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ORIGINAL ARTICLE

Efficacy and safety of weekly intravenous nanoparticle albumin-bound paclitaxel for non-small cell lung cancer patients who have failed at least two prior systemic treatments

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Keywords
Nanoparticle albumin-bound paclitaxel (NAB-paclitaxel); non-small-cell lung cancer (NSCLC); secreted protein acidic and rich in cysteine (SPARC).

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Abstract

Background: The study was conducted to evaluate the efficacy and safety of weekly intravenous nanoparticle albumin-bound paclitaxel (NAB-paclitaxel) treatment in patients with advanced non-small-cell lung cancer (NSCLC) who have undergone multi-line therapy, and to investigate the association of secreted protein acidic and rich in cysteine (SPARC) expression status with clinical outcome.

Methods: Sixty-four patients who received NAB-paclitaxel treatment (130 mg/m^2 on days 1 and 8 of a 21 day cycle) as third line or further systemic treatment from 1 May 2011 to 30 June 2014 were included in this retrospective analysis. Tumor tissue was available in 28 patients for analysis of SPARC expression by immunohistochemistry.

Results: Sixty-two patients had response evaluation and complete survival follow-up data; 83.9% received the weekly NAB-paclitaxel as fourth-line treatment or beyond. The objective response and disease control rates (n = 62) were 16.1% (10/62) and 64.5% (40/62), respectively. The median progression-free and overall survival rates were 3.7 (95% confidence interval 2.6–4.8) and 9.8 months (95% confidence interval 6.9–12.8), respectively. Previous treatment with taxane did not affect the response to NAB-paclitaxel. The main grade 3–4 toxicities experienced were neutropenia (9.4%) and leukopenia (7.8%). Patients with SPARC expression in tumor stroma but not in cancer cells had poorer progression-free survival compared with those with negative SPARC expression in tumor stroma cells (3.3 vs. 5.0 months, P = 0.036).

Conclusion: Weekly NAB-paclitaxel might be effective for heavily pretreated NSCLC patients. SPARC expression in tumor stroma cells might be a potential negative predictor of NAB-paclitaxel.

Introduction

Lung cancer is the most common malignant disease and the leading cause of cancer-related death worldwide.[1] With the development of novel antitumor agents, including targeted and anti-emetic drugs of low toxicities, more and more patients at advanced stage can maintain good performance status in order to continue subsequent treatment after completing standard first and second-line treatments. However, there are few recommendations for third-line chemotherapy or beyond for these patients and palliative care remains the standard approach. Chemotherapy drugs that can present good, well-tolerated clinical outcomes in patients who have failed multi-line therapy are urgently required.

Paclitaxel is one of the most widely used and effective antitumor agents derived from natural sources and plays

an important role in non-small-cell lung cancer (NSCLC).[2–4] Traditional solvent-based paclitaxel is associated with hypersensitivity reactions to the polyoxyethylated castor oil in which it is dissolving. Therefore, pretreatment with a large quantity of drugs, such as corticosteroids and antihistamines, is required. As is universally known, many patients with lung cancer have a series of comorbidities, such as hypertension and diabetes, which limit the use of high dose steroids. Nanoparticle albumin-bound paclitaxel (NAB-paclitaxel) is an albumin-bound formulation of paclitaxel and allows the administration of paclitaxel without the use of lipid-based solvents, which reduces the risk of hypersensitive reactions, and can therefore be administered without the need for corticosteroid and antihistamine premedication.[5,6]

Furthermore, albumin has the potential to increase drug delivery to tumors.[7,8] Equitoxic doses of NAB-paclitaxel have been much higher than those of traditional paclitaxel in both preclinical and clinical studies.[9,10] NAB-paclitaxel has been studied as a first-line therapy and has achieved convincing antitumor activity in advanced NSCLC patients.[11,12] However, compared with the standard first-line regimen of paclitaxel in combination with platinum, NAB-paclitaxel alone did not present a better clinical outcome. As a first-line therapeutic strategy, NAB-paclitaxel failed to demonstrate any advantage beyond previous standard chemotherapy and is less cost-effective than traditional paclitaxel.[13] However, there is currently limited evidence to indicate that NAB-paclitaxel may be a subsequent choice for advanced NSCLC patients who have failed multi-lines of chemotherapy and targeted therapy.[14]

Notably, albumin has the natural ability to promote drug delivery to tumors by initiating albumin receptor (gp60)-mediated transcytosis across endothelial cells, accumulating the drug in tumors by binding to secreted protein acidic and rich in cysteine (SPARC), a well-known matricellular molecule involved in multiple processes in various cancers.[7,9] SPARC may help to facilitate metastasis by increasing the migration and invasion capacity of prostate and breast cells in vitro.[15,16] Several studies have shown that SPARC overexpression is associated with poor prognosis.[17–20] Infante *et al.* investigated whether different distributions of SPARC expression in cancer or tumor stromal cells possessed different clinical significance for resectable pancreatic adenocarcinoma. The results showed that patients whose tumor stromal cells expressed SPARC had poor survival compared with those whose tumor stroma cells did not express SPARC (hazard ratio [HR] 1.89, 95% confidence interval [CI] 1.31–2.74; $P = 0.001$).[21] However, the relationship between the status of SPARC expression in tumor stromal cells and the efficacy of NAB-paclitaxel treatment in advanced NSCLC has been not investigated.

Herein, we retrospectively analyzed clinical outcome and safety in 64 advanced NSCLC patients who received weekly doses of NAB-paclitaxel as subsequent therapy after previous failed multi-line therapy. SPARC expression in cancer or tumor stroma cells and the relationship between SPARC expression and the response to NAB-paclitaxel was evaluated.

Methods

Patients

From 1 May 2011 to 30 June 2014 in our department, 64 consecutive patients received weekly NAB-paclitaxel as third-line (16.1%) or further (83.9%) chemotherapy treatment for recurrent advanced NSCLC. All patients had been histologically or cytologically diagnosed with NSCLC. Prior treatment with epidermal growth factor receptor-tyrosine kinase inhibitors (EGFR-TKIs) or taxanes (paclitaxel or docetaxel) for advanced disease was permitted. All patients had an expected survival of ≥12 weeks with adequate hematologic, hepatic, and renal function. Eastern Cooperative Oncology Group performance status was 0–2. Patients with peripheral neuropathy were excluded. Detailed records of age, gender, smoking history, pathological diagnosis, tumor stage at NAB-paclitaxel administration, prior antitumor therapy, EGFR mutation status, and other clinical data were obtained from all patients. To investigate the relationship between response and SPARC expression in cancer or tumor stroma cells, we collected as many tumor tissue samples as possible. Only 28 patients had tumor tissue available for SPARC analysis. The Institutional Ethic Committee at Peking University Cancer Hospital approved this study.

Methods

Nanoparticle albumin-bound-paclitaxel (Abraxane, Abraxis, Summit, NJ, USA; 100 mg/vial) was used as monotherapy at a dose of 130 mg/m^2 (intravenous infusion for 30 minutes). The drug was administered on days 1 and 8 in a cycle. Treatment was repeated every three weeks until disease progression or unacceptable toxicity. Two patients could not tolerate the continuous NAB-paclitaxel therapy because of serious adverse events, thus we only have an evaluation of their safety data. The remaining 62 patients received at least one cycle of NAB-paclitaxel and were included in the response analyses. Objective efficacy was evaluated using Response Evaluation Criteria in Solid Tumors version 1.1 every two cycles, except when patients' symptoms obviously deteriorated. Tumor responses were analyzed based on the investigator's evaluation of radiologically and clinically detected target

lesions, including complete response (CR), partial response (PR), stable disease (SD), progressive disease (PD), objective response rate (ORR = CR + PR), and disease control rate (DCR = CR + PR + SD). Adverse events (AEs) were graded according to the National Cancer Institute Common Toxicity Criteria for Adverse Events version 4.0. Progression-free survival (PFS) was defined as the time from the first administration of NAB-paclitaxel to the first objective progression of disease. Overall survival (OS) was defined as the time from the first administration of NAB-paclitaxel to death or loss of follow-up. If the patient remained alive at the last follow-up, the data was treated as censored. The authors had access to identifying information during and after data collection.

Immunohistochemistry

Immunohistochemistry (IHC) was used to demonstrate the presence and location of SPARC in tumor tissue samples. Briefly, dried five-micron slides with formalin-fixed and paraffin-embedded tissue were prepared. Antigens were retrieved using ethylene-diamine-tetraacetic acid buffer and incubation at 100°C for 15 minutes. Slides were then incubated overnight at 4°C with monoclonal mouse anti-osteonectin/SPARC antibody (Invitrogen, Carlsbad, CA, USA) at 7 μg/mL. A two-step polymer-horseradish peroxidase method (GTVision, Beijing, China) was used for detection and 3,3′-diaminobenzidine-tetrahydrochloride staining. No staining was observed for the negative control, which was incubated with phosphate buffered saline instead of monoclonal mouse anti-osteonectin/SPARC antibody. Positive IHC was defined if more than 10% of cancer or tumor stroma cells were stained. Two different pathologists independently evaluated the results of IHC staining.

Statistical methods

All data were summarized descriptively, and two-sided 95% CIs were presented. PFS and OS were summarized using Kaplan–Meier methods. The indexes affecting PFS and OS were analyzed using the Cox regression model.

Results

The baseline characteristics of the 62 patients are presented in Table 1 (except the two patients who discontinued chemotherapy as a result of severe adverse events). All patients were categorized as clinical stage IV; 83.9% of patients received NAB-paclitaxel as fourth-line therapy or beyond.

Table 1 Baseline characteristics of patients treated with NAB-paclitaxel (n = 62)

Characteristic	Number of patients	Percentage (%)
Age (years)		
<65	50	80.6
≥65	12	19.4
Gender		
Female	27	43.5
Male	35	56.5
ECOG performance status		
0–1	51	82.3
2	11	17.7
Tumor pathological type		
Adenocarcinoma	46	74.2
Squamous carcinoma	14	22.6
Non-small cell lung cancer	2	3.2
Line of chemotherapy		
3 lines	10	16.1
≥4 lines	52	83.9
Smoking history		
Smoker	30	48.4
Non-smoker	32	51.6
EGFR gene		
Wild-type	39	62.9
Mutant	21	33.9
Unknown	2	3.2
Pre-existing comorbidities		
Yes	27	43.5
No	35	56.5

ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor.

Efficacy

Response evaluation was performed for 62 patients. The ORR for NAB-paclitaxel was 16.1% (10/62) and the DCR (CR + PR + SD) was 64.5% (40/62). Up to 30 November 2016, the median PFS was 3.7 months (95% CI 2.6–4.8) and the median OS was 9.8 months (95% CI 6.9–12.8) (Fig 1). All nine patients with PR were diagnosed with adenocarcinoma, eight had received previous solvent-based paclitaxel or docetaxel therapy, and eight received NAB-paclitaxel as fourth-line or further chemotherapy.

Epidermal growth factor receptor mutation status was detected in 60 patients and 21 (32.3%) cases presented EGFR mutation. No statistically significant differences in PFS and OS after NAB-paclitaxel treatment were observed between EGFR mutated and wild-type patients ($P > 0.05$). Two of the patient samples were insufficient; therefore the pathology could not be further classified. No correlations were observed between age, gender, pathology, PS status, or previous antitumor therapy and clinical outcome of NAB-paclitaxel (Table 2). Cox regression analysis showed that response was related with both OS and PFS (Fig 2).

Pearson's correlation analysis was conducted to further determine whether previous solvent-based paclitaxel or

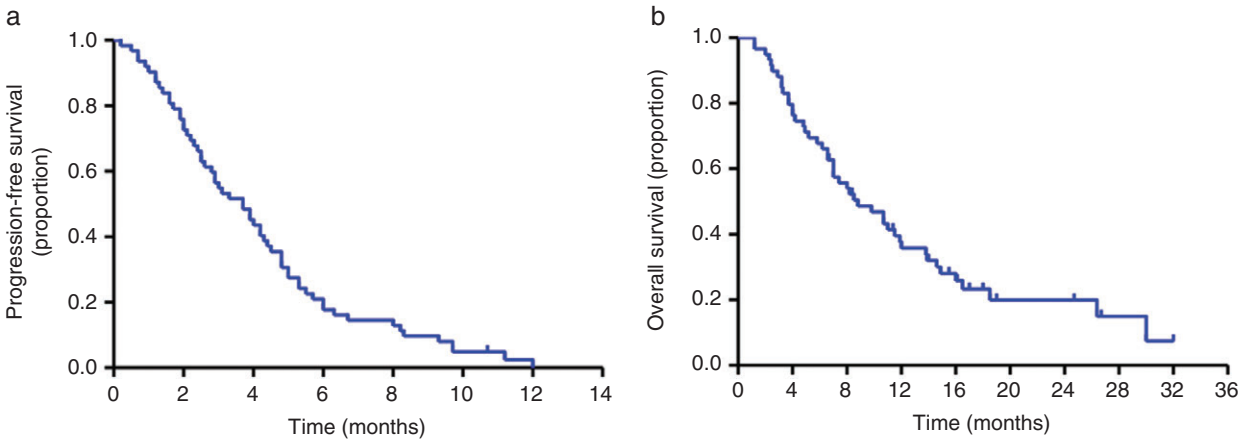

Figure 1 (**a**) Progression-free survival (median PFS 3.7 months, 95% confidence interval 2.6–4.8 months) and (**b**) overall survival (median OS 9.8 months, 95% confidence interval: 6.8–12.8 months) curves of the 62 patients evaluated for response.

docetaxel treatment could influence the response to NAB-paclitaxel. Our results indicated that previous treatment with solvent-based paclitaxel or docetaxel did not affect the response to NAB-paclitaxel. However, patients who achieved disease control after taxane treatment had a tendency to present better efficacy of subsequent NAB-paclitaxel treatment than patients in whom taxane treatment had failed, although the results did not reach statistical significance (DCR 72.4% vs. 47.6%, $P = 0.075$) (Table 3).

Table 2 Analysis of factors related to the efficacy of NAB-paclitaxel in advanced NSCLC patients ($n = 62$)

Characteristic	N	PFS (95% CI)	*P*	OS (95% CI)	*P*
Age (years old)			0.092		0.805
<65	50	3.0 (2.0–4.0)		8.8 (5.9–11.7)	
≥65	12	5.3 (3.8–6.8)		11.0 (0.1–21.9)	
Gender			0.208		0.057
Male	35	2.9 (1.8–4.0)		7.4 (5.5–9.3)	
Female	27	4.4 (3.5–5.2)		13.8 (10.1–17.5)	
Pathology			0.651		0.610
Adenocarcinoma	46	3.3 (1.9–4.7)		10.7 (6.6–14.8)	
Squamous cell carcinoma	14	3.7 (1.5–5.9)		8.0 (3.1–12.9)	
ECOG PS (before NAB-paclitaxel treatment)			0.274		0.536
0 ~ 1	51	3.1 (2.0–4.2)		8.8 (5.4–12.2)	
2	11	5.0 (2.7–7.3)		11.9 (6.2–17.6)	
Response			0.000		0.000
PR + SD	40	4.8 (4.2–5.4)		12.0 (8.7–15.3)	
PD	22	1.6 (1.1–2.1)		4.8 (2.7–6.9)	
Smoking status			0.515		0.055
No	32	4.0 (2.8–5.2)		12.0 (7.9–16.1)	
Current or former smoker	30	2.5 (1.4–3.6)		7.0 (4.8–9.2)	
EGFR-TKI treatment			0.985		0.593
Yes	56	3.7 (2.4–5.0)		9.8 (6.4–13.2)	
No	6	2.1 (0–4.5)		4.9 (0–11.6)	
Previous treatment by paclitaxel or docetaxel			0.557		0.873
Yes	50	3.3 (2.2–4.4)		8.8 (5.5–12.1)	
No	12	3.9 (1.4–6.4)		10.7 (3.9–17.5)	
EGFR mutation			0.291		0.750
Positive	21	4.4 (3.2–5.6)		8.8 (5.1–12.5)	
Negative	39	2.9 (1.6–4.2)		11.0 (6.4–15.6)	

CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR-TKI, epidermal growth factor receptor-tyrosine kinase inhibitor; NSCLC, non-small cell lung cancer; OS, overall survival; PD, progressive disease; PFS, progression free survival; PR, partial response; SD, stable disease.

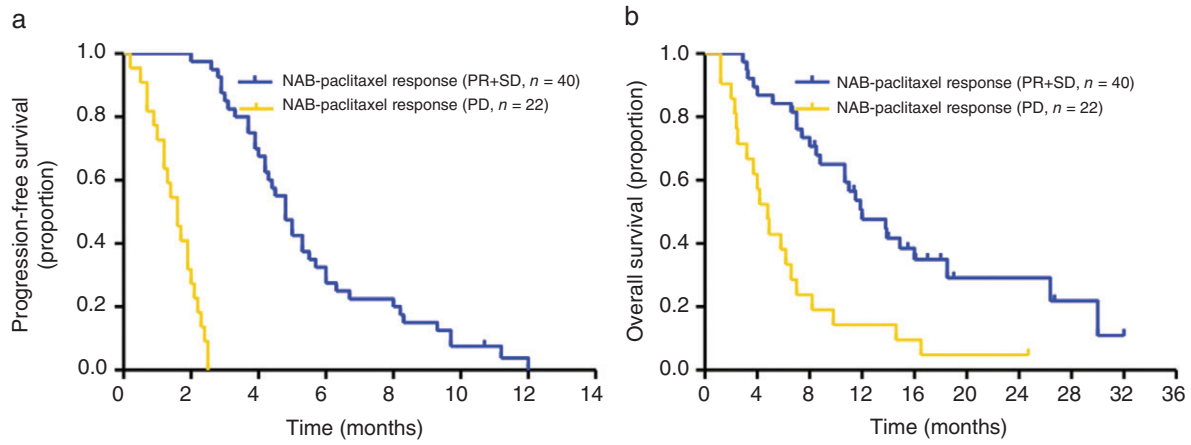

Figure 2 (**a**) Progression-free survival (PFS) and (**b**) overall survival (OS) curves stratified by response to nanoparticle albumin-bound (NAB)-paclitaxel. PD, progressive disease; PR, partial response; SD, stable disease.

Secreted protein acidic and rich in cysteine expression and its correlation to nanoparticle albumin-bound paclitaxel response

Only 28 of the patients included in the study were able to provide enough tumor tissue to test SPARC expression. We investigated SPARC expression in cancer and tumor stroma cells. In tumor stroma cells, SPARC expression was most clearly observed in the cytoplasm of peritumoral fibroblasts. The extracellular matrix and other local inflammatory cells (macrophages and lymphocytes) did not show SPARC expression. Nine patients (32.1%) were classified as cancer cell negative/tumor stroma cell negative, three (10.7%) as cancer cell positive/tumor stroma cell negative, three (10.7%) as cancer cell negative/tumor stroma cell positive, and 13 patients (46.5%) were classified as cancer cell positive/tumor stroma cell positive (Fig 3).

Because of the limited number of patients, we analyzed the associations of SPARC expression in cancer and tumor stroma cells with response to NAB-paclitaxel (Table 4). SPARC expression in tumor stroma cells was correlated with response to NAB-paclitaxel, with 5.0 and 3.3 months for SPARC negative and SPARC positive, respectively (Fig 4); P was statistically significant ($P = 0.036$). However, there was no correlation between SPARC expression in cancer cells and response to NAB-paclitaxel.

Safety

Treatment was well tolerated in most patients receiving NAB-paclitaxel at the full dose (with the exception of two patients). All patients received 0.5–10 cycles (median: four cycles) of NAB-paclitaxel monotherapy, while 10 received only 0.5–1 cycle of NAB-paclitaxel because of worsening symptoms. The most frequent treatment related AEs are presented in Table 5. The major grade 3–4 toxicities were leukopenia (6/64, 9.4%), neutropenia (5/64, 7.8%), and peripheral neuropathy (2/64, 3.1%). Other NAB-paclitaxel associated toxicities, including gastrointestinal AEs, rash, and anemia were mild to moderate and easily managed. Two patients had to discontinue chemotherapy because of drug induced serious fatigue and serious anorexia, respectively.

Discussion

Along with the development of targeted agents based on driver genes related to lung cancer and low toxicity chemotherapy, NSCLC patient survival, particularly in regard to lung adenocarcinoma, has been greatly improved. Prolongation of survival duration increases the opportunity for patients to receive multi-line treatment. Chemotherapy remains an important strategy, not only for EGFR wild-type patients, but also for patients with EGFR mutations.

Table 3 Correlation of previous taxane response and NAB-paclitaxel efficacy in advanced NSCLC ($n = 50$)

		Response of NAB-paclitaxel		
		DCR	PD	Total
Response of previous solvent-based paclitaxel or docetaxel	DCR	21	8	29
	PD	10	11	21
Total		31	19	50

DCR, disease control rate; NAB, nanoparticle albumin-bound; NSCLC, non-small-cell lung cancer; PD, progressive disease.

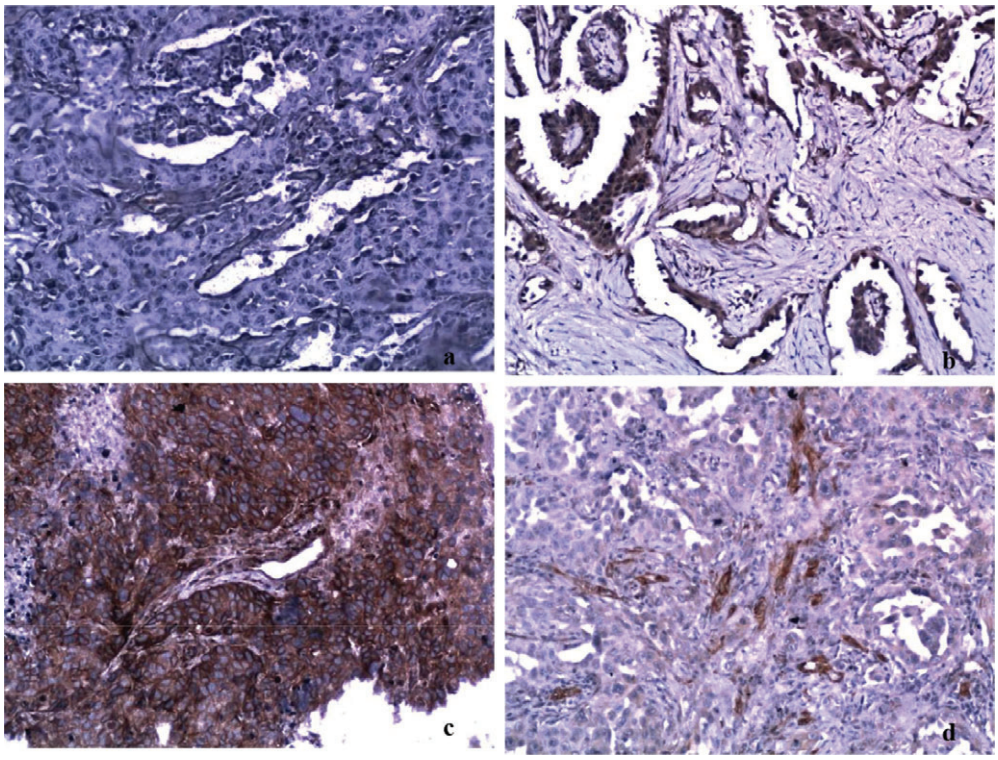

Figure 3 Immunohistochemical expression of secreted protein acidic and rich in cysteine (SPARC): (**a**) cancer and tumor stromal cell negative; (**b**) cancer cell positive, tumor stromal cell negative; (**c**) cancer and tumor stromal cell positive; and (**d**) cancer cell negative, tumor stromal cell positive.

However, to date, a therapeutic regimen after second or third-line treatment failure is still required.

In our study, weekly administration of NAB-paclitaxel displayed convincing therapeutic efficacy in patients who had previously undergone multi-lines of therapy for advanced NSCLC and was well tolerated. More than 80% of the patients in this study received NAB-paclitaxel as fourth-line therapy or beyond, and the ORR and DCR were 16.1% and 64.5%, respectively, with a median PFS of 3.7 months (95% CI 2.6–4.8) and median OS of 9.8 months (95% CI 6.9–12.8). In particular, in the 10 patients who reached PR, eight had received 4–6 previous lines of therapy, including solvent-based paclitaxel or docetaxel, and all were categorized as clinical stage IV at the beginning of NAB-paclitaxel treatment. Similar circumstances occurred in patients who achieved SD. Previous phase III trials for second or third-line therapy of NSCLC patients have reported ORRs of 7.6–9.1%, median PFS of 2.0–2.9 months, and median OS of 6.7–8.3 months.[22–26]

In this study, more than 50% of patients received at least four cycles of NAB-paclitaxel. More than half of the patients had multiple comorbidities, such as hypertension, diabetes, hepatitis B, and heart disease, which inevitably affected functional status, general health, and chemotherapy tolerance. Overall, a weekly dose of 130 mg/m^2 NAB-paclitaxel was well tolerated and no treatment-related death occurred. Patients who were not treated with corticosteroids before NAB-paclitaxel experienced no hypersensitivity. In a randomized phase III trial, compared directly

Table 4 SPARC expression status in cancer or tumor stroma cells with response to NAB-paclitaxel

SPARC expression status	No. of patients	PFS (m) 95% CI	*P*	OS (m) 95% CI	*P*
Positive in cancer cell	16	3.7 (2.9–4.5)	0.342	11.5 (3.0–24.0)	0.627
Negative in cancer cell	12	4.3 (0.7–7.9)		12.0 (3.0–21.0)	
Positive in tumor stroma cell	16	3.3 (0.6–6.0)	0.036	11.5 (1.1–21.9)	0.718
Negative in tumor stroma cell	12	5.0 (2.4–7.6)		12.2 (3.0– 21.0)	

CI, confidence interval; m, months; NAB, nanoparticle albumin-bound; OS, overall survival; PFS, progression-free survival; SPARC, secreted protein acidic and rich in cysteine.

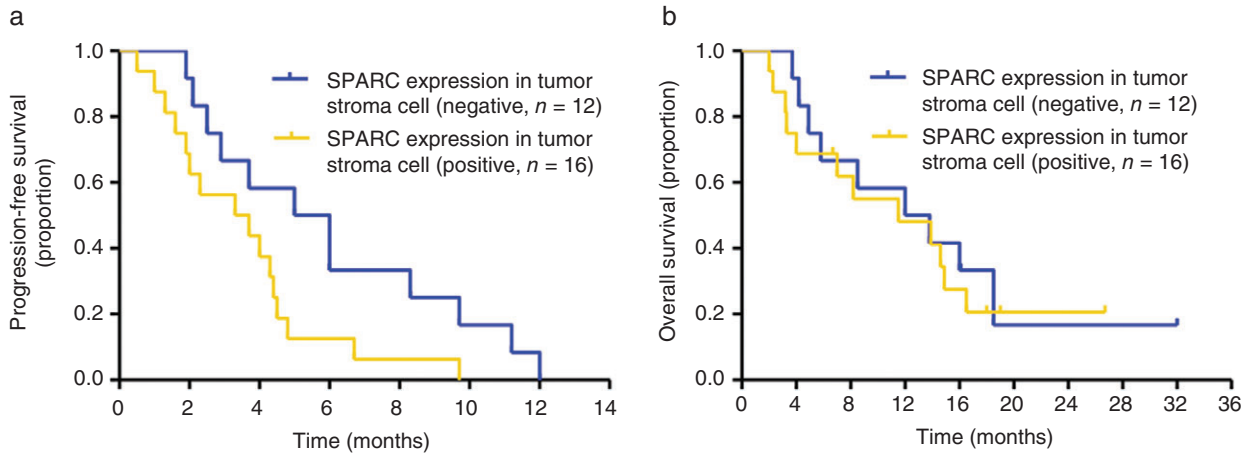

Figure 4 (**a**) Progression-free survival (PFS) and (**b**) overall survival (OS) curves stratified by secreted protein acidic and rich in cysteine (SPARC) expression in tumor stroma cells (n = 28).

with solvent-based paclitaxel plus carboplatin, a weekly dose of 100 mg/m^2 NAB-paclitaxel (on days 1 and 8) plus carboplatin administered every three weeks showed significantly higher response rates and time to progression, with a decreased incidence of grade 4 neutropenia in 1038 untreated patients with stage IIIb–IV NSCLC.[13] However, as anticipated with a higher paclitaxel dose, dose-limiting toxicities included 0.5% grade 3 and 4 peripheral neuropathy in the NAB-paclitaxel group compared with 2.3% in the solvent-based paclitaxel group ($P < 0.001$). In our study, the major grade 3–4 toxicities were leukopenia (6/64, 9.4%), neutropenia (5/64, 7.8%), and peripheral neuropathy (2/64, 3.1%), which were resolved with appropriate support treatment. Peripheral neuropathy was mild to moderate and was alleviated when NAB-paclitaxel treatment was discontinued. Weekly administration of NAB-paclitaxel seems to be an ideal regimen for NSCLC patients, especially when the use of steroids is contraindicated or after multiple lines of treatment.

Because solvent-based paclitaxel or docetaxel is the standard first or second-line therapy regimen, it is necessary to determine whether traditional taxane may influence subsequent NAB-paclitaxel therapy. Our data showed that previous treatment with solvent-based paclitaxel or docetaxel did not affect the response to NAB-paclitaxel. Similar results were observed in several prospective clinical trials, for example, in breast cancer patients who had failed previous taxane treatment received NAB-paclitaxel.[27,28] As such, we conclude that previous taxane therapy does not affect the response to NAB-paclitaxel, which might be attributed to the different action mechanisms of the two kinds of agents. However, we found that the patients who achieved disease control after solvent-based paclitaxel or docetaxel administration benefitted more from NAB-paclitaxel than patients who did not, although the result did not reach statistical significance. This may be a result of NAB technology, which, when albumin with paclitaxel particles are combined, enables a greater amount of NAB-paclitaxel to enter the tumor tissue, with high intra-tumor drug concentration.

Whether SPARC expression is a predictor for NAB-paclitaxel therapy remains controversial. A study by Desal *et al.* showed that SPARC might be a predictive biomarker of response to NAB-paclitaxel.[29] An opposing result was

Table 5 Most frequent treatment-related adverse events (n = 64)

		Maximum grade, no. of patients (%)			
Toxicity	All	1	2	3	4
Leukopenia	23 (35.9%)	8 (12.5%)	9 (14.1%)	2 (3.1%)	4 (6.3%)
Neutropenia	19 (29.7%)	6 (9.4%)	8 (12.5%)	2 (3.1%)	3 (4.7%)
Peripheral neuropathy	16 (25.0%)	12 (18.8%)	2 (3.1%)	2 (3.1%)	0
Nausea/vomiting	7 (10.9%)	6 (9.4%)	1 (1.5%)	0	0
Elevated ALT/AST	4 (6.3%)	2 (3.1%)	2 (3.1%)	0	0
Fatigue	5 (7.8%)	2 (3.1%)	1 (1.5%)	1 (1.5%)	1 (1.5%)
Rash	2 (3.1%)	0	2 (3.1%)	0	0
Anemia	3 (4.7%)	0	2 (3.1%)	1 (1.5%)	0

ALT, alanine transaminase; AST, aspartate transaminase.

reported by Schneeweiss *et al.* in that the efficacy of NAB-paclitaxel did not seem to be associated with SPARC expression in metastatic breast cancer, in either tumor tissues or plasma samples.[30] Koukourakis *et al.* analyzed SPRAC expression in 113 tumor samples from patients with early operable NSCLC.[31] The results showed that stroma SPARC expression was linked with tumor necrosis and SPARC production by stroma cells supported a high degree of vascular maturation. Survival analysis demonstrated a significant association between stroma SPARC and poor prognosis ($P = 0.006$). However, the authors did not collect treatment data for these patients after disease relapse or progression and, thus, could not evaluate the relationship between stroma SPARC expression and response to NAB-paclitaxel. Our study showed that SPARC expression in tumor stroma cells, but not in cancer cells, was correlated with response to NAB-paclitaxel. To the best of our knowledge, this is the first time the relationship between SPARC expression in tumor stroma or cancer cells and response to NAB-paclitaxel has been investigated. However, because of the limited number of patients and the retrospective feature of this study, the predictive role of SPARC expression in tumor stroma cells to NAB-paclitaxel needs to be verified by a large sample study.

There were some limitations to our study. First, this is a retrospective study and all of the patients received NAB-paclitaxel as third-line or further treatment. In the real world, few patients accept subsequent biopsies during their disease course because of multiple reasons, including personal wishes or the difficult location of a nodule for needle biopsy. Therefore, we could only evaluate SPARC expression in the tumor samples available, and these were not real time subsequent biopsies performed before NAB-paclitaxel administration. Second, the number of enrolled patients was limited, which may lead to selection bias. Because of the expense of NAB-paclitaxel and the fact that it is not covered by medical insurance, this treatment is limited to those that can afford it. These factors indicate that we must evaluate the results of our study with caution.

In conclusion, NAB-paclitaxel displays convincing antitumor activity for the management of advanced NSCLC, even in patients who have received multiple lines of treatment. With a high therapeutic index and low side effects, weekly NAB-paclitaxel administration seems to have the ideal clinical benefit-risk ratio. A large-scale, prospective, randomized clinical study is required to provide supportive data for this regimen.

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Disclosure

No authors report any conflict of interest.

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