(group 2); 69 had lung omo/controlateral metastases (group 3, one study) and 20 pts had other sites of disease (pancreas, n = 2; gastrointestinal system, other, n = 5; soft tissue, n = 5; lymph-nodes, n = 1; skin, n = 3; bone, n = 3; kidney, n = 1) (group 4). The average value of median and 5-year survival was of 19.4 months (n = 277, range 11−26.4) and 23.4% (n = 270, range 6.6−70%) for group 1; of 22 months (n = 170, range 12−66) and 26.15% (n = 62, range 23.3−29%) for group 2; 5-year survival of group 3 was 33.4% (n = 69). In group 4 (isolated case reports) MS largely ranged from 2−81 months.
Conclusions: A tailored attempt at curative resection might be a reasonable approach to NSCLC pts with a SSM, especially considering the current availability of novel and refined diagnostic and surgical techniques.

9045 POSTER

Serum metastin is not involved in metastatic potential of non-small cell lung cancer (NSCLC)

E.M. Karapanagiotou[1], K.D. Dilana[1], P.G. Boura[1], I. Gratsias[1], A. Polyzos[1], K.N. Syrigos[1]. *[1]Oncology Unit 3rd Department of Medicine, Sotiria General Hospital, Athens, Greece*

Background: Metastin, the product of the KISS-1 gene, seems to represent a strong suppressant of metastasis for some types of cancer. The aim of this study is to explore whether metastin could be used as diagnostic and prognostic marker in Non-Small Lung Cancer (NSCLC) patients. The serum metastin levels in metastatic and in locally advanced disease were also studied.
Methods: Fasting serum levels of metastin were determined in 96 NSCLC patients (76 with metastatic disease and 21 with locally advanced disease) and 49 healthy volunteers using commercial available ELISA. Metastin serum levels were determined at diagnosis, at the end of first line chemotherapy and at the time of disease progression for those who responded to treatment. Epidemiological, anthropometrical and laboratory data were assessed for patients as well as for healthy volunteers.
Results: Serum metastin levels presented no differences between NSCLC patients and healthy volunteers (1.2±1.0 vs. 1.2±0.4, P = 0.973) as well as between patients with metastatic disease and patients with locally advanced disease (1.2±0.6 vs. 1.2±1.0, P = 0.714). No statistically significant difference in metastin serum levels from the baseline was observed at the end of chemotherapy or at the time of relapse. Multivariate analysis also showed that serum levels of metastin could not be used as predictive factors for Overall Survival or Time to Progression.
Conclusions: There was a lack of direct involvement of metastin in the metastatic potential and prognosis of NSCLC.

9046 POSTER

A phase II retrospective trial of Platinum/Gemcitabine (P/G)-based in first line treatment of advanced NSCLC with genetic polymorphisms analysis

M. Meacci[1], V. Ludovini[1], L. Pistola[1], I. Floriani[2], J. Foglietta[1], R. Chiari[1], F.R. Tofanetti[1], A. Flacco[1], M. Ferraldeschi[1], L. Crinò[1]. *[1]Santa Maria della Misericordia Hospital, Medical Oncology Department, Perugia, Italy; [2]Ist. di Ricerche Farmacologiche M. Negri, Oncology Department, Milano, Italy*

Background: Selecting patients according to key genetic characteristics may help to tailor chemotherapy and optimize the treatment in NSCLC. Genetic variations in drugs metabolism may affect the clinical response, toxicity and prognosis of NSCLC pts treated with P/G-based therapy.
Material and Methods: We evaluated 8 single nucleotide polymorphisms (SNPs) of 6 genes (P53 Arg72Pro (G/C); XRCC3 Thr241Met (C/T); XPD Lys751Gln (A/C); ERCC1 Asn118Asn (C/T); CDA Lys27Gln (A/C), Ala70Thr (G/A), Thr145Thr (C/T) and RRM1 C524T) involved in P/G-based metabolism in a homogeneous population of pts with advanced NSCLC treated with this regime. Genomic DNA was extracted from whole blood samples of pts using the QIAamp DNA estraction kit and automatically purified by Biorobot EZ1 (Qiagen). Polymorphisms were detected with TaqMan-probe based assays using the ABI PRISM 7300 instrument equipped with the Sequence Detection System version 2.0 software (Applied Biosystems, Foster City, CA). Association between SNPs and response, toxicity, progression free survival and overall survival was estimated using logistic regression model, the Kaplan-Meier method, the long-rank test and the Cox proportional hazard model.
Results: We performed a retrospective analysis in 192 chemotherapy-naive pts (median age 63 years), including M/F: 74/26%; stage IIIb/IV: 24/76%; Adeno/Squa/other Ca: 42/27/31%; ECOG PS: 0−1/2−3: 94/6%. Overall response rate was 32.3%, stable disease 25% and disease progression 42.7%. The CDA Thr145Thr T/T genotype significantly correlated with poorer response (partial response in 23.1% of pts versus 42.3% and 34.6% in C/T and C/C genotypes, respectively; p = 0.03). The ERCC1 T/T genotype was significantly associated with hematological toxicity (G1−4) (p = 0.05) compared to ERCC1 C/C and C/T allele. The CDA Thr145Thr C/T genotype was significantly associated with non-hematological toxicity (G3−4) (p = 0.02) compared to CDA Thr145Thr C/C and T/T allele. The median overall survival (OS) time and progression free survival (PFS) were 12.7 and 4.7 months, respectively. None of the analyzed polymorphisms was related to PFS or OS.
Conclusions: These data suggest that genetic polymorphisms in the ERCC1 and CDA genes may modulate the toxicity and response to P/G-based therapy in pts with advanced NSCLC.

9047 POSTER

Intrapleural IL-2 immunotherapy of patients with malignant effusion

I. Shubina[1], K. Titov[2], L. Demidov[2], I. Mikhailova[2], M. Kiselevsky[1]. *[1]Russian N.N. Blokhin Cancer Research Centre, Laboratory of Cell Immunity, Moscow, Russian Federation; [2]Russian N.N. Blokhin Cancer Research Centre, Biotherapy, Moscow, Russian Federation*

Background: Combined intrapleural immunotherapy by IL-2 and lymphokine-activated killer cells of malignant pleural effusion (MPE) showed high effectiveness in patients with some cancer types. The study aimed to assess clinical effectiveness of intrapleural monotherapy by recombinant IL-2 (Proleukin, the Netherlands) for MPE treatment.
Materials and Methods: 25 patients (pts) with metastatic pleural effusion were enrolled in the pilot study: lung cancer 3, breast cancer 17, renal carcinoma 2, ovarian cancer 3, including 4 male and 21 female pts aged 42−73 years. Previously all pts received appropriate complex therapy, namely, surgery combined with chemo-, hormone-, immuno- or radiotherapy. Pleural cavity was drained under anesthesia to provide liquid evacuation every other day and IL-2 infusion for intrapleural immunotherapy. The course included 14-day consequent infusions of Proleukin in the dose of 1m IU in 20 ml of physiological solution. Before and at the end of therapy, effusion was tested cytologically and controlled by x-ray of the chest. X-ray examination was also performed 1, 6, 12 months after the end of treatment.
Results: Prior to the therapy pts had 1000 – 2 400 ml of pleural effusion. Treatment effectiveness was estimated on weeks 4 or 5 after the end of IL-2 infusion. Over this period 11 pts reached complete effect, i.e. no effusion accumulated. Significant reduction of intrapleural effusion was registered in 7 pts, 3 pts had stabilization of the process and 4 pts did not have any effective decrease of effusion accumulation. Recurrences were registered in 5 pts within 2−18 months after the end of treatment. Total efficacy of IL-2 intrapleural immunotherapy of MPE after 4−5 weeks following the last infusion was 84%.
Cytological examination showed that before treatment all MPE samples contained tumor cells and in the last evacuated sample there were no tumor cells in most patients (n = 21) and only 4 patients still had a small number of tumor cells in MPE.
Conclusion: Intrapleural IL-2 immunotherapy of 25 patients with MPE showed high effectiveness (84%), including complete effect −44%, partial effect −28%, stabilization of the process −12% confirmed by cytological and x-ray examination. Considering its good tolerability and high efficacy, intrapleural IL-2 immunotherapy may be recommended for MPE treatment after necessary clinical trials.

9048 POSTER

Aprepitant for the prevention of chemotherapy-induced nausea and vomiting associated with moderately emetogenic (MEC) or highly emetogenic (HEC) chemotherapies in patients with lung cancer

B. Rapoport[1], J.A. Boice[2], C. Brown[3], J.C. Street[4], J.S. Hardwick[5], A.D. Carides[6], R.J. Gralla[7]. *[1]The Medical Oncology Centre of Rosebank, Research, Johannesburg, South Africa; [2]Merck Research Laboratories, Clinical Research, Rahway, USA; [3]Merck Research Laboratories, Clinical Research, North Wales, USA; [4]Reagent, Communications, New York, USA; [5]Merck Research Laboratories, Medical Communications, North Wales, USA; [6]Merck Research Laboratories, Statistics, North Wales, USA; [7]North Shore, Long Island Jewish Health System, Hematology-Oncology, Lake Success, USA*

Background: Aprepitant was shown previously to be effective for prevention of chemotherapy-induced nausea and vomiting (CINV) associated with HEC in patients with solid tumors (including lung cancer) and MEC in breast cancer patients. A recent study (NCT00337727, PN130) assessed aprepitant in patients with a variety of tumor types receiving a broad range of MEC regimens. A post-hoc subgroup analysis of patients with lung cancer was performed and results are reported along with previous CINV data for lung cancer patients receiving HEC.
Materials and Methods: This randomized, gender-stratified, double-blind trial enrolled patients with confirmed malignancies, naïve to HEC or MEC agents, who received at least one MEC agent. Patients

received an aprepitant triple-therapy regimen (aprepitant, ondansetron, and dexamethasone) or a control regimen (ondansetron and dexamethasone) administered orally. Primary and key secondary efficacy endpoints were proportions of patients with No Vomiting and Complete Response (no vomiting/no rescue medication use), respectively, during the 120 hours post-chemotherapy. Treatment group comparisons were based on a logistic regression model with terms for treatment, region, and gender. The proportions displayed for the lung cancer subgroups were not included in the model.
Results: Of 832 patients in the modified intent to treat population, 13% (n = 108) had lung cancer (compared to 43% in previous HEC studies). More patients in the aprepitant groups achieved No Vomiting and Complete Response overall (Table). Regardless of the level of emetogenicity, the antiemetic benefit of aprepitant addition was preserved in the subgroup of patients with lung cancer. Adverse events were generally similar in the aprepitant and control groups.
Conclusions: The aprepitant regimen provided superior efficacy over the control regimen for prevention of CINV for patients receiving HEC or MEC. The benefit of aprepitant triple therapy in patients with lung cancer appears to extend to MEC. Aprepitant was generally well tolerated.

Overall Phase (0−120 hr post-chemotherapy)

	MEC		HEC	
	Aprepitant n/m (%)	Control n/m (%)	Aprepitant n/m (%)	Control n/m (%)
No Vomiting				
All Tumors	324/425 (76.2)*	252/406 (62.1)	374/520 (71.9)*	260/523 (49.7)
Lung Ca	43/52 (82.7)	40/56 (71.4)	174/230 (75.7)	121/217 (55.8)
Complete Response				
All Tumors	292/425 (68.7)*	229/407 (56.3)	352/520 (67.7)*	250/523 (47.8)
Lung Ca	39/52 (75.0)	38/56 (67.9)	169/230 (73.5)	114/216 (52.8)

n/m = patients with favorable response/patients included in subgroup; *p-value < 0.05

9049 POSTER

Intron 8 polymorphism G/T of NFkB2 gene: risk factor for non small cell lung carcinoma

F. Dimitrakopoulos[1], A. Antonacopoulou[1], S.T. Maroussi[1], A. Kottorou[1], C.H. Scopa[2], H.P. Kalofonos[1]. *[1]University of Patras, Clinical Oncology Laboratory, Patras - Rio, Greece; [2]University Hospital of Patras, Department of Pathology, Patras - Rio, Greece*

Background: The members of the NFkB family are among the most important transcription factors in cancer. NFkB1 and the classical pathway have become objects of detailed research in the last years, although, little is known relating to the possible role of NFkB2 (alternative pathway of NFkB) in carcinogenesis. The aim of this study was to define the relation of the NFkB2 single nucleotide polymorphism rs7897947 with non small cell lung carcinoma (NSCLC).
Materials and Methods: We used 37 blood specimens and 89 paraffin-embedded tissue specimens from patients with NSCLC. We also used 129 blood specimens from healthy donors. DNA isolation was performed using the Qiagen DNA blood kit (blood specimens) and the QIAamp DNA FFPE Tissue (tissue-specimens). Samples were genotyped using real-time PCR.
Results: Approximately half of the healthy donors (49.6%) were TT homozygotes, 11.6% were GG homozygotes and 38.8% were GT heterozygotes. The corresponding percentages for the patients were 69%, 24.6% and 6.4%. The difference in allele frequencies between healthy controls and patients was statistically significant (p = 0.007). No correlation was found with age, sex, primary site, histological subtype, grade and maximum diameter. However, patients carrying a G allele had a lower frequency of positive lymph nodes.
Conclusions: The presence of the T allele seems to predispose to NSCLC development and might increase the possibility of lymph node metastatic spread. This study is ongoing and more patients and healthy control donors are currently being recruited to confirm these results.

9050 POSTER

NSCLC in never smokers, a different disease - a single institution retrospective evaluation

V. Minotti[1], R. Chiari[1], C. Molica[1], M. Betti[1], V. Ludovini[1], L. Pistola[1], F.R. Tofanetti[1], A. Flacco[1], A. Hamzaj[1], L. Crinò[1]. *[1]Santa Maria della Misericordia Hospital, Medical Oncology Department, Perugia, Italy*

Background: Although most lung cancers are a result of smoking, approximately 25% of lung cancer cases worldwide are not attributable to tobacco use, accounting for over 300,000 deaths each year. Striking differences in the epidemiological, clinical and molecular characteristics of lung cancers arising in never smokers versus smokers have been identified, suggesting that they are separate entities.
Material and Methods: We report the data of never smokers NSCLC patients (pts) of a single institution experience enrolled from July 2005 to December 2008. Genomic DNA was isolated from paraffin-embedded tumor specimens, amplified for *EGFR* (exons 18, 19, 20 and 21), *KRAS* (exon 2) by nested polymerase chain reaction and sequenced in both sense and antisense directions. RECIST criteria were used to assess response to treatment.
Results:51 of 250 (20.4%) pts with stage IIIB (12 pts) and IV (39 pts) NSCLC treated at our centre were never smokers. Median age was 61.7 years (range 31−84), F/M: 33/18, ECOG PS 0−1/2: 49/2, adeno/squamous/not otherwise specified NSCLC: 40/2/9. Nine of 34 pts (26.5%) evaluated were mutated at the *EGFR* gene: 5 in exon 19 (delE746-A750), 1 in exon 20 (dupl770 insASV) and 3 in exon 21(missense L858R). None of the *EGFR* mutated pts carried a *KRAS* mutation. 1 pt with *KRAS* mutation (G12V) did not responded to tyrosine kinase inhibitor (TKI) treatment. Brain metastases were diagnosed in 9 of 39 pts (23.1%) having stage IV disease with 6 of them being positive at diagnosis. All patients received first line treatment which has been a platinum-based doublet chemotherapy in 42 pts (82.4%), gemcitabine monochemotherapy in 6 pts (11.7%) and first-line (TKI) in 3 pts (5.9%). Response to first line chemotherapy was as follows: 18 (37.5%) stable disease (SD), 19 (39.5%) partial response (RP) and 11 (22.9%) progressive disease (PD). 39 of 51 pts (76.4%) received a small molecule TKI either as second or third line of treatment and 34 of them were evaluable for response. We observed complete response (RC) in 2 pts (5.8%), RP in 15 (44.1%), SD in 12 (35.2%), and PD in 5 (14.7%) with a disease control exceeding 80%. At a median follow-up of 18.5 months, 33.3% (17/51 pts) of the population died. Median estimated PFS was of 7.7 months (95% CI 4.1−11.3 months).
Conclusions: Our data appear to be in line with those that have previously been reported. Never-smokers in whom NSCLC develops are more likely to be young, female, and almost exclusively of adenocarcinoma histology. Never-smokers might have a better prognosis both in terms of PFS and OS respective to smokers NSCLC pts.

9051 POSTER

Reduction of under-reporting of occupational lung cancer (OLC) by lung tissue optical mineralogic analysis (LTOMA) associated to standardised questionnary(SQ) - about fifty-nine cases

M. Vincent[1], S. Vuillermoz-Blas[1], E. Laennec[1], A.S. Blanchet[1], G. Perrin[1], G. Frecon[1], J.F. Alex[1], F. Thivolet[2], E. Roux[1], C. Chemarin[1]. *[1]Hopital Saint Joseph et Saint Luc, Lyon, France; [2]Hôpital Louis Pradel, Lyon, France*

Rational: in France recognition of OLC is insufficient. LTOMA study for operated lung cancer is easy to realize and may contribute to reduce under-reporting.A level upon 1000 asbestos bodies (AB)/gr dry lung identify workers with a high probability of exposure to asbestos in the workplace. [1] The aim of our study is to evaluate OLC recognition level by LTOMA and SQ analysis in a retrospective series of lung cancers.
Patients and Methods: Between December 2004 and December 2008 among 440 new lung cancers cases, 59 patients (51 smokers or ex smokers, 48 males, 11 females, mean age: 63 years) underwent systematically pulmonary biopsy after resection (54) or during diagnostic biopsy by thoracotomy or thoracoscopy(5) for LTOMA. Specimen were digested (sodium hypochlorite) and collected on cellulose membrane filters (pore size: 0.45 μ), dried and fixed on glass slides by fusion in acetone vapors, transmitted and phase contrast light microscopy study (X200) counted: AB, uncoated fiber (UF) larger than 15 μm, ferruginous bodies on opaque particle (FBOP) and on nude particle (FBNP)/gr of dry lung. A SQ of French Pneumology and Occupational medecine societies was submitted to patients. Complete reply SQ was available only in 19/59 cases (32%). However principal occupational work was identified in 55/59 cases (93%).
Result: 10 cases (17%) presented with more 1000 AB/gr of dried lung, all with asbestos occupational exposure. 7 cases (11%) presented suspected professional asbestos exposure with absence elevated level of AB but for two cases high level UF (4284, 3415/gr of dry lung). 3 silicosis cases (5%) were identified with one non smoker with high level of FBOP (10,280/gr of dried lung) and with silicotic nodule on adenopathy. One (1.6%) non smoker handywoman case with two successive lung cancer and construction worker activities had high level dust and granulomatous lesions on adenopathy and a high level UF (1900/gr dry lung).
Discussion and Conclusion: 21/59 cases (35%) were probable OLC. Dumortier [2] reported in a retrospective study of 1931 cases, 13.3% AB level upon 1000/gr dried lung by LOTMA without data concerning SQ. Legrand Cattan [3] with a SQ identify 26% of 122 patients among 207 lung cancers for claiming a compensation. LOTMA combined with SQ is easy to realize and may contribute to reduce under reporting OLC.

References

[1] Henderson DW Pathology 2004;36:517−50