Non Patent Literature 23: Saito T, et al., Nat Med. 2016; 22(6): 679-684.

Non Patent Literature 24: Chari RVJ, et al., Angew Chemie - Int Ed. 2014; 53(15): 3796-3827.

Non Patent Literature 25: Niwa R, et al., Cancer Res. 2004; 64(6): 2127-2133.

Non Patent Literature 26: Ishida T, et al., J Clin Oncol. 2012; 30(8): 837-842.

Non Patent Literature 27: Lo Nigro C, et al., Ann Transl Med. 2019; 7(5): 105-105.

Non Patent Literature 28: Marechal R, et al., BMC Cancer. 2010; 10.

Summary of Invention

[0009a] In one aspect, disclosed herein is a antibody or an antigen binding fragment of the antibody, wherein the antibody or the antigen binding fragment of the antibody comprises

(a) CDRL1, CDRL2, and CDRL3 in any one combination selected from the group consisting of the following combinations (1) and (2):

(1) CDRL1 consisting of the amino acid sequence represented by SEQ ID NO: 1, CDRL2 consisting of the amino acid sequence represented by SEQ ID NO: 2 (KAS), and CDRL3 consisting of the amino acid sequence represented by SEQ ID NO: 3, and

(2) CDRL1 consisting of the amino acid sequence represented by SEQ ID NO: 4, CDRL2 consisting of the amino acid sequence represented by SEQ ID NO: 5 (FVS), and CDRL3 consisting of the amino acid sequence represented by SEQ ID NO: 6, and

CDRH1, CDRH2, and CDRH3 in any one combination selected from the group consisting of the following combinations (3) and (4):

(3) CDRH1 consisting of the amino acid sequence represented by SEQ ID NO: 7, CDRH2 consisting of the amino acid sequence represented by SEQ ID NO: 8, and CDRH3 consisting of the amino acid sequence represented by SEQ ID NO: 9, and

(4) CDRH1 consisting of the amino acid sequence represented by SEQ ID NO: 10, CDRH2 consisting of the amino acid sequence represented by SEQ ID NO: 11, and CDRH3 consisting of the amino acid sequence represented by SEQ ID NO: 12; or

(b) CDRL1, CDRL2, and CDRL3, and CDRH1, CDRH2, and CDRH3 in any one combination selected from the group consisting of the following combinations (1) and (2):

(1) CDRL1 consisting of the amino acid sequence represented by SEQ ID NO: 1, CDRL2 consisting of the amino acid sequence represented by SEQ ID NO: 2 (KAS), and CDRL3 consisting of the amino acid sequence represented by SEQ ID NO: 3, and CDRH1 consisting of the amino acid sequence represented by SEQ ID NO: 7, CDRH2

consisting of the amino acid sequence represented by SEQ ID NO: 8, and CDRH3 consisting of the amino acid sequence represented by SEQ ID NO: 9, and

(2) CDRL1 consisting of the amino acid sequence represented by SEQ ID NO: 4, CDRL2 consisting of the amino acid sequence represented by SEQ ID NO: 5 (FVS), and CDRL3 consisting of the amino acid sequence represented by SEQ ID NO: 6, and CDRH1 consisting of the amino acid sequence represented by SEQ ID NO: 10, CDRH2 consisting of the amino acid sequence represented by SEQ ID NO: 11, and CDRH3 consisting of the amino acid sequence represented by SEQ ID NO: 12.

[0009b] In another aspect, disclosed herein is a humanized antibody or antigen binding fragment of the antibody comprising

(1) a light chain variable region consisting of an amino acid sequence from positions 21 to 127 of SEQ ID NO: 13 and a heavy chain variable region consisting of an amino acid sequence from positions 20 to 146 of SEQ ID NO: 15; or

(2) a light chain consisting of an amino acid sequence from positions 21 to 233 of SEQ ID NO: 13 and a heavy chain consisting of an amino acid sequence from positions 20 to 476 of SEQ ID NO: 15; or

(3) a light chain variable region consisting of an amino acid sequence from positions 21 to 127 of SEQ ID NO: 14 and a heavy chain variable region consisting of an amino

acid sequence from positions 20 to 146 of SEQ ID NO: 16; or

(4) a light chain consisting of an amino acid sequence from positions 21 to 233 of SEQ ID NO: 14 and a heavy chain consisting of an amino acid sequence from positions 20 to 476 of SEQ ID NO: 16.

[0009c] In another aspect, disclosed herein is a polynucleotide encoding the antibody or the antigen binding fragment of the antibody according to the disclosure.

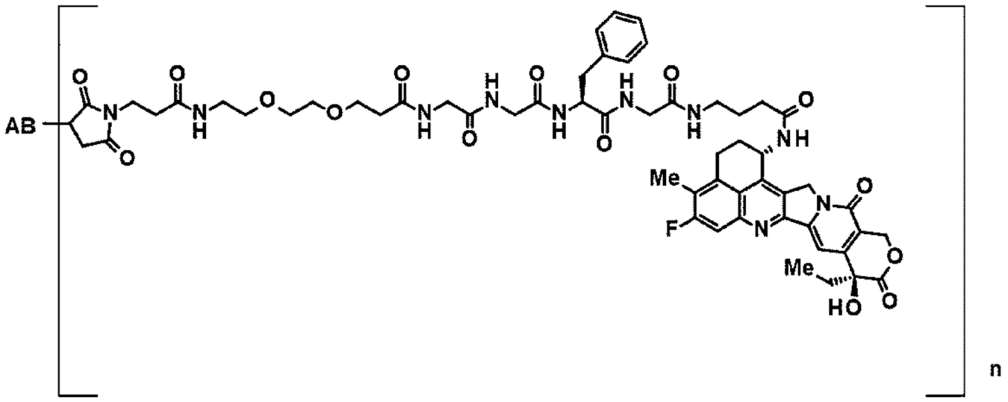
[0009d] In another aspect, disclosed herein is an expression vector comprising the polynucleotide according to the disclosure.

[0009e] In another aspect, disclosed herein is a host cell transformed with the expression vector according to the disclosure.

[0009f] In another aspect, disclosed herein is an antibody-drug conjugate in which the antibody or the antigen binding fragment of the antibody according to the disclosure is conjugated to a drug.

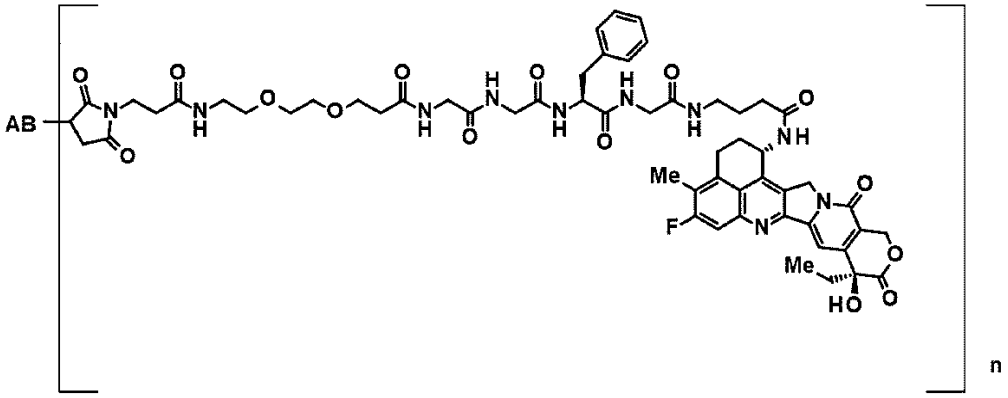
[0009g] In another aspect, disclosed herein is a antibody-drug conjugate having a structure represented by the following formula:

[Formula 5]



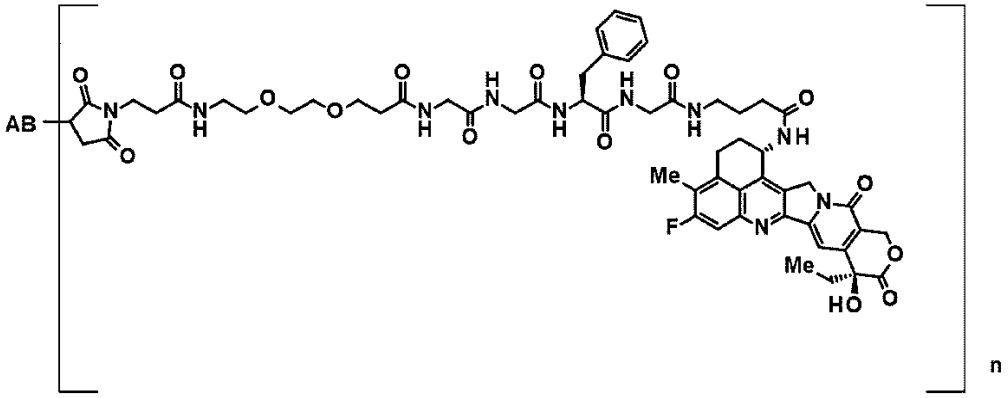
wherein AB represents a humanized antibody or the antigen binding fragment of the antibody comprising a light chain variable region consisting of an amino acid sequence from positions 21 to 127 of SEQ ID NO: 13 and a heavy chain variable region consisting of an amino acid sequence from positions 20 to 146 of SEQ ID NO: 15, n represents an average number of units of the drug-linker structure conjugated to the antibody or the antigen binding fragment of the antibody per antibody or per the antigen binding fragment of the antibody and is in the range of 7 to 8, and the antibody or the antigen binding fragment of the antibody is connected to the linker via a sulfhydryl group derived from the antibody or the antigen binding fragment of the antibody; or

[Formula 6]



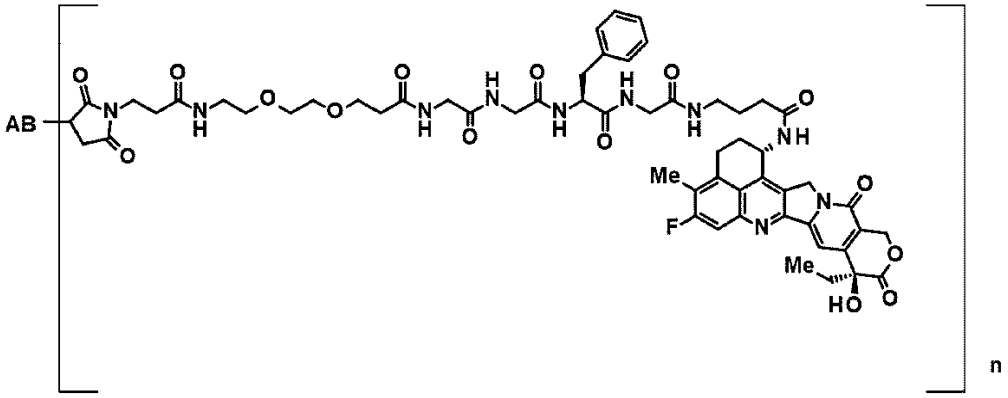
wherein AB represents a humanized antibody or the antigen binding fragment of the antibody comprising a light chain consisting of an amino acid sequence from positions 21 to 233 of SEQ ID NO: 13 and a heavy chain consisting of an amino acid sequence from positions 20 to 476 of SEQ ID NO: 15, n represents an average number of units of the drug-linker structure conjugated to the antibody or the antigen binding fragment of the antibody per antibody or per the antigen binding fragment of the antibody and is in the range of 7 to 8, and the antibody or the antigen binding fragment of the antibody is connected to the linker via a sulfhydryl group derived from the antibody or the antigen binding fragment of the antibody; or

[Formula 7]



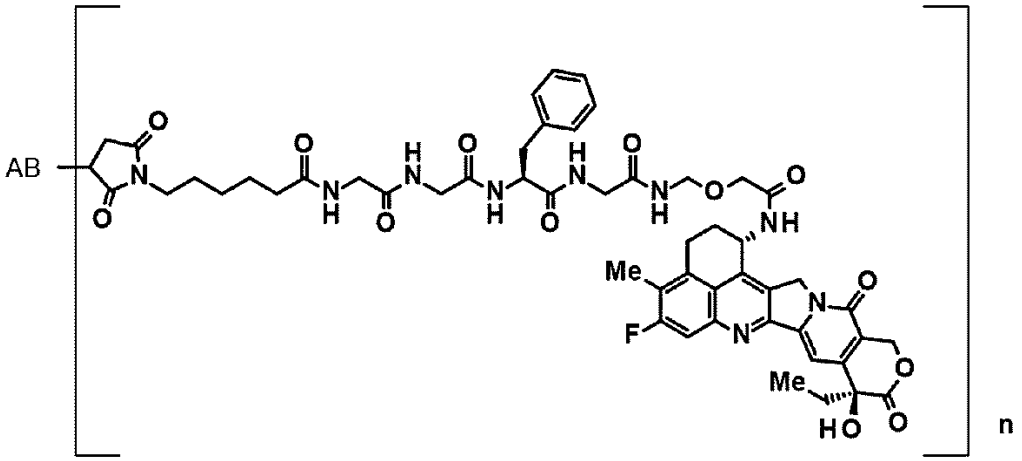

wherein AB represents a humanized antibody or the antigen binding fragment of the antibody comprising a light chain variable region consisting of an amino acid sequence from positions 21 to 127 of SEQ ID NO: 14 and a heavy chain variable region consisting of an amino acid sequence from positions 20 to 146 of SEQ ID NO: 16, n represents an average number of units of the drug-linker structure conjugated to the antibody or the antigen binding fragment of the antibody per antibody or per the antigen binding fragment of the antibody and is in the range of 7 to 8, and the antibody or the antigen binding fragment of the antibody is connected to the linker via a sulfhydryl group derived from the antibody or the antigen binding fragment of the antibody; or

[Formula 8]



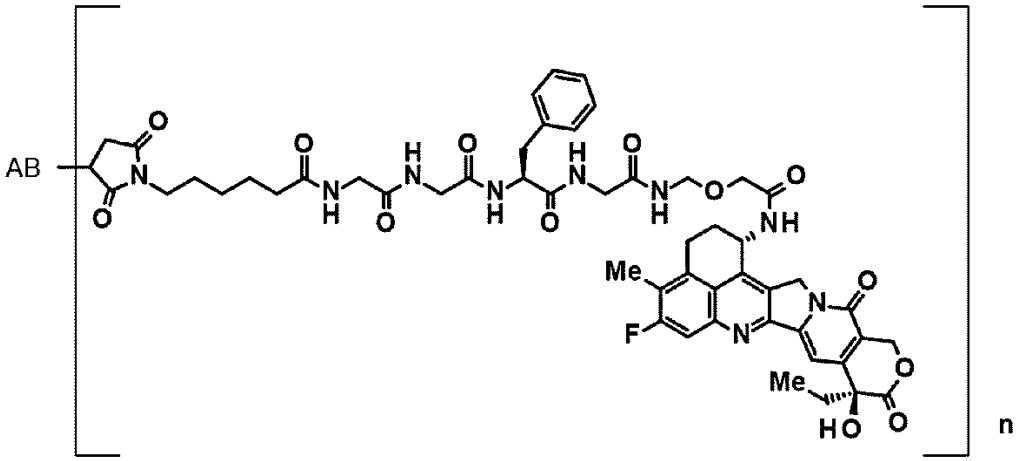
wherein AB represents a humanized antibody or the antigen binding fragment of the antibody comprising a light chain consisting of an amino acid sequence from positions 21 to 233 of SEQ ID NO: 14 and a heavy chain consisting of an amino acid sequence from positions 20 to 476 of SEQ ID NO: 16, n represents an average number of units of the drug-linker structure conjugated to the antibody or the antigen binding fragment of the antibody per antibody or per the antigen binding fragment of the antibody and is in the range of 7 to 8, and the antibody or the antigen binding fragment of the antibody is connected to the linker via a sulfhydryl group derived from the antibody or the antigen binding fragment of the antibody; or

[Formula 9]




wherein AB represents an antibody or the antigen binding fragment of the antibody comprising a light chain variable region consisting of the amino acid sequence of SEQ ID NO: 18 and a heavy chain variable region consisting of the amino acid sequence of SEQ ID NO: 20, n represents an average number of units of the drug-linker structure conjugated to the antibody or the antigen binding fragment of the antibody per antibody or per the antigen binding fragment of the antibody and is in the range of 7 to 8, and the antibody or the antigen binding fragment of the antibody is connected to the linker via a sulfhydryl group derived from the antibody or the antigen binding fragment of the antibody; or

[Formula 10]




wherein AB represents an antibody or the antigen binding fragment of the antibody comprising a light chain consisting of an amino acid sequence from positions 21 to 232 of SEQ ID NO: 26 and a heavy chain consisting of an amino acid sequence from positions 20 to 476 of SEQ ID NO: 27, n represents an average number of units of the drug-linker structure conjugated to the antibody or the antigen binding fragment of the antibody per antibody or per the antigen binding fragment of the antibody and is in the range of 7 to 8, and the antibody or the antigen binding fragment of the antibody is connected to the linker via a sulfhydryl group derived from the antibody or the antigen binding fragment of the antibody.

[0009h] In another aspect, disclosed herein is a pharmaceutical composition comprising the antibody or the antigen binding fragment of the antibody according to the disclosure, a salt of the component, or a hydrate of the component or the salt.

[0009i] In another aspect, disclosed herein is a use of the antibody or the antigen binding fragment of the antibody according to the disclosure, a salt of the component, and a hydrate of the component or the salt in the manufacture of a medicament for treating a tumor.

[0009j] In another aspect, disclosed herein is a use of a pharmaceutical composition comprising the antibody-drug conjugate according to the disclosure in the manufacture of a first medicament and use of an immune checkpoint inhibitor in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy for treating a tumor.

Technical Problem

[0010] An object of the present invention is to provide an antibody that binds to CD25, an antibody-drug conjugate that comprises the antibody and has antitumor activity, a medicament having a therapeutic effect on tumor using the antibody-drug conjugate, and a method for treating tumor using the antibody, the antibody-drug conjugate, or the medicament, etc.

Solution to Problem

[0011] The present inventors have conducted diligent studies to attain the object and consequently found that the particular antibody disclosed in the present

# Claims

[Claim 1]

An antibody or an antigen binding fragment of the antibody, wherein the antibody or the antigen binding fragment of the antibody comprises

(a) CDRL1, CDRL2, and CDRL3 in any one combination selected from the group consisting of the following combinations (1) and (2):

(1) CDRL1 consisting of the amino acid sequence represented by SEQ ID NO: 1, CDRL2 consisting of the amino acid sequence represented by SEQ ID NO: 2 (KAS), and CDRL3 consisting of the amino acid sequence represented by SEQ ID NO: 3, and

(2) CDRL1 consisting of the amino acid sequence represented by SEQ ID NO: 4, CDRL2 consisting of the amino acid sequence represented by SEQ ID NO: 5 (FVS), and CDRL3 consisting of the amino acid sequence represented by SEQ ID NO: 6, and

CDRH1, CDRH2, and CDRH3 in any one combination selected from the group consisting of the following combinations (3) and (4):

(3) CDRH1 consisting of the amino acid sequence represented by SEQ ID NO: 7, CDRH2 consisting of the amino acid sequence represented by SEQ ID NO: 8, and CDRH3 consisting of the amino acid sequence represented by SEQ ID NO: 9, and

(4) CDRH1 consisting of the amino acid sequence represented by SEQ ID NO: 10, CDRH2 consisting of the amino acid sequence represented by SEQ ID NO: 11, and CDRH3 consisting of the amino acid sequence represented by SEQ ID NO: 12; or

(b) CDRL1, CDRL2, and CDRL3, and CDRH1, CDRH2, and CDRH3 in any one combination selected from the group consisting of the following combinations (1) and (2):

(1) CDRL1 consisting of the amino acid sequence represented by SEQ ID NO: 1, CDRL2 consisting of the amino acid sequence represented by SEQ ID NO: 2 (KAS), and CDRL3 consisting of the amino acid sequence represented by SEQ ID NO: 3, and CDRH1 consisting of the amino acid sequence represented by SEQ ID NO: 7, CDRH2 consisting of the amino acid sequence represented by SEQ ID NO: 8, and CDRH3 consisting of the amino acid sequence represented by SEQ ID NO: 9, and

(2) CDRL1 consisting of the amino acid sequence represented by SEQ ID NO: 4, CDRL2 consisting of the amino acid sequence represented by SEQ ID NO: 5 (FVS), and CDRL3 consisting of the amino acid sequence represented by SEQ ID NO: 6, and CDRH1 consisting of the amino acid sequence represented by SEQ ID NO: 10, CDRH2 consisting of the amino acid sequence represented by SEQ ID NO: 11, and CDRH3 consisting of the amino acid sequence represented by SEQ ID NO: 12.

[Claim 2]

The antibody or the antigen binding fragment of the antibody according to claim 1, having the following characteristics:

(1) having no ability to block IL-2; and

(2) exhibiting the ability to remove human regulatory T cells and/or the ability to promote the proliferation of human granzyme-positive CD8-positive cells by conjugation to a cytotoxic active compound.

[Claim 3]

The antibody or the antigen binding fragment of the antibody according to claim 1, wherein the antibody or the antigen binding fragment of the antibody comprises

(a) any one light chain variable region selected from the group consisting of the following light chain variable regions (1) to (4):

(1) a light chain variable region consisting of an amino acid sequence from positions 21 to 127 of SEQ ID NO: 13,

(2) a light chain variable region consisting of an amino acid sequence from positions 21 to 127 of SEQ ID NO: 14,

(3) a light chain variable region consisting of an amino acid sequence having at least 95% or higher sequence identity to the sequences of framework regions except for CDR sequences in each of the amino acid sequences of (1) and (2), and

(4) a light chain variable region consisting of an amino acid sequence derived by the deletion, substitution, or addition of one or several amino acids from the sequences

of framework regions except for CDR sequences in each of the amino acid sequences of (1) and (2), and
any one heavy chain variable region selected from the group consisting of the following heavy chain variable regions (5) to (8):
(5) a heavy chain variable region consisting of an amino acid sequence from positions 20 to 146 of SEQ ID NO: 15,
(6) a heavy chain variable region consisting of an amino acid sequence from positions 20 to 146 of SEQ ID NO: 16,
(7) a heavy chain variable region consisting of an amino acid sequence having at least 95% or higher sequence homology to the sequences of framework regions except for CDR sequences in each of the amino acid sequences of (5) and (6), and
(8) a heavy chain variable region consisting of an amino acid sequence derived by the deletion, substitution, or addition of one or several amino acids from the sequences of framework regions except for CDR sequences in each of the amino acid sequences of (5) and (6); or
(b) any of the following combinations (1) and (2):
(1) a light chain consisting of an amino acid sequence from positions 21 to 233 of SEQ ID NO: 13 and a heavy chain consisting of an amino acid sequence from positions 20 to 476 of SEQ ID NO: 15, and

(2) a light chain consisting of an amino acid sequence from positions 21 to 233 of SEQ ID NO: 14 and a heavy chain consisting of an amino acid sequence from positions 20 to 476 of SEQ ID NO: 16.

[Claim 4]

The antigen binding fragment of the antibody according to claim 1, wherein the antigen binding fragment of the antibody is selected from the group consisting of Fab, F(ab')2, Fab', scFv, and Fv.

[Claim 5]

A humanized antibody or antigen binding fragment of the antibody comprising

(1) a light chain variable region consisting of an amino acid sequence from positions 21 to 127 of SEQ ID NO: 13 and a heavy chain variable region consisting of an amino acid sequence from positions 20 to 146 of SEQ ID NO: 15; or

(2) a light chain consisting of an amino acid sequence from positions 21 to 233 of SEQ ID NO: 13 and a heavy chain consisting of an amino acid sequence from positions 20 to 476 of SEQ ID NO: 15; or

(3) a light chain variable region consisting of an amino acid sequence from positions 21 to 127 of SEQ ID NO: 14 and a heavy chain variable region consisting of an amino acid sequence from positions 20 to 146 of SEQ ID NO: 16; or

(4) a light chain consisting of an amino acid sequence from positions 21 to 233 of SEQ ID NO: 14 and a heavy chain consisting of an amino acid sequence from positions 20 to 476 of SEQ ID NO: 16.

[Claim 6]

A polynucleotide encoding the antibody or the antigen binding fragment of the antibody according to claim 1.

[Claim 7]

The polynucleotide according to claim 6, wherein the polynucleotide comprises

(a) polynucleotides in any one combination selected from the group consisting of the following combinations (1) and (2):

(1) a polynucleotide encoding a light chain variable region comprising CDRL1 consisting of the amino acid sequence represented by SEQ ID NO: 1, CDRL2 consisting of the amino acid sequence represented by SEQ ID NO: 2 (KAS), and CDRL3 consisting of the amino acid sequence represented by SEQ ID NO: 3, and a polynucleotide encoding a heavy chain variable region comprising CDRH1 consisting of the amino acid sequence represented by SEQ ID NO: 7, CDRH2 consisting of the amino acid sequence represented by SEQ ID NO: 8, and CDRH3 consisting of the amino acid sequence represented by SEQ ID NO: 9, and

(2) a polynucleotide encoding a light chain variable region comprising CDRL1 consisting of the amino acid sequence represented by SEQ ID NO: 4, CDRL2 consisting of the amino acid sequence represented by SEQ ID NO: 5 (FVS), and CDRL3 consisting of the amino acid sequence represented by SEQ ID NO: 6, and a polynucleotide encoding a heavy chain variable region comprising CDRH1 consisting of the amino acid sequence represented by SEQ

ID NO: 10, CDRH2 consisting of the amino acid sequence represented by SEQ ID NO: 11, and CDRH3 consisting of the amino acid sequence represented by SEQ ID NO: 12; or

(b) a polynucleotide encoding a light chain consisting of an amino acid sequence from positions 21 to 233 of SEQ ID NO: 13 and a polynucleotide encoding a heavy chain consisting of an amino acid sequence from positions 20 to 476 of SEQ ID NO: 15; or

(c) a polynucleotide encoding a light chain consisting of an amino acid sequence from positions 21 to 233 of SEQ ID NO: 14 and a polynucleotide encoding a heavy chain consisting of an amino acid sequence from positions 20 to 476 of SEQ ID NO: 16.

[Claim 8]

An expression vector comprising the polynucleotide according to claim 6.

[Claim 9]

A host cell transformed with the expression vector according to claim 8.

[Claim 10]

The antibody or the antigen binding fragment of the antibody according to claim 1, wherein:

(a) a heavy chain or a light chain has one or two or more modifications selected from the group consisting of N-linked glycosylation, O-linked glycosylation, N-terminal processing, C-terminal processing, deamidation, isomerization of aspartic acid, oxidation of methionine, addition of a methionine residue to the N terminus,

amidation of a proline residue, conversion of N-terminal glutamine or N-terminal glutamic acid to pyroglutamic acid, and deletion of one or two amino acids from the carboxyl terminus; and/or

(b) one or two amino acids are deleted from the carboxyl terminus of a heavy chain; and/or

(c) one amino acid is deleted from each of the carboxyl termini of both of two heavy chains; and/or

(d) a proline residue at the carboxyl terminus of a heavy chain is further amidated; and/or

(e) wherein the antibody or the antigen binding fragment of the antibody has the modification of a glycan for enhancing antibody-dependent cellular cytotoxic activity.

[Claim 11]

An antibody-drug conjugate in which the antibody or the antigen binding fragment of the antibody according to claim 1 is conjugated to a drug.

[Claim 12]

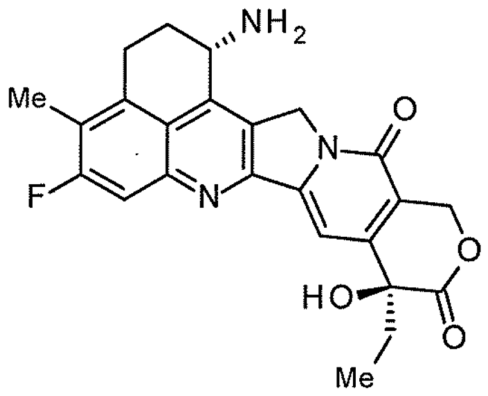
The antibody-drug conjugate according to claim 11, wherein the drug is any one or more drugs selected from the group consisting of a substance having cytotoxic activity, a cytotoxic active compound, a substance having antitumor activity, an antitumor active compound, a chemotherapeutic, a molecular targeting drug, an immunoactivator, an immunosuppressant, a toxin, a photosensitive substance, a drug for diagnosis, a protein, a peptide, an amino acid, a nucleic acid, an antigen, a vitamin, a hormone, a substance effective for

blood disease, a substance effective for autoimmune disease, an anti-inflammatory substance, an antibacterial substance, an antifungal substance, an antiparasitic substance, an antiviral substance, and an anti-anesthetic substance.

[Claim 13]

The antibody-drug conjugate according to claim 12, wherein the cytotoxic active compound is a cytotoxic active compound represented by the following formula:

[Formula 1]




[Claim 14]

The antibody-drug conjugate according to claim 11, wherein the antibody or the antigen binding fragment of the antibody is conjugated to the drug 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)-,

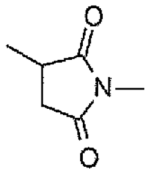
(e)-(Succinimid-3-yl-N)-$CH_2CH_2$-C(=O)-NH-$CH_2CH_2O$-$CH_2CH_2O$-$CH_2CH_2$-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-, and

(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 or the antigen binding fragment of the antibody is connected to the end of -(Succinimid-3-yl-N), the drug is connected to the carbonyl group at another end, 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]

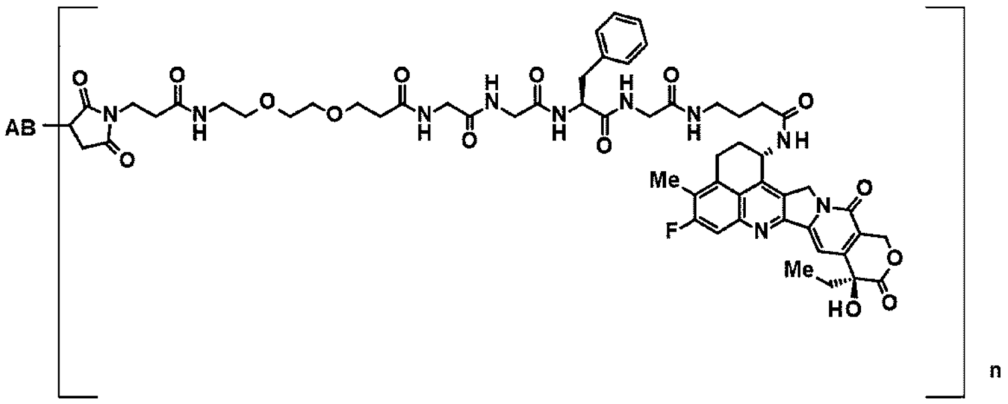


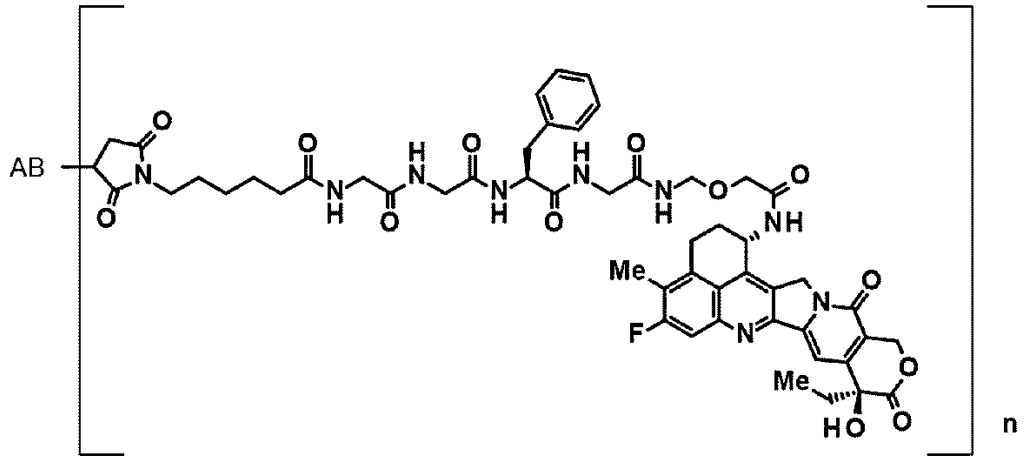
which is connected to the antibody or the antigen binding fragment of the antibody at the 3-position thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at the 1-position.

[Claim 15]

The antibody-drug conjugate according to claim 11, wherein the antibody-drug conjugate has a structure represented by the following formula:

[Formula 3]


AB
O
N
O
O
H
N
O
O
N
H
O
O
O




wherein AB represents the antibody or the antigen binding fragment of the antibody, n represents an average number of units of the drug-linker structure conjugated to the antibody or the antigen binding fragment of the antibody per antibody or per antigen binding fragment of the antibody, and the antibody or the antigen binding fragment of the antibody is connected to the linker via a sulfhydryl group derived from the antibody or the antigen binding fragment of the antibody.

[Claim 16]

The antibody-drug conjugate according to claim 11, wherein the antibody or the antigen binding fragment of the antibody comprises:

(a) a light chain variable region and a heavy chain variable region in any one combination selected from the group consisting of the following combinations (1) and (2):

(1) a light chain variable region consisting of an amino acid sequence from positions 21 to 127 of SEQ ID NO: 13

and a heavy chain variable region consisting of an amino acid sequence from positions 20 to 146 of SEQ ID NO: 15, and

(2) a light chain variable region consisting of an amino acid sequence from positions 21 to 127 of SEQ ID NO: 14 and a heavy chain variable region consisting of an amino acid sequence from positions 20 to 146 of SEQ ID NO: 16,

or an antigen binding fragment of the antibody; or

(b) a light chain and a heavy chain in any one combination selected from the group consisting of the following combinations (1) and (2):

(1) a light chain consisting of an amino acid sequence from positions 21 to 233 of SEQ ID NO: 13 and a heavy chain consisting of an amino acid sequence from positions 20 to 476 of SEQ ID NO: 15, and

(2) a light chain consisting of an amino acid sequence from positions 21 to 233 of SEQ ID NO: 14 and a heavy chain consisting of an amino acid sequence from positions 20 to 476 of SEQ ID NO: 16,

or an antigen binding fragment of the antibody.

[Claim 17]

The antibody-drug conjugate according to claim 11, wherein:

(a) a heavy chain or a light chain has one or two or more modifications selected from the group consisting of N-linked glycosylation, O-linked glycosylation, N-terminal processing, C-terminal processing, deamidation, isomerization of aspartic acid, oxidation of methionine,

addition of a methionine residue to the N terminus, amidation of a proline residue, conversion of N-terminal glutamine or N-terminal glutamic acid to pyroglutamic acid, and deletion of one or two amino acids from the carboxyl terminus; and/or

(b) wherein one or two amino acids are deleted from the carboxyl terminus of a heavy chain; and/or

(c) wherein one amino acid is deleted from each of the carboxyl termini of both of two heavy chains; and/or

(d) wherein a proline residue at the carboxyl terminus of a heavy chain is further amidated; and/or

(e) wherein the antibody-drug conjugate has the modification of a glycan for enhancing antibody-dependent cellular cytotoxic activity.

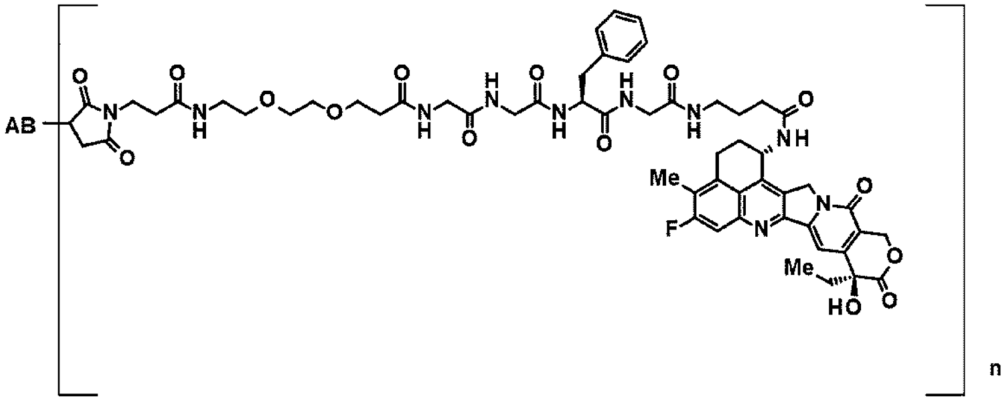
[Claim 18]

The antibody-drug conjugate according to claim 11, wherein the average number of units of the drug-linker structure conjugated per antibody or per the antigen binding fragment of the antibody is in the range of 1 to 10, range of 2 to 8, range of 5 to 8, or range of 7 to 8.

[Claim 19]

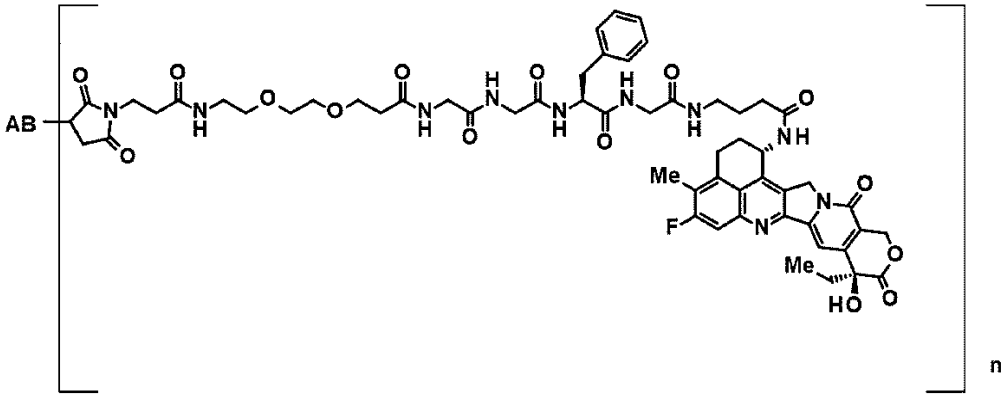
An antibody-drug conjugate having a structure represented by the following formula:

[Formula 5]



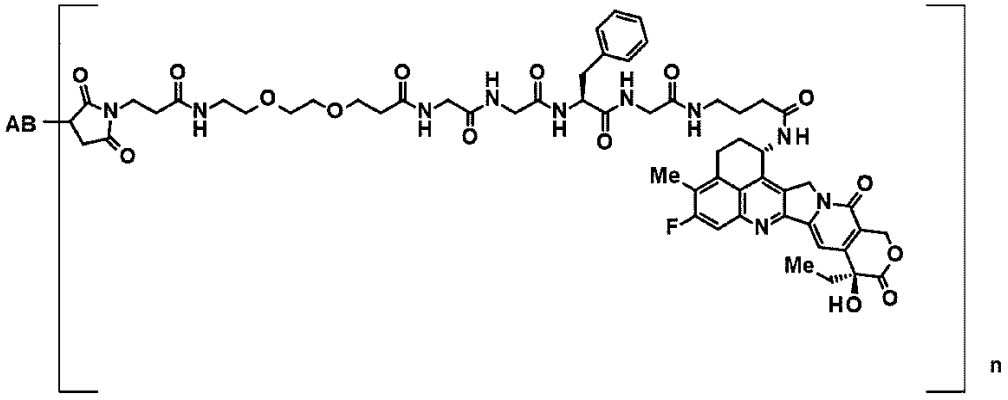
wherein AB represents a humanized antibody or the antigen binding fragment of the antibody comprising a light chain variable region consisting of an amino acid sequence from positions 21 to 127 of SEQ ID NO: 13 and a heavy chain variable region consisting of an amino acid sequence from positions 20 to 146 of SEQ ID NO: 15, n represents an average number of units of the drug-linker structure conjugated to the antibody or the antigen binding fragment of the antibody per antibody or per the antigen binding fragment of the antibody and is in the range of 7 to 8, and the antibody or the antigen binding fragment of the antibody is connected to the linker via a sulfhydryl group derived from the antibody or the antigen binding fragment of the antibody; or

[Formula 6]



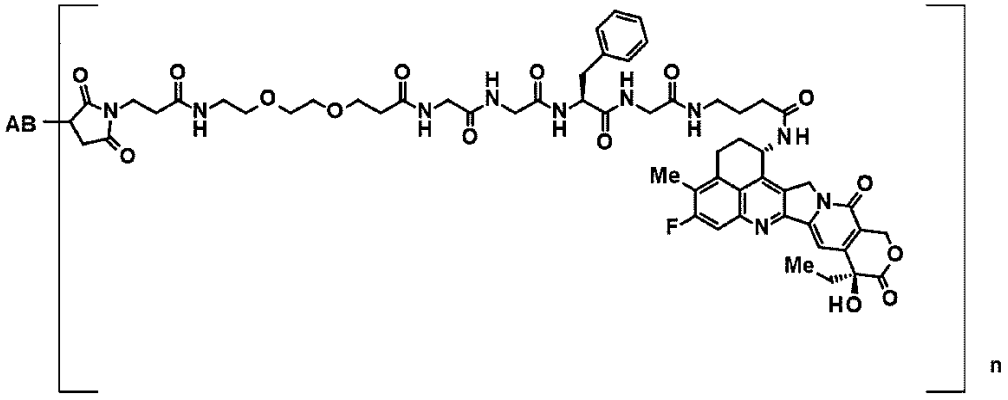
wherein AB represents a humanized antibody or the antigen binding fragment of the antibody comprising a light chain consisting of an amino acid sequence from positions 21 to 233 of SEQ ID NO: 13 and a heavy chain consisting of an amino acid sequence from positions 20 to 476 of SEQ ID NO: 15, n represents an average number of units of the drug-linker structure conjugated to the antibody or the antigen binding fragment of the antibody per antibody or per the antigen binding fragment of the antibody and is in the range of 7 to 8, and the antibody or the antigen binding fragment of the antibody is connected to the linker via a sulfhydryl group derived from the antibody or the antigen binding fragment of the antibody; or

[Formula 7]



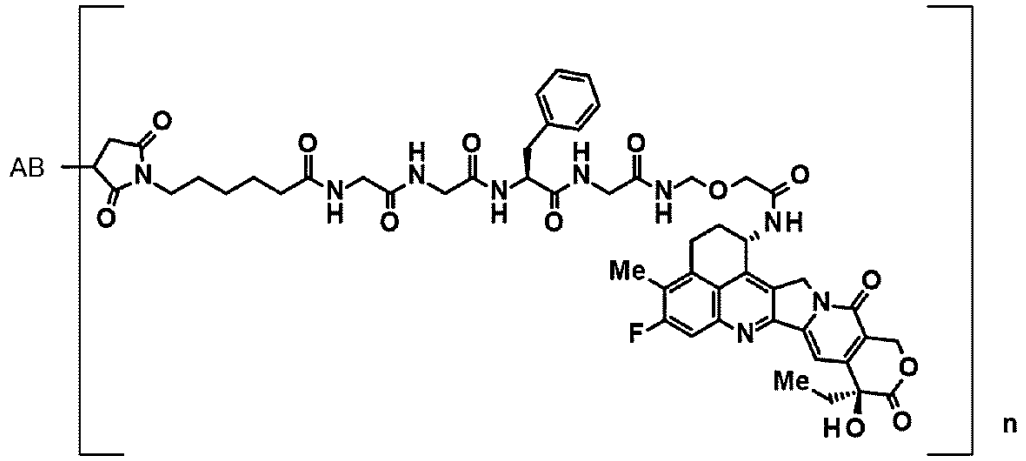
wherein AB represents a humanized antibody or the antigen binding fragment of the antibody comprising a light chain variable region consisting of an amino acid sequence from positions 21 to 127 of SEQ ID NO: 14 and a heavy chain variable region consisting of an amino acid sequence from positions 20 to 146 of SEQ ID NO: 16, n represents an average number of units of the drug-linker structure conjugated to the antibody or the antigen binding fragment of the antibody per antibody or per the antigen binding fragment of the antibody and is in the range of 7 to 8, and the antibody or the antigen binding fragment of the antibody is connected to the linker via a sulfhydryl group derived from the antibody or the antigen binding fragment of the antibody; or

[Formula 8]



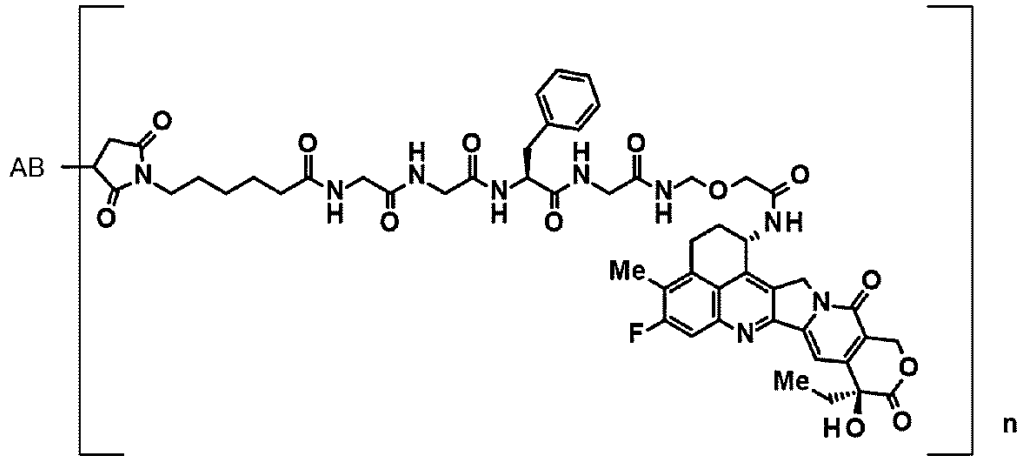
wherein AB represents a humanized antibody or the antigen binding fragment of the antibody comprising a light chain consisting of an amino acid sequence from positions 21 to 233 of SEQ ID NO: 14 and a heavy chain consisting of an amino acid sequence from positions 20 to 476 of SEQ ID NO: 16, n represents an average number of units of the drug-linker structure conjugated to the antibody or the antigen binding fragment of the antibody per antibody or per the antigen binding fragment of the antibody and is in the range of 7 to 8, and the antibody or the antigen binding fragment of the antibody is connected to the linker via a sulfhydryl group derived from the antibody or the antigen binding fragment of the antibody; or

[Formula 9]




wherein AB represents an antibody or the antigen binding fragment of the antibody comprising a light chain variable region consisting of the amino acid sequence of SEQ ID NO: 18 and a heavy chain variable region consisting of the amino acid sequence of SEQ ID NO: 20, n represents an average number of units of the drug-linker structure conjugated to the antibody or the antigen binding fragment of the antibody per antibody or per the antigen binding fragment of the antibody and is in the range of 7 to 8, and the antibody or the antigen binding fragment of the antibody is connected to the linker via a sulfhydryl group derived from the antibody or the antigen binding fragment of the antibody; or

[Formula 10]




wherein AB represents an antibody or the antigen binding fragment of the antibody comprising a light chain consisting of an amino acid sequence from positions 21 to 232 of SEQ ID NO: 26 and a heavy chain consisting of an amino acid sequence from positions 20 to 476 of SEQ ID NO: 27, n represents an average number of units of the drug-linker structure conjugated to the antibody or the antigen binding fragment of the antibody per antibody or per the antigen binding fragment of the antibody and is in the range of 7 to 8, and the antibody or the antigen binding fragment of the antibody is connected to the linker via a sulfhydryl group derived from the antibody or the antigen binding fragment of the antibody.

[Claim 20]

The antibody-drug conjugate according to claim 19, (a) wherein one amino acid is deleted from each of the carboxyl termini of both of two heavy chains of the antibody or the antigen binding fragment of the antibody; or

(b) wherein one amino acid is deleted from each of the carboxyl termini of both of two heavy chains of the antibody or the antigen binding fragment of the antibody and is lysine.

[Claim 21]

A pharmaceutical composition comprising the antibody or the antigen binding fragment of the antibody according to claim 1, a salt of the component, or a hydrate of the component or the salt.

[Claim 22]

Use of the antibody or the antigen binding fragment of the antibody according to claim 1, a salt of the component, and a hydrate of the component or the salt in the manufacture of a medicament for treating a tumor.

[Claim 23]

The use according to claim 22, wherein:

(a) tumor cells express CD25, or tumor immunity is suppressed by regulatory T cells;

(b) the tumor environment and/or the lymph node contains regulatory T cells;

(c) the tumor is blood cancer, breast cancer, small-cell lung cancer, non-small cell lung cancer, head and neck cancer, brain tumor, glioma, eye tumor, esophageal cancer, stomach cancer, colorectal cancer, colon cancer, liver cancer, pancreatic cancer, renal cancer, kidney cancer, urinary bladder cancer, adrenal cortex cancer, prostate cancer, uterine cervical cancer, endometrial cancer, ovary cancer, melanoma, or sarcoma.

[Claim 24]

Use of a pharmaceutical composition comprising the antibody-drug conjugate according to claim 11 in the manufacture of a first medicament and use of an immune checkpoint inhibitor in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy for treating a tumor.

[Claim 25]

The use according to claim 24, wherein the immune checkpoint inhibitor is any one or more members selected from the group consisting of an anti-PD-1 antibody, an anti-PD-L1 antibody, and an anti-CTLA-4 antibody, or

wherein the immune checkpoint inhibitor is any one or more members selected from the group consisting of nivolumab, pembrolizumab, sintilimab, spartalizumab, dostarlimab, serplulimab, tislelizumab, penpulimab, toripalimab, zimberelimab, camrelizumab, retifanlimab, cemiplimab, prolgolimab, geptanolimab, enlonstobart, QL-1604, pucotenlimab, and finotonlimab; or

wherein the immune checkpoint inhibitor is any one or more members selected from the group consisting of atezolizumab, durvalumab, cosibelimab, adebrelimab, sugemalimab, avelumab, socazolimab, KL-A167, and envafolimab; or

wherein the immune checkpoint inhibitor is any one or more members selected from the group consisting of ipilimumab, botensilimab, and tremelimumab.