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.

| Serum concentration (µg/mL) | DARA SC (n=259) | DARA IV (n=257) |
|-----------------------------|-----------------|-----------------|
|                             | ≤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<sub>trough</sub>) | 20     | 69        | 101       | 59         | 4       | 21     | 70        | 102       | 57         | 3      |
| N                           | BQL (NE) | BQL (NE)  | BQL (NE)  | BQL (NE)   | BQL (NE) | BQL (NE) | BQL (NE)  | BQL (NE)  | BQL (NE)   | BQL (NE) |
| Mean (SD)                  | NA      | NA        | NA        | NA         | NA       | 21     | 66        | 100       | 53         | 3      |
| Cycle 1, day 1 (end of dose; C<sub>max</sub> for IV) | NA  | NA        | NA        | NA         | NA       | 21     | 66        | 100       | 53         | 3      |
| N                           | NA      | NA        | NA        | NA         | NA       | 225 (56.3) | 236 (88.5) | 260 (80.6) | 318 (82.0) | 331 (251) |
| 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<sub>max</sub> for SC) | 20     | 67        | 97        | 58         | 4       | NA     | NA        | NA        | NA         | NA     |
| N                           | 151 (79.4) | 145 (58.3) | 124 (58.6) | 96.9 (44.0) | 66.1 (55.5) | 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<sub>trough</sub>) | 20     | 63        | 93        | 58         | 4       | 19     | 61        | 94        | 55         | 3      |
| N                           | 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) |
| 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<sub>trough</sub>) | 17     | 62        | 92        | 56         | 3       | 20     | 65        | 95        | 53         | 3      |
| N                           | 522 (278) | 428 (195)  | 319 (160)  | 296 (131)  | 110 (121)  | 274 (132)  | 287 (125)  | 313 (150)  | 338 (138)  | 363 (153) |
| 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 (end of dose; \( C_{\text{max}} \) for IV) | Cycle 3, day 4 (\( C_{\text{max}} \) for SC) | Cycle 5, day 1 (\( C_{\text{trough}} \)) | Cycle 7, day 1 (\( C_{\text{trough}} \)) | Cycle 12, day 1 (\( C_{\text{trough}} \)) | End of treatment | Follow-up week 8 |
|-----------|----------------------------------------------------------|---------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|-----------------|----------------|
| N         | 17 59 80 45 3                                          | 16 51 74 43 3                                | 13 45 59 38 0                           | 11 35 46 34 0                           | 9 18 26 22 0                           | 9 29 44 32 0    | 10 24 39 24 0 |
| Mean (SD) | 888 (449) 673 (303) 515 (277) 493 (218) 143 (219)     | 1114 (450) 871 (353) 660 (364) 613 (285) 203 (273) | 17 47 70 33 2                           | 14 37 57 25 2                           | 10 23 37 12 1                           | 11 31 38 25 1   | 9 31 35 26 1   |
|           |                                                           | 466 (195) 458 (228) 515 (248) 513 (215) 657 (205) | 714 (235) 727 (279) 763 (283) 846 (265) 1136 (330) | 418 (221) 388 (221) 432 (255) 438 (238) 471 (125) | 470 (196) 429 (250) 464 (269) 457 (263) 427 (163) | 242 (139) 264 (183) 232 (171) 274 (101) 218 (-) | 214 (166) 128 (124) 228 (202) 198 (196) 71.7 (-) |
|           |                                                           |                                              |                                           |                                           |                                           |                 |                 |

DARA SC, daratumumab by subcutaneous administration; DARA IV, daratumumab by intravenous administration; \( C_{\text{trough}} \), trough concentration; SD, standard deviation; BQL, below quantitation limit (0.2 μg/mL); NE, not estimable; \( C_{\text{max}} \), maximum concentration; NA, not available.
Table S2. Efficacy endpoints by baseline body weight subgroup.\textsuperscript{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.

\textsuperscript{a}Baseline body weight was not recorded for one patient in each treatment group.
Table S3. Most common any grade (≥10%) and grade 3/4 (≥5%) TEAEs in the safety-evaluable population by body weight subgroup.

| TEAE, n (%) | DARA SC (n=260) | DARA IV (n=258) |
|-------------|------------------|------------------|
|             | ≤65 kg (n=93)    | >65-85 kg (n=102) | >85 kg (n=65) |
|             | >65-85 kg (n=102) | >85 kg (n=65)    |
| Any event   | 89 (95.7)        | 49 (52.7)        | 51 (50.0)      |
| Grade 3/4   | 92 (90.2)        | 57 (87.7)        | 32 (49.2)      |
| Hematologic |                  |                  |                |
| Anemia      | 28 (30.1)        | 14 (15.1)        | 31 (30.4)      |
|             | 15 (14.7)        | 13 (20.0)        | 7 (10.8)       |
| Neutropenia | 24 (25.8)        | 19 (20.4)        | 16 (15.7)      |
|             | 10 (9.8)         | 12 (18.5)        | 5 (7.7)        |
| Thrombocytopenia | 21 (22.6) | 15 (16.1) | 21 (20.6) |
|             | 16 (15.7)        | 9 (13.8)         | 6 (9.2)        |
| Lymphopenia | 12 (12.9)        | 9 (9.7)          | 5 (4.9)        |
|             | 3 (2.9)          | 4 (6.2)          | 2 (3.1)        |
| Non-hematologic |              |                  |                |
| Upper respiratory infection | 18 (19.4) | 0 | 14 (13.7) |
|             | 0               | 12 (18.5)        | 0              |
| Diarrhea    | 21 (22.6)        | 2 (2.2)          | 6 (5.9)        |
|             | 0               | 14 (21.5)        | 0              |
| Pyrexia     | 17 (18.3)        | 1 (1.1)          | 12 (11.8)      |
|             | 0               | 10 (15.4)        | 1 (1.5)        |
| Fatigue     | 10 (10.8)        | 1 (1.1)          | 10 (9.8)       |
|             | 2 (2.0)          | 13 (20.0)        | 0              |
| Arthralgia  | 15 (16.1)        | 0               | 12 (11.8)      |
|             | 1 (1.0)          | 6 (9.2)          | 2 (3.1)        |
| Back pain   | 15 (16.1)        | 1 (1.1)          | 12 (11.8)      |
|             | 2 (2.0)          | 4 (6.2)          | 2 (3.1)        |
| Nausea      | 14 (15.1)        | 0               | 6 (5.9)        |
|             | 0               | 8 (12.3)         | 1 (1.5)        |
| Hypertension| 7 (7.5)          | 4 (4.3)          | 3 (3.9)        |
|             | 4 (3.9)          | 5 (7.7)          | 3 (4.6)        |
| Pneumonia   | 5 (5.4)          | 5 (5.4)          | 1 (1.0)        |
|             | 1 (1.0)          | 10 (15.4)        | 7 (10.8)       |
| Chills      | 5 (5.4)          | 0               | 7 (6.9)        |
|             | 1 (1.0)          | 3 (4.6)          | 0              |
| Dyspnea     | 7 (7.5)          | 1 (1.1)          | 4 (3.9)        |
|             | 0               | 4 (6.2)          | 1 (1.5)        |

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) |         | Mean difference (DARA SC-DARA IV) |
|---------------|-----------------|---------|-----------------|---------|----------------------------------|
|               | N               | Mean (SD) | N               | Mean (SD) |                                  |
| 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. "Includes all patients who were randomized."