

CLAIMS

1. An in vitro method for the identification of a patient suspected to suffer from gastric cancer and having an equivocal expression level of HER2 protein as a responder for or a patient sensitive to a modulator of the HER2/neu (ErbB2) signaling pathway, said method comprising the following steps:
 - (a) obtaining a sample from said patient; and
 - (b) evaluating
the gene amplification status of the HER2 gene in said sample,
whereby an equivocal expression level of HER2 protein and a high gene amplification status of the HER2 gene is indicative for a responding patient or is indicative for a sensitivity of said patient to said modulator of the HER2/neu (ErbB2) signaling pathway; wherein scoring of said equivocal expression level of HER2 protein is determined in a biopsy sample and wherein said equivocal protein expression level of HER2 is associated with a staining pattern of tumor cell cluster with a weak to moderate complete, basolateral or lateral membranous reactivity irrespective of percentage of tumor cells stained.
2. The method of claim 1, wherein said protein expression level of HER2 is or was determined by an immunohistochemical (IHC) method.
- ~~3. The method of claim 1 or 2, wherein scoring of said equivocal expression level of HER2 protein is determined in a biopsy sample.~~
- ~~43. The method of any of claims 1 to 3 or 2, wherein said equivocal protein expression level of HER2 is HER2(2+), as determined in a biopsy sample.~~
- ~~5. The method of claim 4, wherein said HER2(2+) is associated with a staining pattern in a biopsy sample of tumor cell cluster with a weak to moderate complete, basolateral or lateral membranous reactivity irrespective of percentage of tumor cells stained.~~
- ~~64. The method of claim 1 or 2, wherein said equivocal protein expression level of HER2 is HER2(2+), as determined in a resection sample.~~
- ~~75. The method of any of claims 1 to 64, wherein said gene amplification status of the HER2 gene is detected by an in situ hybridization (ISH) method.~~
- ~~86. The method of any one of claims 1 to 75, wherein said high amplification status of the HER2 gene is an average gene copy number of the HER2 gene of higher than 4 or an average gene copy number of HER2 equal to or higher than 2 per chromosome 17 copy.~~

97. The method of any one of claims 1 to ~~86~~, wherein the response rate of a group of patients identified by the method of any of claims 1 to ~~8-6~~ to a modulator of the HER2/neu (ErbB2) signaling pathway is at least 20 %.
- ~~108~~. The method of any one of claims 1 to 97, wherein said sample is ~~selected from the group consisting of gastric tissue resection, a~~ gastric tissue biopsy, ~~tissue from a metastatic lesion resection and circulating tumor cells.~~
- ~~119~~. The method of claim ~~75~~, wherein said in situ hybridization is selected from the group consisting of fluorescent in situ hybridization (FISH), chromogenic in situ hybridization (CISH) and silver in situ hybridization (SISH).
- ~~1210~~. The method of any one of claims 1 to ~~119~~, wherein said sample is obtained before anti-metastatic, neoadjuvant or adjuvant therapy.
- ~~1311~~. The method of any one of claims 1 to ~~1210~~, wherein said modulator of the HER2/neu (ErbB2) signaling pathway is a HER antibody.

~~14~~12. The method of any one of claims 1 to ~~13~~11, wherein said gastric cancer is invasive gastric cancer.

~~15~~13. The method of claim ~~14~~12, wherein said gastric cancer is selected from the group consisting of intestinal-type adenocarcinoma, mixed-type adenocarcinoma and diffuse-type adenocarcinoma.