

gastric cardia adenocarcinoma have increased, while rates of esophageal squamous cell carcinoma and gastric noncardia adenocarcinoma have decreased, suggesting distinct etiologies (Crew & Neugut, World J Gastroenterol. 2016;354-362).

[0028] Chemotherapy can provide a significant decrease in symptoms for patients with unresectable, locally advanced, or metastatic disease. Single agents that produce partial response (PR) rates (cisplatin, doxorubicin, and mitomycin) are considered the most active in gastrointestinal (GI) cancers (Preusser P et al, Oncology 1998;99-102). Combination regimens employing these agents result in higher response rates (30% to 50%) but are associated with a greater degree of toxicity and produce similar OS (ranging from 6 to 10 months), as compared with single-agent therapy (Preusser P et al, Oncology 1998;99-102). The identification of new agents is therefore essential if prolongation of patient survival is to be reached.

[0029] There is a significant need for additional therapeutic methods for cancers. These include the use of antibodies and antibody drug conjugates as treatment modalities.

3. Summary

[0029a] In one aspect, the present disclosure refers to the use of an antibody drug conjugate in the manufacture of a medicament for treating cancer in a subject, wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and wherein the cancer is locally advanced or metastatic head and neck cancer.

[0029b] In one aspect, the present disclosure refers to the use of an antibody drug conjugate in the manufacture of a medicament for treating cancer in a subject, wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region

comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and wherein the cancer is hormone receptor positive and human epidermal growth factor receptor 2 negative (HR+/HER2-) breast cancer.

[0029c] In one aspect, the present disclosure refers to the use of an antibody drug conjugate in the manufacture of a medicament for treating cancer in a subject, wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and wherein the cancer is ER negative, PR negative, and HER2 negative (ER-/PR-/HER2-) breast cancer (Triple Negative Breast Cancer - TNBC).

[0029d] In one aspect, the present disclosure refers to the use of an antibody drug conjugate in the manufacture of a medicament for treating cancer in a subject, wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and wherein the cancer is squamous non-small cell lung cancer (NSCLC).

[0029e] In one aspect, the present disclosure refers to the use of an antibody drug conjugate in the manufacture of a medicament for treating cancer in a subject, wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region

comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and wherein the cancer is non-squamous NSCLC.

[0029f] In one aspect, the present disclosure refers to the use of an antibody drug conjugate in the manufacture of a medicament for treating cancer in a subject, wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and wherein the cancer is gastric or esophageal cancer.

[0030] In one aspectexample, provided herein is a method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate, wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and wherein the subject has hormone receptor positive and human epidermal growth factor receptor 2 negative (HR+/HER2-) breast cancer.

[0031] In some embodimentexamples of the methods provided herein, the HR+/HER2- breast cancer is estrogen receptor (ER) positive and/or progesterone receptor (PR) positive, and HER2 negative.

[0032] In some embodimentexamples of the methods provided herein, the subject has locally advanced or metastatic cancer.

[0033] In some [embodimentexamples](#) of the methods provided herein, the subject has previously received at least one line of an endocrine therapy and a cyclin-dependent kinase (CDK) 4/6 inhibitor in metastatic or locally advanced setting.

[0034] In some [embodimentexamples](#) of the methods provided herein, the subject has previously received a treatment with a taxane or anthracycline.

[0035] In some [embodimentexamples](#) of the methods provided herein, the subject has a deleterious germline mutation in breast cancer susceptibility gene (BRCA)1 or BRCA2, and wherein the subject has previously been treated with a poly ADP ribose polymerase (PARP) inhibitor.

[0036] In some [aspectexample](#), provided herein is a method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate, wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and wherein the subject has ER negative, PR negative, and HER2 negative (ER-/PR-/HER2-) breast cancer.

[0037] In some [embodimentexamples](#) of the methods provided herein, for example and not by way of limitation, the methods described in the first paragraph before the present paragraph (paragraph [0036]), the subject has locally advanced or metastatic cancer.

[0038] In some [embodimentexamples](#) of the methods provided herein, the subject has previously received at least two lines of systemic therapies.

[0039] In some [embodimentexamples](#) of the methods provided herein, the subject has previously received a treatment with a taxane.

[0040] In some [embodimentexamples](#) of the methods provided herein, for example and not by way of limitation, the methods described in the first to the fourth paragraphs before the present paragraph (paragraphs [0036] to [0039]), the subject has a deleterious germline mutation in breast cancer susceptibility gene (BRCA)1 or BRCA2, and wherein the subject has previously been treated with a poly ADP ribose polymerase (PARP) inhibitor.

[0041] In some [aspectexample](#), provided herein is a method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate, wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and wherein the subject has squamous non-small cell lung cancer (NSCLC).

[0042] In some [embodimentexamples](#) of the methods provided herein, for example and not by way of limitation, the methods described in the first paragraph before the present paragraph (paragraph [0041]), the subject has locally advanced or metastatic cancer.

[0043] In some [embodimentexamples](#) of the methods provided herein, the subject has progressed or relapsed following a platinum-based therapy.

[0044] In some [embodimentexamples](#) of the methods provided herein, the subject has progressed or relapsed within 12 months after a platinum-based therapy.

[0045] In some [embodimentexamples](#) of the methods provided herein, the subject has previously received a therapy with an inhibitor of programmed cell death protein-1 (PD-1) or an inhibitor of programmed cell death-ligand 1 (PD-L1), wherein optionally the inhibitor of PD-1 is nivolumab and wherein optionally the inhibitor of PD-L1 is selected from a group consisting of atezolizumab, avelumab, and durvalumab.

[0046] In some [aspectexample](#), provided herein is a method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate, wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid

sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and wherein the subject has non-squamous NSCLC.

[0047] In some [embodimentexamples](#) of the methods provided herein, the subject has wild-type epidermal growth factor receptor (EGFR) and wild-type anaplastic lymphoma kinase (ALK).

[0048] In some [embodimentexamples](#) of the methods provided herein, for example and not by way of limitation, the methods described in the first to the second paragraphs before the present paragraph (paragraphs [0046] to [0047]), the subject has locally advanced or metastatic cancer.

[0049] In some [embodimentexamples](#) of the methods provided herein, for example and not by way of limitation, the methods described in in the first to the third paragraphs before the present paragraph (paragraphs [0046] to [0048]), the subject has progressed or relapsed following a platinum-based therapy.

[0050] In some [embodimentexamples](#) of the methods provided herein, for example and not by way of limitation, the methods described in in the first to the fourth paragraphs before the present paragraph (paragraphs [0046] to [0049]), the subject has progressed or relapsed within 12 months after a platinum-based therapy.

[0051] In some [embodimentexamples](#) of the methods provided herein, for example and not by way of limitation, the methods described in in the first to the fifth paragraphs before the present paragraph (paragraphs [0046] to [0050]), the subject has previously received a therapy with an inhibitor of programmed cell death protein-1 (PD-1) or an inhibitor of programmed cell death-ligand 1 (PD-L1), wherein optionally the inhibitor of PD-1 is nivolumab and wherein optionally the inhibitor of PD-L1 is selected from a group consisting of atezolizumab, avelumab, and durvalumab.

[0052] In some [aspectexample](#), provided herein is a method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate, wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid

sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and wherein the subject has locally advanced or metastatic head and neck cancer.

[0053] In some [embodimentexamples](#) of the methods provided herein, for example and not by way of limitation, the methods described in in the first paragraph before the present paragraph (paragraph [0052]), the subject has progressed or relapsed following a platinum-based therapy.

[0054] In some [embodimentexamples](#) of the methods provided herein, the subject has progressed or relapsed within 6 months after a platinum-based therapy.

[0055] In some [embodimentexamples](#) of the methods provided herein, for example and not by way of limitation, the methods described in in the first to the third paragraphs before the present paragraph (paragraphs [0052] to [0054]), the subject has previously received a therapy with an inhibitor of programmed cell death protein-1 (PD-1) or an inhibitor of programmed cell death-ligand 1 (PD-L1), wherein optionally the inhibitor of PD-1 is nivolumab and wherein optionally the inhibitor of PD-L1 is selected from a group consisting of atezolizumab, avelumab, and durvalumab.

[0056] In some [aspectexample](#), provided herein is a method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate, wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and wherein the subject has gastric or esophageal cancer.

[0057] In some [embodimentexamples](#) of the methods provided herein, for example and not by way of limitation, the methods described in in the first paragraph before the present paragraph (paragraph [0056]), the subject has locally advanced or metastatic cancer.

[0058] In some [embodimentexamples](#) of the methods provided herein, the subject has progressed or relapsed following a platinum-based therapy or a chemotherapy that included a fluoropyrimidine.

[0059] In some [embodimentexamples](#) of the methods provided herein, the subject has progressed or relapsed within 6 months after the platinum-based therapy or the chemotherapy that included a fluoropyrimidine.

[0060] In some [embodimentexamples](#) of the methods provided herein, the gastric or esophageal cancer is HER2 positive cancer, and wherein the subject has previously received a HER2 directed therapy.

[0061] In some [embodimentexamples](#) of the methods provided herein, the antibody or antigen binding fragment thereof comprises CDR H1 comprising the amino acid sequence of SEQ ID NO:9, CDR H2 comprising the amino acid sequence of SEQ ID NO:10, CDR H3 comprising the amino acid sequence of SEQ ID NO:11; CDR L1 comprising the amino acid sequence of SEQ ID NO:12, CDR L2 comprising the amino acid sequence of SEQ ID NO:13, and CDR L3 comprising the amino acid sequence of SEQ ID NO:14.

[0062] In some [embodimentexamples](#) of the methods provided herein, the antibody or antigen binding fragment thereof comprises CDR H1 comprising the amino acid sequence of SEQ ID NO:16, CDR H2 comprising the amino acid sequence of SEQ ID NO:17, CDR H3 comprising the amino acid sequence of SEQ ID NO:18; CDR L1 comprising the amino acid sequence of SEQ ID NO:19, CDR L2 comprising the amino acid sequence of SEQ ID NO:20, and CDR L3 comprising the amino acid sequence of SEQ ID NO:21.

[0063] In some [embodimentexamples](#) of the methods provided herein, the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:22 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:23.

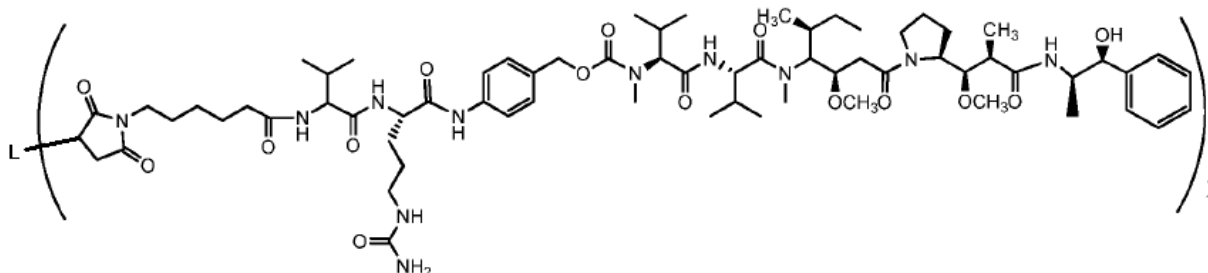
[0064] In some [embodimentexamples](#) of the methods provided herein, the antibody comprises a heavy chain comprising the amino acid sequence ranging from the 20th amino acid (glutamic acid) to the 466th amino acid (lysine) of SEQ ID NO:7 and a light chain comprising the amino acid sequence ranging from the 23rd amino acid (aspartic acid) to the 236th amino acid (cysteine) of SEQ ID NO:8.

[0065] In some [embodimentexamples](#) of the methods provided herein, the antigen binding fragment is an Fab, F(ab')₂, Fv or scFv fragment.

[0066] In some [embodimentexamples](#) of the methods provided herein, the antibody is a fully human antibody.

[0067] In some [embodimentexamples](#) of the methods provided herein, the antibody or antigen binding fragment thereof is recombinantly produced.

[0068] In some [embodimentexamples](#) of the methods provided herein, the antibody drug conjugate has the following structure:



wherein L- represents the antibody or antigen binding fragment thereof and p is from 1 to 10.

[0069] In some [embodimentexamples](#) of the methods provided herein, p is from 2 to 8.

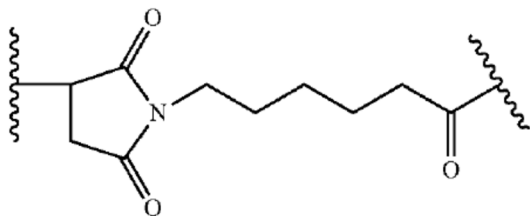
[0070] In some [embodimentexamples](#) of the methods provided herein, p is from 3 to 5.

[0071] In some [embodimentexamples](#) of the methods provided herein, the antibody or antigen binding fragment is linked to each unit of monomethyl auristatin E (MMAE) via a linker.

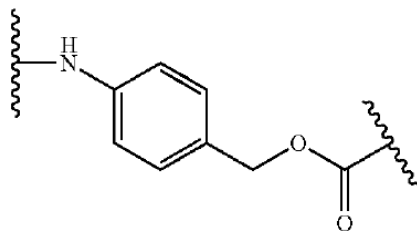
[0072] In some [embodimentexamples](#) of the methods provided herein, the linker is an enzyme-cleavable linker, and wherein the linker forms a bond with a sulfur atom of the antibody or antigen binding fragment thereof.

[0073] In some [embodimentexamples](#) of the methods provided herein, the linker has a formula of: -Aa-Ww-Yy-; wherein -A- is a stretcher unit, a is 0 or 1; -W- is an amino acid unit, w is an integer ranging from 0 to 12; and -Y- is a spacer unit, y is 0, 1, or 2.

[0074] In some [embodimentexamples](#) of the methods provided herein, the stretcher unit has the structure of Formula (1) below; the amino acid unit is valine citrulline; and the spacer unit is a PAB group comprising the structure of Formula (2) below:



Formula (1)



Formula (2).

[0075] In some [embodimentexamples](#) of the methods provided herein, the stretcher unit forms a bond with a sulfur atom of the antibody or antigen binding fragment thereof; and wherein the spacer unit is linked to MMAE via a carbamate group.

[0076] In some [embodimentexamples](#) of the methods provided herein, the antibody drug conjugate comprises from 1 to 10 units of MMAE per antibody or antigen binding fragment thereof.

[0077] In some [embodimentexamples](#) of the methods provided herein, the antibody drug conjugate comprises from 2 to 8 units of MMAE per antibody or antigen binding fragment thereof.

[0078] In some [embodimentexamples](#) of the methods provided herein, the antibody drug conjugate comprises from 3 to 5 units of MMAE per antibody or antigen binding fragment thereof.

[0079] In some [embodimentexamples](#) of the methods provided herein, the antibody drug conjugate is formulated in a pharmaceutical composition, wherein the pharmaceutical composition comprises a pharmaceutically acceptable excipient comprising L-histidine, polysorbate-20 (TWEEN-20), and at least one of trehalose dihydrate and sucrose.

[0080] In some [embodimentexamples](#) of the methods provided herein, the pharmaceutical composition comprises the antibody drug conjugate at a concentration of from 1 to 20 mg/mL, from 5 to 15 mg/mL, from 8 to 12 mg/mL.

[0081] In some [embodimentexamples](#) of the methods provided herein, the antibody drug conjugate is at a concentration of about 10 mg/mL.

[0082] In some [embodimentexamples](#) of the methods provided herein, the L-histidine is present in the range of 5 to 50 mM, 10 to 40 mM, 15 to 35 mM, 15 to 30 mM, or 15 to 25 mM.

[0083] In some [embodimentexamples](#) of the methods provided herein, the L-histidine is present at about 20 mM.

[0084] In some [embodimentexamples](#) of the methods provided herein, the concentration of TWEEN-20 is in the range of from 0.001 to 0.1% (v/v), from 0.0025 to 0.075% (v/v), from 0.005 to 0.05% (v/v), or from 0.01 to 0.03% (v/v).

[0085] In some [embodimentexamples](#) of the methods provided herein, the concentration of TWEEN-20 is about 0.02% (v/v).

[0086] In some [embodimentexamples](#) of the methods provided herein, the pharmaceutical composition comprises trehalose dihydrate.

[0087] In some [embodimentexamples](#) of the methods provided herein, the trehalose dihydrate is present in the range of 1 to 20% (w/v), 2 to 15% (w/v), 3 to 10% (w/v), or 4 to 6% (w/v).

[0088] In some [embodimentexamples](#) of the methods provided herein, the trehalose dihydrate is present at about 5.5% (w/v).

[0089] In some [embodimentexamples](#) of the methods provided herein, the trehalose dihydrate is present in the range of 50 mM to 300 mM, 75 mM to 250 mM, 100 mM to 200 mM, or 130 mM to 150 mM.

[0090] In some [embodimentexamples](#) of the methods provided herein, the trehalose dihydrate is present at about 146 mM.

[0091] In some [embodimentexamples](#) of the methods provided herein, the pharmaceutical composition comprises sucrose.

[0092] In some [embodimentexamples](#) of the methods provided herein, the sucrose is present in the range of 1 to 20% (w/v), 2 to 15% (w/v), 3 to 10% (w/v), or 4 to 6% (w/v).

[0093] In some [embodimentexamples](#) of the methods provided herein, the sucrose is present at about 5.5% (w/v).

[0094] In some [embodimentexamples](#) of the methods provided herein, the sucrose is present in the range of 50 mM to 300 mM, 75 mM to 250 mM, 100 mM to 200 mM, or 130 mM to 150 mM.

[0095] In some [embodimentexamples](#) of the methods provided herein, the sucrose is present at about 146 mM.

[0096] In some [embodimentexamples](#) of the methods provided herein, the pharmaceutical composition has a pH in a range of 5.5 to 6.5 or 5.7 to 6.3.

[0097] In some [embodimentexamples](#) of the methods provided herein, the pharmaceutical composition has a pH of about 6.0.

[0098] In some [embodimentexamples](#) of the methods provided herein, the pH is taken at room temperature, at 15°C to 27°C, at about 4°C, or at about 25°C.

[0099] In some [embodimentexamples](#) of the methods provided herein, the pharmaceutical composition comprises hydrochloric acid (HCl) or succinic acid.

[00100] In some [embodimentexamples](#) of the methods provided herein, the pharmaceutical composition comprises about 20 mM L-histidine, about 0.02% (w/v) TWEEN-20, about 5.5% (w/v) trehalose dihydrate, and HCl; and wherein the pH is about 6.0 at 25°C.

[00101] In some [embodimentexamples](#) of the methods provided herein, the pharmaceutical composition comprises about 20 mM L-histidine, about 0.02% (w/v) TWEEN-20, about 5.5% (w/v) trehalose dihydrate, and succinic acid; and wherein the pH is about 6.0 at 25°C.

[00102] In some [embodimentexamples](#) of the methods provided herein, the pharmaceutical composition comprises about 20 mM L-histidine, about 0.02% (w/v) TWEEN-20, about 5.5% (w/v) sucrose, and HCl; and wherein the pH is about 6.0 at 25°C.

[00103] In some [embodimentexamples](#) of the methods provided herein, the pharmaceutical composition comprises about 20 mM L-histidine, about 0.02% (w/v) TWEEN-20, about 5.5% (w/v) sucrose, and succinic acid; and wherein the pH is about 6.0 at 25°C.

[00104] In some [embodimentexamples](#) of the methods provided herein, wherein the antibody drug conjugate is administered at a dose of 1 to 10 mg/kg of the subject's body weight, 1 to 5 mg/kg of the subject's body weight, 1 to 2.5 mg/kg of the subject's body weight, or 1 to 1.25 mg/kg of the subject's body weight.

[00105] In some [embodimentexamples](#) of the methods provided herein, the antibody drug conjugate is administered at a dose of about 1 mg/kg of the subject's body weight.

[00106] In some [embodimentexamples](#) of the methods provided herein, the antibody drug conjugate is administered at a dose of about 1.25 mg/kg of the subject's body weight.

[00107] In some [embodimentexamples](#) of the methods provided herein, the antibody drug conjugate is administered by an intravenous (IV) injection or infusion.

[00108] In some [embodimentexamples](#) of the methods provided herein, the antibody drug conjugate is administered by an intravenous (IV) injection or infusion over about 30 minutes twice every three-week cycle.

[00109] In some [embodimentexamples](#) of the methods provided herein, the antibody drug conjugate is administered by an intravenous (IV) injection or infusion over about 30 minutes on Days 1 and 8 of every three-week cycle.

[00110] In some [embodimentexamples](#) of the methods provided herein, the antibody drug conjugate is administered by an intravenous (IV) injection or infusion over about 30 minutes three times every four-week cycle.

[00111] In some [embodiment examples](#) of the methods provided herein, the antibody drug conjugate formulated in the pharmaceutical composition is administered by an intravenous (IV) injection or infusion over about 30 minutes on Days 1, 8 and 15 of every four-week cycle.

4. Brief Description of the Drawings

[00112] **FIGS. 1A-E** depict the nucleotide and amino acid sequences of 191P4D12 protein (**FIG. 1A**), the nucleotide and amino acid sequences of the heavy chain (**FIG. 1B**) and light chain (**FIG. 1C**) of Ha22-2(2,4)6.1, and the amino acid sequences of the heavy chain (**FIG. 1D**) and light chain of Ha22-2(2,4)6.1 (**FIG. 1E**).

[00113] **FIG. 2** depicts the efficacy of Ha22-2(2,4)6.1-vcMMAE in subcutaneous established human lung cancer xenograft AG-L4 in SCID mice. The results show that treatment with Ha22-2(2,4)6.1-vcMMAE significantly inhibited the growth of AG-L4 lung cancer xenografts implanted subcutaneously in nude mice compared to both the treated and untreated control.

[00114] **FIG. 3** depicts the efficacy of Ha22-2(2,4)6.1-vcMMAE in subcutaneous established human breast cancer xenograft BT-483 in SCID mice. The results show that treatment with Ha22-2(2,4)6.1-vcMMAE significantly inhibited the growth of BT-483 breast tumor xenografts implanted subcutaneously in SCID mice compared to the treated and untreated control ADCs.

[00115] **FIGS. 4A-H.** Detection of 191P4D12 protein in cancer patient specimens by IHC. **FIGS. 4A-B** show breast cancer specimens. **FIGS. 4C-D** show lung cancer specimens. **FIGS. 4E-F** show esophageal cancer specimens. **FIGS. 4G-H** show head and neck cancer specimens.

5. Detailed Description

[00116] Before the present disclosure is further described, it is to be understood that the disclosure is not limited to the particular embodiments set forth herein, and it is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting.

5.1 Definitions

[00117] Techniques and procedures described or referenced herein include those that are generally well understood and/or commonly employed using conventional methodology by those skilled in the art, such as, for example, the widely utilized methodologies described in Sambrook et al., Molecular Cloning: A Laboratory Manual (3d ed. 2001); Current Protocols in Molecular Biology (Ausubel et al. eds., 2003); Therapeutic Monoclonal Antibodies: From Bench to Clinic

What is Claimed is:

~~1. A method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate;~~

~~wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE); wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and~~

~~wherein the subject has hormone receptor positive and human epidermal growth factor receptor 2 negative (HR+/HER2-) breast cancer.~~

~~2. The method of claim 1, wherein the HR+/HER2- breast cancer is estrogen receptor (ER) positive and/or progesterone receptor (PR) positive, and HER2 negative.~~

~~3. The method of claim 1 or claim 2, wherein the subject has locally advanced or metastatic cancer.~~

~~4. The method of any one of claims 1 to 3, wherein the subject has previously received at least one line of an endocrine therapy and a cyclin dependent kinase (CDK) 4/6 inhibitor in metastatic or locally advanced setting.~~

~~5. The method of any one of claims 1 to 4, wherein the subject has previously received a treatment with a taxane or anthracycline.~~

~~6. The method of any one of claims 1 to 5, wherein the subject has a deleterious germline mutation in breast cancer susceptibility gene (BRCA)1 or BRCA2, and wherein the subject has previously been treated with a poly ADP ribose polymerase (PARP) inhibitor.~~

~~7. A method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate;~~

~~wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E~~

~~(MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and~~

~~wherein the subject has ER negative, PR negative, and HER2 negative (ER-/PR-/HER2-) breast cancer (Triple Negative Breast Cancer-TNBC);~~

~~8. The method of claim 7, wherein the subject has locally advanced or metastatic cancer;~~

~~9. The method of claim 7 or claim 8, wherein the subject has previously received at least two lines of systemic therapies;~~

~~10. The method of claim 9, wherein the subject has previously received a treatment with a taxane;~~

~~11. The method of any one of claims 7 to 10, wherein the subject has a deleterious germline mutation in breast cancer susceptibility gene (BRCA)1 or BRCA2, and wherein the subject has previously been treated with a poly ADP-ribose polymerase (PARP) inhibitor;~~

~~12. A method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate;~~

~~wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and~~

~~wherein the subject has squamous non-small cell lung cancer (NSCLC);~~

~~13. The method of claim 12, wherein the subject has locally advanced or metastatic cancer.~~

~~14. The method of claim 12 or claim 13, wherein the subject has progressed or relapsed following a platinum-based therapy.~~

~~15. The method of claim 14, wherein the subject has progressed or relapsed within 12 months after a platinum-based therapy.~~

~~16. The method of any one of claims 12 to 15, wherein the subject has previously received a therapy with an inhibitor of programmed cell death protein 1 (PD-1) or an inhibitor of programmed cell death ligand 1 (PD-L1), wherein optionally the inhibitor of PD-1 is nivolumab and wherein optionally the inhibitor of PD-L1 is selected from a group consisting of atezolizumab, avelumab, and durvalumab.~~

~~17. A method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate,~~

~~wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and~~

~~wherein the subject has non-squamous NSCLC.~~

~~18. The method of claim 17, wherein the subject has wild-type epidermal growth factor receptor (EGFR) and wild-type anaplastic lymphoma kinase (ALK).~~

~~19. The method of claim 17 or claim 18, wherein the subject has locally advanced or metastatic cancer.~~

~~20. The method of any one of claims 17 to 19, wherein the subject has progressed or relapsed following a platinum-based therapy.~~

~~21. The method of claim 20, wherein the subject has progressed or relapsed within 12 months after a platinum-based therapy.~~

~~22. The method of any one of claims 17 to 21, wherein the subject has previously received a therapy with an inhibitor of programmed cell death protein-1 (PD-1) or an inhibitor of programmed cell death ligand 1 (PD-L1), wherein optionally the inhibitor of PD-1 is nivolumab and wherein optionally the inhibitor of PD-L1 is selected from a group consisting of atezolizumab, avelumab, and durvalumab.~~

231. Use of an antibody drug conjugate in the manufacture of a medicament for A method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate,

wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and

wherein the subject has cancer is locally advanced or metastatic head and neck cancer.

242. The method-use of claim 231, wherein the subject has progressed or relapsed following a platinum-based therapy.

253. The method-use of claim 242, wherein the subject has progressed or relapsed within 6 months after a platinum-based therapy.

264. The method-use of any one of claims 23-1 to 253, wherein the subject has previously received a therapy with an inhibitor of programmed cell death protein-1 (PD-1) or an inhibitor of programmed cell death ligand 1 (PD-L1), wherein optionally the inhibitor of PD-1 is nivolumab and wherein optionally the inhibitor of PD-L1 is selected from a group consisting of atezolizumab, avelumab, and durvalumab.

~~15.~~ Use of an antibody drug conjugate in the manufacture of a medicament for A method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate,

wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and

wherein the ~~subject has~~cancer is hormone receptor positive and human epidermal growth factor receptor 2 negative (HR+/HER2-) breast cancer.

~~26.~~ The ~~method~~use of claim ~~15~~, wherein the HR+/HER2- breast cancer is estrogen receptor (ER) positive and/or progesterone receptor (PR) positive, and HER2 negative.

~~37.~~ The ~~method~~use of claim ~~15~~ or claim ~~26~~, wherein the ~~subject has~~cancer is locally advanced or metastatic cancer.

~~48.~~ The ~~method~~use of any one of claims ~~15~~ to ~~37~~, wherein the subject has previously received at least one line of an endocrine therapy and a cyclin-dependent kinase (CDK) 4/6 inhibitor in metastatic or locally advanced setting.

~~59.~~ The ~~method~~use of any one of claims ~~15~~ to ~~48~~, wherein the subject has previously received a treatment with a taxane or anthracycline.

~~610.~~ The method of any one of claims ~~15~~ to ~~59~~, wherein the subject has a deleterious germline mutation in breast cancer susceptibility gene (BRCA)1 or BRCA2, and wherein the subject has previously been treated with a poly ADP ribose polymerase (PARP) inhibitor.

~~711.~~ Use of an antibody drug conjugate in the manufacture of a medicament for A method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate,

wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E

(MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and

wherein the ~~subject has~~cancer is ER negative, PR negative, and HER2 negative (ER-/PR-/HER2-) breast cancer (Triple Negative Breast Cancer - TNBC).

812. The ~~method~~use of claim 711, wherein the ~~subject has~~cancer is locally advanced or metastatic cancer.

913. The ~~method~~use of claim 711 or claim 812, wherein the subject has previously received at least two lines of systemic therapies.

1014. The method of claim 913, wherein the subject has previously received a treatment with a taxane.

1115. The ~~method~~use of any one of claims 711 to 1014, wherein the subject has a deleterious germline mutation in breast cancer susceptibility gene (BRCA)1 or BRCA2, and wherein the subject has previously been treated with a poly ADP ribose polymerase (PARP) inhibitor.

1216. ~~Use of an antibody drug conjugate in the manufacture of a medicament for~~ A method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate,

wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and

wherein the ~~subject has~~cancer is squamous non-small cell lung cancer (NSCLC).

~~13~~17. The method of claim ~~12~~16, wherein the ~~subject has~~cancer is locally advanced or metastatic cancer.

~~14~~18. The method of claim ~~12~~16 or claim ~~13~~17, wherein the subject has progressed or relapsed following a platinum-based therapy.

~~15~~19. The method of claim ~~14~~18, wherein the subject has progressed or relapsed within 12 months after a platinum-based therapy.

~~16~~20. The method of any one of claims ~~12~~16 to ~~15~~19, wherein the subject has previously received a therapy with an inhibitor of programmed cell death protein-1 (PD-1) or an inhibitor of programmed cell death-ligand 1 (PD-L1), wherein optionally the inhibitor of PD-1 is nivolumab and wherein optionally the inhibitor of PD-L1 is selected from a group consisting of atezolizumab, avelumab, and durvalumab.

~~17~~21. Use of an antibody drug conjugate in the manufacture of a medicament for ~~A method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate,~~

wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and

wherein the ~~subject has~~cancer is non-squamous NSCLC.

~~18~~22. The method of claim ~~17~~21, wherein the subject has wild-type epidermal growth factor receptor (EGFR) and wild-type anaplastic lymphoma kinase (ALK).

~~19~~23. The method of claim ~~17~~21 or claim ~~18~~22, wherein the ~~subject has~~cancer is locally advanced or metastatic cancer.

~~20~~24. The method of any one of claims ~~17~~21 to ~~19~~23, wherein the subject has progressed or relapsed following a platinum-based therapy.

2125. The method of claim 2024, wherein the subject has progressed or relapsed within 12 months after a platinum-based therapy.

2226. The method of any one of claims 1721 to 2125, wherein the subject has previously received a therapy with an inhibitor of programmed cell death protein-1 (PD-1) or an inhibitor of programmed cell death-ligand 1 (PD-L1), wherein optionally the inhibitor of PD-1 is nivolumab and wherein optionally the inhibitor of PD-L1 is selected from a group consisting of atezolizumab, avelumab, and durvalumab.

27. Use of an antibody drug conjugate in the manufacture of a medicament for A method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate,

wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and

wherein the subject has cancer is gastric or esophageal cancer.

28. The method-use of claim 27, wherein the subject has cancer is locally advanced or metastatic cancer.

29. The method-use of claim 27 or claim 28, wherein the subject has progressed or relapsed following a platinum-based therapy and/or a chemotherapy that included a fluoropyrimidine.

30. The method-use of claim 29, wherein the subject has progressed or relapsed within 6 months after the platinum-based therapy or the chemotherapy that included a fluoropyrimidine.

31. The method-use of any one of claims 27 to 30, wherein the gastric or esophageal cancer is HER2 positive cancer, and wherein the subject has previously received a HER2 directed therapy.

32. The ~~method~~-use of any one of claims 1 to 31, wherein the antibody or antigen binding fragment thereof comprises CDR H1 comprising the amino acid sequence of SEQ ID NO:9, CDR H2 comprising the amino acid sequence of SEQ ID NO:10, CDR H3 comprising the amino acid sequence of SEQ ID NO:11; CDR L1 comprising the amino acid sequence of SEQ ID NO:12, CDR L2 comprising the amino acid sequence of SEQ ID NO:13, and CDR L3 comprising the amino acid sequence of SEQ ID NO:14, or

wherein the antibody or antigen binding fragment thereof comprises CDR H1 comprising the amino acid sequence of SEQ ID NO:16, CDR H2 comprising the amino acid sequence of SEQ ID NO:17, CDR H3 comprising the amino acid sequence of SEQ ID NO:18; CDR L1 comprising the amino acid sequence of SEQ ID NO:19, CDR L2 comprising the amino acid sequence of SEQ ID NO:20, and CDR L3 comprising the amino acid sequence of SEQ ID NO:21.

33. The ~~use~~method of any one of claims 1 to 31, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:22 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:23.

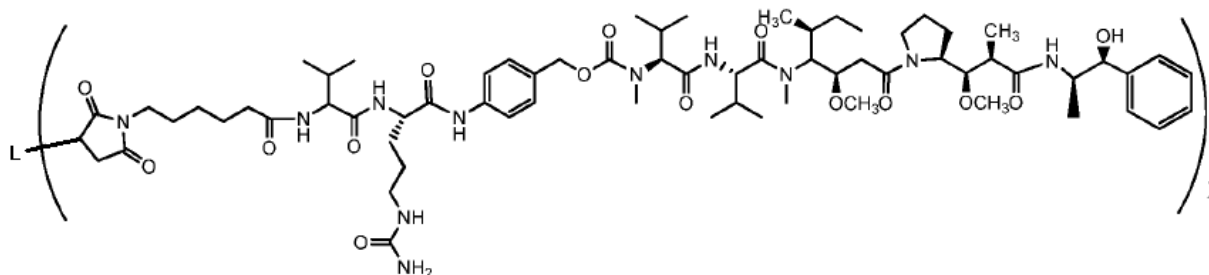
34. The ~~method~~-use of any one of claims 1 to 31, wherein the antibody comprises a heavy chain comprising the amino acid sequence ranging from the 20th amino acid (glutamic acid) to the 466th amino acid (lysine) of SEQ ID NO:7 and a light chain comprising the amino acid sequence ranging from the 23rd amino acid (aspartic acid) to the 236th amino acid (cysteine) of SEQ ID NO:8.

35. The ~~method~~-use of any one of claims 1 to 34, wherein the antigen binding fragment is an Fab, F(ab')₂, Fv or scFv fragment.

36. The ~~method~~-use of any one of claims 1 to 35, wherein the antibody is a fully human antibody.

37. The ~~method~~-use of any one of claims 1 to 36, wherein the antibody or antigen binding fragment thereof is recombinantly produced.

38. The [method-use](#) of any one of claims 1 to 37, wherein the antibody drug conjugate has the following structure:



wherein L- represents the antibody or antigen binding fragment thereof and p is from 1 to 10.

39. The [method-use](#) of claim 38, wherein p is from 2 to 8.

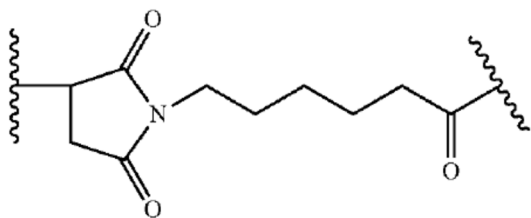
40. The [method-use](#) of claim 38, wherein p is from 3 to 5.

41. The [method-use](#) of any one of claims 1 to 40, wherein the antibody or antigen binding fragment is linked to each unit of monomethyl auristatin E (MMAE) via a linker.

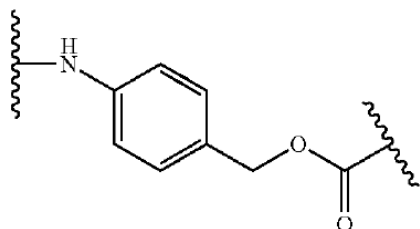
42. The [method-use](#) of claim 41, wherein the linker is an enzyme-cleavable linker, and wherein the linker forms a bond with a sulfur atom of the antibody or antigen binding fragment thereof.

43. The [method-use](#) of claim 41, wherein the linker has a formula of: $-A_a-W_w-Y_y-$; wherein $-A-$ is a stretcher unit, a is 0 or 1; $-W-$ is an amino acid unit, w is an integer ranging from 0 to 12; and $-Y-$ is a spacer unit, y is 0, 1, or 2.

44. The [method-use](#) of claim 43, wherein the stretcher unit has the structure of Formula (1) below; the amino acid unit is valine citrulline; and the spacer unit is a PAB group comprising the structure of Formula (2) below:



Formula (1)



Formula (2).

45. The ~~method-use~~ of claim 43, wherein the stretcher unit forms a bond with a sulfur atom of the antibody or antigen binding fragment thereof; and wherein the spacer unit is linked to MMAE via a carbamate group.

46. The ~~method-use~~ of any one of claims 1 to 37, wherein the antibody drug conjugate comprises from 1 to 10 units of MMAE per antibody or antigen binding fragment thereof.

47. The ~~method-use~~ of any one of claims 1 to 37, wherein the antibody drug conjugate comprises from 2 to 8 units of MMAE per antibody or antigen binding fragment thereof.

48. The ~~method-use~~ of any one of claims 1 to 37, wherein the antibody drug conjugate comprises from 3 to 5 units of MMAE per antibody or antigen binding fragment thereof.

49. The ~~method-use~~ of any one of claims 1 to 48, wherein the ~~antibody drug conjugate~~ ~~medicament~~ is to be administered at a dose of 1 to 10 mg/kg of the subject's body weight, 1 to 5 mg/kg of the subject's body weight, 1 to 2.5 mg/kg of the subject's body weight, or 1 to 1.25 mg/kg of the subject's body weight.

50. The ~~method-use~~ of claim 49, wherein the ~~medicamentantibody drug conjugate~~ is to be administered at a dose of about 1 mg/kg of the subject's body weight.

51. The ~~method-use~~ of claim 49, wherein the ~~medicament antibody drug conjugate~~ is to be administered at a dose of about 1.25 mg/kg of the subject's body weight.

52. The ~~method-use~~ of any one of claims 1 to 51, wherein the ~~medicament antibody drug conjugate~~ is to be administered by an intravenous (IV) injection or infusion.

53. The ~~method-use~~ of any one of claims 1 to 51, wherein the ~~medicament antibody drug conjugate~~ is to be administered by an intravenous (IV) injection or infusion over about 30 minutes twice every three-week cycle.

54. The ~~method-use~~ of any one of claims 1 to 51, wherein the ~~medicament antibody drug conjugate~~ is to be administered by an intravenous (IV) injection or infusion over about 30 minutes on Days 1 and 8 of every three-week cycle.

55. The ~~method-use~~ of any one of claims 1 to 51, wherein the ~~medicament antibody drug conjugate~~ is to be administered by an intravenous (IV) injection or infusion over about 30 minutes three times every four-week cycle.

56. The ~~method-use~~ of any one of claims 1 to 51, wherein the ~~medicament antibody drug conjugate formulated in the pharmaceutical composition~~ is to be administered by an intravenous (IV) injection or infusion over about 30 minutes on Days 1, 8 and 15 of every four-week cycle.