for TGF beta (TGFBR2; $p = 0.014$) and sex-determining region Y-box 9 (SOX9; $p = 0.038$). Tumors in non-smoking females exhibited 4-fold higher PgR expression ($p < 4 \times 10^{-4}$) and 2-fold higher androgen receptor expression (AR; $p < 2 \times 10^{-4}$) compared to their smoking counterparts. NLT in smokers vs. in non-smokers was characterized by higher expression of AHR and RRAD ($p = 0.01$ and $p = 7x10^{-3}$; not corrected). Tumors in smokers exhibited exclusive and significant 44-fold overexpression of aldo keto-reductase (AKR1B10) in contrast to tumors in non-smokers and NLT in both smokers and non-smokers ($p = 7x10^{-6}$). Tumors in both smokers and non-smokers overexpressed survivin (BIRC5; more than 7-fold; $p = 1x10^{-7}$) and nicotine receptor for acetyl-choline subunit A6 (CHRNA6; 4-fold; $p = 1x10^{-7}$) compared to NLT. Expression of CHRNA6 in tumors was higher in non-smokers than in smokers ($p = 0.03$; not corrected). P16 (CDKN2A) was expressed at a low level in NLT in both smokers and non-smokers, however, its expression was 5-fold higher in tumors, particularly in non-smokers ($p = 7 \times 10^{-4}$). Expression of TGFBR3 and TGFBR2 was lower in tumors compared to NLT. TGFBR2 expression in tumor samples was higher in non-smokers than in smokers.
Conclusions: NSCLC is characterized by a specific gene expression profile related to smoking history. Some of the analyzed genes seem to play a role in adaptive response of lung tissue to smoking insult (RRAD, AHR, SOX). The overexpression of PgR and AR in non-smoking women suggests possible hormonal dependence. Some other molecular distinct features (e.g. downregulation of RRAD, TGFR2 and TGFR3) may prompt new therapeutic strategies.

9042 POSTER

Pre-operative radiological staging (CT and PET-CT) compared with pathological staging in patients with resected non-small cell lung cancer attending a regional thoracic centre

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Background: Accurate clinical staging of NSCLC is essential in order to identify resectable patients. Clinical staging is based upon CT and more recently PET/CT in those deemed resectable. We have compared CT and PET/CT staging of NSCLC with pathological staging to determine their impact on pre-operative staging.
Materials and Methods: Patients referred from 10 hospitals (2 tertiary centres, 8 district general hospitals) that underwent lung resections at Birmingham Heartlands Hospital between August 2006 and August 2008 were identified using the pathology database. Medical records including CT and PET/CT, MDT discussions and mediastinoscopies were reviewed. Pre-operative staging using AJCC criteria was compared to pathological staging.
Results: 154 patients were identified and 135 patients were suitable for analysis. 20 patients were excluded (not NSCLC or insufficient data). The mean age of patients was 66 years (46−83); 82 were male, 53 were female. Pathological findings were correlated with CT in 124 patients and with PET/CT in 99 patients. CT correctly T staged 71 patients (57%), 30 patients (24%) were over-staged and 23 patients (19%) were under-staged. CT correctly N staged 67 patients (54%), 25 patients (20%) were over-staged and 32 patients (26%) were under-staged. CT staged 22 patients as T1NO. 15 underwent PET/CT and of these 7 were correctly staged, 3 had upstaged T staging, and 5 had a higher pathological T stage. In the 7 patients who did not undergo PET/CT, 4 had a higher pathological T stage. PET/CT ruled out metastatic disease in 4 patients. 46 (63%) were correctly N staged, 13 (13%) were over-staged (these had negative mediastinoscopy) and 11 (11%) were under-staged. No patient had inappropriate surgery.
Conclusion: Our data confirms the use of CT in T staging and PET/CT in assessing nodal and distant disease. The role of PET-CT in T1N0 disease remains unclear. Targeted mediastinoscopy was useful in 13% of patients. This data emphasises the role of multidisciplinary working in the management of NSCLC.

9043 POSTER

Computer-assisted prediction of microscopic disease extension around non-small cell lung cancer using a pathology-validated PET/CT classifier

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Background: In radiotherapy planning of non-small cell lung cancer (NSCLC), uncertainties exist about potential presence of microscopic disease extension (MDE) around the CT-visible tumor. Prior studies have shown that these additional tumor foci may extent up to 15 mm from the edge of the visible tumor. The primary aim of this study was to develop a computer-assisted prediction model to distinguish between lung cancers of limited extent (MDE absent) and extended lung cancers (MDE present).
Methods and Material: Thirty-four patients undergoing a lobectomy for treatment of NSCLC underwent CT- and PET prior to surgery. The excised lung lobes were examined at pathology for the presence of MDE. The tumor was delineated on the CT scans by an experienced radiotherapist; on the PET scans the tumor was automatically delineated using a threshold of 42% of the maximum value. Imaging features at CT (tumor volume, mean CT Hounsfield unit (HU), shape, irregularity) and at PET (tumor volume, max SUV) were semi-automatically extracted and tested for possible correlations with the presence of MDE. Tumor type (presence/absence) of adenocarcinoma was considered as well. Using multivariate logistic regression with backward feature selection, a subset of features was obtained that is associated with presence or absence of MDE. Receiver operating characteristics (ROC) analysis was performed to quantify the performance of the model.
Results: MDE was found in 18 of the 34 patients. The tumor volume and mean HU within the tumor showed weak, but statistically significant correlation with the presence of MDE ($p = 0.01$ for both CT and PET volume and $p = 0.02$ for the mean HU). Multivariate analysis yielded a two-parameter model (mean HU and tumor circularity) with ability to distinguish between presence (high HU and low circularity) and absence of MDE (area under ROC curve 0.82). At the 90% sensitivity point on the ROC curve, 14 patients were identified by the model who may be potential candidates for smaller treatment margins.
Conclusions: We developed a pathology-validated model based on pre-treatment PET/CT to stratify NSCLC patients into two groups: high-risk and low-risk of microscopic disease extension. Our results suggest that the model may reduce treatment margins in 41% of patients, but further validation in larger clinical study is required.

9044 POSTER

Curative surgery in oligometastatic non-small cell lung cancer patients

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Background: Patients (pts) with metastatic non-small cell lung cancer (NSCLC) have a poor prognosis, with a median survival (MS) usually measured in months. Chemotherapy is considered the standard of care, whereas surgery and radiotherapy are reserved for symptoms relief. Retrospective reports suggest that - in selected pts with a solitary site of metastases (SSM) - radical treatment of the primary disease as well as of the metastatic site may provide long-term survivals. The aim of this review was to investigate the outcomes and extent of adoption of this therapeutic approach.
Methods: MEDLINE search of all the studies published in English between January 1990-December 2008; and ASCO abstract database search over the period 2003−2008. Combinations of the following keywords were used: “non-small cell lung carcinoma”; “NSCLC”; “oligometastatic”; “solitary/isolated metastasis”; “metastasectomy”; “adrenalectomy”; “brain/adrenal/lung metastasis”. A database was created with main pt and disease characteristics, type and site of radical treatment and pt outcomes.
Results: The data of 643 oligometastatic pts were collected. Median age varied between 32−85 years. Three-hundred and fifty-eight pts presented with isolated brain lesions (group 1); 196 pts with adrenal metastases

(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)

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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

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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

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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

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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