1089 PUBLICATION

Chemotherapy with vinorelbine (navelbine: NVB) + carboplatin in advanced non-small cell lung cancer (NSCLC)

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Between Jan. 1995 and May 1996, 75 patients (pts) (56 and 19 from Vila Nova de Gaia Hospital and Coimbra Hospital respectively) with advanced NSCLC were treated with NVB (30 mg/m^2) on days 1 and 8 and Carboplatin (300 mg/m^2) on day 1, every 3 weeks (w). Pts were evaluated after 3 cycles and the treatment was continued for a further 3 cycles in case of tumor response.

Patient's Characteristics: sex F/M: 11/64, median age 59 y (27–73), PS 1: 75%, PS 2: 25%; histology: epidermoid: 52%; adenocarcinoma: 44%; others: 4%. Stage IIIA, IIIB and IV: 1.4%, 69.3%, 29.3% respectively.

Results: The overall response rate was 45.3% with a median duration of 31 w; the median overall survival was 34 w; the median survival of responders was 43.5 w.

Toxicity: 332 cycles were administred and the limiting toxicity was mainly myelosupression: WHO Grade (G) 3 anemia: 4%; G3–4 neutropenia: 23%; G3–4 thrombocytopenia: 4%; acceptable non haematological toxicity: local reaction: 20% and no significative alopecia were observed.

Conclusions: This study confirms that this combination achieves a high response rate, good median survival with acceptable tolerance. This combination should be recommended for the treatment of pts with NSCLC on an outpatient basis.

1090 PUBLICATION

Neoadjuvant chemotherapy with navelbine (NVB) plus cisplatin (C) in stage III_B in non-small cell lung cancer (NSCLC): A phase II trial

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NVB + C has already proven to be one of the most effective regimen in NSCLC in terms of survival for patients (pts) with unresectable disease (Le Chevalier, JCO, 1994). Based on these results we planned to treat pts with stage IIIB NSCLC ≤ 75 years (y) old, in order to determine response rate (RR) and operability of locally advanced disease.

Patient's Characteristics: between Apr. 1996 and Nov. 1996, 30 pts were accrued: 28 of them were evaluable (1 too early, 1 lost to follow-up), median PS 1; median age 61 y (38–75).

Treatment: NVB 30 mg/m^2 on D1 and D8 and C 120 mg/m^2 on D1 in a 21-day schedule for 3 cycles before restaging. G-CSF was permitted in case of severe neutropenia.

Results: A total of 81 cycles have been administered with mainly myelotoxicity: anemia grade (G) 3: 13%, leucopenia G3: 16%; no thrombocytopenia. Clinical toxicity was mainly nausea and vomiting G3 in 66%.

The efficacy after 3 cycles was: 16/28 (57%) partial response, 8 of them were resected, all responders were confirmed by an independent external expert group; 6/28 no change and 6/28 progressive disease.

Conclusions: This NVB + C as a neoadjuvant schema showed a high RR (57%), resulted in patients being able to proceed to resection and will be tried in a Phase III clinical study in order to study its possible effects on survival.

1091 PUBLICATION

Navelbine (NVB) and fractionated doses of cisplatin (CDDP) for the treatment of advanced non-small cell lung cancer (NSCLC)

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Aim: NVB + CDDP has already shown an increased survival rate in randomised trials, resulting in statistically superior survival compared with standard therapy. Based on these results, a phase II study was conducted to assess a new schedule of this combination: NVB 25 mg/m^2 on D1 & 5 and CDDP 20 mg/m^2 daily over 5 days (D1–5) every 21-days (maximum 6 cycles) to ease outpatients administration.

Results: Between 7/94 and 10/95, 50 patients (pts) were included (43 pts evaluable for response) median age 60 y (36–76); PS 0, 1, 2: 15%, 52%, 31% respectively; histology: squamous cell –40%, adenocarcinoma –42%; other 18%; stage IIIB–IV 15%, and 85% respectively. 184 courses were administered (median 4 range 1–8). WHO grade (G) 3–4 neutropenia –10%. The incidence of infection was very low (2% of courses: G 3). G 3 nausea/vomiting –25% (3% of cycles). G 3 constipation –2%; G 3–4 peripheral neuropathy –16% (4% G 4); G 3 alopecia –19%

Response: Overall response rate –42% (95% CI 30–54%) CR-5%; median survival: 8 months; pts alive at 1 year –33%; median TTP: 7 months.

Conclusion: These results confirm that NVB + CDDP has major antitumour activity even in poor prognosis NSCLC (85% with metastatic disease). NVB + fractionated doses of CDDP eases outpatient administration.

1092 PUBLICATION

Radioactive colloid ^{198}Au in combined modality treatment of lung cancer

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Purpose: To evaluate the remote results of colloid ^{198}Au administration in combined modality treatment of lung cancer patients.

Materials and Methods: From 1969 through 1988 ^{198}Au isotope was employed in combined modality therapy of 327 lung cancer patients treated in RIOMR. Of these patients, 160 received preoperative external irradiation of the primary lesion and regional metastasizing areas, the regimen being of enlarged and large dose fractionation (total target dose (TTD) – 20 and 30 Gy), and 55 patients were administered postoperative radiotherapy (conventional dose fractionation at a TTD of 36–40 Gy). 112 patients received radical treatment including surgery and intravenous administration of 1.5–1.9 GBq of ^{198}Au during days 1–5 after surgery.

Squamous-cell lung cancer was in 180 patients, adenocarcinoma – in 75, small-cell – in 41, large-cell – in 21.

Results: The analysis of remote results of radiosurgical treatment of squamous-cell lung cancer and adenocarcinoma demonstrated the efficacy of such a combination at stage I disease (T2NO): 57% of the patients survived for 5 years versus 33% after surgical treatment alone ($t = 2.0$).

In case of metastases in regional lymph nodes (N1,2), a clear superiority of combined three-component treatment including preoperative radiotherapy (TTD 30 Gy), radical surgery and intravenous administration of ^{198}Au in the early postoperative period was registered in patients with non-small-cell lung cancer. 5-year survival rate of squamous-cell lung cancer patients increased by 32% (from 10.3 to 42.1%, $p < 0.05$), of patients with lung adenocarcinoma – by 39% (from 8.1 to 48.0%, $p < 0.05$) compared to that of patients subjected to surgery alone.

1093 PUBLICATION

Oral etoposide plus cisplatin alternating with ifosfamide-epirubicin-vincristine in small cell lung cancer (SCLC)

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Methods: From April 1994 to November 1996, 35 patients (pt) with SCLC were treated. Stage: Limited Disease (LD) in 21 pt and Extensive Disease (ED) in 14 pt. Male 33, Female 2; Mean Age 59; Performance status: ECOG 1 in 22 pt and ECOG 2 in 13 pt. *Treatment* consisted of 6 courses of Alternating Chemotherapy as follows: IFOSFAMIDE 4 g/m2/iv/day 1 + EPIRUBICIN 75 mg/m2/iv/day 1 + VINCRISTINE 2 mg/iv/day 1; (Courses 1, 3 and 5) alternating with CISPLATIN 90 mg/m2/iv/day 1 + ETOPOSIDE 50 mg/m2/PO/day 1 to 14; (Courses 2, 4 and 6). Courses were administered every three weeks. Pt with LD received 45 Gy of chest irradiation during 2nd course of chemotherapy. The pts with LD and complete response, received prophylactic cranial irradiation.

Results: Overall Response (OR) in pt with LD was 81% (Complete Response (CR) in 52% and Partial Response (PR) in 29%.). In pt with ED, OR was 79% (CR 50% and PR 29%). Median Survival was 10 months in pt with ED and 13 months in LD group. **Toxicity:** The major toxicity was myellosuppression. WHO grade 3–4 neutropenia was present in 16% of the courses, and grade 3–4 thrombopenia in 4%. One toxic death due to febrile neutropenia was observed. Other toxicities were rare and when occurred had mild intensity (WHO grade 2 or below).

Conclusions: This regimen is highly active, and well tolerated, in both stages of SCLC. The study is ongoing.