

**S2 Table.** Univariate and multivariate analyses for progression-free survival in 124 evaluable patients with R/M HNSCC receiving ICIs

| Characteristic                               | Univariate                |         | Multivariate              |         |
|--|---------------------------|---------|---------------------------|---------|
|  | Hazards ratio<br>(95% CI) | p-value | Hazards ratio<br>(95% CI) | p-value |
| Age (yr)                                     |                           |         |                           |         |
| > 60 vs. ≤ 60                                | 0.70 (0.47-1.05)          | 0.085   |                           |         |
| Sex  |                           |         |                           |         |
| Male vs. female                              | 0.62 (0.37-1.04)          | 0.068   |                           |         |
| ECOG PS                                      |                           |         |                           |         |
| 2-3 vs. 0-1                                  | 1.06 (0.57-1.96)          | 0.849   |                           |         |
| Smoking history                              |                           |         |                           |         |
| Current or former vs. never                  | 1.02 (0.74-1.41)          | 0.898   |                           |         |
| HPV status                                   |                           |         |                           |         |
| HPV + vs. HPV–                               | 0.64 (0.35-1.15)          | 0.132   |                           |         |
| Unknown vs. HPV–                             | 0.87 (0.54-1.40)          | 0.563   |                           |         |
| Primary tumor location                       |                           |         |                           |         |
| Oropharynx vs. non-oropharynx                | 0.73 (0.46-1.16)          | 0.180   |                           |         |
| Histologic grade                             |                           |         |                           |         |
| Poorly vs. moderate vs. well                 | 1.08 (0.72-1.64)          | 0.708   |                           |         |
| Sum of target lesions (mm)                   |                           |         |                           |         |
| > 40 vs. ≤ 40                                | 1.57 (1.04-2.38)          | 0.034   | 1.53 (1.01-2.33)          | 0.046   |
| Prior lines of systemic therapy              |                           |         |                           |         |
| 0  | 1 <sup>a)</sup>           |         |                           |         |
| 1  | 0.83 (0.43 – 1.58)        | 0.565   |                           |         |
| 2  | 1.16 (0.59 – 2.30)        | 0.661   |                           |         |
| ≥ 3  | 1.33 (0.60 – 2.94)        | 0.486   |                           |         |
| Neutrophil to lymphocyte ratio <sup>b)</sup> |                           |         |                           |         |
| > 4 vs. ≤ 4                                  | 1.78 (1.18 – 2.68)        | 0.006   | 1.75 (1.15-2.65)          | 0.009   |
| Immune-checkpoint inhibitors                 |                           |         |                           |         |
| Anti-PD-1                                    | 1 <sup>a)</sup>           |         |                           |         |
| Anti-PD-L1                                   | 1.48 (0.89 – 2.44)        | 0.716   |                           |         |
| Anti-PD-1/anti-PD-L1+anti-CTLA4              | 1.11 (0.68 – 1.80)        | 0.687   |                           |         |

CI, confidence interval; CTLA-4, cytotoxic T-lymphocyte antigen 4; ECOG, Eastern Cooperative Oncology Group; HPV, human papillomavirus; ICI, immune checkpoint inhibitor; PD-1, programmed cell death protein-1; PD-L1, programmed death-ligand 1; PS, performance status; R/M HNSCC, recurrent or metastatic head and neck squamous cell cancer. <sup>a)</sup>Reference, <sup>b)</sup>The neutrophil-to-lymphocyte ratio is defined as the absolute neutrophil count divided by the absolute lymphocyte count.