CLAIMS

1. Use of a pharmaceutical composition of a radiolabeled gastrin-releasing peptide receptor (GRPR)-antagonist, in the manufacture of a medicament for the treatment of GRPR-positive tumors in a human subject, wherein said pharmaceutical composition comprises

   - a radiolabeled GRPR-antagonist of the following formula:

   MC- S - P

   wherein:

   M is a radiometal suitable for therapy, typically 177-Lutetium, and C is a chelator which binds M;

   S is an optional spacer covalently linked between C and the N-terminal of P;

   P is a GRP receptor peptide antagonist covalently bound with its N-terminal to C or to S; and,

   - one or more pharmaceutically acceptable excipients.

   wherein said subject has been selected for the treatment by positron emitting tomography (PET) / computed tomography (CT) or PET/ magnetic resonance imaging (MRI) with the same GRPR antagonist as defined for the treatment but with ^{68}Ga as radiometal for use as contrast agent.

2. The use according to claim 1, wherein P is of the general formula:

   Xaa1-Xaa2—Xaa3—Xaa4 —Xaa5—Xaa6—Xaa7—Z;

   Xaa1 is not present or is selected from the group consisting of amino acid residues Asn, Thr, Phe, 3- (2-thienyl) alanine (Thi), 4-chlorophenylalanine (Cpa) , α-naphthylalanine (α-Nal) , β-naphthylalanine (β-Nal) , 1,2,3,4-tetrahydronorharman-3-carboxylic acid (Tpi), Tyr, 3-iodo-tyrosine (o-I-Tyr), Trp and pentafluorophenylalanine (5-F-Phe) ;

   Xaa2 is Gln, Asn or His;

   Xaa3 is Trp or 1, 2, 3, 4-tetrahydronorharman-3-carboxylic acid (Tpi);

   Xaa4 is Ala, Ser or Val;

   Xaa5 is Val, Ser or Thr;

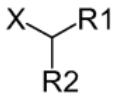
   Xaa6 is Gly, sarcosine (Sar), D-Ala, or β-Ala;

   Xaa7 is His or (3-methyl)histidine (3-Me)His;

all amino acids being independently L- or D- isomer,

Z is selected from -NHOH, -NHNH2, -NH-alkyl, -N(alkyl)2, and -O-alkyl

or Z is

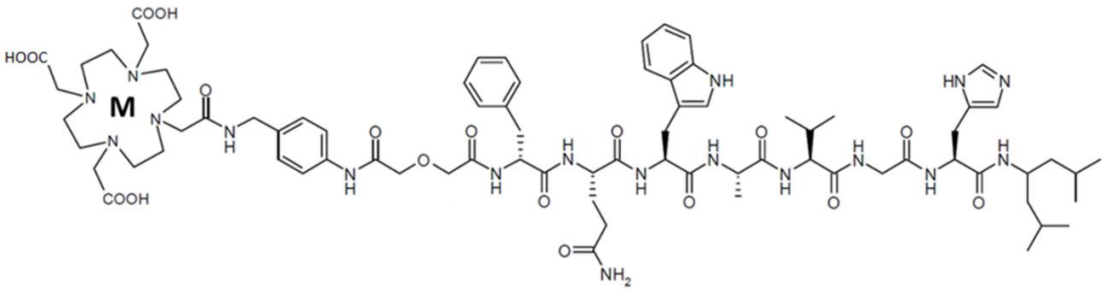


wherein X is NH (forming an amide) or O (forming an ester) and R1 and R2 are the same or different and selected from a proton, an optionally substituted alkyl, an optionally substituted alkyl ether, an aryl, an aryl ether or an alkyl-, halogen, hydroxyl, hydroxyalkyl, amine, amino, amido or amide substituted aryl or heteroaryl group; and,

- one or more pharmaceutically acceptable excipients.

3. The use according to claim 1 or 2, wherein P is DPhe-Gln-Trp-Ala-Val-Gly-His-NH-CH(CH_2-CH(CH_3)$_2$)$_2$.

4. The use according to any one of Claims 1-3; wherein the radiolabelled GRPR-antagonist is the compound of formula (I):



(I)

wherein M is a ^{177}Lu.

5. The use according to any of the preceding claims wherein the pharmaceutical composition is a solution for infusion.

6. The use according to any of claims 1 to 5, wherein, a subject has been selected for the treatment by evaluating [^{68}Ga]-labeled GRPR antagonist uptake in the lesions as determined by PET/MRI or PET/CT imaging in said subject.

7. The use according to Claim 6, wherein a subject selected for the treatment fulfils at last the following condition: at least 50% of the lesions as detected by conventional imaging in said subject, for example by MRI, CT, SPECT or PET, are also identified by [^{68}Ga]-GRPR antagonist uptake as determined by PET/MRI or PET/CT imaging in said subject.

8. The use according to any of claims 1 to 7, wherein said subject has GRPR-positive solid tumors selected from the group consisting of gastrointestinal stromal tumor (GIST), neuroblastoma, glioblastoma, breast, prostate, lung (small cell and non-small cell), colon-rectum, and renal cancer.

9. A pharmaceutical composition of a radiolabeled GRPR-antagonist, for use as a contrast agent for PET/CT or PET/MRI imaging in determining whether a subject can be selected for a treatment with radiolabelled GRPR-antagonist for treating GRPR-positive tumors, wherein said pharmaceutical composition comprises

- a radiolabeled GRPR-antagonist of the following formula:

MC- S - P

wherein:

M is a radiometal for use as contrast agent in PET imaging, for example 68-Gallium and C is a chelator which binds M; e.g. by forming a complex with M;

S is an optional spacer covalently linked between C and the N-terminal of P;

P is a GRP receptor peptide antagonist covalently bound with its N-terminal to C or to S, for example of the general formula:

Xaa1-Xaa2—Xaa3—Xaa4 —Xaa5—Xaa6—Xaa7—Z;

Xaa1 is not present or is selected from the group consisting of amino acid residues Asn, Thr, Phe, 3- (2-thienyl) alanine (Thi), 4-chlorophenylalanine (Cpa) , α-naphthylalanine (α-Nal) , β-naphthylalanine (β-Nal) , 1,2,3,4-tetrahydronorharman-3-carboxylic acid (Tpi), Tyr, 3-iodo-tyrosine (o-I-Tyr) , Trp and pentafluorophenylalanine (5-F-Phe) ;

Xaa2 is Gln, Asn or His;

Xaa3 is Trp or 1, 2, 3, 4-tetrahydronorharman-3-carboxylic acid (Tpi);

Xaa4 is Ala, Ser or Val;

Xaa5 is Val, Ser or Thr;

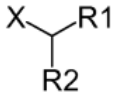
Xaa6 is Gly, sarcosine (Sar), D-Ala, or β-Ala;

Xaa7 is His or (3-methyl)histidine (3-Me)His;

All amino acids being, independently, D- or L- isomers,

Z is selected from -NHOH, -NHNH2, -NH-alkyl, -N(alkyl)2, and -O-alkyl

or Z is



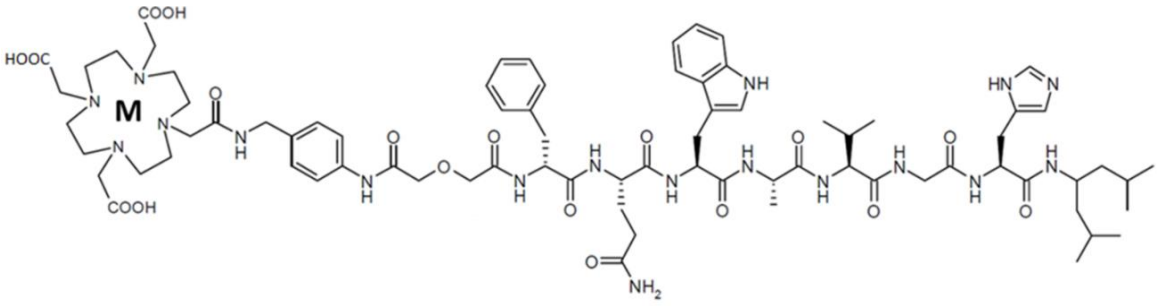
wherein X is NH (amide) or O (ester) and R1 and R2 are the same or different and selected from a proton, an optionally substituted alkyl, an optionally substituted alkyl ether, an aryl, an aryl ether or an alkyl-, halogen, hydroxyl, hydroxyalkyl, amine, amino, amido, or amide substituted aryl or heteroaryl group.; and,

- one or more pharmaceutically acceptable excipients,

wherein said subject is selected for the treatment by evaluating uptake of said radiolabelled GRPR antagonist in GRPR-positive tumors by PET/CT or PET/MRI imaging in said subject.

10. The pharmaceutical composition for use according to claim 9, wherein P is DPhe-Gln-Trp-Ala-Val-Gly-His-NH-CH(CH_2-CH(CH_3)$_2$)$_2$.

11. The pharmaceutical composition for use according to claim 9 or 10 ; wherein the radiolabelled GRPR-antagonist is the compound of formula (I):



(I)

wherein M is a ^{68}Ga.

12. The pharmaceutical composition for use according to any one of Claims 9-11, wherein a subject selected for the treatment fulfils the following condition: at least 30% of the lesions as detected by conventional imaging in said subject, for example by MRI, CT, SPECT or PET, are also identified by [^{68}Ga]-GRPR antagonist uptake as determined by PET/MRI or PET/CT imaging in said subject.

13. The pharmaceutical composition for use according to any of claims 9 to 12, wherein said subject has GRPR-positive solid tumors selected among gastrointestinal stromal tumor (GIST), neuroblastoma, glioblastoma, breast, prostate, lung (small cell and non-small cell), colon-rectum, and renal cancer.

14. A method for determining whether a human patient having tumors can be selected for a treatment with a radiolabelled GRPR antagonist, said method comprising the steps of :

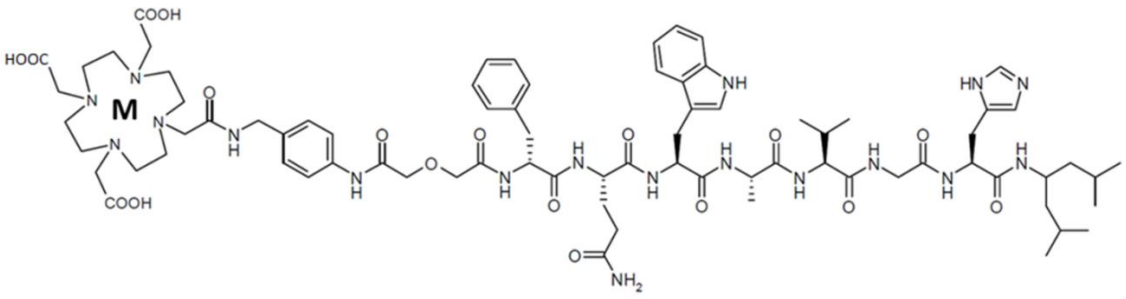
(i) acquiring an image by PET/MRI or PET/CT of said patient, and

(ii) comparing with a control image,

wherein the patient is to be administered an efficient amount of a radiolabelled GRPR antagonist as a contrast agent for imaging the uptake of said radiolabelled GRPR antagonist prior to step (i).

15. The method of Claim 14, further comprising a therapeutically efficient amount of a therapeutic agent which comprises the same GRPR antagonist used prior to step (i) but having a radiometal suitable for therapy to be administered.

16. The method of Claim 14 or 15, wherein the radiolabelled GRPR antagonist for use as contrast agent for imaging is a radiolabelled compound of formula (I):



(I)

wherein M is ^{68}Ga.

17. The method of Claim 15, wherein the radiometal suitable for therapy is 177-Lutetium.

18. The method of any one of Claims 14-17, wherein the therapeutic agent is to be administered at least two weeks after the administration of an efficient amount of a radiolabelled GRPR antagonist as a contrast agent for imaging the uptake of said radiolabelled GRPR antagonist.

19. A pharmaceutical composition of a radiolabeled gastrin-releasing peptide receptor (GRPR)-antagonist, for use in treating GRPR-positive tumors in a human subject, wherein said pharmaceutical composition comprises

a radiolabeled GRPR-antagonist of the following formula:

MC- S - P

wherein:

M is a radiometal suitable for therapy, typically 177-Lutetium, and C is a chelator which binds M;

S is an optional spacer covalently linked between C and the N-terminal of P;

P is a GRP receptor peptide antagonist covalently bound with its N-terminal to C or to S; and,

one or more pharmaceutically acceptable excipients.

wherein said subject has been selected for the treatment by positron emitting tomography (PET) / computed tomography (CT) or PET/ magnetic resonance imaging (MRI) with the same GRPR antagonist as defined for the treatment but with 68-Gallium as radiometal for use as contrast agent.