[2] Dumortier P et al Rev Mal Resp 2009;26:1S92
[3] Legrand Cattan K et al Rev Mal Resp 2000, 17:957−62

9052 POSTER

Single-nucleotide polymorphism K469E G>A in ICAM-1 gene in non-small cell lung cancer

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Background: Non-small cell lung cancer (NSCLC) is the leading cause of cancer death for both men and women. ICAM-1, a cell adhesion molecule that belongs to the Ig-super-family, with a key role in inflammation, has been implicated in cancer. Particularly, the K469E polymorphism (G>A), which affects ICAM-1 mRNA splicing pattern, has been associated with different types of cancer, but not investigated in lung cancer. This polymorphism has also been shown to be related with apoptosis. In addition, we have previously shown that expression of ICAM-1 is transcriptionally regulated by p53. The purpose of this study was to examine the distribution of the K469E polymorphism of ICAM-1 in NSCLC patients and to investigate for potential association(s) with kinetic parameters, such as proliferation index-PI and apoptotic index-AI, and with the p53 status.
Material and Methods: We examined in 188 NSCLC patients, and 127 healthy sex-matched controls, the frequencies of the K469E polymorphism, with PCR-RFLP analysis. Moreover, in 60 of the patients, this polymorphism was examined in relation to tumour kinetic parameters [PI assessed by Ki67 immunohistochemical (IHC) evaluation and AI assessed by Tunel assay], p53 IHC status and clinicopathological data.
Results: The frequency of the GG genotype was significantly higher in NSCLC patients in comparison to the controls ($p = 0.009$). The same genotype was also significantly associated with positive lymph node status ($p = 0.005$). No statistically significant association between the polymorphism and the PI, AI and the p53 status was found.
Conclusions: These findings indicate that individuals carrying the GG genotype may be implicated in NSCLC cancer. Specifically, our results imply that this polymorphism may play a role in the development of metastatic potential of the tumors.

9053 POSTER

Baseline population description of the EPICLIN-Lung epidemiological study in Non-Small Cell Lung Cancer (NSCLC) across Europe

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Background: The lack of well documented local epidemiological and clinical management data, combined with the need of actual data on healthcare consumption, leads to an underestimation of the real burden of NSCLC and its associated unmet medical needs. The aim of this study is to describe the diverse management strategies used across Europe and their impact on clinical outcomes and overall resources burden.
Materials and Methods: The EPICLIN-Lung (NCT00831909) is a multinational, multicentre, non-interventional, prospective cohort study. Patients were recruited from January to March 2009 in Belgium, France, Germany, Greece, Italy, Portugal, Spain and Turkey. Site selection was conducted to obtain a balanced representation of the total number of patients treated in each country. All confirmed NSCLC patients attending the first time the clinical department were included. Data on demographics, diagnosis, clinical management, clinical outcomes and health care resources were collected. Minimum follow-up was 1 year or until death with a maximum of 15 months. Descriptive analysis with common statistics were performed.
Results: A total of 874/3580 patients were recruited as of 24th April 2009. The mean age of patients is 62.4 years old ranging from 59.3 in Turkey and 64.8 in Spain. The overall distribution of sex is 79/21% (male/female) ranging from 89/11% in Turkey and 65/35% in Belgium. The proportion of habitual smokers, ex-smokers and non-smokers is 32.6%, 48.9%, 10.4% respectively. There are some differences in the smoking habits across Europe. The highest proportion of habitual smokers, ex-smokers and non-smokers by country is respectively 41.6% in Turkey, 61.2% in Greece and 24.1% in Portugal. 26.5% of the total patients presented non-advanced disease (stage Ia-IIIa), whereas a 70.2% presented locally advanced/metastatic disease (stage IIIb-IV). In a 3.4% of the patients the stage was unknown. The highest proportion of non-advanced NSCLC patients is in Greece (36.8%), while Portugal presented the highest percentage in stage IIIb-IV disease (91.3%). Histology was adenocarcinoma 36.5%, squamous cell carcinoma 35.4%, large cell carcinoma 7.3%, and another histology 25.4%.
Conclusions: This study will provide a wide description of the management patterns of NSCLC patients across Europe and its impact on resources utilization. Real life NSCLC European basic statistics are presently shown. Updated and more detailed results will be presented at the time of the ECCO-ESMO meeting.

9054 POSTER

Histology classification is not a predictor of clinical outcomes in advanced non-small cell lung cancer (NSCLC) treated with vinorelbine or gemcitabine combinations

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Background: Until recently, histology has not been clearly or consistently described in the literature as a prognostic or predictive variable in advanced NSCLC studies. Recent randomized controlled phase III trials on pemetrexed and TKIs have suggested that these drugs work better in non-squamous subgroups. While a diagnosis of adeno or squamous carcinoma is clear, a significant percentage of patients do not fall into these categories. We compared non-squamous and squamous, and also non-adenocarcinoma and adenocarcinoma histologies in patients with advanced NSCLC, treated with vinorelbine and gemcitabine based first line chemotherapy regimes.
Material and Methods: 503 patients treated at Royal Marsden Hospital with platinum/gemcitabine, platinum/vinorelbine or single agent gemcitabine or vinorelbine as first line chemotherapy for advanced NSCLC between January 2000 and June 2008 were identified. The influence of pathology on progression free survival (PFS) and overall survival (OS) has been invesigated by means of Cox regression analysis. Hazard ratio with 95% CIs has been given for each pathological type after adjusting for the effects of age, gender, stage (III vs IV), PS (0/1 vs 2/3) and treatment type (platinum vs single agent).
Results: Neither univariate nor multivariate analysis suggested that there was a significant difference in the response rates for adenocarcinoma vs non-adenocarcinoma or between squamous and non-squamous pathology. A platinum combination had a better response rate than single agent ($p = 0.007$). There was no difference in PFS between adenocarcinoma and non-adenocarcinoma pathologies ($p = 0.2$), but there was a statistically significant advantage in PFS for squamous vs non-squamous pathologies ($p = 0.009$) and this difference was particularly evident after 6 months. Using multivariate Cox regression analysis to adjust for the effects of age, gender, stage, PS, and tretment type, the path type was not significant. There was no difference in OS in any group.
Conclusions: These results suggest that histology may not be considered as a predictor of clinical outcome using these drugs.

9055 POSTER

Outcome of non-small-cell lung cancer (NSCLC) patients treated for brain metastases (BM) in a single institution

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Introduction: Brain metastases (BM) are a common site of relapse in NSCLC patients (pts), occurring in 25 to 30% of pts. Whole brain radiation therapy (WBRT) is their standard treatment and the respective role of stereotactic radiation surgery (SRS), surgical resection and chemotherapy (CT) remains controversial controversial in the management of BM. Overall survival after development of BM is low with a median survival time less than 6 m in such patients. The aim of this study was to evaluate the long-term outcome of pts with BM treated with at least WBRT, within a multimodal strategy.
Material and Methods: We performed a retrospective analysis of pts treated at Gustave-Roussy Institute, between April 2002 and March 2007. Inclusion criteria were: single or multiple NSCLC BM, WBRT performed in our institution. WBRT planned dose varied according to the PS and the number of BM: 37.5 Gy/15F, 30 Gy/10F or 20 Gy/5F.
Results: We included 96 consecutive NSCLC pts with BM: 64 were male, median age was 57.9 years [31−79]. The histological types were adenocarcinoma in 58 pts (60.4%), squamous cell carcinoma in 18 pts (18.7%), large cell carcinoma in 19 pts (19.7%), neuroendocrine large cell carcinoma in 1 pt. Thirty seven (39%) pts were asymptomatic at the time of diagnosis of BM. The number of BM at diagnosis was as follows: one in 25 pts, 2 in13 pts, 3 in 11 pts and 46 had more than three lesions. Brain was

the only metastatic site in 32 (33.5%) pts or were associated with another site in 36 pts (37.5%) and with at least two other sites in 28 (29%) pts. The Karnofsky Performance Status was > 70% in 77 pts (88%). Radical surgery was performed in 9 pts while 4 pts received a stereotactic radiation surgery. 58 (59%) pts received CT after development of BM: 60% of pts just received one line, 26% had 2 lines, 14% 3 lines or more. 37 pts had synchronous BM, 54% received CT before RT and 57% after, the median time to the beginning WBRT was 3.6 m. The median overall survival was 8.7 m[1.4−56]. 59 pts developed metachronous BM with a median time of 10 m after diagnosis of the primary tumor, the WBRT begins after a median time of 1.15 m. The median overall survival after the diagnosis of BM was 5.7 m [0.4−44.5].
The median overall survival from time of BM diagnosis for all pts was 6.7 m [0.2−69.6]. Median overall survival since the first diagnosis of metastases (watherver the site) was 11.6 m [0.6−69.6].
Conclusion: Our results suggest that in NSCLC pts with synchronous BM, CT may be beneficial and that the sequence with WBRT should be better define.

9056 POSTER

Evaluating the efficacy of zoledronic acid for the prevention of disease progression in patients with non-small cell lung cancer (NSCLC)

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Background: Bisphosphonates are effective inhibitors of bone resorption, and outcomes from preclinical and clinical studies have suggested that they have antitumor activity. Preclinical studies of zoledronic acid (ZOL) have demonstrated its ability to induce tumor cell apoptosis, inhibit angiogenesis, inhibit tumor cell adhesion and invasion, decrease tumor cell proliferation, and activate an immune response. Clinical studies in patients with early stage breast cancer suggest that ZOL improves disease-free survival and recurrence-free survival and may improve bone-metastases-free survival. These findings provide the rationale to investigate whether ZOL can prevent disease progression in patients with early stage NSCLC.
Material and Methods: Study 2419 (NCT00172042) is an ongoing, randomized, phase III trial, sponsored by Novartis, in patients with stage IIIA/B NSCLC who have completed primary treatment (surgery or radiation therapy and chemotherapy) and did not experience disease progression after primary treatment. Patients were randomized within 8 months of diagnosis to treatment with or without ZOL (4 mg q3−4 weeks) for up to 24 months. The primary endpoint of this study is progression-free survival (PFS), which includes disease progression, disease recurrence, and death.
Results: As of January 2009, 407 patients with NSCLC have enrolled and the overall incidence of bone metastases, disease progression, disease recurrence, and death has been evaluated (Table 1).

Table 1: Disease events in patients with NSCLC after primary therapy

	Completed 24 months, n = 58	Ongoing treatment, n = 161	Discontinued treatment, n = 188	Total patients, N = 407
Bone metastases, n (%)	2 (3.4)	4 (2.5)	20 (10.6)	26 (0.6)
Progression/Recurrence, n (%)	19 (32.8)	46 (28.6)	131 (69.7)	196 (48.2)
Death, n (%)	5 (8.6)	0	110 (58.5)	115 (28.3)
Progression/Recurrence/Death, n (%)	21 (36.2)	46 (28.6)	155 (82.4)	222 (54.5)

Currently the median follow-up of patients in this study is 12.9 months (range, 0.03−36.2 months). Updated preliminary safety and efficacy results from this trial will be presented.
Conclusions: Study 2419 is an ongoing trial to evaluate the activity of ZOL in delaying disease progression in patients with NSCLC. The available event profile demonstrates the feasibility of this trial, and updated results will be presented. Results from this trial will complement the growing body of evidence of ZOL for preventing disease recurrence in the early breast cancer setting.

9057 POSTER

New dendritic cell immunotherapy approach: randomized phase II study in IIB-IIIA stage non-small cell lung cancer patients

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Background: Ex vivo-generated dendritic cells (DC) loaded with tumor antigens have been used as vaccines to improve antitumor immunity in patients with different types of cancer since 1996. Currently, extensive studies to improve the immunotherapy approach based on DC-vaccine have been performed. Great emphasis is paid to finding new more efficient ways to load DC with tumor antigens. Our preclinical findings indicate that the mechanically heterogenized tumor cells (MHTC) used for DC loading is a very effective and promising approach. We report a phase II trial in non-small cell lung cancer (NSCLC) patients treated with DC pulsed with MHTC, following successful phase I results.
Material and Methods: Seventy-one patients with IIB-IIIA stage NSCLC, ECOG 0−1, without autoimmune disorders were enrolled. 28 patients had received DC-therapy in adjuvant regimen (4−9x10^6 per injection), 43 patients underwent surgery (lobectomy, pneumonectomy) only. In the trial were used autologous DC of monocytic origin with expression of surface markers CD86 and HLA-DR at least 70%, CD83 – 50% obtained by flow cytometry. Adjuvant therapy with DCs loaded with MHTC was carried out in post-operative period for prevention metastasis development and recurrence of disease. DCs were injected i.v. in 1−2 courses. One course consisted of 5 injections with one-month interval. Groups of comparison were similar by histology forms, stages, age. Clinical and immunological monitoring of DC-vaccine therapy was performed. Special attention was focused on antigen specific antitumor immune response.
Results: DC-immunotherapy was well tolerated without significant toxicity. DC-therapy has improved of 3-year survival of patients. Overall survival of NSCLC patients for 3 year in the group with vaccine therapy was 66% vs 30%. During 3 year follow-up period in a group with DC-vaccine treatment disease progression occurred in 9 patients (32.1%), in a group with surgical treatment alone – in 26 patients (60.5%). 95% of patients showed significant antigen specific immune response after 3−5 DC-vaccinations. In responding to DC-vaccination patients, immunotherapy significantly boosted the IFN-γ and IL-2 producting T-cell response to autologous tumor challenge. Moreover, the increased functionality of T-cells, indicated by increased expression of markers for CTL activation, differentiation and proliferation was revealed.
Conclusions: There was clear evidence of clinical benefit of immunotherapy by DC pulsed with MHTC for NSCLC patients. This approach warrants further study.

9058 POSTER

Analysis of tumor texture on a pre-treatment CT scan predicts treatment outcome in NSCLC patients

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Background: Early identification of patients at risk of treatment failure is an essential step to improve current treatments. We hypothesized that texture and shape attributes of the tumor on a pre-treatment CT scan correlate with patient outcome. We therefore developed a semi-automated recognition system for prediction of 2-years survival, after radiotherapy based on CT scans image traits.
Methods: 129 patients (38 women and 91 men) with inoperable NSCLC (stage I-III), treated with radical (chemo)-radiotherapy were included in this study. The primary gross tumor volume was delineated on a pre-treatment CT scan and was defined as the region of interest (ROI). A set of 30 image traits assessing gray level intensity and spatial distribution, size and shape of the tumor were extracted from the ROI. The cohort was randomly divided into five equally sized groups. In a combinatorial feature selection procedure a support vector machine model was built and validated using a five-fold cross validation approach. The model performance was expressed as the mean AUC assessed by the 5-fold cross validation. The combination of variables with the highest classification accuracy was included in the final model. Patient outcome was defined as 2-years survival calculated from the start of treatment.
Results: From the 30 extracted image features, 5 were included in the final predictive model: contrast, mean gray value, kurtosis, long run emphasis and compactness. These features encode textural and shape information