

The antibody may include a heavy chain variable domain (VH) with an amino acid sequence selected from the group consisting of SEQ ID NOs: 7 and 9; and a light chain variable domain (VL) with an amino acid sequence selected from the group consisting of SEQ ID NOs: 8 and 10. The antibody may be an antibody-drug conjugate. The antibody may be conjugated with monomethyl auristatin E (MMAE). The antibody may be administered intravenously.

[0007a] In a first aspect, there is provided use of an antibody-drug conjugate (ADC) in the manufacture of a medicament for treating cancer in a subject, wherein the subject has at least one cancer cell expressing STn, wherein said ADC comprises: a) an anti-STn antibody, wherein said anti-STn antibody comprises: a heavy chain variable domain (VH) with the amino acid sequence of SEQ ID NO: 7; a light chain variable domain (VL) with the amino acid sequence of SEQ ID NO: 8; b) at least one human IgG constant region; and c) one or more cytotoxic agent, wherein said cytotoxic agent is conjugated to the at least one human IgG constant region via a linker.

[0008] In some examples, the present disclosure provides a method of treating colorectal cancer by administering an anti-STn antibody to a subject with colorectal cancer, wherein the anti-STn antibody includes a heavy chain variable domain (VH) with an amino acid sequence selected from the group consisting of SEQ ID NOs: 7, 9, and 11; and a light chain variable domain (VL) with an amino acid sequence selected from the group consisting of SEQ ID NOs: 8, 10, and 12. The colorectal cancer may be resistant to treatment with at least one of cetuximab, panitumumab, bevacizumab, ramucirumab, trastuzumab, ponatinib, sorafenib, 5-fluorouracil, cisplatin, docetaxel, gemcitabine, irinotecan, paclitaxel, and oxaliplatin. The anti-STn antibody may include an antibody drug conjugate (ADC). The ADC may include at least one conjugate, wherein the at least one conjugate is selected from one or more of an auristatin, a maytansine, a tubulysin, a vinca alkaloid, a pyrrolobenzodiazepine dimer, a camptothecin, a duocarmycin, an amanitin, a phosphoinositide 3-kinase (PI3K) inhibitor, and a mitogen-activated protein kinase kinase (MEK) inhibitor. The ADC may include one or more polymer, wherein the one or more polymer connects the anti-STn antibody and the at least one conjugate. The one or more polymer may include one or more of a poly(ethylene glycol) (PEG), a poly(N-(2-hydroxypropyl)methacrylamide) (polyHPMA), a poly(α -amino acid), a carbohydrate polymer, a glycopolysaccharide, a glycolipid, a glycoconjugate, a polyglycerol, a polyvinyl alcohol, a poly(acrylic acid), a polyketal, and a polyacetal. The one or more polymer may include a poly(1-hydroxymethylethylene hydroxymethylformal) (PHF). The anti-STn

antibody may kill cells expressing STn with a half maximal inhibitory concentration of from about 0.1 nM to about 50 nM.

[0008a] In one example, there is provided use of an anti-STn antibody in the manufacture of a medicament for treating colorectal cancer in a subject with colorectal cancer, wherein said anti-STn antibody comprises: a heavy chain variable domain (VH) comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 7, 9, and 11; and a light chain variable domain (VL) comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 8, 10, and 12.

[0009] Administering the anti-STn antibody may be carried out in combination with at least one other therapeutic treatment. The other therapeutic treatment may include a standard of care therapeutic treatment. The other therapeutic treatment may be selected from one or more of cetuximab, panitumumab, bevacizumab, ramucirumab, trastuzumab, ponatinib, sorafenib, 5-fluorouracil, cisplatin, docetaxel, gemcitabine, irinotecan, paclitaxel, and oxaliplatin. The other therapeutic treatment may also include administration of at least one cell cycle inhibitor. The cell cycle inhibitor may be a cyclin-dependent kinase (CDK)

inhibitor. The CDK inhibitor may inhibit CDK4 and/or CDK6. The CDK inhibitor may be selected from palbociclib, ribociclib, and abemaciclib. The anti-STn antibody may be treated concurrently with the other therapeutic treatment. The anti-STn antibody may be treated sequentially with the other therapeutic treatment.

[0010] In some examples, the present disclosure provides a method of treating cancer, the method comprising administering an anti-STn antibody to a subject with cancer, wherein the anti-STn antibody includes a heavy chain variable domain (VH) with an amino acid sequence selected from the group consisting of SEQ ID NOs: 7, 9, and 11; and a light chain variable domain (VL) with an amino acid sequence selected from the group consisting of SEQ ID NOs: 8, 10, and 12, wherein administering the anti-STn antibody is carried out in combination with at least one cell cycle inhibitor. The cell cycle inhibitor may be a cyclin-dependent kinase (CDK) inhibitor. The CDK inhibitor may inhibit CDK4 and/or CDK6. The CDK inhibitor may be selected from palbociclib, ribociclib, and abemaciclib. The anti-STn antibody may be administered concurrently with the cell cycle inhibitor. The anti-STn antibody may be administered sequentially with the cell cycle inhibitor.

[0010a] In one example, there is provided use of an anti-STn antibody in the manufacture of a medicament for treating cancer in a subject with cancer, wherein said anti-STn antibody comprises: a heavy chain variable domain (VH) comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 7, 9, and 11; and a light chain variable domain (VL) comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 8, 10, and 12, wherein said anti-STn antibody is to be administered in combination with at least one cell cycle inhibitor.

[0011] In some examples, the present disclosure provides an ADC that includes an anti-STn antibody with a VH with an amino acid sequence selected from SEQ ID NOs: 7, 9, and 11; a VL with an amino acid sequence selected from SEQ ID NOs: 8, 10, and 12; and one or more cytotoxic agent. The cytotoxic agent may be selected from at least one of an auristatin, a maytansine, a tubulysin, a vinca alkaloid, a pyrrolobenzodiazepine dimer, a camptothecin, a duocarmycin, an amanitin, a PI3K inhibitor, and a MEK inhibitor. The anti-STn antibody may be conjugated with the one or more cytotoxic agent via a linker. The ADC may include one or more polymer connecting the anti-STn antibody and the one or more cytotoxic agent. The one or more polymer may include one or more of a PEG, a polyHPMA, a poly(α -amino acid), a carbohydrate polymer, a glycopolysaccharide, a glycolipid, a glycoconjugate, a polyglycerol, a polyvinyl alcohol, a poly(acrylic acid), a polyketal, and a polyacetal. The one or more polymer may include a PHF. The one or more polymer may be

attached to the anti-STn antibody via a linker. The one or more cytotoxic agent may be attached to the one or more polymer via a linker. The linker may be a cleavable linker.

[0011a] In one example, there is provided an antibody-drug conjugate (ADC) comprising:

- a. an anti-STn antibody, wherein said anti-STn antibody comprises:
 - a VH comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 7, 9, and 11; and
 - a VL comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 8, 10, and 12; and
- b. one or more cytotoxic agents, wherein said one or more cytotoxic agents is selected from at least one of a pyrrolobenzodiazepine dimer, a camptothecin, an amanitin, a PI3K inhibitor, and a MEK inhibitor.

[0012] In some examples, the present disclosure provides a method of treating cancer in a subject, wherein the subject has at least one cancer cell expressing STn, the method including administering an anti-STn antibody drug conjugate described herein. The at least one cancer cell may be an ovarian cancer cell. The at least one cancer cell may be resistant to treatment with at least one chemotherapeutic agent. The chemotherapeutic agent may be

cisplatin. The anti-STn antibody drug conjugate may be administered at a dose of from about 0.1 mg/kg to about 25 mg/kg. Administration may be by intravenous injection. The anti-STn antibody drug conjugate may be administered daily, weekly, or monthly.

[0012a] In one example, there is provided use of the ADC disclosed herein in the manufacture of a medicament for treating cancer in a subject, wherein the subject has at least one cancer cell expressing STn.

[0013] Some methods of the present disclosure include methods of treating cancer by administering an ADC to a subject, the ADC including: a VH including SEQ ID NO: 7; a VL including SEQ ID NO: 8; at least one human IgG constant region; and a cytotoxic conjugate, wherein the cytotoxic conjugate is conjugated to the at least one human IgG constant region via a linker. The at least one human IgG constant region may be selected from one or more of SEQ ID NOs: 15 and 16. The cytotoxic conjugate may include MMAE. The ADC may be administered at a dose of from about 1 mg/kg to about 6 mg/kg. The ADC may be administered by intravenous bolus injection. The ADC may be administered as part of a composition, wherein the composition includes at least one excipient. The composition may be administered at a volume of from about 0.1 ml/kg to about 10 ml/kg. The composition may be administered at a volume of about 1.2 ml/kg. The composition may include an ADC concentration of from about 0.5 mg/ml to about 10 mg/ml. The ADC may exhibit an apparent terminal elimination half-life of from about 2 days to about 8 days. The ADC may exhibit an apparent clearance rate of from about 10 ml/kg/day to about 20 ml/kg/day. The ADC may exhibit an apparent volume of distribution at steady state of from about 50 ml/kg to about 100 ml/kg. The ADC may exhibit a maximum observed concentration of from about 10 µg/ml to about 200 µg/ml. The ADC may exhibit an area under the concentration versus time curve (AUC) from the start of administration to the last observed quantifiable concentration of from about 50 days*µg/ml to about 500 days*µg/ml.

BRIEF DESCRIPTION OF THE FIGURES

[0014] The foregoing and other objects, features and advantages will be apparent from the following description of particular embodiments of the invention, as illustrated in the accompanying drawings in which like reference characters refer to the same parts throughout the different views. The drawings are not necessarily to scale; emphasis instead being placed upon illustrating the principles of various embodiments of the invention.

[0015] Fig. 1A is a schematic depicting α2,6-sialylated N-acetylgalactosamine (STn) with the largest ellipse indicating the specific region of STn recognized by Group 1 antibodies.

[0016] Fig. 1B is a schematic depicting α2,6-sialylated N-acetylgalactosamine (STn) with the largest ellipse indicating the specific region of STn recognized by Group 2 antibodies.

CLAIMS

What is claimed is:

1. Use of an antibody-drug conjugate (ADC) in the manufacture of a medicament for treating cancer in a subject, wherein the subject has at least one cancer cell expressing STn, wherein said ADC comprises:
 - a) an anti-STn antibody, wherein said anti-STn antibody comprises:
a heavy chain variable domain (VH) with the amino acid sequence of SEQ ID NO: 7;
a light chain variable domain (VL) with the amino acid sequence of SEQ ID NO: 8;
 - b) at least one human IgG constant region; and
 - c) one or more cytotoxic agent, wherein said cytotoxic agent is conjugated to the at least one human IgG constant region via a linker.
2. The use of claim 1, wherein said one or more cytotoxic agent is selected from at least one of an auristatin, a maytansine, a tubulysin, a vinca alkaloid, a pyrrolobenzodiazepine dimer, a camptothecin, a duocarmycin, an amanitin, a phosphoinositide 3-kinase (PI3K) inhibitor, and a mitogen-activated protein kinase kinase (MEK) inhibitor.
3. The use of claim 1 or 2, wherein said linker is a cleavable linker.
4. The use of any one of claims 1-3, wherein said ADC comprises one or more polymer connecting said anti-STn antibody and said one or more cytotoxic agent.
5. The use of claim 4, wherein said one or more polymer comprises one or more of a poly(ethylene glycol) (PEG), a poly(N-(2-hydroxypropyl)methacrylamide) (polyHPMA), a poly(α -amino acid), a carbohydrate polymer, a glycopolysaccharide, a glycolipid, a glycoconjugate, a polyglycerol, a polyvinyl alcohol, a poly(acrylic acid), a polyketal, a polyacetal, or a poly(1-hydroxymethylethylene hydroxymethylformal) (PHF).
6. The use of any one of claims 1-5, wherein the at least one cancer cell is an ovarian cancer cell.
7. The use of any one of claims 1-6, wherein the at least one cancer cell is resistant to treatment with at least one chemotherapeutic agent.
8. The use of claim 7, wherein the at least one chemotherapeutic agent is cisplatin.
9. The use of any one of claims 1-5, wherein the cancer is colorectal cancer.

10. The use of claim 9, wherein said colorectal cancer is resistant to treatment with at least one of cetuximab, panitumumab, bevacizumab, ramucirumab, trastuzumab, ponatinib, sorafenib, 5-fluorouracil, cisplatin, docetaxel, gemcitabine, irinotecan, paclitaxel, and oxaliplatin.
11. The use of any one of claims 1-10, wherein the at least one human IgG constant region is selected from SEQ ID NOs: 15 and 16.
12. The use of any one of claims 1-11, wherein the cytotoxic conjugate comprises MMAE.
13. The use of any one of claims 1-12, wherein the ADC is to be administered at a dose of from 1 mg/kg to 6 mg/kg.