1032 PUBLICATION

Neoadjuvant chemotherapy vs. radiotherapy alone for superior vena cava syndrome (SVCS) due to non-small cell lung cancer (NSCLC): Preliminary results of randomized phase II trial

J.R. Pereira[1,2], S.J. Martins[2], F.K. Ikari[1], S.M. Nikaedo[1], O. Gampel[1]. *[1]Arnaldo Vieira de Carvalho Cancer Institute, Pneumology, Sao Paulo; [2]Paulista Lung Cancer Treatment Group, Clinical Oncology, Sao Paulo, Brazil*

Background: Radiotherapy (RT) is the standard approach to SVCS due to NSCLC but promising results of cisplatin-based chemotherapy (CT) warrant their use as adjuncts in the management of such patients. Moreover, mass reduction induced by cytotoxic drugs could favours local-control of bronchogenic carcinoma by RT.

Methods: The trial design was as follows: arm A, RT alone with 60 Gy (stage III) or 45 Gy (stage IV) administered to the primary tumor, ipsilateral hilum, mediastinum, and supraclavicular areas; arm B, neoadjuvant QT (NCT) with up to 3 cycles of cisplatin (30 mg/m^2/d1–d3), epirubicin (90 mg/m^2/d1), and vinblastine (4 mg/m^2/d1 e d8), followed by the same RT plan and up to 3 additional CT cycles to responders. We intend to proceed partial analysis with 50 pts at all (end of first-stage of enrollment) but we antecipated it because of slow acrual.

Results: From 12/95 to 5/98 31 pts were randomized; 14 were assigned to RT and 17 to NCT. Both groups were balanced according to age, sex, Karnofsky performance status, histologic type, and stage. Treatment toxicity was more frequent in CT arm. With a median follow-up time of 16 weeks (range: 0–68), survival in arm A (12.4 wk) and in arm B (10.0 wk) was similar (logrank p = 0.62).

Conclusion: Additional follow-up time and recruitment is advisable but neoadjuvant CT seems not to confer survival advantage to NSCLC pts with SVCS.

1033 PUBLICATION

Docetaxel (D, Taxotere®) with concurrent radiation in locally advanced non-small cell lung cancer (NSCLC)

S. Aamdal[1], I. Hagen[2], I. Avril[3], G. Lauvvang[1], K. Øwre[1], R. Hatlevoll[1]. *The Norwegian Radium Hospital, Oslo; [2]Rhône-Poulenc Rorer, Østerås, Norway; [3]Rhône-Poulenc Rorer, Antony, France*

Concurrent radiation and chemotherapy play an important role in the treatment of unresectable NSCLC. We performed a phase I/II study of D, 1 h i.v. infusion given at days 1, 8, 22, 29 with concurrent radiotherapy of 2 Gy, 5 days/wk for 5 wks.

Results: 42 patients (pts) entered the study, M/F ratio: 27/15, median age: 59 (41–71), median WHO PS: 1 (0–1), squamous/adeno: 18/21. 12 pts entered the phase I, the MTD was reached at D 40 mg/m^2, oesophagitis was the dose limiting toxicity. 30 pts have been treated in the phase II study with D 30 mg/m^2 as recommended dose. Among the 26 pts evaluable for response, an ORR of 57.7% (95% CI: 38.7–76.7) was observed including 6 Complete Responses and 9 Partial Responses.

	N = 30	95% CI
Median Survival Time (months)	15.9	[7.7–24.8]
1 year survival (%)	51.2	[30.4–71.8]
Median TTP (months)	8.4	[4.7–+]

No hematological toxicity was observed. Non-hematological toxicities: grade 1–2, dysphagia 100% of patients, grade 3–4:1 infection, 1 stomatitis, 1 myocardial infarction (recovered), 1 dyspnea, 1 nausea and 1 neuropathy.

Conclusion: D 30 mg/m^2 weekly for 4 weeks and 50 Gy of concomittant radiotherapy is effective and well tolerated. A randomized comparative trial is warranted.

1034 PUBLICATION

A retrospective survey of anemia in lung cancer (LC) patients receiving cytotoxic chemotherapy (CT)

M. O'Brien[1], P. Barrett-Lee[2]. *[1]Royal Marsden Hospital, Surrey; [2]Velindre Hospital, Cardiff, United Kingdom*

For the UK Anaemia Study Group.

Purpose: Anemia frequently occurs in cancer patients (pts) and can produce symptoms (eg, breathlessness, lethargy) that adversely affect the pts' quality of life. As part of an effort to determine the incidence of anemia in LC pts and to examine some factors that influence anemia, quantitative data were obtained on CT, hemoglobin (Hb) levels, transfusion (TF) requirements, and other parameters in LC pts receiving cyclic platinum-containing (PL) or non-platinum-containing (NPL) CT.

Method: Relevant data from the hospital records of 511 pts treated with PL-CT and 321 treated with NPL-CT were reviewed retrospectively. The LC pts were a subgroup in a previously reported survey of 2715 cancer pts with selected tumor types treated at 28 centers in the UK. The study period was from January 1994 to October 1997. Anemia was defined as Hb less than 11 g/dL.

Results: The prevalence of anemia (expressed as the percentage of pt-courses during which anemia was experienced) increased progressively from baseline rates of 14% for the PLC-CT group and 9% for the NPL-CT group to 50% and 49% for the respective groups at the start of cycle 6 of CT. Corresponding mean Hb levels were 12.8 (range, 7.4–18) g/dL and 13.2 (9.3–17.5) g/dL at baseline versus 11.1 (7.9–13.9) g/dL and 11.3 (7.3–15.5) g/dL at the start of cycle 6. The percentages of pts in each cycle who received TFs increased progressively from baseline to cycle 6, ie, from 6% to 29% in the PL-CT group and from 13% to 28% in the NPL-CT group. Anemia and TFs were associated with the duration of CT.

Conclusion: The results of this survey indicated that anemia frequently develops in LC pts receiving PL- or NP-CT and with repeated courses of CT.

1035 PUBLICATION

The value of cytokeratines as preoperative predictors of survival in NSCLC stages I and II

G. Wagenius[1], M. Bergqvist[1], D. Brattström[1], P. Hesselius[1], K. Lamberg[2], B. Wiklund[3], Å Sillén[4], O. Brodin[1]. *University Hospital Uppsala, Dept of Oncology, Akademiska Sjukhuset, Sjukhusv. 10, S-75185 Uppsala, Sweden*

Lung cancer is the malignancy which causes the highest number of deaths in the world today. Even if the patients are considered operable, less than half of these patients will be cured. The aim of this study was to investigate if preoperative cytokeratin levels in serum of patients could be used as tumormarkers with impact on survival.

Materials and Methods: In this study of 44 patients with NSCLC stage I and II, bloodsamples were collected preoperatively during February 1994 and February 1996. The median age of the patients was 64.2 years (range 39–80 years). The following cytokeratin ELISA tests were used: CK8/1, CK8/2, CK8/3 (three different epitopes of CK8); CK8/18, CK18 and CK19. The cytokeratin levels were included, one by one, in different multivariate analyses together with the clinical parameters gender, smoking habits, performance status, weightloss, histopathology and grade. The cytokeratin levels were considered as continuous variables in these analyses.

Results: During the follow-up time of 30–54 months, 24 patients (54%) died. In the two multivariate analyses in which CK8/18 respective CK18 were included together with the clinical prameters, the cytokeratin tests were the only statistically significant variables, p = 0.033 and p = 0.041, respectively. The other cytokeratin tests were, in this study, not statistically significant associated to survival.

Conclusion: The cytokeratin tests för CK8/18 and CK18 were statistically significant correlated to survival and may therefore be suitable as preoperative markers for identifying high risk patients among operated patients with NSCLC stages I and II.

1036 PUBLICATION

Phase I–II trial of carboplatin (CBDCA) an vinorelbine (VNR) in stage IV non-small cell lung cancer (NSCLC). A pilot study of Spanish Lung Cancer Group

B. Massutí[1], I. Barneto[2], J.A. Meana[1], J. Herrero[1], C. Picó[1], E. Aranda[2], M.A. García[3], I. de la Gándara[3]. *[1]Hospital General Universitario Alicante, Medical Oncology, Alicante; [2]Hospital Universitario Córdoba, Medical Oncology, Alicante; [3]Pierre Fabre Ibérica, Barcelona, Spain*

Aims: Both CBDCA and VNR are active as single agent in advanced NSCLC. Their cytotoxicity is mediated by different mechanism. Subjective toxicity is low and common secondary effect is myelotoxicity. CBDCA-VNR combination may have interest in palliative setting. Best CBDCA dosing is defined using AUC. This association needs to be explored in Phase I–II trial with dose-increasing levels trying to define MTD.

Study Design: Assess toxicity profile and activity. Analysis of VNR dose intensity (DI). Inclusion criteria: Stage IV, chemo-naïvew p, PS 0–1, adequate bone marrow, hepatic and renal functions, informed consent. Symptomatic

CNS metastases were excluded. VNR administered on d1, 8, 15; CBDCA on d1 according Chatelut AUC. Cycles repeated every 28 d. 3 planned dose levels: 1st) VNR 25 mg/m^2 + CBDCA 6, 2nd) VNR 30 mg/m^2 + CBDCA 6, 3rd) VNR 30 mg/m^2 + CBDCA 7. 3–6 p treated at each level according observed toxicity. MTD: G3–4 toxicity CALGB criteria in 2/3 of p (excluding vomiting and alopecia). Weekly CBC. Response assessment after 2nd cycle.

Results: 14 p have been treated. Sex ratio M/F: 13/1. Median age: 58 y (43–69). PS 0/1: 2/12. 39 cycles have been delivered. Non-hematologic toxicity was mild: G3 mucositis in 2/14 p (14%), G2 peripheral neurotoxicity in 3/14 p (21%). Predominant toxicity was myelotoxicity with neutropenia G3 22/39 cycles (56%) and G4 (6/39 cycles (15%), but neutropenic fever occurred only in 4/14 p (28%) or 5/39 cycles (12%). Anemia G3–4 appeared in 1/14 p (7%). Thrombopenia G3 in 4/14 p (28%) and 10/39 cycles (26%). Only 1 p developed G4 thrombopenia. Median neutrophil count was 2100/mm3 d8, 980 d15 and 1310 d21. VNR needs to be reduced in 38/117 (32%) planned doses and omitted in 10 (8%). Delivered VNR DI has been 11 mg/m^2/w (planned 18.75 mg/m^2/w). At 1st level 3/6 evaluable p developed G3–4 toxicity. In 2nd level 4/6 evaluable p suffered G3–4 myelotoxicity. Overall response (PR) in 8/12 evaluable p (66%).

Conclusion: With this schedule CBDCA-VNR combination MTD was reached at 2nd level (VNR 30 mg/m^2 d1, 8, 15 + CBDCA AUC 6 d1 every 28 d). This combination is active but in this subset of p, toxicity seems too high to continue development of this schedule in Phase II trial.

1037 PUBLICATION

A phase II study of irinotecan and infusional cisplatin with recombinant human granulocyte colony-stimulating factor (rG-CSF) support for advanced non-small cell lung cancer (NSCLC)

K. Mori, S. Machida, T. Yoshida, M. Noda, K. Tominaga. *Department of Thoracic Diseases, Tochigi Cancer Center, 4-9-13, Younan, Utsunomiya, Tochigi 320-0834, Japan*

Purpose: We administered chemotherapy consisting of a combination of 5-day continuous infusion of cisplatin (20 mg/m^2/day) plus irinotecan (160 mg/m^2/day, as a bolus, on day 1) with rG-CSF support in previously untreated advanced NSCLC patients, and evaluated the effectiveness and safety of this therapy.

Material: Forty-one NSCLC patients were enrolled.

Results: Twenty-four patients achieved a partial response. The response rate was 58.5% (95% confidence interval, 42.2% to 74.8%), with a median response duration of 32.1 weeks. The median survival time was 44.8 weeks and the 1-year survival rate was 44%. A total of 100 courses of therapy were given. The major toxic effects were grade 3 or 4 diarrhea (23%), granulocytopenia (20%), thrombocytopenia (15%) and anemia (15%). There were no treatment-related deaths.

Conclusions: Combination chemotherapy of irinotecan plus infusional cisplatin with rG-CSF support was well tolerated and effective in patients with advanced NSCLC.

1038 PUBLICATION

Second-line CPT-11 may improve survival in small cell lung cancer

M. Nishio[1], A. Karato[1], S. Okumura[2], S. Tsuchiya[2], K. Nakagawa[2]. *[1]Cancer Institute Hospital, Div. of Internalmedicine, Tokyo; [2]Cancer Institute Hospital, Dept. of Chest surgery, Tokyo, Japan*

Background: We retrospectively analyze prgnosis factors of 134 patients with small cell lung cancer treated at our hospital between 1980 and 1997.

Methods: Case records that contained pretreatment parameters, treatmemet regimens, and survival information were collected. After univariate analysis, the multivariated evaluation of the impact of pretreatment parameters on survival was performed.

Results: Patients were divided into two groups according to initial treatment and second line treatmet: with/without platimun (n = 96/38), with/without CPT-11 (n = 36/82), respectively. The median survival times (MST) of all patients were 17.6 months for limited disease (LD) and 10.1 for extensive disease (ED). For the LD, the MST for those treated with platinum was 23.9 months, for those without platinum treatment was 8.3, showing a significant difference ($P < 0.01$). For ED, the MST of the group which received second-line CPT-11 was 14.7 months, for the group which did not receive CPT-11 was 7.8, showing a significant difference ($P < 0.05$).

Multivariate analysis was also performed to detect variables with significant influence on survival. According to this analysis, the significant prognostic variables were as follows; stage, performance status, lactate dehydrogenase, and second-line with CPT-11.

Conclusion: The improved survival time observed in small cell lung cancer patients treated with second line CPT-11 are notable, but because selection bias cannot be ruled out, the impact of second line CPT-11 on survival needs to be confirmed in prospective randomized trials.

1039 PUBLICATION

Vinorelbine (VNB) + ifosfamide (IFX) in non operable non small cell lung cancer (NSCLC). A phase II study

O. Rivero, M. Lozano, J. Polera, M. Matiewjuk, S. Bonicatto, C. Callejas, E. Torello, A. Zori Comba, D. Lewi, A. Schmilovich. *Grupo Oncológico Argentino Arcos 2626, C.P. (1428), Buenos Aires, Argentina*

Purpose: Though VNB plus Cisplatin (P) is the standard of care in non operable NSCLC, some patients (pts) have previous clinical conditions that increase neurotoxicity. An alternative is the replacement of P by IFX. VNB + IFX have been reported with response rate ranging 32–55%. A prospective multicentric confirmatory phase II trial have been performed at 11 institutions.

Methods: Between 1/96 and 9/98, 50 pts with non operable NSCLC were enrolled. Characteristics of population: median age 59 (r 36–65), male/female: 47/3. Number of metastatic sites: ≥3:18/50. Performance status ECOG 1–2 44/50. Stage IIIB/IV: 26/24. Schedule: VNB 30 mg/sqm IV day 1–8–15, IFX 2 g/sqm day 1 to 3, MESNA standard doses according IFX. Both drags each 28 days. Tumor assessment was done every 3 cycles and responses were confirmed 4 weeks later. Bronchoscopy was performed in complete responders.

Results: Response 43/50 are fully evaluable. CR: 1 PR: 13. Overall 33%. Toxicity (T): 221 cycles of VNB + IFX have been delivered [median 4 (r 2–10)]. T Grade$_{3-4}$ (WHO): leukopenia 13/50 trombocytopenia 1/50, alopecia 19/50, cardiotoxicity 1/50. There were no drug related deaths. Dose intensity: VNB 85% IFX 99%. Survival: median time to progression was: 5 months and median survival was: 9.5 months.

Conclusions: 1) VNB + IFX is an active regimen in non operable NSCLC. 2) T is manageable. 3) Replacement of P by IFX in VNB based chemotherapy seems to not affect survival.

1040 PUBLICATION

Carboplatin & gemcitabine in elderly patients with advanced non small cell lung cancer: Preliminary results

I. Maestu[1], M.D. Torregrosa[2], C. Llorca[3], C. Bosch[4], E. Noguerón[5], V. Giner[6], A. Oltra[1], C. Camps[5], A. Galan[6], D. Almenar[4]. *Oncology departments from Hospitals (H): [1]H. Virgen de los Lirios, Alcoy; [2]H. Luis Alcañiz, Játiva; [3]H. General, Elda; [4]H. Dr Peset Aleixandre & [5]H. General, Valencia; [6]H. General, Sagunto, Spain*

Background: Thirty percent of non small cell carcinomas are diagnosed in patients (pts) over 70 years old. Carboplatin (CBDCA) seems the best tolerated platin in elderly pts. Gemcitabine (GEM) shows activity across lung cancer and tolerance in elderly pts. The aim of the study was to evaluate survival, response and tolerability in pts ≥70 years or younger but frail pts with advanced non small cell carcinoma (ANSCLC) treated with CBDCA & GEM.

Patients and Methods: Between May/1998 and Feb/1999, out 28 untreated ANSCLC entered the study, 25 have been up to now analyzed. Median age was 74 (range 65–81). ECOG performance status (PS) was 0/3 pts; 1/16 and 2/6 pts. Stage was IIIA/2 pts; IIIB/12 pts and IV/11 pts. Treatment consisted of: GEM 1250 mg/m^2 (1000 mg/m^2 in a first step with 6 pts) on day 1 & 8 and CBDCA (AUC = 4) on day 1, every 21 days. PS and symptomatology (pain, dyspnea, hemoptysis, anorexia and asthenia with a easy visual scale) were valuated before and after 3th & 6th cycles.

Results: We have up to now noticed a good tolerability though recruitment and treatment of pts is still ongoing. WHO myelotoxicity in the 62 cycles administered: thrombocytopenia grade I–II/4 & grade III/1; neutropenia grade I–II/19 & grade III/3 and anemia grade I–II/6 & grade III/2. No other major toxicities and no treatment related deaths were reported. At the time of the analysis, only 13 pts were evaluable for response: 5 had partial response/38.4%, 5 stable disease/38.4% and 3 progressed/23%. Up to now improvement in symptoms has been: pain 5/7, dyspnea 5/8, hemoptisis 3/3, anorexia 4/5 and asthenia 6/9.

Conclusions: This schedule shows good tolerability and appears effective in elderly pts with ANSCLC. Definitive results about response, toxicity, symptomatology and survival will be presented.