



XIV ANNUAL MEETING
INTERNATIONAL SOCIETY FOR
ONCODEVELOPMENTAL BIOLOGY
AND MEDICINE

HELSINKI, FINLAND
AUGUST 14-17, 1986

THE PORTHANIA BUILDING
UNIVERSITY OF HELSINKI

TUMOUR IMAGING WITH 111-In AND 131-I LABELLED ANTI-CEA ANTIBODIES (BW 431/31). Vanderick J (1), A Ferrant (2), N Leners (2), G Schulz (3), and C Deckers (1). (1) *Exper. Cancerol.* and (2) *Nucl. Med. Depart., Univ. Louvain Méd. Sch., Brussels, Belgium*; (3) *Res. Lab. Behringwerke AG, Marburg, FRG.*

We have used the murine monoclonal IgG1 BW 431/31 (Bosslet et al., *Int. J. Cancer*, 36, 75-84, 1985) in 14 patients. The first 7 patients received I.V. injection of 0.5 mg monoclonal antibody (Mab) and the 7 others had 3 mg. Ten patients had a colorectal carcinoma, 3 patients an elevated CEA of unknown origin and one had metastatic nodes of an adenocarcinoma of the lung. In 6 patients, intact Mab was given, and in 8 patients F(ab')₂ fragments. Labelling was performed with 111-In in 11 patients and with 131-I in 3 patients. Scintigrams were performed at 24, 48, 72 and in 2 patients at 96 hours after injection. Among the 10 patients with colorectal carcinoma, we found a complete agreement between CTscan and radio-immunoscintigraphy in 3. In 4 other patients, sites of abnormal uptake were seen despite apparently efficient radio- or chemotherapy. One patient with a 14-year complete remission had an increase in serum CEA and a negative scan. Two patients with bulky necrotic tumours showed no uptake in one case and a slight one in the other. We found no abnormal uptake in the lung metastases. In the 3 patients with an elevated CEA of unknown origin, the radio-immunoscintigrams were negative as was the check-up. No side effects were observed after injection of the Mabs. Activity was observed at the site of the kidneys in 5 patients after injection of F(ab')₂ fragments. The testes showed increased uptake in 7 patients. Radioimaging with BW 431/31 may give correct information on the localization and the evolutivity of colorectal carcinoma. F(ab')₂ fragments provided better defined images than those obtained with intact Mab and the quality was further enhanced with 111-In labelling. Adequate uptake is already observed from 24 hours after injection. In our experience, radio-immunoscintigraphy with BW 431/31 alone as diagnosis tool is not satisfactory when investigating the origin of an increased serum CEA in the search of a primary site in patients with CEA of unknown primary.

COMPARISON OF THE RESULTS OBTAINED BY TWENTY MIBG AND BONE DOUBLE SCINTIGRAPHIES IN THE DIAGNOSIS OF NEUROBLASTOMA.

Bouvier JF, Philip T, Chauvot P, Brunat-Mentigny M, Lahnèche B, Centre L. Bérard, Lyon, France.

We wanted to compare the results obtained by scintigraphies performed with 131I-mIBG (metaiodobenzylguanidine) and 99mTc-HMDP (hydroxymethylene sodium diphosphonate) for the detection of neuroblastoma and for the extent of the disease about twenty double scintigraphies.

We performed twenty double scintigraphies on 16 children : 5 girls and 11 boys (average age : 37 months) suffering from neuroblastomas of different grades. The comparative study for the uptake by the tumor was possible only 10 times (in 9 cases before surgery and in one case of incomplete surgery).

In the case of an abdominal mass by a child, we looked for an uptake of 131I-mIBG by the tumor which confirmed a neuroblastoma or for an uptake of 99mTc-HMDP which indicated a very high probability of a neuroblastoma and not a Wilms tumor.

- before surgery (9 cases) : the results were similar for the diagnosis between 131I-mIBG and 99mTc-HMDP in six cases (5 positives cases and one negative case) even if the uptakes were more definite with 131I-mIBG than with 99mTc-HMDP ; for three cases no uptake of 99mTc-HMDP was observed while the tumor took up 131I-mIBG.

- after surgery (7 cases) the positive results were similar between 99mTc-HMDP and 131I-mIBG in one case of partial removal and the negative results were also similar in five of six cases with total ablation of the tumor. For the last case the scintigraphy performed with 131I-mIBG was not interpretable because of undesirable abdominal uptakes.

In determining the extent of the disease all twenty double scintigraphies were useable and we could note :

- in 12 cases the two scintigraphies gave the same result : 5 absence and 7 presence of metastases for which a greater number of spots was revealed by 131I-mIBG in two cases.

- 8 conflicting responses : 5 lesions (3 cases of lymph nodes metastases and 2 cases of bone metastases) were detected only by mIBG and 3 cases of bone metastases took up only HMDP (but for one case anatomopathology revealed the metastase was sterilized after chemotherapy).

In conclusion bone scintigraphy, the easiest technique to perform, remains useful for the detection of neuroblastoma even if mIBG scintigraphy gives better results. In determining the extent of the disease, the two techniques are complementary and essential.

CLINICAL APPLICATION OF MONOCLONAL ANTIBODY DRUG CONJUGATE FOR COLORECTAL CARCINOMA. Takahashi, T., Yamaguchi, T., Yokota, T., Kitamura, K., Suzuyama, H., Noguchi, A., Kitai, S., Otsuji, E., Sawai, K. and Honda, M., Dept. of Surgery, Kyoto Prefectural Univ. of Med., Kyoto, Japan, 602.

207

For targeting chemotherapy of colorectal carcinoma, mitomycin C (MMC) and neocarzinostatin (NCS) were covalently bound to monoclonal antibody A7 which is highly specific to human colon cancer. The *in vitro* cytotoxic effects of the conjugates A7-MMC and A7-NCS on SW1116 were 77 times and 4 times stronger than those of the free MMC and free NCS, respectively. An *in vitro* study in nude mice bearing human colon carcinoma revealed that monoclonal antibody A7 alone had no effect, and that A7-MMC and A7-NCS had greater inhibitory effects than the free MMC and NCS, respectively.

Thirty-five patients with carcinoma of the colon and rectum including 6 with postoperative liver metastasis and one with postoperative peritoneal metastasis, were given the A7-NCS conjugate consisting of between 15 and 90mg of antibody and between 1,000 and 6,000 units of NCS. Immunoperoxidase study of resected specimens revealed selective localization of NCS in the cancer cells. The conjugate had no serious adverse effects. Five of the six patients with postoperative liver metastasis responded favorably to the conjugate, showing a decrease in tumor size on CT scan or relief of pain. The conjugate was of no benefit to patients with multiple lung metastasis or peritoneal metastasis. The effect on other patients with surgically resected carcinoma remains to be determined by a follow-up study.

TUMOUR IMAGING WITH ^{111}In AND ^{125}I ANTI-CEA ANTIBODIES (BW 431/31).

J. Vanderick (1), A. Ferrant (2), N. Leners (2), G. Schulz (3) and C. Deckers (1).

208

(1) Exper. Cancerol. and (2) Nucl. Med. Depart., University of Louvain Medical School, Brussels, Belgium; (3) Research Laboratories Behringwerke AG, Marburg, FRG.

Radioimmunoscintigraphy using the murine monoclonal IgG1, BW 431/31 (Int. J. Cancer, 36, 75-84, 1985) has been performed in 30 patients. The intravenously administered amount of IgG was 0.5 mg (7 patients), 2 mg (4 patients) or 3 mg (19 patients). For labelling of the antibody, either ^{111}In -DTPA (26 cases) or ^{125}I (Iodogen method - 4 cases) was used. F(ab')₂ fragments were given in 20 patients and the whole IgG in 10. The scintigrams were performed 24 and 48 hours after injection. For subtraction of reticuloendothelial radioactivity, $^{99\text{m}}\text{Tc}$ sulfur colloid was used.

19 patients had evolutive primary colorectal carcinoma, 9 had an elevated CEA of unknown origin, one had been operated for lung adenocarcinoma and one patient had a poorly differentiated primary carcinoma of the neck with a high serum CEA level.

The scintigrams showed tumour uptake in 14/19 (74 %) patients with colorectal carcinoma. In 7 patients, radioimmunoscintigraphy showed uptake of antibody despite chemo- or radiotherapy and this uptake was associated with a poor prognosis. The CEA serum level was of no predictive value for tumour uptake.

Uptake in liver metastases was observed in 2 out of 4 patients.

In no patient with an elevated serum CEA level of unknown origin could scintigraphy with the labelled antibody show a site of abnormal uptake.

Testis uptake could be seen in 17 (85 %) of 20 men, and the kidneys were clearly outlined in 17/20 patients who were given F(ab')₂.

We conclude that imaging using labelled anti-CEA antibody (BW 431/31) gives frequently correct information on localization and activity of colorectal carcinoma. The search for the primary of a raised serum CEA level of unknown origin remains disappointing using this antibody.