Comprehensive Support Project

A Randomized Phase II Study of Dose Schedule of S-1 for Metastatic/Advanced Pancreatic Cancer (PAN-01 study)

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Conflict of Interest disclosure slide for representative speakers or investigators

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profit of stock	☑	
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contributions	☑	
fees of testimony, judgment, comment, etc.	☑	
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contributions	☑	
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JSMO Japanese Society of Medical Oncology

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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 alone in advanced PC[1].
- 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.

1, UENO, et al. J Clin Oncol 2013; 31: 1640-1648.

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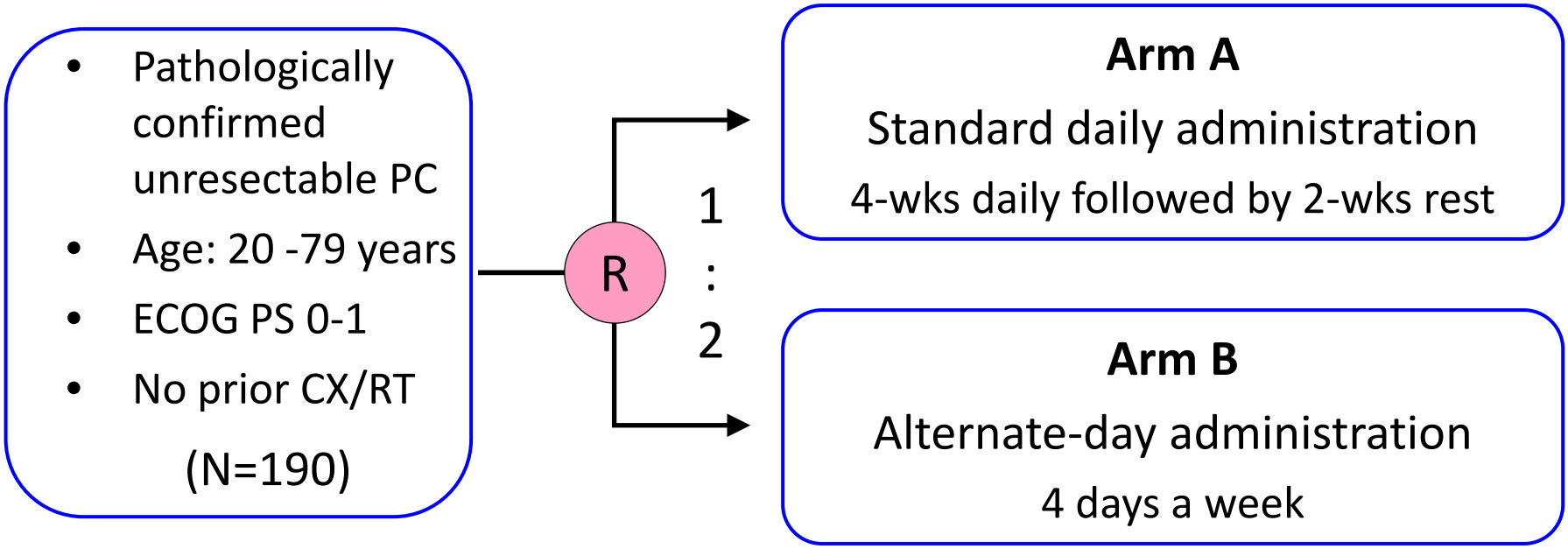
Objective

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

- Primary endpoint: Overall Survival (OS)
- 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)

Study Design



Stratification factors
- Institution
- Locally advanced (LAPC) or Metastatic (MPC)

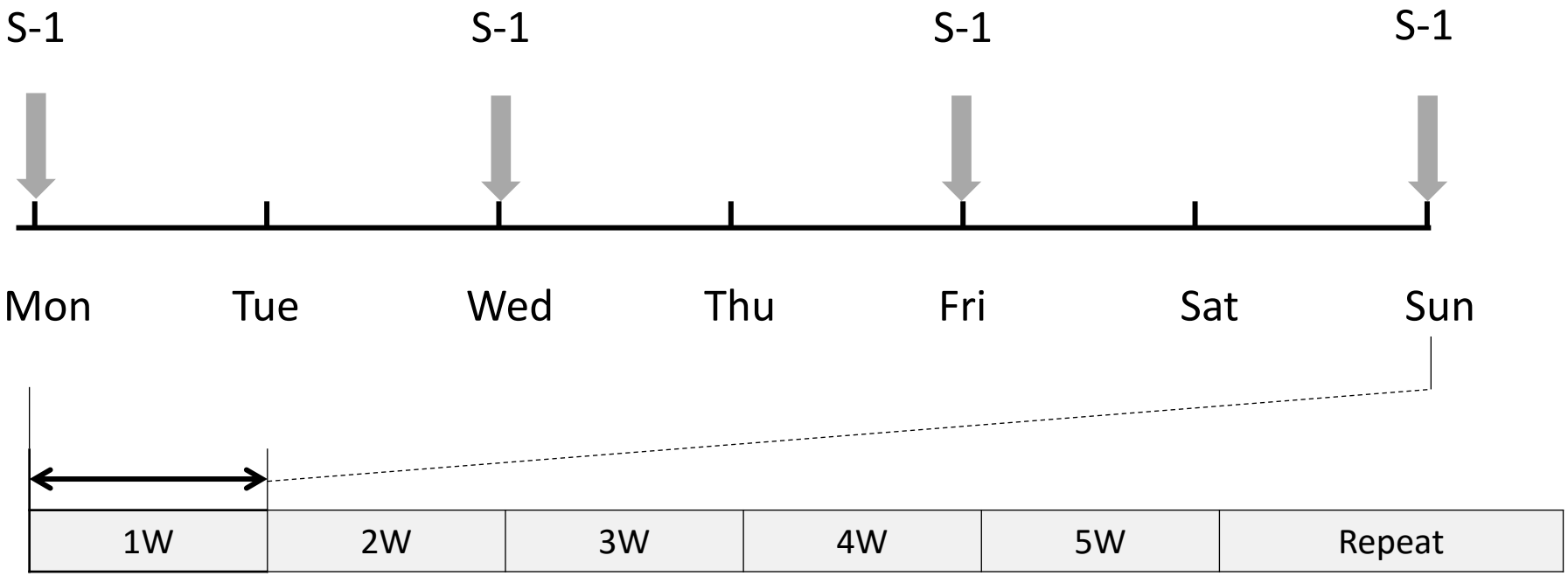
Statistics
- Non-inferiority of alternate-day S-1 to standard administration of S-1 in OS
- One-sided alpha error: 0.05, Power: 80%
- Non-inferiority threshold HR: 1.33
- 180 patients required

UMIN (http://www.umin.ac.jp) Study ID: 000008604

Treatment Schedule (Arm B)

Alternate-day administration

4 days a week



BSA	Dose of S-1
<1.25 m2	80 mg/day
1.25-1.5 m2	100 mg/day
≥ 1.5 m2	120 mg/day

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Results

- From 31 institutions
- Enrollment period: Aug 2012 - Aug 2013
- Median follow-up time: 9.5 months
- Number of enrolled patients: 190
- Number of death events: 169

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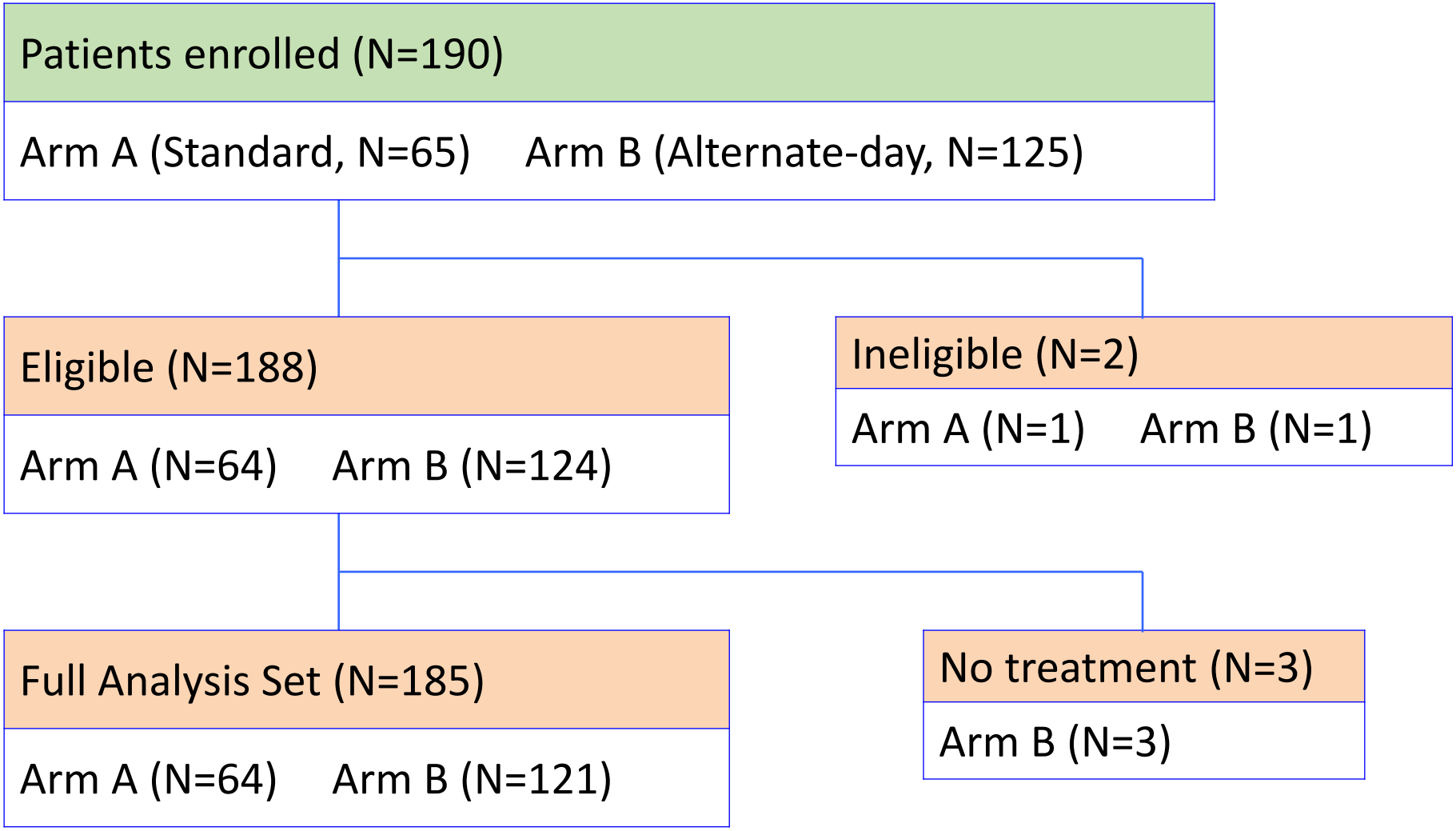
CONSORT Diagram



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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
BSA	1.52 m^2	1.52 m^2	0.921
LAPC/MPC	15/49	28/93	0.964
ECOG PS: 0/1	43/21	77/44	0.630
History of surgery: Yes/No	9/55	16/105	0.874

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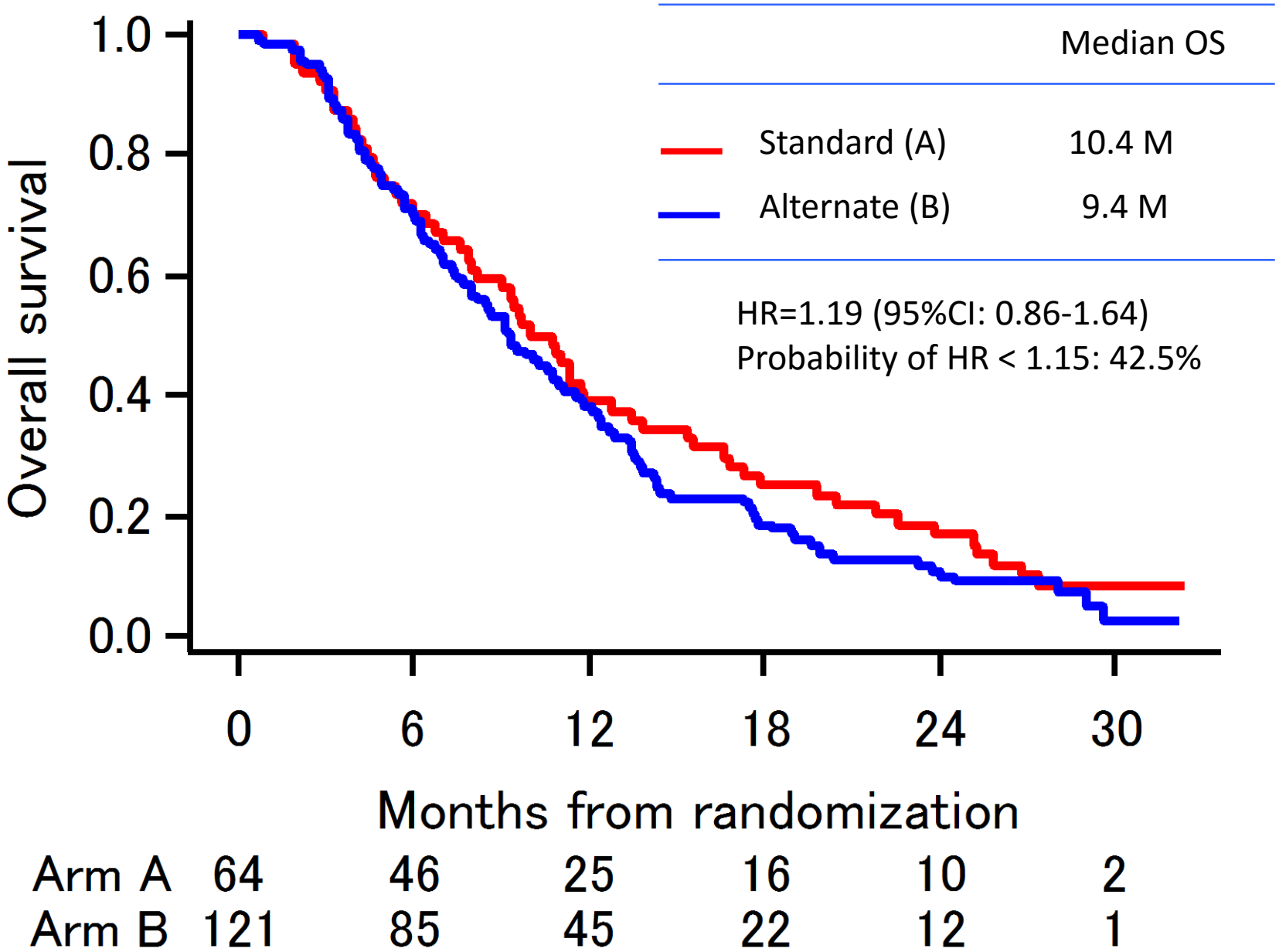
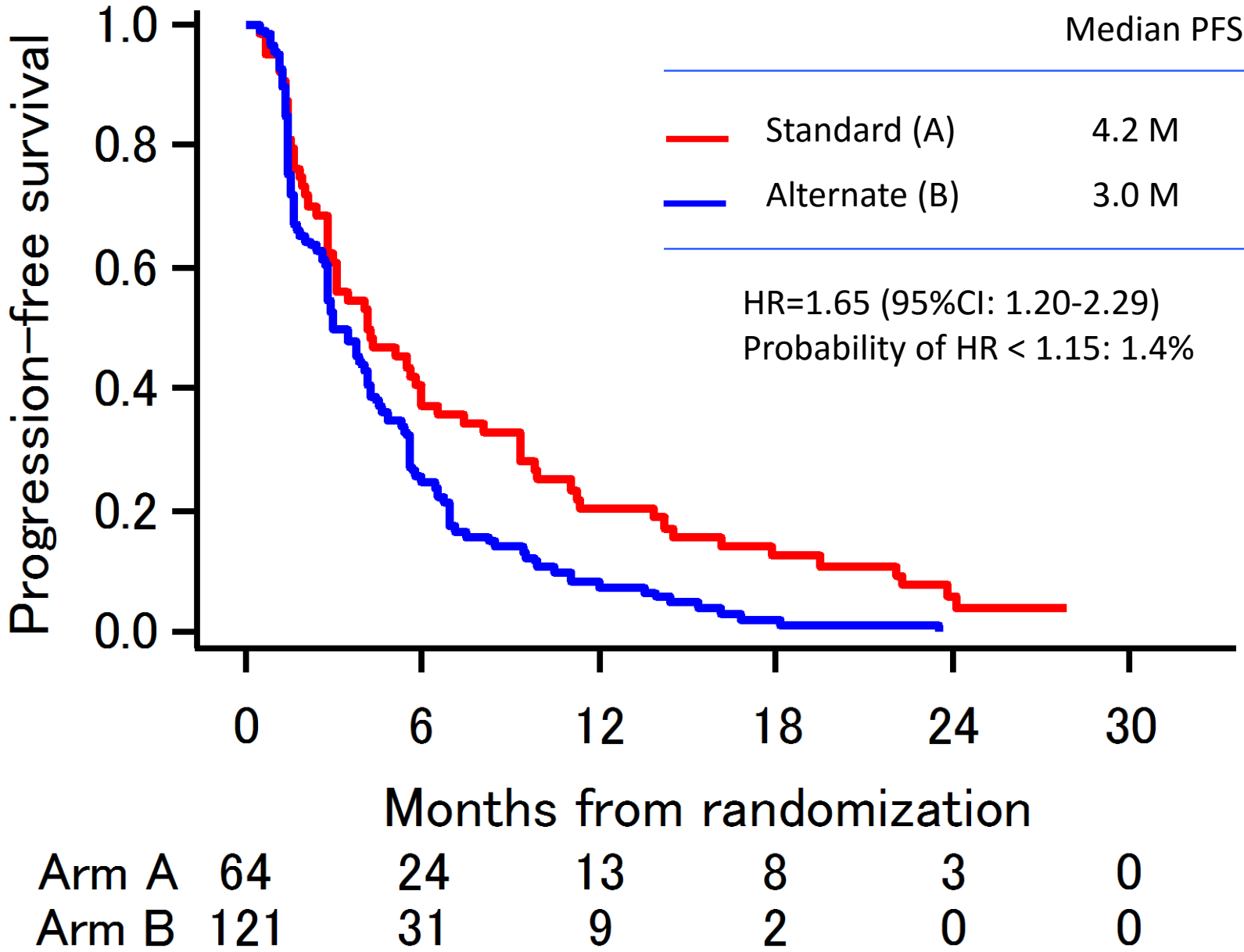
Adverse Events

	Arm A (N=65)		Arm B (N=122)		P_{trend} 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%)	-	9 (7%)	-	<0.001
Pneumonitis	5 (8%)	1 (2%)	2 (2%)	0 (0%)	0.03
Neutropenia	23 (35%)	5 (8%)	28 (23%)	3 (3%)	0.02

Overall Survival



Progression-free Survival



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Objective Response Rate

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

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Summary

- 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).
- 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).
- Anorexia, Fatigue, Pigmentation, and Pneumonitis were more common in standard regimen than alternate-day administration.

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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.

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