Neuroendocrine neoplasms grade 3: prospective overall survival data and survival after platinum-etoposide chemotherapy within an ENETS Center of Excellence


Introduction
Overall survival (OS) and progression-free survival (PFS) data of grade 3 NENs remains limited.

Aim
The aim is to report prospective survival data in grade 3 NENs treated within NETwerk.

Methods
Patient characteristics of all grade 3 NENs treated from April 2016 to May 2018 were prospectively recorded. Median OS (mOS) from diagnosis and mOS and median PFS (mPFS) after start cisplatinum/carboplatinum-etoposide chemotherapy was calculated.

Results
Of 79 included NEN grade 3 patients, there were 46 males (58.2%). Mean age at diagnosis was 68 years [range 22-90y]. In 67% (N=53) of the cases, the primary tumor was a GEP-NEN (of which 18 unknown). In our population 44% (N=35) had metastases at diagnoses, 44% (N=35) had a Ki67 index ≥ 55%, 30% (N=24) had a Ki67 index < 55%. Platinum-etoposide chemotherapy was given in 29% (N=23) of the patients. The majority (N=41) had FDG-PET imaging of which 36 were positive and 14 had somatostatin receptor imaging (SRS) of which 11 were positive. Combined FDG-SRS positivity was seen in 5 of 11 patients (45%). Overall mOS was 10.5m (95%CI: 6.6-NR). In GEP-NEN mOS was 8.3m (95% CI: 6.0-18.7), while in NENs from other origin mOS was 12m (95% CI: 8.3-NR, p = 0.2). The mOS for patients with a Ki67 index < 55% was 14.2m (95% CI: 8.9-NA) vs 8.2m (95% CI: 5.6-NA) for patients with Ki67 index ≥ 55% (p=0.3). In multivariate analysis, age at diagnosis had significant impact on OS (HR 0.95, p=0.003), while tumor origin showed trend towards significance (HR 0.49, p= 0.056). The mPFS and mOS after chemotherapy were 6.5m (95%: 4.8 -NR) and 14.2m (95% CI: 8.3-NR). For the chemotherapy-treated group no significant effect of tumor location, metastasis at diagnosis and age at diagnosis was seen on OS and PFS.

Conclusions
In this grade 3 NEN cohort, non-GEP-NENs have a better OS survival than GEP-NENs. Our results confirm the limited PFS and OS after platinum-etoposide chemotherapy in grade 3 NENs, highlighting the need for better treatment. When performed, FDG-PET and SRS-positivity is frequent and could guide treatment.