

patients (33%) had second-line chemotherapy (the majority received docetaxel) after progression. The median overall survival was 11.0 months (95% CI=7.4, 14.6) in those patients who received chemotherapy after brain radiotherapy. Our results show that only a small fraction of NSCLC patients presenting with synchronous brain metastases are even considered for chemotherapy after WBRT. Although limited by the retrospective nature of the study, good performance status (ECOG 0-2) NSCLC patients with brain metastases who receive chemotherapy after brain radiotherapy have response rates and a median survival comparable to the general Stage IV NSCLC population. We propose that chemo-naïve NSCLC patients who receive radiotherapy treatment for synchronous brain metastases, and maintain an adequate performance status, should be considered for chemotherapy and should not be routinely excluded from clinical trials involving systemic therapy.

P2-242 NSCLC: Cytotoxic Chemotherapy Posters, Tue, Sept 4

First-line treatment with vinorelbine (VRL) plus cisplatin (CDDP) for patients with advanced non-small-cell lung cancer (NSCLC): Molecular correlates

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Background: The combination of cisplatin and vinorelbine is a reference regimen in first-line therapy for advanced NSCLC. The correlation between predictive genetic markers and clinical endpoints may improve the prediction of treatment success and thereby the tailoring of chemotherapy. In this trial, predictive genetic markers of response to CDDP/VRL were examined in genomic DNA and cDNA derived from tumors and circulating tumors.

Methods: 238 chemo-naïve p with stage IIIB (pleural effusion or supraclavicular lymph nodes)-IV or recurrent NSCLC were accrued at 35 sites between April 2004 and January 2006. Treatment consisted of CDDP 75 mg/m² IV day 1 plus VRL 25 mg/m² IV or 60-80 mg/m² oral, days 1, 8 every 21 days. DNA samples were collected from primary tumors for the assessment of microtubule associated protein 4 (MAP4) and from serum for checkpoint forkhead-associated and ring finger (CHFR) methylation.

Results: Data on 207 p is available. Median age 62 years (38-80); males: 84.5%; smokers: 79.2%; PS 0-1: 94.5%; adenocarcinoma, 48.4% / squamous, 34.2%; stage IIIB: 16.9%, IV: 83.1%. Median cycles: 4 (1-12). Hematological toxicities (%p): grade 3/4 neutropenia, 8.7%/7.7%; grade 3/4 thrombocytopenia, 0.5%/1.0%; grade 3 anemia, 2.4%. Febrile neutropenia appeared in 12 p (5.3%). Non-hematological toxicities (%p): pulmonary grade 3/4, 3.4%/2.4%; nausea/vomiting grade 3/4, 7.7%/0.5%; asthenia grade 3, 12.6%; pain grade 3, 5.8%; infection grade 3/4, 3.9%/0.5%; neurotoxicity grade 3, 0.5%. Efficacy in evaluable population: CR, 2.8%; PR, 30.7%; ORR, 33.5% (95% CI, 26.6% to 40.4%); SD, 36.3%. With a median follow up of 6.6 months, median survival for the whole population was 8.9 months (m),

progression free survival 5 m, event free survival 4.8 m, 1-year survival 39.4%.

Conclusions: The tolerability, efficacy and survival results of this trial confirm that CDDP/VRL is effective as first-line therapy, presenting a favourable toxicity profile in p with advanced NSCLC. Complete data on genetic markers will be presented.

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A Phase II study of Carboplatin plus Pemetrexed in previously treated patients with non-small cell lung cancer (NSCLC)

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Aim: This Phase II study was conducted in order to define the efficacy and safety of Carboplatin-Pemetrexed combination as a second-line treatment for NSCLC patients.

Patient and Methods: Twenty six patients with measurable NSCLC and PS 0-1 (ECOG scale) who had failed or relapsed after initial chemotherapy, received Carboplatin AUC4 and Pemetrexed 350mg/m² on day 1 and 15 on up to 6 q28 cycles. Vitamin B12 and folic acid supplementation was given. All patients received GCSF for days 3-5 and 17-19 of cycles. Response to treatment was evaluated by response evaluation criteria in solid tumors (RECIST), and toxicity was graded according to the National Cancer Institute Common Toxicity Criteria version 3.0.

Results: The most common severe hematological adverse events (CTC Grade 3,4) was thrombocytopenia in two patients (7.6%), and anemia in one (3.85%). Serious non hematological toxicity was onycholyses (3.85%), neuropathy (3.85%), stomatitis (3.85%), and fatigue (3.85%). The median number of treatment cycles was 4. Fourteen patients (54%) received all six cycles. One patient reported as complete responder (3.85%), 5 as partial responders (19%) and 4 had stable disease (15.4%), with over all response rate of 38.46%. Median time to progression for 2nd line chemotherapy and overall survival was 6 and 12.6 months respectively.

Conclusions: Second line regimen with carboplatin-pemetrexed in intensive schedule is well tolerate and effective treatment for resistant or relapsed, after initial chemotherapy, NSCLC.

P2-244 NSCLC: Cytotoxic Chemotherapy Posters, Tue, Sept 4

Effect of taxotere combination with celecoxib on proliferation of NSCLC cell

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Objective: To study the effects of Taxotere, Celecoxib and the combination of both on proliferation and apoptosis of NSCLC cell.

Methods: Investigate the effect of Taxotere, Celecoxib and the combination of both on proliferation of NSCLC A549 by MTT assays. Detect the change of apoptosis, cell cycle and the expression of COX-2 protein using flow cytometry analysis and immunocytochemistry, respectively.

Results: Taxotere could inhibit the proliferation of A549 cell by a time and dose-dependent manner and the combination with Celecoxib (12.5 μ mol/l, 25 μ mol/l) could improve the inhibition. After 48h of incubation with Taxotere, the highest inhibitory rate of the cell is 65% and the lowest inhibitory rate is 10%. High-dose celecoxib (>50 μ mol/l) can suppress COX-2 gene expression, while positive response was found in low-dose celecoxib(12.5 μ mol/l,25 μ mol/l) and the combination. Celecoxib can increase the percentage of cell in G0/G1 and decrease that in S and G2/M. The apoptosis rate of cell increased after Celecoxib combined with Taxotere.

Conclusion: Taxotere could inhibit effectively the growth of A549 cell lines in vitro and the combination with Celecoxib could improve the inhibition through inducing apoptosis and influencing the distribution of cell cycle, but had no significant influence in the expression of COX-2 protein.

P2-245 NSCLC: Cytotoxic Chemotherapy Posters, Tue, Sept 4

A phase II trial of pemetrexed in non-small cell lung cancer patients failing previous platinum-based chemotherapy and with/without tyrosine-kinase treatment

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Background: Pemetrexed is an effective salvage agent in NSCLC patients failing previous chemotherapy. Our aim was to evaluate the efficacy of pemetrexed in Chinese NSCLC patients who had failed previous platinum-based chemotherapy and had been salvaged with tyrosine-kinase inhibitor (TKI) treatment or not.

Methods: Treatment consisted of pemetrexed 500 mg/m² intravenous infusion on day 1 of every 3 weeks. Standard premedications, including vitamin B12, folic acid, and dexamethasone were given.

Results: Between June 2005 and November 2006, 44 patients (pts) were enrolled and completed the study. All had been treated with platinum-based chemotherapy. Thirty patients had been treated with TKI after they failed platinum-based chemotherapy. The present treatment was second-line treatment in 10 pts, and third-line or higher in 34 pts. Mean age was 62. Median cycles received was 4, and objective response rates was 18.2% (8 pts had PR). Treatment-related toxicities were mild and few. Grade 3 or 4 haematological toxicities included neutropenia in 18.2%, thrombocytopenia in 6.8%, and anemia in 4.5 pts. Non-haematological toxicities were all less than grade 3. Median time to disease progression was 4.4 months and median survival was 9.1 months. Those received present treatment as second line treatment had a better response than as third line or later treatment (40% vs. 11.8%, p=0.043). Previous treatment with TKI or not did not affect patient's response to present treatment (p=0.782)

Conclusions: This study demonstrated that pemetrexed salvage chemotherapy in NSCLC patients who have failed previous platinum-based chemotherapy produces a relatively lower toxicity profile, and a better compliance and response rate than conventional salvage chemotherapy. Use of pemetrexed as second line agent will have better response rate than as third line or later treatment.

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NSCLC: Cytotoxic Chemotherapy Posters, Tue, Sept 4

Phase II randomized study of vinorelbine alone or plus cisplatin against Chemo-naïve Inoperable Non-small Cell Lung Cancer in the Elderly

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Background: Our aim here was to determine whether or not adding cisplatin into vinorelbine treatment is an appropriate regimen for chemo-naïve NSCLC in patients aged 70 or older.

Methods: After stratification by performance status, patients were randomized into vinorelbine (V) or vinorelbine plus cisplatin (VP) treatment arms. Treatment consisted of vinorelbine 25 mg/m² intravenous infusion on days 1 and 8 of every 3 weeks (V arm), or vinorelbine 22.5 mg/m² intravenous infusion on days 1 and 8, and cisplatin 60 mg/m² intravenous infusion on day 1 of every 3 weeks (VP arm). From May 2005 to December 2006, 68 patients were enrolled. Sixty-three patients went off-study before end of February 2007. Present analysis was based on these 63 patients.

Results: There were 29 patients received V treatment and 34 patients received VP treatment. There was no statistical significant difference in clinical characteristics. In all, 104 cycles of V (median, 4 cycles per patient) and 137 cycles of VP (median, 4 cycles per patient) were given. Objective response rates were 17.2% in V and 32.4% in VP (p=0.175). Control rates were 51.7% in V and 82.4% in VP (p=0.009). Myelosuppression was more common and severe in VP arm. Any grade of anemia and neutropenia were significantly higher in VP arm (p=0.002 and 0.018, respectively). Two patients in VP arm suffered from febrile neutropenia and one patient died in spite of G-CSF and antibiotic treatment. There was only one patient in V arm who had uneventful febrile neutropenia. Non-haematological toxicities was mild and all less than grade 3, except one patient in VP arm who suffered from grade 3 renal function impairment and one patient in V arm who had grade 3 phlebitis. Fatigue sensation was more common and severe in VP arm (p=0.031). Median time to disease progression was 2.7 months in V arm and 5.2 months in VP arm (p=0.0125). One-year survival rate was 49.8% in V arm and 45.4% in VP arm.

Conclusions: Adding cisplatin into vinorelbine treatment is feasible in elderly patients, and has better disease control rate and longer median time to disease progression. However, vinorelbine plus cisplatin treatment was more toxic than vinorelbine treatment alone in elderly patients.

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The effects of NSCLC neoadjuvant therapy on the serum and tumor levels of growth factors, apoptosis and invasiveness markers

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Our aim was to evaluate the effect of neoadjuvant therapy and subsequent surgical treatment of non-small cell lung cancer (NSCLC) on serum markers of tumor growth and expansion: VEGF, TGF- β , bFGF, TIMP-1 and apoptosis marker CD95L assessed by Elisa. 24 NSCLC patients were evaluated: 12 in stage IIIA. 9-IIB, 1-IIA, 1-IB, 1-IA.