49 p (75.3%). 60 p were evaluables for response and 62 p for toxicity. Induction D-C response: 33 PR (RR 55%; 95% CI:43−77), 18 SD (30%) and 9 PD (15%). 4 p went to surgery: 3 pPR and 1 pPD (unresectable). 40 p completed CChRT (5 p in treatment) with 5 CR, 23 PR, 4 SD and 8 PD (RR 70%; 95% CI:56−84). The median to PFS was 11 months (95% CI:7−15) and median OS was 12 months (95% CI:8−16). The PFS and OS at 1 year was 44.5%/48.1% respectively. A total of 175 cycles of D-C were administered (2.8 per p), with the main toxicity (NCI-CTC 3.0) per p Grade (g) 1−2/3−4 (%) was as follows: neutropenia 11.3/29; anemia 30.6/0.5; nausea/vomiting 30.6/4.8; fatigue 27.4/0; diarrhea 14.5/11.2; there were nine episodes of febrile neutropenia and there were one treatment-related death. The main toxicities per p in CChRT (D-C doses: 143, 3.5 per p) were: g1−2 neutropenia/anemia 13/34.7%; g1−2/3 esophagitis in 45.6/2.1% and g1−2 pneumonitis in 26%; there were one treatment-related death.
Conclusions: Induction chemotherapy with D-C plus concurrent TRT and biweekly D-C is a feasible treatment option for locally advanced NSCLC, showing good clinical activity and tolerability with promising survival.

9101 POSTER

Toxicity report of a phase I/II dose escalation study in inoperable locally advanced non-small cell lung cancer with helical tomotherapy and concurrent chemotherapy

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Purpose: To evaluate the feasibility and toxicity of radiation dose escalation using helical tomotherapy (HT) in patients with inoperable stage III non-small cell lung cancer (LANSCLC) with concurrent chemotherapy.
Patients and Methods: This phase I/II study was designed to determine the maximum tolerated dose (MTD) of radiotherapy in patients with LANSCLC, concurrently with docetaxel and cisplatin. Radiotherapy was delivered using HT. A dose per fraction escalation was applied starting at 2 Gy, with an increase of 6% per dose cohort (DC). The RTOG acute radiation morbidity score was used to monitor pulmonary, esophageal and cardiac toxicity. All other adverse events were scored using the NCI CTC version 3.0.
Results: Dose escalation was performed in 34 patients over 5 DCs to a dose per fraction of 2.48 Gy. No differences were found in acute toxicity between the different DCs, but a significant increase in late lung toxicity in DC IV, using a fraction size of 2.36 Gy, necessitated a halt in further dose escalation with the MTD being defined as 2.24 Gy per fraction. The overall incidence of acute $\geqslant$grade 3 esophageal and pulmonary toxicity is 24% and 3% respectively. Overall late lung toxicity was 21%, but an acceptable 13% in DC I-III. Local response rate was 61% on computed tomography.
Conclusion: The use of helical tomotherapy to 67.2 Gy with concurrent cisplatin/docetaxel is feasible and resulted in acceptable toxicity. A full phase II study has been initiated to establish the true local response rate at the MTD of 2.24 Gy per fraction.

9102 POSTER

Toxicity and outcome results of a class solution with moderately hypofractionated radiotherapy in inoperable stage III non-small cell lung cancer using helical tomotherapy

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Purpose: To assess feasibility, toxicity and local control of a class solution protocol of hypofractionated tomotherapy in stage III, inoperable, locally advanced non small cell lung cancer (LANSCLC) patients.
Patients and Methods: Eligible patients were treated according to a uniform class solution (70.5 Gy in 30 fractions) with fixed constraints and priorities using helical tomotherapy (TT). Toxicity monitoring was performed using the RTOG criteria and the NCI CTCAE version 3.0. Pulmonary function tests (PFT) were measured at start and repeated at three months after treatment.
Results: Our class solution resulted in a deliverable plan in all 40 consecutive patients. Acute grade 3 lung toxicity was seen in 10% of patients. Two patients died during acute follow-up with pulmonary toxicity. Correlations were found between changes in PFT and mean lung dose (MLD) or the lung volume receiving 20 Gy (V_{20}). The correlation was strongest for lung diffusion capacity for carbon monoxide (DLCO). A V_{20} of >27% and >32% were predictive for grade 2 and 3 acute lung toxicity respectively ($p < 0.05$). Late grade 3 toxicity was exclusively pulmonary, with an incidence of 16%. Overall grade 3 lung toxicity correlated with a MLD >18 Gy and a median lung dose of > 15 Gy ($p < 0.05$). Median survival was 17 months and the 1y/2y local progression-free survival (LPFS) were 66% and 50% respectively.
Conclusion: The current class solution using hypofractionated TT in patients with LANSCLC is feasible. Toxicity was acceptable and in line with other reports on intensity-modulated radiotherapy. The LPFS was encouraging considering the unselected population.

9103 POSTER

The radioprotective effect of dimethyl sulfoxide in radiation induced acute pulmonary injury: detection by Tc99m-DTPA transalveolar clearance scintigraphy and histopathology

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Purpose: to investigate if radical scavenger and antiapoptotic agent dimethyl sulfoxide can prevent radiation-induced pulmonary injury by Tc^{99m}-DTPA transalveolar clearance scintigraphy, histopathologic assessment, and by TUNEL staining in an animal model.
Material and Method: Twenty white New-Zealand rabbits were grouped as: 1) control (CONT), 2) radiation alone (RT), 3) dimethyl sulfoxide plus radiation (DMSO+RT), and 4) dimethyl sulfoxide, alone (DMSO). Right hemithoraxes of the RT and DMSO+RT groups were irradiated with a single dose of 20 Gy by a Co^{60} treatment unit. Dimethyl sulfoxide (4.5 gr/kg) was given i.p. 30 minutes before irradiation. The Tc^{99m}-DTPA transalveolar clearance scintigraphy was performed on 14^{th} day after irradiation. The rabbits were sacrificed on 15^{th} day and lungs were removed for histopathologic evaluation. Evaluation was performed for the presence of peribronchial inflammatory cell infiltration (PIHI), alveolar septal infiltration (ASI), alveolar exudate (AEX), alveolar edema (AED) interstitial fibrosis (IF), and necrosis formation (NEC) by using a 4-point scale. Apoptotic cells were assessed by TUNEL staining. The reactivity of TUNEL positive cells is scored by 5-point scale.
Results: Administration of dimethyl sulfoxide prior to irradiation caused a marked prolongation in the transalveolar clearance rate of DTPA through the alveolocapillary membrane ($p = 0.028$). In addition, dimethyl sulfoxide administration prior to irradiation revealed better scores for pulmonary parenchyma in histopathologic evaluation compared to radiation alone group. Dimethyl sulfoxide given prior to irradiation markedly decreased the severity of alveolar exudate ($p = 0.042$). TUNEL staining scores of the apoptotic cells in the DMSO administered group prior to irradiation were better than radiation alone group at a statistically significant level ($p = 0.018$).
Conclusion: The results of our study suggest that dimethyl sulfoxide appears to be a protective agent against radiation-induced lung injury. Additional work is needed to better identify the effectiveness of dimethyl sulfoxide as radioprotective agent in radiation associated lung injury.

9104 POSTER

Randomized phase III study of mitomycin/vindesine/cisplatin (MVP) versus weekly irinotecan/carboplatin (IC) or weekly paclitaxel/carboplatin (PC) with concurrent thoracic radiotherapy (CTR) for patients (pts) with unresectable stage III non-small cell lung cancer (NSCLC): West Japan Thoracic Oncology Group (WJTOG) 0105

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Background: Concurrent chemoradiotherapy has become standard treatment of unresectable stage III NSCLC. However, the optimal regimen of concurrent chemoradiotherapy including radiation dose, schedule and chemotherapeutic agents has not been defined. We conducted a

randomized, multicenter phase III trial to assess the efficacy and toxicity of weekly chemotherapy with CTR against MVP with CTR via a non-inferiority design.
Materials and Methods: MVP: mitomycin (8 mg/m^2 on days 1, 29), vindesine (3 mg/m^2 on days 1, 8, 29, 36), and cisplatin (80 mg/m^2 on days 1, 29) with CRT (60 Gy). Pts subsequently received 2 courses of consolidation chemotherapy with MVP; IC: weekly irinotecan (20 mg/m^2)/carboplatin (AUC 2) for 6 weeks and CTR (60 Gy) followed by 2 courses of irinotecan (50 mg/m^2)/carboplatin (AUC 5); PC: weekly paclitaxel (40 mg/m^2)/carboplatin (AUC 2) for 6 weeks and CTR (60 Gy) followed by 2 courses of paclitaxel (200 mg/m^2)/carboplatin (AUC 5). The primary endpoint was overall survival (OS), with secondary endpoints of progression free survival (PFS), response, and toxicity.
Results: From Sep 2001 to Sep 2005, 456 pts were randomized. Pretreatment characteristics were well-balanced among the 3 arms. Major toxicities: Gr 3−4 neutropenia in the MVP, IC, and PC arms was 95.9, 72.1, and 46.9% ($p < 0.001$). Gr 3−4 non-hematologic toxicities in terms of fatigue, febrile neutropenia, and gastrointestinal disorder were 13.0, 6.1, and 4.8% ($p < 0.001$), 37.0, 8.8, and 10.2% ($p < 0.001$), and 24.0, 8.2, and 9.5% ($p < 0.001$) in the MVP, IC and PC arms, respectively. The overall response rates were 66.4, 56.5, and 63.3%, in the MVP, IC and PC arms, respectively. The median survival times were 20.5, 19.8 and 22.0 months and the median PFS (MPFS), 8.2, 8.0 and 9.5 months in the MVP, IC and PC arms, respectively. Non-inferiority of the 2 experimental arms compared with MVP was not achieved, although no significant differences in OS and PFS were apparent among the treatment arms. The PC arm displayed the most favorable MST, MPFS, and hematologic/non- hematologic toxicities.
Conclusions: Weekly PC with CTR displayed similar efficacy, more favorable toxicity profiles compared to MVP with CTR. Therefore, weekly PC with CTR warrants use as the reference regimen in future WJOG studies.

9105 POSTER

Phase III study of concurrent chemoradiotherapy followed by surgery (S) vs. chemotherapy (C) followed by S for stage IIIA (pN2) non-small cell lung cancer (NSCLC): results of prematurely terminated trial, WJTOG9903

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Background: To ascertain whether the addition of concurrent preoperative radiotherapy to induction chemotherapy followed by surgery would improve survival outcome for patients (pts) with stage IIIA NSCLC with mediastinal lymph node metastases. Materials and
Methods: NSCLC pts with pathologically proven N2 disease were randomized either to receive induction chemotherapy (docetaxel 60 mg/m^2 and carboplatin AUC 5×2 cycles) plus concurrent radiation therapy (40 Gy) (CRS arm) or only induction chemotherapy (CS arm). Pts subsequently underwent pulmonary resection if the tumor was determined to be resectable. An original sample size of 180 was used to detect a 20% survival difference (alpha = 0.05) with a power of 0.8. The primary endpoint was overall survival.
Results: From Jan 2001 through Dec 2005, 60 pts were randomized. As accrual of the pts was slow, the study was prematurely terminated in Jan. 2006. Two pts assigned to the CRS arm were ineligible due to staging misconducts. Age ranged from 34 to 70 (median 57), and 66% of the pts were male. The two arms were well balanced in terms of age, gender, smoking status, T stage, and operative procedures. The percentage of squamous cell/adenocarcinoma differed slightly between the two arms (28%/55% for CS, 17%/72% for CRS). Induction therapy was well tolerated and there was no treatment-related death in either arm. Neutropenia (grade 3⩽) was presented by 75% and 89% (P = 0.16) and thrombocytopenia (grade 3⩽) by 0% and 7% of the pts in the CS and CRS arms, respectively. The objective response rate was 25% for both arms (CR/PR/SD/PD was 0%/25%/68%/7% for both groups). The period between induction therapy and surgery was short and shrinkage could not be confirmed for many pts, which resulted in a relatively low response rate and a high SD rate. Surgical resection was performed on 86% and 89% of the pts in the CS and CRS arms, respectively. Progression-free and overall survival were 29.9 months and 9.7 months in the CS arm, respectively, and 39.6 months and 12.4 months in the CRS arm, respectively. Hazard ratios for PFS and OS were 0.68 (95% CI: 0.38−1.21) and 0.77 (95% CI: 0.42−1.41) for CS and CRS. The 3-year survival rate was 39.3% and 51.7% in the CS and CRS arms, respectively. Downstaging was achieved for 21% in the CS arm and 40% in the CRS arm. Recurrent disease at either the hilar or mediastinal lymph node was observed in 58% and 20% in the CS and CRS arms, respectively.
Conclusions: Both the CS and CRS were well tolerated and safe. The addition of induction radiotherapy appeared to confer better local control without adding significant adverse events. The favorable local control, however, did not relate to a statistically significant survival difference probably due to the small number of patients.

9106 POSTER

The role of involved field radiotherapy as a salvage treatment for loco-regional recurrence after complete resection of NSCLC (non-small cell lung cancer)

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Background: In patients with local and/or regional recurrence following initial complete resection of NSCLC, radiation therapy would be an option for salvage treatment. This retrospective study investigated the treatment outcome of salvage radiation therapy in this clinical setting.
Material and Methods: Between 1995 and 2007, 67 patients had local and/or regional recurrences without distant metastasis after complete resection of NSCLC. Median time to recurrence from date of surgery was 10 months. Thirty one patients (46%) had local recurrences, 28 patients (42%) had regional recurrences and 8 patients (12%) had both of local and regional recurrence components. Salvage treatment was done with radiation therapy (79%) or concurrent chemo-radiation therapy (21%) at Samsung Medical Center. All patients received megavoltage radiation therapy with two-dimensional or three-dimensional conformal radiation therapy. Only the recurrence sites were included in the target volume. Elective nodal irradiation was not used. Median radiation dose was 70.2 Gy_{10} (Biologically Effective Dose, 40.8−85.8). Actuarial statistics of local control and survival were estimated using the Kaplan-Meier method.
Results: Median follow-up time from the start of radiation therapy was 15 months. More than half of the patients (66%) had radiographic tumor response after salvage treatment. In-field failure free survival (IFFFS) and loco-regional failure free survival (LRFFS) at 2 years were 50.5% and 32.7%, respectively. Distant metastasis free survival (DMFS) at 2 years was 59.5%. The median survival after radiation therapy was 18 months and 2-year overall survival (OS) was 47.5%, respectively. On multivariate analysis, radiographic tumor response to salvage treatment was predominant prognostic factor for IFFFS, LRFFS and OS. And other prognostic factors associated with failures were the time interval of postoperative recurrence, radiation dose, performance status and tumor histology ($p < 0.05$).
Conclusions: The current study showed superior survival to other published studies for salvage radiotherapy. Responders to salvage treatment showed improved survival. The involved field radiotherapy was effective as a salvage treatment for loco-regional recurrence after complete resection of NSCLC.

9107 POSTER

Dose escalation using Three-Dimensional Conformal Radiotherapy (3D-CRT) in concurrent setting with vinorelbine and a platinum compound, preceeded by induction chemotherapy and followed by consolidation chemotherapy in locally advanced Non-small cell Lung Cancer (NSCLC) - a preliminary report of a modified phase I-II study

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Background and Purpose: local and distant control are poor in locally advanced NSCLC. In order to improve them we aimed to evaluate the maximum-tolerated dose (MTD) and efficacy of dose escalation using 3D-CRT in concurrent setting with vinorelbine and a platinum compound, preceeded by induction chemotherapy (ChT) and followed by consolidation ChT with the same drugs, in locally advanced NSCLC.