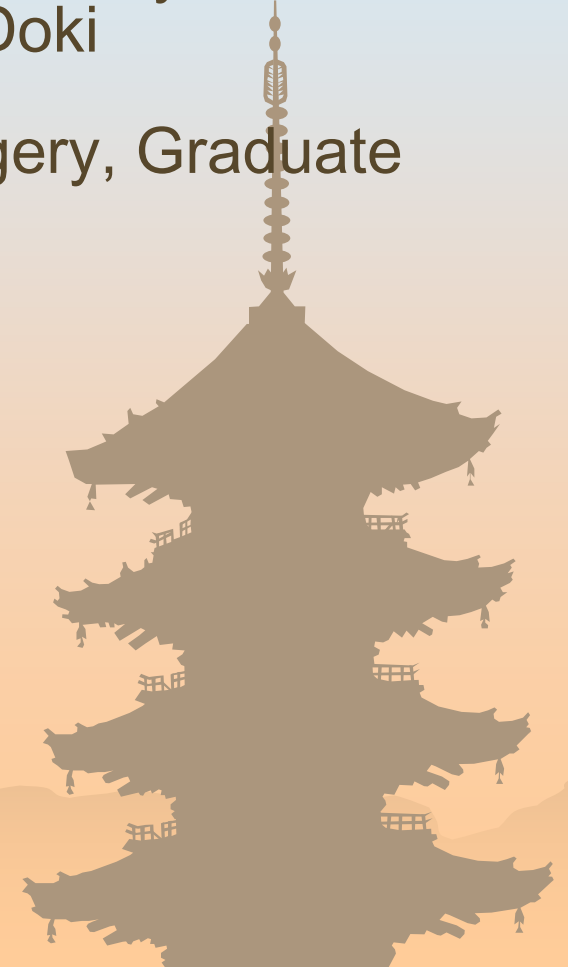


Neoadjuvant intra-peritoneal and systemic chemotherapy for gastric cancer with peritoneal dissemination

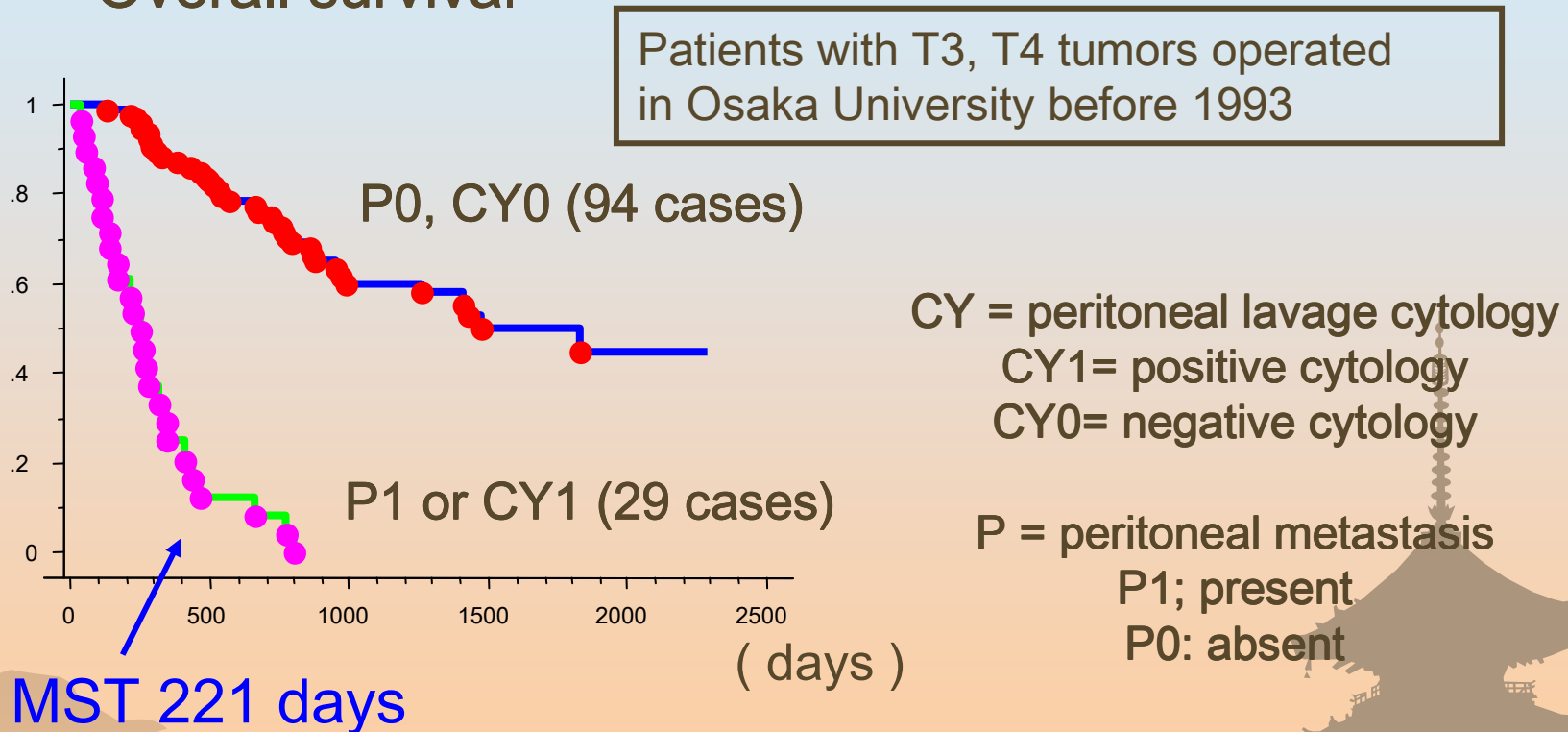
Y. Fujiwara, S. Takiguchi, K. Nakajima, H. Miyata, M. Yamasaki, T. Nishida, M. Mori, and Y. Doki

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Prognosis of GC with peritoneal dissemination at surgery

Overall survival



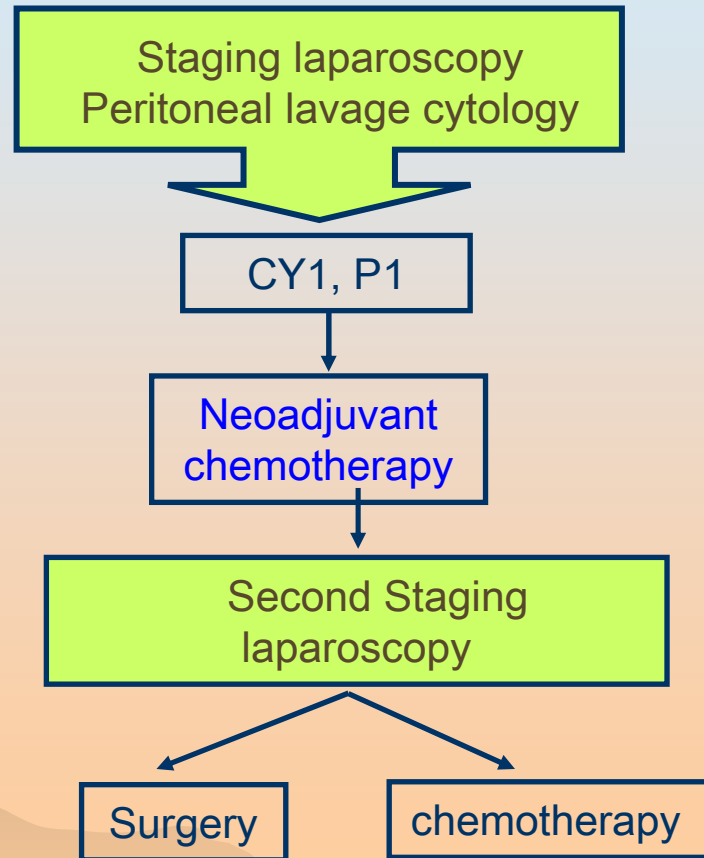
- ◆ Pre-operative diagnosis for PC
- ◆ Introduction of chemotherapy

Pre-operative diagnosis for peritoneal disease in GC

Staging laparoscopy (1994 ~)



Introduction of Neoadjuvant chemotherapy for GC with PC



Treatment protocol I (2000 ~ 2006)

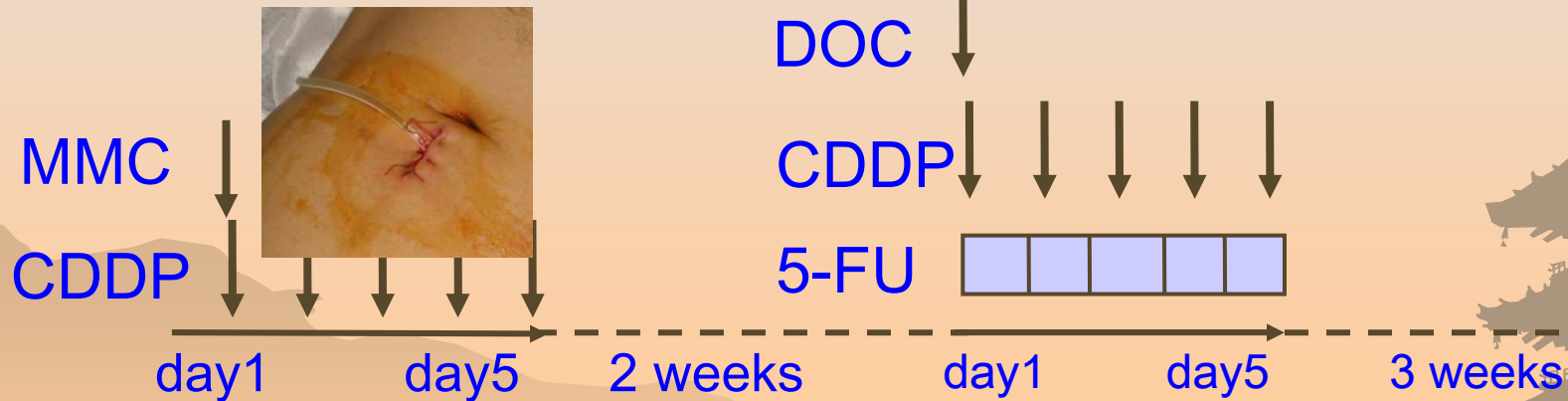
Sequential chemotherapy

MMC, CDDP i.p. + DFP (Docetaxel, 5-FU, CDDP) iv.

Intra-peritoneal chemotherapy

MMC 20 mg day 1
CDDP 20 mg 5 days

Docetaxel 60mg/m² day1
CDDP 10mg/m² day1-5
5FU; 350mg/m² day1-5



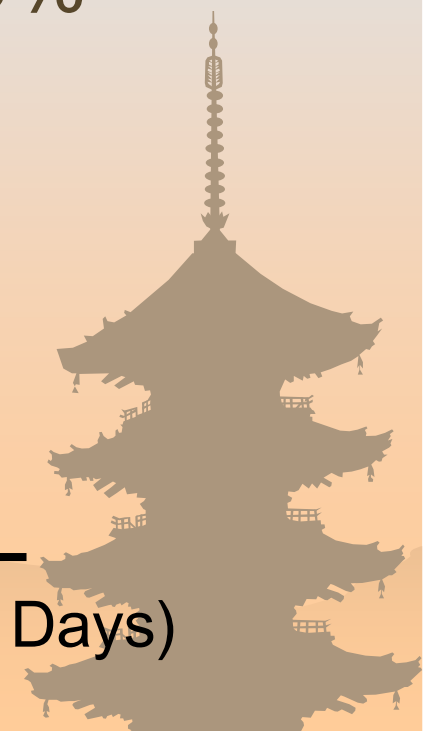
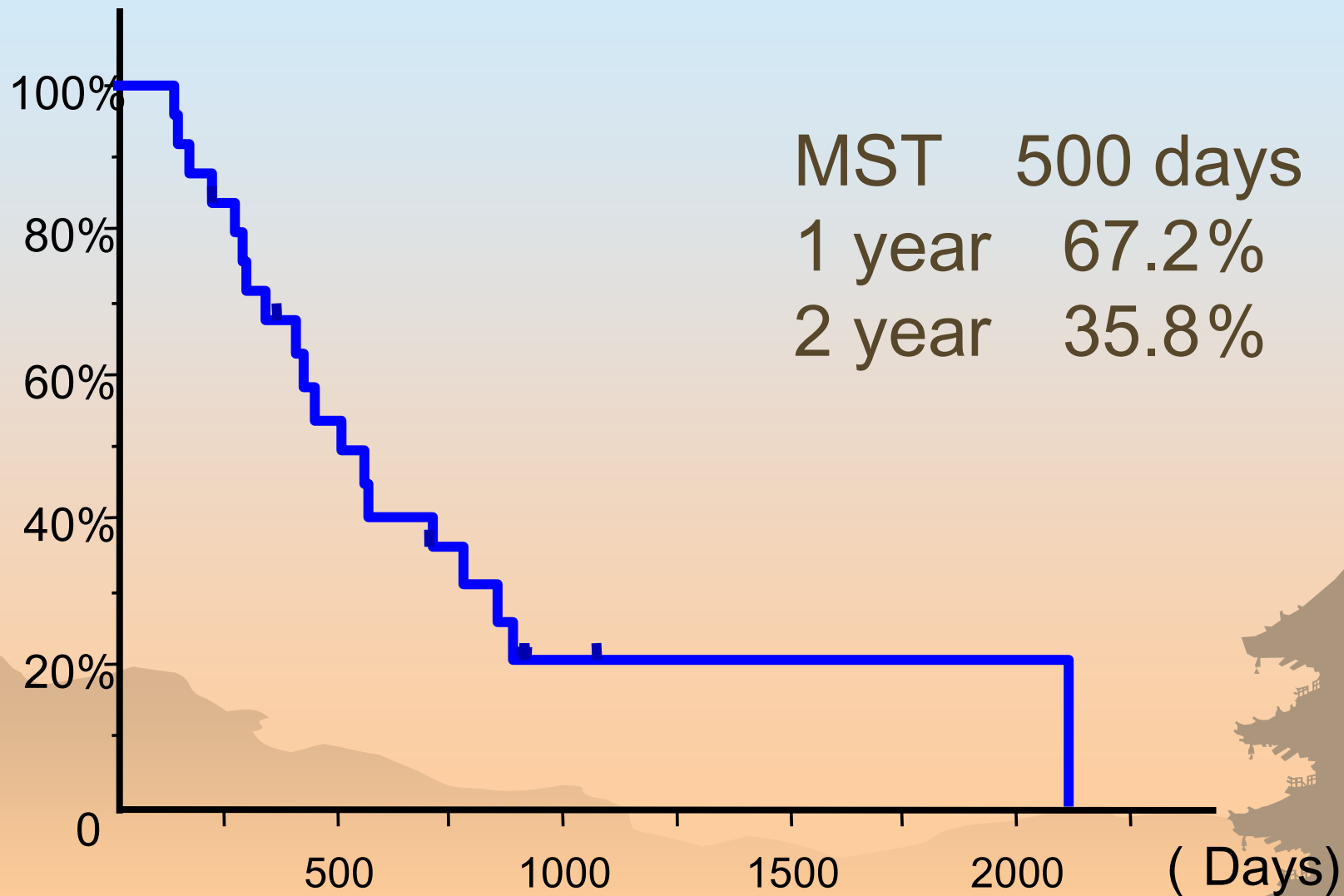
2 cycles before surgery : about 3 months

Patient Characteristics

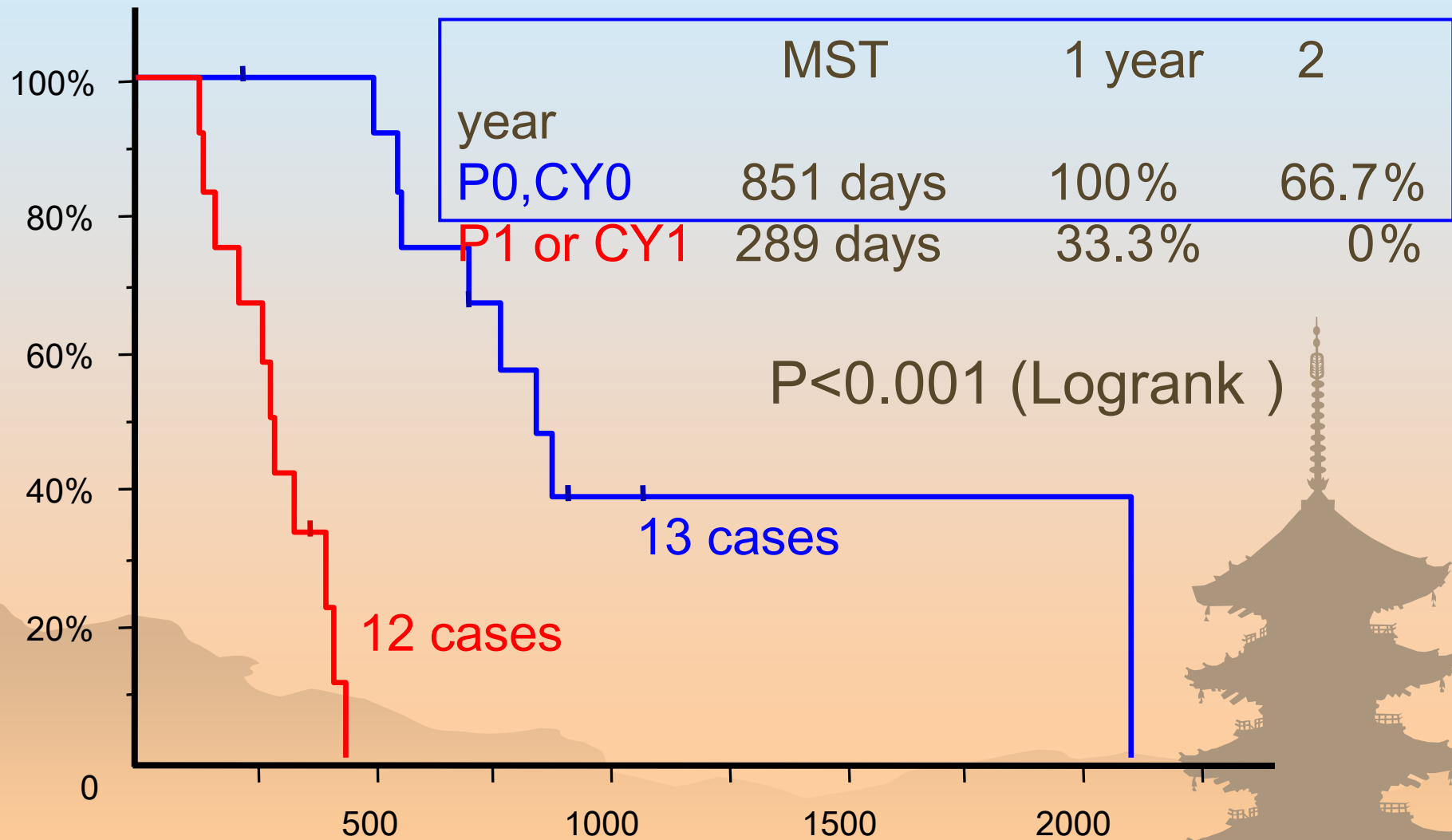
No of cases	25
Age	58.9±11.8 y.o.
Sex	13 : 12
Borrman (Type 1/2/3/4)	1/4/8/12
Histology (Intestinal/diffuse)	5/20
Distant matastasis except of peritoneum (yes/no)	1 (H1) /24



Overall Survival



Survival v.s. Effect for peritoneal disease

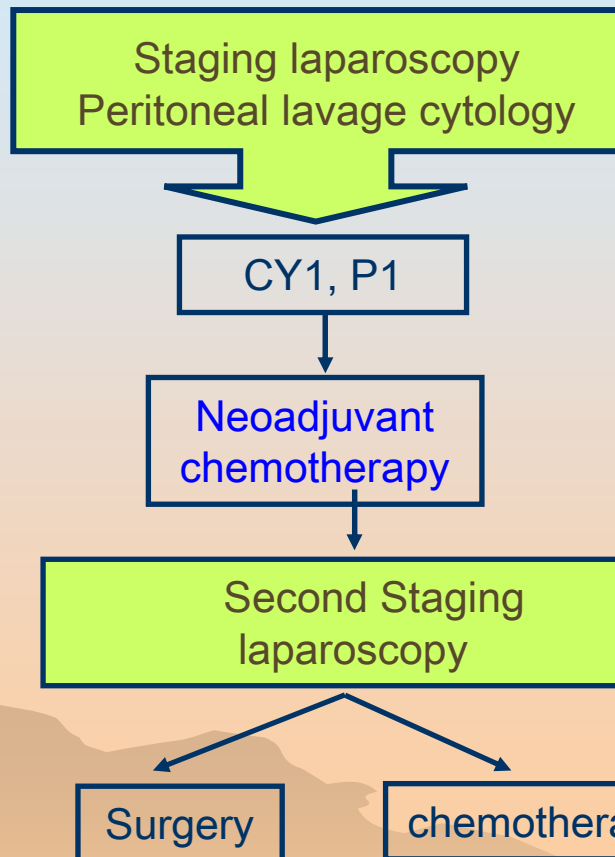


Adverse events (25 cases)

	Grade1 No. (%)	Grade2 No. (%)	Grade3 No. (%)	Grade4 No. (%)
Non hematological				
Fatigue	11(44)	2(8)	0(0)	0(0)
Nausea	6(24)	7(28)	4(16)	0(0)
Diarrhea	2(8)	2(8)	0(0)	0(0)
Alopecia	8(32)	7(28)	0(0)	0(0)
Hematological				
Leucocyte	0(0)	2(8)	17(68)	3(12)
Hb	10(40)	11(44)	0(0)	0(0)
Cr	4(16)	0(0)	0(0)	0(0)
ALT	2(8)	1(4)	1(4)	0(0)

Treatment protocol II (2006 ~ 2008)

Phase I study



Docetaxel i.p.



S-1 80 mg/m²/day

Day1

Day14

Day21

	Docetaxel
Level I	40 mg/m ²
Level II	50 mg/m ²
Level III	60 mg/m ²

2 cycles before surgery : about 1.5 months

Rationale for the protocol

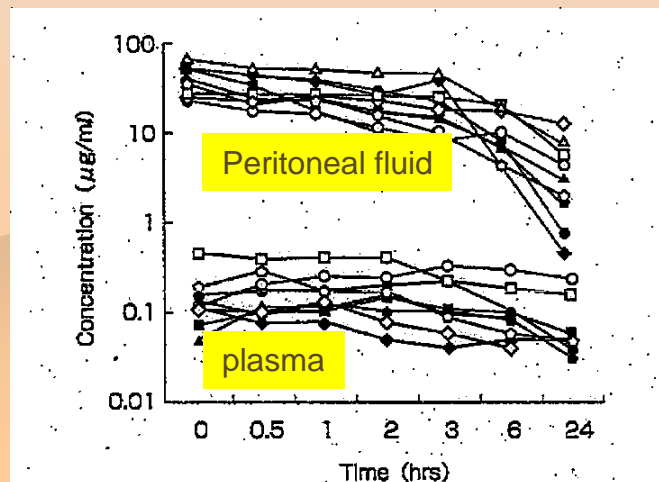
- S-1

An **oral agent** containing tegafur (a prodrug of 5-FU), gimeracil (CDHP): DPD inhibitor and oteracil potassium (Oxo): prevention of GI toxicity.

S-1 has been a key drug for gastric cancer in Japan (N.Engl J Med 2007, Lancet Oncol., 2008)

- ❁ Intra-peritoneal Docetaxel administration

Higher AUC of DOC is achieved in the abdominal cavity



Patient Characteristics

No of cases	Total 12
Level I	3
Level II	6
Level III	3
Ager	64.3±7.1
Sex (male/female)	9/3
Performance Status	
(0/1/2)	9/3/0
Borrman (Type 3/4)	3/9
Histology (intestinal/diffuse)	2/10
Lymph node (N0/N1/N2/N3)	3/6/2/1

Adverse events

(Level I ~ III, n= 12)

Grade 3 Grade 4 \geq G3 (%)

Non hematological toxicity

Fatigue	0	0	0%
Anorexia	1	0	8.3%
Diarrhea	0	0	0%
Rash	0	0	0%
Constipation	0	0	0%
Fever	1	0	8.3%

Hematological toxicity

Leukocytopenia	1	0	8.3%
Neutropeni	1	0	8.3%
Anemia	0	0	0%

Response to peritoneal dissemination

Cases who showed no peritoneal disease after chemotherapy

2/3 cases in Level I (DTX 40mg/m²)

5/6 cases in Level II (DTX 50mg/m²)

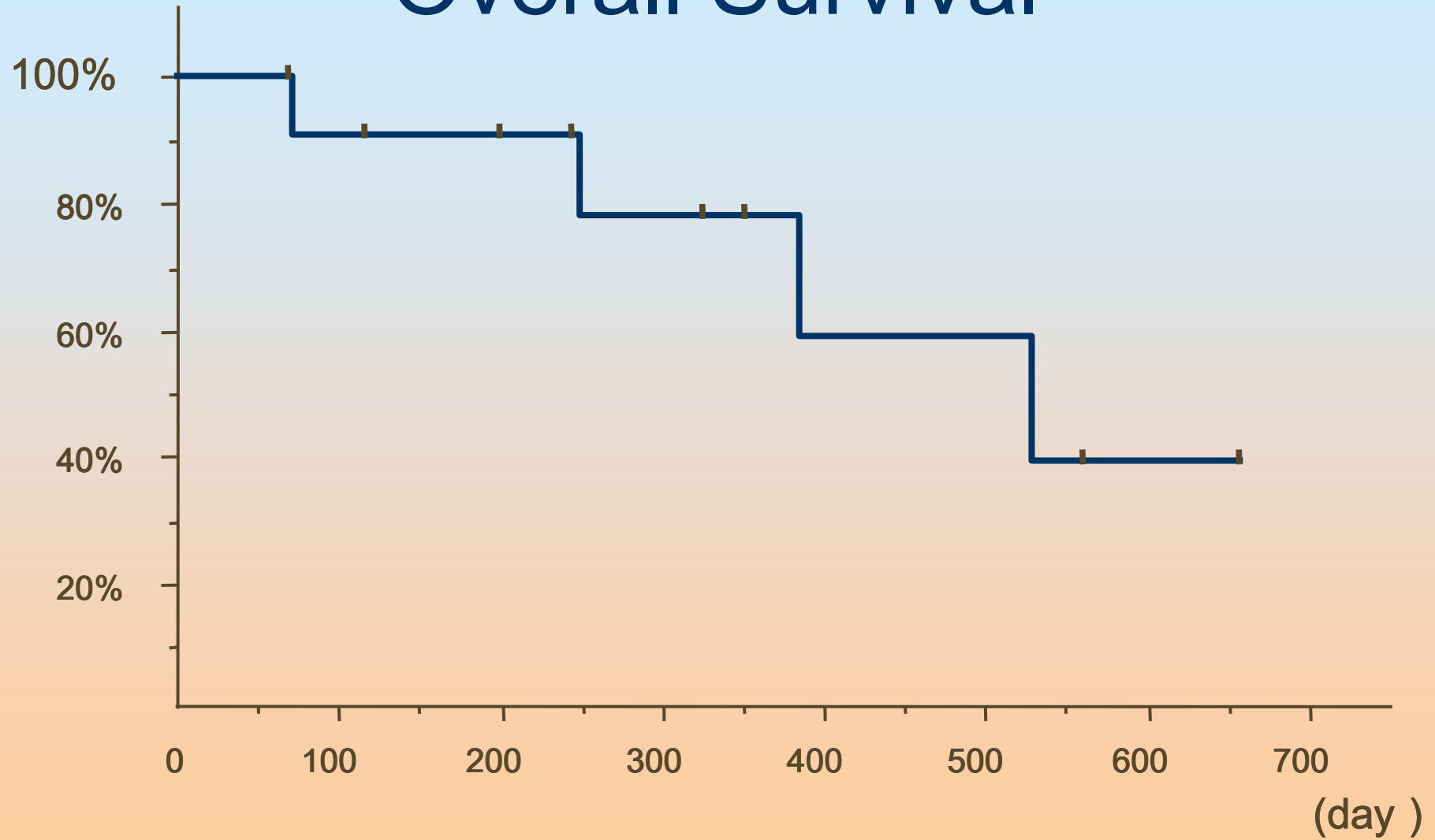
2/3 cases in Level II (DTX 60mg/m²)

Overall response to peritoneal disease

9 cases out of 12 (75 %)

10 cases had gastrectomy after NAC

Overall Survival



MST 530 days 1 year survival 77.9%

Conclusion

- ✓ Pre-operative diagnosis for PC is necessary for T3, T4 gastric cancer.
- ✓ Neoadjuvant chemotherapy for GC with PC is feasible and can be useful to select patients who are needed for surgery.
- ✓ The combination of oral S-1 and intra-peritoneal Docetaxel is safe and effective therapy for GC with peritoneal dissemination
- ✓ NAC combined with intra-peritoneal and systemic chemotherapy will be a promising therapy for GC with peritoneal dissemination

