Supplementary Fig. S1. Assessment of the correlation between TC and IC staining in samples from durvalumab-treated patients.

Pearson Correlation: -0.02

IC, immune cell; TC, tumor cell.
Supplementary Fig. S2. Kaplan–Meier plots of OS in durvalumab-treated patients at a range of PD-L1 (A) TC cutpoints and (B) IC cutpoints. These plots are based on the original PD-L1 scoring data with only 18 months of survival follow-up.

### Table A

| PD-L1 TC Cutpoints | N (Events) | Median OS (mo, 95% CI) | 6-mo OS (95% CI) |
|--------------------|------------|------------------------|-----------------|
| TC ≥50             | 72 (40)    | 9.8 (5.0-13.9)         | 59% (48-71)     |
| TC ≥25             | 111 (65)   | 6.9 (5.0-9.9)          | 55% (46-65)     |
| TC ≥10             | 120 (71)   | 6.9 (5.3-9.9)          | 55% (47-65)     |
| TC ≥1              | 142 (87)   | 6.6 (5.0-9.8)          | 53% (45-62)     |
| TC = 0             | 35 (16)    | NA (3.3-NA)            | 55% (40-75)     |
| All cutpoints      | 179 (103)  | 6.8 (5.0-9.9)          | 54% (47-62)     |

### Table B

| PD-L1 IC Cutpoints | N (Events) | Median OS (mo, 95% CI) | 6-mo OS (95% CI) |
|--------------------|------------|------------------------|-----------------|
| IC ≥50             | 17 (8)     | NA (3.0-NA)            | 52% (32-83)     |
| IC ≥25             | 42 (19)    | 10.2 (5.0-NA)          | 59% (45-76)     |
| IC ≥10             | 94 (49)    | 7.7 (5.0-NA)           | 58% (48-69)     |
| IC ≥1              | 131 (69)   | 7.7 (5.6-11.3)         | 58% (50-67)     |
| IC = 0             | 47 (34)    | 4.5 (2.8-9.9)          | 42% (30-59)     |
| All cutpoints      | 179 (103)  | 6.8 (5.0-9.9)          | 54% (47-62)     |

IC, immune cell; OS, overall survival; PD-L1, programmed cell death ligand-1; TC, tumor cell.
**Supplementary Fig. S3.** Kaplan–Meier plots of PFS in durvalumab-treated patients using a range of PD-L1 (A) TC cutpoints and (B) IC cutpoints. These plots are based on the original PD-L1 scoring data with only 18 months of survival follow-up.

(A) Kaplan–Meier plots of PFS in durvalumab-treated patients using a range of PD-L1 (A) TC cutpoints and (B) IC cutpoints. These plots are based on the original PD-L1 scoring data with only 18 months of survival follow-up.

| PD-L1 TC Cutpoints | N (Events) | Median PFS (mo, 95% CI) | 6-mo PFS (95% CI) |
|---------------------|------------|-------------------------|-------------------|
| TC ≥50              | 72 (56)    | 3.4 (1.9-5.4)           | 27% (18-40)       |
| TC ≥25              | 111 (87)   | 2.0 (1.9-3.7)           | 24% (17-34)       |
| TC ≥10              | 120 (94)   | 2.1 (1.9-3.7)           | 25% (18-34)       |
| TC ≥1               | 142 (115)  | 1.9 (1.8-3.0)           | 21% (15-30)       |
| TC = 0              | 35 (26)    | 2.1 (1.9-5.6)           | 23% (12-44)       |
| All cutpoints       | 179 (143)  | 2.0 (1.9-3.0)           | 21% (16-29)       |

(B) Kaplan–Meier plots of PFS in durvalumab-treated patients using a range of PD-L1 (A) TC cutpoints and (B) IC cutpoints. These plots are based on the original PD-L1 scoring data with only 18 months of survival follow-up.

| PD-L1 IC Cutpoints | N (Events) | Median PFS (mo, 95% CI) | 6-mo PFS (95% CI) |
|---------------------|------------|-------------------------|-------------------|
| IC ≥50              | 17 (12)    | 2.2 (1.8-NA)            | 25% (10-61)       |
| IC ≥25              | 42 (28)    | 3.7 (2.1-5.6)           | 30% (18-50)       |
| IC ≥10              | 94 (70)    | 2.2 (1.9-3.6)           | 27% (19-38)       |
| IC ≥1               | 131 (99)   | 2.1 (1.9-3.6)           | 26% (19-35)       |
| IC = 0              | 47 (43)    | 1.9 (1.7-2.7)           | 11% (5-25)        |
| All cutpoints       | 179 (143)  | 2.0 (1.9-3.0)           | 21% (16-29)       |

IC, immune cell; PD-L1, programmed cell death ligand-1; PFS, progression-free survival; TC, tumor cell.
Supplementary Fig. S4. Bootstrapped OS HR for HAWK and CONDOR combined data for durvalumab monotherapy (n = 190 patients). Data shows overall survival HR [BM+ vs. BM−] unadjusted Cox PH (with Ties handling method=Effron) highlighting optimal cutpoint of TC≥50 or IC≥25% with the lowest HR.

BM, biomarker; CI, confidence interval; HR, hazard ratio; IC, immune cell; OS, overall survival; TC, tumor cell.
**Supplementary Fig. S5.** Kaplan–Meier plots of (A) OS and (B) PFS using the TC50%/IC25% algorithm, based on updated data cutoffs for CONDOR (2018-08-27) and HAWK (2018-06-21).

| Combined algorithm | N (Events) | Median OS (mo, 95% CI) | 6-mo OS (95% CI) | Unadjusted HR (95% CI) | Adjusted HR (95% CI) |
|--------------------|------------|------------------------|------------------|------------------------|---------------------|
| TC ≥50/IC ≥25      | 99 (89)    | 9.8 (5.0–11.5)         | 58% (47–67)      | 0.68 (0.52–0.90)       | 0.71 (0.53–1.04)    |
| TC <50/IC <25      | 80 (71)    | 5.5 (3.8–8.3)          | 49% (37–60)      |                        |                     |

| Combined algorithm | N (Events) | Median PFS (mo, 95% CI) | 6-mo PFS (95% CI) | Unadjusted HR (95% CI) | Adjusted HR (95% CI) |
|--------------------|------------|-------------------------|------------------|------------------------|---------------------|
| TC ≥50/IC ≥25      | 99 (89)    | 2.8 (2.0–5.0)           | 18% (11–22)      | 0.68 (0.52–0.89)       | 0.69 (0.52–0.91)    |
| TC <50/IC <25      | 80 (74)    | 1.9 (1.8–2.1)           | 9% (4–19)        |                        |                     |

CI, confidence interval; HR, hazard ratio; IC, immune cell; OS, overall survival; PFS, progression-free survival; TC, tumor cell.
**Supplementary Table S1.** TC PD-L1 expression levels according to HAWK and CONDOR categories.

| Scoring bin | CONDOR Bin contents | Scoring bin | HAWK Bin contents |
|-------------|----------------------|-------------|-------------------|
| <1%         | <1%                  | 25%         | 25%               |
| ≥1%         | 1–4%                 | 30%         | 26–34%            |
| ≥5%         | 5–9%                 | 40%         | 35–44%            |
| ≥10%        | 10–19%               | 50%         | 45–54%            |
| ≥20%        | 20–24%               | 60%         | 55–64%            |
|             |                      | 70%         | 65–74%            |
|             |                      | 75%         | 75%               |
|             |                      | 80%         | 76–84%            |
|             |                      | 90%         | 85–94%            |
|             |                      | 100%        | 95–100%           |

PD-L1, programmed cell death ligand-1; TC, tumor cell.
Supplementary Table S2. VENTANA PD-L1 (SP263) assay scoring algorithm for HNSCC.

| PD-L1 interpretation | Staining description |
|----------------------|-----------------------|
| PD-L1 status is determined by the percentage of TCs with any membrane staining above background or by the percentage of tumor-associated immune cells (ICs) with staining (IC+) at any intensity above background. The percent of tumor area occupied by any tumor-associated ICs (ICs present; ICP) is used to determine IC+, which is the percent area of ICP exhibiting PD-L1 positive immune cell staining. |
| High status | PD-L1 status is considered high if any of the following are met:  
• ≥50% of TCs exhibit membrane staining; or,  
• ICP >1% and IC+ ≥25%; or,  
• ICP = 1% and IC+ = 100% |
| Low/negative status | PD-L1 status is considered low/negative if:  
• None of the criteria for PD-L1-high status are met |

IC, immune cell; ICP, ICs present; PD-L1, programmed cell death ligand-1; HNSCC, head and neck squamous cell carcinoma; TC, tumor cell.
**Supplementary Table S3.** Design verification study results and analytical validation (interlaboratory reproducibility) at the TC≥50%/IC≥25% cutpoint.

| Study outline                     | Design                                                                 | Results                                                                 |
|-----------------------------------|------------------------------------------------------------------------|-------------------------------------------------------------------------|
| **Reader precision**              | Cohort previously screened for PD-L1 status; consisted of 100 tissue samples (50 PD-L1-high and 50 PD-L1-low/negative) | Between reader, % (95% CI): APA 98.0% (95.4–100.0) ANA 98.0% (95.4–100.0) OPA 98.0% (95.3–100.0) Within reader, % (95% CI): APA 98.7% (97.1–99.7) ANA 98.7% (97.1–99.7) OPA 98.7% (97.3–99.7) |
| **Interlaboratory reproducibility** | Tested in three laboratories with two readers at each site for 5 non-consecutive days; 28 tissue samples enrolled (14 PD-L1-high and 14 PD-L1-low/negative) | Overall, % (95% CI) PPA 99.0% (97.9–100.0) NPA 98.1% (98.0–98.1) OPA 98.6% (98.0–99.0) |
| **Cut-slide stability**           | Four tissue samples sectioned at 4 µm and stored at 2–8°C and 30°C for up to 13 months | Staining results at different storage temperatures and time points up to Month 9 were consistent with results achieved on Day 0. The recommended dating is 7 months. |
| **Tissue thickness**              | Four tissue samples sectioned at various thickness (2, 3, 4, 5, 6, 7 µm) | Demonstrated appropriate antibody staining across all thickness tested. The recommend tissue thickness is 4–5 µm. |

ANA, average negative agreement; APA, average positive agreement; CI, confidence interval; IC, immune cell; NPA, negative percent agreement; OPA, overall percent agreement; PD-L1, programmed cell death ligand-1; PPA, positive percent agreement; TC, tumor cell.