on exponential distribution]. Independently, for each Tx arm, the H_0 6 mo PFS rate $\leqslant$ 25% was tested. RECIST evaluation was performed q6 wks. Secondary outcomes included objective response rate (ORR) and tolerability.
Results: Of 133 pts random. at 15 sites, 130 received Tx (97.7%; P+Cis/P+Car: 65/65). All pts treated were included into the efficacy analyses; 14 pts (10.5%; 5/9) had stage IIIb, 119 (89.5%; 61/58) stage IV tumor (65%/71% male; median age 64/63yrs). Tx groups were balanced (squamous histology 18.5%/20.0%, non-squamous histology 81.5%/80.0%, bone-mets 21.5%/16.9%, brain-mets 3.1%/1.5%). 6 mo PFS rate (P+Cis/P+Car [95% CI]) was 52.8% [40.3;65.3]/39.3% [27.8;50.8]. In the subgroups, the 6 mo PFS rate for pts with squamous hist. was 34.9% [9.4;60.4]/42.0% [16.8;67.3], for pts with non-squamous hist. 57.6% [43.7;71.5]/38.5% [25.6;51.5]. 43.1% /50.8% of pts received all 6 Tx-cycles. Median dose intensity for P (+Cis/+Car [25th, 75th perc.] was 98.2% [92.0;100.0]/98.6 [91.6;99.7]; for Cis 97.8% [91.6;99.8], Car 96.3 [83.1;99.5]. ORR was 32.3% [21.2;45.1; N = 21/65] /20% [11.1;31.8; N = 13/65]. Possibly study drug related, treatment emergent adverse events (TEAE) occurred in 84.6% of pts in either Tx arm; at least 1 serious related TEAE in 16.9%/23.1%. 13 deaths (3/10) occurred; 1/2 due to study drug tox, 0/3 (2 cardiac failures) due to other AEs.
Conclusions: Both regimens showed efficacy according to study hypothesis. Overall, P+Cis revealed more favorable results, especially in the non-squamous histologies.

9080 POSTER

Phase I trial of gemcitabine/carboplatin(GC), followed by pemetrexed/gemcitabine (PG) in chemonaïve patients (pts) with advanced NSCLC

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Background: We performed a Ph I study to establish maximum tolerated dose (MTD) of sequential doublet chemotherapy with GC, followed by PG in chemonaive patients with stage IIIB/IV NSCLC.
Materials and Methods: The starting dose for eligible pts were G(1000 mg/m^2) and C (AUC 4) on Day1, followed by P (500 mg/m^2) with dex/Vit B12/folate supplementation) and G (1000 mg/m^2) on Day14 in a 28 day cycle. Cohorts of 3 pts were expanded to 6, if a dose-limiting toxicity (DLT) was observed. Six dose escalations with a maximum of 6 cycles per patient were planned. Dose adjustments were allowed according to pre-specified criteria. DLTs were recorded if in cylce 1 of chemotherapy: pts had Gr 4 neutropaenia lasting $\geqslant$7 days of febrile neutropaenia, Gr 4/3 thrombocytopaenia (with bleeding), Gr $\geqslant$3 non-haematological toxicity, or if treatment could not be restarted due to unresolved toxicities. At each dose level (DL), if 3/6 pts had any DLT or if 2/6 patients had the same DLT, then that DL was to be considered the MTD.
Results: Of 21 pts entered, 15 (safety population) received $\geqslant$1 cycle of chemotherapy, 6 pts either failed screening or decided not to proceed with treatment. Tumour could be assessed in 13 pts (efficacy population). Three dose levels were administered: DL1:G(1000)/C(AUC4) and G(1000)/P(500), DL2:G(1000)/C(AUC5) and G(1000)/P(500) and DL3:G(1200)/C(AUC5) and G(1200)/P(500). No pts met the pre-defined DLT criteria for MTD. Of 6 patients in DL1, 1/6 pts in the first cohort had a serious AE ischaemic foot, which was not related to study drugs. Of 6 pts who received DL2, 2 DLTs were seen (1 each with $\geqslant$Gr3 ALT and raised creatinine). For DL3, 1/3 had a transient ischaemic attack, which resolved after 2 days. Two pts died due to progressive disease. A partial response was recorded in 2 pts (1 each in DL1 and DL2) and stable disease in 7 pts (2 in DL1, 4 in DL2 and 1 in DL3). The study was closed before MTD was reached because: i) EMEA had issued a new restricted license for pemetrexed in adv NSCLC; ii) high doses of PG combination was shown to have an acceptable risk/benefit profile in other tumours; iii) no further clinical benefit was expected by increasing the dose any further.
Conclusion: Although MTD was not established, an acceptable safety profile was demonstrated. Antitumour activity was seen in 9 pts. Pemetrexed, carboplatin and gemcitabine are 3 of the most active drugs in NSCLC. This new schedule combining all 3 drugs may be worthy of further evaluation.

9081 POSTER

A phase II retrospective trial of Carboplatin (CBDCA) and Alimta in refractory non-small cell lung cancer (NSCLC) with genetic polymorphisms analysis

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Background: Identification of genetic polymorphisms which influence chemotherapy outcome may help towards individually optimized therapy. We investigated the influence of ten single nucleotide polymorphisms (SNPs) of 7 genes (P53 Arg72Pro (G/C); XRCC3 Thr241Met (C/T); XPD Lys751Gln (A/C); ERCC1 Asn118Asn (C/T); GARFT C/G, GARFT C/T, DHFR C/G, DHFR A/G, TS 5′UTR, TS 3′UTR involved with metabolism of CBDCA and Alimta regimen in pts with advanced NSCLC.
Methods: Genomic DNA was extracted from whole blood samples using the QIAamp DNA estraction kit on Biorobot EZ1 (Qiagen). Polymorphisms were detected with TaqMan-probe based assays using the 7300 Real-Time PCR system (Applied Biosystems, Foster City, CA) or PCR followed by RFLP. The results of SNPs were assessed by Cox model for survival/PFS & logistics regression for response/toxicity.
Results: We performed a retrospective analysis in 57 advanced NSCLC pts treated with CBDCA(AUC = 5) + Alimta (500 mg/m^2) after failure of two or three lines of chemotherapy. Median age was 59 years (range 26−79), M/F:63/37%; Adeno/Squa/other Ca:65/20/15%; ECOG PS:0−1/2−3:96/4%. Overall response rate was 38.6%, stable disease 38.6% and disease progression 21.1%. At median follow-up of 7.9 months, 10 pts (17.5%) died, 47 pts (82.5%) are alive. The median progression free survival (PFS) was 7.4 months, the median survival time not reached. P53 Pro72Pro was significantly associated with shorter survival (HR 5.5, 95% CI 1.01−30.5, p = 0.04) when compared to P53 Arg72Arg and P53 Arg72Pro. None of the analyzed polymorphisms was related to response to therapy. No associations were found between the analyzed polymorphisms and toxicity considered either as the maximum observed grade, or as sum of each toxicity pattern grade, probably due to low number of events observed for toxicity within this data set.
Conclusions: P53 Pro72Pro may be associated with shorter survival in pts with advanced NSCLC. Further studies are warranted to validate this finding. Genotype-related differences in common toxicities and in response to therapy were not observed. The small sample size limits interpretation of these data.

9082 POSTER

Phase II study with fractionated schedule of docetaxel and cisplatin in patients with advanced non-small cell lung cancer

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Background: Docetaxel and cisplatin combination chemotherapy is one of the established first line chemotherapy for advanced non-small cell lung cancer (NSCLC). We evaluated the weekly schedule of docetaxel and ciplatin for the efficacy and tolerability in patients with chemotherapy naive NSCLC.
Material and Method: Patients who participated in this study had Stage IIIB or IV NSCLC with measurable disease, no prior chemotherapy, Eastern Cooperative Oncology Group (ECOG) performance status (PS) 0−2. Treatment consisted of docetaxel 40 mg/m^2 and cisplatin 35 mg/m^2 on D1 and D8 every 3 weeks. Patients were evaluated for response every two cycles of treatment.
Result: 35 patients [28 males and 7 females, median age of 61 years old (range 38−68), 31 patients with ECOG PS 0−1 and 4 patients with ECOG PS 2] were enrolled. 57% (20/35) of patients had adenocarcinoma and 74.3% (26/35) had Stage IV disease. Total 153 cycles of chemotherapy were administered. Of the 35 patients, 17 (48.6%) achieved partial response; 11(31.4%) showed stable disease; 7(20%) had progressive disease. Median duration of response was 5.3 months (95% CI: 4.2−6.2 months) and median time to disease progression was 7.43 months (95% CI: 6.41−8.45 months) and estimated overall survival at 1 year was 46.6%. The major hematologic toxicity was myelosuppression. Grade 3 or 4 anemia occured in 6 cycles and grade 3 or 4 neutropenia was observed in 4 cycles. Major non-hematologic toxicities were nausea and fatigue. Grade 3 nausea was observed in 3 patients and grade 3 fatigue was found in 2 patients. 3 patients experienced pneumonia and 1 patient had infectious colitis. There was no treatment related death in this study population.

Conclusion: Weekly schedule of docetaxel and cisplatin in the first-line treatment of NSCLC demonstrated good efficacy and manageable toxicities.

9083 POSTER

Oral vinorelbine in elderly or unfit patients with metastatic NSCLC

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Background: Standard treatment for unfit or elderly patients (PTS) with NSCLC often includes single-agent (not platinum-based) chemotherapy or best supportive care (BSC), rather than a classical chemotherapy doublet. The Elderly Lung Cancer Vinorelbine Italian Study (ELVIS) stated that vinorelbine (VNB) provides both a survival and symptomatic benefit over BSC in elderly pts with NSCLC. The currently available oral formulation of VNB should be handier, with activity and safety profile similar to intravenous formulation.
We aimed to investigate efficacy and safety of oral VNB and its role as the next best in pts with advanced NSCLC not tolerating a classical combination chemotherapy.
Materials and Methods: We enrolled 55 consecutive patients (M/F = 41/14) with median age of 71 years (range 59−84), ECOG PS=1−2, major comorbidities and stage IIIB (n = 23) or IV (n = 32) NSCL (Adenocarcinoma = 51%, Squamous = 31%, NOS = 18%). Patients received oral VNB 60 mg/mq day 1.8 q21 as first-line chemotherapy until progression or unacceptable toxicity, evaluated according to NCI-CTC scale. Time to progression (TTP) was defined as the time between the beginning of treatment and the first evidence of tumor progression. Clinical benefit was evaluated according RECIST score.
Results: The 7% of treated pts had a partial response (RP), 41% stable disease (SD) until the regular treatment suspension and 52% showed a progression disease (PD), with a total clinical benefit of 48%. The median observed TTP was 6 months (range 2−23).
Treatment was well tolerated from the great part of pts and the main toxicities were low-grade (G1-G2). Few pts reported severe (G3-G4) adverse events such as fatigue 4% (n = 2), diarrhea 4% (n = 2), neutropenia 4% (n = 2), vomiting 2% (n = 1), anemia 2% (n = 1).
Conclusions: In our experience, oral VNB represents a safe first line chemotherapy in elderly, unfit pts with metastatic NSCLC not suitable for combination chemotherapy. The oral formulation allows a good compliance to treatment, optimal nausea/vomiting control by oral antiemetics and no required dose adjustment. Furthermore, oral VNB seems to preserve quality of life in the half of treated patients.

9084 POSTER

Pemetrexed vs docetaxel as second-line in NSCLC: is there a difference between adenocarcinoma and squamous cell carcinoma? – a retrospective analysis of a single institution

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Background: Emerging data suggest that chemotherapy with pemetrexed is more effective in patients with adenocarcinoma compared to those with squamous histology, with a longer survival. So the tumor histology should be carefully evaluated in second-line chemotherapy for patients with relapsed or metastatic non-small lung cancer. We retrospectively analysed patients with metastatic NSCLC divided in subgroups on the basis of histology, to evaluate the differential efficacy of pemetrexed and docetaxel.
Materials and Methods: From July 2000 to December 2008 we evaluated 368 patients with NSCLC, treated with pemetrexed or docetaxel, of whom 238 with adenocarcinoma and squamous cell carcinoma. One hundred and ninety-nine (83%) pts were evaluable for PFS and OS. Patients with histology not specified were excluded. Patients characteristics were: median age 63 years, F/M 23/77%, ECOG PS 0−1 86%, current/former/never smokers 37/45/13% (unknown 5%). The most part of pts were previously treated with platinum-based chemotherapy. One hundred and twenty-one pts were treated with pemetrexed, of whom 93 with adenocarcinoma and 28 with squamous cell carcinoma; 78 pts were treated with docetaxel, of whom 53 with adenocarcinoma and 25 with squamous cell carcinoma. Docetaxel was administered at 75 mg/sqm every three weeks (median 3 cycles, range 1−6). Pemetrexed was administered at 500 mg/sqm every three weeks (median 3 cycles, range 1−10).
Results: We analysed the two histologic subgroups and the different type of chemotherapy. The median follow-up is 14 months, median PFS and OS were 2.2 and 8.5 months. The median PFS and OS are presented in the tables below:

	Median PFS (mos)		
	Pemetrexed	Docetaxel	
Adenocarcinoma	2.1	2.3	p = 0.877
Squamous cell carcinoma	2.2	2.3	p = 0.627

	Median OS (mos)		
	Pemetrexed	Docetaxel	
Adenocarcinoma	9.4	8.0	p = 0.860
Squamous cell carcinoma	7.2	9.0	p = 0.636

Conclusions: Our retrospective analysis of adenocarcinoma and squamous cell carcinoma treated with pemetrexed or docetaxel, did not show a statistically significant differences in PFS and OS. Further analyses are needed to validate these data.

9085 POSTER

A platinum based second line rechallenge chemotherapy improves survival in small cell lung cancer patients

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Background: Patients with SCLC that progress after first-line (FL) chemotherapy have a poor prognosis and the evidence of a benefit of SL is still limited. This retrospective analysis evaluates the clinical outcomes of patients who received SL treatment for SCLC.
Methods: Retrospectively we reviewed 166 consecutive patients who progressed after FL and received a second or third-line treatment, between 1993 and 2008 in 17 institutions. In our analysis we divided patients in four subgroups, according to the type of SL treatment: 1) Platinum-based rechallenge (P), 2) Non platinum-based polichemotherapy (NP), 3) Non topotecan monochemotherapy (NT), and 4) topotecan monochemotherapy (T). Our endpoints were Overall survival (OS), Progression free survival (PFS) and Response Rate (RR). Survival curves were designed with Kaplan-Meier method and Cox proportional hazard model was used for investigating factors which influence survival.
Results: Median age was 63 (range 25−86). Median OS from the SL was 6.2 months and PFS 2.9. 163 patients received a platinum based chemotherapy as FL, among them 67% obtained a response (CR = 14%, PR = 53.7%) and 19% had progressive disease (PD). 30% of the complete responders and 22% with partial response after FL had a response in SL, whilst only 16% of patients with SD/PD after FL had a response with SL (test for trend p = 0.03). No statistical differences among regimens groups were found. However, patients receiving platinum-based rechallenge did better than others if they had a long PFS after FL (p = 0.02).
Conclusions: The clinical benefit of SL therapy for SCLC is poor and strictly dependent on response and on duration of response with FL treatment. Consistently with published data, our retrospective analysis confirms that median OS for patients receiving SL is about 6 months and median PFS is 2.9 months. Rechallenge with platinum could be the best options in patients with a long PFS in FL. Single agent topotecan did not show evidence of superiority against other chemotherapy regimens.

9086 POSTER

Pralatrexate plus vitamin B12 and folic acid supplementation in patients with previously-treated, advanced non-small cell lung cancer: safety and efficacy in a phase 1 trial

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Background: Pralatrexate showed activity in previously treated patients (pts) with advanced non-small cell lung cancer (NSCLC) at doses of