1250 mg/m^2 on days 1 and 8 with cisplatin 70 mg/m^2 on day 1 (GC arm) for 4 cycles.
Results: Between July 2001 and January 2003, 102 patients were enrolled (50 on the GV-GI arm; 52 on the GC arm). Patient characteristics were balanced between arms (GV-GI arm: median age 59 years, 84% male, 22 stage IIIB, 24 stage IV, 4 stage IIIA; GC arm: median age 56 years, 87% male, 27 stage IIIB, 23 stage IV, 2 stage IIIA). Of the 101 patients evaluable for response, ORR was significantly higher on the GC arm than the GV-GI arm (25% vs 6%, respectively; p = 0.007). No complete responses occurred. TTP was longer on the GC arm than the GV-GI arm (median 135 and 79 days, respectively), although this difference was not statistically significant (p = 0.065). Survival was not significantly different between arms (median 293 and 197 days, respectively; p = 0.16). Although significantly more thrombocytopenia was reported on the GC arm (21% and 4%, respectively; p = 0.01), it did not lead to more transfusions (15 transfusions in 5 patients vs 14 transfusions in 6 patients, respectively). No other toxicities were significantly different between treatment arms.
Conclusions: GC produced better response in advanced NSCLC than GV-GI, with a trend towards longer TTP. Similar toxicity profiles were observed, with the exception of more thrombocytopenia on the GC arm.

P-583 Clinical parameters predictive of response in advance non-small-cell lung cancer (NSCLC) patients receiving gefitinib in an expanded access program (EAP) after failure of chemotherapy

C. Tibaldi[1], E. Vasile[1], A. Chella[2], F. Russo[1], I. Bernardini[1], A. Nacci[1], A. Falcone[1,3]. [1]*Division of Medical Oncology, Department of Oncology, Livorno, Italy;* [2]*Division of Pneumology, Pisa, Italy;* [3]*University of Pisa, Pisa, Italy*

Background: Epidermal growth factor receptor tyrosine kinase inhibitors as gefitinib (Iressa®) emerged as an accepted treatment in second- or third-line setting in NSCLC. Bronchioloalveolar carcinomas, never or former smokers and female gender were identified as highly sensitive to gefitinib. The objective of this analysis was to evaluate if other clinical parameters, such as response to first-line chemotherapy and time to disease progression to first-line chemotherapy, can predict the response to gefitinib.
Methods: We analyzed the characteristics and the response to gefitinib of 45 pretreated advanced NSCLC patients, who received gefitinib at the dose of 250 mg per day continuously until progression or unacceptable toxicity in an EAP. Patients characteristics were as follows: 30 male and 15 female; 20 adenocarcinomas, 16 squamous carcinomas, 4 bronchioloalveolar carcinomas, 5 NSCLC; performance status (PS) 0: 9 patients, PS 1: 22 patients, PS 2: 14 patients; the median age was 63 yrs (range 35–88); 38 patient were current or former smokers and 7 never smokers.
Results: Up to now 34/45 patients are evaluable for response: 8 patients (23.5%) were responders (partial response + stable disease ⩾6 months) and 26 (76.5%) were non-responders. Predictive factors associated with response were good performance status (responder rate: 60% in PS 0 patients vs 8.3% in PS ⩾1 patients), smoking history (responder rate: 42.8% in never smoking patients vs 18.5% in current or former smokers), histology (responder rate: 66.7% in bronchioloalveolar carcinomas vs 19.3% in other histologies). Response to first-line chemotherapy didn't affect the response to gefitinib. Time to disease progression to first-line chemotherapy was 10.5 months in responder patients and 8.1 months in non-responders.
Conclusion: Never smoking history, performance status 0 and bronchioloalveolar histology were associated with a better response to gefitinib. A longer time to disease progression to first line chemotherapy seems to be correlated with a higher response rate to gefitinib and this could be explained by less aggressive diseases with better biological features. The study is ongoing to better define these features.

P-584 Single agent gemcitabine (GEM) in performance status (PS) 2–3 patients (pts) with advanced non-small cell lung cancer (NSCLC): Effect on disease-related symptoms in a multicenter phase II trial

M. Tiseo[1], A. Tognoni[2], C. Caroti[3], M. Mencoboni[4], M. Pennucci[5], T. Coialbu[6], F. Brema[7], F. Grossi[1], P. Pronzato[2], A. Ardizzoni[8]. [1]*Istituto Nazionale per la Ricerca sul Cancro, Genova, Italy;* [2]*Ospedale S. Andrea, La Spezia, Italy;* [3]*Ospedale Galliera, Genova, Italy;* [4]*Ospedale Villa Scassi, Genova, Italy;* [5]*Ospedale Civile, Carrara, Italy;* [6]*Ospedale Pontedecimo, Italy;* [7]*Ospedale S. Paolo, Savona, Italy;* [8]*Istituto Nazionale per la Ricerca sul Cancro, Genova, Italy;* [9]*Ospedale S. Andrea, La Spezia, Italy;* [10]*Azienda Ospedaliera Universitaria, Parma, Italy*

Background: PS is an independent prognostic factor in NSCLC. Pts with advanced NSCLC and PS ⩾ 2 are generally not considered candidate for standard combination platinum–based chemotherapy. However, there is small evidence in randomized trials that PS ⩾ 2 pts may benefit from chemotherapy. If so, specific treatment strategies must be developed for this group of pts. GEM is well tolerated and improves disease-related symptoms and PS. Therefore, we are conducting a multicenter phase II study with GEM in poor PS pts with advanced NSCLC. Primary objective is to assess impact of treatment on disease-related symptoms palliation, while secondary objectives are to evaluate changes from baseline PS, response rate, toxicity and overall survival.
Methods: pts with stage IIIB and IV NSCLC and PS ⩾ 2 are treated with GEM 1200 mg/m^2 on days 1, 8 of each 21-days cycle plus best supportive care (BSC) for up to 4 cycles. Disease-related symptoms improvement is measured weekly using LCS of FACT-L questionnaire.
Results: from November 2002 to January 2005, 39 pts were enrolled of which 29 are so far fully evaluable. Pts characteristics were: 24 M/5 F, 22 PS2/7 PS3, median age 74 (range 63–86), 17 Adenocarcinoma/8 Squamous/1 Large Cells/3 Unclassified, 9 Stage IIIB/20 IV, all patients were symptomatic. Evaluable baseline questionnaire was received from 26 pts; among these, 21 pts were evaluable for symptom improvement. Median baseline score for LCS was 17 (range 7–24). Symptom improvement (defined as a 2-point or greater improvement in LCS score sustained for 4 weeks or longer, with no worsening at any interim weekly time points) rate was 25%. PS improved in 5 pts. 24 pts completed 2 cycles of GEM and 10 pts completed 4 cycles. For 18 pts who have been evaluated response rate was 20%. GEM was well tolerated. Median survival was 126 days.
Conclusions: Preliminary data of this ongoing study indicate that GEM is well tolerated and effective in disease-related symptoms palliation in pts with advanced NSCLC and PS ⩾ 2.

P-585 Carboplatin plus gemcitabine followed by weekly paclitaxel in advanced and metastatic non-small cell lung cancer (NSCLC): A phase II study

V. Tjan-Heijnen, J. Timmer-Bonte, M. van der Drift, F. van Leeuwen, T. de Boo, M. Wagenaar, L. van Die, J. Bussink. *Radboud University Medical Centre, Nijmegen, Netherlands*

Background: Chemotherapy for advanced NSCLC has gained widespread acceptance since it was demonstrated that cisplatin-based chemotherapy improved survival and quality of life. It was hypothesized that by using a non-cross resistant sequential combination of drugs the response rate might be unaffected or increase, whereas by not giving a three-drug but a sequential combination the toxicities associated with the cumulative amount of drugs might decrease. The primary objective of this sequential study was to determine the best overall response. Secondary endpoints were survival, toxicity and feasibility.
Methods: Patients were eligible if they had measurable advanced NSCLC, no prior chemotherapy, ECOG performance status 0–2 and adequate hepatic, renal and bone marrow function. Treatment consisted of carboplatin (C) AUC 5 day 1 and gemcitabine (G) 1000 mg/m^2 days 1 and 8, every 3 weeks intravenous for maximally 4 cycles, followed by 12 weekly infusions of paclitaxel (P) 80 mg/m^2.
Results: Thirty-six of 40 planned patients have enrolled, with at present 28 patients evaluated: 7 female, 21 male with a median age of 60 years (range 41–74 years). Four had stage IIIB and 24 stage IV disease. Histological subtype: 7 squamous cell carcinoma, 14 adenocarcinoma, 5 undifferentiated large cell carcinoma and 2 not specified. Twenty two patients completed 4 CG-cycles, 21 patients started the 2nd part of treatment of which 14 patients received 6–12 cycles. Of the 28 evaluated patients, 10 had a partial response (PR), 11 stable disease (SD) and 7 progressive disease (PD) on GC-treatment. Of 10 patients with PR on GC, 8 received P-treatment: 1 having PD, 5 continuing PR and 2 improved PR on P-treatment. Of 11 patients with SD on GC, 10 received P-treatment: 3 having PD, 4 continued SD and 3 PR on P-treatment. Of 7 patients with PD on GC, 3 received P-treatment: all 3 having early PD on P-treatment. Overall, 13 (46%) patients achieved a PR and 8 (29%) SD. Median survival was 8.5 months (range 1–38+). Grade 3–4 hematologic toxicity occurred in 46% (ANC) and 36% (PLT) of patients in CG-cycles, not in P-cycles. Grade 3–4 non-hematologic toxicity was seen in 32% of patients (mainly lung and asthenia) during CG-treatment. Grade 3–4 non-hematologic toxicity led to premature treatment discontinuation of P-cycles in 6 of 21 patients, i.e. grade 3–4 liver toxicity in 1 patient, polyneuropathy in 2 patients, perforated peptic ulcer in 1 patient, and interstitial pneumonitis in 2 patients leading to toxic death in one.
Conclusions: CG followed by P is a very active schedule (46% PR and 29% SD), but not easy manageable: 9 of 28 (32%) patients prematurely interrupted treatment because of toxicity. Supported by a grant from Eli Lilly and from Bristol Myers Squibb.

P-586 Phase II study of docetaxel and celecoxib as first or second line therapy in patients with advanced NSCLC

C. Underhill[1], R. Hui[2], M. Links[3], G. Hawson[4], B. Chern[5], D. Yip[6], T. Blackwell[7], C. Crombie[8], M. Boyer[9]. [1]*Border Medical Oncology, Albury-Wodonga, Australia;* [2]*Westmead Hospital, Australia;* [3]*St George Hospital, Australia,* [4]*Nambour Hospital, Australia;* [5]*Redcliffe Hospital, Australia;* [6]*Canberra Hospital, Australia;* [7]*Greenslopes Hospital, Australia;* [8]*Nepean Cancer Centre, Australia;* [9]*Sydney Cancer Centre, Australia*

Background: Overexpression of COX-2 has been found in lung cancers and may play a role in inhibition of apoptosis, promotion of angiogenesis and multi-

drug resistance. In vitro studies shown that COX-2 inhibitors can enhance the cell kill produced by cytotoxics including docetaxel.
Methods: Eligible patients had measurable (RECIST criteria) stage 3b (with pleural effusion) or 4, biopsy proven NSCLC, with adequate renal, hepatic and haematological function Patients with uncontrolled brain metastases or taking COX-2 inhibitors/NSAIDs were excluded. Stratum A was patients age≥70, ECOG PS 0–2 and no prior therapy, or age <70, ECOG PS2 and no prior therapy. Stratum B consisted of patients with one prior therapy and ECOG PS 0 or 1. All patients received celecoxib 100 mg po bd and docetaxel 36 mg/m^2 IV weekly ×6 q 8 weeks. Blood samples were taken for TNF-α, Il-6 and DNA analysis for translational studies. Patients at selected centres underwent PET scans and erythromycin breath testing. IEC approval was given and patients gave written informed consent.
Results: A total of 57 patients were entered on the study, with 39 patients on Stratum B, enrolled between Jan 2002 & Feb 04 reported in this abstract. Median age 60 (range 43–86) Males 28/39, ECOG PS = 0 8/39, PS 1 = 31/39, stage 3b with effusion 14/39, stage 4 25/39. Treatment was well tolerated with a paucity of NCI-CTC (v3.0) grade 3/4 toxicity seen: (grade: pts): neutropenia gr3: 3, gr4: 1; infection gr3: 1, gr4: 1; diarrhoea gr3: 1, gr4: 3, alopecia gr3: 1. No cardiovascular serious adverse events were recorded. Median number of doses of Docetaxel was 6 (range 0–18). There were 5 responses (2CR, 3PR, ORR 12.8%; 95% confidence interval 4.3–27.4%). Median OS was 5 months (range 8 days to 13+ months).
Conclusions: The combination of docetaxel and celecoxib was well tolerated, with response and survival rates similar to those of single agent docetaxel.

P-587 Experience from a large multi-centre expanded access programme (EAP) with gefitinib ('Iressa', ZD1839) as monotherapy in advanced non-small cell lung cancer (NSCLC)

R. van Puijenbroek[1], L. Bosquée[2], G. Tits[3], P. Germonpre[4], E. Strobbe[5], J. Vansteenkiste[1]. [1]*Catholic university, Leuven, Belgium;* [2]*Hospital Citadelle, Liège, Belgium;* [3]*St-Andriesziekenhuis, Tielt, Belgium;* [4]*Univ. Hospital Antwerpen, Belgium;* [5]*AstraZeneca, Belgium*

Background: A worldwide EAP has enabled >221,000 patients with advanced NSCLC to receive Gefitinib ('Iressa', ZD1839) treatment. This paper reports the pattern of use of Gefitinib and the outcome parameters with this treatment in the Belgian EAP. Patients were enrolled at different, university and non-university, hospitals. Data were sampled from all centres that included ten or more patients.
Methods: The series consists of 521 patients with advanced or metastatic NSCLC. Patients received oral Gefitinib 250 mg/day until disease progression, death, or unacceptable toxicity. The patient file listed data on demographics, and effect of Gefitinib on tumour evolution, symptoms and outcome. Detailed information about previous chemotherapy was included: number of previous lines, drugs administered, duration of treatment and treatment-free intervals, and best objective response to each line. Regarding Gefitinib, correlation analysis of potential predictors of response, disease control, symptom improvement and survival analysis was performed.
Results: At the time of submission, 215 questionnaires (41%) were completed for analysis, obtained from five centres that included a high number of patients in the EAP. Baseline demographics: male/female 154/61; stage III/IV/unknown 42/156/17; Performance status (PS) 0–1/2/3–4/unknown 85/70/41/19; histology adeno/BAC/other 112/15/88; smoking never/ever/unknown 15/170/30; prior chemotherapy lines 0/1/2/3+ 19/65/86/43. Best objective response to chemotherapy treatment was 40% for first-line, 23% for second-line, and 15% for third-line. The mean treatment-free survival was 4 months after first-line chemotherapy, 2.3 months after second-line, and 5.8 months after third-line. For all Gefitinib treated patients, disease control rate was 34% (objective response rate 8.4%), median survival 4.5 months, 1-year survival 22.7%, with symptom improvement in 27%. Gefitinib was well tolerated, with grade 3/4 toxicity observed in 9.3% of patients. PS, number of chemotherapy regimens and female gender were predictive for response and disease control. PS and number of chemotherapy regimens were predictive for symptom improvement. Histology and smoking history lacked such an association. Only PS had a highly significant impact of PS on survival.
Conclusions: This study gives detailed information on treatment patterns of advanced NSCLC in a community setting. Gefitinib demonstrated significant antitumor activity in this large set of pre-treated advanced NSCLC patients. Predictive factors for activity were better PS, lower number of chemotherapy regimens and female gender, but not histology or smoking. Prolonged survival was related to better PS only. Final data, including multivariate analysis, will be presented.

P-588 Biweekly docetaxel and vinorelbine as second-line treatment in advanced (stage IIIB+ IV) non-small-cell lung cancer (NSCLC). A phase II study of the Galician Lung Cancer Group

S. Vázquez[1], M. Villanueva[2], M. Amenedo[3], J. Fírvida[4], M. Lázaro[2], L. Del Río[5], G. Huidobro[2], J. Mel[1], M. Ramos[3], C. Grande[2]. [1]*Complexo Hospitalario Xeral-Calde, Lugo, Spain;* [2]*Complexo Hospitalario Universitario de Vigo, Vigo, Spain;* [3]*Centro Oncolóxico de Galicia, A Coruña, Spain;* [4]*Complexo Hospitalario de Ourense, Ourense, Spain;* [5]*Complexo Hospitalario Universitario de Santiago, Santiago, Spain*

Background: To evaluate the efficacy and safety of biweekly docetaxel and vinorelbine in previously treated patients with advanced NSCLC.
Methods: Patients with stage IIIB (with pleural effusion) and IV NSCLC, which progressed after or during first line chemotherapy, measurable disease, ECOG PS = 0–2 and adequate organ function were included. Previous treatment with paclitaxel was allowed. Docetaxel was administered at 40 mg/m^2 and Vinorelbine was administered at 20 mg/m^2, both iv, days 1 and 14. Cycles were repeated every 28 days until disease progression, occurrence of unacceptable toxity or voluntary withdrawal. Both, toxicity and efficacy analyses were performed on the intent-to-treat (ITT) population.
Results: A total of 50 patients were included (M/F, 40/10), with median age 59 years (31–89) and ECOG PS 0–1 in 75% of patients. Tumor histology mainly included epidermoid (50%), adenocarcinoma (25%). Tumor stage was IIIB (35%) and IV (65%). Median number of metastatic lesions was 2 (51% with 2 or more), located mainly in lymph nodes(33%), adrenal glands (31%), lung (31%) and bone (21%).Previous chemotherapy included platinum (97.8%), gemcitabine (82.6%) and paclitaxel (71.3%). A total of 170cycles (median 3, range 1–6) were administered. Median relative dose intensity for biweekly docetaxel and vinorelbine was 89%. Toxicity: Grade III/IV hematologic toxicities per patient were neutropenia (20%) and anemia (4%). One patient died due to neutropenia grade 3 and sepsis. Febrile neutropenia was observed in 3 patients. Grade III/IV non-hematologic toxicities occurred in <5% of patients, and included asthenia (4%), vomiting (2%), mucositis (2%) and diarrhea (2%).Efficacy: Of 49 ITT patients (1 patient have just begun chemotherapy), 1 achieved CR, 4 PR, 11 SD and 23 progressed resulting in an ORR of 10.2% (95%CI: 1.6–18.3%). Ten patients could not be evaluated for response due to early withdrawal (6 tumor-related exitus, 1 P.S. deterioration., 1 toxic death and 2 not-treatment-related pneumonias). Median TTP and OS were 87 days (95%CI: 33.4–140.6) and 198 days (95%CI: 115.1–280.8), respectively.
Conclusion: Biweekly docetaxel and vinorelbine is an active and feasible regimen in previously treated patients with advanced NSCLC.

P-589 Gemcitabine/docetaxel (GD) vs gemcitabine/cisplatin (GC) in stage IIIB/IV advanced non-small cell lung cancer (NSCLC): Grupo gallego de cancer de pulmon (GGCP)

S. Vázquez[1], J. Casal[2], F. Vázquez[3], M. Amenedo[4], J. Fírvida[5], J. Mel[1], G. Huidobro[2], M. Lázaro[6], G. Alonso[7], M. Constela[8]. [1]*Hospital Xeral Calde, Spain;* [2]*Hospital do Meixoeiro, Spain;* [3]*Hospital Arquitecto Marcide, Spain;* [4]*Centro Oncológico de Galicia, Spain;* [5]*Hospital Santa Marta Nai, Spain;* [6]*Hospital Xeral Cies, Spain;* [7]*Hospital Juan Canalejo, Spain;* [8]*Hospital Provincial, Spain*

Background: This trial was designed to compare, in terms of response rates, the standard regimen gemcitabine/cisplatin versus a non-platin regimen, gemcitabine-docetaxel in NSCLC. The chemotherapy regimens administered were: Arm A: gemcitabine 1250 mg/m^2 d1&8 plus cisplatin 75 mg/m^2 d1; Arm B: gemcitabine 1000 mg/m^2 d1&8 plus docetaxel 85 mg/m^2 d1 repeated every three weeks. Eligibility criteria were measurable stage IV or stage IIIB with pleural effusion NSCLC (brain metastases eligible if asymptomatic) and PS (ECOG Scale) = 0–2.
Results: 108 patients (pts) were included between January 2001 and August 2004, 56 in arm A and 52 in arm B. Till the moment 92 patients has been analyzed. For arm A median age was 60 (57–62); PS 0–1: 85.7%, PS 2: 14.3%; Stage IV: 80%, Stage IIIB: 20%. For arm B median age was 62 (59–65); PS 0–1: 85.7%, PS 2: 14.3%; Stage IV: 85.7%, Stage IIIB: 14.3%. Response rates are available in 92 evaluable pts: Arm A (50 pts): CR 2.2%, PR 35.6%, ED 33.3%; Arm B (42 pts): CR 2.8%, PR 47.2%, ED 22.2%. Median overall survival (OS) was 8.9 months (6.3–11.7) in arm A and 8.6 months (5.2–10) in arm B (p = 0.328); median time to progression disease (TTPD) was 6.4 months (4.2–7.6) in arm A and 5.5 months (4.2–10) in arm B (p = 0.973). Toxicities include, in Arms A and B respectively: Grade 3–4 neutropenia 48% and 47.6%, with neutropenic fever in 2% and 2.4%; Grade 3–4 thrombocytopenia 24%, 4.8%; Grade 3–4 anemia 12% and 2.4%. Non-hematological toxicity grades 3–4 were similar in both arms, with the exception of nausea and vomiting, (14% and 2.4% in arm A and B respectively); renal and hepatic toxicity (hepatic 6.1% vs. 17.2% and renal 4.1% vs. 0%), and infection (4% vs. 14.3%).
Conclusions: With the disposable data, overall response rate was higher in the combination gemcitabine-docetaxel, although there are no significant differences in OS and TTPD. GD is an active non-platin regimen and a good first treatment option for advanced NSCLC.