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Randomized phase II study of docetaxel versus paclitaxel in patients with esophageal squamous cell carcinoma refractory to fluoropyrimidine- and platinum-based chemotherapy: OGSG1201

H. Hara[1], S. Yamamoto[2], T Kii[3], R. Kawabata[4,5], J. Kawada[6], A. Takeno[7], J. Matsuyama[8], S. Ueda[9], H. Kawakami[10], Y. Okita[11,12], S. Endo[13], Y. Kimura[5,14], K. Yanagihara[15], T. Okuno[16], Y. Kurokawa[17], T. Shimokawa[18] & T. Satoh[19]†

[1]Department of Gastroenterology, Saitama Cancer Center, Kitaadachi-gun, Saitama, Japan; [2]Department of Gastrointestinal Oncology, Osaka International Cancer Institute, Osaka, Osaka, Japan; [3]Cancer Chemotherapy Center, Osaka Medical College, Takatsuki, Osaka, Japan; [4]Department of Surgery, Osaka Rosai Hospital, Sakai, Osaka, Japan; [5]Department of Surgery, Sakai City Medical Center, Sakai, Osaka, Japan; [6]Department of Surgery, Osaka General Medical Center, Osaka, Osaka, Japan; [7]Department of Surgery, Kansai Rosai Hospital, Amagasaki, Hyogo, Japan; [8]Department of Surgery, Yao Municipal Hospital, Yao, Osaka, Japan; [9]Department of Gastroenterological Surgery and Oncology, Kitano Hospital, Tazuke Kofukai Medical Research Institute, Osaka, Osaka, Japan; [10]Department of Medical Oncology, Kindai University Faculty of Medicine, Osakasayama, Osaka, Japan; [11]Department of Medical Oncology, Kobe City Medical Center General Hospital, Kobe, Hyogo, Japan; [12]Department of Clinical Oncology, Kagawa University Faculty of Medicine, Kita-gun, Kagawa, Japan; [13]Department of Gastroenterological Surgery, Higashiosaka City Medical Center, Higashiosaka, Osaka, Japan; [14]Department of Surgery, Kindai University Faculty of Medicine, Osakasayama, Osaka, Japan; [15]Department of Medical Oncology, Kansai Electric Power Hospital, Osaka, Osaka, Japan; [16]Division of Gastroenterology, Department of Internal Medicine, Graduate School of Medicine, Kobe University, Kobe, Gastrointestinal Cancer Chemotherapy Study Group (OGSG) Hyogo, Japan; [17]Department of Gastroenterological Surgery, Osaka University Graduate School of Medicine, Suita, Osaka, Japan; [18]Department of Medical Data Science, Graduate School of Medicine, Wakayama Medical University, Wakayama, Wakayama, Japan; [19]Department of Frontier Science for Cancer and Chemotherapy, Osaka University Graduate School of Medicine, Suita, Osaka, Japan, †For Osaka Gastrointestinal Cancer Chemotherapy Study Group (OGSG)

Background

There is currently no standard chemotherapy for esophageal squamous cell carcinoma (ESCC) that has become refractory to first-line fluoropyrimidine- and platinum-based chemotherapy. We therefore performed a randomized, selection-design phase II trial to compare docetaxel (DTX) and paclitaxel (PTX) in this setting.

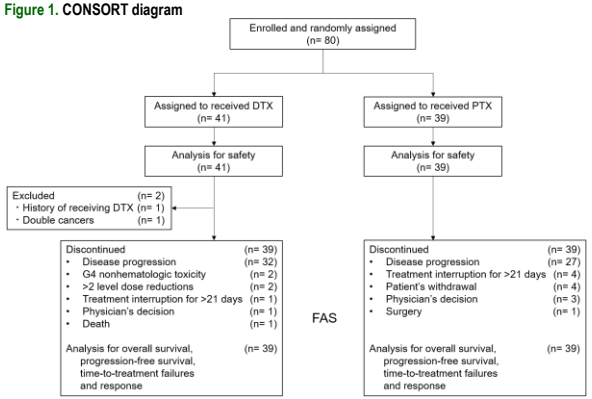
Methods

- Eligible patients with unresectable advanced or recurrent ESCC were randomly assigned to receive either DTX (70 mg/m^2 on day 1 of each 21- day cycle) or PTX (100 mg/m^2 on days 1, 8, 15, 22, 29, and 36 of each 49-day cycle).
- The primary end point of the study was overall survival (OS).
- The secondary end points included progression-free survival (PFS), time to treatment failure (TTF), response rate (RR), and safety.

Results

- 80 patients were randomized to receive DTX (N = 41) or PTX (N = 39), and 78 eligible patients (N = 39 in each group) were included for efficacy analysis.
- The median OS was significantly longer in the PTX group than in the DTX group (8.8 vs. 7.3 months; hazard ratio [HR], 0.62; P = 0.047).
- A significant benefit of PTX over DTX was also apparent in the median PFS (4.4 vs. 2.1 months; HR, 0.49; P = 0.002) and median TTF (3.8 vs. 2.1 months; HR, 0.45; P < 0.001).
- RR (25.6% vs. 7.7%, P = 0.065) as well as disease control rate (74.4% vs. 35.9%, P = 0.0013) were higher in the PTX group than in the DTX group.
- Neutropenia (80% vs. 28%) and leukopenia (76% vs. 28%) of grade ≥3 as well as febrile neutropenia (46% vs. 0%, P < 0.0001) occurred more frequently in the DTX group than in the PTX group.
- 44 individuals received subsequent therapy. Of note, 24 patients, comprising 14 in the DTX group and 10 in the PTX group, received subsequent crossover treatment. Patients who received such crossover therapy showed a significantly longer OS compared with those who received other poststudy treatment (HR of 0.40 [95% CI, 0.23–0.71], P = 0.002), with the survival benefit of such treatment being apparent in the DTX group (HR of 0.30 [95% CI, 0.14–0.65], P = 0.002) but not in the PTX group (HR of 0.58 [95% CI, 0.26–1.28], P = 0.171)

Figure 1. CONSORT diagram



DTX, docetaxel; PTX, paclitaxel; PD, progressive disease; G4, grade 4; FAS, full analysis set.

Table 1. Patient characteristics

Characteristic	DTX (N = 41)	PTX (N = 39)
Age (years) Median (range)	69 (47–83)	67 (48–78)
Sex		
Male	38	35
Female	3	4
ECOG performance status		
0	23	21
1	18	18
Location of primary tumor		
Ce	2	2
Ut	11	10
Mt	16	13
Lt	10	12
Ae	2	2
Histology type		
Well-differentiated SCC	5	6
Moderately differentiated SCC	17	19
Poorly differentiated SCC	9	4
SCC	9	7
Adenosquamous cell carcinoma	0	3
High grade	1	0
Number of organs with metastases		
1	21	21
2	15	14
3	3	3
4	2	1
Sites of metastases		
Lymph node	26	31
Lung	15	8
Liver	8	10
Bone	5	5
Pleura	2	2
Peritoneum	1	3
Other	4	1
History of radiotherapy		
Yes	15	16
No	26	23
Advanced or recurrent		
Advanced	26	21
Recurrent	15	18
Neoadjuvant or adjuvant chemotherapy		
Yes	10	9
No	31	30

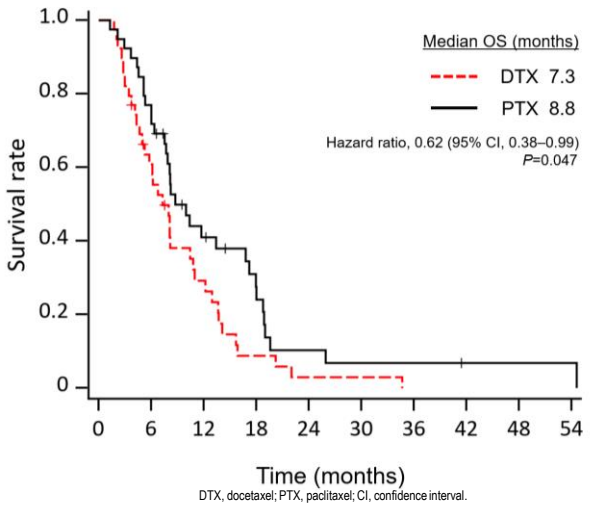
DTX, docetaxel; PTX, paclitaxel; Ce, cervical esophagus; Ut, upper thoracic esophagus; Mt, middle thoracic esophagus; Lt, lower thoracic esophagus; Ae, abdominal esophagus; SCC, squamous cell carcinoma

Table 2. Treatment after study chemotherapy

Treatment	DTX (N = 39)	PTX (N = 39)
No post-treatment	20	14
Third-line treatment	19	25
Systemic therapy		
PTX	14	1
DTX	0	8
S-1	2	10
FP	0	1
Anti PD-1 antibody	2	1
Other	1	3
Unknown	0	1
Fourth-line treatment	7	12
Systemic therapy		
PTX	0	0
DTX	1	2
S-1	6	2
Nedaplatin	0	1
Anti PD-1 antibody	0	1
Other (experimental drug)	0	3
Palliative radiotherapy	0	1
Palliative surgery	0	2
Fifth-line treatment	3	4
Systemic therapy		
PTX	0	1
S-1	1	1
Other (experimental drug)	1	0
Palliative radiotherapy	1	2

DTX, docetaxel; PTX, paclitaxel; FP, 5-fluorouracil (5-FU) + cisplatin.

Figure 2. Kaplan-Meier curves for overall survival



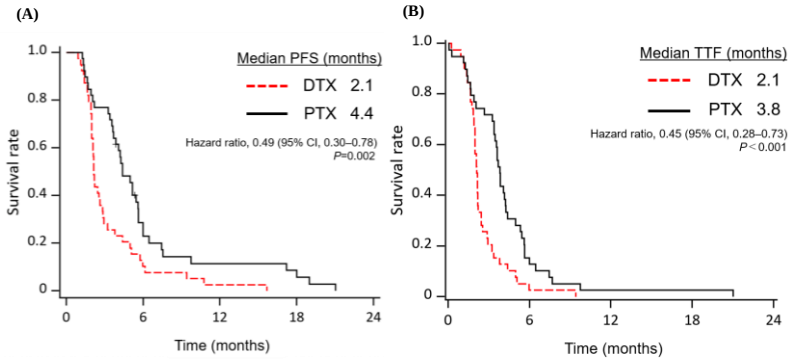
DTX, docetaxel; PTX, paclitaxel; CI, confidence interval.

Table 3. Numbers (%) of patients with main adverse events

Event	DTX (N = 41)					PTX (N = 39)			
	All grade (%)	Grade 3 (%)	Grade 4 (%)	Grade 5 (%)	Grade 3–5 (%)	All grade (%)	Grade 3 (%)	Grade 4 (%)	Grade 3 or 4 (%)
Neutropenia	34 (83)	8 (20)	25 (61)	0	33 (80)	25 (64)	8 (21)	3 (8)	11 (28)
Leukopenia	34 (83)	19 (46)	12 (29)	0	31 (76)	30 (77)	10 (26)	1 (3)	11 (28)
Anemia	36 (88)	11 (27)	0	0	11 (27)	34 (87)	4 (10)	1 (3)	5 (13)
Thrombocytopenia	13 (32)	0	0	0	0	6 (15)	0	0	0
Febrile neutropenia	19 (46)	18 (44)	1 (2)	0	19 (46)	0	0	0	0
Anorexia	31 (76)	6 (15)	0	0	6 (15)	20 (51)	2 (5)	0	2 (5)
Fatigue	30 (73)	5 (12)	0	0	5 (12)	22 (56)	1 (3)	0	1 (3)
Infection	9 (22)	2 (5)	2 (5)	0	4 (10)	9 (23)	2 (5)	0	2 (5)
Neuropathy	5 (12)	0	0	0	0	28 (72)	3 (8)	0	3 (8)
Hyponatremia	8 (20)	3 (7)	0	0	3 (7)	2 (5)	0	0	0
Hypoalbuminemia	31 (76)	2 (5)	0	0	2 (5)	15 (38)	0	0	0
Interstitial pneumonia	3 (7)	0	1 (2)	0	1 (2)	1 (3)	1 (3)	0	1 (3)
Diarrhea	12 (29)	1 (2)	0	0	1 (2)	8 (21)	1 (3)	0	1 (3)
Edema	4(10)	0	0	0	0	4 (10)	1 (3)	0	1 (3)
Myalgia	2 (5)	0	0	0	0	1 (3)	1 (3)	0	1 (3)
AST increased	12 (29)	1 (2)	0	0	1 (2)	8 (21)	0	0	0
Hypokalemia	3 (7)	1 (2)	0	0	1 (2)	1 (3)	0	0	0
Hyperkalemia	5 (12)	1 (2)	0	0	1 (2)	4 (10)	0	0	0
Hypercalcemia	1 (2)	1 (2)	0	0	1 (2)	2 (5)	0	0	0
Alopecia	22 (54)	-	-	-	0	25 (64)	-	-	0
Sudden death	1 (2)	-	-	1 (2)	1 (2)	0	-	-	0
GGT increased	0	0	0	0	0	2 (5)	1 (3)	0	1 (3)
Hyperglycemia	0	0	0	0	0	3 (8)	1 (3)	0	1 (3)
Nausea	10 (24)	0	-	-	0	11 (28)	0	-	0
Anaphylaxis	0 (0)	0	0	0	0	1 (3)	1 (3)	0	1 (3)

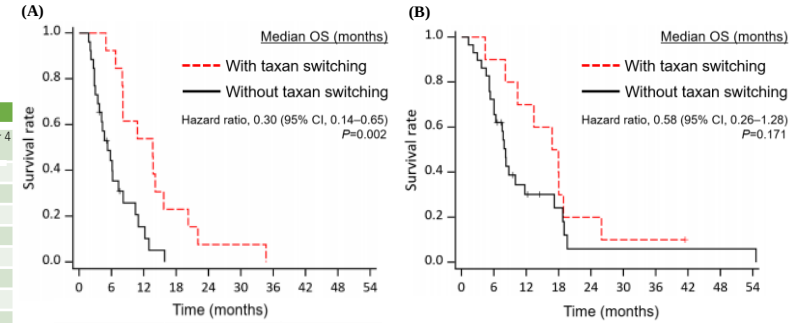
DTX, docetaxel; PTX, paclitaxel; AST, aspartate aminotransferase; GGT, γ-glutamyl transpeptida

Figure 3. Kaplan-Meier curves for progression-free survival (A) and time to treatment failure (B).



DTX, docetaxel; PTX, paclitaxel; CI, confidence interval.

Figure 4. Kaplan-Meier curves for overall survival with and without taxan switching in DTX group (A) and PTX group (B).



DTX, docetaxel; PTX, paclitaxel; CI, confidence interval.

Conclusions

- This is the first to compare PTX to DTX in ESCC refractory to 1st-line fluoropyrimidine- and platinum-based chemotherapy.
- PTX showed a significantly better efficacy as well as a more manageable especially in hematological toxicity compared with DTX.
- With the growing need for 2nd-line treatment not reliant on ICI, our data suggested the validity of PTX in this setting.

Acknowledgments

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