[0012] All references cited herein, including patent applications, patent publications, and scientific literature, are herein incorporated by reference in their entirety, as if each individual reference were specifically and individually indicated to be incorporated by reference.

SUMMARY

[0013] Provided herein are methods of treating cancer in a subject comprising administering to the subject an anti-PD-1 antibody or an antigen-binding fragment thereof, wherein the antibody binds to Programmed Death-1 (PD-1) and inhibits PD-1 activity, wherein the anti-PD-1 antibody or antigen-binding fragment thereof comprises the complementary determining regions (CDRs) of an antibody or antigen-binding fragment selected from the group consisting of nivolumab, Amp-514, tislelizumab, cemiplimab, TSR-042, JNJ-63723283, CBT-501, PF-06801591, JS-001, camrelizumab, PDR001, BCD-100, AGEN2034, IBI-308, BI-754091, GLS-010, LZM-009, AK-103, MGA-012, Sym-021 and CS1003, or a biosimilar thereof, and an antibody-drug conjugate that binds to tissue factor (TF), wherein the antibody-drug conjugate comprises an anti-TF antibody or an antigen-binding fragment thereof conjugated to a monomethyl auristatin or a functional analog thereof or a functional derivative thereof. In one aspect, the present disclosure refers to use of an antibody-drug conjugate that binds to tissue factor (TF) in the manufacture of a medicament for use in combinatorial therapy for treating cancer in a subject, wherein the antibody-drug conjugate comprises an anti-TF antibody or an antigen-binding fragment thereof conjugated to an auristatin or a functional analog thereof or a functional derivative thereof; wherein said medicament is to be administered in combination with an anti-PD-1 antibody or an antigen-binding fragment thereof, wherein the antibody binds to Programmed Death-1 (PD-1) and inhibits PD-1 activity, wherein the anti-PD-1 antibody or antigen-binding fragment thereof comprises the complementary determining regions (CDRs) of an antibody or antigen-binding fragment selected from the group consisting of nivolumab, Amp-514, tislelizumab, cemiplimab, TSR-042, JNJ-63723283, CBT-501, PF-06801591, JS-001, camrelizumab, PDR001, BCD-100, AGEN2034, IBI-308, BI-754091, GLS-010, LZM-009, AK-103, MGA-012, Sym-021 and CS1003, or a biosimilar thereof. In some examples, the anti-PD-1 antibody or antigen-binding fragment thereof comprises the CDRs of an antibody or antigen-binding fragment selected from the group consisting of nivolumab, Amp-514, tislelizumab, cemiplimab, TSR-042, JNJ-63723283, CBT-501, PF-06801591, JS-001,

camrelizumab, PDR001, BCD-100, AGEN2034, IBI-308, BI-754091, GLS-010, LZM-009, AK-103, MGA-012, Sym-021 and CS1003. In some of any of the examples herein, the anti-PD-1 antibody or antigen-binding fragment thereof comprises the heavy chain variable region and the light chain variable region of an antibody or antigen-binding fragment selected from the group consisting of nivolumab, Amp-514, tislelizumab, cemiplimab, TSR-042, JNJ-63723283, CBT-501, PF-06801591, JS-001, camrelizumab, PDR001, BCD-100, AGEN2034, IBI-308, BI-754091, GLS-010, LZM-009, AK-103, MGA-012, Sym-021 and CS1003, or a biosimilar thereof. In some of any of the examples herein, the anti-PD-1 antibody or antigen-binding fragment thereof comprises the heavy chain variable region and the light chain variable region of an antibody or antigen-binding fragment selected from the group consisting of nivolumab, Amp-514, tislelizumab, cemiplimab, TSR-042, JNJ-63723283, CBT-501, PF-06801591, JS-001, camrelizumab, PDR001, BCD-100, AGEN2034, IBI-308, BI-754091, GLS-010, LZM-009, AK-103, MGA-012, Sym-021 and CS1003. In some of any of the examples herein, the anti-PD-1 antibody or antigen-binding fragment thereof is selected from the group consisting of nivolumab, Amp-514, tislelizumab, cemiplimab, TSR-042, JNJ-63723283, CBT-501, PF-06801591, JS-001, camrelizumab, PDR001, BCD-100, AGEN2034, IBI-308, BI-754091, GLS-010, LZM-009, AK-103, MGA-012, Sym-021 and CS1003, or a biosimilar thereof. In some of any of the examples herein, the anti-PD-1 antibody or antigen-binding fragment thereof is selected from the group consisting of nivolumab, Amp-514, tislelizumab, cemiplimab, TSR-042, JNJ-63723283, CBT-501, PF-06801591, JS-001, camrelizumab, PDR001, BCD-100, AGEN2034, IBI-308, BI-754091, GLS-010, LZM-009, AK-103, MGA-012, Sym-021 and CS1003. In some of any of the examples herein, the antibody-drug conjugate is administered at a dose ranging from about 0.9 mg/kg to about 2.1 mg/kg. In some examples, the antibody-drug conjugate is administered at a dose of about 2.0 mg/kg. In some examples, the antibody-drug conjugate is administered at a dose of 2.0 mg/kg. In some of any of the examples herein, the antibody-drug conjugate is administered once about every 1 week, once about every 2 weeks, once about every 3 weeks or once about every 4 weeks. In some examples, the antibody-drug conjugate is administered once about every 3 weeks. In some of any of the examples herein, the anti-PD-1 antibody or antigen-binding fragment thereof comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises:

(i) a CDR-H1 comprising the amino acid sequence of SEQ ID NO:17;

(ii) a CDR-H2 comprising the amino acid sequence of SEQ ID NO:18; and

(iii) a CDR-H3 comprising the amino acid sequence of SEQ ID NO:19; and wherein the light chain variable region comprises:

(i) a CDR-L1 comprising the amino acid sequence of SEQ ID NO:20;

(ii) a CDR-L2 comprising the amino acid sequence of SEQ ID NO:21; and

(iii) a CDR-L3 comprising the amino acid sequence of SEQ ID NO:22. In some of any of the examples herein, the anti-PD-1 antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising an amino acid sequence having at least 85% sequence identity to the amino acid sequence of SEQ ID NO:31 and a light chain variable region comprising an amino acid sequence having at least 85% sequence identity to the amino acid sequence of SEQ ID NO:32. In some of any of the examples herein, the anti-PD-1 antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:31 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:32. In some of any of the examples herein, the anti-PD-1 antibody or antigen-binding fragment thereof is nivolumab. In some of any of the examples herein, the anti-PD-1 antibody or antigen-binding fragment thereof is administered at a dose ranging from about 0.5 mg/kg to about 4.1 mg/kg. In some of any of the examples herein, the anti-PD-1 antibody or antigen-binding fragment thereof is administered at a flat dose ranging from about 50 mg to about 500 mg. In some of any of the examples herein, the anti-PD-1 antibody or antigen-binding fragment thereof is administered at a flat dose of about 240 mg. In some of any of the examples herein, the anti-PD-1 antibody or antigen-binding fragment thereof is administered at a flat dose of about 480 mg. In some of any of the examples herein, the anti-PD-1 antibody or antigen-binding fragment thereof is administered once about every 1 week, once about every 2 weeks, once about every 3 weeks or once about every 4 weeks. In some examples, the anti-PD-1 antibody or antigen-binding fragment thereof is administered once about every 2 weeks. In some of any of the examples herein, the cancer is breast cancer. In some of any of the examples herein, the cancer is cervical cancer. In some of any of the examples herein, the subject is not a candidate for curative therapy. In some examples, curative therapy comprises radiotherapy and/or exenterative surgery. In some of any of the examples herein, the subject has not received prior systemic therapy for the cervical cancer. In some of any of the examples herein, the cervical cancer is an adenocarcinoma, an adenosquamous carcinoma or a squamous cell carcinoma. In some of any of the examples herein, the cervical cancer is an advanced stage cervical cancer. In some examples, the advanced stage cervical cancer is a stage 3 or stage 4 cervical cancer. In some of any of the examples herein, the advanced stage

cervical cancer is metastatic cervical cancer. In some of any of the examples herein, the cervical cancer is recurrent cervical cancer. In some of any of the examples herein, the monomethyl auristatin is monomethyl auristatin E (MMAE). In some of any of the examples herein, the anti-TF antibody or antigen-binding fragment thereof of the antibody-drug conjugate is a monoclonal antibody or a monoclonal antigen-binding fragment thereof. In some of any of the examples herein, the anti-TF antibody or antigen-binding fragment thereof of the antibody-drug conjugate comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises:

(i) a CDR-H1 comprising the amino acid sequence of SEQ ID NO:1;

(ii) a CDR-H2 comprising the amino acid sequence of SEQ ID NO:2; and

(iii) a CDR-H3 comprising the amino acid sequence of SEQ ID NO:3; and

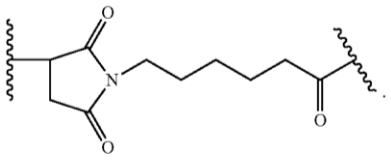
wherein the light chain variable region comprises:

(i) a CDR-L1 comprising the amino acid sequence of SEQ ID NO:4;

(ii) a CDR-L2 comprising the amino acid sequence of SEQ ID NO:5; and

(iii) a CDR-L3 comprising the amino acid sequence of SEQ ID NO:6. In some of any of the examples herein, the anti-TF antibody or antigen-binding fragment thereof of the antibody-drug conjugate comprises a heavy chain variable region comprising an amino acid sequence having at least 85% sequence identity to the amino acid sequence of SEQ ID NO:7 and a light chain variable region comprising an amino acid sequence having at least 85% sequence identity to the amino acid sequence of SEQ ID NO:8. In some of any of the examples herein, the anti-TF antibody or antigen-binding fragment thereof of the antibody-drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:7 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:8. In some of any of the examples herein, the anti-TF antibody of the antibody-drug conjugate is tisotumab. In some of any of the examples herein, the antibody-drug conjugate further comprises a linker between the anti-TF antibody or antigen-binding fragment thereof and the monomethyl auristatin. In some examples, the linker is a cleavable peptide linker. In some examples, the cleavable peptide linker has a formula: -MC-vc-PAB-, wherein:

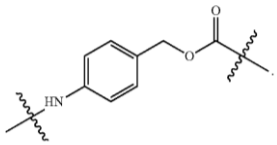
a) MC is:



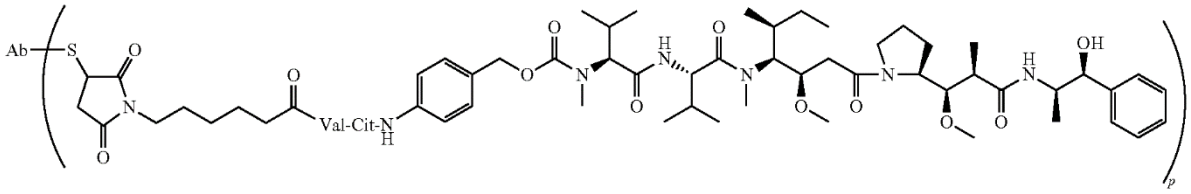
,

b) vc is the dipeptide valine-citrulline, and

c) PAB is:



. In some of any of the examples herein, the linker is attached to sulphydryl residues of the anti-TF antibody obtained by partial reduction or full reduction of the anti-TF antibody or antigen-binding fragment thereof. In some examples, the linker is attached to MMAE (vcMMAE), wherein the antibody-drug conjugate has the following structure:



Ab-MC-vc-PAB-MMAE (vcMMAE)

wherein p denotes a number from 1 to 8, S represents a sulphydryl residue of the anti-TF antibody, and Ab designates the anti-TF antibody or antigen-binding fragment thereof. In some of any of the examples herein, the average value of p in a population of the antibody-drug conjugates is about 4. In some of any of the examples herein, the antibody-drug conjugate is tisotumab vedotin. In some of any of the examplesherein, the route of administration for the antibody-drug conjugate is intravenous. In some of any of the examples herein, the route of administration for the anti-PD-1 antibody or antigen-binding fragment thereof is intravenous. In some of any of the examples herein, the anti-PD-1 antibody or antigen-binding fragment thereof and the antibody-drug conjugate are administered sequentially. In some of any of the examples herein, the anti-PD-1 antibody or antigen-binding fragment thereof and the antibody-drug conjugate are administered simultaneously. In some of any of the examples herein, at least about 0.1%, at least about 1%, at least about 2%, at least about 3%, at least about 4%, at least about 5%, at least about 6%, at

least about 7%, at least about 8%, at least about 9%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 60%, at least about 70%, or at least about 80% of cancer cells from the subject express TF. In some of any of the examples herein, at least about 0.1%, at least about 1%, at least about 2%, at least about 3%, at least about 4%, at least about 5%, at least about 6%, at least about 7%, at least about 8%, at least about 9%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 60%, at least about 70%, or at least about 80% of cancer cells from the subject express PD-L1. In some of any of the examples herein, a tumor derived from the cancer comprises one or more cells that express PD-L1, PD-L2, or both PD-L1 and PD-L2. In some of any of the examples herein, at least about 0.1%, at least about 1%, at least about 2%, at least about 3%, at least about 4%, at least about 5%, at least about 6%, at least about 7%, at least about 8%, at least about 9%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 60%, at least about 70%, or at least about 80% of T-cells from the subject express PD-1. In some of any of the examples herein, one or more therapeutic effects in the subject is improved after administration of the antibody-drug conjugate and the anti-PD-1 antibody or antigen-binding fragment thereof relative to a baseline. In some examples, the one or more therapeutic effects is selected from the group consisting of: size of a tumor derived from the cancer, objective response rate, duration of response, time to response, progression free survival, and overall survival. In some of any of the examples herein, the size of a tumor derived from the cancer is reduced by at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 60%, at least about 70%, or at least about 80% relative to the size of the tumor derived from the cancer before administration of the antibody-drug conjugate and the anti-PD-1 antibody or antigen-binding fragment thereof. In some of any of the embodiments herein, the objective response rate is at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 60%, at least about 70%, or at least about 80%. In some of any of the examples herein, the subject exhibits progression-free survival of at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at

least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years after administration of the antibody-drug conjugate and the anti-PD-1 antibody or antigen-binding fragment thereof. In some of any of the examples herein, the subject exhibits overall survival of at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years after administration of the antibody-drug conjugate and the anti-PD-1 antibody or antigen-binding fragment thereof. In some of any of the examples herein, the duration of response to the antibody-drug conjugate is at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years after administration of the antibody-drug conjugate and the anti-PD-1 antibody or antigen-binding fragment thereof. In some of any of the examples herein, the subject has one or more adverse events and is further administered an additional therapeutic agent to eliminate or reduce the severity of the one or more adverse events. In some of any of the examples herein, the subject is at risk of developing one or more adverse events and is further administered an additional therapeutic agent to prevent or reduce the severity of the one or more adverse events. In some of any of the examples herein, the one or more adverse events is anemia, abdominal pain, hemorrhage, hyperthyroidism, hypothyroidism, hypokalemia, hyponatremia, epistaxis, fatigue, nausea, alopecia, conjunctivitis, keratitis, conjunctival ulceration, constipation, decreased appetite, diarrhea, vomiting, peripheral neuropathy, or general physical health deterioration. In some of any of the examples herein, the one or more adverse events is a grade 3 or greater adverse event. In some of any of the examples herein, the one or more adverse events is a serious adverse event. In some of any of the examples herein, the one or more adverse events is conjunctivitis, conjunctival ulceration, and/or keratitis and the additional agent is a preservative-free lubricating eye drop, an ocular vasoconstrictor, antibiotic, and/or a steroid eye drop. In some of any of the examples herein, the subject is a human. In some of any of the examples herein, the antibody-drug conjugate is in a pharmaceutical composition comprising the antibody-drug conjugate and a pharmaceutical acceptable carrier. In some of

any of the examples herein, the anti-PD-1 antibody or antigen-binding fragment thereof is in a pharmaceutical composition comprising the anti-PD-1 antibody or antigen-binding fragment thereof and a pharmaceutical acceptable carrier.

[0014] In another aspect, the present disclosure provided herein is a kit comprising:

(a) an antibody or an antigen-binding fragment thereof described herein, wherein the antibody binds to Programmed Death-1 (PD-1) and inhibits PD-1 activity;

(b) a dosage ranging from about 0.9 mg/kg to about 2.1 mg/kg of an antibody-drug conjugate described herein that binds to tissue factor (TF), wherein the antibody-drug conjugate comprises an anti-TF antibody or an antigen-binding fragment thereof conjugated to a monomethyl auristatin or a functional analog thereof or a functional derivative thereof; and

(c) instructions for use of the anti-PD-1 antibody or antigen-binding fragment thereof and the antibody drug conjugate according to some of any of the examples herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0015] **FIG. 1** is an image of a Western blot showing phosphorylation of IRE1 and JNK in cell lysates of HeLa cells treated with MMAE (right lane) as compared to HeLa cells not treated with MMAE (left lane). Treatment with MMAE led to phosphorylation of both IRE1 and JNK. pIRE1 indicates phosphorylated IRE1 protein; IRE1 indicated total IRE1 protein; and pJNK indicates phosphorylated JNK protein.

[0016] **FIG. 2A and 2B** are immunofluorescent images of HeLa cells treated with 100 nM MMAE and imaged at the indicated time points in the presence of MMAE. **A)** Top panel shows staining for the ER with the ER-binding dye ER-ID Green and **B)** the lower panel shows RFP-labeled tubulin expressed by the cells.

[0017] **FIG. 3A and 3B** is a series of graphs showing **A)** ATP secretion and **B)** HMGB1 secretion from HeLa cells treated with 100 nM MMAE as compared to HeLa cells not treated with MMAE. Measurements were treated HeLa cells are shown as the fold change over the signal produced by untreated HeLa cells. **p<0.01 and ****p<0.0001.

[0018] **FIG. 4A-4C** is a series of graphs showing that tisotumab vedotin antibody-drug conjugate and MMAE free drug both drove robust **A)** ATP secretion and **C)** HMGB1 release. Activity was specific to the targeted agent (tisotumab vedotin) and free drug (MMAE). The non-targeted isotype ADC (IgG1-MMAE) did not elicit **A)** ATP or **C)** HMGB1 secretion. **B)** Tisotumab vedotin was active on multiple Tissue Factor positive cell lines.

[0019] **FIG. 5** is images of a Western blots showing treatment of HPAFII (pancreatic carcinoma) or MDA-MB-231 (breast carcinoma) cells for 16 hours with tisotumab vedotin or MMAE payloads trigger multiple ER stress pathways including phosphorylation of IRE and its down-stream target JNK as well as cleavage of ATF4. Treatment with the non-targeting H00-MMAE ADC (IgG1 MMAE) did not trigger activation of these ER stress pathways.

[0020] **FIG. 6A and 6B** is a series of graphs in which Tissue Factor positive MDA-MB-231 cells killed with various agents were fed to human peripheral blood mononuclear cells (PBMCs) and immune activation assessed by increased expression of activations markers on innate CD14+ monocyte/macrophages and induction of chemokine and cytokine production. Treatment with tisotumab vedotin ADC or MMAE free drug drove monocyte/macrophage

CLAIMS

WHAT IS CLAIMED IS:

1. Use of an antibody-drug conjugate that binds to tissue factor (TF) in the manufacture of a medicament for use in combinatorial therapy for treating cancer in a subject, wherein the antibody-drug conjugate comprises an anti-TF antibody or an antigen-binding fragment thereof conjugated to an auristatin or a functional analog thereof or a functional derivative thereof; wherein said medicament is to be administered in combination with an anti-PD-1 antibody or an antigen-binding fragment thereof, wherein the antibody binds to Programmed Death-1 (PD-1) and inhibits PD-1 activity, wherein the anti-PD-1 antibody or antigen-binding fragment thereof comprises the complementary determining regions (CDRs) of an antibody or antigen-binding fragment selected from the group consisting of nivolumab, Amp-514, tislelizumab, cemiplimab, TSR-042, JNJ-63723283, CBT-501, PF-06801591, JS-001, camrelizumab, PDR001, BCD-100, AGEN2034, IBI-308, BI-754091, GLS-010, LZM-009, AK-103, MGA-012, Sym-021 and CS1003, or a biosimilar thereof.

2. The use of claim 1, wherein the anti-PD-1 antibody or antigen-binding fragment thereof comprises the CDRs of an antibody or antigen-binding fragment selected from the group consisting of nivolumab, Amp-514, tislelizumab, cemiplimab, TSR-042, JNJ-63723283, CBT-501, PF-06801591, JS-001, camrelizumab, PDR001, BCD-100, AGEN2034, IBI-308, BI-754091, GLS-010, LZM-009, AK-103, MGA-012, Sym-021 and CS1003.

3. The use of claim 1 or 2, wherein the anti-PD-1 antibody or antigen-binding fragment thereof comprises the heavy chain variable region and the light chain variable region of an antibody or antigen-binding fragment selected from the group consisting of nivolumab, Amp-514, tislelizumab, cemiplimab, TSR-042, JNJ-63723283, CBT-501, PF-06801591, JS-001, camrelizumab, PDR001, BCD-100, AGEN2034, IBI-308, BI-754091, GLS-010, LZM-009, AK-103, MGA-012, Sym-021 and CS1003, or a biosimilar thereof.

4. The use of claim 1 or 2, wherein the anti-PD-1 antibody or antigen-binding fragment thereof comprises the heavy chain variable region and the light chain variable region of an antibody or antigen-binding fragment selected from the group consisting of nivolumab, Amp-514, tislelizumab, cemiplimab, TSR-042, JNJ-63723283, CBT-501, PF-06801591, JS-001,

camrelizumab, PDR001, BCD-100, AGEN2034, IBI-308, BI-754091, GLS-010, LZM-009, AK-103, MGA-012, Sym-021 and CS1003.

5. The use of claim 1, wherein the anti-PD-1 antibody or antigen-binding fragment thereof is selected from the group consisting of nivolumab, Amp-514, tislelizumab, cemiplimab, TSR-042, JNJ-63723283, CBT-501, PF-06801591, JS-001, camrelizumab, PDR001, BCD-100, AGEN2034, IBI-308, BI-754091, GLS-010, LZM-009, AK-103, MGA-012, Sym-021 and CS1003, or a biosimilar thereof.

6. The use of claim 1, wherein the anti-PD-1 antibody or antigen-binding fragment thereof is selected from the group consisting of nivolumab, Amp-514, tislelizumab, cemiplimab, TSR-042, JNJ-63723283, CBT-501, PF-06801591, JS-001, camrelizumab, PDR001, BCD-100, AGEN2034, IBI-308, BI-754091, GLS-010, LZM-009, AK-103, MGA-012, Sym-021 and CS1003.

7. The use of any one of claims 1-6, wherein the antibody-drug conjugate is to be administered at a dose ranging from about 0.9 mg/kg to about 2.1 mg/kg.

8. The use of claim 7, wherein the antibody-drug conjugate is to be administered at a dose of about 2.0 mg/kg.

9. The use of claim 7, wherein the antibody-drug conjugate is to be administered at a dose of 2.0 mg/kg.

10. The use of any one of claims 1-9, wherein the antibody-drug conjugate is to be administered once about every 1 week, once about every 2 weeks, once about every 3 weeks or once about every 4 weeks.

11. The use of claim 10, wherein the antibody-drug conjugate is to be administered once about every 3 weeks.

12. The use of any one of claims 1-11, wherein the anti-PD-1 antibody or antigen-binding fragment thereof comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises:

(i) a CDR-H1 comprising the amino acid sequence of SEQ ID NO:17;

(ii) a CDR-H2 comprising the amino acid sequence of SEQ ID NO:18; and

(iii) a CDR-H3 comprising the amino acid sequence of SEQ ID NO:19; and

wherein the light chain variable region comprises:

(i) a CDR-L1 comprising the amino acid sequence of SEQ ID NO:20;

(ii) a CDR-L2 comprising the amino acid sequence of SEQ ID NO:21; and

(iii) a CDR-L3 comprising the amino acid sequence of SEQ ID NO:22.

13. The use of any one of claims 1-12, wherein the anti-PD-1 antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising an amino acid sequence having at least 85% sequence identity to the amino acid sequence of SEQ ID NO:31 and a light chain variable region comprising an amino acid sequence having at least 85% sequence identity to the amino acid sequence of SEQ ID NO:32.

14. The use of any one of claims 1-13, wherein the anti-PD-1 antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:31 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:32.

15. The use of any one of claims 1-14, wherein the anti-PD-1 antibody or antigen-binding fragment thereof is nivolumab.

16. The use of any one of claims 1-15, wherein the anti-PD-1 antibody or antigen-binding fragment thereof is to be administered at a dose ranging from about 0.5 mg/kg to about 4.1 mg/kg.

17. The use of any one of claims 1-15, wherein the anti-PD-1 antibody or antigen-binding fragment thereof is to be administered at a flat dose ranging from about 50 mg to about 500 mg.

18. The use of any one of claims 1-15, wherein the anti-PD-1 antibody or antigen-binding fragment thereof is to be administered at a flat dose of about 240 mg.

19. The use of any one of claims 1-15, wherein the anti-PD-1 antibody or antigen-binding fragment thereof is to be administered at a flat dose of about 480 mg.

20. The use of any one of claims 1-19, wherein the anti-PD-1 antibody or antigen-binding fragment thereof is to be administered once about every 1 week, once about every 2 weeks, once about every 3 weeks or once about every 4 weeks.

21. The use of claim 20, wherein the anti-PD-1 antibody or antigen-binding fragment thereof is to be administered once about every 2 weeks.

22. The use of any one of claims 1-21, wherein the cancer is breast cancer.

23. The use of any one of claims 1-21, wherein the cancer is cervical cancer.

24. The use of claim 23, wherein the subject is not a candidate for curative therapy.

25. The use of claim 24, wherein curative therapy comprises radiotherapy and/or exenterative surgery.

26. The use of claim 23, wherein the subject has not received prior systemic therapy for the cervical cancer.

27. The use of any one of claims 23-26, wherein the cervical cancer is an adenocarcinoma, an adenosquamous carcinoma or a squamous cell carcinoma.

28. The use of any one of claims 23-27, wherein the cervical cancer is an advanced stage cervical cancer.

29. The use of claim 28, wherein the advanced stage cervical cancer is a stage 3 or stage 4 cervical cancer.

30. The use of claim 28 or 29, wherein the advanced stage cervical cancer is metastatic cervical cancer.

31. The use of any one of claims 23-30, wherein the cervical cancer is recurrent cervical cancer.

32. The use of any one of claims 1-31, wherein the auristatin is monomethyl auristatin.

33. The use of any one of claims 1-32, wherein the monomethyl auristatin is monomethyl auristatin E (MMAE).

34. The use of any one of claims 1-33, wherein the anti-TF antibody or antigen-binding fragment thereof of the antibody-drug conjugate is a monoclonal antibody or a monoclonal antigen-binding fragment thereof.

35. The use of any one of claims 1-34, wherein the anti-TF antibody or antigen-binding fragment thereof of the antibody-drug conjugate comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises:

(i) a CDR-H1 comprising the amino acid sequence of SEQ ID NO:1;

(ii) a CDR-H2 comprising the amino acid sequence of SEQ ID NO:2; and

(iii) a CDR-H3 comprising the amino acid sequence of SEQ ID NO:3; and

wherein the light chain variable region comprises:

(i) a CDR-L1 comprising the amino acid sequence of SEQ ID NO:4;

(ii) a CDR-L2 comprising the amino acid sequence of SEQ ID NO:5; and

(iii) a CDR-L3 comprising the amino acid sequence of SEQ ID NO:6.

36. The use of any one of claims 1-35, wherein the anti-TF antibody or antigen-binding fragment thereof of the antibody-drug conjugate comprises a heavy chain variable region comprising an amino acid sequence having at least 85% sequence identity to the amino acid sequence of SEQ ID NO:7 and a light chain variable region comprising an amino acid sequence having at least 85% sequence identity to the amino acid sequence of SEQ ID NO:8.

37. The use of any one of claims 1-36, wherein the anti-TF antibody or antigen-binding fragment thereof of the antibody-drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:7 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:8.

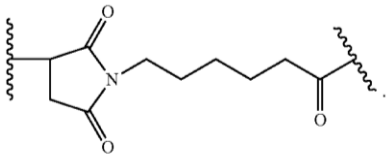
38. The use of any one of claims 1-37, wherein the anti-TF antibody of the antibody-drug conjugate is tisotumab.

39. The use of any one of claims 1-38, wherein the antibody-drug conjugate further comprises a linker between the anti-TF antibody or antigen-binding fragment thereof and the monomethyl auristatin.

40. The use of claim 39, wherein the linker is a cleavable peptide linker.

41. The use of claim 40, wherein the cleavable peptide linker has a formula: -MC-vc-PAB-, wherein:

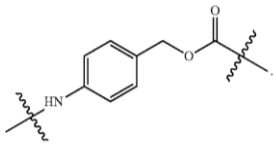
a) MC is:



,

b) vc is the dipeptide valine-citrulline, and

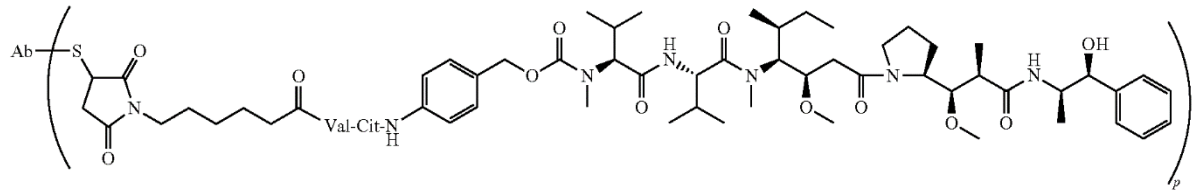
c) PAB is:



.

42. The use of any one of claims 39-41, wherein the linker is attached to sulphydryl residues of the anti-TF antibody obtained by partial reduction or full reduction of the anti-TF antibody or antigen-binding fragment thereof.

43. The use of claim 42, wherein the linker is attached to MMAE (vcMMAE), wherein the antibody-drug conjugate has the following structure:



Ab-MC-vc-PAB-MMAE (vcMMAE)

wherein p denotes a number from 1 to 8, S represents a sulphydryl residue of the anti-TF antibody, and Ab designates the anti-TF antibody or antigen-binding fragment thereof.

44. The use of claim 43, wherein the average value of p in a population of the antibody-drug conjugates is about 4.

45. The use of any one of claims 1-44, wherein the antibody-drug conjugate is tisotumab vedotin.

46. The use of any one of claims 1-45, wherein the route of administration for the antibody-drug conjugate is intravenous.

47. The use of any one of claims 1-46, wherein the route of administration for the anti-PD-1 antibody or antigen-binding fragment thereof is intravenous.

48. The use of any one of claims 1-47, wherein the anti-PD-1 antibody or antigen-binding fragment thereof and the antibody-drug conjugate are to be administered sequentially.

49. The use of any one of claims 1-47, wherein the anti-PD-1 antibody or antigen-binding fragment thereof and the antibody-drug conjugate are to be administered simultaneously.

50. The use of any one of claims 1-49, wherein at least about 0.1%, at least about 1%, at least about 2%, at least about 3%, at least about 4%, at least about 5%, at least about 6%, at least about 7%, at least about 8%, at least about 9%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 60%, at least about 70%, or at least about 80% of cancer cells from the subject express TF.

51. The use of any one of claims 1-50, wherein at least about 0.1%, at least about 1%, at least about 2%, at least about 3%, at least about 4%, at least about 5%, at least about 6%, at least about 7%, at least about 8%, at least about 9%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 60%, at least about 70%, or at least about 80% of cancer cells from the subject express PD-L1.

52. The use of any one of claims 1-51, wherein a tumor derived from the cancer comprises one or more cells that express PD-L1, PD-L2, or both PD-L1 and PD-L2.

53. The use of any one of claims 1-52, wherein at least about 0.1%, at least about 1%, at least about 2%, at least about 3%, at least about 4%, at least about 5%, at least about 6%, at least about 7%, at least about 8%, at least about 9%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 60%, at least about 70%, or at least about 80% of T-cells from the subject express PD-1.

54. The use of any one of claims 1-53, wherein one or more therapeutic effects in the subject is improved after administration of the antibody-drug conjugate and the anti-PD-1 antibody or antigen-binding fragment thereof relative to a baseline.

55. The use of claim 54, wherein the one or more therapeutic effects is selected from the group consisting of: size of a tumor derived from the cancer, objective response rate, duration of response, time to response, progression free survival, and overall survival.

56. The use of any one of claims 1-55, wherein the size of a tumor derived from the cancer is reduced by at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 60%, at least about 70%, or at least about 80% relative to the size of the tumor derived from the cancer before administration of the antibody-drug conjugate and the anti-PD-1 antibody or antigen-binding fragment thereof.

57. The use of any one of claims 1-56, wherein the objective response rate is at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at

least about 45%, at least about 50%, at least about 60%, at least about 70%, or at least about 80%.

58. The use of any one of claims 1-57, wherein the subject exhibits progression-free survival of at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years after administration of the antibody-drug conjugate and the anti-PD-1 antibody or antigen-binding fragment thereof.

59. The use of any one of claims 1-58, wherein the subject exhibits overall survival of at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years after administration of the antibody-drug conjugate and the anti-PD-1 antibody or antigen-binding fragment thereof.

60. The use of any one of claims 1-59, wherein the duration of response to the antibody-drug conjugate is at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years after administration of the antibody-drug conjugate and the anti-PD-1 antibody or antigen-binding fragment thereof.

61. The use of any one of claims 1-60, wherein the subject has one or more adverse events and is further to be administered an additional therapeutic agent to eliminate or reduce the severity of the one or more adverse events.

62. The use of any one of claims 1-61, wherein the subject is at risk of developing one or more adverse events and is further to be administered an additional therapeutic agent to prevent or reduce the severity of the one or more adverse events.

63. The use of claim 61 or claim 62, wherein the one or more adverse events is anemia, abdominal pain, hemorrhage, hyperthyroidism, hypothyroidism, hypokalemia, hyponatremia, epistaxis, fatigue, nausea, alopecia, conjunctivitis, keratitis, conjunctival ulceration, constipation, decreased appetite, diarrhea, vomiting, peripheral neuropathy, or general physical health deterioration.

64. The use of any one of claims 61-63, wherein the one or more adverse events is a grade 3 or greater adverse event.

65. The use of any one of claims 61-63, wherein the one or more adverse events is a serious adverse event.

66. The use of claim 61 or claim 62, wherein the one or more adverse events is conjunctivitis, conjunctival ulceration, and/or keratitis and the additional agent is a preservative-free lubricating eye drop, an ocular vasoconstrictor, antibiotic, and/or a steroid eye drop.

67. The use of any one of claims 1-66, wherein the subject is a human.

68. The use of any one of claims 1-67, wherein the antibody-drug conjugate is in a pharmaceutical composition comprising the antibody-drug conjugate and a pharmaceutical acceptable carrier.

69. The use of any one of claims 1-68, wherein the anti-PD-1 antibody or antigen-binding fragment thereof is in a pharmaceutical composition comprising the anti-PD-1 antibody or antigen-binding fragment thereof and a pharmaceutical acceptable carrier.

70. A kit comprising:

(a) an antibody or an antigen-binding fragment thereof, wherein the antibody binds to Programmed Death-1 (PD-1) and inhibits PD-1 activity;

(b) a dosage ranging from about 0.9 mg/kg to about 2.1 mg/kg of an antibody-drug conjugate that binds to tissue factor (TF), wherein the antibody-drug conjugate comprises an anti-TF antibody or an antigen-binding fragment thereof conjugated to a monomethyl auristatin or a functional analog thereof or a functional derivative thereof; and

(c) instructions for use of the anti-PD-1 antibody or antigen-binding fragment thereof and the antibody drug conjugate according to the use of any one of claims 1-69.