respectively (P value 0.046), indicating that the inclusion of radiographic abnormalities significantly upgrade the toxicity scores.
Conclusion: All patients developed radiographic abnormalities post curative radiotherapy, the extent/severity of which did not correlate with the symptoms. The use of the Symptom Only Scale seems to be more clinically relevant and may be a better tool to evaluate long-term toxicity after curative radiation in the lung.

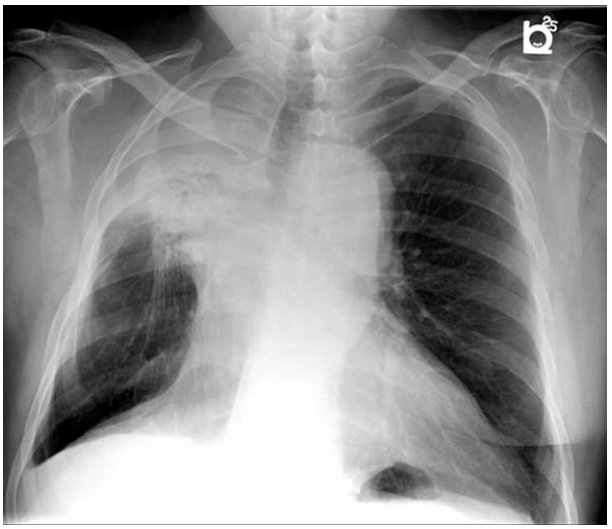


Fig 1. 74 year old male, 16 months post curative radiation, asymptomatic, scoring grade 3 according to RESS and grade 0 according to symptom only system

1139 POSTER

Economic impact of adopting pemetrexed plus cisplatin for malignant pleural mesothelioma into Scottish clinical practice

M. Chetty[1], A. Cordony[2], P. Davey[2], K. Karampela[1], J. Symanowski[3], C. Le Reun[2], M. Watt[1]. *[1]Eli Lilly and Company, Basingsstoke, United Kingdom; [2]M-Tag, Sydney, Australia; [3]Eli Lilly and Company, Indianapolis, United States of America*

Background: The efficacy of pemetrexed + cisplatin (pem/cis) versus cisplatin alone (cis) was evaluated in the largest-ever randomised phase III trial in patients with unresectable malignant pleural mesothelioma (Vogelzang 2003). Emergent data early in the trial led to a decision that all patients be fully supplemented with folic acid and vitamin B12. Survival benefit was assessed in all fully vitamin-supplemented patients (FS) and in those FS patients with advanced disease (stage III/IV). A cost-effectiveness evaluation of pem/cis compared to cis in the treatment of all FS patients and in the FS patients with advanced mesothelioma was conducted for Scotland.
Method: A cost per life-year saved (LYS) analysis using the median survival gain from the clinical trial was undertaken. The above cohorts were chosen because either one could reflect clinical practice in Scotland: vitamin supplementation is mandatory with pemetrexed treatment (ALIMTA* SPC) and most patients treated for mesothelioma in Scotland have advanced disease at presentation (Aziz 2002). Specific unit costs were applied to drug acquisition, administration, supportive care medication, hospitalisations for serious adverse events and post-study chemotherapy, with incidence derived directly from the clinical trial. A discount rate of 3.5% per annum was applied to all outcomes.
Results: The incremental per patient cost for pem/cis compared to cis was £8,196 and the results of the analyses are shown in the table.
The robustness of the model was tested using one-way sensitivity analyses on key variables affecting both cost and outcomes estimates in the cost-effectiveness model. Little variation in the incremental cost/LYS was found with the variables tested for the FS with advanced disease patients (£17,500-£25,000).
Conclusions: The trial demonstrated clear survival gain for the combination therapy, particularly in the cohort of fully supplemented patients with advanced disease. This analysis demonstrates that the pemetrexed/cisplatin combination is a cost-effective treatment for patients with advanced maligant pleural mesothelioma.

	Pem/cis	cis	*P*	Hazard Ratio (95% CI)	Cost/LYS
Fully supplemented (n)	168	163	0.051	0.75 (0.57–1.00)	£30,355
Median survival (months)	13.3	10.0			
Fully supplemented (Stage II/IV) (n)	125	122	0.003	0.63 (0.46–0.86)	£20,844
Median survival (months)	13.2	8.4			

1140 POSTER

First results of long term outcome in patients with inoperable or irresectable Non-small cell lung cancer (NSCLC) treated with high-dose accelerated radiotherapy with or without concurrent or sequential chemotherapy

A. Uitterhoeve, C. Koning, M. Koolen, R. v Os, C. Koedooder, M. v d Kar. *Academic Medical Center, Radiotherapy, Amsterdam, The Netherlands*

Background: Results of high dose radiotherapy (RT) +/− chemotherapy (CT) with curative intent were analyzed in all patients (pts) with NSCLC treated in our department from 1995–2004.
Material: Included are 131 pts with medically inoperable or irresectable NSCLC (TNM stage I: 15 pts, IIB: 15 pts, IIIA: 67 pts, IIIB: 32 pts, X: 2 pts). ECOG performance score was 0, 1 or 2 in 28 pts, 76 pts and 27 pts respectively. Sex distribution: male 89 pts, female 42 pts. Pathology: adenocarcinoma: 18 pts, squamous cell carcinoma (ca): 39 pts, large cell ca: 60 pts, undifferentiated carcinoma 8 pts. No pathologic confirmation could be obtained in 6 pts.
Treatment: Standard curative treatment in our department is 66 Gy /2.75 Gy/ 24 fx/ 33days combined with daily administration of Cisplatin 6 mg/m^2 after completion of the phase II EORTC 08912 study in 1997. If pts fulfilled the inclusion criteria of the EORTC phase III study 08972/22973 they were randomised to either our standard arm or the sequential treatment arm consisting of two courses of a 21-day schedule of CT(Gemcitabin 1250 mg/m^2 d1, Cisplatin 75 mg/m^2 d2) followed by the same RT without daily Cisplatin. Concurrent chemo-radiotherapy was given to 56 pts, 26 pts were treated with sequential chemo-radiotherapy. If administration of CT was not possible, pts received RT only (49 pts).
Results: The 1, 2 and 5 yr actuarial overall survival (OVS) are 46%, 24% and 15%. Factors with a significant influence on OVS are concurrent administration of Cisplatin (1, 2 and 5 yrs OVS 56%, 33% and 24% respectively) and performance status. Older patients (>58 yr) show a trend for a poorer survival, as does advanced stage, but this is apparent only for patients not receiving chemotherapy. The incidence of local recurrence is 36%, the incidence of distant metastases 46%. No late complications are seen in 65 pts, grade 1 or 2 in 22 pts, grade 3 in 19 pts (lung 16x, oes 2x, heart 1x) and grade 4 in 5 pts (spinal cord 1x, lung 2x, oes 2x). One patient had a lethal complication (oes). In 20 patients no sufficient data are present to assess late complications.
Conclusion: In patients with inoperable or irresectable NSCLC radiotherapy 66 Gy/ 24 fx/ 33 days combined with concurrent chemotherapy of daily Cisplatin 6 mg/m^2 results in excellent treatment outcome with a 1, 2 and 5 yr OVS of 56%, 33% and 24%.

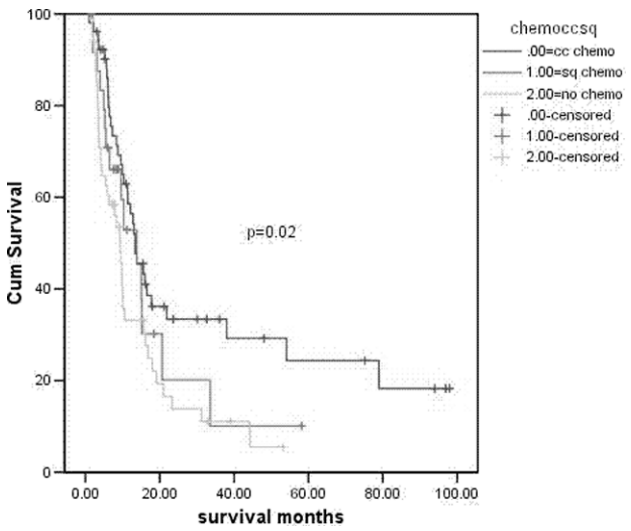
1141 POSTER

Postoperative radiotherapy (PORT) for non-small-cell lung cancer (NSCLC): Results of the 1999–2001 patterns of care study (PCS) nationwide process survey in Japan

T. Uno[1], M. Sumi[2], M. Nakamura[3], Y. Suzumoto[3], A. Kihara[3], H. Kawakami[1], H. Ikeda[2], T. Teshima[3], Japanese pcs Working Subgroup of Lung Cancer. *[1]Chiba University Graduate School of Medicine, Radiology, Chiba, Japan; [2]National Cancer Center, Radiation Oncology, Tokyo, Japan; [3]Osaka University Graduate School of Medicine, Medical Physics and Engineering, Osaka, Japan*

Background: Results of the PORT meta-analysis have considerable impact on the practice pattern for NSCLC after surgery. This study was undertaken to investigate the practice process of PORT for NSCLC in Japan.
Material and Methods: The PCS conducted a nationwide survey of PORT for NSCLC in Japan. The PCS randomly sampled institutions and patients from academic and non-academic institutions (A1: academic, treating ⩾430 patients/year, A2: <430 patients, B1: non-academic, ⩾130 patients/year,

and B2: <130 patients), and conducted an extramural audit survey for 627 stage I-III NSCLC patients.
Results: Ninety-nine (16%) NSCLC patients had received PORT between 1999 and 2001. The median age was 65 years (range, 39–82). The preceding surgery was pneumonectomy in 12%, lobectomy in 79%, and segmentectomy in 9%. Histopathology was squamous cell carcinoma in 46%, adenocarcinoma in 43%, large cell carcinoma in 7%, and adenosquamous carcinoma in 2%. The clinical stage was stage IA in 14%, IB in 13%, IIA in 7%, IIB in 7%, IIIA in 42%, and IIIB in 16%. Location of the primary tumor was the upper lobe in 63%, the middle lobe in 7%, and the lower lobe in 28%. Predominantly involved mediastinal nodes were 7 (34%), 4 (34%), 5 (28%), and 3 (26%) according to the mapping system of Japan Lung Cancer Society. The pathological stage was stage I in 8%, II in 17%, IIIA in 44%, and IIIB in 20%. The median field size of PORT was 9×11 cm, whilst the median total dose was 50 Gy. The photon energy of ⩾6 MV was used for 71% of patients in A1, 78% in A2, and 80% in B1, whereas only 23% in B2 institutions ($p < 0.0001$). The planning target volume included the contralateral mediastinum for more than 70% in A1 to B1 institutions, whereas only 46% in B2 ($p = 0.011$). Thirty patients (31%) received systemic chemotherapy. For 70% of these patients, chemotherapy and PORT were administered concurrently, mainly using platinum based 2-drug combination. For 9 patients, platinum-based chemotherapy was used as an induction therapy. Oral fluorouracil was used in 9 patients. First failure sits were local in 6, regional in 5, and distant metastases in 31, with a median time to first failure of 7 months. Overall survival 3-year for the entire group was 63%.
Conclusions: During the study period, PORT was used mainly for pathologic stage III NSCLC. Obsolete equipments such as Cobalt-60 unit were still used, especially in non-academic institutions treating small patient number/year.



Survival functions

1142 POSTER

Radiation pneumonitis following combined modality therapy in the treatment of locally advanced non-small cell lung cancer (LAD-NSCLC) including three-dimensional conformal radiation therapy (3D-CRT): analysis of clinical and dosimetric prognostic factors

M. Moreno Jiménez[1], J. Aristu[1], L. Arbea[1], C. Garrán[1], M. Cambeiro[1], J.M. López-Picazo[2], G. Nagore[1], R. Martínez-Monge[1]. [1]*Clinica Universitaria, Division of Radiation Oncology, Pamplona, Navarra, Spain;* [2]*Clinica Universitaria, Division of Medical Oncology, Pamplona, Navarra, Spain*

Background: Radiation pneumonitis is the most prominent dose-limiting complication in LAD-NSCLC irradiation. 3D-CRT is a high precision radiation technique that represents a significant advance in the delivery of radiotherapy for LAD-NSCLC, minimizing the exposure to the surrounding normal tissues. This study attempted to identify clinical and dosimetric parameters associated with the development of severe radiation pneumonitis (RP) in patients (pts) with LAD-NSCLC treated with combined modality therapy.
Material and methods: 80 pts (72 males and 8 females; median age: 58 years, range: 32–78) with stage IIIA (20%) and IIIB (80%) NSCLC treated between April 1995 and March 2001 with cisplatin-based induction chemotherapy (IQT) followed by concurrent chemotherapy and hyperfractioned 3D-CRT (1.2 Gy b.i.d.; median dose: 72.41 Gy, range: 54.13–85.89), were evaluated retrospectively. Acute and late (>3 months) RP were scored using the RTOG classification. Potential predictive factors evaluated included clinical parameters (sex, age, performance status, stage, histology, weight loss >5%, tumor site, pre-existing lung disease), therapeutic factors (IQT schedule, 3D-CRT dose, treatment response), and dosimetric factors according to the ICRU definitions (volume and dose of GTV, PTV-2, CTV and PTV-1; pulmonary V20, V30, mean lung dose (MLD) and normal tissue complication probability (NTCP)). The lungs were defined as a whole organ. Univariate and multivariate analyses were performed.
Results: All pts were evaluated for acute RP and 78 pts could be evaluated for late RP. RP (early and late) grade ⩾3 occurred in two pts (2%) and 10 pts (12%), respectively. Five pts (6%) died of pulmonary toxicity, with 3 of them having pre-exisitng moderate-severe cardiopulmonary disease. The median time to diagnosis of late RP was 4.5 months (range: 3–8). Multivariate analysis showed that, pre-existing lung disease (*Odds ratio*= 10.12, $p = 0.01$) and NTCP >30% (OR = 10.54, $p = 0.007$) were independently associated with late pulmonary toxicity grade ⩾3. The incidence of RP grade ⩾3 for pts with pre-existing lung disease and/or NTCP >30% was 25% vs. 4% for pts without pre-existing lung disease or NTCP <30% ($p = 0.01$). The risk of severe RP was higher for pts with pre-existing lung disease and/or NTCP >30% (*Odds ratio*= 7.33; I.C. 95%= 1.44–37.33, $p = 0.016$).
Conclusions: In this study, pre-existing lung disease and NTCP were the best predictors of late severe pulmonary toxicity (grade ⩾3), and should be evaluated in all patients undergoing high-dose 3D-CRT prior to treatment.

1143 POSTER

Lung and heart toxicity analysis of a combined 3D high dose chemoradiation protocol. Recommendations for further studies

F. Mornex[1], A. Belliere[1], O. Chapet[1], M. Khodri[1], P.J. Souquet[2]. [1]*Centre Hospitalier Lyon Sud, Radiation Oncology, Lyon Pierre Bénite, France;* [2]*Centre Hospitalier Lyon Sud, Pneumology, Lyon Pierre Bénite, France*

Background: This work analyzes the toxicity of lung and heart irradiation in patients (pts) presenting with a NSCLC, treated with 3D conformal therapy (74 Gy), in terms of relationship between V_{20} and the incidence and grade of radiation pneumonitis (RP), as well as the assessment of heart events. The ultimate goal is to elaborate recommendations for a future escalation dose phase I trial, based on the observed toxicities.
Patients and Methods: Fifty pts, 41 men, 9 female, median age 63 years (27–80), stage I/II 7%, IIIA 51% and IIIB 42%, squamous carcinoma 58%, adenocarcinoma 24%, large cell indifferenciated 12% and neuroendocrine 6%, have been treated between june 1998 and april 2002. Radiotherapy delivered a mean dose of 72 Gy (range 68–74 Gy), using 3D conformal therapy (2 Gy/day, ICRU point, 5 days/week). The mean PTV was 648 cc (range 220–1876), the mean lung V_{20} 38% (range 19–68%), V_{25} 31%, V_{30} 27.5%. Thirty nine pts (78%) received platinum-based chemotherapy, as an induction (25 pts) and/or as a concurrent (14 pts) scheme. Acute toxicity was scored according to the NCI criteria, late effects using the SOMA/LENT scoring system.
Results: Eight pts experienced a grade 3–4 acute lung toxicity, all of them had a V_{20} ⩾25%, 3 of them presented a late grade 3 fibrosis, with a V_{20}superior 35%. Pts with low FEV1 (<1.5l) presented more frequently a lung toxicity without clear correlation. Three pts died of acute cardiac failure during the first 3 months of the treatment. Grade 4 acute heart toxicity occurred in 1 pt, G3 esophagitis in 3 pts. Eighteen months complete response rate was 45%, median overall survival time 17.3 months, the 12 and 24 months overall survival rates 72% and 37% respectively. A local failure occurred in 55% of pts, either as sole site (21%) or as a component of distant failure. Metastatic rate is 49%, with 18% brain metastases. Four patients are still alive.
Conclusions: The results show a relationship between the V_{20}value and the risk for occurrence of radiation induced lung toxicity. Parameters like FEV1, and V_{20}, $V_{30}$for heart and lung will be integrated in the dose level choice of the future protocol. The heart toxicity is highly difficult to precisely assess, late deaths are rarely documented, responsibility of the treatment is often under-estimated, in smoking patients. These results form a basis for an escalating dose phase I trial, which is under elaboration, integrating these predictive toxicity parameters.