14TH INTERNATIONAL CONGRESS

PERITONEAL SURFACE MALIGNANCIES

A phase II study of Intraperitoneal Paclitaxel combined with Gemcitabine plus Nab-Paclitaxel for Pancreatic Cancer with Peritoneal Metastasis

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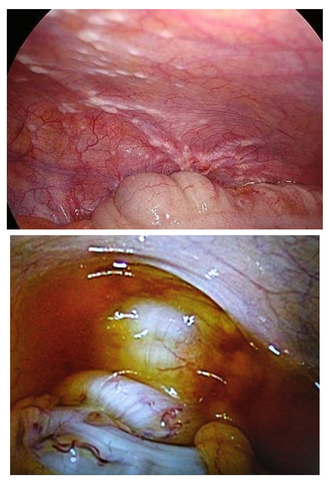
Background

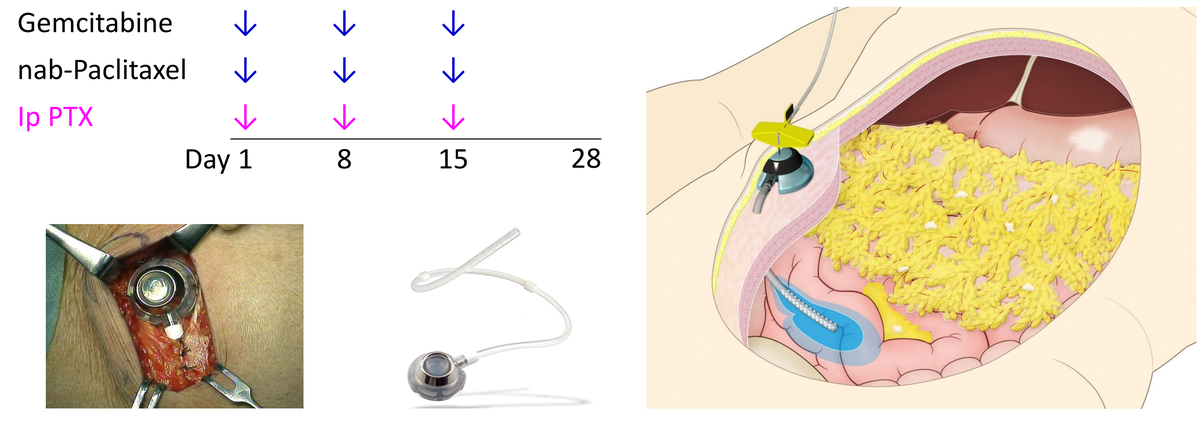
- ✓ Peritoneal metastasis is one of the most life-threatening factors in patients with pancreatic cancer, and no survival improvement has been achieved over time even with recent progress of the intensive chemotherapy. *Takahara N et al. Pancreas 2015.*
- ✓ Intraperitoneal paclitaxel (Ip PTX) combined with systemic chemotherapy has shown promising antitumor activity against peritoneal metastasis in patients with refractory pancreatic cancer. *Takahara N et al. Invest New Drugs 2016.*
- ✓ Therefore, we designed a novel regimen of Ip PTX combined with standard gemcitabine plus nab-paclitaxel (GnP) treatment in chemotherapy-naïve patients with peritoneal metastasis, and determined the recommended doses of this regimen in a phase I trial. *Takahara N et al. Invest New Drugs 2021.*

Study design

★ A multicenter, single-arm, phase II trial between 2019-2022



- ✓ **Primary endpoint:** Overall survival (OS)
- ✓ **Secondary endpoints**
  - Progression-free survival (PFS)
  - Tumor response using RECIST version 1.1
  - Efficacy against peritoneal metastasis (peritoneal cytology)
  - Safety bases on CTCAE version 4.0
- ✓ **Eligibility**
  - Pancreatic cancer with peritoneal metastases
  - No prior treatment other than curative surgery and adjuvant chemotherapy
  - Age of 20-75yrs - ECOG PS of 0-1 - Adequate bone marrow/liver/renal function
- ✓ **Treatment**
  - Ip PTX (30mg/m^2) combined with standard GnP was given on days 1, 8, 15
  - Repeated every 4 weeks until disease progression, unacceptable toxicity, etc.
  - Peritoneal access port allows Ip PTX administration at outpatient clinic repeatedly



- ✓ **Statistics**
  - GnP demonstrated OS of 7.6 months in patients with peritoneal metastasis *Tabernero J, et al. The Oncologist 2015.*
  - Assuming a **null hypothesis (GnP) of 7.0 months** and an **alternative hypothesis (Ip PTX plus GnP) of 12.0 months** with a two-sided type I error of 0.10 and a power of 0.8, a total of **35** fully assessable patients was necessary to enroll.
  - If the lower limit of the 80% confidence interval (CI) for median OS exceeds 7 months , Ip PTX plus GnP can be considered worthy of further investigation in a phase III trial.

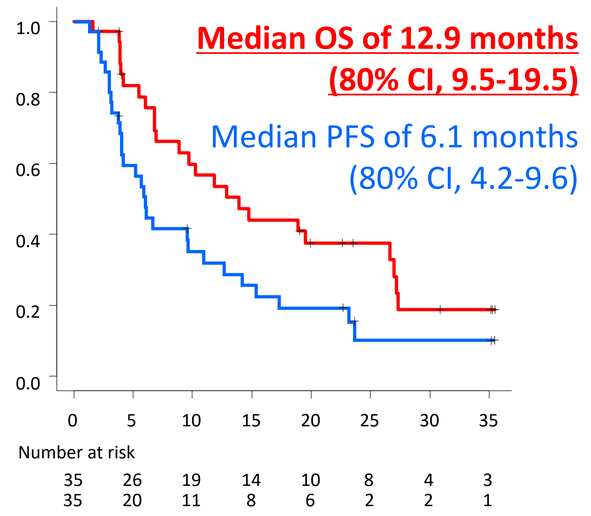
Results

Patient characteristics

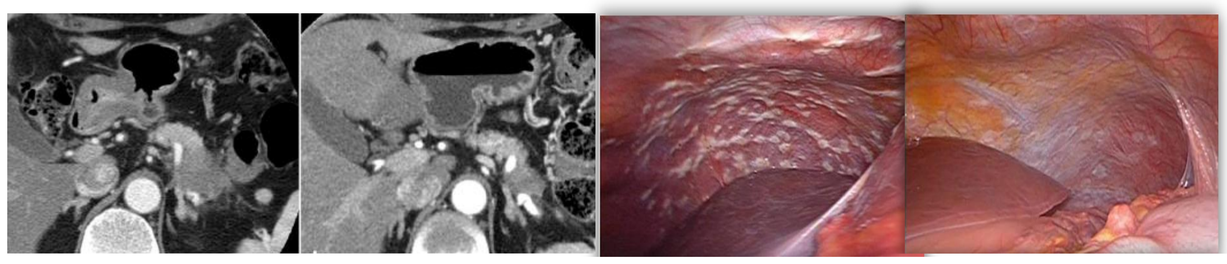
	n = 35
Age, median (range), years	60 (43 - 75)
Sex, male, n (%)	23 (66%)
PS, 0/1, n (%)	19 (54%) / 16 (46%)
Primary tumor location, Head / Body - Tail, n (%)	16 (46%) / 19 (54%)
Metastasis, Liver / Lymph node / Lung, n (%)	12 (34%) / 9 (26%) / 3 (9%)
Metastatic / Recurrence, n (%)	32 (91%) /3 (9%)
CEA, median (range), ng/mL	3.4 (0.6 - 1,452)
CA19-9, median (raneg), IU/mL	495 (11 - 100,029)
Ascites, Small / Moderate - Massive, n (%)	15 (43%) / 4 (11%)
Peritoneal cancer index, median (range)	8 (1 - 33)

Efficacy

Tumor response		
Response rate	26%	
Disease control rate	91%	
Best response		
Complete response	0	
Partial response	9	(26%)
Stable disease	23	(66%)
Progressive disease	3	(9%)
Response in peritoneal cytology	12	(34%)



- ✓ **3 patients (9%) underwent curative surgery** after remarkable response with this chemotherapy, resulting in R0 in 2 patients and R1 in 1 patient.
- ✓ CT and laparoscopic findings in a case who underwent curative surgery



Adverse events

	All grades	Grade 3/4
Hematological		
Leukocytopenia	18 (51%)	9 (26%)
Neutropenia	26 (74%)	16 (46%)
Anemia	14 (40%)	7 (20%)
Thrombocytopenia	13 (37%)	1 (3%)
Febrile neutropenia	5 (14%)	4 (11%)

	All grades	Grade 3/4
Non-hematological		
Ip port infection	4 (11%)	3 (9%)
Ip port obstruction	3 (9%)	2 (6%)
Peripheral neuropathy	30 (86%)	7 (20%)
Upper GI obstruction	4 (11%)	4 (11%)
Colonic obstruction	2 (6%)	2 (6%)
Appendicitis	2 (6%)	2 (6%)
Pneumonia	3 (9%)	2 (6%)
Alopecia	35 (100%)	0%

- ✓ AEs were evaluated in all patients through 251 cycles, with a median 5 (1-24) cycles per patient
- ✓ No treatment-related deaths were observed.

Conclusions

Intraperitoneal paclitaxel combined with gemcitabine plus nab-paclitaxel was safe and effective for pancreatic cancer with peritoneal metastasis. Further studies are warranted.

If you have any questions, please contact me !!
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