Results: Thirty-four patients were enrolled and treated. Patient characteristics were: ECOG performance status 0 in 24 patients, 1 in 10 patients, median age 63 years (range 39-78), and gender male 20, female 14. Dose-escalation was possible to erlotinib 150mg/day for both regimens during chemoradiotherapy. Grade 3/4 leukopenia and neutropenia were noted in both arms. No Grade 4 therapy-related non-hematologic toxicities were noted. For arm A, grade 3 toxicities during chemoradiotherapy were: esophagitis (3), vomiting (1), ototoxicity (1), diarrhea (2), dehydration (3), pneumonitis (1). For arm B, esophagitis (6) was the dominant grade 3 toxicity. Rash developed in 7 patients (21%). Twenty-seven patients (79%) completed their assigned regimen and were evaluable for response (Arm A - 12, Arm B - 15). Reasons for discontinuation were: adverse event (3), withdrawal of consent (2), non-compliance (1) and non-cancer related early death (1). Overall radiologic responses were (Arm A/B): Complete Response (0/1), Partial Response (8/9), Stable Disease (1/2) and Progressive Disease (3/3). Intention-to-treat 1- and 2- overall survivals were 47% and 21%, respectively. Overall and median survivals between the two arms were not significantly different. In the patients who developed a rash (7), 1 complete and 4 partial responses were observed. This group of patients had a trend towards improved overall survival (log-rank 0.07).

Conclusion: The addition of erlotinib to two standard chemoradiotherapy regimens is feasible and does not increase toxicities associated with chemoradiotherapy.

C3-02 Combined Modality Therapy in NSCLC II, Wed, 10:30 - 12:15

Randomized phase II trial using concomitant chemoradiation plus induction (I) or consolidation (C) chemotherapy (CT) for unresectable stage III non-small cell lung cancer (NSCLC) patients (p). Mature results of the SLCG 0008 study

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Background: Neither the optimal sequence of treatment nor the best combination CT is yet well-defined in p receiving concomitant therapy.

Methods: P with unresectable stage III NSCLC with IK > 70 and weight loss < 5% were initially randomized to sequential treatment (arm A), concurrent CT/TRT followed by consolidation (C) CT (arm B) or induction (I) CT followed by CT/TRT (arm C). Based on RTOG 9410 results, arm A was closed and the study continues with two concomitant arms (B, C). All p receive 2 cycles of Docetaxel (D) 40 mg/m^2 d1, 8 plus Gemcitabine (G) 1200 mg/m^2 d1, 8 as I or C therapy. Concomitant treatment includes D 20 mg/m^2 and carboplatin (Cb) AUC 2 weekly plus 60 Gy TRT.

Results: From May 01 to Jun 06, 151 p were included (A: 19, B: 66, C: 66). Due to the early closing of arm A, only data of evaluable arms B and C p are shown: toxicity 127 p (B: 63, C: 64) and response 110 p (B: 53, C: 57). All groups are well-matched for baseline disease characteristics. Toxicity grade 3-4 by CTC and RTOG criteria was: esophagitis 19.5% (arm B) and 14.2% (arm C); pneumonitis 8.8 % (arm B) and 10% (arm C). Neutropenia during I or C therapy: 22 % (B) and 6.2 % (C). Thrombocytopenia 8% (B) and 3% (C). Neutropenia during concomitant therapy: 6.3% (B) and 6% (C). No thrombocytopenia or severe anemia was found during CT/TRT. The reduction CT rate was superior in consolidation (35%) than in induction (15%) and in arm C during concomitant therapy (22.4% C, 6.5% B). Delay of CT dose was similar in B and C arms during I or C (22% B, 20% C) but superior in arm C during concurrent treatment (19.6% B, 30.6% C). The final response rates were 57% (B) and 56.9% (C). A trend for longer time to progression (TTP) was found (B: 7.6 months (m) and C: 9.2 m; p= 0.12) but with similar overall survival (B: 14.3 m and C: 14.7 m; p= 0.38).

Conclusions: Non-platinum CT plus concomitant chemoradiation offer similar response rate and a favorable hematological toxicity profile in unresectable stage III NSCLC p. No differences in OS but a trend for longer TTP in the arm C (I followed by concurrent approach) has been found. Final data are pending in order to select the best sequence for further studies.

C3-03 Combined Modality Therapy in NSCLC II, Wed, 10:30 - 12:15

Randomized, phase III Study of mitomycin/vindesine/cisplatin (MVP) versus weekly irinotecan/carboplatin (IC) or weekly paclitaxel/carboplatin (PC) with concurrent thoracic radiotherapy (TRT) for unresectable stage III non-small-cell lung cancer (NSCLC): WJTOG0105

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Background: Combined modality therapy using both chemotherapy and TRT is the standard treatment option in unrectable stage III NSCLC. Our group demonstrated a superiority of MVP with concurrent TRT over that with sequential TRT (Furuse et al. JCO 17, 1999). Currently, concurrent chemoradiotherapy plays a pivotal role in this patient population. However, the optimal chemotherapy regimen remains unclear. Weekly chemotherapy with concurrent TRT has acceptable toxicities and expected efficacy. We conducted a randomized phase III trial to compare the efficacy and toxicity of weekly chemotherapy with concurrent TRT against MVP by a non-inferiority design.

Methods: Patients (pts) were randomly assigned to 3 regimens; MVP: cisplatin (80 mg/m^2 on days 1, 29), vindesine (3 mg/m^2 on days 1, 8, 29, 36) and mitomycin (8 mg/m^2 on days 1, 29) with concurrent TRT (60 Gy). After then, pts received 2 courses of consolidation chemotherapy with MVP; IC: weekly irinotecan (20 mg/m^2)/carboplatin(AUC 2) for 6 weeks and TRT (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) and TRT (60 Gy) followed by 2 courses of paclitaxel (200 mg/m^2)/carboplatin (AUC 5). The primary endpoint was overall survival; secondary endpoints were time to progression, response, and toxicity.

Results: From Sep 2001 to Sep 2005, 456 pts were randomized; 429 pts had evaluated responses. Pretreatment characteristics were well-balanced between 3 arms (median age 63 years (30-74), PS0/1 41/55 %, Ad/Sq /others 43/ 45/12 %). The achievement rates of full treatment in MVP, IC and PC were 39.9, 29.7, and 49.3 %; those of full-dose TRT /

2 courses of consolidation chemotherapy were 81.1/41.3 %, 41.4/29.7 % and 59.7/50.0 %, respectively. Major toxicities were as follows; G4 neutropenia in MVP, IC, PC were 76.9, 13.1, 4.2 % (p<.001), and G3-4 non-hematological toxicities (decrease in PS, and febrile neutropenia) were 13.3, 6.2, 4.2 % (p=.01), and 29.4, 6.9, 4.9 % (p<.001), respectively. The overall response rates were 65.7 % (95%CI 57.9-73.5), 58.6 % (95%CI 50.5-66.1) and 62.9 % (95%CI 55.0-70.8), in MVP, IC and PC, respectively. Complete analysis will be fixed in Oct 2008.

Conclusions: Weekly PC with TRT appears good compliance with high achievement rate and MVP appears poor compliance with severe hematological and non-hematological toxicities.

C3-04 **Combined Modality Therapy in NSCLC II, Wed, 10:30 - 12:15**

Phase III study comparing a preoperative (PRE) and a perioperative (PERI) chemotherapy (CT) with two different CT regimens in resectable stage I-II non-small cell lung cancer (NSCLC): the IFCT 0002 protocol

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Background: The association of surgery and chemotherapy is now a standard in stages IA-III. The primary objective of this trial was to define the best timing of CT (all before surgery versus perioperative). Another objective was to compare two regimens, gemcitabine-cisplatin (**GP**) and paclitaxel-carboplatin (**TC**) (GP: Gemcitabine 1250 mg/m^2/d1, 8 and cisplatin 75 mg/m^2/d1 q3 wk; TC: Paclitaxel 200 mg/m^2/d1 and carboplatin AUC 6, q3 wk).

Methods: 528 stage I-II resectable NSCLC were randomized to 4 parallel arms: A: 2 GP + in responders, 2 GP, then surgery, B: 2 GP + surgery + in responders, 2 GP, C: 2 TC cycles + in responders, 2 TC then surgery, D: 2 TC + surgery + in responders, 2 TC. Quality of life was evaluated with the EORTC QLQ C30 - LC13 questionnaire at days 1, 42 and 147. Results were analyzed two by two: **PRE** (A+C) versus **PERI** (B+D) and **GP** (A+B) versus **TC** (C+D).

Results: 1) The addition of 2 additionnal preoperative CT cycles in responders did not influence tumor volume, intratumoral necrosis, pleural, venous or intrapulmonary lymphatic invasions. Pathological complete response rates were not statistically different (PRE: 6.3%, PERI: 7.6%, GP: 8.2%, TC: 5.6%). Objective responses were similar (PRE: 50.6%, PERI: 50.9%, GP: 52.2%, TC: 49.2%) 2) 30-day postoperative mortality were identical whether the patient received 2 or 4 cycles before surgery. Similarly, iatrogenic mortality at 6 months did not differ with the number of preoperative CT cycles (PRE:3%, PERI:3.21%). The main toxicities differs betweeen GP and TC only for G ≥2 neuropathy at 6 months (GP: 6.5%, TC: 24.4%, p<10^{-3}) and G ≥2 nausea (GP: 22.17%, TC: 4.22%, p<10^{-3}) .3) Proportions of pts receiving cycles 3 and 4 were higher when they were given before surgery than after surgery (PRE: 90.4%, PERI:75.2 %, p=.0011). Percentages of non operated pts after CT were identical in both groups (PRE: 4.5%, PERI: 4.3%). 4) There was no difference in Quality of Life between the 4 groups. At 6 months, decrease of health status, different functionning and symptoms did not differ between the 4 arms in responding pts (except for alopecia).

Conclusions: **1**- GP and TC were both effective and safe, although with different toxicity profiles. **2**- Results of pathological response suggested that 2 preoperative cycles might be as effective as 4 cycles. **3**- Dose intensity was higher when all chemotherapy was given before surgery compared to both before and after surgery. **4**- Quality of life decrease in the same proportions in each group within the 6 months after randomization.

C3-05 **Combined Modality Therapy in NSCLC II, Wed, 10:30 - 12:15**

Chemotherapy (CT) in addition to surgery or surgery plus radiotherapy (RT) in non-small cell lung cancer (NSCLC): Two meta-analyses using individual patient data (IPD) from randomised controlled trials (RCTs)

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Background: A previous IPD meta-analysis (BMJ 1995;311:899) that suggested cisplatin-based CT may have a role in the treatment of NSCLC has been updated. This includes RCTs, regimens and outcomes that were not available in 1995. The meta-analysis examines the role of CT in 7 treatment comparisons. Here we report on Comparison 1: surgery + CT versus surgery alone and Comparison 3: surgery + RT + CT versus surgery + RT.

Methods: RCTs were identified by comprehensive search strategies. Updated IPD were collected, checked and re-analysed. Results from RCTs were combined using the stratified (by trial) logrank test to calculate individual and pooled hazard ratios (HRs).

Results: Comparison 1

IPD were obtained from 30 RCTs and 8147 patients, representing 95% of all known randomised patients, adding 18 RCTs and 5835 patients to the 1995 analyses. Median follow-up is 5.3 years. 15 RCTs used a cisplatin combination without Tegafur/Tegafur+Uracil (UFT), 8 RCTs used Tegafur/UFT without cisplatin and 7 RCTs used Tegafur/UFT and cisplatin. There is a significant benefit of CT on survival (HR=0.86, 95% CI 0.81-0.93, p<0.0001), with an absolute benefit of 4% (from 60% to 64%) at 5 years. Results were similar for recurrence-free survival (HR=0.83, 95%CI 0.77-0.91, p<0.0001, 14 RCTs) local (HR=0.76, 95% CI 0.66-0.87, p<0.0001, 12 RCTs) and distant recurrence-free interval (HR=0.83, 95% CI 0.74-0.93, p=0.001, 12 RCTs).

Comparison 3

IPD were obtained from 11 RCTs and 2,626 patients (12% with incomplete resection), representing 86% of all known randomised patients, adding 5 RCTs and 1956 patients to the 1995 analysis. Median follow-up is 6.3 years. 10 RCTs used sequential radio-chemotherapy, 8 RCTs used cisplatin + vinca alkaloid/etoposide, 1 used cisplatin + Tegafur and 2 used other cisplatin regimens. There is a significant benefit of CT on overall survival (HR=0.88, 95% CI 0.80-0.96, p=0.0062), with an absolute benefit of 5% (from 29% to 34%) at 5 years. Results were similar for recurrence-free survival (HR=0.84, 0.77-0.93, p=0.0006,