^{124}I-Chimeric monoclonal antibody G250

^{124}I-cG250

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Chemical name:	^{124}I-Chimeric monoclonal antibody G250	
Abbreviated name:	^{124}I-cG250	
Synonym:		
Agent category:	Antibody	
Target:	Carbonic anhydrase IX	
Target category:	Enzyme	
Method of detection:	Positron emission tomography (PET)	
Source of signal:	^{124}I	
Activation:	No	
Studies:	• *In vitro* • Rodents • Humans	Click on protein, nucleotide (RefSeq), and gene for more information about human carbonic anhydrase IX.

Background

[PubMed]

In a variety of solid tumors, hypoxia was found to lead to tumor progression and the resistance of tumors to chemotherapy and radiotherapy (1-3). Tumor oxygenation is heterogeneously distributed within human tumors (4). Hypoxia in malignant tumors is thought to be a major factor limiting the efficacy of chemotherapy and radiotherapy. It would be beneficial to assess tumor oxygenation before and after therapy to provide an evaluation of tumor response to treatment and an insight into new therapeutic treatments (5). Tumor oxygenation is measured invasively using computerized polarographic oxygen-sensitive electrodes, which is regarded as the gold standard (6). Functional and

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non-invasive imaging of intratumoral hypoxia has been demonstrated to be feasible for the measurement of tumor oxygenation (7). This has led to the search for and development of hypoxia-targeted, non-invasive markers of tumor hypoxia.

Chapman proposed the use of 2-nitroimidazoles for hypoxia imaging (8). 2-Nitroimidazole compounds are postulated to undergo reduction in hypoxic condition, forming highly reactive oxygen radicals that subsequently bind covalently to macromolecules inside the cells (9). [^{18}F]Fluoromisonidazole ([^{18}F]FMISO) is the most widely used positron emission tomography (PET) tracer for imaging tumor hypoxia (7). Carbonic anhydrase (CA) IX is one of the most overexpressed genes in cells under hypoxic conditions (10). It is a transmembrane glycoprotein with CA activity in the extracellular domain, and it is found to be overexpressed in renal cell, cervical, lung, and colorectal tumors. Murine monoclonal antibody G250 against CA IX has been developed for *in vitro* and *in vivo* localization of CA IX in cells (11-13). G250 is found to bind to >94% of human clear-cell renal carcinoma. A murine-human chimeric G250 (cG250) has been generated to be less immunogenic in humans (14). ^{124}I-cG250 has been evaluated as a PET imaging agent for renal cell carcinoma in mice (15) and patients (16).

Related Resource Links:

- Chapters in MICAD
- Gene information in NCBI (Carbonic anhydrase IX).
- Articles in OMIM
- Clinical trials (G250)

Synthesis

[PubMed]

The cG250 antibody (~2 nmol) was labeled with 4 MBq (0.108 mCi) ^{124}I in the presence of Iodogen (15). ^{124}I-cG250 was isolated with size-exclusion column chromatography with a radiolabeling efficiency of 67% and a specific activity of 6.2 MBq/nmol (0.16 mCi/nmol). Thin-layer chromatography revealed >97% of ^{124}I was bound to cG250. ^{124}I-cG250 exhibited an immunoreactivity of 95%.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Lawrentschuk et al. (15) performed binding experiments with ^{124}I-cG250 in SK-RC-52 human renal carcinoma cells. The dissociation constant was found to be 2.2 nM with 400,000 antibody molecules per cell.

Animal Studies

Rodents

[PubMed]

Lawrentschuk et al. (15) studied the biodistribution of ^{124}I-cG250 in mice (n = 5/group) bearing SK-RC-52 tumors at days 0 (2 h), 2, 3, and 7 after injection. The tracer accumulation in the tumors was 9.6%, 23.5%, 19.4%, and 7.4% injected dose per gram (ID/g), respectively. The liver and kidneys had lower radioactivity levels than the tumors at days 2–7. The radioactivity in the blood decreased from 32.2% ID/g (day 0) to 0.5% ID/g (day 7). The tumor/blood ratios were 5.0 and 31.0 on day 3 and day 7, respectively. The blood clearance pattern exhibited a two-phase model with a half-life of 2.6 h during the distribution phase and a half-life of 40.5 h during the elimination phase. The control antibody ^{124}I-huA33 exhibited very low tumor accumulation. No blocking experiment was performed.

PET imaging with ^{124}I-cG250 showed localization in the tumors and relatively low activity elsewhere in the mice at 24 h after injection. There was a significant correlation (r^2 = 0.93, $P < 0.0001$) between tumor standard uptake values measured with PET and *ex vivo* measurement (% ID/g). Histoimmunostaining showed CA IX was distributed evenly in the viable tumor cells of the tumor sections.

Other Non-Primate Mammals

[PubMed]

No publication is currently available.

Non-Human Primates

[PubMed]

No publication is currently available.

Human Studies

[PubMed]

Divgi et al. (16) performed PET imaging with ^{124}I-cG250 in 25 patients with renal masses who were scheduled to undergo surgical resection by laparotomy received a single intravenous infusion of 185 MBq (5 mCi (66 nmol)) ^{124}I-cG250 over 20 min in this open-label pilot study. The obtained images were graded as positive (defined as a tumor/healthy kidney ratio >3). Fifteen of 16 clear-cell carcinomas were identified accurately with PET, and all nine non–clear-cell renal masses were negative for the tracer. The sensitivity of ^{124}I-cG250 PET for clear-cell kidney carcinoma was 94%; the negative predictive value was 90%, and specificity and positive predictive accuracy were both 100%.

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