We claim:

1. An ErbB3 inhibitor for treatment of an estrogen receptor positive or negative hormone refractory breast cancer.

2. A method of suppressing growth of an estrogen receptor positive or negative hormone refractory breast cancer cell, the method comprising contacting the cell with an effective amount of an ErbB3 inhibitor.

3. A method of suppressing growth of an estrogen receptor positive or negative hormone refractory breast cancer tumor in a patient, the method comprising administering to the patient an effective amount of an ErbB3 inhibitor.

4. A method of treating a patient for an estrogen receptor positive or negative hormone refractory breast cancer tumor, the method comprising administering to the patient an effective amount of an ErbB3 inhibitor.

5. A method of treating a breast cancer tumor in a patient, the method comprising

selecting a patient with an estrogen receptor positive or negative hormone refractory breast cancer tumor; and

administering to the patient an effective amount of an ErbB3 inhibitor.

6. The method of any one of claims 1 to 5, wherein the ErbB3 inhibitor is an anti-ErbB3 antibody.

7. The method of claim 6, wherein the anti-ErbB3 antibody comprises V_H and/or V_L regions comprising the amino acid sequences set forth in SEQ ID NOs: 1 and 2, respectively.

8. The method of claim 6, wherein the anti-ErbB3 antibody comprises V_H and/or V_L regions comprising the amino acid sequences set forth in SEQ ID NOs: 42 and 43, respectively.

9. The method of claim 6, wherein the anti-ErbB3 antibody comprises, in amino terminal to carboxy terminal order, V_H CDR1, 2 and 3 sequences as shown in SEQ ID NOs: 3-5, respectively, and, in amino terminal to carboxy terminal order, V_L CDR1, 2 and 3 sequences as shown in SEQ ID NOs: 6-8, respectively.

10. The method of any one of claims 3 to 5, further comprising co-administering to the patient an effective amount of at least one additional anti-cancer agent that is not an ErbB3 inhibitor.

11. The method of claim 10, wherein the at least one additional anti-cancer agent comprises at least one chemotherapeutic drug.

12. The method of claim 10, wherein the at least one additional anti-cancer agent is selected from the group consisting of platinum-based chemotherapy drugs, taxanes, tyrosine kinase inhibitors, serine/threonine protein kinase inhibitors, anti-EGFR antibodies, anti-ErbB2 antibodies, and combinations thereof.

13. The method of claim 10, wherein the at least one additional anti-cancer agent comprises an EGFR inhibitor.

14. The method of claim 10, wherein the EGFR inhibitor comprises an anti-EGFR antibody.

15. The method of claim 14, wherein the anti-EGFR antibody comprises cetuximab.

16. The method of claim 13, wherein the EGFR inhibitor is a small molecule inhibitor of EGFR signaling.

17. The method of claim 16, wherein the small molecule inhibitor of EGFR signaling is selected from the group consisting of afatinib gefitinib, lapatinib, canertinib, pelitinib, erlotinib, PKI-166, PD158780, and AG 1478.

18. The method of claim 10, wherein the at least one additional anti-cancer agent comprises a VEGF inhibitor.

19. The method of claim 18, wherein the VEGF inhibitor comprises an anti-VEGF antibody.

20. The method of claim 19, wherein the anti-VEGF antibody is bevacizumab.

21. The method of any one of claims 1 to 20, wherein the hormone refractory breast cancer is estrogen receptor positive (ER+).

22. The method of claim 21 further comprising co-administration of either or both of an estrogen receptor antagonist and an aromatase inhibitor.

23. The method of claim 22, wherein the estrogen receptor antagonist is selected from raloxifene, tamoxifen, afimoxifene (4-hydroxytamoxifen), arzoxifene, lasofoxone, toremifene and fulvestrant; and the aromatase inhibitor is selected from exemestane, anastrozole, letrozole, aminoglutethimide, testolactone, vorozole, formestane and fadrozole.

24. The method of claim 22, wherein the aromatase inhibitor is letrozole.

25. The method of claim 21 further comprising co-administration of either or both of an mTOR inhibitor and an aromatase inhibitor.

26. The method of claim 25, wherein the mTOR inhibitor is selected from temsirolimus, everolimus, sirolimus, and ridaforolimus; and the an aromatase inhibitor is selected from exemestane, anastrozole, letrozole, aminoglutethimide, testolactone, vorozole, formestane and fadrozole.

27. The method of claim 26, wherein the aromatase inhibitor is exemestane.

28. The method of claim 26, wherein the mTOR inhibitor is everolimus.

29. A method of inhibiting heregulin-mediated activation of estrogen receptors in tumor cells, said method comprising 1) selecting a human patient who has been treated for a malignancy with an anti-estrogen therapy and has become resistant to such therapy, which patient has a malignant tumor, which tumor, by analysis of a tumor biopsy taken from the patent after the patient has become resistant, is estrogen receptor positive and overexpresses HER2, and which activation comprises phosphorylation of estrogen receptors, and 2) administering to the patient so selected an antibody that inhibits heregulin binding to ErbB2/ErbB3 heterodimer, wherein the antibody is administered at a dosage that yields a concentration of the antibody in the patient's bloodstream that is a sufficient concentration to inhibit heregulin-induced estrogen receptor phosphorylation in MCF7 cells *in vitro* by at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, or at least 70%, wherein said administration at said dosage is effective to treat the tumor.

30. The method of claim 29, wherein the malignant tumor is a tumor of the breast, ovary lung, or skin.

31. The method of claim 29, wherein the overexpression of HER2 is indicated by the tumor biopsy testing IHER2^{++} or IHER2^{+++} or IHER2 FISH-positive.

32. The method of any one of claims 29 to 31, wherein the anti-estrogen therapy is either or both of a treatment with an estrogen receptor blocker and a treatment with an aromatase inhibitor.

33. The method of claim 32, wherein the administration is by intravenous injection or infusion.

34. The method of any one of claims 31 to 33, wherein the antibody is an anti-ErbB2 antibody.

35. The method of any one of claims 29 to 33, wherein the antibody is an anti-ErbB3 antibody.

36. The method of claim 35, wherein the antibody comprises V_H and/or V_L regions comprising the amino acid sequences set forth in SEQ ID NOs: 1 and 2, respectively.

37. The method of claim 35, wherein the anti-ErbB3 antibody comprises V_H and/or V_L regions comprising the amino acid sequences set forth in SEQ ID NOs: 42 and 43, respectively.

38. The method of any one of claims 29 to 33, wherein the antibody is an anti-ErbB2/antiErbB3 bispecific antibody.

39. The method of claim 38, wherein the bispecific antibody is selected from the group consisting of ALM, A5-HSA-ML3.9, A5-HSA-B1D2, B12-HSA-B1D2, A5-HSA-F5B6H2, H3-HSA-F5B6H2, F4-HSA-F5B6H2 and H3-HSA-B1D2.

40. The method of any one of claims 29 to 39, wherein the administration of the antibody inhibits one or more of growth, invasiveness, and metastasis of the tumor.

41. The method of any one of claims 29 to 40, further comprising co-administration of either or both of an estrogen receptor antagonist and an aromatase inhibitor.

42. The method of claim 41 wherein the estrogen receptor antagonist is selected from raloxifene, tamoxifen, afimoxifene (4-hydroxytamoxifen), arzoxifene, lasofoxone, toremifene and fulvestrant; and the aromatase inhibitor is selected from exemestane, anastrozole, letrozole, aminoglutethimide, testolactone, vorozole, formestane and fadrozole.

43. The method of claim 42 wherein the aromatase inhibitor is letrozole.

44. A composition for inhibition of heregulin-mediated activation of estrogen receptor, said inhibition following selection of a human patient who has been treated for a malignancy with an anti-estrogen therapy and has become resistant to such therapy, which patient has a malignant tumor, which tumor, by analysis of a tumor biopsy taken from the patent after the patient has become resistant, is estrogen receptor positive and overexpresses ErbB2, and which activation comprises phosphorylation of estrogen receptors, said composition comprising an anti-ErbB3 antibody that inhibits heregulin binding to ErbB2/ErbB3 heterodimer.

45. A composition for inhibition of heregulin-mediated activation of estrogen receptor, said inhibition following selection of a human patient who has been treated for a malignancy with an anti-estrogen therapy and has become resistant to such therapy, which patient has a malignant tumor, which tumor, by analysis of a tumor biopsy taken from the patent after the patient has become resistant, is estrogen receptor positive and overexpresses ErbB2, and which activation comprises phosphorylation of estrogen receptors, said composition comprising an anti-ErbB2 antibody that binds to ErbB2 and inhibits heregulin binding to ErbB2/ErbB3 heterodimer.

46. The composition of claim 45, wherein the anti-ErbB2 antibody is pertuzumab.

47. A composition for inhibition of heregulin-mediated activation of estrogen receptor, said inhibition following selection of a human patient who has been treated for a malignancy with an anti-estrogen therapy and has become resistant to such therapy, which patient has a malignant tumor, which tumor, by analysis of a tumor biopsy taken from the patent after the patient has become resistant, is estrogen receptor positive and overexpresses ErbB2, and which activation comprises phosphorylation of estrogen receptors, said composition comprising an anti-ErbB2/antiErbB3 bispecific antibody that inhibits heregulin binding to ErbB2/ErbB3 heterodimer.

48. A composition for treatment of a hormone refractory estrogen-receptor positive cancer, said composition comprising an anti-ErbB3 antibody that inhibits heregulin binding to ErbB2/ErbB3 heterodimer.

49. A composition for treatment of a hormone refractory estrogen-receptor positive cancer, said composition comprising an anti-ErbB2 antibody that binds to ErbB2 and inhibits heregulin binding to ErbB2/ErbB3 heterodimer.

50. The composition of any one of claims 44 to 49 for co-administration with either or both of an estrogen receptor antagonist and an aromatase inhibitor.

51. The composition of claim 45, wherein the anti-ErbB2 antibody is pertuzumab.

52. A composition for treatment of a hormone refractory estrogen-receptor positive cancer, said composition comprising an anti-ErbB2/antiErbB3 bispecific antibody that inhibits heregulin binding to ErbB2/ErbB3 heterodimer.

53. The composition of claim 50, wherein the estrogen receptor antagonist is selected from raloxifene, tamoxifen, afimoxifene (4-hydroxytamoxifen), arzoxifene, lasofoxone, toremifene and fulvestrant; and the aromatase inhibitor is selected from exemestane, anastrozole, letrozole, aminoglutethimide, testolactone, vorozole, formestane and fadrozole.

54. The composition of claim 53, wherein the aromatase inhibitor is letrozole.

55. The method of claim 38, wherein the bispecific antibody is the antibody comprising SEQ ID NO:44.

56. The composition of claim 47 or 52, wherein the bispecific antibody is the antibody comprising SEQ ID NO:44.

57. The composition of any one of claims 44 to 59 for co-administration with either or both of an mTOR inhibitor and an aromatase inhibitor.

58. The composition of claim 57, wherein the mTOR inhibitor is selected from temsirolimus, everolimus, sirolimus, and ridaforolimus; and the an aromatase inhibitor is selected from exemestane, anastrozole, letrozole, aminoglutethimide, testolactone, vorozole, formestane and fadrozole.

59. The method of claim 58, wherein the aromatase inhibitor is exemestane.

60. The method of claim 58, wherein the mTOR inhibitor is everolimus.

CLAIMS

1. Use of an antibody that inhibits heregulin binding to ErbB2/ErbB3 heterodimer in the manufacture of a medicament for treating a malignant tumour by inhibiting heregulin-mediated activation of estrogen receptors in malignant tumor cells in a human patient with a malignant tumor,

wherein the patient has been treated for a malignancy with an anti-estrogen therapy and has become resistant to such therapy,

which tumor, by analysis of a tumor biopsy taken from the patient after the patient has become resistant, is estrogen receptor positive and expresses HER2,

which activation comprises phosphorylation of estrogen receptors, and

wherein said medicament is suitable for administration at a dosage that yields a concentration of the antibody in the patient's bloodstream that is a sufficient concentration to inhibit heregulin-induced estrogen receptor phosphorylation in MCF7 cells in vitro by at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, or at least 70%.