

De Mestier, L., Walter, T., Evrard, C., de Boissieu, P., Hentic, O., Cros, J., Tougeron, D., Lombard-Bohas, C., Rebours, V., Hammel, P., Ruszniewski, P., 2020. **Temozolomide Alone or Combined with Capecitabine for the Treatment of Advanced Pancreatic Neuroendocrine Tumor.** *Neuroendocrinology* 110, 83–91.
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Abstract

Background

The combination of capecitabine (CAP) with temozolomide (TEM) chemotherapy in advanced pancreatic neuroendocrine tumors (PanNET) relies on limited evidence. We compared TEM-CAP to TEM alone in patients with advanced PanNET.

Methods

Consecutive patients with advanced PanNET treated with TEM or TEM-CAP between 2004 and 2017 in three expert centers were included. Progression-free survival (PFS), tolerance, tumor response, and overall survival were compared between the two groups. Propensity-based analyses were performed to reduce confounding bias due to the nonrandomized setting.

Results

TEM and TEM-CAP were administered to 38 patients and 100 patients, respectively, with a median age of 58 years. The patients in the TEM group more often had hormonal syndromes ($p = 0.03$), a longer median delay to diagnosis ($p = 0.001$), and a higher number of pretreatment lines ($p < 0.001$). The performance status was 0 in 58% versus 65% of the patients, and tumor's median Ki-67 index was 8% versus 11%, respectively. Tolerance was

similar, except that there were more cases of asthenia in the TEM group ($p = 0.017$) and more cases of hand-foot syndrome in the TEM-CAP group ($p = 0.025$). The objective response rate was 34% versus 51% ($p = 0.088$). The raw median PFS was similar with TEM and with TEM-CAP (21.4 vs. 19.8 months, $p = 0.84$). Although CAP tended to decrease the risk of progression in Cox multivariate analysis (HR 0.65, $p = 0.12$), it had no effect after adjustment for the propensity score (HR 1.06, $p = 0.80$).

Conclusions

TEM-CAP might not prolong PFS but might achieve a higher response rate than TEM alone. Hence, TEM-CAP might be preferred when tumor shrinkage is the main therapeutic objective. Otherwise, TEM might be adequate for patients with an impaired performance status or in case of extrahepatic metastases.

Keywords: Capecitabine; Chemotherapy; Metastases; Neuroendocrine tumor; Pancreas; Temozolomide.