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<0.001), and G3-4 non-hematological toxicities (decrease in PS, and febrile neutropenia) were 13.3, 6.2, 4.2 % (p<0.01), and 29.4, 6.9, 4.9 % (p<0.001), 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.

G3-04 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

Depierre, Alain1 Milleron, Bernard2 Quoix, Elisabeth1 Puyraveau, Marc1 Braun, Denis1 Breton, Jean-Luc1 Bigay-Game, Laurence1 Pujol, Jean-Louis1 Morin, Franck1 Westeel, Virginie1

1 Centre Hospitalier Universitaire de Besancon, Université de Franche-Comté, Besancon, France 2 Centre Hospitalier Universitaire Tenon, AP-HP, Paris, France 3 Hôpitaux Universitaires de Strasbourg, Strasbourg, France 4 Centre Hospitalier Universitaire de Besancon, Besançon, France 5 Centre Hospitalier de Briey, Briey, France 6 Centre hospitalier de Montbléjar-Belfort, Belfort, France 7 Centre Hospitalier Universitaire de Toulouse, Toulouse, France 8 Centre Hospitalier Universitaire de Montpellier, Montpellier, France 9 Intergroupe Francophone de Cancérologie Thoracique (IFCT), Paris, France

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/m² d1, 8 and cisplatin 75 mg/m²/d1 q3 wk; TC: Paclitaxel 200 mg/m²/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 additional 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 between GP and TC only for G2 neuropathy at 6 months (GP: 6.5%, TC: 24.4%, p<10⁻⁴) and G2 nausea (GP: 22.17%, TC: 4.22%, p<10⁻⁴). 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 functioning 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.

G3-05 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)

Burdett, Sarah1 Arriagada, Rodrigo2 Stewart, Lesley1 Pignon, Jean-Pierre1 Le Pechoux, Cecile2 Tierney, Jayne1 Tribodet, Helene1 On Behalf Of The Nsclc Collaborative Group, 1

1 Meta-analysis Group, MRC Clinical Trials Unit, London, UK 2 Radiation Oncology Department, Institut Gustave Roussy, Villejuif, France 3 Meta-analysis Unit, Institut Gustave Roussy, Villejuif, France

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, regimes 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 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<0.0001, 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,
7 RCTs), local (HR=0.79, 0.67-0.94, p=0.0075, 7 RCTs) and distant recurrence-free interval (HR=0.75, 0.66-0.87, p<0.0001, 7 RCTs).

In both comparisons the results of older and more recent RCTs were comparable. There was no clear evidence of a difference in effect of CT by type of CT, nor that any patient subgroup defined by age, sex or histology benefited more or less from CT. There was a suggestion of a trend in effect of CT by stage for comparison 1 (p=0.047).

Conclusion: Results from 41 RCTs and over 10,000 patients demonstrate conclusively a benefit of adjuvant CT in NSCLC, both in presence or absence of adjuvant radiotherapy. These results are consistent irrespective of the regimen used, the patient subgroup treated or the endpoint assessed, thus providing reliable estimates on which to base future policies and research.

Comparison 1: supported by the UK Medical Research Council
Comparison 3: Unrestricted grants from French PHRC, LNCC and Sanofi-Aventis

C-06 Combined Modality Therapy in NSCLC II, Wed, 10:30 - 12:15

ERCC1 expression as a predictive marker in stage IIIA, N2 positive non-small cell lung cancer patients treated with neoadjuvant concurrent chemoradiotherapy followed by surgery

Hwang, In Gyu1 Ahn, Myung-Ju2 Park, Byeong-Bae2 Park, Sarah Lee, Sang Cheol3 Ahn, Young Chan4 Kim, Kwhanmien5 Kim, Jhingook2 Han, Jung Ho2 Park, Keunchil Choi, Young Soo2 Shim, Young Mog2 Ahn, Jin Seok2

1 Kangwon National University Hospital, Chuncheon-si, Korea 2 Samsung Medical Center, Seoul, Korea

Background: Non-small cell lung cancer patients with excision repair cross-complementation group 1 (ERCC1) overexpression have lower response to cisplatin-based chemotherapy. Preliminary study also suggests that ERCC1 expression was associated with radioresistant in the lung cancer cells. Objective: Aim of our study was to evaluate the predictive value of ERCC1 expression in Stage IIIA, N2 positive non-small cell lung cancer (NSCLC) patients treated with neoadjuvant concurrent chemoradiotherapy (CCRT) followed by surgery.

Method: Seventy-one patients were enrolled between August 1997 and September 2003. We analyzed ERCC1 protein expression from 71 patients who underwent mediastinoscopic biopsy and proven N2 disease before CCRT by immunohistochemistry. All patients were treated with neoadjuvant CCRT followed by surgery. We evaluated the correlation of ERCC1 expression with various clinicopathological factors, including overall survival.

Result: Among 71 specimens, ERCC1 expression was positive in 32 (45.1%) and negative in 39 (54.9%) patients. At a median follow-up of 32.5 months (range: 3.8-99.5), the median disease-free and overall survival were 26.4 months (95% CI: 12.1-40.8) and 42.6 months (95% CI: 23.9-61.3), respectively in all patients. ERCC1-negative group, as compared with ERCC1-positive group, showed significantly prolonged disease free survival (DFS: 34.0 vs 15.8 months, p=0.014) and overall survival (OS: 65.1 vs 20.5 months, p=0.001). In multivariate analyses negative ERCC1 expression (p=0.001), age < 55 yrs at diagnosis (p=0.002) and achieving downstage after CCRT (p=0.003) were statistically significant independent good prognostic factors for survival.

Conclusion: These results suggested that stage IIIA, N2 positive NSCLC patients with ERCC1-negative tumors showed survival benefit from CCRT with cisplatin-containing regimen and ERCC1 expression would be a useful for predictive and prognostic marker.

C-07 Combined Modality Therapy in NSCLC II, Wed, 10:30 - 12:15

Preoperative chemoradiotherapy followed by surgery for stage IIIB non-small cell lung cancer (NSCLC). A multicenter phase II trial of the Swiss Group for Clinical Cancer Research (SAKK)

Stupp, Roger1 Kann, Roger2 Zouhair, Abderrahim1 Mayer, Michael3 Thierstein, Sandra4 Stahel, Rolf5 Betticher, Daniel6 Balmer Majno, Sabine5 Ris, Hans-Beat6 Pless, Miklos6

1 Multidisciplinary Oncology Center, University of Lausanne, Lausanne, Switzerland 2 Department of Radiotherapy, University of Basel, Basel, Switzerland 3 Department of Radiotherapy, University of Lausanne, Lausanne, Switzerland 4 SAKK Coordinating Center, Bern, Switzerland 5 Department of Oncology, University Hospital Zurich, Zurich, Switzerland 6 Department of Medical Oncology, University of Bern/Inselspital, Bern, Switzerland 7 Department of Radiation Oncology, University of Geneva, Geneva, Switzerland 8 Department of Thoracic Surgery, University of Lausanne, Lausanne, Switzerland 9 Department of Medical Oncology, University of Basel, Basel, Switzerland

Background: Outcome of patients (pts) with locally advanced NSCLC treated with radiotherapy- or chemoradiotherapy is poor. Tumor recurrence is observed both locally and distant metastatic sites. Advances in surgery allow considering resection in selected patients with locally advanced tumor stages, in particular after prior neoadjuvant therapy and tumor downstaging. Little prospective data are available on the feasibility, associated toxicity and outcome of such an approach.

Treatment and Methods: This phase II trial aims at evaluating feasibility and outcome of a tri-modality concept of neoadjuvant chemotherapy, radiotherapy (RT) followed by definitive surgery in operable, stage IIIB NSCLC pts. Primary endpoint is progression- and relapse-free survival at 1 year. Treatment consisted of 3 cycles of cisplatin (100 mg/m²) and docetaxel (85 mg/m²) followed by accelerated, concomitant boost RT (44 Gy/22 fx over 3 weeks) and surgery. Operable pts up to age 75 and a performance status of 0-1 with stage IIIB NSCLC (pleural effusion excluded) were eligible.

Results: Forty-five eligible pts (46 accrued) with a median age was 60 years (range 28-70) were treated between September 2001 and May 2006. All patients were staged with PET and/or mediastinoscopy. Tumor localization was right-sided in 28 pts and left-sided in 17 pts. Histology was squamous cell 42%, large cell 11%, adenoc-13% and undifferentiated carcinoma 33%. N3-disease was present in 29%, T4 stage in 78%. Chemotherapy (45 pts) administered as prescribed in >80% of cycles. Thirty-six pts (80%) received RT as planned, RT was omitted in 6 patients due to early progression, and in 3 patients due to complications during the chemotherapy. The objective response rate after chemotherapy was 53% (95% c.i. 38-68%), after additional RT 67% (51-80%).

Thirty-one pts (69%) underwent surgery, the median time from enrollment to surgery was 3.7 months (2.8 - 5.2). Seventeen patients underwent pneumonectomy, in the other patients bilobectomy or lobectomy was performed. A complete (RO) resection was achieved in 24 pts (75% of operated patients, 56% of all pts). Perioperative complications occurred in 13 pts, including 2 pts dying from ARDS and a cerebrovascular event, respectively. Seven pts required a second surgical intervention. The median duration of surgical hospitalization was 12 days (8-134).