Treatment outcomes for well differentiated grade 3 neuroendocrine tumors (NET G3)

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Background: In the most current WHO classification for tumors of the endocrine organs, well differentiated grade 3 neuroendocrine tumors (NET G3) have been distinguished from poorly differentiated grade 3 neuroendocrine carcinomas (NEC G3).
Retrospective data suggest that commonly applied first-line chemotherapy protocols with cisplatin or carboplatin in combination with etoposide (PE) are less effective in NET G3 than NEC G3. Therefore current treatment guidelines suggest alternative first-line treatment with protocols like temozolomide-based (TEM) which have only been evaluated in second-line so far. The aim of this study was to evaluate treatment outcomes for NET G3 with a focus on efficacy of different first-line regimens.

Methods: Retrospective analysis of all patients with NET G3 in the NEN database of our center. All histopathological findings were reviewed by the investigators in order to comply with the most current WHO classification.

Results: A total of 89 patients could be identified. Primary tumors were mainly located in the pancreas. Median overall survival (OS) was not reached during a median follow-up of 18.4 months. 79 patients received palliative first-line therapy: PE 34, FOLFOX 17, TEM 12, other (including streptozotocin-based regimens, targeted agents, peptide receptor radionuclide therapy, somatostatin analogues) 16. Overall response (ORR) and disease control rate (DCR) was 38.2% and 70.6% for PE, 64.7% and 82.4% for FOLFOX, 12% and 58.3% for TEM, 25% and 62.5% for other respectively. Median progression-free survival for PE was 6.7 months. Compared to PE, the other treatment groups showed a trend towards a prolonged PFS (FOLFOX 8.6 months, p = 0.151; TEM 10.8 months; p = 0.333, other 12.0 months, p = 0.085). All non-PE patients combined showed a significantly prolonged PFS vs. PE (10.8 months; p = 0.039).

Conclusions: In this first comparative analysis of first-line treatments for NET G3, patients treated with non-PE regimens show a significantly prolonged PFS. Regarding ORR, FOLFOX seems to be the most active therapeutic regimen. Further prospective evaluation of the optimal therapeutic strategy for this newly defined tumor entity is needed.

Clinical trial identification: The trial was approved by the institutional research ethics committee (approval S-428/2014).

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