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

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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)

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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)

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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.

Conclusions: Induction erlotinib therapy in IIIA-N2 NSCLC with EGFR activating mutation is a promising strategy. The study is planned to start in Sep. 2011.

9036 POSTER

Population-based Outcomes of Limited Stage Small Cell Lung Cancer Patients Treated With Cisplatin-Etoposide vs. Carboplatin-Etoposide

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Purpose: Although a previous randomized control trial did not demonstrate an advantage for Cisplatin-Etoposide (EP) over Carboplatin-Etoposide (EC), cisplatin-based therapy remains standard-of-care in North America. This descriptive study compares overall survival (OS) and locoregional recurrence (LCR) between EP and EC at a population level in patients with limited stage small cell lung cancer (LD-SCLC).
Methods and Materials: All patients with LD-SCLC who were diagnosed from January 2006 to December 2008 and treated with EP or EC and concurrent or sequential radiotherapy were identified. A retrospective review examining prognostic features and outcomes was performed. Demographic comparisons were made using Fisher's exact test for discrete variables and Mann-Whitney non-parametric test for continuous variables. Overall Survival (OS) and locoregional control (LRC) curves were calculated using the Kaplan–Meier method.
Results: A total of 168 patients with LD-SCLC was identified. Ninety-eight patients received EP and 70 received EC. Patients treated with EC were significantly older (median age 74 vs. 62, p value <0.0001). Median follow-up time was 22.3 months. Median OS for the EP and EC patients were 21.5 and 22.1 months (p value = 0.63), and the two year OS rates were 41% and 47%, respectively. LRC rates at 6 and 12 months were 98% and 73% for the EP group and 96% and 68% for the EC group (p value = 0.77). The most common prescription used for the thoracic radiotherapy was 40 Gy/15 fractions in 86% of cases. Concurrent radiation was delivered to 104 patients (89%) treated with EP or EC. Fifty six patients had a thoracic recurrence with 33 (28%) being within the radiation field and 23 (20%) being outside the radiation field. Sixty one patients (52%) recurred distantly as the site of first progression.
Conclusion: Despite the preferential use of EC in a more elderly population, the median survival time, two-year survival rates and locoregional control rates were similar to patients treated with EP.

9037 POSTER

Induction Chemotherapy With Docetaxel (D) and Cisplatin (C) Followed by Concurrent Thoracic Radiotherapy With Biweekly D and C for Stage III Non-Small Cell Lung Cancer (NSCLC) − a Galician Lung Cancer Group Study

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Background: Concurrent chemoradiation (CChRT) is recommended as the evidence-based approach for the management of patients (p) with locally advanced stage III NSCLC and a good performance status, although a clearly superior regimen has not been identified. D has been shown to possess good single agent activity against NSCLC as well as radiosensiziting properties, both alone and sinergisitically with C. The aim of our study was to evaluate the feasibility of induction chemotherapy with D-C followed by CChRT with biweekly D-C.
Methods: 85 p with inoperable locally advanced NSCLC, stage IIIAN2/IIIB (no pleural T4), were included in a phase II study with induction chemotherapy consisting of three cycles of D 75 mg/m^2 on day 1 and C 40 mg/m^2 days 1−2 every 3 weeks and, if no surgery and no progresion, then underwent CChRT with D 30 mg/m^2 and C 30 mg/m^2 every 2 weeks for four courses, during conformal thoracic radiotherapy (60−66 Gys, 180 cGy/day). The primary objective was overall survival (OS); secondary objectives were progression free survival (PFS), response rate (RR) and toxicity. Median follow-up: 17.6 months.
Results: The p characteristics were: mean age 61.1 years (44−75); male/female 77/8; ECOG PS 0/1 in 25/60 p; squamous/adeno/large cell carcinoma: 51.8%/28.2%/20%; stage IIIAN2 20 p (23.5%) and stage IIIB 65 p (76.5%). 78 p were evaluable for response and 82 p for toxicity. Induction D-C response: 2 CR, 46 PR (RR 61.5%; 95% CI:51−72), 21 SD (26.9%) and 9 PD (11.6%). 9 p were treated with surgery: 1 pCR, 5 pPR, 1 pEE and 2 p unresectable. 56 p completed CChRT and 55 p were evaluable (one toxic death) with 8 CR, 37 PR (RR 80%; 95% CI:70−90), 3 SD and 7 PD. The median PFS was 11 months (95% CI:8−14) and median OS was 19 months (95% CI:14.8–23.2). The PFS and OS at 1/3 years were 46%/14% and 63%/15% respectively. A total of 235 cycles of D-C were given (2.8 per p); main toxicities (NCI-CTC 3.0) per p Grade (g) 1−2/3−4 (%) were as follows: neutropenia 10.9/25.6; anemia 30.4/3.5; nausea/vomiting 30.4/7.3; fatigue 28/0; diarrhea 17/9.7; there were ten episodes of febrile neutropenia and there was one treatment-related death. Main toxicities per p in CChRT (D-C doses: 211, 3.6 per p; mean doses RT: 55.4 Gys) were: g1−2 neutropenia/anemia 12/34.4%; g1−2/3 esophagitis in 51.7/1.7% and g1−2 pneumonitis in 24.5%; there was one treatment-related death.
Conclusions: Induction chemotherapy with Docetaxel and Cisplatin followed by concurrent thoracic radiotherapy with biweekly Docetaxel and Cisplatin is a feasible treatment option for locally advanced stage III Non Small Cell Lung Cancer, showing good clinical activity and tolerability with acceptable long-term survival.

9038 POSTER

Radiofrequency Ablation Combined With Conventional Radiotherapy − a Treatment Option for Patients With Medically Inoperable Lung Cancer

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Background: To evaluate the effectiveness of lung radiofrequency ablation (RFA) followed by conventional radiotherapy in medically inoperable stage I non-small cell lung cancer and the extent of treatment related morbidity.
Methods and Materials: Between June 2003 and July 2010 we treated a series of 10 patients with medically unresectable stage I (T1-T2aN0M0) lung cancer: 9 male and 1 female, with a mean age of 75.8 (range: 65−89). The mean follow-up period was 22.1 months (range: 5 to 77). Patients were considered non surgical candidates by an interdisciplinary group because of age, insufficient respiratory reserve and comorbidity (mainly cardiovascular disease). RFA was performed under conscious sedation using CT fluoroscopy guide. Radiation was performed with 25 fractions of 2.5 Gy per fraction for a total of 62.5 Gy. Evaluation of the therapeutic effects was determined using contrast enhanced CT scans taken every 6 months and PET/CT in some cases.
Results: There were minor complications after RFA as pneumothorax (2) and pleural effusion (3) without requiring chest tube. There were no cases of symptomatic pulmonary toxicity secondary to radiotherapy. There were no lung cancer-related deaths. Two patients died of respiratory failure secondary to COPD exacerbation and one case due to bleeding in the upper digestive tract. There was no evidence of local recurrence. Two patients developed metastases in lung (1) and adrenal glands (1) treated with chemotherapy.
Conclusions: Combined CT-guided RFA and conventional radiotherapy in medically inoperable patients is a safe modality for the local control of stage I lung cancer better than radiotherapy alone. Randomized studies are needed to know if there is a survival improvement.

9039 POSTER

The Burden of Mesothelioma Mortality − Estimation as the First Step to Prevention

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Background: Mesothelioma is a rare cancer that principally affects the pleura and is almost always caused by asbestos exposure. The disease is rapidly fatal; most of those affected dying within a year of diagnosis. There is a long latent period between first exposure to asbestos and diagnosis of mesothelioma that is seldom less than 15 years and often exceeds 60 years. Mesothelioma incidence has increased in South East England of which East Kent is a major part, particularly for men aged over 70 years, reflecting areas of asbestos use in shipbuilding and industry in the past.
Methods: Work-related cancers are largely preventable. The aim of the study is to estimate the current burden of cancer in the area of East Kent in the UK attributable to occupational factors, and identify carcinogenic agents, industries and occupations for targeting risk prevention.