

CLAIMS

1. ~~Use of An-an~~ antibody-, or an immunoconjugate comprising the antibody, for the manufacture of a medicament use-infor treating non squamous non-small cell lung cancer (NSQ NSCLC) in a subject in need thereof, wherein the antibody specifically binds to hCEACAM5 and wherein the antibody comprises a VH and a VL, wherein the VH comprises the three complementarity determining regions HCDR1, HCDR2 and HCDR3) and wherein the VL comprises the three CDRs LCDR1, LCDR2 and LCDR3, wherein the HCDR1 comprises the amino acid sequence of SEQ ID NO: 3 (**GFVFSSYD**); the HCDR2 comprises the amino acid sequence of SEQ ID NO: 4 (**ISSGGGIT**); the HCDR3 comprises the amino acid sequence of SEQ ID NO: 5 (**AAHYFGSSGPFAY**); the LCDR1 comprises the amino acid sequence of SEQ ID NO: 6 (**ENIFSY**); the LCDR2 comprises the amino acid sequence of **NTR**; and the LCDR3 comprises the amino acid sequence of SEQ ID NO: 7 (**QHHYGTPFT**), wherein the antibody or the immunoconjugate is administered at a dose level of 5, 10, 20, 30, 40, 60, 80, 100, 120, 150, 180, or 210 mg/m² based on the body surface area of the subject.
2. The ~~antibody, or an immunoconjugate comprising the antibody, for~~ use according to claim 1, wherein the subject is a high carcinoembryonic antigen-related cell adhesion molecule expresser.
3. The ~~antibody, or an immunoconjugate comprising the antibody, for~~ use according to any of claims 1 or 2, wherein the subject was pre-treated with an agent or drug for treatment of non-small cell lung cancer.
4. The ~~antibody, or an immunoconjugate comprising the antibody, for~~ use according to claim 3, wherein the agent or drug is selected from the group consisting of: a chemotherapy agent, an angiogenesis inhibitor, an epidermal growth factor receptor (EGFR) inhibitor, an anaplastic lymphoma kinase (ALK) inhibitor, a receptor tyrosine kinase (ROS1) inhibitor, and an immune checkpoint inhibitor.
5. The ~~antibody, or an immunoconjugate comprising the antibody, for~~ use according to claim 4, wherein the immune checkpoint inhibitor is a PD-1 inhibitor and/or a PD-L1 inhibitor.

6. The ~~antibody, or an immunoconjugate comprising the antibody, for~~ use according to any of claims 1 to 5, wherein the VH comprises SEQ ID NO: 1

(EVQLQESGPGLVKPGGSLSLSCAASG**VF**SSYDMSWVRQTPERGLEWVAYISSGGG**IT**
5 YAPSTVKGRFTVSRDNAKNTLYLQMNSLTSEDTAVYYCAA**HY**FGSSGP**F**AYWGQGT
LTVSS).

7. The ~~antibody, or an immunoconjugate comprising the antibody, for~~ use according to claim 6, wherein the heavy chain comprises SEQ ID NO: 8

10 (EVQLQESGPGLVKPGGSLSLSCAASG**VF**SSYDMSWVRQTPERGLEWVAYISSGGG**ITY**
APSTVKGRFTVSRDNAKNTLYLQMNSLTSEDTAVYYCAA**HY**FGSSGP**F**AYWGQGT**L**VT
VSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL
QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAEL
LGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
15 EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTV
DKSRWQQGNV**F**SCSV**M**HEALHNHYTQKSLSLSPG).

8. The ~~antibody, or an immunoconjugate comprising the antibody, for~~ use according to any of claims 1-7, wherein the VL comprises SEQ ID NO: 2

20 (DIQMTQSPASLSASVGDRVTITCRASE**N**IFSYLAWYQQKPGKSPKLLVYN**TR**TLAEGVP
SRFSGSGSGTDFSLTISS**L**QPEDFATYYC**QH**HYG**T**PFTFGSGTKLEIK).

9. The ~~antibody, or an immunoconjugate comprising the antibody, for~~ use according to claim 8, wherein the light chain comprises SEQ ID NO: 9

25 (DIQMTQSPASLSASVGDRVTITCRASE**N**IFSYLAWYQQKPGKSPKLLVYN**TR**TLAEGVP
SRFSGSGSGTDFSLTISS**L**QPEDFATYYC**QH**HYG**T**PFTFGSGTKLEIK**R**TVAA**P**SVF**I**PPS
DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL
TL**S**KADY**E**KK**H**KVYACEV**T**HQGLSSP**V**TK**S**FN**R**G**E**C).

10. The ~~immunoconjugate comprising the antibody, for~~ use according to any one of claims to 1 to 9, wherein the antibody is conjugated or linked to at least one growth inhibitory agent.

11. The ~~immunoconjugate for~~ use according to claim 10, wherein said growth inhibitory agent is a cytotoxic agent.

12. The ~~immunoconjugate for~~ use according to claim 10 or 11, wherein said growth inhibitory agent is selected from the group consisting of chemotherapeutic agents, enzymes, antibiotics, and toxins such as small molecule toxins or enzymatically active toxins, taxoids, vincas, taxanes, maytansinoid or maytansinoid analogs, tomaymycin or pyrrolobenzodiazepine derivatives, cryptophycin derivatives, leptomycin derivatives, auristatin or dolastatin analogs, prodrugs, topoisomerase II inhibitors, DNA alkylating agents, anti-tubulin agents, and CC-1065 or CC-1065 analogs.

13. The ~~immunoconjugate for~~ use according to claim 10 or 11, wherein said growth inhibitory agent is (N2'-deacetyl-N2'-(3-mercapto-1-oxopropyl)-maytansine) DM1 or N2'-deacetyl-N-2'(4-methyl-4-mercapto-1-oxopentyl)-maytansine (DM4).

14. The ~~immunoconjugate for~~ use according to any one of claims 10 to 13, wherein the antibody is covalently attached via a cleavable or non-cleavable linker to the at least one growth inhibitory agent.

15. The ~~immunoconjugate for~~ use according to claim 14, wherein said linker is selected from the group consisting of N-succinimidyl pyridyldithiobutyrates (SPDB), 4-(Pyridin-2-yl)disulfanyl-2-sulfo-butyric acid (sulfo-SPDB), and succinimidyl (N-maleimidomethyl) cyclohexane-1-carboxylate (SMCC).

16. The ~~immunoconjugate for~~ use according to any of claims 1 to 15, wherein the subject has a hCEACAM5 expression of a percent score greater than or equal to 50 (consisting of 2+ and 3+ intensities) in the tumor cells populations.

~~17. The immunoconjugate for use according to any of claims 1 to 16, wherein the immunoconjugate is administered at a dose level of 5, 10, 20, 30, 40, 60, 80, 100, 120, 150, 180, or 210 mg/m² based on the body surface area of the subject.~~

- 5 ~~1817.~~ The ~~immunoconjugate for~~ use according to any of claims 1 ~~to 17~~16, wherein the immunoconjugate is administered at every 14 days, or every 3 weeks.

18. Use of an immunoconjugate comprising an antibody conjugated or linked to at least one growth inhibitory agent, for the manufacture of a medicament for treating non-squamous non-small cell lung cancer (NSQ NSCLC) in a subject in need thereof,
10 wherein the antibody specifically binds to hCEACAM5 and wherein the antibody comprises a VH and a VL, wherein

the VH comprises SEQ ID NO: 1

15 (EVQLQESGPGLVKPGGSLSLSCAASG**FV**FSSYDMSWVRQTPERGLEWVAYISS
GGGITYAPSTVKGRFTVSRDNAKNTLYLQMNSLTSEDTAVYYCAA**HY**FGSSGP
FAYWGQGTLLTVSS).

the VL comprises SEQ ID NO: 2

(DIQMTQSPASLSASVGDRVITTCRASEN**IF**SYLAWYQQKPGKSPKLLVYN**TR**TL
AEGVPSRFSGSGSGTDFSLTISSLPEDFATYYC**QH**HYG**TP**FTFGSGTKLEIK).

20 wherein the antibody is covalently attached via a cleavable or non-cleavable linker to the at least one growth inhibitory agent, and 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),
wherein the growth inhibitory agent is (N2'-deacetyl-N2'-(3-mercapto-1-oxopropyl)-
25 maytansine) DM1 or N2'-deacetyl-N-2'-(4-methyl-4-mercapto-1-oxopentyl)-maytansine (DM4),
wherein the subject has a hCEACAM5 expression of a percent score greater than or equal to 50 (consisting of 2+ and 3+ intensities) in the tumor cells populations,

the subject having been pre-treated with an agent or a drug for treatment of non-small lung cancer, the chemotherapy agent or the drug being selected from a chemotherapy agent and an
30 immune checkpoint inhibitor.

19. — ~~A method for treating non-squamous non-small cell lung cancer (NSQ-NSCLC) in a subject in need thereof, the method comprising administering an antibody, or an immunoconjugate comprising the antibody, that specifically binds hCEACAM5 wherein the antibody comprises a VH and a VL, wherein the VH comprises the three complementarity determining regions HCDR1, HCDR2 and HCDR3) and wherein the VL comprises the three CDRs LCDR1, LCDR2 and LCDR3, wherein the HCDR1 comprises the amino acid sequence of SEQ ID NO: 3 (GFVFSSYD); the HCDR2 comprises the amino acid sequence of SEQ ID NO: 4 (ISSGGGIT); the HCDR3 comprises the amino acid sequence of SEQ ID NO: 5 (AAHYFGSSGPFAY); the LCDR1 comprises the amino acid sequence of SEQ ID NO: 6 (ENIFSY); the LCDR2 comprises the amino acid sequence of NTR; and the LCDR3 comprises the amino acid sequence of SEQ ID NO: 7 (QHHYGTPFT).~~

20. — ~~The method according to claim 19, wherein the subject is a high-carcinoembryonic antigen-related cell adhesion molecule-expresser.~~

21. — ~~The method according to any of claim 19, wherein the subject was previously treated with an agent or drug for treatment of non-small cell lung cancer.~~

22. — ~~The method according to claim 19, wherein the agent or drug is selected from the group consisting of: a chemotherapy agent, an angiogenesis inhibitor, an epidermal growth factor receptor (EGFR) inhibitor, an anaplastic lymphoma kinase (ALK) inhibitor, a receptor tyrosine kinase (ROS1) inhibitor, and an immune checkpoint inhibitor.~~

23. — ~~The method according to claim 22, wherein the immune checkpoint inhibitor is a PD-1 inhibitor and/or a PD-L1 inhibitor.~~

24. — ~~The method according to any one of claims 19 to 23, wherein the antibody is conjugated or linked to at least one growth inhibitory agent.~~

25. — ~~The method according to claim 24, wherein said growth inhibitory agent is (N2'-deacetyl N2'-(3-mercapto-1-oxopropyl)-maytansine) DM1 or N2'-deacetyl N-2'-(4-methyl-4-mercapto-1-oxopentyl)-maytansine (DM4).~~

5 26. — ~~The method according to any one of claims 19 to 25, wherein the antibody is covalently attached via a cleavable or non-cleavable linker to the at least one growth inhibitory agent.~~

27. — ~~The method according to claim 26, wherein said linker is selected from the group consisting of N-succinimidyl pyridyldithiobutyrate (SPDB), 4-(Pyridin-2-yl)disulfanyl-2-sulfo-~~

10 butyric acid (sulfo-SPDB), and succinimidyl (N-maleimidomethyl)-cyclohexane-1-carboxylate (SMCC).

28. — ~~The method according to any of claims 19 to 27, wherein the subject has a hCEACAM5 expression of a percent score greater than or equal to 50 (consisting of 2+ and 3+ intensities) in~~

15 ~~the tumor cells populations;~~

29. — ~~The method according to any of claims 19 to 28, wherein the antibody is administered at a dose level of 5, 10, 20, 30, 40, 60, 80, 100, 120, 150, 180, or 210 mg/m² based on the body surface area of the subject.~~

20 30. — ~~The method according to any of claims 19 to 29, wherein the antibody is administered at every 14 days, or every 3 weeks.~~