# A prospective Nordic study on the use of chromogranin A for the prediction of progression in patients with pancreatic and small intestinal neuroendocrine tumours.

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## Background

- Retrospective studies showed that changes in plasma chromogranin A (CgA) may predict change in tumour burden in gastroenteropancreatic neuroendocrine tumour (GEP-NET) patients.
- The aim of this prospective study,was to compare the association between changes in plasma CgA and changes in tumor burden on CT in patients with GEP-NET and unknown primary NET with residual disease

## Material & Methods

- In this non-interventional study, patients with GEP-NET and unknown primary NET under treatment with Sandostatin LAR or with non-somatostatin analog anti-tumour treatment, were observed up to a maximum of 24 month.
- 239 patients were included in Denmark, Norway and Sweden from December 2010 to December 2013. A CT was followed by at least one additional CT 1 - 24 months later.
- Matching pairs of CgA and CT assessments were defined for each individual (defined as an event):
  - Primary analysis: CgA within +/- 6 weeks to CT
  - Post-hoc analysis: CgA 3-6 month prior to CT
- Change in tumour size was defined as regression, progression, or stable disease by RECIST1.1. A 25% change in CgA discriminated between increased, unchanged or decreased plasma CgA levels.

**Table 1. Patient demographics and history**

| Category | Statistics | Tumour Location: All | Small Intestine | Pancreas | Other/ Unknown |
|---|---|---|---|---|---|
| Age (years) | n | 239 | 137 | 72 | 30 |
| | Mean (SD) | 64 (10) | 64 (11) | 63 (10) | 67 (8) |
| Sex | | | | | |
| Female | n (%) | 100 (42) | 61 (45) | 27 (38) | 12 (40) |
| Male | n (%) | 139 (58) | 76 (55) | 45 (63) | 18 (60) |
| Number of days from diagnosis to inclusion | n/nmiss | 239/0 | 137/0 | 72/0 | 30/0 |
| | Mean (SD) | 1677 (2012) | 1930 (2225) | 1295 (1762) | 1437 (1290) |
| Octreoscan by Krenning score | n/nmiss | 211/28 | 119/18 | 64/8 | 28/2 |
| 0 | n (%) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| 1 | n (%) | 7 (3) | 5 (4) | 1 (2) | 1 (4) |
| 2 | n (%) | 12 (6) | 10 (8) | 1 (2) | 1 (4) |
| 3 | n (%) | 64 (30) | 39 (33) | 20 (31) | 5 (18) |
| 4 | n (%) | 71 (34) | 35 (29) | 21 (33) | 15 (54) |
| Not done | n (%) | 57 (27) | 30 (25) | 21 (33) | 6 (21) |
| Ki-67 index | n/nmiss | 211/28 | 121/16 | 64/8 | 26/4 |
| | Mean (SD) | 6 (6) | 4 (3) | 8 (6) | 10 (11) |
| Subjects without Baseline CgA | n | 13 | 8 | 3 | 2 |
| CgA ≤ULN | n | 32 | 21 | 7 | 4 |
| CgA>ULN | n | 194 | 108 | 62 | 24 |

Upper Limit of Normal

**Table 2. Correlation analysis between changes in CgA and RECIST1.1, ITT population**

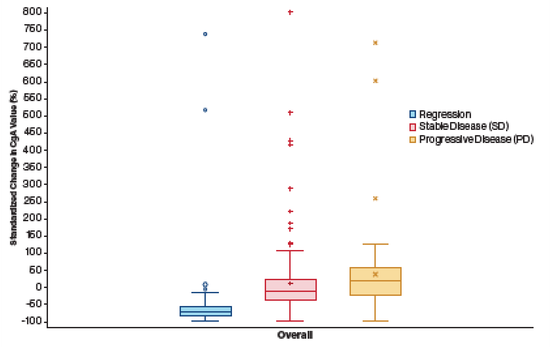
| | Small Intestine | Pancreatic | Unknown | Other | Overall |
|---|---|---|---|---|---|
| Number of events included in analysis | 137 | 123 | 40 | 4 | 304 |
| Spearman's rank correlation coefficient | 0.16 | 0.18 | 0.2 | | 0.17 |
| p-value | 0.07 | 0.04 | 0.21 | | 0.003 |

Only events with CgA test values that were examined 3 to 6 months prior to the CT-scans were included. The category of 'Other' contain too few numbers to perform correlation.

## Results

- Patients demographics and history was similar across subgroups (Table 1)
- Of 304 events in the post-hoc analysis, 58 showed progression, 228 stable disease, and 18 regression (complete and partial response). The median change in plasma CgA was +19(IQR:-20-(+57))%, -12(-37-(+23))% and -73(-83-(-55))%, respectively (Fig. 1)
- The overall Spearman's rank correlation coefficient was 0.17 (p= 0.003), and 0.16 (p=0.07), 0.18 (p=0.04) and 0.20 (p=0.21) for small intestinal (137 events), pancreatic (123 events) and unknown GEP primary (40 events), respectively. (Table 2)

**Figure 1. Boxplot of standardized change in CgA levels by RECIST1.1, Overall, ITT population**




## Conclusion

- This prospective observational study of patients with GEP-NET and unknown primary NET showed a positive correlation between CgA change from baseline and RECIST response. The predictive value of CgA change from baseline of RECIST response, however, remains to be established.
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