Background

- ✓ **S-1 is an active agent for the treatment of pancreatic cancer (PC). GEST study has previously shown the noninferiority of S-1 to gemcitabine in advanced PC.**
- ✓ **The standard regimen of 4 weeks of administration followed by 2 weeks of rest frequently causes adverse effects.**
- ✓ **To induce the effect of S-1 while reducing toxicity, alternate-day administration may be a treatment option.**

Study aim

To clarify the efficacy and toxicity of alternate-day administration of S-1 compared to the standard regimen for advanced PC.

1. **Primary endpoint: Overall Survival (OS)**
2. **Secondary endpoints: Progression-free Survival (PFS), Time to Treatment Failure (TTF), Response rate (RR), Adverse Events (AEs), Quality of Life (EQ-5D, EORTC-QLQ-C30)**

Key eligibility criteria

1. **Pathologically confirmed unresectable PC**
2. **Aged between 20 and 79 years**
3. **PS 0 or 1 (ECOG)**
4. **No prior chemotherapy/radiotherapy**

Statistics

180 patients required

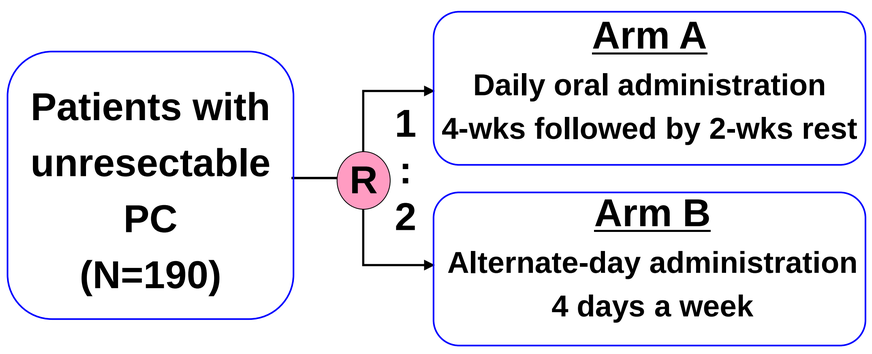
- **Alpha error: 0.05, Power: 80%**
- **Non-inferiority threshold HR: 1.33**

Non-inferiority was considered to be shown if Bayesian posterior probability of HR < 1.15 was at least 90% with non-informative prior

- **95% credible interval was also calculated for HR**

Study design

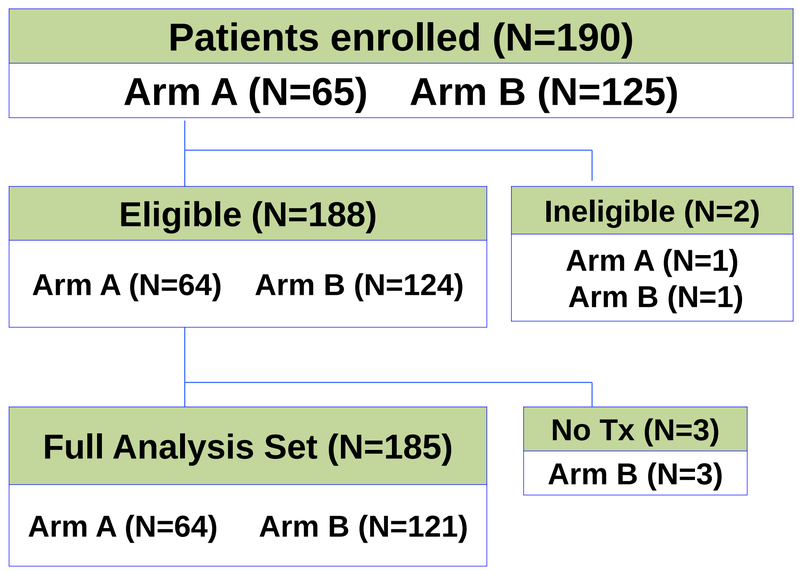
Non-inferiority



Stratification factors

1. **Institution**
2. **Locally advanced (LAPC) or Metastatic (MPC)**

CONSORT diagram

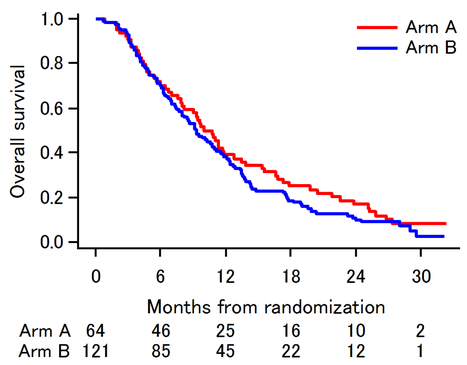


- **From 31 institutions**
- **Enrollment period:**
  Aug 2012 – Aug 2013
- **Median follow-up time: 9.5 months**
- **Number of death events: 169**

Patient characteristics

	Arm A (N=64)	Arm B (N=121)	*P* value
Age: Median (range)	68 (46-78)	66 (40-79)	0.275
Gender: M/F	35/29	72/49	0.528
BMI	20.8	21.2	0.797
LAPC/MPC	15/49	28/93	0.964
PS: 0/1	43/21	77/44	0.630

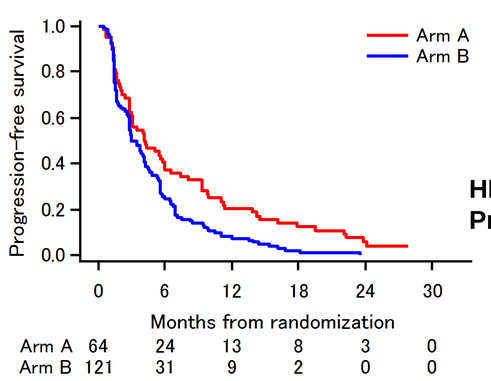
Survival analysis



Median OS

- **Standard (A) 10.4 M**
- **Alternate (B) 9.4 M**

HR=1.19 (95%CI: 0.86-1.64)
Probability of HR < 1.15: 42.5%



Median PFS

- **Standard (A) 4.2 M**
- **Alternate (B) 3.0 M**

HR=1.65 (95%CI: 1.20-2.29)
Probability of HR < 1.15: 1.4%

Median TTF
Arm A: 3.0 M (2.0-4.2)
Arm B: 3.0 M (2.4-3.8)

Response	CR	PR	SD	PD
Arm A	1(2%)	8(13%)	35(56%)	18(29%)
Arm B	0(0%)	12(10%)	64(54%)	43(36%)

Mantel trend test P=0.31

Adverse events

	Arm A (N=65)		Arm B (N=122)		P value
	Any	≧ G3	Any	≧ G3	
Anorexia	38 (59%)	7 (11%)	61 (50%)	5 (4%)	0.04
Fatigue	39 (60%)	3 (5%)	52 (43%)	2 (2%)	0.02
Pigmentation	16 (25%)	0 (0%)	9 (7%)	0 (0%)	<0.001
Pneumonitis	5 (8%)	1 (2%)	2 (2%)	0 (0%)	0.03

Conclusion

This study failed to demonstrate the noninferiority of alternate-day administration of S-1 to standard regimen as a first-line chemotherapy in unresectable pancreatic cancer.

Summary

1. **PAN-01 did not show the noninferiority of alternate-day administration to standard regimen in overall survival.**
   Median OS: 9.4 M vs 10.4 M
   (HR, 1.19; 95% CI, 0.86-1.64)
2. **PAN-01 demonstrated that alternate-day administration was significantly worse than standard regimen in tumor progression .**
   Median PFS: 3.0 M vs 4.2 M
   (HR, 1.65; 95% CI, 1.20-2.29)
3. **Anorexia, Fatigue, Pigmentation, and Pneumonitis were more common in standard regimen than alternate-day administration .**

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COI Disclosure

Shoji Nakamori

The author have no financial conflicts of interest to disclose concerning the presentation.