6616 POSTER

Phase II study of weekly chemotherapy with paclitaxel and gemcitabine as second-line treatment for advanced non-small cell lung cancer after treatment with platinum-based chemotherapy

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Background: Second-line chemotherapy has become almost routine in non-small cell lung cancer (NSCLC) patients (pts) with good performance status (PS). The availability of the new pharmacological agents opens up new possibilities for their use in pts who have retained a good PS following relapse or progression after first-line chemotherapy. Paclitaxel (PTX) and Gemcitabine (GEM) are among the most active new agents in NSCLC and are worth considering for second-line chemotherapy. In phase II study, we evaluated the tolerability and activity of the combination of weekly PTX and GEM in second-line treatment of NSCLC.
Material and Methods: PTX (100 mg/m^2) and GEM (1000 mg/m^2) were administered to NSCLC patients with previous treatment of platinum-based chemotherapy on days 1 and 8 every 3 weeks. A total of 40 pts (M/F, 27/13 pts; median age 59.3 years [33−75]; PS 0/1/2, 7/27/6 pts) were enrolled.
Results: The mean number of cycles administered per patient was 4, and number of cycles ranged from one to twelve. The final efficacy was PR in 13, NC in 26 and PD in 1 for a response rate of 32.5% (95% CI: 18−47%). The median survival time was 41.7 weeks (95% CI: 28.5−54.7 weeks). The median time to progressive disease was 19 weeks. Hematologic toxicities observed included grade 3 or 4 neutropenia in 60%, grade 3 or 4 anemia in 15%, and grade 3 or 4 thrombocytepenia in 12.5%. Non-hematologic toxicities were mild except grade 3 pneumonitis in 1 pt. There were no toxic deaths.
Conclusion: The combination of weekly PTX and GEM is a feasible, well-tolerated, and active scheme for second-line treatment of advanced NSCLC.

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Does the use of erlotinib for the treatment of relapsed stage IIIB/IV NSCLC patients improve quality-adjusted survival compared with docetaxel?

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Background: The main outcome of interest in the treatment of NSCLC is overall survival (OS). However, quality of life (QoL) can also be a significant consideration when selecting the most appropriate treatment strategy. The Quality Adjusted Life Year (QALY) is a measure of the effectiveness of a medical intervention that is increasingly used, especially within the context of pharmaceutical cost/benefit analysis. The QALY is a generic measure of health gain that captures both the quantity and the quality of life experienced by the patient. The following analysis estimated the QALYs for stage IIIB/IV relapsed NSCLC patients receiving erlotinib (Tarceva®) and docetaxel.
Methods: A health state transition model was constructed to stratify patient survival between progression-free survival (PFS) and progressive disease; grade 3/4 adverse events (AEs) were also incorporated. The time in each health state was weighted by published NSCLC utility scores to estimate the QALYs for both erlotinib and docetaxel. This analysis required estimates of survival and health-related QoL (represented by utility scores) for each intervention. QoL was derived from a NSCLC QoL study that estimated utility scores using the EuroQoL 5-Domain (EQ-5D) instrument (Tabberer M et al, Value Health 2006;9:A298). OS was based on phase III randomised, controlled trials, with a mean OS of 9.56 months assumed for erlotinib (Shepherd F et al, NEJM 2005;353:123) and 8.74 months for docetaxel (Hanna N et al, J Clin Oncol 2004;22:1589). Since mean PFS was not reported for docetaxel, the mean time on treatment reported in the trials was used to represent PFS (4.11 and 2.76 months for erlotinib and docetaxel, respectively). The incidences of grade 3/4 treatment-related AEs were also as reported in the clinical trials.
Results: Erlotinib was estimated to produce higher QALYs than docetaxel; 0.277 vs 0.210, which equates to 101 and 77 quality-adjusted days for erlotinib and docetaxel, respectively. When equivalent OS and PFS were assumed, the advantage for erlotinib in terms of QALYs persisted, due to a lower incidence of treatment-related AEs such as febrile neutropenia.
Conclusions: Erlotinib produces greater QALYs compared with docetaxel, and hence provides a valuable alternative to docetaxel in the treatment of relapsed NSCLC. This analysis also illustrates that when NSCLC treatments lead to comparable OS, the QALY can help to differentiate between interventions with different AE and QoL profiles.

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Gemcitabine and docetaxel in non-small cell lung cancer (NSCLC) and study of prognostic factors

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Lung cancer is the most important cancer in the world in term of incidence and mortality. Cisplatin-based chemotherapy represents the cornerstone treatment for advanced and metastatic NSCLC. However, cisplatin has severe toxicity (renal, neural and oto-toxicity) wich remains a significant clinical problem.
We conducted a prospective study to compare the efficacy, the toxicity and survival of two regimens of chemotherapy with and without platinum in stage III and IV non-small cell lung cancer.
Eighty (80) patients were included in this study (72 males, 8 females); the median age was 58.6 years, 40 patients in each arm. They received in:
Arm A: G-D gemcitabine 1250 mg/m^2 D1 and D8 + docetaxel 70 mg/m^2 D8 repeated every 3 weeks for six courses.
Arm B: C-P cisplatin 70 mg/m^2 D1 + paclitaxel 175 mg/m^2 D1 repeated every 3 weeks for six courses.
There was no significant difference in term of response and survival between DC and CP, suggesting the equivalent efficacy of the two regimens. In terms of toxicity, the two arms are comparable except for the asthenia and anemia.
Performans status and nodes status are prognostic factor for survival for patients with non-small-cell lung cancer. Biomarquers such as p53, EGFR, cell proliferation defined by ki67 does not seem to be in correlation with survival.
Larger and longer follow-up studies may be needed to determine the prognostic role of expression of those factors in NSCLC.

6619 POSTER

Efficacy of weekly docetaxel combined with platinum as 1st-line treatment in patients with advanced non-small cell lung cancer

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Background: Docetaxel is a highly effective chemotherapeutic agent with proven efficacy in non-small cell lung cancer (NSCLC). However, myelosuppression can be a substantial concern when docetaxel is administered every 3 weeks. Weekly administration of low-dose docetaxel has demonstrated comparable efficacy together with a distinct toxicity profile with reduced myelosuppression. We conducted a phase II study of weekly docetaxel and cisplatin or carboplatin in patients with advanced NSCLC to evaluate efficacy and safety.
Methods: Twenty-nine patients with advanced or metastatic NSCLC who had not received prior treatment were enrolled. The patients received intravenous infusions of docetaxel (35 mg/m^2, days 1, 8, 15) and cisplatin (75 mg/m^2, day 1) or carboplatin (AUC 6), followed by a week of rest.
Results: Twenty-six patients were assessable for efficacy and all patients assessable for toxicity. The overall response rate was 44.8%. The median survival was 11.3 months, and the 1-year survival rate was 37%. Of the hematologic toxicities, grade 3/4 neutropenia were observed in 12.6%, but there were no episodes of neutropenic fever. Non-hematologic toxicities were mild.
Conclusions: With weekly dosing, though efficacy is comparable, myelosuppression is substantially less, and the overall tolerability profile is better than with every 3 weeks dosing.

6620 POSTER

A phase II study of the combination chemotherapy of docetaxel and carboplatin in advanced non-small cell lung cancer

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Background: To evaluate the efficacy and safety of induction chemotherapy with docetaxel and carboplatin in advanced lung cancer.
Methods: Between January 2005 and January 2007, 54 patients were enrolled and evaluable. Patients were treated with Docetaxel 75 mg/m^2 and Carboplatin AUC 5 on day 1 every 21 days.
Result: Among the 54 patients, 51 were male. The median age was 62 (range 23−79) years old. Pathologically, 20 patients had adenocarcinoma,

19 patients had squamous carcinoma, 3 patients had large cell carcinoma and 12 had unclassfied. Complete responses (CR) were in 2 (3.7%) patients and partial responses (PR) in 26 (48%) patients. The overall response rate was 52% (95% CI, 37−65%) and the median response duration was 5 (range, 1 to 12.7) months. The median progression-free survival was 10.5 (range, 1.4 to 19.5) months. The median overall survival for all patients was 14.8 (range, 1.4 to 23.8) months.
During a total 253 cycles, anemia greater than CTC grade 2 occurred in 51 cycles (20%), leukopenia occurred in 22 cycles (8.7%) and thrombocytopenia occurred in 19 cycles (7.5%). Non-hematologic toxicities were minor and easily controlled.
Conclusion: The combination chemotherapy of docetaxel and carboplatin has moderate efficacy with acceptable toxicities in patients with advanced NSCLC.

6621 POSTER

A bi-weekly administration of gemcitabine and docetaxel in patients with non-small cell lung cancer

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Background: Combination of gemcitabine and docetaxel (GEM/DOC) has shown a favorable activity with its response rate of 34−37.5%, similar to that of cisplatin and docetaxel in chemotherapy-naive patients with stage IIIb or IV non-small cell lung cancer (NSCLC). However, neutropenia and pulmonary toxicities were related to the combination chemotherapy. Especially relatively high rate of pulmonary toxicities have been identified in monthly or weekly administration setting of both combination.
Purpose: We evaluated the feasibility and efficacy of biweekly GEM/DOC chemotherapy in patients with NSCLC.
Patients and Methods: Forty-four patients with post-operative recurrences and eighteen patients with unresectable advanced non-small cell lung cancer were enrolled in this study. Those patients received 1000 mg/m^2 of GEM and 30 mg/m^2 of DOC bi-weekly, q = 2 weeks. Response rate, toxicities, and completion rate are evaluated after 4 cycles. Those patients were basically treated on outpatient basis.
Results: A total of 62 patients were treated with combination of GEM/DOC. Patients characteristics were as follows; recurrent/unresectable: 44/18; male/female: 38/24; median age: 66.1 (range 32−80); performance status 0/1/2: 41/19/2; adeno/squamous/large: 45/15/2; chemo naive/previously treated: 24/38.
Response rate was 20.7% (CR 3, PR 9, SD 34, PD 12, and NE 4). Response rates by tumor pathological type were 25% (11/44) with adenocarcinoma and 8.3% (1/12) with squamous cell carcinoma. Over grade 3 leucopenia occurred in 17.7% (11/62), neutropenia in 32.3% (20/62), skin toxicities in 3.2% (2/62), and pulmonary toxicities in 3.2% (2/62). Treatment completion rate was 93.5% (58/62). The reasons for treatment discontinuation were pneumonia, skin rush, and angiodynia.
Conclusion: GEM/ DOC regimen is a feasible and efficacious regimen against advanced and/or recurrent NSCLC. Biweekly administration of GEM/DOC may decrease hematological toxicities and be well-tolerated regimen. In addition, the rate of pulmonary toxicities in biweekly GEM/DOC may be less compared with other scheduled combination.

6622 POSTER

Chemokine receptors CXCR4 and CX3CR1 in non-small cell lung cancer (NSCLC): pattern of expression and correlation with brain metastases (BM)

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Background: The expression of chemokine receptors has been correlated to the organ-specific metastatic pattern of several tumors, including lung cancer. Aim of this study was to evaluate CXCR4 and CX3CR1 expression in NSCLC and its relation with the occurrence of BM.
Materials and Methods: CXCR4 and CX3CR1 expression was detected by immunohistochemistry in primary tumor specimens of 13 patients (pts) with BM from NSCLC (group A), and in a matched control group of 9 pts with NSCLC and no relapse (group B). Matched group was composed of pts with high-risk of developing BM (stage IIIA-IIIB NSCLC) and adequate follow-up. To evaluate the chemokine staining the percentage of positive neoplastic cells and the intensity of immunoreactivity were considered.
Results: High CX3CR1 expression was detected in 5 (38%) and 4 (44%) cases in group A and B, respectively. The respective figures for CXCR4 were 0 and 5 (56%) in the two groups. No significant difference was observed in the expression of CX3CR1 in patients with and without BM; on the contrary low or no expression of CXCR4 was correlated to the occurrence of BM (p=.005). Interestingly, all pts (n = 3) with high CX3CR1 but negative CXCR4 expression developed BM, and all pts (n = 4) with high CX3CR1 and CXCR4 expression showed no relapse.
Conclusions: These preliminary observations suggest a possible role of chemokine pathway in the development of BM in NSCLC pts. Further studies in NSCLC are warranted to identify pts at high-risk of brain recurrence.

6623 POSTER

Renal safety of prolonged administration of pemetrexed (P)/platinum treatment for advanced malignant mesothelioma

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Background: Maligant mesothelioma is a very rare and aggressive neoplasm of the pleura or pertioneum with a short life expectancy. Standard care of MM is P + cisplatinum (DDP). Best duration of chemotherapy (ctx) for MM remains undetermined. The feasibility of maintenance with P/DDP in patients responding to induction chemotherapy has not been studied. A major obstacle to sustained P/DDP for MM is renal safety beside neurotoxicity. At present, there are no prospective trials with data regarding renal safety in pts receiving >6 cycles of P/DDP in MM.
Methods: We evaluated long term outcome of renal function of P(500 mg/m^2)/DDP(75 mg/m^2) for MM prospectively. Ctx on d1 was repeated on d22 until disease progression or toxicity. Pts with impairment of renal function (Creatinine-Clearance <60 ml/min) switched to P/carboplatinum (CP) AUC 5 for further ctx. P ctx was stopped if Creatinine-Clearance (CrCl) <45 ml/min. Routine folinic acid and vit B12 was administered to prevent AE. Study endpoint was long term renal function for sustained therapy of P/DDP followed by P/CP and/or P-mono.
Results: Between 12/02 and 07/06 86 consecutive pts were treated. Staging procedures revealed abdominal MM (AbM) in 19 pts and pleural MM in another 67. Five pts did not receive ctx. First-line ctx was P/DDP in 66 pts given a mean of 4.9 cycles (range 1−11) for a mean of 120 d (21–397 d) and a mean of 138 mg DDP/cycle. 28 pts received CP/P for maintanance sequentially up to a max of 27 cycles (mean 6.4). A change from P/DDP to P/CP was necessary due to a worsening renal function in all of those pts. Mean S-creatinine/CrCl prior to DDP ctx was 0.87 mg/dl (SD 0.17)/96.0 ml/min (SD 26) and 1.01 mg/dl (SD 0.29)/73.4 ml/min (SD 22) at the end of P/DDP. Median given CP dose was 425 mg (range 175–725 mg). Pts subsequently receiving P/CP had a S-crea of 1.16 mg/dl (CrCl 71.4 ml/min) prior to ctx that did not change during P/CP (1.13 mg/dl and CrCl 69.8 ml/min). 13 pts received P-mono with a mean of 8 cycles (1−26) subsequently. Renal function showed a S-crea(CrCl) of 1.13 mg/dl (71.2 ml/min) prior and 1.11 mg/dl (70.8 ml/min) at the end of P ctx.
Conclusions: Long term maintenance P/DDP of MM is limited by renal impairment due to DDP, while subsequent P/CP or P alone was feasible and not associated with a further deterioration of renal function. Further trials with sustained P/CP or P ctx for MM are warranted to evaluate the efficacy for advanced MM.

6624 POSTER

A plan study on the Iso-NTCP dose escalation of the respiratory-gated intensity-modulated radiation therapy for non-small cell lung cancer

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Background: It has been reported that the local control rate of non-small cell lung cancer is still low in spite of 3D-CRT. It is necessary to escalate the radiation dose and reduce the overall treatment time for improving the treatment results. A plan study was performed to evaluate the dosimetric benefits of the respiratory-gated intensity-modulated radiation therapy (IMRT) for non-small cell lung cancer.
Materials and Methods: Eight lung cancer patients were enrolled who received simulation four-dimensional CT (4DCT) scans. CT data was acquired on a multi-slice spiral CT scanner (Brilliance Big Bore, Philips) with a respiratory gating system (Real-time Position Management, Varian Medial Systems). Two patients were scanned under audio-guidance ('breathe in' and 'breathe out') and the others under free breathing. Planning target volume (PTV) was defined as gross tumor volume plus 5 mm margin. 3DCRT and IMRT plan were performed on Pinnacle ver 7.6c (Philips Radiation Oncology Systems, USA). Three to five coplanar and