

## B3

### New Biomarkers in Neuroendocrine Tumors: A Retrospective Study of Their Diagnostic and Prognostic Value

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**Aims:** In addition to the well-known markers in patients with neuroendocrine tumors (NETs), chromogranin A (CgA) and neuron specific enolase (NSE), two new markers, pro-Gastrin Releasing Peptide (proGRP) and MonoTotal (MT), a cytokeratin marker, were measured in order to evaluate if the established diagnostic and prognostic values improved.

**Methods:** CgA (CIS Bio-international), NSE (Roche Diagnostics), proGRP (Abbott Laboratories) and MT (IDL) were measured in 300 healthy persons, 314 NET not otherwise specified (NETNOS) and 254 small cell cancer (SCC) patients.

#### Results:

	NETNOS	SCC	P-value	Upper reference value
	Median	Median		
	25%-75%	25%-75%		
Chromogranin A (µg/l)	176 66-534	66 42-115	<0.001	98
NSE (µg/l)	8.4 6.0-13.8	17.6 8.3-59.3	<0.001	12.6
proGRP (ng/l)	39 29-56	233 46-1235	<0.001	55
MonoTotal (U/l)	80 49-146	108 60-264	<0.001	127 (M) 84 (F)

CgA was the best marker discriminating NETNOS from healthy (Area under ROC curve (AUC)±SE: 0.857±0.018). ProGRP was the best discriminating marker for SCC (0.846±0.021), but combined with MT, the accuracy was even better (0.937±0.012, p =0.0002). Survival analyses demonstrated that in well differentiated NET (carcinoid), MT and CgA remained associated with survival (p<0.001 and p =0.025, respectively) after correction for age, sex, grade, stage, site and pretreatment. In the moderately differentiated NETNOS (atypical carcinoid), NSE remained the only marker marginally associated with survival (p =0.087). In SCC, NSE and MT remained associated with survival (p<0.001 and p =0.005, respectively).

**Conclusion:** The combination of CgA, NSE, proGRP and MT is a promising marker panel for diagnostics in NET. 1: CgA remains the most useful marker in NETNOS, while the combination of proGRP and MT gives a high accuracy for predicting SCC. 2: CgA and MT are independent prognostic variables for survival in well differentiated NETNOS, while NSE and MT are the prognostic variables in SCC.