Efforts are also being made to incorporate new drugs into established backbones to improve efficacy and reduce toxicity (Borchmann et al., Blood 2015;126).

[0006] CD30 is a characteristic surface antigen expressed on the Reed-Sternberg cells of classical Hodgkin lymphoma (Schwab et al., Nature 1982;299:65-7). Brentuximab vedotin is an antibody-drug conjugate composed of an anti-CD30 monoclonal antibody conjugated by a protease-cleavable linker to the microtubule disrupting agent, monomethyl auristatin E. Brentuximab vedotin has been approved for the treatment of classical Hodgkin lymphoma patients after failure of autologous stem cell transplant (ASCT) or after failure of at least 2 prior multi-agent chemotherapy regimens in patients who are not ASCT candidates, and as consolidation post-ASCT for Hodgkin lymphoma patients at increased risk of relapse/progression (ADCETRIS® (brentuximab vedotin) US Prescribing Information). It has also been approved for systemic anaplastic large cell lymphoma after failure of at least one prior multi-agent chemotherapy regimen. A previous phase 1, dose-escalation study in advanced Hodgkin lymphoma evaluated frontline brentuximab vedotin combined with either ABVD or AVD (doxorubicin, vinblastine, dacarbazine) (Younes et al., Lancet Oncol 2013;14:1348-56).

[0007] Nivolumab is a fully-humanized monoclonal antibody (HuMAb; immunoglobulin G4 [IgG4]) that targets programmed cell death protein 1 (PD-1). In vitro, nivolumab binds to PD-1 with high affinity and inhibits the binding of PD-1 to its ligands PD-L1 and PD-L2 (IC50 ± 1 nM). Nivolumab binds specifically to PD-1 and not to related members of the CD28 family such as CD28, ICOS, CTLA-4 and BTLA. Nivolumab blocks the PD-1 pathway and results in a reproducible enhancement of both proliferation and interferon-gamma (IFN-γ) release in the mixed lymphocyte reaction (MLR). Previous trials have shown that treatment of patients with refractory Hodgkin Lymphoma with a combination of brentuximab vedotin and nivolumab is safe and patients were able to undergo subsequent stem cell transplant (Herrera et al., Blood 131(11): 1183-94.) The combination of nivolumab has also been shown to be well tolerated when combined with doxorubicin, vinblastine, and dacarbazine (N+AVD) (Ramchandren et al., J Clin Oncol 37(23): 1997-2007).

SUMMARY ~~OF THE DISCLOSURE~~

[0008] The present disclosure relates to methods of treating a hematologic cancer comprising administering an anti-CD30 antibody drug conjugate (ADC) in combination with cancer therapeutics as a front line treatment for previously undiagnosed cancers, or as a treatment for relapsed or refractory disease. Additional cancer therapeutics used in combination with the 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, doxorubicin and dacarbazine in the manufacture of a medicament for combination therapy to treat a hematologic cancer in a subject.

[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, 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.

[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, doxorubicin and dacarbazine.

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

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

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

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

[0014] In various ~~embodiment~~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 ~~embodiment~~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

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.

[0016] In various ~~embodiment~~examples, the anti-CD30 antibody of the anti-CD30 antibody drug conjugate is a monoclonal anti-CD30 antibody. In various ~~embodiment~~examples, the anti-CD30 antibody of the anti-CD30 antibody drug conjugate is a chimeric AC10 antibody. In various ~~embodiment~~examples, the antibody drug conjugate comprises monomethyl auristatin E and a protease-cleavable linker. In various ~~embodiment~~examples, the protease cleavable linker is comprises a thiolreactive spacer and a dipeptide. In various ~~embodiment~~examples, the protease cleavable linker consists of a thiolreactive maleimidocaproyl spacer, a valine–citrulline dipeptide, and a p-amino-benzyloxycarbonyl spacer. In various ~~embodiment~~examples, the anti-CD30 antibody drug conjugate is brentuximab vedotin.

[0017] In various ~~embodiment~~examples, the anti-PD-1 antibody is a monoclonal antibody. In various ~~embodiment~~examples, (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. In various ~~embodiment~~examples, the anti-PD-1 antibody is nivolumab or pembrolizumab. In various ~~embodiment~~examples, the anti-PD-1 antibody is nivolumab.

[0018] In various ~~embodiment~~examples, the hematologic cancer comprises one or more cells that express PD-L1, PD-L2, or both PD-L1 and PD-L2.

[0019] In various ~~embodiment~~examples, the hematologic cancer is a CD30-expressing cancer and the CD30 expression is ≥10%. In various ~~embodiment~~examples, the CD30 expression is measured by a FDA approved test.

[0020] In various ~~embodiment~~examples, the anti-CD30 antibody drug conjugate is brentuximab vedotin and is administered at 1.2 mg/kg, and the anti-PD-1 antibody is nivolumab and is administered at 240 mg/dose.

[0021] In various ~~embodiment~~examples, the anti-CD30 antibody drug conjugate is brentuximab vedotin and is administered at 1.2 mg/kg, and the anti-PD-1 antibody is pembrolizumab and is administered at a dose of 1-2 mg/kg, or 100-300 mg.

[0022] In various ~~embodiment~~examples, doxorubicin is administered at dose of 25 mg/m^2, and dacarbazine is administered at a dose of 375 mg/m^2.

[0023] In various ~~embodiment~~examples, the method further comprises administering a granulopoiesis stimulating factor. In various ~~embodiment~~examples, the granulopoiesis stimulating factor is administered from 1 day to 7 days after administration of anti-CD30 antibody drug conjugate. In various

~~embodiment~~examples, the granulopoiesis stimulating factor is administered from 2 days to 5 days after the administration of anti-CD30 antibody drug conjugate. In various ~~embodiment~~examples, the granulopoiesis stimulating factor is administered about 24 hours to about 36 hours after administration of anti-CD30 antibody drug conjugate.

[0024] In various ~~embodiment~~examples, the granulopoiesis stimulating factor is a granulocyte-colony stimulating factor (GCSF). In various ~~embodiment~~examples, the GCSF is a long-acting GCSF or a non long-acting GCSF. In various ~~embodiment~~examples, the GCSF is long-acting GCSF, and is administered 1 day or 2 days after the administration of anti-CD30 antibody drug conjugate. In various ~~embodiment~~examples, the G-CSF is administered about 24 hours to about 36 hours after administration of anti-CD30 antibody drug conjugate. In various ~~embodiment~~examples, the GCSF is not long acting, and is administered 1, 2, 3, 4, 5, 6 or 7 days after the administration of anti-CD30 antibody drug conjugate.

[0025] In various ~~embodiment~~examples, the granulopoiesis stimulating factor is administered in a dose range from 5 to 10 mcg/kg/day, or 300 to 600 mcg/day, or 6 mg/dose.

[0026] In various ~~embodiment~~examples, the granulopoiesis stimulating factor is administered to a subject that has not received anti-CD30 antibody drug conjugate therapy previously.

[0027] In various ~~embodiment~~examples, the subject has not experienced treatment-emergent grade 3-4 neutropenia after anti-CD30 antibody drug conjugate administration. In various ~~embodiment~~examples, the granulopoiesis stimulating factor is given intravenously or subcutaneously. In various ~~embodiment~~examples, the granulopoiesis stimulating factor is given in a single dose or multiple doses.

[0028] In various ~~embodiment~~examples, 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 administered. In various ~~embodiment~~examples, the neuropathy is motor neuropathy or sensory neuropathy. In various ~~embodiment~~examples, the dose of anti-CD30 antibody drug conjugate is delayed by one week if peripheral neuropathy appears, and therapy is continued when the neuropathy is resolved or determined to be Grade 1 or less.

[0029] In various ~~embodiment~~examples, the hematologic cancer is a CD30-expressing hematologic cancer. In various ~~embodiment~~examples, 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).

[0030] In various ~~embodiment~~examples, the hematologic cancer is classical Hodgkin Lymphoma. In various ~~embodiment~~examples, the hematologic cancer is a stage IIA with bulky disease, stage IIB, stage III or stage IV classical Hodgkin Lymphoma.

[0031] In various ~~embodiment~~examples, the anaplastic large cell lymphoma (ALCL) is a systemic anaplastic large cell lymphoma (sALCL).

[0032] In various ~~embodiment~~examples, the cutaneous T-cell lymphoma (CTCL) is a mycosis fungoides (MF). In various ~~embodiment~~examples, the mycosis fungoides (MF) is a CD30-positive mycosis fungoides (MF). In various ~~embodiment~~examples, the cutaneous T-cell lymphoma (CTCL) is a primary cutaneous anaplastic large cell lymphoma (pcALCL).

[0033] In various ~~embodiment~~examples, the hematologic cancer of the subject has not been treated with a checkpoint inhibitor. In various ~~embodiment~~examples, the subject has received prior systemic therapy.

[0034] In various ~~embodiment~~examples, the subject is an adult patient.

[0035] It is specifically provided herein that all aspects of the disclosure described above with the methods of treatment are applicable to the anti-CD30 antibody drug conjugate combination therapy for use in any of the indications described above.

[0036] It is understood that each feature or ~~embodiment~~example, or combination, described herein is a non-limiting, illustrative example of any of the aspects of the disclosure and, as such, is meant to be combinable with any other feature or ~~embodiment~~example, or combination, described herein. For example, where features are described with language such as “one ~~embodiment~~example”, “some ~~embodiment~~examples”, “certain ~~embodiment~~examples”, “further ~~embodiment~~example”, “specific exemplary ~~embodiment~~examples”, and/or “another ~~embodiment~~example”, each of these types of ~~embodiment~~examples is a non-limiting example of a feature that is intended to be combined with any other feature, or combination of features, described herein without having to list every possible combination. Such features or combinations of features apply to any of the aspects of the disclosure. Where examples of values falling within ranges are disclosed, any of these examples are contemplated as possible endpoints of a range, any and all numeric values between such endpoints are contemplated, and any and all combinations of upper and lower endpoints are envisioned.

BRIEF DESCRIPTION OF THE FIGURES

[0037] Figure 1. Details of Brentuximab Vedotin Dose Modifications

WHAT IS CLAIMED:

1. ~~A method for treating a hematologic cancer in a subject comprising administering a therapy comprising~~ Use of an anti-CD30 antibody drug conjugate and an anti-PD-1 antibody, doxorubicin and dacarbazine in the manufacture of a medicament for combination therapy to treat a hematologic cancer in a subject.

2. Use of an anti-CD30 antibody drug conjugate in the manufacture of a first medicament and use of an anti-PD-1 antibody, 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.

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, doxorubicin and dacarbazine.

4. The use ~~method~~ 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.

~~3~~5. The use ~~method~~ of any one of claims 1-4 ~~or 2~~, wherein the anti-PD-1 antibody is to be administered by intravenous infusion for a duration of approximately 60 minutes.

~~4~~6. The use ~~method~~ 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.

~~5. The method of any one of the preceding claims, wherein the anti-CD30 antibody drug conjugate is administered to a subject that has not received anti-CD30 antibody drug conjugate therapy previously.~~

~~6~~7. The use ~~method~~ 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.

~~7~~8. The use ~~method~~ 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.

~~8~~9. The use ~~method~~ 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.

~~9~~10. The use ~~method~~ 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.

~~10. The method of any one of the preceding claims, wherein the anti-CD30 antibody drug conjugate and anti-PD-1 antibody are administered for four to six cycles.~~

11. The use ~~method~~ of any one of the preceding claims further comprising that ~~administering~~ a chemotherapy consisting essentially of doxorubicin and dacarbazine (AD) is to be administered as a combination therapy.

12. The use ~~method~~ of any one of the preceding claims, 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.

13. The use ~~method~~ 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.

14. The use ~~method~~ 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.

~~15. The method of any one of the preceding claims, wherein the anti-CD30 antibody of the anti-CD30 antibody drug conjugate is a chimeric AC10 antibody.~~

~~16~~15. The use ~~method~~ of any one of the preceding claims, wherein the antibody drug conjugate comprises monomethyl auristatin E and a protease-cleavable linker.

~~17~~16. The use ~~method~~ of claim ~~16~~15, i) wherein the protease cleavable linker ~~is~~ 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.

~~18. The method of claim 16 or 17, wherein the protease cleavable linker consists of a thiolreactive maleimidocaproyl spacer, a valine–citrulline dipeptide, and a p-amino-benzyloxycarbonyl spacer.~~

~~19~~17. The use ~~method~~ of any one of the preceding claims, wherein the anti-CD30 antibody drug conjugate is brentuximab vedotin.

~~20~~18. The use ~~method~~ 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.

~~21. The method of any one of the preceding claims, wherein the anti-PD-1 antibody is nivolumab or pembrolizumab.~~

~~22. The method of any one of the preceding claims, wherein the anti-PD-1 antibody is nivolumab.~~

~~23~~19. The use ~~method~~ 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.

2420. The use ~~method~~ of any one of the preceding claims, wherein the hematologic cancer is a CD30-expressing cancer and the CD30 expression is ≥10%.

~~25. The method of claim 24, wherein the CD30 expression is measured by a FDA approved test.~~

2621. The use ~~method~~ 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.

~~27. The method of any one of the preceding claims, wherein the anti-CD30 antibody drug conjugate is brentuximab vedotin and is administered at 1.2 mg/kg, and the anti-PD-1 antibody is pembrolizumab and is administered at a dose of 1-2 mg/kg, or 100-300 mg.~~

2822. The use ~~method~~ of claim ~~26 or 27~~21, 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.

2923. The use ~~method~~ of any one of the preceding claims, further comprising that ~~administering~~ a granulopoiesis stimulating factor is to be administered.

3024. The use ~~method~~ of claim ~~29~~23, 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 about 24 hours to about 36 hours after administration of anti-CD30 antibody drug conjugate.

~~31. The method of any one of claims 29 or 30, wherein the granulopoiesis stimulating factor is administered from 2 days to 5 days after the administration of anti-CD30 antibody drug conjugate.~~

~~32. The method of any one of claims 29 to 31, wherein the granulopoiesis stimulating factor is administered about 24 hours to about 36 hours after administration of anti-CD30 antibody drug conjugate.~~

~~33. The method of any one of claims 29 to 32, wherein the granulopoiesis stimulating factor is a granulocyte-colony stimulating factor (GCSF).~~

~~34. The method of claim 33, wherein the GCSF is a long-acting GCSF or a non long-acting GCSF.~~

~~35. The method of claim 33 or 34, wherein the GCSF is long-acting GCSF, and is administered 1 day or 2 days after the administration of anti-CD30 antibody drug conjugate.~~

~~36. The method of claim 35, wherein the G-CSF is administered about 24 hours to about 36 hours after administration of anti-CD30 antibody drug conjugate.~~

~~37. The method of claim 33 or 34, wherein the GCSF is not long acting, and is administered 1, 2, 3, 4, 5, 6 or 7 days after the administration of anti-CD30 antibody drug conjugate.~~

~~38~~25. The use ~~method~~ of ~~any one of~~ claim~~s 29 to 37~~23 or 24, 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.

~~39~~26. The use ~~method~~ of any one of claims ~~29 to 38~~23 to 25, wherein the granulopoiesis stimulating factor is to be administered to a subject that has not received anti-CD30 antibody drug conjugate therapy previously.

~~40. The method of any one of claims 29 to 39, wherein the subject has not experienced treatment-emergent grade 3-4 neutropenia after anti-CD30 antibody drug conjugate administration.~~

~~41~~27. The use ~~method~~ of any one of claims ~~29~~ 23 to ~~40~~26, wherein the granulopoiesis stimulating factor is to be given intravenously or subcutaneously.

~~42. The method of any one of claims 29 to 41, wherein the granulopoiesis stimulating factor is given in a single dose or multiple doses.~~

43~~28~~. The use ~~method~~ 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.

44~~29~~. The use ~~method~~ of claim 43~~28~~, wherein the neuropathy is motor neuropathy or sensory neuropathy.

~~45. The method of any one of the preceding claims, wherein the dose of anti-CD30 antibody drug conjugate is delayed by one week if peripheral neuropathy appears, and therapy is continued when the neuropathy is resolved or determined to be Grade 1 or less.~~

46~~30~~. The use ~~method~~ 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).

47~~31~~. The use ~~method~~ of claim 46~~30~~, 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).

48~~32~~. The use ~~method~~ of claim 47~~31~~, wherein the hematologic cancer is a stage IIA with bulky disease, stage IIB, stage III or stage IV classical Hodgkin Lymphoma.

~~49. The method of claim 46, wherein the anaplastic large cell lymphoma (ALCL) is a systemic anaplastic large cell lymphoma (sALCL).~~

~~50. The method of claim 46, wherein the cutaneous T-cell lymphoma (CTCL) is a mycosis fungoides (MF).~~

~~51~~33. The use ~~method~~ of claim 32 ~~50~~, wherein the mycosis fungoides (MF) is a CD30-positive mycosis fungoides (MF).

~~52. The method of claim 46, wherein the cutaneous T-cell lymphoma (CTCL) is a primary cutaneous anaplastic large cell lymphoma (pcALCL).~~

~~53. The method of claim 52, wherein the subject has received prior systemic therapy.~~

~~54~~34. The use ~~method~~ of any one of claims ~~45~~ 30 to ~~53~~33, wherein the hematologic cancer of the subject has not been treated with a checkpoint inhibitor.

~~55~~35. The use ~~method~~ of any one of the preceding claims, wherein the subject is an adult patient.