

**Supplementary Table S1.** Baseline patient demographics and disease characteristics for the PD-L1 and tTMB BEPs and the ITT population

|                                | PD-L1 BEP (N = 438) |                     |                 | tTMB BEP (N = 283) |                     |                | ITT population (N = 805) |                     |                 |
|--------------------------------|---------------------|---------------------|-----------------|--------------------|---------------------|----------------|--------------------------|---------------------|-----------------|
|                                | D+EP<br>(n = 152)   | D+T+EP<br>(n = 157) | EP<br>(n = 129) | D+EP<br>(n = 107)  | D+T+EP<br>(n = 105) | EP<br>(n = 71) | D+EP<br>(n = 268)        | D+T+EP<br>(n = 268) | EP<br>(n = 269) |
| Median age (range), years      | 63.0 (40–81)        | 63.0 (36–84)        | 63.0 (38–80)    | 62.0 (40–81)       | 63.0 (36–83)        | 63.0 (38–78)   | 62.0 (28–82)             | 63.0 (36–88)        | 63.0 (35–82)    |
| Age group, n (%)               |                     |                     |                 |                    |                     |                |                          |                     |                 |
| <65 years                      | 89 (58.6)           | 95 (60.5)           | 77 (59.7)       | 65 (60.7)          | 66 (62.9)           | 41 (57.7)      | 167 (62.3)               | 154 (57.5)          | 157 (58.4)      |
| ≥65 years                      | 63 (41.4)           | 62 (39.5)           | 52 (40.3)       | 42 (39.3)          | 39 (37.1)           | 30 (42.3)      | 101 (37.7)               | 114 (42.5)          | 112 (41.6)      |
| Sex, n (%)                     |                     |                     |                 |                    |                     |                |                          |                     |                 |
| Men                            | 111 (73.0)          | 113 (72.0)          | 89 (69.0)       | 78 (72.9)          | 75 (71.4)           | 44 (62.0)      | 190 (70.9)               | 202 (75.4)          | 184 (68.4)      |
| Women                          | 41 (27.0)           | 44 (28.0)           | 40 (31.0)       | 29 (27.1)          | 30 (28.6)           | 27 (38.0)      | 78 (29.1)                | 66 (24.6)           | 85 (31.6)       |
| Race, n (%)                    |                     |                     |                 |                    |                     |                |                          |                     |                 |
| White                          | 133 (87.5)          | 133 (84.7)          | 106 (82.2)      | 102 (95.3)         | 96 (91.4)           | 62 (87.3)      | 229 (85.4)               | 215 (80.2)          | 221 (82.2)      |
| Asian                          | 16 (10.5)           | 23 (14.6)           | 19 (14.7)       | 3 (2.8)            | 7 (6.7)             | 6 (8.5)        | 36 (13.4)                | 47 (17.5)           | 42 (15.6)       |
| Black                          | 2 (1.3)             | 0                   | 2 (1.6)         | 1 (0.9)            | 0                   | 2 (2.8)        | 2 (0.7)                  | 1 (0.4)             | 3 (1.1)         |
| Other or missing data          | 1 (0.7)             | 1 (0.6)             | 2 (1.6)         | 1 (0.9)            | 2 (1.9)             | 1 (1.4)        | 1 (0.4)                  | 5 (1.9)             | 3 (1.1)         |
| Disease stage, n (%)           |                     |                     |                 |                    |                     |                |                          |                     |                 |
| III                            | 18 (11.8)           | 9 (5.7)             | 10 (7.8)        | 12 (11.2)          | 7 (6.7)             | 8 (11.3)       | 28 (10.4)                | 18 (6.7)            | 24 (8.9)        |
| IV                             | 134 (88.2)          | 148 (94.3)          | 119 (92.2)      | 95 (88.8)          | 98 (93.3)           | 63 (88.7)      | 240 (89.6)               | 250 (93.3)          | 245 (91.1)      |
| WHO PS, n (%)                  |                     |                     |                 |                    |                     |                |                          |                     |                 |
| 0                              | 49 (32.2)           | 55 (35.0)           | 41 (31.8)       | 34 (31.8)          | 37 (35.2)           | 23 (32.4)      | 99 (36.9)                | 109 (40.7)          | 90 (33.5)       |
| 1                              | 103 (67.8)          | 102 (65.0)          | 88 (68.2)       | 73 (68.2)          | 68 (64.8)           | 48 (67.6)      | 169 (63.1)               | 159 (59.3)          | 179 (66.5)      |
| Smoking history, n (%)         |                     |                     |                 |                    |                     |                |                          |                     |                 |
| Never smoker                   | 14 (9.2)            | 11 (7.0)            | 7 (5.4)         | 10 (9.3)           | 7 (6.7)             | 3 (4.2)        | 22 (8.2)                 | 15 (5.6)            | 15 (5.6)        |
| Former smoker                  | 70 (46.1)           | 82 (52.2)           | 53 (41.1)       | 43 (40.2)          | 52 (49.5)           | 30 (42.3)      | 126 (47.0)               | 141 (52.6)          | 128 (47.6)      |
| Current smoker                 | 68 (44.7)           | 64 (40.8)           | 69 (53.5)       | 54 (50.5)          | 46 (43.8)           | 38 (53.5)      | 120 (44.8)               | 112 (41.8)          | 126 (46.8)      |
| Brain or CNS metastases, n (%) | 12 (7.9)            | 25 (15.9)           | 12 (9.3)        | 12 (11)            | 17 (16)             | 9 (13)         | 28 (10.4)                | 38 (14.2)           | 27 (10.0)       |
| Liver metastases, n (%)        | 55 (36.2)           | 73 (46.5)           | 52 (40.3)       | 42 (39.3)          | 52 (49.5)           | 36 (50.7)      | 108 (40.3)               | 117 (43.7)          | 104 (38.7)      |
| PD-L1 expression               |                     |                     |                 |                    |                     |                |                          |                     |                 |
| IC <1%                         | 117 (77.0)          | 107 (68.2)          | 101 (78.3)      |                    |                     |                |                          |                     |                 |
| IC ≥1%                         | 35 (23.0)           | 50 (31.8)           | 28 (21.7)       |                    |                     |                |                          |                     |                 |

|               |            |            |            |           |           |           |  |  |
|---------------|------------|------------|------------|-----------|-----------|-----------|--|--|
| TC <1%        | 145 (95.4) | 147 (93.6) | 121 (93.8) |           |           |           |  |  |
| TC ≥1%        | 7 (4.6)    | 10 (6.4)   | 8 (6.2)    |           |           |           |  |  |
| TC and IC <1% | 114 (75.0) | 103 (65.6) | 97 (75.2)  |           |           |           |  |  |
| TC or IC ≥1%  | 38 (25.0)  | 54 (34.4)  | 32 (24.8)  |           |           |           |  |  |
| tTMB score    |            |            |            | 50 (46.7) | 57 (54.2) | 45 (63.4) |  |  |
| <10 mut/Mb    |            |            |            | 57 (53.3) | 48 (45.7) | 26 (36.6) |  |  |
| ≥10 mut/Mb    |            |            |            |           |           |           |  |  |

BEP, biomarker evaluable population; CNS, central nervous system; D, durvalumab; EP, platinum-etoposide; IC, immune cell; ITT, intention-to-treat; mut/Mb, mutation per megabase; PD-L1, programmed cell death ligand-1; PS, performance status; T, tremelimumab; TC, tumor cell; tTMB, tissue tumor mutational burden; WHO, World Health Organization.