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, in one aspect, there is provided a method for determining the efficacy of anti-GPC3 antibody therapy for liver cancer in a patient or determining the continuation of anti-GPC3 antibody therapy for a patient, comprising measuring the number of an immunocyte or an expression level of a molecule expressed on the immunocyte in a 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 at arbitrary points in time between the start and completion of the therapy, 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

determined or the continuation of the anti-GPC3 antibody therapy is determined, and wherein

(i) when the immunocyte is a leukocyte, the predetermined value is selected from the range from 3,000 to 8,000 cells/μL;

(ii) when the immunocyte is a monocyte, the predetermined number is selected from the range from 100 to 1,000 cells/μL;

(iii) when the immunocyte is a lymphocyte, the predetermined number is selected from the range from 450 to 3,000 cells/μL; or

(iv) when the molecule expressed on the immunocyte is CD16, the predetermined value of CD16 expression is selected from a range from 150,000 mesf (molecules of equivalent soluble fluorescence intensity) to 800,000 mesf calculated from flow cytometry measurement value of fluorescence intensity of CD16. In another aspect, there is provided use of an anti-GPC3 antibody in the manufacture of a medicament for treating cancer, wherein the anti-GPC3 antibody is to be administered to a liver cancer patient, wherein the cancer patient has been determined to have (i) a number of an immunocyte which is above a predetermined value, wherein

(a) when the immunocyte is a leukocyte, the predetermined value is selected from the range from 3,000 to 8,000 cells/μL;

(b) when the immunocyte is a monocyte, the predetermined number is selected from the range from 100 to 1,000 cells/μL; or

(c) when the immunocyte is a lymphocyte, the predetermined number is selected from the range from 450 to 3,000 cells/μL;

or (ii) an expression level of a molecule expressed on the immunocyte which is above a predetermined value, wherein, when the molecule expressed on the immunocyte is CD16, the predetermined value of CD16 expression is selected from a range from 150,000 mesf (molecules of equivalent soluble fluorescence intensity) to 800,000 mesf calculated from flow cytometry measurement value of fluorescence intensity of CD16; in a peripheral blood isolated from the cancer patient before or after start of administration of the anti-GPC3 antibody. 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 determining the efficacy of anti-GPC3 antibody therapy for liver cancer in a patient or determining the continuation of anti-GPC3 antibody therapy for a patient, comprising measuring the number of an immunocyte or an expression level of a molecule expressed on the immunocyte in a 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 at arbitrary points in time between the start and completion of the therapy,

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 determined or the continuation of the anti-GPC3 antibody therapy is determined,

and wherein

(i) when the immunocyte is a leukocyte, the predetermined value is selected from the range from 3,000 to 8,000 cells/μL;

(ii) when the immunocyte is a monocyte, the predetermined number is selected from the range from 100 to 1,000 cells/μL;

(iii) when the immunocyte is a lymphocyte, the predetermined number is selected from the range from 450 to 3,000 cells/μL; or

(iv) when the molecule expressed on the immunocyte is CD16, the predetermined value of CD16 expression is selected from a range from 150,000 mesf (molecules of equivalent soluble fluorescence intensity) to 800,000 mesf calculated from flow cytometry measurement value of fluorescence intensity of CD16.

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

(i) when the immunocyte is a $CD45^+$ lymphocyte, the predetermined value is selected from the range from 450 to 3,500 cells/μL;

(ii) when the immunocyte is a $CD3^+$ T cell, the predetermined value is selected from the range from 300 to 2,500 cells/μL;

(iii) when the immunocyte is a $CD4^+$ T cell, the predetermined value is selected from the range from 200 to 1,500 cells/μL;

(iv) when the immunocyte is a $CD8^+$ T cell, the predetermined value is selected from the range from 50 to 300 cells/μL;

(v) when the immunocyte is a CD16+ NK cell, the predetermined value is selected from a range from 50 to 700 cells/μL;

(vi) when the immunocyte is a NKp46+ NK cells, the predetermined value is selected from a range from 30 to 300 cells/μL; or

(vii) when the immunocyte is a CD56-/CD16+ NK cell, the predetermined value number is selected from the range from 2 to 30 cells/μL.

3. The method according to any one of claims 1 to 2, wherein the anti-GPC3 antibody has antibody-dependent cellular cytotoxicity (ADCC) activity, and wherein the 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.

4. The method according to any one of claims 1 to 3, wherein the anti-GPC3 antibody is to be administered to achieve a blood trough level of 200 μg/ml or higher in the cancer patient.

5. The method according to any of claims 1, 2, and 4, wherein the anti-GPC3 antibody has antibody-dependent cellular cytotoxicity (ADCC) activity and/or complement-dependent cytotoxicity (CDC) activity.

6. The method according to claim 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 claim 5, 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 claim 5, wherein the anti-GPC3 antibody is conjugated with a cytotoxic substance.

9. Use of an anti-GPC3 antibody in the manufacture of a medicament for treating cancer, wherein the anti-GPC3 antibody is to be administered to a liver cancer patient,

wherein the cancer patient has been determined to have

(i) a number of an immunocyte which is above a predetermined value, wherein

(a) when the immunocyte is a leukocyte, the predetermined value is selected from the range from 3,000 to 8,000 cells/μL;

(b) when the immunocyte is a monocyte, the predetermined number is selected from the range from 100 to 1,000 cells/μL; or

(c) when the immunocyte is a lymphocyte, the predetermined number is selected from the range from 450 to 3,000 cells/μL;

or

(ii) an expression level of a molecule expressed on the immunocyte which is above a predetermined value, wherein, when the molecule expressed on the immunocyte is CD16, the predetermined value of CD16 expression is selected from a range from 150,000 mesf (molecules of equivalent soluble fluorescence intensity) to 800,000 mesf

calculated from flow cytometry measurement value of fluorescence intensity of CD16;
in a peripheral blood isolated from the cancer patient before or after start of administration of the anti-GPC3 antibody.

10. The use according to claim 9, wherein the lymphocyte is at least one lymphocyte cell selected from a CD45+ lymphocyte, a CD3+ T cell, a CD4+ T cell, and a CD8+ T cell; or at least one lymphocyte cell selected from a CD16+ NK cell, an NKp46+ NK cell, and a CD56-/CD16+ NK cell.

11. The use according to any of claims 9 to 10, wherein the anti-GPC3 antibody has antibody-dependent cellular cytotoxicity (ADCC) activity, and wherein the patient has at least one amino acid polymorphism that results in Val at residue 158 of FcγRIIIA and/or at least one amino acid polymorphism that results in His at residue 131 of FcγRIIA.

12. The use according to any one of claims 9 to 11, wherein the anti-GPC3 antibody is to be administered to achieve a blood trough level of 200 μg/ml or higher in the cancer patient.

13. The use according to any one of claims 9, 10, and 12, wherein the anti-GPC3 antibody has antibody-dependent cellular cytotoxicity (ADCC) activity and/or complement-dependent cytotoxicity (CDC) activity.

14. The use according to claim 13, 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.

15. The use according to claim 13, 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.

16. The use according to claim 13, wherein the anti-GPC3 antibody is conjugated with a cytotoxic substance.