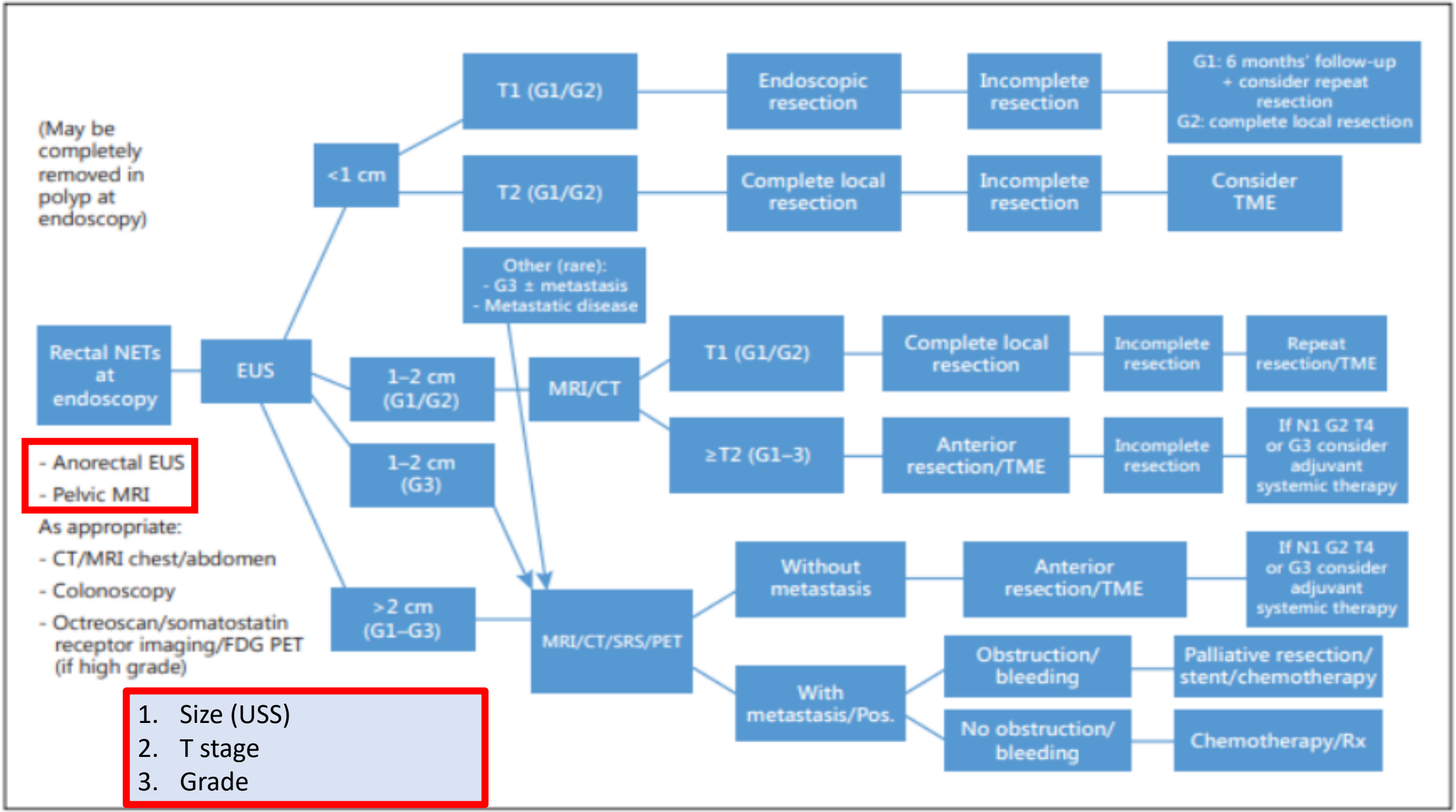
Συστηματική θεραπεία NET ορθού

Γιώργος Ευαγγέλου
Παθολόγος Ογκολόγος
Ογκολογικό Τμήμα Γ’ΠΠ
ΓΝΑ Η Σωτηρία



1. Size (USS)
2. T stage
3. Grade

Outcomes for a Large Cohort of Patients with Rectal Neuroendocrine Tumors: an Analysis of the National Cancer Database

2020

A retrospective cohort study was performed using the National Cancer Database (NCDB)

All patients diagnosed between 2004 and 2015 were included in this analysis.

Patients with metastatic disease and those with missing treatment data were excluded

N = 17.263

16.531 localized + 732 metastatic (4.2%)

Zhao, B., Hollandsworth, H.M., Lopez, N.E. et al. Outcomes for a Large Cohort of Patients with Rectal Neuroendocrine Tumors: an Analysis of the National Cancer Database. J Gastrointest Surg (2020). https://doi.org/10.1007/s11605-020-04525-6

Table 1 Patient demographics stratified by treatment

Variables	All patients	Observation alone	Local excision	Radical resection	*p* valuea
Number of patients	16,531	2057 (12.4)	13,126 (79.4)	1348 (8.2)	
Median age	54	56	54	55	< 0.001
δ50	5132 (31.0)	583 (28.3)	4125 (31.4)	424 (31.5)	
51–55	3819 (23.1)	419 (20.4)	3142 (23.9)	258 (19.1)	
56–65	4475 (27.1)	562 (27.3)	3554 (27.1)	359 (26.6)	
> 65	3105 (18.8)	493 (24.0)	2305 (17.6)	307 (22.8)	
Female sex	8644 (52.3)	1018 (49.5)	6932 (52.8)	694 (51.5)	0.016
Treatment at an academic center	5473 (36.0)	636 (33.7)	4345 (36.0)	492 (39.9)	0.002
Tumor size					< 0.001
δ10 mm	9216 (79.8)	698 (69.7)	7959 (84.1)	559 (51.7)	
11–20 mm	1013 (8.8)	73 (7.3)	755 (8.0)	185 (17.1)	
> 20 mm	1320 (11.4)	230 (23.0)	752 (7.9)	338 (31.2)	
Clinical N stage					< 0.001
cN0	6995 (42.3)	576 (29.1)	6004 (47.1)	415 (31.6)	
cN1	2109 (12.8)	423 (21.4)	1246 (9.8)	440 (33.5)	
cNx	6928 (41.9)	982 (49.6)	5487 (43.1)	459 (34.9)	
Tumor grade differentiation					< 0.001
Well	5542 (33.5)	513 (24.9)	4580 (34.9)	449 (33.3)	
Moderate	701 (4.2)	62 (3.0)	520 (4.0)	119 (8.8)	
Poor/anaplastic	385 (2.3)	157 (7.6)	49 (0.4)	179 (13.3)	
Unknown	9903 (59.9)	1325 (64.4)	7977 (60.8)	601 (44.6)	
Positive resection margins	–	–	1302 (9.9)	107 (7.9)	< 0.001

2020

European ENETS Neuroendocrine Tumor Society

Title: Incidence of Rectal NEN and Adherence to Pathological Classification Rules and Treatment Guidelines: Results of the Population Based Cancer Registry in Belgium

Authors: Geboes K, De Maeyer T, Ribeiro S, De Man M, Carton S, Cuyle P J, Vandamme T, Verslype C, Borbath I, Van Damme N, Van Eycken L, Hoorens A

Institution: UZ Gent, Gent, St Elisabeth Ziekenhuis, Zottegem, Imelda, Bonheiden, Network, UZA, Antwerpen, UZ Leuven, Leuven, UCL, Louvain, Belgian Cancer Registry, Brussels

Institution's Location: Belgium

2020

670 NEN were withheld:

531 (79%) G1 NET:

369 (69%) cases true G1 NET; 4 cases Ki 67 < 5%

53 (8%) G2 NET:

25 cases true NET G2; 28 reclassified cases

11 G3 NET: 2 cases true G3 NET; 8 insufficient data

66 (10%) NEC:

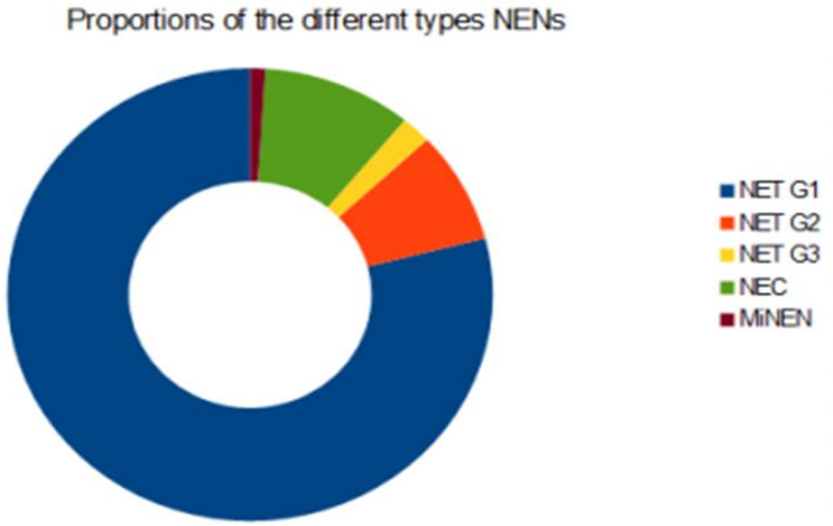
16 cases insufficient data (+ 13 lacking grade of differentiation)

→ Large Cell: 29 cases

(12 correctly classified; 17 cases (G3 NETs) reclassified)

→ Small Cell: 37 cases

(30 correctly classified; 6 cases (G3 NETs) and 1 case (large cell NEC) reclassified)



European ENETS Neuroendocrine Tumor Society

Title: Incidence of Rectal NEN and Adherence to Pathological Classification Rules and Treatment Guidelines: Results of the Population Based Cancer Registry in Belgium

Authors: Geboes K, De Maeyer T, Ribeiro S, De Man M, Carton S, Cuyle P J, Vandamme T, Verslype C, Borbath I, Van Damme N, Van Eycken L, Hoorens A

Institution: UZ Gent, Gent, St Elisabeth Ziekenhuis, Zottegem, Imelda, Bonheiden, Network, UZA, Antwerpen, UZ Leuven, Leuven, UCL, Louvain, Belgian Cancer Registry, Brussels

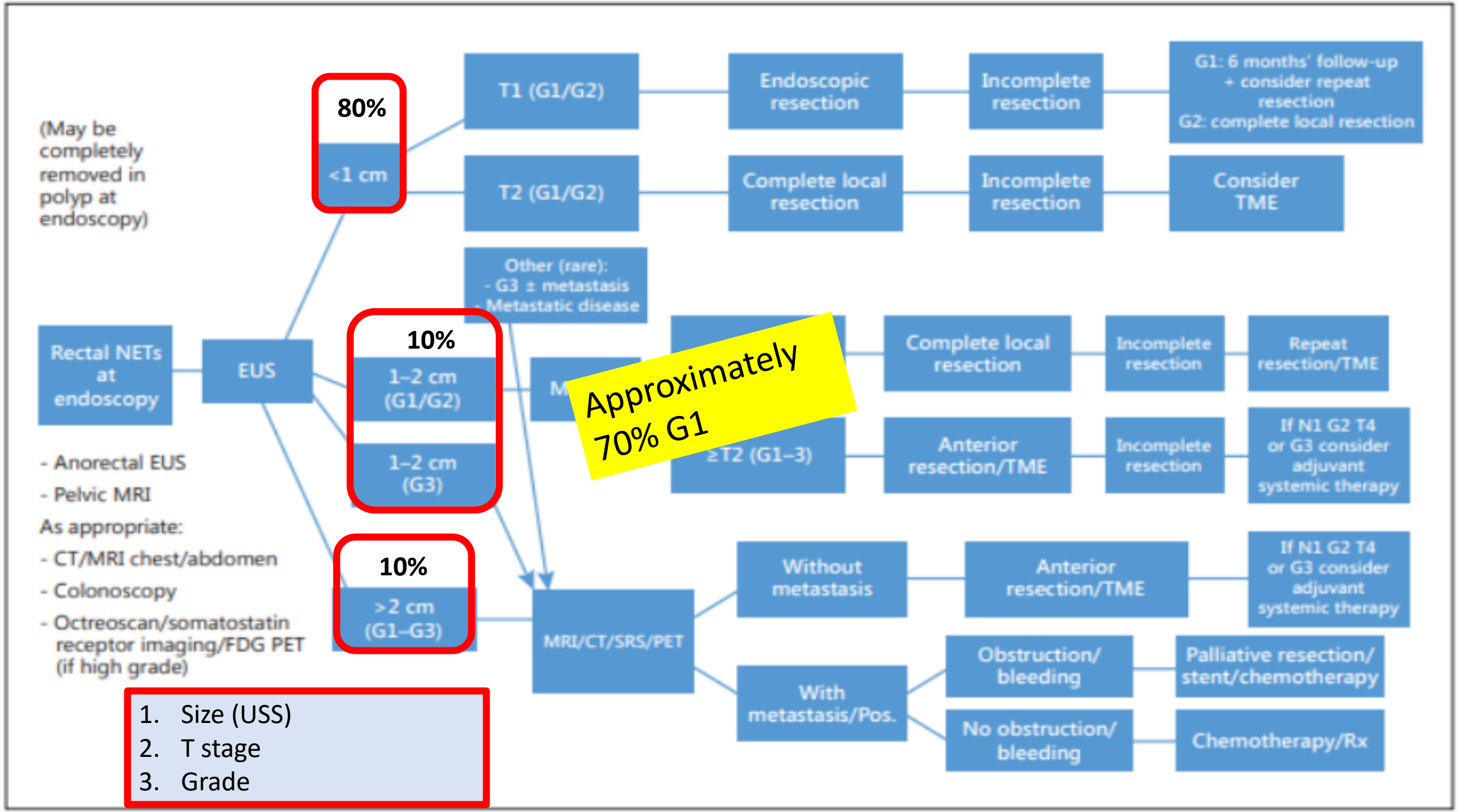
Institution's Location: Belgium

2020

Materials and methods: All pathology reports of rNEN received by the Belgian Cancer Registry, during 2004-2015, were reviewed for clinicopathological data.

Classification was adapted based on the WHO 2019 classification.

Year	Incidence rectal NEN	Ki67 index	Differentiation	Tumor size	Muscularis invasion	Lymphovascular invasion
2004	21	7 (33%)	2 (9%)	7 (33%)	3 (14%)	3 (14%)
2005	24	7 (29%)	4 (17%)	13 (54%)	2 (8%)	1 (4%)
2006	33	10 (30%)	8 (24%)	22 (67%)	5 (15%)	7 (21%)
2007	54	17 (31%)	17 (31%)	26 (48%)	8 (15%)	6 (11%)
2008	56	22 (39%)	18 (32%)	35 (63%)	7 (13%)	13 (23%)
2009	47	27 (57%)	22 (47%)	33 (70%)	10 (21%)	9 (19%)
2010	60	39 (65%)	16 (27%)	23 (38%)	7 (12%)	7 (12%)
2011	72	49 (68%)	33 (46%)	35 (49%)	10 (14%)	10 (14%)
2012	75	60 (80%)	39 (52%)	44 (58%)	14 (19%)	23 (31%)
2013	68	60 (88%)	32 (47%)	46 (68%)	19 (28%)	14 (21%)
2014	91	79 (87%)	51 (56%)	62 (68%)	10 (11%)	14 (15%)
2015	69	59 (85%)	38 (55%)	47 (68%)	18 (26%)	21 (30%)
Total	**670**	**436 (65%)**	**280 (42%)**	**393 (59%)**	**113 (17%)**	**128 (19%)**


Rectal NETs at endoscopy
EUS
- Anorectal EUS
- Pelvic MRI
As appropriate:
- CT/MRI chest/abdomen
- Colonoscopy
- Octreoscan/somatostatin receptor imaging/FDG PET (if high grade)
80%
<1 cm
(May be completely removed in polyp at endoscopy)
T1 (G1/G2)
Endoscopic resection
Incomplete resection
G1: 6 months' follow-up + consider repeat resection
G2: complete local resection
T2 (G1/G2)
Complete local resection
Incomplete resection
Consider TME
Other (rare):
- G3 ± metastasis
- Metastatic disease
10%
1–2 cm (G1/G2)
1–2 cm (G3)
≥T2 (G1–3)
Complete local resection
Incomplete resection
Repeat resection/TME
Anterior resection/TME
Incomplete resection
If N1 G2 T4 or G3 consider adjuvant systemic therapy
Approximately 70% G1
10%
>2 cm (G1–G3)
MRI/CT/SRS/PET
Without metastasis
Anterior resection/TME
If N1 G2 T4 or G3 consider adjuvant systemic therapy
With metastasis/Pos.
Obstruction/ bleeding
Palliative resection/ stent/chemotherapy
No obstruction/ bleeding
Chemotherapy/Rx
1. Size (USS)
2. T stage
3. Grade

Multicenter Study > Ann Surg. 2010 Nov;252(5):750-5. doi: 10.1097/SLA.0b013e3181fb8df6.

Carcinoid Tumors of the Rectum: A Multi-Institutional International Collaboration

N = 100

TABLE 3. Multiple Variable Logistic Regression Analysis of Risk Factors for Lymph Node Metastases*

Variables	Odds Ratio	95% CI	*P*
Tumor size > 10 mm	32.7	14.8–72.3	0.006
Lymphovascular invasion	19.6	12.3–146.0	< 0.001

*Risk factors for nodal involvement calculated in patients who underwent formal surgical resection (n = 100).

TABLE 4. Multiple Variable Logistic Regression Analysis of Risk Factors for Distant Metastases*

Variables	Odds Ratio	95% CI	*P*
Lymph node metastases	12.3	1.8-84.7	0.033
Lymphovascular invasion	74.4	4.6-120.2	0.022

*Risk factors for distant metastases calculated in patients who underwent formal surgical resection (n = 100).

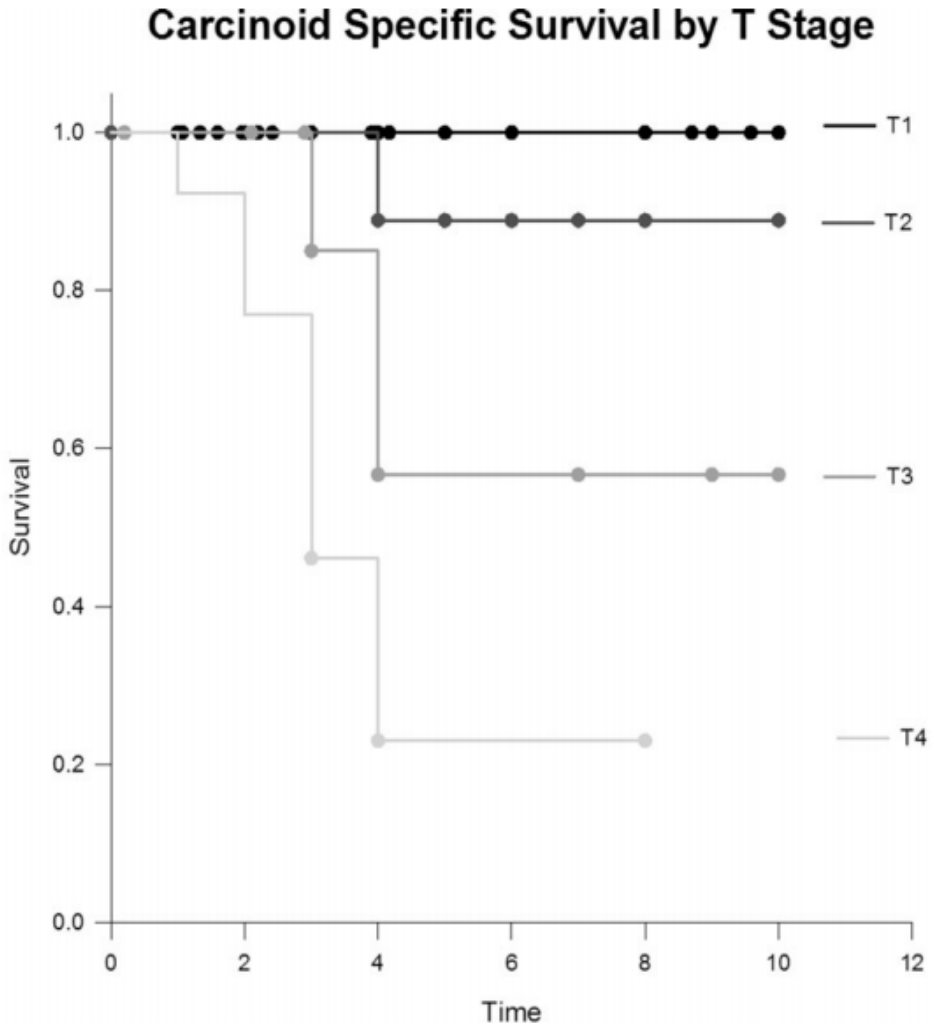


FIGURE 1. Survival by T stage calculated in patients who underwent formal surgical resection (n = 100). Time in years.

European ENETS Neuroendocrine Tumor Society

Title: Incidence of Rectal NEN and Adherence to Pathological Classification Rules and Treatment Guidelines: Results of the Population Based Cancer Registry in Belgium

Authors: Geboes K, De Maeyer F, Ribeiro S, De Man M, Carton S, Cuyle P J, Vandamme T, Verslype C, Borbath I, Van Damme N, Van Eycken L, Hoorens A

Institution: UZ Gent, Gent, St Elisabeth Ziekenhuis, Zottegem, Imelda, Bonheiden, Netwerk, UZA, Antwerpen, UZ Leuven, Leuven, UCL, Louvain, Belgian Cancer Registry, Brussels

Institution's Location: Belgium

Introduction: Classification of rectal NEN (rNEN) changed significantly over the years.
Aim(s): We aimed to have complete epidemiological data on the incidence of rNEN in Belgium and investigated the evolution in reports and treatment decisions.
Materials and methods: All pathology reports of rNEN received by the Belgian Cancer Registry, during 2004-2015, were reviewed for clinicopathological data. Classification was adapted based on the WHO 2019 classification. In order to have an idea about the treatment management, the data were linked with the administrative healthcare database.

Factors associated with lymph node invasion and/or metastatic disease

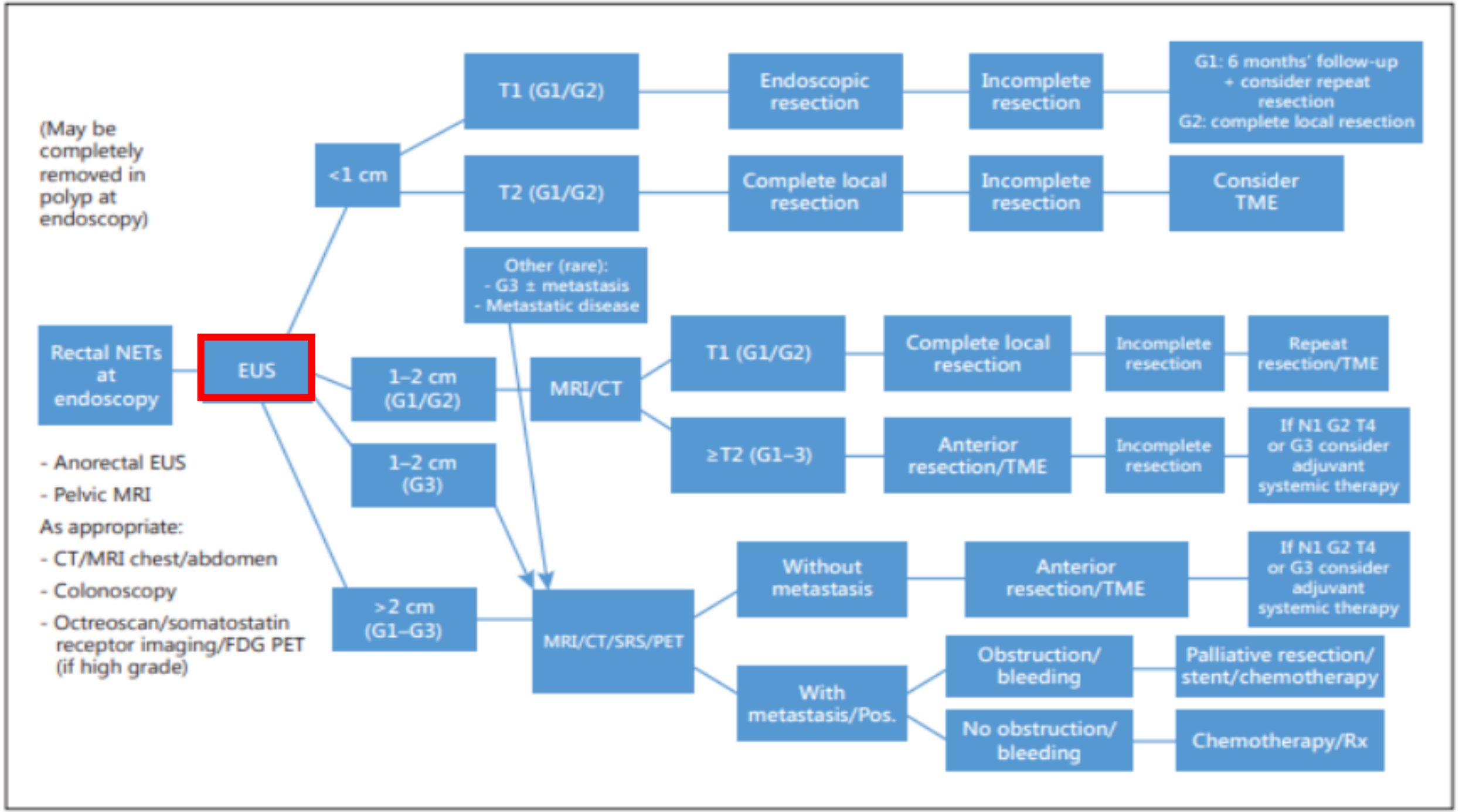
France: Renaten/TENpath: n=345	Univariate analysis	
	OR	p
Tumor size ≥ 10 mm versus < 10 mm	9.1 (3.5-23.5)	10^{-7}
G2,G3 vs G1	4,2 (1,5 – 11,7)	0,03
LV invasion +/-	57,2 (5,6 – 578,9)	0,01
Muscularis invasion +/-	∞ (11,9 - ∞)	10^{-5}

UEG Journal 2019, Volume 7: data on 345 small rNEN

Materials and methods: All pathology reports of rNEN received by the Belgian Cancer Registry, during 2004-2015, were reviewed for clinicopathological data.

Classification was adapted based on the WHO 2019 classification.

Year	Incidence rectal NEN	Ki67 index	Differentiation	Tumor size	Muscularis invasion	Lymphovascular invasion
2004	21	7 (33%)	2 (9%)	7 (33%)	3 (14%)	3 (14%)
2005	24	7 (29%)	4 (17%)	13 (54%)	2 (8%)	1 (4%)
2006	33	10 (30%)	8 (24%)	22 (67%)	5 (15%)	7 (21%)
2007	54	17 (31%)	17 (31%)	26 (48%)	8 (15%)	6 (11%)
2008	56	22 (39%)	18 (32%)	35 (63%)	7 (13%)	13 (23%)
2009	47	27 (57%)	22 (47%)	33 (70%)	10 (21%)	9 (19%)
2010	60	39 (65%)	16 (27%)	23 (38%)	7 (12%)	7 (12%)
2011	72	49 (68%)	33 (46%)	35 (49%)	10 (14%)	10 (14%)
2012	75	60 (80%)	39 (52%)	44 (58%)	14 (19%)	23 (31%)
2013	68	60 (88%)	32 (47%)	46 (68%)	19 (28%)	14 (21%)
2014	91	79 (87%)	51 (56%)	62 (68%)	10 (11%)	14 (15%)
2015	69	59 (85%)	38 (55%)	47 (68%)	18 (26%)	21 (30%)
Total	**670**	**436 (65%)**	**280 (42%)**	**393 (59%)**	**113 (17%)**	**128 (19%)**


Rectal NETs at endoscopy
- Anorectal EUS
- Pelvic MRI
As appropriate:
- CT/MRI chest/abdomen
- Colonoscopy
- Octreoscan/somatostatin receptor imaging/FDG PET (if high grade)
EUS
(May be completely removed in polyp at endoscopy)
<1 cm
T1 (G1/G2)
Endoscopic resection
Incomplete resection
G1: 6 months' follow-up + consider repeat resection
G2: complete local resection
T2 (G1/G2)
Complete local resection
Incomplete resection
Consider TME
Other (rare):
- G3 ± metastasis
- Metastatic disease
1–2 cm (G1/G2)
MRI/CT
T1 (G1/G2)
Complete local resection
Incomplete resection
Repeat resection/TME
≥T2 (G1–3)
Anterior resection/TME
Incomplete resection
If N1 G2 T4 or G3 consider adjuvant systemic therapy
1–2 cm (G3)
>2 cm (G1–G3)
MRI/CT/SRS/PET
Without metastasis
Anterior resection/TME
If N1 G2 T4 or G3 consider adjuvant systemic therapy
With metastasis/Pos.
Obstruction/ bleeding
Palliative resection/ stent/chemotherapy
No obstruction/ bleeding
Chemotherapy/Rx

European ENETS Neuroendocrine Tumor Society

Title: Incidence of Rectal NEN and Adherence to Pathological Classification Rules and Treatment Guidelines: Results of the Population Based Cancer Registry in Belgium

Authors: Geboes K, De Maeyer F, Ribeiro S, De Man M, Carton S, Cuyle P J, Vandamme T, Verslype C, Borbath I, Van Damme N, Van Eycken L, Hoorens A

Institution: UZ Gent, Gent, St Elisabeth Ziekenhuis, Zottegem, Imelda, Bonheiden, Netwerk, UZA, Antwerpen, UZ Leuven, Leuven, UCL, Louvain, Belgian Cancer Registry, Brussels

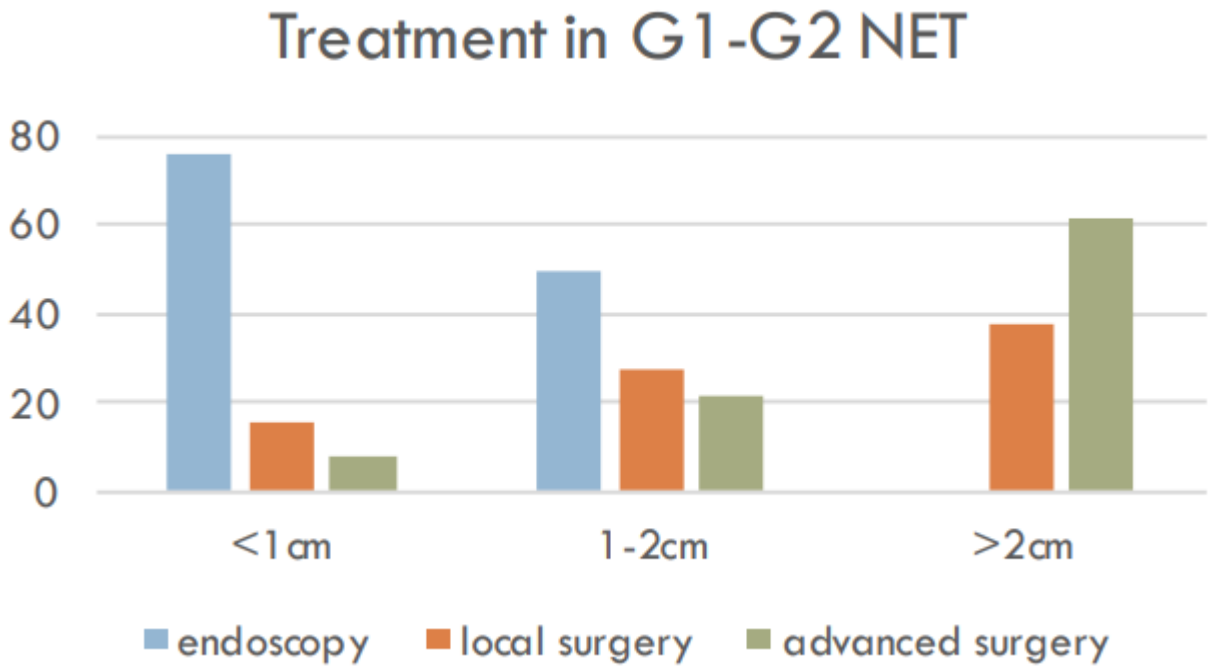
Institution's Location: Belgium

Introduction: Classification of rectal NEN (rNEN) changed significantly over the years.
Aim(s): We aimed to have complete epidemiological data on the incidence of rNEN in Belgium and investigated the evolution in reports and treatment decisions.
Materials and methods: All pathology reports of rNEN received by the Belgian Cancer Registry, during 2004-2015, were reviewed for clinicopathological data. Classification was adapted based on the WHO 2019 classification. In order to have an idea about the treatment management, the data were linked with the administrative healthcare database.

Aim(s): We aimed to have complete epidemiological data on the **incidence of rNEN in Belgium** and investigated the evolution in reports and treatment decisions.

Belgian Cancer Registry, during 2004-2015

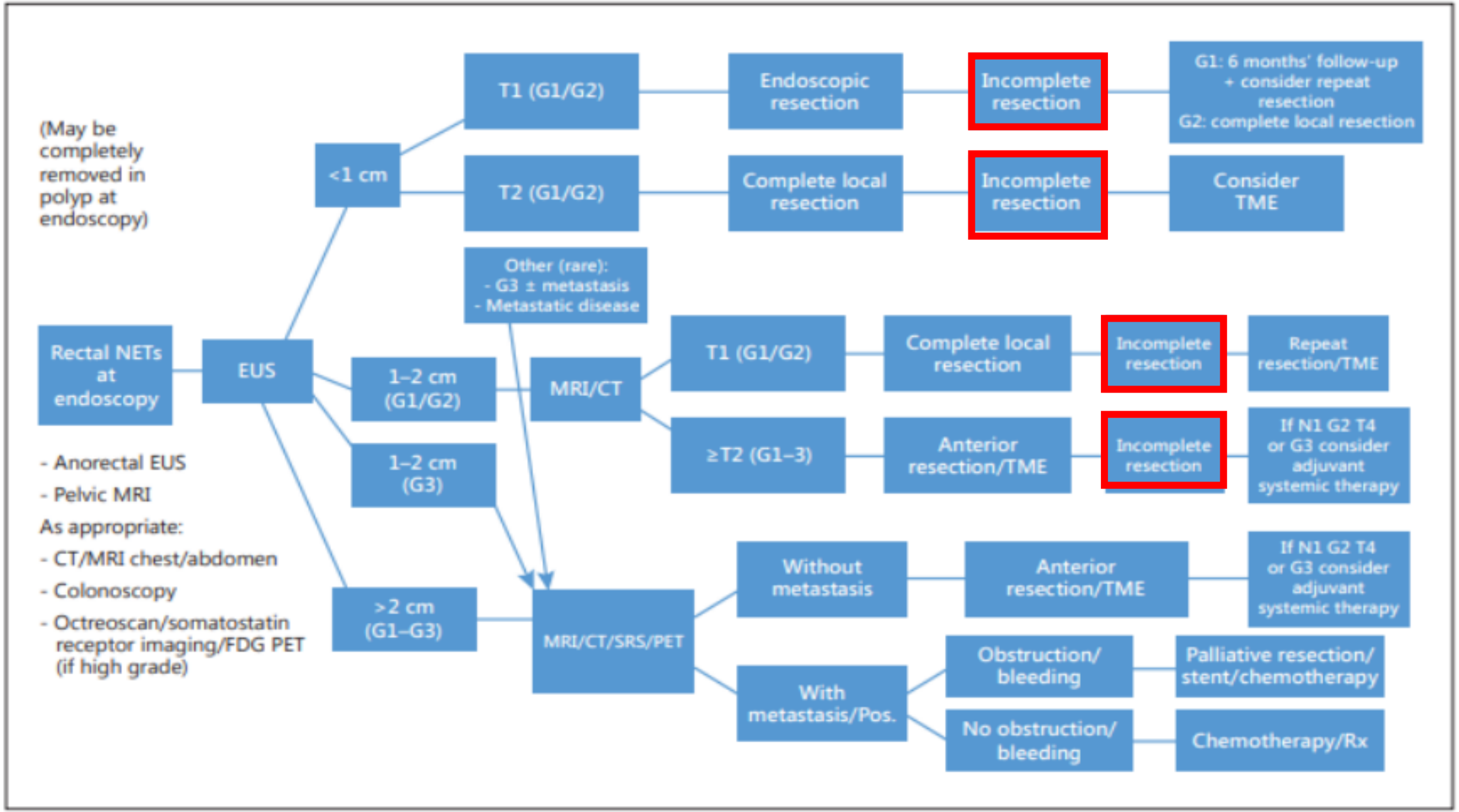
EUS performed in 245/667 (38%) patients (before/after resection?)



Long-term outcomes according to additional treatments after endoscopic resection for rectal small neuroendocrine tumors

	Total (N = 322)	Risk negative (N = 180)	Risk indeterminate (N = 63)	Risk positive (N = 79)	*P*
Characteristics of the patients					
Age at diagnosis (year, mean (SD))	47.67 ± 11.47	46.80 ± 11.14	47.95 ± 12.67	48.62 ± 11.25	0.469
Gender (%)					0.143
Male	207 (64.3)	113 (62.8)	47 (74.6)	47 (59.5)	
Female	115 (35.7)	67 (37.2)	16 (25.4)	32 (40.5)	
How to be diagnosed (%)					0.041
Resected as NET	190 (59.0)	102 (56.7)	46 (73.0)	42 (53.2)	
Diagnosed via biopsy	102 (31.7)	64 (35.6)	13 (20.6)	25 (31.6)	
Resected as Polyps	30 (9.3)	14 (7.8)	4 (6.3)	12 (15.2)	
EUS (%)	44 (13.7)	20 (11.1)	6 (9.5)	18 (22.8)	0.024
Pelvic MRI (%)	15 (4.7)	8 (4.4)	2 (3.2)	5 (6.3)	0.661
Abdominal imaging (yes, %)					
Abdominopelvic CT	299 (92.9)	170 (94.4)	55 (87.3)	74 (93.7)	0.158
Abdominal US	40 (12.4)	19 (10.6)	9 (14.3)	12 (15.2)	0.513
Both	30 (9.3)	13 (7.2)	7 (11.1)	10 (12.7)	0.33
Not performed	13 (4.0)	4 (2.2)	6 (9.5)	3 (3.8)	0.04

Cha, J.H., Jung, D.H., Kim, J. et al. Long-term outcomes according to additional treatments after endoscopic resection for rectal small neuroendocrine tumors. Sci Rep 9, 4911 (2019). https://doi.org/10.1038/s41598-019-40668-6


Rectal NETs at endoscopy
- Anorectal EUS
- Pelvic MRI
As appropriate:
- CT/MRI chest/abdomen
- Colonoscopy
- Octreoscan/somatostatin receptor imaging/FDG PET (if high grade)
EUS
<1 cm
(May be completely removed in polyp at endoscopy)
T1 (G1/G2)
T2 (G1/G2)
Endoscopic resection
Complete local resection
Incomplete resection
Incomplete resection
G1: 6 months' follow-up + consider repeat resection
G2: complete local resection
Consider TME
1–2 cm (G1/G2)
1–2 cm (G3)
>2 cm (G1–G3)
Other (rare):
- G3 ± metastasis
- Metastatic disease
MRI/CT
MRI/CT/SRS/PET
T1 (G1/G2)
≥T2 (G1–3)
Complete local resection
Anterior resection/TME
Incomplete resection
Incomplete resection
Repeat resection/TME
If N1 G2 T4 or G3 consider adjuvant systemic therapy
Without metastasis
With metastasis/Pos.
Anterior resection/TME
Obstruction/ bleeding
No obstruction/ bleeding
If N1 G2 T4 or G3 consider adjuvant systemic therapy
Palliative resection/ stent/chemotherapy
Chemotherapy/Rx

Endoscopic management of 345 small rectal neuroendocrine tumours: a national study from the French group of endocrine tumours (GTE)

	n (%)
Tumour size in mm	
<10 (T1a)	252 (73)
10 to 20 (T1b)	88 (26)
NR	5 (1)
Location	
Low rectum	145 (42)
Medium rectum	81 (23)
High rectum	50 (14)
NR	69 (20)
Ulceration	18 (5)
Diagnosis of r-NET	
Suspected during first endoscopy	61 (18)
Not suspected during first endoscopy	284 (82)
Grade	
G1	309 (90)
G2	32 (9)
G3	4 (1)
Lymphovascular invasion	
Yes	4 (1)
No	124 (26)
NR	217 (63)
Muscular invasion	4 (1)

G: tumour grading; NR: not reported; r-NET: rectal neuroendocrine tumour.

Rectal neuroendocrine tumours ≤2 cm managed from January 2000–June 2018 in 16 French hospitals, were retrospectively analyzed

Endoscopic management of 345 small rectal neuroendocrine tumours: a national study from the French group of endocrine tumours (GTE)

	n (%)
Tumour size in mm	
<10 (T1a)	252 (73)
10 to 20 (T1b)	88 (26)
NR	5 (1)
Location	
Low rectum	145 (42)
Medium rectum	81 (23)
High rectum	50 (14)
NR	69 (20)
Ulceration	18 (5)
Diagnosis of r-NET	
Suspected during first endoscopy	61 (18)
Not suspected during first endoscopy	284 (82)
Grade	
G1	309 (90)
G2	32 (9)
G3	4 (1)
Lymphovascular invasion	
Yes	4 (1)
No	124 (26)
NR	217 (63)
Muscular invasion	4 (1)

G: tumour grading; NR: not reported; r-NET: rectal neuroendocrine tumour.

Table 1. R0 resection improved with subsequent endoscopic salvage resections

	1st endoscopic procedure	2nd endoscopic procedure	3rd Endoscopic procedure	TOTAL
Proportion of R0 resection	54/225 (24%)	60/100 (60%)	20/26 (77%)	134/345 (39%)

Table 2. R0 resection according to the endoscopic technique

	Proportion of R0 resection
Polypectomy	(32/183) 17%
EMR	(40/99) 40%
Advanced-techniques	(62/69) 90%

EMR: endoscopic mucosal resection,
Advanced-techniques included: endoscopic mucosal resection with cap aspiration (EMR-C), endoscopic submucosal resection using a band ligation device (EMR-L), endoscopic submucosal dissection (ESD)

Universitätsklinikum Essen

Molecular Signature of Rectal Neuroendocrine Neoplasia

Unger N[1], Theurer S[2], Herold T[2], Weber F[3], Dralle H[3], Schmid KW[2], Fuehrer D[1], Lahner H[1]

[1]Department of Endocrinology, Diabetes and Metabolism, University Hospital Essen, Essen, Germany
[2]Institute of Pathology, University Hospital Essen, Essen, Germany
[3]Division of Endocrine Surgery, University Hospital Essen, Essen, Germany

	Total NEN	Ileum	Appendix	Rectum
n	**59**	**32**	**12**	**15**
Age at diagnosis	52.41 (16.51 - 81.43)	56.85 (33.36 - 75.61)	37.06 (16.51 - 68.07)	47.50 (25.31 - 81.43)
Gender (f/m)	31/28	13/18	9/3	8/7
Follow-up (years)	3.42 (0.0 -16.31)	4.84 (0.63 - 16.31)	0.69 (0.0 - 10.87)	1.47 (0.0 - 9.65)
Distant metastases	29	23	0	7
G1	42	23	11	8
G2	13	8	1	4
G3	2	1	0	1
NEC	1	0	0	1
Goblet Cell Tumor	1	0	0	1

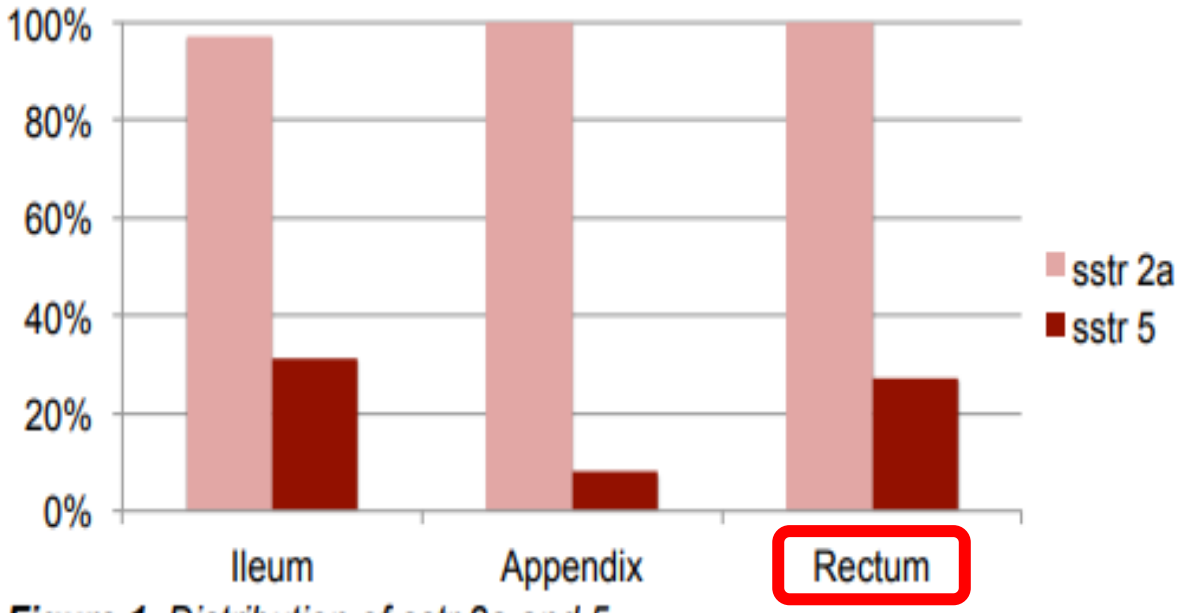


Figure 1. *Distribution of sstr 2a and 5.*

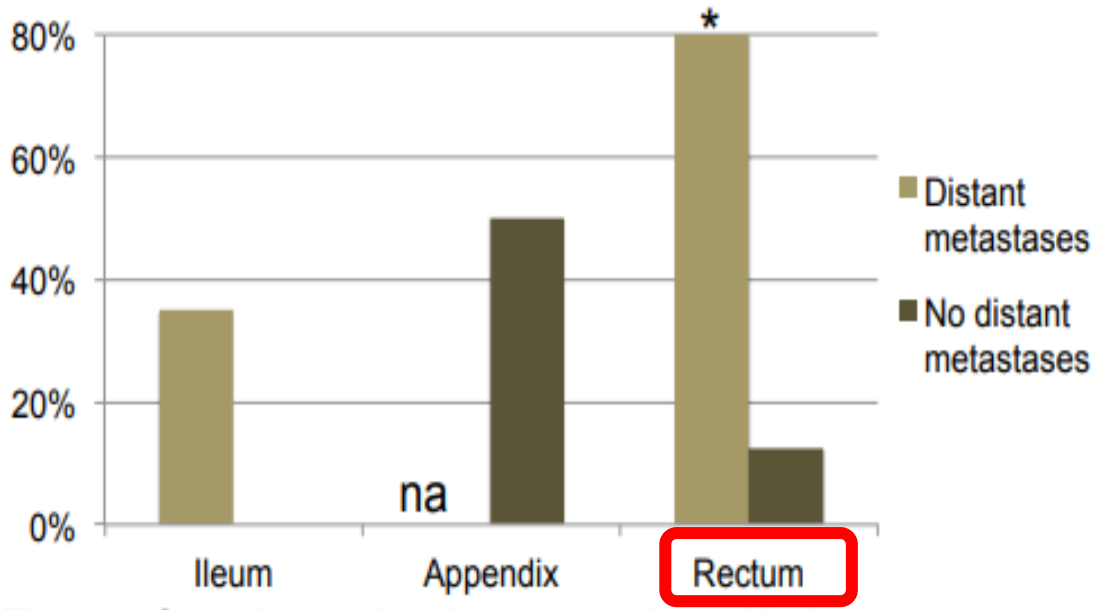


Figure 2. *Somatic mutations in tumour entities with distant metastases vrs non-metastasized tumours. * (p=0.0319).*

Analysis of the molecular features of rectal carcinoid tumors to identify new biomarkers that predict biological malignancy

No BRAF, KRAS, NRAS, or PIK3CA mutations were detected in the carcinoid tumors; moreover,

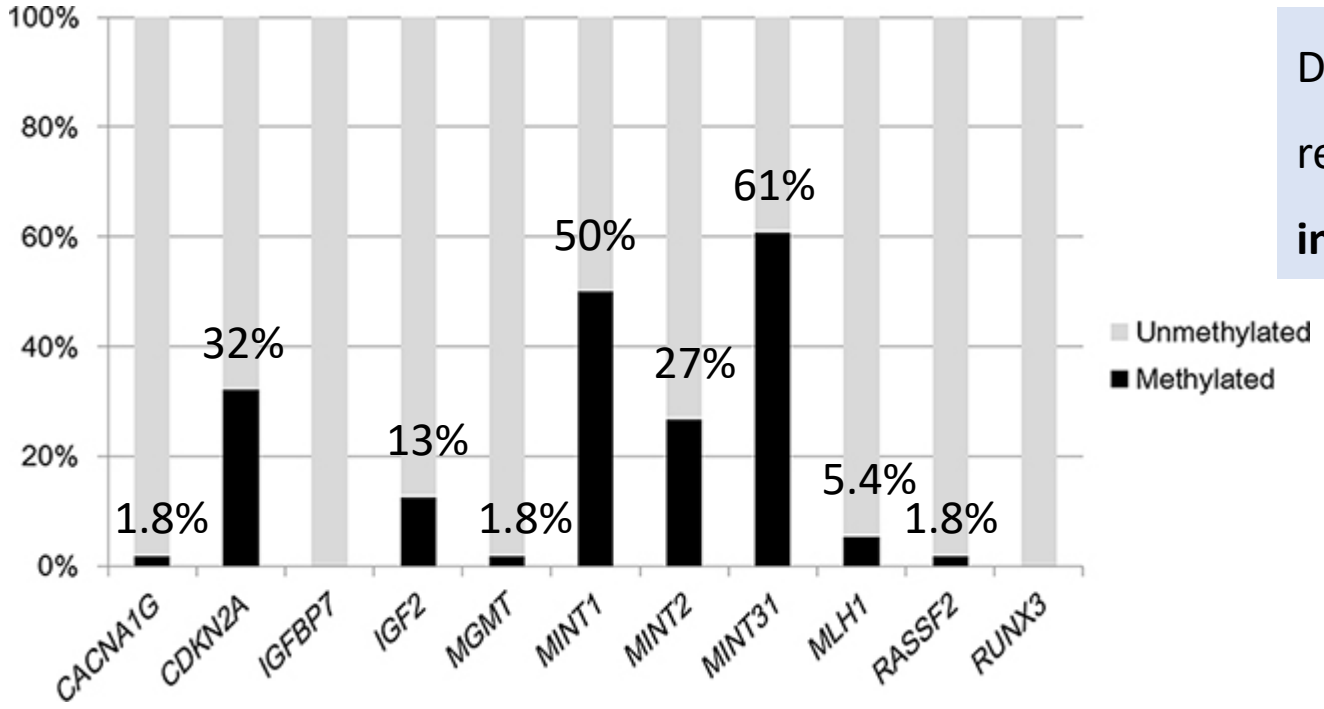
none of the 56 cases exhibited MSI-high status

Clinical and molecular feature	Total	Lymphovascular invasion		*P*
		Negative	Positive	
All cases	56	43	13	
Gender				
Male	29 (52%)	21 (49%)	8 (62%)	0.42
Female	27 (48%)	22 (51%)	5 (38%)	
Age (mean ± SD)	58.9 ± 13.9	58.3 ± 2.1	61.0 ± 3.8	0.53
Tumor size (mm) (mean ± SD)	6.2 ± 2.5	5.9 ± 0.37	7.0 ± 0.68	0.17

Mitsuhashi K, 2015

Mitsuhashi K., Yamamoto I., Kurihara H., Kanno S., Ito M., Igarashi H., Ishigami K., Sukawa Y., Tachibana M., Takahashi H., Tokino T., Maruyama R., Suzuki H., et al Analysis of the molecular features of rectal carcinoid tumors to identify new biomarkers that predict biological malignancy. Oncotarget. 2015; 6: 22114-22125.

Analysis of the molecular features of rectal carcinoid tumors to identify new biomarkers that predict biological malignancy



Detection of high **microRNA-885-5p** expression in rectal carcinoid tumors **with lymphovascular invasion** on miRNA array analysis

Mitsuhashi K, 2015

Mitsuhashi K., Yamamoto I., Kurihara H., Kanno S., Ito M., Igarashi H., Ishigami K., Sukawa Y., Tachibana M., Takahashi H., Tokino T., Maruyama R., Suzuki H., et al Analysis of the molecular features of rectal carcinoid tumors to identify new biomarkers that predict biological malignancy. Oncotarget. 2015; 6: 22114-22125.

Lanreotide in Metastatic Enteropancreatic Neuroendocrine Tumors

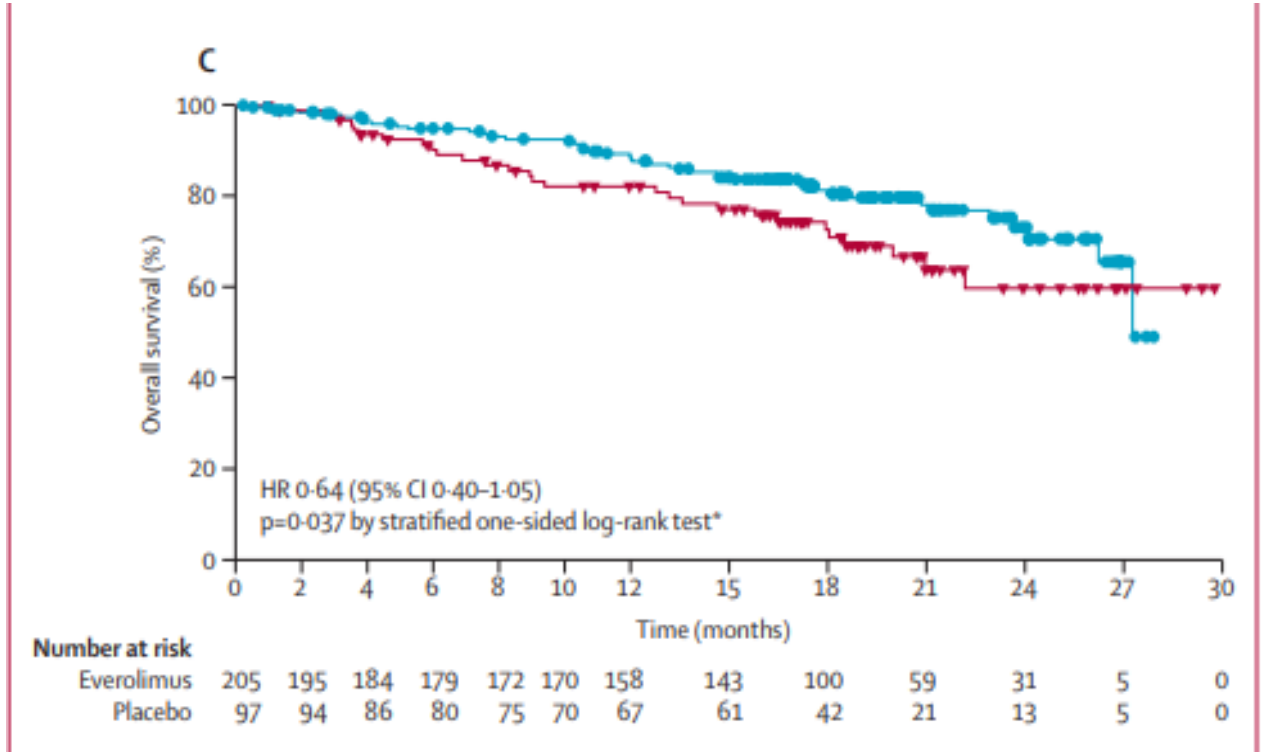
METHODS

PATIENTS

Eligible patients were adults (≥18 years of age) with sporadic neuroendocrine tumors that were confirmed centrally to be well differentiated or moderately differentiated and measurable according to the Response Evaluation Criteria in Solid Tumors (RECIST), version 1.0.12 The tumors had a centrally assessed proliferation index (on staining for the Ki-67 antigen) of less than 10% (or a mitotic index of ≤2 mitoses per 10 high-power fields, if the Ki-67 index could not be quantified reliably). **Primary tumors were located in the pancreas, midgut (defined as the small intestine and appendix), or hindgut (defined as the large intestine, rectum, anal canal, and anus) or were of unknown origin.**

Everolimus for the treatment of advanced, non-functional neuroendocrine tumours of the lung or gastrointestinal tract (RADIANT-4): a randomised, placebo-controlled, phase 3 study

	Everolimus (n=205)	Placebo (n=97)
Age, years	65 (22–86)	60 (24–83)
Sex		
Men	89 (43%)	53 (55%)
Women	116 (57%)	44 (45%)
WHO performance status*		
0	149 (73%)	73 (75%)
1	55 (27%)	24 (25%)
Primary tumour site		
Lung	63 (31%)	27 (28%)
Ileum	47 (23%)	24 (25%)
Rectum	25 (12%)	15 (16%)
Neuroendocrine tumour of unknown primary origin†	23 (11%)	13 (13%)
Jejunum	16 (8%)	6 (6%)
Stomach	7 (3%)	4 (4%)
Duodenum	8 (4%)	2 (2%)
Colon	5 (2%)	3 (3%)
Other‡	6 (3%)	2 (2%)
Caecum	4 (2%)	1 (1%)
Appendix	1 (1%)	0
Tumour grade§		
Grade 1	129 (63%)	65 (67%)
Grade 2	75 (37%)	32 (33%)



Phase 3 Trial of ^{177}Lu-Dotatate for Midgut Neuroendocrine Tumors

Jonathan Strosberg, M.D., Ghassan El-Haddad, M.D., Edward Wolin, M.D., Andrew Hendifar, M.D., James Yao, M.D., Beth Chasen, M.D., Erik Mittra, M.D., Ph.D., Pamela L. Kunz, M.D., Matthew H. Kulke, M.D., Heather Jacene, M.D., David Bushnell, M.D., Thomas M. O'Dorisio, M.D., et al., for the NETTER-1 Trial Investigators*

Table 1. Demographic and Baseline Clinical Characteristics of All Patients Who Underwent Randomization.*

Characteristic	^{177}Lu-Dotatate Group (N=116)	Control Group (N=113)
Sex — no. (%)		
Male	63 (54)	53 (47)
Female	53 (46)	60 (53)
Age — yr	63±9	64±10
Body-mass index†	25±5	26±7
Median time since diagnosis — yr	3.8	4.8
Primary tumor site — no. (%)		
Ileum	86 (74)	82 (73)
Small intestine, not otherwise specified	11 (9)	12 (11)
Midgut, not otherwise specified	9 (8)	7 (6)
Jejunum	6 (5)	9 (8)
Right colon	3 (3)	1 (1)
Appendix	1 (1)	2 (2)

European ENETS Neuroendocrine Tumor Society

Peptide Receptor Radionuclide Therapy in Rectal Neuroendocrine Tumours

Tham WY[A], Huang HL[A] , Tai WMD[B], Yan XS[A], Ng CED[A], Loke SHK[A]
[A]Singapore General Hospital, Singapore; [B]National Cancer Centre Singapore, Singapore

Patient demographics	n=23(%)
Average age at first treatment	55
Gender	
Male	11(48)
Female	12(52)
WHO grade	
1	3(13)
2	15(65)
3	1(4)
unknown	4(17)
Sites of metastasis	
Liver	21(91)
nodes	14(61)
Bone	14(61)
Other sites (e.g. lung, peritoneum)	7(30)
Number of cycles of PRRT administered	68
Lu-177 PRRT	64
Y-90 PRRT	4
Median number of cycles	3
Median cumulative dose of Lu-177(mCi)	593

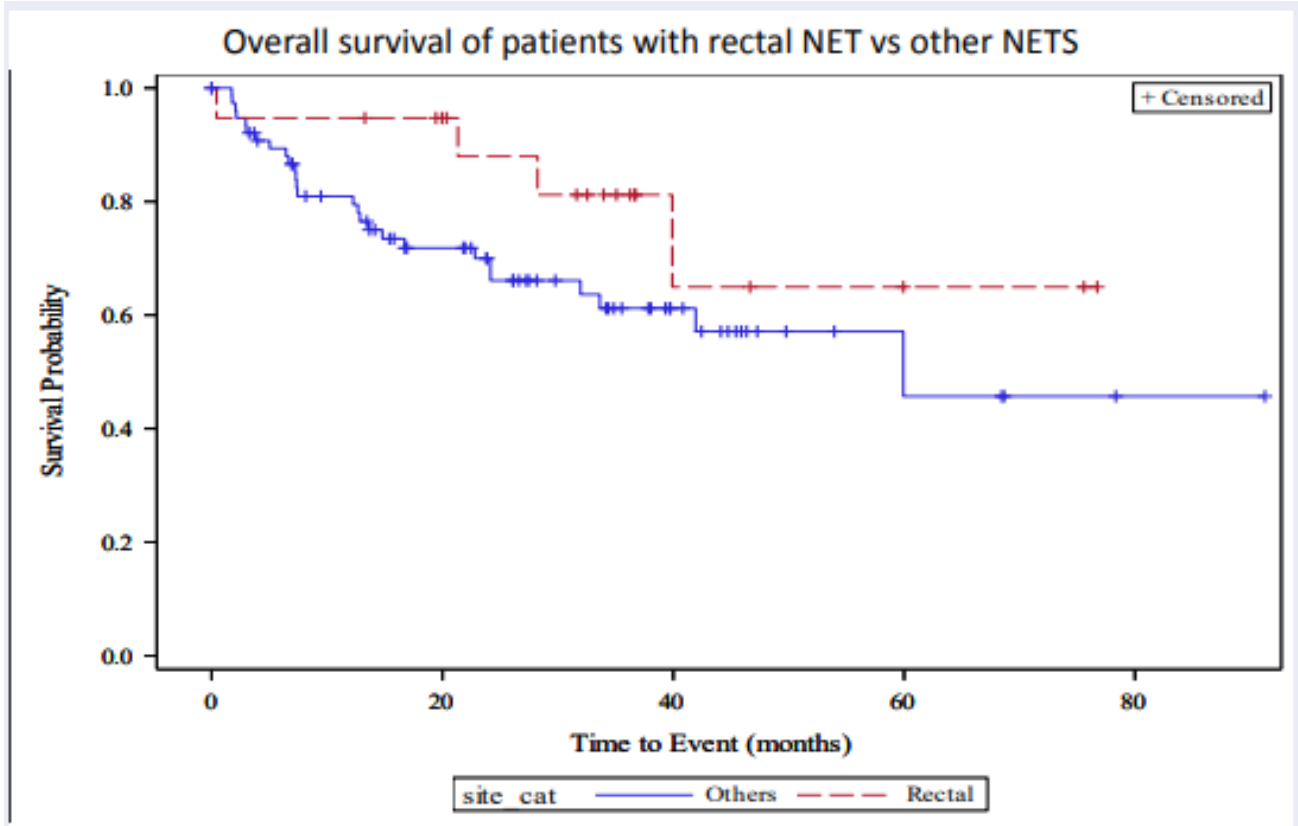


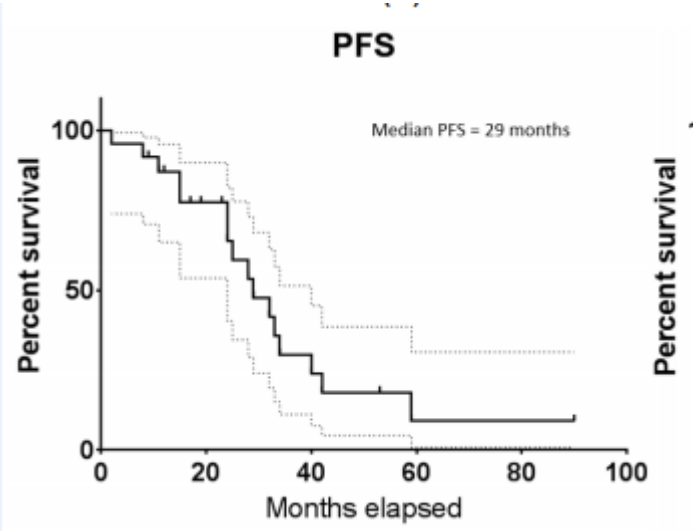
Figure 1: Overall survival of patients with rectal NETs who underwent PRRT vs NETs from other primary sites.

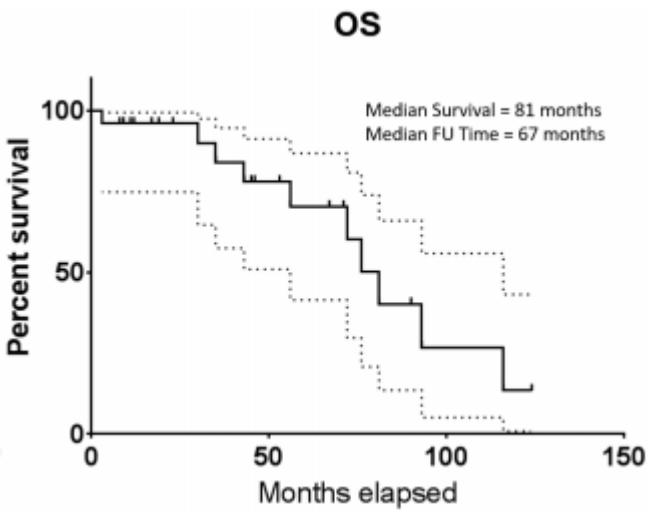
Peter Mac Peter MacCallum Cancer Centre Victoria Australia
European ENETS Neuroendocrine Tumor Society
Hadassah Medical Center

Title: Favourable Outcomes of PRRT for Treatment of Metastatic Rectal Neuroendocrine Neoplasia
Authors: *[1]G. Kong, *[2]S. Grozinsky-Glasberg, [1]T. Akhurst, [1]M.S. Hofman, [3]A. Meirovitz, [3]O. Maimon, [4]Y. Krausz, [4]J Godefroy, [5]M. Michael, [2]D.J. Gross, [1]R.J. Hicks *Co-First authors
Institution: Peter MacCallum Cancer Centre. Hadassah-Hebrew University Medical Centre
Institution's Location: Melbourne, Australia; *and* Jerusalem, Israel

Favourable Outcomes of Peptide Receptor Radionuclide Therapy for Treatment of Metastatic Rectal Neuroendocrine Neoplasia

- **25** consecutive pts (M=18, 31-81yo) were included from 2 institutions
- Tumour origin: rectal (n=23), sigmoid (2)
- The majority 68% had ENETs Grade 2 disease (17/25 pts), three had Grade 3, one Grade 1, and four unavailable grading
- 43% (10pts) had FDG-avid disease (negative in 6 pts; not done in 9)
- 24 pts were treated for disease progression
- 88% (23/25) had prior treatments: chemotherapy (n=1), surgery (2), SSA (7), chemotherapy+surgery (3), chemotherapy+SSA+RT (2), chemotherapy+ SSA+surgery (1), surgery+SSA (4), surgery+SSA+RT (2)
- Most had ^{177}Lu-DOTA-octreotate, median cumulative activity of 30 GBq, median 4 cycles (2-5 cycles)
- 14 pts had radiosensitising chemotherapy: 5FU (n=10) or capecitabine
- At 3 months post-PRRT - CT disease control rate was 96%: 60% (15/25) partial response + 36% stable disease (9/25). All but one had partial SSTR imaging response (Figure 2, 3)
- The median PFS was 29 months. Ten pts died, with median overall survival 81 months, median follow-up of 67 months (Figure 1)
- Toxicity at 3 months: 2 patients had grade 3 lymphopenia. No significant renal toxicity, secondary MDS or leukaemia on follow-up





Ευχαριστώ!

Ερωτήσεις;