

Claims

1. Use of an immunoconjugate that binds to folate receptor 1 (FOLR1) in the manufacture of a medicament for treating cancer in a patient in need thereof, wherein said immunoconjugate comprises (i) an antibody or antigen-binding fragment thereof comprising a heavy chain variable region (VH) complementary determining region (CDR)1 sequence of SEQ ID NO:9 or 19, a VH CDR2 sequence of SEQ ID NO:10 or 11, and a VH CDR3 sequence of SEQ ID NO:12, and a light chain variable region (VL) CDR1 sequence of SEQ ID NO:6, a VL CDR2 sequence of SEQ ID NO:7, and a VL CDR3 sequence of SEQ ID NO:8, and (ii) a maytansinoid, wherein the maytansinoid is linked to the antibody or antigen-binding fragment thereof by sulfo-SPDB, and
wherein the medicament is to be administered in combination with bevacizumab, a platinum-based agent, or doxorubicin, and wherein the platinum-based agent is selected from the group consisting of cisplatin, carboplatin, and oxaliplatin.
2. Use of an immunoconjugate that binds to folate receptor 1 (FOLR1) and one of bevacizumab, a platinum-based agent, or doxorubicin, in the manufacture of a medicament for treating cancer in a patient in need thereof, wherein said immunoconjugate comprises (i) an antibody or antigen-binding fragment thereof comprising a heavy chain variable region (VH) complementary determining region (CDR)1 sequence of SEQ ID NO:9 or 19, a VH CDR2 sequence of SEQ ID NO:10 or 11, and a VH CDR3 sequence of SEQ ID NO:12, and a light chain variable region (VL) CDR1 sequence of SEQ ID NO:6, a VL CDR2 sequence of SEQ ID NO:7, and a VL CDR3 sequence of SEQ ID NO:8, and (ii) a maytansinoid, wherein the maytansinoid is linked to the antibody or antigen-binding fragment thereof by sulfo-SPDB, and wherein the platinum-based agent is selected from the group consisting of cisplatin, carboplatin, and oxaliplatin.
3. The use of claim 1, wherein the immunoconjugate is to be administered in combination with the bevacizumab.
4. The use of claim 1, wherein the immunoconjugate is to be administered in combination with the platinum-based agent.
5. The use of claim 1, wherein the immunoconjugate is to be administered in combination with the doxorubicin.

6. Use of an immunoconjugate that binds to folate receptor 1 (FOLR1) in the manufacture of a medicament for treating cancer in a patient in need thereof, wherein said immunoconjugate comprises (i) an antibody or antigen-binding fragment thereof comprising a heavy chain variable region (VH) complementary determining region (CDR)1 sequence of SEQ ID NO:9, a VH CDR2 sequence of SEQ ID NO:10, and a VH CDR3 sequence of SEQ ID NO:12, and a light chain variable region (VL) CDR1 sequence of SEQ ID NO:6, a VL CDR2 sequence of SEQ ID NO:7, and a VL CDR3 sequence of SEQ ID NO:8, and (ii) a maytansinoid, wherein the maytansinoid is linked to the antibody or antigen-binding fragment thereof by sulfo-SPDB, and

wherein the medicament is to be administered for use in combination with

bevacizumab and a platinum-based agent;

and wherein the platinum-based agent is selected from the group consisting of cisplatin, carboplatin, and oxaliplatin.

7. Use of an immunoconjugate that binds to folate receptor 1 (FOLR1) and one of:

bevacizumab and a platinum-based agent;

in the manufacture of a medicament for treating cancer in a patient in need thereof, wherein said immunoconjugate comprises (i) an antibody or antigen-binding fragment thereof comprising a heavy chain variable region (VH) complementary determining region (CDR)1 sequence of SEQ ID NO:9, a VH CDR2 sequence of SEQ ID NO:10, and a VH CDR3 sequence of SEQ ID NO:12, and a light chain variable region (VL) CDR1 sequence of SEQ ID NO:6, a VL CDR2 sequence of SEQ ID NO:7, and a VL CDR3 sequence of SEQ ID NO:8, and (ii) a maytansinoid, wherein the maytansinoid is linked to the antibody or antigen-binding fragment thereof by sulfo-SPDB; and wherein the platinum-based agent is selected from the group consisting of cisplatin, carboplatin, and oxaliplatin.

8. Use of an immunoconjugate that binds to folate receptor 1 (FOLR1) in the manufacture of a medicament for treating cancer in a patient in need thereof, wherein said immunoconjugate comprises (i) an antibody or antigen-binding fragment thereof comprising a heavy chain variable region (VH) complementary determining region (CDR)1 sequence of SEQ ID NO:9, a VH CDR2 sequence of SEQ ID NO:10, and a VH CDR3 sequence of SEQ ID NO:12, and a light chain variable region (VL) CDR1 sequence of SEQ ID NO:6, a VL CDR2 sequence of SEQ ID NO:7,

and a VL CDR3 sequence of SEQ ID NO:8, and (ii) a maytansinoid, wherein the maytansinoid is linked to the antibody or antigen-binding fragment thereof by sulfo-SPDB, and

wherein the medicament is to be administered for use in combination with

- (i) bevacizumab and doxorubicin; or
- (ii) a platinum based agent and doxorubicin;

and wherein the platinum-based agent is selected from the group consisting of cisplatin, carboplatin, and oxaliplatin.

9. Use of an immunoconjugate that binds to folate receptor 1 (FOLR1) and one of:

- (i) bevacizumab and doxorubicin; or
- (ii) a platinum based agent and doxorubicin

in the manufacture of a medicament for treating cancer in a patient in need thereof, wherein said immunoconjugate comprises (i) an antibody or antigen-binding fragment thereof comprising a heavy chain variable region (VH) complementary determining region (CDR)1 sequence of SEQ ID NO:9, a VH CDR2 sequence of SEQ ID NO:10, and a VH CDR3 sequence of SEQ ID NO:12, and a light chain variable region (VL) CDR1 sequence of SEQ ID NO:6, a VL CDR2 sequence of SEQ ID NO:7, and a VL CDR3 sequence of SEQ ID NO:8, and (ii) a maytansinoid, wherein the maytansinoid is linked to the antibody or antigen-binding fragment thereof by sulfo-SPDB; and wherein the platinum-based agent is selected from the group consisting of cisplatin, carboplatin, and oxaliplatin.

10. The use of any one of claims 1, 2, 4, and 6-9, wherein the platinum-based agent is carboplatin.

11. The use of any one of claims 1, 2, 5, and 6-10, wherein the doxorubicin is pegylated liposomal doxorubicin (PLD).

12. The use of any one of claims 1-11, wherein the immunoconjugate that binds to FOLR1 comprises an antibody or antigen-binding fragment thereof that comprises a VH comprising the sequence of SEQ ID NO:3 and a VL comprising the sequence of SEQ ID NO:5.

13. The use of any one of claims 1-12, wherein the immunoconjugate comprises an antibody comprising (i) a heavy chain comprising the amino acid sequence of SEQ ID NO:13 and (ii) a light chain comprising the amino acid sequence of SEQ ID NO: 15, and wherein the maytansinoid is DM4.
14. The use of any one of claims 1-13, wherein the immunoconjugate comprises an antibody comprising (i) a heavy chain comprising the same amino acid sequence as the amino acid sequence of the heavy chain encoded by the plasmid deposited with the American Type Culture Collection (ATCC) as PTA-10772 and (ii) a light chain comprising the same amino acid sequence as the amino acid sequence of the light chain encoded by the plasmid deposited with the ATCC as PTA-10774, and wherein the maytansinoid is DM4.
15. The use of any one of claims 1-12, wherein the maytansinoid is DM4.
16. The use of any one of claims 1-15, wherein the immunoconjugate is to be administered once every three weeks at a dose of 6 mg/kg adjusted ideal body weight (AIBW).
17. The use of any one of claims 1-15, wherein the immunoconjugate is to be administered once every four weeks at a dose of 5 mg/kg AIBW or once every four weeks at a dose of 6 mg/kg AIBW.
18. The immunoconjugate of any one of claims 1-15, wherein the immunoconjugate is to be administered once every three weeks at a dose of 5 mg/kg AIBW.
19. The use of any one of claims 1-3 and 6-18, wherein the bevacizumab is to be administered once every three weeks at a dose of 15 mg/kg.
20. The use of any one of claims 1-3 and 6-18, wherein the bevacizumab is to be administered twice every four weeks at a dose of 10 mg/kg.
21. The use of any one of claims 1, 2, 4, and 6-20, wherein the carboplatin is to be administered once every three weeks at a dose to obtain an area under the curve (AUC) of 5 mg/ml min or 6 mg/ml min.

22. The use of any one of claims 11-21, wherein the PLD is to be administered once every four weeks at a dose of 40 mg/m^2 or once every four weeks at a dose of 30 mg/m^2 .
23. The use of any one of claims 1-22, wherein the the immunoconjugate comprises from about 1 maytansinoid per antibody to about 8 maytansinoids per antibody, optionally wherein the immunoconjugate comprises from about 3 maytansinoids per antibody to about 4 maytansinoids per antibody.
24. The use of any one of claims 1-23, which further wherein the medicament is to be administered as a steroid to the patient, wherein the steroid is to be administered as an eye drop.
25. The use of any one of claims 1-24, wherein the cancer is ovarian, peritoneal, fallopian, endometrial, or lung cancer.
26. The use of claim 25, wherein the cancer is ovarian cancer, peritoneal cancer, or fallopian cancer, optionally wherein the ovarian cancer is platinum-resistant epithelial ovarian cancer.
27. The use of any one of claims 1-26, wherein the cancer expresses FOLR1.
28. The use of claim 27, wherein the FOLR1 expression is measured by immunohistochemistry (IHC).
29. The use of claim 28, wherein at least 25% of cells in a sample obtained from the patient have an immunohistochemistry (IHC) score of at least 2.
30. The use of claim 28, wherein at least 50% of cells in a sample obtained from the patient have an immunohistochemistry (IHC) score of at least 2.
31. The use of claim 28, wherein at least 75% of cells in a sample obtained from the patient have an immunohistochemistry (IHC) score of at least 2.
32. The use of claim 28, wherein 25%-75% of cells in a sample obtained from the patient have an immunohistochemistry (IHC) score of at least 2.

33. The use of claim 28, wherein at least 50% of cells in a sample obtained from the patient have an immunohistochemistry (IHC) score of at least 3.
34. The use of claim 28, wherein at least 75% of cells in a sample obtained from the patient have an immunohistochemistry (IHC) score of at least 3.
35. The use of any one of claims 1-34, wherein the immunoconjugate and the bevacizumab; platinum-based agent; or doxorubicin; are to be administered in separate pharmaceutical compositions.
36. The use of any one of claims 1-35, wherein the cancer is recurrent.
37. The use of any one of claims 1-36, wherein the cancer has previously been treated with bevacuzimab.
38. The use of any one of claims 1-36, wherein the cancer has not previously been treated with bevacuzimab.
39. The use of any one of claims 1-38, wherein the cancer is primary platinum refractory.
40. The use of any one of claims 1-38, wherein the cancer is platinum resistant.
41. The use of any one of claims 1-38, wherein the cancer is platinum sensitive.
42. The use of any one of claims 1-35 and 38-41, wherein the medicament is to be administered as a first-line therapy.
43. The use of any one of claims 1-41, wherein the medicament is to be administered as a second-line therapy.
44. The use of any one of claims 1-41, wherein the medicament is to be administered as a third-line therapy.
45. The use of any one of claims 1-41, wherein the medicament is to be administered as a fourth-line therapy.

46. The use of any one of claims 1-41, wherein the medicament is to be administered as a fifth-line therapy.
47. The use of any one of claims 1-46, wherein the cancer is advanced cancer.
48. The use of any one of claims 1-47, wherein the administration is an adjuvant therapy.
49. The use of any one of claims 1-47, wherein the administration is a neoadjuvant therapy.