CLAIMS

1) An *in vitro* method for selecting a skin melanoma patient susceptible to responding to treatment with an immune checkpoint inhibitor, said method comprising the steps of:

a) contacting a biological sample from said subject with at least one progastrin-binding antibody, wherein

the biological sample is blood, serum or plasma; and the progastrin-binding antibody is selected in the group consisting of:

- A monoclonal antibody comprising a heavy chain comprising CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°4, 5 and 6, respectively, and a light chain comprising CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°7, 8 and 9, respectively,
- A monoclonal antibody comprising a heavy chain comprising CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°10, 11 and 12, respectively, and a light chain comprising CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°13, 14 and 15, respectively,
- A monoclonal antibody comprising a heavy chain comprising CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°16, 17 and 18, respectively, and a light chain comprising CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°19, 20 and 21, respectively,
- A monoclonal antibody comprising a heavy chain comprising CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°22, 23 and 24, respectively, and a light chain comprising CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°25, 26 and 27, respectively,
- A monoclonal antibody comprising a heavy chain comprising CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°28, 29 and 30, respectively, and a light chain comprising CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°31, 32 and 33, respectively,
- A monoclonal antibody comprising a heavy chain comprising CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°34, 35 and 36, respectively, and a light chain comprising CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°37, 38 and 39, respectively, and

- A monoclonal antibody produced by the hybridoma deposited at the CNCM, Institut Pasteur, 25-28 rue du Docteur Roux, 75724 Paris CEDEX 15, France, on 27 December 2016, under reference I-5158

and

b) determining the concentration of progastrin in said sample, wherein a concentration of progastrin inferior to 3 pM in said biological sample, indicates that the skin melanoma patient is susceptible to responding to treatment with an immune checkpoint inhibitor.

2) The method of claim 1, wherein the method comprises the further steps of:

c) determining a reference concentration of progastrin in a reference sample,

d) comparing the concentration of progastrin in said biological sample with said reference concentration of progastrin,

e) determining, from the comparison of step d), whether said patient is responsive or not to treatment with an immune checkpoint inhibitor.

3) The method of any one of claim 1 or 2, wherein the determination of step a) includes:

(i) contacting said sample with a first progastrin-binding antibody which binds to a first epitope of progastrin, and

(ii) contacting said sample with a second progastrin-binding antibody which binds to a second epitope of progastrin.

4) The method of claim 3, wherein the first progastrin-binding antibody binds an epitope within the C-terminus of progastrin.

5) The method of claim 4, wherein said first progastrin-binding antibody is a monoclonal antibody produced by the hybridoma deposited at the CNCM, Institut Pasteur, 25-28 rue du Docteur Roux, 75724 Paris CEDEX 15, France, on 27 December 2016, under reference I-5158.

6) The method of any one of claims 3 to 5, wherein the second progastrin-binding antibody binds an epitope within the N-terminus of progastrin.

7) The method of any one of claims 3 to 6, wherein said second progastrin-binding antibody is: a monoclonal antibody comprising the

- a heavy chain comprising the following three CDRs, CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°16, 17 and 18, respectively, and
- a light chain comprising the following three CDRs, CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°19, 20 and 21, respectively.

8) The method of any one of claims 1 to 7, wherein the level of progastrin is determined in step a) with an ELISA.

9) Use of an immune checkpoint inhibitor in the manufacture of a medicament for the treatment of skin melanoma, comprising a prior selection of:

a patient responsive to immune checkpoint inhibitors using a method according any one of claims 1 to 8.

10) Use of an immune checkpoint inhibitor in the manufacture of a medicament for the treatment of skin melanoma, comprising:

a) contacting a biological sample from said subject with at least one progastrin-binding antibody, wherein:

- the biological sample is blood, serum or plasma;
- and the progastrin-binding antibody is selected in the group consisting of:
  - A monoclonal antibody comprising a heavy chain comprising CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°4, 5 and 6, respectively, and a light chain comprising CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°7, 8 and 9, respectively,
  - A monoclonal antibody comprising a heavy chain comprising CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°10, 11 and 12, respectively, and a light chain comprising CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°13, 14 and 15, respectively,
  - A monoclonal antibody comprising a heavy chain comprising CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°16, 17 and 18, respectively, and a light chain comprising CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°19, 20 and 21, respectively,

- A monoclonal antibody comprising a heavy chain comprising CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°22, 23 and 24, respectively, and a light chain comprising CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°25, 26 and 27, respectively,
- A monoclonal antibody comprising a heavy chain comprising CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°28, 29 and 30, respectively, and a light chain comprising CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°31, 32 and 33, respectively,
- A monoclonal antibody comprising a heavy chain comprising CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°34, 35 and 36, respectively, and a light chain comprising CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°37, 38 and 39, respectively, and
- A monoclonal antibody produced by the hybridoma deposited at the CNCM, Institut Pasteur, 25-28 rue du Docteur Roux, 75724 Paris CEDEX 15, France, on 27 December 2016, under reference I-5158,

b) determining the concentration of progastrin in said sample, and

c) reducing or stopping the immune checkpoint inhibitor treatment when the concentration of progastrin of step b) is at least 3 pM.

11) An *in vitro* method for prognosing a treatment of skin melanoma with an immune checkpoint inhibitor in a subject, said method comprising the steps of:

a) contacting a biological sample from said subject with at least one progastrin-binding antibody, wherein:

- the biological sample is blood, serum or plasma;
- and the progastrin-binding antibody is selected in the group consisting of:
  - A monoclonal antibody comprising a heavy chain comprising CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°4, 5 and 6, respectively, and a light chain comprising CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°7, 8 and 9, respectively,
  - A monoclonal antibody comprising a heavy chain comprising CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°10, 11 and 12, respectively, and a light chain comprising CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°13, 14 and 15, respectively,

- A monoclonal antibody comprising a heavy chain comprising CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°16, 17 and 18, respectively, and a light chain comprising CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°19, 20 and 21, respectively,
- A monoclonal antibody comprising a heavy chain comprising CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°22, 23 and 24, respectively, and a light chain comprising CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°25, 26 and 27, respectively,
- A monoclonal antibody comprising a heavy chain comprising CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°28, 29 and 30, respectively, and a light chain comprising CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°31, 32 and 33, respectively,
- A monoclonal antibody comprising a heavy chain comprising CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°34, 35 and 36, respectively, and a light chain comprising CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°37, 38 and 39, respectively, and
- A monoclonal antibody produced by the hybridoma deposited at the CNCM, Institut Pasteur, 25-28 rue du Docteur Roux, 75724 Paris CEDEX 15, France, on 27 December 2016, under reference I-5158, and

b) determining the concentration of progastrin in said sample, and

c) determining that the prognosis is negative when the concentration of progastrin of step b) is higher than 3 pM in said biological sample indicates the prognosis is negative.

12) The method of claim 11 wherein the method comprises the further steps of:

a) determining a reference concentration of progastrin in a reference sample,

b) comparing the concentration of progastrin in said biological sample with said reference concentration of progastrin,

c) prognosing, from the comparison of step b), said skin melanoma treatment with an immune checkpoint inhibitor.