

Claims

1. A method of screening a treatment for triple negative breast cancer comprising the use of an androgen receptor inhibitor, the method comprising assaying a biological sample obtained from a subject to determine whether the biological sample obtained from the subject is classified as basal-like subtype or another subtype.
2. The method according to claim 1, wherein assaying the biological sample to determine whether the biological sample is classified as a basal-like subtype or another subtype is performed by detecting the expression of the set of intrinsic genes listed in Table 1.
3. The method according to claim 2, comprising:
 - (a) determining the Basal Centroid classifier score of the sample from the expression of the set of intrinsic genes listed in Table 1;
 - (b) determining the Luminal A Centroid classifier score of the sample from the expression of the set of intrinsic genes listed in Table 1; and
 - (c) calculating a Weighted Basal and Luminal A classifier score from the Basal Centroid classifier score and the Luminal A Centroid classifier score according to the following equation:

$$\text{Weighted Basal and Luminal A classifier score} = -0.25(\text{Basal Centroid classifier score}) + 0.27(\text{Luminal A Centroid classifier score})$$

wherein if the Weighted Basal and Luminal A classifier score is greater than -0.3, the breast cancer treatment comprising an androgen receptor inhibitor is more likely to be effective in the subject than if the Weighted Basal and Luminal A classifier score is less than or equal to -0.3.

4. The method according to claim 3, wherein if the Weighted Basal and Luminal A classifier score is greater than -0.2, the breast cancer treatment comprising an androgen receptor inhibitor is more likely to be effective in the subject than if the Weighted Basal and Luminal A classifier score is less than or equal to -0.2.

5. The method according to claim 4, wherein if the Weighted Basal and Luminal A classifier score is greater than -0.25, the breast cancer treatment comprising an androgen receptor inhibitor is more likely to be effective in the subject than if the Weighted Basal and Luminal A classifier score is less than or equal to -0.25.

6. The method according to claim 2, comprising determining the Basal Centroid classifier score of the sample from the expression of the set of intrinsic genes listed in Table 1, wherein if the Basal Centroid classifier score is less than or equal to 0.9, the breast cancer treatment comprising an androgen receptor inhibitor is likely to be more effective in treating the subject than if the Basal Centroid classifier score is greater than 0.9.

7. The method according to claim 6, wherein if the Basal Centroid classifier score is less than or equal to 0.6, the breast cancer treatment comprising an androgen receptor inhibitor is likely to be effective in treating the subject.

8. The method according to claim 6, wherein if the Basal Centroid classifier score is in the range from 0.2 to 0.8, the breast cancer treatment comprising an androgen receptor inhibitor is likely to be effective in treating the subject.

9. The method according to claim 8, wherein if the Basal Centroid classifier score is in the range from 0.4 to 0.7, the breast cancer treatment comprising an androgen receptor inhibitor is likely to be effective in treating the subject.

10. The method according to any of claims 1 to 9, wherein the breast cancer of the subject is characterized by the presence of androgen receptor-positive tumor cells.

11. The method according to any of claims 1 to 10, wherein the biological sample is selected from the group consisting of a cell, tissue and bodily fluid.

12. The method according to claim 11, wherein the biological sample comprises breast tissue or cells.
13. The method according to claim 11, wherein the tissue is obtained from a biopsy.
14. The method according to claim 11, wherein the bodily fluid is selected from the group consisting of blood, lymph, urine, saliva, fluid from ductal lavage, and nipple aspirate.
15. An androgen receptor inhibitor for use in the treatment of a triple negative breast cancer in a subject wherein a biological sample from the subject has been assayed to determine whether the sample is classified as basal-like subtype or another subtype.
16. The use of an inhibitor according to claim 15, wherein assaying the biological sample to determine whether the biological sample is classified as a basal-like subtype or another subtype is performed by detecting the expression of the intrinsic genes listed in Table 1.
17. The use of an inhibitor according to claim 16, comprising determining the Basal Centroid classifier score and the Luminal A Centroid classifier score of the sample from the expression of the set of intrinsic genes listed in Table 1 and calculating a Weighted Basal and Luminal A classifier score from the Basal Centroid classifier score and the Luminal A Centroid classifier score according to the following equation:

$$\text{Weighted Basal and Luminal A classifier score} = -0.25(\text{Basal Centroid classifier score}) + 0.27(\text{Luminal A Centroid classifier score})$$
wherein the breast cancer treatment is administered to the subject if the Weighted Basal and Luminal A classifier score greater than -0.3.
18. The use of an inhibitor according to claim 17, wherein the breast cancer treatment is administered if the Weighted Basal and Luminal A classifier score is greater than -0.2.

19. The use of an inhibitor according to claim 18, wherein the breast cancer treatment is administered if the Weighted Basal and Luminal A classifier score is greater than -0.25.

20. The use of an inhibitor according to claim 16, comprising determining the Basal Centroid classifier score of the sample from the expression of the set of intrinsic genes listed in Table 1, wherein the breast cancer treatment is administered if the Basal Centroid classifier score is less than or equal to 0.9.

21. The use of an inhibitor according to claim 20, wherein the breast cancer treatment is administered if the Basal Centroid classifier score is less than or equal to 0.6.

22. The use of an inhibitor according to claim 20, wherein the breast cancer treatment is administered if the Basal Centroid classifier score is in the range from 0.2 to 0.8.

23. The use of an inhibitor according to claim 22, wherein the breast cancer treatment is administered if the Basal Centroid classifier score is in the range from 0.4 to 0.7.

24. The use of an inhibitor according to any of claims 15 to 23, wherein the breast cancer of the subject is characterized by the presence of androgen receptor-positive tumor cells.

25. The use of an inhibitor according to any of claims 15 to 24, wherein the androgen receptor inhibitor is selected from the group consisting of enzalutamide, bicalutamide, flutamide, nilutamide, ARN509, ketoconazole, abiraterone acetate, VN/124-1 (TOK-001), orteronel (TAK-700), finasteride, galeterone, cyproterone acetate, andarine and combinations thereof.

26. The use of an inhibitor according to claim 25, wherein the androgen receptor inhibitor is enzalutamide.

27. The use of an inhibitor according to claim 26, wherein the enzalutamide is orally administered once daily at a dose of 160 mg.

28. The use of an inhibitor according to claim 27, wherein the enzalutamide is administered as a single capsule comprising 160 mg enzalutamide.

29. The use of an inhibitor according to claim 27, wherein the enzalutamide is administered as four capsules, each capsule comprising 40 mg enzalutamide.

30. The use of an inhibitor according to any of claims 15 to 29, wherein the breast cancer treatment comprising an androgen receptor inhibitor further comprises one or more other anti-cancer agents that is not an androgen receptor inhibitor.

31. The use of an inhibitor according to claim 30, wherein the one or more other anti-cancer agent that is not an androgen receptor inhibitor is selected from the group consisting of cyclophosphamide, fluorouracil, 5-fluorouracil, methotrexate, thiotepa, carboplatin, cisplatin, taxanes, paclitaxel, protein-bound paclitaxel, docetaxel, vinorelbine, tamoxifen, raloxifene, toremifene, fulvestrant, gemcitabine, irinotecan, ixabepilone, temozolamide, topotecan, vincristine, vinblastine, eribulin, mutamycin, capecitabine, capecitabine, anastrozole, exemestane, letrozole, leuprolide, abarelix, buserlin, goserelin, megestrol acetate, risedronate, pamidronate, ibandronate, alendronate, denosumab, zoledronate, trastuzumab, tykerb or bevacizumab, and combinations thereof.

32. The use according to claim 31 wherein the other anti-cancer agent that is not an androgen receptor inhibitor is paclitaxel.

33. The use of an inhibitor according to any of claims 15 to 32, wherein the biological sample is selected from the group consisting of a cell, tissue and bodily fluid.

34. The use of an inhibitor according to claim 33, wherein the biological sample comprises breast tissue or cells.

35. The use of an inhibitor according to claim 33, wherein the tissue is obtained from a biopsy.

36. The use of an inhibitor according to claim 33, wherein the bodily fluid is selected from the group consisting of blood, lymph, urine, saliva, fluid from ductal lavage, and nipple aspirate.

37. An androgen receptor inhibitor for use in the treatment of triple negative breast cancer in a subject, said subject having a breast cancer comprising breast cancer cells that have been classified as other than basal-like subtype,.

38. An androgen receptor inhibitor for use according to claim 37, wherein the breast cancer cells of the subject are characterized by a Weighted Basal and Luminal A classifier score greater than -0.3 according to the formula:

$$\text{Weighted Basal and Luminal A classifier score} = -0.25(\text{Basal Centroid classifier score}) + 0.27(\text{Luminal A Centroid classifier score})$$

wherein said Basal Centroid classifier score and said Luminal A Centroid classifier score are determined for the breast cancer cells of the subject from the expression by said cells of the set of intrinsic genes listed in Table 1.

39. An androgen receptor inhibitor for use according to claim 38, wherein the breast cancer cells of the subject are characterized by a Weighted Basal and Luminal A classifier score greater than -0.2.

40. An androgen receptor inhibitor for use according to claim 39, wherein the breast cancer cells of the subject are characterized by a Weighted Basal and Luminal A classifier score greater than -0.25.

41. An androgen receptor inhibitor for use according to claim 37, wherein the breast cancer cells of the subject are characterized by a Basal Centroid classifier score of less than or equal to 0.9, determined from the expression by said cells of the set of intrinsic genes listed in Table 1.

42. An androgen receptor inhibitor for use according to claim 41, wherein the breast cancer cells of the subject are characterized by a Basal Centroid classifier score of less than or equal to 0.6.

43. An androgen receptor inhibitor for use according to claim 41, wherein the breast cancer cells of the subject are characterized by a Basal Centroid classifier score is in the range from 0.2 to 0.8.

44. An androgen receptor inhibitor for use according to claim 43, wherein the breast cancer cells of the subject are characterized by a Basal Centroid classifier score is in the range from 0.4 to 0.7.

45. An androgen receptor inhibitor for use according to any of claims 37 to 44, wherein the breast cancer of the subject is characterized by the presence of androgen receptor-positive tumor cells.

46. An androgen receptor inhibitor for use according to any of claims 37 to 45, wherein the androgen receptor inhibitor is selected from the group consisting of enzalutamide, bicalutamide, flutamide, nilutamide, ARN509, ketoconazole, abiraterone acetate, VN/124-1 (TOK-001), orteronel (TAK-700), finasteride, galeterone, cyproterone acetate, andarine and combinations thereof.

47. An androgen receptor inhibitor for use according to claim 46, wherein the androgen receptor inhibitor is enzalutamide.

48. An androgen receptor inhibitor for use according to claim 47, wherein the enzalutamide is orally administered once daily at a dose of 160 mg.

49. An androgen receptor inhibitor for use according to claim 48, wherein the enzalutamide is administered as a single capsule comprising 160 mg enzalutamide.

50. An androgen receptor inhibitor for use according to claim 48, wherein the enzalutamide is administered as four capsules, each capsule comprising 40 mg enzalutamide.

51. An androgen receptor inhibitor for use according to any of claims 37 to 50, wherein the breast cancer treatment comprising an androgen receptor inhibitor further comprises one or more other anti-cancer agents that is not an androgen receptor inhibitor.

52. An androgen receptor inhibitor for use according to claim 51, wherein the other anti-cancer agent that is not an androgen receptor inhibitor is selected from the group consisting of cyclophosphamide, fluorouracil, 5-fluorouracil, methotrexate, thiotepa, carboplatin, cisplatin, taxanes, paclitaxel, protein-bound paclitaxel, docetaxel,

vinorelbine, tamoxifen, raloxifene, toremifene, fulvestrant, gemcitabine, irinotecan, ixabepilone, temozolamide, topotecan, vincristine, vinblastine, eribulin, mutamycin, capecitabine, capecitabine, anastrozole, exemestane, letrozole, leuprolide, abarelix, buserlin, goserelin, megestrol acetate, risedronate, pamidronate, ibandronate, alendronate, denosumab, zoledronate, trastuzumab, tykerb or bevacizumab, and combinations thereof.

53. An androgen receptor inhibitor for use according to claim 52 wherein the other anti-cancer agent that is not an androgen receptor inhibitor is paclitaxel.

54. An androgen receptor inhibitor for use according to claim 37, further comprising a step of testing the subject to determine whether the subject has a breast cancer comprising breast cancer cells that are other than basal-like subtype.

55. An androgen receptor inhibitor for use according to any of claims 38 to 40, further comprising a step of testing the subject to determine the Weighted Basal and Luminal A classifier score of breast cancer cells of the subject.

56. An androgen receptor inhibitor for use according to any of claims 41 to 44, further comprising a step of testing the subject to determine the Basal Centroid classifier score of breast cancer cells of the subject.

57. An androgen receptor inhibitor for use according to claim 40, wherein the subject has received zero or one rounds of prior treatment with an anti-cancer agent, other than an androgen receptor inhibitor, for treatment of triple negative breast cancer.

58. Use of an androgen receptor inhibitor in the manufacture of a medicament for the treatment of triple negative breast cancer in a subject, said subject having a breast cancer comprising breast cancer cells that have been classified as other than basal-like subtype.

59. The use of an inhibitor according to claim 58, wherein the breast cancer cells of the subject are characterized by a Weighted Basal and Luminal A classifier score greater than -0.3 according to the formula:

$$\text{Weighted Basal and Luminal A classifier score} = \\ -0.25(\text{Basal Centroid classifier score}) + 0.27(\text{Luminal A Centroid classifier score})$$

wherein said Basal Centroid classifier score and said Luminal A Centroid classifier score are determined for the breast cancer cells of the subject from the expression by said cells of the set of intrinsic genes listed in Table 1.

60. The use of an inhibitor according to claim 59, wherein the breast cancer cells of the subject are characterized by a Weighted Basal and Luminal A classifier score greater than -0.2.

61. The use of an inhibitor according to claim 60, wherein the breast cancer cells of the subject are characterized by a Weighted Basal and Luminal A classifier score greater than -0.25.

62. The use of an inhibitor according to claim 58, wherein the breast cancer cells of the subject are characterized by a Basal Centroid classifier score of less than or equal to 0.9, determined from the expression by said cells of the set of intrinsic genes listed in Table 1.

63. The use of an inhibitor according to claim 62, wherein the breast cancer cells of the subject are characterized by a Basal Centroid classifier score of less than or equal to 0.6.

64. The use of an inhibitor according to claim 62, wherein the breast cancer cells of the subject are characterized by a Basal Centroid classifier score is in the range from 0.2 to 0.8.

65. The use of an inhibitor according to claim 64, wherein the breast cancer cells of the subject are characterized by a Basal Centroid classifier score is in the range from 0.4 to 0.7.

66. The use of an inhibitor according to any of claims 58 to 65, wherein the breast cancer of the subject is characterized by the presence of androgen receptor-positive tumor cells.

67. The use of an inhibitor according to any of claims 58 to 66, wherein the androgen receptor inhibitor is selected from the group consisting of enzalutamide, bicalutamide, flutamide, nilutamide, ARN509, ketoconazole, abiraterone acetate, VN/124-1 (TOK-001), orteronel (TAK-700), finasteride, galeterone, cyproterone acetate, andarine and combinations thereof.

68. The use of an inhibitor according to claim 67, wherein the androgen receptor inhibitor is enzalutamide.

69. The use of an inhibitor according to claim 68, wherein the enzalutamide is orally administered once daily at a dose of 160 mg.

70. The use of an inhibitor according to claim 69, wherein the enzalutamide is administered as a single capsule comprising 160 mg enzalutamide.

71. The use of an inhibitor according to claim 69, wherein the enzalutamide is administered as four capsules, each capsule comprising 40 mg enzalutamide.

72. The use of an inhibitor according to any of claims 58 to 71, wherein the breast cancer treatment comprising an androgen receptor inhibitor further comprises one or more other anti-cancer agents that is not an androgen receptor inhibitor.

73. The use of an inhibitor according to claim 72, wherein the other anti-cancer agent that is not an androgen receptor inhibitor is selected from the group consisting of cyclophosphamide, fluorouracil, 5-fluorouracil, methotrexate, thiotepa, carboplatin, cisplatin, taxanes, paclitaxel, protein-bound paclitaxel, docetaxel, vinorelbine, tamoxifen, raloxifene, toremifene, fulvestrant, gemcitabine, irinotecan, ixabepilone, temozolmide, topotecan, vincristine, vinblastine, eribulin, mutamycin,

capecitabine, capecitabine, anastrozole, exemestane, letrozole, leuprolide, abarelix, buserlin, goserelin, megestrol acetate, risedronate, pamidronate, ibandronate, alendronate, denosumab, zoledronate, trastuzumab, tykerb or bevacizumab, and combinations thereof.

74. The use of an inhibitor according to claim 73 wherein the other anti-cancer agent that is not an androgen receptor inhibitor is paclitaxel.

75. The use of an inhibitor according to claim 58, further comprising a step of testing the subject to determine whether the subject has a breast cancer comprising breast cancer cells that are other than basal-like subtype.

76. The use of an inhibitor according to any of claims 59 to 61, further comprising a step of testing the subject to determine the Weighted Basal and Luminal A classifier score of breast cancer cells of the subject.

77. The use of an inhibitor according to any of claims 62 to 65, further comprising a step of testing the subject to determine the Basal Centroid classifier score of breast cancer cells of the subject.

78. The use of an inhibitor according to claim 61, wherein the subject has received zero or one rounds of prior treatment with an anti-cancer agent, other than an androgen receptor inhibitor, for treatment of triple negative breast cancer.