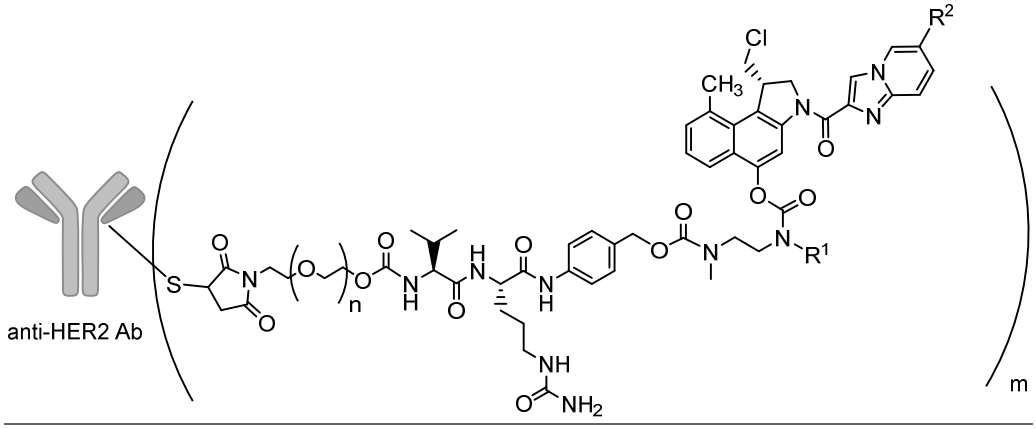
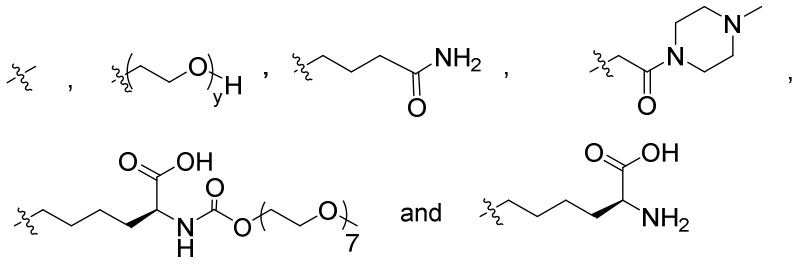
~~BRIEF DESCRIPTION OF THE PRESENT INVENTION~~SUMMARY

The present ~~invention~~ disclosure 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.

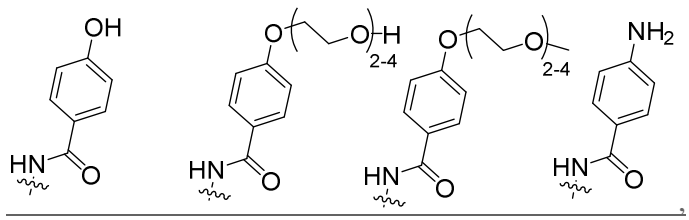
In one aspect, the present invention refers to a use of a compound of formula (I)



wherein anti-HER2 Ab is an anti-HER2 antibody or 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 treating human solid tumours expressing HER2, wherein the human solid tumour expressing HER2 is bladder cancer. In another aspect, the present invention refers to a use of a compound as disclosed herein in the manufacture of a medicament for use in combination therapy with a therapeutic antibody and/or a chemotherapeutic agent for treating bladder cancer. In yet another aspect, the present invention refers to a use of a pharmaceutical composition comprising a compound or a combination therapy 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).

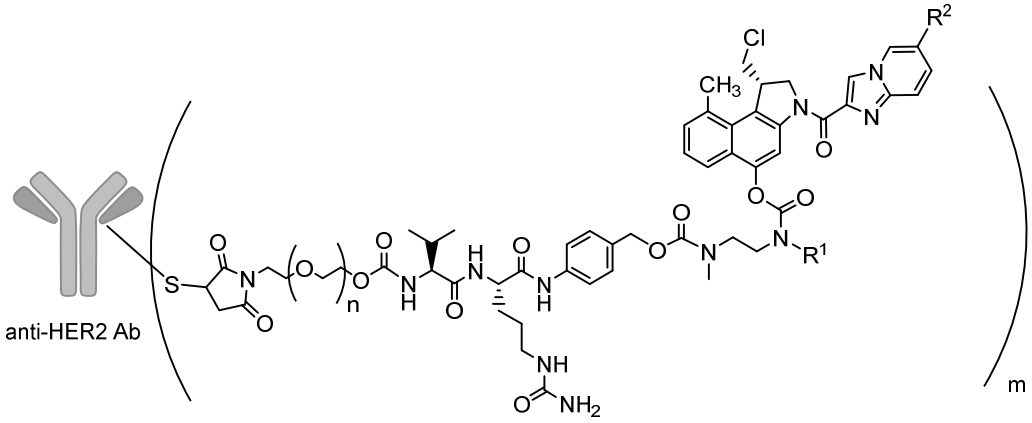
Figure 4. Antitumor activity of SYD985 compared to T-DM1 in HBCx-10 PDX model (breast cancer, ductal adenocarcinoma, HER2 IHC 1+, HER2 FISH negative, ER and PR negative, i.e. triple negative breast cancer) (CRO: XenTech).

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. ~~A~~ Use of a compound of formula (I)



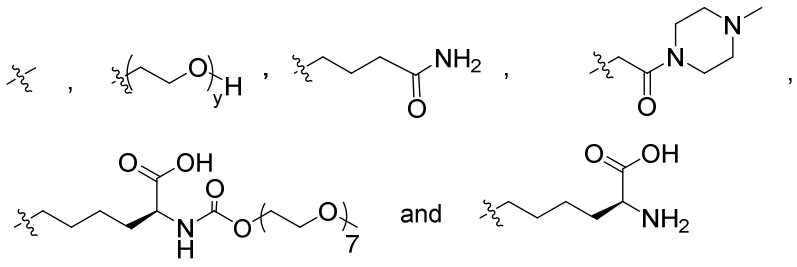
wherein

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

n is 0-3,

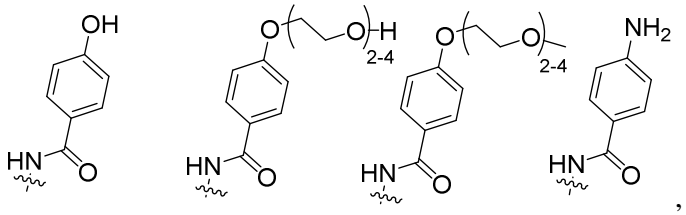
m represents an average DAR of from 1 to 4,

R^1 is selected from



y is 1-16, and

R^2 is selected from



in the manufacture of a medicament for treating ~~for use in the treatment of~~ human solid tumours ~~and haematological malignancies~~ expressing HER2, wherein the human solid tumour expressing HER2 is bladder cancer.

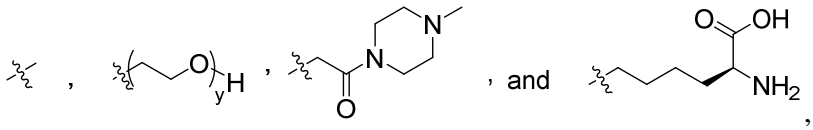
2. ~~A~~ The use ~~compound for use~~ according to claim 1, wherein

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

n is 0-1,

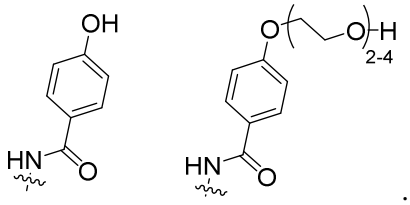
m represents an average DAR of from 1 to 4,

R^1 is selected from

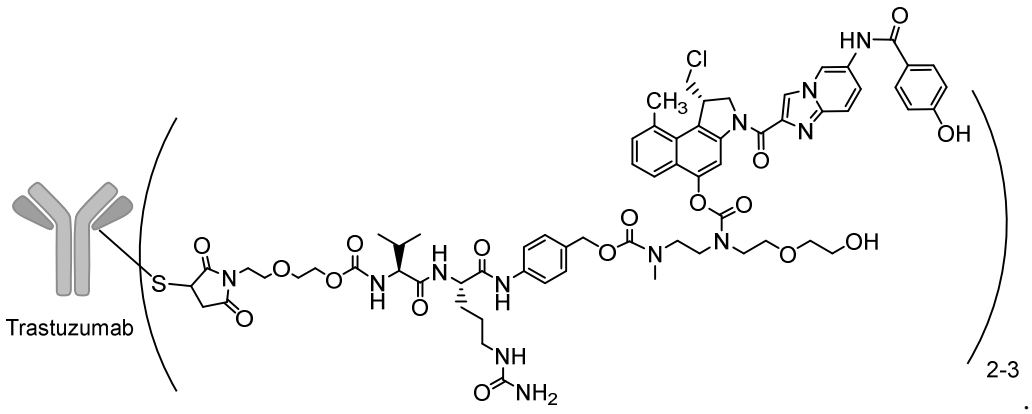


y is 1-16, and

R^2 is selected from



3. ~~A~~ The use ~~compound for use~~ according to claim 1 or 2 of formula (II)



4. ~~A~~ The use ~~compound for use~~ according to ~~any one of~~ claim~~s 1 to~~ 3 of formula (II) having an average DAR of from 2.6 to 2.9~~, for use in the treatment of human solid tumours~~.

~~5. A compound for use according to any one of claims 1 to 4, 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, and the haematological malignancy is acute lymphoblastic leukaemia.~~

~~6. A compound for use according to any one of claims 1 to 5, wherein the HER2 expressing human solid tumour is breast cancer or gastric cancer.~~

~~7. A compound for use according to any one of claims 1 to 6, wherein the breast cancer is hormone receptor positive or negative.~~

~~8.~~5. ~~A~~ The use ~~compound for use~~ according to any one of claims 1 to ~~4~~7, wherein the bladder cancer~~human solid tumour~~ is HER2 IHC 2+ or 1+.

~~9.~~6. ~~A~~ The use ~~compound for use~~ according to any one of claims 1 to ~~5~~8, wherein the bladder cancer~~human solid tumour~~ is HER2 FISH negative.

~~10. A compound for use according to any one of claims 1 to 9, wherein the human solid tumour is triple negative breast cancer.~~

~~11.~~7. ~~A~~ Use of ~~combination of~~ a compound ~~for use~~ according to any one of claims 1 to 6 ~~10~~ in the manufacture of a medicament for use in combination therapy with a therapeutic antibody and/or a chemotherapeutic agent for treating bladder cancer~~, for use in the treatment of human solid tumours and haematological malignancies expressing HER2~~.

~~12. A combination for use according to claim 11, for use in the treatment of breast cancer, particularly triple negative breast cancer.~~

~~13.~~8. ~~A~~ The use ~~combination for use~~ according to claim 7~~11 or 12~~, 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~~.

~~14.~~9. ~~A~~ Use of a pharmaceutical composition comprising a compound ~~for use~~ according to any one of claims 1 to 6~~10~~ or a combination therapy ~~combination for use~~ according to claim 7 or 8~~any one of claims 11 to 13~~, and one or more pharmaceutically acceptable excipients.

~~15.~~10. ~~A~~ The use ~~pharmaceutical composition~~ according to claim 9~~14~~ in the form of a lyophilized powder or a frozen solution.