Phase I dose escalation study of pemetrexed and concurrent thoracic radiation in elderly patients with non-squamous non–small-cell lung cancer

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ABSTRACT

The aim of our study was to determine the maximum tolerated dose (MTD) and recommended dose of pemetrexed with concurrent thoracic radiation therapy for elderly patients with previously untreated locally advanced non-squamous non–small-cell lung cancer (NSCLC). Pemetrexed was administered intravenously on Days 1, 22, 43, 64, 85 and 106. The initial doses of pemetrexed were planned as follows: Level 1 (400 mg/m2) and Level 2 (500 mg/m2). Concurrent thoracic radiation therapy was administered in 2-Gy fractions five times weekly, to a total of 60 Gy. Six patients were enrolled in the current study. The full thoracic radiotherapy dose (60 Gy) was administered for all patients. The full number of cycles (6 cycles) of chemotherapy, including induction and consolidation phases, were administered to 4 of 6 (66%) patients. At Level 1 and Level 2, none experienced a dose-limiting toxicity (DLT). There were no severe toxicities such as pulmonary toxicities, treatment-related death or Grade 2 or more radiation pneumonitis. Therefore, Level 2 was considered the MTD and was also defined as the recommended dose. An objective response was observed in 66.7% of all patients. This regimen was well tolerated and observed to be safe for the treatment of elderly patients with locally advanced non-squamous NSCLC.

Keywords: non–small-cell lung cancer; pemetrexed; radiation; Phase I study; elderly patient

INTRODUCTION

Non–small-cell lung cancer (NSCLC) is a disease with dismal prognosis, as evidenced by the significant number of deaths worldwide. Locally advanced NSCLC (LA-NSCLC) accounts for ~25% of all lung cancer cases [1]. The combination of chemotherapy plus thoracic radiation is the standard treatment for LA-NSCLC [2]. For non-elderly patients with LA-NSCLC, it is known that concurrent chemoradiotherapy prolongs survival compared with chemotherapy followed by radiotherapy [3], although there are no established regimens that include concurrent chemoradiotherapy. Despite this, thoracic radiotherapy alone is considered the standard of care for elderly patients with LA-NSCLC, and it remains unclear whether concurrent chemoradiotherapy significantly improves survival in these patients. Atagi et al. reported that daily low-dose carboplatin with concurrent thoracic radiotherapy significantly prolonged survival compared with thoracic radiotherapy alone in elderly patients with LA-NSCLC [4]. Although this combination is promising in such cases, the daily administration of carboplatin over 1 month as a radio-sensitizer is inconvenient and is not suitable in the outpatient setting. Aoe et al. have demonstrated that a concurrent regimen of S-1 plus thoracic radiotherapy was well tolerated and led to reduction in size of the primary tumor in elderly patients with LA-NSCLC, and also controlled tumor spread [5]. Contrastingly, Harada et al. recommended caution in the use of concurrent...
vinorelbine and thoracic radiotherapy in elderly patients with LA-NSCLC, because this regimen resulted in a high incidence of severe pneumonitis at the standard dose [6]. Thus, it is has not been clear which regimens are suitable as concurrent chemoradiotherapy in elderly patients with LA-NSCLC.

Pemetrexed is a multitargeted antifolate that is approved in combination with platinum in the first-line treatment of advanced non-squamous NSCLC and malignant pleural mesothelioma, and as a single agent for the second-line treatment of advanced or metastatic non-squamous NSCLC [7]. It has been shown that pemetrexed enhances radiation sensitivity in vitro [8], and several clinical trials have revealed that concurrent chemoradiotherapy including pemetrexed–platinum followed by consolidation pemetrexed is well-tolerated and effective for patients with LA-NSCLC [9]. Pemetrexed monotherapy is similar to docetaxel with regards to efficacy in elderly patients with previously treated NSCLC; thus, pemetrexed is thought to be a safe and effective treatment in elderly patients [10]. However, it remains unclear whether concurrent chemoradiotherapy with pemetrexed and thoracic radiation is useful for elderly patients with LA-NSCLC.

As such, we conducted a Phase I dose escalation study to assess the tolerability of concurrent chemoradiotherapy with pemetrexed and thoracic radiation in elderly patients with previously untreated LA-NSCLC. The aim of our study was to determine the optimal dose of pemetrexed.

METHODS
Patient eligibility
Eligible patients were required to meet the following criteria: histologically or cytologically proven unresectable Stage IIIA or IIIB NSCLC; no previous chemotherapy or radiotherapy; a performance status of 0 to 1 as per the Eastern Cooperative Oncology Group (ECOG) scale; aged >70 years; life expectancy of 3 months or more; adequate bone marrow reserves (leukocyte count ≥4000 mm⁻³, neutrophil count ≥2000 mm⁻³, platelet count ≥100 000 mm⁻³, and hemoglobin ≥9.0 g/dl); normal liver function (total serum bilirubin ≤1.5 mg/dl; aspartate transaminase [AST] and alanine transaminase [ALT] <2.5 times the upper limit of the normal range); normal renal function (normal serum creatinine and blood urea nitrogen levels); arterial oxygen pressure ≥70 torr. Patients were excluded if they met any of the following criteria: malignant pericardial or pleural effusions; active double cancer; a concomitant serious illness such as myocardial infarction in the previous 3 months; uncontrolled angina pectoris; heart failure; uncontrolled diabetes mellitus; uncontrolled hypertension; interstitial pneumonia or lung disease; infection or other diseases contraindicating chemotherapy or radiotherapy; pregnancy or breast-feeding. This study was approved by the institutional ethics committee of each participating institute, and written informed consent was obtained from all patients.

STUDY DESIGN
Chemotherapy schedule
This was a single-center, single-arm, Phase I study. All patients were treated with pemetrexed tri-weekly. Pemetrexed was intravenously administered at a starting dose of 400 mg/m²/day (level 1) on Day 1 and Day 22 during the concurrent phase of thoracic radiation. Then, pemetrexed was administered at a fixed dose of 500 mg/m²/day on Days 43, 64, 85 and 106 during the consolidation phase. Subsequent doses were 400 mg/m²/day (Level 1) and 500 mg/m²/day (Level 2) on Day 1 and Day 22, respectively (Table 1). If there were unacceptable toxicities that inhibited Level 1 dose escalation, pemetrexed was administered at a decreased dose of 300 mg/m²/day. In addition, 0.5 g of oral folic acid was administered daily and an intramuscular injection of 1 g of vitamin B12 was administered every 9 weeks; these substances were first given at least 7 days before the initial treatment. Thoracic radiotherapy started on Day 1 at a dose of 2.0 Gy daily, 5 times per week. A total dose of 60 Gy was administered in 30 fractions over a 6-week period.

Radiation therapy
Radiation therapy was administered using 10-MV X-rays in 2-Gy fractions, 5 times weekly. All treatment plans were designed using a commercial treatment planning system (Pinnacle³ version 6.2b or version 9.8, Philips Radiation Oncology Systems, Fitchburg, WI, or Eclipse version 11.0, Varian Medical Systems, Palo Alto, CA). The treatment plan was based on 2.5-mm thick/2.5-mm interval or 5-mm thick/5-mm interval computed tomography (CT) scans obtained in the treatment position. CT images were obtained under normal quiet breathing, and respiratory tumor movement was monitored using X-ray fluoroscopy or four-dimensional CT. The gross tumor volume (GTV) was delineated according to the primary tumor and nodal involvement determined from CT, and 2-[¹⁸F]-fluoro-2-deoxy-D-glucose (¹⁸F-FDG) positron emission tomography (PET)/CT information. The clinical target volume (CTV) was defined and contoured with a 5–10 mm margin around the GTV and contours around regional lymph node regions, i.e. the ipsilateral hilum and the mediastinum. Planning target volume (PTV) 1 included the CTV plus a 5–10-mm margin, and PTV2 included the GTV plus a 5–10-mm margin. An additional margin (typically 5 mm) was added where necessary. Beam shaping was performed using a multileaf collimator. The beam arrangements were antero-posterior parallel-opposed fields followed by off-cord oblique fields in all patients. The standard of practice was to prescribe 60 Gy for the PTV2 and 40 Gy for the PTV1 with concurrent chemotherapy. Other objectives were to restrict the relative volume of normal lung treated at a dose >20 Gy (V20) to <35% and to restrict the maximum spinal cord dose to <50 Gy. The dose was prescribed to the isocenter. Tissue heterogeneity correction was performed, and superposition/convolution dose calculation algorithms such as the collapsed cone convolution (CCC) and the analytical anisotropic algorithm (AAA) were used. The normal lung volume was contoured automatically by CT threshold, the trachea and bronchi were

Table 1. Dose-escalation schedule

<table>
<thead>
<tr>
<th>Level</th>
<th>Pemetrexed (mg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>300</td>
</tr>
<tr>
<td>1</td>
<td>400</td>
</tr>
<tr>
<td>2</td>
<td>500</td>
</tr>
</tbody>
</table>
excluded manually, and the GTV within the lung was excluded automatically. The esophagus was defined from the inferior border of the cricoid cartilage to the gastroesophageal junction. The external surface of the esophagus was contoured on each axial slice of the CT images. The following dosimetric parameters were generated from the dose–volume histogram for the total normal lung: the percentage of the total lung volume exceeding 20 Gy (V20), and the total lung volume mean dose (MLD).

Dose modification
A prophylactic administration of granulocyte-colony stimulating factor (G-CSF) was not permitted. Administration of G-CSF was permitted in patients with Grade 4 neutropenia and/or Grade 3 febrile neutropenia. Subsequent courses of chemotherapy were initiated when the neutrophil counts were 1500 mm$^{-3}$ or more and platelet counts were 100 000 mm$^{-3}$ or more. If the neutrophil or platelet counts had not returned to these levels by Day 1 of the next course of chemotherapy, pemetrexed was withheld until full recovery, and irradiation was also withheld until recovery or continued using G-CSF.

The planned dose levels are shown in Table 1. Doses were escalated according to the frequency of the dose-limiting toxicity (DLT) evaluated during concurrent chemotherapy and thoracic radiation. At least 3 patients were enrolled at each dose level. Initially, 3 patients were treated at Dose Level 1, and no intrapatient dose escalation was allowed. If one DLT was observed in the first 3 patients, 3 more patients were entered at this dose level, and dose escalation continued to the next level if <2 out of 3 or <3 out of 6 patients experienced DLT. The maximum tolerated dose (MTD) was defined as the level before a DLT was observed in 2 out of 3 or 3 out of 6 patients. If 2 out of 3 or 3 out of 6 patients experienced a DLT at Level 1, a dose reduction to Level 0 was planned. DLT was defined as; (i) ≥Grade 3 non-hematological toxicities except nausea/vomiting; (ii) Grade 4 thrombocytopenia; (iii) Grade 4 neutropenia; (iv) Grade 3 or 4 neutropenia complicated by fever; (v) any unresolved toxicity requiring a delay in the administration of a subsequent course exceeding 14 days; (vi) any toxicity requiring a delay in the planning of radiotherapy within 60 days. Toxicities were assessed according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.0. Second-line chemotherapy or other treatments after this study were not prohibited by the protocol.

Treatment evaluation
Prior to treatment, patients were evaluated by complete blood cell count, a differential count, routine chemistry measurements, chest radiography, chest CT, abdominal CT, whole-brain magnetic resonance imaging or CT, and isotope bone scintigraphy. Blood cell count, differential count, routine chemistry measurements, physical examination, and toxicity assessment were performed weekly. Acute toxicity was graded according to CTCAE version 4.0, and late toxicity associated with thoracic radiotherapy was graded according to the Radiation Therapy Oncology Group (RTOG) Late Radiation Morbidity Scoring Schema. Tumor response was evaluated according to Response Evaluation Criteria in Solid Tumor (RECIST) criteria ver. 1.1 [11]. Response based on target (and non-target lesions) was defined as follows: complete response (CR), disappearance of all target (non-target) lesions; partial response (PR), ≥30% reduction in size (or disappearance of one or more non-target lesions); stable disease (SD), <30% decrease and <20% increase in size (or the persistence of one or more non-target lesions); progressive disease (PD), >20% increase in size (or the appearance of new non-target lesions and/or progression of existing non-target lesions). The overall response was defined as the best response recorded from the start of treatment until disease progression or recurrence, confirmed by repeated assessments performed no less than 4 weeks after the criteria for response were first met. Survival was recorded from the first day of pemetrexed treatment to the date of death or last follow-up, and the survival curves were calculated according to the Kaplan–Meier method. Overall survival (OS) was determined as the time from the first day of chemotherapy to death from any cause. Progression-free survival (PFS) was defined as the time between the first day of chemotherapy and the first sign of disease progression or death.

RESULTS
Patients
Between April 2011 and November 2014, a total of six patients (four men, two women; median age 75 years, range 71–78 years) were enrolled in the study. The patients’ characteristics are listed in Table 2. Four patients had a smoking history, two patients were diagnosed with Stage IIIA disease, and four patients were diagnosed with Stage IIIB disease. All patients had adenocarcinoma (AC), and active epidermal growth factor receptor (EGFR) mutation was observed in one patient.

Toxicity and treatment delivery
All treated patients were evaluated for toxicity. Three patients were enrolled at Dose Level 1. Although one patient experienced Grade 3 neutropenia, none of these patients experienced DLT at Level 1. Three patients were started at Dose Level 2. At Dose Level 2, two patients developed Grade 3 neutropenia and one patient experienced Grade 3 nausea. No patients experienced DLT, although three patients developed Grade 3 neutropenia and Grade 3 nausea. In total, none of the six patients developed DLT, although Grade 1 radiation pneumonitis was observed in four patients. No pulmonary toxicities such as interstitial pneumonitis or treatment-related deaths were observed at either Level 1 or 2. The occurrence of hematological and non-hematological toxicities are listed in Table 3. Based on these results, we determined that Dose Level 2 was the MTD, which was subsequently recommended as the dose for the Phase II trial.

Full-dose thoracic radiotherapy (60 Gy) was completed in 100% of patients at both Dose Levels 1 and 2. The complete number of cycles (six cycles) of chemotherapy, including induction and consolidation phases, were administered to four out of six (66%) patients. One patient at Dose Levels 1 and 2 received the complete number of cycles of chemotherapy. At Dose Level 1, one patient received a full cycle of chemotherapy, but two patients did not due to toxicities and/or patient refusal.

Response rate and follow-up
Six patients were evaluable for therapeutic response (Table 4). Of the six patients, four achieved PR, giving an overall response rate of 66.7%. Two patients had SD, but none had PD. The median


**Table 2. Patient characteristics**

<table>
<thead>
<tr>
<th>Different variables</th>
<th>N = 6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>75</td>
</tr>
<tr>
<td>Range</td>
<td>71–78</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>4</td>
</tr>
<tr>
<td>Female</td>
<td>2</td>
</tr>
<tr>
<td><strong>PS (ECOG)</strong></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Disease stage</strong></td>
<td></td>
</tr>
<tr>
<td>IIIB</td>
<td>4</td>
</tr>
<tr>
<td><strong>Histological type</strong></td>
<td></td>
</tr>
<tr>
<td>Ad</td>
<td>6</td>
</tr>
<tr>
<td><strong>Smoking history</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>4</td>
</tr>
<tr>
<td>No</td>
<td>2</td>
</tr>
<tr>
<td><strong>EGFR mutation status</strong></td>
<td></td>
</tr>
<tr>
<td>L858R</td>
<td>1</td>
</tr>
<tr>
<td>Wild type</td>
<td>5</td>
</tr>
<tr>
<td><strong>Comorbid disease</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>5</td>
</tr>
<tr>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td><strong>V20</strong></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>26.2</td>
</tr>
<tr>
<td>Range</td>
<td>21.9–34.8</td>
</tr>
<tr>
<td><strong>MLD</strong></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>14.0</td>
</tr>
<tr>
<td>Range</td>
<td>11.9–19.8</td>
</tr>
</tbody>
</table>

**DISCUSSION**

This was a prospective Phase I dose escalation study of pemetrexed with concurrent thoracic radiation in elderly patients with previously-untreated LA-NSCLC. Our recommended dose was 500 mg/m² with concurrent thoracic radiation. In our study, there were no DLTs, treatment-related deaths or ≥Grade 2 radiation pneumonitis. An optimal assessment of efficacy and survival benefit associated with our regimen is difficult because of the very small sample size. However, the response rate of 66.7% is comparable with that of other studies, and the median overall survival was >5 years. Recently, Takemoto et al. reported the results of a Phase I dose escalation study similar to ours in elderly patients with LA-NSCLC [12]. In their study, two patients were enrolled at pemetrexed Dose Level 1 (400 mg/m²); however, one patient, who experienced prolonged leukopenia and chemoradiotherapy, was discontinued on Day 35. Another patient in their study experienced febrile neutropenia, drug-induced pneumonitis and acute respiratory distress syndrome. At Dose Level 1, DLT was observed in both patients; thus, the investigators deemed Dose Level 1 to be the MTD and concluded that concurrent chemoradiotherapy may be too toxic for elderly patients >75 years with LA-NSCLC. The patients in the study were aged 87 and 83 years, whereas the maximum age in our study was <80 years. Although it is unclear whether the difference in age affected the results of the studies, concurrent chemoradiotherapy seems to be toxic in elderly patients aged ≥80 years with LA-NSCLC. It remains unknown whether concurrent chemoradiotherapy with pemetrexed is suitable for elderly patients; however, pemetrexed at our dose level was a well-tolerated and convenient treatment. Further study is warranted to assess the tolerability of this treatment in elderly patients aged <80 years.

A recent review reported that there are 19 clinical trials evaluating pemetrexed in concurrent chemoradiation regimens, including 11 Phase I studies and 8 Phase II studies, and that pemetrexed can be administered safely at full dose with either cisplatin or carboplatin concomitantly with radical doses of thoracic radiation [9]. All Phase I studies of pemetrexed in LA-NSCLC have evaluated full-dose pemetrexed and platinum without severe toxicities, and adverse events such as hematologic toxicity, radiation pneumonia and esophagitis were acceptable [9]. Recently, the Phase III PROCLAIM study demonstrated that concurrent pemetrexed–cisplatin with thoracic radiation therapy followed by consolidation pemetrexed was not superior to standard chemoradiotherapy for patients with LA-NSCLC, but a significantly lower incidence of drug-associated serious adverse events was observed in patients treated with pemetrexed–cisplatin [13]. Considering this evidence, the combination of full-dose pemetrexed plus concurrent thoracic radiation seems to be well tolerated in Stage III LA-NSCLC.

In elderly patients aged >75, pemetrexed has been shown to be effective and safe [14] when administered as single agent. Weiss et al. reported that elderly patients treated with second-line pemetrexed exhibited longer survival compared with those treated with docetaxel (although the difference was not significant) in patients aged between 70 and 81 years [15]. In patients aged >80 years, little is known about the use of pemetrexed as a single agent. In addition, there is a lack of evidence regarding the administration of pemetrexed in elderly patients with LA-NSCLC. There are no definitive studies to suggest that concurrent radiation therapy with a cytotoxic agent leads to
increased survival of patients aged ≥80 years. Our approach suggests that the combination of pemetrexed with thoracic radiation is safe and effective in elderly patients aged <80 years.

There were several limitations in the current study. First, our study included a very small sample size; thus, bias may exist in the results, particularly with regard to the safety profile. Second, our study lacked data on the tolerability of pemetrexed with concurrent thoracic radiation in patients aged ≥80 years. As such, the population of our study was different from that of Takemoto’s study [14]; they enrolled patients aged >80 years. If patients aged ≤80 were included in their study, the safety profile of pemetrexed may have been different. Although the PROCLAIM Phase III study failed to show the superiority of cisplatin and pemetrexed with concurrent radiation over standard chemoradiotherapy, its considerably lower hematologic toxicities suggest that pemetrexed may be a promising agent for elderly patients [11]. Considering the results of our Phase I study, we believe that pemetrexed is suitable for elderly patients with LA-NSCLC who are candidates for chemoradiotherapy. Future investigation is warranted to assess the usefulness of pemetrexed plus thoracic radiotherapy.

Table 3. Adverse events by dose level in the concurrent chemoradiotherapy of pemetrexed

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Dose Level = 1 (n = 3)</th>
<th>Dose Level = 2 (n = 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade</td>
<td>Grade</td>
</tr>
<tr>
<td></td>
<td>1 2 3 4 3 or 4 (%)</td>
<td>1 2 3 4 3 or 4 (%)</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>0 3 0 0 0%</td>
<td>0 1 0 0 0%</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>0 2 1 0 33%</td>
<td>1 0 2 0 66%</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>0 0 0 0 0%</td>
<td>0 0 0 0 0%</td>
</tr>
<tr>
<td>Anemia</td>
<td>0 0 0 0 0%</td>
<td>1 0 0 0 0%</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>1 0 0 0 0%</td>
<td>0 0 0 0 0%</td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>1 0 0 0 0%</td>
<td>1 0 1 0 33%</td>
</tr>
<tr>
<td>Anorexia</td>
<td>0 1 0 0 0%</td>
<td>0 1 0 0 0%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>0 0 0 0 0%</td>
<td>0 0 0 0 0%</td>
</tr>
<tr>
<td>Stomatitis</td>
<td>1 0 0 0 0%</td>
<td>0 0 0 0 0%</td>
</tr>
<tr>
<td>Infection</td>
<td>0 0 0 0 0%</td>
<td>0 1 0 0 0%</td>
</tr>
<tr>
<td>Skin rash</td>
<td>2 0 0 0 0%</td>
<td>1 0 0 0 0%</td>
</tr>
<tr>
<td>Constipation</td>
<td>0 0 0 0 0%</td>
<td>1 1 0 0 0%</td>
</tr>
<tr>
<td>Fever</td>
<td>0 0 0 0 0%</td>
<td>0 1 0 0 0%</td>
</tr>
<tr>
<td>Neuropathy – sensory</td>
<td>0 0 0 0 0%</td>
<td>0 0 0 0 0%</td>
</tr>
<tr>
<td>Radiation pneumonitis</td>
<td>2 0 0 0 0%</td>
<td>2 0 0 0 0%</td>
</tr>
<tr>
<td>Hyponatremia</td>
<td>0 0 0 0 0%</td>
<td>0 0 0 0 0%</td>
</tr>
<tr>
<td>Vertigo</td>
<td>0 0 0 0 0%</td>
<td>0 0 0 0 0%</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>0 0 0 0 0%</td>
<td>0 0 0 0 0%</td>
</tr>
<tr>
<td>Esophagitis</td>
<td>2 1 0 0 0%</td>
<td>1 0 0 0 0%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>0 0 0 0 0%</td>
<td>0 0 0 0 0%</td>
</tr>
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</table>

Table 4. Response rate according to dose level

<table>
<thead>
<tr>
<th>Dose level</th>
<th>No. of patients</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>CR PR SD PD</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>0 2 1 0</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>0 2 1 0</td>
</tr>
<tr>
<td>Total patients</td>
<td>6</td>
<td>0 4 2 0</td>
</tr>
</tbody>
</table>

Response rate 66.7% (DCR 100%)

CR = complete response, PR = partial response, SD = stable disease, PD = progressive disease, DCR = disease control rate.

increased survival of patients aged >80 years. Our approach suggests that the combination of pemetrexed with thoracic radiation is safe and effective in elderly patients aged <80 years.
3. Furuse K, Fukuoka M, Kawahara M et al. Phase III study of 2. Pfi person or organization that could inappropriately in
well tolerated and less toxic in these patients; therefore, this dose
elderly patients with non-squamous LA-NSCLC. This regimen was
with thoracic radiation is suggested as the recommended dose for

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in patients with previously treated advanced non–small-cell lung

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