

Claims

1. Use of an antibody or functional part, derivative and/or analogue 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 cancer in a subject, wherein the subject has received or is receiving a topoisomerase I inhibitor.
2. Use of a topoisomerase I inhibitor in the manufacture of a medicament for the treatment of cancer in a subject, wherein the subject has received or is receiving a an antibody or functional part, derivative and/or analogue 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, derivative and/or analogue 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 in the manufacture of a medicament for the treatment of cancer in a subject.
4. The use according to any one of the preceding claims, wherein the cancer is colorectal, pulmonary, gastrointestinal or ovarian cancer.
5. The use according to any one of the preceding claims, wherein the cancer is colorectal cancer.
6. The use according to any one of the preceding claims, wherein a VH chain of the variable domain that binds EGFR comprises the amino acid sequence of VH chain MF3755 as depicted in figure 8; or the amino acid sequence of VH chain MF3755 as depicted in figure 8 having at most 15, preferably not more than 10, 9, 8, 7, 6, 5, 4, 3, 2, 1 and preferably having not more than 5, 4, 3, 2 or 1 amino acid modifications, including insertions, deletions, substitutions or a combination thereof with respect said VH; and wherein a VH chain of the variable domain that binds LGR5 comprises the amino acid sequence of VH chain MF5816 as depicted in figure 8; or the amino acid sequence of VH chain MF5816 as depicted in figure 8 having at most 15, preferably not more than 10, 9, 8, 7, 6, 5, 4, 3, 2, 1 and preferably having not more than 5, 4, 3, 2 or 1 amino acid modifications, including insertions, deletions, substitutions or a combination thereof with respect said VH.
7. The use according to any one of the preceding claims, wherein the antibody or functional part, derivative and/or analogue thereof further comprises a common light chain.

8. The use according to claim 7, wherein the common light chain comprises a germline IgV κ 1-39 variable region V-segment.
9. The use according to claim 7 or 8, wherein the light chain comprises the kappa light chain V-segment IgV κ 1-39*01.
10. The use according to any one of claims 1-6, wherein the antibody or functional part, derivative and/or analogue thereof further comprises a common light chain further comprises a light chain variable region comprising an amino acid sequence that is at least 90%, preferably at least 95%, more preferably at least 97%, more preferably at least 98%, more preferably at least 99% identical or 100% identical to the amino acid sequence of set forth in Figure 9.
11. The use according to any one of claims 1-6, wherein the antibody or functional part, derivative and/or analogue thereof further comprises a common light chain further comprises a variable light chain having from 0 to 10, preferably from 0 to 5 amino acid insertions, deletions, substitutions, additions or a combination thereof with respect to a sequence in Figure 9.
12. The use according to any one of claims 1-6, wherein the antibody or functional part, derivative and/or analogue thereof further comprises a common light chain further comprises an LCDR1 comprising the amino acid sequence QSISSY, an LCDR2 comprising the amino acid sequence AAS, and an LCDR3 comprising the amino acid sequence QQSYSTP.
13. The use according to any one of the preceding claims, wherein the topoisomerase I inhibitor is camptothecin or a derivative thereof.
14. The use according to any one of the preceding claims, wherein the topoisomerase I inhibitor is irinotecan or topotecan.
15. The use according to any one of the preceding claims, wherein the antibody is ADCC enhanced.
16. The use according to any one of the preceding claims, wherein the antibody is afucosylated.
17. A 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 topoisomerase I inhibitor and with an antibody or functional part, derivative and/or analogue thereof that comprises a variable domain that binds an extracellular part of EGFR and a variable domain that binds an extracellular part of LGR5.

18. A pharmaceutical composition comprising an antibody or functional part, derivative and/or analogue 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.

19. The pharmaceutical composition according to claim 18, wherein the antibody or functional part, derivative and/or analogue 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.

20. The pharmaceutical composition according to claim 22, wherein the antibody or functional part, derivative and/or analogue 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.

21. A kit comprising an antibody or functional part, derivative and/or analogue 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 topoisomerase I inhibitor and instructions for use of the antibody and the topoisomerase I inhibitor in the treatment of any one of claims 1-16.

22. A product comprising an antibody or functional part, derivative and/or analogue 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 as a combined preparation for simultaneous, separate or sequential use in the treatment of gastrointestinal cancer in a subject.