

CLAIMS

~~What is claimed:~~

1. ~~A method of providing clinically proven safe administration of an anti-CD40 antibody to a human subject diagnosed with an advanced solid tumor, comprising intravenously administering to the subject~~Use of a pharmaceutical composition comprising thean anti-CD40 antibody and a pharmaceutically acceptable carrier in the manufacture of a medicament for the treatment of an advanced solid tumor in a human subject, wherein the pharmaceutical composition is to be administered intravenously to the subject, wherein the antibody comprises a heavy chain variable region and a light chain variable region, the heavy chain variable region comprising heavy chain complementarity determining regions (HCDRs) HCDR1, HCDR2 and HCDR3 amino acid sequences of SEQ ID Nos: 1, 2, and 3, respectively, and the light chain variable region comprising light chain complementarity determining regions (LCDRs) LCDR1, LCDR2 and LCDR3 amino acid sequences of SEQ ID Nos: 4, 5, and 6, respectively, and wherein a total dosage of the antibody to be administered is 50 µg/kg to 2500 µg/kg, preferably 75 µg/kg to 2000 µg/kg, body weight of the subject per administration.
2. The ~~method~~use of claim 1, wherein the antibody comprises a heavy chain variable region (VH) having the amino acid sequence of SEQ ID NO: 7 and a light chain variable region (VL) having the amino acid sequences of SEQ ID NO: 8.
3. The ~~method~~use of claim 1 or 2, wherein the antibody comprises a heavy chain (HC) having the amino acid sequence of SEQ ID NO: 9 and a light chain (LC) having the amino acid sequences of SEQ ID NO: 10.
4. The ~~method~~use of any one of claims 1-3, wherein the total dosage of the anti-CD40 antibody to be administered per administration is 75 µg/kg, 200 µg/kg, 400 µg/kg, 600 µg/kg, 700 µg/kg, 800 µg/kg, 900 µg/kg, 1000 µg/kg, 1100 µg/kg, 1200 µg/kg, 1300 µg/kg, 1400 µg/kg, 1500 µg/kg, 1800 µg/kg, or 2000 µg/kg body weight of the subject, or any dosage in between.
5. The ~~method~~use of any one of claims 1-4, wherein the total dosage of the pharmaceutical composition is to be intravenously administered to the human

subject over about 2 hours, preferably the pharmaceutical composition is to be intravenously administered to the human subject repeatedly, more preferably once every two weeks.

5 6. The methoduse of any one of claims 1-5, further comprising ~~administering to the human subject~~ a therapeutic agent to be administered before or after the administration of the anti-CD40 antibody, preferably the therapeutic agent is selected for the group consisting of corticosteroid, antihistamine, antipyretic, H₂-antagonist, and antiemetic.

10 7. The methoduse of any one of claims 1-6, further comprising ~~administering to the subject~~ an effective amount of at least one of Cetirizine and Montelukast to be administered to the human subject in combination with the anti-CD40 antibody, to thereby reduce infusion-related reactions (IRRS) or reaction of pruritus, preferably cetirizine and montelukast are to be administered no earlier than 3 days before and no later than 3 days after the administration of the anti-CD40 antibody.

15 8. The methoduse of any one of claims 1-7, wherein the anti-CD40 antibody has an in vivo half-life of about 10-16 hours, preferably about 13 hours, when the total dosage of the anti-CD40 antibody to be administered per administration is 600 µg/kg body weight of the subject, , or the anti-CD40 antibody has an in vivo half-life of about 20-28 hours, preferably 24 hours, when the total dosage of the anti-CD40 antibody to be administered per administration is no less than 1200 µg/kg body weight of the subject,.

20 9. The methoduse of any one of claims 1 to 8, wherein the human subject has no accumulation of the anti-CD40 antibody when the pharmaceutical composition is to be intravenously administered to the human subject repeatedly.

25 10. The methoduse of any one of claims 1 to 9, wherein the administration of the anti-CD40 results in target saturation when the total dosage of the anti-CD40 antibody to be administered per administration is about 1000-1400 µg/kg body weight of the subject, preferably 1200 µg/kg body weight of the subject.

30 11. The methoduse of any one of claims 1 to 10, wherein the administration of the anti-CD40 antibody causes, in the peripheral blood of the human subject, a margination

of one or more cells selected from the group consisting of B cells, T cells, and natural killer (NK) cells, and a subsequent recovery thereof.

12. The ~~method~~use of any one of claims 1 to 11, wherein the administration of the anti-CD40 antibody achieves, in the peripheral blood of the human subject, an increase of one or more chemokines selected from the group consisting of MCP-1, IP-10, MIP-1 β , MIP-1 α , and IL-8.
13. The ~~method~~use of any one of claims 1 to 12, wherein the administration of the anti-CD40 antibody achieves, in the peripheral blood of the human subject, an increase of one or more cytokines selected from the group consisting of IFN- γ , TNF- α , and IL12p70.
14. The ~~method~~use of any one of claims 1 to 13, wherein the administration of the anti-CD40 antibody results an increase of one or more activation markers on peripheral blood B lymphocytes, wherein the activation marker is selected from the group consisting of HLA-DR, CD54, CD80, and CD86.
15. The ~~method~~use of any one of claims 1-14, wherein the human subject has at least a partial response or has a prolonged stable disease for 6 or more months.
16. ~~A method of providing clinically proven safe administration of an anti-CD40 antibody to a human subject diagnosed with an advanced solid tumor, comprising intravenously administering to the subject~~Use of a pharmaceutical composition comprising thean anti-CD40 antibody and a pharmaceutically acceptable carrier in the manufacture of a medicament for the treatment of an advanced solid tumor in a human subject, wherein the pharmaceutical composition is to be intravenously administered to the subject, wherein the antibody comprises a heavy chain variable region and a light chain variable region, the heavy chain variable region comprising heavy chain complementarity determining regions (HCDRs) HCDR1, HCDR2 and HCDR3 amino acid sequences of SEQ ID NOs: 1, 2, and 3, respectively, and the light chain variable region comprising light chain complementarity determining regions (LCDRs) LCDR1, LCDR2 and LCDR3 amino acid sequences of SEQ ID NOs: 4, 5, and 6, respectively, wherein a total dosage of the antibody to be administered is about 600 $\mu\text{g/kg}$ to about 1200 $\mu\text{g/kg}$, such as 600 $\mu\text{g/kg}$, 700 $\mu\text{g/kg}$, 800 $\mu\text{g/kg}$, 900 $\mu\text{g/kg}$, 1000 $\mu\text{g/kg}$, 1100 $\mu\text{g/kg}$, 1200 $\mu\text{g/kg}$, body weight of

the subject per administration, preferably the human subject is diagnosed with non-small cell lung cancer (NSCLC), pancreatic cancer, or cutaneous melanoma.

17. The method use of claim 16, wherein the antibody comprises a heavy chain variable region (VH) having the amino acid sequence of SEQ ID NO: 7 and a light chain variable region (VL) having the amino acid sequences of SEQ ID NO: 8.
18. The method use of claim 16 or 17, wherein the antibody comprises a heavy chain (HC) having the amino acid sequence of SEQ ID NO: 9 and a light chain (LC) having the amino acid sequences of SEQ ID NO: 10.
19. A pharmaceutical composition comprising an anti-CD40 antibody and a pharmaceutically acceptable carrier, wherein the antibody comprises a heavy chain variable region and a light chain variable region, the heavy chain variable region comprising heavy chain complementarity determining regions (HCDRs) HCDR1, HCDR2 and HCDR3 amino acid sequences of SEQ ID NOs: 1, 2, and 3, respectively, and the light chain variable region comprising light chain complementarity determining regions (LCDRs) LCDR1, LCDR2 and LCDR3 amino acid sequences of SEQ ID NOs: 4, 5, and 6, respectively, and wherein a total dosage of the antibody to be administered is 50 µg/kg to 2500 µg/kg, preferably 75 µg/kg to 2000 µg/kg, body weight of the subject per administration.
20. An anti-CD40 antibody for use in medicine, wherein the antibody comprises a heavy chain variable region and a light chain variable region, the heavy chain variable region comprising heavy chain complementarity determining regions (HCDRs) HCDR1, HCDR2 and HCDR3 amino acid sequences of SEQ ID NOs: 1, 2, and 3, respectively, and the light chain variable region comprising light chain complementarity determining regions (LCDRs) LCDR1, LCDR2 and LCDR3 amino acid sequences of SEQ ID NOs: 4, 5, and 6, respectively, and wherein a total dosage of the antibody to be administered is 50 µg/kg to 2500 µg/kg, preferably 75 µg/kg to 2000 µg/kg, body weight of the subject per administration.
21. An anti-CD40 antibody for use in the treatment of advanced solid tumors, wherein the antibody comprises a heavy chain variable region and a light chain variable region, the heavy chain variable region comprising heavy chain complementarity determining regions (HCDRs) HCDR1, HCDR2 and HCDR3 amino acid

sequences of SEQ ID NOs: 1, 2, and 3, respectively, and the light chain variable region comprising light chain complementarity determining regions (LCDRs) LCDR1, LCDR2 and LCDR3 amino acid sequences of SEQ ID NOs: 4, 5, and 6, respectively, and wherein a total dosage of the antibody to be administered is 50 µg/kg to 2500 µg/kg, preferably 75 µg/kg to 2000 µg/kg, body weight of the subject per administration.