Online Supplementary Material for Mateos et al. Daratumumab plus bortezomib, melphalan, and prednisone versus bortezomib, melphalan, and prednisone in transplant-ineligible newly diagnosed multiple myeloma: frailty subgroup analysis of ALCYONE.

This file provides supplementary results to expand on results provided in the main article.

Supplementary Table 1. Frailty Assessment Based on the FIRST Study[1]

Category	Score
Age	
≤75 years	0
76-80 years	1
>80 years	2
Charlson Comorbidity Index	
≤1	0
>1	1
ECOG PS score	
0	0
1	1
≥2	2
Sum of scores	
Fit	0
Intermediate	1
Non-frail	0-1
Frail	≥2

ECOG PS = Eastern Cooperative Oncology Group performance status.

Supplementary Table 2. Patient Disposition for Cycle 10+ (Safety Population)[a]

	Non-frail[b]			Frail
	Fit	Intermediate	Total–non-frail[b]	Frail
	D-VMP (16.5%;[c] n=46/278)	D-VMP (42.4%;[c] n=118/278)	D-VMP (59.0%;[c] n=164/278)	D-VMP (41.0%;[c] n=114/278)
Patients who discontinued treatment, n (%)	19 (41.3)	53 (44.9)	72 (43.9)	60 (52.6)
Reason for discontinuation, n (%)				
Progressive disease	19 (41.3)	43 (36.4)	62 (37.8)	43 (37.7)
Adverse event	0	4 (3.4)	4 (2.4)	3 (2.6)
Non-compliance with study drug[d]	0	1 (0.8)	1 (0.6)	3 (2.6)
Death	0	3 (2.5)	3 (1.8)	7 (6.1)
Physician decision	0	1 (0.8)	1 (0.6)	0
Patient withdrawal	0	0	0	3 (2.6)
Other	0	1 (0.8)	1 (0.6)	1 (0.9)

D-VMP = daratumumab plus bortezomib/melphalan/prednisone.

[a]Percentages in the table were calculated using the number of patients in each frailty subgroup who entered Cycle 10 (fit, n=46; intermediate, n=118; total–non-frail, n=164; frail, n=114) as the denominator, unless otherwise indicated.

[b]Non-frail subgroup consists of fit and intermediate patients.

[c]Percentage was calculated using the number of patients in the D-VMP cohort who entered Cycle 10 as the denominator.

[d]Based on reason "Patient refused further study treatment."

Supplementary Table 3. Summary of Relative Dose Intensity (Safety Population)[a]

	Non-frail[b]						Frail	
	Fit (17.4%;[c] n=122/700)		Intermediate (38.1%;[c] n=267/700)		Total–non-frail[b] (55.6%;[c] n=389/700)		Frail (44.4%;[c] n=311/700)	
	D-VMP (13.9%;[d] n=48/346)	VMP (20.9%;[e] n=74/354)	D-VMP (39.9%;[d] n=138/346)	VMP (36.4%;[e] n=129/354)	D-VMP (53.8%;[d] n=186/346)	VMP (57.3%;[e] n=203/354)	D-VMP (46.2%;[d] n=160/346)	VMP (42.7%;[e] n=151/354)
Bortezomib relative dose intensity, %								
N	48	74	138	129	186	203	159	151
Mean (SD)	91.2 (12.2)	89.3 (13.0)	88.0 (15.5)	89.5 (13.0)	88.80 (14.8)	89.5 (13.0)	87.7 (16.5)	87.3 (14.9)
Median (range)	96.8 (54.1-103.2)	95.6 (58.0-105.8)	95.6 (33.8-103.6)	95.0 (36.2-103.9)	95.7 (33.8-103.6)	95.1 (36.2-105.8)	95.3 (12.1-106.3)	92.7 (26.2-110.6)
Melphalan relative dose intensity, %								
N	48	74	137	129	185	203	159	150
Mean (SD)	93.3 (9.7)	93.9 (10.9)	95.1 (9.8)	94.1 (11.4)	94.6 (9.8)	94.0 (11.2)	91.0 (15.1)	91.3 (13.8)
Median (range)	94.8 (70.1-106.8)	96.8 (49.9-119.6)	97.7 (57.9-142.5)	97.2 (37.2-108.1)	97.4 (57.9-142.5)	97.1 (37.2-119.6)	95.9 (25.0-136.9)	95.4 (44.4-107.8)
Prednisone-equivalent relative dose intensity, %								
N	48	74	138	129	186	203	160	150
Mean (SD)	98.9 (3.5)	97.6 (5.8)	97.4 (8.8)	96.4 (10.0)	97.8 (7.8)	96.8 (8.7)	96.9 (10.2)	97.2 (7.0)
Median (range)	99.2 (90.8-110.0)	99.0 (61.0-104.0)	99.0 (24.4-108.9)	98.8 (35.3-106.5)	99.1 (24.4-110.0)	98.8 (35.3-106.5)	99.0 (30.1-129.8)	98.9 (53.7-106.3)
Daratumumab relative dose intensity, %								
N	48		138		186		160	
Mean (SD)	98.2 (5.0)	–	94.9 (14.3)	–	95.7 (12.6)	–	92.3 (19.5)	–
Median (range)	99.4 (70.6-105.4)	–	99.3 (6.9-106.2)	–	99.3 (6.9-106.2)	–	98.5 (1.3-105.9)	–

D-VMP = daratumumab plus bortezomib/melphalan/prednisone; SD = standard deviation; VMP = bortezomib/melphalan/prednisone.

[a]Percentages in the table were calculated using the number of patients in each treatment cohort per frailty subgroup of the safety population (fit: D-VMP, n=48; VMP, n=74; intermediate: D-VMP, n=138; VMP, n=129; total–non-frail: D-VMP, n=186; VMP, n=203; frail: D-VMP; n=160; VMP, n=151) as the denominator, unless otherwise indicated.
[b]Non-frail subgroup consists of fit and intermediate patients.
[c]Percentage was calculated using the number of patients in the safety population as the denominator.
[d]Percentage was calculated using the number of patients in the D-VMP cohort of the safety population as the denominator.
[e]Percentage was calculated using the number of patients in the VMP cohort of the safety population as the denominator.

Supplementary Table 4. Response and MRD-negativity Rates (ITT Population)[a]

	Non-frail[b]									Frail		
	Fit (17.3%;[c] n=122/706)			Intermediate (38.1%;[c] n=269/706)			Total–non-frail[b] (55.4%;[c] n=391/706)			Frail (44.6%;[c] n=315/706)		
	D-VMP (13.7%;[d] n=48/350)	VMP (20.8%;[e] n=74/356)	*P* value	D-VMP (39.7%;[d] n=139/350)	VMP (36.5%;[e] n=130/356)	*P* value	D-VMP (53.4%;[d] n=187/350)	VMP (57.3%;[e] n=204/356)	*P* value	D-VMP (46.6%;[d] n=163/350)	VMP (42.7%;[e] n=152/356)	*P* value
ORR, n (%)	46 (95.8)	59 (79.7)	0.0125	128 (92.1)	94 (72.3)	<0.0001	174 (93.0)	153 (75.0)	<0.0001	144 (88.3)	110 (72.4)	0.0003
≥CR	25 (52.1)	23 (31.1)	0.0209	63 (45.3)	31 (23.8)	0.0002	88 (47.1)	54 (26.5)	<0.0001	72 (44.2)	36 (23.7)	0.0001
sCR	16 (33.3)	7 (9.5)	0.0010	33 (23.7)	6 (4.6)	<0.0001	49 (26.2)	13 (6.4)	<0.0001	32 (19.6)	15 (9.9)	0.0152
CR	9 (18.8)	16 (21.6)		30 (21.6)	25 (19.2)		39 (20.9)	41 (20.1)		40 (24.5)	21 (13.8)	
≥VGPR	34 (70.8)	46 (62.2)	0.3267	104 (74.8)	60 (46.2)	<0.0001	138 (73.8)	106 (52.0)	<0.0001	117 (71.8)	71 (46.7)	<0.0001
VGPR	9 (18.8)	23 (31.1)		41 (29.5)	29 (22.3)		50 (26.7)	52 (25.5)		45 (27.6)	35 (23.0)	
PR	12 (25.0)	13 (17.6)		24 (17.3)	34 (26.2)		36 (19.3)	47 (23.0)		27 (16.6)	39 (25.7)	
SD, n (%)	2 (4.2)	14 (18.9)		7 (5.0)	27 (20.8)		9 (4.8)	41 (20.1)		11 (6.7)	35 (23.0)	
PD, n (%)	0	0		0	1 (0.8)		0	1 (0.5)		0	1 (0.7)	
NE, n (%)	0	1 (1.4)		4 (2.9)	8 (6.2)		4 (2.1)	9 (4.4)		8 (4.9)	6 (3.9)	
MRD-negative (10^{-5}), n (%)	12 (25.0)	6 (8.1)	0.0170	40 (28.8)	7 (5.4)	<0.0001	52 (27.8)	13 (6.4)	<0.0001	47 (28.8)	12 (7.9)	<0.0001

CR = complete response; D-VMP = daratumumab plus bortezomib/melphalan/prednisone; ITT = intent-to-treat; MRD = minimal residual disease; NE = not evaluable; ORR = overall response rate; PD = progressive disease; PR = partial response; sCR = stringent complete response; SD = stable disease; VGPR = very good partial response; VMP = bortezomib/melphalan/prednisone.

[a]Percentages in the table were calculated using the number of patients in each treatment cohort per frailty subgroup of the ITT population (fit: D-VMP, n=48; VMP, n=74; intermediate: D-VMP, n=139; VMP, n=130; total–non-frail: D-VMP, n=187; VMP, n=204; frail: D-VMP; n=163; VMP, n=152) as the denominator, unless otherwise indicated.

[b]Non-frail subgroup consists of fit and intermediate patients.

[c]Percentage was calculated using the number of patients in the ITT population as the denominator.

[d]Percentage was calculated using the number of patients in the D-VMP cohort of the ITT population as the denominator.

[e]Percentage was calculated using the number of patients in the VMP cohort of the ITT population as the denominator.

Supplementary Table 5. Grade 3/4 TEAEs and TEAEs With Outcome of Death (>1 Patient) (Safety Population)[a]

	Non-frail[b]						Frail	
	Fit (17.4%;[c] n=122/700)		Intermediate (38.1%;[c] n=267/700)		Total–non-frail[b] (55.6%;[c] n=389/700)		Frail (44.4%;[c] n=311/700)	
	D-VMP (13.9%;[d] n=48/346)	VMP (20.9%;[e] n=74/354)	D-VMP (39.9%;[d] n=138/346)	VMP (36.4%;[e] n=129/354)	D-VMP (53.8%;[d] n=186/346)	VMP (57.3%;[e] n=203/354)	D-VMP (46.2%;[d] n=160/346)	VMP (42.7%;[e] n=151/354)
Total number of patients with grade 3/4 TEAE, n (%)	35 (72.9)	57 (77.0)	115 (83.3)	94 (72.9)	150 (80.6)	151 (74.4)	127 (79.4)	123 (81.5)
Haematologic, n (%)								
Neutropenia	27 (56.3)	35 (47.3)	46 (33.3)	51 (39.5)	73 (39.2)	86 (42.4)	66 (41.3)	52 (34.4)
Thrombocytopenia	13 (27.1)	31 (41.9)	48 (34.8)	44 (34.1)	61 (32.8)	75 (36.9)	59 (36.9)	59 (39.1)
Lymphopenia	6 (12.5)	2 (2.7)	7 (5.1)	7 (5.4)	13 (7.0)	9 (4.4)	14 (8.8)	13 (8.6)
Anaemia	5 (10.4)	14 (18.9)	21 (15.2)	24 (18.6)	26 (14.0)	38 (18.7)	34 (21.3)	32 (21.2)
Leukopenia	5 (10.4)	4 (5.4)	10 (7.2)	8 (6.2)	15 (8.1)	12 (5.9)	13 (8.1)	18 (11.9)
Febrile neutropenia	1 (2.1)	3 (4.1)	2 (1.4)	2 (1.6)	3 (1.6)	5 (2.5)	1 (0.6)	3 (2.0)
Non-haematologic, n (%)								
Infections	6 (12.5)	11 (14.9)	38 (27.5)	15 (11.6)	44 (23.7)	26 (12.8)	48 (30.0)	27 (17.9)
Pneumonia	2 (4.2)	1 (1.4)	20 (14.5)	6 (4.7)	22 (11.8)	7 (3.4)	23 (14.4)	8 (5.3)
Influenza	1 (2.1)	0	1 (0.7)	1 (0.8)	2 (1.1)	1 (0.5)	2 (1.3)	1 (0.7)
Lower respiratory tract infection	1 (2.1)	1 (1.4)	0	1 (0.8)	1 (0.5)	2 (1.0)	5 (3.1)	2 (1.3)
Bronchitis	0	0	5 (3.6)	2 (1.6)	5 (2.7)	2 (1.0)	5 (3.1)	1 (0.7)
Urinary tract infection	0	0	4 (2.9)	0	4 (2.2)	0	3 (1.9)	1 (0.7)

Upper respiratory tract infection	0	1 (1.4)	3 (2.2)	2 (1.6)	3 (1.6)	3 (1.5)	5 (3.1)	3 (2.0)
Sepsis	0	3 (4.1)	2 (1.4)	1 (0.8)	2 (1.1)	4 (2.0)	2 (1.3)	1 (0.7)
Infection	0	0	2 (1.4)	0	2 (1.1)	0	1 (0.6)	1 (0.7)
Herpes zoster	0	0	2 (1.4)	1 (0.8)	2 (1.1)	1 (0.5)	0	2 (1.3)
Cytomegalovirus infection	0	0	1 (0.7)	0	1 (0.5)	0	2 (1.3)	0
Cystitis	0	0	0	0	0	0	2 (1.3)	0
Viral pneumonia	0	0	0	0	0	0	2 (1.3)	0
Respiratory tract infection	0	0	0	0	0	0	2 (1.3)	0
Septic shock	0	0	0	1 (0.8)	0	1 (0.5)	1 (0.6)	2 (1.3)
Clostridium difficile infection	0	0	0	0	0	0	0	2 (1.3)
Hypertension	3 (6.3)	1 (1.4)	6 (4.3)	3 (2.3)	9 (4.8)	4 (2.0)	10 (6.3)	2 (1.3)
Cataract	2 (4.2)	0	2 (1.4)	0	4 (2.2)	0	3 (1.9)	0
Hyponatraemia	2 (4.2)	0	1 (0.7)	4 (3.1)	3 (1.6)	4 (2.0)	4 (2.5)	5 (3.3)
Spinal compression fracture	2 (4.2)	0	1 (0.7)	1 (0.8)	3 (1.6)	1 (0.5)	1 (0.6)	1 (0.7)
Back pain	1 (2.1)	0	4 (2.9)	2 (1.6)	5 (2.7)	2 (1.0)	2 (1.3)	2 (1.3)
Atrial fibrillation	1 (2.1)	0	3 (2.2)	2 (1.6)	4 (2.2)	2 (1.0)	3 (1.9)	1 (0.7)
Hypokalaemia	1 (2.1)	0	3 (2.2)	0	4 (2.2)	0	3 (1.9)	6 (4.0)
Peripheral sensory neuropathy	1 (2.1)	2 (2.7)	3 (2.2)	4 (3.1)	4 (2.2)	6 (3.0)	1 (0.6)	8 (5.3)
Acute myocardial infarction	1 (2.1)	0	1 (0.7)	0	2 (1.1)	0	2 (1.3)	0
Constipation	1 (2.1)	0	1 (0.7)	1 (0.8)	2 (1.1)	1 (0.5)	1 (0.6)	0
Orthostatic hypotension	1 (2.1)	0	1 (0.7)	0	2 (1.1)	0	0	0

Diabetes mellitus	1 (2.1)	0	1 (0.7)	0	2 (1.1)	0	0	0
Asthenia	1 (2.1)	2 (2.7)	0	3 (2.3)	1 (0.5)	5 (2.5)	4 (2.5)	2 (1.3)
Vomiting	1 (2.1)	1 (1.4)	0	1 (0.8)	1 (0.5)	2 (1.0)	4 (2.5)	4 (2.6)
Nausea	1 (2.1)	1 (1.4)	0	1 (0.8)	1 (0.5)	2 (1.0)	2 (1.3)	2 (1.3)
Blood alkaline phosphatase increased	1 (2.1)	0	0	2 (1.6)	1 (0.5)	2 (1.0)	0	3 (2.0)
Fatigue	0	2 (2.7)	6 (4.3)	2 (1.6)	6 (3.2)	4 (2.0)	6 (3.8)	5 (3.3)
Diarrhea	0	2 (2.7)	5 (3.6)	3 (2.3)	5 (2.7)	5 (2.5)	4 (2.5)	6 (4.0)
Alanine aminotransferase increased	0	1 (1.4)	5 (3.6)	0	5 (2.7)	1 (0.5)	3 (1.9)	4 (2.6)
Aspartate aminotransferase increased	0	1 (1.4)	5 (3.6)	0	5 (2.7)	1 (0.5)	2 (1.3)	3 (2.0)
Hyperglycaemia	0	4 (5.4)	4 (2.9)	2 (1.6)	4 (2.2)	6 (3.0)	7 (4.4)	2 (1.3)
Dyspnea	0	0	4 (2.9)	0	4 (2.2)	0	5 (3.1)	3 (2.0)
Hyperkaliemia	0	0	4 (2.9)	0	4 (2.2)	0	3 (1.9)	3 (2.0)
Syncope	0	1 (1.4)	3 (2.2)	0	3 (1.6)	1 (0.5)	7 (4.4)	0
Hypocalcemia	0	1 (1.4)	3 (2.2)	1 (0.8)	3 (1.6)	2 (1.0)	5 (3.1)	6 (4.0)
Peripheral sensorimotor neuropathy	0	1 (1.4)	2 (1.4)	0	2 (1.1)	1 (0.5)	2 (1.3)	2 (1.3)
Gamma-glutamyltransferase increased	0	0	2 (1.4)	1 (0.8)	2 (1.1)	1 (0.5)	2 (1.3)	2 (1.3)
Pulmonary edema	0	0	2 (1.4)	1 (0.8)	2 (1.1)	1 (0.5)	2 (1.3)	0
Femur fracture	0	0	2 (1.4)	0	2 (1.1)	0	2 (1.3)	2 (1.3)
C-reactive protein increased	0	2 (2.7)	2 (1.4)	0	2 (1.1)	2 (1.0)	1 (0.6)	0

Hyperhidrosis	0	0	2 (1.4)	0	2 (1.1)	0	0	0
Bone pain	0	0	1 (0.7)	0	1 (0.5)	0	3 (1.9)	0
Hypoxia	0	0	1 (0.7)	0	1 (0.5)	0	3 (1.9)	0
Acute kidney injury	0	1 (1.4)	1 (0.7)	3 (2.3)	1 (0.5)	4 (2.0)	2 (1.3)	1 (0.7)
Dehydration	0	1 (1.4)	1 (0.7)	1 (0.8)	1 (0.5)	2 (1.0)	2 (1.3)	3 (2.0)
Bronchospasm	0	0	1 (0.7)	0	1 (0.5)	0	2 (1.3)	1 (0.7)
Peripheral edema	0	0	1 (0.7)	0	1 (0.5)	0	2 (1.3)	1 (0.7)
Chronic obstructive pulmonary disease	0	0	1 (0.7)	0	1 (0.5)	0	2 (1.3)	0
Pyrexia	0	0	1 (0.7)	0	1 (0.5)	0	1 (0.6)	2 (1.3)
Generalized rash	0	3 (4.1)	1 (0.7)	0	1 (0.5)	3 (1.5)	0	0
Cardiac failure	0	1 (1.4)	0	0	0	1 (0.5)	3 (1.9)	3 (2.0)
Renal failure	0	0	0	1 (0.8)	0	1 (0.5)	3 (1.9)	1 (0.7)
Ischemic stroke	0	0	0	0	0	0	3 (1.9)	0
Hypotension	0	0	0	0	0	0	2 (1.3)	2 (1.3)
Decreased appetite	0	0	0	0	0	0	2 (1.3)	1 (0.7)
Acute respiratory failure	0	1 (1.4)	0	0	0	1 (0.5)	2 (1.3)	0
Hyperthermia	0	0	0	1 (0.8)	0	1 (0.5)	2 (1.3)	0
Oxygen saturation decreased	0	0	0	0	0	0	2 (1.3)	0
Chronic cardiac failure	0	0	0	0	0	0	2 (1.3)	0
Muscular weakness	0	0	0	0	0	0	1 (0.6)	3 (2.0)
Insomnia	0	0	0	0	0	0	1 (0.6)	2 (1.3)
Pulmonary embolism	0	1 (1.4)	0	1 (0.8)	0	2 (1.0)	1 (0.6)	1 (0.7)
Toxic skin eruption	0	1 (1.4)	0	1 (0.8)	0	2 (1.0)	0	0
Humerus fracture	0	0	0	0	0	0	0	2 (1.3)

Total number of patients with a TEAE with outcome of death, n (%)	0	2 (2.7)	7 (5.1)	5 (3.9)	7 (3.8)	7 (3.4)	17 (10.6)	13 (8.6)
Cardiac arrest	0	0	1 (0.7)	0	1 (0.5)	0	0	2 (1.3)
Death	0	0	0	0	0	0	2 (1.3)	2 (1.3)
Pneumonia	0	0	0	0	0	0	2 (1.3)	0

D-VMP = daratumumab plus bortezomib/melphalan/prednisone; TEAE = treatment-emergent adverse event; VMP = bortezomib/melphalan/prednisone.

[a] Percentages in the table were calculated using the number of patients in each treatment cohort per frailty subgroup of the safety population (fit: D-VMP, n=48; VMP, n=74; intermediate: D-VMP, n=138; VMP, n=129; total–non-frail: D-VMP, n=186; VMP, n=203; frail: D-VMP; n=160; VMP, n=151) as the denominator, unless otherwise indicated.

[b]Non-frail subgroup consists of fit and intermediate patients.

[c]Percentage was calculated using the number of patients in the safety population as the denominator.

[d]Percentage was calculated using the number of patients in the D-VMP cohort of the safety population as the denominator.

[e]Percentage was calculated using the number of patients in the VMP cohort of the safety population as the denominator.

Supplementary Table 6. Most Common (≥4% of Patients) Serious TEAEs (Safety D-

	Non-frail[b]						Frail	
	Fit (17.4%;[c] n=122/700)		Intermediate (38.1%;[c] n=267/700)		Total–non-frail[b] (55.6%;[c] n=389/700)		Frail (44.4%;[c] n=311/700)	
	D-VMP (13.9%;[d] n=48/346)	VMP (20.9%;[e] n=74/354)	D-VMP (39.9%;[d] n=138/346)	VMP (36.4%;[e] n=129/354)	D-VMP (53.8%;[d] n=186/346)	VMP (57.3%;[e] n=203/354)	D-VMP (46.2%;[d] n=160/346)	VMP (42.7%;[e] n=151/354)
Total number of patients with serious TEAE, n (%)	14 (29.2)	19 (25.7)	66 (47.8)	38 (29.5)	80 (43.0)	57 (28.1)	86 (53.8)	60 (39.7)
Serious TEAE, n (%)								
Infections	7 (14.6)	12 (16.2)	37 (26.8)	14 (10.9)	44 (23.7)	26 (12.8)	44 (27.5)	17 (11.3)
Pneumonia	2 (4.2)	1 (1.4)	20 (14.5)	6 (4.7)	22 (11.8)	7 (3.4)	19 (11.9)	5 (3.3)
Lower respiratory tract infection	1 (2.1)	1 (1.4)	2 (1.4)	1 (0.8)	3 (1.6)	2 (1.0)	7 (4.4)	1 (0.7)
Sepsis	0	3 (4.1)	3 (2.2)	1 (0.8)	3 (1.6)	4 (2.0)	2 (1.3)	1 (0.7)
Spinal compression fracture	2 (4.2)	0	1 (0.7)	0	3 (1.6)	0	1 (0.6)	1 (0.7)
Cardiac failure	0	1 (1.4)	0	1 (0.8)	0	2 (1.0)	2 (1.3)	6 (4.0)

D-VMP = daratumumab plus bortezomib/melphalan/prednisone; TEAE = treatment-emergent adverse event; VMP = bortezomib/melphalan/prednisone.

[a]Percentages in the table were calculated using the number of patients in each treatment cohort per frailty subgroup of the safety population (fit: D-VMP, n=48; VMP, n=74; intermediate: D-VMP, n=138; VMP, n=129; total–non-frail: D-VMP, n=186; VMP, n=203; frail: D-VMP; n=160; VMP, n=151) as the denominator, unless otherwise indicated.

[b]Non-frail subgroup consists of fit and intermediate patients.

[c]Percentage was calculated using the number of patients in the safety population as the denominator.

[d]Percentage was calculated using the number of patients in the D-VMP cohort of the safety population as the denominator.

[e]Percentage was calculated using the number of patients in the VMP cohort of the safety population as the denominator.

Supplementary Table 7. Most Common TEAEs Leading to Treatment Discontinuation (>1 Patient) (Safety Population)[a]

	Non-frail[b]						Frail	
	Fit (17.4%;[c] n=122/700)		Intermediate (38.1%;[c] n=267/700)		Total–non-frail[b] (55.6%;[c] n=389/700)		Frail (44.4%;[c] n=311/700)	
	D-VMP (13.9%;[d] n=48/346)	VMP (20.9%;[e] n=74/354)	D-VMP (39.9%;[d] n=138/346)	VMP (36.4%;[e] n=129/354)	D-VMP (53.8%;[d] n=186/346)	VMP (57.3%;[e] n=203/354)	D-VMP (46.2%;[d] n=160/346)	VMP (42.7%;[e] n=151/354)
Total number of patients with a TEAE leading to treatment discontinuation, n (%)	1 (2.1)	6 (8.1)	9 (6.5)	8 (6.2)	10 (5.4)	14 (6.9)	14 (8.8)	19 (12.6)
Non-haematologic, n (%)								
Fatigue	0	0	0	0	0	0	1 (0.6)	2 (1.3)
Peripheral sensory neuropathy	0	1 (1.4)	0	1 (0.8)	0	2 (1.0)	0	4 (2.6)
Infections	0	3 (4.1)	4 (2.9)	0	4 (2.2)	3 (1.5)	2 (1.3)	3 (2.0)
Pneumonia	0	0	2 (1.4)	0	2 (1.1)	0	1 (0.6)	1 (0.7)

D-VMP = daratumumab plus bortezomib/melphalan/prednisone; TEAE = treatment-emergent adverse event; VMP = bortezomib/melphalan/prednisone.
[a]Percentages in the table were calculated using the number of patients in each treatment cohort per frailty subgroup of the safety population (fit: D-VMP, n=48; VMP, n=74; intermediate: D-VMP, n=138; VMP, n=129; total–non-frail: D-VMP, n=186; VMP, n=203; frail: D-VMP; n=160; VMP, n=151) as the denominator, unless otherwise indicated.
[b]Non-frail subgroup consists of fit and intermediate patients.
[c]Percentage was calculated using the number of patients in the safety population as the denominator.
[d]Percentage was calculated using the number of patients in the D-VMP cohort of the safety population as the denominator.
[e]Percentage was calculated using the number of patients in the VMP cohort of the safety population as the denominator.

Reference

1. Facon T, Dimopoulos MA, Meuleman N, Belch A, Mohty M, Chen WM, et al. A simplified frailty scale predicts outcomes in transplant-ineligible patients with newly diagnosed multiple myeloma treated in the FIRST (MM-020) trial. *Leukemia*. 2020;**34**:224-233.