**Appendix Table 1 Neuroendocrine Cancer Classification** 2

|  |  |  |  |
| --- | --- | --- | --- |
| **Differentiation** | **Grade** | **Gastrointestinal NET**  **(excluding pancreas)** | **Lung and Thymic** |
| **Well-differentiated** | Low Grade (G1) | <2 mitoses/10 HPF AND/OR<3% Ki-67 index | <2 mitoses/10 HPF AND no necrosis |
| Intermediate Grade (G2) | 2-20 mitoses/10 HPF AND/OR 3-20% Ki-67 index | 2-10 mitoses/10 HPF AND/OR foci of necrosis |
| **Poorly differentiated** | High Grade (G3) | >20 mitoses/10 HPF AND/OR >20% Ki-67 index | >10 mitoses/10 HPF |

**Appendix Table 2. Tumor profiling for mutational burden and PD-L1 expression**

**in a distinct cohort of neuroendocrine neoplasms**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Tumor Type** | **TMB (mutations/MB)**  **[Median: range]**  **(N = 361)** | **Odds ratio**  **(95% CI)\*** | **P value** | **PD-L1 positive**  **tumor tissue**  **(%)**  **(N = 446)** | **Odds ratio**  **(95% CI)\*** | **P value** |
| High grade | 8 (1 to 18)  (N = 239) | 4.23 (1.46, 12.31) | **0.004** | 3.5%  (N = 286) | 0.61 (0.24, 1.53) | 0.29 |
| Intermediate or low grade | 6 (1 to 66)  (N = 122) | 5.6%  (N = 160) |
| Lung | 9 (1 to 72)  (N = 97) | 1.46 (0.62, 3.42) | 0.38 | 5.1%  (N = 79) | 2.13 (0.46, 9.80) | 0.32 |
| Non-pancreatic gastrointestinal | 6 (1 to 66)  (N = 85) | 0.46 (0.15, 1.42) | 0.17 | 3.6%  (N = 111) | 1.50 (0.33, 6.83) | 0.60 |
| Gynecological | 7 (1 to 24)  (N = 30) | 0.26 (0.03, 2.08) | 0.17 | 4.3%  (N = 46) | 1.82 (0.29, 11.25) | 0.52 |
| Pancreatic | 6 (1 to 84) (N=65) | 0.23 (0.05, 1.11) | 0,05 | 6.9%  (N=87) | 2.96 (0.72, 12.19) | 0.12 |
| Other (reference) | 7 (1 to 118) (N=84) | Reference | | 2.4%  (N=123) | Reference | |

\*Odds ratio is from a logistic regression with outcome high-grade tumors versus intermediate/low grade tumors and covariate TMB high-level versus low/intermediate-level TMB; for histologic odds ratios, the reference value is “other” tumor types. MB, mega-base pairs

**Appendix Figure 1.** Progression-free survival: Progression-free survival of all 32 patients is shown. Thirty-one percent of patients are progression-free at six months (95% confidence intervals 19% to 52%).



**Appendix Figure 2. Overall survival**

