OV-TL3 F(ab')$_2$ ^{111}In imaging in ovarian cancer

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In 59 patients with ovarian cancer the safety and diagnostic accuracy of radioimmunoscintigraphy (RIS) with OV-TL3 F(ab')$_2$ labelled to ^{111}Indium has been assessed. The murine monoclonal antibody OV-TL3 reacts with a cell surface antigen which is frequently expressed on ovarian cancer cells and not shed into the circulation. Planar images and SPECT were performed between 4 and 96 hours after injection of 140 MBq of the immunoconjugate. Every patient underwent CT of the abdomen and pelvic region and the serum CA 125 levels were determined. 56 patients also underwent ultrasonography. In total, 42 patients underwent explorative surgery 3 to 8 days after intravenous administration of the antibody. The blood clearance followed a bi-exponential curve with a half-life of 3.5 h for the fast component and 30 h for the slow component. Urinary excretion of the radionuclide was at a fairly constant rate of approximately 4% of the injected dose/24 h. Except for the transient rash observed in 2 patients, no side effects were noted.

For the 42 patients who underwent surgery, a correct diagnosis of tumour presence was made in 86% with RIS, in 83% with CA 125, 67% with CT and 63% with ultrasonography. In 17 inoperable patients, clinical and/or radiological signs of tumour recurrence were concordant with RIS findings. The ratios of tumour to background tissue (as fat, muscle or skin) uptake were in the order of 10. The liver uptake, was, however, three times higher than in the tumour. In surgically assessed patients a total of 86 solid tumour localisations were found. The detection sensitivity for these tumour deposits was 60% for RIS, 41% for CT and 27% for ultrasonography.

Immunoscintigraphy with OV-TL3 F(ab')$_2$-^{111}Indium is an accurate diagnostic method for the detection of ovarian cancer. Intestinal and ascites activity and high liver and spleen uptake can intefere with image interpretation.

Session 4. Chairman: D.S. Secher, Slough, UK

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Treatment of B cell malignancies in patients using ^{131}I Lym-1

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Lym-1, a murine IgG2a monoclonal antibody, produced by immunisation with cells from patients with Burkitt's lymphomas, was conjugated with I-131 to image and treat patients with B cell malignancies. Treatment was administered in a fractionated dose (FD) protocol, that is, 30–61 mCi every 2–6 weeks to 28 patients or in a maximum tolerated dose (MTD) protocol wherein each of 10 patients was entered at a dose level of 60, 100 or 150 mCi every 4 weeks until radiation toxicity occurred. In either protocol, treatment was terminated by death, progression, complete remission or development of HAMA. FD was interrupted after one or two doses in eight of the 28 patients. Seventeen of the remaining 20 patients had a partial remission (PR) and 2/20 a complete remission (CR). Tumour regression of 25–50% occurred after each dose of ^{131}I. 2 of 6 patients in the MTD protocol achieved a CR and the remainder a PR. Tumour regression of greater than 50% occurred after each dose.

Cumulative doses as large as 800 mCi were administered in FD compared to 400 mCi in MTD. Grade 3 thrombocytopenia occurred in 10% of patients enrolled in FD and 30% of patients enrolled in MTD. MTD has not been reached despite individual doses of 237 mCi/m^2 and cumulative doses of 292 mCi/m^2. These results suggest more rapid regression with larger doses of ^{131}ILym-1, but controlled studies are required to determine which treatment is more ultimately efficacious.

Dosimetry of antibodies

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In order to develop a dose-response relation for radiolabelled antibody therapy, a reliable determination of the radiation dose is required. The current techniques for dose estimation rely on quantitative planar or SPECT imaging with resolutions typically of about 1 cm. The mean range of most radionuclides considered for therapy is much less than this (even the energetic B-source Y-90 has a mean range in soft tissue of only 4 mm). The usual nonuniformity of radioimmunoconjugate localisation within tumour may result in marked heterogeneities in the tumour dose from one region to another.

We are investigating new dosimetric techniques to quantify the radiolabel distribution after an administration of radiolabelled antibodies at both the cellular and multicellular level. These methods involve the use of image analysis of autoradiographs from tumour sections, and phosphor imaging plates as a high speed moderate resolution (100*100 μm) multi-cellular autoradiography. We are further developing a miniature real-time solid state dosimeter which can be used for *in vivo* studies. This detector has several advantages over TLDs since it can provide information on local tissue dose and in addition of local dose rates.

Chimeric B72.3 antibody for repeated radioimmunotherapy of colorectal carcinoma

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A chimeric antibody with mouse B72.3 variable regions and human IgG4 constant regions (Whittle NR *et al.*, *Protein Eng* 1987, 1, 449–505) has been investigated in patients with colorectal carcinoma. 6 patients have received 10–20 mg of the antibody labelled with 20–50 mCi ^{131}I. Treatment was repeated after 3–4 weeks if no human anti-mouse IgG nor human antichimeric antibody was found in the serum. One to four (mean 2) treatments have been given and 2 patients remain eligible for further treatment. 2 patients produced human antichimeric antibody and human anti-mouse antibody after the first treatment. No anti-antibody response has been found in the other 4 patients. No toxicity was seen. Serial measurements of activity in tumour, blood, liver and lung were made using single photon emission tomography with scatter correction [Green AJ *et al.*, *Eur J Nucl Med* (in press)]. Mean beta half life of clearance of antibody from blood was 145 h, tumour 256 h, liver 230 h and lung 203 h. Antibody localisation was seen in tumours where radioactivity was retained longer than in other tissues. Repeated therapy with chimeric B72.3 antibody is feasible in some patients.