434 PUBLICATION

A PHASE II STUDY OF CISPLATIN (CDDP) AND 96 HOURS CONTINUOUS INFUSION (CI) OF NAVELBINE® (NVB) IN PATIENTS (PTS) WITH ADVANCED SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK (HNT)

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Significant antitumor activity of weekly NVB administration has been previously reported in HNT. As NVB has a cycle specific activity, a CI schedule may increase its therapeutic index. We initiated a trial of CDDP (75 mg/m^2 on d. 1) and NVB (5 mg iv bolus on d. 1 immediately followed by 96 hrs CI of 4 mg/m^2/d) q. 3 weeks. 14 pts (median age 59 y) were included in a first part of the study testing tolerability and efficacy of this association. 12 pts had been previously treated with CT. The median number of courses per pt was 2 (range 1–6). Treatment was generally well tolerated. Hematologic toxicity consisted of neutropenia (gr 1–2: 5 pts, gr 3–4: 2 pts), anemia (gr 1–2: 6 pts, gr 3: 1 pt). No thrombopenia was observed. Non hematological toxicity consisted of nausea/vomiting (gr 1–2: 9 pts, gr 3–4: 1 pt), alopecia (gr 1–2: 3 pts), asthenia (gr 1–2: 2 pts), neuropathy (gr 1: 1 pt), creatinine increase (gr 1–2: 3 pts). One pt developed angina pectoris during the 4th cycle. Antitumor activity was documented in 4 pts (1 CR, 3 PR), giving a 29% response rate. Tumor progression was observed in 9 pts, and disease stabilisation in 1 pt. Present data suggest that CDDP-NVB combination has significant activity in pts with recurrent and/or metastatic HNT. Since toxicity was limited, the study is ongoing with a higher NVB dose (6 mg iv bolus on d. 1 immediately followed by 96 hours CI of NVB 6 mg/m^2/day).

435 PUBLICATION

NEOADJUVANT "BEC" AND "EC" CHEMOTHERAPY (CT) FOR LOCOREGIONALLY ADVANCED UNDIFFERENTIATED NASOPHARYNGEAL CARCINOMA (UCNI)

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From 11/90 to 12/94, 60 UCNT patients (p) (T3–4 and/or N2–3) received 3 courses of either BEC (Bleomycin 15 mg d1 push + 12 mg/m^2 c.i. d1–5, Epirubicin 70 mg/m^2 d1, CDDP 100 mg/m^2 d1—E Cvitkovic, JP Armand—ASCO89), or EC (Epirubicin 60 mg/m^2 d1 and 8, CDDP 100 mg/m^2 d1), followed by RT (64–70 Gy/ 7 wks) on the nasopharyngeal and laterocervical areas. *P. characteristics:* 47 (68%) men; age 41 (10–64); performance status (PS): 0;1–58p 2; 3–10p. TNM distribution: T4–32p (46%), N3–23p (33%). *Activity:* 62/69p (=90%, CI = 83–97%) had an objective response (OR) with 25/69CR (=36%). The OR and CR rate were not influenced by the CT protocol (BEC vs EC: 92% vs 87% OR; 41% vs 30% CR, P = NS), T category (T4 vs others: 34 vs 38% CR) or N category (N3 vs others: 30 vs 39% CR, p = NS). At the end of RT, there were 77% CR (CI: 65–88%) and 94% OR. *Toxicity* was moderate and there were no toxic deaths. We noted gr 4 neutropenia in 6%, anemia in 8%, and vomiting in 12% of cycles. EC resulted in more gr 2–3 mucositis than BEC (19% vs 7%) and 2% gr1 cardiac toxicity. *Compliance:* 7 p refused trt after 2 cycles because of mucositis/vomiting. *Survival:* Medium follow-up is 16 m (2+, 48+). 2 yrs actuarial S is 77%, with 82% for CR to CT vs 73% for the others (p = NS). There was a significant difference in S for p with PS 2:3 (median—13 m) vs PS 0;1 (median not reached), and no differences in respect with sex, T or N categories. As of Febr. 95, 35 p (51%) are CR (3+, 48+ m), 14 PR (2+, 32+ m), and 20 p have failed (5 initially refractory, 15 relapsed after a median OR of 12 m (4, 36)). 11 of the failing p have died: 2 T+, 3 T+ N+ M+, 3 M+. Bone was the main site of metastates (3/6p). *Conclusion:* a) Our results (92% OR, 41% CR with BEC and 87% OR, 30% CR with EC, leading to 94% OR and 77% CR after RT), confirm both neoadjuvant regimens as highly active in UCNT. b) The benefit in terms of survival needs to be defined within prospective randomized trails.

436 PUBLICATION

HIGH-DOSE CARBOPLATIN SUPERSELECTIVE INTRAARTERIAL CHEMOTHERAPY (CT) ± RADIOTHERAPY (RT) IN ADVANCED HEAD AND NECK CANCER: A PHASE I STUDY

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Advances in vascular radiology techniques for superselective transfemoral arterial infusion prompted us to evaluate the effects of high-dose regional carboplatin infusion as neoadjuvant CT for patients with advanced head and neck squamous cell carcinoma. Twenty untreated patients received every 2 weeks three infusions of carboplatin (300–350 mg/m^2) by this method and were subsequently treated by RT (16 pts) and/or surgery (4 pts). All the infusions were performed without any local or general immediate complications. Treatment was well tolerated, with moderate local toxicity non >grade I WHO (stomatitis, dermatitis and alopecia) and minimal myelosupporession non >grade II haematological toxicity. Neoadjuvant CT by superselective rapid infusion of high-dose carboplatin is feasible, relatively nontoxic, effective technique and may have important applications in multimodality treatment of untreated patients with advanced head and neck cancer. The total response rate (CR plus PR) after CT was 94% for the primary tumor and 50% for neck metastases. Thus, further investigations are warranted with specific clinical endpoints (i.e. tumor responses, patients survival and possible enhancement of late toxicity by the combination of CT and RT).

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437 PUBLICATION

PROSTHETIC VOCAL REHABILITATION AFTER TOTAL LARYNGECTOMY. EXPERIENCE ABOUT 185 CASES FROM DECEMBER 1987 TO JUNE 1994

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From December 1987 to June 1994 185 patients have received a vocal rehabilitation by voice prosthesis after a total laryngectomy, whatever the size of the mucous resection may be. Results seem to be far satisfying rather than with the oro-esophageal voice: 79 per cent of the patients have an usable voice as soon as the cicatrization is ended. However only 59 per cent of the patients use commonly their voice. The main complication is due to the fistular enlarging, which can be simply treated in the majority of cases. The prosthesis requires a peculiar maintenance. The reconstruction with a muscolo-cutaneous flap improves quality of voice result.

438 PUBLICATION

M-VAC CHEMOTHERAPY AND GM-CSF IN ADVANCED, RECURRENT AND/OR METASTATIC SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK (SCCHN)

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We evaluated the tolerability and efficacy of M-VAC with GM-CSF in 33 patients (pts) with advanced SCCHN. All pts were males with median age (range): 47 (40–67) years and PS (WHO): 1 (0–2). All pts were chemotherapy naive and 15 pts pretreated by surgery and/or radiotherapy. Treatment: CDDP 70 mg/m^2 and DXR 30 mg/m^2 i.v. on day (D) 2, MTX 30 mg/m^2 and VLB 3 mg/m^2 i.v. on D1, 15, 22, GM-CSF: 5 μg/kg/D, s.c. on D3–14. Cycles (cy) were repeated every 4 weeks. 66 cy were administered, median (range): 2 (1–3). *Efficacy:* 2 CR and 14 PR in 31 evaluable pts were observed for an overall RR of 52% (95% CI: 42–62). The duration of RC was 3 and 2 + months; 14 pts with PR were treated by radiotherapy (9 pts) or other chemotherapy (5 pts). *Toxicity:* Anemia, neutropenia and thrombocytopenia (WHO gr $\geqslant$ 3) occurred in 3, 8 and 3 pts resp. Nausea/vomiting (WHO gr $\leqslant$ 3) were observed in 9 pts, alopecia in 20 pts and skin rash due to GM-CSF (WHO gr1) in 4 pts. There were no treatment-related deaths. *Conclusion:* M-VAC with GM-CSF had a good tolerability and efficacy in chemotherapy naive pts with advanced SCCHN.