therapeutic treatment for cancer, in selecting a treatment or preventive regimen (e.g., in deciding whether or not to administer a particular therapeutic agent to an individual having cancer, or who is at increased risk for developing cancer in the future), or in evaluating an individual's prognosis for disease severity and recovery.

The present invention is based on the finding that certain genotypes for SNPs are associated with sensitivity/insensitivity of cancer towards antibody treatment such as treatment of CLDN18.2 positive cancer, in particular CLDN18.2 positive gastroesophageal cancer with IMAB362. The present invention is further based on the finding that certain genotypes for SNPs are associated with clinical outcome for cancer patients and thus are useful for prognosing cancer.

Therefore, in one aspect, the present invention is directed to a method of assessing (i) if a cancer patient having a tumor antigen-positive tumor is a responder to treatment with an antibody against the tumor antigen, and/or (ii) if a cancer patient having a tumor antigen-positive tumor, will experience progression-free survival, wherein the tumor antigen is the CLDN18.2 protein; said method comprising determining the genotype for one or more single-nucleotide polymorphisms selected from the group consisting of MUC1 rs4072037, IL-10 rs1800896, DNMT3A rs1550117, SMAD4 rs12456284, EGF rs4444903, CDH1 rs16260, and ERCC1 rs11615 in a sample obtained from the patient, wherein (a) the presence of the homozygous MUC1 rs4072037 [AA] genotype indicates a reduced risk of a cancer patient not being a responder to treatment with the antibody and/or a reduced risk of a cancer patient not experiencing progression-free survival; (b) the presence of the homozygous MUC1 rs4072037 [GG] genotype indicates an increased risk of a cancer patient not being a responder to treatment with the antibody and/or an increased risk of a cancer patient not experiencing progression-free survival; (c) the presence of the homozygous IL-10 rs1800896 [GG] genotype indicates a reduced risk of a cancer patient not being a responder to treatment with the antibody and/or a reduced risk of a cancer patient not experiencing progression-free survival; (d) the presence of the heterozygous DNMT3A rs1550117 [GA] genotype indicates a reduced risk of a cancer patient not being a responder to treatment with the antibody and/or a reduced risk of a cancer patient not experiencing progression-free survival; (e) the presence of the heterozygous SMAD4 rs12456284 [GA] genotype indicates a reduced risk of a cancer patient not being a responder to treatment with the antibody and/or a reduced risk of a cancer patient not experiencing progression-free survival; (f) the presence of the homozygous EGF

rs4444903 [AA] genotype indicates a reduced risk of a cancer patient not being a responder to treatment with the antibody and/or a reduced risk of a cancer patient not experiencing progression-free survival; (g) the presence of the homozygous CDH1 rs16260 [AA] genotype indicates a reduced risk of a cancer patient not being a responder to treatment with the antibody and/or a reduced risk of a cancer patient not experiencing progression-free survival; and (h) the presence of the homozygous ERCC1 rs11615 [TT] genotype indicates a reduced risk of a cancer patient not being a responder to treatment with the antibody and/or a reduced risk of a cancer patient not experiencing progression-free survival. In another aspect, the present invention is directed to the use of an antibody binding to CLDN18.2 for the preparation of a medicament for use in a method of treatment of a cancer patient having a tumor which is positive for CLDN18.2, wherein the patient is characterized by having a reduced risk for not being a responder to treatment with the antibody, wherein the reduced risk is indicated in a tumor sample obtained from the patient by (a) the presence of the homozygous MUC1 rs4072037 [AA] genotype; (b) the presence of the homozygous IL-10 rs1800896 [GG] genotype; (c) the presence of the heterozygous DNMT3A rs1550117 [GA] genotype; (d) the presence of the heterozygous SMAD4 rs12456284 [GA] genotype; (e) the presence of the homozygous EGF rs4444903 [AA] genotype; (f) the presence of the homozygous CDH1 rs16260 [AA] genotype; and (g) the presence of the homozygous ERCC1 rs11615 [TT] genotype.

Also disclosed herein is a method of assessing

(i) if a cancer patient having a tumor antigen-positive tumor is a responder to treatment with an antibody against the tumor antigen, and/or

(ii) if a cancer patient, preferably a cancer patient having a tumor antigen-positive tumor, will experience progression-free survival,

said method comprising determining the genotype for one or more single-nucleotide polymorphisms selected from the group consisting of FCGR2A rs1801274, MUC1 rs4072037, IL-10 rs1800896, DNMT3A rs1550117, SMAD4 rs12456284, EGF rs4444903, CDH1 rs16260, ERCC1 rs11615, and FCGR3A rs396991 in a sample obtained from the patient.

In one example, the presence of the heterozygous FCGR2A rs1801274 [CT] genotype indicates a reduced risk of a cancer patient not being a responder to treatment with the antibody and/or a reduced risk of a cancer patient not experiencing progression-free survival.

In one example, the presence of the homozygous FCGR2A rs1801274 [TT] genotype and/or the homozygous FCGR2A rs1801274 [CC] genotype indicates an increased risk of a cancer patient not being a responder to treatment with the antibody and/or an increased risk of a cancer patient not experiencing progression-free survival.

CLAIMS

1. A method of assessing

(i) if a cancer patient having a tumor antigen-positive tumor is a responder to treatment with an antibody against the tumor antigen, and/or

(ii) if a cancer patient having a tumor antigen-positive tumor, will experience progression-free survival,

wherein the tumor antigen is the CLDN18.2 protein;

said method comprising determining the genotype for one or more single-nucleotide polymorphisms selected from the group consisting of MUC1 rs4072037, IL-10 rs1800896, DNMT3A rs1550117, SMAD4 rs12456284, EGF rs4444903, CDH1 rs16260, and ERCC1 rs11615 in a sample obtained from the patient, wherein

(a) the presence of the homozygous MUC1 rs4072037 [AA] genotype indicates a reduced risk of a cancer patient not being a responder to treatment with the antibody and/or a reduced risk of a cancer patient not experiencing progression-free survival;

(b) the presence of the homozygous MUC1 rs4072037 [GG] genotype indicates an increased risk of a cancer patient not being a responder to treatment with the antibody and/or an increased risk of a cancer patient not experiencing progression-free survival;

(c) the presence of the homozygous IL-10 rs1800896 [GG] genotype indicates a reduced risk of a cancer patient not being a responder to treatment with the antibody and/or a reduced risk of a cancer patient not experiencing progression-free survival;

(d) the presence of the heterozygous DNMT3A rs1550117 [GA] genotype indicates a reduced risk of a cancer patient not being a responder to treatment with the antibody and/or a reduced risk of a cancer patient not experiencing progression-free survival;

(e) the presence of the heterozygous SMAD4 rs12456284 [GA] genotype indicates a reduced risk of a cancer patient not being a responder to treatment with the antibody and/or a reduced risk of a cancer patient not experiencing progression-free survival;

(f) the presence of the homozygous EGF rs4444903 [AA] genotype indicates a reduced risk of a cancer patient not being a responder to treatment with the antibody and/or a reduced risk of a cancer patient not experiencing progression-free survival;

(g) the presence of the homozygous CDH1 rs16260 [AA] genotype indicates a reduced risk of a cancer patient not being a responder to treatment with the antibody and/or a reduced risk of a cancer patient not experiencing progression-free survival; and

(h) the presence of the homozygous ERCC1 rs11615 [TT] genotype indicates a reduced risk of a cancer patient not being a responder to treatment with the antibody and/or a reduced risk of a cancer patient not experiencing progression-free survival.

2. The method of claim 1 wherein the antibody acts through recruiting the patient's immune system to destroy tumor cells, preferably through antibody-dependent cell-mediated cytotoxicity (ADCC) and/or complement-dependent cytotoxicity (CDC).

3. The method of claim 1 or 2 wherein the antibody comprises (a) a heavy chain variable region comprising an amino acid sequence represented by SEQ ID NO: 32 and a light chain variable region comprising an amino acid sequence represented by SEQ ID NO: 39 or (b) a heavy chain comprising an amino acid sequence represented by SEQ ID NO: 17 and a light chain comprising an amino acid sequence represented by SEQ ID NO: 24.

4. Use of an antibody binding to CLDN18.2 for the preparation of a medicament for use in a method of treatment of a cancer patient having a tumor which is positive for CLDN18.2, wherein the patient is characterized by having a reduced risk for not being a responder to treatment with the antibody, wherein the reduced risk is indicated in a tumor sample obtained from the patient by

(a) the presence of the homozygous MUC1 rs4072037 [AA] genotype;
(b) the presence of the homozygous IL-10 rs1800896 [GG] genotype;
(c) the presence of the heterozygous DNMT3A rs1550117 [GA] genotype;
(d) the presence of the heterozygous SMAD4 rs12456284 [GA] genotype;
(e) the presence of the homozygous EGF rs4444903 [AA] genotype;
(f) the presence of the homozygous CDH1 rs16260 [AA] genotype; and
(g) the presence of the homozygous ERCC1 rs11615 [TT] genotype.

5. The use of claim 4, wherein said method comprises assessing if the cancer patient is a responder to treatment with an antibody by the method of any one of claims 1 to 3 and treating the cancer patient with the antibody if the patient has a reduced risk for not being a responder to treatment with the antibody.

6. The use of claim 4 or 5 wherein the treatment regimen comprises a treatment with an antibody-drug conjugate and wherein the antibody is directed against the tumor antigen, the

antibody-drug conjugate is preferably an antibody coupled to a radioactive, chemotherapeutic or toxin moiety or wherein the antibody-drug conjugate is an antibody coupled to a cytostatic or cytotoxic compound.

7. The method of any one of claims 1 to 3 or the use of any one of claims 4 to 6 wherein the tumor is a solid tumor.

8. The method of any one of claims 1 to 3 and 7 or the use of any one of claims 4 to 7 wherein the tumor is a gastroesophageal tumor.

9. The method of any one of claims 1 to 3, 7 and 8 or the use of any one of claims 4 to 8 wherein the tumor is an advanced adenocarcinoma of the stomach or the lower esophagus.