similar efficacy to that of intravenous NVB with a dose-equivalence between both formulations demonstrated from pharmacokinetics (PK). The safety profile is almost identical with the exception of more frequent nausea and vomiting, but rarely severe. In order to evaluate the impact of a standard anti-emetic prophylaxis, we compared the UGT toxicity in two NSCLC patient populations treated by oral NVB with/without anti-emetic prophylaxis.

Material and methods: The UGT has been retrospectively analysed from two studies performed in locally advanced or metastatic NSCLC pts receiving NVB oral as a weekly monotherapy at 60mg/m2 for 3 doses, then increased to 80mg/m2 in the absence of grade 3-4 neutropenia. In the 1st study (Ann Oncol 2001;12(10):1375-81), there was no anti-emetic prophylaxis given to the 76 pts treated with oral NVB. In the 2d protocol recently conducted in 56 pts, a systematic anti-emetic prophylaxis was recommended including 5–HT3 antagonists. PK was performed in both studies.

Results: In the 76 NSCLC pts (median age: 64y) without anti-emetic prophylaxis (1st study), nausea and vomiting (CALGB scale) were 83% and 65% respectively; however grade 3-4 were infrequent (10.5% and 7.9% respectively). Median delay between dosing and vomiting was 5 hours with only one occurrence within the 1st hour and 25% vomiting occurring between 2 and 3 hours post dose. Secondary prophylaxis was given to 49% pts (34% with a dopamine antagonist and 14.5% with a 5HT3 antagonist). In the 56 pts (2d study) (median age: 74y) with anti-emetic prophylaxis, 88% received a 5HT3 antagonist. Overall incidence of nausea (54%) and vomiting (24%) were largely reduced compared to their occurrences in the 76 pts without anti-emetic prophylaxis. One pt had grade 3 nausea (2%) and 1 pt (2%) grade 3 vomiting (NCI-CTCv2 scale). No influence of early vomiting (<3h) on NVB oral bioavailability was demonstrated from population PK analysis. The absence of any PK drug-drug interaction between anti-emetics and NVB oral was also well established.

Conclusions: UGT can be controlled in pts treated with oral NVB by a primary anti-emetic prophylaxis with 5HT3 antagonist. This type of prophylaxis is a standard recommendation in the ESMO guidelines. Moreover, neither early vomiting nor associated anti-emetic prophylaxis modify NVB blood exposure.

802 POSTER

Multicenter Phase II trial of weekly Taxol and Paraplatine as first line treatment in elderly patients with non small cell lung cancer (NSCLC): preliminary results

J.-L. Pujol[1], B. Milleron[2], E. Quoix[3], A. Depierre[4], J.-L. Breton[5], R. Gervais[6], D. Debieuvre[7], S. Hominal[8]. [1] *Hopital Arnaud de Villeneuve, Pneumologie, Montpellier, France;* [2] *Hopital Tenon, Pneumologie, Paris, France;* [3] *Hopital Civil, Pneumologie, Starsbourg, France;* [4] *Hopital Jean Minjoz, Pneumologie, Besancon, France;* [5] *Centre Hospitalier de Belfort, Pneumologie, Belfort, France;* [6] *Centre Francois Baclesse, Pneumologie, Caen, France;* [7] *Centre Hospitalier de Vesoul, Pneumologie, Vesoul, France;* [8] *Centre Hospitalier d'Annecy, Pneumologie, Annecy, France*

The use of platinum based chemotherapy in elderly patients with NSCLC is still controversial. The purpose of this phase II trial was to evaluate the efficacy and the safety of 1st line weekly Taxol (T) [paclitaxel] and Paraplatine (P) [carboplatin] in elderly patients with NSCLC.

Eligibility criteria included: age > or = to 70; measurable disease; ECOG PS 0-2; adequate bone marrow, liver, and renal function; no previous chemotherapy; and patient informed consent.

Treatment schedule: T 90 mg/m^2 IV (1h) on days 1, 8 and 15 and P AUC 6 IV on day 1 of a 28-day cycle. Tumor response was evaluated using RECIST criteria and symptoms were evaluated using lung cancer symptoms scale (LCCS).

Results: From March 2002 to March 2003, 51 patients have been included. Data are available for the 40 first patients. They were 29 males and 11 females, median age 74 (range 70-88), ECOG PS: 0 (33%), 1 (56%) and 2 (10%). Tumor histology was squamous cell carcinoma in 13 pts, adenocarcinoma in 23 pts, Large cell Carcinoma in 2. NSCLC was stage IV in 33 pts and IIIb in 7 pts. A total of 156 cycles have been administered (median 4 /pt [range 1-6]). Hematologic toxicity: G3-4 neutropenia in 2 pts (5%) G4 thrombocytopenia in 1 pt (3%) and G3 infection in 2 pt (5%). Non-hematologic toxicity: G3 asthenia in 1 pt (2%), G3 neuropathy in 3 (7%). One toxic death is reported. Objective response was reviewed by an independent committee for 38 first evaluable pts: 1 CR, 17 PR and 12 Stable disease.

Conclusion: Preliminary data suggest that weekly Taxol and Paraplatine is a well tolerated combination with very promising activity in elderly population with NSCLC. Final analysis will be available in September 2003.

803 POSTER

Phase I / II and pharmacokinetic study of Vinflunine (VFL) in combination with cisplatin (CDDP) for treatment of advanced non-small cell lung cancer (NSCLC) in chemonaive patients: Preliminary results.

M. Krzakowski[1], R. Ramlau[2], M. Pinel[3], G. Zorza[3], C. Colin[3], P. Souquet[4]. [1] *The Maria Sklodowska-Curie Memorial Cancer Center, Thoracic Tumours Depertment, Warsaw, Poland;* [2] *Grand Poland Center of Pulmonary Disease abd Tuberculosis, POZNAN, Poland;* [3] *Institut de Recherche Pierre Fabre, Boulogne Billacourt, France;* [4] *Centre Hospitalier Lyon Sud, Pierre Benite, France*

VFL (Javlor®) is a novel semi-synthetic vinca-alkaloid obtained through superacidic chemistry by the selective introduction of two fluorine atoms at the 20'position of vinorelbine (VRL). VFL has shown higher in vivo antitumour activity than VRL in several human tumour models. Platinum-based doublets are the standard of treatment in advanced NSCLC and pre-clinical experiment testing in vitro A549 human NSCLC line has shown synergistic effects of VFL in combination with CDDP. This trial was designed to determine the recommended dose (RD) of the combination (phase I) and, its response rate and safety (phase II) in pts with previously untreated advanced NSCLC. Pharmacokinetic blood sampling was performed to study the absence of mutual interaction VFL-CDDP. Three doses of VFL were investigated 250 mg/m*, 280 mg/m* and 320 mg/m* in combination with CDDP 80 mg/m* once every 3 weeks. Due to the absence of dose limiting toxicities in the first 2 doses of VFL (3 pts per dose), the RD was established at VFL 320 mg/m* plus CDDP 80 mg/m*. Accrual is planned for 40 evaluable pts in phase II (at the RD). As of today, 36 are included and results available for 15 pts with Karnofsky's performance status (KPS) 80 to 100%, measurable disease (WHO) and adequate biological functions. So far, 15 pts (13 males, 2 females; KPS 100%: 5 pts, KPS 90%: 7 pts, KPS 80%: 3 pts; median age: 56 years/range 47-70) are evaluable for response and safety. Five out of these 15 patients achieved partial response (independent radiological review) and, 7 had stable disease. The median number of cycles administered was 5. No grade (G) 3 / 4 anaemia or thrombocytopenia were recorded (NCI-CTC scale), neutropenia G 3 / 4 was seen in 52% of cycles and one episode of febrile neutropenia was reported. Other G 3 non haematological toxicities were: constipation and hiccups 1 episode respectively and abdominal pain 2 episodes. Preliminary pharmacokinetic analysis does not evidence any VFL / CDDP interaction.

Conclusions: VFL / CDDP is a highly active combination in first line treatment of advanced NSCLC, with an excellent tolerance profile; the study accrual is ongoing and updated results will be reported at the meeting. Other combination trials in first line NSCLC have started with carboplatin and gemcitabine.

804 POSTER

Navelbine and Cisplatin with concurrent radiotherapy for unresectable stage III NSCLC

P. Rusu[1], T.E. Ciuleanu[1,2], D. Cernea[1], D. Pelau[1], V. Gaal[1], C. Cebotaru[1], D. Iancu[1], T. Guttman[1], N. Todor[1], N. Ghilezan[1,2]. [1] *Oncology Instinute "Ion Chiricuta", Radiotherapy, Cluj-Napoca, Romania;* [2] *UMF " Iuliu Hatieganu", General Oncology, Cluj-Napoca, Romania*

Purpose: There has been conducted a prospective phase II study to determine the response rate (RR), toxicity and survival (S) of concurrent Navelbine and Cisplatin (2 cycles), with radiotherapy, followed by 2 additional cycles of consolidation chemotherapy with the same drugs, for locally advanced stage III NSCLC. In order to decrease toxicity the role of protectors like amifostine has been evaluated.

Methods and materials: Thirty-three patients with histologically proven NSCLC, unresectable stage IIIA and IIIB, PS=1-2, measurable disease, adequate hematologic, renal and hepatic functions were included the study from 16.11.2000 to 20.11.2002, Patient caracteristics were: median age 59, ranging between 45 - 71, M/F=30/3, PS 1/2=13/20, stage IIIA/IIIB=3/30, squamous cell cc 27, adenocc 2, adenoid chistic cc 1, large cell cc 3. Thetreatment consisted of 2 cycles of chemotherapy with Navelbine (15 mg/sqm, d 1,8, q21) and Cisplatin (80 mg/sqm, d 1, q 21), given concurrently with radiotherapy (60 Gy/30 fractions/ 6 weeks), followed by 2 more cyclesof consolidation chemotherapy with the same drugs (navelbine: 25 mg/sqm d 1,8, cisplatin 100mg/sqm, d1, q 21). Fifteen patients received amifostine (Ethyol WR-272) 740 mg/sqm, d1, 8, q 21, which is an organic thiophosphate, found to have radio and chemoprotective effect. Chemotherapy has been completed by 63% and radiotherapy by 94% patients.