

| VEGF plasma (ng/L) | Sensitivity | FDR | Specificity | Youden index | Below (0) or above (1) cut-off |
|-----------------------|-------------|-------|-------------|-----------------|--------------------------------------|
| 0 | 1.000 | 1.000 | 0.000 | 0.000 | 0 |
| 0.7050 | 1.000 | 0.964 | 0.036 | 0.036 | 0 |
| 2.2800 | 1.000 | 0.927 | 0.073 | 0.073 | 0 |
| 3.3650 | 1.000 | 0.909 | 0.091 | 0.091 | 0 |
| 3.6600 | 1.000 | 0.891 | 0.109 | 0.109 | 0 |
| 4.2100 | 1.000 | 0.855 | 0.145 | 0.145 | 0 |
| 4.6200 | 1.000 | 0.836 | 0.164 | 0.164 | 0 |
| 4.8950 | 1.000 | 0.818 | 0.182 | 0.182 | 0 |
| 5.5600 | 0.950 | 0.818 | 0.182 | 0.173 | 0 |
| 6.2250 | 0.950 | 0.800 | 0.200 | 0.190 | 0 |
| 6.8300 | 0.900 | 0.800 | 0.200 | 0.180 | 0 |
| 7.3950 | 0.900 | 0.782 | 0.218 | 0.196 | 0 |
| 7.7600 | 0.900 | 0.764 | 0.236 | 0.213 | 0 |
| 8.0700 | 0.900 | 0.745 | 0.255 | 0.229 | 0 |
| 8.2400 | 0.900 | 0.727 | 0.273 | 0.245 | 0 |
| 8.4050 | 0.900 | 0.709 | 0.291 | 0.262 | 0 |
| 8.9900 | 0.850 | 0.709 | 0.291 | 0.247 | 0 |
| 10.0700 | 0.850 | 0.691 | 0.309 | 0.263 | 0 |
| 10.7450 | 0.850 | 0.673 | 0.327 | 0.278 | 0 |
| 10.8900 | 0.850 | 0.655 | 0.345 | 0.294 | 0 |
| 11.2450 | 0.800 | 0.636 | 0.364 | 0.291 | 0 |
| 11.8650 | 0.800 | 0.618 | 0.382 | 0.305 | 0 |
| 12.9750 | 0.800 | 0.600 | 0.400 | 0.320 | 0 |
| 13.7900 | 0.800 | 0.582 | 0.418 | 0.335 | 0 |
| 14.3750 | 0.800 | 0.564 | 0.436 | 0.349 | 0 |
| 15.2800 | 0.800 | 0.545 | 0.455 | 0.364 | 0 |
| 15.6500 | 0.800 | 0.527 | 0.473 | 0.378 | 0 |
| 16.4700 | 0.800 | 0.509 | 0.491 | 0.393 | 0 |
| 17.8800 | 0.800 | 0.491 | 0.509 | 0.407 | 0 |
| 18.6100 | 0.800 | 0.473 | 0.527 | 0.422 | 0 |
| 19.0550 | 0.800 | 0.455 | 0.545 | 0.436 | 0 |
| 19.9300 | 0.750 | 0.455 | 0.545 | 0.409 | 0 |
| 20.7550 | 0.750 | 0.436 | 0.564 | 0.423 | 0 |
| 22.2750 | 0.750 | 0.418 | 0.582 | 0.436 | 0 |
| 23.9650 | 0.750 | 0.400 | 0.600 | 0.450 | 0 |
| 25.3700 | 0.750 | 0.382 | 0.618 | 0.464 | 0 |
| 26.4150 | 0.700 | 0.382 | 0.618 | 0.433 | 1 |
| 26.6800 | 0.700 | 0.364 | 0.636 | 0.445 | 1 |
| 28.0550 | 0.650 | 0.364 | 0.636 | 0.414 | 1 |
| 30.1900 | 0.650 | 0.345 | 0.655 | 0.425 | 1 |
| 31.2550 | 0.650 | 0.327 | 0.673 | 0.437 | 1 |
| 31.6250 | 0.600 | 0.327 | 0.673 | 0.404 | 1 |
| 32.0200 | 0.600 | 0.309 | 0.691 | 0.415 | 1 |
| 33.2800 | 0.600 | 0.291 | 0.709 | 0.425 | 1 |
| 36.4750 | 0.600 | 0.273 | 0.727 | 0.436 | 1 |
| 39.1550 | 0.600 | 0.255 | 0.745 | 0.447 | 1 |
| 39.7700 | 0.550 | 0.255 | 0.745 | 0.410 | 1 |
| 39.9300 | 0.500 | 0.255 | 0.745 | 0.373 | 1 |
| 40.6500 | 0.500 | 0.236 | 0.764 | 0.382 | 1 |
| 41.8300 | 0.500 | 0.218 | 0.782 | 0.391 | 1 |
| 42.4500 | 0.450 | 0.218 | 0.782 | 0.352 | 1 |
| 43.9650 | 0.400 | 0.218 | 0.782 | 0.313 | 1 |
| 45.6950 | 0.400 | 0.200 | 0.800 | 0.320 | 1 |
| 48.2200 | 0.400 | 0.182 | 0.818 | 0.327 | 1 |
| 51.2000 | 0.400 | 0.164 | 0.836 | 0.335 | 1 |
| 52.2950 | 0.400 | 0.145 | 0.855 | 0.342 | 1 |
| 53.2800 | 0.400 | 0.127 | 0.873 | 0.349 | 1 |
| 56.0700 | 0.400 | 0.109 | 0.891 | 0.356 | 1 |
| 58.8100 | 0.350 | 0.109 | 0.891 | 0.312 | 1 |
| 60.7100 | 0.300 | 0.109 | 0.891 | 0.267 | 1 |
| 62.5100 | 0.300 | 0.091 | 0.909 | 0.273 | 1 |
| 64.9800 | 0.250 | 0.091 | 0.909 | 0.227 | 1 |
| 68.3000 | 0.250 | 0.073 | 0.927 | 0.232 | 1 |
| 70.1550 | 0.250 | 0.055 | 0.945 | 0.236 | 1 |
| 75.0850 | 0.250 | 0.036 | 0.964 | 0.241 | 1 |
| 83.5250 | 0.200 | 0.036 | 0.964 | 0.193 | 1 |
| 89.9850 | 0.150 | 0.036 | 0.964 | 0.145 | 1 |
| 113.2250 | 0.100 | 0.036 | 0.964 | 0.096 | 1 |
| 136.5650 | 0.100 | 0.018 | 0.982 | 0.098 | 1 |
| 144.0100 | 0.100 | 0.000 | 1.000 | 0.100 | 1 |
| 177.6450 | 0.050 | 0.000 | 1.000 | 0.050 | 1 |
| 206.3200 | 0.000 | 0.000 | 1.000 | 0.000 | 1 |

| VEGF serum (ng/L) | Sensitivity | FDR | Specificity | Youden index | Below (0) or above (1) cut-off |
|----------------------|-------------|-------|-------------|-----------------|--------------------------------------|
| 0 | 1.000 | 1.000 | 0.000 | 0.000 | 0 |
| 9.7800 | 0.950 | 1.000 | 0.000 | 0.000 | 0 |
| 23.0950 | 0.950 | 0.982 | 0.018 | 0.017 | 0 |
| 31.9700 | 0.950 | 0.964 | 0.036 | 0.035 | 0 |
| 43.0950 | 0.950 | 0.945 | 0.055 | 0.052 | 0 |
| 51.5400 | 0.950 | 0.927 | 0.073 | 0.069 | 0 |
| 54.5250 | 0.950 | 0.909 | 0.091 | 0.086 | 0 |
| 56.8150 | 0.950 | 0.891 | 0.109 | 0.104 | 0 |
| 59.4500 | 0.950 | 0.873 | 0.127 | 0.121 | 0 |
| 61.5350 | 0.950 | 0.855 | 0.145 | 0.138 | 0 |
| 63.6200 | 0.950 | 0.836 | 0.164 | 0.155 | 0 |
| 68.7050 | 0.950 | 0.818 | 0.182 | 0.173 | 0 |
| 72.5900 | 0.950 | 0.800 | 0.200 | 0.190 | 0 |
| 74.6900 | 0.950 | 0.782 | 0.218 | 0.207 | 0 |
| 80.8600 | 0.950 | 0.764 | 0.236 | 0.225 | 0 |
| 86.1700 | 0.900 | 0.764 | 0.236 | 0.213 | 0 |
| 93.9750 | 0.900 | 0.745 | 0.255 | 0.229 | 0 |
| 101.1100 | 0.900 | 0.727 | 0.273 | 0.245 | 0 |
| 106.5750 | 0.900 | 0.709 | 0.291 | 0.262 | 0 |
| 113.8200 | 0.900 | 0.691 | 0.309 | 0.278 | 0 |
| 116.6850 | 0.900 | 0.673 | 0.327 | 0.295 | 0 |
| 117.5700 | 0.900 | 0.655 | 0.345 | 0.311 | 0 |
| 119.0450 | 0.900 | 0.636 | 0.364 | 0.327 | 0 |
| 120.8250 | 0.900 | 0.618 | 0.382 | 0.344 | 0 |
| 123.5800 | 0.850 | 0.618 | 0.382 | 0.325 | 0 |
| 127.3400 | 0.850 | 0.600 | 0.400 | 0.340 | 0 |
| 132.6800 | 0.800 | 0.600 | 0.400 | 0.320 | 0 |
| 137.0600 | 0.800 | 0.582 | 0.418 | 0.335 | 0 |
| 140.7150 | 0.800 | 0.564 | 0.436 | 0.349 | 0 |
| 144.5850 | 0.750 | 0.564 | 0.436 | 0.327 | 0 |
| 146.7000 | 0.750 | 0.545 | 0.455 | 0.341 | 0 |
| 148.9850 | 0.750 | 0.527 | 0.473 | 0.355 | 0 |
| 150.5250 | 0.750 | 0.509 | 0.491 | 0.368 | 0 |
| 158.3050 | 0.750 | 0.491 | 0.509 | 0.382 | 0 |
| 166.5000 | 0.750 | 0.473 | 0.527 | 0.395 | 0 |
| 167.8050 | 0.750 | 0.455 | 0.545 | 0.409 | 0 |
| 171.0450 | 0.750 | 0.436 | 0.564 | 0.423 | 0 |
| 176.0900 | 0.750 | 0.418 | 0.582 | 0.436 | 0 |
| 179.7500 | 0.750 | 0.400 | 0.600 | 0.450 | 0 |
| 182.9600 | 0.750 | 0.382 | 0.618 | 0.464 | 0 |
| 187.0150 | 0.700 | 0.382 | 0.618 | 0.433 | 0 |
| 193.0300 | 0.700 | 0.364 | 0.636 | 0.445 | 0 |
| 199.8100 | 0.650 | 0.364 | 0.636 | 0.414 | 0 |
| 208.0700 | 0.600 | 0.364 | 0.636 | 0.382 | 0 |
| 221.5650 | 0.600 | 0.345 | 0.655 | 0.393 | 0 |
| 233.3850 | 0.600 | 0.327 | 0.673 | 0.404 | 0 |
| 236.6700 | 0.550 | 0.327 | 0.673 | 0.370 | 0 |
| 239.4400 | 0.550 | 0.309 | 0.691 | 0.380 | 0 |
| 246.4950 | 0.550 | 0.291 | 0.709 | 0.390 | 0 |
| 251.0900 | 0.550 | 0.273 | 0.727 | 0.400 | 0 |
| 263.6550 | 0.550 | 0.255 | 0.745 | 0.410 | 0 |
| 264.6000 | 0.500 | 0.255 | 0.745 | 0.373 | 1 |
| 265.6450 | 0.450 | 0.255 | 0.745 | 0.335 | 1 |
| 266.5000 | 0.400 | 0.255 | 0.745 | 0.298 | 1 |
| 267.5550 | 0.350 | 0.255 | 0.745 | 0.261 | 1 |
| 275.6050 | 0.300 | 0.255 | 0.745 | 0.224 | 1 |
| 284.7700 | 0.300 | 0.236 | 0.764 | 0.229 | 1 |
| 292.0100 | 0.300 | 0.218 | 0.782 | 0.235 | 1 |
| 298.1000 | 0.300 | 0.200 | 0.800 | 0.240 | 1 |
| 306.2550 | 0.250 | 0.200 | 0.800 | 0.200 | 1 |
| 322.3750 | 0.250 | 0.182 | 0.818 | 0.205 | 1 |
| 332.0100 | 0.200 | 0.182 | 0.818 | 0.164 | 1 |
| 334.3550 | 0.200 | 0.164 | 0.836 | 0.167 | 1 |
| 344.7850 | 0.200 | 0.145 | 0.855 | 0.171 | 1 |
| 354.2600 | 0.200 | 0.127 | 0.873 | 0.175 | 1 |
| 358.8300 | 0.200 | 0.109 | 0.891 | 0.178 | 1 |
| 365.8950 | 0.200 | 0.091 | 0.909 | 0.182 | 1 |
| 397.2250 | 0.200 | 0.073 | 0.927 | 0.185 | 1 |
| 442.7150 | 0.150 | 0.073 | 0.927 | 0.139 | 1 |
| 466.4500 | 0.150 | 0.055 | 0.945 | 0.142 | 1 |
| 473.6150 | 0.150 | 0.036 | 0.964 | 0.145 | 1 |
| 481.2500 | 0.150 | 0.018 | 0.982 | 0.147 | 1 |
| 494.5850 | 0.150 | 0.000 | 1.000 | 0.150 | 1 |
| 593.5100 | 0.100 | 0.000 | 1.000 | 0.100 | 1 |
| 756.3450 | 0.050 | 0.000 | 1.000 | 0.050 | 1 |
| 826.3500 | 0.000 | 0.000 | 1.000 | 0.000 | 1 |

(c)

Figure S1. Receiver-operator characteristics (ROC) of vascular endothelial growth factor (VEGF) concentration in plasma [(a), (c)] and serum [(b), (d)] for event-free survival of therapy-naïve head and neck squamous cell carcinoma patients. (a) ROC for VEGF_{plasma}; (b) ROC for VEGF_{serum}; (c) tabulated sensitivity, false-discovery rate (FDR), specificity, and Youden indices for VEGF_{plasma} to define the cut-off for VEGF_{plasma} of 26 ng/L according the maximum Youden score (underlined); (d) tabulated sensitivity, false-discovery rate (FDR), specificity, and Youden indices for VEGF_{serum} to define the cut-off for VEGF_{serum} of 264 ng/L according the maximum Youden score (underlined).

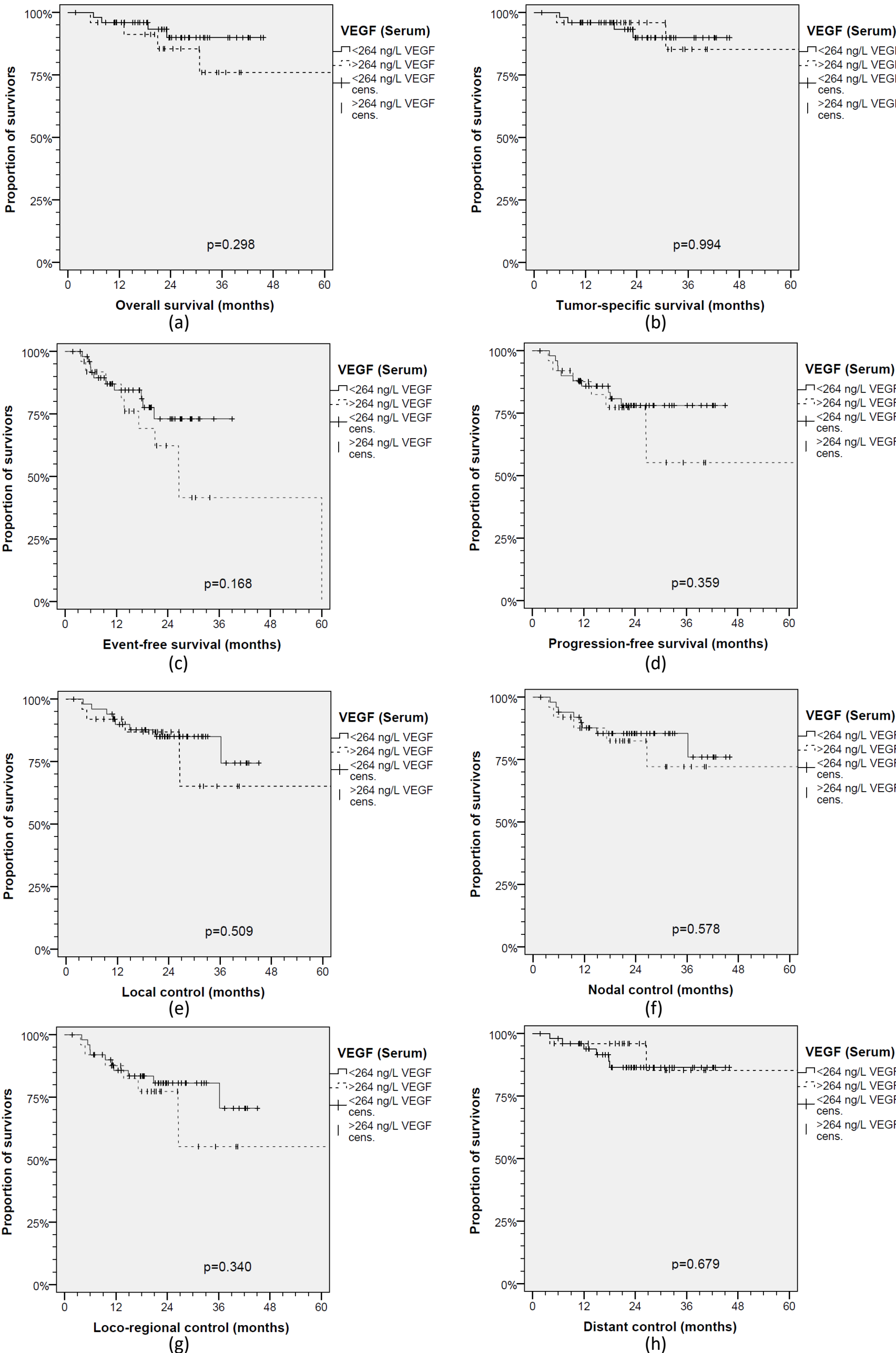


Figure S2. Kaplan-Meier plots for cumulative survival in head and neck squamous cell carcinoma patients from the test cohort stratified according to vascular endothelial growth factor (VEGF) in pre-therapeutic serum. (a) overall survival; (b) tumor-specific survival; (c) event-free survival; (d) progression-free survival; (e) local control; (f) nodal control; (g) loco-regional control; (h) distant control. p values shown are from 2-sided log-rank test.