[0014] In one aspect, provided herein is a use of an antibody-drug conjugate (ADC) in the preparation of a medicine for treating of a patient with Human Epidermal Growth Factor Receptor 2 (HER2)-low expressing breast cancer, wherein the ADC has the structure of the general formula Ab-$(L\text{-}U)_n$, wherein: Ab represents an anti-HER2 antibody, L represents a linker, U represents a conjugated cytotoxic molecule, and n is an integer from 1 to 8 and represents the number of cytotoxic molecules bound to each antibody; wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the CDR sequences of the heavy chain variable region and/or the CDR sequences of the light chain variable region have the same CDR sequences as Disitamab vedotin; wherein the linker L comprises Maleimido-Caproyl-Valine-Citrulline-p-Aminobenzyloxy (mc-vc-pAB), wherein the linker is covalently linked to the anti-HER2 antibody by means of sulfhydryl conjugation, and the linking site is the interchain disulfide bond site of the anti-HER2 antibody; and wherein the cytotoxic molecule U comprises MMAE (monomethyl auristatin E).

[0015] In another example, provided herein is a method for treating a patient with Human Epidermal Growth Factor Receptor 2 (HER2)-low expressing breast cancer, comprising administering to the patient a therapeutically effective amount of an antibody-drug conjugate (ADC), wherein the ADC has the structure of the general formula Ab-$(L\text{-}U)_n$, wherein: Ab represents an anti-HER2 antibody, L represents a linker, U represents a conjugated cytotoxic molecule, and n is an integer from 1 to 8 and represents the number of cytotoxic molecules bound to each antibody; wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the CDR sequences of the heavy chain variable region and/or the CDR sequences of the light chain variable region have the same CDR sequences as Disitamab vedotin; wherein the linker L comprises Maleimido-Caproyl-Valine-Citrulline-p-Aminobenzyloxy (mc-vc-pAB), wherein the linker is covalently linked to the anti-HER2 antibody by means of sulfhydryl conjugation, and the linking site is the interchain disulfide bond site of the anti-HER2 antibody; and wherein the cytotoxic molecule U comprises MMAE (monomethyl auristatin E).

[0016] In some examples, which may be combined with any of the preceding aspects, the HER2-low expressing breast cancer patient is a patient whose HER2 is detected as immunohistochemistry (IHC) 2+/fluorescence in situ hybridization (FISH) negative or IHC1+. In

some examples, which may be combined with any of the preceding aspects or examples, HER2 is detected as IHC 2+/FISH negative or IHC1+ in a sample from the breast cancer. In some examples, which may be combined with any of the preceding aspects or examples, HER2 is detected using an immunohistochemistry (IHC) assay and/or a fluorescence in situ hybridization (FISH) assay.

[0017] In some examples, which may be combined with any of the preceding aspects or examples, the anti-HER2 antibody is a murine, chimeric, humanized or fully human antibody. In some examples, which may be combined with any of the preceding aspects or examples, the anti-HER2 antibody is of the IgG class. In some examples, the anti-HER2 antibody has an IgG1, IgG2, or IgG4 isotype.

[0018] In some examples, which may be combined with any of the preceding aspects or examples, the anti-HER2 antibody comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein: (a) the VH comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:3), a CDR-H2 comprising the amino acid sequence VNPDHGDS (SEQ ID NO:4), and a CDR-H3 comprising the amino acid sequence ARNYLFDH (SEQ ID NO:5), and (b) the VL comprises a CDR-L1 comprising the amino acid sequence QDVGTA (SEQ ID NO:6), a CDR-L2 comprising the amino acid sequence WAS (SEQ ID NO:7), and a CDR-L3 comprising the amino acid sequence HQFATYT (SEQ ID NO:8).

[0019] In some examples, which may be combined with any of the preceding aspects or examples, the anti-HER2 antibody comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein: (a) the VH comprises a CDR-H1 comprising the amino acid sequence DYYIH (SEQ ID NO: 11), a CDR-H2 comprising the amino acid sequence RVNPDHGDSYYNQKFKD (SEQ ID NO: 12), and a CDR-H3 comprising the amino acid sequence ARNYLFDHW (SEQ ID NO: 13), and (b) the VL comprises a CDR-L1 comprising the amino acid sequence KASQDVGTAVA (SEQ ID NO: 14), a CDR-L2 comprising the amino acid sequence WASIRHT (SEQ ID NO: 15), and a CDR-L3 comprising the amino acid sequence HQFATYT (SEQ ID NO: 16).

[0020] In some examples, which may be combined with any of the preceding aspects or examples, the anti-HER2 antibody comprises a heavy chain variable region (VH) comprising the

amino acid sequence of SEQ ID NO: 9, and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 10.

[0021] In some examples, which may be combined with any of the preceding aspects or examples, the anti-HER2 antibody is a human IgG antibody. In some examples, which may be combined with any of the preceding aspects or examples, the anti-HER2 antibody is a human IgG1, IgG2, IgG3, or IgG4 antibody.

[0022] In some examples, which may be combined with any of the preceding aspects or examples, the amino acid sequence of the heavy chain of the antibody is shown in SEQ ID NO:1, and the amino acid sequence of the light chain of the antibody is shown in SEQ ID NO:2.

[0023] In some examples, which may be combined with any of the preceding aspects or examples, the ADC is Disitamab vedotin or a biosimilar thereof.

[0024] In some examples, which may be combined with any of the preceding aspects or examples, the average Drug-to-Antibody Ratio (DAR) value of the ADC is any number from 2 to 7. In some examples, which may be combined with any of the preceding aspects or examples, the average DAR value is 4 ± 0.5.

[0025] In some examples, which may be combined with any of the preceding aspects or examples, the breast cancer is infiltrating locally advanced or metastatic breast cancer as established by histology and/or cytology, and is unresectable.

[0026] In some examples, which may be combined with any of the preceding aspects or examples, the patient has previously received one or more prior treatments. In some examples, the one or more prior treatments are selected from a chemotherapy drug, a targeted therapy, an immunotherapy and an endocrine therapy. In some examples, which may be combined with any of the preceding aspects or examples, the patient has previously received taxane systemic therapy. In some examples, which may be combined with any of the preceding aspects or examples, the patient has previously received systemic therapy with trastuzumab or a biosimilar thereof at least once.

[0027] In some examples, which may be combined with any of the preceding aspects or examples, the medicine or the ADC is administered intranasally, subcutaneously, intradermally, intramuscularly or intravenously.

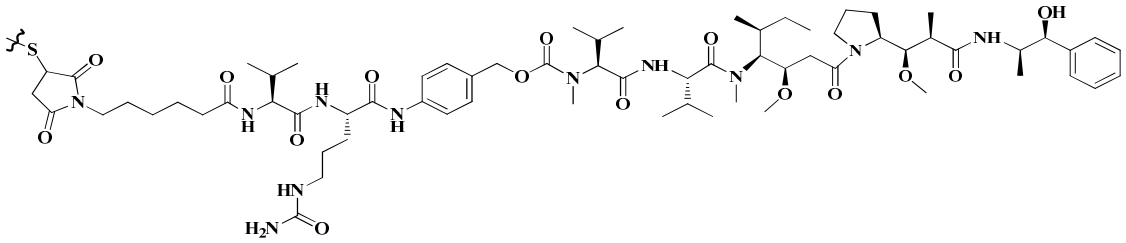
[0028] In some examples, which may be combined with any of the preceding aspects or examples, the ADC is administered at a dose of 2.0 mg/kg every 2 weeks.

[0029] It is to be understood that one, some, or all of the properties of the various examples described herein may be combined to form other examples of the present disclosure. These and other aspects of the disclosure will become apparent to one of skill in the art. These and other examples of the disclosure are further described by the detailed description that follows.

BRIEF DESCRIPTION OF THE DRAWINGS

[0030] FIG. 1 is a schematic diagram of the structure of monomethyl auristatin E (MMAE).

[0031] FIG. 2 is schematic diagram of exemplary structures of an antibody-drug conjugate (ADC) of the general structural formula Ab-(L-U)$_n$ of the present disclosure under one potential set of conjugation conditions (L is linked to one or more interchain disulfide bond sites of the antibody through sulfhydryl conjugation), wherein n is 1, 2, 3, 4, 5, 6, 7, and 8, respectively, L is Maleimido-Caproyl-Valine-Citrulline-p-Aminobenzyloxy (mc-vc-pAB), U is MMAE, and the structure of "-L-U" is as follows:



[0032] FIG. 3 is a flow chart depicting the evaluation criteria of a HER2 dual-probe in situ hybridization (ISH) test.

DETAILED DESCRIPTION

[0033] The present disclosure provides Human Epidermal Growth Factor Receptor 2 (HER2)-targeting antibody-drug conjugates, as well as methods and uses thereof for the treatment of HER2-low expressing breast cancer. The present disclosure is based, at least in part, on data analysis showing that, surprisingly, a HER2-targeting antibody-drug conjugate (ADC) provided by the