treat cancer through the cytotoxic activity of T cells against target cancer tissues containing glypican 3-expressing cells, and are molecular forms that can be produced with high efficiency. Another objective of the present inventions is to provide combination therapies using the multispecific antigen-binding molecules and other pharmaceutical agents.

[Means for Solving the Problems]

The present inventors discovered an L chain common to a domain comprising a glypican 3-binding antibody variable region, and a domain comprising a T-cell receptor complex-binding antibody variable region, where the common L chain is capable of improving affinity to both antigens. This allows preparation of molecular forms that can be produced with high efficiency, and further discovery of novel multispecific antigen-binding molecules that maintain the strong antitumor activity possessed by T-cell redirecting antibodies such as BiTE and the excellent safety property of not inducing a cytokine storm in a cancer antigen-independent manner, and also have long half-lives in blood. Furthermore, the present inventors discovered that the multispecific antigen-binding molecules comprising common L chains target glypican 3-expressing cancer cells and cause cytotoxicity. Based on this discovery, the present inventors elucidated that the multispecific antigen-binding molecules of the present invention cause injury to cancer tissues containing glypican 3-expressing cancer cells. The present inventors revealed anticancer agents that comprise as an active ingredient the multispecific antigen-binding molecule; methods for treating or preventing cancer by combined use of the multispecific antigen-binding molecule and another anticancer agent; multispecific antigen-binding molecules, anticancer agents, or pharmaceutical compositions comprising a combination of a multispecific antigen-binding molecule and an anticancer agent, each of which is used in combination therapies.

Specifically, the present invention provides the following:

[1] Use of an agent in the manufacture of a medicament for treating a glypican 3-positive cancer, wherein the agent comprises as an active ingredient a bispecific antibody of any one of the bispecific antibodies below that comprise an antibody variable region having glypican 3-binding activity and an antibody variable region having CD3-binding activity:

(1) a bispecific antibody in which CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having glypican 3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211, respectively; CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having CD3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 142, respectively; and CDR1, CDR2, and CDR3 comprised in an antibody variable region of a

common L chain are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223, respectively;

(2) a bispecific antibody in which CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having glypican 3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211, respectively; CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having CD3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 144, respectively; and CDR1, CDR2, and CDR3 comprised in an antibody variable region of a common L chain are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223, respectively;

(3) a bispecific antibody in which CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having glypican 3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206, respectively; CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having CD3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 144, respectively; and CDR1, CDR2, and CDR3 comprised in an antibody variable region of a common L chain are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223, respectively;

(4) a bispecific antibody in which CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having glypican 3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206, respectively; CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having CD3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 142, respectively; and CDR1, CDR2, and CDR3 comprised in an antibody variable region of a common L chain are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223, respectively; and

(5) a bispecific antibody in which CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having glypican 3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206, respectively; CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having CD3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 168, respectively; and CDR1, CDR2, and CDR3 comprised in an antibody variable region of a common L chain are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223, respectively

wherein the cancer is gastric cancer, head and neck cancer, esophageal cancer, liver cancer, ovary cancer, breast cancer, colorectal cancer, kidney cancer, skin cancer, pancreas cancer, striated

muscle cancer, prostate cancer, testis cancer, or uterine cervix cancer.

[2] Use of an agent in the manufacture of a medicament for treating a glypican 3-positive cancer, wherein the agent comprises as an active ingredient a bispecific antibody of any one of the bispecific antibodies below:

(1) a bispecific antibody in which an antibody H chain variable region having glypican 3-binding activity is the amino acid sequence of SEQ ID NO: 211; an antibody H chain variable region having CD3-binding activity is the amino acid sequence of SEQ ID NO: 142; and a variable region of a common L chain is the amino acid sequence of SEQ ID NO: 223;

(2) a bispecific antibody in which an antibody H chain variable region having glypican 3-binding activity is the amino acid sequence of SEQ ID NO: 211; an antibody H chain variable region having CD3-binding activity is the amino acid sequence of SEQ ID NO: 144; and a variable region of a common L chain is the amino acid sequence of SEQ ID NO: 223;

(3) a bispecific antibody in which an antibody H chain variable region having glypican 3-binding activity is the amino acid sequence of SEQ ID NO: 206; an antibody H chain variable region having CD3-binding activity is the amino acid sequence of SEQ ID NO: 144; and a variable region of a common L chain is the amino acid sequence of SEQ ID NO: 223;

(4) a bispecific antibody in which an antibody H chain variable region having glypican 3-binding activity is the amino acid sequence of SEQ ID NO: 206; an antibody H chain variable region having CD3-binding activity is the amino acid sequence of SEQ ID NO: 142; and a variable region of a common L chain is the amino acid sequence of SEQ ID NO: 223; and

(5) a bispecific antibody in which an antibody H chain variable region having glypican 3-binding activity is the amino acid sequence of SEQ ID NO: 206; an antibody H chain variable region having CD3-binding activity is the amino acid sequence of SEQ ID NO: 168; and a variable region of a common L chain is the amino acid sequence of SEQ ID NO: 223, wherein the cancer is gastric cancer, head and neck cancer, esophageal cancer, liver cancer, ovary cancer, breast cancer, colorectal cancer, kidney cancer, skin cancer, pancreas cancer, striated muscle cancer, prostate cancer, testis cancer, or uterine cervix cancer.

[3] Use of an agent in the manufacture of a medicament for treating a glypican 3-positive cancer, wherein the agent comprises as an active ingredient a bispecific antibody of any one of the bispecific antibodies below:

(1) a bispecific antibody that has the antibody H chain of SEQ ID NO: 386 having glypican 3-binding activity, the antibody H chain of SEQ ID NO: 398 having CD3-binding activity, and the antibody common L chains of SEQ ID NO: 410;

(2) a bispecific antibody that has the antibody H chain of SEQ ID NO: 386 having glypican 3-binding activity, the antibody H chain of SEQ ID NO: 399 having CD3-binding activity, and the antibody common L chains of SEQ ID NO: 410;

(3) a bispecific antibody that has the antibody H chain of SEQ ID NO: 385 having glypican 3-binding activity, the antibody H chain of SEQ ID NO: 399 having CD3-binding activity, and the antibody common L chains of SEQ ID NO: 410;

(4) a bispecific antibody that has the antibody H chain of SEQ ID NO: 385 having glypican 3-binding activity, the antibody H chain of SEQ ID NO: 398 having CD3-binding activity, and the antibody common L chains of SEQ ID NO: 410; and

(5) a bispecific antibody that has the antibody H chain of SEQ ID NO: 385 having glypican 3-binding activity, the antibody H chain of SEQ ID NO: 402 having CD3-binding activity, and the antibody common L chains of SEQ ID NO: 410, wherein the cancer is gastric cancer, head and neck cancer, esophageal cancer, liver cancer, ovary cancer, breast cancer, colorectal cancer, kidney cancer, skin cancer, pancreas cancer, striated muscle cancer, prostate cancer, testis cancer, or uterine cervix cancer.

[4] Use of a pharmaceutical composition in the manufacture of a medicament for treating a glypican 3-positive cancer or for preventing a glypican 3-positive cancer, wherein the pharmaceutical composition is to be used in combination with another anticancer agent, wherein the pharmaceutical composition comprises as an active ingredient a bispecific antibody of any one of the bispecific antibodies below that comprise an antibody variable region having glypican 3-binding activity and an antibody variable region having CD3-binding activity:

(1) a bispecific antibody in which CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having glypican 3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211, respectively; CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having CD3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 142, respectively; and CDR1, CDR2, and CDR3 comprised in an antibody variable region of a common L chain are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223, respectively;

(2) a bispecific antibody in which CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having glypican 3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211, respectively; CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having CD3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 144, respectively; and CDR1, CDR2, and CDR3 comprised in an antibody variable region of a common L chain are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223, respectively;

(3) a bispecific antibody in which CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having glypican 3-binding activity are the amino acid sequences of the CDR1,

CDR2, and CDR3 regions comprised in SEQ ID NO: 206, respectively; CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having CD3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 144, respectively; and CDR1, CDR2, and CDR3 comprised in an antibody variable region of a common L chain are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223, respectively;

(4) a bispecific antibody in which CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having glypican 3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206, respectively; CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having CD3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 142, respectively; and CDR1, CDR2, and CDR3 comprised in an antibody variable region of a common L chain are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223, respectively; and

(5) a bispecific antibody in which CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having glypican 3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206, respectively; CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having CD3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 168, respectively; and CDR1, CDR2, and CDR3 comprised in an antibody variable region of a common L chain are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223, respectively.

[5] Use of a pharmaceutical composition in the manufacture of a medicament for treating a glypican 3-positive cancer or for preventing a glypican 3-positive cancer, wherein the pharmaceutical composition is to be used in combination with another anticancer agent, wherein the pharmaceutical composition comprises as an active ingredient a bispecific antibody of any one of the bispecific antibodies below:

(1) a bispecific antibody in which an antibody H chain variable region having glypican 3-binding activity is the amino acid sequence of SEQ ID NO: 211; an antibody H chain variable region having CD3-binding activity is the amino acid sequence of SEQ ID NO: 142; and a variable region of a common L chain is the amino acid sequence of SEQ ID NO: 223;

(2) a bispecific antibody in which an antibody H chain variable region having glypican 3-binding activity is the amino acid sequence of SEQ ID NO: 211; an antibody H chain variable region having CD3-binding activity is the amino acid sequence of SEQ ID NO: 144; and a variable region of a common L chain is the amino acid sequence of SEQ ID NO: 223;

(3) a bispecific antibody in which an antibody H chain variable region having glypican

3-binding activity is the amino acid sequence of SEQ ID NO: 206; an antibody H chain variable region having CD3-binding activity is the amino acid sequence of SEQ ID NO: 144; and a variable region of a common L chain is the amino acid sequence of SEQ ID NO: 223;

(4) a bispecific antibody in which an antibody H chain variable region having glypican 3-binding activity is the amino acid sequence of SEQ ID NO: 206; an antibody H chain variable region having CD3-binding activity is the amino acid sequence of SEQ ID NO: 142; and a variable region of a common L chain is the amino acid sequence of SEQ ID NO: 223; and

(5) a bispecific antibody in which an antibody H chain variable region having glypican 3-binding activity is the amino acid sequence of SEQ ID NO: 206; an antibody H chain variable region having CD3-binding activity is the amino acid sequence of SEQ ID NO: 168; and a variable region of a common L chain is the amino acid sequence of SEQ ID NO: 223.

[6] Use of a pharmaceutical composition in the manufacture of a medicament for treating a glypican 3-positive cancer or for preventing a glypican 3-positive cancer, wherein the pharmaceutical composition is to be used in combination with another anticancer agent, wherein the pharmaceutical composition comprises as an active ingredient a bispecific antibody of any one of the bispecific antibodies below:

(1) a bispecific antibody that has the antibody H chain of SEQ ID NO: 386 having glypican 3-binding activity, the antibody H chain of SEQ ID NO: 398 having CD3-binding activity, and the antibody common L chains of SEQ ID NO: 410;

(2) a bispecific antibody that has the antibody H chain of SEQ ID NO: 386 having glypican 3-binding activity, the antibody H chain of SEQ ID NO: 399 having CD3-binding activity, and the antibody common L chains of SEQ ID NO: 410;

(3) a bispecific antibody that has the antibody H chain of SEQ ID NO: 385 having glypican 3-binding activity, the antibody H chain of SEQ ID NO: 399 having CD3-binding activity, and the antibody common L chains of SEQ ID NO: 410;

(4) a bispecific antibody that has the antibody H chain of SEQ ID NO: 385 having glypican 3-binding activity, the antibody H chain of SEQ ID NO: 398 having CD3-binding activity, and the antibody common L chains of SEQ ID NO: 410; and

(5) a bispecific antibody that has the antibody H chain of SEQ ID NO: 385 having glypican 3-binding activity, the antibody H chain of SEQ ID NO: 402 having CD3-binding activity, and the antibody common L chains of SEQ ID NO: 410.

[7] Use of an agent in the manufacture of a medicament for inducing cytotoxicity, for suppressing cell proliferation, for inhibiting cell proliferation, for activating immune response, for treating cancer, or for preventing cancer, wherein the agent comprises the pharmaceutical composition as disclosed herein.

Further, the present examples as disclosed herein are:

[1] An anticancer agent comprising as an active ingredient a bispecific antibody of any one of (a) to (c) below that comprises an antibody variable region having glypican 3-binding activity and an antibody variable region having CD3-binding activity:

(a) a bispecific antibody in which CDR1, CDR2, and CDR3 comprised in the antibody variable region having glypican 3-binding activity are sequences having at least 80% identity to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206, respectively; CDR1, CDR2, and CDR3 comprised in the antibody variable region having CD3-binding activity are sequences having at least 80% identity to the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 168, respectively; and CDR1, CDR2, and CDR3 comprised in an antibody variable region of a common L chain are sequences

Claims

1. Use of an agent in the manufacture of a medicament for treating a glypican 3-positive cancer, wherein the agent comprises as an active ingredient a bispecific antibody of any one of the bispecific antibodies below that comprise an antibody variable region having glypican 3-binding activity and an antibody variable region having CD3-binding activity:

(1) a bispecific antibody in which CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having glypican 3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211, respectively; CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having CD3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 142, respectively; and CDR1, CDR2, and CDR3 comprised in an antibody variable region of a common L chain are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223, respectively;

(2) a bispecific antibody in which CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having glypican 3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211, respectively; CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having CD3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 144, respectively; and CDR1, CDR2, and CDR3 comprised in an antibody variable region of a common L chain are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223, respectively;

(3) a bispecific antibody in which CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having glypican 3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206, respectively; CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having CD3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 144, respectively; and CDR1, CDR2, and CDR3 comprised in an antibody variable region of a common L chain are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223, respectively;

(4) a bispecific antibody in which CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having glypican 3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206, respectively; CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having CD3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 142, respectively; and CDR1, CDR2, and CDR3 comprised in an antibody variable region of a

common L chain are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223, respectively; and

(5) a bispecific antibody in which CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having glypican 3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206, respectively; CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having CD3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 168, respectively; and CDR1, CDR2, and CDR3 comprised in an antibody variable region of a common L chain are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223, respectively,

wherein the cancer is gastric cancer, head and neck cancer, esophageal cancer, liver cancer, ovary cancer, breast cancer, colorectal cancer, kidney cancer, skin cancer, pancreas cancer, striated muscle cancer, prostate cancer, testis cancer, or uterine cervix cancer.

2. Use of an agent in the manufacture of a medicament for treating a glypican 3-positive cancer, wherein the agent comprises as an active ingredient a bispecific antibody of any one of the bispecific antibodies below:

(1) a bispecific antibody in which an antibody H chain variable region having glypican 3-binding activity is the amino acid sequence of SEQ ID NO: 211; an antibody H chain variable region having CD3-binding activity is the amino acid sequence of SEQ ID NO: 142; and a variable region of a common L chain is the amino acid sequence of SEQ ID NO: 223;

(2) a bispecific antibody in which an antibody H chain variable region having glypican 3-binding activity is the amino acid sequence of SEQ ID NO: 211; an antibody H chain variable region having CD3-binding activity is the amino acid sequence of SEQ ID NO: 144; and a variable region of a common L chain is the amino acid sequence of SEQ ID NO: 223;

(3) a bispecific antibody in which an antibody H chain variable region having glypican 3-binding activity is the amino acid sequence of SEQ ID NO: 206; an antibody H chain variable region having CD3-binding activity is the amino acid sequence of SEQ ID NO: 144; and a variable region of a common L chain is the amino acid sequence of SEQ ID NO: 223;

(4) a bispecific antibody in which an antibody H chain variable region having glypican 3-binding activity is the amino acid sequence of SEQ ID NO: 206; an antibody H chain variable region having CD3-binding activity is the amino acid sequence of SEQ ID NO: 142; and a variable region of a common L chain is the amino acid sequence of SEQ ID NO: 223; and

(5) a bispecific antibody in which an antibody H chain variable region having glypican 3-binding activity is the amino acid sequence of SEQ ID NO: 206; an antibody H chain variable region having CD3-binding activity is the amino acid sequence of SEQ ID NO: 168; and a

variable region of a common L chain is the amino acid sequence of SEQ ID NO: 223
wherein the cancer is gastric cancer, head and neck cancer, esophageal cancer, liver cancer, ovary cancer, breast cancer, colorectal cancer, kidney cancer, skin cancer, pancreas cancer, striated muscle cancer, prostate cancer, testis cancer, or uterine cervix cancer.

3. Use of an agent in the manufacture of a medicament for treating a glypican 3-positive cancer, wherein the agent comprises as an active ingredient a bispecific antibody of any one of the bispecific antibodies below:

(1) a bispecific antibody that has the antibody H chain of SEQ ID NO: 386 having glypican 3-binding activity, the antibody H chain of SEQ ID NO: 398 having CD3-binding activity, and the antibody common L chains of SEQ ID NO: 410;

(2) a bispecific antibody that has the antibody H chain of SEQ ID NO: 386 having glypican 3-binding activity, the antibody H chain of SEQ ID NO: 399 having CD3-binding activity, and the antibody common L chains of SEQ ID NO: 410;

(3) a bispecific antibody that has the antibody H chain of SEQ ID NO: 385 having glypican 3-binding activity, the antibody H chain of SEQ ID NO: 399 having CD3-binding activity, and the antibody common L chains of SEQ ID NO: 410;

(4) a bispecific antibody that has the antibody H chain of SEQ ID NO: 385 having glypican 3-binding activity, the antibody H chain of SEQ ID NO: 398 having CD3-binding activity, and the antibody common L chains of SEQ ID NO: 410; and

(5) a bispecific antibody that has the antibody H chain of SEQ ID NO: 385 having glypican 3-binding activity, the antibody H chain of SEQ ID NO: 402 having CD3-binding activity, and the antibody common L chains of SEQ ID NO: 410,

wherein the cancer is gastric cancer, head and neck cancer, esophageal cancer, liver cancer, ovary cancer, breast cancer, colorectal cancer, kidney cancer, skin cancer, pancreas cancer, striated muscle cancer, prostate cancer, testis cancer, or uterine cervix cancer.

4. The use of any one of claims 1 to 3, wherein the glypican 3-positive cancer is a cancer in which the number of glypican 3 antigens on cell surface per cell is 100 or more.

5. The use of any one of claims 1 to 4, wherein the glypican 3-positive cancer is refractory to treatment with an immune checkpoint inhibitor.

6. Use of a pharmaceutical composition in the manufacture of a medicament for treating a glypican 3-positive cancer or for preventing a glypican 3-positive cancer, wherein the

pharmaceutical composition is to be used in combination with another anticancer agent, wherein the pharmaceutical composition comprises as an active ingredient a bispecific antibody of any one of the bispecific antibodies below that comprise an antibody variable region having glypican 3-binding activity and an antibody variable region having CD3-binding activity:

(1) a bispecific antibody in which CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having glypican 3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211, respectively; CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having CD3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 142, respectively; and CDR1, CDR2, and CDR3 comprised in an antibody variable region of a common L chain are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223, respectively;

(2) a bispecific antibody in which CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having glypican 3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 211, respectively; CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having CD3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 144, respectively; and CDR1, CDR2, and CDR3 comprised in an antibody variable region of a common L chain are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223, respectively;

(3) a bispecific antibody in which CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having glypican 3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206, respectively; CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having CD3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 144, respectively; and CDR1, CDR2, and CDR3 comprised in an antibody variable region of a common L chain are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223, respectively;

(4) a bispecific antibody in which CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having glypican 3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206, respectively; CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having CD3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 142, respectively; and CDR1, CDR2, and CDR3 comprised in an antibody variable region of a common L chain are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223, respectively; and

(5) a bispecific antibody in which CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having glypican 3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 206, respectively; CDR1, CDR2, and CDR3 comprised in an antibody H chain variable region having CD3-binding activity are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 168, respectively; and CDR1, CDR2, and CDR3 comprised in an antibody variable region of a common L chain are the amino acid sequences of the CDR1, CDR2, and CDR3 regions comprised in SEQ ID NO: 223, respectively.

7. Use of a pharmaceutical composition in the manufacture of a medicament for treating a glypican 3-positive cancer or for preventing a glypican 3-positive cancer, wherein the pharmaceutical composition is to be used in combination with another anticancer agent, wherein the pharmaceutical composition comprises as an active ingredient a bispecific antibody of any one of the bispecific antibodies below:

(1) a bispecific antibody in which an antibody H chain variable region having glypican 3-binding activity is the amino acid sequence of SEQ ID NO: 211; an antibody H chain variable region having CD3-binding activity is the amino acid sequence of SEQ ID NO: 142; and a variable region of a common L chain is the amino acid sequence of SEQ ID NO: 223;

(2) a bispecific antibody in which an antibody H chain variable region having glypican 3-binding activity is the amino acid sequence of SEQ ID NO: 211; an antibody H chain variable region having CD3-binding activity is the amino acid sequence of SEQ ID NO: 144; and a variable region of a common L chain is the amino acid sequence of SEQ ID NO: 223;

(3) a bispecific antibody in which an antibody H chain variable region having glypican 3-binding activity is the amino acid sequence of SEQ ID NO: 206; an antibody H chain variable region having CD3-binding activity is the amino acid sequence of SEQ ID NO: 144; and a variable region of a common L chain is the amino acid sequence of SEQ ID NO: 223;

(4) a bispecific antibody in which an antibody H chain variable region having glypican 3-binding activity is the amino acid sequence of SEQ ID NO: 206; an antibody H chain variable region having CD3-binding activity is the amino acid sequence of SEQ ID NO: 142; and a variable region of a common L chain is the amino acid sequence of SEQ ID NO: 223; and

(5) a bispecific antibody in which an antibody H chain variable region having glypican 3-binding activity is the amino acid sequence of SEQ ID NO: 206; an antibody H chain variable region having CD3-binding activity is the amino acid sequence of SEQ ID NO: 168; and a variable region of a common L chain is the amino acid sequence of SEQ ID NO: 223.

8. Use of a pharmaceutical composition in the manufacture of a medicament for treating a

glypican 3-positive cancer or for preventing a glypican 3-positive cancer, wherein the pharmaceutical composition is to be used in combination with another anticancer agent, wherein the pharmaceutical composition comprises as an active ingredient a bispecific antibody of any one of the bispecific antibodies below:

(1) a bispecific antibody that has the antibody H chain of SEQ ID NO: 386 having glypican 3-binding activity, the antibody H chain of SEQ ID NO: 398 having CD3-binding activity, and the antibody common L chains of SEQ ID NO: 410;

(2) a bispecific antibody that has the antibody H chain of SEQ ID NO: 386 having glypican 3-binding activity, the antibody H chain of SEQ ID NO: 399 having CD3-binding activity, and the antibody common L chains of SEQ ID NO: 410;

(3) a bispecific antibody that has the antibody H chain of SEQ ID NO: 385 having glypican 3-binding activity, the antibody H chain of SEQ ID NO: 399 having CD3-binding activity, and the antibody common L chains of SEQ ID NO: 410;

(4) a bispecific antibody that has the antibody H chain of SEQ ID NO: 385 having glypican 3-binding activity, the antibody H chain of SEQ ID NO: 398 having CD3-binding activity, and the antibody common L chains of SEQ ID NO: 410; and

(5) a bispecific antibody that has the antibody H chain of SEQ ID NO: 385 having glypican 3-binding activity, the antibody H chain of SEQ ID NO: 402 having CD3-binding activity, and the antibody common L chains of SEQ ID NO: 410.

9. The use of any one of claims 6 to 8, wherein the bispecific antibody is to be administered simultaneously with said another anticancer agent.

10. The use of any one of claims 6 to 8, wherein the bispecific antibody is to be administered before or after administration of said another anticancer agent.

11. The use of any one of claims 6 to 8, wherein said another anticancer agent is a chemotherapeutic agent, a T cell-activating agonist agent, an immune checkpoint inhibitor, or an angiogenic inhibitor.

12. The use of claim 11, wherein the chemotherapeutic agent is an antimetabolite, a plant alkaloid, or a platinum compound.

13. The use of claim 11, wherein the T cell-activating agonist agent is an agonist antibody against TNFRSF.

14. The use of claim 11, wherein the immune checkpoint inhibitor is a PD1 antibody, a PDL1 antibody, a TIM3 antibody, or an LAG3 antibody.

15. The use of claim 11, wherein the angiogenic inhibitor is a VEGFR2 antibody.