often relatively more chemoresistant than the tumor bulk. Since conventional cancer therapies target rapidly proliferating cells (i.e., cells that form the tumor bulk) these treatments are believed to be relatively ineffective at targeting and impairing cancer stem cells. Cancer stem cells can express other features which make them relatively chemoresistant such as multi-drug resistance and anti-apoptotic pathways. The failure to adequately target and eradicate cancer stem cells would constitute a key reason for the failure of standard oncology treatment regimens to ensure long-term benefit in many cancer patients. Thus, the cancer stem cells may not only be the main reason for cancer recurrence after treatment and the ineffectiveness of drugs but also the main reason for malignant cancer metastasis. Thus, one opportunity to cure cancers is to eliminate the cancer stem cells.

Claudins are integral membrane proteins located within the tight junctions of epithelia and endothelia. Claudins are predicted to have four transmembrane segments with two extracellular loops, and N- and C-termini located in the cytoplasm. The claudin (CLDN) family of transmembrane proteins plays a critical role in the maintenance of epithelial and endothelial tight junctions and might also play a role in the maintenance of the cytoskeleton and in cell signaling. CLDN6 is expressed in a series of different human cancer cells while expression in normal tissues is limited to placenta.

Here we present data demonstrating that CLDN6 expression is upregulated during the generation of pluripotent cells. Furthermore, CLDN6 is strongly associated with known markers for cancer stem cells and CLDN6 positve tumor cells show enhanced formation of colonies. It is also demonstrated that therapy using CLDN6 specific antibodies can overcome the chemotherapeutic resistance of tumors such as ovarian cancer and the combination of chemotherapy and CLDN6 antibody therapy has a remarkable synergistic effect.

The findings presented herein indicate that CLDN6 is a novel marker for cancer stem cells and that cancer stem cells can be targeted for diagnostic and therapeutic purposes by targeting CLDN6.

SUMMARY

In one aspect, the present disclosure refers to the use of an antibody for the preparation of a medicament for use in combinatorial therapy for treating or preventing a cancer disease

characterized by cancer cells expressing CLDN6, the antibody having the ability of binding to CLDN6, wherein said medicament is to be administered to a patient in combination with a chemotherapy, wherein the antibody comprises a heavy chain variable region (VH) comprising an amino acid sequence represented by SEQ ID NO: 5 and a light chain variable region (VL) comprising an amino acid sequence represented by SEQ ID NO: 4, and wherein the chemotherapy comprises an agent selected from the group consisting of carboplatin, gemcitabine, paclitaxel, doxorubicin, topotecan and cisplatin.

In another aspect, the present disclosure refers to the use of an antibody drug conjugate for the preparation of a medicament for treating or preventing cancer characterized by cancer cells expressing CLDN6, the use comprising that the antibody drug conjugate is to be administered to a patient, the antibody having the ability of binding to CLDN6 and being covalently attached by a linker to at least one toxin drug moiety, wherein the drug moiety is N2'-deacetyl-N2'(3-mercapto-1-oxopropyl)-maytansine (mertansine or DM1) or monomethyl auristatin E (MMAE), wherein the antibody comprises a heavy chain variable region (VH) comprising an amino acid sequence represented by SEQ ID NO: 5 and a light chain variable region (VL) comprising an amino acid sequence represented by SEQ ID NO: 4.

In yet another aspect, the present disclosure refers to the use of an antibody drug conjugate for the preparation of a medicament for use in combinatorial therapy for treating or preventing cancer characterized by cancer cells expressing CLDN6, the use comprising that the antibody drug conjugate is to be administered to a patient in combination with chemotherapy and/or radiation therapy, the antibody having the ability of binding to CLDN6 and being covalently attached by a linker to at least one toxin drug moiety, wherein the drug moiety is N2'-deacetyl-N2'(3-mercapto-1-oxopropyl)-maytansine (mertansine or DM1) or monomethyl auristatin E (MMAE), wherein the antibody comprises a heavy chain variable region (VH) comprising an amino acid sequence represented by SEQ ID NO: 5 and a light chain variable region (VL) comprising an amino acid sequence represented by SEQ ID NO: 4.

In one example, the present disclosure relates to a method of determining cancer stem cells comprising detecting cells expressing CLDN6.

In one example, the presence of cells expressing CLDN6 indicates the presence of cancer stem cells and/or the amount of cells expressing CLDN6 correlates with the amount of cancer stem

cells. In one example, cells expressing CLDN6 are detected in a sample obtained from a cancer patient such as prior to, during and/or following treatment for cancer. In one example, the method comprises a quantitative and/or qualitative determination of cells expressing CLDN6. In one example, the method comprises comparing the amount of cells expressing CLDN6 to the amount of cells expressing CLDN6 in a reference sample or to a predetermined reference range. The reference sample may be a sample from a patient who has not been diagnosed with cancer. The predetermined reference range may be based on a population of patients who have not been diagnosed with cancer. In one example, the method comprises monitoring the amount of cancer stem cells in a cancer patient, wherein monitoring the amount of cancer stem cells in a cancer patient preferably comprises comparing the amount of cancer stem cells in a sample obtained from the cancer patient to the amount of cancer stem cells in a sample obtained earlier from the cancer patient. In one example, the sample obtained from the cancer patient is a sample taken from the cancer patient during or following the administration of cancer therapy.

In a further example, the present disclosure relates to a method of monitoring the efficacy of a cancer therapy in a cancer patient comprising: (i) determining the amount of cancer stem cells in a sample obtained from the cancer patient during or following the administration of the cancer therapy; and (ii) comparing the amount of cancer stem cells in the sample obtained from the cancer patient to the amount of cancer stem cells in a sample obtained earlier from the cancer patient, wherein determining the amount of cancer stem cells in the sample obtained from the cancer patient and/or determining the amount of cancer stem cells in the sample obtained earlier from the cancer patient comprises determining the amount of cells expressing CLDN6.

In one example, the sample obtained earlier from the cancer patient is a sample taken from the cancer patient prior to, during or following the administration of cancer therapy.

In one example disclosure, a stabilization or a decrease in the amount of cancer stem cells indicates that the cancer therapy is effective. In one example of the disclosure, an increase in the amount of cancer stem cells indicates that the cancer therapy is ineffective. In one example of the disclosure, the cancer therapy is cancer therapy directed against cancer stem cells. In example of the disclosure, the sample obtained from the cancer patient is a biological fluid or a tumor biopsy. In one example of the disclosure, the sample has been subjected to one or more pretreatment steps. In one exampleof the disclosure, the cells expressing CLDN6 are detected or their amount is determined by detecting or determining the amount of CLDN6 protein and/or

CLDN6 mRNA. In one exampleof the disclosure, the cells expressing CLDN6 are detected or their amount is determined by using an immunoassay, wherein the immunoassay is preferably selected from the group consisting of western blots, immunohistochemistry, radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoprecipitation assays, precipitation reactions, gel diffusion precipitation reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, immunofluorescence, protein A immunoassays, flow cytometry and FACS analysis. In one exampleof the disclosure, the cells expressing CLDN6 are detected or their amount is determined by using an antibody having the ability of binding to CLDN6. In one exampleof the disclosure, the cells expressing CLDN6 are cancer cells expressing CLDN6 and/or are cells which are present at a tumor site.

In a further example, the present disclosure relates to a method of treating or preventing cancer comprising inhibiting and/or eliminating cancer stem cells by administering an antibody having the ability of binding to CLDN6 to a cancer patient.

In one example, the cancer stem cells express CLDN6. In one example, the method further comprises administering chemotherapy and/or radiation therapy. In one example, inhibiting and/or eliminating cancer stem cells enhances the anti-cancer effect of chemotherapy and/or radiation therapy, wherein enhancement of the anti-cancer effect of chemotherapy and/or radiation therapy preferably comprises an expansion of the lifespan of a cancer patient undergoing chemotherapy and/or radiation therapy.

In a further example, the present disclosure relates to a method of treating or preventing cancer comprising administering (i) an antibody having the ability of binding to CLDN6 and (ii) chemotherapy to a cancer patient.

In one example, the cancer involves cancer stem cells expressing CLDN6. In one example, administering an antibody having the ability of binding to CLDN6 results in inhibition or elimination of cancer stem cells expressing CLDN6. In one example, administering an antibody having the ability of binding to CLDN6 enhances the anti-cancer effect of chemotherapy, wherein enhancement of the anti-cancer effect of chemotherapy preferably comprises an expansion of the lifespan of a cancer patient undergoing chemotherapy.

In one exampleof the disclosure, elimination of cancer stem cells results in curing of cancer. In one exampleof the disclosure, the antibody having the ability of binding to CLDN6 and the chemotherapy are administered in synergistically effective amounts. In one example of the disclosure, the chemotherapy is administered at a dose which is below the maximum tolerated dose. In one example of the disclosure, the chemotherapy comprises administering an agent selected from the group consisting of taxanes, platinum compounds, nucleoside analogs, camptothecin analogs, anthracyclines, prodrugs thereof, salts thereof, and combinations thereof. In one exampleof the disclosure, the chemotherapy comprises administering an agent selected from the group consisting of paclitaxel, cisplatin, carboplatin, prodrugs thereof, salts thereof, and combinations thereof. In one exampleof the disclosure, the cancer stem cells are at a tumor site of the cancer patient. In one exampleof the disclosure, the cancer is resistant to chemotherapy, in particular if administered as monotherapy. In one exampleof the disclosure, the antibody having the ability of binding to CLDN6 has an inhibitory and/or cytotoxic effect on cancer stem cells, wherein the antibody having the ability of binding to CLDN6 exerts its inhibitory and/or cytotoxic effect on cancer stem cells preferably by mediating one or more of complement dependent cytotoxicity (CDC) mediated lysis, antibody dependent cellular cytotoxicity (ADCC) mediated lysis, induction of apoptosis and inhibition of proliferation. In one exampleof the disclosure, the antibody having the ability of binding to CLDN6 is coupled to a therapeutic moiety and may be an antibody drug conjugate as described herein. In one example, the therapeutic moiety is a cytotoxic agent, a chemotherapeutic agent or a radionuclide. In one example, the therapeutic moiety acts on slow-growing cells. In one exampleof the disclosure, the antibody having the ability of binding to CLDN6 binds to the first extracellular loop of CLDN6. In one exampleof the disclosure, the antibody having the ability of binding to CLDN6 comprises a heavy chain variable region (VH) comprising an amino acid sequence represented by SEQ ID NO: 5 or a fragment thereof and a light chain variable region (VL) comprising an amino acid sequence represented by SEQ ID NO: 4 or a fragment thereof.

In a further example, the present disclosure relates to a method of treating or preventing cancer comprising administering an antibody drug conjugate comprising an antibody having the ability of binding to CLDN6 covalently attached by a linker to at least one toxin drug moiety to a cancer patient.

In one example, the toxin drug moiety is cell membrane-permeable. In one example, at least one of the toxin drug moieties acts on slow-growing cells. In one example, the toxin drug moiety is a

maytansinoid or an auristatin. In one example, the maytansinoid is selected from the group consisting of DM1 and DM4. In one example, the auristatin is selected from the group consisting of monomethyl auristatin E (MMAE) and monomethyl auristatin F (MMAF). In one example, the linker is a cleavable linker, preferably a cathepsin-cleavable linker. In one example, the antibody is attached to the linker through a cysteine thiol of the antibody.

In one example, the cancer involves cancer stem cells expressing CLDN6. In one example, administering the antibody drug conjugate results in inhibition or elimination of cancer stem cells expressing CLDN6. In one example, elimination of cancer stem cells results in curing of cancer. In one example, the cancer stem cells are at a tumor site of the cancer patient. In one example, the antibody drug conjugate has an inhibitory and/or cytotoxic effect on cancer stem cells, wherein the antibody drug conjugate exerts its inhibitory and/or cytotoxic effect on cancer stem cells preferably by induction of apoptosis and/or inhibition of proliferation.

In one example, the method further comprises administering chemotherapy and/or radiation therapy. In one example, administering the antibody drug conjugate enhances the anti-cancer effect of chemotherapy and/or radiation therapy, wherein enhancement of the anti-cancer effect of chemotherapy and/or radiation therapy preferably comprises an expansion of the lifespan of a cancer patient undergoing chemotherapy and/or radiation therapy.

In one example, the antibody drug conjugate and the chemotherapy are administered in synergistically effective amounts. In one example, the chemotherapy is administered at a dose which is below the maximum tolerated dose. In one example, the chemotherapy comprises administering an agent selected from the group consisting of taxanes, platinum compounds, nucleoside analogs, camptothecin analogs, anthracyclines, prodrugs thereof, salts thereof, and combinations thereof. In one example, the chemotherapy comprises administering an agent selected from the group consisting of paclitaxel, cisplatin, carboplatin, prodrugs thereof, salts thereof, and combinations thereof. In one example, the cancer is resistant to chemotherapy, in particular if administered as monotherapy.

In one example, the antibody having the ability of binding to CLDN6, in particular when present in the antibody drug conjugate, has an affinity and/or specificity for CLDN6 appropriate to allow endocytosis of the antibody and/or the antibody drug conjugate. In one example, the antibody having the ability of binding to CLDN6 in the antibody drug conjugate binds to the first

extracellular loop of CLDN6. In one example, the antibody having the ability of binding to CLDN6 in the antibody drug conjugate comprises a heavy chain variable region (VH) comprising an amino acid sequence represented by SEQ ID NO: 5 or a fragment thereof and a light chain variable region (VL) comprising an amino acid sequence represented by SEQ ID NO: 4 or a fragment thereof.

In one exampleof the disclosure, CLDN6 has the amino acid sequence according to SEQ ID NO: 1 or SEQ ID NO: 2. In one exampleof the disclosure, the cancer comprises primary cancer, advanced cancer, metastatic cancer, recurrent cancer or a combination thereof.

In a further example, the present disclosure relates to a method of treating or preventing cancer comprising: (i) determining cancer stem cells in a cancer patient by the method of the disclosure and (ii) administering to the cancer patient cancer therapy directed against cancer stem cells. In one example, the cancer therapy directed against cancer stem cells comprises performing the method of treating or preventing cancer of the disclosure.

In a further example, the present disclosure relates to a method of preventing cancer chemoresistance, cancer recurrence, or cancer metastasis, in particular during or after cancer treatment, comprising treating cancer by the method of the disclosure.

In a further example, the present disclosure provides a medical preparation for treating or preventing cancer comprising (i) an antibody having the ability of binding to CLDN6 and (ii) a chemotherapeutic agent. The antibody having the ability of binding to CLDN6 and the chemotherapeutic agent may be present in the medical preparation in a mixture or separate from each other. The medical preparation may be present in the form of a kit comprising a first container including the antibody having the ability of binding to CLDN6 and a second container including the chemotherapeutic agent. The medical preparation may further include printed instructions for use of the preparation for treatment or prevention of cancer, in particular for use of the preparation in a method of the disclosure. Different examples of the medical preparation, and, in particular, of the antibody having the ability of binding to CLDN6 and the chemotherapeutic agent are as described herein.

In a particular example, the present disclosure provides a medical preparation comprising (i) an antibody having the ability of binding to CLDN6 and (ii) paclitaxel. The antibody having the

ability of binding to CLDN6 and paclitaxel may be present in the medical preparation in a mixture or separate from each other. The medical preparation may be for treating or preventing cancer such as ovarian cancer. The medical preparation may be present in the form of a kit comprising a first container including the antibody having the ability of binding to CLDN6 and a second container including paclitaxel. The medical preparation may further include printed instructions for use of the preparation for treatment or prevention of cancer such as ovarian cancer, in particular for use of the preparation in a method of the disclosure. Different examples of the medical preparation, and, in particular, of the antibody having the ability of binding to CLDN6 are as described herein.

In a further example, the present disclosure provides an antibody drug conjugate comprising an antibody having the ability of binding to CLDN6 covalently attached by a linker to at least one toxin drug moiety.

In one example, the toxin drug moiety is cell membrane-permeable. In one example, at least one of the toxin drug moieties acts on slow-growing cells. In one example, the toxin drug moiety is a maytansinoid or an auristatin. In one example, the maytansinoid is selected from the group consisting of DM1 and DM4. In one example, the auristatin is selected from the group consisting of monomethyl auristatin E (MMAE) and monomethyl auristatin F (MMAF). In one example, the linker is a cleavable linker, preferably a cathepsin-cleavable linker. In one example, the antibody is attached to the linker through a cysteine thiol of the antibody.

In one example, the antibody having the ability of binding to CLDN6, in particular when present in the antibody drug conjugate, has an affinity and/or specificity for CLDN6 appropriate to allow endocytosis of the antibody and/or the antibody drug conjugate. In one example, the antibody having the ability of binding to CLDN6 in the antibody drug conjugate binds to the first extracellular loop of CLDN6. In one example, the antibody having the ability of binding to CLDN6 in the antibody drug conjugate comprises a heavy chain variable region (VH) comprising an amino acid sequence represented by SEQ ID NO: 5 or a fragment thereof and a light chain variable region (VL) comprising an amino acid sequence represented by SEQ ID NO: 4 or a fragment thereof.

In a further example, the present disclosure provides a pharmaceutical formulation comprising the antibody drug conjugate of the disclosure, and a pharmaceutically acceptable diluent, carrier or excipient.

In a further example, the present disclosure provides a medical preparation comprising the antibody drug conjugate of the disclosure, and a chemotherapeutic agent. Preferably, the medical preparation is for treating or preventing cancer. The antibody drug conjugate and the chemotherapeutic agent may be present in the medical preparation in a mixture or separate from each other. The medical preparation may be present in the form of a kit comprising a first container including the antibody drug conjugate and a second container including the chemotherapeutic agent. The medical preparation may further include printed instructions for use of the preparation for treatment or prevention of cancer, in particular for use of the preparation in a method of the disclosure. Different examples of the medical preparation, and, in particular, of the antibody drug conjugate and the chemotherapeutic agent are as described herein.

In a particular example, the present disclosure provides a medical preparation comprising the antibody drug conjugate of the disclosure and paclitaxel. The antibody drug conjugate and paclitaxel may be present in the medical preparation in a mixture or separate from each other. The medical preparation may be for treating or preventing cancer such as ovarian cancer. The medical preparation may be present in the form of a kit comprising a first container including the antibody drug conjugate and a second container including paclitaxel. The medical preparation may further include printed instructions for use of the preparation for treatment or prevention of cancer such as ovarian cancer, in particular for use of the preparation in a method of the disclosure. Different examples of the medical preparation, and, in particular, of the antibody drug conjugate are as described herein.

The present disclosure also provides the agents and compositions described herein such as the antibody drug conjugate, the antibody having the ability of binding to CLDN6 and/or the chemotherapeutic agent for use in the methods described herein. For example, the present disclosure also provides the antibody drug conjugate or the antibody having the ability of binding to CLDN6 for administration in conjunction with a chemotherapeutic agent such as paclitaxel.

In one example, the antibody having the ability of binding to CLDN6 is a monoclonal, chimeric or humanized antibody, or a fragment of an antibody. In one example, the antibody mediates cell

killing when bound to cellular CLDN6, in particular to CLDN6 expressed by cells on their cell surface, wherein the cells are preferably cancer stem cells, such as cancer stem cells of the cancers described herein.

According to the disclosure, a cancer is preferably selected from the group consisting of ovarian cancer, in particular ovarian adenocarcinoma and ovarian teratocarcinoma, lung cancer, including small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC), in particular squamous cell lung carcinoma and adenocarcinoma, large cell carcinoma (LCC), gastric cancer, breast cancer, hepatic cancer, pancreatic cancer, skin cancer, in particular basal cell carcinoma and squamous cell carcinoma, malignant melanoma, head and neck cancer, in particular malignant pleomorphic adenoma, sarcoma, in particular synovial sarcoma and carcinosarcoma, bile duct cancer, cancer of the urinary bladder, in particular transitional cell carcinoma and papillary carcinoma, kidney cancer, in particular renal cell carcinoma including clear cell renal cell carcinoma and papillary renal cell carcinoma, colon cancer, small bowel cancer, including cancer of the ileum, in particular small bowel adenocarcinoma and adenocarcinoma of the ileum, ,placental choriocarcinoma, cervical cancer, testicular cancer, in particular testicular seminoma, testicular teratoma and testicular embryonal carcinoma, uterine cancer, germ cell tumors such as a teratocarcinoma or embryonal carcinoma, in particular germ cell tumors of the testis and ovary, and the metastatic forms thereof.

According to the disclosure, cancer cells and/or cancer stem cells expressing CLDN6 preferably are cells of a cancer described herein.

In one example, a cancer described herein is CLDN6 positive. In one example, cancer cells of a cancer described herein are CLDN6 positive. In one example, cancer cells of a cancer described herein express CLDN6 on their cell surface.

In one example, a cancer described herein comprises primary cancer, advanced cancer, metastatic cancer, recurrent cancer or a combination thereof such as a combination of primary cancer and metastatic cancer. In one example, the cancer is partially or completely refractory to chemotherapy such as paclitaxel monotherapy. In one example, the cancer is ovarian cancer, in particular ovarian cancer partially or completely refractory to chemotherapy such as paclitaxel monotherapy.

Other features and advantages of the instant disclosure will be apparent from the following detailed description and claims.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1: *CLDN6* mRNA is expressed in human iPS cells.

Human foreskin fibroblasts (HFF) were transfected using Lipofectamine RNAiMAX (Life Technologies) either without RNA (no RNA control) or with a reprogramming cocktail (unmod. OSKMNL+EBK+miR-mix) and cells were collected at day 5, 12 and 19 post treatment. RNA was extracted, transcribed into cDNA and afterwards analyzed by quantitative real-time RT-PCR using an ABI PRISM 7300 sequence detection system and software (Applied Biosystems with QuantiTect SYBR green Kit (Qiagen)). Shown is fold induction of *CLDN6* expression of cells treated with the reprogramming cocktail (black bars) relative to HFF cells from day 1 of treatment (grey bars). *CLDN6* mRNA expression was normalized to mRNA expression of the housekeeping gene *HPRT1*. OSKMNL = transcription factors OCT4, SOX2, KLF4, cMYC, NANOG und LIN28, EBK= IFN-*escape* proteins E3, K3 und B18R, miR-mix = miRNA-302a/b/c/d and 367.

CLAIMS

1. Use of an antibody for the preparation of a medicament for use in combinatorial therapy for treating or preventing a cancer disease characterized by cancer cells expressing CLDN6, the antibody having the ability of binding to CLDN6, wherein said medicament is to be administered to a patient in combination with a chemotherapy, wherein the antibody comprises a heavy chain variable region (VH) comprising an amino acid sequence represented by SEQ ID NO: 5 and a light chain variable region (VL) comprising an amino acid sequence represented by SEQ ID NO: 4, and wherein the chemotherapy comprises an agent selected from the group consisting of carboplatin, gemcitabine, paclitaxel, doxorubicin, topotecan and cisplatin.

2. The use of claim 1, wherein the cancer involves cancer stem cells expressing CLDN6.

3. The use of claim 1 or 2 wherein an antibody to be administered having the ability of binding to CLDN6 results in inhibition or elimination of cancer stem cells expressing CLDN6.

4. The use of any one of claims 1 to 3, wherein an antibody to be administered having the ability of binding to CLDN6 enhances the anti-cancer effect of chemotherapy.

5. The use of any one of claims 1 to 4 wherein elimination of cancer stem cells results in curing of cancer.

6. The use of any one of claims 1 to 5 wherein the cancer stem cells are at a tumor site of the cancer patient.

7. The use of any one of claims 1 to 6 wherein the cancer is resistant to chemotherapy.

8. The use of any one of claims 1 to 7 wherein the antibody having the ability of binding to CLDN6 exerts its inhibitory and/or cytotoxic effect on cancer stem cells by mediating one or more of complement dependent cytotoxicity (CDC) mediated lysis, antibody dependent cellular cytotoxicity (ADCC) mediated lysis, induction of apoptosis and inhibition of proliferation.

9. The e use of any one of claims 1 to 8 wherein the antibody having the ability of binding to CLDN6 is coupled to a therapeutic moiety.

10. The use of claim 9 wherein the therapeutic moiety is a cytotoxic agent, a chemotherapeutic agent or a radionuclide.

11. Use of an antibody drug conjugate for the preparation of a medicament for treating or preventing cancer characterized by cancer cells expressing CLDN6, the use comprising that the antibody drug conjugate is to be administered to a patient, the antibody having the ability of binding to CLDN6 and being covalently attached by a linker to at least one toxin drug moiety, wherein the drug moiety is N2'-deacetyl-N2'(3-mercapto-1-oxopropyl)-maytansine (mertansine or DM1) or monomethyl auristatin E (MMAE), wherein the antibody comprises a heavy chain variable region (VH) comprising an amino acid sequence represented by SEQ ID NO: 5 and a light chain variable region (VL) comprising an amino acid sequence represented by SEQ ID NO: 4.

12. The use of claim 11 wherein the linker is a cleavable linker.

13. The use of claim 11 or 12 wherein the linker is a cathepsin-cleavable linker.

14. The use of any one of claims 11 to 13 wherein the antibody is attached to the linker through a cysteine thiol of the antibody.

15. The use of any one of claims 11 to 14 wherein the cancer involves cancer stem cells expressing CLDN6.

16. Use of an antibody drug conjugate for the preparation of a medicament for use in combinatorial therapy for treating or preventing cancer characterized by cancer cells expressing CLDN6, the use comprising that the antibody drug conjugate is to be administered to a patient in combination with chemotherapy and/or radiation therapy, the antibody having the ability of binding to CLDN6 and being covalently attached by a linker to at least one toxin drug moiety, wherein the drug moiety is N2'-deacetyl-N2'(3-mercapto-1-oxopropyl)-maytansine (mertansine or DM1) or monomethyl auristatin E (MMAE), wherein the antibody comprises a heavy chain variable region (VH) comprising an amino acid sequence

represented by SEQ ID NO: 5 and a light chain variable region (VL) comprising an amino acid sequence represented by SEQ ID NO: 4.

17. The use of any one of claims 11 to 16 wherein the antibody drug conjugate to be administered enhances the anti-cancer effect of chemotherapy and/or radiation therapy.

18. The use of any one of claims 1 to 17 wherein CLDN6 has the amino acid sequence according to SEQ ID NO: 1 or SEQ ID NO: 2.

19. The use of any one of claims 1 to 17 wherein the cancer comprises primary cancer, advanced cancer, metastatic cancer, recurrent cancer or a combination thereof.