months since the last course). Treatment consisted of Paclitaxel (80 mg/m$^2$) and Gemcitabine (1250 mg/m$^2$) on days 1 and 15 in a 4-week cycle. Treatment was held until progression or unacceptable toxicity.
**Results:** 145 cycles were administered (median 2 cycles: range 1−6). The overall disease control rate was 35.7%: 3 partial responses (10.7%) and 7 stable disease (25%). Median time to progression was 15 weeks (95% CI 5.4−24.5) and median overall survival was 21 weeks (95% CI 5.4−36.5). Treatment was well tolerated: nausea/vomiting, neurotoxicity and asthenia were the most common non hematological toxicity (grade 2/3/4: 3/0/0, 1/4/0 and 8/1/0, respectively); neurotoxicity was related to a mild-moderate increment of previous treatment toxicity. Neither febrile neutropenia nor mielotoxicity grade IV were recorded. Anemia was the only grade 3 hematological event (grade 2/3/4 anemia 4/1/0, neutropenia 0/0/0, thrombocytopenia (2/1/0). Only one toxicity-related death was registered, due to gastric perforation. Ps was the only factor affecting survival among all analyzed (age >65, gender, PS, LDH, NSE, metastases vs. thoracic disease).
**Conclusions:** Bi-weekly Paclitaxel-Gemcitabine regimen is active in patients with small-cell lung cancer resistant/refractory to platinum-etoposide, with a favorable toxicity profile and easy management.

**9127** POSTER

**The role of thymidylate synthase (TS) and excision repair cross-complementing group 1 (ERCC1) immunohistochemical expression in malignant pleural mesothelioma patients treated with pemetrexed and carboplatin**

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**Background:** The combination cisplatin-pemetrexed has recently become the standard of care in the first-line treatment of malignant pleural mesothelioma (MPM). In unfit patients, carboplatin frequently substitutes cisplatin. However, today there are no data about pemetrexed and/or cisplatin/carboplatin predictors of response in MPM patients. The goal of this study is to retrospectively correlate the expression of ERCC1 and TS in tumor specimens by immunohistochemistry with the outcomes of a series of MPM patients treated with carboplatin plus pemetrexed in first line setting.
**Material and Methods:** TS and ERCC1 expression was detected by immunohistochemistry in tumor specimens of 71 patients. Sections of 2μm were stained with mouse monoclonal antibodies directed against ERCC1 (1:50; clone8F1; Santa Cruz) and TS (clone106; 1:100; DAKO). To evaluate the proteins staining (for TS cytoplasmatic and nuclear; for ERCC1 nuclear) the percentage of positive tumor cells was considered and a proportion score was attributed (TS: 0 $\leqslant$5%, 1 6−29%, 2 $\geqslant$30%; ERCC1: 0 $\leqslant$10%, 1 11−50%, 2 >50%). This proportion score was then multiplied by the staining intensity (1+, 2+, 3+) to obtain a final semiquantitative score (FSC).
**Results:** The increasing FSC of TS (TS-FSC) correlated with a minor probability of disease control (partial response plus stable disease) (OR = 1.57; p = 0.012). Comparing TS-FSC$\geqslant$4 vs TS-FSC$\leqslant$1 progression of disease was significantly increased (OR = 14.4; p = 0.005). The increase of TS-FSC was significantly correlated with a shorter PFS (HR = 1.23; p = 0.004) and OS (HR = 1.21; p = 0.02). In a model corrected for disease control, TS-FSC remained significant correlated with PFS (HR = 1.24; p = 0.005). There was not a significant correlation between ERCC1 expression and disease control, PFS, and OS. Interestingly, ERCC1 was expressed with a percentage $\geqslant$10% in 83.1% of tumor specimens, and with an intensity $\geqslant$2+ in 61.7%.
**Conclusions:** Immunohistochemical TS expression seems to be able to predict the clinical outcomes in MPM patients treated with carboplatin plus pemetrexed. Despite the absence of significant correlation with clinical outcomes, the high ERCC1 expression observed could explain the low response rate of MPM to platinum compounds. Further prospective studies are needed to confirm these results.

**9128** POSTER

**Advanced poorly differentiated neuroendocrine carcinoma arising from miscellaneous organs was less sensitive to chemotherapy and had poorer prognosis than advanced small-cell lung carcinoma**

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**Backgroud:** Neuroendocrine carcinoma is a fairly rare, heterogeneous disease entity, and no standard treatment has been established. The chemotherapy regimen for small-cell lung carcinoma (SCLC) has been adopted for extended or recurrent poorly differentiated neuroendocrine carcinoma (PDNEC) because they share many pathological features and aggressive clinical behavior. However, PDNEC may differ from SCLC with respect to sensitivity to anticancer agents and outcome. The aim of this study was to clarify the efficacy of standard SCLC regimens when used to treat PDNEC arising from various organs and to compare the outcome with that of SCLC.
**Materials and Methods:** We retrospectively reviewed the medical records of 982 patients with a proven diagnosis of neuroendocrine tumor between January 2000 and October 2008 at the National cancer center hospital of Japan. The inclusion criteria were chemotherapy-naïve patients with extended or recurrent PDNEC who had been treated by a combined regimen consisting of cisplatin and etoposide (PE regimen), cisplatin and irinotecan (IP regimen), or carboplatin and etoposide (CE regimen). We investigated patients background, treatment efficacy, and the outcome of the patients according to the organ that was the site of the primary lesion.
**Results:** There were 145 patients who met the above criteria, 41 with PDNEC and 104 with SCLC. The primary site of the PDNEC were gastrointestinal (GI) tract in 18 patients (GI group), hepatobiliary and pancreatic region in 16 patients (HBP group), and another site in 7 patients (other group). Median age was 63.0 (27−84) years, and 108 patients (75%) were male. The response rate of the SCLC patients was 83%, and the response rate of the PDNEC patients was 31%: 38% in the GI group, 13% in the HBP group, and 67% in the other group. Overall survival of the SCLC was 417 days and overall survival of the PDNEC was 281 days: 452 days in the GI group, 237 days in the HBP group, and 270 days in the other group. A multivariate analysis demonstrated that poor performance status, liver involvement, and PE regimen were independent unfavorable prognostic factors.
**Conclusions:** Extended or recurrent PDNEC, especially in the HBP group, was less sensitive to chemotherapy and had a poorer outcome than SCLC. The greater tendency to metastasize to the liver may have affected the outcome in the HBP group.

**9129** POSTER

**Outcomes of malignant pleural mesothelioma patients treated with second-line chemotherapy (SL): a retrospective analysis of 161 patients**

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**Background:** Malignant pleural mesothelioma (MPM) is a disease with a poor prognosis. While a standard first-line therapy (FL) using platinum pemetrexed based regimens is available, no certainty in second-line treatment (SL) exists. In fact, at present, it is unclear whether a SL chemotherapy might improve the outcome and what is the best schedule to be used. For this aim we analyzed the clinical outcomes of patients who received SL treatment for MPM.
**Matherials and Methods:** Retrospectively we reviewed all consecutive patients who progressed after FL and received a SL treatment in 7 italian institutions. In our analysis we divided patients in four subgroups, according to the type of SL treatment: 1) Platinum-based rechallenge, 2) pemetrexed-based rechallenge 3) not platinum based chemotherapy (vinorelbine, gemcitabine, antracyclines, taxanes) and 4) biological agents. Our endpoints were Overall survival (OS), Progression free survival (PFS) and Response Rate (RR). Survival curves were designed with Kaplan-Meier method and Log Rank was used for testing differences.
**Results:** We analyzed 414 patients of whom 161 received a SL. Patients characteristics were: male 63%; median age 62.5 years (range: 41−79).

Median survival (OS) was 24 months (range: 21−29), median progression-free survival (PFS) was 15 months (range: 14−17). Patients achieving a control disease (PR+SD) with a SL regimens were 85 (52.7%).A statistical significant effect was seen for those patients obtaining a response with the FL treatment in terms of PFS ($p < 0.0001$) and OS ($p < 0.0001$) and for those having an epithelial histology ($p = 0.0008$).A significant benefit was seen also for those patients rechallenged with platinum-based regimens versus biological agents and other not platinum-based therapy ($p = 0.0223$) and no differences have been found in pemetrexed containing regimens and among all the other agents.
**Conclusions:** SL chemotherapy seems to be an active treatment in MPM patients. This benefit is more pronounced in patients with epithelial histology and in patients responding to a FL treatment. At present, a rechallenge with platinum based regimens seems the best option, whether no differences among all the other regimens are found.

**9130** POSTER

**An encouraging chemotherapy regimen in progressive small cell lung cancer - Irinotecan and Ifosfamide: an experience from single center**

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**Background:** Recurrent and progressive small cell lung cancer (SCLC) is associated with very short survival and treatment options are limited. Combination of irinotecan with ifosfamide in SCLC has preliminary data. In this study, we evaluated the efficacy of this protocol as well as prognosticators in this patient population.
**Material and Methods:** Twenty five patients were enrolled into this study from March 2006 to December 2008. Inclusion criteria are as follows: Performance status $\leqslant 2$, and documented of progressive disease after cisplatin based chemotherapy. Ifosfamide dose is 1500 mg/m$^2$ per day, days 1−3, irinotecan 60−80 mg/m$^2$ per day days 1, 8 and 15 every four weeks. Granulocyte colony stimulant factor (G-CSF) was administered as indicated by treating physician. Survival data and prognostic factors were analyzed by Kaplan-Maire and Cox regression methods. This study is a retrospective review of these patients.
**Results:** Median age of patients was 55 years (range 42−80). Majority of patients (96%) was male. Median chemotherapy cycles were 3 (range 1−7). Frequency of second, third and fourth line treatments were 68%, 24% and 8% respectively. Partial remission was obtained in 15 patients (60%) and complete remission was obtained in one patient (4%). Median progression free survival and overall survival figures were 7.8 and 11.1 month respectively. G-CSF was used in 40 percent of patients. Grade 3−4 anemia, leukemia, and thrombocytopenia were seen in 20%, 36% and 12% of these cases respectively. Treatment related mortality did not occur. No prognostic factor was associated with treatment outcome.
**Conclusion:** Ifosfamide and irinotecan combination in small cell lung cancer is effective and tolerable after the progression with cisplatin based chemotherapy. Toxicity was manageable and acceptable. Treatment efficacy was not associated with the standard prognostic factors. Proper clinical trials to test this regimen in the first line and maintenance setting are warranted.

**9131** POSTER

**Maintenance semi-metronomic oral cyclophospahamide and oral etoposide regimen in extensive stage small cell lung cancer (SCLC) patients after responding first line treatment**

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**Background:** Although targeted therapies and new molecular agents have started to improve outcomes in some of the cancers, survival figures have not improved recently for small cell lung cancer (SCLC). In particularly, survival of refractory/progressive SCLC is only 3 to 6 months. The aim of this study was to determine whether maintenance semi-metronomic oral cyclophosphamide and oral etoposide regimen, given after standard platinum-based chemotherapy (CT) prolonged survival in responding patients with extensive stage SCLC.
**Patients and Methods:** Between June 2005 and September 2008, we enrolled in to the study 23 patients with extensive stage SCLC after platinum based chemotherapy. Eligibility criteria were complete or partial response to the first line platinum based chemotherapy and, ECOG performance status $\leqslant 2$. Oral cyclophosphamide 50 mg/daily continuously and oral etoposide 50 mg twice daily on days 1−5 every 3 weeks was administered until progression. Kaplan-Meier and Cox regression analyses were used for the survival analysis.
**Results:** Median age was 64 years (range 41−83). Median 9 (range 2−17) cycles of semi-metronomic oral cyclophosphamide and oral etoposide regimen were received. Median progression free survival (PFS) and overall survival (OAS) were 230 day (95% CI, 98−362) and 610 days (95% CI, 547−663), respectively. Factors related with OAS were; age (age $\leqslant$ 58; OAS 778 day vs age $\geqslant$ 58; OAS 487 day, HR:1.07, Cox $P = 0.018$, Long Rank=0.079), response to first line treatment (complete response; OAS 1001 day, others OAS 580 day, Cox $P = 0.079$, Long Rank = 0.064). Tolerance to treatment was very well and there was no grade 3−4 toxicity.
**Conclusion:** Maintenance semi-metronomic oral cyclophosphamide and oral etoposide regimen, given after standard platinum based chemotherapy was found to be effective and minimally toxic. Although the study population was very small, the results of survival and toxicity analyses warrant further research.

**9132** POSTER

**The importance of haematological toxicity on outcomes of small-cell lung cancer patients**

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**Background:** Since the 'state of art' platin-based chemotherapy (CT), for treatment of small-cell lung cancer (SCLC), has important haematological toxicities and that their pre-treatment values have a potential prognostic role, we aimed to evaluate the importance of haematological parameters on outcomes of SCLC patients (pts).
**Material and Methods:** We retrospectively reviewed the clinical data of 109 SCLC pts diagnosed between January 2002 and January 2009 at the Portuguese Institute of Oncology − Porto Centre. Survival rates were calculated by Kaplan-Meier method and overall survival prognostic factors were analyzed with Cox regression model. Determination of prognostic factors for stage of disease [limited disease (LD) *vs* extensive disease (ED)] was performed with logistic regression models. The significance level for all tests was 0.05.
**Results:** From 109 pts diagnosed, 84.4% were male. Median age was 63 years (range, 29−82 years), 85.3% had smoking history and 89% had an ECOG 0−1. Fifteen pts (18.3%) were staged as LD and 94 pts had ED. Eighty per cent of pts were treated with etoposide+cisplatin regimen and 19.8% with etoposide+carboplatin. About 33% of pts had dose delays (DD) by neutropenia, 3% by anaemia, and 2% by thrombocytopenia. The median overall survival was 9 months (95% CI: 8−11). Multivariate analysis results showed that performance status (ECOG >1, OR = 3.2[1.5−6.4]), number of CT cycles (OR=0.63[0.5−0.7]), presence of metastases (OR = 1.9[1.2−3], and more specifically cerebral metastases (OR = 5.9[1.3−26]) influenced overall survival. In addition, male gender obtained an OR = 4.9[1.4−17.8] in relation to ED, revealing gender as a probable independent prognostic factor in ED.
**Conclusion:** Despite the sample size, this study indicated several factors as probable prognostic factors of overall survival in SCLC pts. During the treatment of SCLC, neutropenia is a frequent problem leading to delays of CT and to the reactive use of granulocyte stimulating factors (G-CSF). The use of G-CSF in primary prophylaxis for neutropenia management could be an appropriate supportive care in these subgroups of pts allowing the delivery of full chemotherapy doses on schedule.

**9133** POSTER

**Analysis of treatment effects of erlotinib in non small cell lung cancer patients**

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**Background:** Erlotinib is an orally-active, EGFR-specific quinazoline TK inhibitor that demonstrated antitumour activity in xenograft models. We have had an opportunity to use erlotinib in 111 patients with NSCLC from the year of 2005. Here we provide an evaluation of treatment results in 110 patients evaluable for statistical analysis.
**Methods:** This is a retrospective analysis of the group of 111 patients with NSCLC, who started the treatment with erlotinib from October 2005 to December 2008. Clinical response was evaluated after 2 weeks of treatment. Objective response was evaluated by imaging techniques after 4−6 weeks of erlotinib treatment and had to be confirmed one month later (chest X-ray, CT scanning). At the same time changes of disease symptoms (dyspnea, cough, anorexia, fatique, pain) and adverse events were monitored.