

Supplementary Table 1. Comparison of peripheral blood leukocytes cutoffs identified in the previous HNSCC^a study to those identified in the new cohort of OSCC^b (Group A)

| | Previous HNSCC cohort (n = 824) | OSCC cohort (Group A) (n = 1369) |
|--------------------------------|--|---|
| Neutrophils¹ | ≤ 4.80 4.80–7.99 ≥ 7.99 | ≤ 4.8 4.8–9.1 ≥ 9.1 |
| Monocytes¹ | ≤ 0.58 0.58–1.01 ≥ 1.01 | ≤ 0.3 > 0.3 |
| Lymphocytes¹ | ≤ 1.18 > 1.18 | ≤ 0.8 > 0.8 |
| NLR^c | ≤ 1.35 1.35–3.86 ≥ 3.86 | ≤ 2.9 2.9–5.7 ≥ 5.7 |
| SIRI^d | Not reported | ≤ 1.0 1.0–1.9 ≥ 1.9 |

a-HNSCC: head and neck squamous cell carcinoma; b-OSCC: oral cavity squamous cell carcinoma; c-NLR: neutrophil-to-lymphocyte ratio; d-SIRI: Systemic Inflammation Response Index.

1: Units $\times 10^9/L$.

Supplementary Table 2. Differences in the median values of each hematological parameter between the OSCC^a cohort from MSK^b (Group A) and the OSCC cohort from HSCSP^c (Group B)

| | MSK OSCC (Group A, n = 1369) Median (range) | HSCSP OSCC (Group B, n = 119) Median (range) |
|--------------------------------|--|---|
| Neutrophils¹ | 4.6 (0.8–18.6) | 4.4 (2.1–14.5) |
| Monocytes¹ | 0.4 (0.0–1.7) | 0.6 (0.1–1.7) |
| Lymphocytes¹ | 1.7 (0.3–22.5) | 1.9 (0.5–4.7) |
| NLR^d | 2.6 (0.2–18.8) | 2.3 (0.8–9.5) |
| SIRI^e | 1.0 (0.0–18.8) | 1.4 (0.2–8.7) |

a-OSCC: oral cavity squamous cell carcinoma; b-MSK: Memorial Sloan Kettering; c-HSCSP: Hospital de la Santa Creu i Sant Pau; d-NLR: neutrophil-to-lymphocyte ratio; e-SIRI: Systemic Inflammation Response Index.

1: Units x10⁹/L.

Supplementary Table 3: Mean value of Neutrophils, Monocytes, Lymphocytes, NLR^a, and SIRI^b by clinicopathological variables in Group A patients

| | Neutrophils (x10 ⁹ /L) | P value | Monocytes (x10 ⁹ /L) | P value | Lymphocytes (x10 ⁹ /L) | P value | NLR | P value | SIRI | P value |
|---|--------------------------------------|---------|------------------------------------|---------|--------------------------------------|---------|------|---------|------|---------|
| Age | | 0.035 | | 0.007 | | 0.681 | | 0.003 | | 0.006 |
| < 60 years | 4.86 | | 0.39 | | 1.83 | | 3.01 | | 1.23 | |
| ≥ 60 years | 5.08 | | 0.42 | | 1.81 | | 3.37 | | 1.41 | |
| Sex | | 0.117 | | < 0.001 | | 0.048 | | 0.005 | | < 0.001 |
| Male | 5.06 | | 0.43 | | 1.78 | | 3.36 | | 1.48 | |
| Female | 4.89 | | 0.38 | | 1.87 | | 3.02 | | 1.14 | |
| Tobacco | | 0.003 | | < 0.001 | | 0.128 | | 0.179 | | 0.002 |
| Never | 4.78 | | 0.37 | | 1.77 | | 3.11 | | 1.19 | |
| Ever | 5.10 | | 0.42 | | 1.85 | | 3.28 | | 1.41 | |
| Alcohol | | 0.451 | | < 0.001 | | 0.855 | | 0.937 | | 0.122 |
| Never | 5.04 | | 0.38 | | 1.83 | | 3.21 | | 1.25 | |
| Ever | 4.96 | | 0.42 | | 1.82 | | 3.22 | | 1.36 | |
| WUHNCI^c | | 0.410 | | 0.022 | | 0.411 | | 0.002 | | 0.006 |
| 0 | 4.96 | | 0.40 | | 1.83 | | 3.09 | | 1.27 | |
| ≥ 1 | 5.05 | | 0.42 | | 1.79 | | 3.52 | | 1.48 | |
| Subsite | | < 0.001 | | < 0.001 | | 0.353 | | 0.001 | | < 0.001 |
| OT ^d | 5.22 | | 0.38 | | 1.81 | | 3.06 | | 1.20 | |
| LG ^e | 5.21 | | 0.42 | | 1.83 | | 3.39 | | 1.41 | |
| FOM ^f | 5.50 | | 0.45 | | 1.79 | | 3.54 | | 1.59 | |
| BM ^g | 4.85 | | 0.39 | | 1.90 | | 3.14 | | 1.19 | |
| UG ^h | 4.71 | | 0.42 | | 1.95 | | 3.07 | | 1.29 | |
| RMT ⁱ | 5.54 | | 0.45 | | 1.85 | | 3.30 | | 1.57 | |
| HP ^j | 6.02 | | 0.49 | | 1.50 | | 4.85 | | 2.83 | |
| pT^k Stage^l | | < 0.001 | | < 0.001 | | 0.100 | | < 0.001 | | < 0.001 |
| pT1 | 4.65 | | 0.39 | | 1.82 | | 2.92 | | 1.14 | |
| pT2 | 4.75 | | 0.39 | | 1.82 | | 3.08 | | 1.17 | |
| pT3 | 5.09 | | 0.41 | | 1.83 | | 3.20 | | 1.33 | |
| pT4 | 5.73 | | 0.45 | | 1.70 | | 3.95 | | 1.91 | |
| pN^l Stage^l | | < 0.001 | | 0.039 | | 0.672 | | 0.005 | | 0.001 |
| pN0 | 4.83 | | 0.40 | | 1.84 | | 3.08 | | 1.25 | |
| pN1 | 4.97 | | 0.42 | | 1.78 | | 3.24 | | 1.33 | |
| pN2 | 5.32 | | 0.41 | | 1.79 | | 3.34 | | 1.44 | |
| pN3 | 5.55 | | 0.43 | | 1.77 | | 3.76 | | 1.65 | |
| Grade | | 0.288 | | 0.887 | | 0.023 | | 0.912 | | 0.637 |
| Well diff ^m | 5.09 | | 0.41 | | 1.91 | | 3.18 | | 1.28 | |
| Mod diff ⁿ | 4.93 | | 0.41 | | 1.77 | | 3.26 | | 1.36 | |
| Poorly diff ^o | 5.14 | | 0.40 | | 1.80 | | 3.25 | | 1.33 | |

a-NLR: neutrophil-to-lymphocyte ratio; b-SIRI: Systemic Inflammation Response Index; c-WUHNCI: Washington University Head and Neck Comorbidity Index; d-OT: oral tongue; e-LG: lower gum; f-FOM: floor of mouth; g-BM: buccal mucosa; h-UG: upper gum; i-RMT: retromolar trigone; j-HP: hard palate; k-pT: pathological tumor; l-pN: pathological nodal; m-Well diff: well differentiated; n-Mod diff: moderately differentiated; o-Poorly diff: poorly differentiated.

l Staged according to the AJCC, 8th Edition.

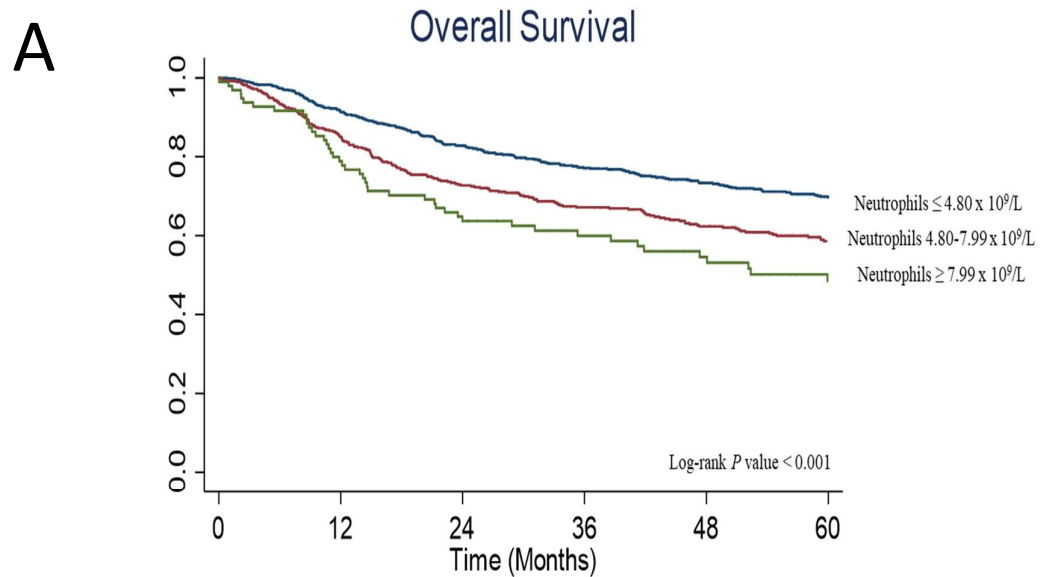
Supplementary Table 4. Survival outcomes in Group A patients by peripheral leukocyte counts using the previous cutoffs

| | Number of patients (n=1369) | 5-year OS ^a (%) | HR ^b (95% CI ^c) | P value | 5-year DSS ^d (%) | HR (95% CI) | P value |
|--------------------------------|-----------------------------|----------------------------|--|---------|-----------------------------|---------------------|---------|
| Neutrophils¹ | | | | | | | |
| ≤ 4.80 | 770 | 69.7 | 1 | < 0.001 | 83.2 | 1 | < 0.001 |
| 4.80–7.99 | 502 | 58.6 | 1.576 (1.324–1.875) | | 76.6 | 1.527 (1.167–1.998) | |
| ≥ 7.99 | 97 | 48.5 | 1.959 (1.465–2.619) | | 67.4 | 2.267 (1.490–3.448) | |
| Monocytes¹ | | | | | | | |
| ≤0.58 | 1179 | 66.2 | 1 | < 0.001 | 80.8 | 1 | 0.099 |
| 0.58–1.01 | 182 | 50.8 | 1.520 (1.222–1.891) | | 72.8 | 1.442 (1.023–2.033) | |
| ≥1.01 | 8 | 40.0 | 1.865 (0.772–4.507) | | 62.5 | 1.529 (0.380–6.158) | |
| Lymphocytes¹ | | | | | | | |
| ≤ 1.18 | 194 | 55.8 | 1 | 0.002 | 78.1 | 1 | 0.591 |
| > 1.18 | 1175 | 65.5 | 0.706 (0.569–0.878) | | 80.0 | 0.905 (0.630–1.301) | |
| NLR^e | | | | | | | |
| ≤ 1.35 | 91 | 70.6 | 1 | < 0.001 | 83.6 | 1 | < 0.001 |
| 1.35–3.86 | 952 | 68.2 | 1.272 (0.880–1.839) | | 81.6 | 1.207 (0.685–2.127) | |
| ≥ 3.86 | 326 | 50.7 | 2.150 (1.466–3.153) | | 72.8 | 2.059 (1.142–3.710) | |

a-OS: overall survival; b-HR: hazard ratio; c-CI: confidence interval; d-DSS: disease-specific survival; e-NLR: neutrophil-to-lymphocyte ratio.

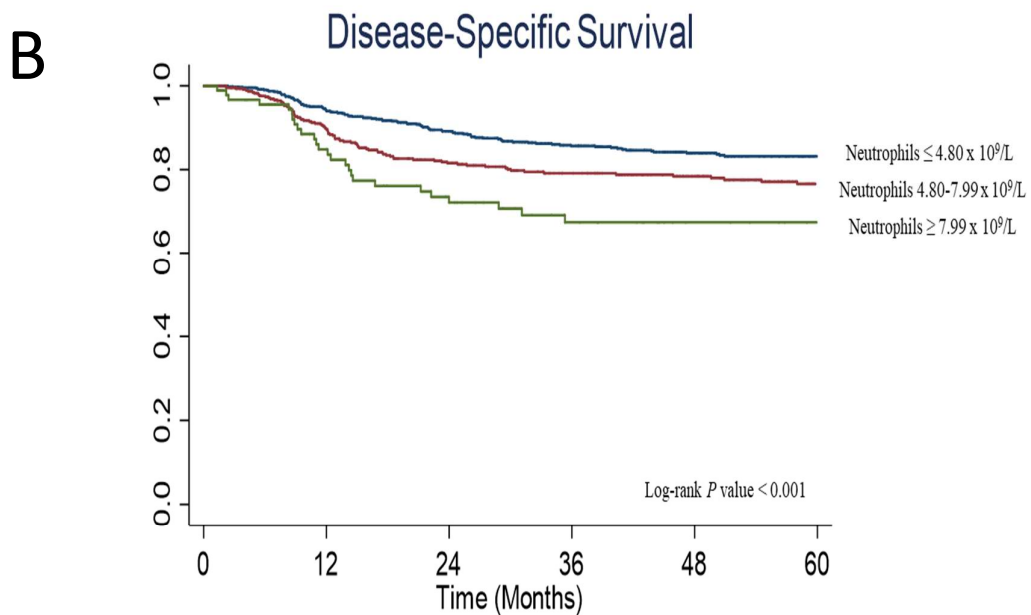
1: Units x10⁹/L.

Supplementary Figure 1. Overall Survival (a) and Disease-Specific Survival (b) in Group A according to neutrophil count categories defined by the previous cutoffs



Number at risk

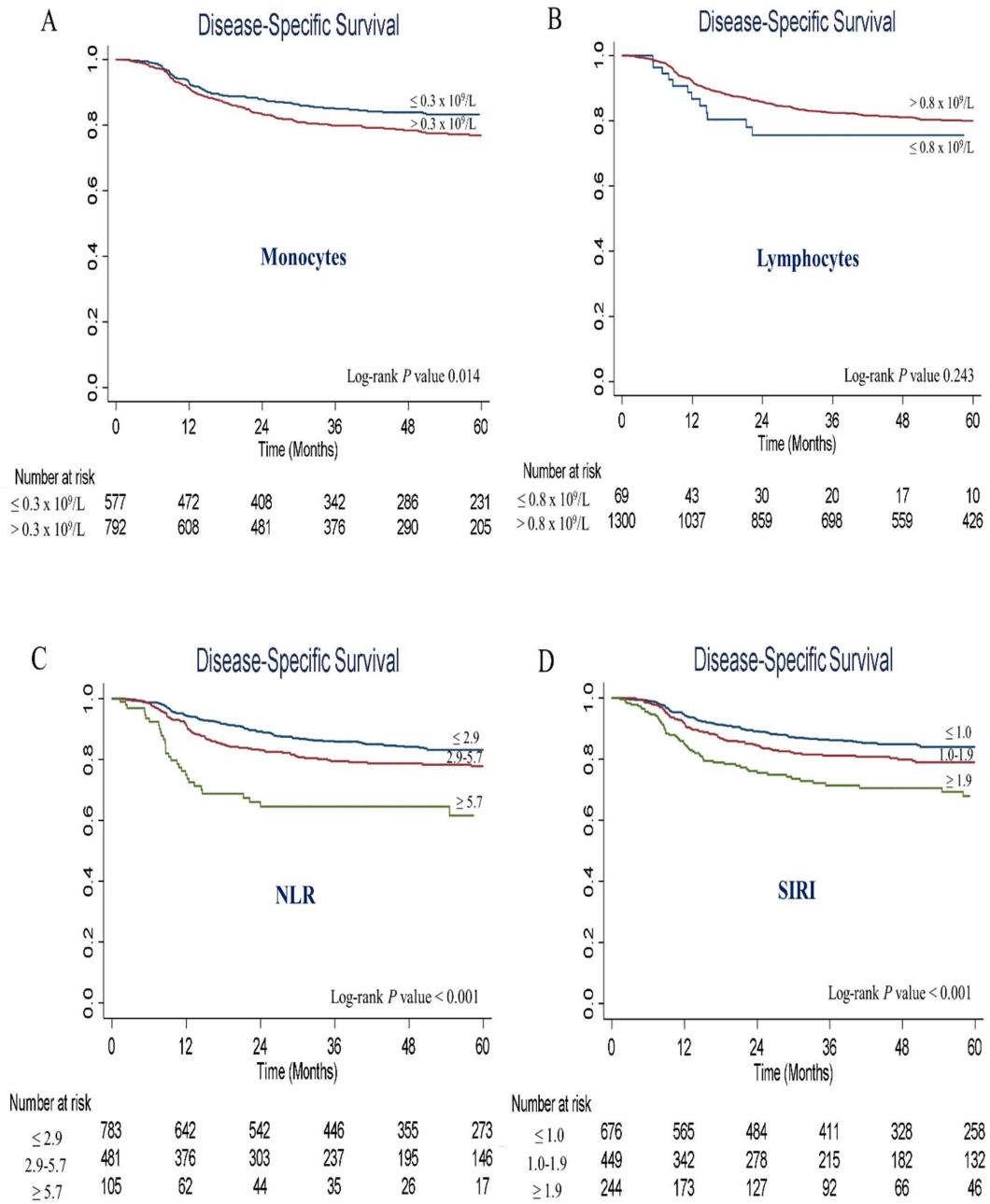
| | 0 | 12 | 24 | 36 | 48 | 60 |
|---------------------------------------|-----|-----|-----|-----|-----|-----|
| Neutrophils $\leq 4.80 \times 10^9/L$ | 770 | 672 | 580 | 487 | 391 | 303 |
| Neutrophils $4.80-7.99 \times 10^9/L$ | 502 | 401 | 322 | 264 | 224 | 170 |
| Neutrophils $\geq 7.99 \times 10^9/L$ | 97 | 73 | 57 | 46 | 37 | 28 |



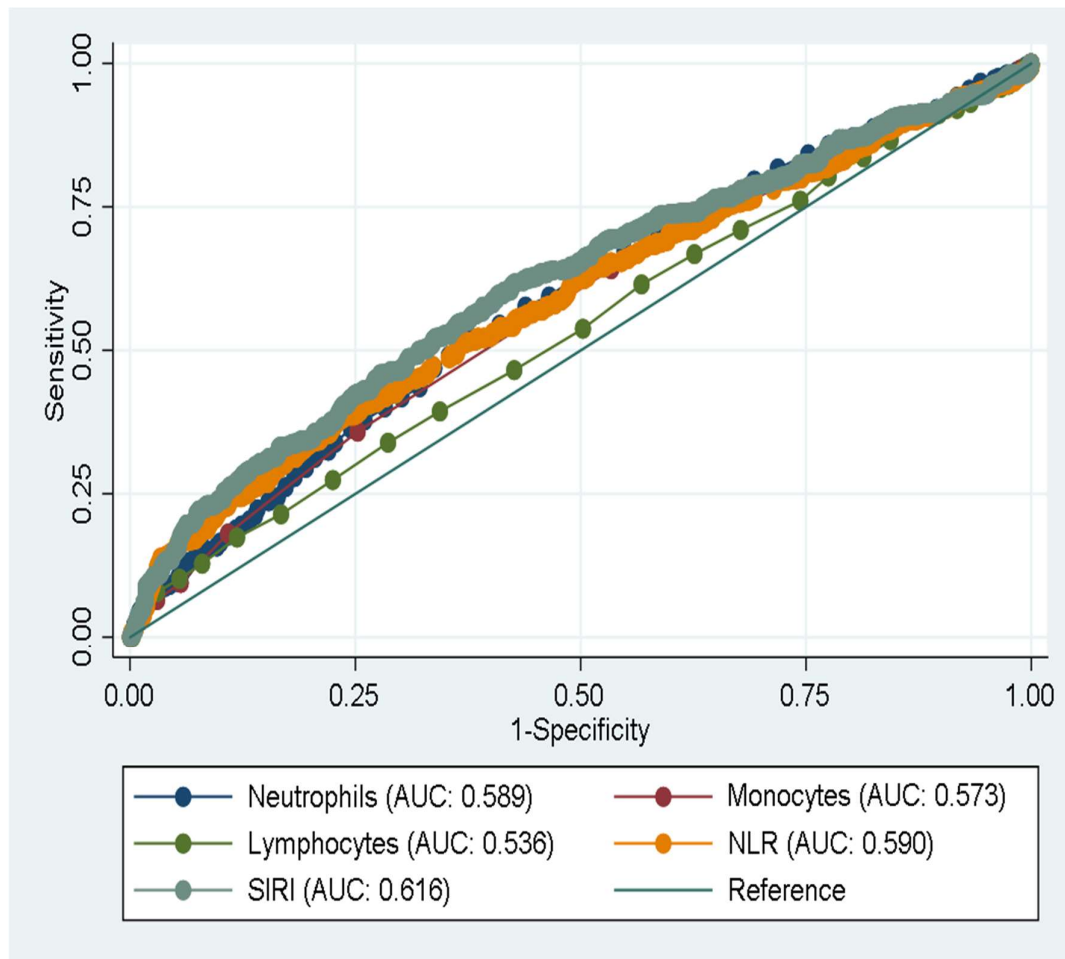
Number at risk

| | 0 | 12 | 24 | 36 | 48 | 60 |
|---------------------------------------|-----|-----|-----|-----|-----|-----|
| Neutrophils $\leq 4.80 \times 10^9/L$ | 770 | 639 | 538 | 442 | 349 | 271 |
| Neutrophils $4.80-7.99 \times 10^9/L$ | 502 | 372 | 297 | 236 | 198 | 142 |
| Neutrophils $\geq 7.99 \times 10^9/L$ | 97 | 69 | 54 | 40 | 29 | 23 |

Supplementary Figure 2. Disease-specific survival in Group A according to (a) Monocytes, (b) Lymphocytes, (c) Neutrophil-to-Lymphocyte Ratio (NLR), and (d) Systemic Inflammation Response Index (SIRI) categories defined by the new oral cavity cutoffs



Supplementary Figure 3. Receiver operating characteristic (ROC) curves and the corresponding area under the curve (AUC) according to Neutrophils, Monocytes, Lymphocytes, Neutrophil-to-Lymphocyte Ratio (NLR), and Systemic Inflammation Response Index (SIRI) values in Group A with overall survival as dependent variable



Supplementary Figure 4. Overall survival in Group B according to (a) Neutrophils, (b) Monocytes, (c) Lymphocytes, (d) Neutrophil-to-Lymphocyte Ratio (NLR), and (e) Systemic Inflammation Response Index (SIRI) categories defined by the new oral cavity cutoffs

