Conclusion: Cisplatin plus S-1 chemotherapy is well tolerated, and our analysis suggests that the risk–benefit profile of this regimen is unaffected by patient age.

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Phase II trial of S-1 with bi-weekly docetaxel for non-small-cell lung cancer previously treated with platinum-based chemotherapy: a North Japan Lung Cancer Study Group (NJLCG0701)

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Background: S-1, a novel oral fluorouracil derivative, is active against non-small-cell lung cancer (NSCLC). A preclinical study showed the synergistic effect of docetaxel and S-1 *in vivo*. On the basis of the findings of the dose-escalation study of bi-weekly administered docetaxel and S-1, we conducted a phase II study to evaluate the efficacy and toxicity of this combination as a second-line treatment for patients (pts) with previously treated NSCLC.
Methods: Pts with NSCLC that was previously treated with one regimen of platinum-based chemotherapy were included. Gefitinib and/or prior surgery followed by adjuvant chemotherapy in addition to first-line treatment were acceptable. Other eligibility criteria were an Eastern Cooperative Oncology Group performance status (PS) of 0/1 and measurable lesions. Pts received S-1 (80 mg/m^2) on days 1−14 and docetaxel (25 mg/m^2) on days 1 and 15 of each 28-day cycle. The primary endpoint was the overall response rate (ORR), and secondary endpoints were progression-free survival (PFS), overall survival, and the toxicity profile. Assuming that 20% ORR in eligible pts indicated potential usefulness and 5% ORR is the lower limit of interest, along with alpha and beta values of 0.05 and 0.10, respectively, the estimated accrual was 34 pts.
Results: We enrolled 35 pts from 7 institutions (Feb. 2007−Sep. 2008). Patient characteristics: male/female, 23/12; median age, 64 years (43−74 years); and PS, 0/1 (17/18). The median number of treatment cycles was 3 (1−7). The objective responses were CR 0; PR 9; SD 14; PD 10; and NE 2, resulting in an ORR of 26% (95% confidence interval (CI), 11−40). The overall disease control rate was 66% (95% CI, 50−81); median PFS, 4.1 months; and overall survival time will be presented. Haematologic grade 3/4 toxicity included neutropenia (31%) and anemia (11%). No febrile neutropenia was observed. Non-haematologic grade 3 toxicity included diarrhoea (17%), infection (8.6%), anorexia (5.7%), rash (5.7%), elevation of serum aspartate aminotransferase (AST) (5.7%). No grade 4 non-haematologic toxicity was observed. There was 1 possible treatment-related death due to pneumonitis and infection after the first chemotherapy cycle.
Conclusion: The combination of S-1 and bi-weekly docetaxel is an active regimen with a tolerable toxicity profile for previously treated NSCLC. Further evaluation of this regimen as compared to the administration of docetaxel alone or pemetrexed is warranted.

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A phase II study of S-1 monotherapy as first-line treatment for elderly patients with advanced non-small cell lung cancer, the Central Japan Lung Study Group trial 0404

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Background: S-1 is an orally active combination of tegafur (a prodrug converted by cells to fluorouracil), gimeracil (an inhibitor of dihydropyrimidine dehydrogenase, which degrades fluorouracil), and oteracil (which inhibits the phosphorylation of fluorouracil in the gastrointestinal tract, thereby reducing its gastrointestinal toxic effects) in a molar ratio of 1:0.4:1. The rate of response to treatment with S-1 was reported to be 22% in patients with advanced non-small cell lung cancer (NSCLC). However, the activity of this drug in elderly patients remains unclear. This study evaluated the efficacy and safety of S-1 as first-line treatment in elderly patients with advanced NSCLC.
Materials and Methods: Elderly chemotherapy-naïve patients (age $\geqslant$70 years) with advanced NSCLC, an ECOG PS of 0−1, and adequate organ functions received oral S-1 for 14 consecutive days, followed by 7 days of no chemotherapy. S-1 was prescribed according to body surface area (BSA) to provide a dose approximately equivalent to 80 mg/m^2/day as follows: BSA < 1.25 m^2, 80 mg daily; BSA $\geqslant$1.25 m^2 but <1.5 m^2, 100 mg daily; and BSA $\geqslant$ 1.5m^2, 120 mg daily. This 3-week cycle was repeated until confirmation of progressive disease or intolerable toxicity. The primary objective of this study was to determine the objective response rate (RR). Secondary endpoints were tolerability, progression-free survival (PFS), and overall survival (OS).
Results: Thirty patients were enrolled, among whom 29 were eligible. Median age was 78 (range, 70−85) years. Twenty-two patients were men (75.9%), and 7 were women (24.1%). Eighteen patients had adenocarcinoma (62.1%), 7 had squamous cell carcinoma (24.1%), and 4 had others (13.8%). The median number of administered cycles was 3 (range, 1−19). Among the 29 patients, there were no complete responses and 8 partial responses for an overall response rate of 27.6% (95% CI, 11.3−43.9%). The median PFS and the median OS time have not yet been reached. Hematologic toxicities of grade 3 was anemia (6.9%). Nonhematologic toxicities of grade 3 consisted of anorexia (3.4%), nausea (3.4%), diarrhea (3.4%), and pneumonia (6.9%). No hematologic and nonhematologic toxicities of grade 4 were observed.
Conclusion: S-1 monotherapy is effective and well tolerated as first-line treatment in elderly patients with advanced NSCLC. The results of the present study warrant further investigations of this regimen, including a randomized controlled trial.

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Phase II study of amrubicin (AMR) in patients (pts) with non-small cell lung cancer (NSCLC) previously treated with platinum-based chemotherapy, a further analysis on adverse effect: WJTOG0401

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Background: AMR is a totally synthetic 9-aminoanthracycline and a novel topoisomerase II inhibitor. AMR has shown promising clinical activity for advanced NSCLC as well as SCLC. This trial was conducted to evaluate the efficacy and safety of AMR for pts with NSCLC previously treated with platinum-based chemotherapy.
Methods: Eligible Pts had a performance status 0 to 1, previous treatment with one platinum-based chemotherapy for advanced NSCLC, and adequate organ function. Pts received AMR 40 mg/m^2 intravenously on days 1−3 every 3 weeks. The primary endpoint was the objective response rate, which determined the sample size based on an optimal two-stage design. With the target activity level of 18% and the lowest response rate of interest set at 5%, 60 eligible patients were required with a 90% power to accept the hypothesis and a 5% significance level to reject the hypothesis.
Results: Sixty-one pts (median age, 63 years; range 51−74 years) were enrolled. The median treatment cycles were 2 (range, 1−15). No complete responses and 7 partial responses were observed, giving an overall response rate of 11.5% (95% CI, 4.7−22.2%). Twenty patients (32.8%) had stable disease and 34 patients (55.7%) had progressive disease as the best response. The overall disease control rate (complete response + partial response + stable disease) was thus 44.3% (95% CI, 31.5−57.6%). The median overall survival and 1-year survival rate were 8.5 months and 32.0%, respectively. Grade 3/4 hematological toxicities were neutropenia (82%), anemia (27.9%) and thrombocytopenia (24.6%). Serious neutropenia was observed in elderly patients. Grade 3/4 non-hematological toxicities were anorexia (9.8%), febrile neutropenia (29.5%) and pneumonitis (1.6%). One case of treatment-related death due to sepsis was observed.