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.

Results: Out of eight eligible trials, one was available only in abstract form and did not report on ILD events. Five trials (4,932 patients, 2,530 gefitinib, 694 erlotinib, 1,708 placebo) were included in the TKI-placebo comparison. Four trials (1,829 patients) comparing two gefitinib doses (250 mg; 909 patients versus 500 mg; 920 patients) were included in the dose effect analysis. We found no evidence of a relationship between TKI treatment and ILD (OR, 1.09; 95% CI, 0.59 to 2.02). This held true when we analyzed erlotinib (OR, 1.14; 95% CI, 0.31 to 4.13) and gefitinib (OR, 1.08; 95% CI, 0.54 to 2.16) trials separately. TKIs were unrelated to ILD, both when given as monotherapy (OR, 0.77; 95% CI, 0.33 to 1.80) or in combination with cytotoxic agents (OR, 1.59; 95% CI, 0.66 to 3.86). We found no evidence of a dose effect relationship (OR, 0.88; 95% CI, 0.33 to 2.34) when comparing the two gefitinib doses regarding ILD incidence. Sensitivity analyses revealed no inconsistencies between different calculation methods.
Conclusion: We found no evidence of increased incidence of ILD events in patients receiving TKIs for advanced NSCLC, when compared to patients receiving placebo. Our observation is strengthened by the lack of a dose effect relationship between gefitinib administration and ILD development. Further study of ILD in NSCLC patients is warranted since there seems to be little evidence in support of the widely held belief in a causal relationship between TKI treatment and ILD.

6579 POSTER

Randomized phase II trial of irinotecan combined with paclitaxel or gemcitabine in untreated advanced non-small cell lung cancer

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Purpose: Patients with advanced non-small cell lung cancer (NSCLC) do not always tolerate cisplatin-based regimens because of its non-hematological toxicities. Given the activity and tolerability of irinotecan-containing regimens in NSCLC, a randomized phase II trial was conducted to evaluate the effects of irinotecan plus paclitaxel or gemcitabine in patients with previously untreated stage IIIB or IV NSCLC.
Patients and Methods: Patients with adequate organ functions, who gave their written informed consent to take part in this clinical trial, were randomly assigned to irinotecan 50 mg/m^2 on days 1, 8, and 15 plus paclitaxel 180 mg/m^2 on day 1 every 4 weeks (arm A) or irinotecan 100 mg/m^2 on days 1 and 8 plus gemcitabine 1000 mg/m^2 on days 1 and 8 every 3 weeks (arm B). The primary end point was response rate.
Results: From January 2004 to April 2006, a total of 80 Japanese patients were enrolled and 78 of them were assessable (38 in arm A and 40 in arm B). Baseline characteristics were comparable. Response rates were 31.6% (95% CI, 17.5 to 48.7) in arm A and 20.0% (95% CI, 9.1 to 35.6) in arm B, respectively. Median time to failure was 86 days in arm A and 145 days in arm B, respectively. Adverse events profiles were, as expected in both arms, no significant additives. The most common grade 3 or 4 adverse events were neutropenia, (78.9% in arm A and 50.0% in arm B).
Conclusion: Both arms are well tolerated in NSCLC patients. In terms of the response rate, irinotecan plus paclitaxel (arm A) may be useful in patients not suitable for cisplatin.

6580 POSTER

Value of lung perfusion in stage III non-small cell lung cancer patients treated with radiotherapy

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Background: To study the value of lung perfusion single photon emission computed tomography (SPECT) scans for patients with stage III non-small cell lung cancer (NSCLC) treated with radiotherapy (RT).
Materials and Methods: 15 patients with stage III NSCLC treated with RT were enrolled. All patients had PET-CT and SPECT scans. The imagings were accurately co-registered in the treatment planning system. The PET-CT images were used to define the gross tumor volume where the standardized uptake value (SUV) > 2.5 was used as the threshold. The SPECT images were used to define the volume of perfused functional lung (FL) and non-functional lung (NFL). FL refers to the region of $\geqslant$30% maximum radioactive counts and the others were categorized as NFL. The degrees of lung perfusion deficit were classified by comparing lung perfusion damaging with area of radiological abnormality as followings. Grade 0: no lung perfusion deficit; Grade 1: the size of radiological abnormality is similar to the area of lung perfusion deficit; Grade 2: the area of lung perfusion is bigger than that of radiological abnormality, and extend to 1 pulmonary lobe; Grade 3: the area of lung perfusion deficit exceed 1 pulmonary lobe. Three dimensional conformal radiotherapy (3DCRT) plans were optimized before lung perfusion. After lung perfusion, to minimize the dose to FL both CT-PET and SPECT lung perfusion imagings were used to optimize 3DCRT and intensity modulation radiotherapy (IMRT) plans. Randomized block analysis of variance was used to analyze the difference of the percentage of whole lung volume received dose $\geqslant$xGy (WLVx) and the percentage of functional lung volume received dose $\geqslant$xGy (FLVx) among the three sets of treatment plans.
Results: All patients had different lung perfusion deficits. Among them 7 patients had grade 1 damage, 4 patients grade 2 damage, and 4 patient grade 3 damage. After the optimization of radiotherapy plans using SPECT perfusion imaging, WLVx and FLVx were decreased significantly both in the 3DCRT plan and in the IMRT plan. Comparing with plans without lung perfusion imaging, there were significant differences in WLV10, WLV15, WLV20, WLV25 ($p < 0.05$) and FLV10, FLV15, FLV20, FLV25 ($p < 0.05$) after the treatment planning was optimized with SPECT imaging. However, there was no significant difference in WLV10, WLV15, WLV20, WLV25 ($P > 0.05$)and FLV10, FLV15, FLV20, FLV25 ($P > 0.05$)between 3DCRT and IMRT arms. When the lung tumor had irregular shape or located in chest wall, IMRT planning had more ascendant than 3DCRT planning. For patients with large perfusion deficits away from lung tumor, the WLVx and FLVx decreased more significantly.
Conclusions: SPECT lung perfusion images were helpful in sparing FL for stage III NSCLC patients treated with RT, especially for ones with large perfusion deficits.

6581 POSTER

Assessment of maintenance oral etopside following induction chemotherapy with gemcitabine and cisplatin in chemo-naive extensive small cell lung cancer patients

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Background: Although vepsid-cisplatin combination is considered the standard treatment for extensive disease SCLC patients yet the majority of patients will relapse with poor long term outcome. So we try the use of gemcitabine-cisplatin combination to evaluate the response and tolerability to treatment, followed by maintenance therapy of oral etopside for non-progressive patients in trial to improve progression free survival and overall survival.
Patients and Methods: Thirty nine patients with extensive SCLC and ECOG $\leqslant$2, were enrolled to receive 4 cycles of chemotherapy consisting of gemcitabine 1000 mg/m^2 (day 1 and 8) and cisplatin 80 mg/m^2 (day 1) every three weeks. Twenty seven non-progressive patients after 4 cycles of chemotherapy were randomized either to receive oral etopside 50 mg/m^2 for consecutive 15days every 3 weeks vs. no therapy until progression.
Results: From January 2003 to September 2005, 39 patients treated with GC, 27 non progressive patients were subsequently randomized to oral etopside (N = 14) or observation (N = 13). Minimum follow up was 18 months. The overall response rate to GC was 59% and toxicity to oral etopside was mild. There was improvement if median PFS favoring the maintenance arm of 10.5 months vs. 7 months ($P < 0.05$). Median OS is improving towards the maintenance arm (13 Vs. 11.5 months). One year survival (60% vs. 24%), 18 months survival (20% vs. 5%) favoring the maintenance. Multivariate analysis revealed that age, performance status, maintenance therapy, and response to treatment were independent prognostic factors for OS ($P < 0.01$) meanwhile age, maintenance therapy, and response to treatment are highly significant factors for PFS ($P < 0.001$).
Conclusion: gemcitabine-cisplatin is an effective and tolerable regiment for extensive disease of SCLC. The addition of 3 months of oral etopside in non progressing patients was associated with a significant improvement of both PFS and OS.

6582 POSTER

Oral vinorelbine concomitantly with thoracic radiotherapy (RT) in locally-advanced or inoperable stage III non-small cell lung cancer (NSCLC): interim results of a phase I dose escalation trial

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Background: In vitro, vinorelbine (NVB) has shown to be a powerful radiosensitizer. The intravenous (IV) formulation led to an encouraging response rate of 75% at a daily dose of 4 mg/m^2 concurrently with 55 Gy