

a cancer therapeutic. Therefore, there is a need for new antibodies against the 5T4 antigen and for corresponding antibody-drug conjugates for cancer therapy. To determine the suitability of these antibodies and corresponding ADCs in a preclinical setting, such antibodies should be cross-reactive for the 5T4 antigen of non-human animal species relevant for the preclinical development of a drug candidate.

SUMMARY

The present disclosure describes antibodies against the human 5T4 oncofoetal antigen and corresponding ADCs that are suitable for testing in clinical trials. Suitable antibodies and corresponding ADCs in a preclinical setting should be cross-reactive for the 5T4 antigen of non-human animal species relevant for preclinical development of a drug candidate.

Preferably, the antibodies are cross-reactive for humans and cynomolgus monkeys and exhibit an affinity for human 5T4 antigen (hu 5T4) which is in the same order of magnitude as their affinity for cynomolgus monkey 5T4 antigen (cyno 5T4).

The disclosure further describes the use of the antibodies and corresponding ADCs in the treatment of solid tumours and haematological malignancies.

In one aspect, the present invention refers to an anti-5T4 antibody comprising heavy chain (HC) and light chain (LC) variable region (VR) complementarity determining regions (CDRs) selected from the group consisting of:

- a. CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:1 and CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:2;
- b. CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:3 and CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:4;
- c. CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:5 and CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:6;
- d. CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:7 and CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:8;

e. CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:9 and CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:10;

f. CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:11 and CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:12;

5 g. CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:13 and CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:14;

h. CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:15 and CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:16;

10 i. CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:17 and CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:18;

j. CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:19 and CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:20;

k. CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:21 and CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:22;

15 l. CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:23 and CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:24;

m. CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:25 and CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:26;

20 n. CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:27 and CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:28;

o. CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:29 and CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:30;

p. CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:31 and CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:32; and

25 q. CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:33 and CDR1, CDR2 and CDR3 amino acid sequences of SEQ ID NO:34.

In another aspect, the present invention refers to an antibody-drug conjugate comprising the antibody as disclosed herein.

30 In yet another aspect, the present invention refers to a pharmaceutical composition comprising the antibody as disclosed herein or the antibody-drug conjugate as disclosed herein and one or more pharmaceutically acceptable excipients, preferably in the form of a lyophilized powder.

In a further aspect, the present invention refers to the antibody as disclosed herein, the antibody-drug conjugate as disclosed herein or the pharmaceutical composition as disclosed herein for use as a medicament.

5 In another aspect, the present invention refers to use of the antibody, the antibody-drug conjugate or the pharmaceutical composition as disclosed herein in the manufacture of a medicament for treating human solid tumours and haematological malignancies.

10 In a further aspect, the present invention refers to use of a combination of the antibody as disclosed herein, the antibody-drug conjugate as disclosed herein or the pharmaceutical composition as disclosed herein with a therapeutic antibody, a chemotherapeutic agent and/or an ADC against a cancer-related target other than the 5T4 antigen in the manufacture of a medicament for treating human solid tumours and haematological malignancies.

BRIEF DESCRIPTION OF THE DRAWINGS

15 Figure 1 shows the binding of chimeric mAbs, humanized mAbs with HC-41C mutation and corresponding anti-5T4 ADCs to hu 5T4-expressing CHO cells (CHOZN) *versus* that of H8 and A1 (Figure 1A clone 789, Figure 1B clone 833, Figure 1C clone 825).

Figure 2 shows the binding of chimeric mAbs, humanized mAbs with HC-41C mutation and corresponding anti-5T4 ADCs to cyno 5T4-expressing CHO cells (CHOZN) *versus* that of H8 and A1 (Figure 2A clone 789, Figure 2B clone 833, Figure 2C clone 825).

c. HCVR amino acid sequence of SEQ ID NO:63 and LCVR amino acid sequence of SEQ ID NO:49;

d. HCVR amino acid sequence of SEQ ID NO:64 and LCVR amino acid sequence of SEQ ID NO:50;

5 e. HCVR amino acid sequence of SEQ ID NO:59 and LCVR amino acid sequence of SEQ ID NO:47; and

f. HCVR amino acid sequence of SEQ ID NO:60 and LCVR amino acid sequence of SEQ ID NO:48;

wherein the linker drug is site-specifically conjugated to the anti-5T4 antibody

10 through the engineered cysteine at heavy chain position 41.

12. A pharmaceutical composition comprising the antibody according to any one of claims 1 to 5 or the antibody-drug conjugate according to any one of claims 6 to 11 and one or more pharmaceutically acceptable excipients, preferably in the form of a lyophilized powder.

15 13. The antibody according to any one of claims 1 to 5, the antibody-drug conjugate according to any one of claims 6 to 11 or the pharmaceutical composition according to claim 12 for use as a medicament.

14. Use of the antibody according to any one of claims 1 to 5, the antibody-drug conjugate according to any one of claims 6 to 11 or the pharmaceutical composition according to claim 12 in the manufacture of a medicament for treating human solid tumours and haematological malignancies.

20 15. The use according to claim 14, wherein the human solid tumours are selected from the group consisting of breast cancer, gastric cancer, colorectal cancer, ovarian cancer, lung cancer, and mesothelioma.

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16. Use of a combination of the antibody according to any one of claims 1 to 5, the antibody-drug conjugate according to any one of claims 6 to 11 or the pharmaceutical composition according to claim 12 with a therapeutic antibody, a chemotherapeutic agent and/or an ADC against a cancer-related target other than the 5T4 antigen in the manufacture of a medicament for treating human solid tumours and haematological malignancies.