Claims

1. Use of a conjugate or a composition comprising the conjugate for the manufacture of a medicament for the treatment of cancer, an infection, an autoimmune disease or an immunodeficiency disorder, wherein the conjugate comprises an antibody conjugated to a cytotoxic agent, and wherein the antibody is capable of binding to MUC1 or TA-MUC1, and wherein the antibody comprises

   (i) a heavy chain variable region comprising the complementarity-determining regions (CDRs) CDR-H1 having the amino acid sequence of SEQ ID NO: 1, CDR-H2 having the amino acid sequence of SEQ ID NO: 2 and CDR-H3 having the amino acid sequence of SEQ ID NO: 3, and

   (ii) a light chain variable region comprising the complementarity-determining regions (CDRs) CDR-L1 having the amino acid sequence of SEQ ID NO: 4, CDR-L2 having the amino acid sequence of SEQ ID NO: 5 and CDR-L3 having the amino acid sequence of SEQ ID NO: 6.

   wherein the amino acid at position 8 of SEQ ID NO: 2 is selected from the group consisting of glutamine, histidine, tryptophan, tyrosine, lysine, arginine, aspartic acid and glutamic acid, or wherein the CDR-H2 has the amino acid sequence of SEQ ID NO: 7.

2. The use according to claim 1, wherein:

   (i) (a) the heavy chain variable region of the antibody has the amino acid sequence of SEQ ID NO: 9 or an amino acid sequence which is at least 90% identical to the amino acid sequence of SEQ ID NO: 9, or the heavy chain variable region of the antibody has the amino acid sequence of SEQ ID NO: 10 or an amino acid sequence which is at least 90% identical to the amino acid sequence of SEQ ID NO: 10, and/or (b) the light chain variable region of the antibody has the amino acid sequence of SEQ ID NO: 12 or an amino acid sequence which is at least 90% identical to the amino acid sequence of SEQ ID NO: 12, or

   (ii) the heavy chain variable region of the antibody has the amino acid sequence of SEQ ID NO: 10 and the light chain variable region of the antibody has the amino acid sequence of SEQ ID NO: 12.

3. The use according to claim 1 or 2 wherein the antibody comprises an Fc region and preferably is an IgG1, IgG2 or IgG4-type antibody.

4. The use according to any one of claims 1 to 3, wherein:

(i) the heavy chain of the antibody has the amino acid sequence of SEQ ID NO: 15, and the light chain of the antibody has the amino acid sequence of SEQ ID NO: 16,

(ii) the heavy chain of the antibody has the amino acid sequence of amino acid numbers 1 to 446 of SEQ ID NO: 15, and the light chain of the antibody has the amino acid sequence of SEQ ID NO: 16,

(iii) the heavy chain of the antibody has the amino acid sequence of SEQ ID NO: 22, and the light chain of the antibody has the amino acid sequence of SEQ ID NO: 16, or

(iv) the heavy chain of the antibody has the amino acid sequence of amino acid numbers 1 to 446 of SEQ ID NO: 22, and the light chain of the antibody has the amino acid sequence of SEQ ID NO: 16.

5. The use according to claim 3 or 4, wherein the antibody comprises a glycosylation pattern having one or more of the following characteristics:

(i) a detectable amount of glycans carrying a bisecting GlcNAc residue;

(ii) a relative amount of glycans carrying at least one galactose residue of at least 25% of the total amount of glycans attached to the Fc glycosylation sites of the antibody in a composition.

6. The use according to any one of claims 1 to 5, wherein the antibody is obtainable by production in a mammalian cell, preferably, wherein the antibody is obtainable by production in a human cell line selected from the group consisting of NM-H9D8 (DSM ACC 2806), NM-H9D8-E6 (DSM ACC 2807), NM-H9D8-E6Q12 (DSM ACC 2856) and cell lines derived therefrom or in a CHO cell line and cell lines derived therefrom.

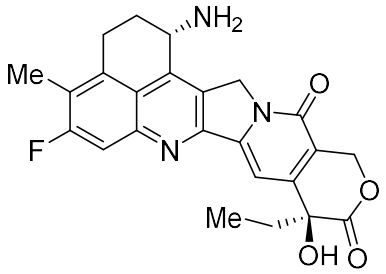
7. The use according to any one of claims 1 to 6, wherein the antibody is obtainable by a production method comprising the steps of (i) providing a host cell comprising a nucleic acid encoding the antibody defined in any one of claims 1 to 4, (ii) culturing the host cell under conditions suitable for expression of the antibody, and (iii) obtaining the antibody expressed by the host cell.

8. The use according to any one of claims 1 to 7, wherein the antibody competes with the antibody comprising a heavy chain variable region with the amino acid sequence of SEQ ID NO: 10 and a light chain variable region with the amino acid sequence of SEQ ID NO:12, or the antibody comprising a heavy chain variable region with the amino acid sequence of SEQ ID NO:11 and a light chain variable region with the amino acid sequence of SEQ ID NO:12 for the binding to TA-MUC1.

9. The use according to any one of claims 1 to 8, wherein the antibody has the activity of being internalized into MUC1- or TA-MUC1 expressing cells through binding to MUC-1 or TA-MUC1.

10. The use according to any one of claims 1 to 9, wherein the cytotoxic agent is an antitumor agent, preferably a chemotherapeutic agent, more preferably wherein the chemotherapeutic agent is selected from the group consisting of a microtubule inhibitor, a topoisomerase I inhibitor, a DNA damaging agent, a DNA alkylating agent and a DNA minor groove binder, more preferably wherein the chemotherapeutic agent is a topoisomerase I inhibitor, and more preferably wherein the topoisomerase I inhibitor is an antitumor compound represented by the following formula:

[Formula 1]



11. The use according to any one of claims 1 to 10, wherein the antibody is conjugated to the cytotoxic agent or antitumor compound via a linker having any structure selected from the group consisting of the following formulas (a) to (f):

(a) -(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-,

(b) -(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-,

(c) -(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-,

(d) -(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-O-CH_2-C(=O)-,

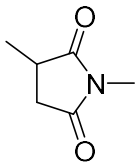
(e) -(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-, and

(f) -(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-,

wherein the antibody is connected to the terminus of -(Succinimid-3-yl-N), the cytotoxic agent or antitumor compound is connected to the carbonyl group in the rightmost of formulas (a) to (f) with the nitrogen atom of the amino group at position 1 as a connecting position, GGFG represents an amino acid sequence consisting of glycine-glycine-phenylalanine-glycine linked through peptide bonds, and

-(Succinimid-3-yl-N)- has a structure represented by the following formula:

[Formula 2]



which is connected to the antibody at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1, preferably wherein the linker is represented by any formula selected from the group consisting of the following formulas (a) to (c):

(a) -(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-,

(b) -(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-O-CH_2-C(=O)-, and

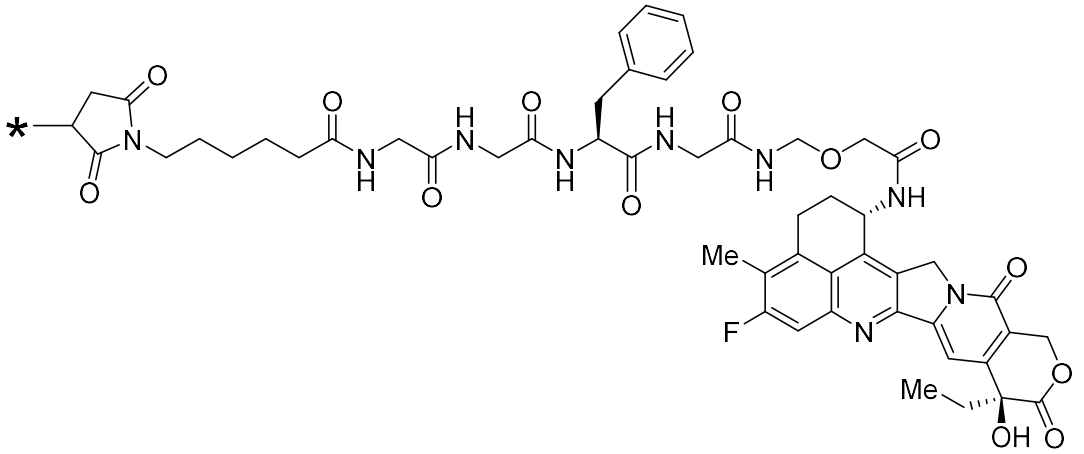
(c) -(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-,

more preferably wherein the linker is represented by the following formula (a):

(a) -(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-.

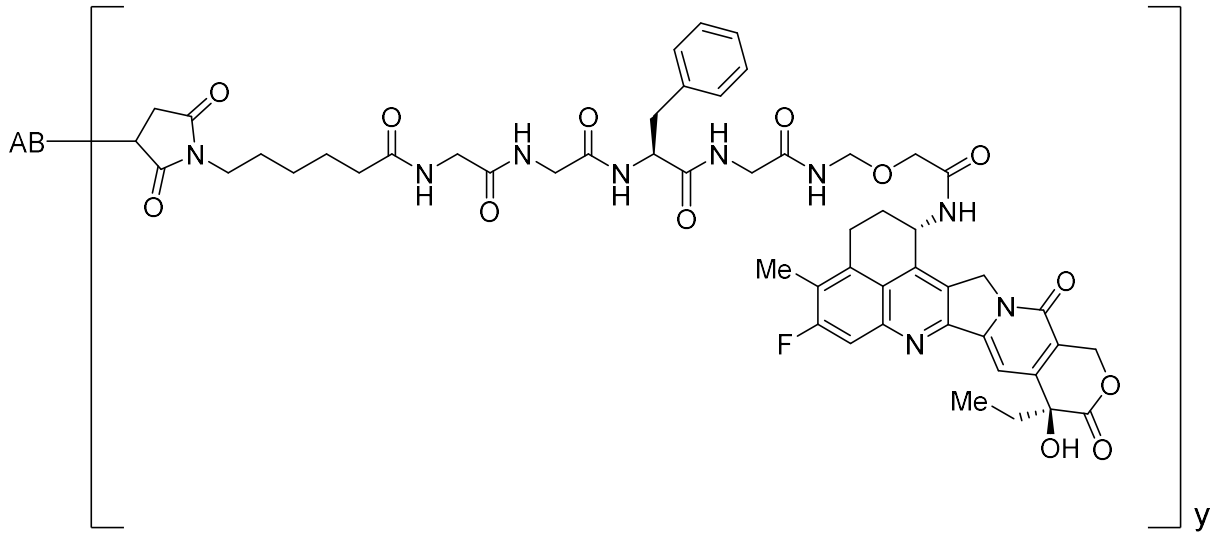
12. The use according to claim 10 or 11, wherein the antibody is conjugated to a drug linker represented by the following formula (wherein asterisk* represents the point of connection to the antibody) by a thioether bond:

[Formula 3]



13. The use according to claim 10 or 11, which is represented by the following formula;

[Formula 4]



wherein AB represents the antibody thereof, y represents an average number of units of the drug-linker structure conjugated to the antibody per itself, and the antibody is conjugated to a drug linker represented by the above formula by a thioether bond.

14. The use according to claim 12 or 13, wherein the antibody comprises any one of the following combinations a) to c) of a heavy chain variable region and a light chain variable region, or heavy chain and light chain:

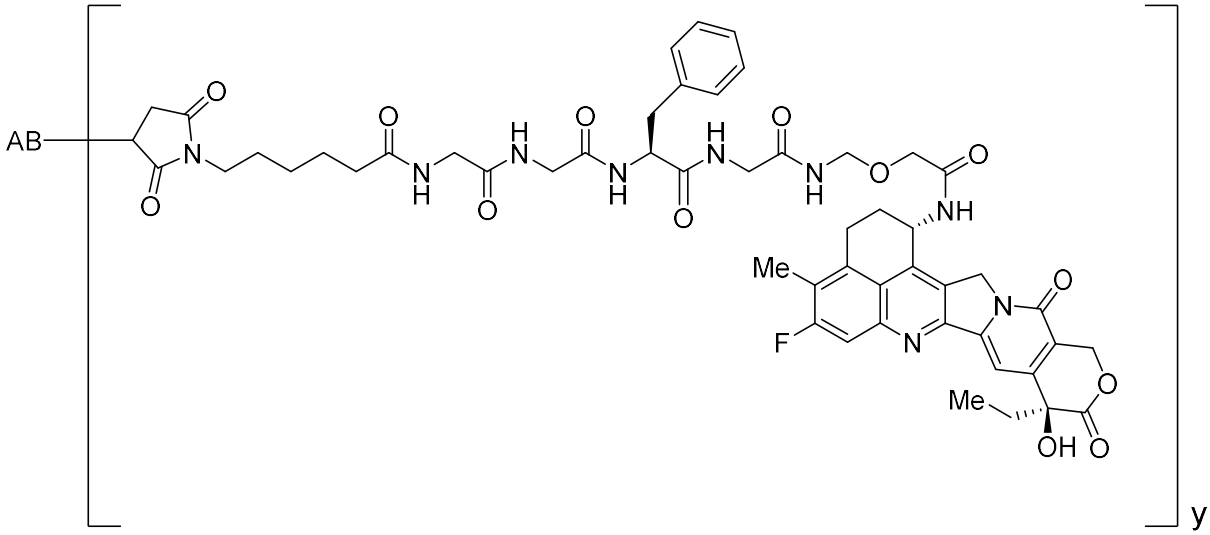
(a) the heavy chain variable region has the amino acid sequence of SEQ ID NO: 10 and the light chain variable region has the amino acid sequence of SEQ ID NO: 12,

(b) the heavy chain has the amino acid sequence of SEQ ID NO: 22 and the light chain has the amino acid sequence of SEQ ID NO: 16, and

(c) the heavy chain has the amino acid sequence of amino acid numbers 1 to 446 of SEQ ID NO: 22 and the light chain has the amino acid sequence of SEQ ID NO: 16.

15. Use of a conjugate or a composition comprising the conjugate for the manufacture of a medicament for the treatment of cancer, an infection, an autoimmune disease or an immunodeficiency disorder, wherein the conjugate is represented by the following formula,

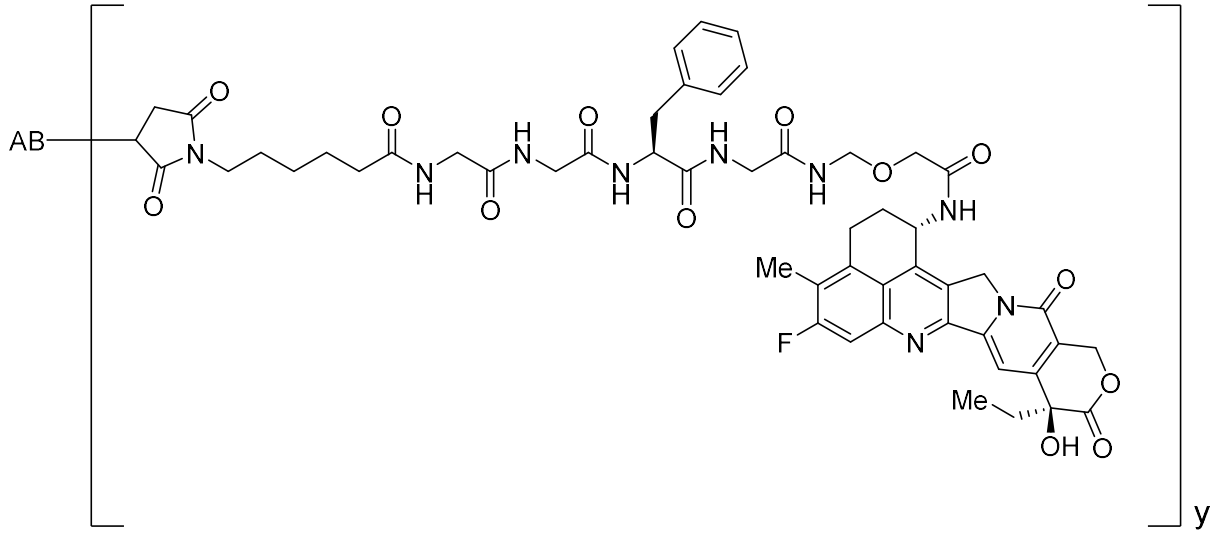
[Formula 5]



wherein AB represents the antibody, the antibody comprises the heavy chain variable region having the amino acid sequence of SEQ ID NO: 10 and the light chain variable region having the amino acid sequence of SEQ ID NO: 12, y represents an average number of units of the drug-linker structure conjugated to the antibody per itself, and the antibody is conjugated to a drug linker represented by the above formula by a thioether bond.

16. Use of a conjugate or a composition comprising the conjugate for the manufacture of a medicament for the treatment of cancer, an infection, an autoimmune disease or an immunodeficiency disorder, wherein the conjugate is represented by the following formula,

[Formula 7]



wherein AB represents the antibody, the antibody comprises (i) the heavy chain having the amino acid sequence of SEQ ID NO: 22 and the light chain having the amino acid sequence of SEQ ID NO: 16 or (ii) the heavy chain having the amino acid sequence of amino acid numbers 1 to 446 of SEQ ID NO: 22 and the light chain having the amino acid sequence of SEQ ID NO: 16, y represents an average number of units of the drug-linker structure conjugated to the antibody per itself, and the antibody is conjugated to a drug linker represented by the above formula by a thioether bond.

17. The use according to any one of claims 1 to 16, wherein the antibody comprises one or more modifications selected from the group consisting of defucosylation, reduced fucose, N-linked glycosylation, O-linked glycosylation, N-terminal processing, C-terminal processing, deamidation, isomerization of aspartic acid, oxidation of methionine, the substitutions of two leucine (L) residues to alanine (A) at position 234 and 235 of the heavy chain (LALA), amidation of a proline residue, and a deletion or lack of one or two amino acids at the carboxyl terminus, preferably wherein the antibody comprises a deletion or lack of one or two amino acid(s) in the carboxyl terminus of the heavy chain, more preferably wherein the antibody comprises two heavy chains, both of which lack one carboxyl-terminal amino acid residue.

18. The use according to any one of claims 1 to 17, wherein the average number y of the cytotoxic agents, in particular drug-linker structures, conjugated per antibody is in a range of from 1 to 10, preferably 2 to 8, more preferably 3 to 8, more preferably 7 to 8, more preferably 7.5 to 8, more preferably wherein the number of conjugated cytotoxic agents per antibody molecule is 8.

19. The use according to any one of claims 1 to 18, wherein the cancer is characterized by expressing TA-MUC1, preferably wherein the cancer is selected from the group consisting of ovarian cancer, breast cancer, pancreatic cancer, lung cancer, colon cancer, stomach cancer, liver cancer, kidney cancer, blood cancer, endometrial cancer, thyroid cancer, leukemias, seminomas, melanomas, carcinomas, teratomas, lymphomas, sarcomas, mesotheliomas, neuroblastomas, gliomas, rectal cancer, adrenal cancer, skin cancer, cancer of the brain, cervical cancer, intestinal cancer, intestine cancer, head and neck cancer, gastrointestinal cancer, lymph node cancer, esophagus cancer, colorectal cancer, ear, nose and throat (ENT) cancer, prostate cancer, bladder cancer, cancer of the uterus and the metastases thereof, more preferably wherein the cancer is ovarian cancer, breast cancer, lung cancer, or bladder cancer

20. The use according to any one of claims 1 to 19, wherein the medicament is used in combination with a further agent.