

# A Case of Metastatic Recurrent Pancreatic Cancer with Sustained Response to 2<sup>nd</sup> Line Chemotherapy Combined with GV1001

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## 1. Case presentation

77세 여환이 폐 결절 증가를 주소로 내원하였다. 환자는 국소 진행성 췌장암 진단되어 2012년 6월부터 8월까지 5-FU 항암화학방사선요법, 2012년 9월부터 2013년 9월까지 13주기의 gemcitabine/cisplatin 병합요법 시행 후, 2013년 11월 유문보존췌십이지장절제술 시행 받았다. 2013년 12월부터 2015년 2월까지 adjuvant aim으로 14주기의 gemcitabine 단독요법 지속하던 중 폐결절 확인되었으며, 재발성 췌장암, 폐 전이로 진단되어 2015년 3월부터 2016년 11월까지 palliative aim의 capecitabine 단독요법을 시행 받았다. 이후 PET-CT에서 폐결절 크기증가 및 신생 결절 소견으로 질병 진행이 확인되었다. 내원시 문진 소견 및 신체 검진상 특이 사항 없었고, performance state는 ECOG 0으로 양호하였다. 실험실 검사는 WBC 3,930/ $\mu$ L, ANC 2,400/ $\mu$ L, Hb 11.7 g/dL, Platelet count 172,000/ $\mu$ L, AST/ALT 32/25 IU/L, Total bilirubin 0.8 mg/dL, Albumin 4.1 g/dL, BUN/Creatinine 14.6/1.06 mg/dL였다.

## 2. Diagnosis

Recurrent pancreatic cancer with lung metastasis

s/p 1<sup>st</sup> line palliative capecitabine (2015.03.03~2016.11.22)

Disease progression

## 3. Therapy and Clinical course

2차 치료로 2016년 12월부터 modified FOLFIRINOX 및 응급 GV1001 시작하였으며, 2개월마다 시행한 CT에서 stable disease로 유지되고 있다. 치료기간 중 grade 3 이상의 neutropenia 발생하여 mFOLFIRINOX의 용량 및 투약 간격 조절하였고, GV 1001의 투약용량은 그대로 유지하였다. 이 외 grade 3 이상의 adverse event 발생 없이 치료에 tolerable하였다. 2017년 11월까지, 총 17주기의 GV 1001 + mFOLFIRINOX 투약을 진행하였고, 약 11개월간 질병 진행 없이 추적 관찰 중이다.

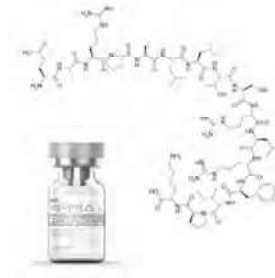
#### 4. Conclusion

폐전이 있는 재발성 췌장암의 2차 치료로 GV1001 + modified FOLFIRINOX 투약에 치료반응이 좋은 증례가 있어 보고하는 바이다.

**Key Words:** Pancreatic cancer, Recurrent, GV1001, Modified FOLFIRINOX

## GV1001

- **A peptide fragment (16 amino acids) derived from hTERT**
- hTERT (Human Telomerase Enzyme)
  - Highly expressed in cancer cell (80-90%)
- Confirmation of GV1001 safety and efficacy in previous clinical trials over 1,600 patients
- Mechanism of action
  - Induces both cytotoxic T-cell and helper T-cell immune responses.
  - GV1001 -specific T-cells to kill cancer cells.



## Case

- **F/78**

- **Chief complaint**

Increased size and number of lung nodules

- **Present illness**

2012년 타병원 건강검진에서 uncinat process의 종괴 발견 후 국소 진행성 췌장암 진단되어 CCRT 및 chemotherapy 후 절제 가능 상태로 PPPD를 시행 받은 환자로, adjuvant chemotherapy 중 다발성 폐 전이로 재발 확인되어 1차 약제로 capecitabine 치료를 하였고, 이후 반응 평가상 폐결절의 크기와 수 증가로 질병 진행 확인되어 치료 계획 수립 위해 본원 내원하였다.

## Case

- **Past medical history**  
Hypertension, DM
- **Social history**  
Smoking: nonsmoker  
Alcohol: nondrinker
- **Review of systems**  
Generalized Weakness (-) Anorexia (-)  
Fever (-) Chill (-)  
Nausea (-) Vomiting (-)

## Case

- **Physical examination**
  - Soft and flat abdomen
  - Abdomen direct tenderness / rebound tenderness (-/-)
- **Vital sign**  
BP : 132/74 mmHg, HR : 65/min, RR : 20/min, BT : 37.1°C
- **Performance status: ECOG 0**

## Case

### • Laboratory study

- WBC 3,930/ $\mu$ L (ANC 2,400/ $\mu$ L)
- Hb 11.7 g/dL
- Platelet count 172,000/ $\mu$ L
- AST/ALT 32/25 IU/L
- Total bilirubin 0.8 mg/dL
- Albumin 4.1 g/dL
- BUN/Creatinine 14.6/1.06 mg/dL
- CA 19-9 1.1 U/mL (Lewis a/b : negative/negative)

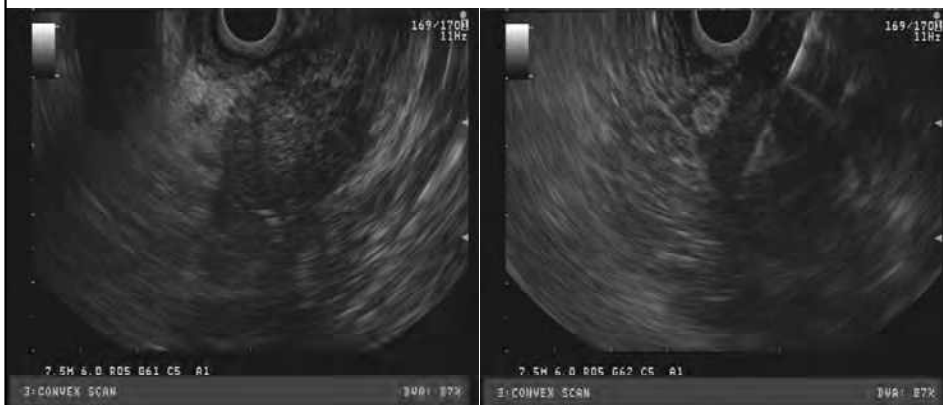
### Progress from diagnosis Abdomen U/S (2012-06-09)



Progress from diagnosis  
**Pancreas CT (2012-06-09)**



Progress from diagnosis  
**EUS-FNA (2012-06-15)**



- **Cytology report**
  - Atypical cell clusters with foamy cytoplasm
  - Consistent with ductal adenocarcinoma

## Progress from diagnosis

- **Initial diagnosis**

Pancreatic cancer, locally advanced (SMV, SMA encasement)

cT4N0M0, Stage III

- **Treatment**

Neoadjuvant CCRT with 5-FU (5,400 cGy, 27fx) (2012.6.27~8.2)

→ Response : SD

Palliative gemcitabine + cisplatin #13 (2012.9.13~2013.9.24)

→ Response : PR

## Progress from diagnosis Pancreas CT (2013-10-30)



**Progress from diagnosis  
PPPD (2013-11-01)**



Status post concurrent chemoradiation therapy with rare residual cancer cells (less than 1%)

**Residual adenocarcinoma, moderately differentiated**

- Size : 500 um
- Tumor extent : Limited to the pancreas
- Lymphovascular invasion / Perineural invasion (-/-)
- Resection margins : Free of carcinoma
- Lymph nodes : total (0/7): Free of carcinoma

**Progress from diagnosis**

• **Diagnosis**

Pancreatic cancer, locally advanced → resectable

s/p CCRT with 5-FU (2012.6.27~8.2)

s/p Gemcitabine + cisplatin #13 (2012.9.13~2013.9.24)

s/p PPPD (2013.11.1)

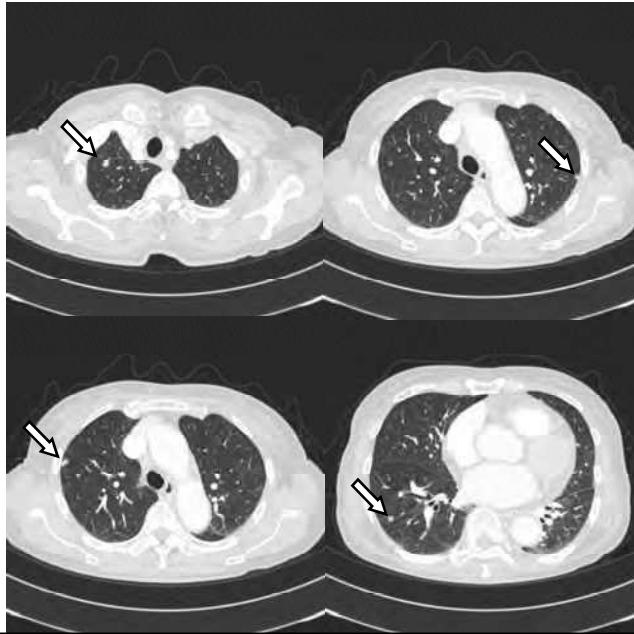
→ **Pancreatic cancer, ypT1N0M0, Stage IA**

• **Next treatment**

Adjuvant gemcitabine #14 (2013.12.3~2015.2.10)



Progress from diagnosis  
**Chest CT (2015-02-12) after #14 Gem**



**Progress from diagnosis**

• **Diagnosis**

Pancreatic cancer, locally advanced → resectable

s/p CCRT with 5-FU (2012.6.27~8.2)

s/p Gemcitabine + cisplatin #13 (2012.9.13~2013.9.24)

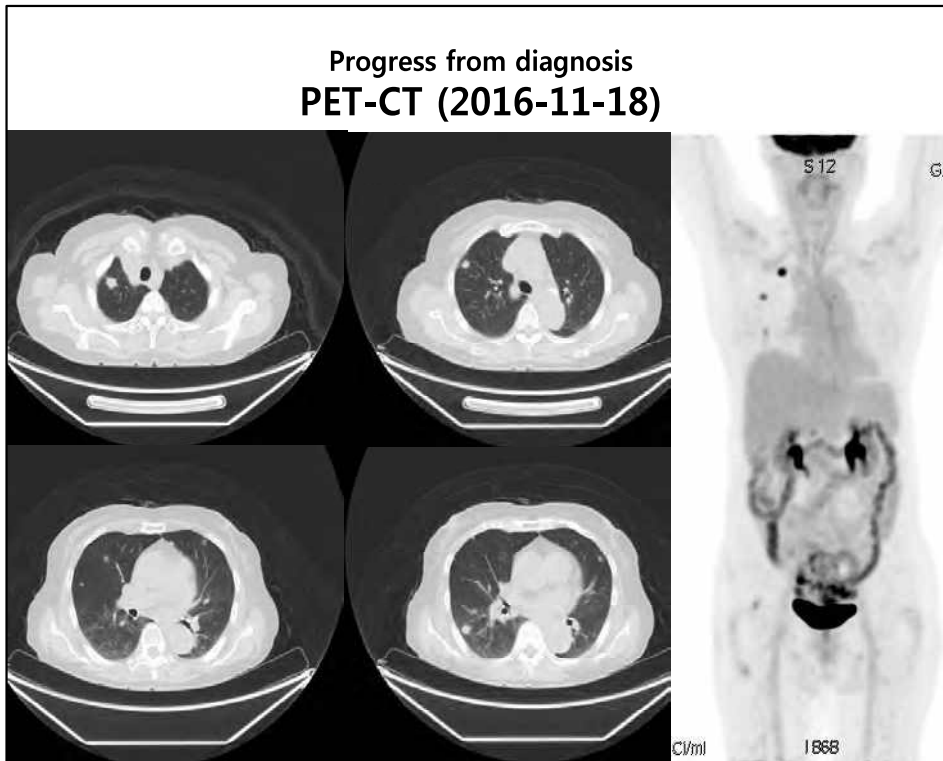
s/p PPPD (2013.11.1) (y/pT1/pN0)

s/p Gemcitabine #14 (2013.12.3~2015.2.10)

→ **Recurrent pancreatic cancer, far advanced (lung metastasis)**

• **Next treatment**

1<sup>st</sup> line palliative capecitabine (2015.03.03~2016.11.22)



### Progress from diagnosis

- **Diagnosis**

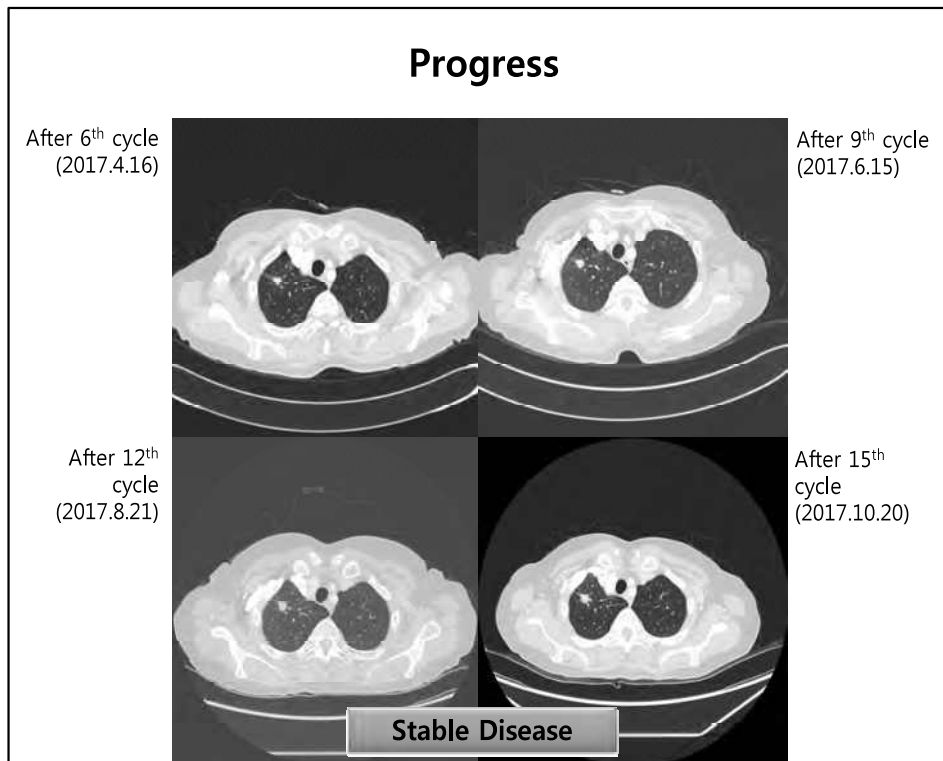
- # Pancreatic cancer, locally advanced → resectable
  - s/p CCRT with 5-FU (2012.6.27~8.2)
  - s/p Gemcitabine + cisplatin #13 (2012.9.13~2013.9.24)
  - s/p PPPD (2013.11.1) (y/pT1/pN0)
  - s/p Gemcitabine #14 (2013.12.3~2015.2.10)

- # Recurrent pancreatic cancer, far advanced (lung metastasis)
  - s/p 1<sup>st</sup> line palliative capecitabine (2015.03.03~2016.11.22)

- **Disease progression**

- **Next treatment**

- 2<sup>nd</sup> line palliative modified FOLFIRINOX + GV1001



### Progress

- Dose and interval modification
  - Q3 wks after #2 d/t G4 neutropenia
  - 25% DR of all drugs from #6 d/t G3 neutropenia
  - 40% DR of 5-FU from #17 d/t G4 neutropenia
  
- No other grade 3 or 4 toxicities were reported

### Progress from diagnosis

• **Final diagnosis**

- # Pancreatic cancer, locally advanced → resectable  
 s/p CCRT with 5-FU (2012.6.27~8.2)  
 s/p Gemcitabine + cisplatin #13 (2012.9.13~2013.9.24)  
 s/p PPPD (2013.11.1) (y/pT1/pN0)  
 s/p Gemcitabine #14 (2013.12.3~2015.2.10)
- # Recurrent pancreatic cancer, far advanced (lung metastasis)  
 s/p 1<sup>st</sup> line palliative capecitabine (2015.03.03~2016.11.22)  
**s/p 2<sup>nd</sup> line palliative mFOLFIRINOX + GV1001 #17  
 (2016.12.15~2017.11.17)**

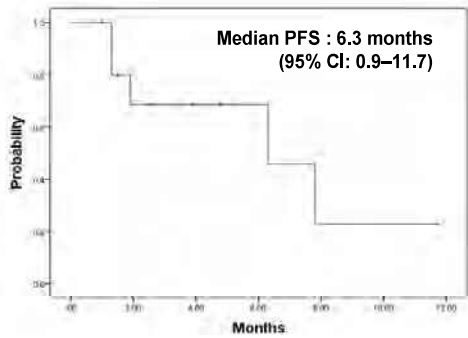
**Next response evaluation : after next chemotherapy cycle**

### 2<sup>nd</sup> line FOLFIRINOX + GV1001 in Severance Hospital

- ✓ GV1001 Enroll: 현재 55명 (ongoing 20명)
- ✓ 2<sup>nd</sup> line FOLFIRINOX + GV1001: 11명

Variables	Patients (n=11)
Age, mean (range)	60.8 (46-78)
Male	73.3%
BMI, mean (range)	21.7 (16.5-23.9)
ECOG 0~1, %	100%
CA 19-9, mean	694
Extent of disease	
Distant metastasis	86.6%
Response	
PR	1 (9.1%)
SD	7 (63.6%)
PD	3 (27.3%)

## 2<sup>nd</sup> line FOLFIRINOX + GV1001 in Severance Hospital



Previous studies focused on FOLFIRINOX as a 2nd-line therapy

Study characteristics			Patients characteristics				Treatment outcomes		
Author	Type	Dose modification	Patients	Age median (range)	ECOG (>=2%)	Cancer status (%)	ORR, %	PFS, months	OS, months
Assaf, 2011	Retro	-	27	63 (45-83)	WHO PS 1-3	MPC (100)	19	3.0	8.5
Lee, 2014	Retro	-	18	57 (44-68)	0-1	MPC (88.9) LAPC (11.1)	27.8	2.8	8.4
Kohayashi, 2017	III	Irinotecan 56% or 67%	18	63 (46-68)	0-1	MPC (100)	22.2	2.8	9.8

## Conclusion

- We experienced a case of
  - Recurrent pancreatic cancer with lung metastasis
  - which shows sustained disease control (over an year)
  - with 2<sup>nd</sup> line treatment of **modified FOLFIRINOX and GV1001**