**Supplementary File 1**

Outcome subgroup analysis

Stratifying the analysis by morphology (Supplementary Tables 1-2), no significant differences were found between the 2 different treatments in the poorly differentiated subgroup (p-value of log-rank test:0.613 for OS [Supplementary Fig. 1A] and 0.982 for PFS [Supplementary Fig. 2A) and the well-differentiated subgroup (p-value of log-rank test:0.687 for OS [Supplementary Fig. 1B] and 0.917 for PFS [Supplementary Fig. 2B]).

**Supplementary Table 1.** Subgroup analysis of OS in patients with poorly differentiated or well-differentiated NENs treated with TEM or CAPTEM

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Variables | No. patients | No. events | Median OS (95%CI) | p- value (log-rank test) |
| TEM & poorly differentiated  | 14 | 12 | 6.2 (3.3-20.0) | 0.613 |
| CAPTEM & poorly differentiated | 12 | 9 | 12.7 (7.5-20.9) |
| TEM & well-differentiated | 54 | 29 | 29.0 (16.5-44.5) | 0.687 |
| CAPTEM & well-differentiated | 13 | 5 | 28.4 (18.2-not estimable) |

**Supplementary Fig. 1**. Comparison of OS in patients with **(A)** poorly differentiated and **(B)** well-differentiated NENs treated with temozolomide (TEM) alone or CAPTEM (TEM + capecitabine)



**B**

**A**

**Supplementary Table 2.** Subgroup analysis of PFS in patients with poorly differentiated or well-differentiated NENs treated with TEM or CAPTEM

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Variables | No. patients | No. events | Median PFS (95%CI) | p-value (log-rank test) |
| TEM & poorly differentiated | 14 | 13 | 2.8 (1.9-5.6) | 0.982 |
| CAPTEM & poorly differentiated | 12 | 11 | 2.9 (2.3-10.5) |
| TEM & well-differentiated | 54 | 40 | 11.5 (10.4-14.9) | 0.917 |
| CAPTEM & well differentiated | 13 | 10 | 10.2 (4.5-17.5) |

**Supplementary Fig. 2.** Comparison of PFS in patients with **(A)** poorly differentiated and **(B)** well-differentiated NENs treated with temozolomide alone (TEM) and CAPTEM (TEM + capecitabine)



**B**

**A**