NSCLC. Blood was sampled regularly, and E and P separated immediately using the MESED instrument (Fabre, Kelmis, Belgium). MMC concentrations were determined using HPLC. Mean P C_0 was 591 ng/ml (SD 40) and mean P $t_{1/2}$ 50 minutes (SD 8). In most samples, MMC levels in E were less than those in P, but concentration time profiles were of a similar shape (E/P ratio 0.77 [SD 0.25]), until approx. 80 minutes after injection, when MMC was no longer detected in E, despite significant quantities in P. This may reflect loss from E, by redistribution, or transformation within E; investigation of this phenomenon is continuing.

† *Clin Biochem*; 27:195–196 (1994).

970 PUBLICATION

AN EVALUATION OF THE NEUROTOXICITY OF A PHASE I DOSE FINDING STUDY OF DOCETAXEL (D) IN COMBINATION WITH VINORELBIN (V)

J.P. Louboutin[1], *C. Maugard-Louboutin*[1], *G. Perrocheau*[2], *M. Gentin*[1], *V. Delecroix*[2], *N. Azli*[3], *P. Fumoleau*[2]

[1]*Centre URA CNRS 1340-Hôpital GR Laënnec, 44305 Nantes, France*

[2]*CRLCC Nantes-Atlantique-ICERC-Site Hospitalier Nord, 44805 Saint, Herblain, France*

[3]*Rhône-Poulenc Rorer, Antony, France*

D, belonging to the taxoid class of anticancer agents, enhances microtubule assembly and inhibits the depolymerization of tubulin. The cytotoxic activity of V is through inhibition of the microtubule assembly. D and V have both shown clinical activity in advanced breast cancer as single agent. Additionally, therapeutic synergism has been observed in preclinical studies when the two drugs are combined simultaneously. Thus, a phase I study of a combination of these 2 drugs commenced in patients with metastatic breast cancer. However, as D. and V. induce mild neurotoxicity, neurological effects of this combination were evaluated. Neurological function at baseline, during (every 2 cycles and at the end of the study), and following treatment, in 13 metastatic breast cancer patients treated with docetaxel (60–85 mg/m^2) and vinorelbine (20–22.5 mg/m^2—D1–D5), none of them treated with vinca-alcaloids and/or CDDP, were prospectively evaluated. Deep tendon reflexes decrease was the most frequent abnormal finding, which occurred in 10 patients (77%). Mild, temporary and reversible grade 1 asymptomatic paresthesia were seen in 4 patients (31%). Pin sensibility, vibration sensation and muscular strength were always normal. Median and peroneal motor nerve conduction velocities, as well as median sensitive nerve conduction velocity, remained in the normal ranges. Peripheral neurotoxicity induced by the docetaxel-vinorelbine combination therapy appears to be mild (grade 1 according to NCI toxicity criteria).

971 PUBLICATION

PRELIMINARY RESULTS OF A RANDOMIZED STUDY OF 1 VS 2 910 MG/M/SQM DOSES OF AMIFOSTINE IN HIGH-RDI CYCLOPHOSPHAMIDE (CPM)-EPIRUBICIN (EDOX) IN PATIENTS WITH HIGH RISK BREAST CARCINOMA

C. Cuvier, A. Ardavanis, J.M. Extra, M. Espie, W. Oster, M. Marty

Department of Medical Oncology, St Louis Hosp., Paris & U.S Bioscience, U.K.

In an effort to reduce hematological toxicity of a dose-intensive regimen (CPM 1200 mg/m^2 & EDOX 75 mg/m^2 every 14 days) given for 6 courses in patients with metastatic, inflammatory or N + > 5, patients received in a randomized parallel design 1 dose (arm A) (910 mg/m^2) or 2 doses (arm B) 4 hours apart. This design aimed at giving the 2nd dose at the expected Cmax of phosphoramide mustard. This exploratory analysis concerns 6 pts and 30 cycles in each arm. No growth factor was allowed. Efficacy was estimated through blood-cell counts (G/l) at d14 (mean), as no recovery period was considered.

	WBC						PLT					
	C1	C2	C3	C4	C5	C6	C1	C2	C3	C4	C5	C6
A	1.2	2.1	1.5	2.4	.9	NA	293	262	384	155	154	NA
B	1.6	1.2	1.9	.8	.9	NA	327	238	222	76	300	NA

While incidence of emesis was similar, hypotension was observed in 15/30 cycles in arm B as compared to 0/30 in arm A.

This preliminary analysis does not suggest increased efficacy of 2 doses of amifostine compared to 1 in patients receiving dose intensive CPM-EDOX while amifostine induced hypotension was observed more often in patients scheduled to receive 2 protective doses.

972 PUBLICATION

PHASE I STUDY OF CYCLOPHOSPHAMIDE AND DOCETAXEL (TAXOTERE®) IN SOLID TUMORS

V. Valero, L. Esparza, S. Patel, R. Theriault, R. Pazdur, J.P. Ayoub, M. Qasim, E. Rodriguez, R. Bellet, G. Hortobagyi

U.T.M.D. Anderson Cancer Center, Houston, TX, U.S.A. and Rhone-Poulenc Rorer, Collegeville, PA, U.S.A.

Twelve patients (pts) received cyclophosphamide (CTX) as a 1 hr infusion followed by Taxotere (TXT) as a 1 hr infusion every 21 days. Dose levels were 0: CTX/TXT 600/60 mg/m^2 (6 pts), 1: CTX/TXT 600/75 mg/m^2 (3 pts), 2: CTX/TXT 700/75 mg/m^2 (3 pts). Pts were premedicated with dexamethasone 8 mg B.I.D. at day 0–4 and oral ondansetron. *Pts characteristics:* tumor types: breast 4, sarcoma 4, colon 3, melanoma 1; med age, 58 yrs (31–72); med Zubrod PS, 1 (0–2); med no. sites 3 (1–5); med no. of prior CT was 1 (0–4). *Response:* 2 PR (breast cancer), 2 SD (breast/sarcoma). *Toxicity:* To date, 9 pts received 18 evaluable courses. Med nadir granulocytes ($\times 10^3$)/d1: 0.7 (med duration 7 days). Neutropenic fever was seen in 3 pts in 3 cycles. *Other GRADE II tox (no. of pts, no. of cycles):* fatigue 4 (9), myalgias 1 (1), nausea 3 (3), diarrhea 2 (2), stomatitis 2 (2), skin (1). *Conclusion:* The results of this ongoing trial showed that the combination of CTX/TXT is well tolerated and with no unexpected toxicities.