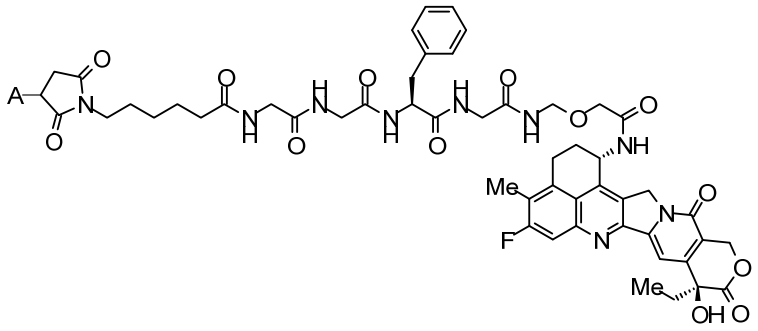
CLAIMS

[Claim 1]

Use of an antibody-drug conjugate and an immune checkpoint inhibitor for the manufacture of a medicament for a therapeutic method for treating cancer wherein the antibody-drug conjugate and the immune checkpoint inhibitor are to be administered in combination, and the antibody-drug conjugate is an antibody-drug conjugate in which a drug-linker represented by the following formula:



wherein A represents the connecting position to an antibody,

is conjugated to the antibody via a thioether bond,

the antibody in the antibody-drug conjugate is an anti-HER2 antibody and the immune checkpoint inhibitor is an anti-PD-1 antibody, an anti-PD-L1 antibody, or an anti-CTLA-4 antibody.

[Claim 2]

The use according to claim 1, wherein the anti-HER2 antibody is an antibody comprising a heavy chain

consisting of an amino acid sequence consisting of amino acid residues 1 to 449 of SEQ ID NO: 1 and a light chain consisting of an amino acid sequence consisting of amino acid residues 1 to 214 of SEQ ID NO: 2.

[Claim 3]

The use according to claim 1, wherein the anti-HER2 antibody is an antibody comprising a heavy chain consisting of the amino acid sequence represented by SEQ ID NO: 1 and a light chain consisting of the amino acid sequence represented by SEQ ID NO: 2.

[Claim 4]

The use according to any one of claims 1 to 3, wherein the average number of units of the drug-linker conjugated per antibody molecule in the antibody-drug conjugate is in the range of from 2 to 8.

[Claim 5]

The use according to any one of claims 1 to 3, wherein the average number of units of the drug-linker conjugated per antibody molecule in the antibody-drug conjugate is in the range of from 7 to 8.

[Claim 6]

The use according to any one of claims 1 to 3, wherein the average number of units of the drug-linker conjugated per antibody molecule in the antibody-drug conjugate is in the range of from 7.5 to 8.

[Claim 7]

The use according to any one of claim 1 to 6, wherein the immune checkpoint inhibitor is an anti-PD-1 antibody.

[Claim 8]

The use according to claim 7, wherein the anti-PD-1 antibody is nivolumab.

[Claim 9]

The use according to claim 7, wherein the anti-PD-1 antibody is pembrolizumab.

[Claim 10]

The use according to any one of claim 1 to 6, wherein the immune checkpoint inhibitor is an anti-PD-L1 antibody.

[Claim 11]

The use according to claim 10, wherein the anti-PD-L1 antibody is atezolizumab.

[Claim 12]

The use according to claim 10, wherein the anti-PD-L1 antibody is durvalumab.

[Claim 13]

The use according to claim 10, wherein the anti-PD-L1 antibody is avelumab.

[Claim 14]

The use according to any one of claim 1 to 6, wherein the immune checkpoint inhibitor is an anti-CTLA-4 antibody.

[Claim 15]

The use according to claim 14, wherein the anti-CTLA-4 antibody is ipilimumab.

[Claim 16]

The use according to claim 14, wherein the anti-CTLA-4 antibody is tremelimumab.

[Claim 17]

The use according to any one of claims 1 to 16, wherein the antibody-drug conjugate and the immune checkpoint inhibitor are separately contained as active components in different formulations, and are to be administered simultaneously or at different times.

[Claim 18]

The use according to any one of claims 1 to 16, wherein the antibody-drug conjugate and the immune checkpoint inhibitor are contained as active components in a single formulation and to be administered.

[Claim 19]

The use according to any one of claims 1 to 18, wherein the cancer is at least one selected from the group consisting of lung cancer, urothelial cancer, colorectal cancer, prostate cancer, ovarian cancer, pancreatic cancer, breast cancer, bladder cancer, gastric cancer, esophagogastric junction adenocarcinoma, gastrointestinal stromal tumor, uterine cervix cancer, esophageal cancer, squamous cell carcinoma, peritoneal cancer, liver cancer, hepatocellular cancer, endometrial

cancer, uterine cancer, salivary gland cancer, kidney cancer, vulval cancer, thyroid cancer, penis cancer, leukemia, malignant lymphoma, plasmacytoma, myeloma, neuroepithelial tissue tumor, nerve sheath tumor, head-and-neck cancer, skin cancer, pharyngeal cancer, gallbladder cancer, bile duct cancer, mesothelioma, Paget's disease, and sarcoma.

[Claim 20]

The use according to claim 19, wherein the cancer is colorectal cancer.

[Claim 21]

The use according to claim 19, wherein the cancer is breast cancer.

[Claim 22]

The use according to claim 19, wherein the cancer is lung cancer.

[Claim 23]

The use according to claim 19, wherein the cancer is urothelial cancer.

[Claim 24]

The use according to claim 19, wherein the cancer is bladder cancer.

[Claim 25]

The use according to claim 19, wherein the cancer is gastric cancer.

[Claim 26]

The use according to claim 19, wherein the cancer is esophagogastric junction adenocarcinoma.

[Claim 27]

The use according to any one of claims 1 to 26, wherein the antibody-drug conjugate has an antitumor immunity-activating effect.

[Claim 28]

The use according to any one of claims 1 to 27, wherein the antibody-drug conjugate has at least one effect selected from the group consisting of:

(1) a promoting effect on growth of intratumor CD8-positive T cells; and

(2) an activating effect on intratumor CD8-positive T cells.

[Claim 29]

The use according to any one of claims 1 to 28, wherein the antibody-drug conjugate has a promoting effect on the formation of immune memory against tumor.

[Claim 30]

The use according to claim 29, wherein the tumor is expressing an antigen for the antibody in the antibody-drug conjugate.

[Claim 31]

The use according to claim 29, wherein a part of the cells of the tumor are not expressing an antigen for the antibody in the antibody-drug conjugate.

[Claim 32]

The use according to any one of claims 1 to 31, wherein the antibody-drug conjugate has at least one effect selected from the group consisting of:

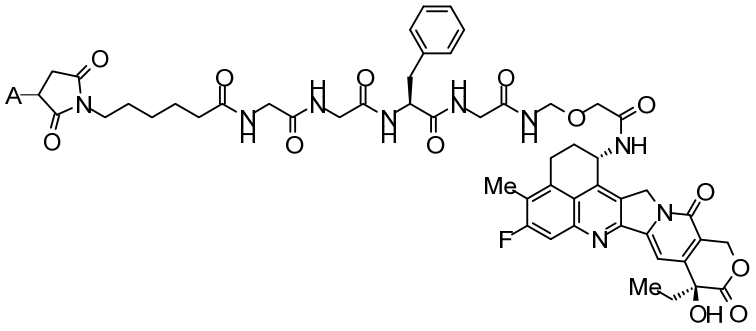
(1) a promoting effect on increase of the number of dendritic cells in a tumor;

(2) an activating effect on dendritic cells; and

(3) a promoting effect on elevation of the expression level of MHC class I on cancer cells.

[Claim 33]

Use of an antibody-drug conjugate for the manufacture of a medicament for a therapeutic method for treating cancer, wherein the antibody-drug conjugate is to be administered in combination with an immune checkpoint inhibitor, wherein a drug-linker represented by the following formula:



wherein A represents the connecting position to an antibody,

is conjugated to the antibody via a thioether bond in the antibody-drug conjugate,

the antibody in the antibody-drug conjugate is an anti-HER2 antibody and
the immune checkpoint inhibitor is an anti-PD-1 antibody, an anti-PD-L1 antibody, or an anti-CTLA-4 antibody.

[Claim 34]
The use according to claim 33, wherein the anti-HER2 antibody is an antibody comprising a heavy chain consisting of an amino acid sequence consisting of amino acid residues 1 to 449 of SEQ ID NO: 1 and a light chain consisting of an amino acid sequence consisting of amino acid residues 1 to 214 of SEQ ID NO: 2.

[Claim 35]
The use according to claim 33, wherein the anti-HER2 antibody is an antibody comprising a heavy chain consisting of the amino acid sequence represented by SEQ ID NO: 1 and a light chain consisting of the amino acid sequence represented by SEQ ID NO: 2.

[Claim 36]
The use according to any one of claim 33 to claim 35, wherein the average number of units of the drug-linker conjugated per antibody molecule in the antibody-drug conjugate is in the range of from 2 to 8.

[Claim 37]
The use according to any one of claim 33 to claim 35, wherein the average number of units of the drug-linker conjugated per antibody molecule in the antibody-drug conjugate is in the range of from 7 to 8.

[Claim 38]
The use according to any one of claim 33 to claim 35, wherein the average number of units of the drug-linker conjugated per antibody molecule in the antibody-drug conjugate is in the range of from 7.5 to 8.
[Claim 39]
The use according to any one of claim 33 to claim 38, wherein the immune checkpoint inhibitor is an anti-PD-1 antibody.
[Claim 40]
The use according to claim 39, wherein the anti-PD-1 antibody is nivolumab.
[Claim 41]
The use according to claim 39, wherein the anti-PD-1 antibody is pembrolizumab.
[Claim 42]
The use according to any one of claim 33 to claim 38, wherein the immune checkpoint inhibitor is an anti-PD-L1 antibody.
[Claim 43]
The use according to claim 42, wherein the anti-PD-L1 antibody is atezolizumab.
[Claim 44]
The use according to claim 42, wherein the anti-PD-L1 antibody is durvalumab.

[Claim 45]

The use according to claim 42, wherein the anti-PD-L1 antibody is avelumab.

[Claim 46]

The use according to any one of claim 33 to claim 38, wherein the immune checkpoint inhibitor is an anti-CTLA-4 antibody.

[Claim 47]

The use according to claim 46, wherein the anti-CTLA-4 antibody is ipilimumab.

[Claim 48]

The use according to claim 46, wherein the anti-CTLA-4 antibody is tremelimumab.

[Claim 49]

The use according to any one of claim 33 to claim 48, wherein the antibody-drug conjugate and the immune checkpoint inhibitor are separately contained as active components in different formulations, and are administered simultaneously or at different times.

[Claim 50]

The use according to any one of claim 33 to claim 49, wherein the antibody-drug conjugate and the immune checkpoint inhibitor are contained as active components in a single formulation and administered.

[Claim 51]

The use according to any one of claim 33 to claim 50, wherein the cancer is at least one selected from the

group consisting of lung cancer, urothelial cancer, colorectal cancer, prostate cancer, ovarian cancer, pancreatic cancer, breast cancer, bladder cancer, gastric cancer, esophagogastric junction adenocarcinoma, gastrointestinal stromal tumor, uterine cervix cancer, esophageal cancer, squamous cell carcinoma, peritoneal cancer, liver cancer, hepatocellular cancer, endometrial cancer, uterine cancer, salivary gland cancer, kidney cancer, vulval cancer, thyroid cancer, penis cancer, leukemia, malignant lymphoma, plasmacytoma, myeloma, neuroepithelial tissue tumor, nerve sheath tumor, head-and-neck cancer, skin cancer, pharyngeal cancer, gallbladder cancer, bile duct cancer, mesothelioma, Paget's disease, and sarcoma.

[Claim 52]

The use according to claim 51, wherein the cancer is colorectal cancer.

[Claim 53]

The use according to claim 51, wherein the cancer is breast cancer.

[Claim 54]

The use according to any one of claim 33 to claim 53, wherein the antibody-drug conjugate has an antitumor immunity-activating effect.

[Claim 55]
The use according to any one of claim 33 to claim 53, wherein the antibody-drug conjugate has at least one effect selected from the group consisting of:
(1) a promoting effect on growth of intratumor CD8-positive T cells; and
(2) an activating effect on intratumor CD8-positive T cells.
[Claim 56]
The use according to any one of claim 33 to claim 53, wherein the antibody-drug conjugate has a promoting effect on the formation of immune memory against tumor.
[Claim 57]
The use according to claim 56, wherein the tumor is expressing an antigen for the antibody in the antibody-drug conjugate.
[Claim 58]
The use according to claim 56, wherein a part of the cells of the tumor are not expressing an antigen for the antibody in the antibody-drug conjugate.
[Claim 59]
The use according to any one of claim 33 to claim 58, wherein the antibody-drug conjugate has at least one effect selected from the group consisting of:
(1) a promoting effect on increase of the number of dendritic cells in a tumor;
(2) an activating effect on dendritic cells; and

(3) a promoting effect on elevation of the expression level of MHC class I on cancer cells.