

Session I

PNET with Extensive Liver Metastases

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1. Case presentation

A 42-year-old woman with epigastric pain and weight loss

2. Diagnosis

Pancreatic neuroendocrine tumors with multiple liver metastases

3. Therapy and Clinical Course

Patient was treated with capecitabine and temozolomide for 53 months, followed by everolimus for 2 months. She has received sunitinib as 3rd-line treatment.

4. Conclusion

Patient continued treatment with exceptionally favorable response to combination therapy with capecitabine and temozolomide.

Key Words: Neuroendocrine Tumors, Pancreatic Neoplasms, Antineoplastic Agents

5. References

1. Strosberg JR, Fine RL, Choi J, et al.: First-line chemotherapy with capecitabine and temozolomide in patients with metastatic pancreatic endocrine carcinomas. *Cancer*. 2011;117(2):268-275. doi:10.1002/cncr.25425
2. Givès M, Ghayouri M, Morse B, et al.: Analysis of potential response predictors to capecitabine/temozolomide in metastatic pancreatic neuroendocrine tumors. *Endocr Relat Cancer*. 2016;23(9):759-767. doi:10.1530/ERC-16-0147

Case (F/42)

- **Chief Complaint: epigastric pain (1WA)**

- Initial visit date: 2015-9-15

- **Present Illness**

- 이전 특이병력 없던 분
- 1주일 전부터 시작된 명치부위 통증으로 타원에서 시행한 복부 CT에서 이상 소견 (multiple liver mass)으로 추가 평가 위하여 본원 내원함

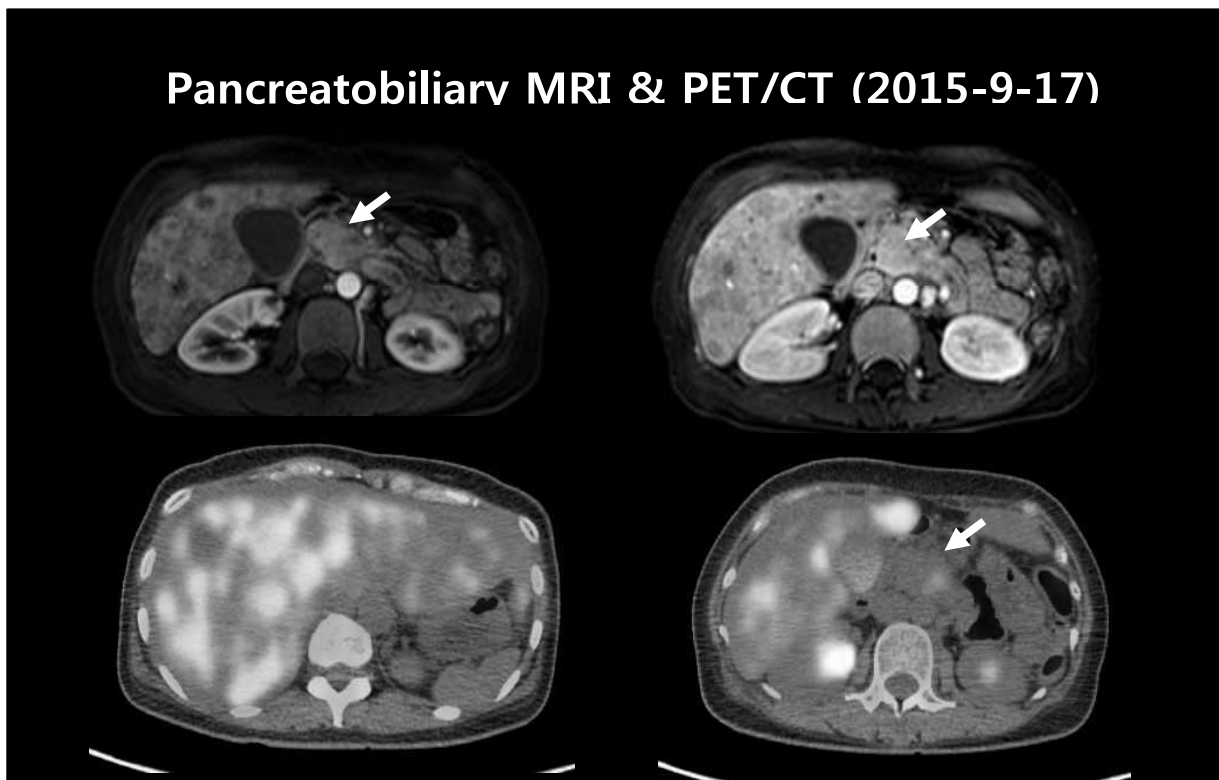
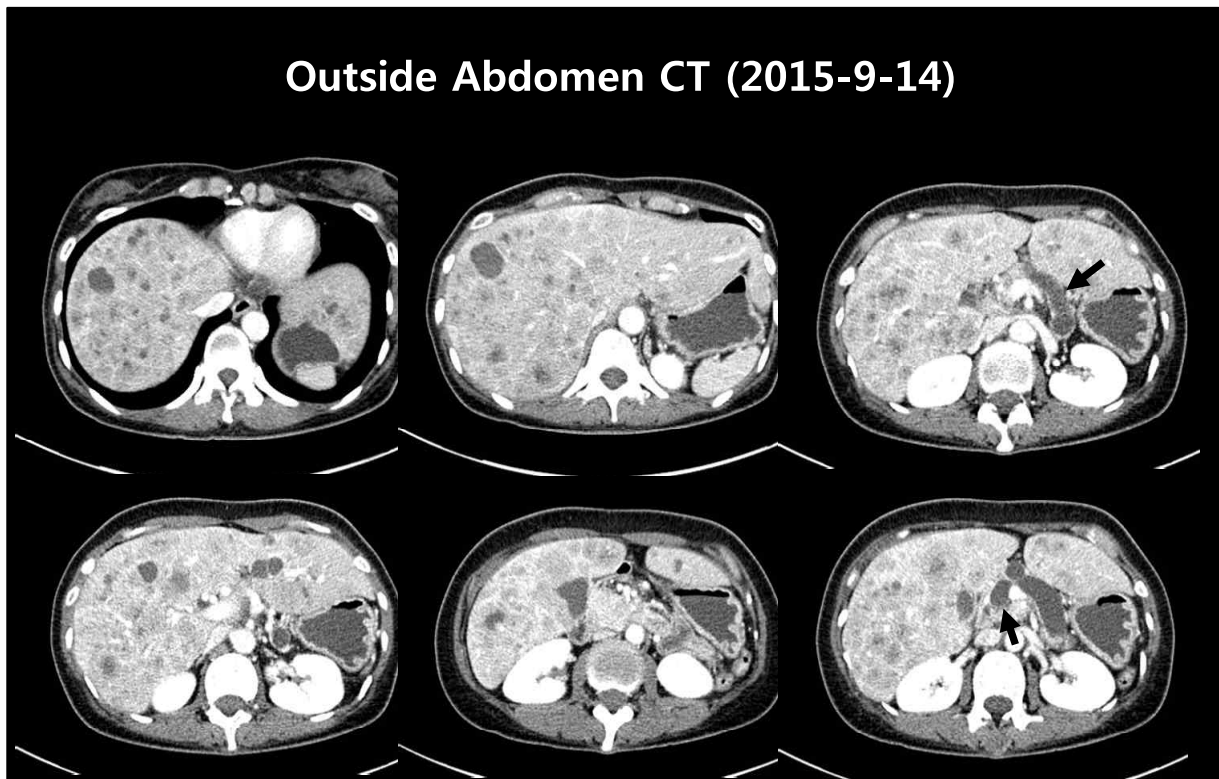
- **Associated symptom**

- Weight loss (9kg/6months)

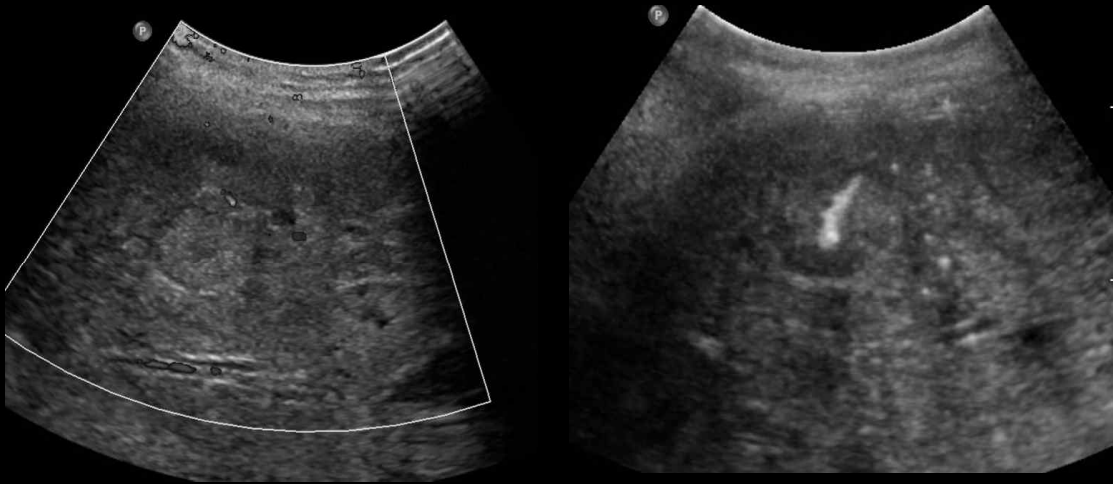
Initial Work-up

- **Laboratory findings**

| | | | |
|-----------------|-----------------|--------|----------------------|
| CBC | 5.73-12.6-305k | Ca/P | 8.7/2.8 mg/dL |
| Protein/albumin | 6.6/3.6 g/dL | BUN | 9 mg/dL |
| Total bil | 0.5 mg/dL | Cr | 0.6 mg/dL |
| ALP | 104 IU/L | AFP | 16.8 ng/mL |
| AST/ALT | 27/28 IU/L | CEA | 9.7 ng/mL |
| GGT | 128 IU/L | CA19-9 | 45.7 U/mL |



Liver Biopsy (2015-9-16)



Diagnosis: **Neuroendocrine tumor, grade 2**
CD56(+), Chromogranin(+), Synaptophysin(+), **Ki-67 3%**

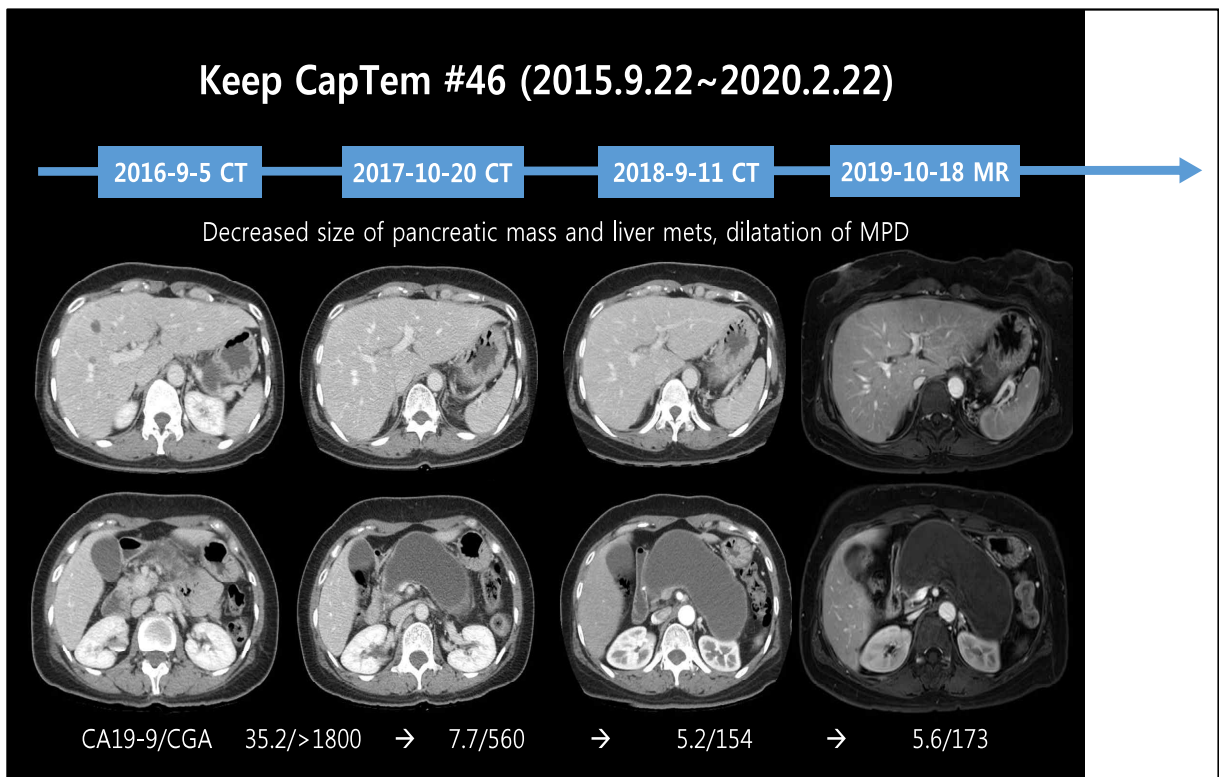
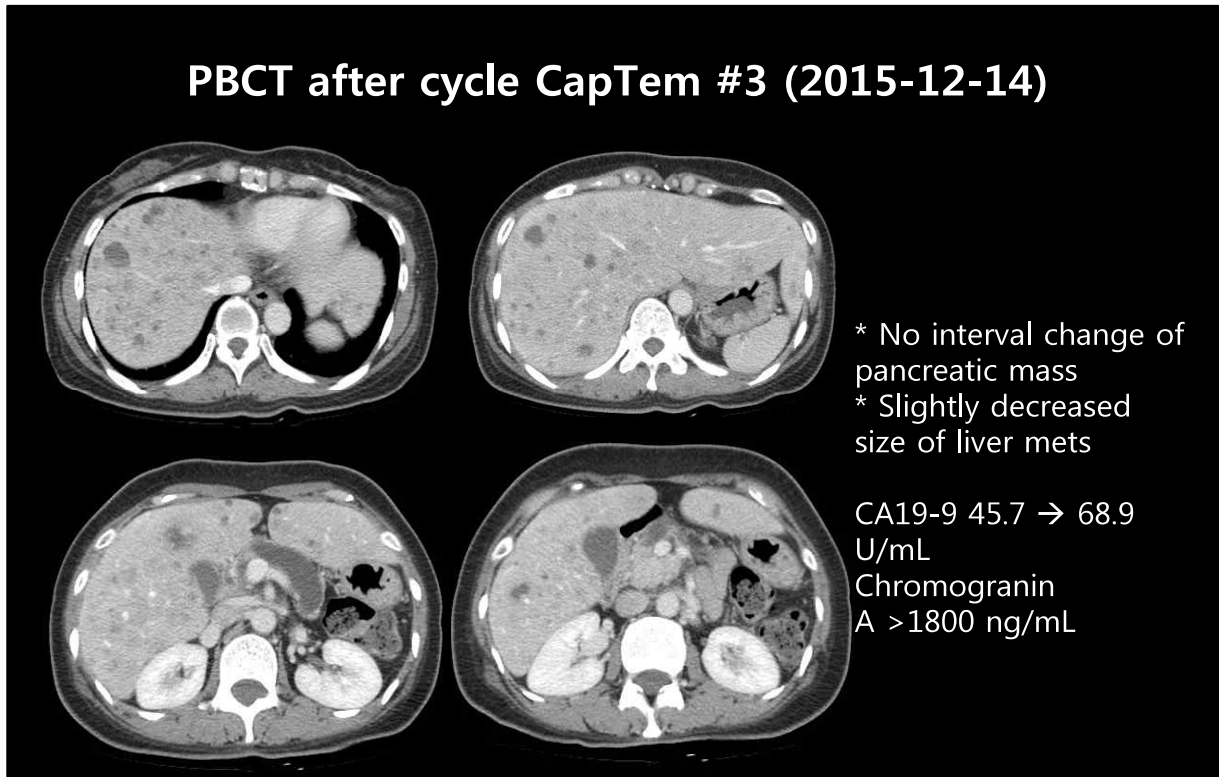
Case (F/42)

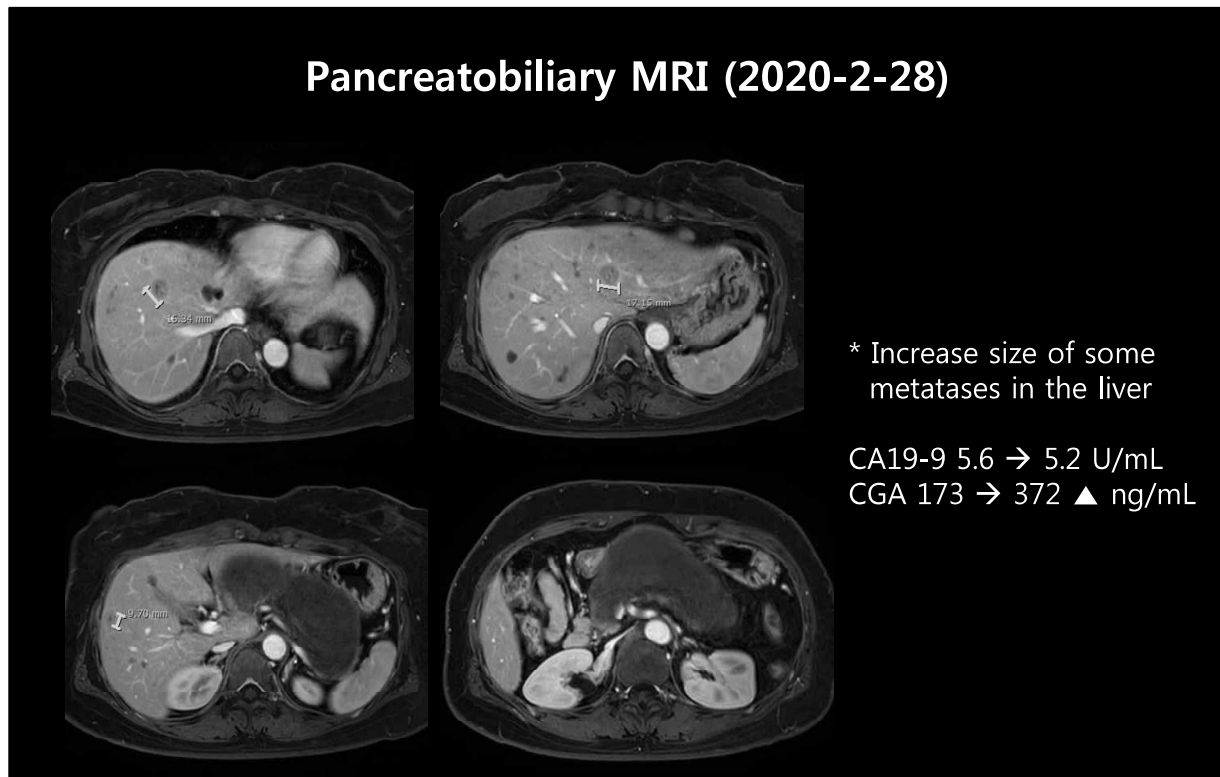
• Assessment>

- PNET, Gr2

• Plan>

- Capicitabine (1000 mg bid, D1-14)
+ temozolomide (300 mg qd, D10-14) #1 (2015.9.22~)





Case (F/42)

- Assessment>
 - PNET, Gr2
 - Disease progression after captem #46 (2015.9.22~2020.2)

- Plan>
 - Stop captem, Liver bx (2020-3-6)

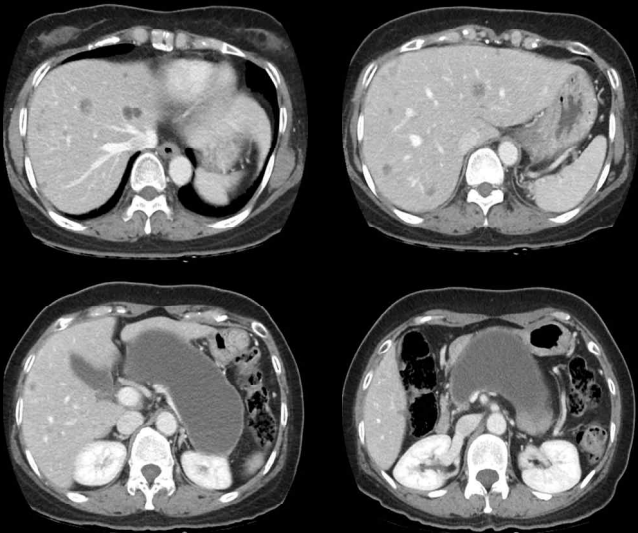
Diagnosis: Neuroendocrine tumor
- Mitotic count: 5/10HPF, Ki-67 19.6%



Afinitor (everolimus 10 mg daily)

Pancreatobiliary CT (2020-5-7)

After everolimus (2020.3.19 ~ 5.14, 8W)



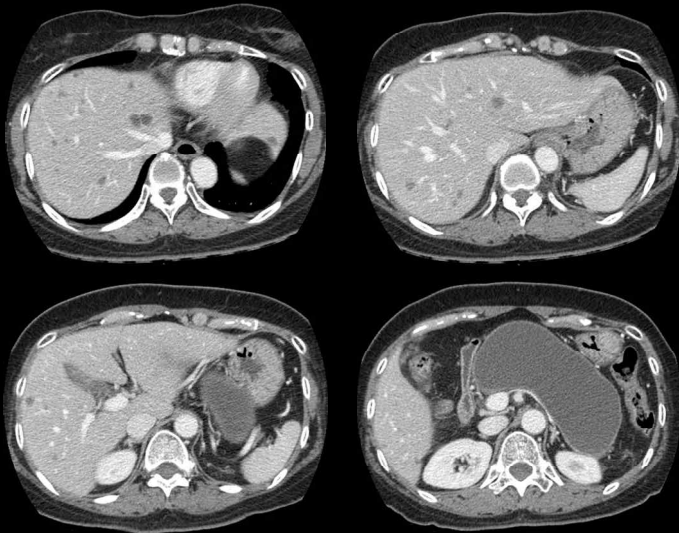
* Increase size of metastases in the liver

PD

Change to Sunitinib (37.5mg daily)

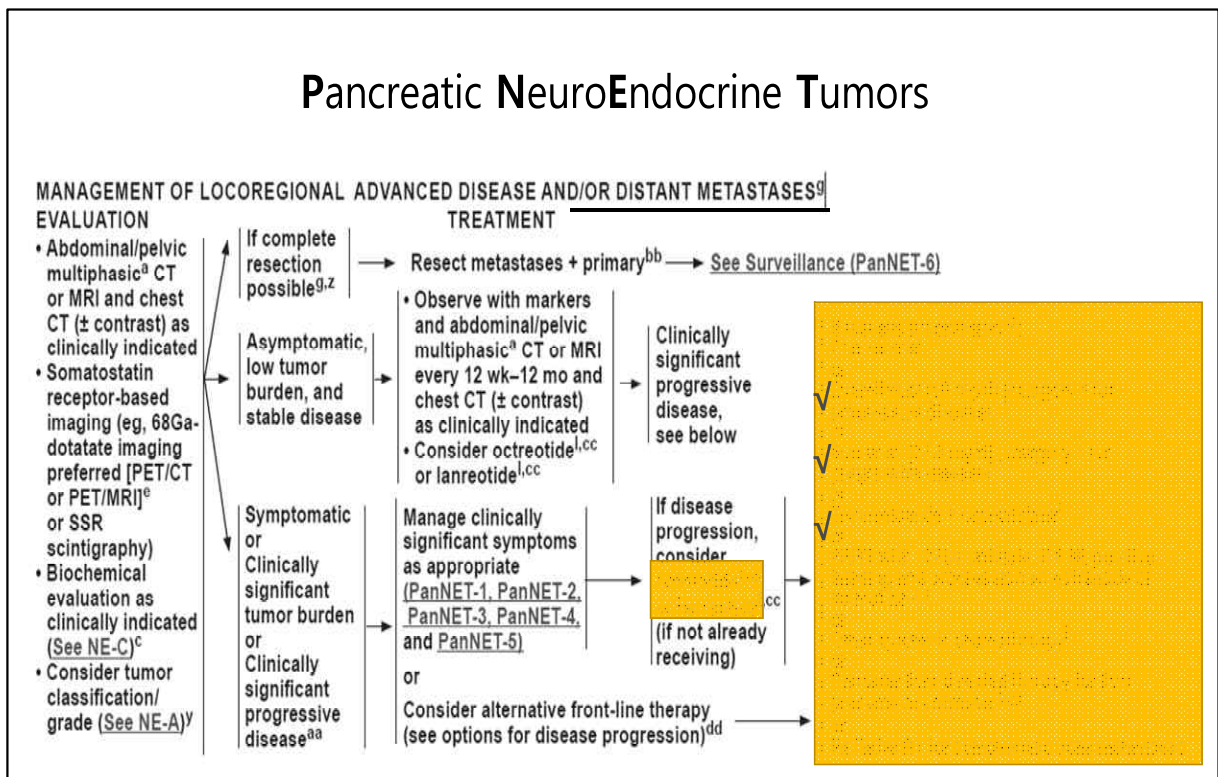
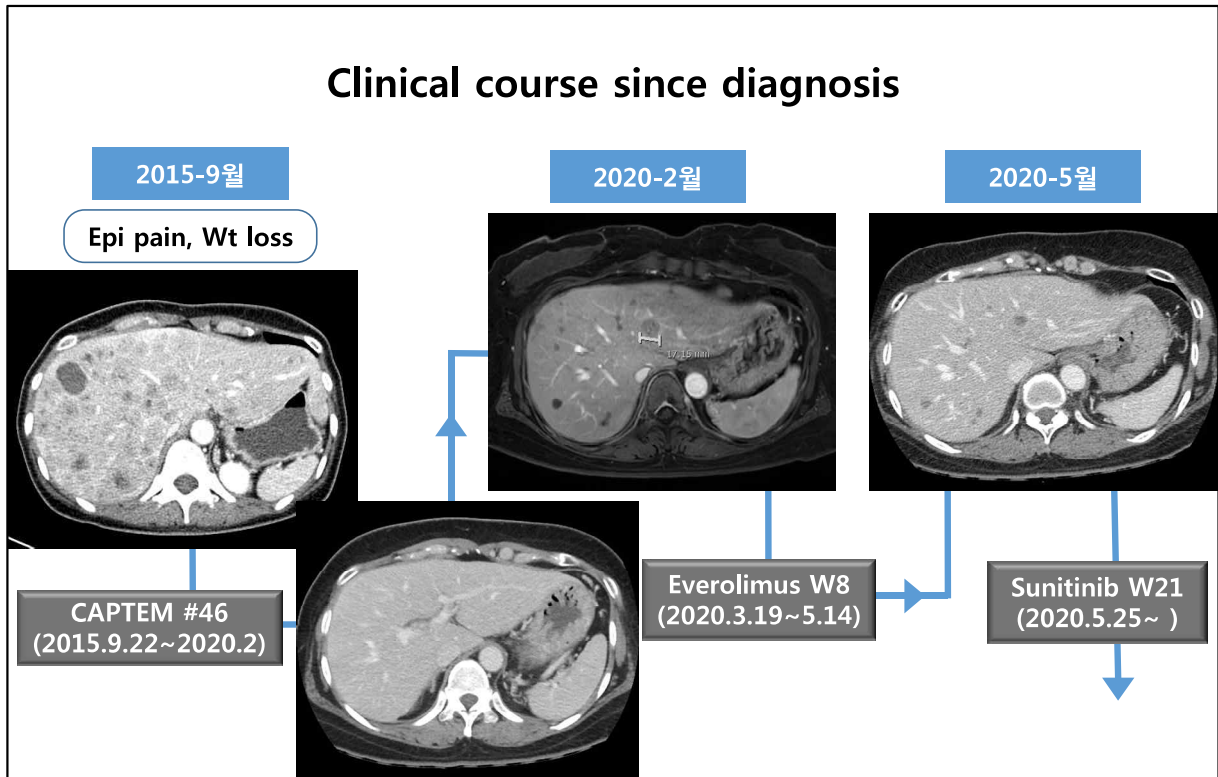
Pancreatobiliary CT (2020-10-6)

After Sunitinib W21 (2020.5.25 ~)



* Stable disease

Sunitinib (37.5 mg daily)
→ Reduce to 25 mg
d/t low PLT since W11
→ Continue treatment



Pancreatic NeuroEndocrine Tumors

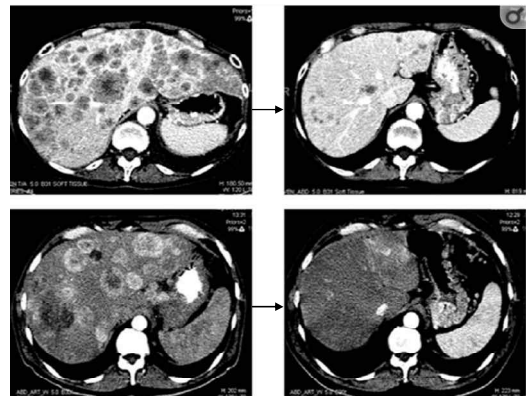
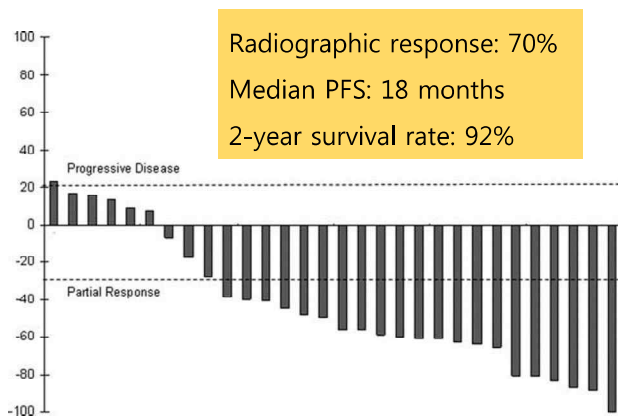
PRINCIPLES OF SYSTEMIC ANTI-TUMOR THERAPY Locoregionally Advanced and/or Metastatic Pancreatic Neuroendocrine Tumors

- Systemic therapy may not be appropriate for every patient with locoregionally advanced or metastatic disease. Consider multidisciplinary discussion to determine the best choice of treatment, including: observation for patients with stable disease with mild tumor burden, hepatic regional therapy for patients with liver-predominant metastases, cytoreductive surgery, or systemic therapy.
- Currently, there are no data to support a specific sequence of regional versus systemic therapy and no data to guide sequencing of the following systemic therapy options.
- There is no known role for systemic treatment in the adjuvant setting for PanNETs.
- Doses and schedules are subject to appropriate modifications depending on the circumstances.
- For management of hormone-related symptoms and complications with octreotide or lanreotide, see [PanNET-1](#) through [PanNET-5](#).

| Pancreatic Neuroendocrine Tumors | | | |
|---|--|--|--|
| | Preferred Regimens | Other Recommended Regimens | Useful in Certain Circumstances |
| Locoregionally Advanced Disease and/or Distant Metastases | <ul style="list-style-type: none"> Everolimus¹² (category 1 for progressive disease) 10 mg by mouth, daily Octreotide^{a,b} LAR or lanreotide^{a,4} (if SSR-positive imaging) Sunitinib¹³ (category 1 for progressive disease) 37.5 mg by mouth, daily Temozolomide + capecitabine¹⁴ (preferred when tumor response is needed for symptoms or debulking) PRRT with ¹⁷⁷Lu-dotatate (if SSR-positive imaging and progression on octreotide or lanreotide)^e | <ul style="list-style-type: none"> Cytotoxic chemotherapy options considered in patients with bulky, symptomatic, and/or progressive disease include: <ul style="list-style-type: none"> 5-FU + doxorubicin + streptozocin (FAS)¹⁵ Streptozocin + doxorubicin¹⁶ Streptozocin + 5-FU¹⁷ FOLFOX (leucovorin + 5-FU + oxaliplatin)¹⁸ CAPEOX (capecitabine + oxaliplatin)¹⁹ | <ul style="list-style-type: none"> None |

Capecitabine and Temozolomide in PNET

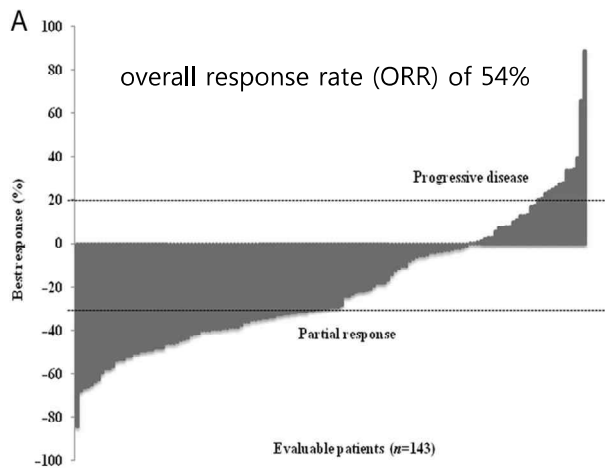
- 30 chemo-naïve patients with metastatic, well, or moderately differentiated pancreatic endocrine carcinomas
- Capecitabine (750 mg/m² twice daily, days 1–14) and temozolomide (200 mg/m² once daily, days 10–14) every 28 days



Cancer. 2011 Jan 15; 117(2): 268–275

Capecitabine and Temozolomide in PNET

- 143 patients with advanced pNET (G1 55%, G2 26%, G3 13%)
- 117/143 (82%) treatment naïve or only one prior line of systemic therapy



Median PFS: 17 months
 Median OS: 73.2 months
 2-year survival rate: 58.6%
 Median DoR: 19months

- Potential response predictors
 → no biomarker-driven selection criteria:
 MGMT (O6-methylguanine DNA methyltransferase) expression, tumor proliferation, ALT (alternative lengthening of telomeres) status

Endocr Relat Cancer. 2016 Sep;23(9):759-67

MEMO

MEMO