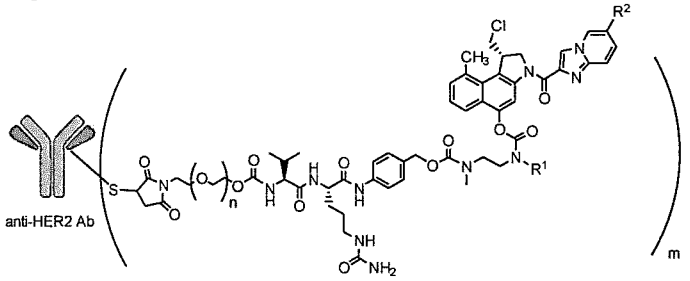
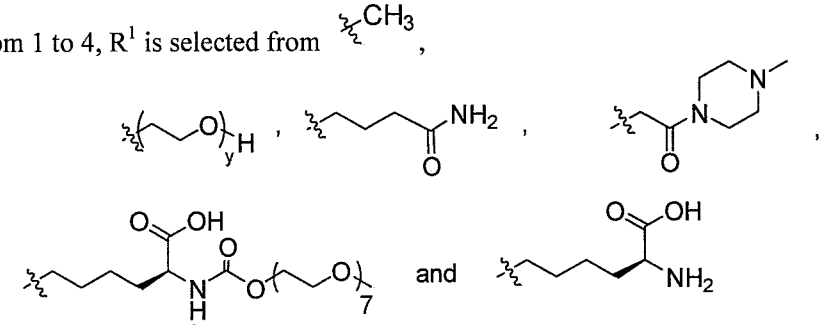
SUMMARY

The present invention relates to duocarmycin-containing antibody-drug conjugates (ADCs) for use in the treatment of human solid tumours and haematological malignancies expressing HER2, in particular breast cancer, gastric cancer, bladder cancer, ovarian cancer, lung cancer, prostate cancer, pancreatic cancer, colorectal cancer, head and neck squamous cell cancer, osteosarcoma, and acute lymphoblastic leukaemia.

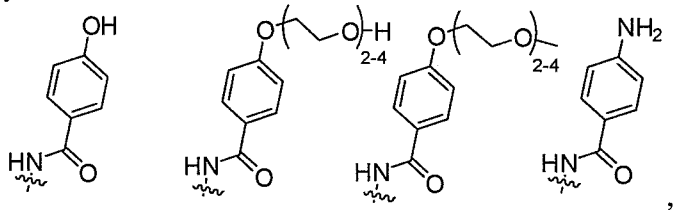
In one aspect, the present invention refers to use of a compound of formula (I)



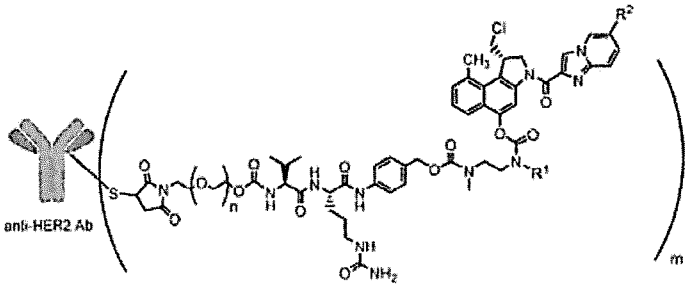
wherein anti-HER2 Ab is an anti-HER2 antibody or an anti-HER2-binding antibody fragment, n is 0-3, m represents an average DAR of from 1 to 4, R^1 is selected from



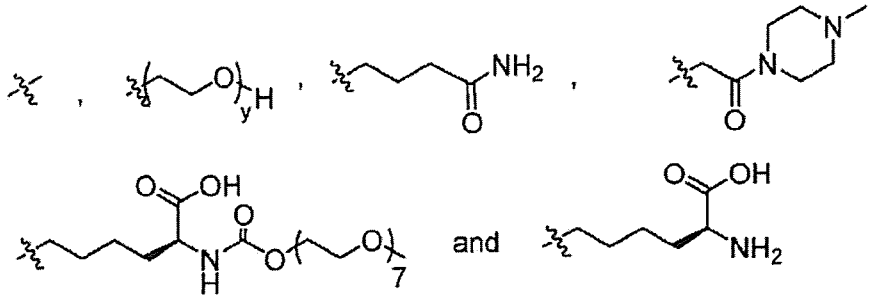
y is 1-16, and R^2 is selected from



, in the manufacture of a medicament for the treatment of human solid tumours expressing HER2, wherein the human solid tumour is HER2 IHC 2+ or 1+. In another aspect, the present invention refers to use of a combination of a compound as defined herein with a therapeutic antibody and/or a chemotherapeutic agent, in the manufacture of a medicament for the treatment of human solid tumours expressing HER2, wherein the human solid tumour is HER2 IHC 2+ or 1+. In yet another aspect, the present invention refers to use of a pharmaceutical composition comprising a compound as defined herein or a combination as defined herein, and one or more pharmaceutically acceptable excipients, in the manufacture of a medicament for the treatment of human solid tumours expressing HER2, wherein the human solid tumour is HER2 IHC 2+ or 1+. In another example, there is disclosed the use of a compound of formula (I)

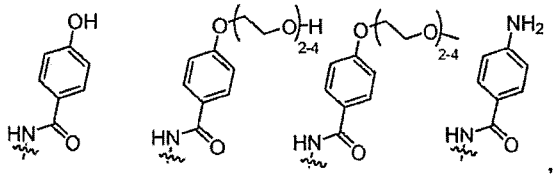


wherein anti-HER2 Ab is an anti-HER2 antibody or an anti-HER2-binding antibody fragment, n is 0-3, m represents an average DAR of from 1 to 4, R^1 is selected from



y is 1-16, and

R^2 is selected from



in the manufacture of a medicament for the treatment of human solid tumours expressing HER2, wherein the human solid tumour is HER2 IHC 2+ or 1+.

In one aspect, there is provided the use of a combination of a compound as disclosed herein with a therapeutic antibody and/or a chemotherapeutic agent, in the manufacture of a medicament for the treatment of human solid tumours expressing HER2.

In one aspect, there is provided a pharmaceutical composition for the treatment of human solid tumours expressing HER2, wherein the human solid tumour is HER2 IHC 2+ or 1+, comprising a compound as disclosed herein or a combination as disclosed herein, and one or more pharmaceutically acceptable excipients.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1. Antitumor activity of SYD985 compared to T-DM1 in MAXF-1162 PDX model (breast cancer, adenocarcinoma, HER2 IHC 3+, HER2 FISH positive) (CRO: Oncotest).

Figure 2. Antitumor activity of SYD985 compared to T-DM1 in HBCx-34 PDX model (breast cancer, ductal carcinoma, HER2 IHC 2+, HER2 FISH negative, ER and PR positive) (CRO: XenTech).

Figure 3. Antitumor activity of SYD985 compared to T-DM1 in MAXF 449 PDX model (breast cancer, invasive ductal carcinoma, HER2 IHC 1+, HER2 FISH negative, ER and PR negative, i.e. triple negative breast cancer) (CRO: Oncotest).

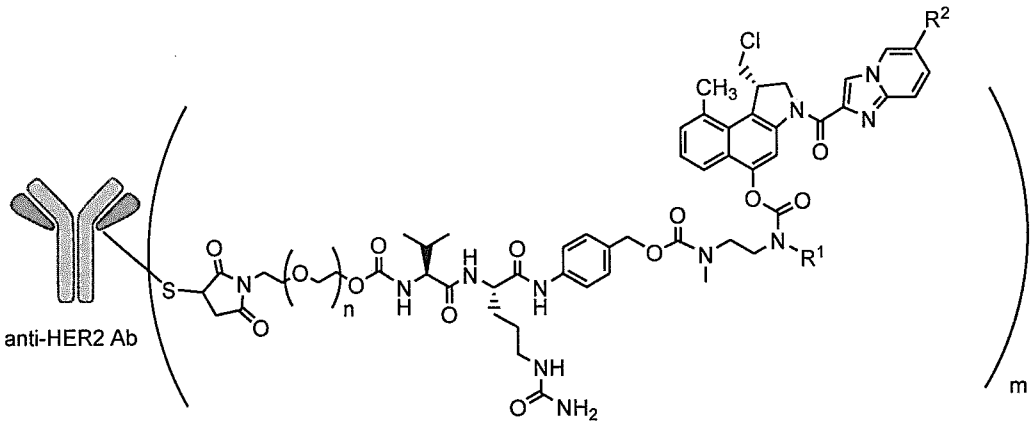
Figure 4. Antitumor activity of SYD985 compared to T-DM1 in HBCx-10 PDX model (breast cancer, ductal adenocarcinoma, HER2 IHC 1+, HER2 FISH negative, ER and PR negative, i.e. triple negative breast cancer) (CRO: XenTech).

Figure 5. Antitumor activity of SYD985 compared to T-DM1 in MAXF-MX1 PDX model (breast cancer, invasive ductal carcinoma, HER2 IHC 1+, HER2 FISH negative, ER and PR negative, i.e. triple negative breast cancer) (CRO: Oncotest).

Figure 6. Antitumor activity of SYD985 compared to T-DM1 in ST313 PDX model (breast cancer, HER2 IHC 2+, HER2 FISH negative, ER and PR positive) (CRO: Start).

CLAIMS

1. Use of a compound of formula (I)



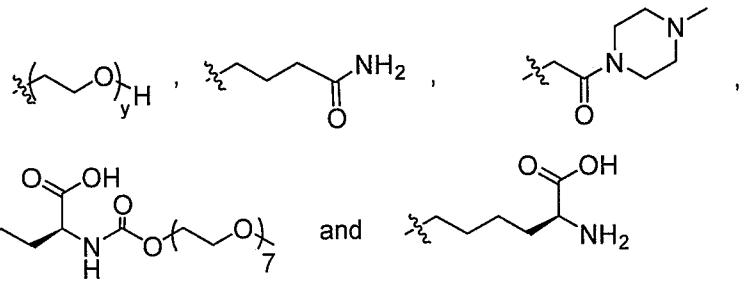
wherein

anti-HER2 Ab is an anti-HER2 antibody or an anti-HER2-binding antibody fragment,

n is 0-3,

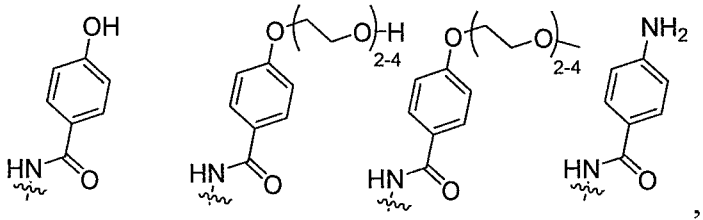
m represents an average DAR of from 1 to 4,

R^1 is selected from ,



y is 1-16, and

R^2 is selected from



in the manufacture of a medicament for the treatment of human solid tumours expressing HER2, wherein the human solid tumour is HER2 IHC 2+ or 1+.

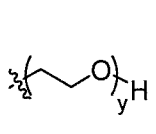
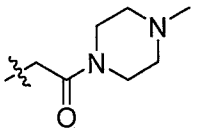
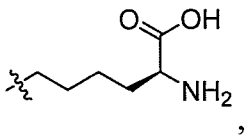
2. The use according to claim 1, wherein

anti-HER2 Ab is an anti-HER2 antibody or an anti-HER2-binding antibody fragment,

n is 0-1,

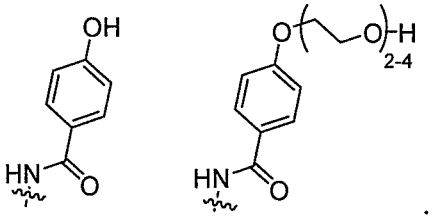
m represents an average DAR of from 1 to 4,

R^1 is selected from ,

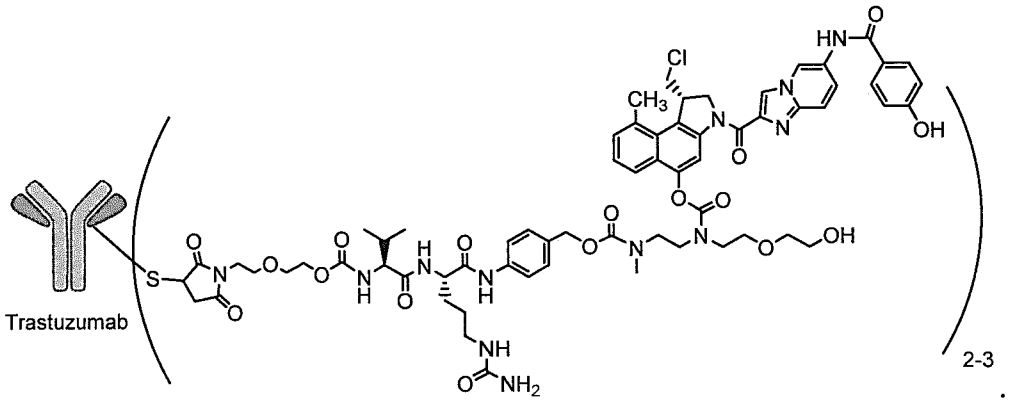
, , and ,

y is 1-16, and

R^2 is selected from

.

3. The use according to claim 1 or 2 of formula (II)



4. The use according to any one of claims 1 to 3, wherein the HER2 expressing human solid tumour is breast cancer, gastric cancer, bladder cancer, ovarian cancer, lung cancer, prostate cancer, pancreatic cancer, colorectal cancer, head and neck squamous cell cancer or osteosarcoma.

5. The use according to any one of claims 1 to 4, wherein the HER2 expressing human solid tumour is breast cancer or gastric cancer.

6. The use according to any one of claims 1 to 5, wherein the breast cancer is hormone receptor positive or negative.

7. The use according to any one of claims 1 to 6, wherein the human solid tumour is HER2 FISH negative.

8. The use according to any one of claims 1 to 7, wherein the human solid tumour is triple negative breast cancer.

9. Use of a combination of a compound as defined in any one of claims 1 to 3 with a therapeutic antibody and/or a chemotherapeutic agent, in the manufacture of a medicament for the treatment of human solid tumours expressing HER2, wherein the human solid tumour is HER2 IHC 2+ or 1+.

10. The use according to claim 9, in the treatment of breast cancer, particularly triple negative breast cancer.

11. The use according to claim 9 or 10, wherein the therapeutic antibody is pertuzumab and the chemotherapeutic agent is a taxane, particularly docetaxel or paclitaxel, or an anthracycline, particularly doxorubicin, epirubicin, daunorubicin or valrubicin.

12. Use of a pharmaceutical composition comprising a compound as defined any one of claims 1 to 3 or a combination as defined in any one of claims 9 or 11, and one or more pharmaceutically acceptable excipients, in the manufacture of a medicament for the treatment of human solid tumours expressing HER2, wherein the human solid tumour is HER2 IHC 2+ or 1+.

13. The use according to claim 12, wherein the pharmaceutical composition is in the form of a lyophilized powder or a frozen solution.