29% of pts, respectively. Non-hematologic side effects were mild. Out of 76 evaluable pts 6 (8%) achieved a complete response and 26 (34%) achieved a partial response, for an overall response rate of 42% (95% CI 31–53%). The median time to progression was 161 days, the median overall survival – 303 days and the one-year overall survival – 32%. QoL analysis showed an improvement of global QoL, physical activity and symptomatic release in 27%, 28% and 34% of pts, respectively. Release of specific symptoms: dyspnoe, chest pain and hemoptysis was achieved in 34%, 22% and 20% of pts, respectively. In conclusion: the combination of G and P, apart of its activity and acceptable toxicity, results in subjective benefit in advanced NSCLC.

This study was supported by a scientific grant from Eli Lilly Poland.

994 POSTER

P53 gene mutations are associated with poor prognosis in adenocarcinoma of the lung

E. Jassem[1], R. Rosell[2], M. Monzo[2], J.-M. De Anta[2], J. Skokowski[1], A. Badzio[1], A. Roszkiewicz[1], J. Jassem[1]. [1]*Medical University, Gdansk, Poland;* [2]*University Hospital, Barcelona, Spain*

Mutation of P53 suppressor gene is the most frequent molecular alteration in NSCLC, but its clinical relevance is a matter of controversy. The aim of study was to determine the prognostic value of this abnormality in 151 NSCLC pts (92 from Poland and 59 from Spain) who underwent radical resection between 1986 and 1992. Major clinical characteristics were: 133 males and 18 females, median age 62 years (range 33–82), 97 squamous cell carcinoma, 46 adenocarcinoma and 8 large cell carcinoma. DNAs from paraffin-embedded tumor tissue samples were screened for mutations in exons 5–8 with the use of PCR/SSCP technique and positive samples were subsequently subjected to direct sequencing. Our previous report on this series showed poor prognosis associated with P53 null mutations (Oncogene 1997; 15: 2951). In the present analysis based on longer follow-up (median 5.1 years) and including more events (90 deaths out of a total of 151 cases) we confirmed negative prognostic impact of null mutations; median survival in pts with and without this abnormality was 10 and 42 months, respectively ($p = 0.027$; log rank). Additionally, in a group of 46 adenocarcinoma pts we noted a significantly shorter overall survival in subjects whose tumors carried P53 mutations (median survival in pts with and without mutation was 5 and 30 months, respectively; $p = 0.011$). The multivariate Cox analysis showed that in this tumor type stage of disease ($p = 0.024$, hazard ratio 1.58; 95% CI 1.06–2.36) and the presence of P53 mutation ($p = 0.026$, hazard ratio 2.75; 95% CI 1.11–5.91) were the only significant determinants of survival. These findings suggest independent prognostic value of P53 mutation in adenocarcinoma of the lung.

995 POSTER

Assessment of the new postsurgical pathological staging classification in NSCLC

J. Jassem[1], R. Dziadziuszko[1], E. Jassem[1], A. Szymanowska[1], W. Rzyman[1], J. Skokowski[1], A. Roszkiewicz[1]. [1]*Medical University, Gdansk, Poland*

Precise staging of primary tumor and regional lymph nodes is of paramount importance in estimating prognosis and selecting a therapeutic strategy in NSCLC. The aim of this analysis was to assess the appropriateness of revised (1997) pTNM stage grouping in a series of 500 patients who underwent complete resection of NSCLC between Jan. 1986 and Dec. 1995. Study group included 399 males and 101 females; mean age 59 years (range: 33–78); 319 squamous cell carcinoma, 125 adenocarcinoma, 37 large cell carcinoma and 19 other types. Median survival and 5-year survival rate (5-SR) for the entire group were 35 months and 41%, respectively. The 5-SR in particular stages (after exclusion of 12 perioperative deaths) were as follows: IA (n = 35): 77%; IB (n = 179): 58%; IIA (n = 4): 50%; IIB (n = 101): 31%; IIIA (n = 123): 16%; IIIB (n = 19): 26%; IV (n = 8): 13%. There was a good distinction between newly split IA and IB (5-SR 77% and 58%, respectively; $p = 0.039$; Wilcoxon test) and between T3N0 and new stage IIIA (34% vs 16%, respectively: $p = 0.007$). No difference was found between T3N0 and T2N1, the categories constituting new stage IIB (5-SR 34% and 29%, respectively; $p = 0.51$). Within stage IIIA there is a striking difference between T3N2 and other TN constellations (5-SR 7% and 19%, respectively; $p = 0.011$). Relatively good results in stage IIIB and IV are probably due to high selection for surgery in these categories and exclusion of perioperative mortality. In new classification stage IIA is underrepresented (<1%). In conclusion: our results confirm the adequacy of the revised stage classification in establishing a prognostic hierarchy in operable NSCLC. T3N2 should be considered as a separate category in future stage groupings.

996 POSTER

Lack of prognostic significance of angiogenesis in non-small-cell lung carcinoma

B.V. Offersen[1], P. Pfeiffer[2], S. Hamilton-Dutoit[3], J. Overgaard[1]. [1]*Danish Cancer Society, Dept. Experimental Clinical Oncology, Aarhus;* [2]*Odense University Hospital, Dept. Oncology, Odense;* [3]*Aarhus University Hospital, Dept. Pathology, Aarhus, Denmark*

Purpose: Tumor angiogenesis plays a pivotal role in tumor growth, maintenance and metastasis. Our aim was to evaluate the prognostic value of tumor angiogenesis in 176 primary tumors from patients operated for non-small-cell lung carcinoma.

Methods: Tumor microvessels were stained by immunohistochemistry for CD34, and angiogenesis was estimated both by a modification of the method described by Weidner (hot spots) and by the use of a Chalkley grid. The vascular data were correlated to other known parameters: overall survival, sex, age, TNM-classification, grade and clinical stage.

Results: The median number of hot spot was 67 (range 27–278) in a counting area of 0.25 mm2, and the median average vascular score by the Chalkley grid was 7.0 (range 3.0–15.0). The counts estimated by the two methods were significantly correlated by Kendall's tau statistics ($P < 0.0001$), and the counts were reproducible. Our data demonstrated significantly prognostic value of stage ($P < 0.0001$), adenocarcinoma ($P = 0.002$), and age ($P = 0.01$). However, none of the estimates of vascular score revealed any prognostic value whatsoever.

Conclusion: In conclusion, our data do not support a significant prognostic role for tumor angiogenesis in patients diagnosed with non-small-cell lung carcinoma after long-term follow-up.

997 POSTER

Response of symptomatic brain metastases of small cell lung cancer (SCLC) to topotecan also after preceeding whole-brain radiation (WBI)

A. Korfel[1], J. v. Pawel[2], E. Oehm[3], U. Keppler[4], M. Deppermann[5], I. Güttler, E. Thiel[1]. [1]*Department of Hematology, Oncology and Transfusion Medicine, University Hospital Benjamin Franklin, Berlin;* [2]*Zentralkrankenhaus Gauting;* [3]*Johanniter Krankenhaus Treuenbritzen;* [4]*Lungenfachklinik Immenhausen;* [5]*SmithKline Beecham Pharma, München, Germany*

Purpose: To evaluate the activity and toxicity of the new topoisomerase-1-inhibitor topotecan in patients with relapsed SCLC with symptomatic brain metastases.

Methods: Eiligible for this phase II study were patients with symptomatic brain metastases of recurrent SCLC after no more than 2 chemotherapy protocols or WBI. Topotecan was administered as a 30-minute intravenous infusion of 1.5 mg/m^2 for 5 consecutive days every 3 weeks.

Results: Fifteen patients were entered and treated with the total of 42 courses. Eight patients were pretreated with WBI. Systemic metastases were found in 12 patients. Response of the brain metastases was reached in 6 (40%) patients: complete response in 2 (13%) and partial response in 4 (27%) patients. Three of these patients were pretreated by WBI. Systemic responses paralleled tumor reduction in the CNS. Median duration of response was 75 days, median overall survival from first diagnosis was 501 days. No neurologic deterioration was observed during the chemotherapy. Toxicity was mainly hematologic with CTC grade 4 leukopenia and thrombopenia occurring in 12 (29%) and 18 (43%) of the courses, respectively.

Conclusion: Topotecan has a significant activity in pretreated patients with symptomatic brain metastases of SCLC. The schedule is well tolerated with myelotoxicity being the most common adverse event.

998 POSTER

Taxol and cisplatin (TP) versus etoposide cisplatin (EP) in advanced non-small cell lung cancer (NSCLC)

T.E. Ciuleanu, C. Cebotaru, I. Radulescu, N. Todor, N. Ghilezan. *Oncological Institute Ion Chiricuta, Cluj, Romania*

Purpose: To assess, in a randomised phase II trial, the results obtained in advanced (st IIIB and IV) NSCLC pts with TP versus the standard EP regimen.