Claims

1. Use of a bispecific antibody or functional part, derivative and/or analogue thereof that comprises a variable domain that binds an extracellular part of EGFR and a second variable domain that binds LGR5, in the manufacture of a medicament for the treatment of a cancer in a human subject, wherein the medicament is to be administered with a fluoropyrimidine, a platinum-based chemotherapeutic agent, a BCL-2 inhibitor, or SN-38.

2. Use of a fluoropyrimidine, a platinum-based chemotherapeutic agent, a BCL-2 inhibitor, or SN-38 in the manufacture of a medicament for the treatment of a cancer in a human subject, wherein the medicament is to be administered with a bispecific antibody or functional part, derivative and/or analogue thereof that comprises a variable domain that binds an extracellular part of EGFR and a second variable domain that binds LGR5.

3. Use of a bispecific antibody or functional part, derivative and/or analogue thereof that comprises a variable domain that binds an extracellular part of EGFR and a second variable domain that binds LGR5, and a fluoropyrimidine, a platinum-based chemotherapeutic agent, a BCL-2 inhibitor, or SN-38 in the manufacture of a medicament for the for the treatment of a cancer in a human subject.

4. The use of any one of claims 1 to 3, wherein:
(i) the variable domain that binds an extracellular part of EGFR is a heavy chain variable region that comprises:
- at least the CDR1, CDR2 and CDR3 sequences of the VH of MF3370; MF3755; MF4280 or MF4289 as depicted in Figure 3; or
- the amino acid sequence of the VH chain of MF3370; MF3755; MF4280 or MF4289 as depicted in Figure 3; and/or

the variable domain that binds LGR5 is a heavy chain variable region that comprises:

- at least the CDR1, CDR2 and CDR3 sequences of the VH of MF5790; MF5803; MF5805; MF5808; MF5809; MF5814; MF5816; MF5817; or MF5818 as depicted in Figure 3; or
- the sequence of the VH chain of MF5790; MF5803; MF5805; MF5808; MF5809; MF5814; MF5816; MF5817; or MF5818 as depicted in Figure 3;

or

(ii) the variable domain that binds an extracellular part of EGFR is a heavy chain variable region that comprises:
- the amino acid sequence of the VH chain of MF3370; MF3755; MF4280 or MF4289 as depicted in Figure 3; and

the variable domain that binds LGR5 is a heavy chain variable region that comprises:
- the sequence of the VH chain of MF5790; MF5803; MF5805; MF5808; MF5809; MF5814; MF5816; MF5817; or MF5818 as depicted in Figure 3.

5. The use of any one of claims 1 to 3, wherein:
(i) the variable domain that binds an extracellular part of EGFR is a heavy chain variable region that comprises:
at least the CDR1, CDR2 and CDR3 sequences of the VH of MF3755 as depicted in Figure 3; and

the variable domain that binds LGR5 is a heavy chain variable region that comprises:
at least the CDR1, CDR2 and CDR3 sequences of the VH of MF5816 as depicted in Figure 3;

or

(ii) the variable domain that binds an extracellular part of EGFR is a heavy chain variable region that comprises:
- the amino acid sequence of the VH chain of MF3755 as depicted in Figure 3; and

the variable domain that binds LGR5 is a heavy chain variable region that comprises:
- the sequence of the VH chain of MF5816 as depicted in Figure 3.

6. The use of any one of claims 1 to 8, wherein:
(i) the antibody comprises a light chain variable region comprising an LCDR1 comprising the amino acid sequence QSISSY, an LCDR2 comprising the amino acid sequence AAS, and an LCDR3 comprising the amino acid sequence QQSYSTPPT; or

(ii) the antibody comprises a light chain variable region comprising an amino acid sequence that is at least 90%, in certain aspects at least 95%, in certain aspects at least 97%, in certain aspects at least 98%, in certain aspects at least 99% identical or in certain aspects 100% identical to the amino acid sequence as set forth in SEQ ID NO: 108; or

(iii) the antibody comprises a light chain variable region comprising a light chain variable region comprising the amino acid sequence of SEQ ID NO: 108.

7. The use of any one of claims 1 to 6, wherein the cancer is an adenocarcinoma or a squamous cell carcinoma; and/or

(i) wherein the cancer is a head and neck cancer, gastric, esophageal, gastro-esophageal-junction cancer, non-small cell lung cancer or colorectal cancer; or
(ii) wherein the cancer is a colorectal cancer.

8. The use of any one of claims 1 to 7, wherein the fluoropyrimidine is fluorouracil.

9. The use of claim 8, wherein:

(i) fluorouracil is to be administered in a range of 200-3000 mg/m^2 intravenously;
(ii) fluorouracil is to be administered at 400 mg/m^2 by intravenous bolus on Day 1, followed by 2400 mg/m^2 to 3000 mg/m^2 intravenously as a continuous infusion over 46 hours every two weeks; or
(iii) fluorouracil is to be administered at 500 mg/m^2 by intravenous bolus on Days 1, 8, 15, 22, 29, and 36 in 8-week cycles.

10. The use of any one of the claims 1 to 7, wherein the platinum-based chemotherapeutic agent is oxaliplatin; or

wherein the platinum-based chemotherapeutic agent is oxaliplatin and oxaliplatin is to be administered at 85 mg/m^2 every two weeks.

11. The use of claim 8, wherein the medicament is to be further administered with oxaliplatin and folinic acid; or

wherein the medicament is to be further administered with oxaliplatin and folinic acid, and oxaliplatin is to be administered at 50-200 mg/m^2 together with folinic acid at 200-600 mg/m^2 intravenously, followed by a fluorouracil at 1200-3600 mg/m^2 intravenously.

12. The use of claim 8, wherein the medicament is to be further administered with irinotecan and folinic acid; or

wherein the medicament is to be further administered with irinotecan and folinic acid, and irinotecan is to be administered at 180 mg/m^2 together with folinic acid at 200-400 mg/m^2 intravenously, followed by fluorouracil at 400-2400 mg/m^2 intravenously.

13. The use of any one of claims 1 to 12, wherein the antibody is afucosylated; and/or wherein the antibody is petosemtamab.

14. The use of any one of claim 1 to 13, wherein the antibody or functional part, derivative and/or analogue thereof is to be administered at 1500 mg.

15. The use of any one of claims 1 to 14, wherein:

(i) the subject to be treated has not received prior anti-cancer therapy; or

(ii) the cancer or subject to be treated has progressed after prior anti-cancer therapy.

16. The use of any one of claims 1 to 15, wherein:

(i) the antibody or functional part, derivative and/or analogue thereof and the fluoropyrimidine, the platinum-based chemotherapeutic agent, the BCL-2 inhibitor, or SN-38 are to be administered to the subject simultaneously, separately, or sequentially; or

(ii) an effective amount of the antibody or functional part, derivative and/or analogue thereof, and an effective amount of the fluoropyrimidine, platinum-based chemotherapeutic agent, BCL-2 inhibitor, or SN-38, are to be administered to the subject.

17. A pharmaceutical composition comprising an antibody or functional part, derivative and/or analogue thereof as defined in any one of claims 1 to 16 and a fluoropyrimidine, a platinum-based chemotherapeutic agent, a BCL-2 inhibitor, or SN-38;

optionally, wherein the antibody or functional part, derivative and/or analogue thereof, and the fluoropyrimidine, a platinum-based chemotherapeutic agent, a BCL-2 inhibitor, or SN-38 are provided in separate formulation.

18. A kit of parts comprising

- an antibody or functional part, derivative and/or analogue thereof, as defined in any one of claims 1 to 16;
- a fluoropyrimidine, a platinum-based chemotherapeutic agent, a BCL-2 inhibitor, or SN-38; and
- instructions for use of said antibody or functional part, derivative and/or analogue thereof and instructions for use of said fluoropyrimidine, platinum-based chemotherapeutic agent, BCL-2 inhibitor, or SN-38.

19. The kit of parts, according to claim 18, wherein:

(i) the instructions for use of the antibody or functional part, derivative/and or analogue thereof comprises instructions for dosing thereof at 1500 mg; and/or

(ii) the kit comprises instructions for use of the antibody or functional part, derivative and/or analogue thereof and fluoropyrimidine, platinum-based chemotherapeutic agent, BCL-2 inhibitor, or SN-38, in the treatment of adenocarcinoma or a squamous cell carcinoma; and/or

(iii) the kit comprises instructions for use of the antibody or functional part, derivative and/or analogue thereof and fluoropyrimidine, platinum-based chemotherapeutic agent, BCL-2 inhibitor, or SN-38, in the treatment of head and neck cancer, gastric, esophageal, gastro-esophageal-junction cancer, non-small cell lung cancer or colorectal cancer; and/or

(iv) the kit comprises instructions for use of the antibody or functional part, derivative and/or analogue thereof and fluoropyrimidine, platinum-based chemotherapeutic agent, BCL-2 inhibitor, or SN-38, in the treatment of colorectal cancer.

20. A combination of:

(i) an antibody or functional part, derivative and/or analogue thereof as defined in any one of the preceding claims, and a fluoropyrimidine, platinum-based chemotherapeutic agent, BCL-2 inhibitor, or SN-38 as defined in any one of claims 1 to 16 for use in the treatment of cancer in a subject in need thereof; or

(ii) an antibody or functional part, derivative and/or analogue thereof, as defined in any one of claims 1 to 16,
instructions for use in the treatment of a cancer in a subject of said antibody, and instructions for use in the treatment of a cancer in a subject of a fluoropyrimidine, a platinum-based chemotherapeutic agent, a BCL-2 inhibitor, or SN-38 as defined in any one of the preceding claims; or

(iii) a fluoropyrimidine, a platinum-based chemotherapeutic agent, a BCL-2 inhibitor, or a SN-38, as defined in any one of claims 1 to 16,
instructions for use in the treatment of a cancer in a subject of a fluoropyrimidine, a platinum-based chemotherapeutic agent, a BCL-2 inhibitor, or a SN-38, and
instructions for use in the treatment of a cancer in a subject of an antibody or functional part, derivative and/or analogue thereof, as defined in any one of the preceding claims.