

CLAIMS

1. Use of an anti-CSF1R antibody and an anti-PD-1 antibody for preparation of a medicament for treatment of cancer in a subject;

wherein the anti-CSF1R antibody and anti-PD-1 antibody are to be administered concurrently or sequentially to the subject; and wherein:

the anti-CSF1R antibody is selected from:

a) an antibody comprising a heavy chain comprising the sequence of SEQ ID NO: 39 and a light chain comprising the sequence of SEQ ID NO: 46;

b) an antibody comprising a heavy chain comprising a heavy chain (HC) CDR1 having the sequence of SEQ ID NO: 15, an HC CDR2 having the sequence of SEQ ID NO: 16, and an HC CDR3 having the sequence of SEQ ID NO: 17, and a light chain comprising a light chain (LC) CDR1 having the sequence of SEQ ID NO: 18, a LC CDR2 having the sequence of SEQ ID NO: 19, and a LC CDR3 having the sequence of SEQ ID NO: 20; and

c) an antibody comprising a heavy chain comprising the sequence of SEQ ID NO: 53 and a light chain comprising the sequence of SEQ ID NO: 60, and

the anti-PD-1 antibody is selected from:

a) an antibody comprising a heavy chain comprising the sequence of SEQ ID NO: 100 and a light chain comprising the sequence of SEQ ID NO: 102;

b) an antibody comprising a heavy chain comprising a heavy chain (HC) CDR1 having the sequence of SEQ ID NO: 105, an HC CDR2 having the sequence of SEQ ID NO: 107, and an HC CDR3 having the sequence of SEQ ID NO: 109, and a light chain comprising a light chain (LC) CDR1 having the sequence of SEQ ID NO: 112, a LC CDR2 having the sequence of SEQ ID NO: 114, and a LC CDR3 having the sequence of SEQ ID NO: 116; and

c) an antibody comprising a heavy chain comprising the sequences of SEQ ID NOs: 100 and 101 and a light chain comprising the sequences of SEQ ID NOs: 102 and 103.

2. The use according to claim 1, wherein the anti-PD-1 antibody is nivolumab.

3. The use according to claim 1 or 2, wherein the anti-CSF1R antibody and the anti-PD-1 antibody are to be administered concurrently.

4. The use according to claim 1 or 2, wherein one or more doses of the anti-PD-1 antibody are to be administered prior to administering the anti-CSF1R antibody.

5. The use according to claim 4, wherein the subject received a complete course of anti-PD-1 antibody therapy prior to administration of the anti-CSF1R antibody and the anti-CSF1R antibody is optionally to be administered during a second course of anti-PD-1 antibody therapy.

6. The use according to any one of claims 3 to 5, wherein at least one dose of the anti-PD-1 antibody is to be administered concurrently with the anti-CSF1R inhibitor.

7. The use according to claim 1 or 2, wherein one or more doses of the anti-CSF1R antibody are to be administered prior to administering the anti-PD-1 antibody.

8. The use according to claim 7, wherein the subject received at least two, at least three, or at least four doses of the anti-CSF1R antibody prior to administration of the anti-PD-1 antibody and optionally at least one dose of the anti-CSF1R antibody is to be administered concurrently with the anti-PD-1 antibody.

9. The use according to any one of the preceding claims, wherein the anti-CSF1R antibody is to be administered at a dose of about 0.1, about 0.3, about 0.5, about 1, about 2, about 3, about 4, about 5, or about 10 mg/kg.

10. The use according to any one of the preceding claims, wherein the anti-PD-1 antibody is to be administered at a dose of about 0.5-10 mg/kg, such as at a dose of about 0.5, about 1, about 2, about 3, about 4, about 5, or about 10 mg/Kg.

11. The use according to any one of the preceding claims, wherein the anti-CSF1R antibody and the anti-PD-1 antibody are to be administered once per 1, 2, 3, 4, or 5 weeks, such as once per week, or such as once every 2 weeks, or once every 3 weeks.

12. The use according to any one of the preceding claims, wherein the cancer is selected from non-small cell lung cancer, melanoma, squamous cell carcinoma of the head and neck, ovarian cancer, pancreatic cancer, renal cell carcinoma, hepatocellular carcinoma, bladder cancer, malignant glioma, colorectal cancer, and endometrial cancer.

13. The use according to any one of the preceding claims, wherein the cancer is recurrent or progressive after a therapy selected from surgery, chemotherapy, radiation therapy, or a combination thereof.

14. The use according to any one of the preceding claims, wherein administration of the anti-CSF1R antibody and the anti-PD-1 antibody in a mouse xenograft model of the cancer results in synergistic inhibition of tumor growth.

15. The use according to claim 14, wherein the cancer is a colon, rectum, or colorectal cancer and the mouse xenograft model comprises colorectal carcinoma cells, such as MC38 colorectal carcinoma cells; or

wherein the cancer is a pancreatic cancer and the mouse xenograft model comprises murine pancreatic ductal adenocarcinoma (PDAC) cells, such as KRas^{G12D}/Ink4a^{-/-} pancreatic ductal adenocarcinoma cells.

16. The use according to any of the preceding claims, wherein the patient has non-

small cell lung cancer, melanoma, squamous cell carcinoma of the head and neck, ovarian cancer, pancreatic cancer, renal cell carcinoma, hepatocellular carcinoma, bladder cancer, malignant glioma, colorectal cancer, or endometrial cancer; and wherein the anti-CSF1R antibody is to be administered at a dose of about 1, about 2, or about 3, or about 4 mg/kg every two weeks and the anti-PD-1 antibody is to be administered at a dose of about 3 mg/kg every two weeks.

17. The use according to any one of claims 1-15, wherein the patient has non-small cell lung cancer, melanoma, squamous cell carcinoma of the head and neck, ovarian cancer, pancreatic cancer, renal cell carcinoma, hepatocellular carcinoma, bladder cancer, malignant glioma, colorectal cancer, or endometrial cancer; and wherein the anti-CSF1R antibody is to be administered at a dose of about 1, about 2, about 3, or about 4 mg/kg every two weeks and the anti-PD-1 antibody is to be administered at a dose of 240 mg every two weeks

18. The use according to any one of claims 1-15, wherein the patient has non-small cell lung cancer, melanoma, squamous cell carcinoma of the head and neck, ovarian cancer, pancreatic cancer, renal cell carcinoma, hepatocellular carcinoma, bladder cancer, malignant glioma, colorectal cancer, or endometrial cancer; and wherein the anti-CSF1R antibody is to be administered at a dose of about 1, about 2, about 3, or about 4 mg/kg every two weeks and the anti-PD-1 antibody is to be administered once every four weeks.

19. The use according to claim 16, 17, or 18, wherein the anti-CSF1R antibody is to be administered at a dose of about 4 mg/kg every two weeks.

20. The use according to claim 16, 17, or 18, wherein the anti-CSF1R antibody is to be administered at a dose of 4 mg/kg every two weeks.

21. The use according to claim 16, 17, or 18, wherein the anti-CSF1R antibody is to be administered at a dose of about 3 mg/kg every two weeks.

22. The use according to claim 16, 17, or 18, wherein the anti-CSF1R antibody is to be administered at a dose of 3 mg/kg every two weeks.

23. The use according to any one of claims 1-15, wherein the patient has non-small cell lung cancer, melanoma, squamous cell carcinoma of the head and neck, ovarian cancer, pancreatic cancer, renal cell carcinoma, hepatocellular carcinoma, bladder cancer, malignant glioma, colorectal cancer, or endometrial cancer; and wherein the anti-CSF1R antibody is to be administered at a dose of about 4 mg/kg every two weeks and the anti-PD-1 antibody is to be administered every four weeks.

24. The use according to any one of claims 1-15, wherein the patient has non-

small cell lung cancer, melanoma, squamous cell carcinoma of the head and neck, ovarian cancer, pancreatic cancer, renal cell carcinoma, hepatocellular carcinoma, bladder cancer, malignant glioma, colorectal cancer, or endometrial cancer; and wherein the anti-CSF1R antibody is to be administered at a dose of 4 mg/kg every two weeks and the anti-PD-1 antibody is to be administered every four weeks.

25. The use according to any one of claims 1-15, wherein the patient has pancreatic cancer, wherein the anti-CSF1R antibody is to be administered at a dose of about 1, about 2, about 3, or about 4 mg/kg every two weeks and the anti-PD-1 antibody is to be administered at a dose of about 3 mg/kg every two weeks.

26. The use according to any one of claims 1-15, wherein the patient has pancreatic cancer, and wherein the anti-CSF1R antibody is to be administered at a dose of about 1, about 2, about 3, or about 4 mg/kg every two weeks and the anti-PD-1 antibody is to be administered at a dose of 240 mg every two weeks.

27. The use according to any one of claims 1-15, wherein the patient has pancreatic cancer, and wherein the anti-CSF1R antibody is to be administered at a dose of about 1, about 2, about 3, or about 4 mg/kg every two weeks and the anti-PD-1 antibody is to be administered once every four weeks.

28. The use according to claim 25, 26, or 27, wherein the anti-CSF1R antibody is to be administered at a dose of about 4 mg/kg every two weeks.

29. The use according to claim 25, 26, or 27, wherein the anti-CSF1R antibody is to be administered at a dose of 4 mg/kg every two weeks.

30. The use according to claim 25, 26, or 27, wherein the anti-CSF1R antibody is to be administered at a dose of about 3 mg/kg every two weeks.

31. The use according to claim 25, 26, or 27, wherein the anti-CSF1R antibody is to be administered at a dose of 3 mg/kg every two weeks.

32. The use according to any one of claims 1-15, wherein the patient has pancreatic cancer, and wherein the anti-CSF1R antibody is to be administered at a dose of about 4 mg/kg every two weeks and the anti-PD-1 antibody is to be administered every four weeks.

33. The use according to any one of claims 1-15, wherein the patient has pancreatic cancer, and wherein the anti-CSF1R antibody is to be administered at a dose of 4 mg/kg every two weeks and the anti-PD-1 antibody is to be administered every four weeks.

34. The use according to any one of claims 1-33, wherein the anti-CSF1R antibody comprises a heavy chain comprising the sequence of SEQ ID NO: 53 and a light

chain comprising the sequence of SEQ ID NO: 60 and the anti-PD-1 antibody is nivolumab.

35. A composition comprising an anti-CSF1R antibody and an anti-PD-1 antibody wherein:

the anti-CSF1R antibody is selected from:

a) an antibody comprising a heavy chain comprising the sequence of SEQ ID NO: 39 and a light chain comprising the sequence of SEQ ID NO: 46;

b) an antibody comprising a heavy chain comprising a heavy chain (HC) CDR1 having the sequence of SEQ ID NO: 15, an HC CDR2 having the sequence of SEQ ID NO: 16, and an HC CDR3 having the sequence of SEQ ID NO: 17, and a light chain comprising a light chain (LC) CDR1 having the sequence of SEQ ID NO: 18, a LC CDR2 having the sequence of SEQ ID NO: 19, and a LC CDR3 having the sequence of SEQ ID NO: 20; and

c) an antibody comprising a heavy chain comprising the sequence of SEQ ID NO: 53 and a light chain comprising the sequence of SEQ ID NO: 60, and

the anti-PD-1 antibody is selected from:

a) an antibody comprising a heavy chain comprising the sequence of SEQ ID NO: 100 and a light chain comprising the sequence of SEQ ID NO: 102;

b) an antibody comprising a heavy chain comprising a heavy chain (HC) CDR1 having the sequence of SEQ ID NO: 105, an HC CDR2 having the sequence of SEQ ID NO: 107, and an HC CDR3 having the sequence of SEQ ID NO: 109, and a light chain comprising a light chain (LC) CDR1 having the sequence of SEQ ID NO: 112, a LC CDR2 having the sequence of SEQ ID NO: 114, and a LC CDR3 having the sequence of SEQ ID NO: 116; and

c) an antibody comprising a heavy chain comprising the sequences of SEQ ID NOs: 100 and 101 and a light chain comprising the sequences of SEQ ID NOs: 102 and 103.

36. The composition of claim 35, wherein the composition provides a dose of about 1, about 2, about 3, or about 4 mg/kg of the anti-CSF1R antibody and a dose of about 3 mg/kg or 240 mg of the anti-PD-1 antibody.

37. The composition of claim 36, wherein the composition provides a dose of about 3 mg/kg of the anti-PD-1 antibody.

38. The composition of claim 37, wherein the composition provides a dose of about 2, about 3, or about 4 mg/kg of the anti-CSF1R antibody.

39. The composition of claim 38, wherein the composition provides a dose of about 4 mg/kg of the anti-CSF1R antibody.

40. The composition of claim 38, wherein the composition provides a dose of 4 mg/kg of the anti-CSF1R antibody.

41. The composition of claim 36, wherein the composition provides a dose of about 240 mg of the anti-PD-1 antibody.

42. The composition of claim 41, wherein the composition provides a dose of about 2, about 3, or about 4 mg/kg of the anti-CSF1R antibody.

43. The composition of claim 42, wherein the composition provides a dose of about 4 mg/kg of the anti-CSF1R antibody.

44. The composition of claim 42, wherein the composition provides a dose of 4 mg/kg of the anti-CSF1R antibody.

45. The composition of any one of claims 35-44, wherein the anti-CSF1R antibody comprises a heavy chain comprising the sequence of SEQ ID NO: 53 and a light chain comprising the sequence of SEQ ID NO: 60 and the anti-PD-1 antibody is nivolumab.