CLAIMS

1. The use of an anti-IL-6R antibody or antigen-binding fragment thereof; and an antigen-specific binding protein that specifically binds VEGF~~a VEGF antagonist~~; in the manufacture of a pharmaceutical composition 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~~ use 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.~~ 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.

3. The use of claim ~~3~~2, 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.~~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~~3, further comprising an EGFR antagonist.

5. The use of claim ~~5~~4, 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~~6. The use of claim ~~8~~1, 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.

~~8~~7. The use of claim ~~9~~6, 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~~8. The use of an anti-IL-6R antibody or antigen-binding fragment thereof in the manufacture of a pharmaceutical composition 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~~9. The use of claim ~~11~~8, 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~~10. The use of claim ~~11~~8, further comprising an antigen-specific binding protein that specifically binds VEGF.

~~12~~11. The use of claim ~~13~~10, 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~~12. The use of claim ~~14~~11, 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.

CLAIMS

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

an antigen-specific binding protein that specifically binds VEGF; in the manufacture of a pharmaceutical composition 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 use 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 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.

3. The use of claim 2, 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 use of any one of claims 1 to 3, further comprising an EGFR antagonist.

5. The use of claim 4, 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 antigen-specific binding protein is a fusion protein comprising Ig domain 2 of VEGFR1, Ig domain 3 of VEGFR2, and a multimerizing domain.

7. The use of claim 6, 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.

8. The use of an anti-IL-6R antibody or antigen-binding fragment thereof in the manufacture of a pharmaceutical composition 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.

9. The use of claim 8, 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.

10. The use of claim 8, further comprising an antigen-specific binding protein that specifically binds VEGF.

11. The use of claim 10, 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.

12. The use of claim 11, 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.