

CLAIMS

1. ~~Bevacizumab for use in improving overall survival of a patient suffering from cancer wherein it is determined from a patient sample if the patient suffering from said cancer has the variant allele of the VEGFR-1 gene corresponding to rs9554316 (SEQ ID NO. 1), wherein position 51 is G, and whereby the bevacizumab is administered to said patient having said variant allele of the VEGFR-1 gene.~~
2. ~~Bevacizumab for use in improving progression-free survival of a patient suffering from cancer wherein it is determined from a patient sample if the patient suffering from said cancer has the variant allele of the VEGFR-1 gene corresponding to rs9554316 (SEQ ID NO. 1), wherein position 51 is G, and whereby the bevacizumab is administered to said patient having said variant allele of the VEGFR-1 gene.~~
3. ~~Bevacizumab for use in an improved chemotherapy regimen for a patient suffering from cancer wherein it is determined from a patient sample if a patient suffering from said cancer has the variant allele of the VEGFR-1 gene corresponding to rs9554316 (SEQ ID NO. 1), wherein position 51 is G, and whereby bevacizumab is administered to the patient having the variant allele of the VEGFR-1 gene.~~
4. ~~The bevacizumab for use in a method according to any one of claims 1 to 3, wherein the patient sample is a blood sample.~~
5. ~~The bevacizumab for use in a method according to any one of claims 1 to 4, wherein bevacizumab is administered as a co-treatment with a chemotherapeutic agent or chemotherapy regimen.~~
6. ~~The bevacizumab for use in a method according to any one of claims 1 to 5, wherein the patient is being co-treated with one or more agents selected from the group consisting of interferon alpha, 5-fluorouracil, leucovorin, irinotecan, gemcitabine-erlotinib and platinum-based chemotherapeutic agents.~~
7. ~~The bevacizumab for use in a method according to any one of claims 1 to 6, wherein the cancer is pancreatic cancer.~~
8. ~~The bevacizumab for use in a method according to claim 7, wherein the patient is being co-treated with is gemcitabine-erlotinib therapy.~~

- ~~9. The bevacizumab for use according to any one of claims 2 to 6, wherein the cancer is renal cell cancer.~~
- ~~10. The bevacizumab for use in a method according to claim 9, wherein the patient is being co-treated with interferon alpha therapy.~~
- ~~11. The bevacizumab for use in a method according to claim 7 or 8, further comprising determining if the patient has more variant alleles of the VEGFR-1 gene selected from the group consisting of:~~
- ~~(a) rs9582036 (SEQ ID NO. 2), wherein position 51 is A;~~
 - ~~(b) rs9513070 (SEQ ID NO. 3), wherein position 51 is A; and~~
 - ~~(c) rs9554320 (SEQ ID NO. 4), wherein position 51 is C.~~
- ~~12. The bevacizumab for use in a method according to claim 9 or 10, further comprising determining if the patient has the variant allele of the VEGFR-1 gene corresponding to rs9513070 (SEQ ID NO. 3), wherein position 51 is A.~~

CLAIMS

- ~~131.~~ Use of bevacizumab in the manufacture of a medicament for the improvement of overall survival of a patient suffering from cancer wherein it is determined from a patient sample if the patient suffering from said cancer has the variant allele of the VEGFR-1 gene corresponding to rs9554316 (SEQ ID NO. 1), wherein position 51 is G, and whereby the bevacizumab is administered to said patient having said variant allele of the VEGFR-1 gene.
- ~~142.~~ Use of bevacizumab in the manufacture of a medicament for the improvement of progression-free survival of a patient suffering from cancer wherein it is determined from a patient sample if the patient suffering from said cancer has the variant allele of the VEGFR-1 gene corresponding to rs9554316 (SEQ ID NO. 1), wherein position 51 is G, and whereby the bevacizumab is administered to said patient having said variant allele of the VEGFR-1 gene.
- ~~153.~~ Use of bevacizumab in the manufacture of a medicament in an improved chemotherapy regimen for a patient suffering from cancer wherein it is determined from a patient sample if a patient suffering from said cancer has the variant allele of the VEGFR-1 gene corresponding to rs9554316 (SEQ ID NO. 1), wherein position 51 is G, and whereby bevacizumab is administered to the patient having the variant allele of the VEGFR-1 gene.

- | ~~164~~. The use according to any one of claims ~~13-1~~ to ~~153~~, wherein the patient sample is a blood sample.
- | ~~175~~. The use according to any one of claims ~~13-1~~ to ~~164~~, wherein bevacizumab is administered as a co-treatment with a chemotherapeutic agent or chemotherapy regimen.
- | ~~186~~. The use according to any one of claims ~~13-1~~ to ~~175~~, wherein the patient is being co-treated with one or more agents selected from the group consisting of interferon alpha, 5-fluorouracil, leucovorin, irinotecan, gemcitabine-erlotinib and platinum-based chemotherapeutic agents.
- | ~~197~~. The use according to any one of claims ~~13-1~~ to ~~186~~, wherein the cancer is pancreatic cancer.
- | ~~208~~. The use according to claim ~~197~~, wherein the patient is being co-treated with is gemcitabine-erlotinib therapy.
- | ~~219~~. The use according to any one of claims ~~14-2~~ to ~~186~~, wherein the cancer is renal cell cancer.
- | ~~2210~~. The use according to claim ~~219~~, wherein the patient is being co-treated with interferon alpha therapy.
- | ~~2311~~. The use according to claim ~~19-7~~ or ~~208~~, wherein the patient sample is further determined for the presence of more variant alleles of the VEGFR-1 gene selected from the group consisting of:
 - (a) rs9582036 (SEQ ID NO. 2), wherein position 51 is A,
 - (b) rs9513070 (SEQ ID NO. 3), wherein position 51 is A; and
 - (c) rs9554320 (SEQ ID NO. 4), wherein position 51 is C.
- | ~~2412~~. The use according to claim ~~21-9~~ or ~~2210~~, wherein the patient sample is further determined for the presence of the variant allele of the VEGFR-1 gene corresponding to rs9513070 (SEQ ID NO. 3), wherein position 51 is A.
- | ~~2513~~. An *in vitro* method for the identification of a responder for or a patient sensitive to bevacizumab, said method comprising determining from a patient sample if a patient suffering from cancer has the variant allele of the VEGFR-1 gene corresponding to rs9554316 (SEQ ID NO. 1), wherein position 51 is G, whereby the presence of said

allele of the VEGFR-1 gene is indicative for a responding patient or is indicative for a sensitivity of the patient to bevacizumab.

~~26~~14. The *in vitro* method according to claim ~~25~~13, wherein the patient sample is a blood sample.

~~27~~15. The *in vitro* method according to claim ~~25~~13 or ~~26~~14, wherein the cancer is pancreatic cancer.

~~28~~16. The *in vitro* method according to claim ~~25~~13 or ~~26~~14, wherein the cancer is renal cell cancer.

~~29~~17. The *in vitro* method according to claim ~~27~~15, further comprising determining if the patient has more variant alleles of the VEGFR-1 gene selected from the group consisting of:

- (a) rs9582036 (SEQ ID NO. 2), wherein position 51 is A,
- (b) rs9513070 (SEQ ID NO. 3), wherein position 51 is A; and
- (c) rs9554320 (SEQ ID NO. 4), wherein position 51 is C.

~~30~~18. The *in vitro* method according to claim ~~28~~16, further comprising determining if the patient has the variant allele of the VEGFR-1 gene corresponding to rs9513070 (SEQ ID NO. 3), wherein position 51 is A.

~~31~~19. Use of primers and/or probes for predicting the response to or sensitivity to bevacizumab therapy of a patient suffering or suspected to suffer from metastatic pancreatic cancer or renal cell cancer wherein the primers and/or probes are capable of detecting the variant allele of rs9554316 (SEQ ID NO. 1), whereby a G at position 51 of rs9554316 (SEQ ID NO. 1) is indicative of a patient response or sensitive to bevacizumab therapy.

~~32~~20. Use of a kit for determining the patient sample according to any one of claims 1 to ~~30~~18, comprising primers or probes capable of determining the presence of the variant allele of the VEGFR-1 gene corresponding to rs9554316 (SEQ ID NO. 1).

~~33~~21. The use of claim ~~32~~20, wherein

- (a) the primers are selected from the group consisting of SEQ ID NO. 25 and SEQ ID NO. 26; or
- (b) the probes is selected from the group consisting of SEQ ID NO. 27, SEQ ID NO. 28 or SEQ ID NO. 29.