RESEARCH ARTICLE

Efficacy of Taxane-Based Regimens in a First-line Setting for Recurrent and/or Metastatic Chinese Patients with Esophageal Cancer

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Abstract

Objective: To compare the efficacy of taxane-based regimens in the first line setting retrospectively in Chinese patients with recurrent and/or metastatic esophageal cancer. Methods: We analyzed 102 recurrent and/or metastatic esophageal cancer patients who received taxanes-based regimens in a first-line setting from January 2009 to December 2013. Sixteen (15.7%) patients were administered Nab-PTX based chemotherapy and 86 patients (84.3%) received paclitaxel (PTX) or docetaxel (DTX) based chemotherapy. Patients in the PTX/DTX group could be further divided into TP (71 patients) and TPF (15 patients) groups. Results: The objective response rate (ORR) of all patients was 20.6%, and the disease control rate (DCR) was 67.6%. The median overall survival (OS) was 10.5 months (95% CI 10.1-16.4) and the median progression-free survival (PFS) was 6.04 months (95% CI 5.09-7.91). The DCR was higher in the TPF group than the TP group (93.3% vs. 59.1%; $p = 0.015$). There were no significant differences in ORR, OS, and PFS among Nab-PTX, TPF and TP groups. Conclusions: The three regimens of Nab-PTX based, TP and TPF proved active in a first line setting of Chinese patients with recurrent and/or metastatic esophageal cancer, and should thus be regarded as alternative treatments.

Keywords: Esophageal cancer - docetaxel - paclitaxel - nanoparticle albumin - bound paclitaxel

Asian Pac J Cancer Prev, **15 (13)**, 5493-5498

Introduction

Esophageal cancer is the eighth most common cancer with a dismal prognosis, which cause the sixth cancer-related mortality worldwide (IARC, 2012). More than two-thirds of patients would be initially diagnosed as unresectable or metastatic disease (Thallinger, et al., 2011). Even patients with resectable disease have a high rate of recurrence with the expected median survival being only 24 months, and 5-year survival rate lower than 30% (Thallinger, et al., 2011; Mirinezhad, et al., 2014). The combination chemotherapy of 5-fluorouracil and cisplatin (PF) is the mainstay of palliative treatment for advanced or recurrent cancer (Nakajima, et al., 2013), however, their poor outcomes require urgently new researches been conducted.

Taxanes, including paclitaxel (PTX) and docetaxel (DTX), have been demonstrated to be effective in advanced and recurrent esophageal cancer as monotherapy (Ajani, et al., 1994; Einzig, et al., 1996). Combinations with taxanes treatment, no matter two or three drugs regiment, including the combination of platinum, fluorouracil, irinotecan or capetabine etc, are elucidated to be more effective than single drug in esophageal cancer (Ilson, et al., 1998; Van Cutsem, et al., 2006; Burtness, et al. 2009; Bang, et al., 2010; Shah, et al., 2011; Gu, et al., 2012). However, the studies to compare taxanes based regimens with PF regimen were not reported except Fujita Y et al. (Fujita, et al., 2008), who reported no significant differences in median survival time between docetaxel plus nedaplatin and cisplatin plus 5-fluorouracil in esophageal cancer patients. However, the low dose design and very small patients' sample in combination of docetaxel and nedaplatin limited its significance (Fujita, et al., 2008). David et al. (Ilson, et al., 1998) reported a triple combination (TPF) of paclitaxel, cisplatin and 5-FU, the response rate was 48%. In the V325 group trial (Van Cutsem, et al., 2006), the addition of docetaxel to the traditional CF (cisplantin/5-FU) regiment also proved to be significantly improved time to progression (5.6 vs. 3.7 months; $p<0.01$), survival (overall survival 9.2 vs. 8.6 months; $p=0.02$) and response rate (37% vs. 25% respectively; $p=0.01$) in GE junction and gastric adenocarcinomas. However, compared with the two

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drug regimens, three drug regimens have more toxicity, including myelosuppression, stomatitis, diarrhea etc.

The nanoparticle albumin-bound paclitaxel (Nab-PTX), a solvent excipients free formulation of paclitaxel, was developed to gain more therapeutic benefits of paclitaxel but eliminate the toxicities associated with Cremophor (Sparreboom, et al., 2005). Several studies elucidated the superiority of Nab-PTX in pharmacokinetics (Al-Hajeili, et al., 2014), particularly the intratumoral accumulation, absorption, binding to the endothelial cells, and transportation were higher compared with paclitaxel as well as better tolerance in breast cancer, lung cancer, ovarian cancer, pancreatic cancer (Desai, et al., 2006; Desai, et al., 2008; Von Hoff, et al., 2013). However, rare effort to study nab-PTX efficacy was focused on metastatic and/or recurrent esophageal cancer (Shi, et al., 2013).

China possesses the highest morbidity and mortality rates in the world (Lu, et al., 2014), and presents distinct characteristics with majority squamous cell cancer (SCC) and midportion location (Jie. and Kang., 2011; Zhao, et al., 2012), which differ from esophageal cancer patients in the western countries where has the rising incidence of adenocarcinoma of the lower esophagus with escalating rates of obesity, gastroesophageal reflux disease, and Barrett's esophagus (Vizcaino, et al., 2002; Dubecz, et al., 2014). To our knowledge, taxanes-based regimens were not fully studied in Chinese esophageal cancer (Huang, et al., 2004; Zhang, et al., 2007; Wang, et al., 2010; Zhang, et al., 2010; Wu, et al., 2012; Ji, et al., 2013), especially Nab-PTX (Shi, et al., 2013), even this new medicine was seldom reported in East Asian countries as Japan and South Korea. This retrospective study was conducted to evaluate the efficacy of taxanes-based regimens in Chinese patients with recurrent and/or metastatic esophageal cancer, compare the efficacy of TP with TPF regimen, and Nab-PTX based regimen with traditional taxanes including PTX and DTX-based regimen separately.

Materials and Methods

Patients

The patients eligibility were 1) with histological and/or pathological diagnoses as esophageal cancer; 2) with radiography and/or pathological evidences that patients had advanced (stage IV) or recurrent/metastatic disease; 3) Patients had an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0-2 with sufficient bone marrow, liver and renal function; 4) received taxane-based chemotherapy in first-line setting at Sun Yat-sen University Cancer Center from January 2009 to December 2013; 5) with complete follow-up data. Patients were excluded if the chemotherapy had been administered as neoadjuvant chemotherapy with radical treatment intent, and if all the lesions were covered by the radiotherapy, palliative surgery or intervention therapy after first line chemotherapy. Written informed consent for chemotherapy was obtained from all patients.

Treatment plan

Patients in PTX/ DTX group were premedicated intravenously (i.v.) 30min before therapy with dexamethasone 10 mg, cimetidine 400 mg (or a comparable histamine H2 receptor blocker) and diphenhydramine hydrochloride 40mg. All patients received 5-HT receptor antagonist before taxanes. PTX and DTX were administered i.v. at a starting dose of 170 mg/m^2 and 60-75mg/m^2 over 1h once every 3 weeks separately. Nab-paclitaxel was administered i.v. at a starting dose of 260 mg/m^2 over 30min each 3 week-period. Twelve patients received molecular targeted agents as cetuximab, nimotuzumab and endostatin (Table 1). In general, chemotherapy was delayed until recovery for a Grade 2 myelosuppression or any significant persisting nonhematologic toxicity. For grade 3-4 myelosuppression, G-CSF or thrombopoietin was administered and the dose of taxanes was adjusted on individual basis. Treatment was discontinued if the tumor progressed, severe toxicity occurred or at the patient's request.

Statistical analysis

Response was assessed according to the Response Evaluation Criteria in Solid Tumors (RECIST 1.1) as complete response (CR), partial response (PR), stable disease (SD) or progressive disease (PD) in patients with measurable lesions. Progression-free survival (PFS) was measured from the initiation of taxanes to the progression, or death without evidence of progression. Overall survival (OS) was measured from the first day of diagnosed with advanced or recurrence to the day of death or to the final day of the follow-up period. Median PFS and median OS were estimated by the Kaplan-Meier method.

The distributions of the baseline characteristics of the patients were assessed by the χ^2 test. Statistical analyses were performed using SPSS software (version 18.0; IBM Corporation, Armonk, NY, USA). All tests were two-sided, and $p<0.05$ was considered statistically significant.

Results

A total of 102 patients were enrolled in this retrospective study. Sixteen were administered Nab-PTX based chemotherapy and 86 received PTX or DTX based chemotherapy. Patients in Nab-PTX group consist of single agent regimen (3 patients) and combination with cisplatin or carboplatin (13 patients). Patients in PTX/DTX group comprise two subgroups: two-drug combination of PTX/DTX and platinum (TP) and triplet regimen TPF with addition of continuous infusion of 5-fluorouracil (5-Fu) or capecitabine (an oral fluoropyrimidine).

Patient characteristics

Clinico-pathological characteristics of patients are exhibited in Table 1. Among all the patients, 87 were male (85.3%). Median age was 59 (range 35-79). The lower esophageal location of the primary tumor was a majority (33.3% in total, 31.3% in Nab-PTX group, 34.4% in TP group, and 46.7% in TPF group), albeit the subsite unbalanced among three groups. Sixty-three (61.8%) patients had relapsed after prior treatment and the remaining 39 were newly diagnosed with metastases. The followed radiotherapy, palliative surgery/interventional therapy were performed more in Nab-PTX group than

Table 1. Patient Characteristics

Characteristics	Nab-PTX group (%)	PTX/ DTX group (%)		*P**	*P***
	(n=16)	TP group (n=71)	TPF group (n=15)		
Gender					
Male	15 (93.8)	61 (85.9)	11 (73.3)		
Female	1 (6.3)	10 (14.1)	4 (26.7)	0.46	0.26
Age (years)					
Median (range)	61.5 (47-79)	59 (35-76)	53 (40-74)		
≥60	8 (50)	33 (46.5)	4 (26.7)		
<60	8 (50)	38 (53.5)	11 (73.3)	0.79	0.36
ECOG PS					
0	1 (6.3)	4 (5.6)	0 (0)		
1	13 (81.3)	57 (80.3)	13 (86.7)		
2	2 (12.5)	10 (14.1)	2 (13.3)	1	0.96
Location					
Cervical †	1 (6.3)	4 (6.3)	2 (13.3)		
Upper thoracic‡	4 (25)	14 (21.9)	3 (20)		
Midthoracic§	4 (25)	22 (34.4)	0 (0)		
Lower thoracic¶	5 (31.3)	22 (34.4)	7 (46.7)		
Multifocal	1 (6.3)	2 (3.1)	0 (0)		
Unknown	1 (6.3)	0 (0)	4 (4.2)	0.99	0.04
Histology					
Squamous cell carcinoma	15 (93.8)	69 (97.2)	15 (100)		
Small cell cancer	1 (6.3)	2 (2.8)	0 (0)	0.4	1
Grade					
1	0 (0)	5 (7)	1 (6.7)		
2	6 (37.5)	35 (49.3)	5 (33.3)		
3	7 (43.8)	24 (33.8)	8 (53.3)		
Unknown	3 (18.8)	7 (9.9)	1 (6.7)	0.44	0.6
Overall evalution					
Initial advanced stage	5 (31.3)	31 (43.7)	3 (20)		
Recurrence and/or metastasis	11 (68.8)	40 (56.3)	12 (80)	0.59	0.19
Target sites before first-line setting					
Primary lesion	6 (37.5)	40 (56.3)	5 (33.3)	0.42	0.19
LN (neck)	5 (31.3)	13 (18.3)	3 (20.0)	0.31	0.55
LN (mediastinal)	7 (43.8)	29 (40.8)	5 (33.3)	0.79	0.86
LN (abdominal)	3 (18.8)	24 (33.8)	2 (13.3)	0.39	0.19
Lung	3 (18.8)	21 (29.6)	6 (40)	0.38	0.47
Liver	7 (43.8)	16 (22.5)	6 (40)	0.23	0.15
Bone	2 (12.5)	5 (7.0)	1 (6.7)	0.61	0.84
Other part (s)	1 (6.3)	8 (11.3)	1 (6.7)	0.7	0.7
Molecular targeted agent	10 (62.5)	2 (2.8)	0 (0)		
Follow-up treatment					
Multi-line Chemotherapy	8 (50)	25 (35.2)	4 (26.7)	0.26	0.41
Chemoradiotherapy	3 (18.8)	9 (12.7)	0 (0)	0.4	0.29
Radiotherapy	6 (37.5)	6 (8.5)	1 (6.7)	0.005	0.01ξ
Palliative surgery/interventional therapy	4 (25)	1 (1.4)	0 (0)	<0.01Þ	<0.01Ÿ
Support care only	1 (6.3)	9 (12.7)	3 (20)	0.47	0.53
Unknown	3 (18.8)	26 (37.1)	4 (26.7)	0.25	0.31

*P** the *P* value of Nab-PTX and PTX+DTX group comparison; *P*** the *P* value of three-group comparison; †Cervical, 15-20 cm from the incisors; ‡ Upper thoracic, 20-25 cm; §Midthoracic, 25-30 cm; ¶Lower thoracic, ≥30 cm, including the gastroesophageal junction; Other part (s): including pleura (1) in Nab-PTX group; brain (1), pleura (3), stomach (1), adrenal gland (2) in TP group; pancreas (1) in TPF group; ξThe difference in number of patients who received radiotherapy between Nab-PTX group and TP group was statistically significant (p=0.007, Bonferroni correction would be to test each of the individual tests at a significance level of 0.017); Þp=0.002; Ÿp=0.003, the difference in number of patients who received palliative surgery/interventional between Nab-PTX group and TP group was statistically significant (p=0.004, Bonferroni correction would be to test each of the individual tests at a significance level of 0.017)

in PTX/DTX group. The three groups were similar in terms of other parameters including age, gender, ECOG performance status, histological type and target sites before first line treatment.

The efficacy of taxanes-based regimens

In the whole group, patients had received 1 cycle to 9 cycles (median 3 cycles) first line chemotherapy. The objective response rate (ORR) among patients with measurable disease was 20.6% in the whole group, and the disease control rate (CR + PR + SD, DCR) was 67.6% (Table 2). Response could not be evaluated in 19 patients for the following reasons: discontinuation before treatment evaluation due to toxicity in 2 patients and refusal by other patients. The median OS was 10.5 months (95% CI 10.1-16.4), and the median PFS was 6.04 months (95% CI 5.09-7.91).

The comparison of efficacy in different groups

The ORR was 25% among patients in Nab-PTX group, 19.7% in TP group, and 20.0% in TPF group (p=0.93). The DCR was 81.3% in Nab-PTX group, 59.1% in TP

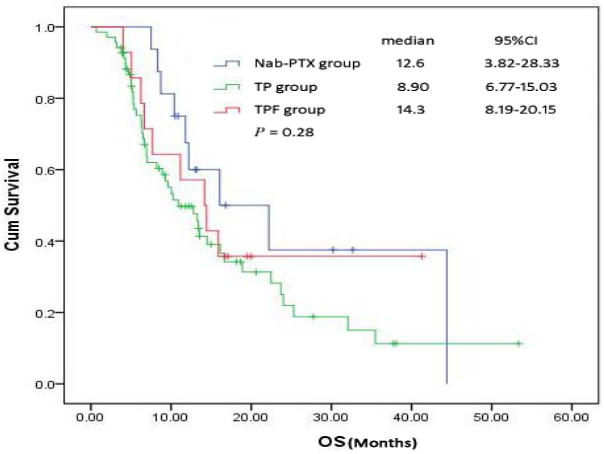

Figure 1. The OS of Nab-PTX Group, TP Group and TPF Group

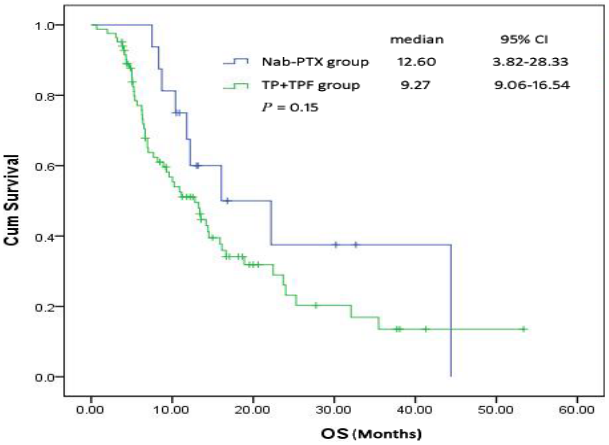

Figure 2. The OS of Nab-PTX Group and TP + TPF Group

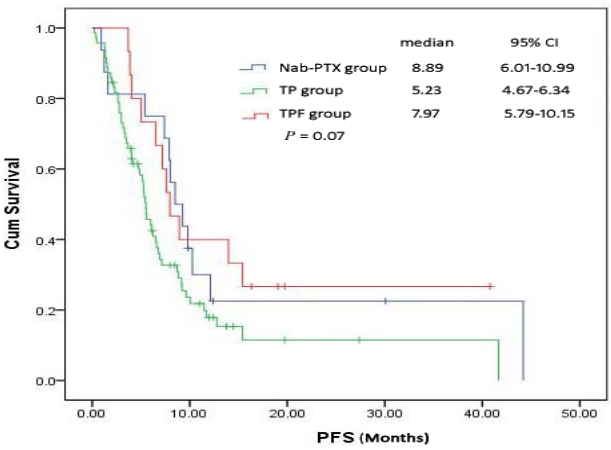

Figure 3. The PFS of Nab-PTX Group, TP Group and TPF Group

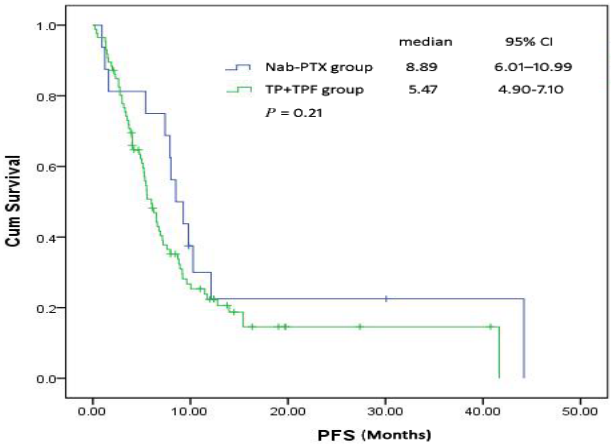

Figure 4. The PFS of Nab-PTX Group and TP + TPF Group

Table 2. Objective Response Rate among Patients with Measurable Lesions

	Nab-PTX group (n=16)	PTX/ DTX group		Total	*P**	*P***
		TP group (n=71)	TPF group (n=15)			
Partial response	4	14	3	21		
Stable disease	9	28	11	48		
Progressive disease	1	13	0	14		
Not evaluated	2	16	1	19		
ORR, %	25	19.7	20	20.6	0.74	0.93
DCR, %	81.3	59.1	93.3	67.6	0.26	0.02[¥]

*According to the Response Evaluation Criteria in Solid Tumors (RECIST); *P** the *P* value of Nab-PTX and PTX+DTX group comparison; *P*** the *P* value of three-group comparison; [¥]The DCR between TP group and TPF group was statistically significant (p=0.015, Bonferroni correction would be to test each of the individual tests at a significance level of 0.017)

group, and 93.3% in TPF group, statistically significant difference among the three groups (p<0.05), however, only the difference between TP group and TPF group was statistically significant (p<0.02) rather than Nab-PTX group and TP group or Nab-PTX group and TPF group (Table 2).

The median OS was 12.6 months (95% CI, 3.8-28.3) in the Nab-PTX group, 8.90 months (95% CI, 6.77-15.03) in the TP group and 14.3 months (95% CI 8.2-20.2; p=0.28) in the TPF group (Figure 1), with no statistical difference. The OS of Nab-PTX group and TP+TPF group (median OS was 9.27 months; 95% CI 9.06-16.54) were insignificant either (p=0.15, Figure 2). The median PFS was 8.89 months (95% CI, 6.01-10.99) in the Nab-PTX group, 5.23 months (95% CI, 4.67-6.34) in the TP group and 7.97 months (95% CI 5.79-10.15; p=0.07) in the TPF group (Figure 3). The PFS of Nab-PTX group and TP+TPF group (median PFS was 5.47 months; 95% CI 4.90-7.10) were insignificant (p=0.21, Figure 4). In the subgroup analyses, both OS and PFS had no statistical difference between any two groups (OS: Nab-PTX group vs. TP group, 12.6 vs. 8.9; p=0.12; TP group vs. TPF group, 8.9 vs. 14.3; p=0.50; Nab-PTX group vs. TPF group, 12.6 vs. 14.3; p=0.42. PFS: Nab-PTX group vs. TP group, 8.89 vs. 5.23; p=0.11; TP group vs. TPF group, 5.23 vs. 7.97; p=0.06; Nab-PTX group vs. TPF group, 8.89 vs. 7.97; p=0.84).

Discussion

Lack of standard second-line therapeutic regimen for patients with advanced and/or recurrent esophageal cancer (Thallinger, et al., 2011) was the reason for chosing the patients treated in the first line setting. In spite of the standard regimens recommended by NCCN guideline as combination of cisplatin and 5-Fu, TP and TPF regimens

including PTX and DTX in the first line setting was settled by several studies (Petrasch, et al., 1998; Ajani, et al., 2005; Van Cutsem, et al., 2006), which had validated high clinical activities and survival advantages in metastatic or recurrent esophageal cancer, this superiority should not be extrapolated to Chinese patients for their different characteristics. In our study, the ORR of 20.6%, DCR of 67.6%, median OS of 10.5 months median PFS of 6.04 months in the whole group were observed.

In regard to the clinical activities, the addition of 5-Fu had been demonstrated a confirmed higher ORR than TP alone (37-43% vs 18-26%) (Ajani, et al., 2005; Roth, et al., 2007). The ORRs in our study were less impressive compared with the previous data (20.0% vs 19.7%). However, the DCR of 93.3% with TPF and 59.1% with TP, revealed that incorporation of 5-Fu produced a higher DCR than TP. Our study showed a tendency to higher ORR and DCR in patients with Nab-PTX than PTX/DTX based regimens (25% vs 19.8%, 81.3% vs 65.1%, respectively), although the differences were not statistically significant. The albumin-bound and nanoparticle technique of Nab-PTX allow higher dose application and cause less adverse events, which may contribute to the potential advantage.

Recently, an one-armed study illuminated the efficacy of Nab-PTX by evaluating the OS, PFS, and ORR in Chinese metastatic esophageal squamous cell cancer patients (Shi, et al., 2013), concluded with a longer median OS (15.5 months) and corresponding ORR and PFS compared with other traditional taxanes based regimens. However, the small patients' sample (33 patients) and subsequent treatments for most patients (87.9% patients receiving subsequent treatment after progression) may have contributed to better OS in the study (Shi, et al., 2013). In our project, albeit the differences in PFS or OS were not statistically significant for all regimens, the two endpoints tended to be better in Nab-PTX based and TPF than TP regimen. Firstly, the efficacy of Nab-PTX based regimen was akin to TPF. Though several studies had illuminated Nab-PTX with high efficacy and mild side effects in breast cancer (O'Shaughnessy, et al., 2013), non-small-cell lung cancer (Xing, et al., 2013) and pancreatic cancer (Zhang, et al., 2013), there is few influential evidence on esophageal cancer. In spite of lacking direct comparison of toxicity, more patients who received Nab-PTX were adminstered target agents compared with TPF in current study, suggesting better tolerance of Nab-PTX. However, the cost-effectivness of Nab-PTX should be taken into account in clinical practice. Secondly, addition of 5-Fu to TP regimen resulted in a trend of longer PFS and OS, which demands another well designed prospective study to confirm as well as the possible subsequent adverse events. Finally, we didn't separate PTX from DTX in the regimens, for there is no consensus in efficacy of these cognate agents for esophageal cancer yet. The efficacy of DTX was confirmed superior to PTX in breast cancer (Jones, et al., 2005), analogous in non-small-cell lung cancer (Esteban, et al., 2003), ovarian cancer (Hsu, et al., 2004) and gastric cancer (Park, et al., 2006). Mizota A et al. (Mizota, et al., 2011) compared PTX with DTX for advanced or recurrent esophageal cancer patients, no significantly different in terms of PFS and OS. Likewise, DTX had not obtained an advantage in second-line treatment (Fujita, et al., 2008).

Since this study was retrospective, non-randomized, small patients' sample, those limitations determined hard to compare the toxicity, quality of life, etc. More patients were included in the TPF group, the results might have been affected.

In conclusion, the three regimens of Nab-PTX based, TP and TPF are active and equal in first line setting of recurrent and/or metastatic esophageal cancer. TPF showed potential activity and, maybe, with more toxicities; Nab-PTX showed potential higher tolerance than TPF, but, less cost-effectiveness; so, the three regimens should become alternative treatments depend on patients' or doctors' consideration.

Acknowledgements

This work was supported by the Science and Technology Planning Project of Guang dong Province, China (2011B061300069) and the National Natural Science Foundation of China (81272641 and 81071872).

References

Ajani JA, Ilson DH, Daugherty K, et al. (1994). Activity of taxol in patients with squamous cell carcinoma and adenocarcinoma of the esophagus. *J Natl Cancer Inst*, **86**, 1086-91.

Ajani JA, Fodor MB, Tjulandin SA, et al. (2005). Phase II multi-institutional randomized trial of docetaxel plus cisplatin with or without fluorouracil in patients with untreated, advanced gastric, or gastroesophageal adenocarcinoma. *J Clin Oncol*, **23**, 5660-7.

Al-Hajeili M, Azmi AS, Choi M (2014). Nab-paclitaxel: potential for the treatment of advanced pancreatic cancer. *Onco Targets Ther*, **7**, 187-92.

Bang YJ, Van Cutsem E, Feyereislova A, et al. (2010). Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. *Lancet*, **376**, 687-97.

Burtness B, Gibson M, Egleston B, et al. (2009). Phase II trial of docetaxel-irinotecan combination in advanced esophageal cancer. *Ann Oncol*, **20**, 1242-8.

Desai N, Trieu V, Yao Z, et al. (2006). Increased antitumor activity, intratumor paclitaxel concentrations, and endothelial cell transport of cremophor-free, albumin-bound paclitaxel, ABI-007, compared with cremophor-based paclitaxel. *Clin Cancer Res*, **12**, 1317-24.

Desai NP, Trieu V, Hwang LY, et al. (2008). Improved effectiveness of nanoparticle albumin-bound (nab) paclitaxel versus polysorbate-based docetaxel in multiple xenografts as a function of HER2 and SPARC status. *Anti-Cancer Grug*, **19**, 899-909.

Dubecz A, Solymosi N, Stadlhuber RJ, et al. (2014). Does the incidence of adenocarcinoma of the esophagus and gastric cardia continue to rise in the twenty-first century? a SEER Database analysis. *J Gastrointest Surg*, **18**, 124-9.

Einzig AI, Neuberg D, Remick SC, et al. (1996). Phase II trial of docetaxel (Taxotere) in patients with adenocarcinoma of the upper gastrointestinal tract previously untreated with cytotoxic chemotherapy: the Eastern Cooperative Oncology Group (ECOG) results of protocol E1293. *Med Oncol*, **13**,

87-93.
Esteban E, Gonzalez de Sande L, Fernandez Y, et al. (2003). Prospective randomised phase II study of docetaxel versus paclitaxel administered weekly in patients with non-small-cell lung cancer previously treated with platinum-based chemotherapy. *Ann Oncol*, **14**, 1640-7.
Fujita Y, Hiramatsu M, Kawai M, et al. (2008). Evaluation of combined docetaxel and nedaplatin chemotherapy for recurrent esophageal cancer compared with conventional chemotherapy using cisplatin and 5-fluorouracil: a retrospective study. *Dis Esophagus*. **21**, 496-501.
Gu M, Li SY, Huang XE, et al. (2012). A phase II study on continuous infusional paclitaxel and 5-Fu as first-line chemotherapy for patients with advanced esophageal cancer. *Asian Pac J Cancer Prev*, **13**, 5587-91.
Hsu Y, Sood AK, Sorosky JI (2004). Docetaxel versus paclitaxel for adjuvant treatment of ovarian cancer: case-control analysis of toxicity. *Am J Clin Oncol*, **27**, 14-8.
Huang J, Cai RG, Meng PJ, et al. (2004). Phase II study of paclitaxel and cisplatin for advanced squamous-cell carcinoma of esophagus. *Chinese J Oncol*, **26**, 753-5.
International Agency for Research on Cancer;GLOBOCAN 2012. Available from URL: http://www-dep.iarc.fr/CancerMondial.htm.
Ilson DH, Ajani J, Bhalla K, et al. (1998). Phase II trial of paclitaxel, fluorouracil, and cisplatin in patients with advanced carcinoma of the esophagus. *J Clin Oncol*, **16**, 1826-34.
Ji FZ, Zhu WG, Yu CH, et al. (2013). A randomized controlled trial of intensity-modulated radiation therapy plus docetaxel and cisplatin versus simple intensity-modulated radiation therapy in II-III stage esophageal carcinoma. *Chinese J Gastrointestinal Surgery*, **16**, 842-5.
Jie. H, Kang. S (2011). The epidemiology, current status of management, challenge and future strategy for esophageal cancer in China. *China Oncology*, **21**, 501-4.
Jones SE, Erban J, Overmoyer B, et al. (2005). Randomized phase III study of docetaxel compared with paclitaxel in metastatic breast cancer. *J Clin Oncol*, **23**, 5542-51.
Lu YF, Liu ZC, Li ZH, et al. (2014). Esophageal/gastric cancer screening in high-risk populations in Henan Province, China. *Asian Pac J Cancer Prev*, **15**, 1419-22.
Mirinezhad SK, Jangjoo AG, Seyednejad F, et al. (2014). Impact of tumor length on survival for patients with resected esophageal cancer. *Asian Pac J Cancer Prev*, **15**, 691-4.
Mizota A, Shitara K, Kondo C, et al. (2011). A retrospective comparison of docetaxel and paclitaxel for patients with advanced or recurrent esophageal cancer who previously received platinum-based chemotherapy. *Oncology*, **81**, 237-42.
Nakajima M, Kato H (2013). Treatment options for esophageal squamous cell carcinoma. *Expert Opinion on Pharmacotherapy*, **14**, 1345-54.
O'Shaughnessy J, Gradishar WJ, Bhar P, Iglesias J (2013). Nab-paclitaxel for first-line treatment of patients with metastatic breast cancer and poor prognostic factors: a retrospective analysis. *Breast Cancer Res Treat*, **138**, 829-37.
Park SH, Lee WK, Chung M, et al. (2006). Paclitaxel versus docetaxel for advanced gastric cancer: a randomized phase II trial in combination with infusional 5-fluorouracil. *Anticancer Drugs*, **17**, 225-9.
Petrasch S, Welt A, Reinacher A, et al. (1998). Chemotherapy with cisplatin and paclitaxel in patients with locally advanced, recurrent or metastatic oesophageal cancer. *Br J Cancer*, **78**, 511-4.
Roth AD, Fazio N, Stupp R, et al. (2007). Docetaxel, cisplatin, and fluorouracil; docetaxel and cisplatin; epirubicin, cisplatin, fluorouracil as systemic treatment for advanced gastric carcinoma: a randomized phase II trial of the Swiss Group for Clinical Cancer Research. *J Clin Oncol*, **25**, 3217-23.
Shah MA, Jhawer M, Ilson DH, et al. (2011). Phase II study of modified docetaxel, cisplatin, and fluorouracil with bevacizumab in patients with metastatic gastroesophageal adenocarcinoma. *J Clin Oncol*, **29**, 868-74.
Shi Y, Qin R, Wang ZK, Dai GH (2013). Nanoparticle albumin-bound paclitaxel combined with cisplatin as the first-line treatment for metastatic esophageal squamous cell carcinoma. *Onco Targets Ther*, **6**, 585-91.
Sparreboom A, Scripture CD, Trieu V, et al. (2005). C omparative preclinical and clinical pharmacokinetics of a cremophor-free, nanoparticle albumin-bound paclitaxel (ABI-007) and paclitaxel formulated in cremophor (Taxol). *Clin Cancer Res*, **11**, 4136-43.
Thallinger CMR, Raderer M, Hejna M (2011). Esophageal Cancer: A Critical Evaluation of Systemic Second-Line Therapy. *J Clin Oncol*, **29**, 4709-14.
Van Cutsem E, Moiseyenko VM, Tjulandin S, et al. (2006). Phase III study of docetaxel and cisplatin plus fluorouracil compared with cisplatin and fluorouracil as first-line therapy for advanced gastric cancer: a report of the V325 Study Group. *J Clin Oncol*, **24**, 4991-7.
Van Cutsem E, Moiseyenko VM, Tjulandin S, et al. (2006). Phase III study of docetaxel and cisplatin plus fluorouracil compared with cisplatin and fluorouracil as first-line therapy for advanced gastric cancer: a report of the V325 Study Group. *J Clin Oncol*, **24**, 4991-7.
Vizcaino AP, Moreno V, Lambert R, Parkin DM (2002). Time trends incidence of both major histologic types of esophageal carcinomas in selected countries, 1973-1995. *Int J Cancer* **99**, 860-8.
Von Hoff DD, Ervin T, Arena FP, et al. (2013). Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. New Engl. *J Med*, **369**, 1691-703.
Wang T, Zhang SF, Wang L (2010). A 24-hour continuous infusion of paclitaxel in the treatment of advanced esophageal cancer. *Natl Medical J China*, **90**, 1986-8.
Wu S, Chen MY, Luo JC, Wei L, Chen Z (2012). Comparison between docetaxel plus cisplatin and cisplatin plus fluorouracil in the neoadjuvant chemoradiotherapy for local advanced esophageal squamous cell carcinoma. *Chinese J Oncol*, **34**, 873-6.
Xing PY, Li JL, Wang Y, et al. (2013). Efficacy and safety of albumin-bound paclitaxel in treating recurrent advanced non-small-cell lung cancer. *Chin J Cancer Res*, **25**, 200-5.
Zhang DS, Wang DS, Wang ZQ, et al. (2013). Phase I/II study of albumin-bound nab-paclitaxel plus gemcitabine administered to Chinese patients with advanced pancreatic cancer. *Cancer Chemother Pharmacol*, **71**, 1065-72.
Zhang P, Xie CY, Wu SX (2007). Concurrent chemoradiation with paclitaxel and platinum for locally advanced esophageal cancer. *Chinese J Oncol*, **29**, 773-7.
Zhang TR, Zhao T, Xu X, Gu XW, Pan YK (2010). Efficacy and side-effects of docetaxel combined with cisplatin on the treatment of local advanced esophageal cancer with concomitant radiation therapy. *Chinese J Oncol*, **32**, 791-4.
Zhao J, He YT, Zheng RS, Zhang SW, Chen WQ (2012). Analysis of esophageal cancer time trends in China, 1989- 2008. *Asian Pac J Cancer Prev*, **13**, 4613-7.