generated by multiple covariates and analysed on SPSS software (version 15.0; SPSS, Inc., Chicago, IL).
Results: Median age of the cohort was 60 years (range, 35−85) where 65(89%) were male, with 11 (15.1%) patients having SVCO at presentation. Karnofsky performance score (KPS) of <70 was seen in 22 (30.1%) patients at the time of registration. Squamous histology was seen in 16 (22%) while non squamous was established in 67 (78.1%) patients. Complete AJCC staging work up revealed stage II A (1 patient, 1.4%), II B (1, 1.4%), III A (21, 28.8%), III B (18, 24.7%) and IV (32, 43.8%). At presentation bone metastasis was seen in 16 (22%), and visceral metastasis in 9 (12.4%) patients. Upfront chemotherapy was infused in 50 (68.5%) patients while 73 (100%) received adjuvant radical radiation therapy to the primary lesion. None of the patients received any curative or palliative surgical intervention. Median OS of the population was 5 months (range,0−28 mths). Amongst the multiple covariates tested like age, sex, KPS, histology, AJCC stage, chemotherapy and radiation therapy parameters, only factors related to chemotherapy had shown a significant relation to OS. Superior median survival was seen in patients who received chemotherapy than otherwise (8.02±5.24 mths vs. 3.74±5.21 mths, p = 0.03). Partial responders to chemotherapy had better survival outcome than those with progressive disease during the course of chemotherapy ((9.45±5.4 mths vs.5.56±5.4 mths, p = 0.02).
Conclusions: Role of chemotherapy is well evident in the overall dismal outcome of lung cancer in our study. However, factors like patient preference and financial constraints do have an indirect effect in our set up on the application of chemotherapy. Similar effect is reflected for adoption of radical surgical approach which is glaringly lacking. Additionally, advanced stage presentation could be seen as a probable failure of adequate screening and early diagnosis. Overall, the concept of multidisciplinary approach towards lung cancer management needs to be rigidly followed.

9030 POSTER

An Expression Profile Classifies Early Stage Non-small Cell Lung Cancer Into Two Groups With Good and Poor Disease-free Survival Rates

J. Sanz[1], S. Hernandez[1], A. Romera[2], M. Ferrer[1], B. Perez-Villamil[2], J.R. Jarabo[3], A. Gomez[3], F. Hernando[3], J. Puente[2], J.L. Gonzalez-Larriba[2]. *[1]Hospital Clinico San Carlos, Anatomia Patologica, Madrid, [2]Hospital Clinico San Carlos, Oncologia, Madrid, [3]Hospital Clinico San Carlos, Cirugia, Madrid, Spain*

Introduction: In Spain, 20,000 new cases diagnosed annually of lung cancer. In this disease, the overall survival rate at 5 years is 14%. Of all patients diagnosed in early stages (I and II), 25−30% develop recurrence within 5 years. The aim of our study was to identify molecular subgroups with poor prognosis using gene expression profiles.
Materials and Methods: 84 surgically resected cases (with mediastinal lymph node dissection and negative margins) of stage I (n = 60) or II (n = 24) NSCLC from our institution (40 squamous cell carcinoma (SCC), 39 adenocarcinomas, 3 adenosquamous and 2 large cell), without previous tumours and without neoadjuvant or adjuvant therapy. Recurrence rate was 34.5%. RNA was extracted from frozen samples with more than 70% tumour cells. Tumours were analyzed using microarray expression 4x44 K (Agilent). The data were normalized (LOWESS) and subjected to unsupervised analysis (clustering and k-means) to classify samples based on expression profiles. The association of identified molecular subgroups with clinicopathological (age, sex, smoking, stage, differentiation, inflammation, . . .), molecular variables (mutations of EGFR, k-Ras and B-Raf) and disease free survival (DFS) was analyzed. An external dataset was used to validate our molecular classification.
Results: In our series, neither the histological subtype nor tumour stage was associated with DFS. We have identified two molecular subgroups of NSCLC whose Kaplan–Meier curves show a statistically significant association with DFS (Log-rank test p = 0.004). The better prognosis subgroup includes one third of patients with both adenocarcinomas and SCC, stage I and II. Moreover, pathway analysis points out to a key role of the immune system in the prognosis value of molecular groups. A predictor was obtained to classify samples into low and high risk groups. Prognostic value of the classifier was validated in an external series of 162 patients (p = 0.001). Predictor was associated with DFS independently of the stage.
Conclusions: In our series, classical histopathological subtypes and tumour stage did not show statistical significant associations with DFS while our expression profile subtypes did. This association was confirmed in an external dataset. This classification could allow selecting patients at low risk of recurrence of patients who may require adjuvant treatment in addition to surgery.

9031 POSTER

Does the "Two Week-Wait" Target Improve Survival in Patients With Lung Cancer in the UK?

M. Kumari[1], I. Nikolopoulos[1], S. Huf[1], K. Thakur[1]. *[1]Queen Elizabeth Hospital, General Surgery, London, United Kingdom*

Backround: Incidence and mortality rates for men have fallen sharply since peaking in 1974. Incidence of lung cancer has risen by 76 per cent for women between 1971 and 2000, while mortality rates are falling slightly after peaking in 1994. Lung cancer 5-year survival rates are poor and have been largely static over time. Cancer waiting time targets were introduced to monitor service performance via process improvement. The intention was to improve the outcome (survival) of the disease. The aim of the study was to assess whether the "two week-wait" target can improve survival in patients with lung cancer.
Materials and Methods: 753 patients were diagnosed with lung cancer between January 2002 and December 2006. Data were retrospectively collected from the cancer database at Queen Elizabeth Hospital, London. Survival was compared in patients that were referred via the "two week-wait" rule (Group 1) and those not referred via this pathway (Group 2).
Results: Only 27% of patients were referred under the "two week-wait" rule and of the remainder a significant proportion came from the Accident & Emergency (A&E) or referred from other specialities (221 and 188 patients respectively).
Kaplan–Meier comparison showed survival to be 16% for Group 1 and 9% for Group 2.
The mean survival for lung cancer patients referred via the "two week-wait" route is 0.82 years (301 days, 95% confidence interval, 246–356 days) and the same for patients referred via non two-week route which was 0.41 years (134 days, 95% confidence interval 108–260 days), (p value $\leqslant$0.005).
Conclusions: The "two week-wait" rule significantly improves the survival in patients with lung cancer. However the underutilisation of two week route cannot be ignored as an unacceptably high percentage of lung cancer patients come via A&E (40%) and other specialities (36%).

9032 POSTER

A Feasibility Study of Induction Pemetrexed Plus Cisplatin Followed by Extrapleural Pneumonectomy (EPP) and Postoperative Hemithoracic Radiation (H-RT) for Malignant Pleural Mesothelioma (MPM) − First All Japan Trial

Y. Miyata[1], S. Hasegawa[2], F. Tanaka[3], M. Okada[1], T. Yamanaka[4], T. Soejima[5], N. Kamikonya[6], K. Fukuoka[7], K. Yokoi[8], T. Nakano[7]. *[1]Hiroshima University, General Thoracic Surgery, Hiroshima, [2]Hyogo College of Medicine, Thoracic Surgery, Nishinomiya, [3]University of Occupational and Environmental Health, Surgery, Kitakyushu, [4]National Kyushu Cancer Center, Institute for Clinical Research, Fukuoka, [5]Hyogo Cancer Center, Radiation Oncology, Kobe, [6]Hyogo College of Medicine, Radiation Oncology, Kobe, [7]Hyogo College of Medicine, Internal Medicine, Nishinomiya, [8]Nagoya University, Thoracic Surgery, Nagoya, Japan*

Background: Feasibility and efficacy of trimodality therapy for MPM is still under controversy mainly due to the lack of clinical evidence. In this context, a prospective multi-institutional study has been planned to evaluate the feasibility of trimodality therapy for MPM with support by the Special Coordination Funds for Promoting Science and Technology from the Japanese Ministry of Education, Culture, Sports, Science and Technology.
Methods: Eligibility criteria: a histologically confirmed diagnosis of MPM, including all subtypes clinical T0−3, N0−2, M0 disease considered to be completely resectable; no prior treatment with chemotherapy, surgery or radiotherapy for the disease; age between 20 and 75 years; ECOG performance status of 0 or 1; a predicted postoperative forced expiratory volume in 1 s of >1000 ml; adequate bone marrow, hepatic, renal, cardiac and respiratory functions; a life expectancy of >12 weeks; and written informed consent. Treatment methods: Induction chemotherapy of pemetrexed 500 mg/m^2 plus cisplatin 60 mg/m^2 with vitamin supplementation for 3 cycles, followed by EPP and postoperative H-RT (54 Gy). Primary endpoints: macroscopic complete resection rate by EPP and treatment-related mortality for trimodality therapy.
Results: A total of 17 institutions in Japan with certified specialists in oncology, surgery and radiation therapy participated in this trial. The study was initiated in May 2008 and patient enrollment was completed in November 2010 with 42 eligible patients. Median age 64.5 (range 43−74), M: F = 39:3, Clinical stage I:II:III = 14:13:15, Histological type epithelial: sarcomatous; biphasic; others = 28: 1: 9: 4. Of 42, 33 patients underwent surgery. Three patients received thoracotomy only due to extensive disease, and macroscopic complete resection with EPP was achieved in 30 patients (71% of ITT).

Conclusions: Results of the present trial will be the foundation of a future treatment strategy for resectable MPM.

9033 POSTER

Induction Chemotherapy in Non Small Cell Lung Cancer Patients − Evolution of Common Practice During Last 25 Years

E. Fabre[1], F. Le Pimpec Barthes[2], A. Cazes[3], P. Berna[2], A. Arame[2], A. Dujon[4], G. Meyer[5], H. Blons[6], C. Foucault[2], M. Riquet[2]. *[1]HEGP, Medical Oncology, Paris Cedex 15, [2]HEGP, Thoracic Surgery, Paris Cedex 15, [3]HEGP, Pathology, Paris Cedex 15, [4]Centre Médico-Chirurgical du Cèdre, Thoracic Surgery, Boisguillaume, [5]HEGP, Pneumology, Paris Cedex 15, [6]HEGP, Molecular Biology, Paris Cedex 15, France*

Background: As a means of reducing the risk of recurrence after surgery, there has been a growing interest in combining chemotherapy (CT) with surgical resection in non small cell lung cancer (NSCLC) patients. Induction CT offers theoretical advantages over adjuvant CT chemotherapy, including improved patient compliance, a smaller primary tumour, and pathologic evaluation of treatment efficacy. But meta-analyses showed comparable efficacy. The purpose of the present study is to assess the place of induction CT in common practice and over time.
Material and Methods: We reviewed the prospective database of all NSCLC patients (pts) who underwent surgical resection for lung cancer from 1983 to 2006 in two centres i) Laennec university hospital transferred in 2000 to European hospital Georges Pompidou, Paris, France and ii) Cedar Centre, Boisguillaume, France. Patients were referred by 9 french medical centres. The database included pts' complete medical history; staging was performed according to 1997 Mountain's revision. We analyzed the tolerance, efficacy and use of induction CT, comparing 4 time-periods of 6 years.
Results: 4668 pts entered the study: 832, 1148, 1493 and 1195 pts respectively during the periods 1983–1988, 1989–1994, 1995–2000 and 2001–2006. Indications for induction CT were: clinical trial, N2 involvement or lung sparing in case of respiratory insufficiency, metastasis, initially unresectable tumour, other. Induction CT consisted in platinum-based association in 95%. Median number of cycles was 2 (ranging from to 1 to 8) and $\geqslant$3 side effects were found in 12%.
Time trend analyses showed increasing number of old patients (>75 yrs pts rose from 5.3% to 11%), females (9.6 to 23.7%), previous cancer (10.6 to 22.6%) and /or cardio-vascular disease (22.7 to 43.3%). There were also more adenocarcinomas (30.4 to 49.4%), earlier stage of disease and smaller size of tumour: T1 + T2: 71.64 to 80.09%; N0 + N1: 69.5 to 78.4%. Multimodal treatment evolved over time: induction CT was more frequently performed during last period 2001–2006 (24.8% pts) than previously (3.8% during 1983–1988), whereas the use of adjuvant CT decreased from 48.5% to 29.7%.
Multivariate analysis showed that induction and adjuvant CT are independent factor of overall survival (respectively $p = 0.00086$ and $p = 0.048$).
Conclusion: Our study demonstrated that the use of induction CT has increased during last 25 years despite evolution of clinicopathological features showing earlier stage of disease, older pts and more co-morbidity in operated pts. The changing pattern of multi-modal treatment is explained by induction CT good tolerance and efficacy that we observed.

9034 POSTER

Determination of Standard Dose Cetuximab Together With Concurrent Individualised, Isotoxic Accelerated Radiotherapy (RT) and Cisplatin-vinorelbine for Patients (pts) With Stage III Non-small Cell Lung Cancer (NSCLC): a Phase I Study (NCT00522886)

A. Dingemans[1], G. Bootsma[2], A. van Baardwijk[3], B. Reijmen[3], R. Wanders[3], M. Hochstenbag[1], A. van Belle[1], R. Houben[4], P. Lambin[3], D. de Ruysscher[3]. *[1]University Hospital of Maastricht, Pulmonology, Maastricht, [2]Atrium Medical Center, Pulmonology, Heerlen, [3]MAASTRO-Clinic, Radiation Oncology, Maastricht, [4]MAASTRO, Biostatistics, Maastricht, The Netherlands*

Background: Concurrent chemo-radiotherapy (C-RT) is the treatment of choice for stage III NSCLC. As cetuximab improves survival in head and neck cancer when added to RT and has activity in NSCLC, we investigated the maximum tolerated dose (MTD) of cetuximab with C-RT in stage III NSCLC. Individualised, isotoxic accelerated RT was chosen to allow the maximal tolerable radiation dose for individual pts based on normal tissue constraints.
Methods: Open label phase I study (NCT00522886). Main inclusion criteria: stage III NSCLC, WHO-PS 0−1, FEV1 >50%, DLCO >50%, weight loss <10%, no severe cardiac disease, normal renal function. Pts without progression after 2 cycles of gemcitabine 1250 mg/m^2 day (d)1−8; carboplatin AUC 5 d1 every 3 weeks (wks) were included and treated with cetuximab 400 mg/kg d-7 and 250 mg/kg weekly together with RT and cisplatin (50 mg/m^2 d1−8; 40 mg/m^2 d22)-vinorelbine for 5 wks. Vinorelbine was escalated in 3 steps; 1) 10 mg/m^2 d1−8 and 8 mg/m^2 d22−29; 2) 20 mg/m^2 d1−8 and 8 mg/m^2 d22−29; 3) 20 mg/m^2 d1−8; 15 mg/m^2 d22−29. RT: 3 wks 1.5 Gy BID (45 Gy) followed by 2 Gy QD to a MLD of 19 Gy. Max 69 Gy in 5.5 wks.
Toxicity (tox) (CTCAEv3.0) was scored till 3 months (mts) after RT. FDG-PET-CT was done 3 mts after RT. Primary endpoint: MTD 3 mts after C-RT. MTD was defined as: 2/6 pts had grade 3 pneumonitis, diarrhoea, liver or renal toxicity or 3/6 pts had grade 3 oesophagitis. When 1/6 pts developed grade 4 skin or neurological or grade 5 haematological tox the dose level was extended with 6 pts. Pts were included in a next dose level when all pts were followed for 3 mts and MTD was not reached. The trial was approved by the required authorities, all pts gave informed consent.
Results: Between 09/07 and 10/10 24 pts (12 males, 12 females, mean age 62.2 years) were included. The dose could be escalated to dose level 3. Full data are available from the first 18 pts. Grade 3 tox: 8/18 pts (fatigue 2, oesophagitis 1, skin tox 1, diarrhoea 1, cough 1, dyspnea 1, vomiting 1, pulmonary embolism 1). DLT was not reached. One patient with a complete PET response in dose level 3 developed a fatal hemoptoe 4 mts after RT. Although not in MTD period, 6 extra pts were enrolled at dose level 3. PET responses in the first 18 pts: 8 complete response, 8 partial response, 1 progressive disease, 1 missing.
Conclusion: C-RT with cetuximab, cisplatin-vinorelbine seems feasible with acceptable tox and promising PET responses. Final results will be presented.

9035 POSTER

A National, Multi Center, Randomized, Open-label, Phase II Study of Erlotinib Versus Gemcitabine (GEM) Plus Cisplatin as Neoadjuvant Treatment in Stage IIIA-N2 Non-small-cell Lung Cancer (NSCLC) Patients (pts) With Activating EGFR Mutations (C-TONG 1103)

W. Zhong[1], Y. Wu[1], C. Wang[2], W. Mao[3], L. Xu[4], Y. Cheng[5], X. Yang[1], K. Chen[6]. *[1]Guangdong Lung Cancer Institute, Chinese Thoracic Oncology Group, Guangzhou, [2]Tianjin Medical University Cancer Institute and Hospital, Chinese Thoracic Oncology Group, Tianjin, [3]Zhejiang Cancer Hospital, Chinese Thoracic Oncology Group, Hangzhou, [4]Jiangsu Cancer Hospital, Chinese Thoracic Oncology Group, Nanjing, [5]Jilin Cancer Hospital, Chinese Thoracic Oncology Group, Changchun, [6]Beijing Cancer Hospital, Chinese Thoracic Oncology Group, Beijing, China*

Background: Stage IIIA NSCLC represents a relatively heterogeneous group of pts with ipsilateral mediastinal (N2) lymph node involvement. The relative roles of treatment modalities are not clearly defined. Concurrent chemoradiation therapy remains an important treatment for stage IIIA disease, but its treatment-related life threatening toxicity limits its use. The EGFR tyrosine kinase inhibitor (TKI) may provide a dramatic response in pts with pulmonary adenocarcinoma carrying EGFR activating mutations in the metastatic setting. In the OPTIMAL study, first-line erlotinib versus carboplatin/GEM in advanced NSCLC pts with EGFR activating mutations, the primary analysis showed significantly prolonged progressive free survival (PFS) was with erlotinib vs carboplatin/GEM ($p < 0.0001$). The aim of this study is to investigate the efficacy and safety of erlotinib versus GEM plus cisplatin (GC) as neoadjuvant treatment in pts with stage IIIA-N2 NSCLC with EGFR activating mutations and to explore a new treatment strategy for this subset.
Materials and Methods: This is a multi center, randomized, phase II study evaluating efficacy and safety of erlotinib vs GC as neoadjuvant therapy for stage IIIA-N2 NSCLC pts with EGFR activating mutations. *Target population and neo-adjuvant treatment phase*: Pts with resectable stage IIIA-N2 NSCLC confirmed by mediastinoscopy or EBUS or PET/CT and proved to process EGFR activating mutations in exon 19 deletion or exon 21 L858R will be randomized to the induction erlotinib therapy arm (150 mg erlotinib taken once daily and continued uninterrupted for 42 days until evaluation) or the induction GC arm (GEM 1250 mg/m^2 IV on day 1 and day 8, and cisplatin 75 mg/m^2 on day 1 of a 3-week schedule) for 2 cycles. *Surgery treatment phase*: Tumour response will be evaluated after 6 weeks of induction treatment (during day 43 to day 49). The pts considered to be technically resectable will undergo thoracotomy. *Adjuvant phase*: After complete resection, pts will receive erlotinib 150 mg/day for 1 year or GC for 2 cycles at the same dose as neoadjuvant. *Duration of Trial Recruitment*: 18 months. *The total sample size*: 90 cases.
Results: *Primary outcome measure*: The objective response rate (ORR) in neoadjvant treatment. *Secondary Outcome Measures*: To evaluate lymph node downgrade rate, complete resection rate, pathological complete response (pCR) rate, PFS, 3 year overall survival (OS) rate, safety and quality of life (QOL). *Follow-up*: Pts after surgery will receive long-term follow-up including chest CT scan every 3 months, brain MRI every 6 months, bone scan (ECT) every 12 months for up to 2 years.