

SUMMARY

The present disclosure relates to methods of treating a subject having cancer (e.g., lung cancer, e.g., NSCLC, e.g., squamous or non-squamous NSCLC, e.g., locally advanced unresectable NSCLC (e.g., Stage IIIB NSCLC), or recurrent or metastatic NSCLC (e.g., Stage IV NSCLC)) by administering a combination of an anti-TIGIT antagonist antibody (e.g., an anti-TIGIT antagonist antibody as disclosed herein, e.g., tiragolumab) and a PD-1 axis binding antagonist (e.g., an anti-PD-L1 antagonist antibody (e.g., atezolizumab)).

In one aspect, the present disclosure refers to use of tiragolumab and atezolizumab in the manufacture of a medicament for treating a subject having a lung cancer, wherein one or more dosing cycles of the medicament is to be administered to the subject, wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 30%, and the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with atezolizumab without tiragolumab; and wherein:

- (i) tiragolumab is to be administered at a fixed dose of about 600 mg every three weeks and atezolizumab is to be administered at a fixed dose of about 1200 mg every three weeks,
- (ii) tiragolumab is to be administered at a fixed dose of about 420 mg every two weeks and atezolizumab is to be administered at a fixed dose of about 840 mg every two weeks, or
- (iii) tiragolumab is to be administered at a fixed dose of about 840 mg every four weeks and atezolizumab is to be administered at a fixed dose of about 1680 mg every four weeks.

In another aspect, the present disclosure refers to use of tiragolumab in the manufacture of a medicament for treating a subject having a lung cancer, wherein one or more dosing cycles of the medicament and atezolizumab are to be administered to the subject, wherein the medicament is formulated for administration of tiragolumab in combination with atezolizumab, wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 30%, and the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with atezolizumab without tiragolumab, and wherein:

- (i) tiragolumab is to be administered at a fixed dose of about 600 mg every three weeks and atezolizumab is to be administered at a fixed dose of about 1200 mg every three weeks,
- (ii) tiragolumab is to be administered at a fixed dose of about 420 mg every two weeks and atezolizumab is to be administered at a fixed dose of about 840 mg every two weeks, or
- (iii) tiragolumab is to be administered at a fixed dose of about 840 mg every four weeks and atezolizumab is to be administered at a fixed dose of about 1680 mg every four weeks.

In yet another aspect, the present disclosure refers to use of atezolizumab in the manufacture of a medicament for treating a subject having a lung cancer, wherein one or more dosing cycles of the medicament and tiragolumab are to be administered to the subject, and wherein the medicament is formulated for administration of atezolizumab in combination with tiragolumab, wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 30%, and the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with the atezolizumab without the tiragolumab, and wherein:

- (i) tiragolumab is to be administered at a fixed dose of about 600 mg every three weeks and atezolizumab is to be administered at a fixed dose of about 1200 mg every three weeks,

- (ii) tiragolumab is to be administered at a fixed dose of about 420 mg every two weeks and atezolizumab is to be administered at a fixed dose of about 840 mg every two weeks, or
- (iii) tiragolumab is to be administered at a fixed dose of about 840 mg every four weeks and atezolizumab is to be administered at a fixed dose of about 1680 mg every four weeks.

5 In another aspect, the present disclosure refers to use of tiragolumab and atezolizumab in the manufacture of a medicament for treating a subject having a lung cancer, wherein one or more dosing cycles of tiragolumab and atezolizumab are to be administered to the subject, wherein the subject previously received concurrent chemoradiotherapy (cCRT) for lung cancer, wherein the subject has not had disease progression after the cCRT, and wherein:

- 10 (i) tiragolumab is to be administered at a fixed dose of about 600 mg every three weeks and atezolizumab is to be administered at a fixed dose of about 1200 mg every three weeks,
- (ii) tiragolumab is to be administered at a fixed dose of about 420 mg every two weeks and atezolizumab is to be administered at a fixed dose of about 840 mg every two weeks, or
- (iii) tiragolumab is to be administered at a fixed dose of about 840 mg every four weeks and
- 15 atezolizumab is to be administered at a fixed dose of about 1680 mg every four weeks.

 In another aspect, the present disclosure refers to use of tiragolumab in the manufacture of a medicament for treating a subject having a lung cancer, wherein one or more dosing cycles of the medicament and atezolizumab are to be administered to the subject, wherein the medicament is formulated for administration of tiragolumab in combination with atezolizumab, wherein the subject

20 previously received concurrent chemoradiotherapy (cCRT) for lung cancer, wherein the subject has not had disease progression after the cCRT, and wherein:

- (i) tiragolumab is to be administered at a fixed dose of about 600 mg every three weeks and atezolizumab is to be administered at a fixed dose of about 1200 mg every three weeks,
- (ii) tiragolumab is to be administered at a fixed dose of about 420 mg every two weeks and
- 25 atezolizumab is to be administered at a fixed dose of about 840 mg every two weeks, or
- (iii) tiragolumab is to be administered at a fixed dose of about 840 mg every four weeks and atezolizumab is to be administered at a fixed dose of about 1680 mg every four weeks.

 In yet another aspect, the present disclosure refers to use of atezolizumab in the manufacture of a medicament for treating a subject having a lung cancer, wherein one or more dosing cycles of the medicament and tiragolumab are to be administered to the subject, wherein the medicament is

30 formulated for administration of atezolizumab in combination with tiragolumab, wherein the subject previously received concurrent chemoradiotherapy (cCRT) for lung cancer, wherein the subject has not had disease progression after the cCRT, and wherein:

- (i) tiragolumab is to be administered at a fixed dose of about 600 mg every three weeks and
- 35 atezolizumab is to be administered at a fixed dose of about 1200 mg every three weeks,
- (ii) tiragolumab is to be administered at a fixed dose of about 420 mg every two weeks and atezolizumab is to be administered at a fixed dose of about 840 mg every two weeks, or
- (iii) tiragolumab is to be administered at a fixed dose of about 840 mg every four weeks and atezolizumab is to be administered at a fixed dose of about 1680 mg every four weeks.

In a first example, the disclosure features a method for treating a subject having a lung cancer comprising administering to the subject one or more dosing cycles of an anti-TIGIT antagonist antibody (e.g., at a fixed dose of between about 30 mg to about 1200 mg every three weeks, at a fixed dose of between about 300 mg to about 800 mg every two weeks, or at a fixed dose of between about 700 mg to about 1000 mg every four weeks) and a PD-1 axis binding antagonist (e.g., an anti-PD-L1 antagonist antibody) (e.g., at a fixed dose of between about 80 mg to about 1600 mg every three weeks, at a fixed dose of between about 200 mg to about 1200 mg every two weeks, or at a fixed dose of between about 400 mg to about 2000 mg every four weeks), wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 30% (e.g., greater than, or equal to, 50%), and the treatment results in (a) a complete response (CR) or a partial response (PR) and/or (b) an increase in progression-free survival (PFS) as compared to treatment with the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) without the anti-TIGIT antagonist antibody.

In some examples of the first example, the method comprises administering to the subject an anti-TIGIT antagonist antibody at a fixed dose of between about 30 mg to about 600 mg every three weeks. In some examples, the method comprises administering to the subject an anti-TIGIT antagonist antibody at a fixed dose of about 600 mg every three weeks. In some examples of the first example, the method comprises administering to the subject an anti-TIGIT antagonist antibody at a fixed dose of between about 400 mg to about 500 mg every two weeks. In some examples, the method comprises administering to the subject an anti-TIGIT antagonist antibody at a fixed dose of about 420 mg every two weeks. In some examples of the first example, the method comprises administering to the subject an anti-TIGIT antagonist antibody at a fixed dose of between about 800 mg to about 900 mg every two weeks. In some examples, the method comprises administering to the subject an anti-TIGIT antagonist antibody at a fixed dose of about 840 mg every two weeks.

In some examples of the first example, the anti-TIGIT antagonist antibody comprises the following hypervariable regions (HVRs): an HVR-H1 sequence comprising the amino acid sequence of SNSAAWN (SEQ ID NO: 1); an HVR-H2 sequence comprising the amino acid sequence of KTYRFRKWYSYAVSVKG (SEQ ID NO: 2); an HVR-H3 sequence comprising the amino acid sequence of ESTTYDLLAGPFDY (SEQ ID NO: 3); an HVR-L1 sequence comprising the amino acid sequence of KSSQTVLYSSNNKKYLA (SEQ ID NO: 4); an HVR-L2 sequence comprising the amino acid sequence of WASTRES (SEQ ID NO: 5); and an HVR-L3 sequence comprising the amino acid sequence of QQYYSTPFT (SEQ ID NO: 6). In some examples, the anti-TIGIT antagonist antibody further comprises the following light chain variable region framework regions (FRs): an FR-L1 comprising the amino acid sequence of DIVMTQSPDSLAVSLGERATINC (SEQ ID NO: 7); an FR-L2 comprising the

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amino acid sequence of WYQQKPGQPPNLLIY (SEQ ID NO: 8); an FR-L3 comprising the amino acid sequence of GVPDRFSGSGSGTDFLTISLQAEDVAVYYC (SEQ ID NO: 9); and an FR-L4 comprising the amino acid sequence of FGPGTKVEIK (SEQ ID NO: 10). In some examples, the anti-TIGIT antagonist antibody further comprises the following heavy chain variable region FRs: an FR-H1 comprising the amino acid sequence of X₁VQLQQSGPGLVKPSQTLTLTCAISGDSVS (SEQ ID NO: 11), wherein X₁ is Q or E; an FR-H2 comprising the amino acid sequence of WIRQSPSRGLEWLG (SEQ ID NO: 12); an FR-H3 comprising the amino acid sequence of RITINPDTSKNQFSLQLNSVTPEDTAVFYCTR (SEQ ID NO: 13); and an FR-H4 comprising the amino acid sequence of WGQGTLTVSS (SEQ ID NO: 14). In some examples, X₁ is Q. In some examples, X₁ is E.

In some examples of the first example, the anti-TIGIT antagonist antibody comprises: (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 17 or 18; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 19; or (c) a VH domain as in (a) and a VL domain as in (b).

In some examples of the first example, the anti-TIGIT antagonist antibody comprises: a VH domain comprising the amino acid sequence of SEQ ID NO: 17 or 18 and a VL domain comprising the amino acid sequence of SEQ ID NO: 19.

In some examples of the first example, the anti-TIGIT antagonist antibody is a monoclonal antibody. In some examples, the anti-TIGIT antagonist antibody is a human antibody (e.g., a monoclonal human antibody).

In some examples of the first example, the anti-TIGIT antagonist antibody is a full-length antibody. In some examples of the first example, the anti-TIGIT antagonist antibody is tiragolumab.

In some examples of the first example, the anti-TIGIT antagonist antibody is an antibody fragment that binds TIGIT selected from the group consisting of Fab, Fab', Fab'-SH, Fv, single chain variable fragment (scFv), and (Fab')₂ fragments.

In some examples of the first example, the anti-TIGIT antagonist antibody is an IgG class antibody. In some examples, the IgG class antibody is an IgG1 subclass antibody.

In some examples of the first example, the method comprises administering to the subject a PD-1 axis binding antagonist (e.g., an anti-PD-L1 antibody) at a fixed dose of about 1200 mg every three weeks. In some examples of the first example, the method comprises administering to the subject a PD-1 axis binding antagonist (e.g., an anti-PD-L1 antibody) at a fixed dose of about 840 mg every two weeks. In some examples of the first example, the method comprises administering to the subject a PD-1 axis binding antagonist (e.g., an anti-PD-L1 antibody) at a fixed dose of about 1680 mg every four weeks.

In some examples of the first example, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is atezolizumab (MPDL3280A), MSB0010718C, MDX-1105, or MEDI4736. In some examples, the anti-PD-L1 antagonist antibody is atezolizumab.

In some examples of the first example, the anti-PD-L1 antagonist antibody comprises the following HVRs: an HVR-H1 sequence comprising the amino acid sequence of GFTFSDSWIH (SEQ ID

NO: 20); an HVR-H2 sequence comprising the amino acid sequence of AWISPYGGSTYYADSVKG (SEQ ID NO: 21); an HVR-H3 sequence comprising the amino acid sequence of RHWPGGFDY (SEQ ID NO: 22); an HVR-L1 sequence comprising the amino acid sequence of RASQDVSTAVA (SEQ ID NO: 23); an HVR-L2 sequence comprising the amino acid sequence of SASFLYS (SEQ ID NO: 24); and an HVR-L3 sequence comprising the amino acid sequence of QQYLYHPAT (SEQ ID NO: 25). In some examples, the anti-PD-L1 antagonist antibody comprises: (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 26; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 27; or (c) a VH domain as in (a) and a VL domain as in (b).

In some examples of the first example, the anti-PD-L1 antagonist antibody comprises: a VH domain comprising the amino acid sequence of SEQ ID NO: 26 and a VL domain comprising the amino acid sequence of SEQ ID NO: 27.

In some examples of the first example, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is a monoclonal antibody. In some examples, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is a humanized antibody (e.g., a monoclonal humanized antibody).

In some examples of the first example, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is a full-length antibody.

In some examples of the first example, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is an antibody fragment that binds PD-L1 selected from the group consisting of Fab, Fab', Fab'-SH, Fv, single chain variable fragment (scFv), and (Fab')₂ fragments.

In some examples of the first example, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is an IgG class antibody. In some examples, the IgG class antibody is an IgG1 subclass antibody.

In some examples of the first example, the method comprises administering to the subject the anti-TIGIT antagonist antibody at a fixed dose of about 600 mg every three weeks and the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) at a fixed dose of about 1200 mg every three weeks.

In some examples of the first example, the length of each of the one or more dosing cycles is 21 days.

In some examples of the first example, the method comprises administering to the subject the anti-TIGIT antagonist antibody and the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) on about Day 1 of each of the one or more dosing cycles.

In some examples of the first example, the method comprises administering to the subject the anti-TIGIT antagonist antibody at a fixed dose of about 420 mg every two weeks and the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) at a fixed dose of about 820 mg every two weeks. In some examples of the first example, the length of each of the one or more dosing cycles is 28 days. In some examples of the first example, the method comprises administering to the subject the anti-TIGIT antagonist antibody and the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) on about Day 1 and Day 15 of each of the one or more dosing cycles.

In some examples of the first example, the method comprises administering to the subject the anti-TIGIT antagonist antibody at a fixed dose of about 840 mg every four weeks and the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) at a fixed dose of about 1680 mg every four weeks. In some examples of the first example, the length of each of the one or more dosing cycles is 28 days. In some examples of the first example, the method comprises administering to the subject the anti-TIGIT antagonist antibody and the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) on about Day 1 of each of the one or more dosing cycles.

In some examples of the first example, the method comprises administering to the subject the anti-TIGIT antagonist antibody before the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody). In some examples, the method comprises a first observation period following administration of the anti-TIGIT antagonist antibody and second observation period following administration of the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody). In some examples, the first observation period and the second observation period are each between about 30 minutes to about 60 minutes in length.

In some examples of the first example, the method comprises administering to the subject the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) before the anti-TIGIT antagonist antibody. In some examples, the method comprises a first observation period following administration of the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) and second observation period following administration of the anti-TIGIT antagonist antibody. In some examples, the first observation period and the second observation period are each between about 30 minutes to about 60 minutes in length.

In some examples of the first example, the method comprises administering to the subject the anti-TIGIT antagonist antibody and the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) simultaneously.

In some examples of the first example, the method comprises administering to the subject the anti-TIGIT antagonist antibody and PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) intravenously. In some examples, the method comprises administering to the subject the anti-TIGIT antagonist antibody by intravenous infusion over 60 ± 10 minutes. In some examples, the method comprises administering to the subject the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) by intravenous infusion over 60 ± 15 minutes.

In some examples of the first example, the PD-L1-positive tumor cell fraction has been determined by an immunohistochemical (IHC) assay. In some examples, the IHC assay uses anti-PD-L1 antibody SP263, 22C3, SP142, or 28-8. In some examples, the PD-L1-positive tumor cell fraction is determined by positive staining with an anti-PD-L1 antibody (e.g., SP263, 22C3, SP142, or 28-8). In some examples, the PD-L1-positive tumor cell fraction is greater than, or equal to, 50%, as determined by positive staining with the anti-PD-L1 antibody SP263 (e.g., wherein the PD-L1-positive tumor cell fraction is calculated using the Ventana SP263 IHC assay). In some examples, the PD-L1-positive tumor cell fraction is greater than, or equal to, 50%, as determined by positive staining with the anti-PD-L1 antibody 22C3 (e.g., wherein the PD-L1-positive tumor cell fraction is calculated using the pharmDx 22C3 IHC assay). In some examples, the PD-L1-positive tumor cell fraction is greater than,

or equal to, 30%, as determined by positive staining with the anti-PD-L1 antibody SP142 (e.g., wherein the PD-L1-positive tumor cell fraction is calculated using the Ventana SP142 IHC assay). In some examples, the PD-L1-positive tumor cell fraction is greater than, or equal to, 50%, as determined by positive staining with the anti-PD-L1 antibody 28-8.

5 In some examples of the first example, a tumor sample obtained from the subject has been determined to have a detectable nucleic acid expression level of PD-L1. In some examples, the detectable nucleic acid expression level of PD-L1 has been determined by RNA-seq, RT-qPCR, qPCR, multiplex qPCR or RT-qPCR, microarray analysis, SAGE, MassARRAY technique, ISH, or a combination thereof.

10 In some examples of the first example, the lung cancer is a non-small cell lung cancer (NSCLC). In some examples, the NSCLC is a squamous NSCLC. In some examples, the NSCLC is a non-squamous NSCLC. In some examples, the NSCLC is a locally advanced unresectable NSCLC. In some examples, the NSCLC is a Stage IIIB NSCLC. In some examples, the NSCLC is a recurrent or metastatic NSCLC. In some examples, the NSCLC is a Stage IV NSCLC. In some examples, the subject has not
15 been previously treated for Stage IV NSCLC.

In some examples of the first example, the subject does not have a sensitizing epidermal growth factor receptor (*EGFR*) gene mutation or anaplastic lymphoma kinase (*ALK*) gene rearrangement.

In some examples of the first example, the subject does not have a pulmonary lymphoepithelioma-like carcinoma subtype of NSCLC.

20 In some examples of the first example, the subject does not have an active Epstein-Barr virus (EBV) infection or a known or suspected chronic active EBV infection. In some examples, the subject is negative for EBV IgM or negative by EBV PCR. In some examples, the subject is negative for EBV IgM and negative by EBV PCR. In some examples, the subject is positive for EBV IgG or positive for Epstein-Barr nuclear antigen (EBNA). In some examples, the subject is positive for EBV IgG and positive for
25 EBNA.

In some examples of the first example, the subject is negative for EBV IgG or negative for EBNA. In some examples, the subject is negative for EBV IgG and negative for EBNA.

In some examples, the subject is likely to have an increase in the PFS of the subject as compared to a reference PFS time. In some examples, the reference PFS time is the median PFS time
30 of a population of subjects who have received a treatment comprising an PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) without an anti-TIGIT antagonist antibody.

In a second example, the disclosure features a method for treating a subject having a NSCLC comprising administering to the subject one or more dosing cycles of an anti-TIGIT antagonist antibody (e.g., at a fixed dose of about 600 mg every three weeks, at a fixed dose of about 420 mg every two
35 weeks, or at a fixed dose of about 840 mg every four weeks) and a PD-1 axis binding antagonist (e.g., an anti-PD-L1 antagonist antibody) (e.g., at a fixed dose of about 1200 mg every three weeks, at a fixed dose of about 840 mg every two weeks, or at a fixed dose of about 1680 mg every four weeks), wherein the anti-TIGIT antagonist antibody comprises: a VH domain comprising the amino acid sequence of SEQ ID NO: 17 or 18 and a VL domain comprising the amino acid sequence of SEQ ID NO: 19, and wherein
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the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 30% (e.g., greater than, or equal to, 50%), and the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with atezolizumab without the anti-TIGIT antagonist antibody.

In a third example, the disclosure features a method for treating a subject having a NSCLC comprising (a) obtaining a tumor sample from the subject; (b) detecting the protein expression level of PD-L1 in the tumor sample by staining tumor cells from the tumor sample with anti-PD-L1 antibody SP263 and determining a PD-L1-positive tumor cell fraction therefrom, wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 50%; and (c) administering to the subject a therapy comprising one or more dosing cycles of an anti-TIGIT antagonist antibody (e.g., at a fixed dose of 600 mg every three weeks, at a fixed dose of 420 mg every two weeks, or at a fixed dose of 840 mg every four weeks) and atezolizumab (e.g., at a fixed dose of 1200 mg every three weeks, at a fixed dose of 840 mg every two weeks, or at a fixed dose of 1680 mg every four weeks), wherein the anti-TIGIT antagonist antibody comprises: a VH domain comprising the amino acid sequence of SEQ ID NO: 17 or 18; and a VL domain comprising the amino acid sequence of SEQ ID NO: 19, and wherein the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with atezolizumab without the anti-TIGIT antagonist antibody.

In a fourth example, the disclosure features a method for treating a subject having a NSCLC comprising (a) obtaining a tumor sample from the subject; (b) detecting the protein expression level of PD-L1 in the tumor sample by staining tumor cells from the tumor sample with anti-PD-L1 antibody 22C3 and determining a PD-L1-positive tumor cell fraction therefrom, wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 50%; and (c) administering to the subject a therapy comprising one or more dosing cycles of an anti-TIGIT antagonist antibody (e.g., at a fixed dose of 600 mg every three weeks, at a fixed dose of 420 mg every two weeks, or at a fixed dose of 840 mg every four weeks) and atezolizumab (e.g., at a fixed dose of 1200 mg every three weeks, at a fixed dose of 840 mg every two weeks, or at a fixed dose of 1680 mg every four weeks), wherein the anti-TIGIT antagonist antibody comprises: a VH domain comprising the amino acid sequence of SEQ ID NO: 17 or 18; and a VL domain comprising the amino acid sequence of SEQ ID NO: 19, and wherein the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with atezolizumab without the anti-TIGIT antagonist antibody.

In a fifth example, the disclosure features a method for treating a subject having a NSCLC comprising administering to the subject one or more dosing cycles of tiragolumab (e.g., at a fixed dose of 600 mg every three weeks, at a fixed dose of 420 mg every two weeks, or at a fixed dose of 840 mg every four weeks) and atezolizumab (e.g., at a fixed dose of 1200 mg every three weeks, at a fixed dose of 840 mg every two weeks, or at a fixed dose of 1680 mg every four weeks), wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 30% (e.g., greater than, or equal to, 50%), and the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with atezolizumab without tiragolumab.

In a sixth example, the disclosure features a method for treating a subject having a NSCLC comprising (a) obtaining a tumor sample from the subject; (b) detecting the protein expression level of PD-L1 in the tumor sample by an IHC assay using anti-PD-L1 antibody SP263 and determining a PD-L1-

positive tumor cell fraction therefrom, wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 50%; and (c) administering to the subject a therapy comprising one or more dosing cycles of an anti-TIGIT antagonist antibody (e.g., at a fixed dose of 600 mg every three weeks, at a fixed dose of 420 mg every two weeks, or at a fixed dose of 840 mg every four weeks) and atezolizumab (e.g., at a fixed dose of 1200 mg every three weeks, at a fixed dose of 840 mg every two weeks, or at a fixed dose of 1680 mg every four weeks), wherein the anti-TIGIT antagonist antibody comprises: a VH domain comprising the amino acid sequence of SEQ ID NO: 17 or 18; and a VL domain comprising the amino acid sequence of SEQ ID NO: 19, and wherein the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with atezolizumab without the anti-TIGIT antagonist antibody.

In a seventh example, the disclosure features a method for treating a subject having a NSCLC comprising (a) obtaining a tumor sample from the subject; (b) detecting the protein expression level of PD-L1 in the tumor sample by an IHC assay using anti-PD-L1 antibody 22C3 and determining a PD-L1-positive tumor cell fraction therefrom, wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 50%; and (c) administering to the subject a therapy comprising one or more dosing cycles of an anti-TIGIT antagonist antibody (e.g., at a fixed dose of 600 mg every three weeks, at a fixed dose of 420 mg every two weeks, or at a fixed dose of 840 mg every four weeks) and atezolizumab (e.g., at a fixed dose of 1200 mg every three weeks, at a fixed dose of 840 mg every two weeks, or at a fixed dose of 1680 mg every four weeks), wherein the anti-TIGIT antagonist antibody comprises: a VH domain comprising the amino acid sequence of SEQ ID NO: 17 or 18; and a VL domain comprising the amino acid sequence of SEQ ID NO: 19, and wherein the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with atezolizumab without the anti-TIGIT antagonist antibody.

In an eighth example, the disclosure features an anti-TIGIT antagonist antibody and a PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) for use in a method of treating a subject having a lung cancer, the method comprising administering to the subject one or more dosing cycles of the anti-TIGIT antagonist antibody (e.g., at a fixed dose of between about 30 mg to about 1200 mg every three weeks, at a fixed dose of between about 300 mg to about 800 mg every two weeks, or at a fixed dose of between about 700 mg to about 1000 mg every four weeks) and a PD-1 axis binding antagonist (e.g., an anti-PD-L1 antagonist antibody) (e.g., at a fixed dose of between about 80 mg to about 1600 mg every three weeks, at a fixed dose of between about 200 mg to about 1200 mg every two weeks, or at a fixed dose of between about 400 mg to about 2000 mg every four weeks), wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 30% (e.g., greater than, or equal to, 50%), and the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) without the anti-TIGIT antagonist antibody.

In some examples of the eighth example, the anti-TIGIT antagonist antibody is to be administered to the subject at a fixed dose of between about 30 mg to about 600 mg every three weeks. In some examples, the anti-TIGIT antagonist antibody is to be administered to the subject at a fixed dose of about 600 mg every three weeks. In some examples, the anti-TIGIT antagonist antibody is to

be administered at a fixed dose of between about 400 mg to about 500 mg every two weeks. In some examples, the anti-TIGIT antagonist antibody is to be administered at a fixed dose of about 420 mg every two weeks. In some examples, the anti-TIGIT antagonist antibody is to be administered at a fixed dose of between about 800 mg to about 900 mg every two weeks. In some examples, the anti-TIGIT antagonist antibody is to be administered at a fixed dose of about 840 mg every two weeks.

In some examples of the eighth example, the anti-TIGIT antagonist antibody comprises the following HVRs: an HVR-H1 sequence comprising the amino acid sequence of SNSAAWN (SEQ ID NO: 1); an HVR-H2 sequence comprising the amino acid sequence of KTYRFRKWYSDYAVSVKG (SEQ ID NO: 2); an HVR-H3 sequence comprising the amino acid sequence of ESTTYDLLAGPFDY (SEQ ID NO: 3); an HVR-L1 sequence comprising the amino acid sequence of KSSQTVLYSSNNKKYLA (SEQ ID NO: 4); an HVR-L2 sequence comprising the amino acid sequence of WASTRES (SEQ ID NO: 5); and an HVR-L3 sequence comprising the amino acid sequence of QQYYSTPFT (SEQ ID NO: 6). In some examples, the anti-TIGIT antagonist antibody further comprises the following light chain variable region FRs: an FR-L1 comprising the amino acid sequence of DIVMTQSPDSLAVSLGERATINC (SEQ ID NO: 7); an FR-L2 comprising the amino acid sequence of WYQQKPGQPPNLLIY (SEQ ID NO: 8); an FR-L3 comprising the amino acid sequence of GVPDRFSGSGSGTDFTLTISLQAEDVAVYYC (SEQ ID NO: 9); and an FR-L4 comprising the amino acid sequence of FGPGTKVEIK (SEQ ID NO: 10). In some examples, the anti-TIGIT antagonist antibody further comprises the following heavy chain variable region FRs: an FR-H1 comprising the amino acid sequence of X₁VQLQQSGPGLVKPSQTLSTCAISGDSVS (SEQ ID NO: 11), wherein X₁ is Q or E; an FR-H2 comprising the amino acid sequence of WIRQSPSRGLEWLG (SEQ ID NO: 12); an FR-H3 comprising the amino acid sequence of RITINPDTSKNQFSLQLNSVTPEDTAVFYCTR (SEQ ID NO: 13); and an FR-H4 comprising the amino acid sequence of WGQGTLVTVSS (SEQ ID NO: 14). In some examples, X₁ is Q. In some examples, X₁ is E.

In some examples of the eighth example, the anti-TIGIT antagonist antibody comprises: (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 17 or 18; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 19; or (c) a VH domain as in (a) and a VL domain as in (b).

In some examples of the eighth example, the anti-TIGIT antagonist antibody comprises: a VH domain comprising the amino acid sequence of SEQ ID NO: 17 or 18 and a VL domain comprising the amino acid sequence of SEQ ID NO: 19.

In some examples of the eighth example, the anti-TIGIT antagonist antibody is a monoclonal antibody. In some examples, the anti-TIGIT antagonist antibody is a human antibody (e.g., a monoclonal human antibody).

In some examples of the eighth example, the anti-TIGIT antagonist antibody is a full-length antibody. In some examples of the eighteenth example, the anti-TIGIT antagonist antibody is tiragolumab.

In some examples of the eighth example, the anti-TIGIT antagonist antibody is an antibody fragment that binds TIGIT selected from the group consisting of Fab, Fab', Fab'-SH, Fv, single chain variable fragment (scFv), and (Fab')₂ fragments.

In some examples of the eighth example, the anti-TIGIT antagonist antibody is an IgG class antibody. In some examples, the IgG class antibody is an IgG1 subclass antibody.

In some examples of the eighth example, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is to be administered to the subject at a fixed dose of about 1200 mg every three weeks. In other examples, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is to be administered to the subject at a fixed dose of about 840 mg every two weeks. In other examples, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is to be administered to the subject at a fixed dose of about 1680 mg every four weeks.

In some examples of the eighth example, the PD-1 axis binding antagonist is a PD-L1 binding antagonist or a PD-1 binding antagonist. In some examples, the PD-L1 binding antagonist is an anti-PD-L1 antagonist antibody (e.g., atezolizumab (MPDL3280A), MSB0010718C, MDX-1105, or MEDI4736). In some examples, the PD-L1 antagonist is atezolizumab. In some examples, the PD-1 binding antagonist is an anti-PD-1 antagonist antibody (e.g., nivolumab (MDX-1106) or pembrolizumab (formerly lambrolizumab (MK-3475))). In some examples, the PD-1 binding antagonist is AMP-224. In some examples of the eighth example, the anti-PD-L1 antagonist antibody comprises the following HVRs: an HVR-H1 sequence comprising the amino acid sequence of GFTFSDSWIH (SEQ ID NO: 20); an HVR-H2 sequence comprising the amino acid sequence of AWISPYGGSTYYADSVKG (SEQ ID NO: 21); an HVR-H3 sequence comprising the amino acid sequence of RHWPGGFDY (SEQ ID NO: 22); an HVR-L1 sequence comprising the amino acid sequence of RASQDVSTAVA (SEQ ID NO: 23); an HVR-L2 sequence comprising the amino acid sequence of SASFLYS (SEQ ID NO: 24); and an HVR-L3 sequence comprising the amino acid sequence of QQYLYHPAT (SEQ ID NO: 25). In some examples, the anti-PD-L1 antagonist antibody comprises: (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 26; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 27; or (c) a VH domain as in (a) and a VL domain as in (b).

In some examples of the eighth example, the anti-PD-L1 antagonist antibody comprises: a VH domain comprising the amino acid sequence of SEQ ID NO: 26 and a VL domain comprising the amino acid sequence of SEQ ID NO: 27.

In some examples of the eighth example, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is a monoclonal antibody. In some examples, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is a humanized antibody (e.g., a monoclonal humanized antibody).

In some examples of the eighth example, PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is a full-length antibody.

In some examples of the eighth example, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is an antibody fragment that binds PD-L1 or PD-1 selected from the group consisting of Fab, Fab', Fab'-SH, Fv, single chain variable fragment (scFv), and (Fab')₂ fragments.

In some examples of the eighth example, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is an IgG class antibody. In some examples, the IgG class antibody is an IgG1 subclass antibody.

In some examples of the eighth example, the anti-TIGIT antagonist antibody is to be administered to the subject at a fixed dose of about 600 mg every three weeks and the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is to be administered to the subject at a fixed dose of about 1200 mg every three weeks.

In some examples of the eighth example, the length of each of the one or more dosing cycles is 21 days.

In some examples of the eighth example, the anti-TIGIT antagonist antibody and PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) are to be administered to the subject on about Day 1 of each of the one or more dosing cycles.

In some examples, the anti-TIGIT antagonist antibody is to be administered at a fixed dose of about 420 mg every two weeks and the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is to be administered at a fixed dose of about 820 mg every two weeks. In some examples, the length of each of the one or more dosing cycles is 28 days. In some examples, the anti-TIGIT antagonist antibody and the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) are to be administered on about Day 1 and Day 15 of each of the one or more dosing cycles.

In some examples, the anti-TIGIT antagonist antibody is to be administered at a fixed dose of about 840 mg every four weeks and the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is to be administered at a fixed dose of about 1680 mg every four weeks. In some examples, the length of each of the one or more dosing cycles is 28 days. In some examples, the anti-TIGIT antagonist antibody and the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) are to be administered on about Day 1 of each of the one or more dosing cycles.

In some examples of the eighth example, the anti-TIGIT antagonist antibody is to be administered to the subject before the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody). In some examples, a first observation period is to follow administration of the anti-TIGIT antagonist antibody and second observation period is to follow administration of the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody). In some examples, the first observation period and the second observation period are each between about 30 minutes to about 60 minutes in length.

In some examples of the eighth example, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is to be administered to the subject before the anti-TIGIT antagonist antibody. In some examples, a first observation period is to follow administration of the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) and second observation period is to follow administration of the anti-TIGIT antagonist antibody. In some examples, the first observation period and the second observation period are each between about 30 minutes to about 60 minutes in length.

In some examples of the eighth example, the anti-TIGIT antagonist antibody is to be administered to the subject simultaneously with the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody).

In some examples of the eighth example, the anti-TIGIT antagonist antibody and PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) are to be administered to the subject intravenously. In some examples, the anti-TIGIT antagonist antibody is to be administered to the subject by intravenous infusion over 60 ± 10 minutes. In some examples, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is to be administered to the subject by intravenous infusion over 60 ± 15 minutes.

In some examples of the eighth example, the PD-L1-positive tumor cell fraction has been determined by an immunohistochemical (IHC) assay. In some examples, the IHC assay uses anti-PD-L1 antibody SP263, 22C3, SP142, or 28-8. In some examples, the PD-L1-positive tumor cell fraction is determined by positive staining with an anti-PD-L1 antibody (e.g., SP263, 22C3, SP142, or 28-8). In some examples, the PD-L1-positive tumor cell fraction is greater than, or equal to, 50%, as determined by positive staining with the anti-PD-L1 antibody SP263 (e.g., wherein the PD-L1-positive tumor cell fraction is calculated using the Ventana SP263 IHC assay). In some examples, the PD-L1-positive tumor cell fraction is greater than, or equal to, 50%, as determined by positive staining with the anti-PD-L1 antibody 22C3 (e.g., wherein the PD-L1-positive tumor cell fraction is calculated using the pharmDx 22C3 IHC assay). In some examples, the PD-L1-positive tumor cell fraction is greater than, or equal to, 30%, as determined by positive staining with the anti-PD-L1 antibody SP142 (e.g., wherein the PD-L1-positive tumor cell fraction is calculated using the Ventana SP142 IHC assay). In some examples, the PD-L1-positive tumor cell fraction is greater than, or equal to, 50%, as determined by positive staining with the anti-PD-L1 antibody 28-8.

In some examples of the eighth example, the IHC assay uses anti-PD-L1 antibody SP263. In some examples, the IHC assay uses anti-PD-L1 antibody 22C3.

In some examples of the eighth example, a tumor sample obtained from the subject has been determined to have a detectable nucleic acid expression level of PD-L1. In some examples, the detectable nucleic acid expression level of PD-L1 has been determined by RNA-seq, RT-qPCR, qPCR, multiplex qPCR or RT-qPCR, microarray analysis, SAGE, MassARRAY technique, ISH, or a combination thereof.

In some examples of the eighth example, the lung cancer is a non-small cell lung cancer (NSCLC). In some examples, the NSCLC is a squamous NSCLC. In some examples, the NSCLC is a non-squamous NSCLC. In some examples, the NSCLC is a locally advanced unresectable NSCLC. In some examples, the NSCLC is a Stage IIIB NSCLC. In some examples, the NSCLC is a recurrent or metastatic NSCLC. In some examples, the NSCLC is a Stage IV NSCLC. In some examples, the subject has not been previously treated for Stage IV NSCLC.

In some examples of the eighth example, the subject does not have a sensitizing epidermal growth factor receptor (*EGFR*) gene mutation or anaplastic lymphoma kinase (*ALK*) gene rearrangement.

In some examples of the eighth example, the subject does not have a pulmonary lymphoepithelioma-like carcinoma subtype of NSCLC.

In some examples of the eighth example, the subject does not have an active EBV infection or a known or suspected chronic active EBV infection. In some examples, the subject is negative for

EBV IgM or negative by EBV PCR. In some examples, the subject is negative for EBV IgM and negative by EBV PCR. In some examples, the subject is positive for EBV IgG or positive for EBNA. In some examples, the subject is positive for EBV IgG and positive for EBNA.

5 In some examples of the eighth example, the subject is negative for EBV IgG or negative for EBNA. In some examples, the subject is negative for EBV IgG and negative for EBNA.

In some examples of the eighth example, the PFS of the subject is increased as compared to a reference PFS time. In some examples, the reference PFS time is the median PFS time of a population of subjects who have received a treatment comprising a PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) without an anti-TIGIT antagonist antibody.

10 In a ninth example, the disclosure features an anti-TIGIT antagonist antibody and atezolizumab for use in a method of treating a subject having a NSCLC, the method comprising administering to the subject one or more dosing cycles of an anti-TIGIT antagonist antibody (e.g., at a fixed dose of 600 mg every three weeks, at a fixed dose of 420 mg every two weeks, or at a fixed dose of 840 mg every four weeks) and atezolizumab (e.g., at a fixed dose of 1200 mg every three weeks, at a fixed dose of 840 mg
15 every two weeks, or at a fixed dose of 1680 mg every four weeks), wherein the anti-TIGIT antagonist antibody comprises: a VH domain comprising the amino acid sequence of SEQ ID NO: 17 or 18 and a VL domain comprising the amino acid sequence of SEQ ID NO: 19., and wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 30% (e.g., greater than, or equal to, 50%), and the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as
20 compared to treatment with atezolizumab without the anti-TIGIT antagonist antibody

In a tenth example, the disclosure features tiragolumab and atezolizumab for use in a method of treating a subject having a NSCLC, the method comprising administering to the subject one or more dosing cycles of tiragolumab (e.g., at a fixed dose of 600 mg every three weeks, at a fixed dose of 420 mg every two weeks, or at a fixed dose of 840 mg every four weeks) and atezolizumab (e.g., at a fixed
25 dose of 1200 mg every three weeks, at a fixed dose of 840 mg every two weeks, or at a fixed dose of 1680 mg every four weeks), and wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 30% (e.g., greater than, or equal to, 50%), and the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with atezolizumab without tiragolumab.

30 In an eleventh example, the disclosure features a use of an anti-TIGIT antagonist antibody and a PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) in the manufacture of a medicament for use in a method of treating a subject having a lung cancer, the method comprising administering to the subject one or more dosing cycles of the medicament, wherein the medicament is formulated for administration of the anti-TIGIT antagonist antibody (e.g., at a fixed dose of between about 30 mg to
35 about 1200 mg every three weeks, at a fixed dose of between about 300 mg to about 800 mg every two weeks, or at a fixed dose of between about 700 mg to about 1000 mg every four weeks) and a PD-1 axis binding antagonist (e.g., an anti-PD-L1 antagonist antibody) (e.g., at a fixed dose of between about 80 mg to about 1600 mg every three weeks, at a fixed dose of between about 200 mg to about 1200 mg every two weeks, or at a fixed dose of between about 400 mg to about 2000 mg every four weeks), wherein the
40 subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to,

30% (e.g., greater than, or equal to, 50%), and the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) without the anti-TIGIT antagonist antibody.

5 In a twelfth example, the disclosure features a use of an anti-TIGIT antagonist antibody in the manufacture of a medicament for use in a method of treating a subject having lung cancer, the method comprising administering to the subject one or more dosing cycles of the medicament and a PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody), wherein the medicament is formulated for administration of the anti-TIGIT antagonist antibody (e.g., at a fixed dose of between about 30 mg to about 1200 mg every three weeks, at a fixed dose of between about 300 mg to about 800 mg every two weeks, or at a fixed dose of between about 700 mg to about 1000 mg every four weeks) and a PD-1 axis binding antagonist (e.g., an anti-PD-L1 antagonist antibody) (e.g., at a fixed dose of between about 80 mg to about 1600 mg every three weeks, at a fixed dose of between about 200 mg to about 1200 mg every two weeks, or at a fixed dose of between about 400 mg to about 2000 mg every four weeks), wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 15 30% (e.g., greater than, or equal to, 50%), and the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) without the anti-TIGIT antagonist antibody.

In a thirteenth example, the disclosure features a use of a PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) in the manufacture of a medicament for use in a method of treating a 20 subject having lung cancer, the method comprising administering to the subject one or more dosing cycles of the medicament and an anti-TIGIT antagonist antibody, wherein the medicament is formulated for administration of the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) (e.g., at a fixed dose of between about 80 mg to about 1600 mg every three weeks, at a fixed dose of between about 200 mg to about 1200 mg every two weeks, or at a fixed dose of between about 400 mg to about 2000 mg every four weeks) and the anti-TIGIT antagonist antibody is to be administered (e.g., at a fixed dose of between about 30 mg to about 1200 mg every three weeks, at a fixed dose of between about 300 mg to about 800 mg every two weeks, or at a fixed dose of between about 700 mg to about 1000 mg every four weeks), wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 30% (e.g., greater than, or equal to, 50%), and the treatment results in (a) a 25 CR or a PR and/or (b) an increase in PFS as compared to treatment with the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) without the anti-TIGIT antagonist antibody. 30

In some examples of any of the eleventh, twelfth, and thirteenth examples, the anti-TIGIT antagonist antibody is to be administered to the subject at a fixed dose of between about 30 mg to about 600 mg every three weeks. In some examples, the anti-TIGIT antagonist antibody is to be administered 35 to the subject at a fixed dose of about 600 mg every three weeks. In some examples, the anti-TIGIT antagonist antibody is to be administered at a fixed dose of between about 400 mg to about 500 mg every two weeks. In some examples, the anti-TIGIT antagonist antibody is to be administered at a fixed dose of about 420 mg every two weeks. In some examples, the anti-TIGIT antagonist antibody is to be administered at a fixed dose of between about 800 mg to about 900 mg every

two weeks. In some examples, the anti-TIGIT antagonist antibody is to be administered at a fixed dose of about 840 mg every two weeks.

In some examples of any of the eleventh, twelfth, and thirteenth examples, the anti-TIGIT antagonist antibody comprises the following hypervariable regions (HVRs): an HVR-H1 sequence comprising the amino acid sequence of SNSAAWN (SEQ ID NO: 1); an HVR-H2 sequence comprising the amino acid sequence of KTYRFRKWYSDYAVSVKG (SEQ ID NO: 2); an HVR-H3 sequence comprising the amino acid sequence of ESTTYDLLAGPFDY (SEQ ID NO: 3); an HVR-L1 sequence comprising the amino acid sequence of KSSQTVLYSSNNKKYLA (SEQ ID NO: 4); an HVR-L2 sequence comprising the amino acid sequence of WASTRES (SEQ ID NO: 5); and an HVR-L3 sequence comprising the amino acid sequence of QQYYSTPFT (SEQ ID NO: 6). In some examples, the anti-TIGIT antagonist antibody further comprises the following light chain variable region framework regions (FRs): an FR-L1 comprising the amino acid sequence of DIVMTQSPDSLAVSLGERATINC (SEQ ID NO: 7); an FR-L2 comprising the amino acid sequence of WYQQKPGQPPLLIIY (SEQ ID NO: 8); an FR-L3 comprising the amino acid sequence of GVPDRFSGSGSGTDFTLTISLQAEDVAVYYC (SEQ ID NO: 9); and an FR-L4 comprising the amino acid sequence of FGPGTKVEIK (SEQ ID NO: 10). In some examples, the anti-TIGIT antagonist antibody further comprises the following heavy chain variable region FRs: an FR-H1 comprising the amino acid sequence of X₁VQLQQSGPGLVKPSQTLSTCAISGDSVS (SEQ ID NO: 11), wherein X₁ is Q or E; an FR-H2 comprising the amino acid sequence of WIRQSPSRGLEWLG (SEQ ID NO: 12); an FR-H3 comprising the amino acid sequence of RITINPDTSKNQFSLQLNSVTPEDTAVFYCTR (SEQ ID NO: 13); and an FR-H4 comprising the amino acid sequence of WGQGTLTVSS (SEQ ID NO: 14). In some examples, X₁ is Q. In some examples, X₁ is E.

In some examples of any of the eleventh, twelfth, and thirteenth examples, the anti-TIGIT antagonist antibody comprises: (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 17 or 18; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 19; or (c) a VH domain as in (a) and a VL domain as in (b).

In some examples of any of the eleventh, twelfth, and thirteenth examples, the anti-TIGIT antagonist antibody is a monoclonal antibody. In some examples, the anti-TIGIT antagonist antibody is a human antibody (e.g., a monoclonal human antibody).

In some examples of any of the eleventh, twelfth, and thirteenth examples, the anti-TIGIT antagonist antibody is a full-length antibody. In some examples of any of the twenty-first, twenty-second, and twenty-third examples, the anti-TIGIT antagonist antibody is tiragolumab.

In some examples of any of the eleventh, twelfth, and thirteenth examples, the anti-TIGIT antagonist antibody is an antibody fragment that binds TIGIT selected from the group consisting of Fab, Fab', Fab'-SH, Fv, single chain variable fragment (scFv), and (Fab')₂ fragments.

In some examples of any of the eleventh, twelfth, and thirteenth examples, the anti-TIGIT antagonist antibody is an IgG class antibody. In some examples, the IgG class antibody is an IgG1 subclass antibody.

In some examples of any of the eleventh, twelfth, and thirteenth examples, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is to be administered to the subject at a fixed dose of about 1200 mg every three weeks. In some examples of any of the eleventh, twelfth, and thirteenth examples, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is to be administered to the subject at a fixed dose of about 840 mg every two weeks. In some examples of any of the eleventh, twelfth, and thirteenth examples, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is to be administered to the subject at a fixed dose of about 1680 mg every four weeks.

In some examples of any of the eleventh, twelfth, and thirteenth examples, the PD-1 axis binding antagonist is a PD-L1 binding antagonist or a PD-1 binding antagonist. In some examples, the PD-L1 binding antagonist is an anti-PD-L1 antagonist antibody (e.g., atezolizumab (MPDL3280A), MSB0010718C, MDX-1105, or MEDI4736). In some examples, the PD-L1 antagonist is atezolizumab. In some examples, the PD-1 binding antagonist is an anti-PD-1 antagonist antibody (e.g., nivolumab (MDX-1106) or pembrolizumab (formerly lambrolizumab (MK-3475))). In some examples, the PD-1 binding antagonist is AMP-224.

In some examples of any of the eleventh, twelfth, and thirteenth examples, the anti-PD-L1 antagonist antibody comprises the following HVRs: an HVR-H1 sequence comprising the amino acid sequence of GFTFSDSWIH (SEQ ID NO: 20); an HVR-H2 sequence comprising the amino acid sequence of AWISPYGGSTYYADSVKG (SEQ ID NO: 21); an HVR-H3 sequence comprising the amino acid sequence of RHWPGGFDY (SEQ ID NO: 22); an HVR-L1 sequence comprising the amino acid sequence of RASQDVSTAVA (SEQ ID NO: 23); an HVR-L2 sequence comprising the amino acid sequence of SASFLYS (SEQ ID NO: 24); and an HVR-L3 sequence comprising the amino acid sequence of QQYLYHPAT (SEQ ID NO: 25). In some examples, the anti-PD-L1 antagonist antibody comprises: (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 26; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 27; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the anti-PD-L1 antagonist antibody comprises: a VH domain comprising the amino acid sequence of SEQ ID NO: 26 and a VL domain comprising the amino acid sequence of SEQ ID NO: 27.

In some examples of any of the eleventh, twelfth, and thirteenth examples, the anti-PD-L1 antagonist antibody is a monoclonal antibody. In some examples, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is a humanized antibody (e.g., a monoclonal humanized antibody).

In some examples of any of the eleventh, twelfth, and thirteenth examples, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is a full-length antibody.

In some examples of any of the eleventh, twelfth, and thirteenth examples, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is an antibody fragment that binds PD-L1 or PD-1 selected from the group consisting of Fab, Fab', Fab'-SH, Fv, single chain variable fragment (scFv), and (Fab')₂ fragments.

In some examples of any of the eleventh, twelfth, and thirteenth examples, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is an IgG class antibody. In some examples, the IgG class antibody is an IgG1 subclass antibody.

5 In some examples of any of the eleventh, twelfth, and thirteenth examples, the anti-TIGIT antagonist antibody is to be administered to the subject at a fixed dose of about 600 mg of every three weeks and the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is to be administered to the subject at a fixed dose of about 1200 mg every three weeks. In some examples of any of the eleventh, twelfth, and thirteenth examples, the anti-TIGIT antagonist antibody is to be administered to the subject at a fixed dose of about 420 mg of every two weeks and the PD-1 axis binding antagonist (e.g.,
10 anti-PD-L1 antagonist antibody) is to be administered to the subject at a fixed dose of about 840 mg every two weeks. In some examples of any of the eleventh, twelfth, and thirteenth examples, the anti-TIGIT antagonist antibody is to be administered to the subject at a fixed dose of about 840 mg of every two weeks and the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is to be administered to the subject at a fixed dose of about 1680 mg every three weeks.

15 In some examples of any of the eleventh, twelfth, and thirteenth examples, the length of each of the one or more dosing cycles is 21 days.

In some examples of any of the eleventh, twelfth, and thirteenth examples, the anti-TIGIT antagonist antibody and PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) are to be administered to the subject on about Day 1 of each of the one or more dosing cycles.

20 In some examples of any of the eleventh, twelfth, and thirteenth examples, the anti-TIGIT antagonist antibody is to be administered to the subject before the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody). In some examples, a first observation period is to follow administration of the anti-TIGIT antagonist antibody and second observation period is to follow administration of the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody). In some examples, the first observation
25 period and the second observation period are each between about 30 minutes to about 60 minutes in length.

In some examples of any of the eleventh, twelfth, and thirteenth examples, the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is to be administered to the subject before the anti-TIGIT antagonist antibody. In some examples, a first observation period is to follow administration of the
30 PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) and second observation period is to follow administration of the anti-TIGIT antagonist antibody. In some examples, the first observation period and the second observation period are each between about 30 minutes to about 60 minutes in length.

35 In some examples of the eleventh, the anti-TIGIT antagonist antibody is to be administered to the subject simultaneously with the PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody).

In some examples of any of the eleventh, twelfth, and thirteenth examples, the anti-TIGIT antagonist antibody and PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) are to be administered to the subject intravenously. In some examples, the anti-TIGIT antagonist antibody is to be administered to the subject by intravenous infusion over 60 ± 10 minutes. In some examples, the
40

PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) is to be administered to the subject by intravenous infusion over 60 ± 15 minutes.

In some examples of any of the eleventh, twelfth, and thirteenth examples, the anti-TIGIT antagonist antibody and PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) are to be administered to the subject subcutaneously.

In some examples of any of the eleventh, twelfth, and thirteenth examples, the PD-L1-positive tumor cell fraction has been determined by an immunohistochemical (IHC) assay. In some examples, the IHC assay uses anti-PD-L1 antibody SP263, 22C3, SP142, or 28-8. In some examples, the PD-L1-positive tumor cell fraction is determined by positive staining with an anti-PD-L1 antibody (e.g., SP263, 22C3, SP142, or 28-8). In some examples, the PD-L1-positive tumor cell fraction is greater than, or equal to, 50%, as determined by positive staining with the anti-PD-L1 antibody SP263 (e.g., wherein the PD-L1-positive tumor cell fraction is calculated using the Ventana SP263 IHC assay). In some examples, the PD-L1-positive tumor cell fraction is greater than, or equal to, 50%, as determined by positive staining with the anti-PD-L1 antibody 22C3 (e.g., wherein the PD-L1-positive tumor cell fraction is calculated using the pharmDx 22C3 IHC assay). In some examples, the PD-L1-positive tumor cell fraction is greater than, or equal to, 30%, as determined by positive staining with the anti-PD-L1 antibody SP142 (e.g., wherein the PD-L1-positive tumor cell fraction is calculated using the Ventana SP142 IHC assay). In some examples, the PD-L1-positive tumor cell fraction is greater than, or equal to, 50%, as determined by positive staining with the anti-PD-L1 antibody 28-8.

In some examples of any of the eleventh, twelfth, and thirteenth examples, the IHC assay uses anti-PD-L1 antibody SP263. In some examples, the IHC assay uses anti-PD-L1 antibody 22C3.

In some examples of any of the eleventh, twelfth, and thirteenth examples, a tumor sample obtained from the subject has been determined to have a detectable nucleic acid expression level of PD-L1. In some examples, the detectable nucleic acid expression level of PD-L1 has been determined by RNA-seq, RT-qPCR, qPCR, multiplex qPCR or RT-qPCR, microarray analysis, SAGE, MassARRAY technique, ISH, or a combination thereof.

In some examples of any of the eleventh, twelfth, and thirteenth examples, the lung cancer is a non-small cell lung cancer (NSCLC).

In some examples of any of the ninth, tenth, eleventh, twelfth, and thirteenth examples, the NSCLC is a squamous NSCLC. In some examples, the NSCLC is a non-squamous NSCLC. In some examples, the NSCLC is a locally advanced unresectable NSCLC. In some examples, the NSCLC is a Stage IIIB NSCLC. In some examples, the NSCLC is a recurrent or metastatic NSCLC. In some examples, the NSCLC is a Stage IV NSCLC. In some examples, the subject has not been previously treated for Stage IV NSCLC.

In some examples of any of the ninth, tenth, eleventh, twelfth, and thirteenth examples, the subject does not have a sensitizing epidermal growth factor receptor (*EGFR*) gene mutation or anaplastic lymphoma kinase (*ALK*) gene rearrangement.

In some examples of any of the ninth, tenth, eleventh, twelfth, and thirteenth examples, the subject does not have a pulmonary lymphoepithelioma-like carcinoma subtype of NSCLC.

In some examples of any of the ninth, tenth, eleventh, twelfth, and thirteenth examples, the subject does not have an active EBV infection or a known or suspected chronic active EBV infection. In some examples, the subject is negative for EBV IgM or negative by EBV PCR. In some examples, the subject is negative for EBV IgM and negative by EBV PCR. In some examples, the subject is positive for EBV IgG or positive for EBNA. In some examples, the subject is positive for EBV IgG and positive for EBNA.

In some examples of any of the ninth, tenth, eleventh, twelfth, and thirteenth examples, the subject is negative for EBV IgG or negative for EBNA. In some examples, the subject is negative for EBV IgG and negative for EBNA.

In some examples of any of the eleventh, twelfth, and thirteenth examples, the PFS of the subject is increased as compared to a reference PFS time. In some examples, the reference PFS time is the median PFS time of a population of subjects who have received a treatment comprising a PD-1 axis binding antagonist (e.g., anti-PD-L1 antagonist antibody) without an anti-TIGIT antagonist antibody.

In a fourteenth example, the disclosure features a use of an anti-TIGIT antagonist antibody and atezolizumab in the manufacture of a medicament for use in a method of treating a subject having a NSCLC, the method comprising administering to the subject one or more dosing cycles of the medicament, wherein the medicament is formulated for administration of the anti-TIGIT antagonist antibody (e.g., at a fixed dose of 600 mg every three weeks, at a fixed dose of 420 mg every two weeks, or at a fixed dose of 840 mg every four weeks) and atezolizumab (e.g., at a fixed dose of 1200 mg every three weeks, at a fixed dose of 840 mg every two weeks, or at a fixed dose of 1680 mg every four weeks), wherein the anti-TIGIT antagonist antibody comprises: a VH domain comprising the amino acid sequence of SEQ ID NO: 17 or 18 and a VL domain comprising the amino acid sequence of SEQ ID NO: 19, and wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 30% (e.g., greater than, or equal to, 50%), and the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with atezolizumab without the anti-TIGIT antagonist antibody.

In a fifteenth example, the disclosure features a use of an anti-TIGIT antagonist antibody in the manufacture of a medicament for use in a method of treating a subject having a NSCLC, the method comprising administering to the subject one or more dosing cycles of the medicament and atezolizumab, wherein the medicament is formulated for administration of the anti-TIGIT antagonist antibody (e.g., at a fixed dose of 600 mg every three weeks, at a fixed dose of 420 mg every two weeks, or at a fixed dose of 840 mg every four weeks) and atezolizumab (e.g., at a fixed dose of 1200 mg every three weeks, at a fixed dose of 840 mg every two weeks, or at a fixed dose of 1680 mg every four weeks), wherein the anti-TIGIT antagonist antibody comprises: a VH domain comprising the amino acid sequence of SEQ ID NO: 17 or 18 and a VL domain comprising the amino acid sequence of SEQ ID NO: 19, and wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 30% (e.g., greater than, or equal to, 50%), and the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with atezolizumab without the anti-TIGIT antagonist antibody.

In a sixteenth example, the disclosure features a use of atezolizumab in the manufacture of a medicament for use in a method of treating a subject having a NSCLC, the method comprising

administering to the subject one or more dosing cycles of the medicament and an anti-TIGIT antagonist antibody, wherein the medicament is formulated for administration of atezolizumab (e.g., at a fixed dose of 1200 mg every three weeks, at a fixed dose of 840 mg every two weeks, or at a fixed dose of 1680 mg every four weeks) and the anti-TIGIT antagonist antibody is to be administered (e.g., at a fixed dose of 600 mg every three weeks, at a fixed dose of 420 mg every two weeks, or at a fixed dose of 840 mg every four weeks) , wherein the anti-TIGIT antagonist antibody comprises: a VH domain comprising the amino acid sequence of SEQ ID NO: 17 or 18 and a VL domain comprising the amino acid sequence of SEQ ID NO: 19, and wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 30% (e.g., greater than, or equal to, 50%), and the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with atezolizumab without the anti-TIGIT antagonist antibody.

In a seventeenth example, the disclosure features a use of tiragolumab and atezolizumab in the manufacture of a medicament for use in a method of treating a subject having a NSCLC, the method comprising administering to the subject one or more dosing cycles of the medicament, wherein the medicament is formulated for administration of tiragolumab (e.g., at a fixed dose of 600 mg every three weeks, at a fixed dose of 420 mg every two weeks, or at a fixed dose of 840 mg every four weeks) and atezolizumab (e.g., at a fixed dose of 1200 mg every three weeks, at a fixed dose of 840 mg every two weeks, or at a fixed dose of 1680 mg every four weeks), and wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 30% (e.g., greater than, or equal to, 50%), and the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with atezolizumab without tiragolumab.

In an eighteenth example, the disclosure features a use of tiragolumab in the manufacture of a medicament for use in a method of treating a subject having a NSCLC, the method comprising administering to the subject one or more dosing cycles of the medicament and atezolizumab, wherein the medicament is formulated for administration of tiragolumab (e.g., at a fixed dose of 600 mg every three weeks, at a fixed dose of 420 mg every two weeks, or at a fixed dose of 840 mg every four weeks) and atezolizumab is to be administered (e.g., at a fixed dose of 1200 mg every three weeks, at a fixed dose of 840 mg every two weeks, or at a fixed dose of 1680 mg every four weeks), and wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 30% (e.g., greater than, or equal to, 50%), and the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with atezolizumab without tiragolumab.

In a nineteenth example, the disclosure features a use of atezolizumab in the manufacture of a medicament for use in a method of treating a subject having a NSCLC, the method comprising administering to the subject one or more dosing cycles of the medicament and tiragolumab, wherein the medicament is formulated for administration of atezolizumab (e.g., at a fixed dose of 1200 mg every three weeks, at a fixed dose of 840 mg every two weeks, or at a fixed dose of 1680 mg every four weeks) and tiragolumab is to be administered (e.g., at a fixed dose of 600 mg every three weeks, at a fixed dose of 420 mg every two weeks, or at a fixed dose of 840 mg every four weeks) , and wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 30% (e.g.,

greater than, or equal to, 50%), and the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with atezolizumab without tiragolumab.

In some examples of any of the fourteenth, fifteenth, sixteenth, seventeenth, eighteenth, and nineteenth examples, the subject does not have a pulmonary lymphoepithelioma-like carcinoma subtype of NSCLC.

In some examples of any of the fourteenth, fifteenth, sixteenth, seventeenth, eighteenth, and nineteenth examples, the subject does not have a sensitizing epidermal growth factor receptor (*EGFR*) gene mutation or anaplastic lymphoma kinase (*ALK*) gene rearrangement.

In some examples of any of the fourteenth, fifteenth, sixteenth, seventeenth, eighteenth, and nineteenth examples, the subject does not have an active EBV infection or a known or suspected chronic active EBV infection. In some examples, the subject is negative for EBV IgM or negative by EBV PCR. In some examples, the subject is negative for EBV IgM and negative by EBV PCR. In some examples, the subject is positive for EBV IgG or positive for EBNA. In some examples, the subject is positive for EBV IgG and positive for EBNA.

In some examples of any of the fourteenth, fifteenth, sixteenth, seventeenth, eighteenth, and nineteenth examples, the subject is negative for EBV IgG or negative for EBNA. In some examples, the subject is negative for EBV IgG and negative for EBNA.

In some examples of any of the preceding examples, the treatment results in an increase in PFS of at least about 3.1 months (e.g., at least about 4.9 months), as compared to treatment with atezolizumab without tiragolumab.

In some examples of any of the preceding examples, the treatment results in an increase in OS of at least about 5.7 months (e.g., at least about 9 months), as compared to treatment with atezolizumab without tiragolumab.

In a twentieth example, the disclosure features a method for treating a subject having a lung cancer, the method comprising administering to the subject one or more dosing cycles of an anti-TIGIT antagonist antibody and a PD-1 axis binding antagonist, wherein the subject previously received concurrent chemoradiotherapy (cCRT) for lung cancer, and wherein the subject has not had disease progression after the cCRT (e.g., the subject has not had radiographic disease progression after the cCRT). In some examples, the subject previously received at least two cycles of the cCRT (e.g., at least three cycles of the cCRT, at least four cycles of the cCRT, at least five cycles of the cCRT, at least six cycles of the cCRT, or more). In some examples, the cCRT comprises a platinum-based chemotherapy (e.g., the cCRT comprises a concurrent platinum-based CRT, e.g., a concurrent CRT comprising administration of cisplatin (e.g., cisplatin-etoposide or cisplatin-vinorelbine) or a concurrent CRT comprising administration of carboplatin (e.g., carboplatin-paclitaxel)). In some examples, the cCRT comprises a thoracic radiotherapy. In some examples, the radiotherapy was administered to the subject at 60-66 Gy in 30-33 fractions. In some examples, the cCRT was administered with curative intent. In some examples, the cCRT was administered as a consolidation therapy.

In some examples, the anti-TIGIT antagonist antibody comprises the following hypervariable regions (HVRs): an HVR-H1 sequence comprising the amino acid sequence of SNSAAWN (SEQ ID NO: 1); an HVR-H2 sequence comprising the amino acid sequence of KTYRFRKWYSDYAVSVKG (SEQ ID

NO: 2); an HVR-H3 sequence comprising the amino acid sequence of ESTTYDLLAGPFDY (SEQ ID NO: 3); an HVR-L1 sequence comprising the amino acid sequence of KSSQTVLYSSNNKKYLA (SEQ ID NO: 4); an HVR-L2 sequence comprising the amino acid sequence of WASTRES (SEQ ID NO: 5); and an HVR-L3 sequence comprising the amino acid sequence of QQYYSTPFT (SEQ ID NO: 6). In some examples, the anti-TIGIT antagonist antibody further comprises the following light chain variable region framework regions (FRs): an FR-L1 comprising the amino acid sequence of DIVMTQSPDSLAVSLGERATINC (SEQ ID NO: 7); an FR-L2 comprising the amino acid sequence of WYQQKPGQPNNLLIY (SEQ ID NO: 8); an FR-L3 comprising the amino acid sequence of GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC (SEQ ID NO: 9); and an FR-L4 comprising the amino acid sequence of FGPGTKVEIK (SEQ ID NO: 10). In some examples, the anti-TIGIT antagonist antibody further comprises the following heavy chain variable region FRs: an FR-H1 comprising the amino acid sequence of X₁VQLQQSGPGLVKPSQTLSTCAISGDSVS (SEQ ID NO: 11), wherein X₁ is Q or E; an FR-H2 comprising the amino acid sequence of WIRQSPSRGLEWLG (SEQ ID NO: 12); an FR-H3 comprising the amino acid sequence of RITINPDTSKNQFSLQLNSVTPEDTAVFYCTR (SEQ ID NO: 13); and an FR-H4 comprising the amino acid sequence of WGQGTLVTVSS (SEQ ID NO: 14). In some examples, X₁ is Q. In other examples, X₁ is E. In some examples, the anti-TIGIT antagonist antibody comprises: (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 17 or 18; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 19; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the anti-TIGIT antagonist antibody comprises: a VH domain comprising the amino acid sequence of SEQ ID NO: 17 or 18; and a VL domain comprising the amino acid sequence of SEQ ID NO: 19.

In some examples, the anti-TIGIT antagonist antibody is a monoclonal antibody. In some examples, the anti-TIGIT antagonist antibody is a human antibody. In some examples, the anti-TIGIT antagonist antibody is a full-length antibody. In some examples, the anti-TIGIT antagonist antibody is tiragolumab.

In some examples, the anti-TIGIT antagonist antibody is an antibody fragment that binds TIGIT selected from the group consisting of Fab, Fab', Fab'-SH, Fv, single chain variable fragment (scFv), and (Fab')₂ fragments.

In some examples, the anti-TIGIT antagonist antibody is an IgG class antibody (e.g., an IgG1 subclass antibody).

In some examples, the PD-1 axis binding antagonist is a PD-L1 binding antagonist or a PD-1 binding antagonist. In some examples, the PD-L1 binding antagonist is an anti-PD-L1 antagonist antibody is atezolizumab (MPDL3280A), MSB0010718C, MDX-1105, or MEDI4736. In some examples, the anti-PD-L1 antagonist antibody is atezolizumab. In some examples, the PD-1 binding antagonist is an anti-PD-1 antagonist antibody. In some examples, the anti-PD-1 antagonist antibody is nivolumab (MDX-1106), pembrolizumab (MK-3475). In some examples, the PD-1 binding antagonist is AMP-224.

In some examples, the anti-PD-L1 antagonist antibody comprises the following HVRs: an HVR-H1 sequence comprising the amino acid sequence of GFTFSDSWIH (SEQ ID NO: 20); an HVR-H2 sequence comprising the amino acid sequence of AWISPYGGSTYYADSVKG (SEQ ID NO: 21); an HVR-H3 sequence comprising the amino acid sequence of RHWPGGFDY (SEQ ID NO: 22); an HVR-L1 sequence comprising the amino acid sequence of RASQDVSTAVA (SEQ ID NO: 23); an HVR-L2 sequence comprising the amino acid sequence of SASFLYS (SEQ ID NO: 24); and an HVR-L3 sequence comprising the amino acid sequence of QQYLYHPAT (SEQ ID NO: 25). In some examples, the anti-PD-L1 antagonist antibody comprises: (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 26; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 27; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the anti-PD-L1 antagonist antibody comprises: a VH domain comprising the amino acid sequence of SEQ ID NO: 26; and a VL domain comprising the amino acid sequence of SEQ ID NO: 27.

In some examples, the PD-1 axis binding antagonist is a monoclonal antibody. In some examples, the PD-1 axis binding antagonist is a humanized antibody. In some examples, the PD-1 axis binding antagonist is a full-length antibody.

In some examples, the PD-1 axis binding antagonist is an antibody fragment that binds PD-L1 selected from the group consisting of Fab, Fab', Fab'-SH, Fv, single chain variable fragment (scFv), and (Fab')₂ fragments. In some examples, the PD-1 axis binding antagonist is an IgG class antibody. In some examples, the IgG class antibody is an IgG1 subclass antibody.

In some examples, the method comprises administering to the subject the anti-TIGIT antagonist antibody at a fixed dose of between about 30 mg to about 1200 mg every three weeks, e.g., at a fixed dose of between about 30 mg to about 600 mg every three weeks, e.g., at a fixed dose of about 600 mg every three weeks. In some examples, the method comprises administering to the subject the PD-1 axis binding antagonist at a fixed dose of between about 80 mg to about 1600 mg every three weeks, e.g., at a fixed dose of about 1200 mg every three weeks. In some examples, the method comprises administering to the subject the anti-TIGIT antagonist antibody at a fixed dose of about 600 mg every three weeks and the PD-1 axis binding antagonist at a fixed dose of about 1200 mg every three weeks. In some examples, the length of each of the one or more dosing cycles is 21 days. In some examples, the method comprises administering to the subject the anti-TIGIT antagonist antibody and the PD-1 axis binding antagonist on about Day 1 of each of the one or more dosing cycles.

In some examples, the method comprises administering to the subject the anti-TIGIT antagonist antibody at a fixed dose of between about 300 mg to about 800 mg every two weeks, e.g., at a fixed dose of between about 400 mg to about 500 mg every two weeks, e.g., at a fixed dose of about 420 mg every two weeks. In some examples, the method comprises administering to the subject the PD-1 axis binding antagonist at a fixed dose of between about 200 mg to about 1200 mg every two weeks, e.g., at a fixed dose of about 840 mg every two weeks. In some examples, the method comprises administering to the subject the anti-TIGIT antagonist antibody at a fixed dose of about 420 mg every two weeks and the PD-1 axis binding antagonist at a fixed dose of about 840 mg every two weeks. In some

examples, the length of each of the one or more dosing cycles is 28 days. In some examples, the method comprises administering to the subject the anti-TIGIT antagonist antibody and the PD-1 axis binding antagonist on about Days 1 and 15 of each of the one or more dosing cycles.

5 In some examples, the method comprises administering to the subject the anti-TIGIT antagonist antibody at a fixed dose of between about 700 mg to about 1000 mg every four weeks, e.g., at a fixed dose of between about 800 mg to about 900 mg every four weeks, e.g., at a fixed dose of about 840 mg every four weeks. In some examples, the method comprises administering to the subject the PD-1 axis binding antagonist at a fixed dose of between about 400 mg to about 2000 mg every four weeks, e.g., at a fixed dose of about 1680 mg every four weeks. In some examples, the method comprises
10 administering to the subject the anti-TIGIT antagonist antibody at a fixed dose of about 840 mg every four weeks and the PD-1 axis binding antagonist at a fixed dose of about 1680 mg every four weeks. In some examples, the length of each of the one or more dosing cycles is 28 days. In some examples, the method comprises administering to the subject the anti-TIGIT antagonist antibody and the PD-1 axis binding antagonist on about Day 1 of each of the one or more dosing cycles.

15 In some examples, the method comprises administering to the subject the PD-1 axis binding antagonist before the anti-TIGIT antagonist antibody. In some examples, the method comprises a first observation period following administration of the PD-1 axis binding antagonist and second observation period following administration of the anti-TIGIT antagonist antibody. In some examples, the first observation period and the second observation period are each between about 30 minutes to about 60
20 minutes in length.

In some examples, the method comprises administering to the subject the anti-TIGIT antagonist antibody before the PD-1 axis binding antagonist. In some examples, the method comprises a first observation period following administration of the anti-TIGIT antagonist antibody and second observation period following administration of the PD-1 axis binding antagonist. In some examples, the first
25 observation period and the second observation period are each between about 30 minutes to about 60 minutes in length.

In some examples, the method comprises administering to the subject the anti-TIGIT antagonist antibody and the PD-1 axis binding antagonist simultaneously.

30 In some examples, the method comprises administering to the subject the anti-TIGIT antagonist antibody and PD-1 axis binding antagonist intravenously, e.g., by intravenous infusion over 60 ± 10 minutes. In some examples, the method comprises administering to the subject the PD-1 axis binding antagonist by intravenous infusion over 60 ± 15 minutes.

In some examples, the method comprises administering to the subject the anti-TIGIT antagonist antibody and PD-1 axis binding antagonist subcutaneously.

35 In some examples, a PD-L1-positive tumor cell fraction of the subject is determined. In some examples, the PD-L1-positive tumor cell fraction is determined by positive staining with an anti-PD-L1 antibody, wherein the anti-PD-L1 antibody is SP263, 22C3, SP142, or 28-8. In some examples, the staining is part of an IHC assay. In some examples, the PD-L1-positive tumor cell fraction is greater than or equal to 1% tumor cell (TC), as determined by positive staining with an anti-PD-L1 antibody SP263 or
40 22C3. In some examples, the PD-L1-positive tumor cell fraction is less than 1% TC (e.g.,

from 0% to 1% TC, e.g., PD-L1-negative), as determined by positive staining with an anti-PD-L1 antibody SP263 or 22C3. In some examples, the PD-L1 expression is calculated using the Ventana SP263 IHC assay. In some examples, the PD-L1 expression is calculated using the pharmDx 22C3 IHC assay.

In some examples, a detectable nucleic acid expression level of PD-L1 has been determined by RNA-seq, RT-qPCR, qPCR, multiplex qPCR or RT-qPCR, microarray analysis, SAGE, MassARRAY technique, ISH, or a combination thereof.

In some examples, the lung cancer is a non-small cell lung cancer (NSCLC). In some examples, the NSCLC is a squamous NSCLC. In other examples, the NSCLC is a non-squamous NSCLC. In some examples, the NSCLC is a locally advanced unresectable NSCLC (e.g., a locally advanced unresectable NSCLC having a PD-L1-positive tumor cell fraction less than 1% TC or a locally advanced unresectable NSCLC having a PD-L1-positive tumor cell fraction greater than, or equal to, 1% TC). In some examples, the NSCLC is a Stage III NSCLC (e.g., Stage IIIA NSCLC, Stage IIIB NSCLC, or Stage IIIC NSCLC), e.g., a Stage III NSCLC having a PD-L1-positive tumor cell fraction less than 1% TC (e.g., a Stage IIIA NSCLC having a PD-L1-positive tumor cell fraction less than 1% TC, a Stage IIIB NSCLC having a PD-L1-positive tumor cell fraction less than 1% TC, or a Stage IIIC NSCLC having a PD-L1-positive tumor cell fraction less than 1% TC) or a Stage III NSCLC having a PD-L1-positive tumor cell fraction greater than, or equal to, 1% TC (e.g., a Stage IIIA NSCLC having a PD-L1-positive tumor cell fraction greater than, or equal to, 1% TC, a Stage IIIB NSCLC having a PD-L1-positive tumor cell fraction greater than, or equal to, 1% TC, or a Stage IIIC NSCLC having a PD-L1-positive tumor cell fraction greater than, or equal to, 1% TC). In some examples, the NSCLC (e.g., the squamous NSCLC, the non-squamous NSCLC, or the locally advanced unresectable NSCLC) is not a Stage IV NSCLC.

In some examples, the subject does not have a sensitizing epidermal growth factor receptor (*EGFR*) gene mutation or anaplastic lymphoma kinase (*ALK*) gene rearrangement. In some examples, the subject does not have an active Epstein-Barr virus (EBV) infection or a known or suspected chronic active EBV infection. In some examples, the subject is negative for EBV IgM or negative by EBV PCR. In some examples, the subject is negative for EBV IgM and negative by EBV PCR. In some examples, the subject is positive for EBV IgG or positive for Epstein-Barr nuclear antigen (EBNA). In some examples, the subject is positive for EBV IgG and positive for EBNA. In some examples, the subject is negative for EBV IgG or negative for EBNA. In some examples, the subject is negative for EBV IgG and negative for EBNA.

In some examples, the PFS is increased as compared to a reference PFS time, e.g., the median PFS time of a population of subjects who have received a treatment comprising a PD-1 axis binding antagonist (e.g., durvalumab) without an anti-TIGIT antagonist antibody.

In a twenty-first example, provided herein is a method for treating a subject having a NSCLC, the method comprising administering to the subject one or more dosing cycles of an anti-TIGIT antagonist antibody and atezolizumab, wherein the anti-TIGIT antagonist antibody comprises: a VH domain comprising the amino acid sequence of SEQ ID NO: 17 or 18; and a VL domain comprising the amino acid sequence of SEQ ID NO: 19, and wherein the subject previously received cCRT for lung cancer, and

wherein the subject has not had disease progression after the cCRT, and wherein the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with durvalumab without the anti-TIGIT antagonist antibody. In some examples, the anti-TIGIT antagonist antibody is administered at a fixed dose of 600 mg every three weeks and atezolizumab is administered at a fixed dose of 1200 mg every three weeks. In other examples, the anti-TIGIT antagonist antibody is administered at a fixed dose of 420 mg every two weeks and atezolizumab is administered at a fixed dose of 840 mg every two weeks. In other examples, the anti-TIGIT antagonist antibody is administered at a fixed dose of 840 mg every four weeks and atezolizumab is administered at a fixed dose of 1680 mg every four weeks.

In some examples, the subject previously received at least two cycles of the cCRT. In some examples, the cCRT comprises a platinum-based chemotherapy. In some examples, the cCRT comprises a thoracic radiotherapy, e.g., a thoracic radiotherapy administered to the subject at 60-66 Gy in 30-33 fractions. In some examples, the cCRT was administered with curative intent. In some examples, the cCRT was administered as a consolidation therapy.

In a twenty-second example, the disclosure features a method for treating a subject having a NSCLC, the method comprising administering to the subject one or more dosing cycles of tiragolumab and atezolizumab, wherein the subject previously received cCRT for lung cancer, and wherein the subject has not had disease progression after the cCRT, and the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with durvalumab without tiragolumab. In some examples, tiragolumab is administered at a fixed dose of 600 mg every three weeks and atezolizumab is administered at a fixed dose of 1200 mg every three weeks. In other examples, tiragolumab is administered at a fixed dose of 420 mg every two weeks and atezolizumab is administered at a fixed dose of 840 mg every two weeks. In other examples, tiragolumab is administered at a fixed dose of 840 mg every four weeks and atezolizumab is administered at a fixed dose of 1680 mg every four weeks.

In some examples, the subject previously received at least two cycles of the cCRT. In some examples, the cCRT comprises a platinum-based chemotherapy. In some examples, the cCRT comprises a thoracic radiotherapy, e.g., a thoracic radiotherapy administered to the subject at 60-66 Gy in 30-33 fractions. In some examples, the cCRT was administered with curative intent. In some examples, the cCRT was administered as a consolidation therapy.

In a twenty-third example, provided herein is an anti-TIGIT antagonist antibody and an anti-PD-L1 antagonist antibody for use in a method of treating a subject having a lung cancer, wherein the method is according to any one of the preceding examples.

In a twenty-fourth example, the disclosure features a use of an anti-TIGIT antagonist antibody in the manufacture of a medicament for treating a subject having a lung cancer in combination with an anti-PD-L1 antagonist antibody, wherein the treatment is according to the method of any one of the preceding examples. In some examples, the anti-TIGIT antagonist antibody and the anti-PD-L1 antagonist antibody are formulated separately. In other examples, the anti-TIGIT antagonist antibody and the anti-PD-L1 antagonist antibody are formulated together.

In a twenty-fifth example, the disclosure features a use of an anti-PD-L1 antagonist antibody in the manufacture of a medicament for treating a subject having a lung cancer in combination with an anti-TIGIT antagonist antibody, wherein the treatment is according to the method of any one of the preceding examples. In some examples, the anti-TIGIT antagonist antibody and the anti-PD-L1 antagonist antibody are formulated separately. In other examples, the anti-TIGIT antagonist antibody and the anti-PD-L1 antagonist antibody are formulated together.

In some examples of any of the preceding examples, the subject is a human (e.g., an adult patient).

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a schematic diagram of the study design showing the parameters for the selection of subjects, randomization into treatment arms, and treatment endpoints.

FIG. 2 is a table showing minor imbalances in sex, race, and ECOG in baseline demographics divided by TPS (TPS $\geq$ 50% and TPS 1-49%) at the interim analysis timepoint.

FIG. 3 is a table showing differences in treatment outcomes and study discontinuations across the PD-L1 TPS $\geq$ 50% and PD-L1 TPS 1-49% populations and monotherapy and combination therapy arms at the interim analysis timepoint.

FIG. 4 is a table showing the difference in best overall response (BOR) observed in the primary population (PD-L1 TPS $\geq$ 1%), the PD-L1 TPS $\geq$ 50% population, and the PD-L1 TPS 1-49% population receiving either an atezolizumab monotherapy or a combination therapy of tiragolumab and atezolizumab at the interim analysis timepoint.

FIG. 5 is a series of tables showing an improved BOR in squamous cell cancer patients in the intent-to-treat (ITT) population at the interim analysis timepoint.

FIG. 6 is a table and accompanying graph showing the relative frequency and type of adverse events recorded for patients receiving either an atezolizumab monotherapy or a combination therapy of tiragolumab and atezolizumab at the interim analysis timepoint. Adverse events with an asterisk were observed at higher frequency in the combination therapy arm than the monotherapy arm.

FIG. 7 is a table showing observed treatment-related and immune-related adverse events (AEs) were imbalanced between the treatment arms due to rash and IRR at the interim analysis timepoint.

FIGS. 8A and 8B are a pair of tables showing subgroup analysis of the objective response rate (ORR) at the primary endpoint analysis timepoint.

FIG. 9A is a table showing the difference in ORR observed in the primary population (PD-L1 TPS $\geq$ 1%) receiving either an atezolizumab monotherapy or a combination therapy of tiragolumab and atezolizumab at the primary endpoint analysis timepoint.

FIG. 9B is a pair of tables showing the difference in ORR observed in the PD-L1 TPS $\geq$ 50% population and the PD-L1 TPS 1-49% population receiving either an atezolizumab monotherapy or a combination therapy of tiragolumab and atezolizumab at the primary endpoint analysis timepoint.

FIGS. 10A and 10B are a pair of tables showing subgroup analysis of progression-free survival (PFS) at the primary endpoint analysis timepoint.

CLAIMS

WHAT IS CLAIMED IS:

1. Use of tiragolumab and atezolizumab in the manufacture of a medicament for treating a subject having a lung cancer, wherein one or more dosing cycles of the medicament is to be administered to the subject, wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 30%, and the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with atezolizumab without tiragolumab; and wherein:

(i) tiragolumab is to be administered at a fixed dose of about 600 mg every three weeks and atezolizumab is to be administered at a fixed dose of about 1200 mg every three weeks,

(ii) tiragolumab is to be administered at a fixed dose of about 420 mg every two weeks and atezolizumab is to be administered at a fixed dose of about 840 mg every two weeks, or

(iii) tiragolumab is to be administered at a fixed dose of about 840 mg every four weeks and atezolizumab is to be administered at a fixed dose of about 1680 mg every four weeks.

2. Use of tiragolumab in the manufacture of a medicament for treating a subject having a lung cancer, wherein one or more dosing cycles of the medicament and atezolizumab are to be administered to the subject, wherein the medicament is formulated for administration of tiragolumab in combination with atezolizumab, wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 30%, and the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with atezolizumab without tiragolumab, and wherein:

(i) tiragolumab is to be administered at a fixed dose of about 600 mg every three weeks and atezolizumab is to be administered at a fixed dose of about 1200 mg every three weeks,

(ii) tiragolumab is to be administered at a fixed dose of about 420 mg every two weeks and atezolizumab is to be administered at a fixed dose of about 840 mg every two weeks, or

(iii) tiragolumab is to be administered at a fixed dose of about 840 mg every four weeks and atezolizumab is to be administered at a fixed dose of about 1680 mg every four weeks.

3. Use of atezolizumab in the manufacture of a medicament for treating a subject having a lung cancer, wherein one or more dosing cycles of the medicament and tiragolumab are to be administered to the subject, and wherein the medicament is formulated for administration of atezolizumab in combination with tiragolumab, wherein the subject has been determined to have a PD-L1-positive tumor cell fraction of greater than, or equal to, 30%, and the treatment results in (a) a CR or a PR and/or (b) an increase in PFS as compared to treatment with the atezolizumab without the tiragolumab, and wherein:

(i) tiragolumab is to be administered at a fixed dose of about 600 mg every three weeks and atezolizumab is to be administered at a fixed dose of about 1200 mg every three weeks,

(ii) tiragolumab is to be administered at a fixed dose of about 420 mg every two weeks and atezolizumab is to be administered at a fixed dose of about 840 mg every two weeks, or

(iii) tiragolumab is to be administered at a fixed dose of about 840 mg every four weeks and atezolizumab is to be administered at a fixed dose of about 1680 mg every four weeks.

4. The use of any one of claims 1-3, wherein tiragolumab is to be administered to the subject at a fixed dose of about 600 mg every three weeks and atezolizumab is to be administered to the subject at a fixed dose of about 1200 mg every three weeks and the length of each of the one or more dosing cycles is 21 days.

5. The use of claim 4, wherein tiragolumab and atezolizumab are to be administered to the subject on about Day 1 of each of the one or more dosing cycles.

6. The use of any one of claims 1-3, wherein tiragolumab is to be administered to the subject at a fixed dose of about 420 mg every two weeks and atezolizumab is to be administered to the subject at a fixed dose of about 840 mg every two weeks and the length of each of the one or more dosing cycles is 28 days.

7. The use of claim 6, wherein tiragolumab and atezolizumab are each to be administered on about Days 1 and 15 of each of the one or more dosing cycles.

8. The use of any one of claims 1-3, wherein tiragolumab is to be administered to the subject at a fixed dose of about 840 mg every four weeks and atezolizumab is to be administered to the subject at a fixed dose of about 1680 mg every four weeks and the length of each of the one or more dosing cycles is 28 days.

9. The use of claim 8, wherein tiragolumab and atezolizumab are each to be administered on about Day 1 of each of the one or more dosing cycles.

10. The use of any one of claims 1-9, wherein tiragolumab and atezolizumab are to be administered to the subject intravenously.

11. The use of any one of claims 1-9, wherein tiragolumab and atezolizumab are to be administered to the subject subcutaneously.

12. The use of any one of claims 1-11, wherein the PD-L1-positive tumor cell fraction has been determined by an immunohistochemical (IHC) assay.

13. The use of any one of claims 1-12, wherein the PD-L1-positive tumor cell fraction is determined by positive staining with an anti-PD-L1 antibody, wherein the anti-PD-L1 antibody is SP263, 22C3, SP142, or 28-8.

14. The use of claim 13, wherein the PD-L1-positive tumor cell fraction is greater than, or equal to, 50%, as determined by positive staining with the anti-PD-L1 antibody SP263.

15. The use of claim 14, wherein the PD-L1-positive tumor cell fraction is calculated using the Ventana SP263 IHC assay.

16. The use of claim 13, wherein the PD-L1-positive tumor cell fraction is greater than, or equal to, 50%, as determined by positive staining with the anti-PD-L1 antibody 22C3.

17. The use of claim 16, wherein the PD-L1-positive tumor cell fraction is calculated using the pharmDx 22C3 IHC assay.

18. The use of claim 13, wherein:

(a) the PD-L1-positive tumor cell fraction is greater than, or equal to, 30%, as determined by positive staining with the anti-PD-L1 antibody SP142; or

(b) the PD-L1-positive tumor cell fraction is greater than, or equal to, 50%, as determined by positive staining with the anti-PD-L1 antibody 28-8.

19. The use of any one of claims 1-11, wherein a tumor sample obtained from the subject has been determined to have a detectable nucleic acid expression level of PD-L1.

20. The use of claim 19, wherein the detectable nucleic acid expression level of PD-L1 has been determined by RNA-seq, RT-qPCR, qPCR, multiplex qPCR or RT-qPCR, microarray analysis, SAGE, MassARRAY technique, ISH, or a combination thereof.

21. The use of any one of claims 1-20, wherein the lung cancer is a non-small cell lung cancer (NSCLC).

22. The use of claim 21, wherein the NSCLC is a squamous NSCLC or a non-squamous NSCLC.

23. The use of claim 21, wherein the NSCLC is:

(a) a locally advanced unresectable NSCLC; or

(b) a recurrent or metastatic NSCLC.

24. The use of claim 23, wherein:

(a) the locally advanced unresectable NSCLC is a Stage IIIB NSCLC; or

(b) the recurrent or metastatic NSCLC is a Stage IV NSCLC.

25. The use of claim 23 or 24, wherein the subject has not been previously treated for Stage IV NSCLC.

26. The use of any one of claims 1-25, wherein the subject does not have a sensitizing epidermal growth factor receptor (*EGFR*) gene mutation or anaplastic lymphoma kinase (*ALK*) gene rearrangement.

27. The use of any one of claims 1-26, wherein the PFS is increased as compared to a reference PFS time.

28. The use of claim 27, wherein the reference PFS time is the median PFS time of a population of subjects who have received a treatment comprising atezolizumab without tiragolumab.

29. The use of any one of claims 1-28, wherein the treatment results in an increase in PFS of at least about 3.1 months, as compared to treatment with atezolizumab without tiragolumab.

30. The use of any one of claims 1-29, wherein the treatment results in an increase in OS of at least about 5.7 months, as compared to treatment with atezolizumab without tiragolumab.

31. Use of tiragolumab and atezolizumab in the manufacture of a medicament for treating a subject having a lung cancer, wherein one or more dosing cycles of tiragolumab and atezolizumab are to be administered to the subject, wherein the subject previously received concurrent chemoradiotherapy (cCRT) for lung cancer, wherein the subject has not had disease progression after the cCRT, and wherein:

(i) tiragolumab is to be administered at a fixed dose of about 600 mg every three weeks and atezolizumab is to be administered at a fixed dose of about 1200 mg every three weeks,

(ii) tiragolumab is to be administered at a fixed dose of about 420 mg every two weeks and atezolizumab is to be administered at a fixed dose of about 840 mg every two weeks, or

(iii) tiragolumab is to be administered at a fixed dose of about 840 mg every four weeks and atezolizumab is to be administered at a fixed dose of about 1680 mg every four weeks.

32. Use of tiragolumab in the manufacture of a medicament for treating a subject having a lung cancer, wherein one or more dosing cycles of the medicament and atezolizumab are to be administered to the subject, wherein the medicament is formulated for administration of tiragolumab in combination with atezolizumab, wherein the subject previously received concurrent chemoradiotherapy (cCRT) for lung cancer, wherein the subject has not had disease progression after the cCRT, and wherein:

(i) tiragolumab is to be administered at a fixed dose of about 600 mg every three weeks and atezolizumab is to be administered at a fixed dose of about 1200 mg every three weeks,

(ii) tiragolumab is to be administered at a fixed dose of about 420 mg every two weeks and atezolizumab is to be administered at a fixed dose of about 840 mg every two weeks, or

(iii) tiragolumab is to be administered at a fixed dose of about 840 mg every four weeks and atezolizumab is to be administered at a fixed dose of about 1680 mg every four weeks.

33. Use of atezolizumab in the manufacture of a medicament for treating a subject having a lung cancer, wherein one or more dosing cycles of the medicament and tiragolumab are to be administered to the subject, wherein the medicament is formulated for administration of atezolizumab in combination with tiragolumab, wherein the subject previously received concurrent chemoradiotherapy (cCRT) for lung cancer, wherein the subject has not had disease progression after the cCRT, and wherein:

(i) tiragolumab is to be administered at a fixed dose of about 600 mg every three weeks and atezolizumab is to be administered at a fixed dose of about 1200 mg every three weeks,

(ii) tiragolumab is to be administered at a fixed dose of about 420 mg every two weeks and atezolizumab is to be administered at a fixed dose of about 840 mg every two weeks, or

(iii) tiragolumab is to be administered at a fixed dose of about 840 mg every four weeks and atezolizumab is to be administered at a fixed dose of about 1680 mg every four weeks.