namely inhibiting topoisomerase I rather than disrupting microtubules. Unlike monomethyl auristatin E, camptothecin-based therapies do not cause peripheral neuropathy clinically.

[0008] There remains a need for therapies, such as combination therapies, with an acceptable safety profile and high efficacy for the treatment of cancer. The present invention meets this need by providing methods of treating cancer with a combination of ADCs targeting the same antigen, but comprising different cytotoxic agents, such as a combination of BV and SGN-CD30C. We theorized using a reduced dose of BV in combination with SGN-CD30C could provide a dual mechanism of action to retain or enhance anti-tumor activity while decreasing the incidence of non-overlapping toxicities (i.e. peripheral neuropathy).

[0009] 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

[0010] In one aspect, the present disclosure provides a use of a first antibody-drug conjugate that binds to CD30 and a second antibody-drug conjugate that binds to CD30 in the manufacture of a medicament for combination therapy for treating cancer in a subject, wherein the first antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to an auristatin or a functional analog thereof or a functional derivative thereof, and the second antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to a camptothecin or a functional analog thereof or a functional derivative thereof. In another aspect, the present disclosure provides a use of a first antibody-drug conjugate that binds to CD30 in the manufacture of a medicament for use in combinatorial therapy for treating cancer in a subject, wherein said medicament is to be administered to the subject in combination with a second antibody-drug conjugate that binds to CD30, wherein the first antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to an auristatin or a functional analog thereof or a functional derivative thereof, and the second antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to a camptothecin or a functional analog thereof or a functional derivative thereof. In yet another aspect, the present disclosure provides a use of a first antibody-drug conjugate that binds to CD30 in the manufacture of a first medicament

and use of a second antibody-drug conjugate that binds to CD30 in the manufacture of a second medicament, wherein the first and the second medicaments are to be used in combination therapy to treat cancer in a subject, wherein the first antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to an auristatin or a functional analog thereof or a functional derivative thereof, and the second antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to a camptothecin or a functional analog thereof or a functional derivative thereof.

[0010a] Provided herein is a method of treating cancer in a subject, the method comprising administering to the subject a first antibody-drug conjugate that binds to CD30, wherein the first antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to an auristatin or a functional analog thereof or a functional derivative thereof, and a second antibody-drug conjugate that binds to CD30, wherein the second antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to a camptothecin or a functional analog thereof or a functional derivative thereof. In some examples, the cancer is a hematologic cancer. In some examples, the cancer is selected from the group consisting of Hodgkin lympohoma, non-Hodgkin lymphoma, anaplastic large cell lymphoma, peripheral T-cell lymphoma, or mycosis fungoides. In some examples, the cancer is Hodgkin lymphoma. In some examples, the Hodgkin lymphoma is classical Hodgkin lymphoma. In some examples, the cancer is non-Hodgkin lymphoma. In some examples, the non-Hodgkin lymphoma is diffuse large B-cell lymphoma (DLBCL). In some examples, the DLBCL is relapsed DLBCL. In some examples, the DLBCL is refractory DLBCL. In some examples, the DLBCL is germinal-center B-cell like (GCB). In some examples, the DLBCL is non-GCB. In some examples, the cancer is anaplastic large cell

lymphoma. In some examples, the anaplastic large cell lymphoma is systemic anaplastic large cell lymphoma. In some examples, the anaplastic large cell lymphoma is primary cutaneous anaplastic large cell lymphoma. In some examples, the cancer is peripheral T-cell lymphoma. In some examples, the peripheral T-cell lymphoma is angioimmunoblastic T-cell lymphoma. In some examples, the subject has been previously treated with one or more therapeutic agents and did not respond to the treatment. In some examples, the subject has been previously treated with one or more therapeutic agents and relapsed after the treatment. In some examples, the subject has been previously treated with one or more therapeutic agents and has experienced disease progression during treatment. In some examples, the subject has not been previously treated with an antibody-drug conjugate that binds to CD30. In some examples, the subject has previously received allogenic stem cell transplant to treat the cancer. In some examples, the subject has previously received autologous stem cell transplant to treat the cancer. In some examples, the subject relapsed following stem cell transplant. In some examples, the subject has previously received CAR-T therapy. In some examples, the subject relapsed after CAR-T therapy. In some examples, the cancer is an advanced stage cancer. In some examples, the advanced stage cancer is a stage 3 or stage 4 cancer. In some examples, the advanced stage cancer is metastatic cancer. In some examples, the cancer is recurrent cancer. In some examples, the anti-CD30 antibody of the first and/or second 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:

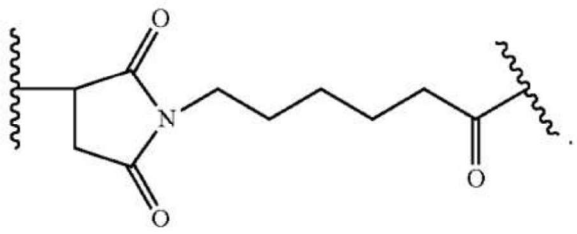
(i) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 4;

(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 examples, the anti-CD30 antibody of the first and/or second antibody-drug conjugate comprises a heavy chain variable region comprising an amino acid sequence at least 85% identical to the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising an amino acid sequence at least 85% identical to the amino acid sequence of SEQ ID

NO: 8. In some examples, the anti-CD30 antibody of the first and/or second antibody-drug conjugate comprises a heavy chain variable region comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 8. In some examples, the anti-CD30 antibody of the first and/or second antibody-drug conjugate comprises a heavy chain variable region comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 8. In some examples, the anti-CD30 antibody 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 examples, the anti-CD30 antibody of the first and/or second antibody-drug conjugate is cAC10. In some examples, the first antibody-drug conjugate further comprises a linker between the anti-CD30 antibody or antigen-binding portion thereof and the 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:

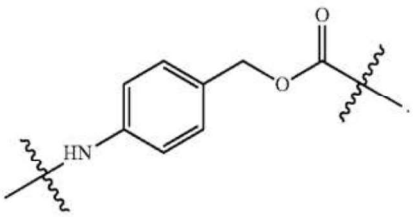
a) MC is:



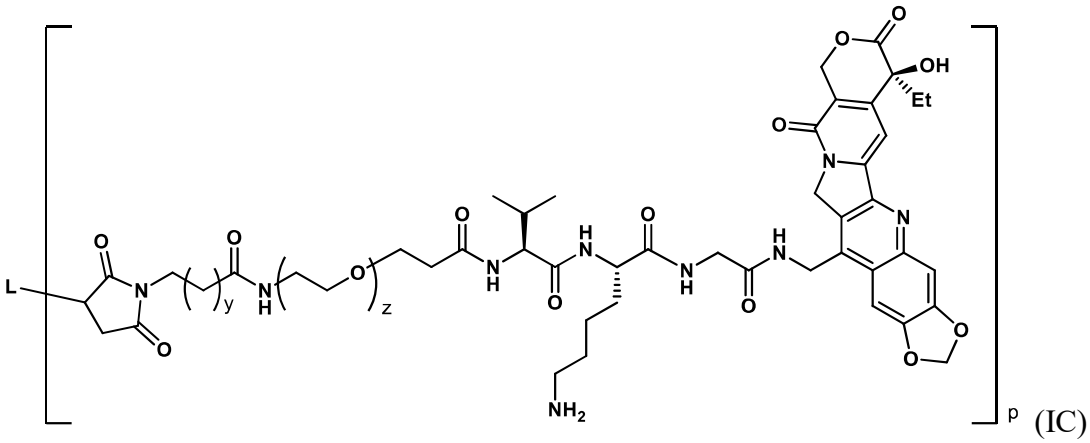
,

b) vc is the dipeptide valine-citrulline, and

c) PAB is:



. In some examples, the auristatin is a monomethyl auristatin. In some examples, the monomethyl auristatin is monomethyl auristatin E (MMAE). In some examples, the monomethyl auristatin is monomethyl auristatin F (MMAF). In some examples, the first antibody-drug conjugate is brentuximab vedotin or a biosimilar thereof. In some examples, the first antibody-drug conjugate is brentuximab vedotin. In some examples, the second antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to a camptothecin or a functional analog thereof or a functional derivative thereof forming a camptothecin conjugate of Formula (IC):



(IC)

or a pharmaceutically acceptable salt thereof, wherein:

L is the anti-CD30 antibody or an antigen-binding fragment thereof,

y is 1, 2, 3, or 4, or is 1 or 4,

z is an integer from 2 to 12, or is 2, 4, 8, or 12, and

p is 1-16, or is 2, 3, 4, 5, 6, 7, 8, 9, or 10, or is 2, 4 or 8. In some examples, y is 1. In some examples, z is 8. In some examples, p is 8. In some examples, the second

antibody-drug conjugate is SGN-CD30C. In some examples, the first antibody-drug conjugate is administered at a dose of 0.1 mg/kg to 1.8 mg/kg of the subject's bodyweight. In some examples, the first antibody-drug conjugate is administered at a dose of about 0.2 mg/kg of the subject's bodyweight. In some examples, the first antibody-drug conjugate is administered at a dose of about 0.3 mg/kg of the subject's bodyweight. In some examples, the first antibody-drug conjugate is administered at a dose of about 0.4 mg/kg of the subject's bodyweight. In some examples, the first antibody-drug conjugate is administered to a subject having a bodyweight of greater than 100 kg as if the subject had a bodyweight of 100 kg. In some examples, the first antibody-drug conjugate is administered to the subject once about every 3 weeks. In some examples, the first antibody-drug conjugate is administered to the subject once every 3 weeks. In some examples, the first antibody-drug conjugate is administered to the subject on about day 1 of about a 21-day treatment cycle. In some examples, the first antibody-drug conjugate is administered to the subject on day 1 of a 21-day treatment cycle. In some examples, the first antibody-drug conjugate is administered by intravenous infusion. In some examples, the second antibody-drug conjugate is administered at a dose of 0.01 mg/kg to 5 mg/kg of the subject's bodyweight. In some examples, the second antibody-drug conjugate is administered at a dose of 0.1 mg/kg to 2 mg/kg of the subject's bodyweight. In some examples, the second antibody-drug conjugate is administered at a dose of about 0.1 mg/kg of the subject's bodyweight. In some examples, the second antibody-drug conjugate is administered at a dose of about 0.5 mg/kg of the subject's bodyweight. In some examples, the second antibody-drug conjugate is administered to the subject once about every 3 weeks. In some examples, the second antibody-drug conjugate is administered to the subject once every 3 weeks. In some examples, the second antibody-drug conjugate is administered to the subject on about day 1 of about a 21-day treatment cycle. In some examples, the second antibody-drug conjugate is administered to the subject on day 1 of a 21-day treatment cycle. In some examples, the second antibody-drug conjugate is administered by intravenous infusion. In some examples, the method further comprises administration of granulocyte-colony stimulating factor (G-CSF) to the subject. In some examples, the G-CSF is administered 1 to 3 days after the administration of the first and/or second anti-CD30 antibody-drug conjugate. In some examples, the G-CSF is selected from the group consisting of filgrastim, PEG-filgrastim, lenograstim, and tbo-filgrastim. In some

examples, administering the first and second antibody-drug conjugates to the subject results in a depletion of cancer cells by 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%, at least about 80%, at least about 90%, at least about 95%, or about 100% compared to the amount of cancer cells before administering the first and second antibody-drug conjugates to the subject. In some examples, one or more therapeutic effects in the subject is improved after administration of the first and second antibody-drug conjugates relative to a baseline. In some examples, the one or more therapeutic effects is selected from the group consisting of: objective response rate, duration of response, time to response, progression free survival and overall survival. In some examples, 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 examples, 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 first and second antibody-drug conjugates. In some examples, 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 first and second antibody-drug conjugates. In some examples, the duration of response to the first and second antibody-drug conjugates 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 first and second antibody-drug conjugates. In some examples, the subject is a human.

[0011] In a further aspect, the present disclosure provides a pharmaceutical composition for use in the treatment of cancer in a subject, the composition comprising a first antibody-drug conjugate that binds to CD30, wherein the first antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to an auristatin or a functional analog thereof or a functional derivative thereof, and a second antibody-drug conjugate that binds to CD30, wherein the second antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to a camptothecin or a functional analog thereof or a functional derivative thereof. Also provided herein is a pharmaceutical composition for the treatment of cancer in a subject, the composition comprising a first antibody-drug conjugate that binds to CD30, wherein the first antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to an auristatin or a functional analog thereof or a functional derivative thereof, and a second antibody-drug conjugate that binds to CD30, wherein the second antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to a camptothecin or a functional analog thereof or a functional derivative thereof, wherein the composition is for use in a method of any of the examples herein.

[0012] In a further aspect, the present disclosure provides a kit comprising a first antibody-drug conjugate that binds to CD30 and a second antibody-drug conjugate, wherein the first antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to an auristatin or a functional analog thereof or a functional derivative thereof, and the second antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to a camptothecin or a functional analog thereof or a functional derivative thereof, and instructions for using the kit to treat cancer in a subject. Also provided herein is a kit comprising a first antibody-drug conjugate that binds to CD30, wherein the first antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to an auristatin or a functional analog thereof or a functional derivative thereof, a second antibody-drug conjugate that binds to CD30, wherein the second antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to a camptothecin or a functional analog thereof or a

functional derivative thereof, and instructions for using the kit in the method of any of the examples herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] FIG. 1A-1E is a series of graphs showing tumor volumes over time for individual animals treated with SGN-CD30C alone (FIG. 1A), BV alone (FIG. 1B) and a combination of SGN-CD30C + BV (FIG. 1C), mean tumor volumes over time for animals that were untreated, treated with SGN-CD30C alone, treated with BV alone, or treated with a combination of SGN-CD30C + BV (FIG. 1D), and tumor quadrupling time for animals that were untreated, treated with SGN-CD30C alone, treated with BV alone, or treated with a combination of SGN-CD30C + BV (FIG. 1E).

[0014] FIG. 2A-2D is a series of graphs showing tumor volumes over time for individual animals treated with SGN-CD30C alone (FIG. 2A), BV alone (FIG. 2B) and a combination of SGN-CD30C + BV (FIG. 2C) and percent survival over time for animals that were untreated,

CLAIMS

What is claimed is:

1. Use of a first antibody-drug conjugate that binds to CD30 and a second antibody-drug conjugate that binds to CD30 in the manufacture of a medicament for combination therapy for treating cancer in a subject, wherein the first antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to an auristatin or a functional analog thereof or a functional derivative thereof, and the second antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to a camptothecin or a functional analog thereof or a functional derivative thereof.

2. Use of a first antibody-drug conjugate that binds to CD30 in the manufacture of a medicament for use in combinatorial therapy for treating cancer in a subject, wherein said medicament is to be administered to the subject in combination with a second antibody-drug conjugate that binds to CD30, wherein the first antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to an auristatin or a functional analog thereof or a functional derivative thereof, and the second antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to a camptothecin or a functional analog thereof or a functional derivative thereof.

3. Use of a first antibody-drug conjugate that binds to CD30 in the manufacture of a first medicament and use of a second antibody-drug conjugate that binds to CD30 in the manufacture of a second medicament, wherein the first and the second medicaments are to be used in combination therapy to treat cancer in a subject, wherein the first antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to an auristatin or a functional analog thereof or a functional derivative thereof, and the second antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to a camptothecin or a functional analog thereof or a functional derivative thereof.

4. The use of any one of claims 1-3, wherein the cancer is a hematologic cancer.

5. The use of claim 4, wherein the cancer is selected from the group consisting of Hodgkin lympohoma, non-Hodgkin lymphoma, anaplastic large cell lymphoma, peripheral T-cell lymphoma, or mycosis fungoides.

6. The use of claim 5, wherein the cancer is Hodgkin lymphoma or non-Hodgkin lymphoma.

7. The use of claim 6, wherein the Hodgkin lymphoma is classical Hodgkin lymphoma.

8. The use of claim 7, wherein the non-Hodgkin lymphoma is diffuse large B-cell lymphoma (DLBCL).

9. The use of claim 8, wherein the DLBCL is relapsed and/or refractory DLBCL.

10. The use of claim 8 or claim 9, wherein the DLBCL is germinal-center B-cell like (GCB).

11. The use of claim8 or claim 9, wherein the DLBCL is non-GCB.

12. The use of claim 5, wherein the cancer is anaplastic large cell lymphoma.

13. The use of claim 12, wherein the anaplastic large cell lymphoma is systemic anaplastic large cell lymphoma.

14. The use of claim 12, wherein the anaplastic large cell lymphoma is primary cutaneous anaplastic large cell lymphoma.

15. The use of claim 5, wherein the cancer is peripheral T-cell lymphoma.

16. The use of claim 15, wherein the peripheral T-cell lymphoma is angioimmunoblastic T-cell lymphoma.

17. The use of claim 5, wherein the cancer is mycosis fungoides.

18. The use of any one of claims 1-17, wherein the subject has been previously treated with one or more therapeutic agents and did not respond to the treatment.

19. The use of any one of claims 1-17, wherein the subject has been previously treated with one or more therapeutic agents and relapsed after the treatment.

20. The use of any one of claims 1-17, wherein the subject has been previously treated with one or more therapeutic agents and has experienced disease progression during treatment.

21. The use of any one of claims 1-20, wherein the subject has not been previously treated with an antibody-drug conjugate that binds to CD30.

22. The use of any one of claims 1-21, wherein the subject has previously received allogenic stem cell transplant to treat the cancer.

23. The use of any one of claims 1-21, wherein the subject has previously received autologous stem cell transplant to treat the cancer.

24. The use of claim 22 or claim 23, wherein the subject relapsed following stem cell transplant.

25. The use of any one of claims 1-24, wherein the subject has previously received CAR-T therapy.

26. The use of claim 25, wherein the subject relapsed after CAR-T therapy.

27. The use of any one of claims 1-26, wherein the cancer is an advanced stage cancer.

28. The use of claim 27, wherein the advanced stage cancer is a stage 3 or stage 4 cancer.

29. The use of claim 27 or claim 28, wherein the advanced stage cancer is metastatic cancer.

30. The use of any one of claims 1-29, wherein the cancer is recurrent cancer.

31. The use of any one of claims 1-30, wherein at least 1% of the cancer cells in the subject express CD30.

32. The use of any one of claims 1-31, wherein the anti-CD30 antibody of the first and/or second 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.

33. The use of any one of claims 1-32, wherein the anti-CD30 antibody of the first and/or second antibody-drug conjugate comprises a heavy chain variable region comprising an amino acid sequence at least 85% identical to the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising an amino acid sequence at least 85% identical to the amino acid sequence of SEQ ID NO: 8.

34. The use of any one of claims 1-33, wherein the anti-CD30 antibody of the first and/or second antibody-drug conjugate comprises a heavy chain variable region comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 8.

35. The use of any one of claims 1-34, wherein the anti-CD30 antibody of the first and/or second antibody-drug conjugate comprises a heavy chain variable region comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 8.

36. The use of any one of claims 1-35, wherein the anti-CD30 antibody 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.

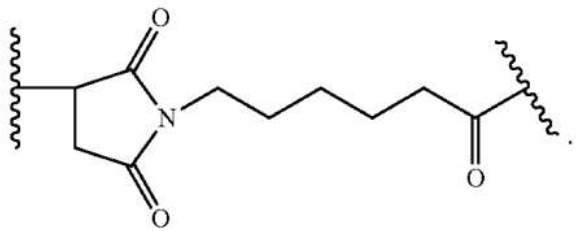
37. The use of any one of claims 1-36, wherein the anti-CD30 antibody of the first and/or second antibody-drug conjugate is cAC10.

38. The use of any one of claims 1-37, wherein the first antibody-drug conjugate further comprises a linker between the anti-CD30 antibody or antigen-binding portion thereof and the auristatin.

39. The use of claim 38, wherein the linker is a cleavable peptide linker.

40. The use of claim 39, wherein the cleavable peptide linker has a formula: -MC-vc-PAB-, wherein:

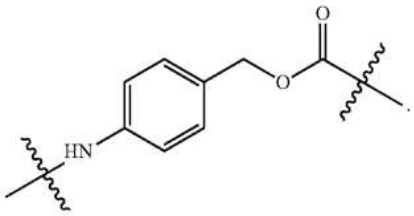
a) MC is:



,

b) vc is the dipeptide valine-citrulline, and

c) PAB is:



.

41. The use of any one of claims 1-40, wherein the auristatin is a monomethyl auristatin.

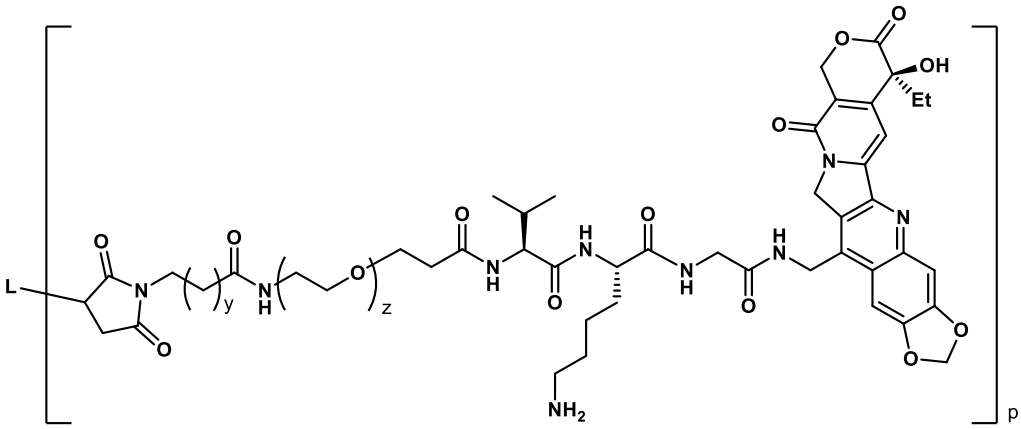
42. The use of claim 41, wherein the monomethyl auristatin is monomethyl auristatin E (MMAE).

43. The use of claim 41, wherein the monomethyl auristatin is monomethyl auristatin F (MMAF).

44. The use of any one of claims 1-42, wherein the first antibody-drug conjugate is brentuximab vedotin or a biosimilar thereof.

45. The use of any one of claims 1-42, wherein the first antibody-drug conjugate is brentuximab vedotin.

46. The use of any one of claims 1-45, wherein the second antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to a camptothecin or a functional analog thereof or a functional derivative thereof forming a camptothecin conjugate of Formula (IC):



(IC)

or a pharmaceutically acceptable salt thereof, wherein:

L is the anti-CD30 antibody or an antigen-binding fragment thereof,

y is 1, 2, 3, or 4, or is 1 or 4,

z is an integer from 2 to 12, or is 2, 4, 8, or 12, and

p is 1-16, or is 2, 3, 4, 5, 6, 7, 8, 9, or 10, or is 2, 4 or 8.

47. The use of claim 46, wherein y is 1.

48. The use of claim 46 or 47, wherein z is 8.

49. The use of any one of claims 46-48, wherein p is 8.

50. The use of any one of claims 1-45, wherein the second antibody-drug conjugate is SGN-CD30C.

51. The use of any one of claims 1-50, wherein the first antibody-drug conjugate is to be administered at a dose of 0.1 mg/kg to 1.8 mg/kg of the subject's bodyweight.

52. The use of claim 51, wherein the first antibody-drug conjugate is to be administered at a dose of about 0.2 mg/kg of the subject's bodyweight.

53. The use of claim 51, wherein the first antibody-drug conjugate is to be administered at a dose of about 0.3 mg/kg of the subject's bodyweight.

54. The use of claim 51, wherein the first antibody-drug conjugate is to be administered at a dose of about 0.4 mg/kg of the subject's bodyweight.

55. The use of any one of claims 51-54, wherein the first antibody-drug conjugate is to be administered to a subject having a bodyweight of greater than 100 kg as if the subject had a bodyweight of 100 kg.

56. The use of any one of claims 1-55, wherein the first antibody-drug conjugate is to be administered to the subject once about every 3 weeks.

57. The use of any one of claims 1-55, wherein the first antibody-drug conjugate is to be administered to the subject once every 3 weeks.

58. The use of any one of claims 1-56, wherein the first antibody-drug conjugate is to be administered to the subject on about day 1 of about a 21-day treatment cycle.

59. The use of any one of claims 1-56, wherein the first antibody-drug conjugate is to be administered to the subject on day 1 of a 21-day treatment cycle.

60. The use of any one of claims 1-59, wherein the first antibody-drug conjugate is to be administered by intravenous infusion.

61. The use of any one of claims 1-60, wherein the second antibody-drug conjugate is to be administered at a dose of 0.01 mg/kg to 5 mg/kg of the subject's bodyweight.

62. The use of claim 61, wherein the second antibody-drug conjugate is to be administered at a dose of 0.1 mg/kg to 2 mg/kg of the subject's bodyweight.

63. The use of claim 61, wherein the second antibody-drug conjugate is to be administered at a dose of about 0.1 mg/kg of the subject's bodyweight.

64. The use of claim 61, wherein the second antibody-drug conjugate is to be administered at a dose of about 0.5 mg/kg of the subject's bodyweight.

65. The use of any one of claims 1-64, wherein the second antibody-drug conjugate is to be administered to the subject once about every 3 weeks.

66. The use of any one of claims 1-64, wherein the second antibody-drug conjugate is to be administered to the subject once every 3 weeks.

67. The use of any one of claims 1-65, wherein the second antibody-drug conjugate is to be administered to the subject on about day 1 of about a 21-day treatment cycle.

68. The use of any one of claims 1-65, wherein the second antibody-drug conjugate is to be administered to the subject on day 1 of a 21-day treatment cycle.

69. The use of any one of claims 1-68, wherein the second antibody-drug conjugate is to be administered by intravenous infusion.

70. The use of any one of claims 1-69 further comprising that granulocyte-colony stimulating factor (G-CSF) is to be administered to the subject.

71. The use of claim 70, wherein the G-CSF is to be administered 1 to 3 days after the first and/or second anti-CD30 antibody-drug conjugate is to be administered.

72. The use of claim 70 or 71, wherein the G-CSF is selected from the group consisting of filgrastim, PEG-filgrastim, lenograstim, and tbo-filgrastim.

73. The use of any one of claims 1-72, wherein the first and second antibody-drug conjugates to be administered to the subject results in a depletion of cancer cells by 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%,

at least about 80%, at least about 90%, at least about 95%, or about 100% compared to the amount of cancer cells before the first and second antibody-drug conjugates to be administered to the subject.

74. The use of any one of claims 1-73, wherein one or more therapeutic effects in the subject is improved after the first and second antibody-drug conjugates to be administered relative to a baseline.

75. The use of claim 74, wherein the one or more therapeutic effects is selected from the group consisting of: objective response rate, duration of response, time to response, progression free survival and overall survival.

76. The use of any one of claims 1-75, 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%.

77. The use of any one of claims 1-76, 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 the first and second antibody-drug conjugates to be administered.

78. The use of any one of claims 1-77, 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 the first and second antibody-drug conjugates to be administered.

79. The use of any one of claims 1-78, wherein the duration of response to the first and second antibody-drug conjugates 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 the first and second antibody-drug conjugates to be administered.

80. The use of any one of claims 1-79, wherein the subject is a human.

81. A pharmaceutical composition for use in the treatment of cancer in a subject, the composition comprising a first antibody-drug conjugate that binds to CD30, wherein the first antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to an auristatin or a functional analog thereof or a functional derivative thereof, and a second antibody-drug conjugate that binds to CD30, wherein the second antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to a camptothecin or a functional analog thereof or a functional derivative thereof.

82. A kit comprising a first antibody-drug conjugate that binds to CD30 and a second antibody-drug conjugate, wherein the first antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to an auristatin or a functional analog thereof or a functional derivative thereof, and the second antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to a camptothecin or a functional analog thereof or a functional derivative thereof, and instructions for using the kit to treat cancer in a subject.