

## Biomarkers in Late Stage Neuroendocrine Tumors of the Small Bowel

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**Background:** Small bowel neuroendocrine tumors (SB-NETs) comprise 20-25% of all neuroendocrine tumors (NETs). They present early with obstruction or later with diarrhoea, flushing and in some, right sided heart lesions (CHD). Biomarkers for MGC include serotonin or urinary 5 hydroxy indole acetic acid (U5HIAA), the general NET marker chromogranin A (CGA) and a specific marker, neurokinin A (NKA). We have shown that NKA >50ng/l indicates poor prognosis. Many treatment options for MGC exist.

**Methods:** We reviewed clinical notes from 20 patients who died from SB-NETs to identify useful markers for late stage disease. We noted biomarkers for 2 years prior to death, at 24, 18, 12 & 6m.

**Results:** All patients were symptomatic, 20/20 with diarrhoea, 19/20 with flushing and 10/20 with CHD. All received somatostatin analogue therapy. Thirteen had surgery (5/20 right hemi-colectomy, 4/20 tumor resection). Eight received radio nucleotide therapy, 3 hepatic embolization and 7 IFA therapy.

From 24-6m median U5HIAA (with ranges) rose through 285 (54.3-1,230), 274 (82.4-704), 397 (62-1,985) to 701 (78.1-1,995) umol/l, CGA 375 (140->1,200), 1,200 (40->1,200), >1,200 (220->1,200) to >1,200 175->1,200)U/l and NKA 57 (20-580), 109 (22-917), 112 (23-1,350) to 134 (30-2,425)ng/l. (Ref Ranges: U5HIAA <47umol/l, CGA <30U/l, NKA<20ng/l).

In 20 patients with 4 sample times, 4 specimens were missed for NKA, 6 for CGA and 15 for 5HIAA.

In 2 patients U5HIAA remained  $<150\mu\text{mol/l}$  throughout and 6 had no sample at 6m. In 4 patients CGA remained  $<500\text{U/l}$  throughout, 47% of CGAs were  $>1,200\text{U/l}$ . In 2 patients NKA remained  $<50\text{ng/l}$  throughout and in all others NKA was  $>50\text{ng/l}$  from 6m.

**Conclusion:** The DACO Assay for CGA does not dilute parallel to standards above  $1,200\text{U/l}$  making CGA difficult to measure in advanced disease. Missed sampling for U5HIAA is a problem in late disease. NKA and U5HIAA are both reliable tests for heralding terminal disease.