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