SUMMARY

[8] In one example, the present disclosure provides for a method of decreasing the activity of $CD30^+$ T regulatory (Treg) cells in a subject having cancer comprising administering to the subject an antibody-drug conjugate, wherein the antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding portion thereof conjugated to a monomethyl auristatin.

[8a] In one aspect, the present disclosure refers to use of an antibody-drug conjugate in the manufacture of a medicament for decreasing the activity of CD30+ T regulatory (Treg) cells for treatment of cancer in a subject, wherein the antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding portion thereof conjugated to a monomethyl auristatin, wherein decreasing the activity of $CD30^+$ Treg cells comprises a decrease in the number of $CD30^+$ Treg cells relative to the number of one or more other types of $CD4^+$ T cells, wherein the one or more other types of $CD4^+$ T cells comprise Th1 cells, Th2 cells or Th17 cells, and wherein the CD30+ Treg cells are CD30+ inducible T regulatory (iTreg) cells or CD30+ peripheral T regulatory (pTreg) cells.

[9] In some examples, decreasing the activity of $CD30^+$ Treg cells comprises a decrease in the number of $CD30^+$ Treg cells. In some examples, the number of $CD30^+$ Treg cells is decreased relative to the number of one or more other types of $CD4^+$ T cells. In some examples, the one or more other types of $CD4^+$ T cells comprise Th1 cells, Th2 cells or Th17 cells. In some examples, the one or more other types of $CD4^+$ T cells comprise Th1 $CD30^+$ cells, Th2 $CD30^+$ cells or Th17 $CD30^+$ cells. In some examples, the number of $CD30^+$ Treg cells is decreased relative to the number of $CD30^+$ Treg cells in the subject prior to administration of the antibody-drug conjugate.

[10] In some examples, decreasing the activity of $CD30^+$ Treg cells comprises a decrease in the function of $CD30^+$ Treg cells. In some examples, the decrease in the function of $CD30^+$ Treg cells is relative to the function of $CD30^+$ Treg cells in a subject prior to administration of the antibody-drug conjugate.

[11] In some examples, the $CD30^+$ Treg cells are $CD30^+$ inducible T regulatory (iTreg) cells or $CD30^+$ peripheral T regulatory (pTreg) cells.

[12] In some examples, the monomethyl auristatin is monomethyl auristatin E (MMAE). In some examples, the monomethyl auristatin is monomethyl auristatin F (MMAF).

[13] In some examples, the anti-CD30 antibody is monoclonal anti-CD30 antibody AC10. In some examples, the anti-CD30 antibody is cAC10. In some examples, the antibody-drug conjugate is brentuximab vedotin.

[14] In some examples, the anti-CD30 antibody 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

CLAIMS

WHAT IS CLAIMED IS:

1. Use of an antibody-drug conjugate in the manufacture of a medicament for decreasing the activity of CD30+ T regulatory (Treg) cells for treatment of cancer in a subject, wherein the antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding portion thereof conjugated to a monomethyl auristatin, wherein decreasing the activity of $CD30^+$ Treg cells comprises a decrease in the number of $CD30^+$ Treg cells relative to the number of one or more other types of $CD4^+$ T cells, wherein the one or more other types of $CD4^+$ T cells comprise Th1 cells, Th2 cells or Th17 cells, and wherein the CD30+ Treg cells are CD30+ inducible T regulatory (iTreg) cells or CD30+ peripheral T regulatory (pTreg) cells.

2. The use of claim 1, wherein the one or more other types of $CD4^+$ T cells comprise Th1 $CD30^+$ cells, Th2 $CD30^+$ cells or Th17 $CD30^+$ cells.

3. The use of claim 1 or 2, wherein the number of $CD30^+$ Treg cells is decreased relative to the number of $CD30^+$ Treg cells in the subject prior to administration of the antibody-drug conjugate.

4. The use of any one of claims 1-3, wherein decreasing the activity of $CD30^+$ Treg cells comprises a decrease in the function of $CD30^+$ Treg cells.

5. The use of claim 4, wherein the decrease in the function of $CD30^+$ Treg cells is relative to the function of $CD30^+$ Treg cells in a subject prior to administration of the antibody-drug conjugate.

6. The use of any one of claims 1-5, wherein the anti-CD30 antibody is an IgG1 antibody.

7. The use of any one of claims 1-6, wherein the monomethyl auristatin is monomethyl auristatin E (MMAE).

8. The use of any one of claims 1-6, wherein the monomethyl auristatin is monomethyl auristatin F (MMAF).

9. The use of any one of claims 1-8, wherein the anti-CD30 antibody is a chimeric anti-CD30 antibody.

10. The use of claim 9, wherein the chimeric anti-CD30 antibody comprises variable regions derived from a mouse antibody and constant regions derived from a human antibody.

11. The use of any one of claims 1-10, wherein the anti-CD30 antibody 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.

12. The use of any one of claims 1-11, 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.

13. The use of any one of claims 1-11, wherein the anti-CD30 antibody of the 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.

14. The use of any one of claims 1-13, wherein the antibody-drug conjugate further comprises a linker between the anti-CD30 antibody or antigen-binding portion thereof and the monomethyl auristatin.

15. The use of claim 14, wherein the linker is a cleavable peptide linker.

16. The use of claim 15, wherein the cleavable peptide linker has a formula: -MC-vc-PAB-.

17. The use of any one of claims 1-16, wherein the antibody-drug conjugate is brentuximab vedotin.

18. The use of any one of claims 1-17, wherein the subject is a human patient.

19. The use of claim 18, wherein the subject has been previously treated for the cancer.

20. The use of claim 19, wherein the subject did not respond to treatment or relapsed after first-line treatment.

21. The use of claim 18, wherein the subject has not previously been treated for the cancer.

22. The use of any one of claims 18-21, wherein the cancer is a lymphoma.

23. The use of claim 22, wherein the lymphoma is a T-cell lymphoma.

24. The use of claim 22, wherein the lymphoma is a B-cell lymphoma.

25. The use of claim 22, wherein the lymphoma is a non-Hodgkin lymphoma.

26. The use of claim 25, wherein the non-Hodgkin lymphoma is a mature T-cell lymphoma.

27. The use of claim 25, wherein the non-Hodgkin lymphoma is diffuse large B-cell lymphoma (DLBCL), peripheral T-cell lymphoma (PTCL), anaplastic large cell lymphoma (ALCL) or cutaneous T-cell lymphoma (CTCL).

28. The use of claim 27, wherein the non-Hodgkin lymphoma is cutaneous T-cell lymphoma (CTCL).

29. The use of claim 27, wherein the non-Hodgkin lymphoma is anaplastic large cell lymphoma (ALCL).

30. The use of claim 22, wherein the lymphoma is a Hodgkin lymphoma.

31. The use of claim 30, wherein the subject has been previously treated for the Hodgkin lymphoma and the subject did not respond to treatment or relapsed after first-line treatment.

32. The use of claim 31, wherein the subject relapsed after autologous stem cell transplant.

33. The use of claim 31, wherein the subject relapsed after first-line treatment and the subject is ineligible for autologous stem cell transplant.

34. The use of claim 30, wherein the subject has not been previously treated for the Hodgkin lymphoma.

35. The use of claims 30-34, wherein the Hodgkin lymphoma is classical Hodgkin lymphoma (cHL).

36. The use of claim 35, wherein the classical Hodgkin lymphoma (cHL) is advanced cHL.

37. The use of any one of claims 1-36, wherein one or more additional therapeutic agents capable of modulating the immune response is to be further administered.

38. The use of claim 37, wherein the one or more additional therapeutic agents is not an antibody or antigen-binding fragment thereof.

39. The use of claim 37, wherein the one or more additional therapeutic agents is an antibody or antigen-binding fragment thereof.

40. The use of any one of claims 1-36, wherein one or more additional therapeutic agents is to be further administered.

41. The use of claim 40, wherein the one or more additional therapeutic agents is a chemotherapy regimen consisting essentially of doxorubicin, vinblastine, and dacarbazine (AVD).

42. The use of claim 40, wherein the one or more additional therapeutic agents is a chemotherapy regimen consisting essentially of Cyclophosphamide, Doxorubicin, and Prednisone (CHP).

43. The use of claim 40, wherein the one or more additional therapeutic agents is an alkylating agent, an anthracycline, an antibiotic, an antifolate, an antimetabolite, an antitubulin agent, an auristatin, a chemotherapy sensitizer, a DNA minor groove binder, a DNA replication inhibitor, a duocarmycin, an etoposide, a fluorinated pyrimidine, a lexitropsin, a nitrosourea, a platinol, a purine antimetabolite, a puromycin, a radiation sensitizer, a steroid, a taxane, a topoisomerase inhibitor, and/or a vinca alkaloid.

44. The use of claim 40, wherein the one or more additional therapeutic agents is selected from the group consisting of adriamycin, an androgen, anthramycin (AMC), asparaginase, 5-azacytidine, azathioprine, bleomycin, busulfan, buthionine sulfoximine, camptothecin, carboplatin, carmustine (BSNU), CC-1065, chlorambucil, cisplatin, colchicine, cyclophosphamide, cytarabine, cytidine arabinoside, cytochalasin B, dacarbazine, dactinomycin (formerly actinomycin), daunorubicin, docetaxel, doxorubicin, an estrogen, 5-fluordeoxyuridine, 5-fluorouracil, gramicidin D, hydroxydaunorubicin, hydroxyurea, idarubicin, ifosfamide, irinotecan, lomustine (CCNU), mechlorethamine, melphalan, 6-mercaptopurine, methotrexate, mithramycin, mitomycin C, mitoxantrone, nitroimidazole, paclitaxel, plicamycin, prednisone, prednisolone, procarbizine, streptozotocin, tenoposide, 6-thioguanine, thioTEPA, topotecan, vinblastine, vincristine, vinorelbine, VP-16 and VM-26.

45. The use of claim 18, wherein the subject has cHL that has not been previously treated and wherein the medicament is for use in combination with adriamycin, dacarbazine and vinblastine.

46. The use of claim 45, wherein the cHL is advanced cHL.

47. The use of claim 18, wherein the subject has a mature T-cell lymphoma that has not been previously treated and wherein the medicament is for use in combination with cyclophosphamide, hydroxydaunorubicin and prednisone.

48. The use of claim 18, wherein the subject has a mature T-cell lymphoma that has not been previously treated and wherein the medicament is for use in combination with cyclophosphamide, hydroxydaunorubicin and prednisolone.

49. The use of claim 40, wherein the one or more additional therapeutic agents is an antibody or antigen-binding fragment thereof.

50. The use of any one of claims 18-49, wherein the subject is to be further irradiated.

51. The use of claim 29, wherein the anaplastic large cell lymphoma (ALCL) is a systemic anaplastic large cell lymphoma (sALCL).

52. The use of claim 28, wherein the cutaneous T-cell lymphoma (CTCL) is a mycosis fungoides (MF).

53. The use of claim 52, wherein the mycosis fungoides (MF) is a CD30-positive mycosis fungoides (MF).

54. The use of claim 28, wherein the cutaneous T-cell lymphoma (CTCL) is a primary cutaneous anaplastic large cell lymphoma (pcALCL).

55. The use of claim 54, wherein the subject has received prior systemic therapy.