

conducted with the oral formulation of NVB aiming to evaluate equal efficacy/tolerability.

**Material and methods:** Pts to be recruited were  $\sim 70$ y with unresectable localised or metastatic NSCLC. Oral NVB was given weekly 60mg/m<sup>2</sup> (1 cycle/cy) and then escalated to 80mg/m<sup>2</sup> if no gr 4 neutropenia/no more than 1 gr 3 during first cy. At 80mg/m<sup>2</sup>, if 1 gr 4/2 consecutive gr 3 neutropenia occurred, dose was reduced to 60mg/m<sup>2</sup>. All pts had anti-emetic prophylaxis. Primary endpoint was response rate (OR) with secondary endpoints being response duration (MDR), progression-free survival (PFS), median survival (MS), tolerance and pharmacokinetics (PK).

**Results:** 56 pts were recruited from April 2001 to March 2002 in 6 European countries. Median age was 74 (range: 70-82), 75% were male with a KPS of 80 in 48%, 90 in 34% and 100 in 18%. 43 pts (76.8%) had metastatic disease at inclusion with 1/2 organs involved in 64.3% and \* 3 in 35.7%. Co-morbidities were present in 87.5% of pts: 39 (69.6%) had 1 or 2 and 10 (17.9%) had \* 3 co-morbidities. Cardiovascular morbidity was present in 36 (64.3%). 200 cy were given (median 3cy/pt, range: 1-10), median dose intensity (DI): 47.2mg/m<sup>2</sup>/w with RDI of 66%. 472 doses were administered (median=7). Out of 45 pts receiving 2d cy, 29 (64%) were escalated to 80mg/m<sup>2</sup>. 13 pts received  $\sim 6$ cy. Considering the intent-to-treat population (ITT): 6 PR (10.7%, 95% CI [2.6-18.8]) and 25 NC (disease control/DC=55.4%) were reported. MDR was 5.2 months (95% CI [4.3-9.1]), PFS 3.7 months (95% CI [2.5-4.5]) and MS 8.2 months (95% CI [6.2-11.3]). In the evaluable population (47pts/56), OR was 12.8% (DC=66%). A total of 125 doses (20.9%) were cancelled, 91 (72.8%) due to haematological toxicity. Grade 3/4 neutropenia was present in 61cy (30.8%), infection with neutropenia in 5cy (2.5%), leucopenia in 43cy (21.5%) and anemia in 2cy (1%). Grade 3 non-haematological toxicities were only fatigue (4%cy), nausea (2.5%cy), diarrhoea (1.5%cy). 1 pt had a grade 4 thrombosis (0.5%). PK performed in 52/56 pts reported similar bio-availability and blood profiles when compared to a large adult database.

**Conclusion:** Oral NVB given as weekly monotherapy was easy to administer and well tolerated, offering an optimal disease control in such elderly population leading to a favourable activity /toxicity ratio.

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POSTER

### Malignant pleural mesothelioma (MPM): analysis of consecutive 65 patients (pts)

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**Introduction:** MPM is a rare but raising neoplasia characterized by poor prognosis in the majority of cases. Surgery plays a pivotal role in the treatment of this disease in early stages; the role of chemotherapy (CT) and local irradiation (RT) is controversial, even if the introduction of new drugs is very promising.

**Patients and methods:** We analyzed 65 cases of MPM collected by the Department of Medical Oncology and of Thoracic Surgery of the Civic Hospital of Verona from 1983 to 2003. We considered 3 groups of pts: pts with early MPM treated only with surgery (#49); pts treated with surgery plus adjuvant CT/RT (#11) and pts with advanced MPM treated only with CT (#5).

**Results:** The characteristics of pts were: median age 56.7 years; M/F 52/13; histology: epithelial 50, biphasic 13, sarcomatous 2. Stage I #28, II #23, III #12, IV #2 (Brigham's stadition). Asbestos exposure was registered in 35 cases (53%); 22 of these (33%) were related to smoke and asbestos. 60 pts (pts) with good PS (ECOG 0-1) underwent pleuropneumectomy; 49 pts underwent only radical surgery, with macroscopic residual of disease in 4 pts; 9 pts had adjuvant CT-RT, 2 adjuvant RT and 5 palliative CT. Intraoperative mortality was 7.5%; surgical accidents occurred in 39% of pts. In adjuvant setting 3 pts were treated with CAP schedule (CTX 600 mg/m<sup>2</sup>; ADM 50 mg/m<sup>2</sup>; CDDP 70 mg/m<sup>2</sup>) and 6 pts with CBDCA (AUC 6) and TXL (200 mg/m<sup>2</sup>) followed by RT (50 Gy); 5 pts were treated with palliative CT (CDDP and GEM). In the group of pts treated with CAP scheme only 1 patient completed adjuvant treatment (4 cycles of CT followed by sequential RT). Neutropenia G3-4 occurred in 2 pts Nausea and vomiting G3 and alopecia G3 occurred in all pts. In the group of pts treated with CBDCA and TXL timing of CT was respected in all cases. Asymptomatic neutropenia occurred in 3 pts (G4 in 2 cases and G3 in 1 case); 1 febrile neutropenia was observed; Alopecia G2-3 occurred in all pts; arthralgias were referred by 2 pts. No cases of nausea or vomiting were registered. OS at 1, 3 and 5 years for pts treated only with surgery was respectively 49%, 23 and 14%; OS at 1, 3 and 5 years for epithelial subtype was 61%, 30 and 18%; for biphasic and sarcomatous histotype it was 8% at 1 year, 0% at 3 years. Median Survival for pts treated with adjuvant CT + RT was 22 months; for pts with advanced disease treated only with CT it was 10 months.

**Conclusions:** In our experience surgery maintains a pivotal role in the treatment of early MPM; about adjuvant CT the association of CBDCA and TXL seems to be better tolerated than CAP and can be considered the standard therapy in the adjuvant setting in association with sequential RT. Prognosis of pts with MPM relapsed after surgery remains very poor, above all for non epithelial histotypes.

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POSTER

### Optimized schedule of gemcitabine (G), paclitaxel (T) and cisplatin (P) in the treatment of stage IIIB/IV non-small cell lung cancer (NSCLC): results of a phase II study

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**Background:** The combination of G, T and P has been proposed as one of the most active regimen in advanced NSCLC (Fraschi et al, J Clin Oncol 1999;17:2316-25). However, the best schedule and sequence have not been yet determined. Preclinical and clinical evidences show that G should be administered at least 4 hours before P, whereas T is well known to have a better toxicity profile when administered before P. Moreover, no drug-interaction has been observed between G and T. With the aim to optimize the schedule proposed by Frasci et al., we undertook this phase II trial to evaluate the activity and toxicity of the following schedule: G 1000 mg/m<sup>2</sup> days 1-8, T 125 mg/m<sup>2</sup> days 1-8, P 50 mg/m<sup>2</sup> days 1-8, every 21 days.

**Patients and Methods:** From 06/01 to 10/02, 43 untreated patients (pts) with stage IIIB/IV NSCLC were enrolled. Pts characteristics were: M/F ratio 28/15; PS 0/1/2 = 15/18/10; histology: adenocarcinoma 19, squamous-cell 10, undifferentiated/large cell 14; stage IIIB/IV 28/15.

**Results:** all pts were evaluable for toxicity and 41 for response. PR were observed in 27 pts, for a RR of 62.8%; SD was reported in 7 (16.3%), whereas 5 (11.6%) pts progressed. Hematological toxicity was moderate with WHO grade (Gr) 3-4 neutropenia, thrombocytopenia and anemia occurring in only 16 (37.2%), 5 (11.6%), and 4 (9.3%), respectively. Febrile neutropenia occurred in 2 pts and RBC transfusion was required in 2 cases. Non-hematological toxicity was mild with only asthenia (9.3%) and emesis (4.6%) reaching Gr 3. To date, 19 pts progressed with a median time-to-progression of 5 months. Data on 1-year and median survival are still premature.

**Conclusion:** In comparison with the original schedule, the modification of drug sequence, based on pharmacokinetic evidences, led to a reduction of hematological toxicity without reducing the activity of the treatment. Data on survival, after longer follow-up, will confirm these findings.

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### Results of postoperative radiotherapy for pathological stage III and surgical margin close or positive T3N0 NSCLC

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**Background:** A retrospective analysis is performed in order to evaluate the local control, survival outcomes, relapse patterns and prognostic factors in patients with NSCLC who had postoperative radiotherapy.

**Methods and Materials:** We evaluated 85 patients; 64 patients with p stage 3 and 21 with surgical margin close or positive T3N0 patients with NSCLC and had postoperative radiotherapy between 1978-2000 in Cerrahpasa Medical Faculty, Department of Radiation Oncology. All of the pathological specimens were reviewed in Department of Pathology of our faculty. Female male ratio was as 4/81. Histology was squamous in 56 and nonsquamous in 29 patients. Operation types were lobectomy in 38, pneumonectomy in 38, bilobectomy in 6, wedge resection in 3 patients. There were 4 T1, 23 T2, 50 T3, 8 T4, 25 N0, 18 N1, 40 N2, 2 N3 patients. Radiotherapy dose differed between 46-66 Gy. Dose was increased after 45-50 Gy when there were close or positive margins. Age, type of operation, histology, grade, primary tumor size, T stage, N stage, perinodal invasion, number and level of nodal lymph node invasion, lymphatic invasion, surgical margins, thorax wall invasion, pleural invasion, interval between surgery-radiotherapy, radiotherapy dose were the factors used for univariate and multivariate analysis.

**Results:** Median follow-up time was 42 months (3-102months) in alive patients. Twenty-eight patients locally recurred and 38 patients had distant