Final analysis of the phase III non-inferiority COLUMBA study of subcutaneous *versus* intravenous daratumumab in patients with relapsed or refractory multiple myeloma

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Supplemental Materials

Table S1. Serum concentration of daratumumab by baseline body weight subgroup.

	DARA SC (n=259)					DARA IV (n=257)				
Serum concentration (μg/mL)	≤50 kg	>50-65 kg	>65-85 kg	>85-120 kg	>120 kg	≤50 kg	>50-65 kg	>65-85 kg	>85-120 kg	>120 kg
Pharmacokinetic analysis set, N	21	71	102	61	4	21	70	105	58	3
Cycle 1, day 1 (C_{trough})										
N	20	69	101	59	4	21	70	102	57	3
Mean (SD)	BQL (NE)	BQL (NE)	BQL (NE)	BQL (NE)	BQL (NE)	BQL (NE)	BQL (NE)	BQL (NE)	BQL (NE)	BQL (NE)
Cycle 1, day 1 (end of dose; C_{max} for IV)										
N	NA	NA	NA	NA	NA	21	66	100	53	3
Mean (SD)	NA	NA	NA	NA	NA	225 (56.3)	236 (88.5)	260 (80.6)	318 (82.0)	331 (251)
Cycle 1, day 4 (C_{max} for SC)										
N	20	67	97	58	4	NA	NA	NA	NA	NA
Mean (SD)	151 (79.4)	145 (58.3)	124 (58.6)	96.9 (44.0)	66.1 (55.5)	NA	NA	NA	NA	NA
Cycle 1, day 15 (C_{trough})										
N	20	63	93	58	4	19	61	94	55	3
Mean (SD)	325 (181)	250 (92.6)	191 (95.9)	176 (72.5)	77.5 (75.7)	159 (69.9)	167 (74.5)	186 (78.4)	208 (87.1)	221 (115)
Cycle 2, day 1 (C_{trough})										
N	17	62	92	56	3	20	65	95	53	3
Mean (SD)	522 (278)	428 (195)	319 (160)	296 (131)	110 (121)	274 (132)	287 (125)	313 (150)	338 (138)	363 (153)
Cycle 3, day 1 (C_{trough})										

N	17	59	80	45	3	20	56	90	45	2
Mean (SD)	888 (449)	673 (303)	515 (277)	493 (218)	143 (219)	466 (195)	458 (228)	515 (248)	513 (215)	657 (205)
Cycle 3, day 1 (end of dose; C_{max} for IV)										
N	NA	NA	NA	NA	NA	19	54	84	45	2
Mean (SD)	NA	NA	NA	NA	NA	714 (235)	727 (279)	763 (283)	846 (265)	1136 (330)
Cycle 3, day 4 (C_{max} for SC)										
N	16	51	74	43	3	NA	NA	NA	NA	NA
Mean (SD)	1114 (450)	871 (353)	660 (364)	613 (285)	203 (273)	NA	NA	NA	NA	NA
Cycle 5, day 1 (C_{trough})										
N	13	45	59	38	0	17	47	70	33	2
Mean (SD)	871 (419)	591 (338)	458 (304)	423 (211)	-	418 (221)	388 (221)	432 (255)	438 (238)	471 (125)
Cycle 7, day 1 (C_{trough})										
N	11	35	46	34	0	14	37	57	25	2
Mean (SD)	1069 (356)	589 (334)	474 (296)	464 (205)	-	470 (196)	429 (250)	464 (269)	457 (263)	427 (163)
Cycle 12, day 1 (C_{trough})										
N	9	18	26	22	0	10	23	37	12	1
Mean (SD)	679 (219)	378 (250)	254 (180)	206 (112)	-	242 (139)	264 (183)	232 (171)	274 (101)	218 (-)
End of treatment										
N	9	29	44	32	0	11	31	38	25	1
Mean (SD)	315 (405)	260 (224)	238 (284)	163 (137)	-	214 (166)	128 (124)	228 (202)	198 (196)	71.7 (-)
Follow-up week 8										
N	10	24	39	24	0	9	31	35	26	1
Mean (SD)	128 (213)	153 (173)	146 (218)	111 (158)	-	179 (147)	118 (196)	141 (160)	146 (209)	BQL (NE)

DARA SC, daratumumab by subcutaneous administration; DARA IV, daratumumab by intravenous administration; C_{trough}, trough concentration; SD, standard deviation; BQL, below quantitation limit (0.2 µg/mL); NE, not estimable; C_{max}, maximum concentration; NA, not available.

Table S2. Efficacy endpoints by baseline body weight subgroup.[a]

	DARA SC (n=263)			DARA IV (n=259)		
	≤65 kg (n=94)	>65-85 kg (n=102)	>85 kg (n=66)	≤65 kg (n=92)	>65-85 kg (n=105)	>85 kg (n=61)
Overall response rate, n (%)	46 (48.9)	38 (37.3)	31 (47.0)	39 (42.4)	44 (41.9)	20 (32.8)
Overall survival, median (95% CI), months	NR (18.5-NE)	28.1 (18.4-NE)	28.8 (22.8-NE)	23.8 (20.5-NE)	NR (19.9-NE)	23.0 (16.9-NE)

DARA SC, daratumumab by subcutaneous administration; DARA IV, daratumumab by intravenous administration; CI, confidence interval; NR, not reached; NE, not estimable.

[a]Baseline body weight was not recorded for one patient in each treatment group.

Table S3. Most common[a] any grade (≥10%) and grade 3/4 (≥5%) TEAEs in the safety-evaluable population by body weight subgroup.

	DARA SC (n=260)						DARA IV (n=258)					
	≤65 kg (n=93)		>65-85 kg (n=102)		>85 kg (n=65)		≤65 kg (n=92)		>65-85 kg (n=105)		>85 kg (n=61)	
TEAE, n (%)	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4
Any event	89 (95.7)	49 (52.7)	92 (90.2)	51 (50.0)	57 (87.7)	32 (49.2)	87 (94.6)	52 (56.5)	98 (93.3)	54 (51.4)	55 (90.2)	30 (49.2)
Hematologic												
Anemia	28 (30.1)	14 (15.1)	31 (30.4)	15 (14.7)	13 (20.0)	7 (10.8)	22 (23.9)	15 (16.3)	30 (28.6)	16 (15.2)	14 (23.0)	8 (13.1)
Neutropenia	24 (25.8)	19 (20.4)	16 (15.7)	10 (9.8)	12 (18.5)	5 (7.7)	13 (14.1)	8 (8.7)	13 (12.4)	9 (8.6)	9 (14.8)	3 (4.9)
Thrombocytopenia	21 (22.6)	15 (16.1)	21 (20.6)	16 (15.7)	9 (13.8)	6 (9.2)	17 (18.5)	12 (13.0)	20 (19.0)	14 (13.3)	13 (21.3)	9 (14.8)
Lymphopenia	12 (12.9)	9 (9.7)	5 (4.9)	3 (2.9)	4 (6.2)	2 (3.1)	7 (7.6)	6 (6.5)	7 (6.7)	7 (6.7)	3 (4.9)	3 (4.9)
Non-hematologic												
Upper respiratory infection	18 (19.4)	0	14 (13.7)	0	12 (18.5)	0	6 (6.5)	0	12 (11.4)	2 (1.9)	12 (19.7)	0
Diarrhea	21 (22.6)	2 (2.2)	6 (5.9)	0	14 (21.5)	0	15 (16.3)	1 (1.1)	15 (14.3)	0	3 (4.9)	0
Pyrexia	17 (18.3)	1 (1.1)	12 (11.8)	0	10 (15.4)	1 (1.5)	16 (17.4)	0	13 (12.4)	1 (1.0)	10 (16.4)	1 (1.6)
Fatigue	10 (10.8)	1 (1.1)	10 (9.8)	2 (2.0)	13 (20.0)	0	8 (8.7)	1 (1.1)	14 (13.3)	2 (1.9)	6 (9.8)	0
Arthralgia	15 (16.1)	0	12 (11.8)	1 (1.0)	6 (9.2)	0	3 (3.3)	0	11 (10.5)	0	4 (6.6)	0
Back pain	15 (16.1)	1 (1.1)	12 (11.8)	2 (2.0)	4 (6.2)	2 (3.1)	17 (18.5)	3 (3.3)	12 (11.4)	2 (1.9)	9 (14.8)	2 (3.3)
Nasopharyngitis	14 (15.1)	0	6 (5.9)	0	8 (12.3)	1 (1.5)	11 (12.0)	0	10 (9.5)	0	0	0
Cough	9 (9.7)	1 (1.1)	9 (8.8)	1 (1.0)	7 (10.8)	0	11 (12.0)	0	15 (14.3)	0	10 (16.4)	0
Nausea	11 (11.8)	0	7 (6.9)	0	6 (9.2)	0	14 (15.2)	1 (1.1)	11 (10.5)	1 (1.0)	7 (11.5)	0
Hypertension	7 (7.5)	4 (4.3)	4 (3.9)	4 (3.9)	5 (7.7)	3 (4.6)	7 (7.6)	4 (4.3)	10 (9.5)	6 (5.7)	6 (9.8)	5 (8.2)
Pneumonia	5 (5.4)	5 (5.4)	1 (1.0)	1 (1.0)	10 (15.4)	7 (10.8)	10 (10.9)	7 (7.6)	4 (3.8)	3 (2.9)	5 (8.2)	3 (4.9)
Chills	5 (5.4)	0	7 (6.9)	1 (1.0)	3 (4.6)	0	9 (9.8)	0	8 (7.6)	0	15 (24.6)	2 (3.3)
Dyspnea	7 (7.5)	1 (1.1)	4 (3.9)	0	4 (6.2)	1 (1.5)	6 (6.5)	0	13 (12.4)	0	9 (14.8)	2 (3.3)

TEAEs, treatment-emergent adverse events; DARA SC, daratumumab by subcutaneous administration; DARA IV, daratumumab by intravenous administration; [a]Occurring among the total DARA SC and DARA IV groups.

Table S4. Modified-CTSQ satisfaction with therapy domain scores among the intent-to-treat population[a]

	DARA SC (n=263)		DARA IV (n=259)		
	N	Mean (SD)	N	Mean (SD)	Mean difference (DARA SC-DARA IV)
Cycle 1, day 8	230	76.9 (14.64)	227	70.5 (15.98)	6.4
Cycle 1, day 15	238	78.8 (14.95)	226	72.1 (16.72)	6.7
Cycle 1, day 22	239	78.7 (15.75)	226	72.8 (16.20)	5.9
Cycle 2, day 1	238	79.7 (16.58)	239	74.2 (16.44)	5.5
Cycle 2, day 8	232	80.1 (17.24)	227	74.8 (15.57)	5.3
Cycle 2, day 15	224	80.0 (17.37)	228	74.3 (16.94)	5.6
Cycle 2, day 22	214	79.3 (18.65)	221	75.2 (16.47)	4.1
Cycle 3, day 1	224	80.4 (17.78)	217	76.0 (17.39)	4.4
Cycle 4, day 1	209	79.5 (19.88)	205	76.6 (17.22)	2.9
Cycle 5, day 1	188	79.6 (18.95)	187	77.1 (17.11)	2.5
Cycle 6, day 1	159	81.9 (18.34)	169	76.1 (17.79)	5.8
Cycle 7, day 1	137	85.0 (16.87)	150	78.6 (16.01)	6.4
Cycle 8, day 1	128	85.0 (15.13)	135	79.2 (15.54)	5.8
Cycle 9, day 1	118	85.0 (15.10)	124	79.3 (15.60)	5.7
Cycle 10, day 1	109	84.8 (15.35)	114	79.0 (15.02)	5.8
Cycle 11, day 1	100	84.1 (15.26)	103	78.5 (15.70)	5.6
Cycle 12, day 1	88	84.6 (16.53)	91	79.1 (16.48)	5.5
Cycle 13, day 1	82	83.4 (17.07)	87	79.0 (16.49)	4.4
Cycle 14, day 1	74	82.8 (17.18)	71	80.0 (14.77)	2.7
Cycle 15, day 1	64	84.9 (15.84)	64	79.4 (14.81)	5.5
Cycle 16, day 1	59	85.8 (14.90)	58	79.3 (14.42)	6.5
Cycle 17, day 1	54	85.9 (15.33)	54	80.8 (15.05)	5.2
Cycle 18, day 1	54	85.7 (16.25)	49	81.6 (13.68)	4.1
Cycle 19, day 1	49	85.3 (16.34)	46	81.2 (14.65)	4.1
Cycle 20, day 1	46	85.0 (14.75)	45	81.6 (13.41)	3.4
Cycle 21, day 1	45	85.4 (15.13)	44	79.9 (15.65)	5.5
Cycle 22, day 1	45	87.1 (13.65)	39	82.5 (13.08)	4.6
Cycle 23, day 1	42	85.7 (15.68)	34	81.5 (14.05)	4.2
Cycle 24, day 1	42	87.4 (14.89)	33	81.1 (14.38)	6.4
Cycle 25, day 1	40	88.2 (13.61)	30	81.2 (12.86)	7.0
Cycle 26, day 1	36	86.4 (19.54)	27	79.2 (14.89)	7.2
Cycle 27, day 1	31	87.2 (12.67)	26	78.8 (13.21)	8.4
Cycle 28, day 1	33	89.5 (13.06)	24	77.4 (11.13)	12.1
Cycle 29, day 1	31	88.6 (13.34)	24	80.2 (14.59)	8.4
Cycle 30, day 1	27	86.9 (14.49)	20	80.0 (10.65)	6.9
Cycle 31, day 1	24	84.7 (15.10)	20	80.4 (14.45)	4.3
Cycle 32, day 1	20	84.1 (14.31)	17	82.4 (12.47)	1.8
Cycle 33, day 1	13	87.4 (11.35)	11	78.6 (14.46)	8.8

Cycle 34, day 1	12	89.3 (13.79)	8	84.4 (14.78)	4.9
Cycle 35, day 1	7	90.8 (12.69)	6	84.5 (13.30)	6.3
Cycle 36, day 1	5	92.1 (9.58)	2	92.9 (10.10)	-0.7
Cycle 37, day 1	3	95.2 (5.46)	1	85.7	9.5
Cycle 38, day 1	3	89.3 (15.57)	0	NE	NE

CTSQ, Cancer Therapy Satisfaction Questionnaire; DARA SC, daratumumab by subcutaneous administration; DARA IV, daratumumab by intravenous administration; SD, standard deviation; NE, not estimable. [a]Includes all patients who were randomized.