



Determinants of Clinical Outcome of Poorly Differentiated Gastroenteropancreatic (Neuro-) Endocrine Carcinomas in a Multi-Center Cohort from Germany

U.-F. Pape¹, S. Maasberg¹, A. König², A. Starke³, S. Ezzidin⁴, N. Begum⁵, F. Scheerer⁶, C. Fottner⁷, M. Bläker⁸, M. Pavel¹

¹Med. Dept., Div. of Hepatology & Gastroenterology, Charité Campus Virchow Clinic, University Medicine Berlin, ²Dept. f. Gastroenterology, Endocrinology & Metabolism, University Clinic Marburg, ³Dept. of Medicine, Lukas-Hospital, Neuss and University Clinic Düsseldorf, ⁴Dept. of Nuclear Medicine, University Clinic Bonn, ⁵Dept. of General Surgery, University Clinic Schleswig-Holstein, Lübeck, ⁶Klinikum Neuperlach, Munich, ⁷Dept. Of Endocrinology, University Clinic Mainz, ⁸Practice for Gastroenterology, Hamburg all Germany for the participating centers of the German Registry of Neuroendocrine Gastrointestinal Tumours (NET-Registry)

Background:

Prognosis of poorly differentiated neuroendocrine carcinomas (PDEC) – a relatively small but biologically and clinically very aggressive subset of neuroendocrine neoplasms (NEN) - has been difficult to predict due to heterogenous tumour biology, various classification systems, and lack of reliable and recent data due to the rarity of these tumours. Some prognostic factors have been identified¹⁻³, however, either mostly single center-based surveys or focus on single subentities of these analyses limit the value of their results. On the other hand, population-based analyses⁴⁻⁶ NEN are limited by the inclusion of cases with differently classified NEN and a lack of NEN-specific details. In recent years neuroendocrine tumor (NET)-registries have been founded in several countries^{7,8} and here we report the results from the German NET-registry, which is associated with the German Society for Endocrinology (DGE)⁹. In a nationwide survey including solely data from NET diagnosed since 1999 the German registry for gastrointestinal NET has strived to accumulate and analyze factors which influence prognosis in NET.

Aim of the study:

The German NET-registry collected data from patients (pts) with histologically proven NET from all over Germany (figure 1). Epidemiological, histopathological and clinical data of the PDEC-subgroup as well as information on outcome results were analyzed.

Results:

Figure 1: Participating centers of the German NET-registry



Table 1: Basic data in the German NET-registry

| | |
|----------------------------------|----------------------------------|
| number of all NET: | 2009 |
| number of PDEC: | 188 (9.4%) |
| ♀:♂ | 83:105 |
| mean age at initial diagnosis: | 59.4 yrs |
| median age at initial diagnosis: | 62 yrs (range 15-83) |
| mean follow-up: | 21.3 months |
| median follow-up: | 11.0 months (range 1-117 months) |

Figure 2: Primary tumor localization of PDEC

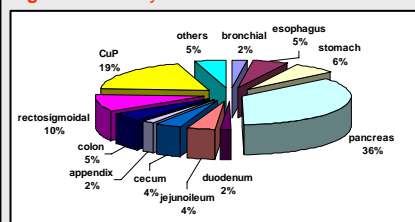
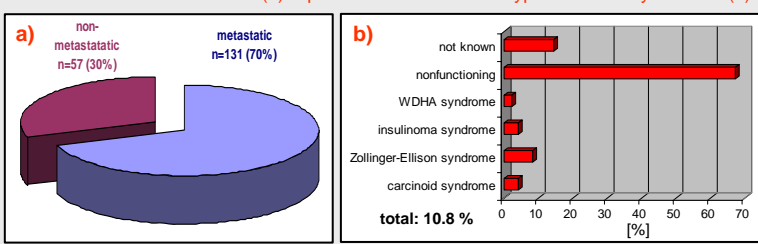


Figure 3: Metastatic rate & localizations (a) & prevalence of hormone hypersecretion syndromes (b)



References:

- 1 Pape UF et al. *Endocr Rel Cancer* 2008
- 2 Pape UF et al. *Cancer* 2008
- 3 Panzutto et al. *Endocr Rel Cancer* 2005
- 4 Yao J et al. *J Clin Oncol* 2008
- 5 Plöckinger U et al. The German NET-Registry: An audit on the diagnosis and therapy of neuroendocrine tumors. *Neuroendocrinology* 2009
- 5 Quaedvlieg PFHJ et al. *Ann Oncol* 2001
- 6 Lepage C et al. *Int J Cancer* 2009
- 7 Lombard-Bohas C et al. *Neuroendocrinology* 2009
- 8 Ahmed A et al. *Endocr Rel Cancer* 2009

Acknowledgements:

The German NET-registry receives support through scientific grants from IPSEN Pharma GmbH and Novartis Pharma GmbH, both Germany.

Figure 4: Results of survival analysis of PDEC in the whole cohort

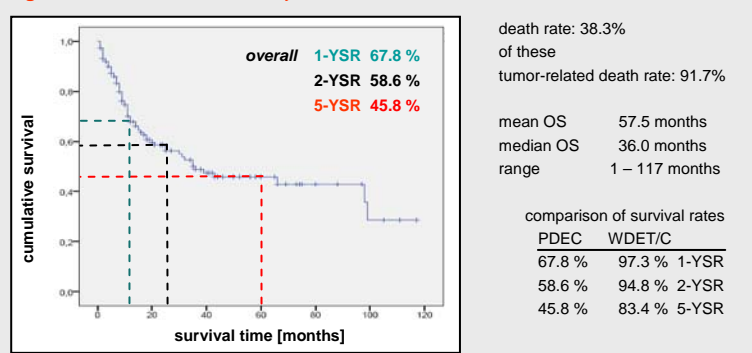


Figure 5: Results of survival analysis according to limited LD vs. extensive ED disease and survival analysis of LD-pts according to surgical treatment (b)

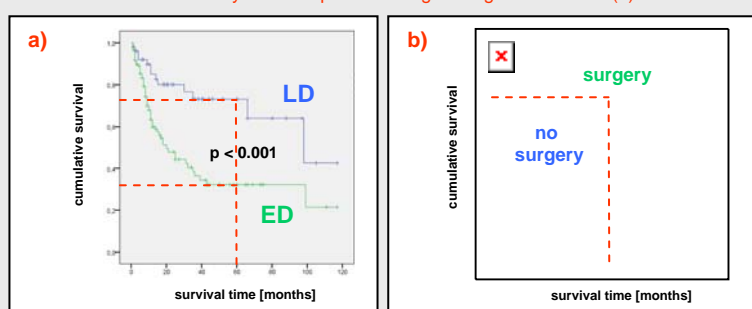
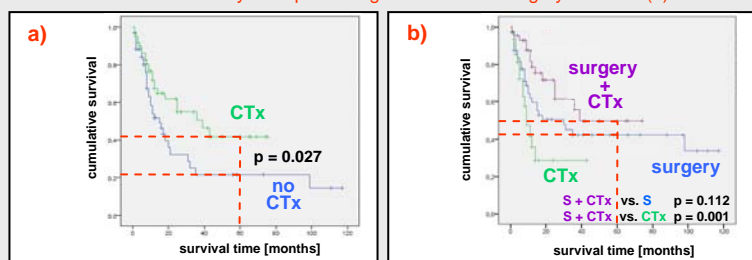


Figure 6: Results of survival analysis according CTx vs. no CTx in ED-pts (a) and survival analysis of pts having received both surgery and CTx (b)



Conclusions:

- The German NET-registry reports data from > 2000 pts. with 188 PDEC from 28 centers in Germany.
- A preference of metastatic as well as pancreatic, rectosigmoidal or unknown primaries PDEC is reported.
- Carcinoid syndrome, hyperinsulinemic hypoglycemic neuroglycopenia (insulinoma syndrome) and Zollinger-Ellison syndrome are rarely observed functional syndromes.
- Survival is poor in comparison to well differentiated NET.
- Survival is significantly influenced by
 - extent of metastasis (LD vs. ED),
 - performance of surgery,
 - performance of CTx
 - or both.
- Tx strategies should be tailored according to these factors.

Methods:

Data from 2009 patients with NET were collected by specifically trained study nurses by structured extraction from clinical source documents after informed consent had been obtained and entered into a data base (Microsoft Access)⁹. Data analysis was performed after structured data extraction and statistical assessment using SPSS Version 16.0.