First line chemotherapy with sequential administration of gemcitabine followed by docetaxel in elderly advanced non-small-cell lung cancer (NSCLC) patients: a multicenter phase II study

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Background: Single-agent chemotherapy (gemcitabine or vinorelbine) is currently the standard treatment for elderly advanced NSCLC patients. The combination of gemcitabine+docetaxel was active but not well tolerated in this subset (Hainsworth et al, Clin Lung Cancer 2003). Modified schedule of docetaxel (37.5 mg/m² on day 1 and 8 every 3 weeks) is active and well tolerated in pre-treated elderly advanced NSCLC patients (Tibaldi et al, Clin Lung Cancer 2006). Aim of this study was to evaluate the activity and the toxicity of a sequential regimen of gemcitabine followed by docetaxel in elderly advanced NSCLC patients.

Methods: Chemo-naïve elderly patients (> 70 years old) with histologically or cytologically confirmed stage IIIB (positive pleural effusion or metastatic supraclavear lymph nodes) or IV NSCLC and a performance status (PS) 0-2 were treated with gemcitabine 1200 mg/m² on Day 1 and 8 every 3 weeks for 3 cycles followed by, in case of no progression, docetaxel 37.5 mg/m² on Day 1 and 8 every 3 weeks for further 3 cycles.

Results: Fifty-six patients were enrolled into the study: 46 male and 10 women; 13 stage IIIB and 43 stage IV; 7 PS 0, 38 PS1, 11 PS2; median age was 75 years (range 70-84). The median number of major comorbidities was 2. All the patients were evaluable for toxicity and 45 were evaluable for response. Toxicity was mild; afebrile grade 3-4 neutropenia was observed in 4 patients (7.1%) and grade 3 thrombocytopenia in 2 patients (3.6%); no grade 3-4 anaemia was observed. Non-haematological grade 3-4 toxicities were: fatigue in 5 patients (8.9%), diarrhea in 1 patient (1.8%) and mucositis in 2 patients (3.6%). Nine of the 45 evaluable patients showed a partial response (20%, 95% CI 9.6% - 34.4%), 17 had a stable disease (37.8%) and 19 a progression (42.2%). Five patients had a conversion from stable disease to partial response by docetaxel.

Conclusion: Sequential chemotherapy with gemcitabine and docetaxel seems active and well tolerated in elderly advanced NSCLC patients. The final analysis will be presented at the meeting.

Dose-Finding and Phase II Study of Weekly Docetaxel and Cisplatin as First-Line Chemotherapy in Advanced Non-Small Cell Lung Cancer (NSCLC)

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Objectives: The aim of the present study is to evaluate the efficacy and toxicity of weekly docetaxel combined with cisplatin as first-line chemotherapy in patients with locally advanced or metastatic NSCLC and to identify the optimal dose of weekly docetaxel to be administered.

Methods: Chemonaive patients over 18 years of age with NSCLC stage IIIB and malignant pleural effusion, or stage IV were enrolled in this study. In the dose finding portion, patients received docetaxel once weekly at an initial dose of 25 mg/m² for three weeks with cisplatin added on day 15 at a fixed dose of 75 mg/m². The dose of docetaxel was escalated by 3 mg/m² for each level to a maximum dose of 34 mg/m². Treatment was repeated every 4 weeks for 6 cycles unless progressive disease, unacceptable toxicity, or consent withdrawal were present. Patients were enrolled in cohorts of 3 to receive combination chemotherapy. If a dose-limiting toxicity (DLT) occurred in 1 of the 3 patients, additional patients would be enrolled at that dose level. DLT was defined as any grade 3-4 non-hematological toxicity (except alopecia, nausea and vomiting), grade 4 hematologic toxicity, or grade 3 hematologic toxicity with complications (e.g. neutropenic fever or bleeding). The maximum-tolerated dose (MTD) was defined as the dose immediately below the level associated with the occurrence of DLT in more than one-third of treated patients.

Results: Forty-nine patients were enrolled into this phase I/II study. In the dose-finding portion, the MTD of docetaxel was not reached since no patient developed DLT when docetaxel was given at the highest dose of 34 mg/m². In the phase II portion, 18 patients received docetaxel at 34 mg/m² and 14 patients received 31 mg/m². Of the 49 eligible patients, none had a complete response and 19 achieved a partial response. The overall response rate was 38.8% (95% CI: 26.7-55.6%). Twenty-one patients (42.9%) had stable disease (37.8%) and 19 a progression (42.2%). Five patients had a conversion from stable disease to partial response by docetaxel.

Conclusions: Weekly docetaxel combined with cisplatin on day 15 has an acceptable toxicity profile and is an effective regimen as first-line chemotherapy in NSCLC. No dose-limiting toxicities were observed even when weekly docetaxel was given at 34 mg/m².