

Supplementary Table S2: Adjusted Cox proportional hazards model for anti-PD-(L)1 monotherapy real-world progression free survival (rwPFS) and overall survival (OS) in the monotherapy validation cohort (n=352)

| Covariate | rwPFS | | OS | |
|--|---------------------------|---------|---------------------------|---------|
| | HR (95% CI) | p-value | HR (95% CI) | p-value |
| Age (yrs; continuous) | 0.995 (0.9809 to 1.0093) | 0.4913 | 0.9937 (0.9779 to 1.0099) | 0.4451 |
| Sex (Male vs. Female) | 0.7307 (0.5308 to 1.0060) | 0.0544 | 0.7522 (0.5239 to 1.0801) | 0.1229 |
| Line of Therapy (continuous) | 1.1471 (0.9612 to 1.3689) | 0.1282 | 1.1857 (0.9841 to 1.4286) | 0.0732 |
| Tumor Type (Bladder vs. Other) | 1.314 (0.6808 to 2.5361) | 0.4156 | 1.2523 (0.5596 to 2.8024) | 0.5841 |
| Tumor Type (CUP vs. Other) | 1.1033 (0.6087 to 2.0000) | 0.7459 | 1.5385 (0.8092 to 2.9252) | 0.1888 |
| Tumor Type (Esophagogastric vs. Other) | 1.8144 (0.9607 to 3.4267) | 0.0663 | 3.2582 (1.6792 to 6.3220) | 0.0005 |
| Tumor Type (Head and Neck vs. Other) | 1.3932 (0.7394 to 2.6252) | 0.3049 | 2.0698 (1.0431 to 4.1070) | 0.0375 |
| Tumor Type (Melanoma vs. Other) | 0.7624 (0.3582 to 1.6227) | 0.4815 | 0.516 (0.1762 to 1.5111) | 0.2275 |
| Tumor Type (NSCLC vs. Other) | 2.0562 (1.3541 to 3.1223) | 0.0007 | 2.0547 (1.2671 to 3.3317) | 0.0035 |
| anti-PD-(L)1 therapy (Pembrolizumab vs. other) | 0.8367 (0.5554 to 1.2606) | 0.394 | 0.7593 (0.4758 to 1.2119) | 0.2484 |
| IRS status (High vs. Low) | 0.4078 (0.2903 to 0.5730) | <0.0001 | 0.4742 (0.3211 to 0.7003) | 0.0002 |

Associations of covariates with pembrolizumab rwPFS and OS was performed using Cox proportional hazards modeling adjusting for age (years [yrs]; continuous), sex assigned at birth, line of systemic therapy (continuous), Tumor Type (all tumor types with >15 samples were considered separately; remaining tumor types were grouped into a single category [Other]), anti-PD-(L)1 therapy (pembrolizumab vs. other) and Immunotherapy Response Score (IRS) status (-High vs. -Low). The hazard ratio (HR) for each covariate in the full model in the overall 352 patient cohort (see Fig. 1B&C) is shown, along with 95% confidence interval (CI), and p-values.