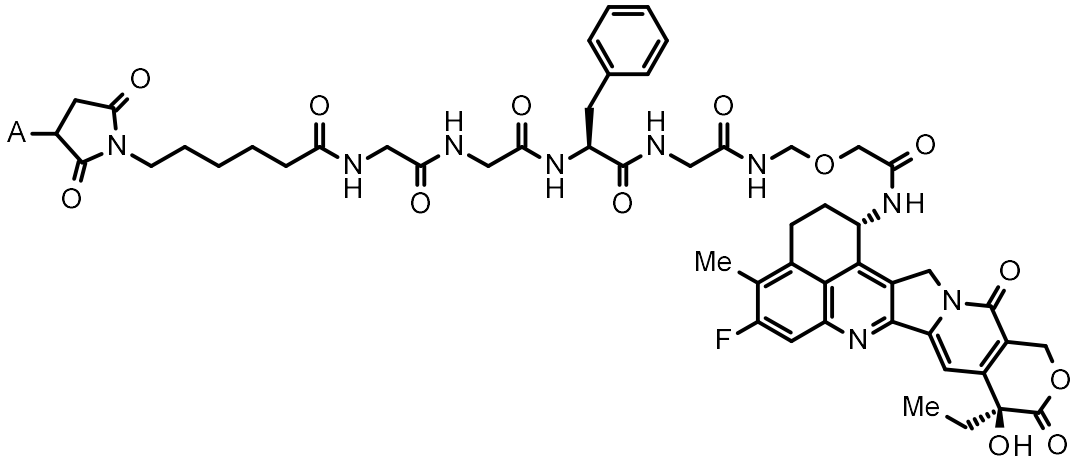
Claims

[Claim 1]

A pharmaceutical combination comprising

an anti-HER2 antibody-drug conjugate and a HER dimerization inhibitor, and

the anti-HER2 antibody-drug conjugate is an anti-HER2 antibody-drug conjugate in which a drug-linker represented by the following formula:



wherein A represents a connecting position to an anti-HER2 antibody,

is conjugated to the anti-HER2 antibody via a thioether bond.

[Claim 2]

The pharmaceutical combination according to claim 1, wherein the anti-HER2 antibody is an antibody comprising a heavy chain comprising CDRH1 consisting of an amino acid sequence represented by SEQ ID NO: 3, CDRH2 consisting of an amino acid sequence represented by SEQ ID NO: 4, and CDRH3 consisting of an amino acid sequence represented by SEQ ID NO: 5, and a light chain comprising CDRL1 consisting of an amino acid sequence represented by SEQ ID NO: 6, CDRL2 consisting of an amino acid sequence represented by amino acid residues 1 to 3 of SEQ ID NO: 7, and CDRL3 consisting of an amino acid sequence represented by SEQ ID NO: 8.

[Claim 3]

The pharmaceutical combination according to claim 1, wherein the anti-HER2 antibody is an antibody comprising a heavy chain comprising a heavy chain variable region consisting of an amino acid sequence represented by SEQ ID NO: 9 and a light chain comprising a light chain variable region consisting of an amino acid sequence represented by SEQ ID NO: 10.

[Claim 4]

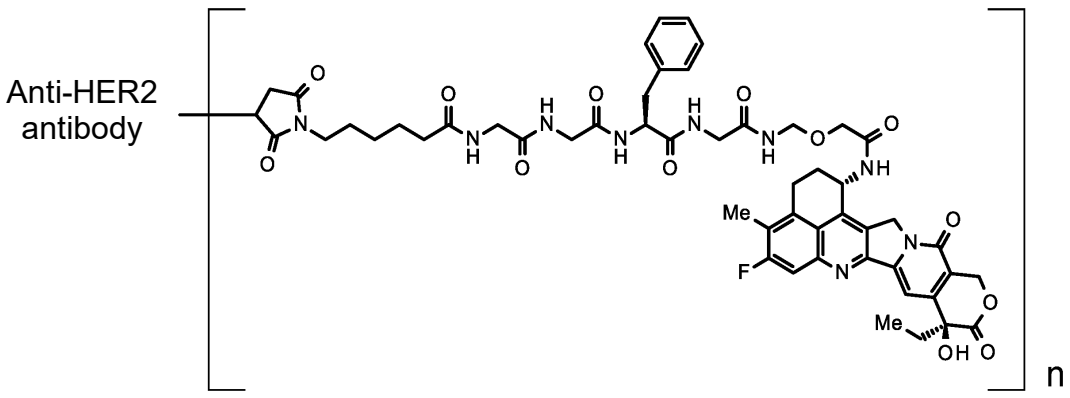
The pharmaceutical combination according to claim 1, wherein the anti-HER2 antibody is an antibody comprising a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 1 and a light chain consisting of an amino acid sequence represented by SEQ ID NO: 2.

[Claim 5]

The pharmaceutical combination according to claim 1, wherein the anti-HER2 antibody is an antibody comprising a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 11 and a light chain consisting of an amino acid sequence represented by SEQ ID NO: 2.

[Claim 6]

The pharmaceutical combination according to any one of claims 1 to 5, wherein the anti-HER2 antibody-drug conjugate is an anti-HER2 antibody-drug conjugate represented by the following formula:



wherein a drug-linker is conjugated to the anti-HER2 antibody via a thioether bond; and n represents the average number of units of the drug-linker conjugated per antibody molecule, wherein n is in the range of from 7 to 8.

[Claim 7]

The pharmaceutical combination according to any one of claims 1 to 6, wherein the anti-HER2 antibody-drug conjugate is trastuzumab deruxtecan.

[Claim 8]

The pharmaceutical combination according to any one of claims 1 to 7, wherein the HER dimerization inhibitor is an antibody capable of binding to subdomain II of an extracellular domain of HER2 protein.

[Claim 9]

The pharmaceutical combination according to any one of claims 1 to 7, wherein the HER dimerization inhibitor is pertuzumab.

[Claim 10]

The pharmaceutical combination according to any one of claims 1 to 9, wherein the anti-HER2 antibody-drug conjugate and the HER dimerization inhibitor are separately contained as active components in different formulations, and are administered simultaneously or at different times.

[Claim 11]

The pharmaceutical combination according to any one of claims 1 to 9, wherein the anti-HER2 antibody-drug conjugate and the HER dimerization inhibitor are contained as active components in a single formulation and administered.

[Claim 12]

A pharmaceutical combination according to any one of claims 1 to 11 for use in treating cancer.

[Claim 13]

The pharmaceutical combination for use according to claim 12, wherein the cancer is at least one selected from the group consisting of breast cancer, gastric cancer,

colorectal cancer, lung cancer, esophageal cancer, head-and-neck cancer, gastroesophageal junction adenocarcinoma, biliary tract cancer, Paget's disease, pancreatic cancer, ovarian cancer, uterine carcinosarcoma, bladder cancer, prostate cancer, urothelial cancer, gastrointestinal stromal tumor, uterine cervix cancer, squamous cell carcinoma, peritoneal cancer, liver cancer, hepatocellular cancer, endometrial cancer, kidney cancer, vulval cancer, thyroid cancer, penis cancer, leukemia, malignant lymphoma, plasmacytoma, myeloma, glioblastoma multiforme, sarcoma, osteosarcoma, and melanoma.

[Claim 14]

The pharmaceutical combination for use according to claim 12, wherein the cancer is at least one selected from the group consisting of breast cancer, gastric cancer, colorectal cancer, lung cancer, esophageal cancer, head-and-neck cancer, gastroesophageal junction adenocarcinoma, biliary tract cancer, Paget's disease, pancreatic cancer, ovarian cancer, uterine carcinosarcoma, bladder cancer, and prostate cancer.

[Claim 15]

The pharmaceutical combination for use according to claim 12, wherein the cancer is breast cancer.

[Claim 16]

The pharmaceutical combination for use according to claim 12, wherein the cancer is colorectal cancer.

[Claim 17]

The pharmaceutical combination for use according to any one of claims 12 to 16, wherein the cancer is HER2-overexpressing cancer.

[Claim 18]

The pharmaceutical combination for use according to claim 17, wherein the HER2-overexpressing cancer is cancer given a score of 3+ for the expression of HER2 in an immunohistochemical method.

[Claim 19]

The pharmaceutical combination for use according to claim 17, wherein the HER2-overexpressing cancer is cancer given a score of 2+ for the expression of HER2 in an immunohistochemical method and determined as positive for the expression of HER2 in an *in situ* hybridization method.

[Claim 20]

The pharmaceutical combination for use according to any one of claims 12 to 16, wherein the cancer is HER2 low-expressing cancer.

[Claim 21]

The pharmaceutical combination for use according to claim 20, wherein the HER2 low-expressing cancer is cancer given a score of 2+ for the expression of HER2 in an immunohistochemical method and determined as negative for the expression of HER2 in an *in situ* hybridization method.

[Claim 22]

The pharmaceutical combination for use according to claim 20, wherein the HER2 low-expressing cancer is cancer given a score of 1+ for the expression of HER2 in an immunohistochemical method.

[Claim 23]

The pharmaceutical combination for use according to claim 20, wherein the HER2 low-expressing cancer is cancer given a score of >0 and <1+ for the expression of HER2 in an immunohistochemical method.

[Claim 24]

The pharmaceutical combination for use according to any one of claims 12 to 23, wherein the pharmaceutical combination exerts a significantly superior antitumor effect than single administration of the anti-HER2 antibody-drug conjugate.

[Claim 25]

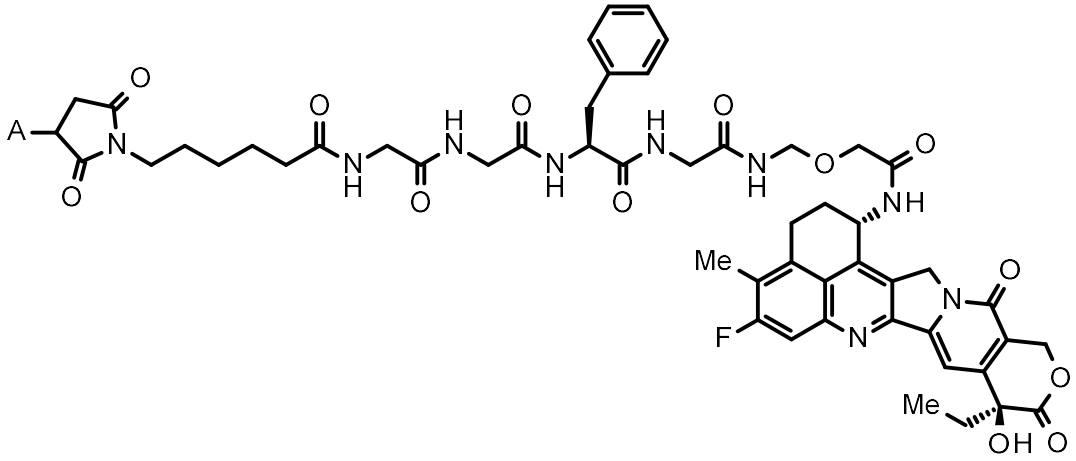
The pharmaceutical combination for use according to any one of claims 12 to 24, wherein the cancer is untreatable with single administration of the anti-HER2 antibody-drug conjugate.

[Claim 26]

The pharmaceutical combination for use according to any one of claims 12 to 25, wherein the anti-HER2 antibody-drug conjugate and the HER dimerization inhibitor exert a synergistic antitumor effect.

[Claim 27]

Use of an anti-HER2 antibody-drug conjugate in the manufacture of a medicament for treating cancer, , wherein the anti-HER2 antibody-drug conjugate is for use in combination with a HER dimerization inhibitor, wherein the anti-HER2 antibody-drug conjugate is an anti-HER2 antibody-drug conjugate in which a drug-linker represented by the following formula:



wherein A represents a connecting position to an anti-HER2 antibody,

is conjugated to the anti-HER2 antibody via a thioether bond.

[Claim 28]

The use according to claim 27, wherein the anti-HER2 antibody is an antibody comprising a heavy chain comprising CDRH1 consisting of an amino acid sequence represented by SEQ ID NO: 3, CDRH2 consisting of an amino acid sequence

represented by SEQ ID NO: 4, and CDRH3 consisting of an amino acid sequence represented by SEQ ID NO: 5, and a light chain comprising CDRL1 consisting of an amino acid sequence represented by SEQ ID NO: 6, CDRL2 consisting of an amino acid sequence represented by amino acid residues 1 to 3 of SEQ ID NO: 7, and CDRL3 consisting of an amino acid sequence represented by SEQ ID NO: 8.

[Claim 29]

The use according to claim 27, wherein the anti-HER2 antibody is an antibody comprising a heavy chain comprising a heavy chain variable region consisting of an amino acid sequence represented by SEQ ID NO: 9 and a light chain comprising a light chain variable region consisting of an amino acid sequence represented by SEQ ID NO: 10.

[Claim 30]

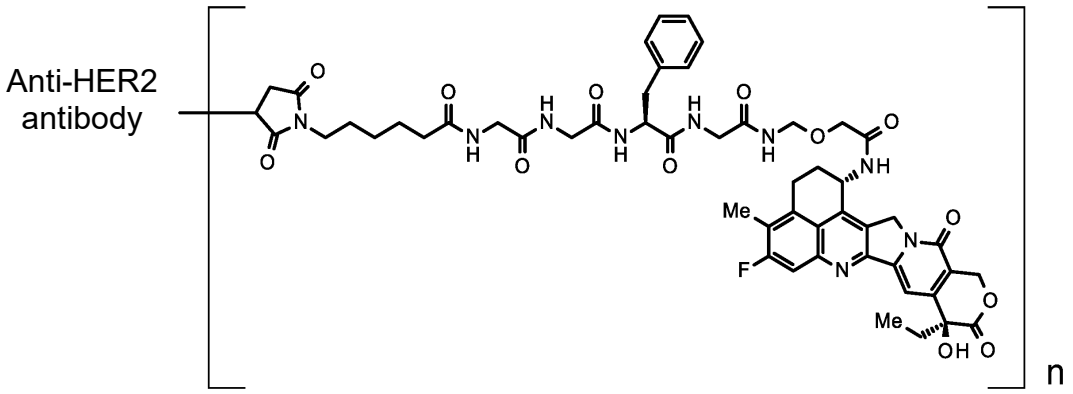
The use according to claim 27, wherein the anti-HER2 antibody is an antibody comprising a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 1 and a light chain consisting of an amino acid sequence represented by SEQ ID NO: 2.

[Claim 31]

The use according to claim 27, wherein the anti-HER2 antibody is an antibody comprising a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 11 and a light chain consisting of an amino acid sequence represented by SEQ ID NO: 2.

[Claim 32]

The use according to any one of claims 27 to 31, wherein the anti-HER2 antibody-drug conjugate is an anti-HER2 antibody-drug conjugate represented by the following formula:



wherein a drug-linker is conjugated to the anti-HER2 antibody via a thioether bond; and n represents the average number of units of the drug-linker conjugated per antibody molecule, wherein n is in the range of from 7 to 8.

[Claim 33]

The use according to any one of claims 27 to 32, wherein the anti-HER2 antibody-drug conjugate is trastuzumab deruxtecan.

[Claim 34]

The use according to any one of claims 27 to 33, wherein the HER dimerization inhibitor is an antibody capable of binding to subdomain II of an extracellular domain of HER2 protein.

[Claim 35]

The use according to any one of claims 27 to 33, wherein the HER dimerization inhibitor is pertuzumab.

[Claim 36]

The use according to any one of claims 27 to 35, wherein the anti-HER2 antibody-drug conjugate and the HER dimerization inhibitor are separately contained as active components in different formulations, and are administered simultaneously or at different times.

[Claim 37]

The use according to any one of claims 27 to 35, wherein the anti-HER2 antibody-drug conjugate and the HER dimerization inhibitor are contained as active components in a single formulation and administered.

[Claim 38]

The use according to any one of claims 27 to 37, wherein the cancer is at least one selected from the group consisting of breast cancer, gastric cancer, colorectal cancer, lung cancer, esophageal cancer, head-and-neck cancer, gastroesophageal junction adenocarcinoma, biliary tract cancer, Paget's disease, pancreatic cancer, ovarian cancer, uterine carcinosarcoma, bladder cancer, prostate cancer, urothelial cancer, gastrointestinal stromal tumor, uterine cervix cancer, squamous cell carcinoma, peritoneal cancer, liver cancer, hepatocellular cancer, endometrial cancer, kidney cancer, vulval cancer, thyroid cancer, penis cancer, leukemia, malignant lymphoma, plasmacytoma, myeloma, glioblastoma multiforme, sarcoma, osteosarcoma, and melanoma.

[Claim 39]

The use according to claim 38, wherein the cancer is at least one selected from the group consisting of breast cancer, gastric cancer, colorectal cancer, lung cancer, esophageal cancer, head-and-neck cancer, gastroesophageal junction adenocarcinoma, biliary tract cancer, Paget's disease, pancreatic cancer, ovarian cancer, uterine carcinosarcoma, bladder cancer, and prostate cancer.

[Claim 40]

The use according to claim 39, wherein the cancer is breast cancer.

[Claim 41]

The use according to claim 39, wherein the cancer is colorectal cancer.

[Claim 42]

The use according to any one of claims 27 to 41, wherein the cancer is HER2-overexpressing cancer.

[Claim 43]

The use according to claim 42, wherein the HER2-overexpressing cancer is cancer given a score of 3+ for the expression of HER2 in an immunohistochemical method.

[Claim 44]

The use according to claim 42, wherein the HER2-overexpressing cancer is cancer given a score of 2+ for the expression of HER2 in an immunohistochemical method and determined as positive for the expression of HER2 in an *in situ* hybridization method.

[Claim 45]

The use according to any one of claims 27 to 41, wherein the cancer is HER2 low-expressing cancer.

[Claim 46]

The use according to claim 45, wherein the HER2 low-expressing cancer is cancer given a score of 2+ for the expression of HER2 in an immunohistochemical method and determined as negative for the expression of HER2 in an *in situ* hybridization method.

[Claim 47]

The use according to claim 45, wherein the HER2 low-expressing cancer is cancer given a score of 1+ for the expression of HER2 in an immunohistochemical method.

[Claim 48]

The use according to claim 45, wherein the HER2 low-expressing cancer is cancer given a score of >0 and <1+ for the expression of HER2 in an immunohistochemical method.

[Claim 49]

The use according to any one of claims 27 to 48, wherein administration of a combination of the anti-HER2 antibody-drug conjugate and the HER dimerization

inhibitor exerts a significantly superior antitumor effect than single administration of the anti-HER2 antibody-drug conjugate.

[Claim 50]

The use according to any one of claims 27 to 49, wherein the cancer is untreatable with single administration of the anti-HER2 antibody-drug conjugate.

[Claim 51]

The use according to any one of claims 27 to 50, wherein the anti-HER2 antibody-drug conjugate and the HER dimerization inhibitor exert a synergistic antitumor effect.