

Claims

1. An *in vitro* method for the prognosis of overall breast cancer survival, breast cancer recurrence or response to HER2 antagonist treatment for a patient suffering from breast cancer, the method comprising:

5 (a) examining a sample from the patient to determine whether the patient is human epidermal growth factor receptor 2 (HER2) positive or negative based on a predetermined level of HER2; and

(b) measuring WW domain-binding protein 2 (WBP2) levels in the patient's sample,

10 wherein a result in step (a) and a result in step (b) are compared to a set of predetermined expression level results from a comparison population wherein the comparison population is stratified into a plurality of four subgroups determining the aggressiveness of a breast cancer and provides a prognosis of overall breast cancer survival, breast cancer recurrence or response to
15 treatment for the patient, the subgroups comprising:

(i) a reference group of HER2 negative patients comprising WBP2 expression below a predetermined level;

(ii) a group of HER2 negative patients comprising WBP2 expression above a predetermined level;

20 (iii) a group of HER2 positive patients comprising WBP2 expression below a predetermined level; or

(iv) a group of HER2 positive patients comprising WBP2 expression above a predetermined level.

25 2. The method of claim 1, wherein each subgroup (ii) to (iv) is referenced from the reference group (i).

3. The method of claim 2, wherein a sample with WBP2 expression levels above the predetermined level and a HER2 positive patient provides the
30 prognosis that the patient has an approximate 4 to 5 times lower chance of overall survival compared to the reference group.

4. The method of claim 2, wherein a sample with WBP2 expression levels below the predetermined level and a HER2 positive patient provides the prognosis that the patient has an approximate 1 to 2 times lower chance of overall survival compared to the reference group.

5. The method of claim 2, wherein a sample with WBP2 expression levels above the predetermined level and a HER2 negative patient provides the prognosis that the patient has an approximate 2 to 3 times lower chance of overall survival compared to the reference group.

6. The method of claim 2, wherein a sample with WBP2 expression levels above the predetermined level and a HER2 positive patient provides the prognosis that the patient has an approximate 2 to 3 times higher chance of cancer recurrence compared to the reference group.

7. The method of claim 2, wherein a sample with WBP2 expression levels below the predetermined level and a HER2 positive patient provides the prognosis that the patient has an approximate 1 times higher chance of cancer recurrence compared to the reference group.

8. The method of claim 2, wherein a sample with WBP2 expression levels above the predetermined level and a HER2 negative patient provides the prognosis that the patient has an approximate 1 to 2 times higher chance of cancer recurrence compared to the reference group.

9. The method of claim 1 or 2, wherein a sample with WBP2 expression level above the predetermined level and a HER2 positive result predicts that the patient is likely to respond to treatment.

10. The method of claim 1 or 2, wherein a sample with WBP2 expression level below the predetermined level and a HER2 positive result predicts that the patient is less likely to respond to treatment.

5 11. The method of claim 1, wherein the HER2 antagonist comprises Herceptin (Trastuzumab), Pertuzumab, Lapatinib, Lapatinib in combination with capecitabine, Trastuzumab emtansin, Ado-trastuzumab, Neratinib, or Dasatinib.

10 12. The method of any one of the preceding claims, wherein the WBP2 levels in the patient's sample are measured with at least one probe adapted to target a WBP2 protein.

13. The method of claim 12, wherein the probe is an antibody.

15 14. The method of claim 12, wherein the probe is an aptamer.

15. The method of claim 12, wherein the probe is a peptide.

20 16. A kit for identifying in a sample the amount of human epidermal growth factor receptor 2 (HER2) and the amount of WW domain-binding protein 2 (WBP2) in the sample, the kit comprising:

(a) at least one first probe adapted to detect and measure a human epidermal growth factor receptor 2 (HER2) level in the sample to determine
25 whether the sample is HER2 positive or HER2 negative;

(b) at least one second probe adapted to detect and measure WW domain-binding protein 2 (WBP2) levels in the sample; and

(c) written instructions for examining a sample to determine a population stratified into a plurality of four subgroups prognostic of overall
30 breast cancer survival, breast cancer recurrence or response to HER2

antagonist treatment for a patient suffering from breast cancer, wherein the subgroups comprise:

(i) a reference group of HER2 negative patients comprising WBP2 expression below a predetermined level;

5 (ii) a group of HER2 negative patients comprising WBP2 expression above a predetermined level;

(iii) a group of HER2 positive patients comprising WBP2 expression below a predetermined level; or

10 (iv) a group of HER2 positive patients comprising WBP2 expression above a predetermined level.

17. The kit of claim 16, wherein the first probe is adapted target a HER2 protein.

15 18. The kit of claim 16, wherein the second probe is adapted to target a WBP2 protein.

19. The kit of claim 17 or 18, wherein the first and second probe is an antibody.

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20. The kit of claim 17 or 18, wherein the first and second probe is an aptamer.

21. The kit of claim 17 or 18, wherein the first and second probe is a peptide.

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22. An *in vitro* method for determining the prognosis of overall survival, cancer recurrence or response to HER2 antagonist treatment, the method comprising:

30 (a) measuring the level of human epidermal growth factor receptor 2 (HER2) in a sample;

(b) measuring the level of WW domain-binding protein 2 (WBP2) in the sample; and

(c) determining whether the level of HER2 and WBP2 are above or below a predetermined level

5 (d) stratifying the sample into one of four subgroups to provide a prognosis of overall breast cancer survival, breast cancer recurrence or response to breast cancer treatment, wherein the subgroups comprise:

(i) a reference group of HER2 negative patients comprising WBP2 expression below a predetermined level;

10 (ii) a group of HER2 negative patients comprising WBP2 expression above a predetermined level;

(iii) a group of HER2 positive patients comprising WBP2 expression below a predetermined level; or

15 (iv) a group of HER2 positive patients comprising WBP2 expression above a predetermined level.