Results: No grade 4 acute toxicity (RTOG/SWOG scales) event was reported. 1 pt had a 1 week treatment break because of a grade 3 oesophagitis. With a 6.5 months follow-up, Grade 2 long-term oesophageal toxicity occurred in 2 pts. 1 pt died from massive haemoptysis not scored as treatment-related death. 13 pts were evaluable for tumour response. 6 complete and 3 partial response, 2 stable and 2 progressive disease occurred.

Table 1: Biological effect of the experimental and standard regimen

	Experimental Regimen	Standard Regimen
Total Dose/Number of fr	72 Gy/24 fr	60 Gy/30 fr
BED (acute effect/anti-tumour effect)*	102	77
BED(long-term effect)**	137	78
Overall treatment Time (weeks)	5	6

BED denotes for Biological Effective Dose, Gy for Gray, * alpha/beta ratio = 7, ** alpha/beta ratio = 3.3

Conclusions: More data are needed to confirm the feasibility of this strategy, but early toxicity data and tumour response rate are encouraging. This radiobiologically intense high-dose accelerated strategy also has practical and economical advantages

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Gemcitabine-cisplatin (GP) vs gemcitabine-carboplatin (GC) in advanced non-small cell lung cancer (NSCLC): a multicenter phase II randomized trial

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Background: In this randomized study we explored a 21-day schedule of both GP and GC regimens to assess toxicity and activity in advanced NSCLC patients (pts).

Patients and Methods: From Jan 1998 to Mar 2001, 115 untreated IIIB-IV NSCLC pts were randomized either to GP (62 pts) or to GC arm (53 pts). Before randomization, pts were stratified according to stage (IIIB vs IV) and PS (ECOG 0-1 vs 2). Treatment consisted of G 1.2 gr/sqm, d 1,8; P 80 mg/sqm or C AUC 5, d 2; every 21 days. Response rate (RR) was calculated according to the intent-to-treat principle. We utilized the Kaplan-Meier product-limit method to estimate time to progression (TTP) and overall survival (OS) rates.

Results: Characteristics of pts were as follow: median age 63 (40-75); M/F ratio 90/25; PS 0/1/2 in 24/71/20 pts; stage IIIB/IV in 45/70. Among pts with stage IV disease, metastatic sites were: bone 46%, lung/pleura 40%, adrenals 26%; distant nodes 18%, liver 13%, asymptomatic CNS 7%; others 7%; more than or equal to 2 sites in 26 (37%) pts. To date 36/115 pts are still alive, with a median follow-up of 11 months (mo). A total of 499 courses were delivered (262 GP, 237 GC), with a median number of 4 (1-6). All pts were evaluable for toxicity, 107 for response. WHO recorded toxicities at each course were generally moderate and overlapping for the two arms, except for: G1-2/G3-4 thrombocytopenia in 26/15 pts with GP and 15/5 with GC; G1-2/G3-4 leucopenia in 55/4 GP and 19/3 GC; G1-2/G3-4 emesis in 71/12 GP and 28/5 GC; G1-2/G3 peripheral neurotoxicity in 27/2 GP and 3/0 GC; G1/G2 renal toxicity in 13/2 GP and 1/0 GC; G1-2/G3 hair loss in 23/1 GP and 11/0 GC. Responses were as follows: 37 PR (23 in GP arm, 14 in GC) for an overall RR of 35%, 41% and 26% in GP and GC arm respectively. We observed a RR of 40% for pts with stage IIIB, and 27% with stage IV. Thirty seven (35%) pts had SD, with 20 (19%) lasted more than 6 mo, and 33 (30%) pts progressed. Median response duration was 7 mo (3-30+), (GP, 7 mo; GC, 6 mo). Median TTP and OS was 5 and 11 mo respectively. Although not directly comparable, we observed a higher TTP and OS in GP arm (7 and 11 mo respectively) than GC arm (5 and 10 mo).

Conclusions: Data of this study indicated both these 21-day regimens effective in advanced NSCLC. GC had a more favourable toxicity profile, but a possible higher activity was suggested for the GP regimen. Final results will be presented.

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A randomised phase II study of gemcitabine/cisplatin alone and with herceptin in patients with HER2-positive non-small cell lung cancer (nsclc)

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Herceptin has demonstrated improvements in survival and time to progression when added to chemotherapy in treating HER2-positive breast cancer. Improvements in treatment for NSCLC are needed and some lung cancers do show HER2 positivity. A randomised phase II study recruited 103 patients with stage IIIB-IV NSCLC. Median age was 59 and 72% of patients had adenocarcinoma. Patients were all HER2-positive as measured by immunohistochemistry (2+, 3+), FISH or high serum HER2 levels (>15ng/mL). Approximately 4% of patients were positive by high serum HER2 only. Patients were randomised to treatment with gemcitabine (1250mg/m2 days 1+8) and cisplatin (75mg/m2 day 1) 3 weekly cycles (control) or gem/cis 3 weekly cycles plus Herceptin (2mg/kg) weekly.

Patients in both the control and Herceptin arms have received a median of 6 cycles of therapy. The incidence of grade III/IV toxicity in the control vs Herceptin arms was: nausea, 52 vs 47%; stomatitis, 6 vs 6%; asthenia, 12 vs 13%; headache, 16 vs 32%; anaemia, 12 vs 16%; thrombocytopenia, 35 vs 36%; and leucopenia, 37 vs 34%. Clinically significant cardiac adverse events were limited to 2 patients (1 grade IV, 1 grade V) in the Herceptin arm.

Investigator-assessed response rates in the control/Herceptin arms were (95%CI) 41% (28-56) and 32% (20-47), respectively. Median TTP was (months; 95%CI) 7.2 months (6.4-9.7) and 6.3 months (5.5-7.2), respectively. Overall, there were 7 FISH-positive patients and 5 of these responded to treatment. Time to progression in the control arm patient was 5.4 months and in the Herceptin arm patients 4.6, 8.5, 9.6 and 11.1 months.

Herceptin and gem/cis appears to be a well-tolerated regimen. There was no evidence in this study that Herceptin adds to the efficacy of gem/cis in NSCLC. In the small numbers of patients who were FISH-positive and treated with Herceptin, the TTP was generally longer than the median. However, the majority of tumours were moderate overexpressors (90% 2+ by IHC) and a benefit in patients whose tumours overexpress/amplify HER2 at very high levels cannot be excluded.

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HER2 status in non-small cell lung cancer (NSCLC): results from the patient screening for enrolment to a phase 2 study of herceptin

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Purpose: Lung cancer is the major cause of cancer-related death in North America and Europe. About 75% of lung cancer is non-small-cell lung cancer (NSCLC). Overexpression of HER2 is associated with poor prognosis in NSCLC. The objective of this phase 2 study was to explore whether treatment with Herceptin would benefit patients with advanced NSCLC. For the enrolment in the pivotal Herceptin NSCLC trial patients were screened for HER2 overexpression at the 2+ or 3+ level by immunohistochemistry (IHC), and/or HER2 gene amplification of >2 by fluorescence in situ hybridization (FISH) and/or for shed antigen concentration >15 ng/mL by enzyme-linked immuno sorbent assay (ELISA).

Methods: 568 advanced and/or metastatic non-small cell lung carcinomas of stage IIIB and IV were evaluated. Of these 568 tumours, 164 were adenocarcinomas, 76 squamos cell carcinomas, 49 not further characterized large cell carcinomas, 2 signet ring carcinomas, and 279 tumours NSCLC not otherwise specified. 374 of the above tumours were examined with all three techniques.

Results: Adenocarcinomas were more frequently HER2 positive by IHC than squamous cell carcinomas and large cell carcinomas (31% vs. 19% vs. 14%, respectively). The HER2 gene amplification rate was low in all three tumour types (3.4% vs. 0% vs. 2.7%). Serum levels of >15 ng/mL were evident in 12 (19%) adenocarcinomas, 2 (3%) squamos cell carcinomas, and 5 (14%) large cell carcinomas. Out of 35 HER2 positive adenocarcinomas (by at least one method), 26 (74%) were poorly differentiated (G3). Overall, 29% of the evaluated tumours showed a positive HER2 status by at least one