P2-281   NSCLC: Cytotoxic Chemotherapy Posters, Tue, Sept 4

Retrospective study on patients diagnosed with advanced Non-Small Cell Lung Cancer treated with the combination of gemcitabine and vinorelbine: assessment of therapeutic efficacy and prognosis factors

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Introduction: Gemcitabine (G), vinorelbine (V) and their combination (GV) have shown to be useful in patients with Non-Small Cell Lung Cancer (NSCLC). The purpose of this study has been to confirm the effectiveness (activity) of GV and to identify prognostic factors related with clinical outcomes.

Methods: A retrospective analysis was carried out relating to 144 patients with NSCLC treated between October 1996 and April 2005 with G (1000-1250 mg/m^2) +V (25-30 mg/m^2) both administered on days 1 and 8 every three weeks.

Results: Treatment was well tolerated neutropenia grade 3-4 being registered as the worse toxicity in 18% of cases, including 7% of neutropenic fever. The objective response rate was 36.8% (95% CI: 28.9-44.7) and the median progression free survival and overall survival rates were 21 (18-25) and 33 (26-40) weeks respectively. In multivariate analysis only the histology of adenocarcinoma (HR 3; p<.0001), less than two metastatic sites (HR 1.7; p =.02)and Karnofsky index (KI) above 70 % (HR 1.5; p=.02) showed a significant association with longer survival.

Conclusion: The combination of GV is well tolerated and active in patients with advanced NSCLC. The histology of adenocarcinoma, less than two metastatic sites and KI above 70 % have been identified as independent variables related with longer survival.

P2-282   NSCLC: Cytotoxic Chemotherapy Posters, Tue, Sept 4

Gemcitabine and vinorelbine combination as second-line therapy in previously taxane and platinum-treated non-small cell lung cancer

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Background: Gemcitabine (G) and vinorelbine (V) combination showed tolerable toxicities with response rate of 10-30% as second-line chemotherapy at several phase II studies. We evaluated its efficacy and toxicity in previously taxane and platinum-treated refractory NSCLC.

Methods: From July 2004 to February 2007, 25 evaluable patients were enrolled. All patients were refractory or resistant NSCLC after taxane and platinum combination as first-line therapy for advanced NSCLC and ECOG PS 0-2. Treatment consisted of gemcitabine 1000 mg/m^2 plus vinorelbine 25 mg/m^2 i.v. on days 1 & 8 of a 21-day cycle.

Results: Among a total of 25 patients, 23 patients were evaluable for response and all 25 patients for toxicity. Median age was 58 years (range 44-79) and gender ratio was 19 males/6 females. Objective responses were seen in 5 of 23 evaluable patients (22%). four patients (18%) had stable disease and 14 patients (60%) progressive disease. Median overall survival was 5.3 months. A median of 2 cycles per patients were administered (range 1-8). The median delivered dose was 538.5 mg/m^2/week of gemcitabine and 13.3 mg/m^2/week of vinorelbine and relative dose intensity was 81% and 80%, respectively. Grade 3/4 neutropenia occurred in 68% but, febrile neutropenia only occurred in 12%. Nausea, vomiting, anorexia, neuropathy and liver dysfunction were mild in most of patients. Grade 3 asthenia occurred in 20%. There was no predictive factor for tumor response of second-line therapy. For univariate analysis for overall survival, the responder of first-line, good performance status, and disease-stabilized patients of GV chemotherapy were significantly analyzed (p<0.05).

Conclusions: Gemcitabine and vinorelbine combination therapy showed modest efficacy with disease stability of 40% and tolerable toxicity profile in patients with previously taxane and platinum-treated refractory NSCLC.

P2-283   NSCLC: Cytotoxic Chemotherapy Posters, Tue, Sept 4

Dose individualization of Carboplatin in elderly patients with advanced non small cell lung cancer (ANSCLC): an exploratory analysis

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Background: Application of population pharmacokinetic modelling to the routine therapeutic drug monitoring in elderly patients help to individualize the dosage of anticancer drugs. The aim of this study was to explore, by means of the individual pharmacokinetic parameters, the Calvert's formula bias for establishing the Carboplatin (Cb) dose in elderly patients. Creatinine (Cr) Cl was calculated by Cockdroft-Gault equation.

Methods: Between December 2005 and September 2006, 19 chemonaive ANSCLC patients were included in two groups: 9 adult patients < 65 years and 10 aged patients > 75 years. Treatment consisted in Cb day 1 and gemcitabine 1250 mg/m^2 days 1 and 8 every 21 days. Cb dose was calculated for a foreseen AUC= 5 in young adults and AUC= 4 in aged patients. Three blood samples were collected between 1-2 hours (h), 3-5 h and 12-24 h post infusion. Ultrafiltrated Carboplatin (Cbu) was determined using a flameless atomic absorption spectrometer. For pharmacokinetic analysis non lineal effects models implemented in NONMEM program were used. Individual pharmacokinetic parameters were calculated and predictors in the structural model were analysed.

Results: Mean and variation coefficient of some biometric characteristics and pharmacokinetic (PK) parameters are as follow:

Group	Cb Administered Dose (mg)	Age (years)	Cbu Cl Calvert (mL/min)	Cbu Cl Estimated (mL/min)	Cbu Calculated Dose (mg)
Young	662(23.4)	58(7.51)	129.62(25.2)	137(15.1)	741(19.9)
Elderly	323(16.1)	77.7(1.88)	81.61(8.21)	59.7(15.1)	234(20.9)