Grade 3/4 anemia occurred in 1 pt (5%) and grade 3 thrombocytopenia in 3 pts (14%). Non hematological toxicity was mild; 3 pts (14%) developed grade 3 neuropathy and 7 pts (34%) grade 2/3 asthenia. Mild hypersensitivity reactions occurred in 2 pts (10%). A total of 62 cycles were administered (median number: 3 cycles/pt). The median administered dose intensity was 100% of the planned dose for P and 85% for C. Three pts (17%) achieved partial response, 5 pts (28%) stable disease and 10 pts (55%) progressive disease Two of the responding patients had refractory disease and responses lasted for 4.5 months (2 pts) and 2.5 months (1 pt). The median TTP was 5.5 months (range: 3–10) and the median overall survival was 7 months (range: 1–14.5).

Conclusion: The P + C combination is a well tolerated and active regimen as second line therapy in patients with SCLC.

1028 PUBLICATION

Phase II multi-institutional study of Irinotecan (CPT-11) and Cisplatin (CDDP) on a three-week schedule in patients with advanced non-small cell lung cancer (NSCLC)

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Introduction: Irinotecan (CPT-11) is a promising new drug in non-small-cell lung cancer (NSCLC). The combination of CPT-11 and CDDP is being developed with the aim of having a regimen with potential effectiveness for NSCLC and other solid tumours as well. The optimal schedule of the combination is not established.

Patients and Methods: Patients eligible had histologically confirmed NSCLC, measurable disease, stage IV or IIIB non suitable for radiotherapy, age = <71 years, ECOG performance status = <2. Patients previously treated with chemotherapy for advanced disease or with symptomatic brain metastases were not eligible. CPT-11 200 mg/m^2, given as a 60 minute i.v infusion, was immediately followed by CDDP 80 mg/m^2 i.v. on day 1. Cycles were repeated every 21 days. In case of delayed diarrhoea immediate therapy with loperamide was started. Prophylactic use of haematopoyetic growth factors was not permitted.

Preliminary Results: From July 98 to February 99, 48 patients have been recruited. 43 are currently evaluable for toxicity and 32 for efficacy. 125 cycles have been administrated (median: 3, range: 1–8). Median age: 59 (43–71) years; M/F: 37/6. 18% IIIB, 82% IV.

Histology: 33% squamous cell carcinoma, 37% adenocarcinoma, 22% large cell carcinoma, 8% non differentiated carcinoma. Main toxicities (% patients) were neutropaenia (NCI grade 4) 11.6%, diarrhoea (NCI grade 4) 9.3%, nausea and vomiting (NCI grade 3) 16.2%, asthenia (NCI grade 3) 8.1%.

32 patients are available for efficacy after 3 cycles. 13/32 achieved partial response, 11/32 stable disease and 8/32 progressed. Updated results will be presented.

Conclusion: Preliminary data suggest that irinotecan and cisplatin on this particular schedule have a manageable toxicity profile and that this combination is fairly active in NSCLC.

1029 PUBLICATION

Gemcitabine-cisplatin-vinorelbine phase II trial in stage III non small cell lung cancer

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Purpose: To assess efficacy and toxicity of Gemcitabine (GZ)-Cisplatin (CP)-Vinorelbine (VN) in stage II non small cell lung cancer (NSCLC).

Methods: From Jan/98 to Jan/99 46 patients (pts) were enrolled, 43 were male and 3 female, median age 63.5 years (42–75), ECOG PS 0/1/2 was 10/35/1, stage IIIA/IIIB were 11/35, and histology squamous/adenocarcinoma/large cell was 32/9/5. It was required to have histologically proven NSCLC subsidiary of radical management. Treatment was GZ 1000 mg/m^2 on days 1 and 8, CP 100 mg/m^2 on day 1 and VN 25 mg/m^2 on days 1 and 8, every 21 days.

Results: To Feb/99 37 pts were evaluable for response and all for toxicity. Overall response rate was 62% (95% CI: 47–77%) with 2 clinical CR (5%) and 21 PR (57%), 12 SD (33%) and 2 PD (5%). After treatment 7 pts were sent to surgery and 27 to radiotherapy. Even with a short follow-up, 7 pts are death (2 due to toxicity) and 39 are alive. A median of 3 cycles per pts (1–6) were administered. In % over total sessions CTC grade 3 toxicity was anemia in 2.2%, neutropenia in 14%, thrombocytopenia in 5.1%, nausea in 2.9%, vomiting in 7.4%, creatinine in 1.4%, pulmonary edema and stomatitis in 0.7% each one. Grade 4 toxicity was neutropenia in 13.3% (6 febrile), thrombocytopenia and vomiting in 1.4% each one and dyspnea in 0.7%. Moderate and severe fatigue were reported in 11 and 6 pts. 16 hospitalizations and 2 toxic deaths were observed, and 3 pts left treatment due toxicity.

Conclusion: Although results toxic, these findings suggest that this regimen is very active in locally advanced NSCLC.

1030 PUBLICATION

Blood cell mitochondrial DNA (mtDNA) damage related to treatment in small cell lung cancer (SCLC) patients

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Purpose: Evidence of accumulation of the carcinogen agents in the mitochondria have been reported. To explore *in vivo* the effect of exogen agents, like chemotherapy (CT) or radiotherapy (RT) on mtDNA, we undertook the present study in SCLC patients.

Methods: 19 patients with SCLC (limited disease) were studied. All patients underwent the same treatment, based on four CT courses of carboplatin and oral etoposide, and chest RT. Blood samples were taken before and inmediatly after CT and every 12 weeks during the patients follow-up. Variations of three mtDNA mutations (mutations in tRNA genes of mtDNA) were detected by mutation specific PCR and assess them by a semiquantitative method, in mtDNA of blood cells; the ratio between mtDNA and nuclear DNA was also analyzed by the same semiquantitative method.

Results: The higher ratio of each mutation studied was observed inmediatly after the CT, decreasing to basal values during RT treatment and post-treatment visits. The top deviation of mtDNA with mutations, respect to basal values was between 3-fold to 80-fold. The correlation between ratio of mtDNA mutations and the total mtDNA showed that a low ratio of mutations correlates to increased mtDNA and viceversa.

Conclusion: Mitochondrial DNA of blood cells is damaged during CT administration and this injury is reverted after CT treatment. The amount of mtDNA increases with a low ratio of mtDNA mutations, and clearly decreases when a very high ratio of mtDNA mutations are present.

1031 PUBLICATION

A multi-centre phase II trial of gemcitabine (GEM) and vinorelbine (VRL) in patients (PTS) with stage III–IV non small cell lung cancer (NSCLC)

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Purpose: A multi-centre phase II study was conducted to evaluate the efficacy and toxicity of VRL plus GEM in pts with stage IIIb or IV NSCLC.

Patients and Methods: From March 1998 to September 1998, 40 pts were enrolled on study. VRL 20 mg/m^2 was given as a 10 minutes I.V., followed by a 30 minutes I.V. of GEM 800 mg/m^2 on days 1, 8, and 15 of each 28-day cycle.

Results: Twenty-two (55%) pts were stage IV and 7 IIIB (17.5%). The majority of pts were male (80%). Median age was 68 (range 39 to 84). Two pts achieved a complete response, and 27 pts achieved a partial response: overall response rate of 72.5%. (95% CI, 58.7%–86.3%). Median survival was 12 months. Significant (WHO grade 3/4) toxicities were myelosuppression, which included leucopenia (47.5% of pts), anemia (17.5% of pts), and thrombocytopenia (12.5% of pts). However, febrile neutropenia occurred only in 3 pts and accounted for one treatment-related death. Chronic fatigue syndrome, or flu-like syndrome, occurred in 17 pts and the symptoms recovered spontaneously one to two days after injections in 10 pts. Another 7 pts needed dose reduction to relieve symptoms. Interstitial pneumonitis occurred in 6 pts and recovered after steroid treatment. No patient experienced grade 3 or 4 nausea/vomiting.

Conclusion: The combination of VRL and GEM in advanced NSCLC is a highly active non-cisplatin containing regimen with acceptable toxicity profile.