

Claims

1. An antibody-drug conjugate comprising a monoclonal antibody or an antigen-binding fragment thereof and a drug, wherein the monoclonal antibody or the antigen-binding fragment thereof binds to Nectin-4 and comprises:

- 5 (a) a variable heavy chain (VH) region comprising complementarity-determining regions (CDRs) CDR-H1, CDR-H2 and CDR-H3, wherein
- (i) the CDR-H1 comprises an amino acid sequence according to SEQ ID NO: 7,
- (ii) the CDR-H2 comprises an amino acid sequence according to SEQ ID NO: 8,
- 10 (iii) the CDR-H3 comprises an amino acid sequence according to SEQ ID NO: 9,
- and
- (b) a variable light chain (VL) region comprising complementarity-determining regions (CDRs) CDR-L1, CDR-L2 and CDR-L3, wherein
- 15 (i) the CDR-L1 comprises an amino acid sequence according to SEQ ID NO: 10,
- (ii) the CDR-L2 comprises an amino acid sequence according to SEQ ID NO: 11,
- 20 (iii) the CDR-L3 comprises an amino acid sequence according to SEQ ID NO: 12,

and the drug is a topoisomerase I inhibitor.

2. The antibody-drug conjugate of claim 1, comprising an antibody selected from a chimeric antibody, a multispecific antibody, a human antibody, a humanized antibody, or an antigen-binding fragment thereof.

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3. The antibody-drug conjugate of claim 1 or 2, comprising an antibody selected from an antibody of class IgG, of class IgM, of class IgA or an antigen-binding fragment thereof, or a single-chain antibody, or an antibody Fv fragment.

4. The antibody-drug conjugate of claim 3, wherein the antibody has a heavy chain constant domain having a reduced effector function.

5. The antibody-drug conjugate of claim 4, wherein the reduced effector function is a reduced binding to the Fc receptor.

6. The antibody-drug conjugate of any one of claims 1-5, comprising an antibody, which specifically binds to Nectin-4 expressed by tumors with a higher affinity in comparison to Nectin-4 expressed by human differentiated keratinocytes, or an antigen-binding fragment thereof.

7. The antibody-drug conjugate of any one of claims 1-6, comprising an antibody or antigen-binding fragment thereof comprising:

(a) (i) a VH region comprising an amino acid sequence according to SEQ ID NO:13 or an amino acid sequence having an identity thereof of at least 85%, at least 90%, at least 95% or at least 99%,

and

(ii) a VL region, particularly a VL region comprising an amino acid sequence according to SEQ ID NO:14 or an amino acid sequence having an identity thereof of at least 85%, at least 90%, at least 95% or at least 99%.

8. The antibody-drug conjugate of any one of claims 2-7, wherein the antibody is a chimeric antibody or an antigen-binding fragment thereof.

9. The antibody-drug conjugate of any one of claims 2-7, wherein the antibody is a humanized antibody or an antigen-binding fragment thereof.

10. The antibody-drug conjugate of any one of claims 3-9, wherein the antibody of class IgG, has a subclass selected from the group consisting of IgG1, IgG2, IgG3 and IgG4.

11. The antibody-drug conjugate of claim 10, wherein the antibody of class IgG is subclass IgG1 or an antigen-binding fragment thereof.
12. The antibody-drug conjugate of claim 10, wherein the antibody of class of IgG is subclass IgG2 or an antigen-binding fragment thereof.
- 5 13. The antibody-drug conjugate of claim 10, wherein the antibody of class IgG is subclass IgG3 or an antigen-binding fragment thereof.
14. The antibody-drug conjugate of claim 10, wherein the antibody of class IgG is subclass IgG4 or an antigen-binding fragment thereof.
- 10 15. The antibody-drug conjugate of any one of claims 1-14, wherein the topoisomerase I inhibitor is a camptothecin or analog thereof.
16. The antibody-drug conjugate of any one of claims 1-14, wherein the topoisomerase I inhibitor is exatecan.
17. The antibody-drug conjugate of any one of claims 1-14, wherein the topoisomerase I inhibitor is deruxtecan.
- 15 18. A pharmaceutical composition comprising an active agent, which is the antibody-drug conjugate of any one of claims 1-17, and a pharmaceutically acceptable carrier and/or excipient.
19. An antibody-drug conjugate of any one of claims 1-17 or the pharmaceutical composition of claim 18, for use in medicine.
- 20 20. Use of the antibody-drug conjugate of any one of claims 1-17 or the pharmaceutical composition of claim 18 in the manufacture of a medicament for the prevention and/or treatment of a Nectin-4 associated disorder.
21. The use of claim 20, wherein the Nectin-4 associated disorder is a Nectin-4 positive cancer.

22. The use of claim 21, wherein the cancer is selected from bladder, urothelial, endometrial, cervical, colorectal, liver, thyroid, breast, pancreatic, lung, ovarian, head and neck and/or esophagus cancer.