

Claims

1. Use of a first bispecific antibody, comprising a first binding part specifically binding to human CEACAM5 and a second binding part specifically binding to human CD47, characterized in that
- 5 a) the first binding part comprises a heavy chain variable region comprising a CDRH1 of SEQ ID NO:23, a CDRH2 of SEQ ID NO:24 and a CDRH3 of SEQ ID NO:25, and a light chain variable region comprising a CDRL1 of SEQ ID NO:35, CDRL2 of SEQ ID NO:36, and CDRL3 of SEQ ID NO:37,
- b) the second binding part comprises a heavy chain variable region comprising a CDRH1 of SEQ ID NO:23, a CDRH2 of SEQ ID NO:24, and a CDRH3 of SEQ ID NO:25,
- 10 and as light chain variable region a light chain variable region comprising a CDRL1 of SEQ ID NO:29, a CDRL2 of SEQ ID NO:30, and a CDRL3 of SEQ ID NO:31,
- in the manufacture of a first medicament and
- use of a second bispecific antibody comprising a first binding part specifically binding to human CEACAM5 and a second binding part specifically binding to human CD3ε, characterized in that:
- 15 a) the first binding part comprises a heavy chain variable region comprising a CDRH1 of SEQ ID NO:2, a CDRH2 of SEQ ID NO:3 and a CDRH3 of SEQ ID NO:4, and a light chain variable region comprising a CDRL1 of SEQ ID NO:18, CDRL2 of SEQ ID NO:19, and CDRL3 of SEQ ID NO:20, and
- b) the second binding part comprises a heavy chain variable region comprising a CDRH1 of SEQ ID NO:2, a CDRH2 of SEQ ID NO:3 and a CDRH3 of SEQ ID NO:4, and a light chain variable region comprising a CDRL1 of SEQ ID NO:6, a CDRL2 of SEQ ID NO:7, and a CDRL3 of SEQ ID NO:8
- 20 in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy to treat cancer.
- 25 2. Use of a first bispecific antibody comprising a first binding part specifically binding to human CEACAM5 and a second binding part specifically binding to human CD47 characterized in that:
- a) the first binding part comprises a heavy chain variable region of SEQ ID NO:26 and a light chain variable region of SEQ ID NO:38, and
- b) the second binding part comprises a heavy chain variable region of SEQ ID NO:26,
- 30 and a light chain variable region of SEQ ID NO:32,
- in the manufacture of a first medicament, and use of a second bispecific antibody comprising a first binding part specifically binding to human CEACAM5 and a second binding part specifically binding to human CD3ε characterized in that:
- a) the first binding part comprises a heavy chain variable region of SEQ ID NO:1 and a light chain variable region of SEQ ID NO:21, and
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b) the second binding part comprises a heavy chain variable region of SEQ ID NO:1, and a light chain variable region of SEQ ID NO:5 in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy to treat cancer.

3. Use of a first bispecific antibody comprising a first binding part specifically binding to human CEACAM5 and a second binding part specifically binding to human CD47 characterized in that:

a) the first binding part comprises a heavy chain region of SEQ ID NO:27 and a light chain of SEQ ID NO: 39, and

b) the second binding part comprises a heavy chain region of SEQ ID NO:27, and a light chain of SEQ ID NO:33, in the manufacture of a first medicament, and use of

a second bispecific antibody comprising a first binding part specifically binding to human CEACAM5 and a second binding part specifically binding to human CD3ε characterized in that:

a) the first binding part comprises a heavy chain region of SEQ ID NO:15 and a light chain of SEQ ID NO:22, and

b) the second binding part comprises a heavy chain region of SEQ ID NO:15, and a light chain of SEQ ID NO:9, in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy to treat cancer.

4. The use according to anyone of claims 1 to 3, characterized in that the cancer is a solid cancer.

5. The use according to claim 4, characterized in that the cancer is a colorectal cancer, NSCLC (non-small cell lung cancer), gastric cancer, pancreatic cancer, breast cancer, or another CEACAM5 expressing cancer.

6. The use according to anyone of claims 1 to 3, characterized by a ratio of the KD values for the binding to recombinant CEACAM3 and recombinant CEACAM5 of a factor of 100 or more.

7. The use according to anyone of claims 1 to 3, characterized by a ratio of the KD values for the binding to recombinant CEACAM3 and recombinant CEACAM5 of a factor of between 100 and 200.

8. The the use according to anyone of claims 1 to 7, characterized in that the first bispecific antibody and the second bispecific antibody are administered to said subject simultaneously in 2 to 15 day intervals.

9. A combination of a first bispecific antibody comprising a first binding part specifically binding to human CEACAM5 and a second binding part specifically binding to human CD47, characterized in that:

a) the first binding part comprises a heavy chain variable region comprising a CDRH1 of SEQ ID NO:23, a CDRH2 of SEQ ID NO:24 and a CDRH3 of SEQ ID NO:25, and a light chain variable

region comprising a CDRL1 of SEQ ID NO:35, CDRL2 of SEQ ID NO:36, and CDRL3 of SEQ ID NO:37,

b) the second binding part comprises a heavy chain variable region comprising a CDRH1 of SEQ ID NO:23, a CDRH2 of SEQ ID NO:24, and a CDRH3 of SEQ ID NO:25,

5 and as light chain variable region a light chain variable region comprising a CDRL1 of SEQ ID NO:29, a CDRL2 of SEQ ID NO:30, and a CDRL3 of SEQ ID NO:31, and

a second bispecific antibody comprising a first binding part specifically binding to human CEACAM5 and a second binding part specifically binding to human CD3ε characterized in that:

10 a) the first binding part comprises a heavy chain variable region comprising a CDRH1 of SEQ ID NO:2, a CDRH2 of SEQ ID NO:3 and a CDRH3 of SEQ ID NO:4, and a light chain variable region comprising

a CDRL1 of SEQ ID NO:18, CDRL2 of SEQ ID NO:19, and CDRL3 of SEQ ID NO:20, and b) the second binding part comprises a heavy chain variable region comprising a CDRH1 of SEQ ID NO:2, a CDRH2 of SEQ ID NO:3 and a CDRH3 of SEQ ID NO:4, and a light chain variable region
15 comprising a CDRL1 of SEQ ID NO:6, a CDRL2 of SEQ ID NO:7, and a CDRL3 of SEQ ID NO:8.

10. A combination of a first bispecific antibody comprising a first binding part specifically binding to human CEACAM5 and a second binding part specifically binding to human CD47 characterized in that:

20 a) the first binding part comprises a heavy chain variable region of SEQ ID NO:26 and a light chain variable region of SEQ ID NO:38, and

b) the second binding part comprises a heavy chain variable region of SEQ ID NO:26, and a light chain variable region of SEQ ID NO:32, and

a second bispecific antibody comprising a first binding part specifically binding to human CEACAM5 and a second binding part specifically binding to human CD3ε characterized in that:

25 a) the first binding part comprises a heavy chain variable region of SEQ ID NO:1 and a light chain variable region of SEQ ID NO:21, and

b) the second binding part comprises a heavy chain variable region of SEQ ID NO:1, and a light chain variable region of SEQ ID NO:5.

30 11. A combination of a first bispecific antibody comprising a first binding part specifically binding to human CEACAM5 and a second binding part specifically binding to human CD47 characterized in that:

a) the first binding part comprises a heavy chain region of SEQ ID NO:27 and a light chain of SEQ ID NO: 39, and b) the second binding part comprises a heavy chain region of SEQ ID NO:27, and a light
35 chain of SEQ ID NO:33, and

a second bispecific antibody comprising a first binding part specifically binding to human CEACAM5 and a second binding part specifically binding to human CD3ε characterized in that:

a) the first binding part comprises a heavy chain region of SEQ ID NO:15 and a light chain of SEQ ID NO:22, and b) the second binding part comprises a heavy chain region of SEQ ID NO:15, and a light chain of SEQ ID NO:9.

12. A pharmaceutical composition comprising the combination of any one of claims 9 to 11 and a pharmaceutically acceptable excipient or carrier.

13. The pharmaceutical composition of claim 12, for use as a medicament.

14. Use of the pharmaceutical composition of claim 12 or 13 in the manufacture of a medicament for treating a solid cancer.

15. Use of the pharmaceutical composition of any one of claims 12 to 14, in the manufacture of a medicament for treating colorectal cancer, NSCLC (non-small cell lung cancer), gastric cancer, pancreatic cancer, or breast cancer.

16. Use of the combination of any one of claims 9 to 11 or the pharmaceutical composition of any one of claims 12 to 15 in the manufacture of a medicament for treating a cancer that expresses CEACAM5 in a patient, wherein the patient is to be administered a therapeutically effective amount of the medicament.

17. The use of claim 16, wherein the antibodies are to be administered simultaneously.

18. The use of claim 16 or 17, wherein the patient is to be administered one or more doses of 0.01 to 10 mg/kg of the combination or composition of any one of claims 9 to 15.

19. The use of claim 16 or 17, wherein the patient is to be administered one or more doses of 0.01 to 10 mg/kg of the second bispecific antibody and one or more doses of 1 to 20 mg/kg of the first bispecific antibody.

20. Use of the combination or composition of any one of claims 7 to 11 in the manufacture of a medicament for increasing survival time in a patient having a cancer that expresses CEACAM5, wherein said patient is to be administered a therapeutically effective amount of the medicament.