Methods: Eligible pts had histologic or cytologic diagnosis of PM not amenable to curative surgery. P 500 mg/m^2 alone or in combination with either Cis 75 mg/m^2 or carboplatin (Cb) AUC 5 was given on day 1 of each 21-day cycle, with vitamin B_{12}, folic acid, and dexamethasone. Investigator-determined best response and survival data (with censoring) were recorded at the end of study participation. Myelosuppression data (NCI CTC, version 2.0) were also collected.
Results: In this nonrandomized, open-label study 109 pts received $\geqslant$1 dose of P, P+Cis, or P+Cb and were evaluable for safety; 91 pts were evaluable for efficacy. Baseline characteristics, efficacy, and safety data are summarized in the table. A higher percentage of pts on the P arm received prior therapy, which generally corresponded to greater toxicity.
Conclusions: The results of this large, nonrandomized study confirm that P and P+platinum are efficacious in the treatment of pts with PM. The response results are comparable to those previously reported for the EAP in pts with pleural mesothelioma.

6572 POSTER

Stereotactic body radiotherapy (SBRT) for lung cancer: Clinical experience for medically inoperable lung tumours with excellent local control

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Background: To report clinical results from ours first patients with resecable lung tumours, but clinically inoperable patients, treated with stereotactic body radiotherapy (SBRT) employing hypofractionated high dose fraction schedule.
Material and Methods: Between July 2002 and February 2007, 21 lung tumours patients have been treated using SBRT, all of them resecable, 20 medically inoperable, one operable but with 1 brain metastasis treated with radiosurgery. After immobilization with Stereotactic Body Frame (ELEKTA) we have made 3 CT simulation studies in 1 week and measured the variations in CTV and organs and calculated the position statistical variability to determine the PTV for each patient. All patients have been treated with 6 to 12 coplanar or no coplanar conformed beams (average 8.2 beams), 3 fractions in 1 week, the dose was prescribed to cover PTV with no more margin, T1 with 16 Gy each fraction and total dose of 48 Gy and T2−3 with 14 Gy/fraction and total dose of 42 Gy. Dose calculation included heterogeneity corrections. Follow-up was at 4−6 weeks and then every 3 months.
Results: For 21 patients, median age was 73 years (range 55−84). There were 19 males and 15 (83.3%) smokers. The mean follow-up was 15.8 months (range 1.5−56). All have pathology diagnosis: 8 SCC, 6 ADC, 1 SCLC and 6 non-specifics NSCLC. Pretreatment PET was made in 15 (71.4%) patients. Tumor stages were 10 T1, 9 T2, 1 T3, 1 metastasis, 1 local relapse. Four patients (19%) received previous cisplatin-based chemotherapy. All lesions were resecable, but 20 patients (95.2%) were medically inoperable. All SBRT was completed without interruptions. GTV mean volume was 16.2 ml (95% CI: 8.8−23.6), PTV mean volume was 52.2 ml (95% CI: 30.5−73.9). There was no acute esophagitis, one patient develops acute pneumonitis and no delayed lung toxicities were found. At the moment, only 10 patients were evaluated for response: 7 (70%) complete responses, 2 (20%) partial responses and 1 (10%) stable disease. No patient failed locally and only 2 patients (9.5%) developed distant metastasis.
Median survival was 30 month (95% CI: 9.2−50.8). Overall survival at 12 and 18 months were 83.9% (95% CI: 83.7−84.1) and 67.1% (95% CI: 66.8−67.4), respectively.
Conclusions: SBRT for lung cancer demonstrates a high response rate and excellent local control and survival. There are minimal toxicities and no treatment related deaths.

6573 POSTER

Clinical evidence for the radiosensitivity of mesothelioma following postoperative image-guided radiotherapy

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Background: The increasing incidence of mesothelioma presents a serious problem around the world with no standard therapy and no treatment proven to offer durable benefit. The high mortality rate has not significantly improved with radical surgery or new systemic therapies, but there is growing evidence that a trimodality approach using postoperative radiotherapy may be curative in selected patients. Mesothelioma is characterized by relentless locoregional growth that spreads beyond the scope of surgery, and it is timely to evaluate newer techniques of image-guided radiotherapy (IGRT) in this disease.
Objective: To document locoregional control from high dose postoperative radiotherapy in pleural mesothelioma patients who have PET scans accurately reflecting disease distribution.
Materials and Methods: Thirteen consecutive patients were treated with postoperative radiotherapy to regions of residual disease with doses of 45 to 60 Gy, after pleurectomy/decortications from 2003 to 2006. 3D-conformal or intensity-modulated radiotherapy techniques were used with PET/CT fusion IGRT. All had pre-treatment PET scans showing ^{18}FDG-avid disease, and post-treatment imaging including followup PET or PET/CT scans in 10 cases. All but one received intraoperative phototherapy. Ten had epithelioid and 3 had biphasic mesothelioma.
Results: There were no in-field relapses within the planning target volume (PTV) confirmed with PET scan co-registration, resulting in a local control rate of 100% at a median followup of 10 months post-radiotherapy. Relapses outside the PTV were found in 11 cases, all in multiple sites. Many were in areas deemed at moderate risk but not included in the PTV due to strict dose constraint criteria required to minimize the risk of major radiation toxicities.
No patient died as a consequence of radiotherapy. Radiation morbidity was seen in two cases, with transient grade 2 pneumonitis and liver injury, both patients remaining well and disease-free 30 months after surgery. Six received palliative chemotherapy for distant relapse and only 1 had neoadjuvant chemotherapy. Additional palliative radiotherapy was given in 2 cases.
Conclusions: Mesothelioma appears to be a radiosensitive disease that can be locally controlled by radiation doses of 50 Gy in conjunction with debulking surgery. Using modern technological advances in planning and delivery, radiotherapy can be administered safely and accurately without significantly damaging surrounding tissues.

6574 POSTER

A phase I/II study on stereotactic body radiotherapy for stage I non-small cell lung cancer

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Background: The outcome of stage I non-small cell lung cancer (NSCLC) patients treated with conventional radiotherapy is inferior to that of the patients treated with surgery. The aim of this study is to evaluate the clinical outcome of stereotactic body radiotherapy (SBRT) in the treatment of stage I NSCLC.
Materials and Methods: We performed SBRT on 31 patients with stage I NSCLC. Of the 31 patients, 20 were medically inoperable, and 11 refused surgery. Nineteen tumors were T1 stage masses and 12 tumors were T2. The median tumor size was 25 mm. SBRT was delivered at 45 Gy/3 fractions except in cases in which the tumor was close to an organ at risk, in which case we used 60 Gy/8 fractions. The radiation target was the primary tumor, and photon energy was 6 MV in all cases.
Results: The median duration of observation for all patients was 32 months (range 4−87 months). The 5-year overall and cause-specific survival rates were 48.9% and 62.6%, respectively. In 9 of the 31 cases, there was evidence of local recurrence. The local control rate of T1 tumors was 84.2% (16/19 cases) and of T2 tumors, 50.0% (6/12 cases). Five patients developed acute pulmonary toxicity greater than grade 2, although the symptoms improved with medical treatment.
Conclusions: SBRT was shown to be an effective treatment for stage I NSCLC patients, although the local control rate for T2 tumors was low. A more intensive treatment regimen should be considered for T2 tumors because no severe toxicity occurred.

6575 POSTER

Is there still a place for surgery in the treatment of locally-advanced non-small cell lung cancer (IIIA, N2)?

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Background: Surgical resection for patients with stage IIIA (N2) non-small cell lung cancer (NSCLC) results in disappointing 5-year survival

rates (<10%). Most of these patients develop distant metastases, and this rationalizes the use of induction chemotherapy. There is ongoing discussion about the role of surgical resection (vs. radiotherapy) as local treatment modality after induction therapy. The aim of this retrospective analysis was to evaluate results of surgery and radiotherapy after neoadjuvant chemotherapy in the clinical setting.
Methods: Patients with stage IIIA NSCLC treated with neoadjuvant chemotherapy from 1994 to 2006 were identified from registration databases. During this period all treatment proposals (or trial participation) were discussed by a multidisciplinary thoracic oncology committee. Response to induction therapy, definitive local therapy, recurrence of disease, and overall survival were reviewed.
Results: Ninety-nine patients, 66 men and 33 women, were identified. The mean age was 61 (36−77), 40 tumors were left-sided. Neoadjuvant chemotherapy consisted of platin-based doublets/triplets. Clinical mediastinal downstaging was achieved in 32 patients. Thirty-nine patients underwent surgery: 19 lobectomies, 19 pneumonectomies, and one thoracotomy without resection. Microscopic complete resection was achieved in 26 patients (69%). Thirty-days mortality was 3% (n = 1 after pneumonectomy). Forty-two patients received radiotherapy with radical intent. Radiation doses actually delivered ranged from 51 to 81 Gy, median dose given was 60 Gy. The 2- and 5-year overall survival after surgery was 58% and 29% respectively, survival in lobectomy patients being significantly higher (p = 0.03). The 2- and 5-year overall survival after radiotherapy was 40% and 16%. The cumulative incidence of locoregional recurrence at 2 and 5 years was 27 and 41% for surgically treated patients and 45 and 54% for irradiated patients (p = 0.39). Mortality within 6 months after local treatment was high in patients who underwent pneumonectomy (21%), and much lower in patients who underwent lobectomy or radiotherapy (5%).
Conclusions: Radiotherapy is being regarded as the standard local treatment modality after neoadjuvant chemotherapy for stage IIIA NSCLC. Our retrospective data show that in selected patients complete surgical resection is associated with favorable locoregional control and long-term survival. Due to excess early mortality, pneumonectomy should be avoided.

6576 POSTER

Extent of mediastinal lymph-nodes resection as prognostic factor for survival in stage I−IIIA non-small-cell lung cancer (NSCLC) patients undergone surgery: a retrospective analysis of a mono-institutional series

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Background: The role of mediastinal lymphoadenectomy in patients undergoing lobectomy or pneumonectomy for early stage (I-IIIA) NSCLC as prognostic factor is still under debate. A non significant effect of such approach on both progression-free and overall-survival (PFS/OS) has been reported. Although adjuvant chemotherapy has recently demonstrated to significantly improve survival, different extents of mediastinal surgery across all adjuvant trials are reported; for this reason an update regarding the supposed independent prognostic role of this intervention is required.
Methods: A retrospective database of surgically resected NSCLC patients who referred to the Regina Elena National Cancer Institute was gathered. A panel of known prognostic factors (sex, type of surgery, histology, tumor size, node involvement, grading) plus the number of resected mediastinal nodes (#RMNs) was correlated to clinical outcomes (PFS and OS) by using the Cox regression model (considering #RMNs as quantitative variable; significance cut-off <0.10) as well as classification and regression trees (CART) analysis.
Results: A data-set of 191 stage I-IIIA NSCLC patients undergone surgery was built. Patients with more than 26 removed nodes had better outcome according to the CART analysis; by using this cut-off, #RMNs was considered as categorical variable too. Multivariate analysis is shown in the table.

		HR	95% CI	p
PFS	Nodal involvement	1.90	1.16, 3.12	0.01
	Type of surgery	3.24	1.33, 7.91	0.01
	#RMNs	2.59	1.17, 5.72	0.018
OS	Nodal involvement	1.86	1.00, 3.44	0.048
	Type of surgery	3.21	1.05, 9.75	0.04
	#RMNs	3.05	1.11, 8.38	0.03
	Grading G2−3	1.88	0.99, 3.57	0.053

Conclusions: The presented data suggest that prognosis of stage I-IIIA NSCLC patients can be conditioned by the extent of mediastinal nodes resection. Further prospective trials are needed to confirm this result.

6577 POSTER

Prospective phase II trial of a combination of gemcitabine, cisplatin and UFT as first-line treatment in patients with advanced, unresectable, non-small cell lung carcinoma

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Background: Most patients with advanced non small cell lung cancer (NSCLC) receive either single agents or chemotherapy doublet. Meta-analysis have showed combination chemotherapy consisting of cisplatin plus new agent yielded a substantial survival advantage compared with carboplatin plus new agent in patients with advanced NSCLC. And also combination chemotherapy comprised of oral UFT and cisplatin was shown to be an effective and safe regimen. Therefore a Phase II study was conducted using the combination of gemcitabine, cisplatin and UFT in patients with advanced NSCLC.
Materials and Methods: Eligible patients had histologically or cytologically confirmed stage IIIB or IV NSCLC and good performance status. Patients who had recieved prior cytotoxic treatment were excluded. Gemcitabine (1,250 mg/m^2, 10 mg/kg/min on days 1 and 8) and cisplatin (75 mg/m^2 on day 1) were injected intravenously and UFT (400 mg/day) was administered orally on day 1−14. Treatment was repeated every 3 weeks. Primary end points was overall response rate and secondary end points were overall survival, time to progression and toxicity.
Results: Thirty seven patients with advanced NSCLC were enrolled. The median age of the patients was 60 years (range: 44 to 72). The performance status (WHO) was 0 for 4 (11%), 1 for 30 (81%) and 2 for 3 (8%) patients. Twenty three patients did complete six cycles. The median number of cycles of gemcitabine was 6 (range 1−6). Complete response was achieved in 1 (3%) patient, partial response in 17 (46%) patients, stable disease in 9 (24%) patients. Overall response rate was 49%. Among response available patients (33 patients), response rate was 55%. The mean survival time was 16.0 months (95% CI: 13.2, 18.9) and the 1-year survival rate was 40% and then median time to progression was 3.4 months. Toxicity was moderate and mostly hematologic. Grade 3/4 neutropenia occurred in 37%, 5 patients with febrile neutropenia. Grade 3/4 anemia and thrombocypenia was occurred in 37% and 5%. Nonhematologic toxicity was mild.
Conclusion: The combination therapy comprising gemcitabine, cisplatin and UFT is active and tolerated first line regimen in NSCLC patients.

6578 POSTER

No evidence of an association between EGFR inhibitor treatment and interstitial lung disease in patients with advanced lung cancer

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Background: The EGFR tyrosine kinase inhibitors (TKIs), erlotinib and gefitinib, have been evaluated for the treatment of advanced non-small-cell lung cancer (NSCLC), both as monotherapies and in combination with cytotoxic agents. Interstitial lung disease (ILD) has been reported as a rare and unexpected adverse event of TKI therapy. To investigate if TKIs are associated with ILD, we conducted a meta-analysis to compare the incidence of ILD events in the treatment and placebo arms of randomized trials of TKI treatment. We also investigated the potential dose effect relationship between drug administration and ILD development.
Methods: We searched the MEDLINE database to identify trials randomizing patients with advanced NSCLC to either TKI therapy or placebo. For the dose effect analysis, we identified trials randomizing patients to different doses of TKIs. For both comparisons, trials were considered eligible only if treatment arms differed solely regarding the administration of TKIs. We abstracted data on the incidence of ILD. Fixed effects meta-analysis was performed to estimate a pooled odds ratio (OR) and its confidence interval, with values higher than one indicating that ILD is more common in patients receiving TKIs or in those receiving higher TKI doses (for the dose effect assessment). Continuity correction, propotional to the relative size of the opposite of the study, was used for studies with zero events in one arm. Sensitivity analyses were performed using different correction methods or no correction. Results are presented in accordance with the QUOROM guidelines.