BRIEF SUMMARY

[0008] 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] 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 an anti-PD-L1 antibody and an anti-CD20 antibody for the manufacture of a first medicament comprising the anti-PD-L1 antibody and a second medicament comprising the anti-CD20 antibody for treating or delaying progression of a CD20-expressing lymphoma in an individual, wherein the first and second medicaments are to be used in combination.

[0010] In another aspect, provided herein is use of an effective amount of an anti-PD-L1 antibody in the manufacture of a medicament for treating or delaying progression of a CD20-expressing lymphoma in an individual, wherein the anti-PD-L1 antibody is to be 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 a CD20-expressing lymphoma in an individual, wherein the anti-CD20 antibody is to be used in combination with an anti-PD-L1 antibody. 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 an anti-PD-L1 antibody in combination with an anti-CD20 antibody for use in treating or delaying progression of a lymphoma.

[0012] 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] 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 an anti-PD-L1 antibody and an anti-CD20 antibody for the manufacture of a first medicament comprising the anti-PD-L1 antibody and a second medicament comprising the anti-CD20 antibody for enhancing immune function in an individual having a CD20-expressing lymphoma, wherein the first and second medicaments are to be used in combination.

[0014] In another aspect, provided herein is use of an effective amount of an anti-PD-L1 antibody in the manufacture of a medicament for enhancing immune function in an individual having a CD20-expressing lymphoma, wherein the anti-PD-L1 antibody is to be 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 a CD20-expressing lymphoma, wherein the anti-CD20 antibody is to be used in combination with an anti-PD-L1 antibody. 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.

[0023] Provided herein are kits comprising an anti-PD-L1 antibody and a package insert comprising instructions for using the anti-PD-L1 antibody in combination with an anti-CD20 antibody to treat or delay progression of a lymphoma in an individual. Provided herein are kits comprising an anti-PD-L1 antibody 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. Provided herein are kits comprising an anti-CD20 antibody and a package insert comprising instructions for using the anti-CD20 antibody in combination with an anti-PD-L1 antibody to treat or delay progression of a lymphoma in an individual. 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. 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. 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 disclosure. These and other aspects of the invention will become apparent to one of skill in the art. These and other embodiments of the disclosure are further described by the detailed description that follows.

CLAIMS

What is claimed is:

1. Use of an effective amount of an anti-PD-L1 antibody and an anti-CD20 antibody for the manufacture of a first medicament comprising the anti-PD-L1 antibody and a second medicament comprising the anti-CD20 antibody for treating or delaying progression of a CD20-expressing lymphoma in an individual, wherein the first and second medicaments are to be used in combination.

2. Use of an effective amount of an anti-PD-L1 antibody in the manufacture of a medicament for treating or delaying progression of a CD20-expressing lymphoma in an individual, wherein the anti-PD-L1 antibody is to be 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 a CD20-expressing lymphoma in an individual, wherein the anti-CD20 antibody is to be used in combination with an anti-PD-L1 antibody.

4. A pharmaceutical composition comprising an anti-PD-L1 antibody in combination with an anti-CD20 antibody for use in treating or delaying progression of a lymphoma.

5. The use or pharmaceutical composition for use according to any one of claims 1-4, wherein the anti-PD-L1 antibody inhibits the binding of PD-L1 to PD-1.

6. The use or pharmaceutical composition for use according to any one of claims 1-4, wherein the anti-PD-L1 antibody inhibits the binding of PD-L1 to B7-1.

7. The use or pharmaceutical composition for use according to any one of claims 1-4, wherein the anti-PD-L1 antibody inhibits the binding of PD-L1 to both PD-1 and B7-1.

8. The use or pharmaceutical composition for use according to any one of claims 1-7, wherein the anti-PD-L1 antibody is a monoclonal antibody.

28. The use or pharmaceutical composition for use according to any one of claims 1-27, wherein the treatment results in a sustained response in the individual after cessation of the treatment.

29. The use or pharmaceutical composition for use according to any of claims 1-28, wherein the anti-CD20 antibody or the anti-PD-L1 antibody is to be administered continuously or intermittently.

30. The use or pharmaceutical composition for use according to any of claims 1-29, wherein the anti-CD20 antibody is to be administered before the anti-PD-L1 antibody.

31. The use or pharmaceutical composition for use according to any of claims 1-29, wherein the anti-CD20 antibody is to be administered simultaneous with the anti-PD-L1 antibody.

32. The use or pharmaceutical composition for use according to any of claims 1-29, wherein the anti-CD20 antibody is to be administered after the anti-PD-L1 antibody.

33. Use of an effective amount of an anti-PD-L1 antibody and an anti-CD20 antibody for the manufacture of a first medicament comprising the anti-PD-L1 antibody and a second medicament comprising the anti-CD20 antibody for enhancing immune function in an individual having a CD20-expressing lymphoma, wherein the first and second medicaments are to be used in combination.

34. Use of an effective amount of an anti-PD-L1 antibody in the manufacture of a medicament for enhancing immune function in an individual having a CD20-expressing lymphoma, wherein the anti-PD-L1 antibody is to be used in combination with an anti-CD20 antibody.

35. Use of an effective amount of an anti-CD20 antibody in the manufacture of a medicament for enhancing immune function in an individual having a CD20-expressing lymphoma, wherein the anti-CD20 antibody is to be used in combination with an anti-PD-L1 antibody.

36. A pharmaceutical composition comprising an anti-PD-L1 antibody in combination with an anti-CD20 antibody for use in enhancing immune function in an individual having a lymphoma.

65. The use or pharmaceutical composition for use according to any one of claims 33-64, wherein the anti-CD20 antibody is to be administered before the anti-PD-L1 antibody.

66. The use or pharmaceutical composition for use according to any one of claims 33-64, wherein the anti-CD20 antibody is to be administered simultaneous with the anti-PD-L1 antibody.

67. The use or pharmaceutical composition for use according to any one of claims 33-64, wherein the anti-CD20 antibody is to be administered after the anti-PD-L1 antibody.

68. The use or pharmaceutical composition for use according to any one of claims 1-67, wherein the anti-PD-L1 antibody 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.

69. The use or pharmaceutical composition for use according to any one of claims 12, 13, 48, and 49, wherein the anti-PD-L1 antibody is to be administered to the individual intravenously at a dose of 1200 mg once every three weeks.

70. The use or pharmaceutical composition for use according to any one of claims 17-21 and 53-57, 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.