**Supplemental table 4: Prognostic factors for overall survival in patients with metastatic grade 2 neuroendocrine neoplasms (cohort national cancer registry)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | N | Univariable  HR (95% CI) | P-value | Multivariable  HR (95% CI) | P-value |
| Sex |  |  |  |  |  |
| Male | 312 | Ref. |  |  |  |
| Female | 292 | 1.14 (0.92 – 1.41) | 0.25 | - | - |
| Age |  |  |  |  |  |
| ≤65 | 314 | Ref. |  | Ref. |  |
| >65 | 290 | 1.73 (1.40 – 2.15) | <0.001 | 2.00 (1.60 – 2.49) | **<0.001** |
| Primary tumor |  |  |  |  |  |
| GE | 263 | Ref. |  | Ref. |  |
| Pancreas | 147 | 2.01 (1.52 – 2.66) | <0.001 | 2.28 (1.70 – 3.06) | **<0.001** |
| Lung | 74 | 3.58 (2.59 – 4.96) | <0.001 | 3.87 (2.73 – 5.50) | **<0.001** |
| Other | 11 | 2.14 (1.11 – 4.11) | 0.023 | 1.52 (0.75 – 3.08) | 0.246 |
| Unknown | 109 | 1.79 (1.31 – 2.43) | <0.001 | 1.74 (1.26 – 2.39) | **0.001** |
| Number of organs with metastases |  |  |  |  |  |
| 1 | 320 | Ref. |  | Ref. |  |
| 2-3 | 260 | 1.15 (0.92 – 1.43) | 0.21 | 0.84 (0.61 – 1.17) | 0.31 |
| ≥4 | 24 | 1.59 (0.94 – 2.70) | 0.087 | 1.16 (0.56 – 2.40) | 0.69 |
| Location metastases |  |  |  |  |  |
| Liver | 503 | 1.12 (0.83 – 1.51) | 0.45 | 1.41 (1.00 – 1.99) | 0.051 |
| Brain | 12 | 3.07 (1.63 – 5.78) | 0.001 | 2.54 (1.24 – 5.21) | **0.011** |
| Lung | 38 | 1.47 (0.98 – 2.21) | 0.061 | 3.41 (1.87 – 6.20) | **<0.001** |
| Bone | 138 | 1.33 (1.04 – 1.70) | 0.024 | 1.30 (0.91 – 1.84) | 0.15 |
| Lymph nodes (distant) | 119 | 1.22 (0.94 – 1.59) | 0.13 | 1.52 (1.06 – 2.18) | **0.022** |
|  |  |  |  |  |  |
| Lung\*Bone1 |  | - | - | 0.29 (0.13 – 0.68) | **0.004** |
| Lung\*Lymph nodes1 |  | - | - | 0.29 (0.08 – 1.02) | 0.053 |

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

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

*Events = 335.*