

Claims

1. 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
5 binds an extracellular part of LGR5 for use in the treatment of head and neck cancer in a subject, wherein said use comprises providing the subject with a flat dose of 1500 mg of the antibody or functional part, derivative and/or analogue thereof.
2. The antibody or functional part, derivative and/or analogue thereof for use
10 according to claim 1, wherein the subject is a human subject.
3. The antibody or functional part, derivative and/or analogue thereof for use according to any of the preceding claims, wherein the antibody or functional part, derivative and/or analogue thereof is provided intravenously.
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4. The antibody or functional part, derivative and/or analogue thereof for use according to any of the preceding claims, wherein the head and neck cancer is a squamous cell cancer or adenocarcinoma.
- 20 5. The antibody or functional part, derivative and/or analogue thereof for use according to any of the preceding claims, wherein the head and neck cancer is a squamous cell cancer.
6. The antibody or functional part, derivative and/or analogue thereof for use
25 according to any of the preceding claims, wherein the head and neck cancer is nasopharyngeal cancer, laryngeal cancer, hypopharyngeal cancer, nasal cavity cancer, paranasal sinus cancer, oral cancer and oropharyngeal cancer.
7. The antibody or functional part, derivative and/or analogue thereof for use
30 according to any of the preceding claims, wherein the head and neck cancer is oropharyngeal squamous cell cancer.

8. The antibody or functional part, derivative and/or analogue thereof for use according to any of the preceding claims, wherein the head and neck cancer has one or more mutations in the LGR5 and/or EGFR pathway present in models selected from HN5124, HN5125, HN2579, HN2590 and HN2167.

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9. The antibody or functional part, derivative and/or analogue thereof for use according to any one of the preceding claims, wherein the cancer is characterized by expression of LGR5 and/or EGFR.

10. The antibody or functional part, derivative and/or analogue thereof for use according to any 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 3; or the amino acid sequence of VH chain MF3755 as depicted in figure 3 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 3; or the amino acid sequence of VH chain MF5816 as depicted in figure 3 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.

11. The antibody or functional part, derivative and/or analogue thereof for use according to any of the preceding claims, wherein the variable domain that binds LGR5 binds an epitope that is located within amino acid residues 21-118 of the human LGR5 sequence depicted in figure 1.

12. The antibody or functional part, derivative and/or analogue thereof for use according to claim 11, wherein amino acid residues at positions 43, 44, 46, 67, 90, and 91 of human LGR5 are involved in the binding of the LGR5 binding variable domain to LGR5.

13. The antibody or functional part, derivative and/or analogue thereof for use according to claim 11 or 12, wherein the LGR5 binding variable domain binds less to an LGR5 protein comprising one or more of the amino acid residue variations selected from 43A, 44A, 46A, 67A, 90A, and 91A.

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14. The antibody or functional part, derivative and/or analogue thereof for use according to any of the preceding claims, wherein the variable domain that binds EGFR binds an epitope that is located within amino acid residues 420-480 of the human EGFR sequence depicted in figure 2.

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15. The antibody or functional part, derivative and/or analogue thereof for use according to claim 14, wherein amino acid residues at positions I462, G465, K489, I491, N493 and C499 of human EGFR are involved in the binding of the EGFR binding variable domain to EGFR.

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16. The antibody or functional part, derivative and/or analogue thereof for use according to claim 14 or 15, wherein the EGFR binding variable domain binds less to an EGFR protein comprising one or more of the amino acid residue substitutions selected from I462A, G465A, K489A, I491A, N493A and C499A.

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17. The antibody or functional part, derivative and/or analogue thereof for use according to any of the preceding claims, wherein the antibody is ADCC enhanced.

18. The antibody or functional part, derivative and/or analogue thereof for use

25 according to any of the preceding claims, wherein the antibody is afucosylated.

19. ~~A method of treating head and neck cancer comprising administering to a subject~~

~~in need thereof~~ Use of an antibody or functional part, derivative and/or analogue

thereof that comprises a variable domain that binds an extracellular part of EGFR

30 and a variable domain that binds an extracellular part of LGR5 in the manufacture of a medicament for treating head and neck cancer.