BRIEF SUMMARY

[0008] ~~In one aspect, p~~Provided herein are methods for treating or delaying progression of cancer in an individual comprising administering to the individual an effective amount of a PD-1 axis binding antagonist and an anti-CD20 antibody.

[0009] ~~In another aspect,~~Also provided herein are methods of enhancing immune function in an individual having cancer comprising administering an effective amount of a combination of a PD-1 axis binding antagonist and an anti-CD20 antibody. In some embodiments, CD8 T cells in the individual have enhanced priming, activation, proliferation and/or cytolytic activity relative to prior to the administration of the combination. In some embodiments, the CD8 T cell activation is characterized by an elevated frequency of γ-IFN$^+$ CD8 T cells and/or enhanced cytolytic activity relative to prior to administration of the combination. In some embodiments, the number of CD8 T cells is elevated relative to prior to administration of the combination. In some embodiments, the CD8 T cell is an antigen-specific CD8 T cell.

[0009a] In one aspect, provided herein is use of an effective amount of a PD-1 axis binding antagonist and an anti-CD20 antibody for the manufacture of a first medicament comprising the PD-1 axis binding antagonist and a second medicament comprising the anti-CD20 antibody for treating or delaying progression of cancer in an individual.

[0010] In another aspect, provided herein is use of an effective amount of a PD-1 axis binding antagonist in the manufacture of a medicament for treating or delaying progression of cancer in an individual, wherein the PD-1 axis binding agent is used in combination with an anti-CD20 antibody. In one embodiment, there is provided use of a human PD-1 axis binding antagonist in the manufacture of a medicament for treating or delaying progression of cancer in an individual, wherein the medicament comprises the human PD-1 axis binding antagonist and an optional pharmaceutically acceptable carrier, and wherein the treatment comprises administration of the medicament in combination with a composition comprising an anti-CD20 antibody and an optional pharmaceutically acceptable carrier.

[0011] In another aspect, provided herein is use of an effective amount of an anti-CD20 antibody in the manufacture of a medicament for treating or delaying progression of cancer in an individual, wherein the anti-CD20 antibody is used in combination with a PD-1 axis binding antagonist. In one embodiment, there is provided use of an anti-CD20 antibody in the manufacture of a medicament for treating or delaying progression of cancer in an individual, wherein the medicament comprises the anti-CD20 antibody and an optional pharmaceutically acceptable carrier, and wherein the treatment comprises administration of the medicament in combination with a composition comprising a human PD-1 axis binding antagonist and an optional pharmaceutically acceptable carrier.

[0011a] In one aspect, provided herein is a pharmaceutical composition comprising a PD-1 axis binding antagonist in combination with an anti-CD20 antibody for use in treating or delaying progression of cancer.

[0012] In another aspect, provided herein is a pharmaceutical composition comprising a PD-1 axis binding antagonist for use in treating or delaying progression of cancer in combination with an anti-CD20 antibody. In one embodiment, there is provided a composition comprising a human PD-1 axis binding antagonist and an optional pharmaceutically acceptable carrier for use in treating or delaying progression of cancer in an individual, wherein the treatment comprises administration of said composition in combination with a second composition, wherein the second composition comprises an anti-CD20 antibody and an optional pharmaceutically acceptable carrier.

[0013] In another aspect, provided herein is a pharmaceutical composition comprising an anti-CD20 antibody for use in treating or delaying progression of cancer in combination with a PD-1 axis binding antagonist. In one embodiment, there is provided a composition comprising an anti-CD20 antibody and an optional pharmaceutically acceptable carrier for use in treating or delaying progression of

cancer in an individual, wherein the treatment comprises administration of said composition in combination with a second composition, wherein the second composition comprises a human PD-1 axis binding antagonist and an optional pharmaceutically acceptable carrier.

[0013a] In one aspect, provided herein is use of an effective amount of a PD-1 axis binding antagonist and an anti-CD20 antibody for the manufacture of a first medicament comprising the PD-1 axis binding antagonist and a second medicament comprising the anti-CD20 antibody for enhancing immune function in an individual having cancer.

[0014] In another aspect, provided herein is use of an effective amount of a PD-1 axis binding antagonist in the manufacture of a medicament for enhancing immune function in an individual having cancer, wherein the PD-1 axis binding agent is used in combination with an anti-CD20 antibody. In one embodiment, there is provided use of a human PD-1 axis binding antagonist in the manufacture of a medicament for enhancing immune function in an individual having cancer, wherein the medicament comprises the human PD-1 axis binding antagonist and an optional pharmaceutically acceptable carrier, and wherein the treatment comprises administration of the medicament in combination with a composition comprising an anti-CD20 antibody and an optional pharmaceutically acceptable carrier. In some embodiments, CD8 T cells in the individual have enhanced priming, activation, proliferation and/or cytolytic activity relative to prior to the administration of the combination. In some embodiments, the CD8 T cell activation is characterized by an elevated frequency of γ-IFN$^+$ CD8 T cells and/or enhanced cytolytic activity relative to prior to administration of the combination. In some embodiments, the number of CD8 T cells is elevated relative to prior to administration of the combination. In some embodiments, the CD8 T cell is an antigen-specific CD8 T cell.

[0015] In another aspect, provided herein is use of an effective amount of an anti-CD20 antibody in the manufacture of a medicament for enhancing immune function in an individual having cancer, wherein the anti-CD20 antibody is used in combination with a PD-1 axis binding antagonist. In one embodiment, there is provided use of an anti-CD20 antibody in the manufacture of a medicament for enhancing immune function in an individual having cancer, wherein the medicament comprises the anti-CD20 antibody and an optional pharmaceutically acceptable carrier, and wherein the treatment comprises administration of the medicament in combination with a composition comprising a human PD-1 axis binding antagonist and an optional pharmaceutically acceptable carrier. In some embodiments, CD8 T cells in the individual have enhanced priming, activation, proliferation and/or cytolytic activity relative to prior to the administration of the combination. In some embodiments, the CD8 T cell activation is characterized by an elevated frequency of γ-IFN$^+$ CD8 T cells and/or enhanced cytolytic activity relative to prior to administration of the combination. In some embodiments, the number of CD8 T cells is elevated relative to prior to administration of the combination. In some embodiments, the CD8 T cell is an antigen-specific CD8 T cell.

[0015a] In one aspect, provided herein is a pharmaceutical composition comprising a PD-1 axis binding antagonist in combination with an anti-CD20 antibody for use in enhancing immune function.

[0016] In another aspect, provided herein is a pharmaceutical composition comprising a PD-1 axis binding antagonist for use in enhancing immune function in combination with an anti-CD20 antibody. In one embodiment, there is provided a composition comprising a human PD-1 axis binding antagonist and an optional pharmaceutically acceptable carrier for use in enhancing immune function in an individual having cancer, wherein the treatment comprises administration of said composition in combination with a second composition, wherein the second composition comprises an anti-CD20 antibody and an optional pharmaceutically acceptable carrier. In some

embodiments, CD8 T cells in the individual have enhanced priming, activation, proliferation and/or cytolytic activity relative to prior to the administration of the combination. In some embodiments, the CD8 T cell activation is characterized by an elevated frequency of γ-IFN$^+$ CD8 T cells and/or enhanced cytolytic activity relative to prior to administration of the combination. In some embodiments, the number of CD8 T cells is elevated relative to prior to administration of the combination. In some embodiments, the CD8 T cell is an antigen-specific CD8 T cell.

[0017] In another aspect, provided herein is a pharmaceutical composition comprising an anti-CD20 antibody for use in enhancing immune function in combination with a PD-1 axis binding antagonist. In one embodiment, there is provided a composition comprising an anti-CD20 antibody and an optional pharmaceutically acceptable carrier for use in enhancing immune function in an individual having cancer, wherein the treatment comprises administration of said composition in combination with a second composition, wherein the second composition comprises a human PD-1 axis binding antagonist and an optional pharmaceutically acceptable carrier. In some embodiments, CD8 T cells in the individual have enhanced priming, activation, proliferation and/or cytolytic activity relative to prior to the administration of the combination. In some embodiments, the CD8 T cell activation is characterized by an elevated frequency of γ-IFN$^+$ CD8 T cells and/or enhanced cytolytic activity relative to prior to administration of the combination. In some embodiments, the number of CD8 T cells is elevated relative to prior to administration of the combination. In some embodiments, the CD8 T cell is an antigen-specific CD8 T cell.

[0018] In some embodiments of the methods, uses, compositions, and kits described above and herein, the cancer is a non-solid tumor. In some embodiments, the cancer is a lymphoma or a leukemia. In some embodiments, the leukemia is chronic lymphocytic leukemia (CLL) or acute myeloid leukemia (AML). In some embodiments, the lymphoma is follicular lymphoma (FL), diffuse large B-cell lymphoma (DLBCL), or Non-Hodgkin's lymphoma (NHL).

[0019] In some embodiments of the methods, uses, compositions, and kits described above and herein, the PD-1 axis binding antagonist is selected from the group consisting of a PD-1 binding antagonist, a PD-L1 binding antagonist and a PD-L2 binding antagonist. In some embodiments, the PD-1 axis binding antagonist is a PD-1 binding antagonist. In some embodiments, the PD-1 binding antagonist inhibits the binding of PD-1 to its ligand binding partners. In some embodiments, the PD-1 binding antagonist inhibits the binding of PD-1 to PD-L1, PD-1 to PD-L2, or PD-1 to both PD-L1 and PD-L2. In some embodiments, the PD-1 binding antagonist is an antibody. In some embodiments, the PD-1 binding antagonist is MDX-

[0023] In another aspect, provided herein are kits comprising a PD-1 axis binding antagonist and a package insert comprising instructions for using the PD-1 axis binding antagonist in combination with an anti-CD20 antibody to treat or delay progression of cancer in an individual. In another aspect, provided herein are kits comprising a PD-1 axis binding antagonist and an anti-CD20 antibody. In some embodiments, the kits further comprise a package insert comprising instructions for using the PD-1 axis binding antagonist and the anti-CD20 antibody to treat or delay progression of cancer in an individual. In another aspect, provided herein are kits comprising an anti-CD20 antibody and a package insert comprising instructions for using the anti-CD20 antibody in combination with a PD-1 axis binding antagonist to treat or delay progression of cancer in an individual. ~~In another aspect,~~ Also provided herein are kits comprising a PD-1 axis binding antagonist and a package insert comprising instructions for using the PD-1 axis binding antagonist in combination with an anti-CD20 antibody to enhance immune function in an individual having cancer. ~~In another aspect,~~Further provided herein are kits comprising a PD-1 axis binding antagonist and an anti-CD20 antibody, and a package insert comprising instructions for using the PD-1 axis binding antagonist and the anti-CD20 antibody to enhance immune function in an individual having cancer. ~~In another aspect,~~Yet further provided herein are kits comprising an anti-CD20 antibody and a package insert comprising instructions for using the anti-CD20 antibody in combination with a PD-1 axis binding antagonist to enhance immune function in an individual having cancer.

[0024] In some embodiments the methods, uses, compositions and kits described above and herein, the individual is a human. In some embodiments, the individual has cancer or has been diagnosed with cancer. In some embodiments, the individual is suffering from replaced or refractory cancer (e.g., a non-solid tumor). In some embodiments, the individual is suffering from leukemia (e.g., CLL, AML) or lymphoma (e.g., NHL). In some embodiments, the individual is suffering from relapsed or refractory or previously untreated CLL. In some embodiments, the individual is suffering from refractory or relapsed follicular lymphoma or diffuse large B-cell lymphoma (DLBCL).

[0025] It is to be understood that one, some, or all of the properties of the various embodiments described herein may be combined to form other embodiments of the present ~~invention~~disclosure. These and other aspects of the invention will become apparent to one of skill in the art. These and other embodiments of the ~~invention~~ disclosure are further described by the detailed description that follows.

CLAIMS

What is claimed is:

1. A method for treating or delaying progression of cancer in an individual comprising administering to the individual an effective amount of a PD-1 axis binding antagonist and an anti-CD20 antibody.

2. The method of claim 1, wherein the PD-1 axis binding antagonist is selected from the group consisting of a PD-1 binding antagonist, a PD-L1 binding antagonist and a PD-L2 binding antagonist.

3. The method of claim 2, wherein the PD-1 axis binding antagonist is a PD-1 binding antagonist.

4. The method of claim 3, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to its ligand binding partners.

5. The method of claim 4, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to PD-L1.

6. The method of claim 4, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to PD-L2.

7. The method of claim 4, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to both PD-L1 and PD-L2.

8. The method of claim 4, wherein the PD-1 binding antagonist is an antibody.

9. The method of claim 8, wherein the PD-1 binding antagonist is MDX-1106.

10. The method of claim 8, wherein the PD-1 binding antagonist is Merck 3745.

11. The method of claim 8, wherein the PD-1 binding antagonist is CT-011.

12. The method of claim 4, wherein the PD-1 binding antagonist is AMP-224.

13. The method of claim 2, wherein the PD-1 axis binding antagonist is a PD-L1 binding antagonist.

14. The method of claim 13, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to PD-1.

15. The method of claim 13, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to B7-1.

16. The method of claim 13, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to both PD-1 and B7-1.

17. The method of claim 13, wherein the PD-L1 binding antagonist is an anti-PD-L1 antibody.

18. The method of claim 17, wherein the anti-PD-L1 antibody is a monoclonal antibody.

19. The method of claim 17, wherein the anti-PD-L1 antibody is an antibody fragment selected from the group consisting of Fab, Fab'-SH, Fv, scFv, and $(Fab')_2$ fragments.

20. The method of any one of claims 17-19, wherein the anti-PD-L1 antibody is a humanized antibody or a human antibody.

21. The method of claim 13, wherein the PD-L1 binding antagonist is selected from the group consisting of: YW243.55.S70, MPDL3280A, MDX-1105, and MEDI4736.

22. The method of claim 17, wherein the anti-PD-L1 antibody comprises a heavy chain comprising HVR-H1 sequence of SEQ ID NO:15, HVR-H2 sequence of SEQ ID NO:16, and HVR-H3 sequence of SEQ ID NO:3; and a light chain comprising HVR-L1 sequence of SEQ ID NO:17, HVR-L2 sequence of SEQ ID NO:18, and HVR-L3 sequence of SEQ ID NO:19.

23. The method of claim 17, wherein the anti-PD-L1 antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:24 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:21.

24. The method of claim 2, wherein the PD-1 axis binding antagonist is a PD-L2 binding antagonist.

25. The method of claim 24, wherein the PD-L2 binding antagonist is an antibody.

26. The method of claim 24, wherein the PD-L2 binding antagonist is an immunoadhesin.

27. The method of any one of claims 8, 17-23, and 25, wherein the antibody is a human IgG1 having Asn to Ala substitution at position 297 according to EU numbering.

28. The method of any one of claims 1-27, wherein the anti-CD20 antibody is a humanized B-Ly1 antibody.

29. The method of any one of claims 1-27, wherein the anti-CD20 antibody is a GA101 antibody.

30. The method of claim 29, wherein the GA101 is an anti-human CD20 antibody comprising an HVR-H1 comprising the amino acid sequence of SEQ ID NO:50, an HVR-H2 comprising the amino acid sequence of SEQ ID NO:51, an HVR-H3 comprising the amino acid sequence of SEQ ID NO:52, an HVR-L1 comprising the amino acid sequence of SEQ ID NO:53, an HVR-L2 comprising the amino acid sequence of SEQ ID NO:54, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO:55.

31. The method of claim 30, wherein the GA101 antibody comprises a VH domain comprising the amino acid sequence of SEQ ID NO:56 and a VL domain comprising the amino acid sequence of SEQ ID NO:57.

32. The method of claim 30, wherein the GA101 antibody comprises an amino acid sequence of SEQ ID NO:58 and an amino acid sequence of SEQ ID NO:59.

33. The method of claim 30, wherein the GA101 antibody is obinutuzumab.

34. The method of claim 30, wherein the GA101 antibody comprises an amino acid sequence that has at least 95% sequence identity with amino acid sequence of SEQ ID NO:58 and that comprises an amino acid sequence that has at least 95% sequence identity with an amino acid sequence of SEQ ID NO:59.

35. The method of any one of claims 1-27, wherein the anti-CD20 antibody is a multispecific antibody.

36. The method of any one of claims 1-27, wherein the anti-CD20 antibody is a bispecific antibody.

37. The method of any one of claims 1-36, wherein the individual is a human.

38. The method of any one of claims 1-37, wherein the individual has cancer or has been diagnosed with cancer.

39. The method of any one of claims 1-38, wherein the cancer is a CD20-expressing cancer.

40. The method of any one of claims 1-39, wherein the cancer is a non-solid tumor.

41. The method of claim 40, wherein the cancer is a lymphoma or a leukemia.

42. The method of claim 41, wherein the leukemia is chronic lymphocytic leukemia (CLL) or acute myeloid leukemia (AML).

43. The method of claim 41, wherein the lymphoma is Non-Hodgkin's lymphoma (NHL).

44. The method of claim 39 or 40, wherein the individual is suffering from relapsed or refractory or previously untreated chronic lymphocytic leukemia.

45. The method of claim 44, wherein the individual is suffering from refractory or relapsed follicular lymphoma or diffuse large B-cell lymphoma (DLBCL).

46. The method of any one of claims 1-45, wherein the treatment results in a sustained response in the individual after cessation of the treatment.

47. The method of any of claims 1-46, wherein the anti-CD20 antibody or the PD-1 axis binding antagonist is administered continuously or intermittently.

48. The method of any of claims 1-47, wherein the anti-CD20 antibody is administered before the PD-1 axis binding antagonist.

49. The method of any of claims 1-47, wherein the anti-CD20 antibody is administered simultaneous with the PD-1 axis binding antagonist.

50. The method of any of claims 1-47, wherein the anti-CD20 antibody is administered after the PD-1 axis binding antagonist.

51. A method of enhancing immune function in an individual having cancer comprising administering an effective amount of a combination of a PD-1 axis binding antagonist and an anti-CD20 antibody.

52. The method of claim 51, wherein CD8 T cells in the individual have enhanced priming, activation, proliferation and/or cytolytic activity relative to prior to the administration of the combination.

53. The method of claim 51, wherein the CD8 T cell activation is characterized by an elevated frequency of γ-IFN$^+$ CD8 T cells and/or enhanced cytolytic activity relative to prior to administration of the combination.

54. The method of claim 51, wherein the number of CD8 T cells is elevated relative to prior to administration of the combination.

55. The method of any one of claims 51-54, wherein the CD8 T cell is an antigen-specific CD8 T cell.

56. The method of any one of claims 51-55, wherein the PD-1 axis binding antagonist is selected from the group consisting of a PD-1 binding antagonist, a PD-L1 binding antagonist and a PD-L2 binding antagonist.

57. The method of claim 56, wherein the PD-1 axis binding antagonist is a PD-1 binding antagonist.

58. The method of claim 57, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to its ligand binding partners.

59. The method of claim 57, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to PD-L1.

60. The method of claim 57, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to PD-L2.

61. The method of claim 57, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to both PD-L1 and PD-L2.

62. The method of claim 57, wherein the PD-1 binding antagonist is an anti-PD-1 antibody.

63. The method of claim 62, wherein the PD-1 binding antagonist is MDX-1106, Merck 3745, or CT-011.

64. The method of claim 57, wherein the PD-1 binding antagonist is AMP-224.

65. The method of claim 56, wherein the PD-1 axis binding antagonist is a PD-L1 binding antagonist.

66. The method of claim 65, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to PD-1.

67. The method of claim 65, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to B7-1.

68. The method of claim 65, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to both PD-1 and B7-1.

69. The method of claim 65, wherein the PD-L1 binding antagonist is an anti-PD-L1 antibody.

70. The method of claim 69, wherein the anti-PD-L1 antibody is a monoclonal antibody.

71. The method of claim 69, wherein the anti-PD-L1 antibody is an antibody fragment selected from the group consisting of Fab, Fab'-SH, Fv, scFv, and $(Fab')_2$ fragments.

72. The method of any one of claims 69-71, wherein the anti-PD-L1 antibody is a humanized antibody or a human antibody.

73. The method of claim 65, wherein the PD-L1 binding antagonist is selected from the group consisting of: YW243.55.S70, MPDL3280A, MDX-1105, and MEDI4736.

74. The method of any one of claims 69-72, wherein the anti-PD-L1 antibody comprises a heavy chain comprising HVR-H1 sequence of SEQ ID NO:15, HVR-H2 sequence of SEQ ID

NO:16, and HVR-H3 sequence of SEQ ID NO:3; and a light chain comprising HVR-L1 sequence of SEQ ID NO:17, HVR-L2 sequence of SEQ ID NO:18, and HVR-L3 sequence of SEQ ID NO:19.

75. The method of claim 74, wherein the anti-PD-L1 antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:24 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:21.

76. The method of claim 56, wherein the PD-1 axis binding antagonist is a PD-L2 binding antagonist.

77. The method of claim 76, wherein the PD-L2 binding antagonist is an antibody.

78. The method of claim 76, wherein the PD-L2 binding antagonist is an immunoadhesin.

79. The method of any one of claims 62, 69-75, and 77, wherein the antibody is a human IgG1 having Asn to Ala substitution at position 297 according to EU numbering.

80. The method of any one of claims 51-79, wherein the anti-CD20 antibody is a humanized B-Ly1 antibody.

81. The method of any one of claims 51-79, wherein the anti-CD20 antibody is a GA101 antibody.

82. The method of claim 81, wherein the GA101 is an anti-human CD20 antibody comprising an HVR-H1 comprising the amino acid sequence of SEQ ID NO:50, an HVR-H2 comprising the amino acid sequence of SEQ ID NO:51, an HVR-H3 comprising the amino acid sequence of SEQ ID NO:52, an HVR-L1 comprising the amino acid sequence of SEQ ID NO:53, an HVR-L2 comprising the amino acid sequence of SEQ ID NO:54, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO:55.

83. The method of claim 81, wherein the GA101 antibody comprises a VH domain comprising the amino acid sequence of SEQ ID NO:56 and a VL domain comprising the amino acid sequence of SEQ ID NO:57.

84. The method of claim 81, wherein the GA101 antibody comprises an amino acid sequence of SEQ ID NO:58 and an amino acid sequence of SEQ ID NO:59.

85. The method of claim 81, wherein the GA101 antibody is obinutuzumab.

86. The method of claim 81, wherein the GA101 antibody comprises an amino acid sequence that has at least 95% sequence identity with amino acid sequence of SEQ ID NO:58 and that comprises an amino acid sequence that has at least 95% sequence identity with an amino acid sequence of SEQ ID NO:59.

87. The method of any one of claims 51-79, wherein the anti-CD20 antibody is a multispecific antibody.

88. The method of any one of claims 51-79, wherein the anti-CD20 antibody is a bispecific antibody.

89. The method of any one of claims 51-88, wherein the individual is a human.

90. The method of any one of claims 51-89, wherein the individual has cancer or has been diagnosed with cancer.

91. The method of any one of claims 51-90, wherein the cancer is a CD20-expressing cancer.

92. The method of any one of claims 51-91, wherein the cancer is a non-solid tumor.

93. The method of claim 92, wherein the cancer is a lymphoma or a leukemia.

94. The method of claim 93, wherein the leukemia is chronic lymphocytic leukemia (CLL) or acute myeloid leukemia (AML).

95. The method of claim 93, wherein the lymphoma is Non-Hodgkin's lymphoma (NHL).

96. The method of claim 91, wherein the individual is suffering from relapsed or refractory or previously untreated chronic lymphocytic leukemia.

97. The method of claim 96, wherein the individual is suffering from refractory or relapsed follicular lymphoma or diffuse large B-cell lymphoma (DLBCL).

98. The method of any of claims 51-97, wherein the anti-CD20 antibody or the PD-1 axis binding antagonist is administered continuously or intermittently.

99. The method of any of claims 51-98, wherein the anti-CD20 antibody is administered before the PD-1 axis binding antagonist.

100. The method of any of claims 51-98, wherein the anti-CD20 antibody is administered simultaneous with the PD-1 axis binding antagonist.

101. The method of any of claims 51-98, wherein the anti-CD20 antibody is administered after the PD-1 axis binding antagonist.

102. The method of any one of claims 1-101, wherein the PD-1 axis binding antagonist or the anti-CD20 antibody is administered intravenously, intramuscularly, subcutaneously, topically, orally, transdermally, intraperitoneally, intraorbitally, by implantation, by inhalation, intrathecally, intraventricularly, or intranasally.

103. The method of any one of claims 23, 24, 74, and 75, wherein the anti-PD-L1 antibody is administered to the individual intravenously at a dose of 1200 mg once every three weeks.

104. The method of any one of claims 30-34 and 82-85, wherein the anti-CD20 antibody is administered to the individual intravenously at a dose of 1000 mg once on days 1, 8, and 15 of cycle 1 and on day 1 of cycles 2 to 8.

105. A kit comprising a PD-1 axis binding antagonist and a package insert comprising instructions for using the PD-1 axis binding antagonist in combination with an anti-CD20 antibody to treat or delay progression of cancer in an individual.

106. A kit comprising a PD-1 axis binding antagonist and an anti-CD20 antibody.

107. The kit of claim 106, wherein the kit further comprises a package insert comprising instructions for using the PD-1 axis binding antagonist and the anti-CD20 antibody to treat or delay progression of cancer in an individual.

108. A kit comprising an anti-CD20 antibody and a package insert comprising instructions for using the anti-CD20 antibody in combination with a PD-1 axis binding antagonist to treat or delay progression of cancer in an individual.

CLAIMS

What is claimed is:

1. Use of an effective amount of a PD-1 axis binding antagonist and an anti-CD20 antibody for the manufacture of a first medicament comprising the PD-1 axis binding antagonist and a second medicament comprising the anti-CD20 antibody for treating or delaying progression of cancer in an individual.

2. Use of an effective amount of a PD-1 axis binding antagonist in the manufacture of a medicament for treating or delaying progression of cancer in an individual, wherein the PD-1 axis binding agent is used in combination with an anti-CD20 antibody.

3. Use of an effective amount of an anti-CD20 antibody in the manufacture of a medicament for treating or delaying progression of cancer in an individual, wherein the anti-CD20 antibody is used in combination with a PD-1 axis binding antagonist.

4. A pharmaceutical composition comprising a PD-1 axis binding antagonist in combination with an anti-CD20 antibody for use in treating or delaying progression of cancer.

5. A pharmaceutical composition comprising a PD-1 axis binding antagonist for use in treating or delaying progression of cancer in combination with an anti-CD20 antibody.

6. A pharmaceutical composition comprising an anti-CD20 antibody for use in treating or delaying progression of cancer in combination with a PD-1 axis binding antagonist.

7. The use or pharmaceutical composition of any one of claims 1-6, wherein the PD-1 axis binding antagonist is selected from the group consisting of a PD-L1 binding antagonist, a PD-1 binding antagonist and a PD-L2 binding antagonist.

8. The use or pharmaceutical composition of claim 7, wherein the PD-1 axis binding antagonist is a PD-L1 binding antagonist.

9. The use or pharmaceutical composition of claim 8, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to PD-1.

10. The use or pharmaceutical composition of claim 8, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to B7-1.

11. The use or pharmaceutical composition of claim 8, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to both PD-1 and B7-1.

12. The use or pharmaceutical composition of claim 8, wherein the PD-L1 binding antagonist is an anti-PD-L1 antibody.

13. The use or pharmaceutical composition of claim 12, wherein the anti-PD-L1 antibody is a monoclonal antibody.

14. The use or pharmaceutical composition of claim 12, wherein the anti-PD-L1 antibody is an antibody fragment selected from the group consisting of Fab, Fab'-SH, Fv, scFv, and (Fab')2 fragments.

15. The use or pharmaceutical composition of any one of claims 12-14, wherein the anti-PD-L1 antibody is a humanized antibody or a human antibody.

16. The use or pharmaceutical composition of claim 7, wherein the PD-L1 binding antagonist is selected from the group consisting of: YW243.55.S70, MPDL3280A, MDX-1105, and MEDI4736.

17. The use or pharmaceutical composition of claim 12, wherein the anti-PD-L1 antibody comprises a heavy chain comprising HVR-H1 sequence of SEQ ID NO:15, HVR-H2 sequence of SEQ ID NO:16, and HVR-H3 sequence of SEQ ID NO:3; and a light chain comprising HVR-L1 sequence of SEQ ID NO:17, HVR-L2 sequence of SEQ ID NO:18, and HVR-L3 sequence of SEQ ID NO:19.

18. The use or pharmaceutical composition of claim 12, wherein the anti-PD-L1 antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:24 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:21.

19. The use or pharmaceutical composition of claim 7, wherein the PD-1 axis binding antagonist is a PD-1 binding antagonist.

20. The use or pharmaceutical composition of claim 19, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to its ligand binding partners.

21. The use or pharmaceutical composition of claim 20, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to PD-L1.

22. The use or pharmaceutical composition of claim 20, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to PD-L2.

23. The use or pharmaceutical composition of claim 20, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to both PD-L1 and PD-L2.

24. The use or pharmaceutical composition of claim 20, wherein the PD-1 binding antagonist is an antibody.

25. The use or pharmaceutical composition of claim 24, wherein the PD-1 binding antagonist is MDX-1106.

26. The use or pharmaceutical composition of claim 24, wherein the PD-1 binding antagonist is Merck 3745.

27. The use or pharmaceutical composition of claim 20, wherein the PD-1 binding antagonist is AMP-224.

28. The use or pharmaceutical composition of claim 7, wherein the PD-1 axis binding antagonist is a PD-L2 binding antagonist.

29. The use or pharmaceutical composition of claim 28, wherein the PD-L2 binding antagonist is an antibody.

30. The use or pharmaceutical composition of claim 28, wherein the PD-L2 binding antagonist is an immunoadhesin.

31. The use or pharmaceutical composition of any one of claims 12-18, 24, and 29, wherein the antibody is a human IgG1 having Asn to Ala substitution at position 297 according to EU numbering.

32. The use or pharmaceutical composition of any one of claims 1-31, wherein the anti-CD20 antibody is a humanized B-Ly1 antibody.

33. The use or pharmaceutical composition of any one of claims 1-31, wherein the anti-CD20 antibody is a GA101 antibody.

34. The use or pharmaceutical composition of claim 33, wherein the GA101 is an anti-human CD20 antibody comprising an HVR-H1 comprising the amino acid sequence of SEQ ID NO:50, an HVR-H2 comprising the amino acid sequence of SEQ ID NO:51, an HVR-H3 comprising the amino acid sequence of SEQ ID NO:52, an HVR-L1 comprising the amino acid sequence of SEQ ID NO:53, an HVR-L2 comprising the amino acid sequence of SEQ ID NO:54, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO:55.

35. The use or pharmaceutical composition of claim 33 or 34, wherein the GA101 antibody comprises a VH domain comprising the amino acid sequence of SEQ ID NO:56 and a VL domain comprising the amino acid sequence of SEQ ID NO:57.

36. The use or pharmaceutical composition of claim 33 or 34, wherein the GA101 antibody comprises an amino acid sequence of SEQ ID NO:58 and an amino acid sequence of SEQ ID NO:59.

37. The use or pharmaceutical composition of claim 33, wherein the GA101 antibody is obinutuzumab.

38. The use or pharmaceutical composition of claim 33 or 34, wherein the GA101 antibody comprises an amino acid sequence that has at least 95% sequence identity with amino acid sequence of SEQ ID NO:58 and that comprises an amino acid sequence that has at least 95% sequence identity with an amino acid sequence of SEQ ID NO:59.

39. The use or pharmaceutical composition of any one of claims 1-31, wherein the anti-CD20 antibody is a multispecific antibody.

40. The use or pharmaceutical composition of any one of claims 1-31, wherein the anti-CD20 antibody is a bispecific antibody.

41. The use or pharmaceutical composition of any one of claims 1-40, wherein the individual is a human.

42. The use or pharmaceutical composition of any one of claims 1-41, wherein the individual has cancer or has been diagnosed with cancer.

43. The use or pharmaceutical composition of any one of claims 1-42, wherein the cancer is a CD20-expressing cancer.

44. The use or pharmaceutical composition of any one of claims 1-43, wherein the cancer is a non-solid tumor.

45. The use or pharmaceutical composition of claim 44, wherein the cancer is a lymphoma or a leukemia.

46. The use or pharmaceutical composition of claim 45, wherein the leukemia is chronic lymphocytic leukemia (CLL) or acute myeloid leukemia (AML).

47. The use or pharmaceutical composition of claim 45, wherein the lymphoma is Non-Hodgkin's lymphoma (NHL).

48. The use or pharmaceutical composition of claim 43 or 44, wherein the individual is suffering from relapsed or refractory or previously untreated chronic lymphocytic leukemia.

49. The use or pharmaceutical composition of claim 48, wherein the individual is suffering from refractory or relapsed follicular lymphoma or diffuse large B-cell lymphoma (DLBCL).

50. The use or pharmaceutical composition of any one of claims 1-49, wherein the treatment results in a sustained response in the individual after cessation of the treatment.

51. The use or pharmaceutical composition of any of claims 1-50, wherein the anti-CD20 antibody or the PD-1 axis binding antagonist is to be administered continuously or intermittently.

52. The use or pharmaceutical composition of any of claims 1-51, wherein the anti-CD20 antibody is to be administered before the PD-1 axis binding antagonist.

53. The use or pharmaceutical composition of any of claims 1-51, wherein the anti-CD20 antibody is to be administered simultaneous with the PD-1 axis binding antagonist.

54. The use or pharmaceutical composition of any of claims 1-51, wherein the anti-CD20 antibody is to be administered after the PD-1 axis binding antagonist.

55. Use of an effective amount of a PD-1 axis binding antagonist and an anti-CD20 antibody for the manufacture of a first medicament comprising the PD-1 axis binding antagonist and a second medicament comprising the anti-CD20 antibody for enhancing immune function in an individual having cancer.

56. Use of an effective amount of a PD-1 axis binding antagonist in the manufacture of a medicament for enhancing immune function in an individual having cancer, wherein the PD-1 axis binding agent is used in combination with an anti-CD20 antibody.

57. Use of an effective amount of an anti-CD20 antibody in the manufacture of a medicament for enhancing immune function in an individual having cancer, wherein the anti-CD20 antibody is used in combination with a PD-1 axis binding antagonist.

58. A pharmaceutical composition comprising a PD-1 axis binding antagonist in combination with an anti-CD20 antibody for use in enhancing immune function.

59. A pharmaceutical composition comprising a PD-1 axis binding antagonist for use in enhancing immune function in combination with an anti-CD20 antibody.

60. A pharmaceutical composition comprising an anti-CD20 antibody for use in enhancing immune function in combination with a PD-1 axis binding antagonist.

61. The use or pharmaceutical composition of any one of claims 55-60, wherein CD8 T cells in the individual have enhanced priming, activation, proliferation and/or cytolytic activity relative to prior to the administration of the combination.

62. The use or pharmaceutical composition of any one of claims 55-60, wherein the CD8 T cell activation is characterized by an elevated frequency of γ-IFN$^+$ CD8 T cells and/or enhanced cytolytic activity relative to prior to administration of the combination.

63. The use or pharmaceutical composition of any one of claims 55-60, wherein the number of CD8 T cells is elevated relative to prior to administration of the combination.

64. The use or pharmaceutical composition of any one of claims 55-63, wherein the CD8 T cell is an antigen-specific CD8 T cell.

65. The use or pharmaceutical composition of any one of claims 55-64, wherein the PD-1 axis binding antagonist is selected from the group consisting of a PD-L1 binding antagonist, a PD-1 binding antagonist and a PD-L2 binding antagonist.

66. The use or pharmaceutical composition of claim 65, wherein the PD-1 axis binding antagonist is a PD-L1 binding antagonist.

67. The use or pharmaceutical composition of claim 66, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to PD-1.

68. The use or pharmaceutical composition of claim 66, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to B7-1.

69. The use or pharmaceutical composition of claim 66, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to both PD-1 and B7-1.

70. The use or pharmaceutical composition of claim 66, wherein the PD-L1 binding antagonist is an anti-PD-L1 antibody.

71. The use or pharmaceutical composition of claim 70, wherein the anti-PD-L1 antibody is a monoclonal antibody.

72. The use or pharmaceutical composition of claim 70, wherein the anti-PD-L1 antibody is an antibody fragment selected from the group consisting of Fab, Fab'-SH, Fv, scFv, and (Fab')2 fragments.

73. The use or pharmaceutical composition of any one of claims 70-72, wherein the anti-PD-L1 antibody is a humanized antibody or a human antibody.

74. The use or pharmaceutical composition of claim 66, wherein the PD-L1 binding antagonist is selected from the group consisting of: YW243.55.S70, MPDL3280A, MDX-1105, and MEDI4736.

75. The use or pharmaceutical composition of any one of claims 70-73, wherein the anti-PD-L1 antibody comprises a heavy chain comprising HVR-H1 sequence of SEQ ID NO:15, HVR-H2 sequence of SEQ ID NO:16, and HVR-H3 sequence of SEQ ID NO:3; and a light chain comprising HVR-L1 sequence of SEQ ID NO:17, HVR-L2 sequence of SEQ ID NO:18, and HVR-L3 sequence of SEQ ID NO:19.

76. The use or pharmaceutical composition of claim 75, wherein the anti-PD-L1 antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:24 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:21.

77. The use or pharmaceutical composition of claim 65, wherein the PD-1 axis binding antagonist is a PD-1 binding antagonist.

78. The use or pharmaceutical composition of claim 77, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to its ligand binding partners.

79. The use or pharmaceutical composition of claim 77, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to PD-L1.

80. The use or pharmaceutical composition of claim 77, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to PD-L2.

81. The use or pharmaceutical composition of claim 77, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to both PD-L1 and PD-L2.

82. The use or pharmaceutical composition of claim 77, wherein the PD-1 binding antagonist is an anti-PD-1 antibody.

83. The use or pharmaceutical composition of claim 82, wherein the PD-1 binding antagonist is MDX-1106 or Merck 3745.

84. The use or pharmaceutical composition of claim 77, wherein the PD-1 binding antagonist is AMP-224.

85. The use or pharmaceutical composition of claim 65, wherein the PD-1 axis binding antagonist is a PD-L2 binding antagonist.

86. The use or pharmaceutical composition of claim 85, wherein the PD-L2 binding antagonist is an antibody.

87. The use or pharmaceutical composition of claim 85, wherein the PD-L2 binding antagonist is an immunoadhesin.

88. The use or pharmaceutical composition of any one of claims 70-76, 82, and 86, wherein the antibody is a human IgG1 having Asn to Ala substitution at position 297 according to EU numbering.

89. The use or pharmaceutical composition of any one of claims 55-88, wherein the anti-CD20 antibody is a humanized B-Ly1 antibody.

90. The use or pharmaceutical composition of any one of claims 55-88, wherein the anti-CD20 antibody is a GA101 antibody.

91. The use or pharmaceutical composition of claim 90, wherein the GA101 is an anti-human CD20 antibody comprising an HVR-H1 comprising the amino acid sequence of SEQ ID NO:50, an HVR-H2 comprising the amino acid sequence of SEQ ID NO:51, an HVR-H3 comprising the amino acid sequence of SEQ ID NO:52, an HVR-L1 comprising the amino acid sequence of SEQ ID NO:53, an HVR-L2 comprising the amino acid sequence of SEQ ID NO:54, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO:55.

92. The use or pharmaceutical composition of claim 90, wherein the GA101 antibody comprises a VH domain comprising the amino acid sequence of SEQ ID NO:56 and a VL domain comprising the amino acid sequence of SEQ ID NO:57.

93. The use or pharmaceutical composition of claim 90, wherein the GA101 antibody comprises an amino acid sequence of SEQ ID NO:58 and an amino acid sequence of SEQ ID NO:59.

94. The use or pharmaceutical composition of claim 90, wherein the GA101 antibody is obinutuzumab.

95. The use or pharmaceutical composition of claim 90, wherein the GA101 antibody comprises an amino acid sequence that has at least 95% sequence identity with amino acid sequence of SEQ ID NO:58 and that comprises an amino acid sequence that has at least 95% sequence identity with an amino acid sequence of SEQ ID NO:59.

96. The use or pharmaceutical composition of any one of claims 55-88, wherein the anti-CD20 antibody is a multispecific antibody.

97. The use or pharmaceutical composition of any one of claims 55-88, wherein the anti-CD20 antibody is a bispecific antibody.

98. The use or pharmaceutical composition of any one of claims 55-97, wherein the individual is a human.

99. The use or pharmaceutical composition of any one of claims 55-98, wherein the individual has cancer or has been diagnosed with cancer.

100. The use or pharmaceutical composition of any one of claims 55-99, wherein the cancer is a CD20-expressing cancer.

101. The use or pharmaceutical composition of any one of claims 55-100, wherein the cancer is a non-solid tumor.

102. The use or pharmaceutical composition of claim 101, wherein the cancer is a lymphoma or a leukemia.

103. The use or pharmaceutical composition of claim 102, wherein the leukemia is chronic lymphocytic leukemia (CLL) or acute myeloid leukemia (AML).

104. The use or pharmaceutical composition of claim 102, wherein the lymphoma is Non-Hodgkin's lymphoma (NHL).

105. The use or pharmaceutical composition of claim 100, wherein the individual is suffering from relapsed or refractory or previously untreated chronic lymphocytic leukemia.

106. The use or pharmaceutical composition of claim 105, wherein the individual is suffering from refractory or relapsed follicular lymphoma or diffuse large B-cell lymphoma (DLBCL).

107. The use or pharmaceutical composition of any of claims 55-106, wherein the anti-CD20 antibody or the PD-1 axis binding antagonist is to be administered continuously or intermittently.

108. The use or pharmaceutical composition of any of claims 55-107, wherein the anti-CD20 antibody is to be administered before the PD-1 axis binding antagonist.

109. The use or pharmaceutical composition of any of claims 55-107, wherein the anti-CD20 antibody is to be administered simultaneous with the PD-1 axis binding antagonist.

110. The use or pharmaceutical composition of any of claims 55-107, wherein the anti-CD20 antibody is to be administered after the PD-1 axis binding antagonist.

111. The use or pharmaceutical composition of any one of claims 1-110, wherein the PD-1 axis binding antagonist or the anti-CD20 antibody is to be administered intravenously, intramuscularly, subcutaneously, topically, orally, transdermally, intraperitoneally, intraorbitally, by implantation, by inhalation, intrathecally, intraventricularly, or intranasally.

112. The use or pharmaceutical composition of any one of claims 17, 18, 75, and 76, wherein the anti-PD-L1 antibody is to be administered to the individual intravenously at a dose of 1200 mg once every three weeks.

113. The use or pharmaceutical composition of any one of claims 34-38 and 91-95, wherein the anti-CD20 antibody is to be administered to the individual intravenously at a dose of 1000 mg once on days 1, 8, and 15 of cycle 1 and on day 1 of cycles 2 to 8.

114. A kit comprising a PD-1 axis binding antagonist and a package insert comprising instructions for using the PD-1 axis binding antagonist in combination with an anti-CD20 antibody to treat or delay progression of cancer in an individual.

115. A kit comprising a PD-1 axis binding antagonist and an anti-CD20 antibody.

116. The kit of claim 115, wherein the kit further comprises a package insert comprising instructions for using the PD-1 axis binding antagonist and the anti-CD20 antibody to treat or delay progression of cancer in an individual.

117. A kit comprising an anti-CD20 antibody and a package insert comprising instructions for using the anti-CD20 antibody in combination with a PD-1 axis binding antagonist to treat or delay progression of cancer in an individual.