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.

Characteristics of patients: There were 65 men (58.6%) and 46 women (41.4%). Mean age was 61.0 years (27.0−86.0). Twenty three patiens (20.7%) were neversmokers, 64 (57.7%) former smokers and 22 (19.8%) smokers. Adenocarcinoma was diagnosed in 48 patiens (43.2%), bronchoalveolar carcinoma (BAC) in 10 (9.0%), squamous cell carcinoma in 37 (33.3%), NSCLC without further details in 13 (11.7%) and large cell carcinoma in 3 (2.7%). Performance status (PS) at the start of treatment was 0 in 12 patient (10.8%), 1 in 79 (71.1%) and 2 in 20 patients (18%). Erlotinib treatment was started after failure of preceding chemotherapy in almost all patients (93.5%).
Results: Only 36 from 111 patients (32.4%) have active therapy of erlotinib and they have therapeutical response. The treatment was stopped in 75 patients (67.6%) for progression of disease in 52 patients (68%), in 9 patients (12%) stopped for adverse events, eight patients (10.6%) died during follow up. In 50 patients (45.0%) was started therapy with erlotinib in second line therapy, in 54 patients (48.6%) in third line therapy, in 6 patients (5.4%) in first line therapy. Best objective response was PR in 13 patiens (11.7%) and SD in 45 (40.5%). Progression of the disease was found in 52 patients (46.8%). It was interesting that improvement in at least one of symptoms was noticed sooner than objective response. Median survival time was 5, 7 months from the beginning of erlotinib treatment for part of died patiens, while one-year live 33% patients and six month live 47.9% patients.
Conclusions: Our results are in comparison with published data. Several phase II and III clinical trials with 150 mg erlotinib testing its efficacy in advanced NSCLC patients have been performed. In 57 previously treated patients with EGFR-expressing NSCLC, the response rate (RR) to erlotinib was 12.3%. Responses were seen regardless of the number of prior chemotherapy regimens. The median survival was 8.4 months, and the 1-year survival was 40%. Till the present time there have been no method to determine the group of patient with NSCLC, that has clear benefit from erlotinib treatment.

9134 POSTER

Phase II study of topotecan and bevacizumab in patients with metastatic non-small cell lung cancer who have failed prior systemic chemotherapy – interim analysis

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Background: Previous studies have suggested improved outcomes for chemotherapy naïve advanced non-small cell lung Cancer (NSCLC) treated with topoisomerase I inhibitor. Bevacizumab in combination with carboplatin and paclitaxel is approved for NSCLC in first line therapy. There is no clinical data describing safety and efficacy of topotecan and bevacizumab combination. The objective of this study was to evaluate the response rate and toxicities of the combination of IV topotecan and bevacizumab in patients with stage IIIB/IV NSCLC who have failed prior systemic chemotherapy.
Materials and Methods: Twenty-six patients were enrolled between 10/2006−1/2009 in this Phase II trial. All patients received topotecan 4.0 mg/m^2 IV per day on days 1, day 8 and day 15 and bevacizumab 10 mg/kg IV was given day 1 and 15. Treatment was repeated every 28 days Treatment was repeated every 28 days in the absence of disease progression or unacceptable toxicity. Response assessment (using RECIST) was performed every two cycles.

Table 1

Characteristics	No.	%
Male/female	12/14	46/54%
Age (yrs), median (range)	66 (38−81)	
Race		
White	24	92
Asian	2	8
Histology		
Adenocarcinoma	26	100
Stage IV	26	100
Smoking (smoker = 20 PY)		
Current smoking	1	4
Quit >20 yrs	2	8
Quit <20 yrs	12	46
Non smoker	11	42
Previous lines of chemotherapy (range)	2.5 (1−5)	
Treated Brain Mets	6	23
# months elapsed since brain Tx (range)	10.5 (2−31)	
Total	26	

Results: Patients' characteristics were shown in table 1. There were 6/26 (23%) partial responses and 15/26 (58%) stable diseases with an overall response rate of 81%. Median progression free survival in responder was 8.9 months and 4.4 months in patients with stable disease. Median overall survival of 12.5 months (95% CI, 9.4−15). The most common nonhematologic toxicities were fatigue, headache, nausea and hypertension and most of <3 grade (G). One patient had G 3 fatigue; one had G 4 hyperuricemia and one patient with Gaucher's disease and thrombocytopenia had G V hemoptysis. Hematological toxicities were manageable with G 3 neutropenia in 5 (19%), G 3 thrombocytopenia in 4 (16%), and G3 anemia in 1 (4%). The treatment combination was tolerable even in patients with history of brain metastatic disease (23%) and patients 70 yrs or older (39%).
Conclusions: The combination of topotecan and bevacizumab appears to be effective and safe for patients with metastatic non-squamous non small cell lung carcinoma. Further accrual to this study is warranted.

9135 POSTER

Erlotinib as maintenance therapy after platinun-based chemotherapy in advanced non-small-cell lung cancer (NSCLC): a phase II trial

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Background: We conducted this prospective phase II trial to evaluate the efficacy and toxicity of the sequential therapy of erlotinib in advanced NSCLC patients (pts) without progression after platinum-based chemotherapy (CT).
Material and Methods: Eligibility criteria: advanced NSCLC, Performance status (PS) 0 or 1, adequate renal, hepatic and bone marrow function, no progressive disease after ending chemotherapy. Treatment consisted on: erlotinib 150 mg/day starting 3−4 weeks after last day of CT until progression or unacceptable toxicity. Safety and Response was evaluated monthly.
Results: 47 pts were enrolled, 42 (89%) stage IV and 5 (11%) wet stage IIIB, all valid for response and toxicity. The median age was 62 years (range: 39–77) with 39 (83%) males and 8 (17%) females. Histology subtypes: adenocarcinoma 28 pts (61.7%), bronquioloalveolar 3 pts (6.4%), large cell 3 pts (6.4%) and squamous cell 12 pts (25.5%). PS 0 was found in 23 pts (49%) and PS 1 in 24 pts (51%). 38 pts (81.9%) completed at least six cycles of chemotherapy. The response to CT was: CR: 1 pt (2.1%), PR: 24 pts (51.1%), ED: 22 pts (46%). Sequential erlotinib improved response in 6 pts (12.8%), in 23 pts (48.9) prolonged stabilization, and 18 pts (38.3%) had progression. The median time to progression (TTP) and survival (OS) were 9.4 months (m) (95% CI, 4.96−13−84), and 19.23 m (95% CI, 8.82−29.64) respectively. No significant differences in TTP were found according to age, sex, PS, histology or previous response to chemotherapy, but yes depending on response to erlotinib: PR: 31.5 m (95% CI 15.37−47.63), EE: 12.8 m (95% CI, 10.58−15.03), Progression: 6.3 m (95% CI, 5.36−7.3), $p < 0.001$; and moreover depending on smoking status: Never: 21.67 m(95% CI, 5.39−37.94), previous smoker > 5 years: 14.03 m(95% CI, 10.77−17.30), previous smoker 1 year: 7.77 m(95% CI, 7.62−7.91), current smoker: 5.9 m(95% CI, 5.12−6.34), $p < 0.001$. In Cox-regression model, again smoking status ($p < 0.001$), and response to erlotinib ($p = 0.002$) were associated with a significant difference in TTP. Very similar results respect OS, although in Cox-regression model only never smoker or more than 5 years previous smoker patients had a significant better survival. Toxicity: The most frequent side effect was skin rash, grade (g) 1 in 11 pts (23.4%), g 2 in 16 pts (34%) and g 3 in 3 pts (6.4%). Only 1 pt had diarrea g 3, and no other significant side effects were observed. We found a significant benefit in pts with g 2−3 skin toxicity respect those with g 0−1, in both TTP($p = 0.0003$) and OS ($p = 0.0014$).
Conclusion: Erlotinib administered as maintenance therapy after platinum-based CT had promising results. Pts with the best benefit were those with response to erlotinib, in never or past (more than 5 years) smokers and with g 2−3 skin toxicity