Supplementary Figure 11

Baseline - OS

| Variable | | N | Hazard ratio | | р |
|----------------|----------------|----|--------------|-------------------|-------|
| CMC | Above median | 38 | • | Reference | |
| | Below median | 36 | | 0.57 (0.33, 1.00) | 0.048 |
| Cohort | A: Head & Neck | 15 | • | Reference | |
| | B: Breast | 18 | | 0.89 (0.41, 1.93) | 0.775 |
| | C: Ovarian | 18 | — — | 0.48 (0.21, 1.07) | 0.071 |
| | D: Melanoma | 11 | | 0.18 (0.05, 0.73) | 0.016 |
| | E: Other | 12 | | 0.37 (0.16, 0.89) | 0.027 |
| PD-L1 fraction | | 74 | | 0.22 (0.08, 0.61) | 0.004 |
| log TMB | | 74 | | 0.99 (0.68, 1.43) | 0.938 |

Baseline - PFS

| Variable | | N | Hazard ratio | | р |
|----------------|----------------|----|-------------------|-------------------|-------|
| CMC | Above median | 38 | | Reference | |
| | Below median | 36 | ■ | 0.54 (0.31, 0.93) | 0.028 |
| Cohort | A: Head & Neck | 15 | • | Reference | |
| | B: Breast | 18 | | 2.84 (1.29, 6.23) | 0.009 |
| | C: Ovarian | 18 | — ; ■— | 1.42 (0.66, 3.06) | 0.371 |
| | D: Melanoma | 11 | | 0.39 (0.11, 1.41) | 0.150 |
| | E: Other | 12 | | 0.47 (0.20, 1.14) | 0.094 |
| PD-L1 fraction | | 74 | | 0.30 (0.11, 0.81) | 0.017 |
| log TMB | | 74 | | 0.79 (0.55, 1.14) | 0.208 |

Cycle 3 - OS

| Variable | | N | Hazard ratio | | р |
|----------------|----------------|----|---------------------------------------|-------------------|-------|
| CMC | Above median | 23 | • | Reference | |
| | Below median | 30 | ·- | 0.50 (0.22, 1.13) | 0.096 |
| Cohort | A: Head & Neck | 12 | • | Reference | |
| | B: Breast | 10 | | 0.59 (0.24, 1.47) | 0.259 |
| | C: Ovarian | 10 | | 0.32 (0.11, 0.90) | 0.031 |
| | D: Melanoma | 10 | | 0.09 (0.02, 0.47) | 0.004 |
| | E: Other | 11 | | 0.30 (0.12, 0.77) | 0.012 |
| PD-L1 fraction | | 53 | · · · · · · · · · · · · · · · · · · · | 0.31 (0.09, 1.05) | 0.060 |
| log TMB | | 53 | - ja | 1.19 (0.79, 1.80) | 0.412 |

Cycle 3 - PFS

| Variable | | N | Hazard ratio | | р |
|----------------|----------------|----|--------------|-------------------|------|
| CMC | Above median | 23 | • | Reference | |
| | Below median | 29 | ■ | 0.52 (0.25, 1.07) | 0.08 |
| Cohort | A: Head & Neck | 12 | • | Reference | |
| | B: Breast | 10 | - | 2.14 (0.87, 5.27) | 0.10 |
| | C: Ovarian | 10 | ⊢ | 1.14 (0.44, 2.90) | 0.79 |
| | D: Melanoma | 9 | | 0.14 (0.03, 0.78) | 0.02 |
| | E: Other | 11 | ⊢ ■; | 0.43 (0.17, 1.09) | 0.08 |
| PD-L1 fraction | | 52 | | 0.45 (0.14, 1.39) | 0.17 |
| log TMB | | 52 | ⊢ | 0.94 (0.62, 1.41) | 0.75 |

Supplementary Figure 11. Multivariable analysis of OS and PFS using cancer mutation concentration (CMC) at baseline and cycle 3 of pembrolizumab. CMC was determined using a bespoke targeted approach across the trial cohort. At both baseline and cycle 3, patients were split into above- or below-median groups. Survival outcomes are shown in a multivariable analysis including cohort, PD-L1 expression, and tumor mutation burden (TMB).