anti-CD30 ADC include anti-PD-1 antibodies and a chemotherapeutic regimen comprising doxorubicin and dacarbazine.

[0009] Provided herein is a method for treating a hematologic cancer in a subject comprising administering a therapy comprising an anti-CD30 antibody drug conjugate and an anti-PD-1 antibody, doxorubicin and dacarbazine.

[0009a] In one aspect, the present disclosure provides the use of an anti-CD30 antibody drug conjugate and an anti-PD-1 antibody, and a chemotherapeutic regimen consisting essentially of doxorubicin and dacarbazine in the manufacture of a medicament for combination therapy to treat a hematologic cancer in a subject, wherein the anti-CD30 antibody of the anti-CD30 antibody drug conjugate comprises i) a heavy chain CDR1 set out in SEQ ID NO: 4, a heavy chain CDR2 set out in SEQ ID NO: 6, a heavy chain CDR3 set out in SEQ ID NO: 8; and ii) a light chain CDR1 set out in SEQ ID NO: 12, a light chain CDR2 set out in SEQ ID NO: 14, and a light chain CDR13 set out in SEQ ID NO: 16.

[0009b] In another aspect, the present disclosure provides the use of an anti-CD30 antibody drug conjugate in the manufacture of a first medicament and use of an anti-PD-1 antibody, and a chemotherapeutic regimen consisting essentially of doxorubicin and dacarbazine in the manufacture of a second medicament, the third medicament, and the fourth medicament, and wherein the first, the second, the third, and the fourth medicaments are to be used in combination therapy to treat a hematologic cancer in a subject, wherein the anti-CD30 antibody of the anti-CD30 antibody drug conjugate comprises i) a heavy chain CDR1 set out in SEQ ID NO: 4, a heavy chain CDR2 set out in SEQ ID NO: 6, a heavy chain CDR3 set out in SEQ ID NO: 8; and ii) a light chain CDR1 set out in SEQ ID NO: 12, a light chain CDR2 set out in SEQ ID NO: 14, and a light chain CDR13 set out in SEQ ID NO: 16.

[0009c] In another aspect, the present disclosure provides the use of an anti-CD30 antibody drug conjugate in the manufacture of a medicament for use in combinatorial therapy for treating a hematologic cancer in a subject, wherein said medicament is to be administered in combination with an anti-PD-1 antibody, and a chemotherapeutic regimen consisting essentially of doxorubicin and dacarbazine, wherein the anti-CD30 antibody of the anti-CD30 antibody drug conjugate comprises i) a heavy chain CDR1 set out in SEQ ID NO: 4, a heavy chain CDR2 set out in SEQ ID NO: 6, a heavy chain CDR3 set out in SEQ ID NO: 8; and ii) a light chain CDR1 set out in SEQ ID NO: 12, a light chain CDR2 set out in SEQ ID NO: 14, and a light chain CDR13 set out in SEQ ID NO: 16.

[0010] In various examples, the anti-PD-1 antibody is administered at least 30 minutes after each administration of anti-CD30 antibody drug conjugate. In various examples, the anti-CD30-antibody drug conjugate is administered by intravenous infusion over a period of about 30 minutes. In various examples, the anti-PD-1 antibody is administered by intravenous infusion for a duration of approximately 60 minutes.

[0011] In various examples, the anti-PD-1 antibody is administered to a subject that has not received anti-CD30 antibody drug conjugate therapy previously. In various examples, the anti-CD30 antibody drug conjugate is administered to a subject that has not received anti-CD30 antibody drug conjugate therapy previously. In various examples, the subject has not received checkpoint inhibitor therapy or an anti-PD-1 antibody previously.

[0012] In various examples, the anti-CD30 antibody drug conjugate and anti-PD-1 antibody are administered every 2 weeks. In various examples, the anti-PD-1 antibody is administered beginning with cycle 1 of the administration of anti-CD30 antibody drug conjugate. In various examples, the anti-CD30 antibody drug conjugate and anti-PD-1 antibody are administered on day 1 and day 15 of a 28-day cycle. In various examples, the anti-CD30 antibody drug conjugate and anti-PD-1 antibody are administered for no more than six cycles. In various examples, the anti-CD30 antibody drug conjugate and anti-PD-1 antibody are administered for four to six cycles.

[0013] In various examples, the method further comprises administering a chemotherapy consisting essentially of doxorubicin and dacarbazine (AD) as a combination therapy.

[0014] In various examples, the anti-CD30 antibody of the anti-CD30 antibody drug conjugate comprises i) a heavy chain CDR1 set out in SEQ ID NO: 4, a heavy chain CDR2 set out in SEQ ID NO: 6, a heavy chain CDR3 set out in SEQ ID NO: 8; and ii) a light chain CDR1 set out in SEQ ID NO: 12, a light chain CDR2 set out in SEQ ID NO: 14, and a light chain CDR13 set out in SEQ ID NO: 16.

[0015] In various examples, the anti-CD30 antibody of the anti-CD30 antibody drug conjugate comprises i) an amino acid sequence at least 85% identical to a heavy chain variable

WHAT IS CLAIMED:

1. Use of an anti-CD30 antibody drug conjugate and an anti-PD-1 antibody, and a chemotherapeutic regimen consisting essentially of doxorubicin and dacarbazine in the manufacture of a medicament for combination therapy to treat a hematologic cancer in a subject, wherein the anti-CD30 antibody of the anti-CD30 antibody drug conjugate comprises

i) a heavy chain CDR1 set out in SEQ ID NO: 4, a heavy chain CDR2 set out in SEQ ID NO: 6, a heavy chain CDR3 set out in SEQ ID NO: 8; and

ii) a light chain CDR1 set out in SEQ ID NO: 12, a light chain CDR2 set out in SEQ ID NO: 14, and a light chain CDR13 set out in SEQ ID NO: 16.

2. Use of an anti-CD30 antibody drug conjugate in the manufacture of a first medicament and use of an anti-PD-1 antibody, and a chemotherapeutic regimen consisting essentially of doxorubicin and dacarbazine in the manufacture of a second medicament, the third medicament, and the fourth medicament, and
wherein the first, the second, the third, and the fourth medicaments are to be used in combination therapy to treat a hematologic cancer in a subject, wherein the anti-CD30 antibody of the anti-CD30 antibody drug conjugate comprises

i) a heavy chain CDR1 set out in SEQ ID NO: 4, a heavy chain CDR2 set out in SEQ ID NO: 6, a heavy chain CDR3 set out in SEQ ID NO: 8; and

ii) a light chain CDR1 set out in SEQ ID NO: 12, a light chain CDR2 set out in SEQ ID NO: 14, and a light chain CDR13 set out in SEQ ID NO: 16.

3. Use of an anti-CD30 antibody drug conjugate in the manufacture of a medicament for use in combinatorial therapy for treating a hematologic cancer in a subject, wherein said medicament is to be administered in combination with an anti-PD-1 antibody, and a chemotherapeutic regimen consisting essentially of doxorubicin and dacarbazine, wherein the anti-CD30 antibody of the anti-CD30 antibody drug conjugate comprises

i) a heavy chain CDR1 set out in SEQ ID NO: 4, a heavy chain CDR2 set out in SEQ ID NO: 6, a heavy chain CDR3 set out in SEQ ID NO: 8; and

ii) a light chain CDR1 set out in SEQ ID NO: 12, a light chain CDR2 set out in SEQ ID NO: 14, and a light chain CDR13 set out in SEQ ID NO: 16.

4. The use of any one of claims 1-3, wherein the anti-PD-1 antibody is to be administered at least 30 minutes after each administration of anti-CD30 antibody drug conjugate.

5. The use of any one of claims 1-4, wherein the anti-PD-1 antibody is to be administered by intravenous infusion for a duration of approximately 60 minutes.

6. The use of any one of the preceding claims, wherein the anti-PD-1 antibody is to be administered to a subject that has not received anti-CD30 antibody drug conjugate therapy previously, and/or

wherein the anti-CD30 antibody drug conjugate is to be administered to a subject that has not received anti-CD30 antibody drug conjugate therapy previously.

7. The use of any one of the preceding claims, wherein the anti-CD30 antibody drug conjugate and anti-PD-1 antibody are to be administered every 2 weeks.

8. The use of any one of claims 1-3, wherein the anti-PD-1 antibody is to be administered beginning with cycle 1 of the administration of anti-CD30 antibody drug conjugate.

9. The use of any one of the preceding claims, wherein the anti-CD30 antibody drug conjugate and anti-PD-1 antibody are to be administered on day 1 and day 15 of a 28-day cycle.

10. The use of any one of the preceding claims, wherein the anti-CD30 antibody drug conjugate and anti-PD-1 antibody are to be administered for no more than six cycles, or are to be administered for four to six cycles.

11. The use of any one of the preceding claims, wherein the anti-CD30 antibody of the anti-CD30 antibody drug conjugate comprises

i) an amino acid sequence at least 85% identical to a heavy chain variable region set out in SEQ ID NO: 2 and

ii) an amino acid sequence at least 85% identical to a light chain variable region set out in SEQ ID NO: 10.

12. The use of any one of the preceding claims, wherein the anti-CD30 antibody of the anti-CD30 antibody drug conjugate is a monoclonal anti-CD30 antibody, optionally wherein the anti-CD30 antibody of the anti-CD30 antibody drug conjugate is a chimeric AC10 antibody.

13. The use of any one of the preceding claims, wherein the antibody drug conjugate comprises monomethyl auristatin E and a protease-cleavable linker.

14. The use of claim 13, i) wherein the protease cleavable linker comprises a thiolreactive spacer and a dipeptide, or ii) wherein the protease cleavable linker consists of a thiolreactive maleimidocaproyl spacer, a valine–citrulline dipeptide, and a p-amino-benzyloxycarbonyl spacer.

15. The use of any one of the preceding claims, wherein the anti-CD30 antibody drug conjugate is brentuximab vedotin.

16. The use of any one of the preceding claims, wherein (i) the anti-PD-1 antibody cross-competes with nivolumab or pembrolizumab for binding to human PD-1; (ii) the anti-PD-1 antibody binds to the same epitope as nivolumab or pembrolizumab; (iii) the anti-PD-1 antibody is nivolumab; or (iv) the anti-PD-1 antibody is pembrolizumab.

17. The use of any one of the preceding claims, wherein the hematologic cancer comprises one or more cells that express PD-L1, PD-L2, or both PD-L1 and PD-L2.

18. The use of any one of the preceding claims, wherein the hematologic cancer is a CD30-expressing cancer and the CD30 expression is ≥10%.

19. The use of any one of the preceding claims, wherein i) the anti-CD30 antibody drug conjugate is brentuximab vedotin and is to be administered at 1.2 mg/kg, and the anti-PD-1 antibody is nivolumab and is to be administered at 240 mg/dose, and/or ii) the anti-CD30 antibody drug conjugate is brentuximab vedotin and is to be administered at 1.2 mg/kg, and the anti-PD-1 antibody is pembrolizumab and is to be administered at a dose of 1-2 mg/kg, or 100-300 mg.

20. The use of claim 19, wherein doxorubicin is to be administered at dose of 25 mg/m^2, and dacarbazine is administered at a dose of 375 mg/m^2.

21. The use of any one of the preceding claims, further comprising that a granulopoiesis stimulating factor is to be administered.

22. The use of claim 21, i) wherein the granulopoiesis stimulating factor is to be administered prophylactically from 1 day to 7 days after administration of anti-CD30 antibody drug conjugate; ii) wherein the granulopoiesis stimulating factor is to be administered from 2 days to 5 days after the administration of anti-CD30 antibody drug conjugate; or iii) wherein the granulopoiesis stimulating factor is to be administered 24 hours to 36 hours after administration of anti-CD30 antibody drug conjugate.

23. The use of claim 21 or 22, wherein the granulopoiesis stimulating factor is to be administered in a dose range from 5 to 10 mcg/kg/day, or 300 to 600 mcg/day, or 6 mg/dose.

24. The use of any one of claims 21 to 23, wherein the granulopoiesis stimulating factor is to be administered to a subject that has not received anti-CD30 antibody drug conjugate therapy previously.

25. The use of any one of claims 21 to 24, wherein the granulopoiesis stimulating factor is to be given intravenously or subcutaneously.

26. The use of any one of the preceding claims, wherein if the subject exhibits Grade 3 or Grade 4 neuropathy, the administration of anti-CD30 antibody drug conjugate therapy is withheld until peripheral neuropathy decreases to Grade 2 or less and then 0.9 mg/kg anti-CD30 antibody drug conjugate therapy is to be administered.

27. The use of claim 26, wherein the neuropathy is motor neuropathy or sensory neuropathy.

28. The use of any one of the preceding claims, wherein the hematologic cancer is selected from the group consisting of classical Hodgkin Lymphoma, non-Hodgkin Lymphoma, cutaneous T-cell lymphoma (CTCL), and anaplastic large cell lymphoma (ALCL).

29. The use of claim 28, wherein i) the hematologic cancer is classical Hodgkin Lymphoma; ii) the anaplastic large cell lymphoma (ALCL) is a systemic anaplastic large cell lymphoma (sALCL); iii) the cutaneous T-cell lymphoma (CTCL) is a mycosis fungoides (MF); or iv) the cutaneous T-cell lymphoma (CTCL) is a primary cutaneous anaplastic large cell lymphoma (pcALCL).

30. The use of claim 29, wherein the hematologic cancer is a stage IIA with bulky disease, stage IIB, stage III or stage IV classical Hodgkin Lymphoma.

31. The use of claim 30, wherein the mycosis fungoides (MF) is a CD30-positive mycosis fungoides (MF).

32. The use of any one of claims 28 to 31, wherein the hematologic cancer of the subject has not been treated with a checkpoint inhibitor.

33. The use of any one of the preceding claims, wherein the subject is an adult patient.