1168 PUBLICATION

A phase II study of biweekly irinotecan plus cisplatin in patients with extensive stage small cell lung cancer

S. Bae[1], M. Kim[2], S. Shin[2], K. Lee[2], M. Hyun[2], Y. Do[3], H. Song[3], K. Kwon[3], K. Park[4], W. Lee[5]. [1]*Daegu Catholic University Hospital, Internal Medicine, Daegu, Korea;* [2]*Yeungnam University Hospital, Internal Medicine, Daegu, Korea;* [3]*Keimyung University Dongsan Hospital, Internal Medicine, Daegu, Korea;* [4]*Dongguk University Hospital, Internal Medicine, Daegu, Korea;* [5]*Fatima Hospital, Internal Medicine, Daegu, Korea*

Background: Superiority of irinotecan/cisplatin (IP) combination over etoposide/cisplatin has recently been suggested in a phase III study in patients with small cell lung cancer (SCLC). But about 70% of patients in the study recieved assigned IP treatment with modified doses or delivery schedule due to the adverse events (N Engl J Med 2002; 346: 85–91).
Aim: This multicenter, phase II trial was designed to confirm these results in chemo-naïve pts with ES SCLC using a modified biweekly regimen of IP to improve tolerability with acceptable response.
Patients and methods: 37 chemotherapy-naïve patients with ED-SCLC received irinotecan (d1, d15: 60 mg/m^2)/cisplatin (d1, d15: 30 mg/m^2)(biweekly IP). Pts were restaged every 2 cycles. Eligibility criteria included: measurable disease, ECOG PS 0–2, adequate organ function, no active brain metastases, and informed consent.
Results: 37 pts were enrolled between 09/03 and 01/05. Baseline characteristics include: median age 66 years (49–78); male/female, 31/6; ECOG PS 0,1,2: 13/18/5. Grade(G) 3 non-hematologic toxicity included: nausea (21%), vomiting (5%) and diarrhea (5%). G3 hematologic toxicity included: neutropenia (10%) and thrombocytopenia (3%). There were no treatment-related deaths. Response data are available for 30 pts. Complete/partial response were observed in 4 pts (13%)/21 pts (70%), respectively, for an overall RR of 83%. One pt (3%) had stable disease, and 4 pts (13%) had progressive disease (7 pts were unevaluable because of intercurrent illness, poor compliance, or treatment toxicity.) Median progression-free (PFS) and overall survival (OS) were: 33 weeks (95% CI, 22–44) and 76 weeks (95% CI, 43–109), respectively.
Conclusions: modified IP is a safe and well-tolerated regimen with acceptable RR in the first-line treatment of extensive-stage SCLC.

1169 PUBLICATION

A pharmacoeconomic feasibility study of three chemotherapy regimens for advanced non small cell lung cancer (NSCLC) in India

L. Abraham Jacob, P. Bapsy, H. Dadhich, T. Sahoo, J. George. *Kidwai Memorial Institute of Oncology, Medical Oncology, Bangalore, India*

Background: Incidence of lung cancer in Bangalore among men is 495 per 1,000,000 population. Majority of these patients present with stage IIIB/IV disease. Hence palliation of symptoms and prolongation of life are the primary goals of treatment. Newer third generation platinum-based regimens have emerged as the mainstay of chemotherapy for such patients with an absolute increase in survival of 4% at 1yr over second generation platinum based regimens. This study was undertaken to compare the efficacy, toxicity, pharmacoeconomics and feasibility of the newer third generation regimens as against the second generation in our set up.
Materials and methods: The study population included previously untreated stage IIIB/ IV NSCLC patients with an ECOG performance status of $\geqslant$2. The study arms included: 1) Gemcitabine + Cisplatin (G + C), 2) Paclitaxel + Cisplatin (P + C) and 3) Etoposide + Cisplatin (E + C). Twenty patients were recruited into each arm and prospectively studied for response rates (RR), median time to progression (TTP), toxicity profile and cost of therapy.
Dosages of drugs were as follows: Gemcitabine – 1250 mg/m^2 on days 1&8; Paclitaxel – 175 mg/m^2 on day 1; Etoposide – 100 mg/m^2 on days 1, 2, 3 and Cisplatin – 75–100 mg/m^2 on day 1 of three weekly cycle. Chemotherapy was administered for a maximum of six cycles or till progression. Pharmacoeconomics was calculated for the three arms based on cost of drug, hospital stay, loss of wages and management of toxicity.

Results:

	G + C	P + C	E + C
RR (%)	35	30	15
TTP (months)	4.5	4	2.7
GradeIII/IV hematological toxicity (%)	45	30	15
Pharmacoeconomics per patient per cycle in Indian Rupee	30,000	20,000	6,000

Third generation agents (Gemcitabine and Paclitaxel) were associated with better respose rates and time to progression. However cost of therapy in the Gemcitabine arm was 5 times more as compared to Etoposide arm and cost of therapy in Paclitaxel arm was 3.3 times more as compared to Etoposide arm. Cost of the drug and management of toxicity resulted in the higher pharmacoeconomics of third generation agents.
Conclusion: With a percapita income of only Rs. 10000–13000 and with more than 80% being rural poor, third generation agents do not appear to be economically viable for the management of advanced NSCLC in India.

1170 PUBLICATION

Radiochemotherapy in the treatment of small cell lung carcinoma. Results and evaluation of acute toxicity

N. Rodriguez de Dios[1], A.L. Manuel[1,3], S.L. Xavier[1], F.A. Palmira[1], M.B. Carlos[2], G. David[1], R.C. Anna[1], V. Pedro[1], A.S. Carmen[1]. [1]*Hospital De La Esperanza, Radiation Oncology Institute, Barcelona, Spain;* [2]*Hospital Del Mar, Clinical Oncology, Barcelona, Spain;* [3]*Universidad Pompeu Fabra, Barcelona, Spain*

Background: The schedules of concurrent chemo-radiation in the treatment of small cell lung carcinoma (SCLC) are leading to improved survival when compared to sequential treatments but also with a considerable increase in acute toxicities. We analized the acute toxicity and the efficacy of concurrent chemotherapy and radiotherapy in the treatment of limited stage of small cell lung carcinoma.
Methods: Since 1999, sixty patients affected of limited small cell lung carcinoma were included. In 98.3% of patients the chemotherapy administrated was Cisplatin (80 mg/m^2), on day 1 and Etoposide (100 mg/m^2), on days 1–3, and in 88.4% of cases the radiotherapy began between the first to third cycles of chemotherapy. All patients were treated with standard technique, administering 45 Gy in 25 fractions to the mediastinum plus a boost of 9–10 Gy to the tumor. The fractionation was 180 cGy/day, five days/ week; in 19 patients (31.7%) accelerated radiotherapy was used administering twice daily 150 cGy fractions separated 6 hours each other. The 78.3% of patients had profilactic cranial irradiation.
Results: The most common toxicity was the esophagitis, followed by dermitis. Three patients presented pneumonitis grade II. In any case the radiochemoterapy was interrupted. A complete response was observed in 62.7% of cases, a partial response in 25.4%, stable disease in 5.1% and 6.8% had local progression. After a mean follow-up of 24 months the overall survival, cause specific survival and local recurrence free survival at two years was 49.5$\pm$7.3%, 55.2$\pm$7.5% and 69.3$\pm$7.6% respectively.
Conclusions: Radiochemotherapy improve the results in patients with SCLC, despite an increased toxicity. The acute side effects seems acceptable and controlled with standard treatments. The twice-daily schedule has worse side effects as compared with concurrent once-daily radiotherapy. Despite of the limited number of patients and the shorter follow-up these data are promissing, beacuse they represent an improve in the response rates.

1171 PUBLICATION

What is the role of radiotherapy in advanced mesothelioma?

P.G. Niblock, G.R. Kerr, S.C. Erridge, J.A.D. Ironside, F.A. Little, A. Price. *Western General Hospital, Edinburgh Cancer Centre, Edinburgh, United Kingdom*

Background: Adjuvant radiotherapy (RT) to prevent biopsy site metastases in patients with mesothelioma is standard practice in the UK based on one randomised trial of 40 patients carried out in the pre-chemotherapy era. In Edinburgh, between 2000 and 2003, patients were offered chemotherapy (CT) within the context of a series of clinical trials and the use of adjuvant RT was not routine.
Aim: To evaluate our use of RT in patients with advanced pleural mesothelioma.
Methods: Between January 2000 and December 2003 116 patients were referred to the Edinburgh Cancer Centre with pathologically confirmed mesothelioma. Nine patients had primary peritoneal disease and were excluded from further analysis. Six patients had an extrapleural pneumonectomy for early mesothelioma and are also excluded, leaving 101 for this review. Data was extracted on age, gender, stage, use of CT and RT (including site) from the data base. The case notes of 95 were available for review and data was extracted on histology, surgical intervention, performance status (PS) and indication for RT.
Results: The median age of the cohort was 68 (range 46–91) years and 95 were male. 27 patients had epithelioid tumours, 10 sarcomatoid, 4 mixed and the remainder were unspecified. PS was not documented in 15 cases. Of the remainder 8 were PS 0, 42 PS 1, 21 PS 2, and 10 PS 3. 67 patients had pleural aspiration, 83 closed pleural biopsy, 39 thoracoscopy and 13 thoracotomy.

60 patients were offered and 39 received CT. 38 received RT, which was given adjuvantly in only 5 patients (one of whom later required 2 further courses for the development of biopsy site metastases). RT was given to 12 patients for biopsy site metastases (4 of which were also painful) and to 16 patients for chest wall pain alone.
The median age of those receiving RT was 70 years, 36 were male, 8 (21%) had epithelioid and 5 (13%) sarcomatoid histology. Two were PS 0, 14 PS 1, 10 PS 2 and 4 PS 3. 24 (73%) patients had pleural aspiration, 28 (85%) closed pleural biopsy, 14 (42%) thoracoscopy and 4 (12%) thoracotomy. 13 (39%) also received CT.
Conclusion: Age, gender, histology, PS and biopsy procedure did not influence the requirement for RT in our centre. RT was more often delivered for the palliation of pain rather than biopsy site metastases. In our cohort of patients the development of a mass was a relatively uncommon event and this supports a recent Australian study. We suggest that routine prophylactic irradiation to biopsy sites may not be necessary.

1172 PUBLICATION

First results of a prospective study on safety and feasibility of navigated brachytherapy as a new treatment option for peripheral lung cancer

W. Harms[1], R. Krempien[1], C. Grehn[1], F. Hensley[1], J. Debus[1], H.D. Becker[2]. [1]*University of Heidelberg, Radiation Oncology, Heidelberg, Germany;* [2]*Thoraxclinic, University of Heidelberg, Interdisciplinary Bronchoscopy, Heidelberg, Germany*

Introduction: The aim of this prospective study was to prove feasibility and safety of endobronchial high dose rate (HDR) brachytherapy applied as a highly conformal boost for inoperable peripheral non-small-cell lung cancer (NSCLC).
Material and Methods: Patients with medically or surgically inoperable stage I-III peripheral NSCLC were prospectively treated with combined external beam radiotherapy (EBRT, 50–66 Gy, depending on nodal status) and navigated brachytherapy (15 Gy). Inclusion criteria comprised tumor localization distant to the second segmental bronchus, tumor diameter <5 cm, written informed consent, and histologically proven NSCLC. Navigated bronchoscopy was performed with an electromagnetic navigation system (superDimension, Israel) for localization of a micro-sensor mounted on the tip of a bronchoscope. The probe can be actively guided by a steering mechanism to the targeted lesion displayed on reconstructed chest CTs. After localization of the NSCLC and placement of a catheter, endobronchial ultrasound (EBUS) was performed to confirm the exact position in the center of the lesion. Then, a 6 french brachytherapy catheter was placed within the tumor and fixed at the nose of the patient for the 5 day treatment period. Primary CT based 3D brachytherapy treatment planning (PLATO, Nucletron, Netherlands) was performed on chest CTs acquired with the inserted brachytherapy catheter loaded with a dummy probe. The brachytherapy PTV comprised the peripheral NSCLC and the draining boncho-vascular bundle. Prior to every brachytherapy repeated CTs were performed to ensure a stable positioning of the brachytherapy catheter. HDR brachytherapy (single dose 5 Gy, 370 GBq 192-Iridium, Nucletron, Netherlands) was applied three times a week. Primary endpoints of this study were safety and feasibility of brachytherapy as well as navigated bronchoscopical catheter placement and primary CT based 3D-treatment planning.
Results: After approval of the ethics committee 6 patients have been enrolled so far. Navigated bronchoscopy, catheter placement and CT based brachytherapy proved to be feasible and safe. All patients tolerated the brachytherapy catheter well during the treatment period. Repeated CTs prior to brachytherapy revealed a stable positioning of the catheters with a maximum deviation <2 mm. After a median follow up of 3 months (2 weeks to 9 months) no major side effects or complications have been observed. The first patient treated revealed a partial remission on EBUS and CT, respectively and demonstrated only minor cytological residuals on histology.
Conclusion: Navigated brachytherapy of inoperable peripheral NSCLC proved to be safe and feasible. The major advantage of this new approach compared to other highly conformal techniques is the possibility to easily encompass the draining broncho-vascular bundle and to apply highly fractionated treatment schedules with a broad therapeutic index in curative situations or single dose treatments in palliative situations.

1173 PUBLICATION

Phase II trial of neo-adjuvant gemcitabine-carboplatin-paclitaxel (GCP) chemotherapy for operable non-small cell lung cancer (NSCLC)

R.P. Abratt[1], J.S. Lee[2], J.Y. Han[3], C.M. Tsai[4], M. Boyer[5], T. Mok[6], S.W. Kim[2], J.S. Lee[3], A.J.M. Brnabic[7], M. Lehnert[8]. [1]*Groote Schuur Hospital, Department of Radiation Oncology, Cape Town, South Africa;* [2]*Asan Medical Center, Division of Oncology, Seoul, Korea;* [3]*National Cancer Center, Center of Lung Cancer, Goyang-Si, Korea;* [4]*Taipei Veterans General Hospital, Taipei, Taiwan;* [5]*Royal Prince Alfred Hospital, Sydney Cancer Centre, Sydney, Australia;* [6]*Prince of Wales Hospital, Department of Clinical Oncology, Hong Kong, Hong Kong;* [7]*Eli Lilly Australia, Clinical Outcomes and Research Institute, Sydney, Australia;* [8]*Eli Lilly Asian Operations, Hong Kong, Hong Kong*

Background: The aim of this open-label single-arm phase II study (B9E-MC-S179) was to evaluate the efficacy, feasibility and safety of the GCP combination as neo-adjuvant chemotherapy in patients with operable stage NSCLC.
Material and Methods: Major eligibility criteria included histologic or cytologic diagnosis of NSCLC; Stage IB, II or IIIA disease; tumor amenable to curative surgical resection; no prior tumor therapy; ECOG performance status (PS) 0 or 1; and written informed consent. Patients were given 3 cycles of chemotherapy followed by tumor resection. Each 21-day cycle consisted of gemcitabine 1000 mg/m^2 on days 1 and 8, carboplatin AUC 5 on day 1 and paclitaxel 175 mg/m^2 on day 1. The primary endpoint was response rate and secondary endpoints included safety and time-to-event variables.
Results: Forty-four patients were enrolled in this multi-national, multi-center study: 39 males, 5 females; mean age 56.4 yr, range 37–67 yr; 18% Stage IB, 16% Stage II, 66% Stage IIIA. All 44 patients received 3 cycles of treatment: 33 patients had a partial response to chemotherapy, for a response rate of 75% (95% CI: 60, 87%). 3 patients did not undergo surgery (1 patient had brain metastases discovered, 1 patient died from the study disease and the tumor of 1 patient was no longer amenable to surgery). 36 patients had a complete tumor resection, 5 of whom had a complete pathological response with no viable tumor cells in the resected tumor on histological examination. Median time to progression and median time to treatment failure were both 13.6 months (95% CI: 8.9, >16 months) and 26/44 patients (59%) have progressed. The one-year survival rate was 86% (95% CI: 72, 95%). Grade 3/4 hematological toxicity was reported for 37 patients (84%), most commonly neutropenia (34 patients, 77%) and thrombocytopenia (11 patients, 25%). Other toxicities included grade 3/4 anemia (4 patients, 9%), febrile neutropenia (1 patient, 2%), bleeding (1 patient, 2%), vomiting (1 patient, 2%), rash (1 patient, 2%), increased alanine aminotransferase (3 patients, 7%) and grade 2 alopecia (35 patients, 80%). Toxicity caused a reduction or delay in gemcitabine for 32 patients (73%) (23% had a reduction or delay at day 1 and 68% at day 8), in carboplatin for 12 patients (27%) and in paclitaxel for 11 patients (25%).
Conclusion: The GCP combination showed promising efficacy and appears to be safe and feasible as neo-adjuvant chemotherapy in patients with operable stage NSCLC.

1174 PUBLICATION

Intrafractional movement of the oesophagus in patients with Non-Small Cell Lung Cancer (NSCLC)

N. Panakis[1], J. McClelland[2], A. Chandler[3], J. Blackall[2], S. Ahmad[4], S. Hughes[4], D. Hawkes[2], D. Landau[4], M. Brada[1]. [1]*The Institute of Cancer Research, Academic Department of Radiotherapy, Sutton, United Kingdom;* [2]*University College London, Centre for Medical Image Computing, London, United Kingdom;* [3]*King's College London, Division of Imaging Sciences, London, United Kingdom;* [4]*Guy's and St Thomas' Hospitals NHS Trust, Department of Radiotherapy, London, United Kingdom*

Background: Concomitant chemo-radiation appears to result in a survival advantage in patients with NSCLC compared to sequential therapy. This is at the expense of increased radiation-induced oesophageal toxicity. The extent of oesophageal movement on dose delivered to the oesophagus is not known and needs to be determined before introducing techniques to avoid it.
Materials and Methods: CT scans were performed in 7 patients with NSCLC prior to undergoing radical radiotherapy. 2 CT images were acquired of the thorax in inhale and exhale positions. A rigid registration was performed relative to the spine to account for global patient movement. This was followed by non-rigid registration to account for organ motion and deformation. The oesophagus was manually identified on the exhale image and its central point was identified at 4 cm intervals along its length from