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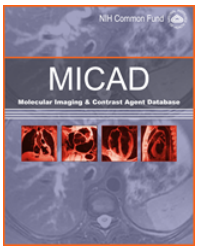

^{111}In-Capromab pendetide

^{111}In-CYT-356

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Chemical name:	^{111}In-Capromab pendetide	
Abbreviated name:	^{111}In-CYT-356, ^{111}In-GYK-DTPA-7E11-C5.3, ^{111}In-DTPA-7E11-C5.3, ^{111}In-7E11-C5.3	
Synonym:	ProstaScint®	
Agent Category:	Antibody	
Target:	Prostate-specific membrane antigen (PSMA)	
Target Category:	Antibody-antigen binding	
Method of detection:	SPECT	
Source of signal:	^{111}In	
Activation:	No	
Studies:	• *In vitro* • Rodents • Humans	Click on protein, nucleotide (RefSeq), and gene for more information about PSMA.

Background

[PubMed]

Prostate-specific membrane antigen (PSMA) is a unique type II, transmembrane-bound glycoprotein that is overexpressed on prostate tumor cells and in the neovasculature of most of the solid tumors, but not in the vasculature of normal tissues (1, 2). This unique expression of PSMA makes it an important biomarker as well as a large extracellular target of imaging agents (3, 4). 7E11-C5, a monoclonal antibody against the cytoplasmic domain of PSMA, was found to be specific to prostate tumor tissues in humans when conjugated with glycyl-tyrosyl-(*N*-ε-diethylenetriamine pentacetic acid)-lysine (GYK-DTPA). Tumors often contain dying or necrotic cells with permeable membranes, allowing the binding of antibodies to the intracellular epitope of PSMA. The antibody conjugate (Capromab pendetide or CYT-365) was radiolabeled with ^{111}Indium. ^{111}In-CYT-356 was approved by the US Food and Drug Administration in 1996 for the detection of prostate carcinoma and soft tissue metastases in prostate cancer patients. Newer antibodies against the extracellular domain of PSMA are being developed for immunotherapy of prostate cancer (5, 6).

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Synthesis

[PubMed]

Purified monoclonal antibody 7E11-C5.3 was coupled with GYK-DTPA by site-specifically generated reactive aldehyde groups on the oligosaccharides found on the heavy chain of the antibody (7). A mixture of $^{111}InCl_3$ (37 MBq, 1 mCi) and the conjugated antibody (100 µg) was incubated for 1 h at 37°C. ^{111}In-CYT-356 was purified by high performance chromatography (8). The specific activity was 55.5-210.9 MBq/mg (1.5-5.7 mCi/mg).

^{111}In-CYT-356 can be easily prepared from a commercially available kit consisting of two vials to be mixed: 1) a sterile solution of 185 MBq/ml (5 mCi/ml) ^{111}In-choride in sodium acetate buffer; and 2) a sterile solution of 0.5 mg of CYT-356. The mixture was incubated at room temperature for 30 min and filtered through a 0.22-µm filter.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

LNCaP human prostate cancer cells were reported to have a K_d of 6.69 nM with [^{131}I]7E11-C5 and B_{max} of 95,000 sites/cell in saturation binding studies (9) using intact cells. The binding was accounted for by a subpopulation of permeated cells produced when the cells were trypsinized and washed. Little internalization of the tracer was found over a period of 48 h at 37°C. When permeated cells were used, the number of binding sites/cell was similar to [^{131}I]J591, an antibody against the extracellular domain of PSMA. Using nonpermeated cells, [^{131}I]J591 has a K_d of 1.83 nM and a B_{max} of 600,000-800,000 sites/cell.

Various immunohistochemical studies indicate that 7E11-C5 reacts weakly with normal prostate epithelial cells and strongly with malignant prostate epithelial cells but does not react with non-prostate tumors or most normal tissues (8, 10-14). It also stains endothelial cells in solid tumors, such as lung, renal, colon, and breast carcinomas but not in normal vascular endothelial cells (15, 16).

Animal Studies

Rodents

[PubMed]

Biodistribution of ^{111}In-CYT-356 was studied in LNCaP tumor-bearing nude mice by *ex vivo* tissue radioactivity measurements (8). ^{111}In-CYT-356 uptake in tumor was high with 14% injected dose/g (ID/g) on day 1 after injection of 11.7 µg of the tracer (0.59 MBq, 16 µCi). It increased to 30% ID/g on days 3 and 7. Tumor image was visible by scintigraphic scan on day 4. Uptake in the lung, spleen, liver, and kidney was 4-6% ID/g, whereas the muscle showed an uptake of <1% ID/g. Uptake in non-tumor organs was similar in tumor-bearing mice and normal mice. ^{111}In-CYT-356 did not accumulate in PC-3 and Du-145 prostate tumor lines (PSMA negative). Furthermore, ^{111}In-labeled GYK-DTPA-conjugated, nonspecific antibody did not localize to the LNCaP tumor.

Other Non-Primate Mammals

[PubMed]

No publication is currently available.

Non-Human Primates

[PubMed]

No publication is currently available.

Human Studies

[PubMed]

Human dosimetry of ^{111}In-CYT-356 was estimated in 25 prostate cancer patients (17). Dynamic whole-body positron emission tomography (PET) scans were acquired after the injection of 185 MBq (5 mCi) of ^{111}In-CYT-356 over a 7-10-day period. The organ that received the highest absorbed dose was the liver (1.0 mGy/MBq or 3.7 rad/mCi), followed by the spleen (0.88 mGy/MBq or 3.3 rad/mCi), and the kidneys (0.67 mGy/MBq or 2.5 rad/mCi). The prostate was estimated at 0.44 mGy/MBq (1.63 rad/mCi). The effective dose was calculated as 0.25-0.29 mSv/MBq (0.93-1.07 rem/mCi).

In one of the pivotal studies, ^{111}In-CYT-356 scans (152 patients with prostate cancer) had a sensitivity, specificity, and overall accuracy of 62, 72, and 68%, respectively (18). The sensitivity of computed tomography (CT) and magnetic resonance imaging (MRI) was 4% and 15%, respectively.

Sodee et al. (19) reported the results of a retrospective study of 2,290 ^{111}In-CYT-356 scans of 2,154 patients with prostate cancer performed at 15 institutions. ^{111}In-CYT-356 scans identified positive uptake in the prostate or fossa (70.4%), pelvic nodes (31.5%), pelvic and extrapelvic nodes (23.9%), and extrapelvic nodes only (11.0%). In patients with newly diagnosed prostate cancer (n = 487), there was a significant correlation ($p < 0.001$) of prostate-specific antigen (PSA) level with positive ^{111}In-CYT-356 scans in the prostate bed and pelvic metastases. The association between PSA level and positive ^{111}In-CYT-356 scans in the fossa recurrence was weaker ($p < 0.033$) in patients after surgery (n = 1,225) and was not significant for pelvic and extrapelvic metastases. There was no association between PSA level and ^{111}In-CYT-356 scans in patients with radiation therapy (n = 340) or hormonal therapy (n = 238).

^{111}In-CYT-356 imaging has been studied in the detection of nodal metastases, detection of recurrent prostate cancer, detection of occult extraprostatic fossa, and evaluation before definitive therapy in patients with prostate cancer [PubMed]. Fusion studies of ^{111}In-CYT-356 scans with CT or MRI improve the prediction of lymph node metastases in patients for definitive local therapy (20, 21).

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