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.

Patients and Methods: Forty-nine patients (pts) were included from 14.02.2005 to 23.07.2008: median age 56(41−73), M/F = 4/45, PS 1/2 = 32/17, stage IIIA/IIIB = 10/39, squamous cell cc 36, large cell cc 2, adenocc 7, "non-small" carcinoma 4. Treatment consisted of 2 cycles of induction ChT, followed by concurrent chemoradiotherapy and consolidation ChT. When given as induction or consolidation chemotherapy, drugs were given in full doses: Vrb (25 mg/sqm, d1, 8, q21) and Cis (100 mg/sqm, d1, q21), or Carbo (AUC 5, d1, q21), in concurrent setting, doses were reduced: Vrb 15 mg/sqm, d1, 8, q21, Cis 80 mg/sqm, d1, q21 or Carbo AUC 4, d1, q21. Pre and post-induction ChT computed tomography defined the target volumes for radiotherapy. Patients who fulfilled the dose-volume histogram constraints, underwent dose escalation of radiotherapy, in cohorts of 7 pts, if no more than two grade 3 or one grade 4 toxicities occurred, until MTD. If one grade 3 and one grade 4 toxicities occurred, further expansion continued by 5 more pts.
Results: Forty pts underwent dose escalation in five cohorts: 64 Gy, 66 Gy, 68 Gy, 70 Gy, 72 Gy, without dose-limiting toxicity. For each dose level up to 7 pts were enrolled, with further expansion by five pts at 70 Gy dose level. Acute toxicities, in the 49 evaluable pts, were preponderantly mild, of grade 1 and 2. Severe grade 3 and 4 toxicities were: esophagitis in 4(10%), pulmonary toxicity in 7(14%), neutropenia in 8(16%) pts. There were 43% CR, 41% PR, 8% SD, 8%PD. RR.was 84%. With a median follow-up of 15.9 months, the 1-year survival rate was 83% (95% CI: 70−91). The mS has not been reached yet. Locoregional progression-free survival at 1 year was 77% (95% CI: 61−88).
Conclusions: As no MTD was reached during dose escalation this strategy has to be continued. RR and Survival data were promissing.

9108 POSTER

Mature results of an individualized radiation dose prescription trial based on normal tissue constraints in stage I-III non-small cell lung cancer (NSCLC)(NCT00573040)

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Background: We previously showed in a modeling and a phase I trial that individualized radiation dose escalation based on normal tissue contraints would allow safe administration of high radiation doses (van Baardwijk, Int J Radiat Oncol Biol Phys 2008). Here, we report the mature results of a prospective trial applying this individualized maximal tolerable dose approach.
Materials and Methods: Patients with stage III or medically inoperable stage I-II NSCLC, WHO-PS 0−2, an FEV1 and DLCO $\geqslant$30% were included. Patients were irradiated using an individualized prescribed total tumor dose (TTD) using normal tissue dose constraints (mean lung dose, MLD 10 to 19 Gy dependent on FEV1/DLCO, maximal spinal cord dose 54 Gy) up to a TTD between 54 Gy and 79.2 Gy in 1.8 Gy fractions BID. No concurrent chemo-radiation was administered; stage III patients received induction chemotherapy. The primary tumor and the initially PET-positive mediastinal lymph nodes were irradiated. Primary endpoint was overall survival (OS), secondary endpoints progression free survival (PFS) and toxicity (CTCAE v3.0). Results are expressed as median $\pm$ SD.
Results: 166 patients were included (115 males, 51 females; age 69 $\pm$ 10.4 years). Stage distribution: I 29%, II 10%, IIIA 22%, IIIB 39%. The gross tumor volume (GTV) was 50.3 $\pm$ 194.8 cc. The TTD was 64.8$\pm$11.4 Gy (EQD2 corrected for proliferation 62.5$\pm$9.0 Gy) with an MLD of 14.8$\pm$4.6 Gy, given in 36$\pm$6.3 fractions in an overall treatment time of 25.5$\pm$5.8 days. With a median FU of 31.6 months, the median OS was 21.0 months with a 1-yr OS of 68.7% and a 2-yr OS of 45.6%. Median PFS was 21.6 months; 75 patients (45%) had a recurrence (33% isolated loco-regional failure (LRR), 51% M+, 16% LRR and M+ as first event). OS and PFS was higher in tumors with a GTVmedian (resp p = 0.022 and p = 0.09) and EQD2> median (resp p = 0.012 and p = 0.013) and showed a trend in favor of stage I-II vs stage III (resp p = 0.05 and 0.17) and resectable vs unresectable tumors (resp p = 0.09 and p = 0.06). Based on multivariable analysis a higher GTV significantly decreased OS and PFS (both p < 0.001), while a higher TTD and EQD2 increased PFS (resp p = 0.017 and 0.008). Both acute and late toxicity were mainly mild. Acute dysphagia grade 3 was observed in 5% and was transient (late grade 3: 0%), while acute dyspnea grade 3−4 was seen in 10% (resp 8% and 2%) and late grade 3−4 in 5% (resp 3% and 2%). No myelitis was observed.
Conclusions: Individualized prescribed radical radiotherapy based on normal tissue constraints shows survival rates similar to concurrent chemoradiation schedules with mild toxicity.

9109 POSTER

Concomitant chemo-radiation (CRT) of locally-advanced NSCLC using weekly docetaxel: toxicity profile

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Background: Concomitant chemo-radiation (CRT) has been shown to be superior to radiotherapy (RT) without chemotherapy (CT) and to neoadjuvant chemotherapy followed by RT (NeoCTRT). It is not known which chemo-regimen is the optimal regimen. We have used concomitant weekly docetaxel. In this study we report the toxicity experienced with this regimen compared with patients treated with RT without concurrent CT treated at our institution.
Methods and Material: Data from patient files of a) 113 patients treated with RT in planned doses of 60−66 Gy without CT, b) 183 patients treated with NeoCTRT 60−66 Gy, and c) 37 patients treated with neoadjuvant CT followed by concomitant weekly docetaxel 20 mg/m^2 to a radiation dose of 60 Gy. All RT was applied 1995−2008 as 3-D RT in 2 Gy/F without elective nodal irradiation.
Results: The median survival in RT alone, NeoCTRT and CRT was 16.3, 15.6, and 20.5 months. The1 year survival was 60%, 61%, and 79%. However, the differences were not statistically significant. No grade 3+ hematological toxicity was found in the CRT group. Dyspnoe grade 3+ was not significant more prevalent in the CRT group, while esophagitis grade 3+ was. In a logistic regression analyses using dyspnoe grade 3+ as endpoint, only PS 2+ was a statistically significant factor, while analyzing esophagitis grade 3+ CRT and stage were of significance.
Conclusion: Use of concurrent docetaxel with RT resulted in an increased frequency of esophagitis grade 3−4 while the risk of pneumonitis did not change significantly. Although a trend for better survival with CRT was demonstrated, this was not statistically significant.

	N	Dyspnoe g3+	Dysphagia g3+	Treatment related deaths
a) RT alone	113	17.6%	1.9%	8
b) Neoadjuvant CT	183	22.8%	0.6%	5
c) CRT	37	27.8%	8.3%	3
p value CRT vs no-CRT		ns	<0.02	ns

9110 POSTER

Temozolomide as concomitant treatment to radiotherapy in non-small cell lung cancer patients with brain metastasis: a Galician lung cancer group study

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Background: Phase II and phase III trials have shown higher response and survival to radiotherapy when it is administered with temozolomide, in patients with brain metastasis from various primary tumors. We conducted a study to evaluate radiological response, toxicity, neurological progression, and survival of patients with brain metastasis secondary to a non-small cell lung cancer undergoing radiotherapy with concomitant temozolomide as compassionate use.
Materials and Methods: We included 24 patients aged >18, with non-small cell lung cancer and brain metastasis, who had not received previous holocraneal radiotherapy. They were administered 30 Gy of radiotherapy, in daily fractions of 300 cGy for 10 days, together with 72 mg/m^2 of temozolomide daily for 14 days. Metastasis progression and survival were estimated using Kaplan-Meier curves.
Results: Patients were mostly men (79%), with a mean age of 56.7 years, and histological diagnostic of adenocarcinoma or epidermoid tumor