

Claims

1. An method of determining susceptibility of a patient to developing hypertension associated with a therapy by 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 rs2305949 (SEQ ID NO. 3), and

(b) identifying a patient as more or less susceptible to developing hypertension associated with a therapy by an angiogenesis inhibitor comprising bevacizumab or an antibody that binds essentially the same epitope on VEGF as bevacizumab based on said genotype, wherein the
10 presence of CC genotype at polymorphism rs2305949 (SEQ ID NO. 3) indicates that said patient is more susceptible to developing hypertension than a patient having a genotype of CT or TT at polymorphism rs2305949 (SEQ ID NO. 3), or the presence of CT or TT genotype at polymorphism rs2305949 (SEQ ID NO. 3) indicates that said patient is less susceptible to developing hypertension than a patient having a genotype of CC at polymorphism rs2305949
15 (SEQ ID NO. 3).

2. The method of claim 1, wherein the therapy further comprises a chemotherapeutic agent or chemotherapy regimen.

20 3. The method of any one of claims 1 to 2, wherein the angiogenesis inhibitor is ~~administered~~ formulated for administration with one or more agents selected from the group consisting of taxanes, interferon alpha, 5-fluorouracil, leucovorin, irinotecan, gemcitabine-erlotinib and platinum-based chemotherapeutic agents.

25 4. The method of any one of claims 1 to 3, wherein the cancer is pancreatic cancer, renal cell cancer, colorectal cancer, breast cancer or lung cancer.

5. The method of any one of claims 1 to 4, wherein the sample is a blood sample.

30 6. The method of any one of claims 1 to 5, wherein the genotype is determined by means of MALDI-TOF mass spectrometry.

7. ~~The method of any one of claims 1 to 6, further comprising administering the therapy to the patient.~~

87. A pharmaceutical composition comprising an angiogenesis inhibitor as defined in claims 1 to ~~7~~6 for the treatment of a patient in need thereof, wherein said patient has been determined to be less susceptible to developing hypertension associated with a therapy comprising the angiogenesis inhibitor in accordance with the method of any one of claims 1 to ~~7~~6.

98. A kit for carrying out the method of any one of claims 1 to ~~7~~6, comprising oligonucleotides capable of determining the genotype at polymorphism rs2305949 (SEQ ID NO. 3).

~~109~~. A method of reducing the risk of developing hypertension associated with a therapy 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 rs2305949 (SEQ ID NO. 3);

(b) identifying a patient as less susceptible to developing hypertension associated with a therapy by an angiogenesis inhibitor comprising bevacizumab or an antibody that binds essentially the same epitope on VEGF as bevacizumab, wherein the presence of CT or TT genotype at polymorphism rs2305949 (SEQ ID NO. 3) indicates that said patient is less susceptible to developing hypertension than a patient having a genotype of CC at polymorphism rs2305949 (SEQ ID NO. 3); and

(c) ~~administering~~ formulating said angiogenesis inhibitor for administration to a patient with the CT or TT genotype at polymorphism rs2305949 (SEQ ID NO. 3) identified as less susceptible to developing hypertension in accordance with (b).

~~110~~. The method of claim ~~109~~, wherein the therapy further comprises a chemotherapeutic agent or chemotherapy regimen.

~~111~~. The method of any one of claims ~~109~~ to ~~110~~, 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, leucovorin, irinotecan, gemcitabine-erlotinib and platinum-based chemotherapeutic agents.

1312. The method of any one of ~~claims 10-9~~ to 12-11 wherein the cancer is pancreatic
5 cancer, renal cell cancer, colorectal cancer, breast cancer or lung cancer.

1413. The method of any one of claims 10-9 to 1312, wherein the sample is a blood sample.

10 1514. The method of any one of claims 10-9 to 1413, wherein the genotype is determined by means of MALDI-TOF mass spectrometry.

1615. ~~An method of treating a patient, the method comprising administering to the patient therapy comprising an~~ angiogenesis inhibitor comprising bevacizumab or an antibody
15 that binds essentially the same epitope on VEGF as bevacizumab wherein the patient genotype at polymorphism rs2305949 (SEQ ID NO. 3) has been determined to be CT or TT for use in treating a patient.

1716. An method of determining susceptibility of a patient to developing hypertension
20 associated with a therapy 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 rs4444903 (SEQ ID NO. 4), and

25 (b) identifying a patient as more or less susceptible to developing hypertension associated with a therapy by 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 GA genotype at polymorphism rs rs4444903 (SEQ ID NO. 4) indicates that said patient is more susceptible to developing hypertension than a patient having a genotype of GG or
30 AA at polymorphism rs4444903 (SEQ ID NO. 4), or the presence of GG or AA genotype at polymorphism rs4444903 (SEQ ID NO. 4) indicates that said patient is less susceptible to developing hypertension than a patient having a genotype of GA at polymorphism rs4444903 (SEQ ID NO. 4).

1817. The method of claim 1716, wherein the therapy further comprises a chemotherapeutic agent or chemotherapy regimen.

1918. The method of any one of claims 1716 to 1817, 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, leucovorin, irinotecan, gemcitabine-erlotinib and platinum-based chemotherapeutic agents.

2019. The method of any one of claims 1716 to 1918, wherein the cancer is pancreatic cancer, renal cell cancer, colorectal cancer, breast cancer or lung cancer.

2120. The method of any one of claims 1716 to 2019, wherein the sample is a blood sample.

2221. The method of any one of claims 1716 to 2120 wherein the genotype is determined by means of MALDI-TOF mass spectrometry.

~~23. The method of any one of claims 17 to 22, further comprising administering the therapy to the patient.~~

2422. A pharmaceutical composition comprising an angiogenesis inhibitor as defined in claims 1716 to 2321 for the treatment of a patient in need thereof, wherein said patient has been determined to be less susceptible to developing hypertension associated with a therapy by the angiogenesis inhibitor in accordance with the method of any one of claims 1716 to 2321.

2523. A kit for carrying out the method of any one of claims 1716 to 2321, comprising oligonucleotides capable of determining the genotype at polymorphism rs4444903 (SEQ ID NO. 4).

2624. A method of reducing the risk of developing hypertension associated with a therapy 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 rs4444903 (SEQ ID NO. 4);

(b) identifying a patient as less susceptible to developing hypertension associated with a therapy by an angiogenesis inhibitor comprising bevacizumab or an antibody that binds essentially the same epitope on VEGF as bevacizumab, wherein the presence of GG or AA genotype at polymorphism rs4444903 (SEQ ID NO. 4) indicates that said patient is less susceptible to developing hypertension than a patient having a genotype of GA at polymorphism rs4444903 (SEQ ID NO. 4); and

(c) ~~administering~~ formulating said angiogenesis inhibitor for administration to a patient with the GG or AA genotype at polymorphism rs4444903 (SEQ ID NO. 4) identified as less susceptible to developing hypertension in accordance with (b).

~~2725~~. The method of claim ~~2624~~, wherein the therapy further comprises a chemotherapeutic agent or chemotherapy regimen.

~~2826~~. The method of any one of claims ~~2624~~ to ~~2725~~, 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, leucovorin, irinotecan, gemcitabine-erlotinib and platinum-based chemotherapeutic agents.

~~2927~~. The method of any one of claims ~~2624~~ to ~~2826~~, wherein the cancer is pancreatic cancer, renal cell cancer, colorectal cancer, breast cancer or lung cancer.

~~3028~~. The method of any one of claims ~~2624~~ to ~~2927~~, wherein the sample is a blood sample.

~~3129~~. The method of any one of claims ~~2624~~ to ~~3028~~, wherein the genotype is determined by means of MALDI-TOF mass spectrometry.

~~3230~~. ~~An method of treating a patient, 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 rs4444903 (SEQ ID NO. 4) has been determined to be GG or AA for use in treating a patient.