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.

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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.

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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.