**Supplemental table 5: Prognostic factors for overall survival in patients with metastatic grade 3 neuroendocrine neoplasms (cohort national cancer registry)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | N | UnivariableHR (95% CI) | P-value | MultivariableHR (95% CI) | P-value |
| Sex  |  |  |  |  |  |
| Male | 1,689 | Ref. |  |  |  |
| Female | 1,296 | 0.98 (0.91 – 1.06) | 0.64 | - | - |
| Age |  |  |  |  |  |
| ≤65 | 1,271 | Ref. |  | Ref. |  |
| >65 | 1,714 | 1.48 (1.38 – 1.60) | <0.001 | 1.53 (1.42 – 1.65) | **<0.001** |
| Primary tumor |  |  |  |  |  |
| GE | 631 | Ref. |  | Ref. |  |
| Pancreas | 188 | 0.76 (0.64 – 0.90) | 0.002 | 0.72 (0.61 – 0.86) | **<0.001** |
| Lung | 1,069 | 1.05 (0.95 – 1.16) | 0.33 | 1.22 (1.09 – 1.36) | **0.001** |
| Other | 314 | 0.88 (0.77 – 1.01) | 0.077 | 1.00 (0.87 – 1.16) | 0.99 |
| Unknown | 783 | 1.05 (0.94 – 1.17) | 0.38 | 1.16 (1.04 – 1.30) | **0.009** |
| Number of organs with metastases |  |  |  |  |  |
| 1 | 1,527 | Ref.  |  | Ref. |  |
| 2-3 | 1,362 | 1.39 (1.29 – 1.50) | <0.001 | 1.29 (1.16 – 1.43) | **<0.001** |
| ≥4 | 96 | 1.76 (1.43 – 2.17) | <0.001 | 1.60 (1.22 – 2.11) | **0.001** |
| Location metastases |  |  |  |  |  |
| Liver | 1,763 | 1.53 (1.42 – 1.65) | <0.001 | 1.64 (1.46 – 1.84) | **<0.001** |
| Brain | 304 | 0.91 (0.81 – 1.03) | 0.13 | 1.02 (0.88 – 1.18) | 0.79 |
| Lung | 476 | 1.18 (1.07 – 1.31) | 0.001 | 1.07 (0.96 – 1.20) | 0.24 |
| Bone | 761 | 1.12 (1.03 – 1.22) | 0.007 | 1.16 (1.00 – 1.34) | 0.051 |
| Lymph nodes (distant) | 874 | 0.86 (0.80 – 0.93) | <0.001 | 0.83 (0.75 – 0.92) | **0.001** |
|  |  |  |  |  |  |
| Liver\*Bone1 |  | - | - | 0.75 (0.63 – 0.90) | **0.002** |

*Abbreviations: HR = Hazard Ratio; 95% CI = 95% Confidence Interval; Ref. = Reference; GE = gastroenteral.*

*1Interaction terms included in the final multivariable model.*

*Events = 2,842.*