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Prospective Phase II Trial of a Combination of Gemcitabine and UFT as First-line Treatment in Elderly Patients With Advanced Non-small Cell Lung Cancer

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Background: The standard regimen in elderly patients with non-small-cell lung cancer (NSCLC) is still uncertain. Gemcitabine is one of the most widely used drugs for the treatment of NSCLC, and several phase II trials specifically designed for elderly patients with advanced NSCLC have confirmed the role of gemcitabine in this setting. In addition, oral uracil-tegafur (UFT®) was associated with a survival advantage in the adjuvant setting. Therefore, we performed a phase II study using the combination of gemcitabine and UFT as first-line therapy in elderly patients with advanced NSCLC.
Materials and Methods: Elderly (⩾ 70 years) patients who had histologically or cytologically confirmed stage IIIB or IV NSCLC with a performance status of 1−2 were eligible. Gemcitabine (1250 mg/m^2 on days 1 and 8, respectively) was injected intravenously and UFT® (400 mg/day) was administered orally on days 1−14. Treatment was repeated every 3 weeks for up to four cycles. Patients who had not progressed after four cycles continued UFT® monotherapy until progression. Primary endpoint was overall response rate and secondary endpoints were overall survival, time to progression and safety profiles.
Results: Between March 2008 and November 2010, 48 patients were enrolled. The median age was 74.5 years (range: 70−84 years), and there were 29 males and 19 females. The performance status was 1 in 41 and 2 in 7 patients. Thirty-one (64.6%) patients were stage IV and seventeen (35.4%) patients were stage IIIB. Thirty patients (62.5%) completed four cycles of chemotherapy. Response was evaluated in 44 patients, with the remaining 4 being lost to follow-up or patient refusal. All efficacy data are reported using the intention-to-treat patient population. Partial response was achieved in twelve (25.0%) patient and stable disease in 23 (47.9%) patients. Disease control rate was 72.9%. The median duration of response in the 12 responding patients was 2.4 months (95% confidence interval [CI]; 1.2−4.6 months), while the median time to progression for all patients was 4.3 months (95% CI; 3.7−5.5 months) at a median follow-up duration of 174.5 days (range; 19–875 days)Thirty-five patients had died at the time of the present evaluation. The median survival time was 5.7 months (95% CI; 5.1−7.0 months) with a 1-year survival rate of 29.1%. A total of 154 cycles (median 4, range 1−4 cycles) for gemcitabine and 225 cycles (median 4.5, range 1−20 cycles) for UFT® were administrated in 48 patients assessable for toxicity. Toxicities were mild and mostly hematological adverse events. Grade 3/4 neutropenia occurred in 10.3% of patients and one patients experienced febrile neutropenia. All cases were successfully treated with antibiotics and G-CSF, and there were no treatment-related deaths during this study. Grade 3/4 anemia and thrombocytopenia occurred in 2.6% and 2.6% of patients, respectively. Non-hematological toxicities were mild.
Conclusions: The combination of gemcitabine and UFT is an active and well-tolerated first-line regimen in elderly patients with advanced NSCLC.

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EGFR-targeting Chimeric Monoclonal IgG-1 Antibody Cetuximab in a Phase II/III Study Added Either to Gemcitabine Followed by Docetaxel or Carboplatin Plus Gemcitabine for Chemonaïve Patients With Advanced Non-small Cell Lung Cancer (NSCLC) − Results of the Phase II Study Part

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Background: In this randomized phase II/III trial the efficacy and safety of cetuximab in combination with two different chemotherapy regimens is assessed. Primary study endpoints: Clinically relevant toxicities (phase II) and overall survival (phase III).
Material and Methods: Chemonaïve patients with histologically confirmed stage IIIB or IV NSCLC and performance status (WHO) 0−2 received cetuximab 400 mg/m^2 as loading dose and then 250 mg/m^2 weekly either combined with gemcitabine 1000 mg/m^2 days 1+8 for 2 cycles (3qw) followed by docetaxel 75 mg/m^2 day 1 for 2 cycles (q3w) (arm A) or carboplatin AUC5 day 1 and gemcitabine 1200 mg/m^2 days 1+8 for 4 cycles (q3w) (arm B). If patients did not progress single agent cetuximab was continued until tumour progression or unacceptable toxicity.
Results: In total 352 patients were enrolled; 345 patients received study medication (173/172 arm A/B). 2914 infusions of cetuximab combined with chemotherapy and 2666 infusions without chemotherapy were given. Toxicities per patient requiring clinical intervention are shown below. 162 patients on single agent cetuximab received up to 39 cycles without significant toxicity (arm A: 75 patients, range 1−35 cycles, median 4, mean 5.9, and 13 patients ⩾10 cycles; arm B: 87 patients, range 1−39 cycles, median 4, mean 6.0 and 12 patients ⩾10 cycles). Under cetuximab in combination with chemotherapy, grade 3 or 4 hematological toxicity was more common in patients receiving carboplatin/gemcitabine (arm A/B: anemia 3%/10%, leukopenia 17%/29%, neutropenia 25%/38%, and thrombopenia 2%/40%, all $p < 0.01$, χ^2-test). Skin reactions were common and occurred in 79% of patients in both treatment arms. 32%/42% in arm A/B completed the protocol treatment, and overall response rates were 19%/31% in arm A/B, respectively. Overall survival as a secondary aim of the Phase II part showed no statistically significant differences between treatment arms (hazard ratio 1.102, $p = 0.4284$, χ^2-test).

Clinically relevant toxicities	Arm A		Arm B	"Maintenance"
	Cetuximab/ gemcitabine, n = 173 (pts)	Cetuximab/ docetaxel, n = 112 (pts)	Cetuximab/ carboplatin/ gemcitabine, n = 172 (pts)	Single-agent cetuximab, n = 162 (pts)
Total number of cycles (3qw)	312	203	547	962
Median number of cycles per patient	2	2	4	4
Anemia + ⩾ 1 blood transfusion	1%	4%	10%	–
Thrombopenia + ⩾ 1 platelet transfusion	<1%	–	11%	–
Febrile neutropenia + IV antibiotics	<1%	6%	3%	–
Skin reaction (any/grade 3)	80%/6%	25%/6%	79%/9%	34%/6%

Conclusions: Cetuximab in combination with single agent gemcitabine-docetaxel and with carboplatin//gemcitabine is well tolerated. Patients on weekly single agent cetuximab received up to 39 cycles. The toxicity was as expected and slightly higher under carboplatin/gemcitabine. The study continues as a Phase III trial with a total of 608 patients.

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Effect of Somatostatin Analogs in the Control of Tumour Growth in Patients With Metastatic Lung Carcinoid Tumours

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Background: Antitumour effect of somatostatin analogs has been poorly documented in metastatic typical or atypical lung carcinoid tumours (LCT). In this study our purpose was the evaluation of disease control rate and progression-free survival (PFS) of metastatic LCT patients treated with long-acting somatostatin analogs alone.
Materials and Methods: Eighteen out of 39 metastatic LCT patients followed between 2000 and 2009, and treated with somatostatin analogs alone were retrospectively reviewed. Response rates were evaluated according to RECIST criteria. Median PFS was estimated by the Kaplan–Meier method and compared between groups (typical or atypical CT) using the Log-Rank test.
Results: Fifty percent of patients had a typical CT. Fourteen patients (78%) achieved stable disease for 6 months or more as best response. Median PFS was 17 months (3.5–30.5 months). PFS of patients with typical and atypical LCT was 50 and 10 months respectively ($p = 0.2$). PFS of twelve patients (66%) with a progressive disease before treatment was 21 months.
Conclusion: Our study demonstrate that long-term tumour stabilizations can be obtained with long-acting somatostatin analogs alone in patient with metastatic LCT.