

Chromogranin A

(Pilot study)

**O. Topolcan, J. Vrzalova, L. Holubec jr.,
M. Casova, M. Prazakova,
S. Svobodova and M. Pesek**

Charles University in Prague Faculty of Medicine in Pilsen,
Faculty hospital Pilsen

Czech Republic

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Introduction

Characteristic

- Highly hydrophilic protein
- M.w. 49 kDA
- Genes located on chromosome 14
- Granins family
 - Chromogranin A (CgA)
 - Chromogranin B
 - Secretogranin II

Introduction

Extracellular biologic functions

- Precursor of biologic active peptides
- CgA tissue specific proteolysis yields e.g. :
 - Pancreastatin: ↓ production of insulin
glucagon and
parathyroide hormone (PTH)
 - Vasostatin: ↓ vasoconstriction
 - Parastatin: ↓ production of PTH
 - Chromastatin: ↓ production of catecholamines

Introduction

Intracellular biologic functions

- Regulation of production and secretion of
 - Peptidic hormones
 - Neuropeptides
- Binding of Calcium
- Clustering together with hormones and neurotransmitters
 - formation of granules – exocytosis after impulse
 - regulation of secretion

Aim of study

- To find the clinical use of Chromogranin for:
 - Diagnosis and follow-up at carcinoid syndrome
 - Follow-up at NSCLC

Groups of patients

- Control group:
57 patients without oncologic disease
- Non small cell lung cancer group (NSCLC):
112 patients with NSCLC
 - 54 – in remission
 - 58 – in progression (partial or complete)
- Carcinoid group:
31 patients with carcinoid (lung or GIT)
 - 15 – in remission
 - 16 – in progression

Methods

- Biologic material - serum
- Kits producer Schering company – CIS Bio (France)
 - Immunoradiometric assay IRMA
 - Units: ng/mL
 - Calibration curve range : 1.5 – 1210 ng/mL
 - Quality control - internal

Quality control

- Control material (Producer control)
 - 1 control - level ~ 170 ng/mL
- Interassay CV in our laboratory
 - 2.74 %
- Intraassay CV in our laboratory
 - 4.02 %

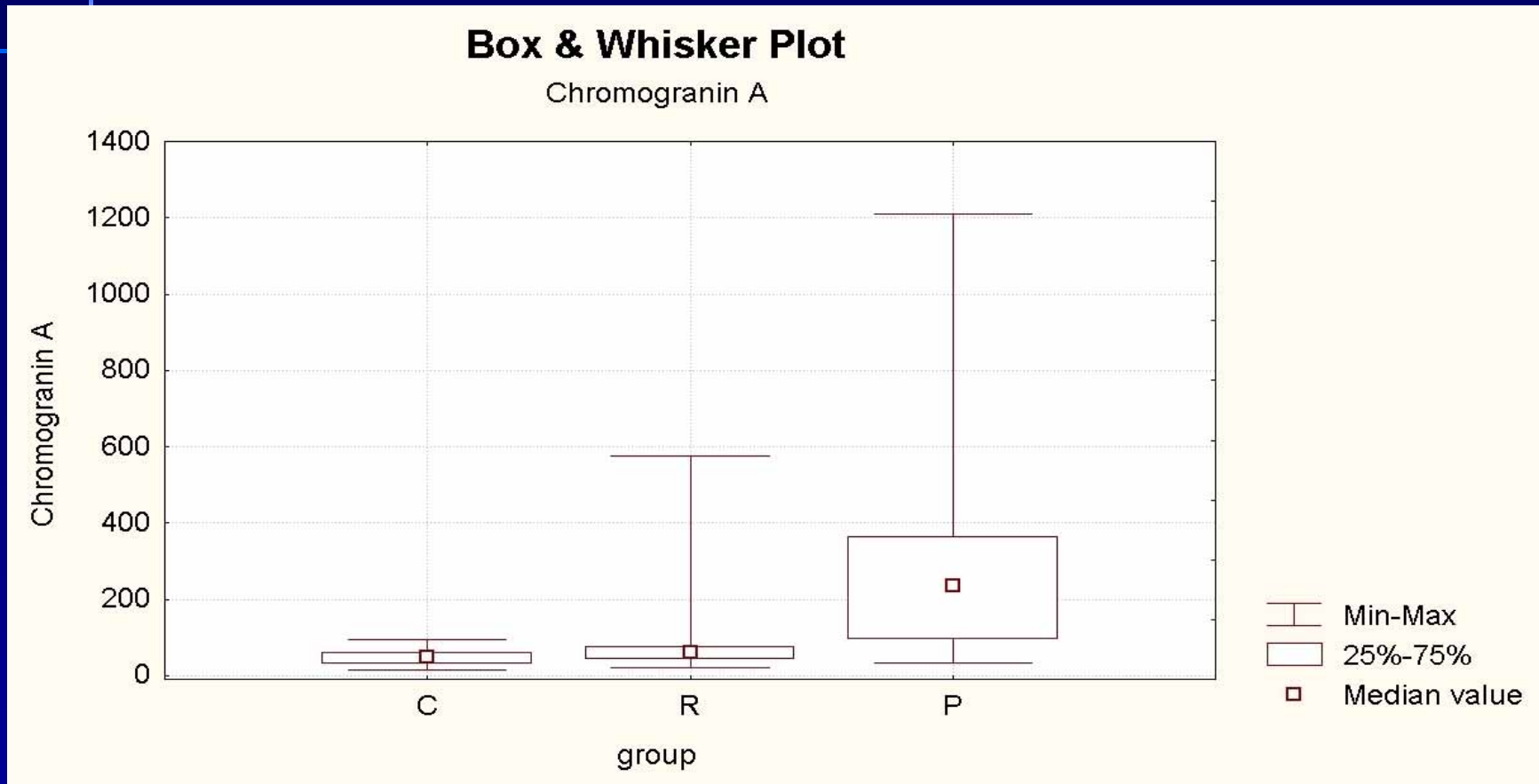
NSCLC group

Parameters	Chromogranin A (ng/mL)		
Group	Control	NSCLC	
		Remission	Progression
n =	57	54	58
Median	47	59	234
95% percentile	78	184.2	1210
5% percentile	16.7	25.1	44
Min.	14.4	21.6	31
Max.	94.8	576	1210

Carcinoid group

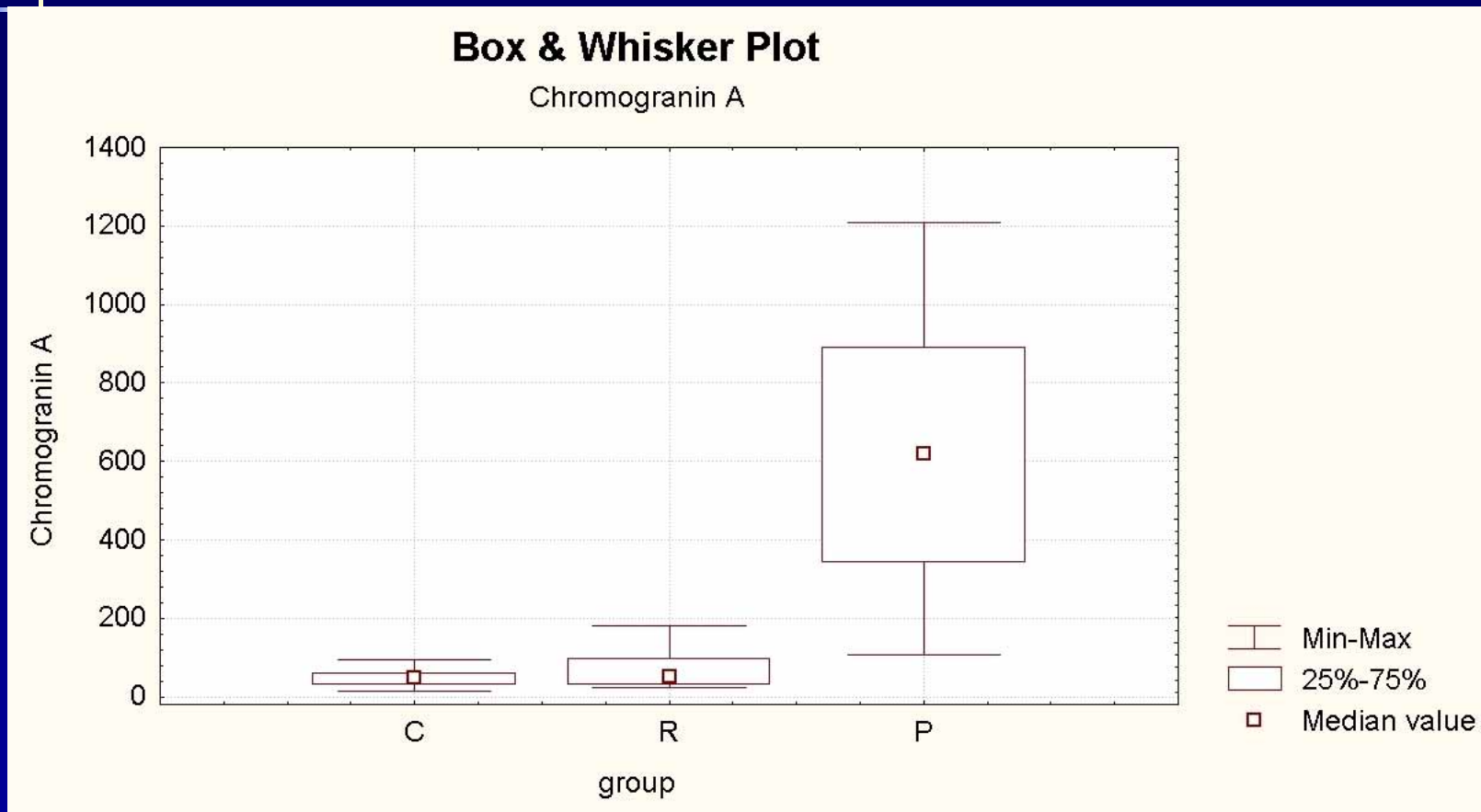
Parameters	Chromogranin A (ng/mL)		
Group	Control	Carcinoid	
		Remission	Progression
n =	57	15	16
Median	47	59.4	619.9
percentile 95%	78	181.5	1210
percentile 5%	16.7	22.9	27.8
Min.	14.4	22.9	107
Max.	94.8	181.6	1210

NSCLC group



C-control, R-remission, P-progression

Carcinoid



C - control, R - remission, P - progression

Significant differences

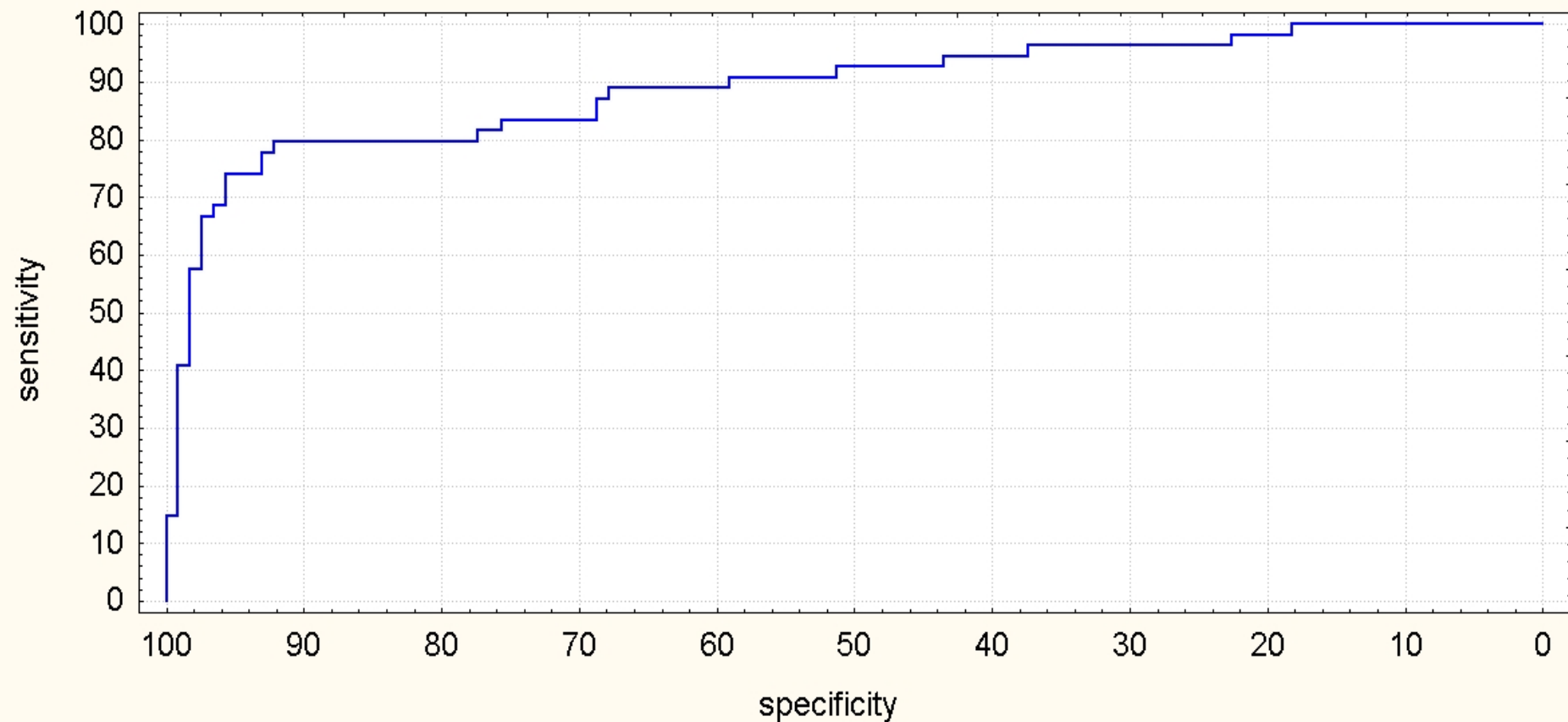
Group	NSCLC	Carcinoid
control versus remission	$p \leq 0.05$	NS
control versus progresion	$p \leq 0.00001$	$p \leq 0.0001$
remission versus progresion	$p \leq 0.0001$	$p \leq 0.0001$

Non small cell lung cancer control + remission versus progression

ROC CURVE

Chromogranin A

C + R vs. P



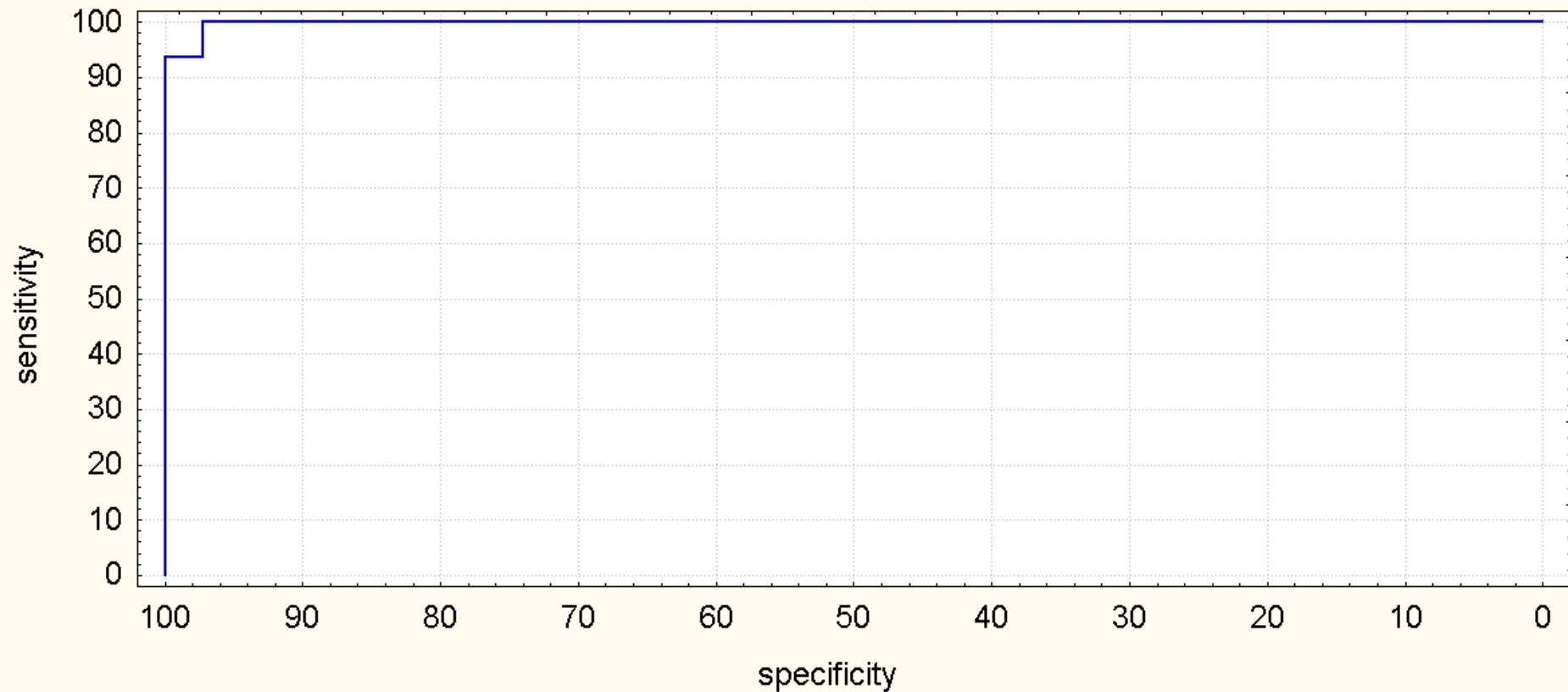
Carcinoid group

control + remission versus progression

ROC CURVE

Chromogranin A

C + R vs. P



Case report 1

Diagnostic use (44 year old man)

3.01.2007 - Computer Tomography
- multiple metastases into liver
(primary origin unknown)

1.02.2007 – cytology

low differentiated adenocarcinoma

Therapy CIS-DDP + 5-FU - without success

1.03.2007 Chromogranin A – 1200 ng/mL

Case report 1

Diagnostic use (44 year man)

2.03.2007 - PET /CT

multiple metastases into liver and
metastasis in mesenterium, susp. carcinoid

4.04.2007 - ¹¹¹In Octreoscan

small intestine carcinoid

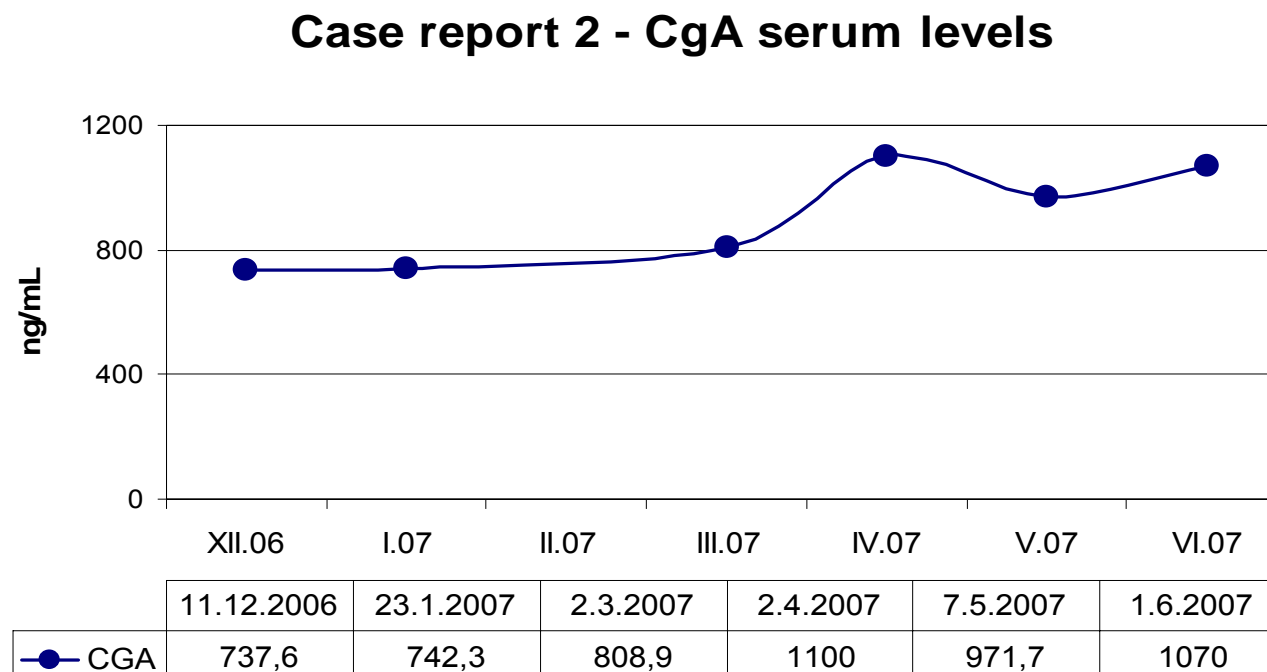
Therapy changed – Sandostatin

19.07.2007 - Partial remission

21.07. 2007 Chromogranin A – 512 ng/mL

Case report 2

Monitoring therapy (unsuccessful)



Front mediastinum carcinoid, therapy - Sandostatin

Case report 3

Interfering benign diseases

Disease	n	Median	Min - max
Renal failure	7	1000	800 - 1200
Chronic liver disease	12	540	126 - 800

Conclusion

Higher serum levels **Chromogranin A:**

- Patients with NSCLC in progression
 - Sensitivity 74 % (specificity 95 %)
- Patients with carcinoid sy in progression
 - Sensitivity 99 % (specificity 95 %)
- Patients with renal failure and chronic liver diseases

Chromogranin A

Clinical use

- To distinguish remission from progression at patients with malignant tumours with neuroendocrine activity
- To confirm the diagnosis of carcinoid

Studies proposed

- Study on larger groups of patients
- Correlations between CgA levels and:
 - Diagnosis
 - Clinical status
 - Stage of disease
 - Prognosis (DFI and OS)
 - Therapy
 - Immunohistochemistry