

# Sharing the Experience of GEP-NEN based on KSGC Multicenter Study



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\* The author has nothing to declare.

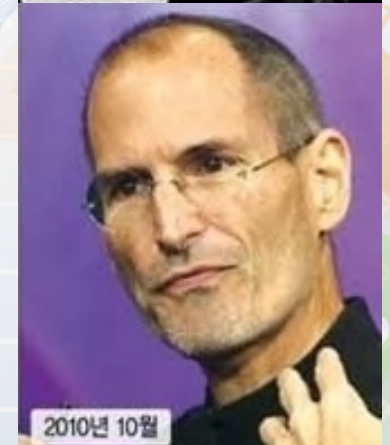
# Contents

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- Korean retrospective GEP-NET registry

## ➤ Korean multicenter study

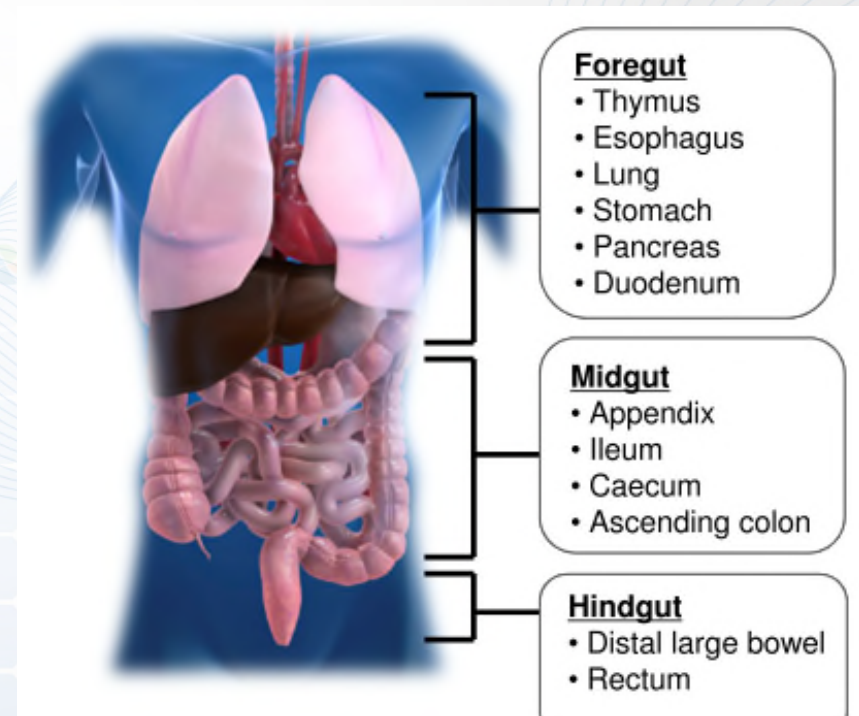
- Epidemiology and clinical manifestation according to different sites
  - Therapeutic outcomes and introduction of novel therapeutic approach in Korea
- 
- Current situation & future direction





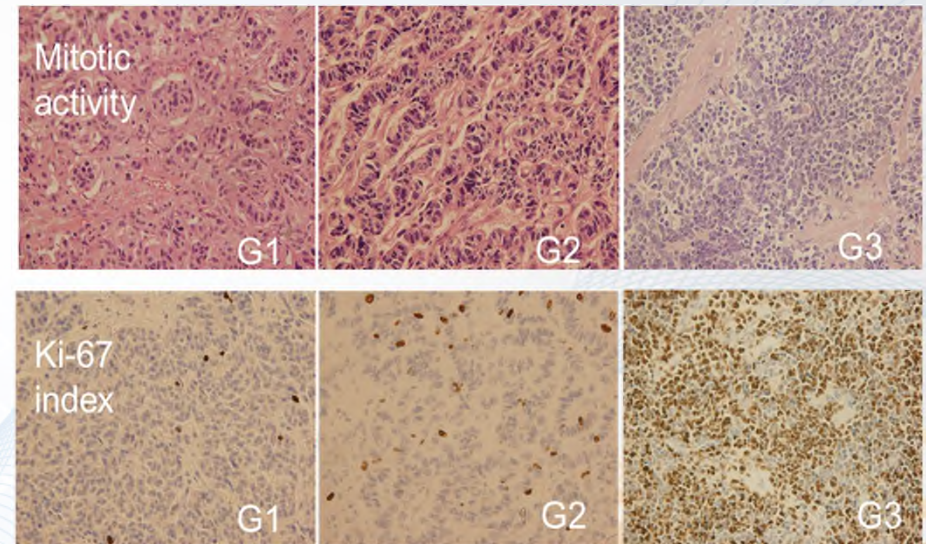
# Neuroendocrine neoplasm

- Epithelial neoplasms with predominant neuroendocrine differentiation
- Relatively rare & not familiar disease
- Several terms with confusion
- Heterogenous group of cancers
- Diverse disease with different prognosis
- Classification
  - Site and embryonic origin
  - Functional status
  - Hereditary disease; MEN-1, MEN-2, VHLS



# NEN classification

- Histologic grades : WHO 2010 → 2017
- Attempting to stratify patients into different prognostic groups
- Low grade (G1), intermediate grade (G2), and high grade (G3) NET vs. G3 NEC
- Based on cell morphology and proliferation rate using mitotic index and Ki-67 index



Grade (WHO 2017)	Ki-67 index	Mitoses/10 hpfs
Neuroendocrine tumor G1	<3 %	< 2/10 HPF
Neuroendocrine tumor G2	3-20 %	2-20/10 HPF
Neuroendocrine tumor G3	>20 %	>20/10 HPF
Neuroendocrine carcinoma G3 (small, large cell type)	>20 %	>20/10 HPF
Mixed neuroendocrine-nonneuroendocrine neoplasm (MiNEN)		



# History of GEP-NEN research

➤ The Korean Society of Gastrointestinal Cancer,  
Council of the Neuroendocrine Tumor Research

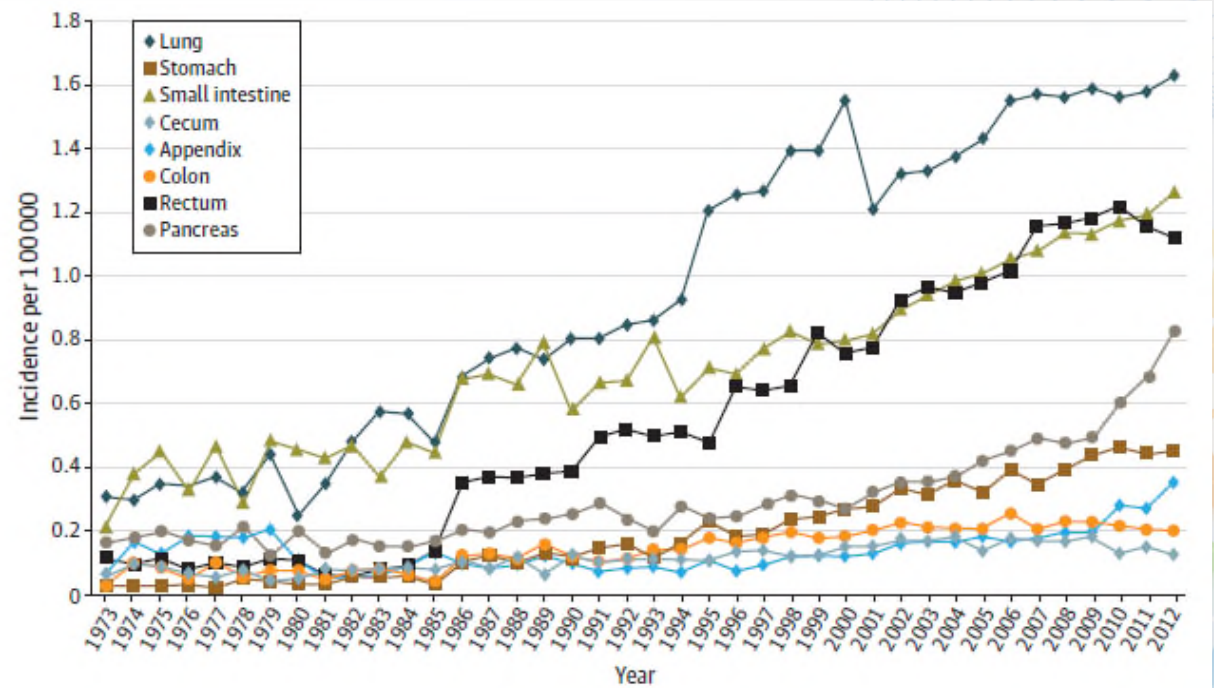
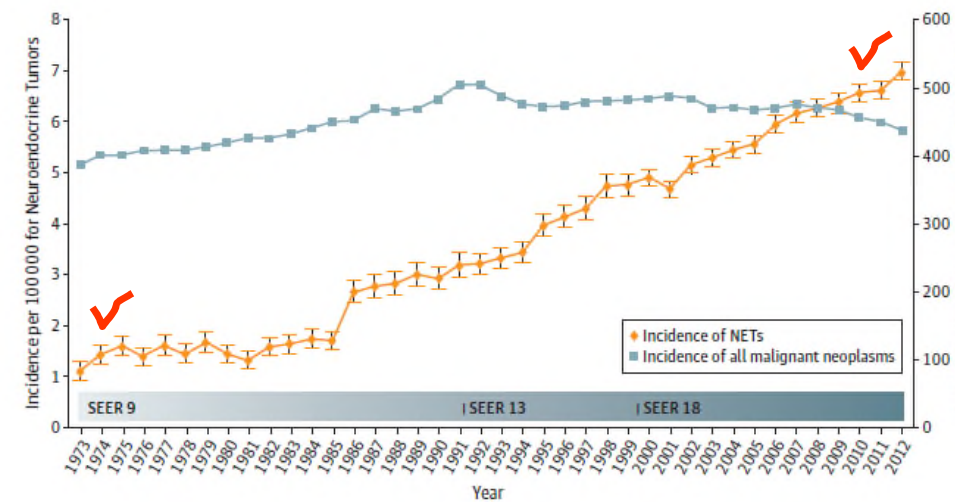
➤ History of GEP-NET research in KSGC

- Publication of the Korean textbook of “Gastroenteropancreatic Neuroendocrine Tumor” (52 authors, 1<sup>st</sup> ed. 2012)
- Korean GEP-NET tumor registry (KGNTR, 2002-2012)
  - Esophageal NET (BMC Cancer. 2014 7;14:569)
  - pNET (Pancreas. 2016 45(7):941-6.)
  - Biliary NET (Scand J Gastroenterol. 2017 52(4):437-441)
  - Everlimus in pNETs (Cancer Chemother Pharmacol. 2017 80(4):799-805)
  - Gastric NET (Journal of Digestive Cancer Reports. 2017 5(2):86-90)



# Incidence of GEP-NET (US SEER Data)

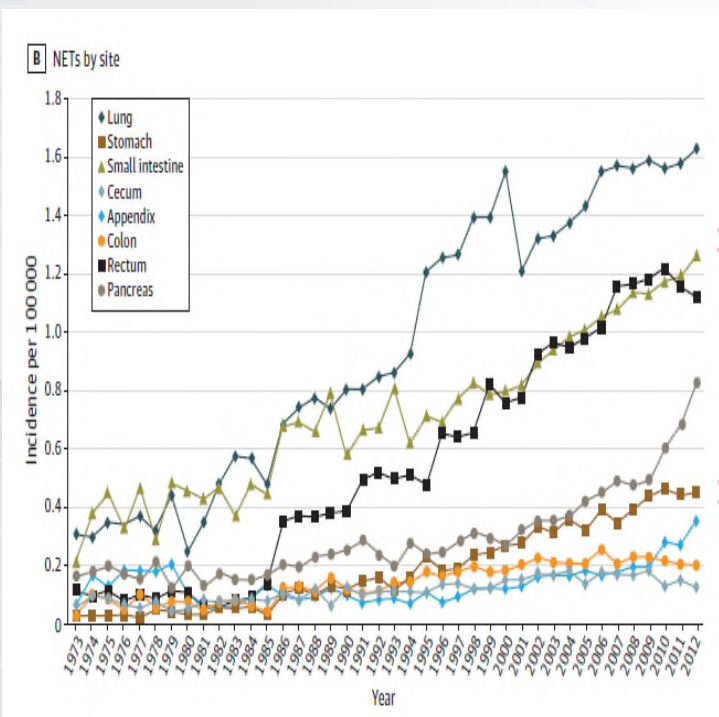
64,971 US GEP-NETs (1973-2012)





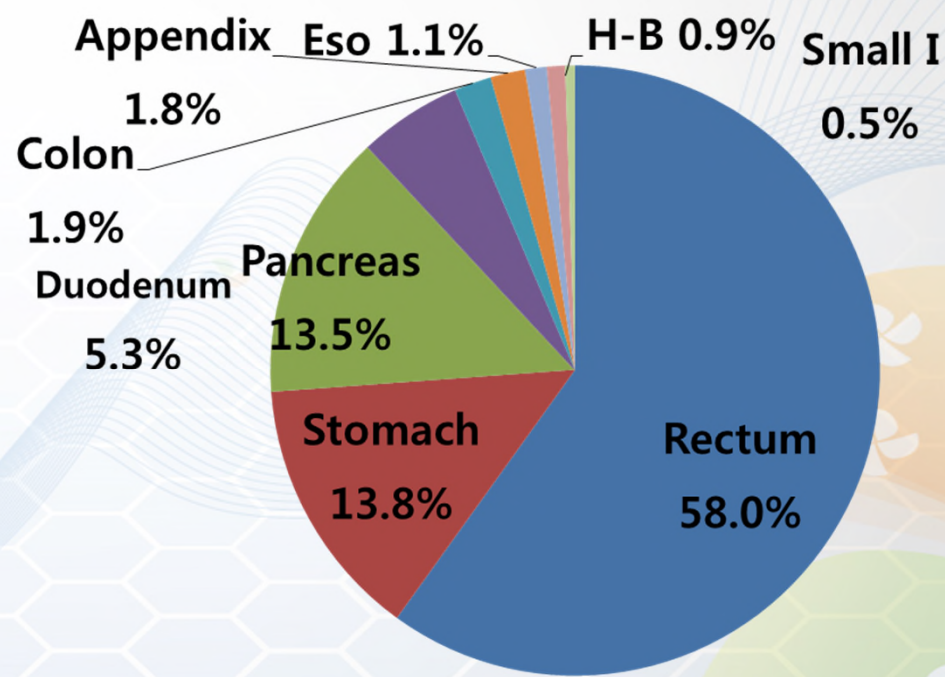
# Distribution according to primary site (KGNTNTR)

US SEER data GEP-NETs (1973-2012)



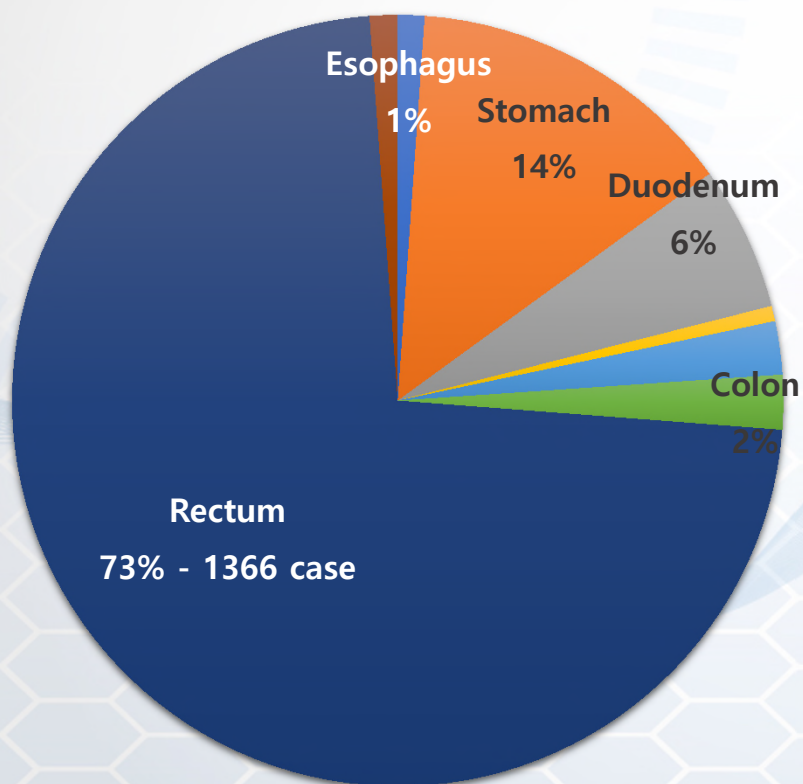
Small intestine  
Rectum  
Pancreas  
Stomach

2,345 Korea GEP-NETs from KGNTNTR

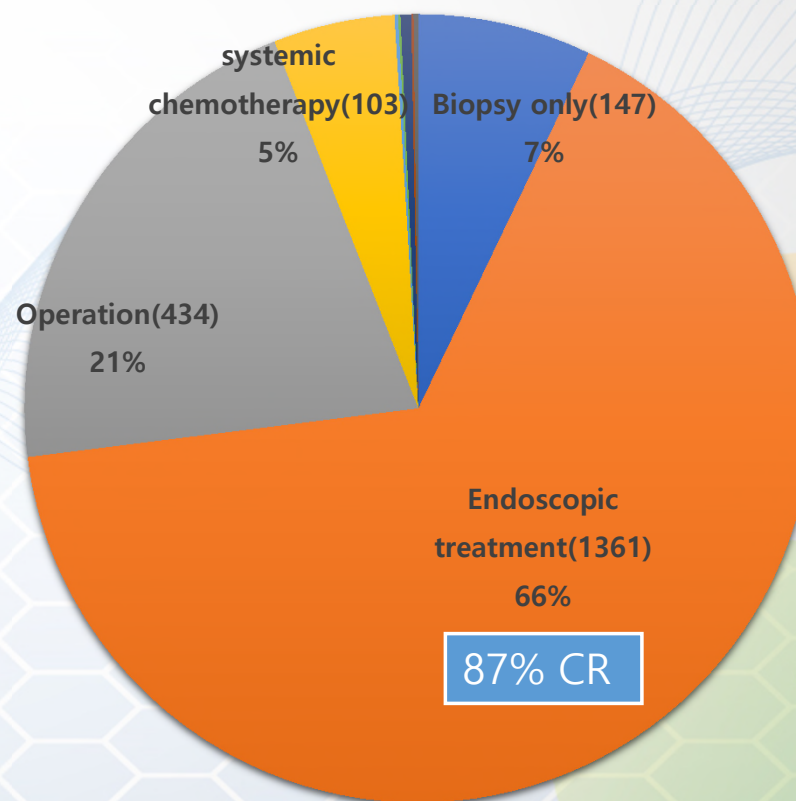


# Gastrointestinal NET

- 25 hospital, 2037 patients



## Treatment modality & outcomes





# Esophageal NET

- 26 cases of esophageal NET
- Characteristics
  - Site: lower third of esophagus (76.9%), size : 2.34 cm
  - P/D 38.5% , W/D 11.5%
  - Regional LN metastasis: 57.7%
  - Endoscopic treatment: only 3 small cases (< 1.0 cm)
- Advanced esophageal NET has unfavorable prognosis compared to other site GEP-NETs

## RESEARCH ARTICLE

Open Access

### The clinical features and treatment modality of esophageal neuroendocrine tumors: a multicenter study in Korea

Chang Geun Lee<sup>1</sup>, Yun Jeong Lim<sup>1\*</sup>, Seun Ja Park<sup>2</sup>, Byung Ik Jang<sup>3</sup>, Seok Reyo Choi<sup>4</sup>, Jae Kwang Kim<sup>5</sup>, Yong-Tae Kim<sup>6</sup>, Joo Young Cho<sup>7</sup>, Chang Hun Yang<sup>1</sup>, Hoon Jai Chun<sup>8</sup>, Si Young Song<sup>9</sup> and Neuroendocrine tumor study group

#### Abstract

**Background:** Neuroendocrine tumors (NETs) of the esophagus are extremely rare, and few cases have been reported worldwide. Thus, a comprehensive nationwide study is needed to understand the characteristics of and treatment strategy for esophageal NETs.

**Methods:** We collected data on esophageal NET patients from 25 hospitals in Korea from 2002–2012. The incidence, location, clinical symptoms, histopathology, treatment response, and the biochemical, radiologic and endoscopic characteristics of esophageal NETs were surveyed.

**Results:** Among 2,037 NETs arising in different gastrointestinal sites, esophageal NETs were found in 26 cases (1.3%). The mean patient age was  $60.12 \pm 9.30$  years with a 4:1 male predominance. In endoscopic findings, 76.9% (20/26) of NETs were located in the lower third of the esophagus and the mean size was  $2.34 \pm 1.63$  cm. At diagnosis, more than half the patients (15/26, 57.7%) had regional lymph node metastasis or widespread metastasis. Endoscopic resection was conducted in three cases, and in all three of them, lymph node metastasis was not found and tumor size was below 1.0 cm. All tumors were completely removable through endoscopic procedures and there was no recurrence during the follow-up period. Eighteen other patients received an operation, chemotherapy or both. Among them, nine patients (50.0%) expired because of the progression of their cancer or post-operative complications. In Kaplan-Meier survival analysis, only tumor size (more than 2.0 cm) showed prognostic significance ( $P = 0.045$ ).

**Conclusions:** Despite the general assumption that gastrointestinal NETs are benign and slow-growing tumors, the prognosis of advanced esophageal NETs is not favorable.

**Keywords:** Esophagus, Neuroendocrine tumor, Treatment, Prognosis

# Gastric NET

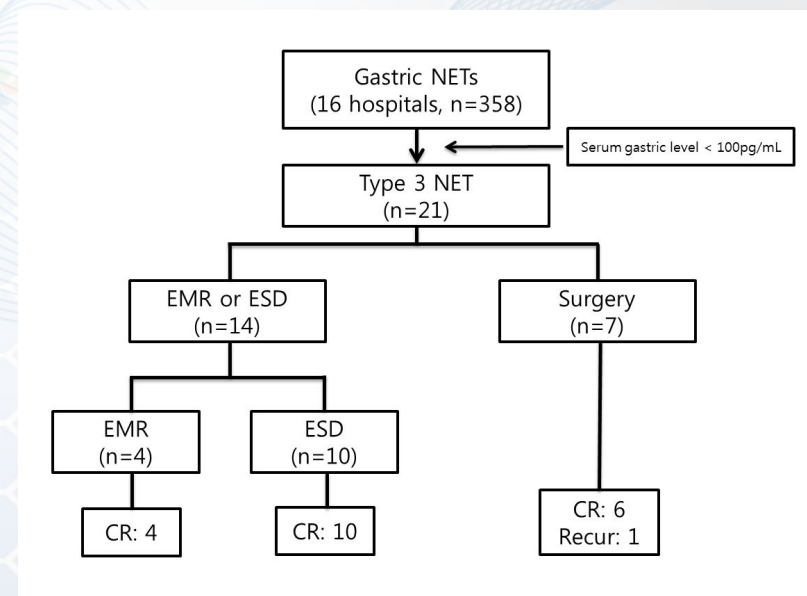
- Type 3 gastric NET (n=21)
  - TG vs. endoscopic treatment
  - Site : body (85.7%), size (9.5mm)
  - WHO 2010 G1 (61.9%) G2 (33.4%), G3 (1%)

- Endoscopic treatment
  - Small sized type 3 gastric NET (n=14)
  - no recurrence (median fu 27 months)

➤ Endoscopic treatment can be an alternative safe modality in selected cases of type 3 gastric NET.

## Type 3 Gastric Neuroendocrine Neoplasm Clinical Features: A Multicenter Study in Korea

Kyong Joo Lee<sup>1</sup>, Hee Man Kim<sup>1</sup>, Sang Kil Lee<sup>2</sup>, Ho Sun Choi<sup>3</sup>, Jie-Hyun Kim<sup>4</sup>,  
Seun Ja Park<sup>5</sup>, Sung Chul Park<sup>6</sup>, Byung Ik Jang<sup>7</sup>, Jin Tae Jung<sup>8</sup>, Tae Joo Jeon<sup>9</sup>,  
Jong Hun Lee<sup>10</sup>, Jae Kyu Sung<sup>11</sup>, Semi Park<sup>12</sup>, Yoon Jae Kim<sup>13</sup>, Jae Hee Cho<sup>13</sup>





# Biliary NET

## ORIGINAL ARTICLE

### Clinicopathological characteristics of biliary neuroendocrine neoplasms: a multicenter study

Kyong Joo Lee<sup>a\*</sup>, Jae Hee Cho<sup>b\*</sup>, Sang Hyub Lee<sup>c</sup>, Kwang Hyuk Lee<sup>d</sup>, Byung Kyu Park<sup>e</sup>, Jun Kyu Lee<sup>f</sup>, Sang Myung Woo<sup>g</sup>, Ji Kon Ryu<sup>c</sup>, Jong Kyun Lee<sup>d</sup>, Yeon Suk Kim<sup>b</sup>, Jae Woo Kim<sup>h</sup> and Woo Jin Lee<sup>g</sup>

<sup>a</sup>Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, South Korea; <sup>b</sup>Department of Internal Medicine, Gachon university, Gil Medical Center, Incheon, South Korea; <sup>c</sup>Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, South Korea; <sup>d</sup>Department of Internal Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; <sup>e</sup>National Health Insurance Corporation Ilsan Hospital, Goyang, South Korea; <sup>f</sup>Department of Internal Medicine, Dongguk University Ilsan Hospital, Dongguk University, Goyang, South Korea; <sup>g</sup>Center for Liver Cancer, National Cancer Center, Goyang, South Korea

#### ABSTRACT

**Objectives:** This study assessed the clinicopathological features, therapeutic approaches, and prognosis of patients with biliary neuroendocrine neoplasm (NENs).

**Materials and methods:** Multicenter retrospective study of patients with biliary tract NENs in the gallbladder, the extrahepatic bile duct, or the ampulla of Vater between 2005 and 2014.

**Results:** Total of 43 patients were included in the study. The median age was 62 years (range: 29–84 years) and 58.1% of the patients were male. The tumors occurred in the gallbladder ( $n=11$ ), the extrahepatic bile duct ( $n=5$ ) or the ampulla of Vater ( $n=27$ ). The liver was the most common metastatic site. Based on the 2010 World Health Organization classification, more patients with gallbladder NENs (11/11 (100%)) had neuroendocrine carcinoma G3 than those with NENs in the ampulla of Vater (10/27 (37.1%)). The median progression-free survival time (39.3 vs 5.1 months;  $p=0.001$ ) and median overall survival time (46.9 vs 7.1 months;  $p=0.001$ ) were significantly longer in patients with biliary tract NENs than gallbladder NENs. WHO 2010 grade 3 was independent prognostic factor for survival (hazard ratio [CI], 2.81–26.0).

**Conclusion:** The 2010 WHO classification is the only factor related to prognosis.

#### ARTICLE HISTORY

Received 26 October 2016  
Accepted 12 November 2016

#### KEYWORDS

World Health Organization classification; biliary tract; neuroendocrine neoplasm; neuroendocrine carcinoma; prognosis

## ➤ Biliary NET

- 43 cases from 7 institutes
- GB ( $n=11$ ), EHBD ( $n=5$ ), AoV ( $n=27$ )

## ➤ Poor prognostic factor after univariate analysis

- GB > AoV + EHBD
- Metastasis
- WHO grade 3
- No chemotherapy

## ➤ Biliary WHO grade 3 was the only significant

WHO 2010 grade is most important prognostic factor regardless of site and metastasis

# Pancreas NET

## ➤ US SEER data

- 11.5% of GEP-NET (29,664 cases, 1973-2007)
- Lowest 5 year survival (37.6%) (Rectal NET 88.5%)

## ➤ Taiwan multicenter study

- 6% of GEP-NET (2,187 cases, 1996-2008)

## ➤ Korean multicenter study

- 13.5% of GEP-NET (2,354 cases, 2002-2012)

n= 299	
Follow-up duration, median months (range)	Not available
Progression free survival (PFS), median months (95% C.I.)	91.0 (78.8 – 103.2)

n= 317	
Median age, year (IQR)	56 (47 – 65)
Sex, n (%)	
M / F	162 / 155
Family history of NET	4 (1.3 %)
Function	
Non-functioning tumor	174 (78.7 %)
Functioning tumor	47 (21.3 %)
Insulinoma	33 (14.9 %)
Gastrinoma	2 (0.9%)
Somatostatinoma	4 (1.8%)
Glucagonoma	3 (1.4%)
Others	5 (2.3%)



### Prognostic Validity of the American Joint Committee on Cancer and the European Neuroendocrine Tumors Staging Classifications for Pancreatic Neuroendocrine Tumors

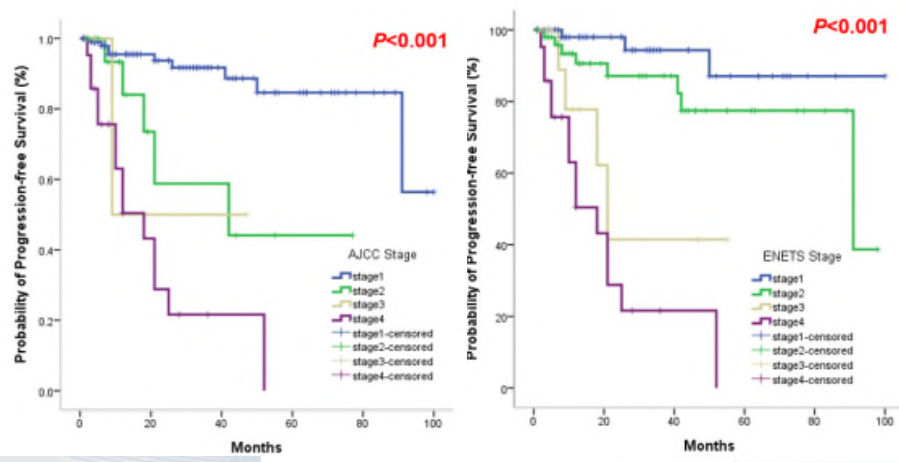
A Retrospective Nationwide Multicenter Study in South Korea

Jae Hee Cho, MD, PhD,\* Ji Kon Ryu, MD, PhD,† Si Young Song, MD, PhD,‡ Jin-Hyeok Hwang, MD, PhD,§ Dong Ki Lee, MD, PhD,|| Sang Myung Woo, MD, PhD,¶ Young-Eun Joo, MD, PhD,# Seok Jeong, MD, PhD,\*\* Seung-Ok Lee, MD, PhD,†† Byung Kyu Park, MD, PhD,‡‡ Young Koog Cheon, MD, PhD,§§ Jinin Han, MD, PhD,|||| Tae Nyeun Kim, MD, PhD,¶¶ Jin Kyu Lee, MD, PhD,## Sung-Hoon Moon, MD, PhD,\*\*\* Hyunjin Kim, MD, PhD,††† Eun Taek Park, MD, PhD,‡‡‡ Jae Chul Hwang, MD, PhD,§§§ Tae Hyeon Kim, MD, PhD,||||| Tae Joo Jeon, MD, PhD,¶¶¶ Chang-Min Cho, MD, PhD,### Ho Soon Choi, MD, PhD,\*\*\*\* and Woo Jin Lee, MD, PhD\*

# AJCC vs. ENETS vs. WHO 2010 (153 cases from 15 institutes)

TABLE 3. Univariate and Multivariate Analysis of Prognostic Factors for pNETs

	Mean Survival, mo	Univariate Analysis			AJCC Multivariate Analysis			ENETS Multivariate Analysis		
		HR	95% CI	P	HR	95% CI	P	HR	95% CI	P
AJCC stage				<0.001			<0.001			
I	87									
II	47	4.64	1.51–14.23	0.007	2.87	0.83–9.89	0.096			
III	28	6.18	0.77–49.90	0.087	4.62	0.56–38.41	0.157			
IV	18	17.01	7.13–40.56	<0.001	10.23	3.66–25.56	<0.001			
ENETS stage				<0.001						<0.001
I	92									
II	79	2.86	0.76–10.86	0.122				2.37	0.62–9.01	0.205
III	32	10.35	2.30–46.64	0.002				5.30	1.07–26.38	0.042
IV	18	27.38	7.857–95.51	<0.001				15.37	3.88–60.91	<0.001
WHO				<0.001			0.074			0.062
Grade I	83									
Grade II	47	2.94	1.19–7.25	0.019	1.72	0.63–4.66	0.290	1.66	0.63–4.41	0.307
Grade III	21	12.55	5.12–30.79	<0.001	3.55	1.17–10.79	0.025	3.61	1.21–10.79	0.021
Age		1.02	0.99–1.05	0.315						
Sex										
Male	64									
Female	74	0.73	0.36–1.48	0.384						



AJCC and ENETS TNM stages better reflect the prognosis of pNETs compared to WHO 2010 grade

# Contents

## ➤ Introduction

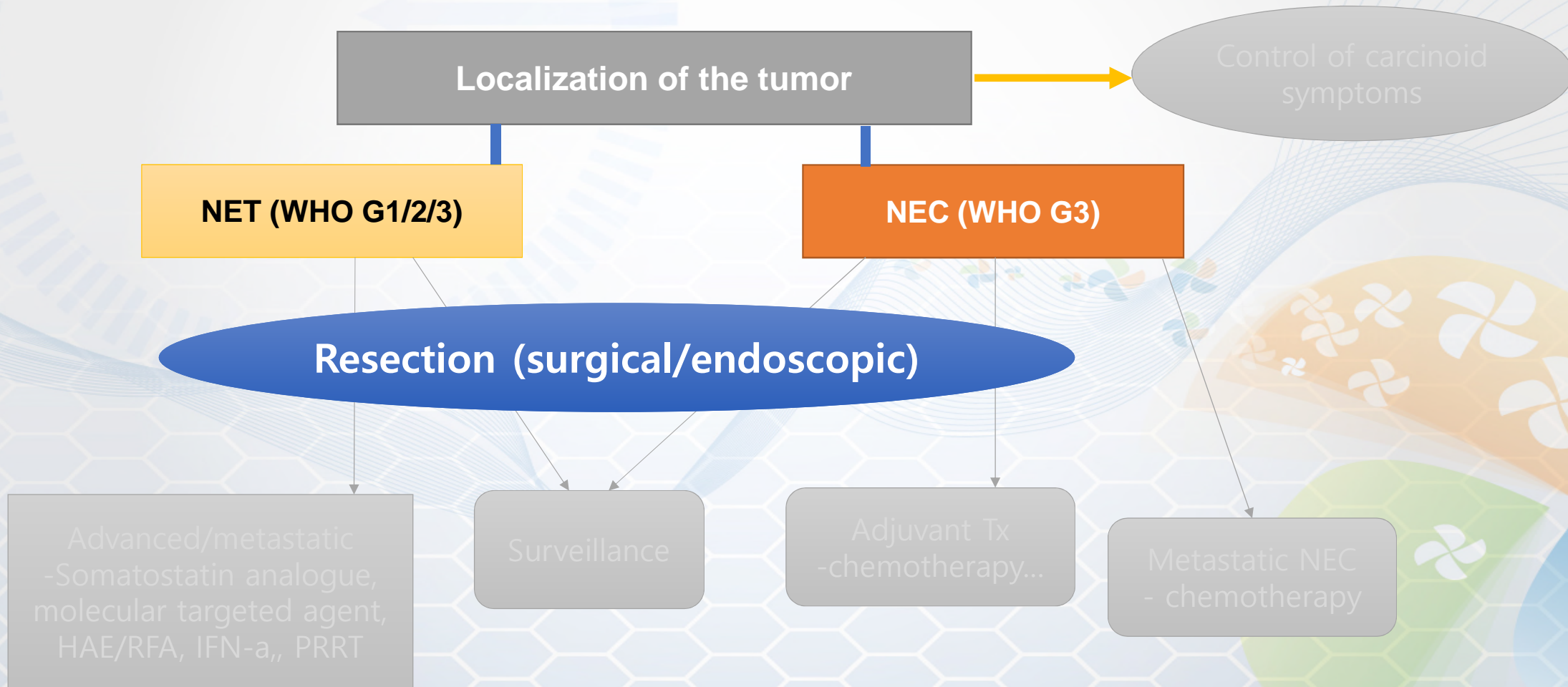
- Korean retrospective GEP-NEN registry

## ➤ Korean multicenter study

- Epidemiology and clinical manifestation according to different sites
  - Therapeutic outcomes and introduction of novel therapeutic approach in Korea
- 
- Current situation & future direction



# Overview of treatment algorithm

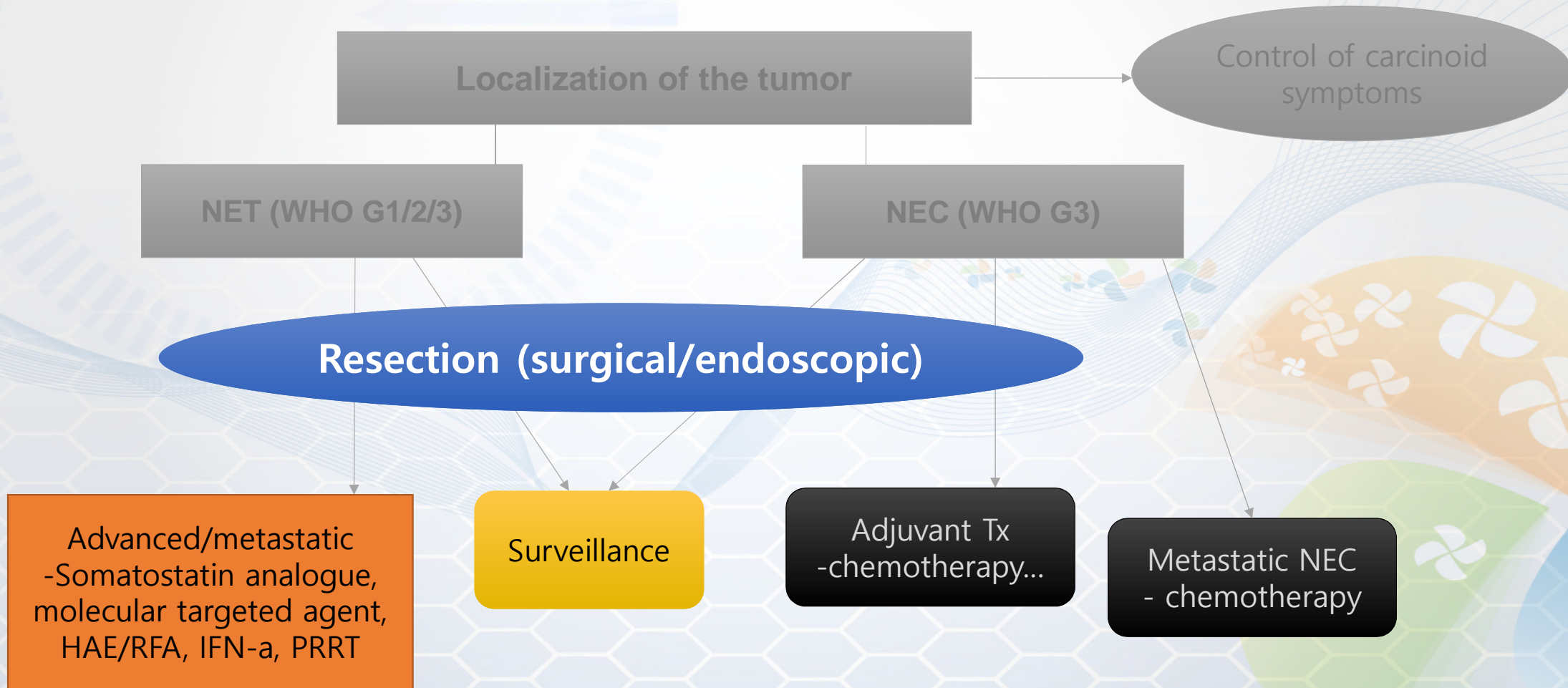


# Management of GEP-NEN

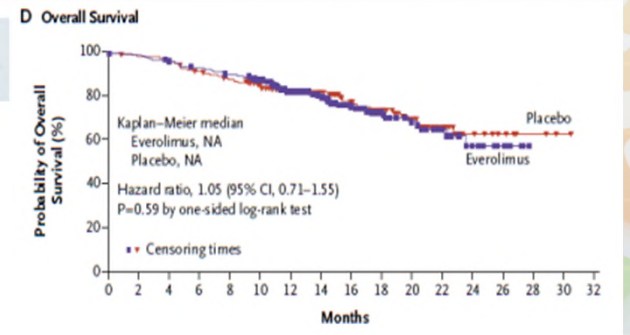
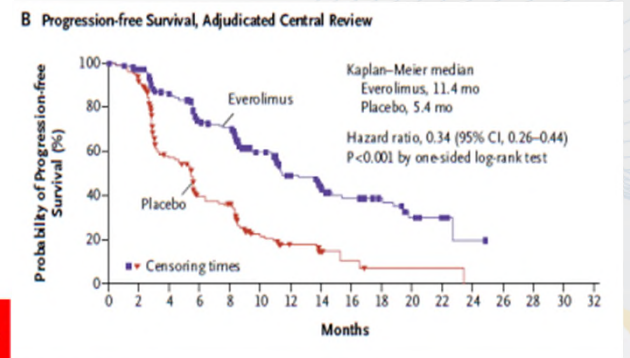
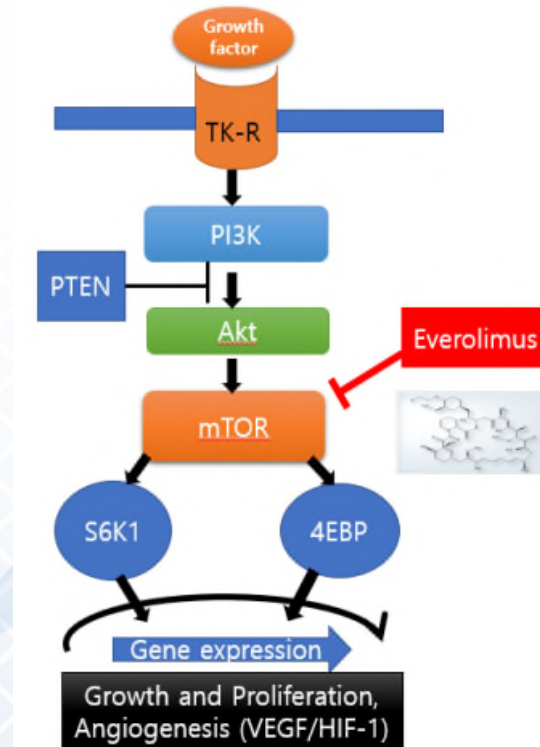
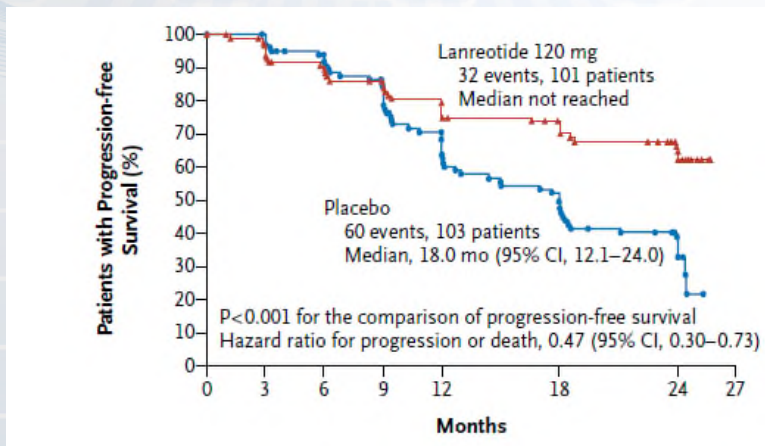
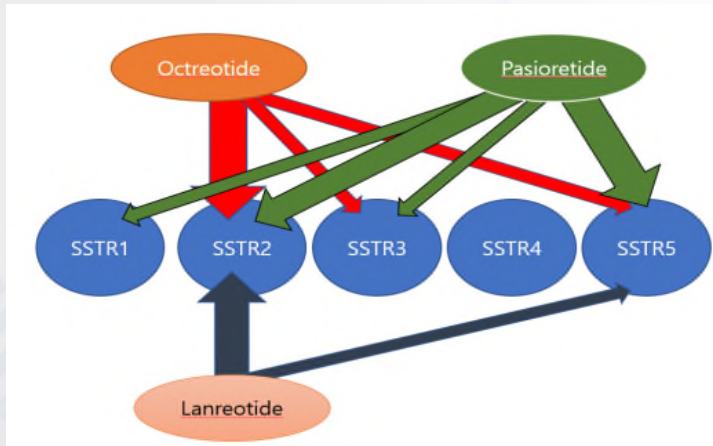
Site	Criteria	Management		
<b>Appendix</b>	$\leq 2$ cm and confined to the appendix $>2$ cm, Incomplete resection (nodes, margin)	Simple appendectomy Re-exploration, Rt hemicolectomy		Simple appendectomy Re-exploration, Right hemicolectomy
<b>Small bowel</b>	Irrespective of size	En-bloc bowel resection with regional lymphadenectomy		
<b>Duodenum</b>	Locoreginal disease (noninvasive or invasive)	Endoscopic resection Local excision (Transduodenal) Pancreaticoduodenectomy		
<b>Colon</b>	Irrespective of size	Partial colectomy and regional lymphadenectomy		
<b>Rectum</b>	$\leq 1$ cm incidental tumors <b>All other rectal tumors</b>	Completely resected <b>Endorectal MRI or EUS (T1 vs T2-4)</b>	No additional f/u $\leq 2$ cm $>2$ cm	No additional f/u <b>T1: Transanal or endoscopic resection</b> <b>T2: LAR, APR</b>
<b>Stomach</b>	Type 1 (atrophic gastritis, Gastrin $\uparrow$ ) Type 2 (Gastrin $\uparrow$ ), Zollinger Ellison <b>Type 3 (Gastrin NL)</b>	Endoscopic resection, antrectomy Endoscopic or surgical resection <b>Radical gastric resection with lymphadenectomy</b> <b>Consider endoscopic or surgical wedge resection (EUS no LN)</b>		
<b>Pancreas</b>	Nonfunctional Functional	<b>Surgical resection</b> , symptomatic treatment		



# Overview of treatment algorithm



# Somatostatin analogue / molecular targeted agent





# Korean experience of everolimus for pNET

Cancer Chemother Pharmacol (2017) 80:799–805  
DOI 10.1007/s00280-017-3421-7



ORIGINAL ARTICLE

## Clinical outcomes of everolimus in patients with advanced, nonfunctioning pancreatic neuroendocrine tumors: a multicenter study in Korea

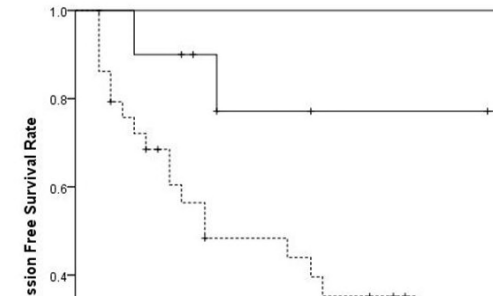
Kyong Joo Lee<sup>1</sup> · Jae Hee Cho<sup>2</sup> · Sang Hyub Lee<sup>3</sup> · Si Young Song<sup>4</sup> · Kwang Hyuk Lee<sup>5</sup> · Seok Jeong<sup>6</sup> · Ji Kon Ryu<sup>3</sup> · Sang Myung Woo<sup>7</sup> · Seungmin Bang<sup>4</sup> · Jong Kyun Lee<sup>5</sup> · Tae Hoon Lee<sup>8</sup> · Woo Hyun Paik<sup>3</sup> · Yong Tae Kim<sup>3</sup> · Woo Jin Lee<sup>7</sup>

- Efficacy of everolimus for pNET
- 40 patients of metastatic or recurrent pNETs
- Median PFS was 20 months (2–38 mo)

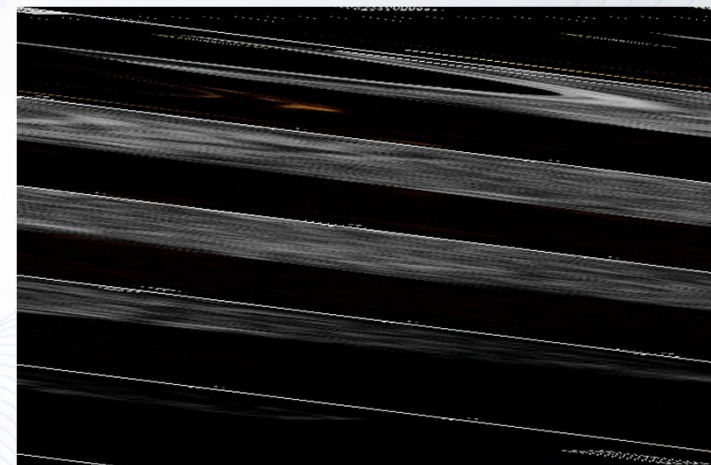
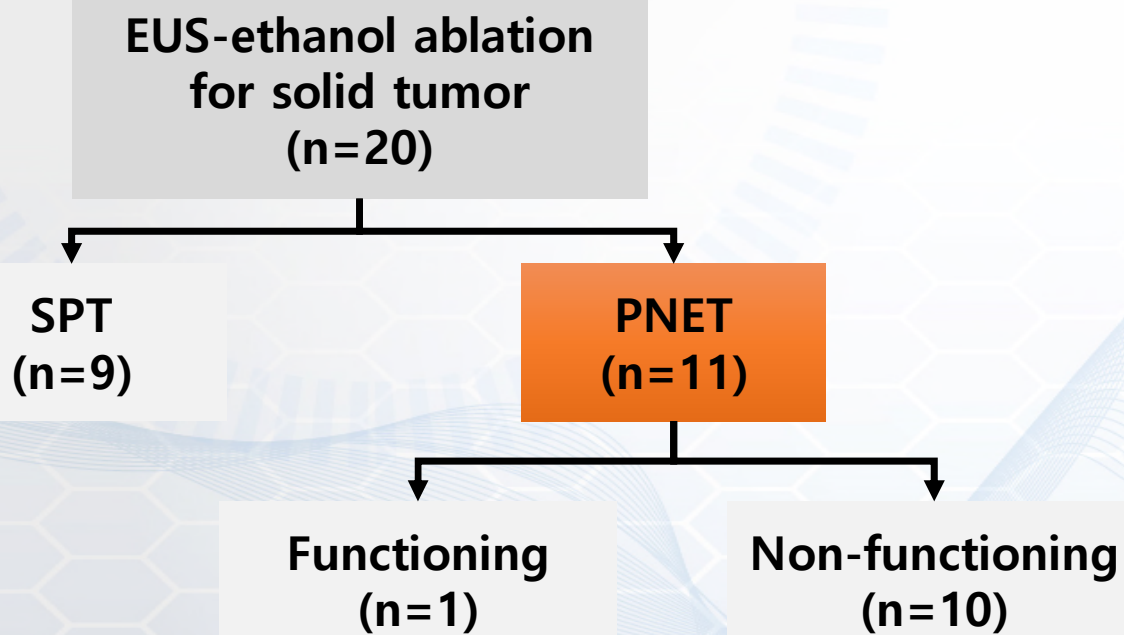
WHO grade act as the most important factor for everolimus response  
Everolimus has similar therapeutic effects in Korean patients

Table 4. Treatment-related adverse event after everolimus

Toxicity	Grade	
	All grades	Grade 3 or 4
Stomatitis	19 (47.5%)	2 (5%)
Skin rash	13 (32.5%)	1 (2.5%)
Anemia	5 (12.5%)	1 (2.5%)
Diarrhea	4 (10%)	1 (2.5%)
Thrombocytopenia	3 (7.5%)	0
Pneumonitis	1 (2.5%)	0
Cough	1 (2.5%)	0
Hyperglycemia	1 (2.5%)	0



# Endoscopic ablation Tx for pNET

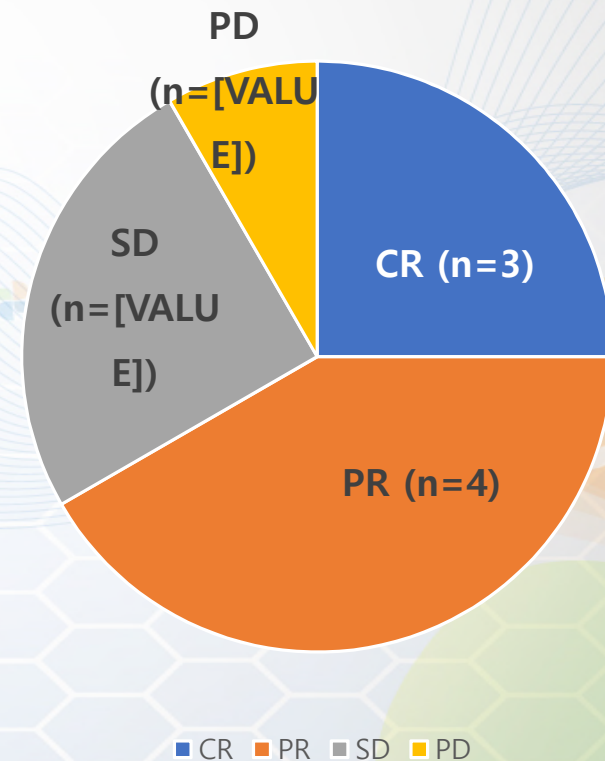




# Therapeutic outcomes

EUS guided ethanol ablation fo pNET		N = 11
Sex	Male Female	5 6
Site	Head Body/tail	6 5
Size (median, mm)	Initial Post-ablation size (median 192 days)	12 (8-21) 10 (0-14)
EtOH dose	(mean±SD, ml)	1.05 ± 0.86
Adverse events	Acute pancreatitis (necrotizing pancreatitis) Abdominal pain	2 (1) 5
FU duration (median, day)		322 (126-552)
Surgical resection after ablation		0

Therapeutic outcomes  
(median 322 days)



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- Korean retrospective GEP-NEN registry

## ➤ Korean multicenter study

- Epidemiology and clinical manifestation according to different sites
- Therapeutic outcomes and novel therapeutic approach in Korea

## • Conclusion & future direction

# International GEP-NET network

## ➤NEGO symposium

- 2014, 2015, 2016(IASGO presymposium)
- International expert consensus meeting
- Sharing the GEP-NET experience from clinical research in Asian Pacific region

## ➤NET case reports

- International e-news letter
- Case reports: sharing the experience of GEP-NET



대한소화기암학회  
Issue 3 / July 29, 2015

대한소화기암학회에서 제공하는 NET Report입니다.  
NET 관련된 국내 임상 사례, 최신의 임상논문 정보를 제공합니다.

**Case Report**

**A case of gastric neuroendocrine tumor misdiagnosed as adenocarcinoma**  
In Ji Seung, Myoung Chung, Jun Chul Park, Sang Keon Shin, Yong Chan Lee, Sang Kil Lee

A 70-year-old man visited the private clinic due to right upper quadrant pain for 2 weeks. His EGD showed an ulcerative mass in antrum suspected as advanced gastric cancer. Histopathology of the lesion revealed adenocarcinoma with poorly differentiated histology. He was referred to our clinic for further management. He had essential hypertension 10 years ago. He had been recently diagnosed with coronary artery occlusive disease and initiated on aspirin and antiplatelet agent once daily. His family history was unremarkable. Blood pressure was normal. He was afebrile with pulse rate of 76 per minute, respiration 20 per minute. Abdominal examination showed normal bowel sound and mild tenderness at epigastric area without rebound tenderness or palpable mass. White blood cell count was 4,520/mm<sup>3</sup>, hemoglobin 9.4 g/dL and normal platelet count. Serum alanine aminotransferase was 30 U/L, aspartate aminotransferase 20 U/L, total bilirubin 0.5 mg/dL, and alkaline phosphatase 134 U/L. Serum tumor marker such as CEA and CA 19-9 were all normal. ...

[Case Download](#)

**Amputary neuroendocrine tumor diagnosed by endoscopic papillectomy in previously confirmed amputary adenoma**  
Tae Hwon Lee, Se-Hyung Jang

A 53-year-old female patient visited our hospital for dyspepsia of 3-month duration, he had no specific medical or surgical history. Her vital signs at admission were blood pressure 110/70 mmHg, pulse rate 62/min, respiratory rate 20/min, and body temperature 36.3°C. Physical examination revealed no marked features. The laboratory data also showed no abnormalities, including tumor markers CEA 1.0 ng/mL, CA 19-9 2.0 U/mL. Screening upper gastrointestinal endoscopy showed protruding major papilla and subsequent endoscopic biopsy of the major papilla revealed low-grade adenoma. A duodenoscopic image showed an enlarged major papilla with central umbilication and fine nodularity. EUS at the major ampulla revealed a 1.1 × 0.9 cm, slightly hypoechoic round amputary mass confined to the submucosa without definite wall disruption or adjacent invasion (Fig. 1). Abdomen CT did not show an abnormally dilated pancreatic or biliary duct, ductal invasion, or enlarged lymph nodes. ...

[Case Download](#)

**Original Article**

**Subgroup analysis of patients with G2 gastroenteropancreatic neuroendocrine tumors**  
G2 소화기 신경내분비종양(GEP-NET) 환자의 하위그룹 분석





Vol. 03

# Professional Leaders of Asia in **NEUROENDOCRINE TUMORS**

Welcome  
Message

PLANET

About PLANET



PLANET  
Vol. 01

PLANET  
Vol. 02

## Sharing of NET Experience in Korea

- Clinicopathological characteristics of biliary neuroendocrine neoplasm: a multicenter study

VIEW

- Small well-differentiated rectal neuroendocrine tumor with multiple regional lymph node metastasis

VIEW

- A case of pancreatic neuroendocrine tumor with massive cystic degeneration misdiagnosed as a pancreatic pseudocyst

VIEW

## Sharing of NET Experience in China

- A case of type 1 gastric neuroendocrine tumor

VIEW

- A case of multiple endocrine neoplasia type 2B (MEN2B)

VIEW

## Sharing of NET Experience in Japan

- Usefulness of somatostatin receptor scintigraphy in the diagnosis of pancreatic neuroendocrine tumors

VIEW

## Sharing of NET Experience in USA

- Update on Non-Surgical Management of GEP-NETS in the US

VIEW

- Metastatic midgut carcinoid presenting with right sided heart failure and carcinoid heart disease

VIEW

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GEP-Net cases of each countries for sharing of experience and academic and clinical survey

Vol. 02

## Professional Leaders of Asia in



Congratulations on opening and starting PLANET.

I'm really pleased that we have the opportunity to share information on neuroendocrine neoplasms (NEN) among Asian countries. I would like to appreciate the Korean Society of Gastrointestinal Cancer. It is a great honor for Japanese specialists to participate in PLANET.

Well, several new developments have occurred in the field of neuroendocrine tumors (NET) in Japan. First, the utility of chromogranin A (CgA), useful for the diagnosis and monitoring of the treatment response of NET, has been demonstrated in Japan. For NEN diagnosis and treatment, grading and correct histological diagnosis according to the WHO 2010 classification is important. Regarding the histological diagnosis, the advent of EUS-FNA has enabled correct pathological diagnosis and suitable treatment for the affected tissue. Furthermore, EUS-FNA has also facilitated the assessment of the presence or absence of gene mutations. Additionally, somatostatin receptor type 2 is expressed in several cases of NET. Somatostatin receptor scintigraphy (<sup>111</sup>In-octreoscan) has also been approved in Japan, and this advancement will undoubtedly contribute to the localization diagnosis, the identification of remote metastasis, and assessments of the treatment responses of NEN. Finally, regarding the treatment strategy for NEN, the management of liver metastasis is important. The advent of novel molecular-targeted drugs has dramatically improved the prognosis of advanced NEN. Multimodality therapy that accounts for the tumor stage, degree of tumor differentiation, tumor volume, and speed of tumor growth is required.

This April, I moved to Neuroendocrine Tumor Center, Fukuoka Sanno Hospital, International University of Health and Welfare from Kyushu University Hospital. From now on, I think that it will be easier to work harder more about NET. Therefore, I look forward to working with the readers. Thank you.

Director of Japan Neuroendocrine Tumors Society  
Professor Tetsuhide Ito



### Title of Case

## Gastrinomas coexisting with hyperparathyroidism in a patient with multiple endocrine neoplasia type 1

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**Category**  Upper GI  Lower GI  Pancreatobiliary tract  Others

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### CASE DESCRIPTION

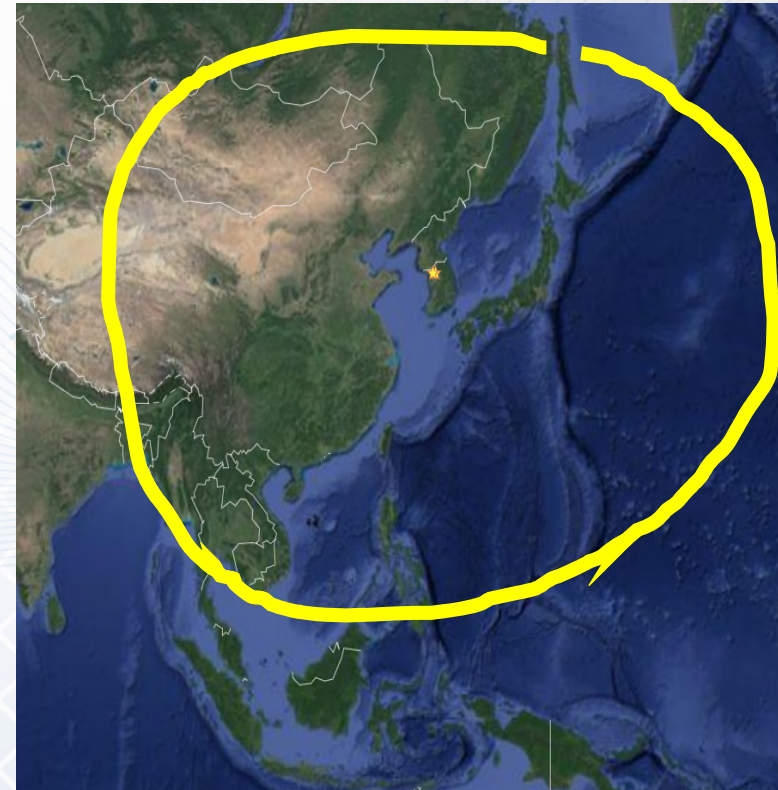
A 51-year-old man with a family history of pancreatic neuroendocrine tumor (PNET) had been treated for reflux esophagitis. In 20XX, the patient underwent surgery for duodenal NET, and 7 years later, he underwent another surgery for thymic carcinoid tumor. The patient had been regularly followed-up after the completion of adjuvant chemotherapy. However, 9 years later, contrast-enhanced computed tomography (CT) showed an 8 mm tumor in the pancreatic tail. The following year, the patient was referred to our hospital. He was not suffering from either vomiting or diarrhea. Moreover, physical examination showed neither thyromegaly nor abdominal symptoms. After discontinuation of proton pump inhibitor administration, an increased serum gastrin level of 346 pg/mL was observed. Furthermore, in response to intravenous administration of calcium gluconate, a significant reactive increase (1.5-fold) in the gastrin level was observed. In addition, an increased intact-parathyroid hormone (PTH) level of 105.7 pg/mL and an increased serum calcium level of 11.2 mg/dL were observed. With regard to tumor markers, the neuron specific enolase (NSE) level was 13.8 ng/mL, and the pro-gastrin releasing peptide (pro-GRP) level was 40.6 pg/mL. Contrast-enhanced CT showed 10 mm and 13 mm round tumors, which exhibited early enhancement (Figures 1A and B). Besides the pancreatic tail lesions observed on the CT images, endoscopic ultrasonography (EUS) showed at least 9 hypochoic tumors of approximately 5 - 10 mm, including 1 lesion in the pancreatic head, 4 lesions in the pancreatic body, and 2 lesions in the pancreatic tail (Figures 1C-E). The upper gastrointestinal endoscopy showed multiple erosions, ulcer scars, and submucosal tumors of approximately 10 mm in the duodenum (Figures 1F-H). Moreover, methoxyisobutylisonitrile (MIBI) scintigraphy showed abnormal accumulation in the parathyroid gland (Figure 1I). Pituitary magnetic resonance imaging (MRI) showed a pituitary adenoma, which was found to be non-functional based on various challenge tests. Thus, the patient was diagnosed with gastrinoma, hyperparathyroidism, and non-functional pituitary adenoma, which were associated with multiple endocrine neoplasia type 1 (MEN1).

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# Conclusion

- Clinical course of GEP-NET is highly variable according to site of origin.
- Multidisciplinary team approach, evolving clinical/basic research are essential for overcoming GEP-NET.
- For the accurate diagnosis and proper treatment of rare disease of GEP-NET, disease network by international communication are needed in Asian pacific countries.
- This symposium will be valuable foundation for the next steps of international cooperation and collaboration.





Vol. 03

# Professional Leaders of Asia in NEUROENDOCRINE TUMORS

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## Sharing of NET Experience in Korea



- Clinicopathological characteristics of biliary neuroendocrine neoplasm: a multicenter study
- Small well-differentiated rectal neuroendocrine tumor with multiple regional lymph node metastasis
- A case of pancreatic neuroendocrine tumor with massive cystic degeneration misdiagnosed as a pancreatic pseudocyst

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## Sharing of NET Experience in China



- A case of type 1 gastric neuroendocrine tumor
- A case of multiple endocrine neoplasia type 2B (MEN2B)

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## Sharing of NET Experience in Japan



- Usefulness of somatostatin receptor scintigraphy in the diagnosis of pancreatic neuroendocrine tumors

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## Sharing of NET Experience in USA



- Update on Non-Surgical Management of GEP-NETS in the US
- Metastatic midgut carcinoid presenting with right sided heart failure and carcinoid heart disease

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# 소화기 신경내분비종양

Gastroenteropancreatic Neuroendocrine Tumor (NET)

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