Pilot Radioimmunotherapy Trial with $^{131}$I-labeled Murine Monoclonal Antibody CC49 and Deoxyspergualin in Metastatic Colon Carcinoma

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ABSTRACT

An antitumor immune response is invariable following administration of murine monoclonal antibody (mAb), precluding effective multidose therapy. In advanced colorectal cancer patients, we carried out a pilot study with multiple doses of $^{131}$I-labeled CC49 administered with deoxyspergualin (DSG), an immunomodulator, to determine its effect on immune response. Cumulative toxicity and efficacy were also evaluated.

Six patients with tumor-associated glycoprotein 72-expressing colorectal cancer were treated i.v. with 15 mCi/m$^2$ $^{131}$I-labeled to 20 mg mAb CC49 biweekly, along with concurrent DSG 200 mg/m$^2$ daily for 5 days, for a maximum of four courses. None had received prior murine mAbs.

All patients had targeting of radioactivity to known tumor sites following initial infusion. Four of six patients received all four courses of therapy, three without any acute side effects. In these patients, there was no change in serum clearance with variable tumor targeting following repeat infusions. Two patients had grade II anaphylactoid reactions, which were treated without sequelae. One of these had faster serum clearance of radioactivity following repeat infusions of $^{131}$I-labeled CC49. Human antitumor antibody titers in all patients were significantly less compared to concurrent times in patients receiving CC49 without DSG ($p < 0.05$). There was no correlation between the human antitumor antibody titer and serum clearance or tumor targeting of $^{131}$I-labeled CC49. There were no clinical responses.

We concluded that multiple doses of murine antibody $^{131}$I-labeled CC49 can be safely administered with no change in serum or whole-body kinetics in 50% of patients treated biweekly. DSG may reduce the human immune response to the murine mAb.

INTRODUCTION

A major limitation of murine antibodies has been the invariable development of a host immune response, resulting in faster serum and whole-body clearance and reduced or absent targeting following repeat administration. In our experience with 43 patients with colon cancer, 20 patients with breast cancer and 8 patients with prostate cancer who received a single dose of 20 mg mAb CC49, almost all patients develop an immune response following murine antibody administration, which precludes repeat administration of the murine mAb (1). HAMA$^1$ titers are usually seen by 2 weeks and are invariable at 4 weeks.

DSG is a synthetic analogue of the antitumor antibiotic spergualin first isolated from culture filtrates of Bacillus laterosporus (2, 3). The compound has been studied for both its antitumor properties and as an immunomodulatory compound. Although DSG contains the polyamine spermidine within its structure, and therefore can be considered a spermidine analogue, its biological activity has not been duplicated by spermidine or spermine administration. DSG exhibits immunomodulatory properties in experimental animals (4–6) and has shown immune suppression in multiple models including experimental allergic encephalomyelitis, tissue graft rejection, and humoral immunity. Although the mechanisms are not established, DSG has been shown to increase interleukin 2 production in mixed lymphocyte culture, to enhance natural killer cell activity in spleen cells of tumor-bearing mice, and to activate T lymphocytes (7). It also suppresses certain macrophage/monocyte functions (8). Clinical trials using DSG as an immunosuppressor have shown impressive activity in aborting or preventing renal and hepatic graft rejection (9, 10). The highest drug dosage used in these trials was 220 mg/m$^2$/day for 5 days, each infusion being over a period of 3 h. At these doses side effects were mild, consisting of perioral numbness during the infusion and minor leukocytosis and platelet depression, as well as alopecia. A Phase

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Abbreviations used: HAMA, human antitumor antibody; DSG, deoxyspergualin; TAG-72, tumor-associated glycoprotein 72; mAb, monoclonal antibody; CT, computed tomographic; SPECT, single-photon emission computed tomography.
I trial carried out at this Center to assess the antitumor properties of DSG concluded that a safe dose for Phase II studies would be 1440 mg/m²/day for 7 days, at which dose the principal side effects were hypotension when the infusion rate was too rapid and thrombocytopenia (11). Pharmacokinetic studies during this trial demonstrated that a terminal half-life from the plasma for this drug was between 53 and 106 min.

TAG-72 is a tumor-associated mucin that is widely expressed in adenocarcinomas, particularly colorectal, ovary, breast, prostate, and lung cancers (12). Radiolabeled antibodies which target TAG-72 have been used extensively for possible improved tumor diagnosis and treatment (13, 14). The “first generation” anti-TAG-72 mAb B72.3 has been used in radioimmunodiagnosis and radioimmunotherapy trials in >1000 patients (14).

mAb CC49 is a murine IgG, that reacts against the TAG-72 antigen found in most differentiated adenocarcinomas (15). CC49 is a “second generation” mAb developed against the TAG-72 antigen and has been shown to localize in antigen-expressing tumors. Because its antigen affinity is high (about 2 × 10¹⁰ M⁻¹; Ref.15), it is being studied for its potential usefulness in the diagnosis and treatment of adenocarcinomas (16).

In our hands, mAb CC49 has been somewhat better than B72.3 for localizing to colorectal carcinoma. In 10 patients who received both mAbs simultaneously prior to surgery, there was a 60% improvement in tumor:serum ratios with CC49 (P < 0.05) 1 week after infusion, with absolute tumor concentration of CC49 being greater, albeit not statistically significant in this small group of patients, than that of B72.3 (17). We also found that absolute tumor uptake of CC49 was better at the 20-mg dose than at the 1-mg dose, and decided that the optimum mass amount of mAb CC49 for clinical use would be 20 mg.

Subsequently, we carried out a Phase I trial with 131I-labeled CC49 in patients with metastatic colon carcinoma and found the maximum tolerated single dose to be 75 mCi/m² 131I. Although there were no major therapeutic responses in this Phase I trial (1), we did find a minor response in a patient who was treated twice with 30 mCi/m² 131I-labeled CC49.

Experimental data (18) have shown that fractionated delivery of radioimmunotherapy may be more effective than a single large dose. This trial was therefore designed to evaluate suppression of the human immune response to mouse antibody by DSG. We decided to undertake a radioimmunotherapy schedule that fulfilled the following characteristics: (a) a cumulative dose of radioactivity that had therapeutic potential (1); (b) an outpatient schedule (i.e., ≤29 mCi ¹³¹I/dose); and (c) a fractionated schedule at time points where HAMA formation was seen in the majority of patients treated with comparable mass amounts of mAb CC49 without concurrent DSG. Suppression was evaluated by: (a) clinical observation; (b) estimation of HAMA titers; and (c) serial imaging of ¹³¹I distribution.

MATERIALS AND METHODS

Patients. Six patients with measurable metastatic colorectal carcinoma were studied (Table 1). Patient selection requirements included no prior radiotherapy or mouse mAb and tumor tissue reactivity (≥50% reactivity with CC49 in an average high-power field). All patients had, at the time of entry into the study, serum bilirubin ≤ 2 mg/dl, serum creatinine ≤ 1.5 mg/dl, total WBC ≥ 3,500/μl, and platelet count ≥ 100,000/μl. The pilot radioimmunotherapy study was approved by the Institution Review Board and the Committee on Radiation at this Center. Informed consent was obtained from all patients. All patients underwent standard imaging modalities including CT scans within 2 weeks prior to and 4 weeks after therapy.

Patients received 20 mg CC49 labeled with 15 mCi/m² ¹³¹I biweekly for a total of four doses, or until symptom-limiting toxicity was seen. Patient characteristics are summarized in Table 1. All patients had failed 5-fluorouracil and leucovorin therapy prior to the mAb infusion. None had received any therapy for at least 4 weeks prior to entry into this protocol. The median time elapsed between prior therapy and entry into this trial was 8 weeks. All patients received a saturated solution of potassium iodide (10 drops p.o. three times daily), starting the day of and prior to radiolabeled mAb administration and continuing until 2 weeks after the last dose of ¹³¹I. A test dose of 0.5 mg unlabeled CC49 was injected i.v. prior to every dose of radioimmunotherapy, and the patient was observed for at least 30 min. The radioantibody was then administered only if there were no side effects.

Starting the day of and prior to radioantibody administration, patients received 200 mg/m² DSG administered i.v. in 500 ml normal saline over 3 h daily for 5 days. This therapy was repeated with every dose of radioantibody.

All pre- and postradioimmunotherapy CT scans were evaluated by a radiologist familiar with the clinical history. Responses were graded as follows: progression, increase in size and/or number of lesions; partial response, ≥50% reduction in sum of greatest diameters of measurable lesions, with no increase in size of any lesion; minor response, <50% reduction in sum of greatest diameters of measurable lesions, with no increase in size of any lesion; and stable disease, no change in lesion size or number.

mAb CC49. Clinical grade CC49 was provided by the Division of Cancer Therapy, National Cancer Institute. CC49 was labeled with ¹³¹I using the iodogen (Pierce, Inc., Rockford, IL) method. In brief, the requisite amount of the mAb and radiiodine were mixed in sterile 10-ml glass vials precoated with iodogen and incubated at room temperature for 15 min. The radiolabeled mAb was separated from the mixture by passage through a sterile BioGel P6 (Bio-Rad Inc., Melville, NY) size exclusion column. TLC of an aliquot was carried out and the preparation utilized only if the percentage of protein-bound radioactivity was ≥95%.

Radioimmunoreactivity. In every patient, the radiolabeled mAb was assayed for radioimmunoreactivity using the method described by Lindmo et al. (19). In brief, appropriate dilutions of each mAb were added in triplicate to wells of microtiter plates precoated with antigen-positive (LS174T) and antigen-negative (A435) cell extract and incubated at 4°C overnight. The percentage of bound radioactivity was plotted against dilution to obtain the percentage of binding at conditions of antigen excess.

Administration of Radiolabeled mAb. All mAb preparations were administered after passage through a 0.2-μm filter. Unlabeled CC49 (0.5 mg) was initially administered as an i.v. slow bolus, and patients were monitored for symptoms with
vital signs being measured every 15 min. If there was no adverse reaction noticed within 0.5 h of this test dose, the radiolabeled mAb diluted in 100 ml 5% human serum albumin in normal saline was administered as an i.v. infusion over 1 h. The radiolabeled mAb was injected into the patient prior to determination of radioimmunoreactivity. The 1-h infusion was felt to be slow enough to monitor for possible anaphylactoid and other unknown adverse events. Patients’ vital signs were monitored for at least 4 h after completion of antibody infusion.

Whole-body measurements of radiation were obtained using an ionization chamber calibrated to measure radiation dose (in mR/h) both at the body surface and 1 m from the patient. These measurements were obtained whenever the patient returned for DSG and/or imaging.

**Pharmacokinetics, Whole-Body Counting and Radio-immunoscintigraphy.** Anterior and posterior whole-body 131I images were obtained at multiple time points to estimate biodistribution following each antibody infusion. SPECT images of relevant areas were obtained whenever possible, usually 3 days after each mAb infusion. Whenever possible, similar imaging parameters, especially with respect to time postinfusion and speed of camera motion for whole-body images, were maintained for all imaging studies after each infusion of radioantibody. All images were obtained with a known quantity of 131I (standard) placed within the field of view. Coregistration of CT and SPECT images enabled more precise anatomical identification of sites of increased radioactive uptake (20). To determine changes in biodistribution attributable to the development of an antimouse response subsequent to the mAb administration, images were visually assessed for increase in liver or spleen radioactivity and changes in blood pool radioactivity. Images were also assessed for thyroid and stomach visualization, bearing in mind the inherent variability in uptake in these organs consequent to the patients’ taking stable iodide. These were compared to baseline appearance.

Blood was obtained for determination of the radiolabeled mAb clearance following antibody infusion and at multiple time points daily to enable determination of pharmacokinetics of radiolabeled CC49.

**In Vitro Studies.** Samples of serum (0.5 ml each) were counted in a gamma counter along with appropriate dilutions of the standards and biopsy specimens. All serum and standard counts were obtained at the same time. Samples were counted in the 131I window in a gamma well scintillation counter (LKB Wallac, Piscataway, NJ). Samples were counted to <1% relative error, according to the criteria of Loewinger and Berman (21). Measurements were then converted to percentage of injected dose of radiiodine per liter of serum.

Samples of preinfusion, 2-week, and 4-week sera were incubated with 125I-labeled CC49 (10 ng 125I-labeled CC49 added to 50 μl serum) and analyzed by high pressure liquid chromatography to determine the presence of HAMA. These assays were carried out at least 4 weeks after infusion to minimize the contribution of 131I-labeled CC49. The percentage of immune complexes was measured as that proportion of radioactivity seen at Mr 300,000, as a fraction of total radioactivity present.

To further define the nature of the HAMA, a sandwich radioassay was utilized to determine the amount of HAMA reactive against an isotype-matched control murine mAb (B6.2) and expressed in μg/ml HAMA. Microtiter plates (96-well), each coated with 100 ng mAb B6.2, were incubated for 24 h at 4°C with appropriate dilutions of patient sera. Fifty μl 125I-labeled B6.2 were then added to each well and incubated for 24 h at 4°C. The individual wells were counted after washing along with aliquots of added 125I-labeled B6.2, and the percentage of bound radioactivity was plotted against serial dilution on a semilogarithmic graph to obtain the amount of anti-B6.2 antibody present in serum.

**Computer Analysis.** Serum clearance data were entered into a computer program (BLD, NIH, Bethesda, MD), and exponential fits were used to approximate the y-axis intercept and half-life (t1/2) for serum and whole-body clearances. For serum data both monoexponential and biexponential fits could be fit with r2 > 0.9. For whole-body clearance data, the radiation dose at 1 m from the patient was not high, especially at later time points. Perhaps for this reason, whole-body clearance of seven doses of 131I-labeled CC49 could not be fit with r2 > 0.9. For all other doses, sufficiently accurate fits for monoexponential clearance were obtained.

**RESULTS**

Six patients with measurable metastatic colorectal carcinoma were studied (Table 1). The labeling method was simple and efficient. The procedure reproducibly resulted in >90% incorporation of radiiodine to antibody as determined by TLC. Radioimmunoreactivity of 131I-labeled CC49 was always >55%. None of the patients had side effects during infusion of the test dose. All patients experienced fatigue, which was felt to be due to the vigorous schedule of therapy and perhaps to the radioantibody itself. There was no nonhematological toxicity. Hematological toxicity was limited to grade 2 leukopenia in one patient (patient 3) following the third course of radioantibody/DSG, necessitating halving the last dose of 131I-labeled CC49. The leukopenia resolved spontaneously. There was no other toxicity. No major responses were seen in this pilot study.

All patients showed targeting to known tumor following the first radioantibody infusion. Radionuclide scans were interpreted as positive if there were focal persistent areas of increased tracer concentration in the liver. Nodal areas of increased radiotracer concentration were interpreted as positive only if the uptake was intense and persistent, or if nondraining mesenteric nodes were involved. SPECT delineated lesion extent better than did the planar images. Patients with lung me-
Table 2  Serum and whole-body clearance using monoexponential approximations

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*Only data with fits of r ≥ 0.9 are presented.

*A, y-axis intercept; % D, percentage of injected dose; NA, not available (see text for details).

*Monoexponential fit could not be approximated with accuracy ≥0.9.

tastases had multiple lesions <1 cm in diameter, visualized as diffusely increased uptake. All known lesions ≥2 cm in diameter in the liver and abdomen (a total of 16 lesions) were visualized by initial radioimmunoscinography. Lesion visualization was best at 1 week after the mAb infusion. Splenic uptake of 131I-labeled CC49 was greater than could be accounted for by vascular distribution.

Serum clearances were fitted to monoexponential and biexponential clearances. The whole-body data could not be approximated to a monoexponential clearance satisfactorily in 7 of 22 infusions, with no correlation observed between serum and body clearances. To better evaluate whole-body clearances, semi-quantitative methods are being used to determine whole-body and organ clearances in each patient. Table 2 details serum and whole-body clearances in the patients. These will be discussed individually below.

Fig. 1 shows HAMA titers over time in the patients who received 131I-labeled CC49 with DSG, along with a mean curve obtained from a group of 24 patients with metastatic colon carcinoma who received a single dose of 131I-labeled CC49 without concurrent DSG. Fig. 1a details the percentage of immune complexes seen when serum at the various time points was incubated with radiolabeled CC49 and then passed through a size exclusion column; it therefore represents the total humoral response to murine CC49. Fig. 1b graphs that quantity of human IgG reactive with an isotype-matched control murine mAb and therefore all but the anti-idiotypic and non-IgG response. HAMA titers, including (expressed as percentage of immune complexes) or excluding (expressed as μg/ml anti-B6.2) the anti-idiotypic response, were considerably decreased in patients receiving DSG (P < 0.05). There was no correlation between the HAMA titer and biological behavior of 131I-labeled CC49.

Patient 1 tolerated the first two doses of 131I-labeled CC49 without any acute side effects. This patient had urticaria (grade I) 30 min into the third infusion. The symptoms resolved promptly upon cessation of therapy and administration of i.v. diphenhydramine. 131I-labeled CC49 was therefore discontinued, and this patient did not receive any further therapy. Targeting of radioantibody to known tumor in the liver and (diffusely) in the lungs was excellent following the first dose of radioantibody; the second and third doses showed increased thyroid and stomach uptake with no tumor uptake. This patient had significantly faster serum and whole-body clearance of repeat antibody infusions (doses 2 and 3) and a larger volume of distribution (manifest by a lower serum y-axis intercept: Table 2). However, this patient had no serum evidence of HAMA (Fig. 1).

Patient 2 tolerated the first three doses of radioantibody without any acute side effects. This patient had a grade II reaction about 15 min upon starting the fourth dose of radioantibody, which resolved on administration of diphenhydramine. Shortness of breath returned upon restarting the radioantibody, necessitating discontinuation after about two-thirds of the 131I-labeled CC49 had been administered. Patient 2 had bleeding from the colonic recurrence during the fourth course of therapy, and therefore did not receive the full dose of DSG; this patient also required emergent therapy for the bleeding (at this time the


platelet count was >150,000/µl, and consequently images or serum for pharmacokinetics could not be obtained. Targeting to liver and colon disease was excellent after the first infusion, with increased hepatosplenic uptake noticed after the second infusion; the colon recurrence was visualized after the second infusion, although the liver metastases were not (either as areas of increased or decreased radioactivity). Serum kinetics (Table 2) did not change. In this patient, whole-body data could not be approximated well. There was no evidence of tumor targeting after the third infusion, with increased hepatosplenic uptake accompanied by thyroid and stomach visualization. Again, this patient had no serum evidence of HAMA (Fig. 1).

The third patient received all four courses of therapy without acute side effects. There were no anaphylactoid reactions during any course of radioantibody. This patient had grade II leukopenia following the third course of therapy, consistent with DSG toxicity, and received one-half (i.e., 7.5 mCi/m²) of the last dose of 131I-labeled CC49. This patient had lung disease visualized as diffusely increased pulmonary uptake, seen as discrete small foci on SPECT. There was essentially no change in imaging characteristics following each infusion and no change in serum clearance characteristics; this patient’s whole-body clearance was faster after each infusion (Table 2). Patient 3 had steadily increasing minimal HAMA titers (Fig. 1).

Patient 4 received three courses of 131I-labeled CC49 and DSG without incident. This patient had shortness of breath, pleuritic chest pain, and fever ≥ 40°C 1 week after administration of the third dose of 131I-labeled CC49. A perfusion/ventilation study was consistent with multiple pulmonary emboli;
this patient was placed off-study and treated for pulmonary problems. This patient had faster serum clearance (Table 2) of the second and third infusions; imaging did not reveal any appreciable change. Patient 4 did not develop any HAMA titers (Fig. 1) following the infusions.

Patient 5 received all courses of radioantibody and DSG without acute incident. Fig. 2 shows anterior and posterior whole-body images obtained immediately (upper images) and 1 week after (lower images) the first radioantibody infusion. The initial images show blood pool distribution of radioactivity, with hepatic tumors clearly visualized 1 week later. Fig. 3 has comparable images obtained immediately (upper images) and 1 week after (lower images) the fourth infusion of $^{131}$I-labeled CC49. These are virtually identical to the images in Fig. 2, showing that tumor targeting was comparable. However, increased stomach and thyroid radioactivity suggested increased dehalogenation. Patient 5 had faster serum clearance only of the fourth infusion of antibody, with minimal increase in volume of distribution of the second (compared to the first) and fourth infusions. This patient had steadily increasing low HAMA titers (Fig. 1).

Patient 6 also received all courses of radioantibody and DSG without acute incident. Fig. 4 shows anterior whole-body images obtained immediately following each infusion in this patient. There is no appreciable uptake in any normal organ other than the spleen. Fig. 5 shows anterior whole-body images obtained 1 week after each infusion of $^{131}$I-labeled CC49. Although organ biodistribution is comparable among the images, tumor uptake is minimal following infusions 3 and 4, with image 4 showing reduced whole-body radioactivity. This patient had no change in serum clearance half-time (Table 2), with a steady increase in the volume of distribution after each infusion. There was no evidence (Fig. 1) of HAMA.

**DISCUSSION**

Six patients with metastatic colon cancer were treated with repeated outpatient infusions of $^{131}$I-labeled CC49 administered concurrently with DSG, administered biweekly for a maximum of four doses. In four of the six patients treated, there was comparable targeting of radioactivity to tumor following repeat $^{131}$I-labeled CC49 administration. HAMA titers in all patients were considerably lower than those seen in patients with metastatic colon carcinoma receiving comparable mass amounts of CC49 without DSG. Of the 24 possible doses in these patients, 22 were administered. There were two anaphylactoid reactions.

The total dose of $^{131}$I-labeled CC49 (60 mCi/m²) administered in this trial was the same dose that resulted in a minor response in a patient treated in an earlier Phase I trial with $^{131}$I-labeled CC49 (3). However, there were no responses seen in this group of patients. The immunohistochemical characteristics of these patients were not different from the earlier responders. The patient in the earlier trial had disease limited to the liver; it is possible that no responses were seen in this group of patients because their tumor burdens were greater than those in the earlier responders. The earlier responder had been treated with two doses of 30 mCi/m² $^{131}$I-labeled CC49 given 7 weeks apart, whereas this patient population was treated with four doses of 15 mCi/m² $^{131}$I-labeled CC49 given 2 weeks apart. These differences in dose schedule may also account for the lack of responses in this trial.

This trial showed that DSG can considerably reduce the human immune response to the murine mAb. Multiple infusions of $^{131}$I-labeled CC49 could be given safely with, in most instances, comparable targeting to tumor. The therapy was well tolerated, with fatigue, presumably secondary to infusion and imaging schedules, being the most common side effect. No
dose-limiting toxicity was noted. Despite a potentially therapeutic quantity of $^{131}$I-labeled CC49 being given, there were no responses seen.

The development of nonimmunogenic (e.g., humanized) forms of antibody that will permit multiple administrations is likely to be essential for effective radioimmunotherapy (22). Both chimeric (consisting of murine Fv attached to human Fc regions) and humanized (murine complementarity-determining region attached to a human framework) antibodies do consist of murine regions and can theoretically evoke an immune response. Immunomodulators such as DSG could successfully ameliorate such immune responses. This trial demonstrated that DSG reduced the host immune response to murine antibody and may therefore well abrogate an immune response following chimeric (about 33% murine) or humanized (about 5% murine) antibodies.

Similar results have been obtained using cyclosporine, another compound with immunomodulatory properties (23, 24). However, all of the trials utilizing cyclosporine have studied the safety of one repeat administration of the murine mAb administered at varying times following the initial murine mAb therapy. None of the trials examined immunomodulatory effectiveness following more than two infusions of the radiolabeled murine mAb, changes if any in antibody kinetics, or tumor targeting. Every trial utilized a different temporal and dose schedule of cyclosporine. However, all of the studies showed that cyclosporine therapy resulted in safe repeat administration of the radiolabeled murine mAb.

This trial also demonstrated that the HAMA titer and serum clearance are not the only parameters that determine successful repeat administration of the radiolabeled murine mAb. One patient with no evidence of HAMA prior to the third infusion of $^{131}$I-labeled CC49 nonetheless had anaphylactoid symptoms. This may have been due to the presence of circulating levels of IgM too small to be detected by high pressure liquid chromatography. The host immune response may also have a cellular component that is not reflected in any of the serological tests for HAMA outlined above; this would probably account for the decreased tumor targeting seen following some repeat infusions. Although these effects may not account for more than a small proportion of the overall host immune response, it is not possible to postulate whether the nature of the response would change following “less immunogenic” (e.g., chimeric or humanized) antibody administration.

DSG may reduce the human immune response to multiple infusions of $^{131}$I-labeled CC49, a radiolabeled murine mAb, administered to patients with metastatic colon cancer. This was evidenced by no acute side effects following most repeat infusions of $^{131}$I-labeled CC49, and no change in serum clearance or tumor targeting following most repeat administrations. There was no apparent relationship between the HAMA titers and symptomatology or tumor targeting, suggesting that the human response to xenogeneic antibody may consist of multiple humoral and cellular components. DSG was safe at the dose schedule used.

DSG may well abrogate any immune response to genetically engineered chimeric or humanized antibody.

REFERENCES


Fig. 5 Anterior whole-body images obtained 1 week after infusion of $^{131}$I-labeled CC49 in patient 6, who had liver metastases. Left to right, infusions 1–4.


Pilot radioimmunotherapy trial with 131I-labeled murine monoclonal antibody CC49 and deoxyspergualin in metastatic colon carcinoma.

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