CANCER

Stratification of patients with GEP NET tumors

Patients with metastatic gastroenteropancreatic neuroendocrine tumors (GEP NETs) can be stratified into distinct risk categories that have different prognoses and thus require different therapeutic approaches, according to a French research group. The main predictors for overall survival are age at diagnosis of metastases, the number of metastases in the liver, spontaneous tumor progression slope, and initial surgery.

GEP NETs, which mostly include carcinoids and pancreatic endocrine tumors, are a very heterogeneous group of tumors that share some cellular characteristics but have a diverse natural history and behavior. Because of this heterogeneity, defining factors that determine the prognosis of patients with GEP NETs is particularly important for choosing the appropriate therapy and interpreting results. Previous studies, however, have provided controversial results, in part owing to the heterogeneity of their participants.

In order to identify the main prognostic factors of patients with GEP NETs, Durante and colleagues performed a retrospective, single-center analysis of a specific and relatively homogeneous subgroup of patients ($n=118$, 60 men, mean age 57 years). All participants had distant, stage IV metastases from a well-differentiated endocrine carcinoma and

had not received any previous therapy other than surgery. Investigations included histological examination of the tumoral tissue, laboratory examinations and conventional imaging studies (CT and MRI). After the first complete imaging work-up of the metastases, the patients were followed up for an average of 4.6 years.

By the end of the study, 54% of participants had died, which was attributable to tumor progression in 95% of cases. A multivariate analysis revealed four parameters that were markedly associated with increased mortality: advanced age (>65 years) at the diagnosis of distant metastases, having more than 10 metastases in the liver, a progressive tumor-progression slope, and the absence of previous surgery. The authors suggest adjustment of the therapeutic and monitoring strategies according to the predicted outcomes: whereas a 'wait-and-see' strategy might be sufficient for patients with no risk factors, an early and aggressive intervention is recommended for those who have at least three risk factors.

Interestingly, the location of the primary tumor, the number of metastases at extrahepatic sites, the proliferative index, and the presence of a functioning endocrine carcinoma—which had previously been suggested as prognostic factors—were not found to be significantly

associated with overall survival. Although the evaluation of the tumor-progression slope using MRI or CT scans, which is not routinely performed in patients with endocrine tumors, proved to be useful in this study, the authors note that it delays prognostic classification, which might be stressful for patients.

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Original article Durante, C. *et al.* Prognostic factors influencing survival from metastatic (stage IV) gastroenteropancreatic well-differentiated endocrine carcinoma. *Endocr. Relat. Cancer* **16**, 585–597 (2009).