

CLAIMS

1. A method of identifying a cancer patient for treatment with an antibody drug conjugate (ADC) that includes an ADC payload and an ADC antibody that targets a protein on cancer cells, wherein the protein is calcium signal transducer trophoblast antigen 2 (TROP2), comprising:
 - staining a tissue sample obtained from the cancer patient immunohistochemically using a dye linked to a diagnostic antibody, wherein the diagnostic antibody binds to the protein on the cancer cells in the tissue sample;
 - acquiring a digital image of the tissue sample;
 - detecting cancer cells in the digital image;
 - determining for each cancer cell a mean optical density of staining by the dye in the membrane of the cancer cell;
 - determining for each cancer cell a mean optical density of staining by the dye in the cytoplasm of the cancer cell;
 - computing a normalized membrane optical density (nmOD) for each cancer cell in the digital image;
 - identifying each cancer cell as nmOD positive if the nmOD of the cancer cell is equal to or less than a nmOD threshold;
 - identifying the tissue sample as nmOD positive if the percentage of cancer cells that are nmOD positive is equal to or greater than a nmOD percentage threshold; and
 - identifying the cancer patient as one who will likely benefit from administration of the ADC if the tissue sample is nmOD positive.
2. Use of an antibody drug conjugate (ADC) that includes an ADC payload and an ADC antibody that targets a protein on a cancer cell in the manufacture of a medicament for the treatment of cancer,
 - wherein the protein is calcium signal transducer trophoblast antigen 2 (TROP2),
 - wherein the use comprises:
 - staining a tissue sample obtained from a cancer patient immunohistochemically using a dye linked to a diagnostic antibody, wherein the diagnostic antibody binds to the protein on the cancer cells in the tissue sample;

acquiring a digital image of the tissue sample;
detecting cancer cells in the digital image;
determining for each cancer cell a mean optical density of staining by the dye in the membrane of the cancer cell;
determining for each cancer cell a mean optical density of staining by the dye in the cytoplasm of the cancer cell;
computing a normalized membrane optical density (nmOD) for each cancer cell in the digital image;
identifying each cancer cell as nmOD positive if the nmOD of the cancer cell is equal to or less than a nmOD threshold;
identifying the tissue sample as nmOD positive if the percentage of cancer cells that are nmOD positive is equal to or greater than a nmOD percentage threshold; and
wherein the ADC is to be administered to the cancer patient if the tissue sample is nmOD positive.

3. Use of an antibody drug conjugate (ADC) that includes an ADC payload and an ADC antibody that targets a protein in cancer cells in the manufacture of a medicament for the treatment of cancer,

wherein the protein is calcium signal transducer trophoblast antigen 2 (TROP2),
wherein the ADC is to be administered to a cancer patient if a tissue sample obtained from the cancer patient was determined to be normalized membrane optical density (nmOD) positive, wherein the tissue sample was stained using a diagnostic antibody that binds to the protein in membranes and cytoplasm of cancer cells in the tissue sample, wherein for each cancer cell in a digital image of the tissue sample a mean optical density of membrane staining and a mean optical density of cytoplasm staining were determined, wherein for each cancer cell in the digital image a normalized membrane optical density (nmOD) was computed, wherein each cancer cell in the digital image was identified as nmOD positive if the normalized membrane optical density of the cancer cell was equal to or less than a nmOD threshold, and wherein the tissue sample was identified as nmOD positive if the percentage of cancer cells that were nmOD positive was equal to or greater than a nmOD percentage threshold.

4. The method of claim 1, or the use of claim 2 or claim 3, wherein the detecting of cancer cells involves (or involved) detecting for each cancer cell the pixels that belong to the membrane and the pixels that belong to the cytoplasm.
5. The method of claim 1, further comprising:
recommending a therapy involving the ADC to the cancer patient when the tissue sample is nmOD positive.
6. The method of claim 1, or the use of claim 2 or claim 3, wherein the normalized membrane threshold is (or was) in a range of 0.45 to 0.50.
7. The method of claim 1, or the use of claim 2 or claim 3, wherein the normalized membrane threshold is (or was) 0.486.
8. The method of claim 1, or the use of claim 2 or claim 3, wherein the percentage threshold is (or was) in a range of 3% to 7%.
9. The method of claim 1, or the use of claim 2 or claim 3, wherein the percentage threshold is (or was) 5%.
10. The method of claim 1, or the use of claim 2 or claim 3, wherein the detecting of cancer cells involves (or involved) detecting for each cancer cell the pixels that belong to the membrane using a cell center determined for each cancer cell.
11. The method of claim 1, or the use of claim 2 or claim 3, wherein the staining intensity of each membrane is (or was) computed based on an average optical density of a brown diaminobenzidine (DAB) signal in pixels of the membrane, and wherein the staining intensity of each cytoplasm is computed based on the average optical density of the brown DAB signal in pixels of the cytoplasm.
12. The method of claim 1, or the use of claim 2 or claim 3, wherein the dye is 3,3'-Diaminobenzidine (DAB).

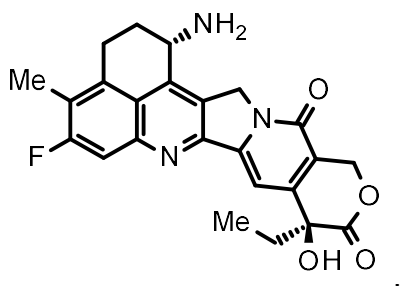
13. The method of claim 1, or the use of claim 2 or claim 3, wherein the ADC is datopotamab deruxtecan (DS-1062).

14. The method of claim 1, or the use of claim 2 or claim 3, wherein the ADC antibody is hTINA1-H1L1.

15. The method of claim 1, or the use of claim 2 or claim 3, wherein the ADC antibody is a humanized IgG1 monoclonal antibody.

16. The method of claim 1, or the use of claim 2 or claim 3, wherein the ADC payload is a topoisomerase I inhibitor.

17. The method or use of claim 16, wherein the topoisomerase I inhibitor is represented by the following formula:



18. The method of claim 1, or the use of claim 2 or claim 3, wherein the diagnostic antibody is Abcam EPR 20043.

19. The method of claim 1, or the use of claim 2 or claim 3, wherein the cancer patient has a cancer selected from the group consisting of: breast cancer, gastric cancer, colorectal cancer, lung cancer, esophageal cancer, head-and-neck cancer, esophagogastric junction cancer, biliary tract cancer, Paget's disease, pancreatic cancer, ovarian cancer, uterine cancer sarcoma, bladder cancer, prostate cancer, urothelial cancer, gastrointestinal stromal tumor, uterine cervix cancer, squamous cell carcinoma, peritoneal cancer, liver cancer, hepatocellular cancer, endometrial cancer, kidney cancer, vulval cancer, thyroid

cancer, penis cancer, leukemia, malignant lymphoma, plasmacytoma, myeloma, glioblastoma multiforme, sarcoma, osteosarcoma, and melanoma.

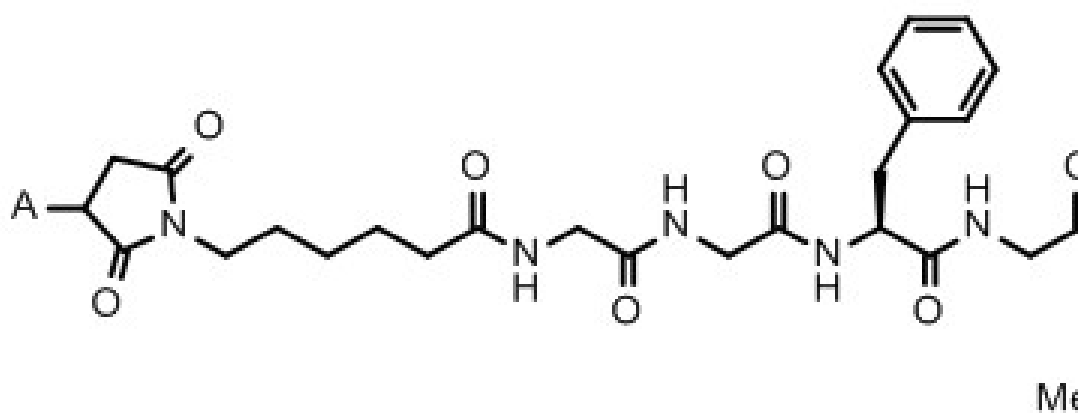
20. The method of claim 1, or the use of claim 2 or claim 3, wherein the cancer patient has a cancer selected from the group consisting of: breast cancer, gastric cancer, colorectal cancer, lung cancer, pancreatic cancer, ovarian cancer, prostate cancer, and kidney cancer.

21. The method of claim 1, or the use of claim 2 or claim 3, wherein the cancer patient has breast cancer.

22. The method of claim 1, or the use of claim 2 or claim 3, wherein the cancer patient has lung cancer.

23. The method of claim 1, or the use of claim 2 or claim 3, wherein the cancer patient has non-small cell lung cancer.

24. The method of claim 1, or the use of claim 2 or claim 3, wherein the ADC is an anti-TROP2 antibody conjugated to a drug-linker via a thioether bond, wherein the drug-linker is represented by the following formula:



, and

wherein A represents a connecting position to the anti-TROP2 antibody.

25. The method of claim 1, or the use of claim 2 or claim 3, wherein the ADC includes an anti-TROP2 antibody comprising:

a heavy chain comprising CDRH1 consisting of an amino acid sequence represented by SEQ ID NO: 3, CDRH2 consisting of an amino acid sequence represented by SEQ ID NO: 4, and CDRH3 consisting of an amino acid sequence represented by SEQ ID NO: 5; and

a light chain comprising CDRL1 consisting of an amino acid sequence represented by SEQ ID NO: 6, CDRL2 consisting of an amino acid sequence represented by SEQ ID NO: 7, and CDRL3 consisting of an amino acid sequence represented by SEQ ID NO: 8.

26. The method of claim 1, or the use of claim 2 or claim 3, wherein the ADC includes an anti-TROP2 antibody comprising:

a heavy chain variable region consisting of the amino acid sequence represented by SEQ ID NO: 9; and

a light chain variable region consisting of the amino acid sequence represented by SEQ ID NO: 10.

27. The method of claim 1, or the use of claim 2 or claim 3, wherein the ADC includes an anti-TROP2 antibody comprising:

a heavy chain consisting of the amino acid sequence represented by SEQ ID NO: 11; and

a light chain consisting of the amino acid sequence represented by SEQ ID NO: 2.

28. The method or use of claim 13, wherein the ADC includes an anti-TROP2 antibody comprising:

a heavy chain consisting of the amino acid sequence represented by SEQ ID NO: 1; and

a light chain consisting of the amino acid sequence represented by SEQ ID NO: 2.

29. Use of an antibody drug conjugate (ADC) that includes an ADC payload and an ADC antibody that targets a protein on a cancer cell in the manufacture of a medicament for the treatment of cancer,

wherein the protein is calcium signal transducer trophoblast antigen 2 (TROP2),

wherein the ADC is to be administered to a cancer patient if a tissue sample obtained from the cancer patient is normalized membrane optical density (nmOD) positive.

30. Use of an antibody drug conjugate (ADC) that includes an ADC payload and an ADC antibody that targets a protein in cancer cells in the manufacture of a medicament for the treatment of cancer,

wherein the protein is calcium signal transducer trophoblast antigen 2 (TROP2),

wherein the ADC is to be administered to a cancer patient if a tissue sample obtained from the cancer patient was determined to be normalized membrane optical density (nmOD) positive.