Advances in the applications of monoclonal antibodies in clinical oncology

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TUMOUR IMAGING WITH $^{111}$In AND $^{131}$I LABELLED ANTI-CEA ANTIBODIES (BW 431/31).
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The murine anti-CEA monoclonal antibody BW 431/31 (Bosslet et al, Int. J. Cancer 36:75-84, 1985) has been used in 10 patients. Eight had colorectal carcinoma and two had elevated CEA of unknown origin. The first 7 patients had injection of 0.5 mg monoclonal antibody (Mab), and the 3 others received 3 mg. In 6 patients, intact Mab was given, and in 4 $F(ab')_2$ fragments.

BW 431/31 was labelled with $^{111}$In in 8 patients and with $^{131}$I in 2 patients. Scintigrams were performed 24, 48, 72 and, in 3 patients, 96 h after injection. In 3 out of 8 patients with colorectal carcinoma, the findings of radioimmunoscinintigraphy and CT scan were in agreement. In 3 other patients, in apparent clinical remission, sites of abnormal uptake were seen. Two patients had bulky necrotic masses. No uptake was observed in one and a slight uptake in the other. In 2 patients with elevated CEA of unknown origin, the radioimmunoscinintigrams were negative. No side-effects were observed after injection of the Mabs. In 3 patients, activity was observed at the site of the kidneys after injection of labelled $F(ab')_2$, fragments. Radioimmunoscintigraphy using BW 431/31 may give correct information on the localisation of colorectal carcinoma. Adequate uptake can be observed from 24 h after injection. $F(ab')_2$, fragments provided better defined images than those obtained with intact Mab and the quality was further enhanced with $^{111}$In labelling. Further work is needed to show if there is an advantage in using 3 mg instead of 0.5 mg Mab.

THE EFFECT OF INCREASING UNLABELLED MONOCLONAL ANTIBODY (MoAb) DOSES ON METASTASES DETECTION AND ON BODY DISTRIBUTION OF VARIOUS $^{111}$In MoAbs.

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We have studied four different murine MoAbs, all labelled with 5 mCi of $^{111}$In. These include 96.5 (anti-P97, melanoma), ZME-018 (anti-high molecular weight antigen of melanoma), ZCE-025 (anti-CEA) and PAY-276 (anti-prostatic acid phosphatase). Twenty to 25 patients were studied using each MoAb. In each study, patients were divided into groups of 5 patients according to the amount of unlabelled MoAb injected with the 1 mg $^{111}$In-labelled MoAb.

Unlabelled MoAb dose varied from 1 mg to 80 mg. Images, digital and analogue, were acquired at 24, 72 and in most cases at 120 and 168 hours. Lesion detection was compared with clinical, radiographic, and other scintigraphic results. Regions of interest were used to analyse relative non-tumour body distribution of labelled MoAb at 72 h.

In all four MoAb results, detection rate of metastatic lesions improved with increasing MoAb dose but the 'saturation' point differed with each of them, ranging from 20 to 80 mg.

The non-tumour body distribution also varied with increasing MoAb dose. The liver uptake fell as the bone, kidney and blood pool increased with increasing MoAb dose. The level at which statistical significance occurred, however, varied with each antibody. Spleen uptake was variable.

The 'blocking' effect of unlabelled MoAb influences the non-specific distribution of labelled MoAb primarily through reduction of liver uptake and increases the sensitivity of metastases detection.