

CLAIMS

1. Use of a combination of (i) an antibody-drug conjugate (ADC) comprising an anti-CEACAM5 antibody and (ii) an anti-PD-1 antibody or anti-PD-L1 antibody, in an effective amount, in the manufacture of a medicament for the treatment of a cancer in a subject in need thereof, wherein the cancer expresses CEACAM5.
2. The use according to claim 1, wherein the anti-CEACAM5 antibody comprises a HCDR1 having the amino acid sequence of SEQ ID NO: 1, a HCDR2 having the amino acid sequence of SEQ ID NO: 2, a HCDR3 having the amino acid sequence of SEQ ID NO: 3, a LCDR1 having the amino acid sequence of SEQ ID NO: 4, a LCDR2 having the amino acid sequence NTR, and a LCDR3 having the amino acid sequence of SEQ ID NO: 5, and/or wherein the anti-CEACAM5 antibody comprises a variable domain of a heavy chain (VH) consisting of SEQ ID NO: 6 and a variable domain of a light chain (VL) consisting of SEQ ID NO: 7, and/or wherein the anti-CEACAM5 antibody is tusamitamab.
3. The use according to claim 1 or 2, wherein the ADC comprises at least one cytotoxic agent, optionally wherein the cytotoxic agent is selected from the group consisting of radioisotopes, protein toxins, small molecule toxins, and any combination thereof, optionally wherein the cytotoxic agent is a small molecule toxin selected from the group consisting of antimetabolites, DNA-alkylating agents, DNA-cross-linking agents, DNA-intercalating agents, anti-microtubule agents, topoisomerase inhibitors, and any combination thereof, optionally wherein the cytotoxic agent is a small molecule toxin being an anti-microtubule agent selected from the group consisting of taxanes, vinca alkaloids, maytansinoids, colchicine, podophyllotoxin, griseofulvin, and any combination thereof, and optionally wherein the cytotoxic agent is a maytansinoid selected from the group consisting of N2'-deacetyl-N2'-(3-mercapto-1-oxopropyl)-maytansine (DM1), N2'-deacetyl-N2'-(4-methyl-4-mercapto-1-oxopentyl)-maytansine (DM4), and any combination thereof.
4. The use according to claim 3, wherein the anti-CEACAM5 antibody is covalently attached via a cleavable or non-cleavable linker to the at least one cytotoxic agent, optionally wherein said linker is selected from the group consisting of N-succinimidyl pyridyldithiobutyrate (SPDB), 4-(pyridin-2-yl-disulfanyl)-2-sulfo-butyric acid (sulfo-SPDB), and succinimidyl(N-maleimidomethyl) cyclohexane-1-carboxylate (SMCC).
5. The use according to any one of claims 1 to 4, wherein the ADC is characterized by a drug-to-antibody ratio (DAR) ranging from 1 to 10.
6. The use according to any one of claims 1 to 5, wherein the ADC is tusamitamab ravtansine.

7. The use according to any one of claims 1 to 6, wherein the cancer expresses CEACAM5 with moderate or high intensity defined by immunohistochemistry, optionally wherein the cancer expresses CEACAM5 with moderate intensity (immunohistochemistry intensity $\geq 2+$ in $\geq 1\%$ to $< 50\%$ of tumor cells), or wherein the cancer expresses CEACAM5 with high intensity (immunohistochemistry intensity $\geq 2+$ in $\geq 50\%$ of tumor cells).
8. The use according to any of claims 1 to 7, wherein the cancer is a solid tumor.
9. The use according to any one of claims 1 to 8, wherein the cancer is selected from the group consisting of colorectal cancer, gastric cancer, gastroesophageal junction cancer, esophageal cancer, lung cancer, uterine cervix cancer, pancreatic cancer, ovarian cancer, thyroid cancer, bladder cancer, endometrial cancer, breast cancer, liver cancer, biliary tract cancer (e.g. cholangiocarcinoma), prostate cancer, and skin cancer.
10. The use according to claim 9, wherein the cancer is gastric cancer, gastroesophageal junction cancer, pancreatic cancer, prostate cancer, or esophageal cancer.
11. The use according to any one of claims 1 to 10, wherein the subject has received no prior systemic chemotherapy for treatment of the cancer.
12. The use according to any one of claims 1 to 11, wherein the anti-PD-1 antibody is selected from the group consisting of pembrolizumab, nivolumab, cemiplimab, sintilimab, dostarlimab, and tislelizumab, optionally wherein the anti-PD-1 antibody is pembrolizumab.
13. The use according to any one of claims 1 to 11, wherein the anti-PD-L1 antibody is selected from the group consisting of atezolizumab, avelumab, and durvalumab.
14. The use according to any one of claims 1 to 13, wherein the anti-PD-1 antibody or the anti-PD-L1 antibody and the ADC are to be administered sequentially, optionally wherein the anti-PD-1 antibody or the anti-PD-L1 antibody is to be administered before the ADC, or wherein the anti-PD-1 antibody or the anti-PD-L1 antibody and the ADC are to be administered simultaneously.
15. The use according to any one of claims 1 to 14, wherein anti-PD-1 antibody or the anti-PD-L1 antibody is to be administered to the subject intravenously in a dose of 200 mg to 400 mg, optionally wherein the anti-PD-1 antibody or the anti-PD-L1 antibody is to be administered to the subject intravenously in a dose selected from 200 mg, 350 mg, 360 mg, and 400 mg.

16. The use according to any one of claims 6 to 15, wherein the tusamitamab ravtansine is to be administered to the subject intravenously in a dose of 60 mg/m² to 190 mg/m², optionally wherein the tusamitamab ravtansine is to be administered to the subject intravenously in a dose of 120 mg/m² to 170 mg/m².

17. The use according to any one of claims 15-16, wherein the anti-PD-1 antibody or the anti-PD-L1 antibody is to be administered to the subject intravenously in a dose of about 200 mg and the tusamitamab ravtansine is to be administered to the subject intravenously in a dose of 120 mg/m² to 170 mg/m², optionally wherein the anti-PD-1 antibody or the anti-PD-L1 antibody and the tusamitamab ravtansine are to be administered once every three weeks.

18. The use according to any one of claims 15-17, wherein the anti-PD-1 antibody or the anti-PD-L1 antibody is to be administered to the subject intravenously in a dose of about 400 mg and the tusamitamab ravtansine is to be administered to the subject intravenously in a dose of 120 mg/m² to 170 mg/m², optionally wherein the anti-PD-1 antibody or the anti-PD-L1 antibody is to be administered once every six weeks and the tusamitamab ravtansine is to be administered once every three weeks.

19. The use according to any one of claims 1 to 18, wherein the ADC is tusamitamab ravtansine and the anti-PD-1 antibody is pembrolizumab.

20. The use according to any one of claims 1 to 18, wherein the anti-PD-1 antibody or the anti-PD-L1 antibody and the ADC are to be administered about once every three weeks, wherein the ADC is tusamitamab ravtansine and is to be administered to the subject intravenously in a dose of about 120 mg/m², or in a dose of about 150 mg/m².

21. The use according to claim 20, wherein the anti-PD-1 antibody is pembrolizumab, optionally wherein the anti-PD-1 antibody is to be administered to the subject intravenously in a dose of about 200 mg.

22. The use according to any one of claims 1 to 19, wherein (iii) a platinum-based chemotherapy is to be administered to the subject, optionally wherein the platinum-based chemotherapy is selected from the group consisting of cisplatin and carboplatin.

23. The use according to claim 22, wherein the anti-PD-1 antibody or the anti-PD-L1 antibody is to be administered before the ADC and the platinum-based chemotherapy.

24. The use according to claim 22, wherein the anti-PD-1 antibody or the anti-PD-L1 antibody, the ADC, and the platinum-based chemotherapy are to be administered to the subject for at least four cycles.

25. The use according to claim 22, wherein cisplatin is to be administered to the subject, optionally wherein the cisplatin is to be administered intravenously to the subject in a dose from 38 mg/m² to 75 mg/m², optionally wherein the cisplatin is to be administered intravenously to the subject in a dose of about 75 mg/m².

26. The use according to claim 22, wherein carboplatin is to be administered to the subject, optionally wherein the carboplatin is to be administered intravenously to the subject in a dose of about $(\text{target AUC}) \times [(140 - \text{age}) \times (\text{weight in kg}) / \text{serum creatinine (mg/dL)} \times 72 (\times 0.85 \text{ if female}) + 25]$, wherein the target AUC is from AUC 2.5 to AUC 5, optionally wherein the target AUC is AUC 5.

27. The use of any one of the preceding claims, wherein pemetrexed is to be administered to the subject, optionally wherein the pemetrexed is to be administered intravenously at a dose from 250 mg/m² to 500 mg/m², optionally wherein the pemetrexed is to be administered intravenously at a dose about 500 mg/m², optionally wherein the pemetrexed is to be administered intravenously after a vitamin supplementation.

28. The use according to claim 27, wherein the anti-PD-1 antibody or the anti-PD-L1 antibody and the ADC are to be administered about once every three weeks, wherein the ADC is tusamitamab ravtansine and is to be administered to the subject intravenously in a dose of about 120 mg/m², or in a dose of about 150 mg/m², optionally wherein the anti-PD-1 antibody is pembrolizumab, optionally wherein the anti-PD-1 antibody is to be administered to the subject intravenously in a dose of about 200 mg.