

CLAIMS

1. Use of a pharmaceutical composition comprising (a) an antibody, or antigen-binding portion thereof, that specifically binds to CD40, and (b) an immunotherapeutic agent that inhibits PD-1 function in the preparation of a medicament for treating a solid tumour in a subject, wherein the immunotherapeutic agent that inhibits PD-1 function is an anti-PD-1 antibody or anti-PD-L1 antibody; and wherein the antibody or antigen-binding portion thereof that specifically binds to CD40 comprises the following CDRs

V _L CDR1: CTGSSSNIGAGYNVY	[SEQ ID NO:1];
V _L CDR2: GNINRPS	[SEQ ID NO:2];
V _L CDR3: CAAWDKSIISGLV	[SEQ ID NO:3];
V _H CDR1: GFTFSTYGMH	[SEQ ID NO:4];
V _H CDR2: GKGLEWLSYISGGSSYIFYADSVRGR	[SEQ ID NO:5]; and
V _H CDR3: CARILRGGSGMDL	[SEQ ID NO:6].

2. The use according to Claim 1, wherein the immunotherapeutic agent that inhibits PD-1 function is an anti-PD-1 antibody which blocks the interaction between PD1 and PD-L1.

3. The use according to Claim 1 or 2, wherein the pharmaceutical composition provides a synergistic benefit in the treatment of a solid tumour in a subject.

4. The use according to one of the preceding claims, wherein the solid tumour is selected from the groups consisting of an adenoma, a blastoma, a carcinoma, a desmoid tumour, a desmoplastic small round cell tumour, an endocrine tumour, a germ cell tumour, a lymphoma, a sarcoma, a Wilms tumour, a lung tumour, a colon tumour, a lymph tumour, a breast tumour and a melanoma.

5. The use to any one of the preceding claims, wherein the solid tumour is a melanoma.

6. The use according to any one of the preceding claims, wherein the antibody or antigen-binding portion thereof that specifically binds to CD40 comprises or consists of an intact antibody.

7. The use according to any one of Claims 1 to 5, wherein the antibody or antigen-binding portion thereof that specifically binds to CD40 comprises or consists of an antigen-binding fragment selected from the group consisting of: an Fv fragment and a Fab-like fragment.

8. The use according to any one of the preceding claims, wherein the antibody or antigen-binding portion thereof is human or humanised.

9. The use according to any one of the preceding claims, wherein the antibody or antigen-binding portion thereof that specifically binds to CD40 comprises the light chain variable region of SEQ ID NO: 7 and the heavy chain variable region of SEQ ID NO: 8.

10. The use according to any one of the preceding claims, wherein the antibody or antigen-binding portion thereof that specifically binds to CD40 comprises the light chain constant region of SEQ ID NO: 11 and the heavy chain constant region of SEQ ID NO: 12.

11. The use according to any one of the preceding claims, wherein the antibody or antigen-binding portion thereof that specifically binds to CD40 comprises or consists of the light chain of SEQ ID NO: 7 plus SEQ ID NO:11, and the heavy chain of SEQ ID NO: 8 plus SEQ ID NO:12.

12. The use according to any one of Claims 2 to 11, wherein the anti-PD-1 antibody is selected from the group consisting of Nivolumab, Pembrolizumab, Lambrolizumab, and Pidilizumab.

13. Use of an antibody, or antigen-binding portion thereof, that specifically binds to CD40 in the preparation of a medicament for treating a solid tumour in a subject, wherein the antibody or antigen-binding portion thereof that specifically binds to CD40 is to be used in combination with an immunotherapeutic agent that inhibits PD-1 function selected from the group consisting of an anti-PD-1 antibody and an anti-PD-L1 antibody; and wherein the antibody or antigen-binding portion thereof that specifically binds to CD40 comprises the following CDRs:

V _L CDR1: CTGSSSNIGAGYNVY	[SEQ ID NO:1];
V _L CDR2: GNINRPS	[SEQ ID NO:2];
V _L CDR3: CAAWDKSIISGLV	[SEQ ID NO:3];
V _H CDR1: GFTFSTYGMH	[SEQ ID NO:4];
V _H CDR2: GKGLEWLSYISGGSSYIFYADSVRGR	[SEQ ID NO:5]; and
V _H CDR3: CARILRGGSGMDL	[SEQ ID NO:6].

14. The use according to Claim 13, wherein the antibody or antigen-binding portion thereof that specifically binds to CD40 is to be used in combination with an anti-PD-1 antibody which blocks the interaction between PD1 and PD-L1.

15. The use according to Claim 13, wherein the antibody or antigen-binding portion thereof is as defined in any one of Claims 6 to 11.

16. The use according to Claim 14 or 15, wherein the immunotherapeutic agent that inhibits PD-1 function is as defined in Claim 12.

17. A pharmaceutical composition comprising (a) an antibody, or antigen-binding portion thereof, that specifically binds to CD40, and (b) an immunotherapeutic agent that inhibits PD-1 function, wherein the immunotherapeutic agent that inhibits PD-1 function is an anti-PD-1 antibody or anti-PD-L1 antibody; and wherein the antibody or antigen-binding portion thereof that specifically binds to CD40 comprises the following CDRs:

V _L CDR1: CTGSSSNIGAGYNVY	[SEQ ID NO:1];
V _L CDR2: GNINRPS	[SEQ ID NO:2];
V _L CDR3: CAAWDKSIISGLV	[SEQ ID NO:3];
V _H CDR1: GFTFSTYGMH	[SEQ ID NO:4];
V _H CDR2: GKGLEWLSYISGGSSYIFYADSVRGR	[SEQ ID NO:5]; and
V _H CDR3: CARILRGGSGMDL	[SEQ ID NO:6].

18. The pharmaceutical composition according to Claim 17, comprising an anti-PD-1 antibody which blocks the interaction between PD1 and PD-L1.

19. The pharmaceutical composition according to Claim 17, wherein the antibody or antigen-binding portion thereof is as defined in any one of Claims 6 to 11.

20. The pharmaceutical composition according to Claim 18 or 19, wherein the further immunotherapeutic agent that inhibits PD-1 function is as defined in Claim 12.

21. The use according to any one of Claims 13 to 16, wherein the antibody or antigen-binding portion thereof that specifically binds to CD40 and the immunotherapeutic agent that inhibits PD-1 function are to be administered simultaneously or wherein the immunotherapeutic agent that inhibits PD-1 function is to be administered between 24 hours and two weeks, between 24 hours and one week, between 24 and 72 hours, or between 24 and 48 hours after the antibody or antigen-binding portion thereof that specifically binds to CD40 is to be administered.

22. The use according to any one of Claims 13 to 16 and 21, wherein the antibody or antigen-binding portion thereof that specifically binds to CD40 is to be administered locally to the tumour site.

23. The use according to any one of Claims 13 to 16 and 21 to 22, wherein at least 30% of the amount of the antibody or antigen-binding portion thereof that specifically binds to CD40 to be administered is to be retained at the tumour site at four hours after administration, preferably wherein at least 40% of the said amount is to be retained at the tumour site at four hours after administration.

24. The use according to any one of Claims 13 to 16 and 21 to 23, wherein the immunotherapeutic agent that inhibits PD-1 function is formulated as a composition suitable for systemic administration with at least one pharmaceutically acceptable diluent or carrier.

25. The use according to any one of Claims 13 to 16 and 21 to 24, wherein the antibody or antigen-binding portion thereof that specifically binds to CD40 is to be administered on multiple separate occasions and the immunotherapeutic agent that inhibits PD-1 function is to be administered such that exposure of the subject to the immunotherapeutic agent that inhibits PD-1 function is continuous for the duration of the treatment.

26. The use according to any one of Claims 1 to 16 and 21 to 25, wherein the subject is a human.