Initial Experience Evaluating $^{90}$Yttrium-Radiolabeled Anti-Carcinoembryonic Antigen Chimeric T84.66 in a Phase I Radioimmunotherapy Trial

Jeffrey Y. C. Wong, Lawrence E. Williams, David M. Yamauchi, Tamara Odom-Maryon, Jose M. Esteban, Michael Neumaier, Anna M. Wu, David K. Johnson, F. James Primus, John E. Shively, and Andrew A. Rautbatschek


Abstract

Chimeric T84.66 (cT84.66) is a high-affinity ($5 \times 10^{10} \text{ M}^{-1}$) anti-carcinoembryonic antigen (CEA) IgG1. In a recently completed pretherapy imaging trial, $^{111}$In-labeled cT84.66 demonstrated targeting of CEA-producing metastatic sites and low immunogenicity, with human anti-chimeric antibody (HACA) response in only 1 of 15 patients after a single administration. The purpose of the present study was to evaluate cT84.66-diethylenetriaminepentaacetic acid labeled with $^{90}$Y in a dose-escalation Phase I trial. Patients with metastatic CEA-producing malignancies received imaging doses of 5 mCi $^{111}$In-labeled cT84.66 first, followed 1–2 weeks later by 5 mg cT84.66 labeled with the therapeutic dose of $^{90}$Y. Immediately following the therapeutic infusion, diethylenetriaminepentaacetic acid was administered by continuous i.v. infusion over 3 days at 250 mg/m$^2$ body surface area/24 h. Biodistribution, tumor targeting, absorbed radiation dose estimates, antibody clearance, and HACA response were evaluated through blood samples, 24-h urine collections, and nuclear images performed at serial time points after infusion. To date, three patients with metastatic colorectal cancer have been evaluated at the first dose level of 5 mCi/m$^2$. No side effects were associated with antibody administration. Localization of the antibody to nonhepatic metastatic sites was observed. Size-exclusion high-performance liquid chromatography demonstrated the formation of CEA:antibody complexes in serum in all three patients. A significant variation among patients in the clearance rate of the antibody and complexes from blood to liver was seen, which resulted in a reciprocal relationship between estimated liver dose and red marrow dose. Patients who demonstrated faster clearance to liver demonstrated greater excretion of a low-molecular-weight metabolite through the urine. Two patients developed HACA responses, which persisted at 4 months after therapy. At this first dose level, no tumor responses were seen and reversible grade 1 thrombocytopenia was observed in 2 patients.

cT84.66 demonstrated effective localization in CEA-producing tumors. Its low immunogenicity after a single administration makes it attractive for further evaluation as a radioimmunotherapeutic agent. However, further evaluation is needed to determine whether its immunogenicity will remain low after multiple administrations. Additionally, in two of the three patients, we identified rapid clearance of the antibody to the liver. This underscores the need to identify, characterize, and understand further those factors that influence the biodistribution and clearance of anti-CEA antibodies to allow for better selection of patients for therapy and rational planning of radioimmunotherapy.

Introduction

The use of radiolabeled monoclonal antibodies to deliver therapeutically doses of radiation to tumors is undergoing active investigation as a potential form of cancer therapy. Antibodies to a number of tumor-associated antigens have been and continue to be studied in Phase I and Phase II clinical trials (1–8). Several groups have evaluated antibodies directed against CEA as agents for radioimmunomaging (9–14) and radioimmunotherapy (15).

1 Presented at the “Fifth Conference on Radioimmunodetection and Radioimmunotherapy of Cancer,” October 6–8, 1994, Princeton, NJ. This work was supported by NIH Grant PO1 CA-43904.

2 To whom reprint requests should be sent, at City of Hope National Medical Center, 1500 East Duarte Road, Duarte, CA 91010.

3 The abbreviations used are: CEA, carcinoembryonic antigen; HACA, human anti-chimeric antibody; HAMA, human anti-murine antibody; DTPA, diethylenetriaminepentaacetic acid; mT84.66, murine T84.66; cT84.66, chimeric T84.66; ID, injected dose; CF, computed tomography; HPLC, high-performance liquid chromatography.

Materials and Methods

Antibody Production and Conjugation. Chimeric T84.66 is an intact IgG1 antibody derived from murine T84.66, an IgG1 monoclonal antibody developed at the City of Hope National Medical Center with high specificity and affinity (approximately $2 \times 10^{10} \text{ M}^{-1}$) for CEA (36, 37). It recognizes the A3 B3 domain of CEA and has little cross-reactivity with normal tissues. As reported by Neumaier et al. (38), genomic clones encoding for the heavy and light chains of T84.66 were isolated from the murine hybridoma. Chimeric genes were constructed by fusing the murine variable regions to the human constant regions, using restriction endonuclease cleavage sites located in the J–C introns. Chimeric light-chain (κ) and heavy-chain (γ1) genes were inserted into the expression vector pSV2-neo to yield the dual expression vector pSV2J3, containing both the heavy- and light-chain transcription units. Murine myeloma Sp2/0 cells were then transfected with the pSV2J3 plasmid by electroporation. Transfectomomas were then subcloned to yield a stable, virable, high producer. The affinity constant of the chimeric antibody was comparable ($5 \times 10^{10} \text{ M}^{-1}$) to the murine antibody. Large-scale production was accomplished using a hollow-fiber bioreactor. The antibody was purified through a two-step purification process, which included protein A affinity and anion exchange chromatography.

Purified antibody was conjugated to the isothiocyanatobenzoyl DTPA chelate of Sumerdon et al. (39). The ratio of chelate:antibody was determined to be 1:4:1 using the method of Meares et al. (40). Characterization of the purified product was assessed by SDS-PAGE (reducing and nonreducing conditions).
and by gel filtration chromatography. The immunoreactivity of cT84.66-DTPA conjugate was >90% by solid-phase CEA RIA.

Immunospecificity was evaluated by immunohistochemistry in more than 100 human colorectal cancers and 40 gastric cancers. Ninety-three % of tumors stained positive with cT84.66, which was similar to its murine antecedent. In addition, the percentage of stained cells, as well as the intensity and location of staining observed, were comparable to murine T84.66, with the majority of tumors demonstrating intense staining of >75% of cells. Seventy-five normal tissues were also evaluated by immunohistochemistry. No staining was seen with normal granulocytes, gallbladder, lung, kidney, spleen, liver, and stomach. There was weak staining at the apex of some of the cells of the intestinal tract.

The final avidal lot of purified antibody conjugate used in this study met standards set by Food and Drug Administration guidelines. An Investigational New Drug application for 111In- and 99mTc-labeled cT84.66 is currently on file with the Food and Drug Administration.

**Radiolabeling of Antibody.** Radiolabeling was performed by incubating the cT84.66-DTPA conjugate with 111In (Medi-Physics, Arlington Heights, IL) or 99mTc (Nordion International, Kanata, Ontario, Canada) for 30 min at room temperature, with the reaction stopped by the addition of 0.01 M sodium EDTA. Preclinical human serum stability testing demonstrated <4% of 111In activity dissociating from the antibody out to 216 h. Preclinical murine antibody biodistribution studies of 111In-labeled cT84.66-DTPA demonstrated targeting to CEA-producing colon carcinoma xenografts (LS174T) and normal organ biodistributions that were comparable with other intact 111In-labeled antibodies (35). Tumor uptakes in the range of 70%/ID/g at 48—72 h after infusion were observed. These studies also demonstrated comparable biodistributions between the 111In- and 99mTc-labeled cT84.66-DTPA.

Prior to each administration, the sample was purified by size-exclusion HPLC (TSK-G3000 column) and tested for endotoxin by limulus amoebocyte lysate assay (BioWhittaker, Walkersville, MD) and isoipe binding by instant TLC before patient administration. For all administered doses, radiolabeling of >90% and endotoxin levels of <1 units/ml was demonstrated. Immunoreactivity by solid-phase CEA RIA was consistently >95%.

**Clinical Trial Design.** Chimeric T84.66, radiolabeled with 111In or 99mTc, was evaluated in a Phase I dose escalation radionuclide ablative trial, which is currently ongoing. The primary objective of this trial was to determine the maximum tolerated dose of 99mTc-cT84.66 when administered i.v. and to characterize the associated toxicities. Biodistribution, tumor targeting, absorbed radiation dose estimates, and clearance of the antibody were also evaluated through blood samples, 24-h urine collections, and nuclear scans performed at time points out to 7 days after antibody infusion.

Patients were eligible if they were 18 years of age or older and had evidence of metastatic disease that was CEA producing and refractory to conventional therapies. Tumor CEA production was documented by either an elevated serum CEA or positive CEA immunohistochemistry staining of tumor biopsy specimens. Serum CEA was assayed using a commercially available enzyme immunoassay (Hoffmann LaRoche Inc., Nutley, New Jersey). Blood CEA levels were compared with pharmacokinetic parameters of antibody clearance from the plasma. All patients had to demonstrate a Karnofsky performance status of >60%, a predicted life expectancy of at least 3 months, completion of any previous therapy 4 weeks prior to antibody therapy, and adequate renal, pulmonary, and hepatic function. Patients with histories of previous antibody exposure and positive HAMA or HACA responses were excluded from the study. In addition, patients with active brain or leptomeningeal metastatic disease, previous radiotherapy to the whole pelvis or to >50% of the bone marrow, or previous exposure to nitrosoureas or mitomycin-c were excluded. The following studies were performed prior to antibody administration: differential blood count; Sequential Multiple Analysis-18; creatinine clearance; electrocardiogram; pulmonary function tests; urinalysis; serum HIV testing; serum pregnancy testing, if indicated; plasma CEA levels; serum HACA response; chest X-ray; and CT scans of relevant anatomic locations corresponding to areas of metastatic or suspected metastatic disease. CT scans were obtained using a General Electric BiSpeed Advantage system. If clinically indicated, bone scans or magnetic resonance imaging scans were performed to assess disease location and extent. All blood studies were done within 2 weeks, and all radiological studies were done within 6 weeks of antibody infusion.

Each patient received first an imaging dose of 111In-cT84.66, which was radiolabeled at a ratio of 5 mCi 111In:5 mg protein. Initially, a test dose of 100 μg radiolabeled antibody was administered i.v. over 5 min. After 15 min, if there were no side effects, the remainder of the antibody was administered. Antibody was delivered i.v. at a rate of 2 ml/min (0.2 mg/min) to deliver the entire antibody dose (50-ml volume) over approximately 25 min. Serial blood samples were taken for pharmacokinetics at 30 min, 1, 2, and 6 h, and at each scan time after antibody infusion. Urine collections (24 h) were done daily for 5 consecutive days after antibody administration for pharmacokinetic analysis. Blood and urine samples were counted for 111In activity on a Packard gamma counter (model 5530; Packard, Inc., Downers Grove, IL) with a window setting of 150—500 keV and were processed on a size-exclusion HPLC Superose 6 column. Planar and whole-body imaging studies were performed at 6, 24, and 48 h and 4—7 days after antibody administration using a Toshiba 901 HG camera with single-photon emission CT capability. In all cases, 20% energy windows were set over each of the two γ-ray energies of 111In. A medium-energy, high-resolution collimator was used throughout. A scan speed of 20 cm/min over a distance of 200 cm was used for the whole-body imaging. Single-photon emission CT scans were performed of relevant areas at 48 h and 4—7 days after antibody administration. A bowel cathartic was administered to patients prior to each scan to reduce normal bowel uptake, unless it was thought that the patient could not tolerate such a preparation.

For this trial, a maximum of three therapy cycles at 6—7 weeks intervals was planned for each patient. Toxicity was scored using the Southwest Oncology Group toxicity criteria. Informed written consent was obtained for each patient prior to protocol entry. This protocol had full review and approval from the City of Hope Institutional Review Board.

**Analysis of HACA Response.** The serum HACA response to cT84.66 and cT84.66-DTPA was assayed prior to infusion and at planned time points of 2 weeks and 1, 3, and 6 months after infusion using a double-capture, solid-phase, quantitative RIA, similar to that published by LoBuglio et al. (32). Briefly, patients’ sera were diluted 1:4 or 1:5 in normal saline, and 100 μl each dilution were pipetted into quadruplicate glass tubes. To each tube, 100 μl 111In-labeled cT84.66 (approximately 100,000 cpm) were added. Polystyrene beads coated with cT84.66 or cT84.66-DTPA were then added to the tubes, incubated at room temperature for 90 min, and then washed. The beads were counted on a Packard gamma counter (model BS5003) with a window setting of 150—500 keV. Serial dilutions of a goat antihuman Fc preparation of known concentration was used to generate a standard curve from 12.5 to 200 ng/ml. One % BSA in PBS was used as a negative control. A sample was scored positive if it was >12.5 ng/ml, the limit of sensitivity of this particular RIA.

**Pharmacokinetic Analysis and Dosimetry Estimates.** Whole-body and normal organ absorbed radiation doses were estimated from serial 111In scans of the whole body and local anatomical areas. Opposed images were used to construct the geometric mean uptake as a function of time for those organs seen in both projections. Otherwise, single-view images were acquired. All resultant curves on 111In activity versus time were corrected for background and patient attenuation. Attenuation was estimated using a separate series of experiments involving gamma camera efficiency in counting a 111In phantom source as a function of tissue-equivalent absorber thickness.

Given the geometric mean or single-view uptake values, residence times for 99mTc (41) were calculated. Using the ADAPT II software (42), a five-compartment model was used to fit the biodistribution data for the blood, liver, urine, and total body. In the model, blood served as the central (mamillary) compartment, with liver, residual body, urine, and fecal excretion as the other compartments. Modeling of the data was done separately for the imaging and therapeutic 111In infusions. A single rate input into the blood compartment was specified. Residual activity was constrained to be equal to the difference between the total-body activity and the sum of the blood and liver activity.
Results

Patient Results. To date, three patients have been entered in this trial at the first dose level of 5 mCi/m² 99Y-cT84.66. The clinical courses of these patients are summarized in Table 1. All three patients had extensive metastatic colorectal cancer with elevated CEA levels ranging from 97 to 302 ng/ml. CEA immunohistochemistry also was performed on tumor samples from patients 1 and 2 and demonstrated intense and diffuse (>90% cells) tumor staining. All three patients had received two regimens of chemotherapy previously but had not received radiotherapy or monoclonal antibodies previously. Antibody localization to metastatic sites in the abdominal wall, mesentery, and pelvis was seen in patient 1 (Fig. 1). Patients 2 and 3 had only liver metastases, which were imaged as photopenic lesions due to uptake of activity by normal liver, as has been observed with other 111In-labeled antibodies (10, 22, 34). Nuclear images were similar after the first and second antibody infusions.

There were no side effects or changes in vital signs associated with the antibody infusion. Two of the three patients developed grade 1 thrombocytopenia, which recovered to baseline. Patient 1 developed headaches and nausea 24 h after initiation of DTPA, which resolved with reduction of the DTPA dose. No other toxicities related to the therapy were observed. At this first dose level, all patients demonstrated tumor progression at 6–10 weeks after therapy, preventing the administration of a second cycle of radiolabeled antibody.

Evaluation of Immunogenicity. Patients 1 and 2 developed HACA responses as early as 2 weeks after the therapeutic infusions. Two of the three patients developed grade 1 thrombocytopenia, headaches, and nausea from DTPA. Patient 1 had a negative HACA response when evaluated at 1 month after the therapeutic infusion. He died prior to the planned 3-month sample.

Pharmacokinetics and Dosimetry Estimates. As observed in the pilot imaging trial (35), significant differences between patients in the rate of antibody clearance from the blood to the liver were observed. Fig. 3 shows antibody uptake and clearance as a function of time for blood, liver, and urine for patients 1 and 3. Patient 1 demonstrated relatively slow blood clearance of the antibody to the liver, whereas patient 3 demonstrated rapid clearance to the liver. Pharmacokinetics for patient 2 was similar to that of patient 3, with rapid clearance of antibody from the blood to the liver. This interpatient variation in clearance kinetics resulted in variations in projected organ doses and a reciprocal relationship between liver and red marrow doses (Table 2). Size-exclusion HPLC demonstrated the formation of CEA:antibody complexes in serum after antibody infusion (Fig. 4). In patients with high liver accumulation, the CEA complexes disappeared quickly from the serum, whereas in those patients with lower liver accumulation, serum CEA levels remained elevated beyond 3 months after infusion and continue to be followed. Patient 3 had a negative HACA response when evaluated at 1 month after the therapeutic infusion.

Table 1 Clinical summary of patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)/sex</th>
<th>Diagnosis</th>
<th>Pre-infusion CEA (ng/ml)</th>
<th>Previous therapy</th>
<th>Administered 90Y activity (mCi)</th>
<th>Tumor response</th>
<th>Toxicities</th>
<th>HACA response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>47/female</td>
<td>Colorectal cancer with abdominal wall, mesenteric, and pelvic metastases</td>
<td>97</td>
<td>5-FU/leucovorin, i.p. IUdR*</td>
<td>7.5</td>
<td>Progression at 6 wk</td>
<td>Reversible grade 1 thrombocytopenia, headaches and nausea from DTPA</td>
<td>Positive beginning at 2 wk after infusion</td>
</tr>
<tr>
<td>2</td>
<td>57/female</td>
<td>Colorectal cancer with liver metastases</td>
<td>294</td>
<td>5-FU/leucovorin, hydroxyurea</td>
<td>9.5</td>
<td>Progression at 10 wk</td>
<td>None</td>
<td>Positive beginning at 2 wk after infusion</td>
</tr>
<tr>
<td>3</td>
<td>55/male</td>
<td>Colorectal cancer with liver metastases</td>
<td>302</td>
<td>cis-platinum/FludR/leucovorin, CPT-11</td>
<td>9.9</td>
<td>Progression at 8 wk</td>
<td>Reversible grade 1 thrombocytopenia</td>
<td>Negative at 1 mo after infusion</td>
</tr>
</tbody>
</table>

\* 5-FU, 5 Fluorouracil; IUdR, iododeoxyuridine; FludR, fluoroodeoxyuridine; CPT-11, irinotecan.
Table 2 Estimated total radiation doses to normal organs

<table>
<thead>
<tr>
<th>Patient</th>
<th>Liver (cGy)</th>
<th>Marrow (cGy)</th>
<th>Spleen (cGy)</th>
<th>Total Body (cGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>234.1</td>
<td>67.0</td>
<td>245.8</td>
<td>14.7</td>
</tr>
<tr>
<td>2</td>
<td>471.2</td>
<td>37.7</td>
<td>258.2</td>
<td>16.6</td>
</tr>
<tr>
<td>3</td>
<td>432.4</td>
<td>42.6</td>
<td>197.1</td>
<td>16.8</td>
</tr>
</tbody>
</table>

*Radiation dose estimates to normal organs from the therapeutic infusions are presented for the three patients. Contributions from both 111In and 90Y were taken into account in estimating doses. Details of the dosimetry methods used are presented in "Materials and Methods."
done on 4 patients going to surgery 1–2 weeks after antibody infusion, during which biopsies were performed to evaluate tumor uptake. Primary tumor doses ranged from 2.2 to 47.0 cGy/mCi 90Y, for an average of 20.6 cGy/mCi 90Y, which is comparable to what has been reported for murine T84.66 (46).

Based on these results, a Phase 1 dose escalation therapy trial was initiated. Both the imaging and therapy antibody administrations were well tolerated, and the antibody localized to CEA-producing metastatic sites. Formation of antigen:antibody complexes was observed by HPLC soon after antibody administration. As with the imaging trial, variations in antibody clearance and metabolism between patients were noted. These differences were primarily in the clearance rate of antigen:antibody complexes from the blood to the liver. Patients 2 and 3, for example, demonstrated faster serum clearance and higher liver uptake of the antibody compared with patient 1. The reasons for such interpatient variability are unclear but may, in part, be related to the degree of metastatic tumor burden in the liver. Of the 29 patients evaluated with cT84.66 in this and other imaging protocols at this institution, there have been 3 patients, including the 2 patients in this trial, with unusually rapid clearance of antibody to the liver. All 3 of these patients had significant metastatic tumor burden in the liver. Patients with smaller liver metastases did not show rapid clearance to the liver. In addition, at this time, liver clearance does not seem to be related to total-body tumor burden or to elevations in liver function studies.

Intepatient variability in blood clearance resulted in a reciprocal relationship between radiation dose estimates to the red marrow and liver, which correlated with the toxicities observed. Patient 1 had typical clearance kinetics and received the highest radiation-absorbed dose to the marrow. This resulted in grade 1 thrombocytopenia, with a count nadir at 4 weeks and recovery to baseline by 8 weeks. The time course of thrombocytopenia is similar to what has been observed with other radioimmunotherapeutic agents (1–8). Patients 2 and 3 had more rapid clearance of antibody to the liver, resulting in lower marrow doses. Patient 2 had no observed hematological toxicity. Patient 3 had grade 1 thrombocytopenia soon after therapy, with a nadir at 1 week after infusion and recovery to baseline by 6 weeks. The time course of thrombocytopenia, however, was not typical of radioimmunotherapy-induced marrow toxicity at the activities administered in this trial. The observed thrombocytopenia in patient 3 may be due in part to hepatic irradiation, because a rapid drop in platelet count has been observed after whole-liver irradiation, as reported by Vriesendorp et al. (47) in the beagle dog model, and is thought to be secondary to trapping of platelets in the liver.

Intepatient variation in the rate of activity cleared through the urine was also observed. Urinary activity was in the form of a low-molecular-weight metabolite. Patients 2 and 3, with higher and more rapid uptake of antibody to the liver, demonstrated greater excretion of this low-molecular-weight metabolite, which was enhanced after the therapeutic infusion. These observations suggest that 111In-cT84.66 undergoes formation of antigen:antibody complexes in serum, which are cleared to and metabolized by the liver and excreted out through the urine as a low-molecular-weight metabolite. Patients 2 and 3 demonstrated greater liver uptake, more rapid metabolism, and, therefore, a greater and more rapid excretion of the low-molecular-weight metabolite through the urine.

In our previous imaging trial, a HACA response after single administration of chimeric T84.66 was observed in only 1 of 15 patients. In the current therapy trial, two of the three patients have developed HACA. This may indicate that the immunogenicity of the antibody is increased after more than one administration, because each patient in the therapy trial received an imaging followed by a therapy infusion of the antibody. However, more patients need to be evaluated to characterize fully the frequency and titer of the HACA response after multiple cT84.66 administrations.

Rapid clearance of radiolabeled antibody to the liver may lessen marrow toxicity but can compromise tumor uptake and increase the risk of hepatic toxicity. One possible strategy to improve antibody biodistribution is to administer unlabeled or "cold" antibody prior to the radiolabeled antibody. Beatty et al. (48) demonstrated up to a 3-fold reduction in liver uptake without compromising tumor uptake if up to 0.2 mg unlabeled mT84.66 was administered prior to a 2-µg dose of 111In-labeled mT84.66 in nude mice bearing LS174T colon cancer xenografts. Blood uptake also was increased up to 3-fold by cold antibody infusion, reflecting the delayed clearance of antibody: antigen complexes to the liver. The effect seemed to be saturable, because higher doses of unlabeled mT84.66 (2.0 mg) resulted in no further decrease in hepatic uptake and began to decrease tumor uptake. Based on these results, we have initiated an imaging trial in patients with colorectal cancer in which unlabeled cT84.66 is given prior to the radiolabeled dose. The unlabeled dose is escalated in cohorts of five patients. We are currently at a level of 25 mg unlabeled cT84.66 and have yet to observe significant differences in liver uptake or clearance kinetics of the radiolabeled antibody. As predicted from the initial murine experiments, we anticipate that hundreds of µg monoclonal antibody may be needed to alter human antibody biodistribution of this construct, particularly in those patients demonstrating unusually rapid clearance of the antibody to the liver.

cT84.66 is a high-affinity anti-CEA antibody that demonstrates localization to CEA-producing tumors. Although the incidence of HACA seems to be low after a single administration, further evaluation is needed to determine whether its immunogenicity will remain low after multiple administrations. Finally, two of three patients demonstrated unusually rapid clearance of the antibody to the liver, leading potentially to unfavorable biodistributions. This underscores the need to identify, characterize, and understand further those factors that influence the biodistribution of radiolabeled anti-CEA antibodies, to allow for better selection of patients for therapy and rational planning of radioimmunotherapy.

Acknowledgments

We thank Lupe Ettinger, R.N. (protocol nurse); Gina Farino, B.S. (data manager); James Kao, M.S., and Randall Woo, M.S. (radiopharmacy); George Lopatin, B.S. (dosimetry); Akiko Chai, M.S. (biostatistics); and Kathleen Thomas, C.N.M.T., Ron Fomin, C.N.M.T., and Joy Bright, C.N.M.T. (nuclear medicine) for their contributions.
Initial Experience Evaluating $^{90}$Yttrium-Radiolabeled Anti-Carcinoembryonic Antigen Chimeric T84.66 in a Phase I Radioimmunotherapy Trial

Jeffrey Y. C. Wong, Lawrence E. Williams, David M. Yamauchi, et al.

*Cancer Res* 1995;55:5929s-5934s.

Updated version Access the most recent version of this article at: http://cancerres.aacrjournals.org/content/55/23_Supplement/5929s

E-mail alerts Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.