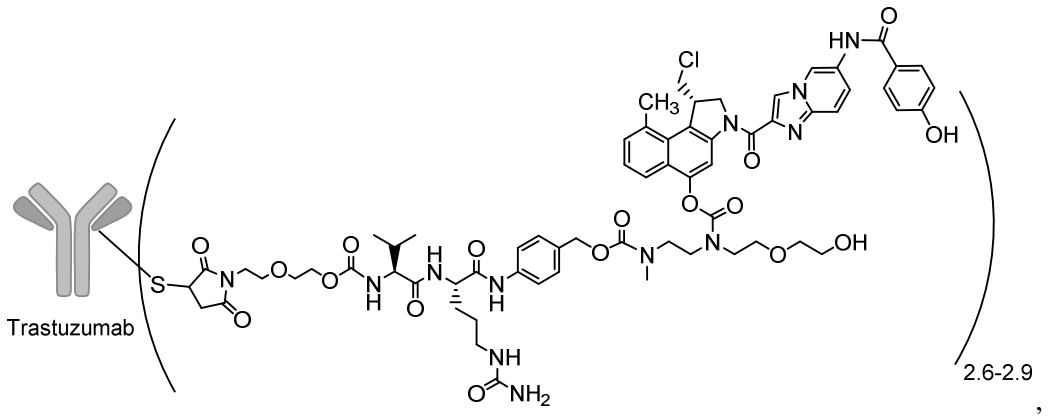
related reactions, bleeding, low platelet count, nerve damage and skin reactions around the infusion site. Consequently, treatment with T-DM1 may have to be discontinued because of (unacceptable) toxicity.

Furthermore, cancer patients, particularly (metastatic) breast cancer patients, may become refractory to T-DM1 treatment, meaning that after an initial positive response to T-DM1 such treatment is discontinued because of disease progression. Hence, there is a high medical need for new HER2-targeted therapies for the treatment of T-DM1 refractory cancer patients.

SUMMARY

Surprisingly, it was found that it is possible to treat patients that do no longer respond to trastuzumab conjugated to a DM1 payload, with trastuzumab conjugated to a duocarmycin payload, in spite of the fact that both conjugates use the same antibody for delivering the payload.

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



,

wherein 2.6-2.9 represent an average DAR for the compound in the manufacture of a medicament for treating a trastuzumab emtansine refractory HER2 IHC 3+ or HER2 IHC 2+/FISH positive cancer patient. In one example, there is disclosed a compound of formula (I) for use in the treatment of T-DM1 refractory cancer patients.

In another example, there is disclosed a pharmaceutical composition comprising the compound of formula (I) and one or more pharmaceutically acceptable excipients for use in the treatment of T-DM1 refractory cancer patients.

In yet another example, there is disclosed a method of treating a T-DM1 refractory cancer patient, particularly a T-DM1 refractory breast cancer patient, comprising administering to the patient a therapeutically effective amount of a compound of formula (I).

In yet another examples, there is disclosed a combination therapy of a compound of formula (I) with an immune checkpoint inhibitor.

In yet another example, there is disclosed a method of treating a T-DM1 refractory cancer patient, particularly a T-DM1 refractory breast cancer patient, comprising administering to the patient a therapeutically effective amount of a compound of formula (I), followed by administering a therapeutically effective amount of an immune checkpoint inhibitor.

Other aspects and advantages of the invention will be readily apparent from the following detailed description of the invention. The embodiments and advantages of the disclosure will be realized and attained by means of the elements and combinations particularly pointed out in the appended claims.

It is to be understood that both the foregoing summary and the following detailed description are exemplary and explanatory only, and are not restrictive of the invention as claimed.

BRIEF DESCRIPTION OF THE DRAWING

Figure 1 shows computed tomography (CT) scans (A: baseline, B: after 6 i.v. infusions of 1.2 mg/kg SYD985 every 3 weeks) of the lung of a 59-year-old HER2-positive breast cancer patient with lung and bone metastases.

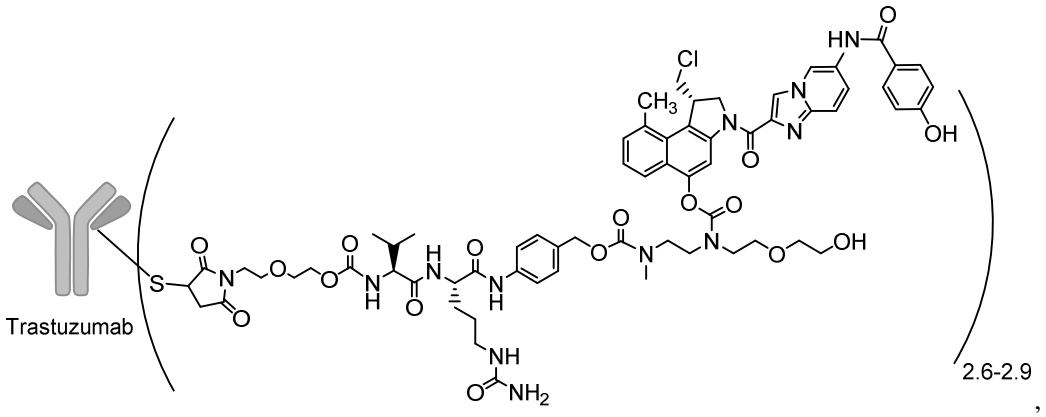
DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to trastuzumab vc-*seco*-DUBA (SYD985) for use in the treatment of trastuzumab emtansine (T-DM1) refractory cancer patients, particularly T-DM1 refractory breast cancer patients.

The present invention provides a compound of formula (I)

CLAIMS

1. Use of a therapeutically effective amount of a compound of formula (I)



,

wherein 2.6-2.9 represent an average DAR for the compound in the manufacture of a medicament for treating a trastuzumab emtansine refractory HER2 IHC 3+ or HER2 IHC 2+/FISH positive cancer patient.

2. The use of claim 1, wherein the average DAR for the compound is about 2.8.

3. The use of claim 1 or 2, wherein the patient is refractory to both trastuzumab and trastuzumab emtansine.

4. The use of claim 3, wherein the patient is refractory to all of trastuzumab, lapatinib and trastuzumab emtansine.

5. The use of any one of claims 1 to 4, wherein said cancer patient is a breast cancer patient.

6. The use of any one of claims 1 to 5, wherein the compound of formula (I) is to be administered, preferably every 3 weeks, with a dose in the range of from 0.9 mg/kg to 2.1 mg/kg of patient body weight per intravenous administration, preferably of from 1.2 to 1.8 mg/kg of patient body weight per intravenous administration.

7. The use of claim 6, wherein the dose is about 0.9 mg/kg, about 1.2 mg/kg, about 1.5 mg/kg, about 1.8 mg/kg, or about 2.1 mg/kg of patient body weight, preferably about 1.2 mg/kg of patient body weight.