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1. (**Currently Amended**) The use of ~~A pharmaceutical composition, comprising:~~

an anti-IL-6R antibody or antigen-binding fragment thereof**; and**

a VEGF antagonist;

in the manufacture of a medicament for use in inhibiting or attenuating the growth of an anti-VEGF-resistant tumor in a subject **wherein the tumor exhibits increased IL-6/STAT3 signaling**.

~~2. (Cancelled) A pharmaceutical composition comprising an anti-IL-6R antibody or antigen-binding fragment thereof for use in inhibiting or attenuating the growth of a tumor in a subject, wherein the tumor exhibits increased IL-6/STAT3 signaling.~~

3. (Currently Amended) The ~~pharmaceutical composition~~method of claim 1 ~~or 2~~, wherein the anti-IL-6R antibody or antigen-specific binding fragment thereof comprises a heavy chain variable region (HCVR) and a light chain variable region (LCVR), wherein the HCVR comprises the complementarity determining regions (CDRs) of SEQ ID NO:2, and wherein the LCVR comprises the CDRs of SEQ ID NO:3.

4. (**Original**) The ~~pharmaceutical composition~~use of claim 3, wherein the HCVR comprises CDRs having the amino acid sequences of SEQ ID NOs:4, 5, and 6; and wherein LCVR comprises CDRs having the amino acid sequences of SEQ ID NOs:7, 8 and 9.

5. (**Original**) The ~~pharmaceutical composition~~use of any one of claims 1 to 4, further comprising an EGFR antagonist.

6. The ~~pharmaceutical composition~~use of claim 5, wherein the EGFR antagonist is selected from the group consisting of an anti-EGFR antibody, an anti-EGFRvIII antibody, an anti-ErbB2 antibody, an anti-ErbB3 antibody, and an anti-ErbB4 antibody.

~~7. (Cancelled) The pharmaceutical composition of any one of claims 1 to 4, further comprising a VEGF antagonist.~~

8. (**Currently Amended**) The ~~pharmaceutical composition~~use of claim**1** ~~7~~, wherein the VEGF antagonist is an antigen-specific binding protein that specifically binds VEGF.

9. The ~~pharmaceutical composition~~use of claim 8, wherein the antigen-specific binding protein is fusion protein comprising Ig domain 2 of VEGFR1, Ig domain 3 of VEGFR2, and a multimerizing domain.

10. The ~~pharmaceutical composition~~use of claim 9, wherein the Ig domain 2 of VEGFR1 comprises amino acids 27 to 129 of SEQ ID NO:11, the Ig domain 3 of VEGFR2 comprises amino acids 130 to 231 of SEQ ID NO:11, and the multimerizing domain comprises amino acids 232 to 457 of SEQ ID NO:11.

11. ~~A pharmaceutical composition comprising~~The use of an anti-IL-6R antibody or antigen-binding fragment thereof ~~for use~~ in the manufacture of a medicament for inhibiting or attenuating the growth of an anti-VEGF-resistant tumor in a subject wherein the tumor exhibits increased IL-6/STAT3 signaling,

wherein the anti-IL-6R antibody or antigen-specific binding fragment thereof comprises a heavy chain variable region (HCVR) and a light chain variable region (LCVR),

wherein the HCVR comprises CDRs having the amino acid sequences of SEQ ID NOs:4, 5, and 6; and wherein LCVR comprises CDRs having the amino acid sequences of SEQ ID NOs:7, 8 and 9.

12. The ~~pharmaceutical composition~~use of claim ~~11~~9, further comprising an EGFR antagonist selected from the group consisting of an anti-EGFR antibody, an anti-EGFRvIII antibody, an anti-ErbB2 antibody, an anti-ErbB3 antibody, and an anti-ErbB4 antibody.

13. The ~~pharmaceutical composition~~use of claim ~~11~~9, further comprising an antigen-specific binding protein that specifically binds VEGF.

14. The ~~pharmaceutical composition~~use of claim ~~13~~11, wherein the antigen-specific binding protein is a fusion protein comprising Ig domain 2 of VEGFR1, Ig domain 3 of VEGFR2, and a multimerizing domain.

15. The ~~pharmaceutical composition~~use of claim ~~14~~12, wherein the Ig domain 2 of VEGFR1 comprises amino acids 27 to 129 of SEQ ID NO:11, the Ig domain 3 of VEGFR2 comprises amino acids 130 to 231 of SEQ ID NO:11, and the multimerizing domain comprises amino acids 232 to 457 of SEQ ID NO:11.

What is claimed is:

1. A pharmaceutical composition comprising an anti-IL-6R antibody or antigen-binding fragment thereof for use in inhibiting or attenuating the growth of an anti-VEGF-resistant tumor in a subject.

2. A pharmaceutical composition comprising an anti-IL-6R antibody or antigen-binding fragment thereof for use in inhibiting or attenuating the growth of a tumor in a subject, wherein the tumor exhibits increased IL-6/STAT3 signaling.

3. The pharmaceutical composition of claim 1 or 2, wherein the anti-IL-6R antibody or antigen-specific binding fragment thereof comprises a heavy chain variable region (HCVR) and a light chain variable region (LCVR), wherein the HCVR comprises the complementarity determining regions (CDRs) of SEQ ID NO:2, and wherein the LCVR comprises the CDRs of SEQ ID NO:3.

4. The pharmaceutical composition of claim 3, wherein the HCVR comprises CDRs having the amino acid sequences of SEQ ID NOs:4, 5, and 6; and wherein LCVR comprises CDRs having the amino acid sequences of SEQ ID NOs:7, 8 and 9.

5. The pharmaceutical composition of any one of claims 1 to 4, further comprising an EGFR antagonist.

6. The pharmaceutical composition of claim 5, wherein the EGFR antagonist is selected from the group consisting of an anti-EGFR antibody, an anti-EGFRvIII antibody, an anti-ErbB2 antibody, an anti-ErbB3 antibody, and an anti-ErbB4 antibody.

7. The pharmaceutical composition of any one of claims 1 to 4, further comprising a VEGF antagonist.

8. The pharmaceutical composition of claim 7, wherein the VEGF antagonist is an antigen-specific binding protein that specifically binds VEGF.

9. The pharmaceutical composition of claim 8, wherein the antigen-specific binding protein is fusion protein comprising Ig domain 2 of VEGFR1, Ig domain 3 of VEGFR2, and a multimerizing domain.

10. The pharmaceutical composition of claim 9, wherein the Ig domain 2 of VEGFR1 comprises amino acids 27 to 129 of SEQ ID NO:11, the Ig domain 3 of VEGFR2 comprises amino acids 130 to 231 of SEQ ID NO:11, and the multimerizing domain comprises amino acids 232 to 457 of SEQ ID NO:11.

11. A pharmaceutical composition comprising an anti-IL-6R antibody or antigen-binding fragment thereof for use in inhibiting or attenuating the growth of an anti-VEGF-resistant tumor in a subject wherein the tumor exhibits increased IL-6/STAT3 signaling,

wherein the anti-IL-6R antibody or antigen-specific binding fragment thereof comprises a heavy chain variable region (HCVR) and a light chain variable region (LCVR),

wherein the HCVR comprises CDRs having the amino acid sequences of SEQ ID NOs:4, 5, and 6; and wherein LCVR comprises CDRs having the amino acid sequences of SEQ ID NOs:7, 8 and 9.

12. The pharmaceutical composition of claim 11, further comprising an EGFR antagonist selected from the group consisting of an anti-EGFR antibody, an anti-EGFRvIII antibody, an anti-ErbB2 antibody, an anti-ErbB3 antibody, and an anti-ErbB4 antibody.

13. The pharmaceutical composition of claim 11, further comprising an antigen-specific binding protein that specifically binds VEGF.

14. The pharmaceutical composition of claim 13, wherein the antigen-specific binding protein is a fusion protein comprising Ig domain 2 of VEGFR1, Ig domain 3 of VEGFR2, and a multimerizing domain.

15. The pharmaceutical composition of claim 14, wherein the Ig domain 2 of VEGFR1 comprises amino acids 27 to 129 of SEQ ID NO:11, the Ig domain 3 of VEGFR2 comprises amino acids 130 to 231 of SEQ ID NO:11, and the multimerizing domain comprises amino acids 232 to 457 of SEQ ID NO:11.

CLAIMS

1. The use of an anti-IL-6R antibody or antigen-binding fragment thereof; and

a VEGF antagonist; in the manufacture of a medicament for use in inhibiting or attenuating the growth of an anti-VEGF-resistant tumor in a subject wherein the tumor exhibits increased IL-6/STAT3 signaling.

2. The method of claim 1, wherein the anti-IL-6R antibody or antigen-specific binding fragment thereof comprises a heavy chain variable region (HCVR) and a light chain variable region (LCVR), wherein the HCVR comprises the complementarity determining regions (CDRs) of SEQ ID NO:2, and wherein the LCVR comprises the CDRs of SEQ ID NO:3.

3. The use of claim 3, wherein the HCVR comprises CDRs having the amino acid sequences of SEQ ID NOs:4, 5, and 6; and wherein LCVR comprises CDRs having the amino acid sequences of SEQ ID NOs:7, 8 and 9.

4. The use of any one of claims 1 to 4, further comprising an EGFR antagonist.

5. The use of claim 5, wherein the EGFR antagonist is selected from the group consisting of an anti-EGFR antibody, an anti-EGFRvIII antibody, an anti-ErbB2 antibody, an anti-ErbB3 antibody, and an anti-ErbB4 antibody.

6. The use of claim 1, wherein the VEGF antagonist is an antigen-specific binding protein that specifically binds VEGF.

7. The use of claim 8, wherein the antigen-specific binding protein is fusion protein comprising Ig domain 2 of VEGFR1, Ig domain 3 of VEGFR2, and a multimerizing domain.

8. The use of claim 9, wherein the Ig domain 2 of VEGFR1 comprises amino acids 27 to 129 of SEQ ID NO:11, the Ig domain 3 of VEGFR2 comprises amino acids 130 to 231 of SEQ ID NO:11, and the multimerizing domain comprises amino acids 232 to 457 of SEQ ID NO:11.

9. The use of an anti-IL-6R antibody or antigen-binding fragment thereof in the manufacture of a medicament for inhibiting or attenuating the growth of an anti-VEGF-resistant tumor in a subject wherein the tumor exhibits increased IL-6/STAT3 signaling,

wherein the anti-IL-6R antibody or antigen-specific binding fragment thereof comprises a heavy chain variable region (HCVR) and a light chain variable region (LCVR),

wherein the HCVR comprises CDRs having the amino acid sequences of SEQ ID NOs:4, 5, and 6; and wherein LCVR comprises CDRs having the amino acid sequences of SEQ ID NOs:7, 8 and 9.

10. The use of claim 9, further comprising an EGFR antagonist selected from the group consisting of an anti-EGFR antibody, an anti-EGFRvIII antibody, an anti-ErbB2 antibody, an anti-ErbB3 antibody, and an anti-ErbB4 antibody.

11. The use of claim 9, further comprising an antigen-specific binding protein that specifically binds VEGF.

12. The use of claim 12, wherein the antigen-specific binding protein is a fusion protein comprising Ig domain 2 of VEGFR1, Ig domain 3 of VEGFR2, and a multimerizing domain.

13. The use of claim 13, wherein the Ig domain 2 of VEGFR1 comprises amino acids 27 to 129 of SEQ ID NO:11, the Ig domain 3 of VEGFR2 comprises amino acids 130 to 231 of SEQ ID NO:11, and the multimerizing domain comprises amino acids 232 to 457 of SEQ ID NO:11.