

Claims

1. Use of an antibody or functional part thereof that comprises a variable domain that binds an extracellular part of EGFR and a variable domain that binds an extracellular part of LGR5 in the manufacture of a medicament for the treatment of colorectal cancer in a subject, wherein the subject has received or is receiving a human topoisomerase I inhibitor.
2. Use of a human topoisomerase I inhibitor in the manufacture of a medicament for the treatment of colorectal cancer in a subject, wherein the subject has received or is receiving an antibody or functional part thereof that comprises a variable domain that binds an extracellular part of EGFR and a variable domain that binds an extracellular part of LGR5.
3. Use of an antibody or functional part thereof that comprises a variable domain that binds an extracellular part of EGFR and a variable domain that binds an extracellular part of LGR5, and a human topoisomerase I inhibitor in the manufacture of a medicament for the combination therapy of colorectal cancer in a subject.
4. Use of an antibody or functional part thereof that comprises a variable domain that binds an extracellular part of EGFR and a variable domain that binds an extracellular part of LGR5 in the manufacture of a medicament for preventing metastasis or tumor recurrence in a subject, wherein the subject has received or is receiving a human topoisomerase I inhibitor and wherein the tumor is colorectal cancer.
5. Use of a human topoisomerase I inhibitor in the manufacture of a medicament for preventing metastasis or tumor recurrence in a subject, wherein the subject has received or is receiving an antibody or functional part thereof that comprises a variable domain that binds an extracellular part of EGFR and a variable domain that binds an extracellular part of LGR5 and wherein the tumor is colorectal cancer.
6. Use of an antibody or functional part thereof that comprises a variable domain that binds an extracellular part of EGFR and a variable domain that binds an extracellular part of LGR5, and a human topoisomerase I inhibitor in the manufacture of a medicament for preventing metastasis or tumor recurrence in a subject and wherein the tumor is colorectal cancer.
7. The use according to any of the preceding claims, wherein the variable domain that binds an extracellular part of EGFR comprises a heavy chain variable

region comprising CDR1, CDR2 and CDR3 sequences of the variable region MF3755 (SEQ ID NO: 89) and wherein the variable domain that binds an extracellular part of LGR5 comprises a heavy chain variable region comprising CDR1, CDR2 and CDR3 sequences of the variable region of MF5816 (SEQ ID NO: 107) and wherein both variable domains comprise CDR1, CDR2 and CDR3 sequences of the light chain variable region as set forth in SEQ ID NO: 113.

8. The use according to any of the preceding claims, wherein the variable domain that binds an extracellular part of EGFR comprises a heavy chain variable region comprising a CDR1 having SEQ ID NO: 17, a CDR2 having SEQ ID NO: 19, and a CDR3 having SEQ ID NO: 21, wherein the variable domain that binds an extracellular part of LGR5 comprises a heavy chain variable region comprising a CDR1 having SEQ ID NO: 69, a CDR2 having SEQ ID NO: 71, and a CDR3 having SEQ ID NO: 73 and wherein both variable domains comprise a light chain variable region comprising a CDR1 having SEQ ID NO: 118, a CDR2 having SEQ ID NO: 119, and a CDR3 having SEQ ID NO: 120.

9. The use according to any of the preceding claims, wherein the variable domain that binds an extracellular part of EGFR comprises the heavy chain variable region of VH chain MF3755 (SEQ ID NO: 89); and wherein the variable domain that binds an extracellular part of LGR5 comprises the heavy chain variable region of VH chain MF5816 (SEQ ID NO: 107) and wherein both variable domains comprise the light chain variable region as set forth in SEQ ID NO: 113.

10. The use according to any one of the preceding claims, wherein the topoisomerase I inhibitor is camptothecin or a derivative thereof.

11. The use according to any one of the preceding claims, wherein the topoisomerase I inhibitor is irinotecan or topotecan.

12. The use according to any one of the preceding claims, wherein the topoisomerase I inhibitor is irinotecan.

13. The use according to any one of the preceding claims, wherein the antibody is ADCC enhanced.

14. The use according to any one of the preceding claims, wherein the antibody is afucosylated.

15. An in vitro method for inhibiting proliferation of a cell that expresses EGFR and LGR5 in a system permissive for proliferation of the cell, the method comprising providing the system with a human topoisomerase I inhibitor and with an antibody or functional part thereof that comprises a variable domain that binds

an extracellular part of EGFR and a variable domain that binds an extracellular part of LGR5.

16. A pharmaceutical composition comprising an antibody or functional part thereof that comprises a variable domain that binds an extracellular part of EGFR and a variable domain that binds an extracellular part of LGR5; and a human topoisomerase I inhibitor.

17. The pharmaceutical composition according to claim 16 wherein the antibody or functional part thereof that comprises a variable domain that binds an extracellular part of EGFR and a variable domain that binds an extracellular part of LGR5; and a topoisomerase I inhibitor are provided in a single formulation.

18. The pharmaceutical composition according to claim 16, wherein the antibody or functional part thereof that comprises a variable domain that binds an extracellular part of EGFR and a variable domain that binds an extracellular part of LGR5; and a topoisomerase I inhibitor are provided in separate formulations.

19. A kit comprising an antibody or functional part thereof that comprises a variable domain that binds an extracellular part of EGFR and a variable domain that binds an extracellular part of LGR5; a human topoisomerase I inhibitor and instructions for use of the antibody and the topoisomerase I inhibitor in the treatment of any one of claims 1-14.

20. A product comprising an antibody or functional part thereof that comprises a variable domain that binds an extracellular part of EGFR and a variable domain that binds an extracellular part of LGR5 and a human topoisomerase I inhibitor as a combined preparation for simultaneous, separate or sequential use in the treatment of colorectal cancer in a subject.