

Anti-CEA mouse MoAb, produced by JP Mach (Ludwig Inst., Lausanne, Switzerland) were injected IV as 500 µg of intact immunoglobulins, ¹³¹I labeled according to the iodogen technique to a specific activity of 5 to 10 µCi/µg. Mouse MoAb 19-9 and 17-1-A provided by H. Koprowski (Wistar Inst., Philadelphia, USA) labeled with ¹³¹I to a specific activity of 2 µCi/µg were injected IV as 1 mg of F(ab')₂ fragments. A mixture of 2 out of the three antibodies mentioned above was infused 22 out of 27 times, and scanning was performed up to 7 days after injection. Final diagnosis was obtained by pathology (14/27) or on clinical evolution (13/27). Overall specificity of the method was 100% (10/10) with no false positive results, sensitivity yielded to 59% (10/17) with 7 false negative results and accuracy happened to be 74% (20/27). According to our limited experience, three major indications could be selected prospectively: 1) Isolated elevation of serum tumor markers, 2) Non convincing evidence on conventional methods, 3) Staging of GI carcinoma prior to surgery. In most cases, failure of the method was observed in peritoneal carcinomatosis (4/7) or when recurrence occurred behind the bladder, making image analysis difficult due to urinary clearance of ¹³¹I. Improvement of the technique could be expected from more appropriated radiolabel than Iodine and possibly from single photon emission tomography along with the association of several MoAb sharing similar tumor cell specificity but reacting with distinct epitopes.

12.

ESTIMATION OF CIRCULATING IMMUNE COMPLEXES IN CANCER PATIENTS: SENSE OR NONSENSE? M. Bertschmann, J.P. Späth, U.E. Nydegger and E.F. Lüscher, Theodor Kocher Institute, University of Berne and Blood Transfusion Service, Swiss Red Cross, Central Laboratory, CH-3000 Bern 9, Switzerland.

Since the detection of blocking factors in serum of cancer patients and the identification of circulating tumor-antigen-antibody complexes (CIC) as the active entities a large body of data has accumulated from experimental animal models and cancer patients in the hope to use levels of CIC as parameters for diagnosis and/or prognosis of malignancies. In the present experiments CIC were sequentially determined in serum samples from DBA/2 mice bearing histocompatible P-815 mastocytomas. 125I-C1q binding assays and Raji cell binding assays were used according to standard procedures. The tumor model is characterized by a transient phase of spontaneous regression correlated with proliferation and differentiation of cytotoxic T cells. However, regression normally changes to progression and not only T- but also B cell proliferation is observed. Since no functional correlate of B cell stimulation in the form of circulating or tumor cell bound antibody could be detected so far, tests were performed for detecting antibody in the form of CIC and for correlating CIC levels with tumor development. Despite the wide variation in tumor development elevated levels of CIC were not detected, neither in the 125I-C1q binding nor in the Raji cell binding assay. Reference complexes formed between soluble tumor cell membrane proteins and allo-antibody, however, were easily detected. These negative results are in accordance with recent negative results in mammary cancer patients (Krieger et al., Int. J. Cancer 31, 207, 1983). They support a more critical evaluation of the usefulness of CIC determination for diagnosis and/or prognosis of malignancies.

13.

MONOCLONAL ANTIBODIES AGAINST HUMAN LUNG CARCINOMAS. R. Stahel and S. Bernal, Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA 02115, U.S.A.

Mouse monoclonal antibodies were generated against cell lines of human lung adenocarcinoma (SLC40) and small cell carcinoma (OHI). SLC40 grows as cellular aggregates in suspension culture and forms glandular structures in nude mice. The antibodies LAM2 and LAM3 are strongly reactive with the surface membrane of SLC40, as demonstrated by indirect immunofluorescence and radioimmunoassay. LAM3 is also reactive with several lung adenocarcinomas growing as adherent or suspension cells in culture, but not with other adenocarcinomas, including colon and pancreas. LAM3 may be helpful in distinguishing adenocarcinomas of the lung from other carcinomas. In contrast, LAM2 is reactive with several carcinomas that grow as suspension cells in culture, including small cell carcinomas, lung adenocarcinomas, mesothelioma and seminoma. Little or no reactivity was observed with 18 carcinoma cell lines that grow adherent to the culture dish. Thus, LAM2 recognizes a surface membrane antigen that is present primarily in carcinoma cells that lack anchorage dependence in vitro. Model systems are being used to evaluate the correlation between LAM2 reactivity and metastatic potential in vivo. The antibody SMI1 is strongly reactive with cell lines and tissues from small cell carcinoma of the lung but not with most other cancer cells and normal tissues. We have found SMI1 to be useful in identifying small cell carcinoma in tissue sections and in bone marrow aspirates. Since SMI1 is highly cytotoxic to small cell carcinoma in the presence of complement, it may also be useful for therapy. SMI1, LAM2 and LAM3 are unreactive with normal bronchus, normal bone

marrow cells and leukemic cells. These antibodies may be useful in studies of differentiation and biologic behavior of lung cancer cells; they could also be important in the diagnosis, staging and treatment of lung cancers.

14.

COMBINATION CHEMOTHERAPY WITH CISPLATIN, ADRIAMYCIN, ETOPOSIDE AND CYCLOPHOSPHAMIDE FOR SMALL CELL CARCINOMA OF THE LUNG (SCLC). J.P. Dumont, J. Klasterky, J.P. Sculier, D. Bequart, G. Vandermoten, P. Rocmans, P. Libert, P. Ravez, J. Michel, E. Longueval, A. Fiesale, P. Mommen, Institut Jules Bordet, Université Libre de Bruxelles, Bruxelles, Belgique

Combinations of cisplatin (C), adriamycin (A) and etoposide (Vepesid - V) (Cancer 50, 652, 1982) or A, V and cyclophosphamide (Endoxan - E) (Cancer Treat. Rep. 66, 221, 1982) are effective in the management of SCLC. We evaluate a 4-drug combination consisting of C (60mg/m²), A (45mg/m²), V (80 mg/m² di,2,3) and E (1g/m²) every 3 to 4 weeks in patients with proven SCLC; 40 patients were evaluated so far after 3 courses of therapy. The median age was 54 years and the initial median performance status was 75 (Karnofsky's scale):

| | Limited disease | Extensive disease |
|-------------------------|-----------------|-------------------|
| Evaluable patients | 24 | 16 |
| Complete remission (CR) | 6 (25%) | 0 (0%) |
| Partial remission (PR) | 15 (62%) | 9 (56%) |
| CR + PR | 21 (87%) | 9 (56%) |

Toxicity was moderate: leucopenia grade IV was observed in 11 (27%) and grade III in 10 (25%); serious (grade III and IV) extra-hematologic toxicity (nausea, vomiting, alopecia, diarrhea, stomatitis, infection and metabolic abnormalities) was rare, except for alopecia.

Treatment was continued for a total of 10 courses or until progression. Patients with LD and PR received thoracic irradiation (5000r) and those with CR prophylactic brain irradiation. Six months after therapy 5/6 patients with CR after 3 courses of CAVE are still alive without evidence of progressive disease; the corresponding figure for PR's is 14/24.

Although final conclusions can only be drawn after evaluation of more patients and longer follow up, it appears that CAVE does not result in an increase rate of response as compared to CAV or AVE.

15.

AUTOLOGOUS MARROW TRANSPLANTATION (AUTO M.T.) IN ACUTE LEUKEMIAS: MARSEILLE EXPERIENCE IN 28 PATIENTS (PTS). D. Mazoni, B. Mascaret, J.A. Gastaut, G. Sebahoun, N. Tubiana, G. Novakovich and Y. Carcassonne, Marrow Transplant Unit and Blood Bank, Institut Paoli-Calmettes (IPC) Marseille 13273 - France -

18 pts received auto MT after high dose Melphalan (HDM 140mg/m² I.V. n=17 pts) or BACT (n=1 pt): all these pts were in relapse and had measurable disease. In AML 10/12 achieved complete remission (CR), in ALL 2/3 achieved CR, in blast crisis of CML 2/2 achieved PR. The pt receiving BACT for ALL in relapse achieved CR. Thus high dose chemotherapy is able to induce new CR or PR in high proportion of pts with leukemia in relapse (15/18 evidence of response - 83%, 13/18 CR-72%). 10 pts received auto MT after HDM (8) or BACT (n=2) as a consolidation of previous remission and are not evaluable for response. In 13 pts no attempt was done to purge marrow, and no maintenance therapy was done after the graft: all relapsed except one with AML in relapse who is in second non maintained CR 17 mths+. 8 pts had new marrow aspiration, received second course of HDM and auto MT as a consolidation and in vivo treatment of their marrow: 2 pts died in CR, 2 relapsed, 4 are in continuous CR 29 mths+, 28 mths+, 15 mths+, 9 mths+ after the first auto MT, 4 pts with ALL received I.V. Methotrexate (MTX) after auto MT (Seattle protocol for allogeneic MT): one died from pneumonia, 3 are in continuous CR 4 mths+, 3 mths+, 2 mths+. 3 pts received BACT and auto MT after complement + CALLA treatment of their marrow: all engrafted, one relapsed at 4 mths and is alive 9 mths+, one died from pneumonia within one mth, one is alive in continuous CR 3 mths+. High dose chemotherapy followed by auto MT is an efficient treatment for leukemic pts. Marrow contamination of the graft has to be considered as a limiting factor; marrow contamination might be treated by immunological, pharmacological means...

16.

TOTAL BODY IRRADIATION (TBI) AND CYCLOPHOSPHAMIDE (Cy) AS A CONDITIONING REGIMEN OF ALLOGENEIC MARROW TRANSPLANTATION (ALLO M.T.): INVESTIGATION OF SINGLE DOSE VERSUS FRACTIONATED REGIMEN OF TBI. D. Maraninchi, D. Baume, J.A. Gastaut, B. Mascaret, J.P. Guillet, R. Amalric and Y. Carcassonne, Marrow Transplant Unit, Institut Paoli-Calmettes (IPC) Marseille 13273 - France -

We investigated in 33 patients (pts) with hematologic malignancies different TBI regimen as a preparation of allo M.T.. 5 pts received 1000 rads TBI (lungshielding 800). 4 pts received 200 rads per day for 5 days. 11 pts received 220 rads per day for 5 days, 7 pts received 240 per day for 5 days. Irradiation source was linear accelerator saturne. Lungshielding

was done in each pt (lung dose ≤ 800 rads). Dose rate was during each irradiation ≤ 4 rads/mm. Immediate tolerance to TBI was better in pts receiving fractionated TBI rather than one set TBI. 3 pts out of 5 receiving one set TBI died from interstitial pneumonia. One pt out of 28 died from pneumonia in pts receiving fractionated regimen. No relapse was observed in pts grafted in complete remission. Aplasia was slightly longer in pts receiving fractionated TBI (gr ≤ 500 /ml: 22 ± 4 days) than in pts receiving single dose TBI (16 ± 4). Despite that difference, morbidity by infection was the same in both groups. Fractionated regimen of TBI seem to limit complications of marrow transplantation. Our current protocols investigate 220 rads x 5 in standard risk pts and 240 x 5 in high risk pts. 15/20 pts (75%) are alive in the standard risk, 4/13 pts (31%) are alive in the high risk group.

17.

RANDOMIZED TRIAL OF CISPLATIN (C), METHOTREXATE (A), BLEOMYCIN (B) AND VINCRISTINE (O) vs ABO IN SQUAMOUS CELL HEAD AND NECK CANCER. M.Clavel, J.Wildiers, F.Cognetti, M.Van Rijnant, R. Rosso, A.Rossi, A.Kirkpatrick, O.Dalesio, M.Rozencweig. EORTC Head and Neck Cooperative Group.

This ongoing trial was initiated to assess the role of C in CABO. Of 216 patients (pts) randomized, 211 were eligible, 127 were evaluable and 66 were too early. All pts had measurable a/o evaluable lesions, a performance status (WHO) ≤ 2 , no prior chemotherapy and normal hematologic and renal functions. The distribution of pts in the 2 arms was well balanced in terms of performance status, presentation, and prior therapy. The CABO regimen consisted of C : 50 mg/sq m on d4, A = 40 mg/sq m on d1 & 15, B : 10 mg on d1, 8, 15 and O : 2 mg on d1, 8, 15. O was withdrawn after 6 injections. In the other arm, A, B and O were given on d1, 8, 15 at the same dosage as in the CABO regimen. Both treatments were administered on an ambulatory basis. Patients received three 3-wk courses of CABO or ABO as induction therapy. Among 71 pts in the CABO arm, there were 14 complete and 29 partial responses for an overall response rate of 61%. Among 56 pts in the ABO arm, there were 4 complete and 15 partial remissions for an overall response rate of 34%. The corresponding overall response rates were 68 vs 35% in pts with measurable lesions, 65 vs 45 % in those with previously untreated stage III/IV disease and 60 vs 31% in those with recurrent a/o metastatic disease. At this point, there are no differences between the two treatment arms in terms of time to progression and survival. Toxic effects were essentially mild to moderate and consisted mainly of leukopenia, nausea and vomiting, constipation or diarrhea, cutaneous alterations, drug fever, neurologic manifestations and minor renal function impairment. As expected, ABO was better tolerated than CABO with particular respect to gastrointestinal distress. The apparently superior efficacy of CABO remains to be documented.

18.

COMPUTED TOMOGRAPHY (CT) GUIDED PERCUTANEOUS BIOPSY OF MALIGNANCIES : USE IN DIAGNOSIS AND TREATMENT. B.Ody, D.Mirescu and H.Hauser, Division of Radiodiagnosis, HSpital cantonal universitaire, CH 1211 Geneva 4, Switzerland.

During the last 5 years (November 1978-November 1983), 255 patients have been biopsied under CT control to obtain speci-

men for histological and cytological examination. 190 of them had before the puncture a suspicion of malignant masses (103 males and 87 females, all between 20 to 84 years of age, mean 59,5 ($\pm 13,5$ SD). Fine or large bored needles were used to perform percutaneous punctures in various organs under local anaesthesia. 2/3 of the biopsies were abdominal, particularly in the liver and in the retroperitoneum, the remainder concerned mainly the bone (vertebral column and pelvis), soft tissues and the chest. In 92 % of the cases, sufficient probe material was obtained. Minor complications were observed in 8 patients and only one serious, non lethal, abdominal hemorrhage. The main indications to the CT controlled percutaneous biopsies were : confirmation of malignant nature of a mass, confirmation of metastatic spread, proof of the histological type of malignancy before chemotherapy and/or radiotherapy, search of tumoral tissues after unsuccessful biopsies by other methods (endoscopy, cytology of excretions, blind puncture). 40 % of our biopsies were adenocarcinoma, hepatocarcinoma 14 %, squamous cell carcinoma 10 %, undifferentiated carcinoma and lymphoma (9 % of each). 12 patients have had iterative punctures in the following period either to determine the efficiency of the treatment or to prove the malignant nature of new lesions. Thus, the CT guided biopsy is a safe, useful, precise and quick method to allow histological diagnosis of cancer, especially for small and/or deep thoracic and abdominal tumours. Its cost and morbidity are inferior to those of exploratory surgery.

19.

RADIOISOTOPIC EVALUATION BEFORE INTRAPERITONEAL CHEMOTHERAPY. D.X.SLOMAN, M.FORNI, M.AAPRO, PA.BRIOSCHI, A.DONATH, F.KNAUER Nuclear Medicine Division, Oncohaematology division, Gynecology Division, University Hospital of Geneva.

Evidence from the peritoneal dialysis literature suggests that the peritoneal permeability of many hydrophilic antineoplastic drugs may be considerably less than plasma clearance. The concentration difference between the peritoneal cavity and plasma offers a potentially exploitable advantage. The aim of this study was to evaluate the drug distribution in the peritoneal cavity with scintigraphic photoimaging technique. 3 evaluable patients who were refractory to systemic chemotherapy were included : 2 ovarian tumors (stage III) and 1 peritoneal mesothelioma. Semipermanent Tenckhoff silastic dialysis catheters were implanted surgically in the peritoneal cavity under local anesthesia. The patients received a single 1 hour instillation of 2,000 ml isotonic sterile dialysed solution (HAUSMAN lab. St-Gall) in which 2 mCi of MAA (macroaggregate albumin) labeled with Tc99m were diluted. An antero-posterior static scintigraphic image was performed in all patients. Furthermore in one case, tomoscintigraphy was performed too. In all cases the intraperitoneal space was completely demonstrated. The distribution appeared to be very uncompleted. To achieve wide distribution a large volume of fluid was administered. Nevertheless static images and tomoscintigraphy pointed out very heterogeneous distribution of activity suggesting that all tumor-bearing areas were not adequately exposed. Among the important factors of failure in the "belly bath" technique for intraperitoneal infusion and delivery of drugs : the lack of a wide and homogenous distribution may reduce the accessibility of drug to all surfaces and represent probably an important variable for inadequate penetration of the tumor by the drug.