

A Phase II Study of S-1 and Paclitaxel Combination Therapy as a First-Line Treatment in Elderly Patients with Advanced Non-Small Cell Lung Cancer

AKIHIRO YOSHIMURA,^{a,†} YUSUKE CHIHARA,^{a,†} KOJI DATE,^b NOBUYO TAMIYA,^a YOSHIZUMI TAKEMURA,^c TATSUYA IMABAYASHI,^a YOSHIKO KANEKO,^a TADAOKI YAMADA,^a MIKIO UEDA,^d TAICHIRO ARIMOTO,^e JUNJI UCHINO,^a YOSHINOBU IWASAKI,^f KOICHI TAKAYAMA^a

^aDepartment of Pulmonary Medicine, Kyoto Prefectural University of Medicine, Kyoto, Japan; ^bDepartment of Pulmonary Medicine, Kyoto Chubu Medical Center, Kyoto, Japan; ^cDepartment of Pulmonary Medicine, Kyoto Kuramaguchi Medical Center, Kyoto, Japan;

^dDepartment of Pulmonary Medicine, Nishijin Hospital, Kyoto, Japan; ^eKyoto Industrial Health Association, Kyoto, Japan; ^fDepartment of Pulmonary Medicine, Showa General Hospital, Tokyo, Japan

[†]Contributed equally

TRIAL INFORMATION

- **ClinicalTrials.gov Identifier:** UMIN000003782
- **Sponsor(s):** Kyoto Prefectural University of Medicine
- **Principal Investigator:** Yoshinobu Iwasaki
- **IRB Approved:** Yes

LESSONS LEARNED

- Coadministration of S-1 and paclitaxel in elderly patients with advanced non-small cell lung cancer showed favorable efficacy.
- Coadministration of S-1 and paclitaxel in elderly patients with advanced non-small lung cancer showed tolerable toxicity.

ABSTRACT

Background. Although monotherapy with cytotoxic agents including docetaxel or vinorelbine are recommended for elderly patients with advanced non-small cell lung cancer (NSCLC), the outcome is not satisfactory. We evaluated the efficacy and safety of S-1 and paclitaxel (PTX) as a first-line cotreatment in elderly patients with advanced NSCLC.

Methods. Oral S-1 was administered on days 1–14 every 3 weeks at 80, 100, and 120 mg per day for patients with body surface area < 1.25 m², 1.25–1.5 m², and > 1.5 m², respectively. PTX was administered at 80 mg/m² on days 1 and 8. The primary endpoint was response rate, and secondary endpoints were progression-free survival (PFS), overall survival (OS), and safety.

Results. Seventeen patients were enrolled with response and disease control rates of 47.1% and 88.2%, respectively. Median PFS and OS were 5.6 and 35.0 months, respectively. Hematological grade 3 or 4 toxicities included leukopenia (55.8%), neutropenia (52.9%), febrile neutropenia (11.8%), and anemia (11.8%). Nonhematological grade 3 toxicities included stomatitis (23.5%), diarrhea (5.9%),

and interstitial lung disease (5.9%), and grade 5 toxicities included interstitial lung disease (5.9%).

Conclusion. This S-1 and PTX cotherapy dose and schedule showed satisfactory efficacy with mild toxicities in elderly patients with advanced NSCLC. *The Oncologist* 2019;24:459–e131

DISCUSSION

Coadministration of S-1 and PTX is expected to be especially effective in patients with NSCLC with epidermal growth factor receptor (*EGFR*) mutations, and four such patients included in this study showed prolonged survival in a subgroup analysis with a median OS of 49.8 months. In a pooled analysis of elderly patients with *EGFR* mutations, the median OS was 30.8 months [1]. Thus, the OS in our study was much longer than that reported previously, although our findings were obtained in a small sample in a subgroup analysis. Previous studies reported an inverse relationship between thymidylate synthase expression and fluorouracil (5-FU) sensitivity in colorectal and gastric

Correspondence: Junji Uchino, M.D., Ph.D., Department of Pulmonary Medicine, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, 465 Kajii-cho, Kamigyo-ku, Kyoto, Japan 6028566. Telephone: 81-75-251-5513; e-mail: uchino@koto.kpu-m.ac.jp Received October 2, 2018; accepted for publication November 23, 2018; published Online First on December 21, 2018. © AlphaMed Press; the data published online to support this summary are the property of the authors. <http://dx.doi.org/10.1634/theoncologist.2018-0858>

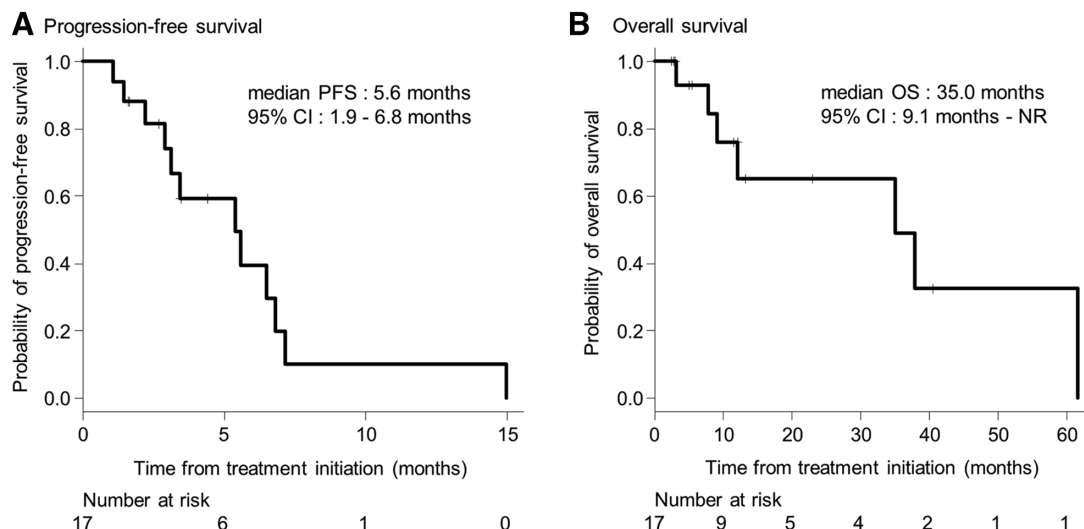


Figure 1. Kaplan-Meier plots. **(A):** Kaplan-Meier estimation of progression-free survival. **(B):** Kaplan-Meier estimation of overall survival. Abbreviations: CI, confidence interval; NR, not reached; PFS, progression-free survival.

cancers [2], and the thymidylate synthase expression in patients with NSCLC with *EGFR* mutations has been reported to be significantly lower than that in wild-type cases [3]. Moreover, thymidine phosphorylase converts 5-FU to its more active form, fluorodeoxyuridylate, and a correlation between the expression of thymidine phosphorylase and efficacy of 5-FU-based chemotherapy has been observed [4]. Because PTX upregulated the expression of thymidine phosphorylase mRNA in human gastric cancer xenografts [5], we hypothesized that the

combination of S-1 with PTX would provide good anticancer effects.

In conclusion, cotherapy with S-1 and PTX for elderly patients with advanced NSCLC showed favorable efficacy and tolerable toxicity. The results of this study met the criteria for the primary endpoint, suggesting that this regimen could be a treatment option for those patients. However, further studies are needed to compare this regimen with conventional therapy for elderly patients with advanced NSCLC.

TRIAL INFORMATION

Disease	Lung cancer – NSCLC
Stage of Disease/Treatment	Metastatic/advanced
Prior Therapy	None
Type of Study – 1	Phase II
Type of Study – 2	Single arm
Primary Endpoint	Overall response rate
Secondary Endpoint	Progression-free survival
Secondary Endpoint	Overall survival
Secondary Endpoint	Safety

Additional Details of Endpoints or Study Design

The sample size was calculated at an α error of 0.05 and β error of 0.2. The expected response rate and threshold response rate are determined to be 35% and 10%, respectively. The estimated minimum sample size was 16, and considering the potential patient dropout, we planned to enroll 18 patients.

Investigator's Analysis	Active and should be pursued further
--------------------------------	--------------------------------------

DRUG INFORMATION**Drug 1**

Generic/Working Name	S-1
Company Name	Taiho Pharmaceutical Co., Ltd.
Dose	40, 50, and 60 milligrams (mg) per squared meter (m ²)
Route	Oral (p.o.)
Schedule of Administration	S-1 was administered twice daily from day 1 to day 14. The dose of S-1 was calculated according to the patient's body surface area as follows: 40, 50, and 60 mg/m ² S-1 for body surface areas of <1.25, 1.25–1.50, and ≥ 1.50 m ² , respectively.

Drug 2

Generic/Working Name	Paclitaxel
Company Name	Bristol-Myers Squibb
Dose	PTX was fixed as 80 mg/m ²
Route	IV
Schedule of Administration	PTX was fixed as 80 mg/m ² on days 1 and 8

PATIENT CHARACTERISTICS

Number of Patients, Male	13
Number of Patients, Female	4
Stage	IIIB or IV
Age	Median (range): 79 (range, 72–84) years
Number of Prior Systemic Therapies	Median (range): not collected
Performance Status: ECOG	0 — 9 1 — 8 2 — 0 3 — 0 Unknown —
Cancer Types or Histologic Subtypes	Adenocarcinoma, 8; squamous cell carcinoma, 5; non-small cell lung carcinoma, 4.

PRIMARY ASSESSMENT METHOD

Title	Total patient population
Number of Patients Enrolled	17
Number of Patients Evaluable for Toxicity	17
Number of Patients Evaluated for Efficacy	17
Evaluation Method	RECIST 1.1
Response Assessment – CR	<i>n</i> = 0 (0%)
Response Assessment – PR	<i>n</i> = 8 (47.1%)
Response Assessment – SD	<i>n</i> = 7 (41.2%)
Response Assessment – PD	<i>n</i> = 2 (11.8%)
(Median) Duration Assessments – PFS	5.6 months; 95% CI, 1.6–6.8
(Median) Duration Assessments – OS	35.0 months; 95% CI, 9.1–NR

ADVERSE EVENTS

Name	NC/NA, %	Grade 1, %	All Cycles				All grades, %
			Grade 2, %	Grade 3, %	Grade 4, %	Grade 5, %	
Anemia	11	24	53	12	0	0	89
Febrile neutropenia	88	0	0	12	0	0	12
Neutrophil count decreased	29	0	18	35	18	0	71

Gastritis	47	35	18	0	0	0	53
Diarrhea	23	53	18	6	0	0	77
Pneumonitis	76	6	6	6	0	6	24

Adverse Events Legend

The grade 3 or higher adverse events were leukopenia (58.9%), neutropenia (52.9%), anemia (11.8%), febrile neutropenia (11.8%), stomatitis (23.5%), diarrhea (5.9%), and interstitial pneumonia (11.8%). The median number of cotherapy cycles with S-1 and PTX cycles was 4 (range 2–4). Four cycles of combination chemotherapy were completed by 52.9% (9/17) of the patients. The main reason for discontinuation was prolonged neutropenia. Dose reduction was necessary in 35.3% (6/17) of the patients. Abbreviation: NC/NA, no change from baseline/no adverse event.

Grade 3–5 adverse events	n (%)
Neutropenia	9 (52.9)
Anemia	2 (11.8)
Febrile neutropenia	2 (11.8)
Stomatitis	4 (23.5)
Diarrhea	1 (5.9)
Interstitial lung disease	1 (5.9)

SERIOUS ADVERSE EVENTS

Name	Grade	Attribution
Pneumonitis	5	Possible

Serious Adverse Events Legend

One patient who developed pneumonitis exhibited respiratory failure, and the chest computed tomography showed ground-glass opacity after 22 days of the four-cycle treatment. He died after 28 days of the four-cycle treatment, although he discontinued all suspected drugs, including S-1, and received pulsed methylprednisolone therapy. The relationship between this event and the combination therapy cannot be ruled out.

ASSESSMENT, ANALYSIS, AND DISCUSSION**Completion**

Study completed

Investigator's Assessment

Active and should be pursued further

Lung cancer is the leading cause of cancer-related deaths worldwide, and the number of elderly patients with lung cancer is increasing [6]. Non-small cell lung cancer (NSCLC) accounts for approximately 85% of lung cancer cases, and nearly 50% of patients with NSCLC are aged ≥ 70 years [7]. Approximately 50% of patients with NSCLC show metastasis at diagnosis [8], and platinum doublet therapy is recommended for patients with advanced NSCLC with good performance status. However, although platinum doublet therapy is effective in some elderly patients, it may not show adequate efficacy in others because of an unfavorable side effect profile [9, 10].

For elderly patients with advanced NSCLC without driver oncogene mutation, monotherapy with cytotoxic agents such as docetaxel, vinorelbine, or gemcitabine (GEM) are recommended, but the efficacy of these regimens has not been satisfactory [11–13]. Therefore, these patients require a more effective and safe treatment approach. Although platinum-based combination therapy has been shown to improve the overall response rate (ORR) and prolonged progression-free survival (PFS) or overall survival (OS) more than monotherapy does, coadministration may be intolerable for elderly patients because of severe toxicities [9]. Therefore, for elderly patients, it is important to select drugs without platinum agents to obtain better effects with less toxicity.

S-1 (Taiho Pharmaceutical Co., Ltd, Tokyo, Japan) is an oral fluorinated pyrimidine formulation composed of

tegafur, 5-chloro-2,4-dihydroxy-pyridine, a reversible inhibitor of dihydropyrimidine dehydrogenase, and potassium oxonate. In a phase II study of elderly patients with advanced NSCLC, S-1 monotherapy as a first-line treatment was reported to be effective and well tolerated [14] with an ORR and median OS of 27.6% and 12.1 months and no grade 4 toxicity.

Paclitaxel (PTX; Bristol-Myers Squibb, NY) is a microtubule-stabilizing taxane drug. It enhances tubulin polymerization and inhibits spindle fiber function, resulting in inhibition of mitosis and cell division. Several phase II studies on the efficacy and safety of PTX monotherapy for elderly patients with advanced NSCLC have been reported, with ORRs of 23%–41.2% and median OS values of 9.8–10.3 months [15, 16]. However, for elderly patients with advanced NSCLC, the combination of carboplatin and PTX was not significantly superior to PTX monotherapy and also showed more toxicity than the monotherapy did [9].

The combination of S-1 and PTX is expected to show a greater synergistic effect than that of either drug alone. Thymidine phosphorylase (TP) converts fluorouracil (5-FU) to fluorodeoxyuridylate, the more active metabolite. The efficacy of 5-FU-based anticancer agents is correlated with the expression of TP mRNA [4]. The expression levels of TP mRNA were upregulated by PTX in human gastric cancer xenografts [17], and significant tumor reduction was observed with PTX in combination with S-1 in a mouse

model of human breast cancer [18]. Moreover, some clinical studies have already reported that the combination of S-1 and PTX is effective and tolerable for the treatment of patients with advanced NSCLC [19] as well as advanced gastric cancer [20–22].

We previously reported the results of a phase I study of S-1 and PTX coadministration for elderly patients with advanced NSCLC [23]. We determined that the recommended dose of S-1 and PTX was 80 mg/m² during days 1–14 and days 1 and 8, respectively. In this study, we conducted a phase II study of S-1 and PTX cotherapy for elderly patients with advanced NSCLC.

The results of this phase II study revealed that it met the criteria for the primary endpoint. The S-1 and PTX cotherapy was the treatment option for elderly patients with advanced NSCLC.

Combination chemotherapy regimens, both platinum- and non-platinum-based, improve patient prognoses significantly compared with monotherapy [9, 24]. However, compared with non-platinum-based chemotherapy, platinum-based chemotherapy shows severe toxicities in elderly patients [25]. Therefore, non-platinum-based combination chemotherapies are promising for the treatment of elderly patients. In fact, non-platinum-based cotherapy such as S-1 plus GEM has been reported to be effective and well tolerated [26, 27].

Furthermore, previous studies have reported ORR, median PFS, and median OS of 27.0%–40.0%, 4.2–6.4 months, and 12.9–17.8 months, respectively, in elderly patients who received cotherapy with S-1 and GEM [26, 27], and these results were not superior to those of our study (Fig. 1). Therefore, cotherapy with S-1 and PTX seemed to be effective and well tolerated. The results of this study indicate that it met the criteria for the primary endpoint of ORR. In this study, the patients received a combination of S-1 and PTX and developed several adverse events, with hematological toxicities such as neutropenia occurring frequently. However, the rates of adverse events were similar to those with docetaxel monotherapy [28], which has been recommended for elderly patients with advanced NSCLC. Moreover, the reported grade 3 or 4 hematological toxicities in elderly patients who received a combination of S-1 with GEM were leukopenia (27.0%–29.0%), neutropenia (24.0%–45.9%), and anemia (0%–13.5%) [26, 27]. These results were equivalent to the findings of our study, indicating mild toxicities with S-1 and PTX cotherapy.

REFERENCES

- Morikawa N, Minegishi Y, Inoue A et al. First-line gefitinib for elderly patients with advanced NSCLC harboring EGFR mutations. A combined analysis of North-East Japan Study Group studies. *Expert Opin Pharmacother* 2015;16:465–472.
- Salonga D, Danenberg KD, Johnson M et al. Colorectal tumors responding to 5-fluorouracil have low gene expression levels of dihydropyrimidine dehydrogenase, thymidylate synthase, and thymidine phosphorylase. *Clin Cancer Res* 2000;6:1322–1327.
- Ren S, Chen X, Kuang P et al. Association of *EGFR* mutation or *ALK* rearrangement with expression of DNA repair and synthesis genes in never-smoker women with pulmonary adenocarcinoma. *Cancer* 2012;118:5588–5594.
- de Bruin M, van Capel T, Van der Born K et al. Role of platelet-derived endothelial cell growth factor/thymidine phosphorylase in fluoropyrimidine sensitivity. *Br J Cancer* 2003;88:957–964.
- Sakurai Y, Yoshida I, Kamoshida S et al. Changes of gene expression of thymidine phosphorylase, thymidylate synthase, dihydropyrimidine dehydrogenase after the administration of 5'-deoxy-5-fluorouridine, paclitaxel and its combination in human gastric cancer xenografts. *Anticancer Res* 2008;28:1593–1602.
- Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. *CA Cancer J Clin* 2015;65:5–29.
- Provencio M, Camps C, Alberola V et al. Lung cancer and treatment in elderly patients: The Achilles Study. *Lung Cancer* 2009;66:103–106.
- Kocher F, Hilbe W, Seeber A et al. Longitudinal analysis of 2293 NSCLC patients: A comprehensive study from the TYROL registry. *Lung Cancer* 2015;87:193–200.

Coadministration of S-1 and PTX is expected to be especially effective in patients with NSCLC with epidermal growth factor receptor (*EGFR*) mutations, and four such patients included in this study showed prolonged survival in a subgroup analysis with a median OS of 49.8 months. In a pooled analysis of elderly patients with *EGFR* mutations, the median OS was 30.8 months [1]. Thus, the OS in our study was much longer than that reported previously, although our findings were obtained for a small sample in a subgroup analysis.

Previous studies reported an inverse relationship between thymidylate synthase expression and 5-FU sensitivity in colorectal and gastric cancers [2]. Thymidylate synthase expression in patients with NSCLC with *EGFR* mutations has been reported to be significantly lower than that in wild-type cases, suggesting that tumors in these patients may show greater sensitivity [3]. Moreover, thymidine phosphorylase converts 5-FU to its more active form, fluorodeoxyuridylate, and a correlation between the expression of thymidine phosphorylase and efficacy of 5-FU-based chemotherapy has been observed [4]. In several phase II studies, the S-1 plus paclitaxel combination was effective and tolerated by patients with advanced gastric cancer [20–22], and a retrospective study by Aono et al. showed that S-1 and paclitaxel combination therapy is effective for pretreated advanced NSCLC, with a response rate of 32.6% and median PFS of 253 days [19]. Because PTX upregulated the expression of thymidine phosphorylase mRNA in human gastric cancer xenografts [5], the combination of S-1 with PTX would provide good anticancer effects.

In conclusion, coadministration of S-1 and PTX for elderly patients with advanced NSCLC showed favorable efficacy and tolerable toxicity. The results of this study met the criteria for the primary endpoint, suggesting that this regimen could be a treatment option for those patients. However, further studies are needed to compare this regimen with conventional therapy for elderly patients with advanced NSCLC.

DISCLOSURES

Junji Uchino: Eli Lilly Japan K.K. (RF); **Koichi Takayama:** Chugai-Roche Co. and Ono Pharmaceutical Co. (RF), AstraZeneca, Chugai-Roche Co., MSD-Merck Co., Eli Lilly Co., Boehringer-Ingelheim Co., Daiichi-Sankyo Co. (H). The other authors indicated no financial relationships.

(C/A) Consulting/advisory relationship; (RF) Research funding; (E) Employment; (ET) Expert testimony; (H) Honoraria received; (OI) Ownership interests; (IP) Intellectual property rights/inventor/patent holder; (SAB) Scientific advisory board

9. Quoix E, Zalcman G, Oster JP et al. Carboplatin and weekly paclitaxel doublet chemotherapy compared with monotherapy in elderly patients with advanced non-small-cell lung cancer: IFCT-0501 randomised, phase 3 trial. *Lancet* 2011;378:1079–1088.
10. Abe T, Takeda K, Ohe Y et al. Randomized phase III trial comparing weekly docetaxel plus cisplatin versus docetaxel monotherapy every 3 weeks in elderly patients with advanced non-small-cell lung cancer: The intergroup trial JCOG0803/WJOG4307L. *J Clin Oncol* 2015;33:575–581.
11. Kudoh S, Takeda K, Nakagawa K et al. Phase III study of docetaxel compared with vinorelbine in elderly patients with advanced non-small-cell lung cancer: Results of the West Japan Thoracic Oncology Group Trial (WJTOG 9904). *J Clin Oncol* 2006;24:3657–3663.
12. Effects of vinorelbine on quality of life and survival of elderly patients with advanced non-small-cell lung cancer. The Elderly Lung Cancer Vinorelbine Italian Study Group. *J Natl Cancer Inst* 1999;91:66–72.
13. Gridelli C, Perrone F, Gallo C et al. Chemotherapy for elderly patients with advanced non-small-cell lung cancer: The Multicenter Italian Lung Cancer in the Elderly Study (MILES) phase III randomized trial. *J Natl Cancer Inst* 2003;95:362–372.
14. Nishiyama O, Taniguchi H, Kondoh Y et al. Phase II study of S-1 monotherapy as a first-line treatment for elderly patients with advanced non-small-cell lung cancer. *Anticancer Drugs* 2011;22:811–816.
15. Fidiás P, Supko JG, Martins R et al. A phase II study of weekly paclitaxel in elderly patients with advanced non-small cell lung cancer. *Clin Cancer Res* 2001;7:3942–3949.
16. Nakamura Y, Sekine I, Furuse K et al. Retrospective comparison of toxicity and efficacy in phase II trials of 3-h infusions of paclitaxel for patients 70 years of age or older and patients under 70 years of age. *Cancer Chemother Pharmacol* 2000;46:114–118.
17. Sakurai Y, Yoshida I, Kamoshida S et al. Changes of gene expression of thymidine phosphorylase, thymidylate synthase, dihydropyrimidine dehydrogenase after the administration of 5'-deoxy-5-fluorouridine, paclitaxel and its combination in human gastric cancer xenografts. *Anticancer Res* 2008;28:1593–1602.
18. Nukatsuka M, Fujioka A, Nakagawa F et al. Antimetastatic and anticancer activity of S-1, a new oral dihydropyrimidine-dehydrogenase-inhibiting fluoropyrimidine, alone and in combination with paclitaxel in an orthotopically implanted human breast cancer model. *Int J Oncol* 2004;25:1531–1536.
19. Aono N, Ito Y, Nishino K et al. A retrospective study of the novel combination of paclitaxel and S1 for Pretreated advanced non-small cell lung cancer. *Chemotherapy* 2012;58:454–460.
20. Nakajo A, Hokita S, Ishigami S et al. A multicenter phase II study of biweekly paclitaxel and S-1 combination chemotherapy for unresectable or recurrent gastric cancer. *Cancer Chemother Pharmacol* 2008;62:1103–1109.
21. Mochiki E, Ohno T, Kamiyama Y et al. Phase I/II study of S-1 combined with paclitaxel in patients with unresectable and/or recurrent advanced gastric cancer. *Br J Cancer* 2006;95:1642–1647.
22. Sugimoto N, Narahara H, Sakai D et al. The effectiveness of S-1 based sequential chemotherapy as second-line treatment for advanced/recurrent gastric cancer [in Japanese]. *Gan To Kagaku Ryoho* 2009;36:417–424.
23. Chihara Y, Date K, Takemura Y et al. Phase I study of S-1 plus paclitaxel combination therapy as a first-line treatment in elderly patients with advanced non-small cell lung cancer. *Invest New Drugs* 2018 [Epub ahead of print].
24. Frasci G, Lorusso V, Panza N et al. Gemcitabine plus vinorelbine versus vinorelbine alone in elderly patients with advanced non-small-cell lung cancer. *J Clin Oncol* 2000;18:2529–2536.
25. Santos FN, de Castria TB, Cruz MR et al. Chemotherapy for advanced non-small cell lung cancer in the elderly population. *Cochrane Database Syst Rev* 2015;(10):CD010463.
26. Seto T, Yamanaka T, Wasada I et al. Phase I/II trial of gemcitabine plus oral TS-1 in elderly patients with advanced non-small cell lung cancer: Thoracic Oncology Research Group study 0502. *Lung Cancer* 2010;69:213–217.
27. Kaira K, Yanagitani N, Sunaga N et al. Prospective exploratory study of gemcitabine and S-1 against elderly patients with advanced non-small cell lung cancer. *Oncol Lett* 2017;14:1123–1128.
28. Kudoh S, Takeda K, Nakagawa K et al. Phase III study of docetaxel compared with vinorelbine in elderly patients with advanced non-small-cell lung cancer: Results of the West Japan Thoracic Oncology Group Trial (WJTOG 9904). *J Clin Oncol* 2006;24:3657–63.

TABLE

Table 1. Baseline characteristics of patients (*n* = 17)

Characteristics	<i>n</i> (%)
Age at enrollment, yr	
Mean ± SD	78.5 ± 3.0
Median (range)	79.0 (72–84)
Gender	
Male	13 (76.5)
Female	4 (23.5)
PS	
0	9 (52.9)
1	8 (47.1)
Tissue type	
Adenocarcinoma	8 (47.1)
Squamous cell carcinoma	5 (29.4)
Non-small cell lung carcinoma	4 (23.5)
Disease stage	
IIIB	3 (17.6)
IV	10 (58.8)
Postoperative recurrence	4 (23.5)
EGFR gene mutation	
Negative	9 (52.9)
Positive	4 (23.5)
Unknown	0 (0.0)
Not assessed	4 (23.5)

Abbreviations: EGFR, epidermal growth factor receptor; PS, performance status.

[Click here to access other published clinical trials.](#)