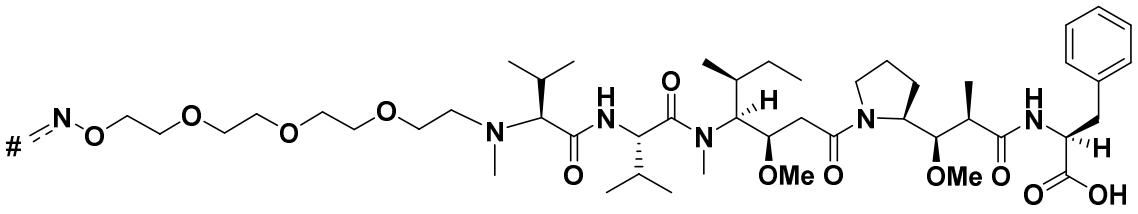
Claims

WHAT IS CLAIMED IS:

1. A formulation comprising: (i) about 20 mg/mL antibody-drug conjugate (ADC); (ii) about 5 mM histidine buffer at about pH 6.0, (iii) about 6% w/v trehalose, and (iv) about 0.02% w/v polysorbate 80, wherein the ADC comprises:

a cytotoxic tubulin analog having the structure



; and

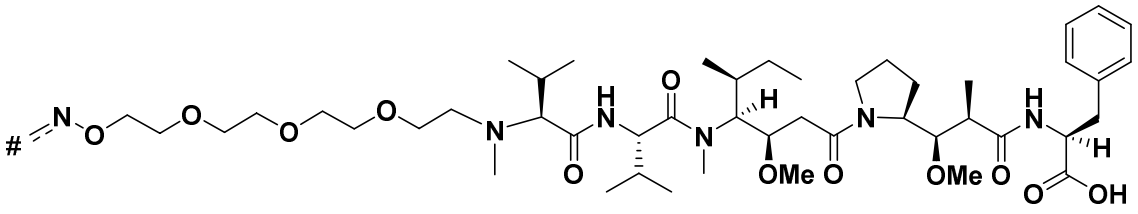
an anti-HER2 antibody or antibody fragment comprising SEQ ID NO: 2 and SEQ ID NO: 3,

wherein ---- represents a single bond or a double bond, and wherein # represents a connection to the anti-HER2 antibody or antibody fragment.

2. The formulation of claim 1, wherein the anti-HER2 antibody or antibody fragment comprises one or more non-naturally encoded amino acids incorporated in a heavy chain, a light chain, or both the heavy chain and the light chain of the ADC.

3. A formulation comprising: (i) about 20 mg/mL antibody-drug conjugate (ADC); (ii) about 5 mM histidine buffer at about pH 6.0, (iii) about 6% w/v trehalose, and (iv) about 0.02% w/v polysorbate 80, wherein the ADC comprises:

a cytotoxic tubulin analog having the structure



; and

an anti-HER2 antibody or antibody fragment comprising SEQ ID NO: 2,

wherein the anti-HER2 antibody or antibody fragment comprises one or more non-naturally encoded amino acids incorporated in a heavy chain, a light chain, or both the heavy chain and the light chain, wherein ---- represents a single bond or a double bond, and wherein # represents a connection to the anti-HER2 antibody or antibody fragment.

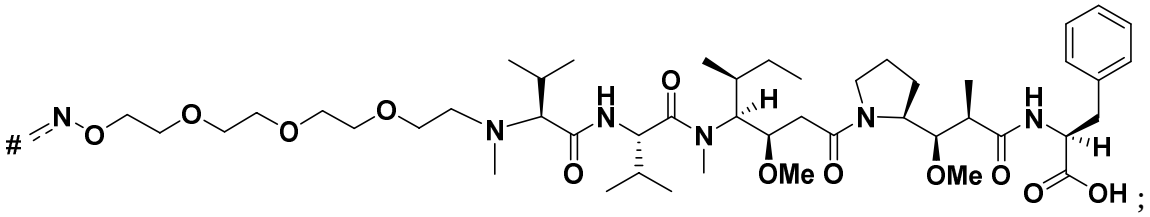
4. The formulation of any one of claims 1-3, wherein the anti-HER2 antibody or antibody fragment comprises one or more non-naturally encoded amino acids incorporated in the heavy chain.

5. The formulation of any one of claims 1-4, wherein ==== represents a double bond, and wherein the tubulin analog is covalently bonded to the anti-HER2 antibody via the double bond,

optionally wherein the double bond is between the tubulin analog and a member of the one or more non-naturally encoded amino acids.

6. The formulation of any one of claims 1-5, wherein:

(a) the ADC comprises two heavy chains, wherein each heavy chain comprises SEQ ID NO: 2, and wherein each heavy chain is individually conjugated to a different tubulin analog having the structure



;

wherein # represents a connection to the anti-HER2 antibody or antibody fragment;

(b) the anti-HER2 antibody or antibody fragment is humanized; and/or

(c) the one or more non-naturally encoded amino acids are para-acetyl phenylalanine.

7. The formulation of claim 3, or of any one of claims 4-6 when dependent from claim 3, wherein a light chain of the anti-HER2 antibody or antibody fragment is any one of SEQ ID NOs: 4, 5, 6, 7, 8, 9, 10, 11, 12 and 13.

8. The formulation of any one of claims 1-7, wherein the histidine is L-histidine.

9. The formulation of any one of claims 1-8, further comprising an additional therapeutic agent,

optionally wherein the additional therapeutic agent is:

(a) an immunotherapeutic agent, chemotherapeutic agent, hormonal agent, antitumor agent, immunostimulatory agent or immunomodulator, or a combination thereof;

(b) a HER2 targeted therapeutic; or

(c) a checkpoint inhibitor, a HER2 kinase inhibitor, cyclin-dependent kinase inhibitor, tyrosine kinase inhibitor, small-molecule kinase inhibitor or a platinum-based therapeutic, or a combination thereof.

10. Use of the formulation of any one of claims 1-8 in the manufacture of a medicament for treating a tumor or cancer in a human subject in need thereof, wherein the medicament comprises an effective amount of the ADC.

11. The use according to claim 10, wherein:

(a) the effective amount is about 0.22, 0.33, 0.44, 0.55, 0.66, 0.77, 0.88, 0.99, 1.0, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9 or 2.0 mg per kilogram body weight (mg/kg) of the human subject,

optionally wherein the effective amount is about 0.33, 0.66, 0.88, 1.1, 1.3, 1.5, 1.6, 1.7 or 1.8 mg/kg of the human subject;

(b) the medicament is to be administered once every 1, 2, 3, 4, 5, 6, 7 or 8-week;

(c) the medicament is to be administered over a period lasting two or more 1, 2, 3, 4, 5, 6, 7 or 8-week cycles;

(d) the medicament is to be administered over a period lasting at least four weeks, or the medicament is to be administered over a period lasting at least three weeks;

(e) the medicament is to be administered more than once within a 1, 2, 3, 4, 5, 6, 7 or 8-week cycle, optionally

(i) wherein the medicament is to be administered more than once within a 4-week cycle, or

(ii) wherein the medicament is to be administered more than once within a 3-week cycle;

(f) the dosage to be administered is the same on different days, or the dosage to be administered is different on different days;

(g) the medicament is to be administered once every two weeks for more than 8 weeks, or the medicament is to be administered once every four weeks for more than 8 weeks; and/or

(h) the tumor or cancer is breast cancer, ovarian cancer, gastric cancer, gastro-esophageal junction adenocarcinoma, cervical cancer, uterine cancer, endometrial cancer, testicular cancer, prostate cancer, colorectal cancer, esophageal cancer, bladder cancer, non-small cell lung cancer (NSCLC), urothelial carcinoma, cholangiocarcinoma, colon biliary tract cancer, pancreatic cancer, or solid tumor,

optionally wherein the tumor or cancer is breast cancer, ovarian cancer or gastric cancer.

12. The use according to any one of claim 11 parts (c)-(e)(i) and (f)-(h), wherein:

(a) the medicament is to be administered at about 1.8 mg/kg dosage on day 1 of the first 4-week cycle,

optionally wherein the medicament is to be further administered at about 1.7 mg/kg, 1.5 mg/kg, 1.3 mg/kg or lower dosage on day 1 of the second 4-week cycle;

(b) the medicament is to be administered at about 1.7 mg/kg dosage on day 1 of the first 4-week cycle,

optionally wherein the medicament is to be further administered at about 1.5 mg/kg, 1.3 mg/kg or lower dosage on day 1 of the second 4-week cycle;

(c) the medicament is to be administered at about 1.6 mg/kg dosage on day 1 of the first 4-week cycle,

optionally wherein the medicament is to be further administered at about 1.5 mg/kg, 1.3 mg/kg, 1.1 mg/kg or lower dosage on day 1 of the second 4-week cycle; or

(d) the medicament is to be administered at about 1.5 mg/kg dosage on day 1 of the first 4-week cycle,

optionally wherein the medicament is to be further administered at about 1.3 mg/kg, 1.1 mg/kg or lower dosage on day 1 of the second 4-week cycle.

13. The use according to any one of claim 11 parts (c)-(e) and (e)(ii)-(h), wherein the medicament is to be administered over a period lasting two or more 3-week cycles,

optionally wherein:

(a) the medicament is to be administered at about 1.8 mg/kg dosage on day 1 of the first 3-week cycle;

(b) the medicament is to be administered at about 1.7 mg/kg dosage on day 1 of the first cycle of 3-week;

(c) the medicament is to be administered at about 1.5 mg/kg dosage on day 1 of the first cycle of 3-week;

(d) the medicament is to be administered at about 1.3 mg/kg dosage on day 1 of the first cycle of 3-week;

(e) the medicament is to be administered at about 1.1 mg/kg dosage on day 1 of the first cycle of 3-week;

(f) the medicament is to be administered at about 0.88 mg/kg dosage on day 1 of the first cycle of 3-week; or

(g) the medicament is to be administered at about 0.66 mg/kg dosage on day 1 of the first cycle of 3-week.

14. The use according to any one of claims 10-13, further comprising formulating the medicament to be administered with an effective amount of an additional therapeutic agent,

optionally wherein the additional therapeutic agent is:

(a) a chemotherapeutic agent, a hormonal agent, an antitumor agent, an immunostimulatory agent, an immunomodulator or an immunotherapeutic agent, or a combination thereof;

(b) a checkpoint inhibitor, a HER2 kinase inhibitor, cyclin-dependent kinase inhibitor, tyrosine kinase inhibitor, small-molecule kinase inhibitor or a platinum-based therapeutic, or a combination thereof; or

(c) a HER2 targeted therapeutic.

15. The use according to any one of claims 10-14, wherein:

(a) the medicament is to be administered orally, intradermally, intratumorally, intravenously, or subcutaneously;

(b) the tumor or cancer is a HER2 expressing cancer;

(c) the cancer is a HER2 low expressing cancer, HER2 moderate expressing cancer, or HER2 high expressing cancer; and/or

(d) the subject to be treated has a HER2 expressing cancer and/or cancer metastases from a same or different cancer.