DARA Monotherapy Studies



- ≥18 years of age, ECOG status ≤2^{1,2}
- GEN501¹
 - Open-label, multicenter, phase 1/2, dose-escalation and dose-expansion study
 - Relapsed from or refractory to ≥2 prior lines of therapy including PIs and IMiDs
- SIRIUS²
 - Open-label, multicenter, phase 2 study
 - Patients had received ≥3 prior lines of therapy, including a PI and an IMiD, or were double refractory to a PI and an IMID
- DARA was approved by the FDA on November 16, 2015, based on these studies

Baseline Characteristics

		16 mg/kg	
	GEN501, Part 2	SIRIUS	Combined
	n = 42	n = 106	N = 148
Median (range) age, y	64.0 (44-76)	63.5 (31-84)	64 (31-84)
≥65 years of age, n (%)	20 (48)	48 (45)	68 (46)
Female/male sex, %	36/64	51/49	53/47
ECOG score, n (%) 0 1 2	12 (29) 28 (67) 2 (5)	29 (27) 69 (65) 8 (8)	41 (28) 97 (66) 10 (7)
Median (range) time since diagnosis, y	5.8 (0.8-23.7)	4.8 (1.1-23.8)	5.1 (0.8-23.8)
Median (range) number of prior lines of therapy >3 prior lines of therapy, n (%)	4 (2-12)	5 (2-14)	5 (2-14)
	26 (62)	87 (82)	113 (76)
Prior ASCT, n (%)	31 (74)	85 (80)	116 (78)
Prior PI, n (%)	42 (100)	106 (100)	148 (100)
Bortezomib	42 (100)	105 (99)	147 (99)
Carfilzomib	8 (19)	53 (50)	61 (41)
Prior IMiD, n (%)	40 (95)	106 (100)	146 (99)
Lenalidomide	40 (95)	105 (99)	145 (98)
Pomalidomide	15 (36)	67 (63)	82 (55)
Thalidomide	19 (45)	47 (44)	66 (45)

Baseline Refractory Status

	16 mg/kg			
Refractory to,	GEN501, Part 2	SIRIUS	Combined	
n (%)	11 - 42	11 – 100	IN - 140	
Last line of therapy	32 (76)	103 (97)	135 (91)	
Both PI and IMiD	27 (64)	101 (95)	128 (86)	
Plonly	3 (7)	3 (3)	6 (4)	
IMiD only	4 (10)	1 (1)	5 (3)	
PI + IMiD + alkylating agent	21 (50)	79 (75)	100 (68)	
Bortezomib	30 (71)	95 (90)	125 (84)	
Carfilzomib	7 (17)	51 (48)	58 (39)	
Lenalidomide	31 (74)	93 (88)	124 (84)	
Pomalidomide	15 (36)	67 (63)	82 (55)	
Thalidomide	12 (29)	29 (27)	41 (28)	
Alkylating agent only	25 (60)	82 (77)	107 (72)	

Relapsed and Refractory MM

Median overall survival in the combined eligible population from the IMS LifeLink and OPTUM datasets (N = 662) and double refractory (n = 350) and triple/quadruple refractory (n = 93) patients.



Efficacy in Combined Analysis

Median Follow up 20.7 months

		16 mg/kg (N = 148)		
	Response	n (%)	95% CI	
	ORR	46 (31.1)	23.7-39.2	
	Clinical benefit (ORR + MR)	55 (37.2)	29.4-45.5	
ſ	VGPR or better (sCR+CR+VGPR)	20 (13.5)	8.5-20.1	
	CR or better (sCR+CR)	7 (4.7)	1.9-9.5	
83.1 %	sCR CR VGPR PR MR SD PD NE	3 (2.0) 4 (2.7) 13 (8.8) 26 (17.6) 9 (6.1) 68 (45.9) 18 (12.2) 7 (4.7)	0.4-5.8 0.7-6.8 4.8-14.6 11.8-24.7 2.8-11.2 37.7-54.3 7.4-18.5 1.9-9.5	

- Median DOR = 7.6 (95% CI, 5.6-NE) months
- ORR = 31% and was consistent in subgroups including age, number of prior lines of therapy, refractory status, or renal function
- Time to response = 0.95 (0.5-5.6) months

Efficacy in Combined Analysis - Subgroups



Responses were seen across all subgroups regardless of prior lines of therapy, refractory status, renal function, and baseline percentage of plasma cells in the bone marrow

PFS

median follow-up 20.7 months



OS



- For the combined analysis, median OS = 20.1 months (95% CI, 16.6-NE months)
- 18-month and 24-month OS rate = 56.5% and 45% respectively

Usmani, SZ. Blood. 2016. http://dx.doi.org/10.1182/blood-2016-03-705210.

The Breakthrough (BT) population outcome



Months from Start of Treatment

mOS 5-8 months in patients
relapsed or refractory MM after ≥3
prior lines of therapy, including
IMID and PI

Pomalidomide: mOS

13,1months in patients relapsed or refractory MM after ≥2 prior lines of therapy, including IMID and PI

Daratumumab: mOS of 20

months in patients with relapsed or refractory, double refractory or relapsed after ≥3 L, including pomalidomide and carfilzomib

Usmani et al., Oncologist 2016; *doi:10.1634/theoncologist.2016-0104* Usmani, SZ. Blood. 2016. http://dx.doi.org/10.1182/blood-2016-03-705210. *Jesus San Miguel et.al, Lancet 2013*

Comparative Efficacy of Daratumumab Monotherapy and Pomalidomide Plus Low-dose Dexamethasone (POM+LoDex) in the Treatment of Multiple Myeloma: A Matching Adjusted Indirect Comparison (MAIC)

Suzy Van Sanden,¹ Tetsuro Ito,^{3*} Martin Vogel,³ Joris Diels¹

"Jamaen Health Economics & Market Access & MEA 32 atolics & Modeling, Beene, Belgium, "Jamaen Health Economics & Market Access & MEA, High Wycombe, UK;

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*Jansen EMEA Medical Alfairs, Neuro, Germany

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OBJECTIVE

METHODS

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POSTER PRESENTED AT THE 19TH ANNUAL EUROPEAN CONGRESS OF THE INTERNATIONAL SOCIETY FOR

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MAIC of OS among patients treated with DARA versus POM+LoDex in the ITT population and POM-naïve population

Due to the high percentage of POM-refractory patients (55%) treated with DARA in GEN501 and SIRIUS who were not included in the POM-naïve MM-003 study, the OS advantage of DARA may be a conservative estimate



HR 0.56 (0.38-0.83);p= 0.0041

HR 0.33 (0.17-0.66);p= 0.0017

- The primary analysis suggests a 44% reduction in the risk of death compared with POM+LoDex
- Comparison of POM-naïve patients from both studies suggests a 67% reduction in the risk of death compared with POM+LoDex

Suzy van sanden, et al. Poster 19th annual european congress of the international society for pharmacoeconomics and outcomes research (ispor-eu); 29 october-2 november 2016; vienna, austria.

CASTOR: Study Design

Multicenter, randomized, open-label, active-controlled phase 3 study



Daratumumab IV administered in 1000 mL to 500 mL; gradual escalation from 50 mL to 200 mL/hour permitted

Baseline Demographics and Clinical Characteristics

Characteristic	DVd (n = 251)	Vd (n = 247)	Characteri	stic	DVd (n = 251)	Vd (n = 247)
Age, years			Prior lines of therap	oy, n (%)		
Median (range)	64 (30-88)	64 (33-85)	1		122 (49)	113 (46)
≥75, n (%)	23 (9)	35 (14)	2		70 (28)	74 (30)
ISS staging n (%) ^a			3		37 (15)	32 (13)
	98 (39)	96 (39)	>3		22 (9)	28 (11)
	94 (38)	100 (41)	Prior ASCT, n (%)		156 (62)	149 (60)
III	59 (24)	51 (21)	Prior PI, n (%)		169 (67)	172 (70)
Cytogenetic profile, n (%) ^b			Prior IMiD, n (%)		179 (71)	198 (80)
Del17p	28 (16)	21 (12)	Prior PI + IMiD, n (%)	112 (45)	129 (52)
t(4;14)	14 (8)	15 (9)	Refractory to IMiD,	, n (%)	74 (30)	90 (36)
Time from diagnosis, years	3.87	3.72	Refractory to			
Median (range)	(0.7-20.7)	(0.6-18.6)	last line of therapy,	n (%)	76 (30)	85 (34)

Updated Efficacy



- Median (range) follow-up: 13.0 (0-21.3) months
- An additional 7% of patients receiving DVd achieved ≥CR with longer follow-up

Responses continue to deepen in the DVd group with longer follow-up

ITT, intent-to-treat. Note: PFS = ITT population; ORR = response-evaluable population. ^aKaplan-Meier estimate. ^bP <0.0001 for DVd versus Vd.

PFS: Prior Lines of Treatment



with greatest benefit observed in 1 prior line

Maria-Victoria Mateos, Abstract 1150 ASH 2016

ORR by Prior Lines^a



More patients achieve a deeper response with DVd after 1 prior line of treatment

^aResponse-evaluable population. ^bP = 0.0006 for DVd vs Vd. ^cP <0.0001 for DVd vs Vd. ^dP = 0.0133 for DVd vs Vd.

Maria-Victoria Mateos, Abstract 1150 ASH 2016



MRD rates by prior lines of therapy

 MRD was evaluated by ClonoSEQ-NGS—based assay in a central laboratory at 3 sensitivity thresholds, for patients with suspected CR and also for patients who maintain CR at Cycle 9 and Cycle 15

MRD-negative rates for DVd were ≥3-fold higher across all thresholds

***P <0.0001. **P <0.01. NS, not significant; NGS, next-generation sequencing. P values calculated using likelihood-ratio chi-square test. MRD-negativity rate = proportion of patients with negative MRD test results at any time during treatment.

PFS: MRD Status (10⁻⁵)



MRD negativity is associated with better outcomes

PFS: Cytogenetic Risk in All Evaluable Patients^a



DVd improves outcomes regardless of cytogenetic risk

NR, not reached.

^aITT/Biomarker risk–evaluable analysis set. ^bCentral NGS. High-risk patients had any of t(4;14), t(14;16), or del17p. Standard-risk patients had an absence of high-risk abnormalities.

Maria-Victoria Mateos, Abstract 1150 ASH 2016



Median OS was NR; results did not cross the prespecified stopping boundary.

Time to Response



Palumbo, A. N Engl J Med 2016.375(8):754-766.

Palumbo A, et al. ASCO 2016. Abstract LBA4.

Most Common TEAEs (All Patients): Updated Analysis

	DVd (n = 243)		Vd (n =	= 237)
Homotologic n (%)	All grade	Grade 3/4	All grade	Grade 3/4
nematologic, n (<i>%</i>)	≥25% ^a	≥5% ^a	≥25% ª	≥5% ^a
Thrombocytopenia	145 (60)	110 (45)	105 (44)	78 (33)
Anemia	67 (28)	36 (15)	75 (32)	38 (16)
Neutropenia	45 (19)	32 (13)	23 (10)	11 (5)
Lymphopenia	32 (13)	24 (10)	9 (4)	6 (3)
Nonhematologic, n (%)				
Peripheral sensory neuropathy	120 (49)	11 (5)	90 (38)	16 (7)
Diarrhea	83 (34)	9 (4)	53 (22)	3 (1)
Upper respiratory tract infection	72 (30)	6 (3)	43 (18)	1 (0.4)
Cough	66 (27)	0	30 (13)	0
Fatigue	53 (22)	12 (5)	58 (25)	8 (3)
Pneumonia	33 (14)	22 (9)	28 (12)	23 (10)
Hypertension	22 (9)	16 (7)	8 (3)	2 (0.8)

- Grade 3/4 TEAEs: 79% of DVd patients versus 63% of Vd patients
- Discontinuations due to TEAEs: 9% of DVd patients versus 9% of Vd patients^b
- No new IRRs; incidence remains stable with longer follow-up (45%)

Infusion-related Reactions (IRRs)

	Safety Analysis Set (n = 243)		
	All grades	Grade 3	
Patients with IRRs, %	45	9	
Most common (>5%) IRRs			
Dyspnea	11	2	
Bronchospasm	9	3	
Cough	7	0	

- No grade 4 or 5 IRRs observed
- 98% of patients with IRRs experienced the event on the first infusion
- 2 patients discontinued due to IRRs
 - Bronchospasm in the first patient
 - Bronchospasm, laryngeal edema, and skin rash in the second patient

Preinfusion: dexamethasone 20 mg, paracetamol 650-1000 mg, diphenhydramine 25-50 mg Stop infusion immediately for mild symptoms; once resolved, resume at half the infusion rate

POLLUX: Study Design

Multicenter, randomized (1:1), open-label, active-controlled phase 3 study



Pre-medication for the DRd treatment group consisted of dexamethasone 20 mg^a, paracetamol, and an antihistamine

Dimopoulos MA, et al. N Engl J Med 2016;375:1319-1331.

Baseline Demographics and Clinical Characteristics (cont.)

Characteristic	DRd (n = 286)	Rd (n = 283)
Prior ASCT, %	63	64
Prior PI, %	86	86
Prior IMiD, % Prior lenalidomide, %	55 18	55 18
Prior PL + IMiD %	44	44
	44	44
Refractory to PI, %	20	16
Refractory to last line of therapy, %	28	27

Updated Efficacy

Median (range) follow-up: 17.3 (0-24.5) months



Responses continue to deepen in the DRd group with longer follow-up

HR, hazard ratio; CI, confidence interval; sCR, stringent complete response; PR, partial response; ITT, intent-to-treat. Note: PFS = ITT population; ORR = response-evaluable population. ^aKaplan-Meier estimate. ^bP <0.0001 for DRd vs Rd.

MRD-negative Rate



MRD-negative rates were >3-fold higher at all thresholds

ITT population. *P* values are calculated using likelihood-ratio chi-square test.

Usmani abstract 489 ASH meeting 2016

Refractory to Last Line of Therapy



DRd benefits patients refractory to last line of therapy

^aKaplan-Meier estimate. ^bResponse-evaluable population. ^c*P* <0.0001 for DRd vs Rd.

Usmani abstract 489 ASh meeting 2016

PFS: Cytogenetic Risk in All Evaluable Patients^a



NR, not reached; NS, not significant.

aITT/Biomarker risk-evaluable analysis set. High-risk patients had any of t(4;14), t(14;16), or del17p. Standard-risk patients had an absence of high-risk abnormalities.

OS

Median (range) follow-up: 17.3 (0-24.5) months

ITT population.

Median OS was not reached; results did not cross the prespecified stopping boundary.

PFS: Prior Lenalidomide Treatment

No Prior Lenalidomide Treatment Prior Lenalidomide Treatment 18-month 18-month **PFS**^a **PFS**^a 79% % surviving without progression % surviving without progression 76% 🔁 DRd DRd 59% 60 -Rd 49% 40 -Rd Median: 17.1 months HR: 0.45 (95% CI, 0.20-0.99; P = 0.042) (95% CI, 0.26-0.51; *P* <0.0001) HR: 0.37 27 24 a Months Months No. at risk No. at risk 37 30 38 37 Rd Rd DRd DRd

Treatment effect is consistent regardless of prior lenalidomide exposure

Philippe Moreau, abstract 1151 ASH 2016

Time to Response

Dimopoulos MA, et al. *N Engl J Med* 2016;375:1319-1331.

Most Common AEs (All Patients): Updated Analysis

	DRd (n = 283)		Rd (n	= 281)
Hematologic, %	All grade ≥25%ª	Grade 3/4 ≥5% ^a	All grade ≥25%ª	Grade 3/4 ≥5% ^a
Neutropenia Febrile neutropenia	60 6	53 6	44 3	38 3
Anemia Thrombocytopenia	34 28	14 13	36 30	21 15
Lymphopenia	6	5	5	4
Nonhematologic, %				
Diarrhea	47	6	28	3
Fatigue	35	6	29	3
Upper respiratory tract infection	33	1	23	1
Cough	30	0	13	0
Constipation	30	1	26	0.7
Muscle spasms	27	0.7	20	2
Nasopharyngitis	26	0	17	0
Nausea	25	1	16	0.4
Pneumonia	16	9	13	8

No new safety signals reported

AE, adverse event. ^aCommon treatment-emergent AEs listed are either ≥25% all grade OR ≥5% grade 3/4.

Infusion-related Reactions (IRRs)

IRRs ≥2%	Safety Analysis Set (n = 283)		
	All grades (%)	Grade 3 (%)	
Patients with IRRs	48	5	
Cough	9	0	
Dyspnea	9	0.7	
Vomiting	6	0.4	
Nausea	5	0	
Chills	5	0.4	
Bronchospasm	5	0.4	
Pruritus	3	0.4	
Throat irritation	3	0	
Headache	3	0	
Nasal congestion	3	0	
Wheezing	2	0.7	
Laryngeal edema	2	0.4	
Rhinorrhea	2	0	
Pyrexia	2	0	

- No grade 4 or 5 IRRs were reported
- 92% of all IRRs occurred during the first infusion
- 1 patient discontinued daratumumab due to an IRR

Dimopoulos MA, et al. N Engl J Med 2016;375:1319-1331.

Lenalidomide-based Studies

	POLLUX DRd vs Rd	ASPIRE KRd vs Rd ¹	ELOQUENT-2 ERd vs Rd ^{2,3}	TOURMALINE-MM1 NRd vs Rd⁴
PFS HR (95% CI)	0.37 (0.27-0.52)	0.69 (0.57-0.83)	0.73 (0.60-0.89)	0.74 (0.59-0.94)
ORR	93%	87%	79%	78%
≥VGPR	76%	70%	33%	48%
≥CR	43%	32%	4%	14%
Duration of response, mo	D NE	28.6	20.7	20.5
OS HR (95% CI)	0.64 (0.40-1.01)	0.79 (0.63-0.99)	0.77 (0.61-0.97)	NE

1. Stewart AK, et al. *N Engl J Med*. 2015;372(2):142-152.

2. Lonial S, et al. N Engl J Med. 2015;373(7):621-631.

3. Dimopoulos MA, et al. *Blood*. 2015;126(23):Abstract 28.

4. Moreau P, et al. N Engl J Med. 2016;374(17):1621-1634.

Dimopoulos MA, et al. *N Engl J Med* 2016;375:1319-1331.

Phase 1b Study of Daratumumab Plus Pomalidomide and Dexamethasone in Relapsed and/or Refractory Multiple Myeloma (RRMM) With ≥2 Prior Lines of Therapy

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Rationale for DARA + POM-D

- In a randomized, phase 3 study, pomalidomide plus low-dose dexamethasone (POM-D) in patients relapsed from or refractory to previous treatment with bortezomib or lenalidomide resulted in the following¹:
 - Overall response rate (ORR) = 31%
 - Median progression-free survival (PFS) = 4.0 months
 - Median overall survival (OS) = 12.7 months
- Pomalidomide increases CD38 expression in a time- and dose-dependent fashion in multiple myeloma (MM) cells²
- Increases in T-cell clonality were observed with DARA plus lenalidomide and dexamethasone (Rd) but not with Rd alone in POLLUX³

1. San Miguel J, et al. *Lancet Oncol.* 2013;14(11):1055-1066.

2. Boxhammer R, et al. Presented at: 51st American Society of Clinical Oncology (ASCO) Annual Meeting; May 29-June 2, 2015; Chicago, IL. Abstract 8588.

3. Chiu, C. et al. Presented at: 58th American Society of Hematology (ASH) Annual Meeting & Exposition; December 3-6, 2016; San Diego, CA. Abstract 4531

MMY1001: DARA + POM-D Cohort

Eligibility criteria

- Refractory to last line of therapy
- ≥2 prior lines of therapy, including
 2 consecutive cycles of lenalidomide
 and bortezomib
- Pomalidomide naïve
- Eastern Cooperative Oncology Group (ECOG) score ≤2
- Absolute neutrophil count ≥1.0×10⁹/L, and platelet count ≥75×10⁹/L for patients with >50% plasma cells
- Calculated creatinine clearance (CrCl) ≥45 mL/min/1.73 m²

Open-label, multicenter, 6-arm, phase 1b study (28-day cycles)

DARA* IV 16 mg/kg + Pomalidomide 4 mg (Days 1-21) + Dexamethasone 40 mg QW

*QW for Cycles 1-2, Q2W for Cycles 3-6, and Q4W thereafter

Treat 6 patients with DARA + POM-D

Expansion cohort of an additional 97 patients (N = 103 total)

Baseline Demographics and Clinical Characteristics

Characteristic	DARA + POM-D N = 103
Age, y	
Median (range)	64 (35-86)
Category, n (%)	
<65	52 (51)
65-<75	43 (42)
≥75	8 (8)
Female/male, %	45/55
ECOG score, n (%)	
0	28 (27)
1	63 (61)
2	12 (12)
Cytogenetic profile, n (%)*	n = 87
Standard risk	65 (75)
High risk	22 (25)
del17p	16 (18)
t(4;14)	6 (7)
t(14;16)	1 (1)
Time from diagnosis, y	
Median (range)	5.13 (0.4-16.0)

Characteristic	DARA + POM-D N = 103
Prior lines of therapy, n (%)	
Median (range)	4 (1-13)
1	3 (3)
2	22 (21)
3	25 (24)
>3	53 (52)
Prior ASCT, n (%)	76 (74)
Prior PI, n (%)	102 (99)
Prior BORT	101 (98)
Prior CARF	34 (33)
Prior LEN, n (%)	103 (100)
Prior PI + IMiD, n (%)	102 (99)
Refractory to, n (%)	
LEN	92 (89)
BORT	73 (71)
CARF	31 (30)
Refractory to PI + IMiD, n (%)	73 (71)

ISS, International Staging System; ASCT, autologous stem cell transplant; PI, proteasome inhibitor; BORT, bortezomib; CARF, carfilzomib; LEN, lenalidomide; IMiD, immunomodulatory drug. *Based on FISH or karyotyping. Percentages based on n = 87 as denominator.

Patient Disposition: DARA + POM-D*

- Median follow-up: 13.1 months (range: 0.2-25.8)
- Median duration of treatment: 6.7 months (range: 0.03-20.0+)

Safety Summary: DARA + POM-D

Most common (>25%) TEAEs

N = 103	n (%)
Neutropenia ^a	82 (80)
Anemia	56 (54)
Fatigue	54 (52)
Diarrhea	44 (43)
Thrombocytopenia	43 (42)
Cough	39 (38)
Leukopenia	38 (37)
Constipation	35 (34)
Dyspnea	33 (32)
Nausea	32 (31)
Pyrexia	31 (30)
Back pain	29 (28)
Upper respiratory tract infection	29 (28)
Muscle spasms	28 (27)

- 44% of patients had baseline grade 1/2 neutropenia
- 15% of patients discontinued due to treatment-emergent adverse events (TEAEs)
 - None of the TEAEs occurred in >1 patient
 - 3% were related to DARA
- 9% of patients had a TEAE leading to death
 - None were related to DARA
- No patients reported secondary primary malignancies

No new safety signals were reported with longer follow-up

Most Common (>5%) Grade 3/4 Adverse Events (AEs)

- Serious adverse events (SAEs) occurred in 53% of patients
 - 18% were related to DARA per investigator discretion
- The most common grade 3 or 4 infection/infestation TEAE was pneumonia (10%)
- There were relatively low rates of febrile neutropenia (8%)

Other than neutropenia, rates of grade ≥3 AEs were similar to those observed historically with POM-D alone

IRRs in >5% Patients: DARA + POM-D

	N = 103		
IRR	Any grade, %	Grade 3, %	
Any event	50	4	
Chills	15	0	
Cough	11	0	
Dyspnea	11	0	
Nausea	9	0	
Nasal congestion	7	0	
Throat irritation	7	0	

- 4 (4%) patients had grade 3 infusion-related reactions (IRRs)
 - Hypertension (n = 2), hypoxia (n = 1), and increased blood pressure (n = 1)
- No grade 4 or 5 IRRs occurred
- 1 patient discontinued due to an IRR (grade 3 hypoxia)
- All IRRs occurred during the first infusion, except for 1 instance of laryngeal edema, which occurred during the second infusion

IRRs were mostly grade ≤2 and occurred predominantly during the first infusion

ORR^a: DARA + POM-D

			•	PR 📕	VGPR CF	R sCR
	DARA + POM-D (N = 103)		ر 70			
	n (%)	95% CI	60 -	ORR = 60%		
ORR (sCR+CR+VGPR+PR)	62 (60)	50.1-69.7	17	%	8	
Best response	- (-)		bet	ter	9	
sCR CR VGPR PR MR SD PD NE	8 (8) 9 (9) 26 (25) 19 (18) 2 (2) 26 (25) 3 (3) 10 (10)	3.4-14.7 4.1-15.9 17.2-34.8 11.5-27.3 0.2-6.8 17.2-34.8 0.6-8.3 4.8-17.1	* 40 - * 30 - 20 -	L	25	42% VGPR or better
VGPR or better (sCR+CR+VGPR)	43 (42)	32.1-51.9	10 -		18	
CR or better (sCR+CR)	17 (17)	9.9-25.1	0			
DARA + POM-D (N = 103)						

- Among patients with CR or better, the minimal residual disease negative rate at:
 - 10⁻⁴ threshold = 6/17 (35%)
 - 10⁻⁵ threshold = 5/17 (29%)
 - 10⁻⁶ threshold = 1/17 (6%)

Deep responses were observed with DARA + POM-D

ORR Subgroup Analysis: DARA + POM-D

	ORR (95% CI)	Ν	ORR 95% CI
All patients	⊢•⊣	103	60.2 (50.1-69.7)
Sex Male	⊢ −−4	57	54.4 (40.7-67.6)
Female	▶ ● → ●	46	67.4 (52.0-80.5)
Age, y <65	F	52	57.7 (43.2-71.3)
≥65	▶− −− 1	51	62.7 (48.1-75.9)
Renal function (baseline C	CrCI):		
<60 mL/min		31	58.1 (39.1-75.5)
≥60 mL/min		72	61.1 (48.9-72.4)
Baseline hepatic function:		0.4	
Normai		84	05.5 (54.3-75.5)
		19	36.8 (16.3-61.6)
Number of prior lines of the	nerapy:		
2 lines		22	63.6 (40.7-82.8)
3 lines		26 ^b	65.4 (44.3-82.8)
>3 lines	┣━━━●┿═┫	53	54.7 (40.4-68.4)
Refractoriness:			
PI + IMiD		73	57.5 (45.4-69.0)
Measurable type of MM:			
lgG		56	53.6 (39.7-67.0)
Non-IgG		17	58.8 (32.9-81.6)
Cytogenetic risk:		65	
Standard IISK Light rick		20	50.5 (45.0-70.0)
		22	Ja. 1 (JU.4-79.J)
0 20	40 60 80 100		
	%		

High response rate maintained across clinically relevant subgroups

^aClassified as mild, moderate, or severe; 17% had mild impairment; 1% had moderate impairment; 0% had severe impairment. Patients with impaired hepatic function received fewer doses of DARA versus patients with normal hepatic function. ^bDiscrepancy from demographics table due to update of concomitant medication data.

PFS: DARA + POM-D

- Median PFS: 8.8 months (95% CI, 4.6-15.4)
- 6-month PFS rate: 57.8% (95% CI, 47.3-66.9)
- 12-month PFS rate: 41.9% (95% CI, 31.5-51.9)

~40% of patients maintain PFS after 1 year

OS: DARA + POM-D

OS by Response Category OS ___ ≥PR -A SD/MR - PD/NE 80 · % surviving patients % surviving patients Median: NE (95% CI, 17.5-NE) Median: 17.5 months 40 -(95% CI, 13.3-NE) Median: 8.5 months (95% CI, 5.0-12.3) Median: 2.3 months (95% CI, 0.6-5.4) 0 -Months Months No. at risk 6 0 ≥PR 62 11 1 No. at risk 103 SD/MR 28 PD/NE 13

12-month OS rate: 66.2% (95% CI, 55.6-74.8)

Patients with SD/MR derive survival benefit with DARA + POM-D

Conclusions: DARA + POM-D

- DARA can be safely combined with POM-D
 - High neutropenia rates in a population with 44% baseline neutropenia
 - Febrile neutropenia rates were consistent with POM-D alone
- DARA (16 mg/kg) + POM-D induced deep responses, including MRD negativity, in a heavily pretreated patient population
 - Median of 4 prior lines of therapy
 - 71% of patients were double refractory to a PI and an IMiD
 - High response rate is maintained in double-refractory and high-risk patients
- 40% of patients remain progression-free after 1 year
- The addition of DARA to POM-D is associated with encouraging OS

A phase 3 study is being planned