Production and Characterization of 188Re-C595 Antibody for Radioimmunotherapy of Transitional Cell Bladder Cancer

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Bladder cancer was responsible for >12,000 deaths in the United States in 1999. The high-molecular-weight glycoprotein MUC1 mucin is overexpressed on bladder tumors and represents a useful target for radioimmunoscintigraphy and radioimmunotherapy. We report on the production and initial tracer studies of a 188Re-antibody complex directed against this target and intended for intravesical radioimmunotherapy of superficial bladder cancer. Methods: 188Re perrhenate was eluted from a 188W/188Re generator. C595 antibody was reduced with 2-mercaptoethanol and was labeled in the presence of stannous tartrate. The final reaction mixture contained high-molecular-weight contamination, which was removed from the complex using an affinity separation technique. The specificity and integrity of the antibody complex were tested by radioimmunoassay and size exclusion chromatography. Tumor localization was investigated using an ex vivo model in human cystectomy specimens. Tracer amounts of the complex were also administered intravesically to three patients with bladder cancer, who were then imaged by γ scintigraphy. Results: The complex was immunoreactive (70% ± 17%) and specific for MUC1 antigens. A peak corresponding to a protein of 150 kDa was observed on size exclusion chromatography, showing that the complex was homogeneous. Binding to bladder tumors was observed in an ex vivo model in which tumors were successfully imaged in four specimens. The mean tumor-to-normal tissue ratio in ex vivo bladders was 7:1. Tumor uptake after intravesical administration was confirmed in three patients with bladder cancer (mean tumor-to-normal tissue ratio, 4:1). Conclusion: The C595 antibody was labeled with 188Re, providing a radioimmunconjugate with high immunoreactivity and specificity. Its ability to localize in tumors both in an ex vivo model and after intravesical administration to patients has been shown. This approach will now be extended for the therapy of superficial bladder cancer. Key Words: monoclonal antibody; radioimmunotherapy; 188Re; bladder cancer


B bladder cancer is the fourth most common cancer in men in the United States (1). Most patients have superficial disease (Ta, T1) that has not invaded muscle, but up to 70% of these tumors will recur. Around 12% of superficial tumors will ultimately progress to invasive disease, requiring radical treatment such as cystectomy or radiotherapy, which has a poor prognosis. Most superficial tumors can be controlled by transurethral resection with or without intravesical chemotherapy or immunotherapy. Undoubtedly, intravesical instillations can reduce tumor recurrence; however, there is no evidence that these adjuvant therapies can prevent progression to life-threatening invasive disease (2).

Radioimmunotherapy, which involves the conjugation of cytotoxic nuclides to tumor-specific antibodies to deliver a lethal dose of radiation specifically to tumor cells, is an attractive concept. In practice, there have been many difficulties when immunoconjugates of murine origin have been given intravenously to treat solid tumors. However, intracavitary therapy to regions such as the peritoneum or ventricles of the brain allows direct delivery of a radioimmunoconjugate to the site of tumor and may overcome some of the difficulties encountered when the intravenous route is used. The intracavitary approach may be applied to the bladder, where there is a natural port of access through the urethra allowing radioimmunoconjugates to be delivered easily through a catheter. In addition, minimal systemic leakage occurs when radioimmunoconjugates are instilled into the bladder, which negates the Human Anti-Mouse Antibody (HAMA) response (3), thereby potentially allowing multiple treatments.

MUC1 mucin is a high-molecular-weight glycoprotein that is found on normal urothelium, where it has a protective function (4,5). Most of the molecule is comprised of up to 100 repeats of a 20–amino acid sequence known as the variable number tandem repeat (VNTR) sequence (6). MUC1 mucin is both upregulated and abnormally glycosylated in bladder cancer, which exposes novel regions of the protein core, giving it potential as a tumor target antigen (7).
The monoclonal antibody C595 (8) has been well characterized and found to recognize a tetrapeptide motif (RPAP) within the VNTR region of the protein core (9).

Previous studies involving conjugates of C595 include 111In (10), 67Cu (3,11), and 99mTc (12) radiolabels and have shown that it is possible to target bladder tumors after intravesical administration. 188Re is a dual β- and γ-emitting radionuclide that has many advantages over other therapeutic nuclides for use in the system we describe. The physical half-life of 188Re is 17 h, and its maximum particle range of 11 mm will just penetrate through the thickness of the bladder wall. The γ emission of 188Re will also allow imaging and dosimetric estimations to be performed. Most important, however, from a practical point of view, is that 188Re can be obtained from a 188W/188Re generator in a carrier-free form as sodium perrhenate (7).

The aim of this study was to achieve efficient labeling of C595 antibody with 188Re and then to characterize the antibody complex to assess its suitability for intravesical radioimmunotherapy of bladder cancer.

MATERIALS AND METHODS

Monoclonal Antibodies

Monoclonal antibody C595 (anti-MUC1 mucin, IgG3) was originally produced using conventional hybridoma technology (14) with spleen cells from a BALB/c mouse immunized against purified MUC1 urinary mucin (8). Production of C595 containing supernatant was performed by Serotec Ltd. (Oxford, U.K.) using standard tissue culture media and incorporating the use of hollow fiber cell culture methods (CELLine membrane technology; Integra Biosciences, Letchworth, U.K.). Cell-free supernatants were clarified by ultracentrifugation (40,000 rpm) and ultrafiltration (0.45 μm) and purified by epitope affinity chromatography (15). The nonspecific control monoclonal antibody 1H11 (anti-dust mite antigen) was prepared from exhausted media from static cultures of its hybridoma and purified by antigen affinity chromatography.

Labeling Procedures

188Re was obtained from the decay of 188W on an aluminum oxide column in a bench-top generator (Medigen-Re generator; MAP Medical Technologies, Tikkakoski, Finland). The 188Re was eluted from the generator in sterile NaCl (0.9% w/v) at room temperature in the form of sodium perrhenate solution.

A direct reduction-mediated technique was used to label the C595 antibody with 188Re (16). Antibody was initially reduced by the addition of 2-mercaptoethanol ([2ME] Sigma Chemical Co., Dorset, UK) at a molar ratio of 1,000:1 (2ME:antibody). After a 30-min incubation at room temperature, excess thiol was removed using a prepacked Sephadex G25 desalting column (PD-10 column; Pharmacia Biotech, Uppsala, Sweden) pre-equilibrated with phosphate-buffered saline (PBS), pH 7.4. The protein concentration was determined spectrophotometrically at 280 nm (Ε1% 1cm , 14.3) and the antibody was stored in 0.5-mg fractions at −80°C until it was required.

A solution of stannous tartrate was prepared in acetate-buffered saline at the appropriate pH (range, 3.9–5.2) such that the molar ratio of sodium tartrate (Sigma) to stannous chloride (Sigma) was 9:1. Stannous tartrate was added to an aliquot of reduced antibody to a final molar ratio of 1:150 stannous ions to one antibody. The required amount of 188Re–sodium perrhenate was then added, and the reaction was allowed to proceed under anaerobic conditions at room temperature with agitation for 2 h. Free 188Re was separated from radiolabeled antibody by gel filtration chromatography using a prepacked PD-10 column. Carrier protein in the form of bovine serum albumin ([BSA] 1% w/v), ascorbic acid (0.2% w/v), or both were then added to appropriate samples for stability analysis.

Monoclonal antibody 1H11 for use as the negative control in ex vivo experiments was labeled with 99mTc after first being partially reduced with 2ME as described. The labeling procedure was performed according to the method of Mather and Ellison (17). Briefly, a vial of Medronate II Agent (Nycomed Amersham, Amersham, U.K.) was reconstituted with sterile saline for injection (5 mL). An aliquot (100 μL) was then added to the partially reduced antibody solution, followed by addition of the required quantity of 99mTc–sodium pertechnetate. The reaction was allowed to proceed at room temperature for 10 min, followed by separation of the 99mTc-antibody complex from free 99mTc using a PD-10 column. In all cases, labeling efficiency was calculated as the amount of activity in the antibody-containing fractions eluted from the PD-10 column expressed as a percentage of the total activity added to the column.

Immunoreactivity Determination

Synthetic target antigen was produced by conjugating a MUC1-related peptide (APDTRPAPG) to CNBr-activated Sepharose 4B (Pharmacia Biotech) at a ratio of 1 μmol peptide per milliliter gel according to the manufacturer’s instructions. Slurries (25%) of peptide-coated Sepharose beads and unconjugated Sepharose beads in PBS containing BSA (1% w/v) were prepared. These were then used to produce a set of antigen standards by mixing peptide-conjugated Sepharose with unconjugated beads to a final volume of 200 μL. Synthetic antigen tubes contained 25, 50, 100, or 200 μL peptide-coated beads, and negative control tubes (to test for nonspecific binding) that contained 200 μL unconjugated Sepharose or 200 μL buffer were included. PBS containing BSA (1% w/v) was added as a blocking agent to a final volume of 0.5 mL. 188Re-labeled antibody was diluted to 100 ng/mL in blocking buffer, and 0.5 mL was added to each antigen tube. The tubes were incubated at 4°C for 4 h with agitation, followed by centrifugation for 1 min at 13,000 rpm (Microcentaur; Sanyo Gallenkamp PLC, Loughborough, U.K.) to sediment the Sepharose beads. An aliquot (200 μL) of supernatant from each reaction was removed and placed in a fresh tube. All pellet and supernatant tubes were analyzed for 188Re activity by scintillation counting (1282 Compu gamma; LKB Wallac, Turku, Finland). The immunoreactivity of the labeled antibody was calculated as the proportion of antibody bound to antigen at theoretic infinite antigen excess by linear regression analysis, plotting the reciprocal of the amount of antigen-coated Sepharose against the reciprocal of the fraction of bound antibody complex (18).

Affinity Separation of 188Re-C595 from High-Molecular-Weight Contamination

An aliquot (0.5 mL) of MUC1-related peptide conjugated to Sepharose beads (as described) was mixed with the 188Re-C595 crude preparation and rolled at 4°C for 1 h. The Sepharose was then layered on top of a PD-10 column, and an AC-16 adapter end net (Pharmacia Biotech) was placed on top of the affinity/gel filtration column composite. The system was then washed with 12 mL PBS; this was followed by washing with NaSCN (3 mol/L, 2
Gel Filtration Chromatography of each well was measured by scintillation counting.

After tapping the plate dry on tissue paper, it was cut into individual wells and the activity containing Tween 20 (0.1% v/v; Sigma). After incubation at room temperature for 1 h. The fluid was then aspirated from each well and the plate was washed four times in PBS (0.3 mL/min). Blue dextran (5 mg/mL; Sigma) was placed 1 cm from the bottom of the strip, which was placed in PBS. Each well was blocked with PBS containing BSA (1% w/v, 75 μL per well) for 1 h at room temperature. Serial dilutions of the radiolabeled antibody (0.01–10 μg/mL) were prepared and dispensed into the wells of the plate (50 μL per well), followed by incubation at room temperature for 1 h. The fluid was then aspirated from each well and the plate was washed four times in PBS containing Tween 20 (0.1% v/v; Sigma). After tapping the plate dry on tissue paper, it was cut into individual wells and the activity of each well was measured by scintillation counting.

**Antibody Complex Specificity**

The specificity of the antibody complex was investigated by measuring its binding to a selection of antigenic materials that had been adsorbed to the surface of a microtiter plate. Antigens used were affinity-purified urinary MUC1 mucin, MUC1-related peptide (APDTRPAPG) conjugated to BSA, MUC2-related peptide (PTPTPTGTPTQT) conjugated to BSA, and BSA alone (1% w/v in PBS). Each well was blocked with PBS containing BSA (1% w/v, 75 μL per well) for 1 h at room temperature. Serial dilutions of the radiolabeled antibody (0.01–10 μg/mL) were prepared and dispensed into the wells of the plate (50 μL per well). After incubation at room temperature for 1 h, the fluid was then aspirated from each well and the plate was washed four times in PBS containing Tween 20 (0.1% v/v; Sigma). After tapping the plate dry on tissue paper, it was cut into individual wells and the activity of each well was measured by scintillation counting.

**Gel Filtration Chromatography**

The molecular homogeneity of the affinity-purified 188Re-C595 was analyzed by gel filtration chromatography. A chromatography column (1.6 × 90 cm) was packed with Sephacryl S300 HR (Pharmacia Biotech) and equilibrated with 300 mL PBS. Analytes were loaded onto the column and fractions were collected throughout elution in PBS (0.3 mL/min). Blue dextran (5 mg/mL; Sigma) was used to determine the void volume of the column. Unlabeled C595 antibody (10 mg/mL) was applied to the column and the fractions were analyzed spectrophotometrically at 280 nm. Affinity-purified 188Re-C595 was then applied to the column, followed by rhenum perphenate; the elution fractions were analyzed for radioactivity by scintillation counting.

**Analysis of Stability of 188Re-C595**

The stability of the labeled antibody preparation was assessed by instant thin-layer chromatography (ITLC). Silica gel–impregnated glass fire sheets (Gelman Sciences, Ann Arbor, MI) were cut into 10 × 1 cm strips. An aliquot of the labeled antibody was placed 1 cm from the bottom of the strip, which was placed in a solvent (NaCl, 0.9% w/v) that allowed free 188Re to migrate with the solvent front while 188Re-C595 complex remained at the origin. The strip was analyzed with a scintillation counter that plotted activity against the length of the strip. Analysis of the peaks yielded a labeling efficiency of 25.8% and a mean labeling efficiency was 59.9% ± 22.9% (n = 12). However, a significant level of high-molecular-weight contaminating material that observed strongly at 280 nm was observed at this pH and could not be separated from the antibody complex using G25 gel filtration chromatography. Subsequent labeling reactions were performed at pH 4.5 and yielded a labeling efficiency of 62.1% ± 25.8% (n = 14). The level of high-molecular-weight contamination in samples of antibody complex labeled at this pH was reduced. The mean immunoreactive fraction of the complex labeled at pH 6.0 was 58.8% ± 11.6% and was lower than that of antibody labeled at pH 4.5 (70.4% ± 16.9%), reflecting the degree of contamination with labeled species that was non-reactive. No evidence of nonspecific binding was observed for complexes labeled at either pH during immunoreactivity testing.

**RESULTS**

**188Re Labeling of C595 Antibody**

Initial labeling reactions were performed at pH 6.0. The mean labeling efficiency was 59.9% ± 22.9% (n = 12). However, a significant level of high-molecular-weight contaminating material that absorbed strongly at 280 nm was observed at this pH and could not be separated from the antibody complex using G25 gel filtration chromatography. Subsequent labeling reactions were performed at pH 4.5 and yielded a labeling efficiency of 62.1% ± 25.8% (n = 14). The level of high-molecular-weight contamination in samples of antibody complex labeled at this pH was reduced. The mean immunoreactive fraction of the complex labeled at pH 6.0 was 58.8% ± 11.6% and was lower than that of antibody labeled at pH 4.5 (70.4% ± 16.9%), reflecting the degree of contamination with labeled species that was non-reactive. No evidence of nonspecific binding was observed for complexes labeled at either pH during immunoreactivity testing.

The chromatogram resulting from the purification on the combined affinity/gel filtration column is shown in Figure 1. It could be seen that a peak of active material that had an absorbance at 280 nm was washed from the column with PBS. This was assumed to be high-molecular-weight con-
taminating species. On addition of 3 mol/L NaSCN to the column, a second peak of material with a high absorbance was eluted and was subsequently found to bind to MUC1 mucin by radioimmunoassay. The third peak of material that was not radioactive was identified as NaSCN, which had been separated from the antibody complex while passing through the gel filtration component of the system. The mean increase in immunoreactivity of affinity-treated complex compared with nontreated material was 24.5% (n = 4).

In Vitro Characterization of 188Re-C595

The specificity of the 188Re-C595 complex was investigated by measuring the level of binding to a range of antigens using a radioimmunoassay. We observed a high level of binding to the MUC1-related antigens that titrated out at low antibody concentration. However, no reactivity with the irrelevant antigens was observed (data not shown).

The molecular homogeneity of the 188Re-C595 complex was analyzed by gel filtration chromatography on a Sephacryl S300 HR column (Fig. 2). The void volume of the column was determined to be 102 mL. The major peak of unlabeled C595 antibody was found to elute at 132 mL, with a smaller peak of material (presumably aggregated protein) eluting in the void volume. Affinity-purified 188Re-C595 was found to elute in a single peak that corresponded with the major peak of unlabeled C595 antibody (138 mL). The peak was followed by a small shoulder of radioactive material. This peak had a molecular weight of >66 kDa and was therefore not dissociated antibody heavy or light chains. However, it may have been caused by larger antibody fragments, such as associated heavy and light chains (75 kDa).

Stability of 188Re-C595

The stability of 188Re-C595 was analyzed by ITLC and immunoreactivity testing over a period of 22 h after labeling. Figure 3 illustrates the stability of the antibody complex during storage at room temperature together with data showing the effect of the addition of a carrier protein (BSA), ascorbic acid, or both on stability. Immediately after labeling, all radioactivity was bound to antibody, and the antibody complex was determined to be 66% immunoreactive at this time. Subsequent ITLC analyses revealed that the 188Re became dissociated from the antibody with storage at room temperature, with the degree of dissociation being reduced slightly in the presence of BSA and ascorbic acid. However, the most marked effect was observed when both BSA and ascorbic acid were added to the preparation after labeling. The proportion of activity remaining bound to the antibody 22 h after labeling was 54% with both additives present and 26% with the untreated antibody complex. In addition, at 24 h after labeling, the immunoreactive fraction...
fell to 30% in the presence of BSA and ascorbic acid and 8% with no additives.

Tumor Targeting in Ex Vivo Model

Tumor localization was examined in five ex vivo cystectomy specimens. The mean immunoreactive fraction of \(^{188}\)Re-C595 preparations used was 64\% ± 8.7\%. Binding to tumors was observed in four bladders, with the mean tumor-to-normal tissue ratio being 7.1:1. The mean tumor uptake was 7.9\% ± 5.4\% of the injected dose per gram tissue. An example of the image obtained by \(\gamma\) scintigraphy is shown in Figure 4A; Figure 4B shows the cystectomy specimen from which the image was taken, dissected to reveal the tumor in the lumen. A fifth bladder with no evidence of carcinoma after pathologic examination showed no uptake of \(^{188}\)Re-C595, although the immunoreactivity of this preparation was 74\%.

To determine whether tumor localization was associated with a specific immune recognition event or merely associated with nonspecific binding of protein, an irrelevant antibody (1H11) was compared with that of \(^{188}\)Re-C595 in an ex vivo experiment. \(^{99m}\)Tc-1H11 antibody was instilled into the cystectomy specimen. After washout and gamma-camera imaging, the \(^{188}\)Re-C595 complex was instilled into the same bladder. The imaging procedure was repeated and no tumor localization of the irrelevant antibody occurred, whereas the \(^{188}\)Re-C595 showed positive tumor uptake (data not shown). The tumor-to-normal tissue ratio was calculated from weighing and counting the dissected tissue and was found to be 2.5:1 after instillation of \(^{188}\)Re-C595.

Intravesical Tracer Studies

To confirm that the \(^{188}\)Re-C595 complex could localize in tumors in patients, a tracer dose was administered to a small group of patients (\(n = 3\)) with transitional cell carcinoma who were about to undergo transurethral resection of a bladder tumor. The mean immunoreactive fraction of the antibody complex preparations instilled was 66\% ± 15.9\%. The intravenous pyelogram obtained before the investigation of one of these patients is shown in Figure 5A and reveals a large filling defect on the left-hand side of the bladder. Histologic examination of tissue from this area confirmed it as a G3pT1 transitional cell carcinoma. The gamma-camera image obtained after instillation and washout of the \(^{188}\)Re-C595 complex (Fig. 5B) shows localized uptake at the site of the tumor. The mean tumor-to-normal tissue ratio in this group of patients was 3.9:1 and the mean percentage injected dose per gram tissue was 0.24 ± 0.19 for tumor and 0.06 ± 0.05 for normal tissue.

DISCUSSION

The monoclonal antibody C595, which binds to a protein core epitope on MUC1 mucin, has a proven track record in both in vitro (19) and in vivo (12, 20) cancer diagnostics. We report on application of the partial reduction method (16) to the labeling of C595 with \(^{188}\)Re to produce an antibody complex with potential therapeutic use. Partial reduction methodologies used previously in this laboratory to label C595 antibody with \(^{99m}\)Tc resulted in an antibody complex with high stability, which was found to localize in bladder tumors in an ex vivo model (12). Because \(^{188}\)Re and \(^{99m}\)Tc (from the same periodic group) have similar chemical properties, this method of direct labeling was used to produce a pair of comparable antibody complexes, one with diagnostic applications and the other to be used for intravesical therapy of bladder cancer.

The labeling efficiency of the reaction was satisfactory for the intended clinical use and resulted in an antibody complex.
complex with high immunoreactivity, which retained its specificity for MUC1-related antigens. At pH 6.0, the labeled product was contaminated with high-molecular-weight material that could not be separated from the antibody complex using Sephadex G25 gel filtration chromatography. The level of contamination was reduced by labeling at lower pH. Although a highly pure preparation may not necessarily be required for intravesical administration, a peptide affinity chromatography technique was applied to remove high-molecular-weight contamination. This was a simple procedure, taking about 1.5 h to perform and involving the use of peptide affinity and gel filtration matrices in tandem to effect purification and desalting in a one-step process. Sephacryl S300 gel filtration analysis of the affinity-purified antibody complex revealed that it was free from high-molecular-weight contamination. The peak of labeled material was followed by a shoulder of material of size >66 kDa. This may be caused by fragmentation of the antibody to produce heavy and light chain dimers. A small amount of fragmentation, as we observed, is inevitable when one begins to reduce the interchain disulfide bonds. However, the amount of fragmentation was small and cannot account totally for the observed loss of immunoreactivity of this complex over time.

The ex vivo model allows tumor localization to be examined in a human bladder without the need for laboratory animals. These studies showed that $^{188}$Re-C595 has the ability to localize in tumors and deliver its therapeutic $\beta$ energy. The negative control experiment using a $^{99m}$Tc-labeled irrelevant antibody showed that the tumor localization of $^{188}$Re-C595 is caused by a specific immunologic interaction of the antibody with MUC1 mucin that is overexpressed on transitional cell carcinoma of the bladder rather than nonspecific binding of protein. One might argue that a specimen that had been removed surgically would not be an accurate model of a living human bladder. However, tumor localization was confirmed in tracer studies in three patients with bladder cancer. Mean tumor-to-normal tissue ratios were similar to those observed in ex vivo studies, suggesting that the model gives an accurate reflection of tumor localization after intravesical administration of antibody complexes.

The main problem encountered with the $^{188}$Re-C595 antibody complex was its lack of stability during storage at room temperature. Serial ITLC analysis of the complex showed that perrhenate became dissociated from the antibody. This was considered to be associated with the tendency of rhenium to return to its higher oxidation states in the absence of a suitable reducing agent. In addition, reduction of interchain disulfide bonds within the antibody molecule may result in perturbation of the molecular stability of the protein. However, improvement in stability when carrier protein and a free radical scavenger were added to the antibody complex suggests that it may be associated with radiolysis. If radiolysis were the cause, lowering the specific activity of the complex might improve its stability; however, this would require the use of very large amounts of antibody for the ultimate therapeutic application. The main concern raised by the release of the nuclide from the antibody is the possible irradiation of noncancerous tissue. There is no evidence either in the literature or from our own experiences that free perrhenate is taken up by normal urothelial cells as is the case with nuclides of iodine ($^{211}$); therefore, such irradiation would arise from perrhenate released into the bladder lumen from antibody that had not yet been internalized. However, patients undergoing intravesical radioimmunotherapy would have a urinary catheter in place, and it is envisaged that free perrhenate would be washed out of the bladder in the urine. Further work is necessary to try to alleviate the problems of stability.

**FIGURE 5.** (A) Intravenous pyelogram shows large filling defect on left-hand side of bladder, which was confirmed as G3pT1 transitional cell carcinoma at operation. (B) Gamma-camera image shows localized uptake of $^{188}$Re-C595 complex at site of tumor.
Although the radioimmuno therapy of solid tumors using the systemic approach remains fraught with difficulties, the use of intravesical administration of antibody for the treatment of superficial bladder cancer is a practical possibility. The route of administration is simple, convenient, and well tolerated by patients. In addition, unlike systemic therapy, the intravesical approach allows the complex direct access to the tumor without exposure to serum proteases or the human immune system. This reduces the time required for tumor localization and increases the amount of active antibody available for tumor cell binding. In addition, retention of radiometals within tumor cells is well documented (22,23); thus, breakdown of the antibody complex may not be problematic once it has been internalized. Preliminary work (data not shown) supports anecdotal evidence that the MUC1 mucin (24) and, indeed, $^{188}$Re-C595 is internalized.

CONCLUSION

The $^{188}$Re-C595 antibody complex is a reagent with high immunoreactivity and specificity for MUC1 mucin and is suitable for use in intravesical radioimmunotherapy of superficial bladder cancer. Further clinical studies are now underway to investigate the tumor localization and therapeutic efficacy of this complex in MUC1-expressing cancers.

ACKNOWLEDGMENTS

The authors thank Dr. Malcolm Frier for radiopharmacy advice and Dr. Martin L. Wastei for radiologic support with this work. This work was supported by the British Cancer Research Campaign and the British Urological Foundation.

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