

Claims

1. Use of a combination of a ErbB-2 targeting agent; a chemotherapeutic drug, and a bispecific antibody that comprises a first antigen-binding site that can bind an epitope on domain I of ErbB-2 and a second antigen-binding site that can bind an epitope on domain III of ErbB-3, in the manufacture of a medicament for the treatment of an individual that has an ErbB-2, ErbB-3 or ErbB-2/ErbB-3 positive tumor, wherein the ErbB-2 targeting agent is a bivalent monospecific antibody that comprises antigen binding sites that can bind an epitope on ErbB-2 extracellular domain IV.
2. The use of claim 1, wherein the monospecific antibody or bispecific antibody comprises a drug conjugate
3. The use of claim 1, wherein the monospecific antibody is Trastuzumab.
4. The use of claim 1, wherein the monospecific antibody is Trastuzumab emtansine.
5. The use of any one of claims 1-4, wherein said individual is afflicted with ErbB-2 positive metastatic breast cancer.
6. The use of any one of claims 1-5, wherein said individual is ErbB-2 ++ or ErbB-2 +++,
7. The use of any one of claims 1-6, wherein said individual has an ErbB-2 therapy resistant phenotype and/or a heregulin resistance phenotype, or an ErbB-2 monoclonal antibody therapy resistant phenotype.
8. A pharmaceutical composition comprising a ErbB-2 targeting agent, a chemotherapeutic drug, and a bispecific antibody that comprises an antigen-binding site that can bind an epitope on domain I of ErbB-2 and an antigen-binding site that can bind an epitope on domain III of ErbB-3, wherein the ErbB-2 targeting agent is a bivalent monospecific antibody that comprises antigen binding sites that can bind an epitope on ErbB-2 extracellular domain IV.
9. A kit of parts, comprising a ErbB-2 targeting agent, a chemotherapeutic drug, and a bispecific antibody that comprises an antigen-binding site that can bind an epitope on domain I of ErbB-2 and an antigen-binding site that can bind an epitope on domain III of ErbB-3, wherein the ErbB-2 targeting agent is a bivalent monospecific antibody that comprises antigen binding sites that can bind an epitope on ErbB-2 extracellular domain IV.
10. The use, pharmaceutical composition, or kit of parts of any one of claims 1-9, wherein said chemotherapeutic drug is selected from vinorelbine, paclitaxel, docetaxel, gemcitabine, eribulin, capecitabine and carboplatin.

11. The use, pharmaceutical composition, or kit of parts of claim 10, wherein said chemotherapeutic drug is vinorelbine.
12. The use, pharmaceutical composition, or kit of parts of any one of claims 1-11, wherein said bispecific antibody comprises at least the CDR1, CDR2 and CDR3 sequences of an ErbB 2 specific heavy chain variable region selected from the group consisting of MF2973, MF3004, MF3958, MF2971, MF3025, MF2916, MF3991, MF3031 and MF3003 and the CDR1, CDR2 and CDR3 sequences of an ErbB 3 specific heavy chain variable region selected from the group consisting of MF3178; MF3176; MF3163; MF6055; MF6056; MF6057; MF6058; MF6059; MF6060; MF6061; MF6062; MF6063; MF6064; MF 6065; MF6066; MF6067; MF6068; MF6069; MF6070; MF6071; MF6072; MF6073 and MF6074, and wherein the first antigen binding site and the second antigen binding site of said bispecific antibody comprise a light chain variable region comprising the rearranged germline human kappa light chain IgV κ 1-39*01/IGJ κ 1*01.
13. The use, pharmaceutical composition, or kit of parts of claim 12, wherein said bispecific antibody comprises at least the CDR1, CDR2 and CDR3 sequences of MF3958 comprising AYYIN, RIYPGSGYTSYAQKFQG, and PPVYYDSAWFAY, respectively, and at least the CDR1, CDR2 and CDR3 sequences of MF3958 and the CDR1, CDR2 and CDR3 sequences of MF3178 comprising GYYMH, WINPNSGGTNYAQKFQG, and DHGSRHFWSYWGFYD, respectively.
14. The use, pharmaceutical composition, or kit of parts of claim 13, wherein said bispecific antibody comprises the ErbB 2 specific heavy chain variable region of MF3958 and the ErbB 3 specific heavy chain variable region of MF3178.
15. The use, pharmaceutical composition, or kit of parts of any one of claims 12-14, wherein said first antigen binding site and said second antigen binding site of said bispecific antibody comprise at least the CDR1, CDR2 and CDR3 sequences of a light chain variable region of SEQ ID No: 74.
16. The use, pharmaceutical composition, or kit of parts of claim 15, wherein the light chain variable region comprises SEQ ID NO: 74.