of the GPC3-targeting drug therapy is determined or the continuation of the GPC3-targeting drug therapy is determined. The present inventors have also created a GPC3-targeting drug or a preparation which is to be administered to a patient for which the efficacy of the GPC3-targeting drug therapy has been determined or the continuation of the GPC3-targeting drug therapy has been determined.

[0015]

More specifically, the present invention provides the following aspects:

In one aspect, the present disclosure refers to a method for predicting the efficacy of anti-GPC3 antibody therapy for hepatocellular cancer in a patient, comprising measuring the number of an immunocyte or an expression level of a molecule expressed on the immunocyte in peripheral blood isolated from the patient before the start of anti-GPC3 antibody therapy and/or the patient treated with the anti-GPC3- antibody therapy, wherein the anti-GPC3 antibody has antibody-dependent cellular cytotoxic (ADCC) activity,

wherein when the number of an immunocyte or the expression level of a molecule expressed on the immunocyte is above a predetermined value, the efficacy of the anti-GPC3 antibody therapy is predicted,

and wherein

(i) when the immunocyte is a leukocyte, the predetermined value is higher than 5750 cells/μL;
(ii) when the immunocyte is a monocyte, the predetermined number is higher than 550 cells/μL;
(iii) when the immunocyte is a neutrophil, the predetermined value is higher than 3750 cells/μl;
(iv) when the immunocyte is a lymphocyte, the predetermined number is higher than 1250 cells/μL; or
(v) when the molecule expressed on the immunocyte is CD16 on NK cells, the predetermined value of CD16 expression is higher than 375000 mesf.

In another aspect, the present disclosure refers to a method for determining the continuation of anti-GPC3 antibody therapy for a patient having hepatocellular cancer, comprising measuring the number of an immunocyte or an expression level of a molecule expressed on the immunocyte in peripheral blood isolated from the patient treated with anti-GPC3 antibody therapy at arbitrary points in time between the start and completion of the therapy, wherein the anti-GPC3 antibody has antibody dependent cellular cytotoxic (ADCC) activity, wherein when the number of an immunocyte or the expression level of a molecule expressed on the immunocyte is above a predetermined value, the continuation of the anti-GPC3 antibody therapy is determined, wherein
(i) when the immunocyte is a leukocyte, the predetermined value is higher than 5750 cells/μL;

(ii) when the immunocyte is a monocyte, the predetermined value is higher than 550 cells/μL;
(iii) when the immunocyte is a neutrophil, the predetermined value is higher than 3750 cells/μL;
(iv) when the immunocyte is a lymphocyte, the predetermined value is higher than 1250 cells/μL; or
(v) when the molecule expressed on the immunocyte is CD16 on NK cells, the predetermined value of CD16 expression is higher than 375000 mesf.

In another aspect, the present disclosure refers to a use of an anti-GPC3 antibody having antibody-dependent cellular cytotoxic (ADCC) activity in the manufacture of a medicament for treating hepatocellular cancer in a patient, wherein the anti-GPC3 antibody is to be administered to the patient, in which the number of an immunocyte or an expression level of a molecule expressed on the immunocyte in peripheral blood isolated from the patient is above a predetermined value, wherein
(i) when the immunocyte is a leukocyte, the predetermined value is higher than 5750 cells/μL;
(ii) when the immunocyte is a monocyte, the predetermined value is higher than 550 cells/μL;
(iii) when the immunocyte is a neutrophil, the predetermined value is higher than 3750 cells/μL;
(iv) when the immunocyte is a lymphocyte; the predetermined value is higher than 1250 cells/μL; or

(v) when the molecule expressed on the immunocyte is CD16 on NK cells, the predetermined value of CD16 expression is higher than 375000 mesf.

Furthermore, the present disclosure describes:

[1] a method for determining the efficacy of GPC3-targeting drug therapy for cancer in a patient or determining the continuation of GPC3-targeting drug therapy for a patient, comprising measuring the number of an immunocyte or an expression level of a molecule expressed on the immunocyte in a biological sample isolated from the patient before the start of GPC3-targeting drug therapy and/or the patient treated with the GPC3-targeting drug therapy, wherein when the number of an immunocyte or the expression level of a molecule expressed on the immunocyte is a predetermined value, the efficacy of the GPC3-targeting drug therapy is determined or the continuation of the GPC3-targeting drug therapy is determined,

[2] the method according to [1], wherein the biological sample is peripheral blood isolated from the patient,

Claims

1. A method for predicting the efficacy of anti-GPC3 antibody therapy for hepatocellular cancer in a patient, comprising measuring the number of an immunocyte or an expression level of a molecule expressed on the immunocyte in peripheral blood isolated from the patient before the start of anti-GPC3 antibody therapy and/or the patient treated with the anti-GPC3- antibody therapy, wherein the anti-GPC3 antibody has antibody-dependent cellular cytotoxic (ADCC) activity,

wherein when the number of an immunocyte or the expression level of a molecule expressed on the immunocyte is above a predetermined value, the efficacy of the anti-GPC3 antibody therapy is predicted,

and wherein

(i) when the immunocyte is a leukocyte, the predetermined value is higher than 5750 cells/μL;

(ii) when the immunocyte is a monocyte, the predetermined number is higher than 550 cells/μL;

(iii) when the immunocyte is a neutrophil, the predetermined value is higher than 3750 cells/μl;

(iv) when the immunocyte is a lymphocyte, the predetermined number is higher than 1250 cells/μL; or

(v) when the molecule expressed on the immunocyte is CD16 on NK cells, the predetermined value of CD16 expression is higher than 375000 mesf.

2. A method for determining the continuation of anti-GPC3 antibody therapy for a patient having hepatocellular cancer, comprising measuring the number of an immunocyte or an expression level of a molecule expressed on the immunocyte in peripheral blood isolated from the patient treated with anti-GPC3 antibody therapy at arbitrary points in time between the start and completion of the therapy, wherein the anti-GPC3 antibody has antibody dependent cellular cytotoxic (ADCC) activity, wherein when the number of an immunocyte or the expression level of a molecule expressed on the immunocyte is above a predetermined value, the continuation of the anti-GPC3 antibody therapy is determined, wherein

(i) when the immunocyte is a leukocyte, the predetermined value is higher than 5750 cells/μL;

(ii) when the immunocyte is a monocyte, the predetermined value is higher than 550 cells/μL;

(iii) when the immunocyte is a neutrophil, the predetermined value is higher than 3750 cells/μL;

(iv) when the immunocyte is a lymphocyte, the predetermined value is higher than 1250 cells/μL; or

(v) when the molecule expressed on the immunocyte is CD16 on NK cells, the predetermined value of CD16 expression is higher than 375000 mesf.

3. Use of an anti-GPC3 antibody having antibody-dependent cellular cytotoxic (ADCC) activity in the manufacture of a medicament for treating hepatocellular cancer in a patient, wherein the anti-GPC3 antibody is to be administered to the patient, in which the number of an immunocyte or an expression level of a molecule expressed on the immunocyte in peripheral blood isolated from the patient is above a predetermined value, wherein
(i) when the immunocyte is a leukocyte, the predetermined value is higher than 5750 cells/μL;
(ii) when the immunocyte is a monocyte, the predetermined value is higher than 550 cells/μL;
(iii) when the immunocyte is a neutrophil, the predetermined value is higher than 3750 cells/μL;
(iv) when the immunocyte is a lymphocyte; the predetermined value is higher than 1250 cells/μL; or
(v) when the molecule expressed on the immunocyte is CD16 on NK cells, the predetermined value of CD16 expression is higher than 375000 mesf.

4. The method according to claim 1 or 2, or the use according to claim 3, wherein the lymphocyte comprises at least one lymphocyte cell selected from a CD45+ lymphocyte, a CD3+ T cell, a CD4+ T cell, and a CD8+ T cell; or wherein the lymphocyte comprises at least one lymphocyte cell selected from a CD16+ NK cell, an NKp46+ NK cell, and a CD56-/CD16+ NK cell.

5. The method according to claim 1, 2 or 4, or the use according to claim 3 or 4,wherein the hepatocellular cancer patient has a polymorphism, at least one allele having Val at amino acid residue 158 of FcγRIIIA and/or at least one allele having His at amino acid residue 131 of FcγRIIA.

6. The method according to any one of claims 1, 2, 4, and 5, or the use according to any one of claims 3 to 5, wherein the anti-GPC3 antibody is an anti-GPC3 chimeric antibody or a humanized anti-GPC3 antibody comprising any of the following (1) to (5):

(1) heavy chain CDR1, heavy chain CDR2, and heavy chain CDR3 represented by SEQ ID NOs: 4, 5, and 6, respectively, and light chain CDR1, light chain CDR2, and light chain CDR3 represented by SEQ ID NOs: 7, 8, and 9, respectively;

(2) heavy chain CDR1, heavy chain CDR2, and heavy chain CDR3 represented by SEQ ID NOs: 12, 13, and 14, respectively, and light chain CDR1, light chain CDR2, and light chain CDR3 represented by SEQ ID NOs: 15, 16, and 17, respectively;

(3) heavy chain CDR1, heavy chain CDR2, and heavy chain CDR3 represented by SEQ ID NOs: 20, 21, and 22, respectively, and light chain CDR1, light chain CDR2, and

light chain CDR3 represented by SEQ ID NOs: 23, 24, and 25, respectively;
(4) heavy chain CDR1, heavy chain CDR2, and heavy chain CDR3 represented by SEQ ID NOs: 28, 29, and 30, respectively, and light chain CDR1, light chain CDR2, and light chain CDR3 represented by SEQ ID NOs: 31, 32, and 33, respectively; and
(5) heavy chain CDR1, heavy chain CDR2, and heavy chain CDR3 represented by SEQ ID NOs: 36, 37, and 38, respectively, and light chain CDR1, light chain CDR2, and light chain CDR3 represented by SEQ ID NOs: 39, 40, and 41, respectively.

7. The method according to any one of claims 1, 2, and 4 to 6, or the use according to any one of claims 3 to 6, wherein the anti-GPC3 antibody comprises any of the following (1) to (6):
(1) a heavy chain variable region selected from the group of heavy chain variable regions represented by SEQ ID NOs: 44, 45, 46, 47, 48, 49, and 50 and a light chain variable region represented by SEQ ID NO: 51;
(2) a heavy chain variable region selected from the group of heavy chain variable regions represented by SEQ ID NOs: 44, 45, 46, 47, 48, 49, and 50 and a light chain variable region selected from the group of light chain variable regions represented by SEQ ID NOs: 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, and 66;

(3) a heavy chain variable region represented by SEQ ID NO: 67 and a light chain variable region represented by SEQ ID NO: 68;
(4) a heavy chain variable region represented by SEQ ID NO: 69 and a light chain variable region represented by SEQ ID NO: 70;
(5) a heavy chain variable region represented by SEQ ID NO: 71 and a light chain variable region represented by SEQ ID NO: 72; and
(6) a heavy chain variable region represented by SEQ ID NO: 71 and a light chain variable region represented by SEQ ID NO: 73.

8. The method according to any one of claims 1 to 2, and 4 to 7, or the use according to any one of claims 3, and 4 to 7, wherein the anti-GPC3 antibody is to be administered to achieve a blood trough level of 230 ug/mL or higher in the cancer patient.