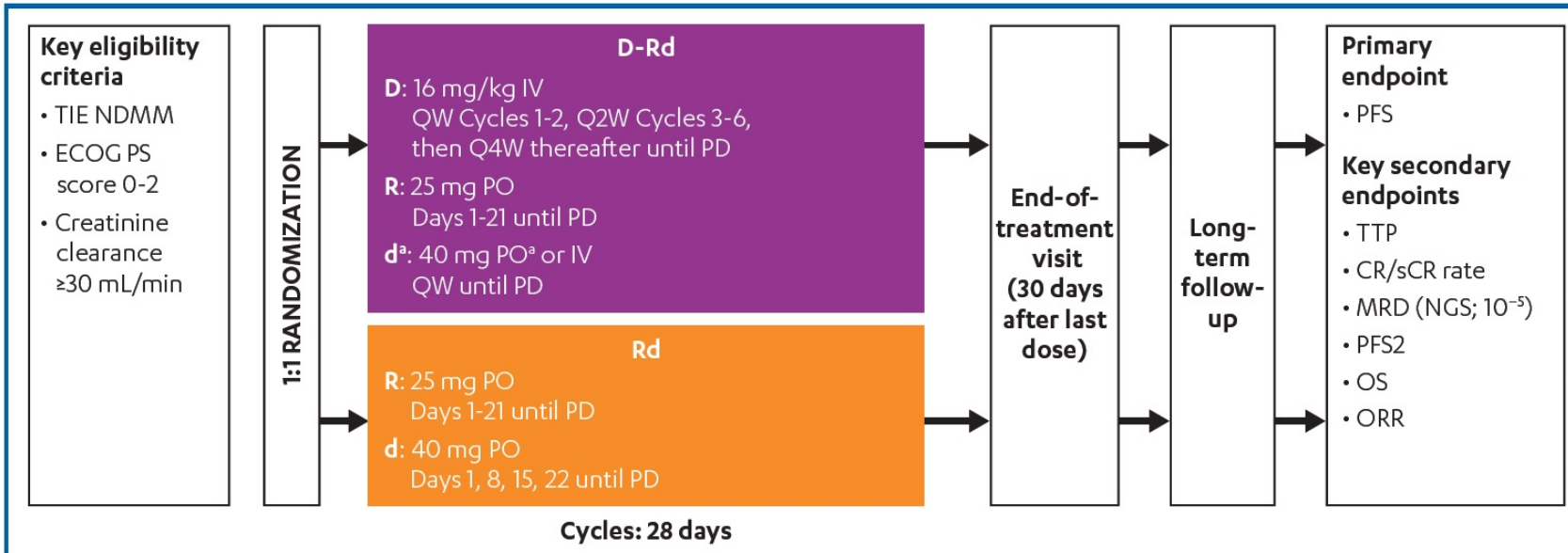
# Poster 1875: Daratumumab Plus Lenalidomide and Dexamethasone (D-Rd) Versus Lenalidomide and Dexamethasone (Rd) in Patient with Newly Diagnosed Multiple Myeloma (NDMM) Ineligible for Transplant: Updated Analysis of MAIA

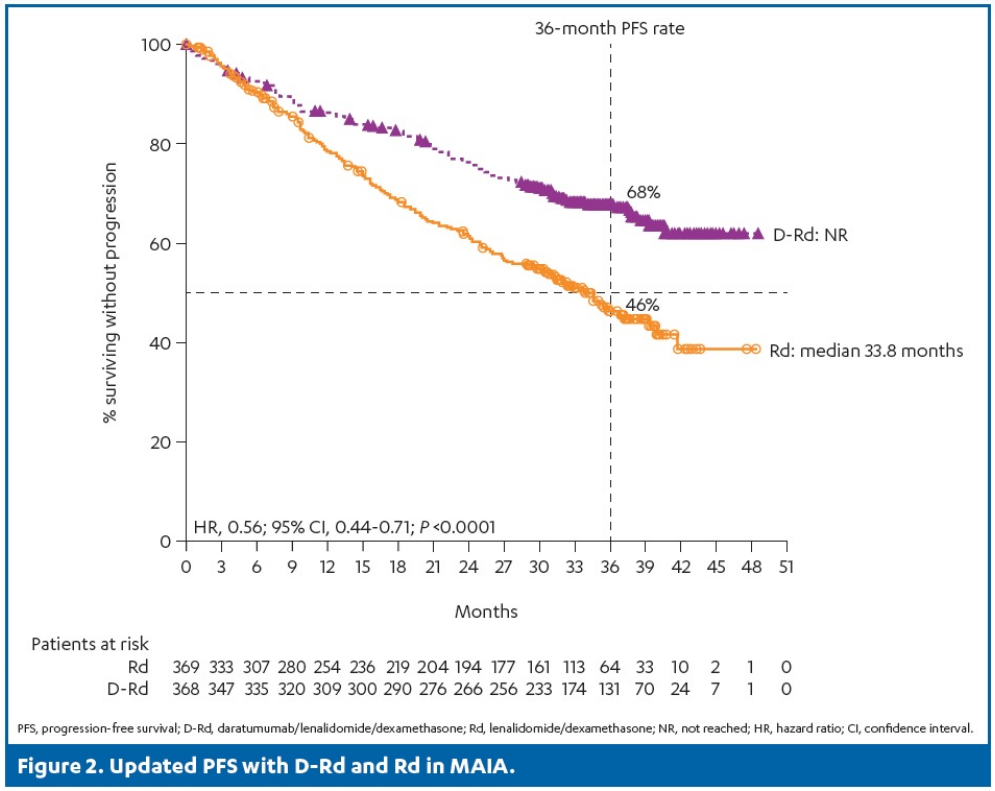



TIE, transplant-ineligible; NDMM, newly diagnosed multiple myeloma; ECOG PS, Eastern Cooperative Oncology Group performance status; Rd, lenalidomide/dexamethasone; PO, oral; PD, progressive disease; D-Rd, daratumumab/lenalidomide/dexamethasone; IV, intravenous; QW, once weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; 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 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.

**Figure 1. MAIA study design.**

*Bahlis et al, ASH 2019 Poster 1875*

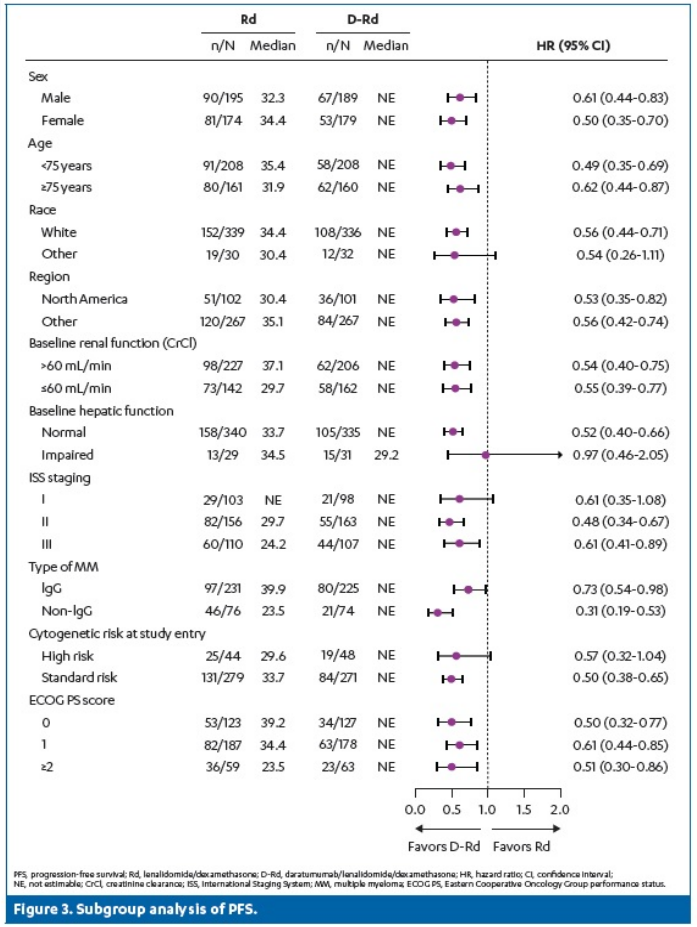
# Poster 1875: Daratumumab Plus Lenalidomide and Dexamethasone (D-Rd) Versus Lenalidomide and Dexamethasone (Rd) in Patient with Newly Diagnosed Multiple Myeloma (NDMM) Ineligible for Transplant: Updated Analysis of MAIA




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

**Figure 2. Updated PFS with D-Rd and Rd in MAIA.**

- After a median follow-up of 36.4 months, median PFS was NR with D-Rd versus 33.8 months with Rd (HR, 0.56; 95% CI, 0.44-0.71; P<0.0001)
  - The estimated 36-month rate was 68% with D-Rd versus 46% with Rd



| | Rd n/N | Rd Median | D-Rd n/N | D-Rd Median | HR (95% CI) |
|---|---|---|---|---|---|
| Sex | | | | | |
| Male | 90/195 | 32.3 | 67/189 | NE | 0.61 (0.44-0.83) |
| Female | 81/174 | 34.4 | 53/179 | NE | 0.50 (0.35-0.70) |
| Age | | | | | |
| <75 years | 91/208 | 35.4 | 58/208 | NE | 0.49 (0.35-0.69) |
| ≥75 years | 80/161 | 31.9 | 62/160 | NE | 0.62 (0.44-0.87) |
| Race | | | | | |
| White | 152/339 | 34.4 | 108/336 | NE | 0.56 (0.44-0.71) |
| Other | 19/30 | 30.4 | 12/32 | NE | 0.54 (0.26-1.11) |
| Region | | | | | |
| North America | 51/102 | 30.4 | 36/101 | NE | 0.53 (0.35-0.82) |
| Other | 120/267 | 35.1 | 84/267 | NE | 0.56 (0.42-0.74) |
| Baseline renal function (CrCl) | | | | | |
| >60 mL/min | 98/227 | 37.1 | 62/206 | NE | 0.54 (0.40-0.75) |
| ≤60 mL/min | 73/142 | 29.7 | 58/162 | NE | 0.55 (0.39-0.77) |
| Baseline hepatic function | | | | | |
| Normal | 158/340 | 33.7 | 105/335 | NE | 0.52 (0.40-0.66) |
| Impaired | 13/29 | 34.5 | 15/31 | 29.2 | 0.97 (0.46-2.05) |
| ISS staging | | | | | |
| I | 29/103 | NE | 21/98 | NE | 0.61 (0.35-1.08) |
| II | 82/156 | 29.7 | 55/163 | NE | 0.48 (0.34-0.67) |
| III | 60/110 | 24.2 | 44/107 | NE | 0.61 (0.41-0.89) |
| Type of MM | | | | | |
| IgG | 97/231 | 39.9 | 80/225 | NE | 0.73 (0.54-0.98) |
| Non-IgG | 46/76 | 23.5 | 21/74 | NE | 0.31 (0.19-0.53) |
| Cytogenetic risk at study entry | | | | | |
| High risk | 25/44 | 29.6 | 19/48 | NE | 0.57 (0.32-1.04) |
| Standard risk | 131/279 | 33.7 | 84/271 | NE | 0.50 (0.38-0.65) |
| ECOG PS score | | | | | |
| 0 | 53/123 | 39.2 | 34/127 | NE | 0.50 (0.32-0.77) |
| 1 | 82/187 | 34.4 | 63/178 | NE | 0.61 (0.44-0.85) |
| ≥2 | 36/59 | 23.5 | 23/63 | NE | 0.51 (0.30-0.86) |



PFS, progression-free survival; Rd, lenalidomide/dexamethasone; D-Rd, daratumumab/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.

**Figure 3. Subgroup analysis of PFS.**

*Bahlis et al, ASH 2019 Poster 1875*

# Poster 1875: Daratumumab Plus Lenalidomide and Dexamethasone (D-Rd) Versus Lenalidomide and Dexamethasone (Rd) in Patient with Newly Diagnosed Multiple Myeloma (NDMM) Ineligible for Transplant: Updated Analysis of MAIA

## CONCLUSIONS

- After a median follow-up of 36.4 months, the addition of DARA to Rd continues to demonstrate a significant PFS benefit and improved rates of deeper and more durable responses, including a tripling of the MRD-negativity rate, versus Rd alone in patients with TIE NDMM
  - The estimated 36-month PFS rate was substantially higher for D-Rd than Rd
  - Importantly, 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
  - PFS2 may be considered a surrogate for overall survival; longer overall survival is anticipated in patients receiving D-Rd versus Rd
- No new safety concerns were observed
- These results continue to support the use of D-Rd in the first line of treatment for TIE patients with NDMM



*Bahlis et al, ASH 2019 Poster 1875*

# Daratumumab Data:

# Phase III POLLUX & CASTOR Update

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

Genmab

# Poster 1866: Four-Year Follow-up of the Phase 3 POLLUX Study of Daratumumab Plus Lenalidomide and Dexamethasone (D-Rd) Versus Lenalidomide and Dexamethasone (Rd) Alone in Relapsed or Refractory Multiple Myeloma (RRMM)

Jonathan L. Kaufman,[1,*] Saad Z. Usmani,[2] Jesus San-Miguel,[3] Nizar J. Bahlis,[4] Darrell White,[5] Lotfi Benboubker,[6] Gordon Cook,[7] Merav Leiba,[8] P. Joy Ho,[9] Kihyun Kim,[10] Naoki Takezako,[11] Philippe Moreau,[12] Maria Krevvata,[13] Huiling Pei,[14] Jon Ukropec,[15] Thomas Renaud,[16] Sonali Trivedi,[13] Rachel Kobos,[16] Meletios A. Dimopoulos[17]

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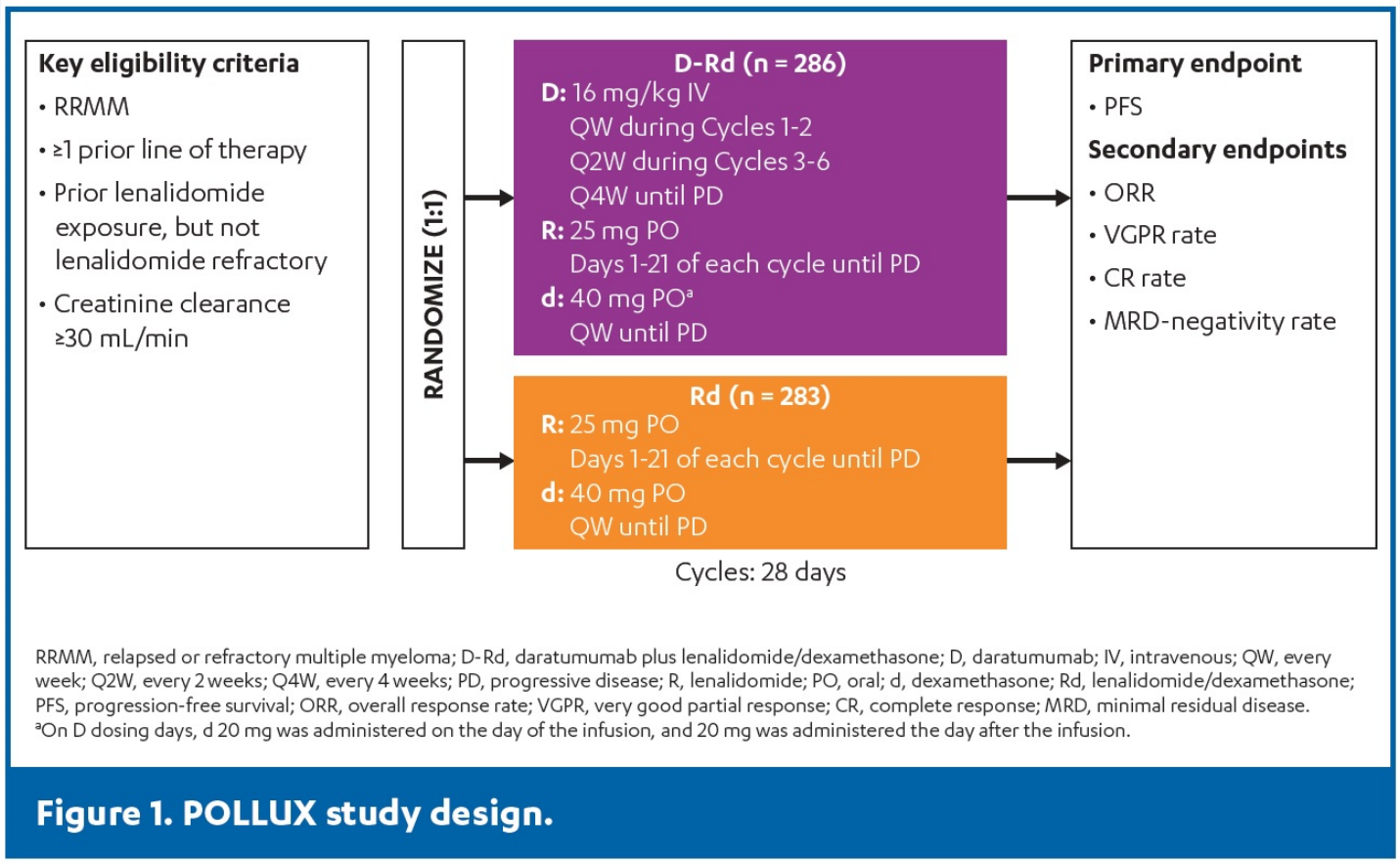
# Poster 1866: Four-Year Follow-up of the Phase 3 POLLUX Study of Daratumumab Plus Lenalidomide and Dexamethasone (D-Rd) Versus Lenalidomide and Dexamethasone (Rd) Alone in Relapsed or Refractory Multiple Myeloma (RRMM)



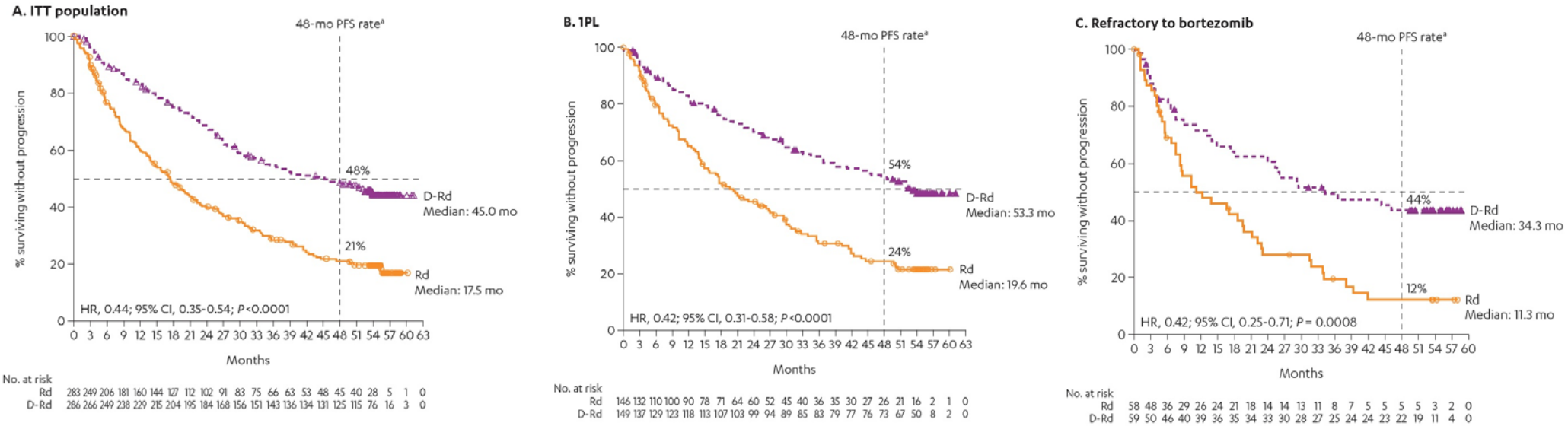

RRMM, relapsed or refractory multiple myeloma; D-Rd, daratumumab plus lenalidomide/dexamethasone; D, daratumumab; IV, intravenous; QW, every week; Q2W, every 2 weeks; Q4W, every 4 weeks; PD, progressive disease; R, lenalidomide; PO, oral; d, dexamethasone; Rd, lenalidomide/dexamethasone; PFS, progression-free survival; ORR, overall response rate; VGPR, very good partial response; CR, complete response; MRD, minimal residual disease.
[a]On D dosing days, d 20 mg was administered on the day of the infusion, and 20 mg was administered the day after the infusion.

**Figure 1. POLLUX study design.**



*Kaufman et al, ASH 2019 Poster 1866*

# Poster 1866: Four-Year Follow-up of the Phase 3 POLLUX Study of Daratumumab Plus Lenalidomide and Dexamethasone (D-Rd) Versus Lenalidomide and Dexamethasone (Rd) Alone in Relapsed or Refractory Multiple Myeloma (RRMM)




PFS, progression-free survival; ITT, intent-to-treat; 1PL, 1 prior line of therapy; D-Rd, daratumumab plus lenalidomide/dexamethasone; Rd, lenalidomide/dexamethasone; HR, hazard ratio; CI, confidence interval.
[a]Kaplan–Meier estimate.

- After a median (range) follow-up of 54.8 (0-61.9) months, D-Rd significantly prolonged PFS versus Rd in the ITT population (median: 45.0 vs 17.5 months; HR, 0.44; 95% CI, 0.35-0.54; P<0.0001; Figure 2A)
  - D-Rd prolonged PFS versus Rd among patients who received 1 prior line of therapy (1PL; Figure 2B)
  - D-Rd also prolonged PFS versus Rd among patients who were refractory to bortezomib (Figure 2C)



*Kaufman et al, ASH 2019 Poster 1866*

# Poster 1866: Four-Year Follow-up of the Phase 3 POLLUX Study of Daratumumab Plus Lenalidomide and Dexamethasone (D-Rd) Versus Lenalidomide and Dexamethasone (Rd) Alone in Relapsed or Refractory Multiple Myeloma (RRMM)

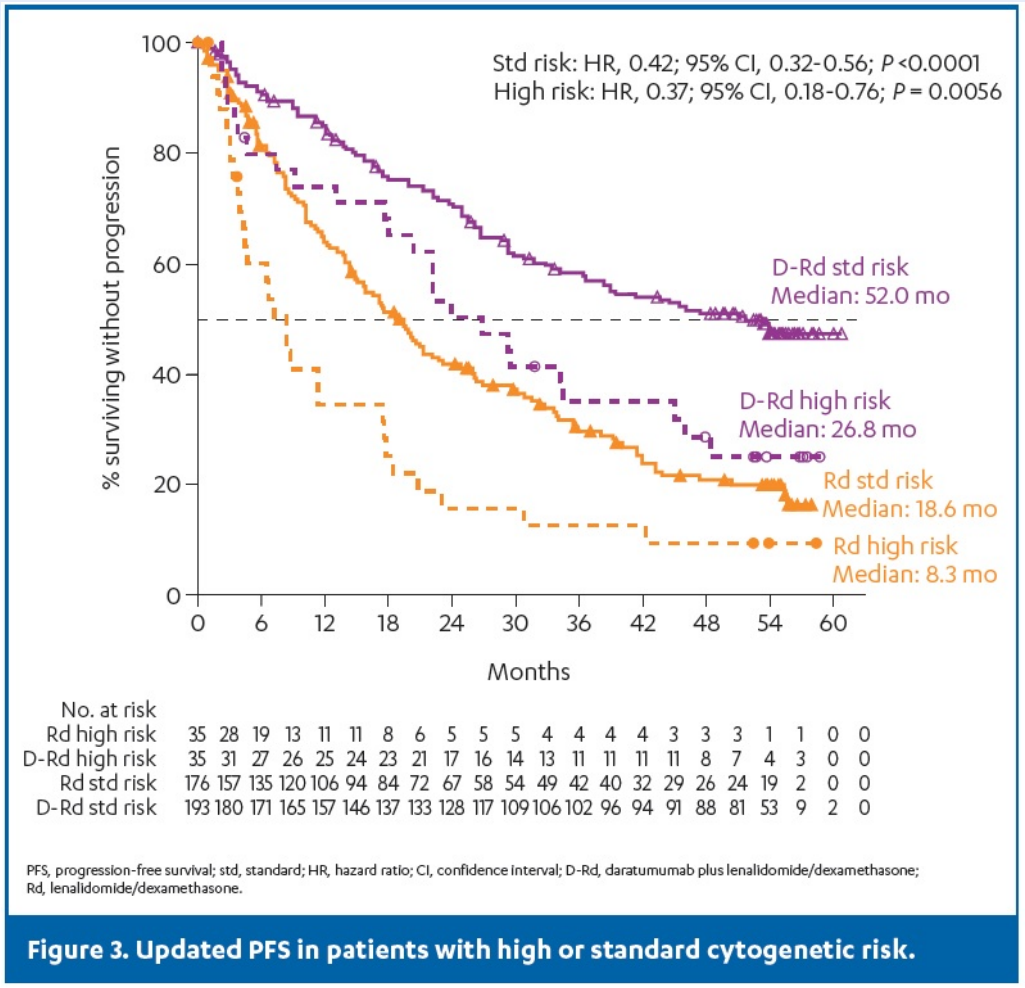



**Figure 3. Updated PFS in patients with high or standard cytogenetic risk.**

*Kaufman et al, ASH 2019 Poster 1866*

# Poster 1866: Four-Year Follow-up of the Phase 3 POLLUX Study of Daratumumab Plus Lenalidomide and Dexamethasone (D-Rd) Versus Lenalidomide and Dexamethasone (Rd) Alone in Relapsed or Refractory Multiple Myeloma (RRMM)

## CONCLUSIONS

- After >4 years of median follow-up, D-Rd continued to demonstrate significant efficacy benefits versus Rd alone in RRMM patients
  - PFS benefit was seen among patients who had 1PL and those with high or standard cytogenetic risk, as well as among patients with bortezomib refractoriness
  - D-Rd versus Rd achieved higher ORRs and deeper responses
  - D-Rd improved the rate of MRD negativity and was associated with sustained MRD negativity
- No new safety concerns were identified with longer follow-up
- These updated results continue to support the use of daratumumab combination therapies in patients with RRMM after 1PL

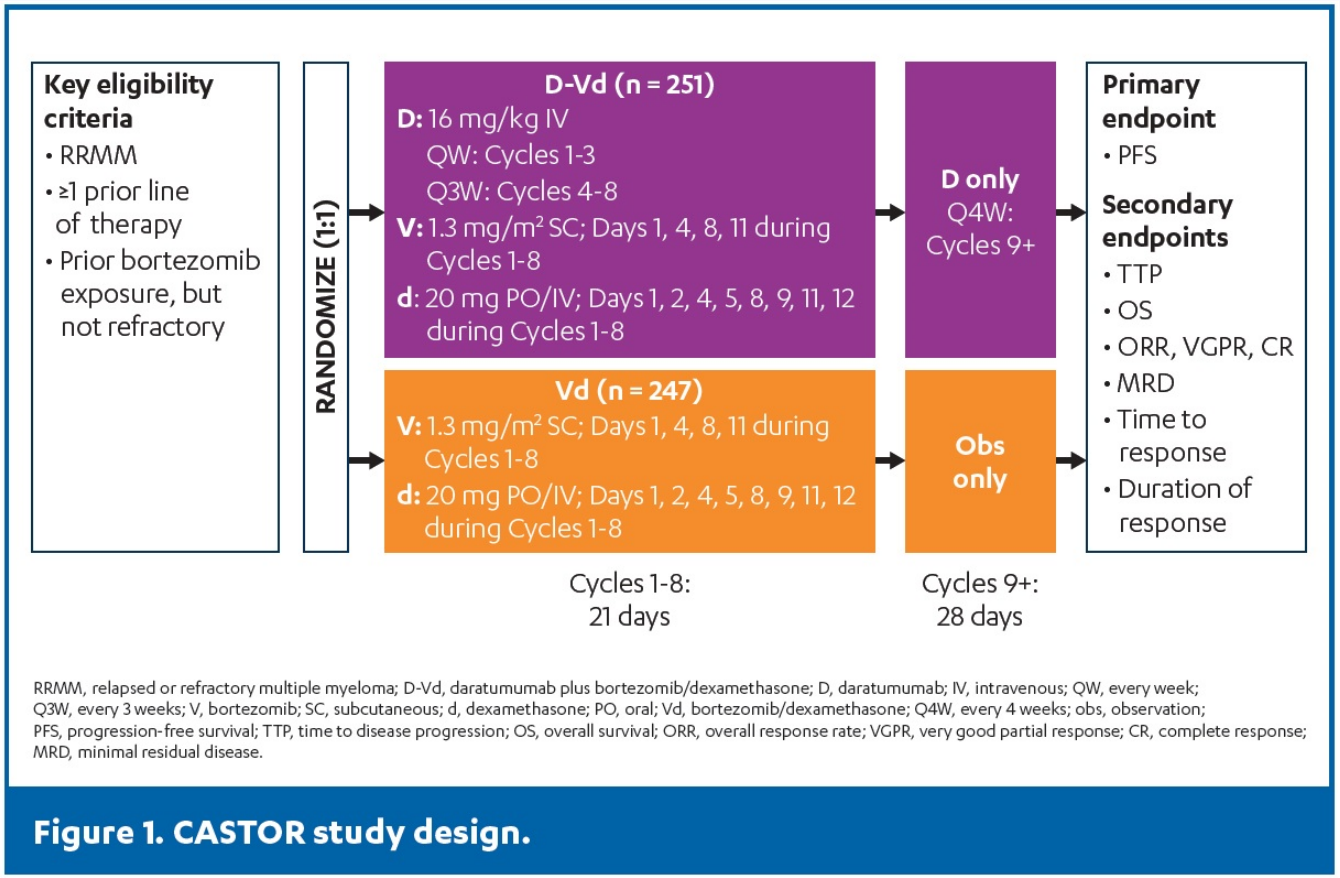
*Kaufman et al, ASH 2019 Poster 1866*

# Poster 3192: Efficacy and Safety of Daratumumab, Bortezomib and Dexamethasone (D-Vd) Versus Bortezomib and Dexamethasone (Vd) in First Relapse Patients (pts) with Multiple Myeloma (MM): Four-Year update of CASTOR

Katja Weisel,[1,*] Pieter Sonneveld,[2] Maria-Victoria Mateos,[3] Vania Hungria,[4] Andrew Spencer,[5] Jane Estell,[6] Wolney Barreto,[7] Paolo Corradini,[8] Chang-Ki Min,[9] Eva Medvedova,[10] Maria Krevvata,[11] Sonali Trivedi,[11] Xiang Qin,[11] Huiling Pei,[12] Jon Ukropec,[13] Rachel Kobos,1[4] Ming Qi,1[1] Ajay K. Nooka[15]

1University Medical Center of Hamburg-Eppendorf, Hamburg, Germany, and University of Tuebingen, Tuebingen, Germany; 2Erasmus MC, Rotterdam, The Netherlands; 3University Hospital of Salamanca/IBSAL, Salamanca, Spain; 4Santa Casa Medical School, São Paulo, Brazil; 5Malignant Haematology and Stem Cell Transplantation Service, Alfred Health-Monash University, Melbourne, Australia; 6Haematology Department, Concord Cancer Centre, Concord Hospital, Concord, NSW, Australia; 7Hospital Santa Marcelina, São Paulo, Brazil; 8Fondazione IRCCS Instituto Nazionale dei Tumori, Milan, Italy; 9Seoul St. Mary's Hospital, Seoul, The Republic of Korea; 10Oregon Health & Science University, Portland, OR, USA; 11Janssen Research & Development, LLC, Spring House, PA, USA; 12Janssen Research & Development, LLC, Titusville, NJ, USA; 13Janssen Global Medical Affairs, Horsham, PA, USA; 14Janssen Research & Development, LLC, Raritan, NJ, USA; 15Winship Cancer Institute, Emory University, Atlanta, GA, USA.

# Poster 3192: Efficacy and Safety of Daratumumab, Bortezomib and Dexamethasone (D-Vd) Versus Bortezomib and Dexamethasone (Vd) in First Relapse Patients (pts) with Multiple Myeloma (MM): Four-Year update of CASTOR

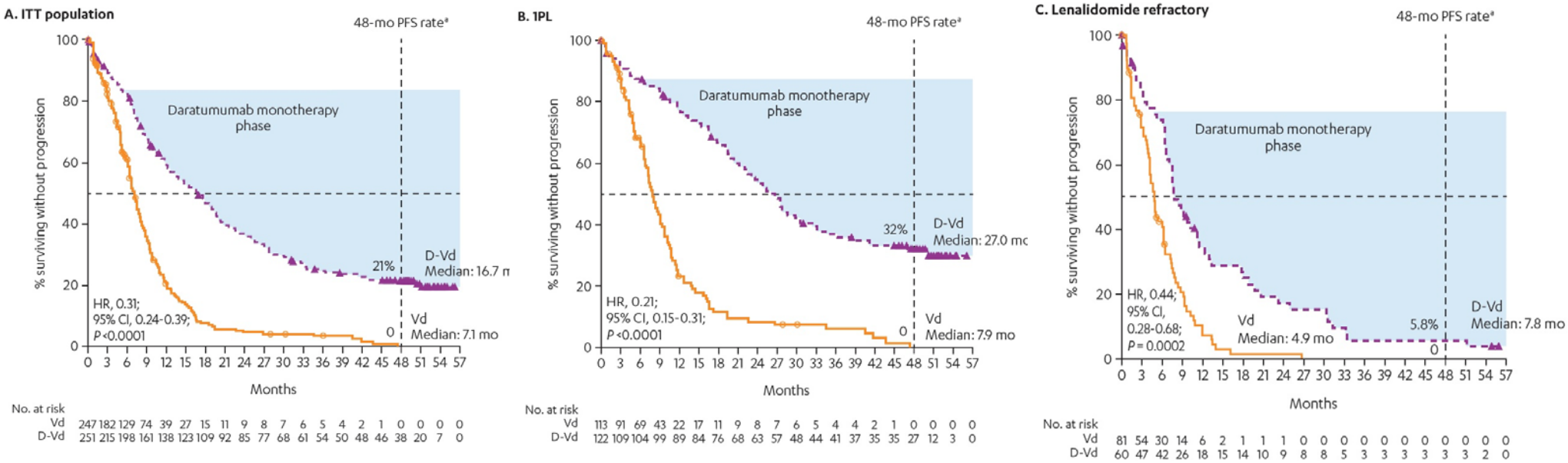



RRMM, relapsed or refractory multiple myeloma; D-Vd, daratumumab plus bortezomib/dexamethasone; D, daratumumab; IV, intravenous; QW, every week; Q3W, every 3 weeks; V, bortezomib; SC, subcutaneous; d, dexamethasone; PO, oral; Vd, bortezomib/dexamethasone; Q4W, every 4 weeks; obs, observation; PFS, progression-free survival; TTP, time to disease progression; OS, overall survival; ORR, overall response rate; VGPR, very good partial response; CR, complete response; MRD, minimal residual disease.

**Figure 1. CASTOR study design.**

*Weisel et al, ASH 2019 Poster 3192*

# Poster 3192: Efficacy and Safety of Daratumumab, Bortezomib and Dexamethasone (D-Vd) Versus Bortezomib and Dexamethasone (Vd) in First Relapse Patients (pts) with Multiple Myeloma (MM): Four-Year update of CASTOR




PFS, progression-free survival; ITT, intent-to-treat; 1PL, 1 prior line of therapy; D-Vd, daratumumab plus bortezomib/dexamethasone; HR, hazard ratio; CI, confidence interval; Vd, bortezomib/dexamethasone.
[a]Kaplan–Meier estimate.

- After a median follow-up of 50.2 months, PFS was significantly prolonged with D-Vd versus Vd in the ITT population (median: 16.7 vs 7.1 months; HR, 0.31; 95% CI, 0.24-0.39; P<0.0001; Figure 2A)
  - In patients receiving 1PL, D-Vd versus Vd improved PFS (Figure 2B)
  - PFS was also improved with D-Vd versus Vd among patients who were refractory to lenalidomide (Figure 2C)



*Weisel et al, ASH 2019 Poster 3192*

# Poster 3192: Efficacy and Safety of Daratumumab, Bortezomib and Dexamethasone (D-Vd) Versus Bortezomib and Dexamethasone (Vd) in First Relapse Patients (pts) with Multiple Myeloma (MM): Four-Year update of CASTOR

## CONCLUSIONS

- With >4 years of median follow-up, D-Vd continued to demonstrate significant efficacy benefits versus Vd alone in RRMM patients
  - D-Vd induced deeper and more durable responses and improved MRD-negativity rates
  - PFS benefit with D-Vd was seen in both standard and high cytogenetic risk groups
- Efficacy benefits with D-Vd were especially pronounced in patients who received 1PL of therapy regardless of prior treatment with lenalidomide
  - Patients with 1PL of therapy had a 79% reduction in risk of disease progression or death versus Vd
- The safety profile of D-Vd remained consistent with longer follow-up, with no new safety concerns identified
  - A higher rate of invasive secondary primary malignancies was noted for patients who received D-Vd versus Vd, similar to previously reported CASTOR results[8,13]; other phase 3 studies of daratumumab combination therapy reported balanced rates of secondary primary malignancies in both the daratumumab and control groups[9,11-14]
- These updated results continue to support the use of daratumumab combination therapies in patients with RRMM after 1PL

*Weisel et al, ASH 2019 Poster 3192*

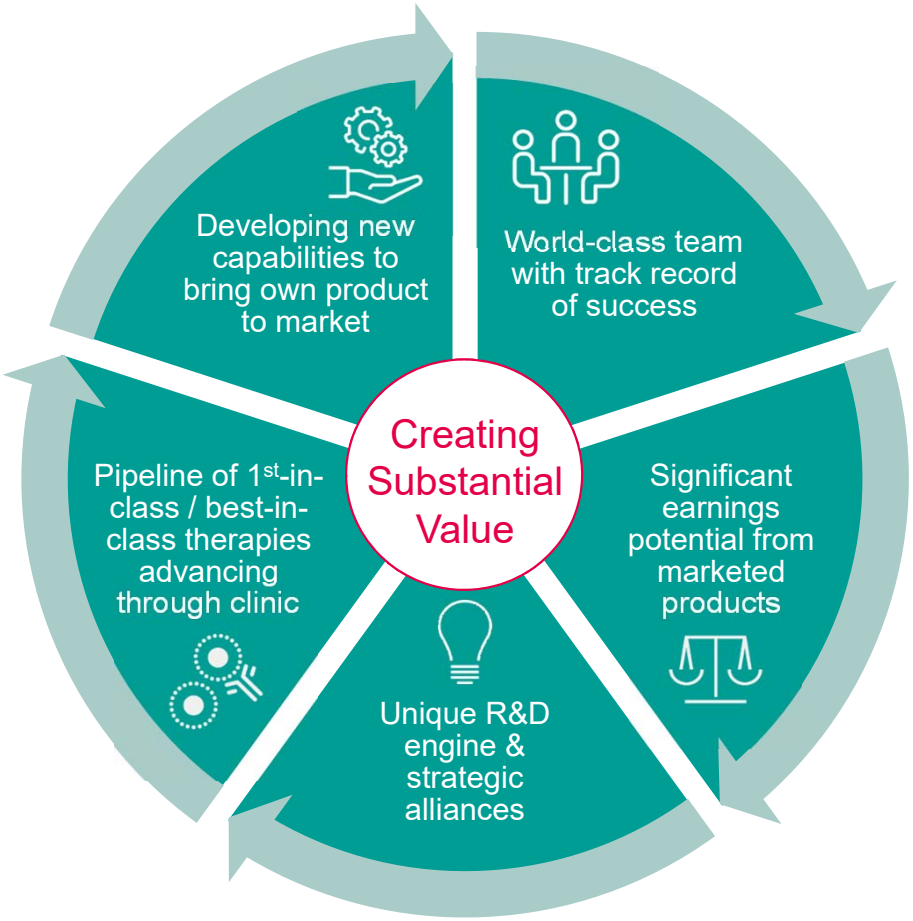
# Daratumumab Q&A

# 2020 & Beyond: Positioned for Success

Dr. Jan van de Winkel
President & CEO

Genmab

# Delivering on Genmab's Promise: Innovating Antibodies, Improving Lives



# Key 2020 Priorities

## Building a Strong Differentiated Product Pipeline

| Priority | ✓ | Targeted Milestones |
|---|---|---|
| Genmab proprietary* products | | » Tisotumab vedotin[1] - Phase II innovaTV 204 safety & efficacy analysis in recurrent/metastatic cervical cancer and engage U.S. FDA for BLA submission subject to trial results<br>» Tisotumab vedotin - data on other solid tumor types<br>» Enapotamab vedotin – data to support late stage development<br>» DuoBody-CD3xCD20 Phase I/II – decision on recommended Phase II dose & initiate expansion cohorts<br>» HexaBody-DR5/DR5 Phase I/II - advance dose escalation<br>» DuoBody-PD-L1x4-1BB[2] Phase I/II – initiate expansion cohorts<br>» File INDs and/or CTAs for 2 new products |
| Daratumumab[3] | | » U.S. FDA and EMA decision on Phase III COLUMBA multiple myeloma SubQ submission<br>» sBLA and MAA Submission Phase III ANDROMEDA amyloidosis<br>» sBLA and MAA submission Phase III APOLLO multiple myeloma |
| Ofatumumab[4] | | » U.S. FDA decision on regulatory dossier submission in multiple sclerosis |
| Teprotumumab[5] | | » U.S. FDA decision on Phase III OPTIC active thyroid eye disease submission |

*Certain product candidates in development with partners, as noted.
1. 50:50 dev. w/ Seattle Genetics; 2. 50:50 dev. w/ BioNTech; 3. In dev. w/ Janssen; 4. In dev. by Novartis; 5. In dev. w/ Horizon Therapeutics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