

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 combination therapy 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 complete response (CR) or a partial response (PR) and/or (b) an increase in progression-free survival (PFS) as compared to treatment with atezolizumab without tiragolumab; and wherein:

- (i) 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
- (ii) 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 complete response (CR) or a partial response (PR) and/or (b) an increase in progression-free survival (PFS) as compared to treatment with atezolizumab without tiragolumab, and wherein:

- (i) 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
- (ii) 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 complete response (CR) or a partial response (PR) and/or (b) an increase in progression-free survival (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 420 mg every two weeks and atezolizumab is to be administered at a fixed dose of about 840 mg every two weeks, or
- (ii) 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.

CLAIMS

WHAT IS CLAIMED IS:

1. Use of tiragolumab and atezolizumab in the manufacture of a medicament for combination therapy 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 complete response (CR) or a partial response (PR) and/or (b) an increase in progression-free survival (PFS) as compared to treatment with atezolizumab without tiragolumab; and wherein:

(i) 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

(ii) 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 complete response (CR) or a partial response (PR) and/or (b) an increase in progression-free survival (PFS) as compared to treatment with atezolizumab without tiragolumab, and wherein:

(i) 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

(ii) 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 complete response (CR) or a partial response (PR) and/or (b) an increase in progression-free survival (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 420 mg every two weeks and atezolizumab is to be administered at a fixed dose of about 840 mg every two weeks, or

(ii) 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 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.

5. The use of claim 4, wherein tiragolumab and atezolizumab are each to be administered on Days 1 and 15 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 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.

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

8. The use of any one of claims 1-7, wherein tiragolumab and atezolizumab are to be administered to the subject intravenously.

9. The use of any one of claims 1-7, wherein tiragolumab and atezolizumab are to be administered to the subject subcutaneously.

10. The use of any one of claims 1-9, wherein the PD-L1-positive tumor cell fraction has been determined by an immunohistochemical (IHC) assay.

11. The use of any one of claims 1-10, 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.

12. The use of claim 11, 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.

13. The use of claim 12, wherein the PD-L1-positive tumor cell fraction is calculated using the Ventana SP263 IHC assay.

14. The use of claim 11, 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.

15. The use of claim 14, wherein the PD-L1-positive tumor cell fraction is calculated using the pharmDx 22C3 IHC assay.

16. The use of claim 11, 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.

17. The use of any one of claims 1-9, wherein a tumor sample obtained from the subject has been determined to have a detectable nucleic acid expression level of PD-L1.

18. The use of claim 17, 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.

19. The use of any one of claims 1-18, wherein the lung cancer is a non-small cell lung cancer (NSCLC).

20. The use of claim 19, wherein the NSCLC is a squamous NSCLC or a non-squamous NSCLC.

21. The use of claim 19, wherein the NSCLC is:

- (a) a locally advanced unresectable NSCLC; or
- (b) a recurrent or metastatic NSCLC.

22. The use of claim 21, wherein:

- (a) the locally advanced unresectable NSCLC is a Stage IIIB NSCLC; or
- (b) the recurrent or metastatic NSCLC is a Stage IV NSCLC.

23. The use of claim 21 or 22, wherein the subject has not been previously treated for Stage IV NSCLC.

24. The use of any one of claims 1-23, wherein the subject does not have a sensitizing epidermal growth factor receptor (*EGFR*) gene mutation or anaplastic lymphoma kinase (*ALK*) gene rearrangement.

25. The use of any one of claims 1-24, wherein the PFS is increased as compared to a reference PFS time.

26. The use of claim 25, wherein the reference PFS time is the median PFS time of a population of subjects who have received a treatment comprising atezolizumab without tiragolumab.

27. The use of any one of claims 1-26, wherein the treatment results in an increase in PFS of at least 3.1 months, as compared to treatment with atezolizumab without tiragolumab.

28. The use of any one of claims 1-27, wherein the treatment results in an increase in overall survival (OS) of at least 5.7 months, as compared to treatment with atezolizumab without tiragolumab.