The approach for gastric NETs: The clinician`s contribution

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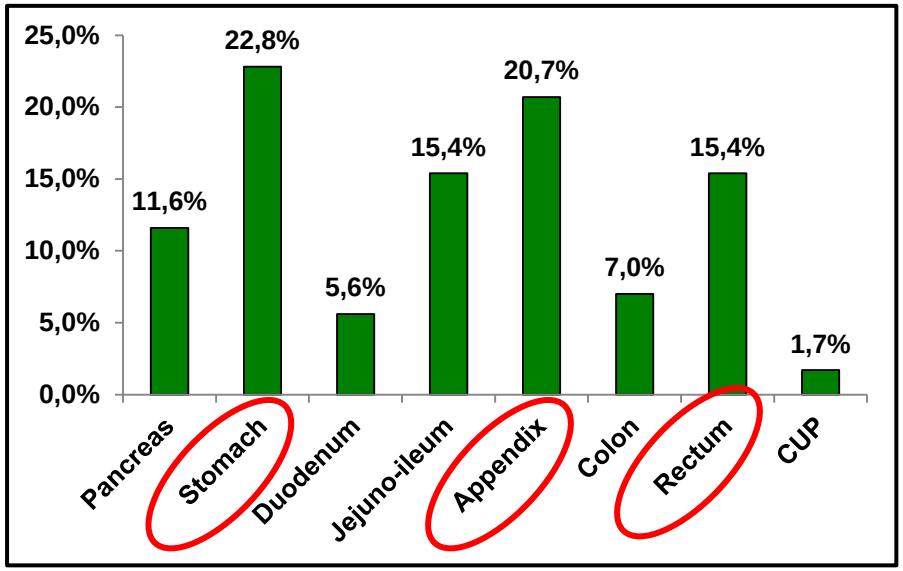
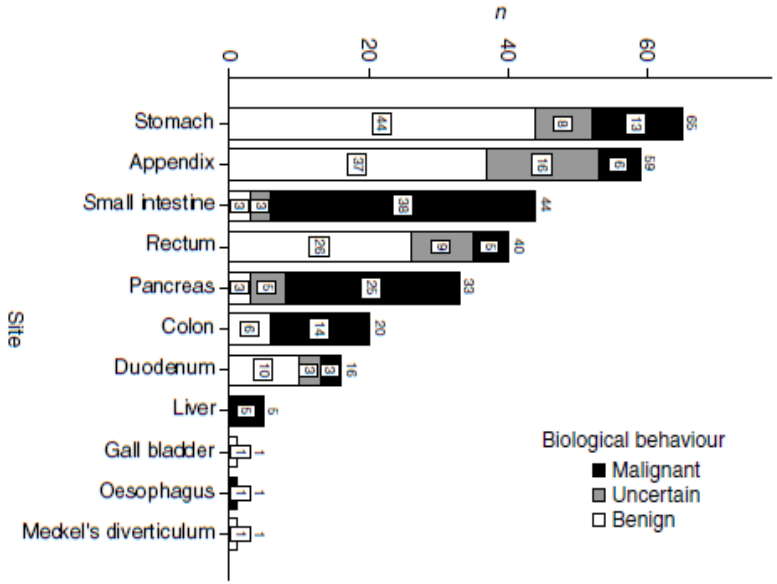
- No conflicts of interest

Frequency and potential malignancy of gastric NET (gNET)

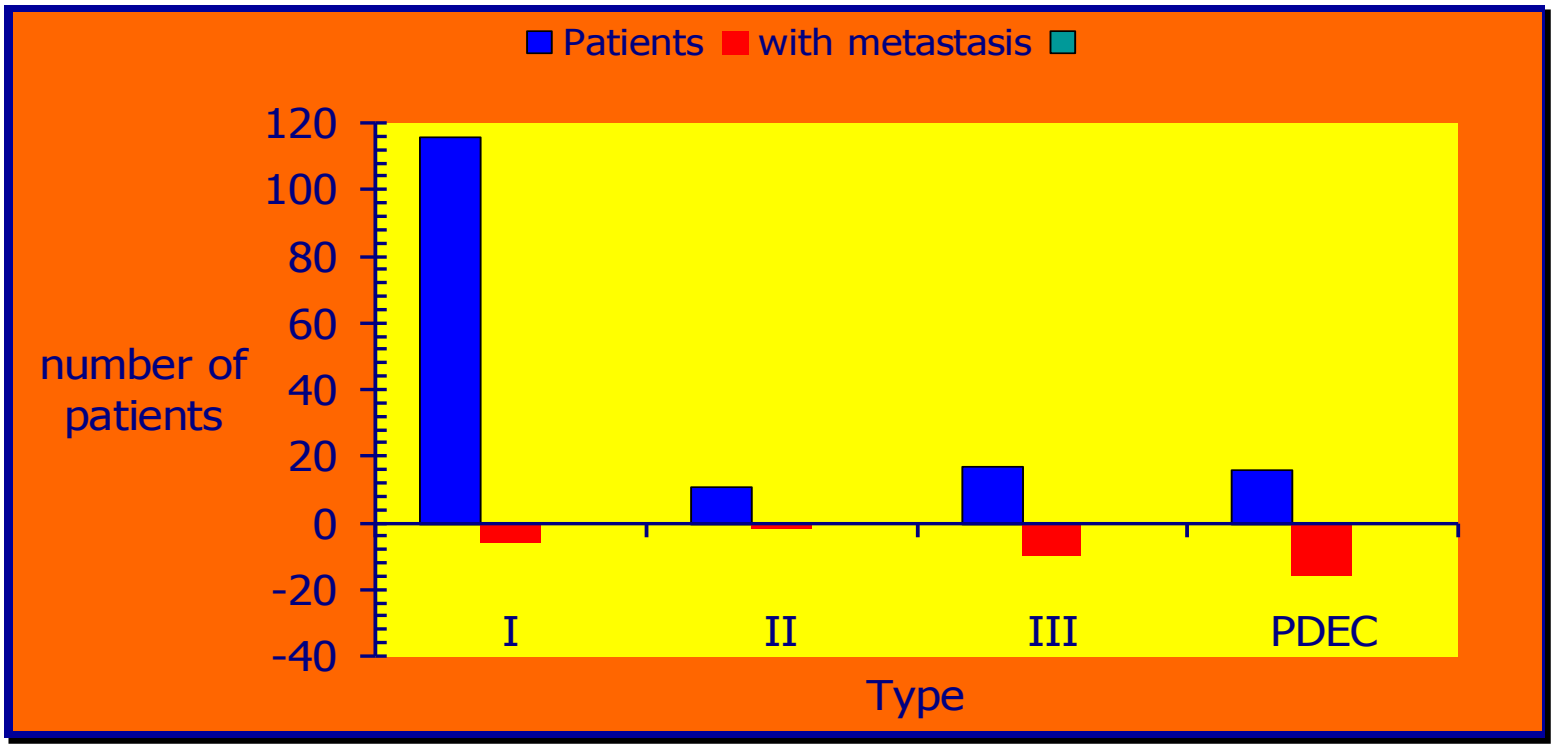




n = 285 in 12 months

Niederle et al, Endocr Rel Cancer 2010

Gastric NEN/T/C
G. Rindi 1999

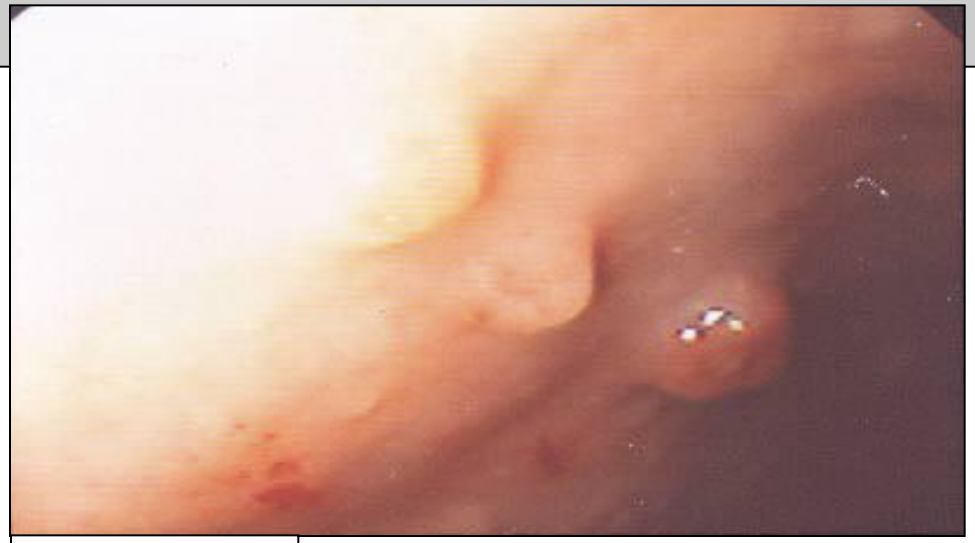


PDEC: Poorly differentiated NEC

Gastric Neuroendocrine Tumors/Neoplasias

	Pathophysiology	Disease severity
Type 1 Type 2	Hypergastrinemia + « adjuvant factor »	Usually mild
Type 3	Sporadic tumor disease	Often severe

Gastric NET



Type 1, CAG

Type 3

Type 2, ZES and MEN 1

Classification of g-NENs subtypes

	Type 1	Type 2	Type 3
Proportion among g-NENs, %	70–80	5–6	14–25
Tumor characteristics	Often small (<1–2 cm), multiple in 65% of cases, polypoid in 78% of cases	Often small (<1–2 cm) and multiple, polypoid	Unique, often large (>2 cm) polypoid and ulcerated
Associated conditions	Atrophic body gastritis	Gastrinoma/MEN-1	None
Pathology	G1–G2 NET	G1–G2 NET	G3 NEC
Serum gastrin levels	↑	↑	Normal
Gastric pH	↑↑	↓↓	Normal
Metastases, %	2–5	10–30	50–100
Tumor-related deaths, %	0	<10	25–30

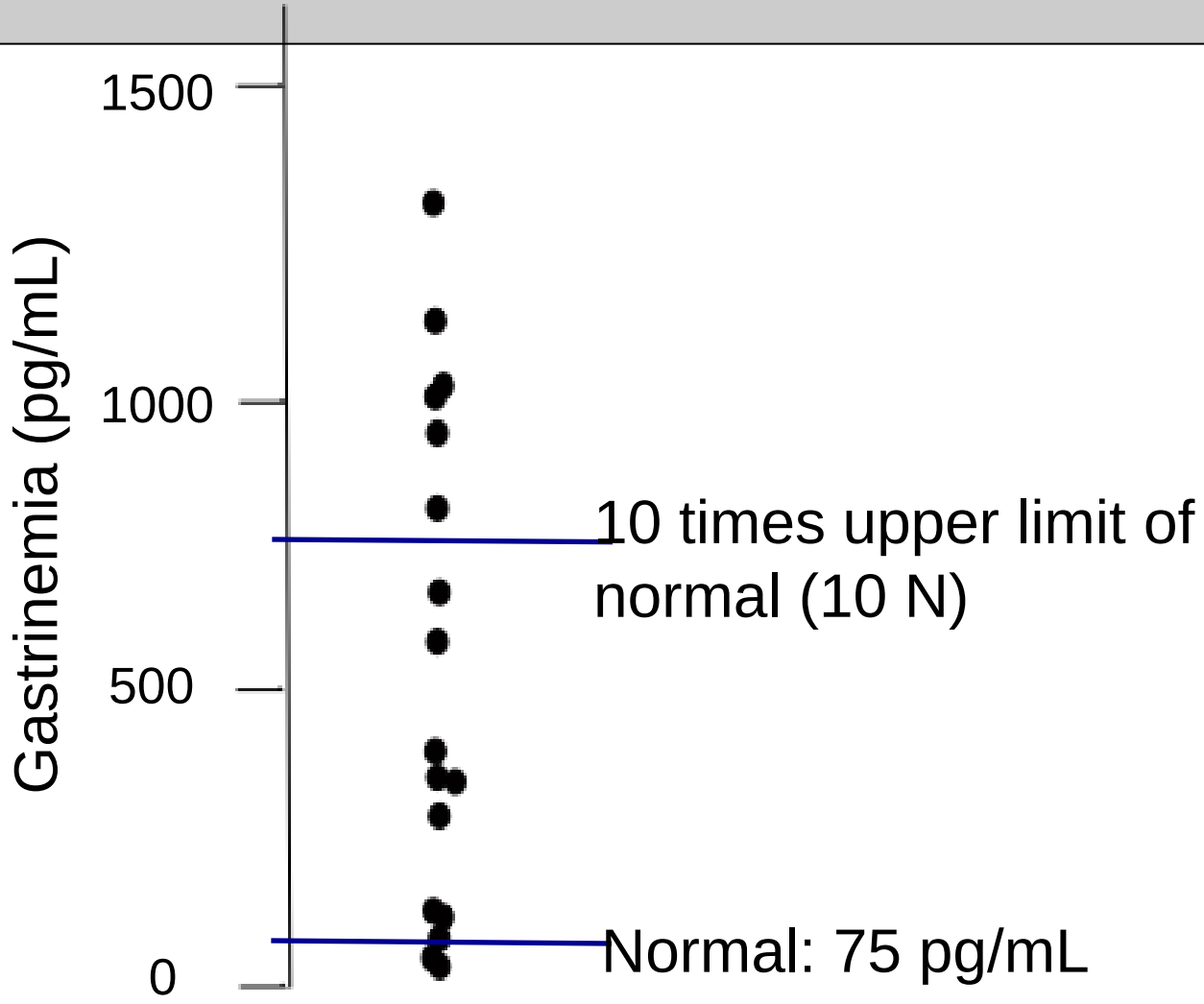
Delle Fave et al.
Neuroendocrinology 2016;103:119-124

Upper GI endoscopy

Loss of gastric folds

Fundic biopsies

Hypergastrinemia in patients with fundic chronic atrophic gastritis



Roucayrol and Cattan, Gastroenterology, 1990

Comorbidities gNET Type 1

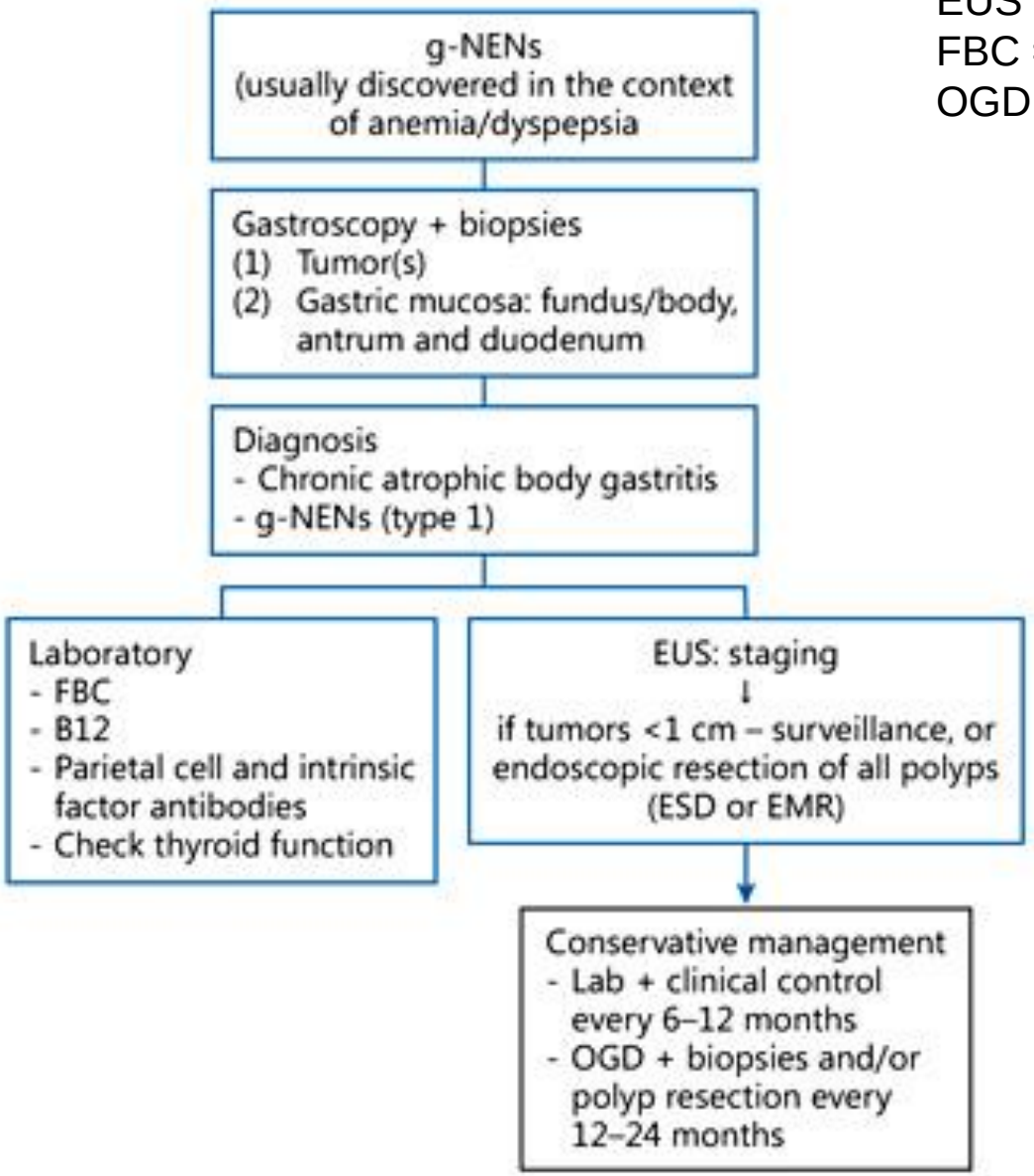
Table 2 Common medical comorbidities encountered in the 111 patients with type 1 gastric carcinoids.

Benign diseases	*n*	Percentage (%)	Tumor-related diseases	*n*	Percentage (%)	Incidence (cases/100 000 per year) Current study	Incidence (cases/100 000 per year) European community[a]
Medical comorbidities							
Anemia (B12 deficiency)	47	42.3	Parathyroid adenoma	6	5.4	853.9	2
Hashimoto's thyroiditis	41	36.9	Papillary thyroid carcinoma	3	2.7	426.9	10
Hypertension	22	19.8	Colon cancer	2	1.8	284.6	75
Hyperlipidemia	12	10.8	Breast cancer			287.8	110.3
Diabetes mellitus type 2	11	9.9	Lung cancer			284.6	23.9
Anemia (iron deficiency) and osteoporosis	10	9	Prolactinoma				30
Diabetes mellitus type 1	7	6.3	Endometrial carcinoma	1	0.9	143.9	5
Multinodular goiter	6	5.4	Acute myelogenic leukemia			142.3	8
Obesity, rheumatoid arthritis, and coronary heart disease	4	3.6	Prostate cancer			137.7	78.9
Ischemic attack, Sjögren's syndrome, and systemic lupus erythematous	3	2.7	Medullary thyroid carcinoma			142.3	1
Premature ovarian failure, impaired fasting glucose, renal transplantation, and psoriasis	2	1.8	Hepatocellular carcinoma				8.9
Addison's disease, Graves' disease, vitiligo, depression, chronic autoimmune hepatitis, and lymphocytic colitis	1	0.9	Midgut carcinoid				0.9

[a]Data retrieved from reference 2 and European Society of Medical Oncology (references (18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29)).

Thomas et al., EJE 2013

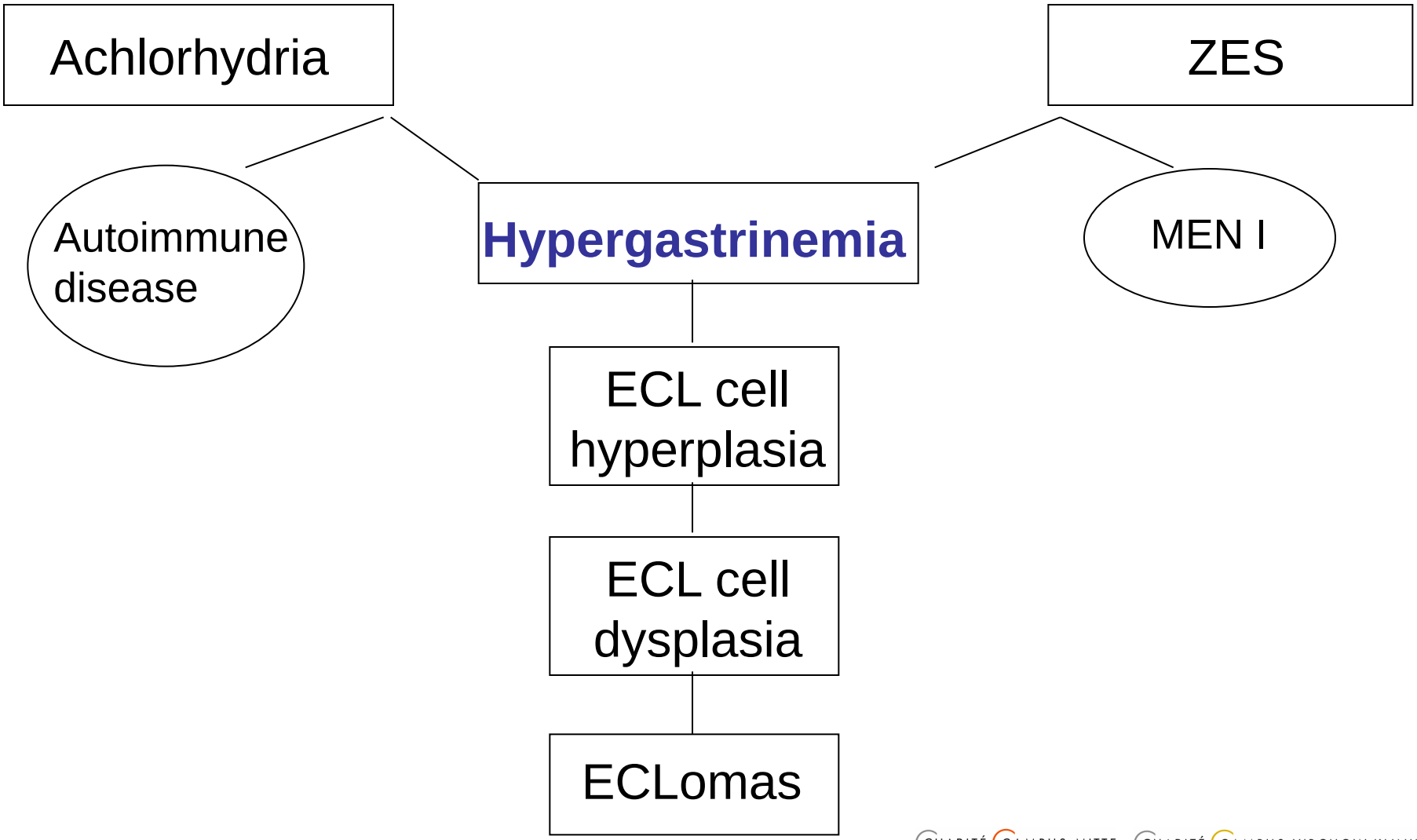
Algorithm for type 1 g-NET management



EUS = endoscopic ultrasonography
FBC = full blood count
OGD = oesophageal gastroduodenal endoscopy

Delle Fave et al.
Neuroendocrinology 2016;103:119-124

Gastric NET


Type 1
Type 2
Achlorhydria
ZES
Autoimmune disease
Hypergastrinemia
MEN I
ECL cell hyperplasia
ECL cell dysplasia
ECLomas

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Delle Fave et al.
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Treatment of gastric NET, Type 1 and 2

- None
- Endoscopy mucosal resection (EMR)
- Surgery
  - local resection
  - antrectomy
  - total gastrectomy

- Others
  - Somatostatin analogues…

Complete resection rate in endoscopic mucosal resection and endoscopic submucosal dissection groups

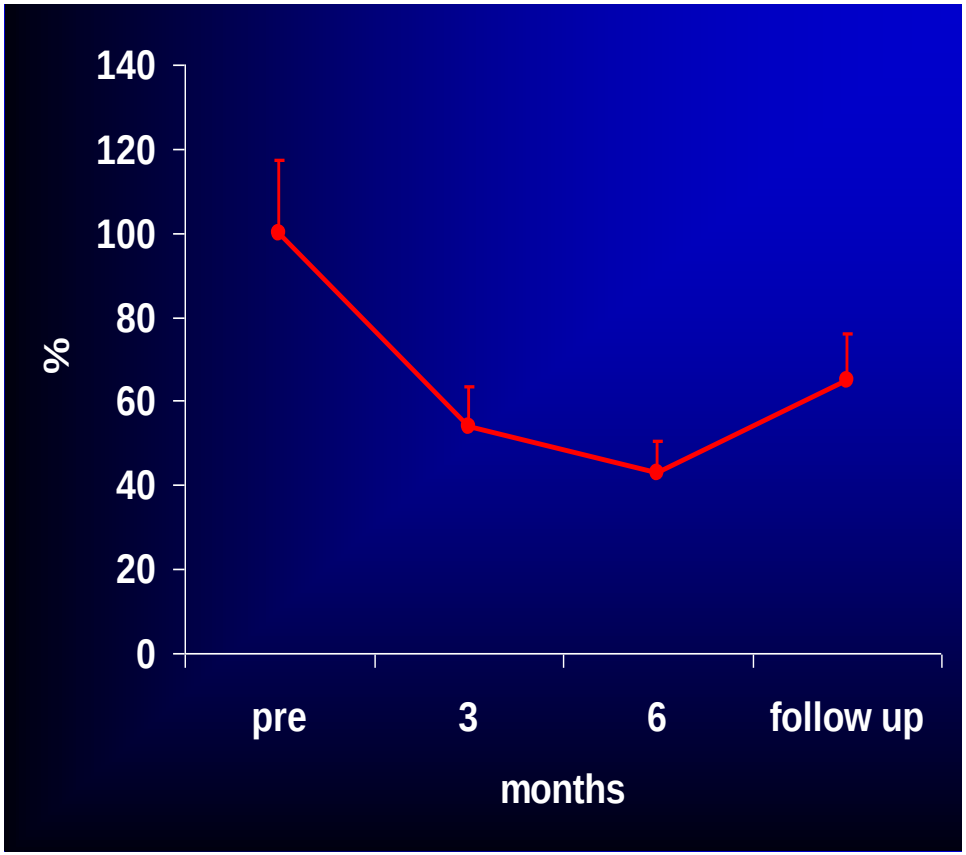
	EMR ( )	ESD ( )	value
Endoscopic complete resection, (%)	45 (93.7)	38 (97.4)	0.624
Histologic complete resection, (%)	40 (83.3)	37 (94.9)	0.174
Lateral margin involvement, (%)	2 (4.2)	1 (2.6)	>0.999
Vertical margin involvement, (%)	8 (16.7)	1 (2.6)	0.038*

EMR: endoscopic mucosal resection and ESD: endoscopic submucosal dissection; *odd ratio was 7.6.

HH Kim at al. *Gastroenterol Res Pract.* 2014; 2014: 253860.

gNET, Type 1: SSA treatment

Octreotide: n° cells ECL



P.Tomassetti: NEJM, 2000

"Complete regression of gastric carcinoids (polyps) in MEN 1 pts by LAR 30 mg 1 yr"

Aliment. Pharm. Ther.: 1994

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Delle Fave et al.
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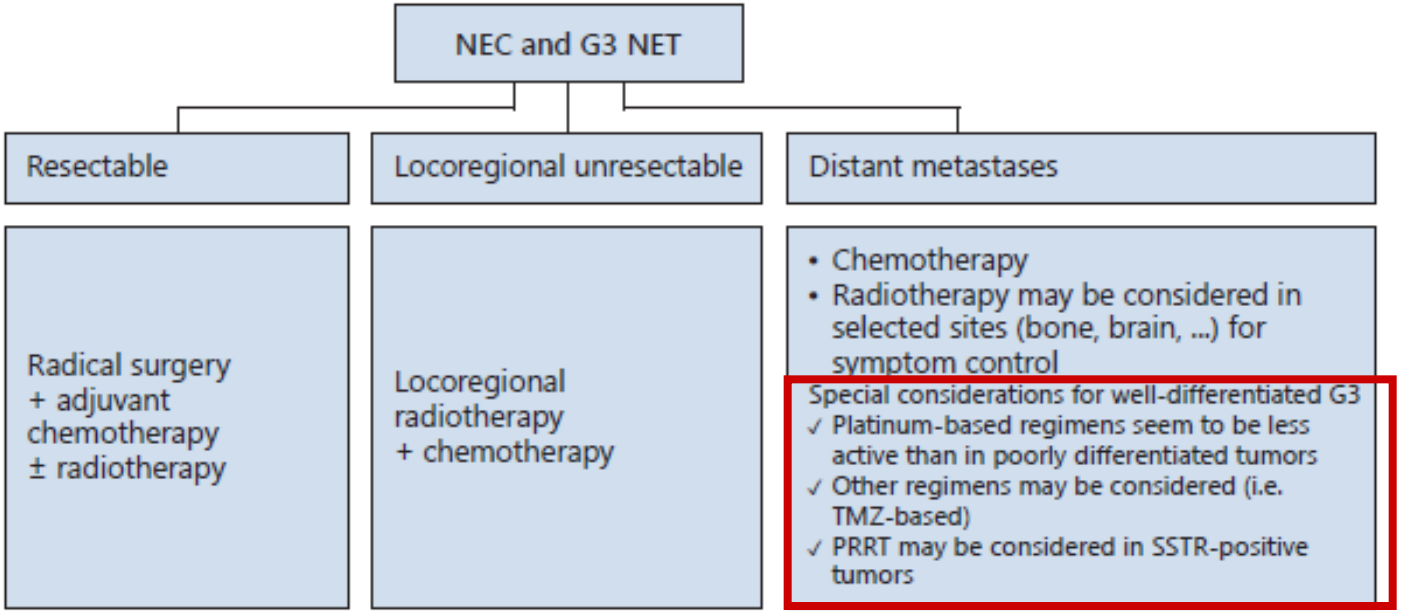
Treatment of Gastric NET, Type 3

- Follow treatment principles of gastric adenocarcinomas
- Endoscopy mucosal resection (EMR) only in T1 tumors
- Surgery
  - total gastrectomy
- Others
  - Chemotherapy according to grading and tumor extent

Therapeutic algorithm for NEC and NET/G3



- Chemotherapy; radiotherapy
  - ✓ Cisplatin or carboplatin and etoposide are generally recommended in the adjuvant setting or as first-line therapy in advanced disease. Alternative regimens substituting irinotecan for etoposide may also be employed as first-line therapy in advanced disease.
  - ✓ Irinotecan or oxaliplatin-based regimens may be considered as second-line therapy.
- Clinical judgement should be used.

Garcia-Carbonero et al.
Neuroendocrinology 2016;103:186-194

Summary: gNET treatment options

Types	I Atrophic gastritis	II MEN I	III Sporadic
Gastrin	+++	++++	-
Metastases	-	+/-	++ Size > 1 cm Invasive
Therapy (SSA or (netazepide))	yes (?)	yes	No
Resection Size and n° of lesions (*Endoscopic * Surgical #*)	yes *	yes *	yes #

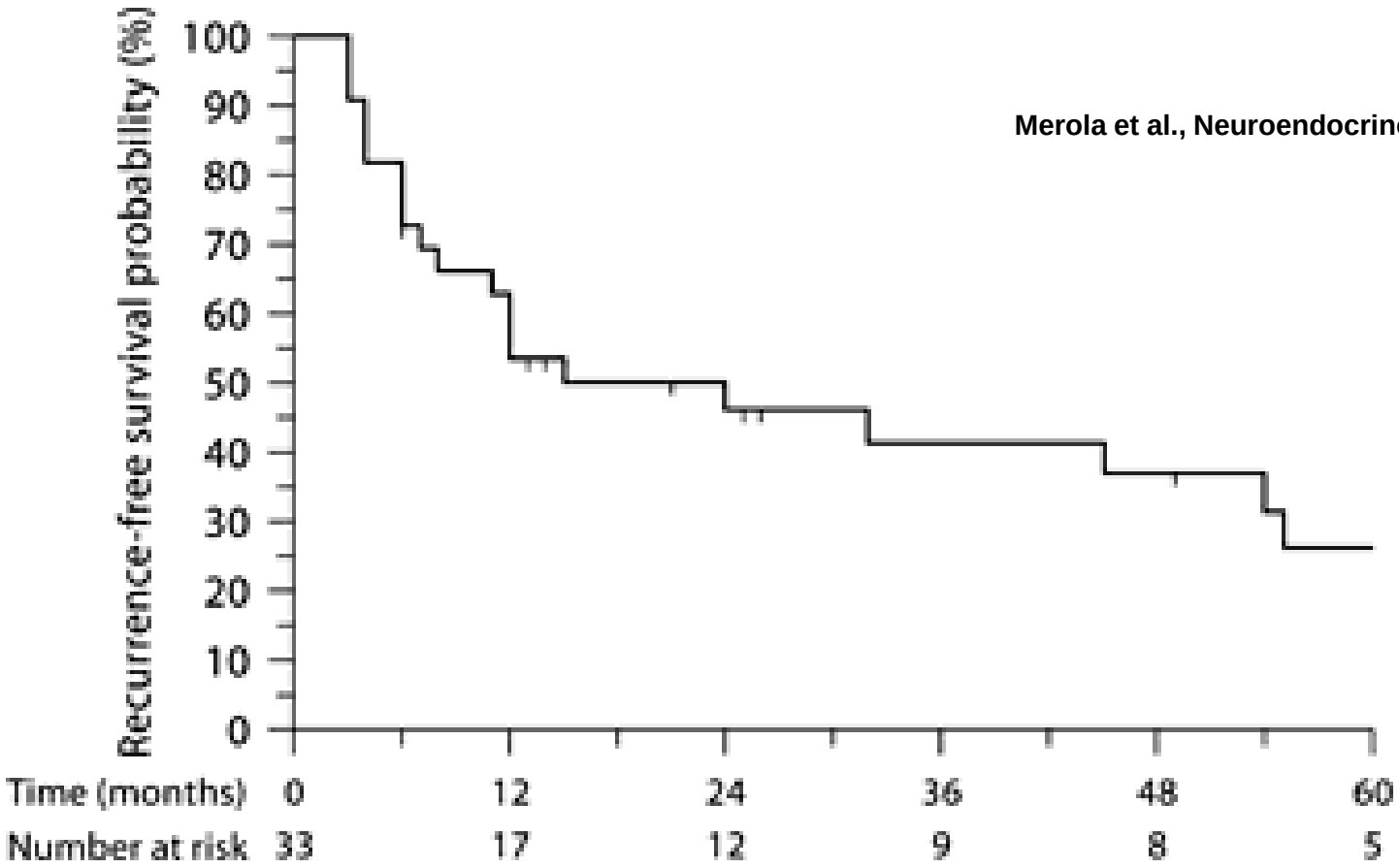
Follow-up for Type 1 and 2

NET < 1 cm

A – Endoscopy (1x / year)

B - Gastrin/CGA (1x / year)

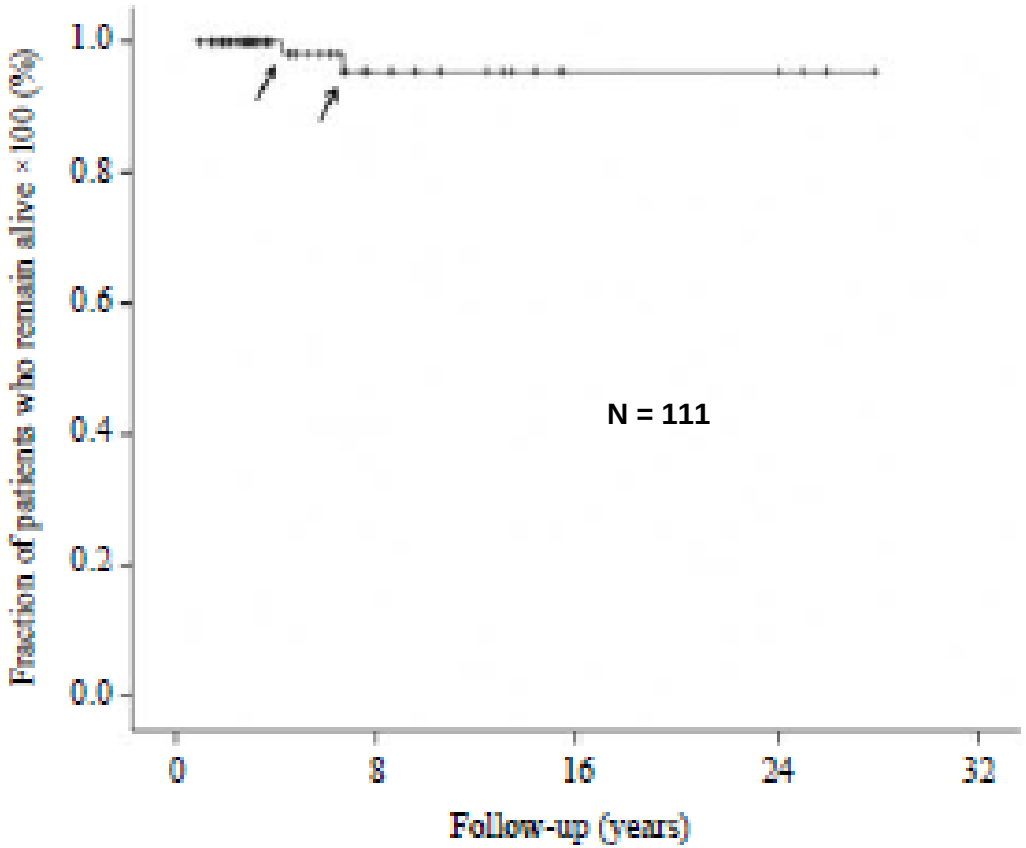
gNET, type 1:
Recurrence-free survival during follow-up



Merola et al., Neuroendocrinology, 2012

2/3 of patients had tumor recurrence after endoscopic resection, with a median time to recurrence of 8 months (range 3–55).

Survival according to Kaplan-Meir analysis of gNET type 1 patients



Thomas et al., EJE, 2013

Reminder

1.) Gastric NET are increasingly diagnosed worldwide

2.) First diagnosis is almost exclusively made by gastroenterologists

3.) Expertise of MDT is absolutely necessary

Gastric NET, type I, < 1cm

Charite, Universitätsmedizin, Berlin, CVK/CCM

Thanks