

SUMMARY

[0010] The present disclosure describes a combination treatment comprising a PD-1 axis binding antagonist and an agent that decreases or inhibits TIGIT expression and/or activity.

[0010a] In one aspect, there is provided use of an anti-PD-L1 antagonist antibody or antigen-binding fragment thereof in the manufacture of a medicament for treating or delaying progression of cancer in an individual, wherein the medicament is to be administered with an anti-TIGIT antagonist antibody or antigen-binding fragment thereof.

[0011] 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 agent that decreases or inhibits TIGIT expression and/or activity.

[0011a] In one aspect, there is provided use of an anti-PD-L1 antagonist antibody or antigen-binding fragment thereof in the manufacture of a medicament for reducing or inhibiting cancer relapse or cancer progression in an individual, wherein the medicament is to be administered with an anti-TIGIT antagonist antibody or antigen-binding fragment thereof.

[0012] Provided herein are also methods for reducing or inhibiting cancer relapse or cancer progression in an individual comprising administering to the individual an effective amount of a PD-1 axis binding antagonist and an agent that decreases or inhibits TIGIT expression and/or activity.

[0012a] In one aspect, there is provided use of an anti-PD-L1 antagonist antibody or antigen-binding fragment thereof in the manufacture of a medicament for treating or delaying progression of an immune related disease in an individual, wherein the medicament is to be administered with an anti-TIGIT antagonist antibody or antigen-binding fragment thereof and the immune related disease is a viral infection.

[0013] Provided herein are also methods for treating or delaying progression of an immune related disease in an individual comprising administering to the individual an effective amount of a PD-1 axis binding antagonist and an agent that decreases or inhibits TIGIT expression and/or activity.

[0013a] In one aspect, there is provided use of an anti-PD-L1 antagonist antibody or antigen-binding fragment thereof in the manufacture of a medicament for reducing or inhibiting progression of an immune related disease in an individual, wherein the medicament is to be administered with an anti-TIGIT antagonist antibody or antigen-binding fragment thereof and the immune related disease is a viral infection.

[0014] Provided herein are also methods for reducing or inhibiting progression of an immune related disease in an individual comprising administering to the individual an effective amount of a PD-1 axis binding antagonist and an agent that decreases or inhibits TIGIT expression and/or activity.

[0015] In some embodiments, the immune related disease is associated with a T cell dysfunctional disorder. In some embodiments, the T cell dysfunctional disorder is characterized by decreased responsiveness to antigenic stimulation. In some embodiments, the T cell dysfunctional disorder is characterized by T cell anergy or decreased ability to secrete cytokines, proliferate or execute cytolytic activity. In some embodiments, the T cell dysfunctional disorder is characterized by T cell exhaustion. In some embodiments, the T cells are CD4+ and CD8+ T cells. In some embodiments, the immune related disease is selected from the group consisting of unresolved acute infection, chronic infection and tumor immunity.

[0015a] In one aspect, there is provided use of an anti-PD-L1 antagonist antibody or antigen-binding fragment thereof in the manufacture of a medicament for increasing, enhancing or stimulating an immune response or function in an individual having cancer, wherein the medicament is to be administered with an anti-TIGIT antagonist antibody or antigen-binding fragment thereof.

[0016] Provided herein are also methods of increasing, enhancing or stimulating an immune response or function in an individual by administering to the individual an effective amount of a PD-1 axis binding antagonist and an agent that decreases or inhibits TIGIT expression and/or activity.

agent that inhibits and/or blocks the intracellular signaling mediated by TIGIT binding to PVR.

[0025] In some embodiments, the agent that inhibits and/or blocks the interaction of CD226 with TIGIT is a small molecule inhibitor, an inhibitory antibody or antigen-binding fragment thereof, an aptamer, an inhibitory nucleic acid, and an inhibitory polypeptide. In some embodiments, the agent that inhibits and/or blocks the interaction of CD226 with TIGIT is an anti-TIGIT antibody or antigen-binding fragment thereof.

[0026] In some embodiments, the antagonist of TIGIT expression and/or activity is a small molecule inhibitor, an inhibitory antibody or antigen-binding fragment thereof, an aptamer, an inhibitory nucleic acid, and an inhibitory polypeptide. In some embodiments, the antagonist of TIGIT expression and/or activity is an anti-TIGIT antibody or antigen-binding fragment thereof.

[0027] In some embodiments, the antagonist of PVR expression and/or activity is a small molecule inhibitor, an inhibitory antibody or antigen-binding fragment thereof, an aptamer, an inhibitory nucleic acid, and an inhibitory polypeptide.

[0028] In some embodiments, the agent that inhibits and/or blocks the interaction of TIGIT with PVR is a small molecule inhibitor, an inhibitory antibody or antigen-binding fragment thereof, an aptamer, an inhibitory nucleic acid, and an inhibitory polypeptide.

[0029] In some embodiments, the agent that inhibits and/or blocks the intracellular signaling mediated by TIGIT binding to PVR is a small molecule inhibitor, an inhibitory antibody or antigen-binding fragment thereof, an aptamer, an inhibitory nucleic acid, and an inhibitory polypeptide.

[0030] The present disclosure also describes a combination treatment comprising an agent that decreases or inhibits TIGIT expression and/or activity and an agent that decreases or inhibits one or more additional immune co-inhibitory receptors.

[0031] Provided herein are methods of increasing, enhancing or stimulating an immune response or function in an individual by administering to the individual an effective amount of an agent that decreases or inhibits TIGIT expression and/or activity and an agent that decreases or inhibits one or more additional immune co-inhibitory receptors.

[0032] In some embodiments, the one or more additional immune co-inhibitory receptor is selected from the group consisting of PD-1, CTLA-4, LAG3, TIM3, BTLA and VISTA. In some embodiments, the one or more additional immune co-inhibitory receptor is selected from the group of PD-1, CTLA-4, LAG3 and TIM3.

[0063] Provided is 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 agent that decreases or inhibits TIGIT expression and/or activity to treat or delay progression of cancer in an individual.

[0064] Disclosed is a kit comprising a PD-L1 binding antagonist that inhibits the binding of PD-L1 to PD-1, a PD-1 binding antagonist that inhibits the binding of PD-1 to PD-L1 and/or PD-L2, or a PD-L2 binding antagonist that inhibits the binding of PD-L2 to PD-1 and an agent that decreases or inhibits TIGIT expression and/or activity, and a package insert comprising instructions for using the PD-L1 binding antagonist, the PD-1 binding antagonist, or the PD-L2 binding antagonist and the agent that decreases or inhibits TIGIT expression and/or activity to treat or delay progression of cancer in an individual.

[0065] Provided is a kit comprising an agent that decreases or inhibits TIGIT expression and/or activity and a package insert comprising instructions for using the agent that decreases or inhibits TIGIT expression and/or activity in combination with a PD-1 axis binding antagonist to treat or delay progression of cancer in an individual.

[0066] Provided is 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 agent that decreases or inhibits TIGIT expression and/or activity to enhance immune function of an individual having cancer.

[0067] Disclosed is a kit comprising a PD-L1 binding antagonist that inhibits the binding of PD-L1 to PD-1, a PD-1 binding antagonist that inhibits the binding of PD-1 to PD-L1 and/or PD-L2, or a PD-L2 binding antagonist that inhibits the binding of PD-L2 to PD-1 and an agent that decreases or inhibits TIGIT expression and/or activity, and a package insert comprising instructions for using the PD-L1 binding antagonist, the PD-1 binding antagonist, or the PD-L2 binding antagonist and the agent that decreases or inhibits TIGIT expression and/or activity to enhance immune function of an individual having cancer.

[0068] Provided is a kit comprising an agent that decreases or inhibits TIGIT expression and/or activity and a package insert comprising instructions for using the agent that decreases or inhibits TIGIT expression and/or activity in combination with a PD-1 axis binding antagonist to enhance immune function of an individual having cancer.

[0069] Provided is 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 agent that modulates the CD226 expression and/or activity to treat or delay progression of cancer in an individual.

[0070] Provided is a kit comprising a PD-1 axis binding antagonist and an agent that modulates the CD226 expression and/or activity, and a package insert comprising instructions for using the PD-1 axis binding antagonist and the agent that modulates the CD226 expression and/or activity to treat or delay progression of cancer in an individual.

(SEQ ID NO:19); and a light chain comprising HVR-L1 sequence of RASQDVSTAVA (SEQ ID NO:20), HVR-L2 sequence of SASFLYS (SEQ ID NO:21), and HVR-L3 sequence of QQYLYHPAT (SEQ ID NO:22). In certain embodiments that may be combined with any of the preceding embodiments, the anti-PD-L1 antibody comprises a heavy chain variable region comprising the amino acid sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDSWIHWRQAPGKGLEWVAWISPYGG
STYYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCARRHWPGGFDYWGQG
TLVTVSA (SEQ ID NO:23),

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDSWIHWRQAPGKGLEWVAWISPYGG
STYYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCARRHWPGGFDYWGQG
TLVTVSSASTK (SEQ ID NO:40), or

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDSWIHWRQAPGKGLEWVAWISPYGG
STYYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCARRHWPGGFDYWGQG
TLVTVSS (SEQ ID NO:41), and a light chain variable region comprising the amino acid sequence of

DIQMTQSPSSLSASVGDRVTITCRASQDVSTAVAWYQQKPGKAPKLLIYSASFLYSG
VPSRFSGSGSGTDFLTISLQPEDFATYYCQQYLYHPATFGQGTKVEIKR (SEQ ID

NO:24). In certain embodiments that may be combined with any of the preceding embodiments, the PD-1 axis binding antagonist is an anti-PD-1 antibody. In certain embodiments that may be combined with any of the preceding embodiments, the anti-PD-1 antibody is MDX-1106, MK-3475, or CT-011. In certain embodiments that may be combined with any of the preceding embodiments, the PD-1 axis binding antagonist is AMP-224. In certain embodiments that may be combined with any of the preceding embodiments, the PD-1 axis binding antagonist is a PD-L2 binding antagonist. In certain embodiments that may be combined with any of the preceding embodiments, the PD-L2 binding antagonist is an antibody. In certain embodiments that may be combined with any of the preceding embodiments, the PD-L2 binding antagonist is an immunoadhesin.

[0109] Provided is a kit comprising an agent that decreases or inhibits TIGIT expression and/or activity and a package insert comprising instructions for using the agent that decreases or inhibits TIGIT expression and/or activity in combination with an agent that decreases or inhibits one or more additional immune co-inhibitory receptors to treat or delay progression of cancer in an individual. Disclosed is a kit comprising an agent that decreases or inhibits TIGIT expression and/or activity and an agent that decreases or inhibits one or more additional

immune co-inhibitory receptors, and a package insert comprising instructions for using the agent that decreases or inhibits TIGIT expression and/or activity and the agent that decreases or inhibits one or more additional immune co-inhibitory receptors to treat or delay progression of cancer in an individual, wherein the one or more additional immune co-inhibitory receptors are selected from the group consisting of PD-1, CTLA-4, LAG3, TIM3, BTLA, VISTA, B7H4, and CD96. Provided is a kit comprising an agent that decreases or inhibits one or more additional immune co-inhibitory receptors and a package insert comprising instructions for using the agent that decreases or inhibits one or more additional immune co-inhibitory receptors in combination with an agent that decreases or inhibits TIGIT expression and/or activity to treat or delay progression of cancer in an individual. Provided is a kit comprising an agent that decreases or inhibits TIGIT expression and/or activity and a package insert comprising instructions for using the agent that decreases or inhibits TIGIT expression and/or activity in combination with an agent that decreases or inhibits one or more additional immune co-inhibitory receptors to enhance immune function of an individual having cancer. Disclosed is a kit comprising an agent that decreases or inhibits TIGIT expression and/or activity and an agent that decreases or inhibits one or more additional immune co-inhibitory receptors, and a package insert comprising instructions for using the agent that decreases or inhibits TIGIT expression and/or activity and the agent that decreases or inhibits one or more additional immune co-inhibitory receptors to enhance immune function of an individual having cancer, wherein the one or more additional immune co-inhibitory receptors are selected from the group consisting of PD-1, CTLA-4, LAG3, TIM3, BTLA, VISTA, B7H4, and CD96. Provided is a kit comprising an agent that decreases or inhibits one or more additional immune co-inhibitory receptors and a package insert comprising instructions for using the agent that decreases or inhibits one or more additional immune co-inhibitory receptors in combination with an agent that decreases or inhibits TIGIT expression and/or activity to enhance immune function of an individual having cancer. In certain embodiments that may be combined with any of the preceding embodiments, the one or more additional immune co-inhibitory receptor is selected from the group consisting of PD-1, CTLA-4, LAG3, TIM3, BTLA, VISTA, B7H4, and CD96. In certain embodiments that may be combined with any of the preceding embodiments, the one or more additional immune co-inhibitory receptor is selected from the group consisting of PD-1, CTLA-4, LAG3 and TIM3.

[0110] Provided is a kit comprising an agent that decreases or inhibits TIGIT expression and/or activity and a package insert comprising instructions for using the agent that decreases or inhibits TIGIT expression and/or activity in combination with an agent that increases or activates one or more additional immune co-stimulatory receptors to treat or delay progression of cancer in an individual.

CLAIMS

What is claimed is:

1. Use of an anti-PD-L1 antagonist antibody or antigen-binding fragment thereof in the manufacture of a medicament for treating or delaying progression of cancer in an individual, wherein the medicament is to be administered with an anti-TIGIT antagonist antibody or antigen-binding fragment thereof.
2. Use of an anti-PD-L1 antagonist antibody or antigen-binding fragment thereof in the manufacture of a medicament for reducing or inhibiting cancer relapse or cancer progression in an individual, wherein the medicament is to be administered with an anti-TIGIT antagonist antibody or antigen-binding fragment thereof.
3. Use of an anti-PD-L1 antagonist antibody or antigen-binding fragment thereof in the manufacture of a medicament for treating or delaying progression of an immune related disease in an individual, wherein the medicament is to be administered with an anti-TIGIT antagonist antibody or antigen-binding fragment thereof and the immune related disease is a viral infection.
4. Use of an anti-PD-L1 antagonist antibody or antigen-binding fragment thereof in the manufacture of a medicament for reducing or inhibiting progression of an immune related disease in an individual, wherein the medicament is to be administered with an anti-TIGIT antagonist antibody or antigen-binding fragment thereof and the immune related disease is a viral infection.
5. The use of claim 3 or 4, wherein the viral infection is an unresolved acute viral infection or a chronic viral infection.
6. Use of an anti-PD-L1 antagonist antibody or antigen-binding fragment thereof in the manufacture of a medicament for increasing, enhancing, or stimulating an immune response or function in an individual having cancer, wherein the medicament is to be administered with an anti-TIGIT antagonist antibody or antigen-binding fragment thereof.
7. The use of any one of claims 1-6, wherein the medicament is to be administered with at least one chemotherapeutic agent.
8. The use of any one of claims 1-7, wherein CD4 and/or CD8 T cells in the individual have increased or enhanced priming, activation, proliferation, cytokine release, and/or cytolytic activity relative to prior to the administration of the combination.
9. The use of any one of claims 1-8, wherein the number of CD4 and/or CD8 T cells is elevated relative to prior to administration of the combination.

10. The use of any one of claims 1-9, wherein the number of activated CD4 and/or CD8 T cells is elevated relative to prior to administration of the combination.
11. The use of any one of claims 1-10, wherein activated CD4 and/or CD8 T cells are characterized by γ -IFN⁺ producing CD4 and/or CD8 T cells and/or enhanced cytolytic activity relative to prior to the administration of the combination.
12. The use of any one of claims 8-11, wherein the CD4 and/or CD8 T cells exhibit increased release of cytokines selected from the group consisting of IFN- γ , TNF- α , and interleukins relative to prior to administration of the combination.
13. The use of any one of claims 8-12, wherein the CD4 and/or CD8 T cells are effector memory T cells.
14. The use of claim 13, wherein the CD4 and/or CD8 effector memory T cells are characterized by γ -IFN⁺ producing CD4 and/or CD8 T cells and/or enhanced cytolytic activity.
15. The use of claim 13, wherein the CD4 and/or CD8 effector memory T cells are characterized by having the expression of CD44^{high} CD62L^{low}.
16. The use of any one of claims 1, 2, and 6-15, wherein the cancer has elevated levels of T cell infiltration.
17. The use of any one of claims 1-16, wherein the anti-TIGIT antagonist antibody or antigen-binding fragment thereof comprises (1) an HVR-L1 sequence of KSSQSLYYSGVKENLLA (SEQ ID NO:1), an HVR-L2 sequence of ASIRFT (SEQ ID NO:2), an HVR-L3 sequence of QQGINNPLT (SEQ ID NO:3), an HVR-H1 sequence of GFTFSSFTMH (SEQ ID NO:4), an HVR-H2 sequence of FIRSGSGIVFYADAVRG (SEQ ID NO:5), and an HVR-H3 sequence of RPLGHNTFDS (SEQ ID NO:6); or
(2) an HVR-L1 sequence of RSSQSLVNSYGNTFLS (SEQ ID NO:7), an HVR-L2 sequence of GISNRFS (SEQ ID NO:8), an HVR-L3 sequence of LQGTHQPPT (SEQ ID NO:9), an HVR-H1 sequence of GYSFTGHLMN (SEQ ID NO:10), an HVR-H2 sequence of LIIPYNGGTSYNQKFKG (SEQ ID NO:11), and an HVR-H3 sequence of GLRGFYAMDY (SEQ ID NO:12).
18. The use of claim 17, wherein the anti-TIGIT antagonist antibody or antigen-binding fragment thereof comprises a light chain comprising the amino acid sequence set forth in
DIVMTQSPSSLAVSPGKVTMTCK**S**SSQSLYYSGVKENLLAWYQQKPGQS
PKLLIYY**ASIRFT**GVPDRFTGSGSGTDYTLTITSVQAEDMGQYFC**QQGINNPLT**FGDGTKLEIKR (SEQ ID NO:13) or

DVVLQTPLSLSVSFGDQVSISCRSSQSLVNSYGN~~T~~FLSWYLHKPGQSPQLLIFG**ISNR**FSGVPDRFS
GSGSGTDFTLKISTIKPEDLGMYCY**CLQGTHQPPT**FGPGTKLEVK (SEQ ID NO:14); or a heavy chain
comprising an amino acid sequence set forth in

EVQLVESGGGLTQPGKSLKLSCEASG**FTFS**FTMHWVRQSPGKGLEWVAFIR**SGSGIVFYADAVRG**
RFTISRDNANKLLFLQMNDLKSEDTAMYYCARR**PLGHNTFDS**WGQGTTLTVSS (SEQ ID NO:15) or
EVQLQQSGPELVKPGTSMKISCKAS**GYSTGHLMN**WVKQSHGKNLEWIGLIIPY**NGGTSYNQKFKG**
KATLTVDKSSSTAYMELLSTSDDSAVYFC**SRGLRGFYAMD**YWGGGTSVTVSS (SEQ ID NO:16).

19. The use of claim 17 or 18, wherein the anti-TIGIT antagonist antibody or antigen-binding
fragment thereof comprises a light chain comprising the amino acid sequence set forth in

DIVMTQSPSSSLAVSPGEKVTMTCKSSQSLY**SGV**KENLLAWYQKPGQS
PKLLIYY**ASIRFT**GVDPDRFTGSGSGTDYTLTITSVQAEDMGQYFC**QQGINNPLTF**GDG**TKLEIKR** (SEQ
ID NO:13) or

DVVLQTPLSLSVSFGDQVSISCRSSQSLVNSYGN~~T~~FLSWYLHKPGQSPQLLIFG**ISNR**FSGVPDRFS
GSGSGTDFTLKISTIKPEDLGMYCY**CLQGTHQPPT**FGPGTKLEVK (SEQ ID NO:14), and a heavy
chain comprising the amino acid sequence set forth in

EVQLVESGGGLTQPGKSLKLSCEASG**FTFS**FTMHWVRQSPGKGLEWVAFIR**SGSGIVFYADAVRG**
RFTISRDNANKLLFLQMNDLKSEDTAMYYCARR**PLGHNTFDS**WGQGTTLTVSS (SEQ ID NO:15) or
EVQLQQSGPELVKPGTSMKISCKAS**GYSTGHLMN**WVKQSHGKNLEWIGLIIPY**NGGTSYNQKFKG**
KATLTVDKSSSTAYMELLSTSDDSAVYFC**SRGLRGFYAMD**YWGGGTSVTVSS (SEQ ID NO: 16).

20. The use of any one of claims 1-19, wherein the anti-TIGIT antagonist antibody or antigen-
binding fragment thereof is a humanized antibody, a chimeric antibody, a bispecific antibody, a
heteroconjugate antibody, an immunotoxin.

21. The use of any one of claims 1-20, wherein the anti-PD-L1 antagonist antibody or antigen-
binding fragment thereof is selected from the group consisting of MPDL3280A, YW243.55.S70, MDX-
1105, and MEDI4736.

22. The use of any one of claims 1-20, wherein the anti-PD-L1 antagonist antibody or antigen-
binding fragment thereof comprises a heavy chain comprising an HVR-H1 sequence of
GFTFSDSWIH (SEQ ID NO:17), an HVR-H2 sequence of AWISPYGGSTYYADSVKG (SEQ ID
NO:18), and an HVR-H3 sequence of RHWPGGFDY (SEQ ID NO:19); and a light chain comprising
an HVR-L1 sequence of RASQDVSTAVA (SEQ ID NO:20), an HVR-L2 sequence of SASFLYS (SEQ
ID NO:21), and an HVR-L3 sequence of QQYLYHPAT (SEQ ID NO:22).

23. The use of claim 22, wherein the anti-PD-L1 antagonist antibody or antigen-binding fragment
thereof comprises a heavy chain variable region comprising the amino acid sequence of
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDSWIHWVRQAPGKGLEWVAVISPYGG

STYYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCARRHWPGGFDYWGQGLTVTVSA (SEQ ID NO:23),

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDSWIHWRQAPGKGLEWVAWISPYGGSTYYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCARRHWPGGFDYWGQGLTVTVSSASTK (SEQ ID NO:40), or

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDSWIHWRQAPGKGLEWVAWISPYGGSTYYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCARRHWPGGFDYWGQGLTVTVSS (SEQ ID NO:41), or a light chain variable region comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVTITCRASQDVSTAVAWYQQKPGKAPKLLIYSASFLYSGVPSRFSGSGS GTDFTLTISLQPEDFATYYCQYLYHPATFGQGTKVEIKR (SEQ ID NO:24).

24. The use of claim 22 or 23, wherein the anti-PD-L1 antagonist antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDSWIHWRQAPGKGLEWVAWISPYGGSTYYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCARRHWPGGFDYWGQGLTVTVSA (SEQ ID NO:23),

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDSWIHWRQAPGKGLEWVAWISPYGGSTYYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCARRHWPGGFDYWGQGLTVTVSSASTK (SEQ ID NO:40), or

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDSWIHWRQAPGKGLEWVAWISPYGGSTYYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCARRHWPGGFDYWGQGLTVTVSS (SEQ ID NO:41), and a light chain variable region comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVTITCRASQDVSTAVAWYQQKPGKAPKLLIYSASFLYSGVPSRFSGSGS GTDFTLTISLQPEDFATYYCQYLYHPATFGQGTKVEIKR (SEQ ID NO:24).

25. The use of any one of claims 22-24, wherein the anti-PD-L1 antagonist antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDSWIHWRQAPGKGLEWVAWISPYGGSTYYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCARRHWPGGFDYWGQGLTVTVSS (SEQ ID NO:41), and a light chain variable region comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVTITCRASQDVSTAVAWYQQKPGKAPKLLIYSASFLYSGVPSRFSGSGS GTDFTLTISLQPEDFATYYCQYLYHPATFGQGTKVEIKR (SEQ ID NO:24).

26. The use of any one of claims 1, 2, and 6-25, wherein the cancer is selected from the group consisting of a non-small cell lung cancer, a small cell lung cancer, a renal cell cancer, a colorectal cancer, an ovarian cancer, a breast cancer, a pancreatic cancer, a gastric carcinoma, a bladder cancer, an esophageal cancer, a mesothelioma, a melanoma, a head and neck cancer, a thyroid cancer, a sarcoma, a prostate cancer, a glioblastoma, a cervical cancer, a thymic carcinoma, a

leukemia, a lymphoma, a myeloma, mycosis fungoides, a Merkel cell cancer, and a hematologic malignancy.

27. The use of any one of claims 1-26, wherein the anti-TIGIT antagonist antibody or antigen-binding fragment thereof is to be administered continuously.

28. The use of any one of claims 1-26, wherein the anti-TIGIT antagonist antibody or antigen-binding fragment thereof is to be administered intermittently.

29. The use of any one of claims 1-28, wherein the anti-TIGIT antagonist antibody or antigen-binding fragment thereof is to be administered before the anti-PD-L1 antagonist antibody or antigen-binding fragment thereof.

30. The use of any one of claims 1-28, wherein the anti-TIGIT antagonist antibody or antigen-binding fragment thereof is to be administered simultaneously with the anti-PD-L1 antagonist antibody or antigen-binding fragment thereof.

31. The use of any one of claims 1-28, wherein the anti-TIGIT antagonist antibody or antigen-binding fragment thereof is to be administered after the anti-PD-L1 antagonist antibody or antigen-binding fragment thereof.