

Claims

1. An method of determining whether a patient is suitably treated by a therapy comprising an angiogenesis inhibitor comprising bevacizumab or an antibody that binds essentially the same epitope on VEGF as bevacizumab, said method comprising:

5 (a) determining in a sample derived from a patient suffering from cancer the genotype at polymorphism rs699946 (SEQ ID NO. 1), and

(b) identifying a patient as more or less suitably treated by a therapy comprising an angiogenesis inhibitor comprising bevacizumab or an antibody that binds essentially the same epitope on VEGF as bevacizumab based on said genotype, wherein the presence of each A allele
10 at polymorphism rs699946 (SEQ ID NO. 1) indicates an increased likelihood that said patient is more suitably treated, or the presence of each G allele at polymorphism rs699946 (SEQ ID NO. 1) indicates an increased likelihood that said patient is less suitably treated.

2. The method of claim 1, wherein whether a patient is suitably treated by a therapy
15 comprising an angiogenesis inhibitor is determined in terms of progression-free survival.

3. The method of any one of claims 1 to 2, wherein the therapy further comprises a chemotherapeutic agent or chemotherapy regimen.

20 4. The method of any one of claims 1 to 3, wherein the angiogenesis inhibitor is formulated for administration ~~administered~~ with one or more agents selected from the group consisting of taxanes, interferon alpha, 5-fluorouracil, capecitabine, leucovorin, gemcitabine, erlotinib and platinum-based chemotherapeutic agents.

25 5. The method of any one of claims 1 to 4, wherein the cancer is pancreatic cancer, renal cell cancer, colorectal cancer, breast cancer or lung cancer.

6. The method of any one of claims 1 to 5, wherein the sample is a blood sample.

30 7. The method of any one of claims 1 to 6, wherein the genotype is determined by means of MALDI-TOF mass spectrometry.

~~8. The method of any one of claims 1 to 7, further comprising administering the therapy to the patient.~~

98. A pharmaceutical composition comprising an angiogenesis inhibitor as defined in
5 claims 1 to ~~8~~7 for the treatment of a patient in need thereof, wherein said patient has been
determined to be more suitably treated with the therapy comprising the angiogenesis inhibitor in
accordance with the method of any one of claims 1 to ~~8~~7.

109. A kit for carrying out the method of any one of claims 1 to ~~8~~7, comprising
10 oligonucleotides capable of determining the genotype at polymorphism rs699946 (SEQ ID NO.
1).

110. A method for improving the treatment effect of a chemotherapeutic agent or
chemotherapy regimen of a patient suffering from cancer by adding an angiogenesis inhibitor
15 comprising bevacizumab or an antibody that binds essentially the same epitope on VEGF as
bevacizumab, said method comprising:

(a) determining in a sample derived from a patient suffering from cancer the genotype at
polymorphism rs699946 (SEQ ID NO. 1);

(b) identifying a patient as more suitably treated by the addition of an angiogenesis
20 inhibitor comprising bevacizumab or an antibody that binds essentially the same epitope on
VEGF as bevacizumab based on said genotype, wherein the presence of each A allele at
polymorphism rs699946 (SEQ ID NO. 1) indicates an increased likelihood that said patient is
more suitably treated; and

(c) ~~administering~~ formulating said angiogenesis inhibitor in combination with a
25 chemotherapeutic agent or chemotherapy regimen for administration to a patient identified as
more suitably treated in accordance with (b).

1211. The method of claim ~~11~~10, wherein whether a patient is suitably treated by a
therapy comprising an angiogenesis inhibitor is determined in terms of progression-free survival.
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1312. The method of any one of claims ~~11~~10 to ~~12~~11, wherein the angiogenesis
inhibitor is formulated for administration ~~administered~~ with one or more agents selected from the
group consisting of taxanes, interferon

alpha, 5-fluorouracil, capecitabine, leucovorin, gemcitabine, erlotinib and platinum-based chemotherapeutic agents.

1413. The method of any one of claims 1110 to 1312, wherein the cancer is pancreatic
5 cancer, renal cell cancer, colorectal cancer, breast cancer or lung cancer.

1414. The method of any one of claims 1110 to 1413, wherein the sample is a blood sample.

10 1415. The method of any one of claims 1110 to 1514, wherein the genotype is determined by means of MALDI-TOF mass spectrometry.

~~1716. An method of treating a patient suffering from cancer, the method comprising administering to the patient therapy comprising an angiogenesis inhibitor comprising~~
15 bevacizumab or an antibody that binds essentially the same epitope on VEGF as bevacizumab wherein the patient genotype at polymorphism rs699946 (SEQ ID NO. 1) has been determined to be an A allele for use in treating a patient suffering from cancer.

1817. An method of determining whether a patient is suitably treated by a therapy
20 comprising an angiogenesis inhibitor comprising bevacizumab or an antibody that binds essentially the same epitope on VEGF as bevacizumab, said method comprising:

(a) determining in a sample derived from a patient suffering from cancer the genotype at polymorphism rs12505758 (SEQ ID NO. 2), and

(b) identifying a patient as more or less suitably treated by a therapy with an angiogenesis
25 inhibitor comprising bevacizumab or an antibody that binds essentially the same epitope on VEGF as bevacizumab based on said genotype, wherein the presence of each T allele at polymorphism rs12505758 (SEQ ID NO. 2) indicates an increased likelihood that said patient is more suitably treated, or the presence of each C allele at polymorphism rs12505758 (SEQ ID NO. 2) indicates an increased likelihood that said patient is less suitably treated.

30 1918. The method of claim 1817, wherein whether a patient is suitably treated by a therapy comprising an angiogenesis inhibitor is determined in terms of overall survival.

2019. The method of any one of claims 18-17 to 1918, wherein the therapy further comprises a chemotherapeutic agent or chemotherapy regimen.

5 2120. The method of any one of claims 18-17 to 2019, wherein the angiogenesis inhibitor is formulated for administration ~~administered~~ with one or more agents selected from the group consisting of taxanes, interferon alpha, 5-fluorouracil, capecitabine, leucovorin, gemcitabine, erlotinib and platinum-based chemotherapeutic agents.

10 2221. The method of any one of claims 18-17 to 2120, wherein the cancer is pancreatic cancer, renal cell cancer, colorectal cancer, breast cancer or lung cancer.

2322. The method of any one of claims 18-17 to 2221, wherein the sample is a blood sample.

15 2423. The method of any one of claims 18-17 to 2322, wherein the genotype is determined by means of MALDI-TOF mass spectrometry.

~~25. The method of any one of claims 18 to 24, further comprising administering the therapy to the patient.~~

20 2624. A pharmaceutical composition comprising an angiogenesis inhibitor as defined in claims 18-17 to 25-23 for the treatment of a patient in need thereof, wherein said patient has been determined to be more suitably treated with the angiogenesis inhibitor in accordance with the method of any one of claims 18-17 to 2523.

25 2725. A kit for carrying out the method of any one of claims 18-17 to 2523, comprising oligonucleotides capable of determining the genotype at polymorphism rs12505758 (SEQ ID NO. 2).

30 2826. A method for improving the treatment effect of a chemotherapeutic agent or chemotherapy regimen of a patient suffering from cancer by adding an angiogenesis inhibitor comprising bevacizumab or an antibody that binds essentially the same epitope on VEGF as bevacizumab, said method comprising:

(a) determining in a sample derived from a patient suffering from cancer the genotype at polymorphism rs12505758 (SEQ ID NO. 2);

(b) identifying a patient as more suitably treated by the addition of an angiogenesis inhibitor comprising bevacizumab or an antibody that binds essentially the same epitope on VEGF as bevacizumab based on said genotype, wherein the presence of each T allele at polymorphism rs12505758 (SEQ ID NO. 2) indicates an increased likelihood that said patient is more suitably treated; and

(c) ~~administering~~ formulating said angiogenesis inhibitor in combination with a chemotherapeutic agent or chemotherapy regimen for administration to a patient identified as more suitably treated in accordance with (b).

~~2927.~~ The method of claim ~~2826~~, wherein whether a patient is suitably treated by a therapy comprising an angiogenesis inhibitor is determined in terms of overall survival.

~~3028.~~ The method of any one of claims ~~28-26~~ to ~~2927~~, wherein the angiogenesis inhibitor is formulated for administration ~~administered~~ with one or more agents selected from the group consisting of taxanes, interferon alpha, 5-fluorouracil, capecitabine, leucovorin, gemcitabine, erlotinib and platinum-based chemotherapeutic agents.

~~3129.~~ The method of any one of claims ~~28-26~~ to ~~3028~~, wherein the cancer is pancreatic cancer, renal cell cancer, colorectal cancer, breast cancer or lung cancer.

~~3230.~~ The method of any one of claims ~~28-26~~ to ~~3129~~, wherein the sample is a blood sample.

~~3331.~~ The method of any one of claims ~~28-26~~ to ~~3230~~, wherein the genotype is determined by means of MALDI-TOF mass spectrometry.

~~3432.~~ ~~An method of treating a patient suffering from cancer, the method comprising administering to the patient therapy comprising an angiogenesis inhibitor comprising bevacizumab or an antibody that binds essentially the same epitope on VEGF as bevacizumab wherein the patient genotype at polymorphism rs12505758 (SEQ ID NO. 2) has been determined to be a T allele~~ for use in treating a patient suffering from cancer.

3533. An method of determining whether a patient is suitably treated by a therapy comprising an angiogenesis inhibitor comprising bevacizumab or an antibody that binds essentially the same epitope on VEGF as bevacizumab, said method comprising:

5 (a) determining in a sample derived from a patient suffering from cancer the genotype at polymorphism rs11133360 (SEQ ID NO. 5), and

(b) identifying a patient as more or less suitably treated by a therapy comprising an angiogenesis inhibitor comprising bevacizumab or an antibody that binds essentially the same epitope on VEGF as bevacizumab based on said genotype, wherein the presence of each T allele at polymorphism rs11133360 (SEQ ID NO. 5) indicates an increased likelihood that said patient is more suitably treated, or the presence of each C allele at polymorphism rs11133360 (SEQ ID NO. 5) indicates an increased likelihood that said patient is less suitably treated.

15 3634. The method of claim 3533, wherein whether a patient is suitably treated by a therapy comprising an angiogenesis inhibitor is determined in terms of progression-free survival.

3735. The method of any one of claims 3533 to 3634, wherein the therapy further comprises a chemotherapeutic agent or chemotherapy regimen.

20 3836. The method of any one of claims 3533 to 3735, wherein the angiogenesis inhibitor is formulated for administration ~~administered~~ with one or more agents selected from the group consisting of taxanes, interferon alpha, 5-fluorouracil, capecitabine, leucovorin, gemcitabine, erlotinib and platinum-based chemotherapeutic agents.

25 3937. The method of any one of claims 3533 to 3836, wherein the cancer is pancreatic cancer, renal cell cancer, colorectal cancer, breast cancer or lung cancer.

4038. The method of any one of claims 3533 to 3937, wherein the sample is a blood sample.

30 4139. The method of any one of claims 3533 to 4038, wherein the genotype is determined by means of MALDI-TOF mass spectrometry.

~~42. The method of any one claims 35 to 41, further comprising administering the therapy to the subject.~~

4340. A pharmaceutical composition comprising an angiogenesis inhibitor as defined in claims ~~35-33~~ to ~~42-39~~ for the treatment of a patient in need thereof, wherein said patient has been determined to be more suitably treated with the angiogenesis inhibitor in accordance with the method of any one of claims ~~35-33~~ to ~~42-39~~.

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4441. A kit for carrying out the method of any one of claims ~~35-33~~ to ~~42-39~~, comprising oligonucleotides capable of determining the genotype at polymorphism rs11133360 (SEQ ID NO. 5).

10 4542. A method for improving the treatment effect of a chemotherapeutic agent or chemotherapy regimen of a patient suffering from cancer by administering an angiogenesis inhibitor comprising bevacizumab or an antibody that binds essentially the same epitope on VEGF as bevacizumab, said method comprising:

15 (a) determining in a sample derived from a patient suffering from cancer the genotype at polymorphism rs11133360 (SEQ ID NO. 5);

(b) identifying a patient as more suitably treated by the addition of an angiogenesis inhibitor comprising bevacizumab or an antibody that binds essentially the same epitope on VEGF as bevacizumab based on said genotype, wherein the presence of each T allele at polymorphism rs11133360 (SEQ ID NO. 5) indicates an increased likelihood that said patient is
20 more suitably treated; and

(c) ~~administering~~ formulating said angiogenesis inhibitor in combination with a chemotherapeutic agent or chemotherapy regimen for administration to a patient identified as more suitably treated in accordance with (b).

25 4643. The method of claim ~~45-42~~, wherein whether a patient is suitably treated by a therapy comprising an angiogenesis inhibitor is determined in terms of progression-free survival.

4744. The method of any one of claims ~~45-42~~ to ~~46-43~~, wherein the angiogenesis inhibitor is formulated for administration ~~administered~~ with one or more agents selected from the
30 group consisting of taxanes, interferon alpha, 5-fluorouracil, capecitabine, leucovorin, gemcitabine, erlotinib and platinum-based chemotherapeutic agents.

4845. The method of any one of claims 45-42 to 4744, wherein the cancer is pancreatic cancer, renal cell cancer, colorectal cancer, breast cancer or lung cancer.

5 4946. The method of any one of claims 45-42 to 4845, wherein the sample is a blood sample.

5047. The method of any one of claims 45-42 to 4946, wherein the genotype is determined by means of MALDI-TOF mass spectrometry.

10 5148. ~~An method of treating a patient suffering from cancer, the method comprising administering to the patient therapy comprising an angiogenesis inhibitor comprising bevacizumab or an antibody that binds essentially the same epitope on VEGF as bevacizumab wherein the patient genotype at polymorphism rs11133360 (SEQ ID NO. 5) has been determined to be a T allele~~ for use in treating a patient suffering from cancer.

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