^{68}Ga-DOTA-4-amino-1-carboxymethyl-piperidine-D-Phe-Gln-Trp-Ala-Val-Gly-His-Sta-Leu-NH_2

^{68}Ga-RM2

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Chemical name:	^{68}Ga-DOTA-4-amino-1-carboxymethyl-piperidine-D-Phe-Gln-Trp-Ala-Val-Gly-His-Sta-Leu-NH_2	
Abbreviated name:	^{68}Ga-RM2	
Synonym:		
Agent category:	Peptide	
Target:	Gastrin-releasing peptide receptor (GRPR)	
Target category:	Receptor	
Method of detection:	Positron emission tomography (PET)	
Source of signal\contrast:	^{68}Ga	
Activation:	No	
Studies:	• *In vitro* • Rodents	Click on protein, nucleotide (RefSeq), and gene for more information about gastrin-releasing peptide receptor.

Background

[PubMed]

The amphibian bombesin (BBN or BN, a peptide of 14 amino acids) is an analog of human gastrin-releasing peptide (GRP, a peptide of 27 amino acids) that binds to GRP

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receptor (GRPR) with high affinity and specificity (1). Both GRP and BBN share an amidated C-terminus sequence homology of seven amino acids, Trp-Ala-Val-Gly-His-Leu-Met-NH_2. BBN-Like peptides have been shown to induce various biological responses in diverse tissues, including the central nervous system (CNS) and the gastrointestinal (GI) system. They also act as potential growth factors for both normal and neoplastic tissues (2). Specific BBN receptors have been identified on CNS and GI tissues, including the pancreas, and on a number of tumor cell lines. The BBN-receptor superfamily includes at least four different subtypes, namely neuromedin B (NMB or BB1), the GRPR subtype (BB2), the BB3 subtype, and the BB4 subtype (3). The findings of GRPR overexpression in various human tumors, such as breast, prostate, lung, colon, ovarian, and pancreatic cancers, provide opportunities for tumor imaging by designing specific molecular imaging agents to target the GRPR.

Currently used targeting GRPR peptides are primarily agonists. Therefore, there is a need for GRPR antagonist radioligands. Llinares et al. (4) developed a series of GRPR peptide antagonists. One of them, D-Phe-Gln-Trp-Ala-Val-Gly-His-Sta-Leu-NH_2 (RM26), has been found to be a selective GRPR antagonist. A DOTA-Gly-benzoyl group was added to the C-terminus to form DOTA-Gly-benzoyl-D-Phe-Gln-Trp-Ala-Val-Gly-His-Sta-Leu-NH_2 (RM1). For evaluation as a single-photon emission computed tomography (SPECT) imaging agent for GRPR, ^{111}In has been attached to RM1 to form ^{111}In-RM1 (5). A new GRPR peptide antagonist, DOTA-4-amino-1-carboxymethyl-piperidine-D-Phe-Gln-Trp-Ala-Val-Gly-His-Sta-Leu-NH_2 (RM2), has been found to have a higher affinity for GRPR than RM1 and has been labeled with ^{68}Ga for positron emission tomography (PET) imaging (6).

Related Resource Links:

- Chapters in MICAD (GRPR)
- Gene information in NCBI (GRPR).
- Articles in OMIM (GRPR)
- Clinical trials (GRPR)
- Drug information in FDA (GRPR)

Synthesis

[PubMed]

RM2 was prepared by solid-phase peptide synthesis with >70% yield (6). $^{68}GaCl_3$ was added to a solution of RM2 (~12 nmol) in aqueous solution (pH 4). The mixture was heated for 2 min at 95°C. The product, ^{68}Ga-RM2, had a specific activity of 10 GBq/μmol (0.27 Ci/μmol).

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Mansi et al. (6) performed *in vitro* inhibition studies of RM1 and RM2 in cultured, GRPR-rich, PC-3 human prostate cells with ^{125}I-BBN; Mansi et al. recorded 50% inhibition concentration (IC_{50}) values of 35.0 ± 13.0 and 7.7 ± 3.3, respectively. RM2 was able to inhibit the calcium release and receptor internalization induced by BBN.

Animal Studies

Rodents

[PubMed]

Mansi et al. (6) performed *ex vivo* biodistribution studies of ~0.2 MBq (5.4 μCi) ^{68}Ga-RM2 in nude mice (n = 3/group) bearing PC-3 tumors. Tumor accumulation values for ^{68}Ga-RM2 were 9.6 ± 1.5, 14.1 ± 1.9, 14.7 ± 2.1, and 13.6 ± 0.6% injected dose per gram (ID/g) at 20, 60, 80, and 120 min after injection, respectively. ^{68}Ga-RM2 exhibited a fast blood clearance, with 0.5% ID/g at 80 min after injection. The tumor/blood ratios were 6, 18, 29, and 43 at 20, 60, 80, and 120 min after injection, respectively. The initial accumulation was high in the pancreas, kidney, pituitary, adrenal, stomach, and intestine at 20 min after injection, with rapid washout by 120 min. The accumulation was low in other tissues. No blocking studies were reported

PET imaging in nude mice bearing LNCaP or PC-3 xenografts was performed with 7 MBq (0.19 mCi) ^{68}Ga-RM2 at 60 min after injection. The tumors, kidneys, and urinary bladder were clearly visualized. Preinjection of excess RM2 peptide (20 nmol, 5 min) inhibited the visualization of the tumors at 60 min after injection.

Other Non-Primate Mammals

[PubMed]

No publication is currently available.

Non-Human Primates

[PubMed]

No publication is currently available.

Human Studies

[PubMed]

No publication is currently available.

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