

SUMMARY

The present disclosure relates generally to methods of treating breast cancer patients with the antibody-drug conjugate, trastuzumab emtansine (T-DM1).

In one aspect, the present disclosure refers to a use of trastuzumab emtansine (T-DM1) in the manufacture of a medicament for the treatment of HER2-positive early breast cancer as an adjuvant therapy, wherein the patient is to be administered an effective amount of trastuzumab emtansine (T-DM1) as a monotherapy, wherein the patient has residual disease after a pre-operative systemic treatment;

(a) wherein the residual disease is present:

- i) in a breast;
- ii) a lymph node; or
- iii) in a breast and lymph node;

(b) wherein the pre-operative systemic treatment comprises a HER2 target therapy, optionally where the HER2 target therapy comprises:

- i) trastuzumab;
- ii) trastuzumab and pertuzumab;
- iii) trastuzumab, pertuzumab, and an agent selected from the group consisting of lapatinib, neratinib, dacomitinib, afatinib and combinations thereof; or
- iv) a taxane in combination with: trastuzumab; trastuzumab and pertuzumab; or trastuzumab, pertuzumab, and an agent selected from the group consisting of lapatinib, neratinib, dacomitinib, afatinib and combinations thereof; and/or

(c) wherein the patient:

- i) is an adult;
- ii) is subjected to a definitive surgery prior to the administration of T-DM1;
- iii) is administered T-DM1 no more than 12 weeks after the definitive surgery;
- iv) has completed at least 16 weeks of pre-operative systemic treatment with a taxane-containing chemotherapy regimen and HER2 targeted therapy;
- v) has completed at least 6 cycles of taxane-containing chemotherapy;
- vi) is administered T-DM1 at a dose of 3.6 mg/kg every 3 weeks; or
- vii) is administered T-DM1 for fourteen cycles at a dose of 3.6 mg/kg every 3 weeks.

In another aspect, the present disclosure refers to trastuzumab emtansine (T-DM1) for use in an adjuvant therapy HER2-positive early breast cancer in a patient, wherein the

adjuvant is a monotherapy and wherein the patient has residual disease after a pre-operative systemic treatment;

(a) wherein the residual disease is present:

- i) in a breast;
- ii) a lymph node; or
- iii) in a breast and lymph node;

(b) wherein the pre-operative systemic treatment comprises a HER2 target therapy, optionally where the HER2 target therapy comprises:

- i) trastuzumab;
- ii) trastuzumab and pertuzumab;
- iii) trastuzumab, pertuzumab, and an agent selected from the group consisting of lapatinib, neratinib, dacomitinib, afatinib and combinations thereof; or
- iv) a taxane in combination with: trastuzumab; trastuzumab and pertuzumab; or trastuzumab, pertuzumab, and an agent selected from the group consisting of lapatinib, neratinib, dacomitinib, afatinib and combinations thereof; and/or

(c) wherein the patient:

- i) is an adult; and/or
- ii) is subjected to a definitive surgery prior to the administration of T-DM1.

In another aspect, the present disclosure refers to a use of trastuzumab emtansine (T-DM1) in the manufacture of a medicament for use in an adjuvant therapy HER2-positive early breast cancer in a patient, wherein the adjuvant is a monotherapy and wherein the patient has residual disease after a pre-operative systemic treatment;

(a) wherein the residual disease is present:

- i) in a breast;
- ii) a lymph node; or
- iii) in a breast and lymph node;

(b) wherein the pre-operative systemic treatment comprises a HER2 target therapy, optionally where the HER2 target therapy comprises:

- i) trastuzumab;
- ii) trastuzumab and pertuzumab;
- iii) trastuzumab, pertuzumab, and an agent selected from the group consisting of lapatinib, neratinib, dacomitinib, afatinib and combinations thereof; or

iv) a taxane in combination with: trastuzumab; trastuzumab and pertuzumab; or trastuzumab, pertuzumab, and an agent selected from the group consisting of lapatinib, neratinib, dacomitinib, afatinib and combinations thereof; and/or

5 (c) wherein the patient:

i) is an adult patient; and/or

ii) is subjected to a definitive surgery prior to the administration of T-DM1.

In yet another aspect, the present disclosure refers to a use of trastuzumab emtansine (T-DM1) in the manufacture of a medicament for the treatment of breast cancer in a patient
10 with HER2-positive early breast cancer who has residual disease in the breast or axillary lymph nodes after neoadjuvant therapy with chemotherapy and HER2 targeted therapy, wherein

(a) all clinically evident tumor cells in the breast and axillary lymph nodes are to be removed by definitive surgery; and

15 (b) the patient is to be subjected to monotherapy adjuvant therapy with trastuzumab emtansine (T-DM1).

In yet another aspect, the present disclosure refers to a use of trastuzumab emtansine (T-DM1) in the manufacture of a medicament for the treatment of HER2-positive early breast cancer in a patient with residual disease following neoadjuvant therapy, wherein trastuzumab
20 emtansine (T-DM1) is to be administered to the patient in an effective amount after the patient is subjected to definitive surgery, and wherein the residual disease is a pathological residual invasive disease in:

(a) a lymph node; and/or

(b) in a breast.

25 In yet another aspect, the present disclosure refers to a use of trastuzumab emtansine (T-DM1) in the manufacture of a medicament for reducing the risk of cancer recurrence in a patient with HER2-positive early breast cancer, wherein trastuzumab emtansine (T-DM1) is to be administered to the patient an effective amount, wherein the patient did not achieve pathologic complete response with neoadjuvant therapy and the patient had definitive surgery
30 prior to the administering of T-DM1.

In one example, the present disclosure concerns a method of adjuvant therapy comprising administering to a patient with HER2-positive early breast cancer an effective amount of trastuzumab emtansine (T-DM1) as a monotherapy, wherein the patient has residual disease after a pre-operative systemic treatment. In certain examples,

the residual disease is present in a breast, in a lymph node, or present in a breast and a lymph node. In certain examples, the pre-operative systemic treatment comprises a HER2 targeted therapy, such as trastuzumab. In certain examples, the HER2 targeted therapy further comprises pertuzumab, lapatinib, neratinib, dacomitinib and/or afatinib. In certain examples, the HER2 targeted therapy comprises trastuzumab and pertuzumab. In certain examples, the HER2 targeted therapy comprises trastuzumab and further comprises an agent selected from the group consisting of lapatinib, neratinib, dacomitinib and afatinib. In certain examples, the pre-operative systemic treatment further comprises a taxane. In certain examples, the patient is an adult patient. In certain examples, the patient is subjected to a definitive surgery prior to the administration of T-DM1. In certain examples, the patient is administered T-DM1 no more than 12 weeks after the definitive surgery. In certain examples, the patient has completed at least 16 weeks of pre-operative systemic treatment with a taxane-containing chemotherapy regimen and HER2 targeted therapy. In certain examples, the patient has completed at least 6 cycles of taxane-containing chemotherapy. In certain examples, the patient is administered T-DM1 at a dose of 3.6 mg/kg every 3 weeks. In certain examples, the patient is administered T-DM1 for fourteen cycles at a dose of 3.6 mg/kg every 3 weeks. In certain examples, the adjuvant therapy substantially increases invasive disease-free survival (IDFS) as compared to adjuvant therapy with trastuzumab. In certain examples, the adjuvant therapy provides a 50% reduction in the risk of invasive disease recurrence as compared to adjuvant therapy with trastuzumab. In certain examples, the adjuvant therapy leads to a decrease in distant recurrence as compared to adjuvant therapy with trastuzumab. In certain examples, the adjuvant therapy provides a 40% reduction in the risk of distant recurrence as compared to adjuvant trastuzumab.

In one example, the present disclosure concerns trastuzumab emtansine (T-DM1) for use in an adjuvant therapy of HER2-positive early breast cancer in a patient, wherein the adjuvant therapy is a monotherapy and wherein the patient has residual disease after a pre-

operative systemic treatment. In certain examples, the residual disease is present in a breast, present in a lymph node, or present in a breast and a lymph node. In certain examples, the pre-operative systemic treatment comprises a HER2 targeted therapy. In certain examples, the HER2 targeted therapy comprises trastuzumab. In certain examples, the HER2 targeted therapy further comprises pertuzumab, lapatinib, neratinib, dacomitinib and/or afatinib. In certain examples, the HER2 targeted therapy comprises trastuzumab and pertuzumab. In certain examples, the HER2 targeted therapy comprises trastuzumab and further comprises an agent selected from the group consisting of lapatinib, neratinib, dacomitinib and afatinib. In certain examples, the pre-operative systemic treatment further comprises a taxane. In certain examples, the patient is an adult patient. In certain examples, the patient is subjected to a definitive surgery prior to the administration of T-DM1. In certain examples, the adjuvant therapy substantially increases invasive disease-free survival (IDFS) as compared to adjuvant therapy with trastuzumab. In certain examples, the adjuvant therapy provides a 50% reduction in the risk of invasive disease recurrence as compared to adjuvant therapy with trastuzumab. In certain examples, the adjuvant therapy leads to a decrease in distant recurrence as compared to adjuvant therapy with trastuzumab. In certain examples, the adjuvant therapy provides a 40% reduction in the risk of distant recurrence as compared to adjuvant trastuzumab.

In one example, the present disclosure concerns the use of trastuzumab emtansine (T-DM1) in the manufacture of a medicament for use in an adjuvant therapy of HER2-positive early breast cancer in a patient, wherein the adjuvant therapy is a monotherapy and wherein the patient has residual disease after a pre-operative systemic treatment. In certain examples, the residual disease is present in a breast, present in a lymph node, or present in a breast and a lymph node. In certain examples, the pre-operative systemic treatment comprises a HER2 targeted therapy. In certain examples, the HER2 targeted therapy comprises trastuzumab. In certain examples, the HER2 targeted therapy further comprises pertuzumab, lapatinib, neratinib, dacomitinib and/or afatinib. In certain examples, the HER2 targeted therapy comprises trastuzumab and pertuzumab. In certain examples, the HER2 targeted therapy comprises trastuzumab and further comprises an agent selected from the group consisting of lapatinib, neratinib, dacomitinib and afatinib. In certain examples, the pre-operative systemic treatment further comprises a taxane. In certain examples, the patient is an adult patient. In certain examples, the patient is subjected to a definitive surgery prior to the administration of T-DM1. In certain examples, the

adjuvant therapy substantially increases invasive disease-free survival (IDFS) as compared to adjuvant therapy with trastuzumab. In certain examples, the adjuvant therapy provides a 50% reduction in the risk of invasive disease recurrence as compared to adjuvant therapy with trastuzumab. In certain examples, the adjuvant therapy leads to a decrease in distant recurrence as compared to adjuvant therapy with trastuzumab. In certain examples, the adjuvant therapy provides a 40% reduction in the risk of distant recurrence as compared to adjuvant trastuzumab.

In one example, the present disclosure concerns a method for the treatment of breast cancer in a patient with HER2-positive early breast cancer who has residual disease in the breast or axillary lymph nodes after neoadjuvant therapy with chemotherapy and HER2 targeted therapy comprising (i) removing all clinically evident tumor cells in the breast and axillary lymph nodes by definitive surgery; and (ii) subjecting the patient to adjuvant treatment with T-DM1 in the absence of prior or concurrent adjuvant treatment with chemotherapy. In certain examples, the patient has residual disease in the breast or axillary lymph nodes after neoadjuvant therapy with a taxane and HER2 targeted therapy. In certain examples, the patient has completed at least 16 weeks of neoadjuvant therapy with a taxane-containing chemotherapy regimen and HER2 targeted therapy. In certain examples, the patient has completed at least 6 cycles of a taxane-containing chemotherapy regimen. In certain examples, the patient is subjected to adjuvant treatment with T-DM1 no more than 12 weeks after definitive surgery. In certain examples, the definitive surgery is performed at least 14 days following the completion of neoadjuvant therapy. In certain examples, definitive surgery is performed no later than 9 weeks following the completion of neoadjuvant therapy. In certain examples, the patient is subjected to adjuvant treatment with an infusion of T-DM1 at a dose of 3.6 mg/kg every 3 weeks. In certain examples, the patient is subjected to adjuvant treatment for fourteen cycles of an infusion of T-DM1 at a dose of 3.6 mg/kg every 3 weeks. In certain examples, the treatment substantially increases invasive disease-free survival (IDFS) as compared to adjuvant treatment with trastuzumab. In certain examples, the treatment leads to a decrease in distant recurrence as compared to adjuvant treatment with trastuzumab. In certain examples, the adjuvant therapy provides a 50% reduction in the risk of invasive disease recurrence as compared to adjuvant therapy with trastuzumab. In certain examples, the adjuvant therapy provides a 40% reduction in the risk of distant recurrence as compared to adjuvant trastuzumab.

In one example, the present disclosure concerns a method for the treatment of HER2-

positive early breast cancer in a patient with residual disease following neoadjuvant therapy, the method comprising administering to the patient an effective amount of T-DM1 after the patient is subjected to definitive surgery. In one example, the residual disease is a pathological residual invasive disease. In certain examples, the residual disease is a pathological residual invasive disease in the breast and/or axillary node. In certain examples, the method does not comprise prior or concurrent adjuvant treatment with chemotherapy. In certain examples, the neoadjuvant therapy comprises a taxane and HER2 targeted therapy. In certain examples, the neoadjuvant therapy comprises a taxane and trastuzumab. In certain examples, the patient has completed at least 16 weeks of neoadjuvant therapy. In certain examples, the patient has completed at least 6 cycles of taxane-containing neoadjuvant chemotherapy. In certain examples, the patient is subjected to treatment with T-DM1 no more than 12 weeks after definitive surgery. In certain examples, the definitive surgery is performed at least 14 days following the completion of neoadjuvant therapy. In certain examples, the definitive surgery is performed no later than 9 weeks following the completion of neoadjuvant therapy. In certain examples, the patient is subjected to treatment with an infusion of T-DM1 at a dose of 3.6 mg/kg every 3 weeks. In certain examples, the patient is subjected to treatment for fourteen cycles of an infusion of T-DM1 at a dose of 3.6 mg/kg every 3 weeks. In certain examples, treatment substantially increases invasive disease-free survival (IDFS) as compared to adjuvant treatment with trastuzumab. In certain examples, the treatment leads to a decrease in distant recurrence as compared to adjuvant treatment with trastuzumab. In certain examples, the adjuvant therapy provides a 50% reduction in the risk of invasive disease recurrence as compared to adjuvant therapy with trastuzumab. In certain examples, the adjuvant therapy provides a 40% reduction in the risk of distant recurrence as compared to adjuvant trastuzumab.

In another example, the present disclosure concerns a method for reducing the risk of cancer recurrence in a patient with HER2-positive early breast cancer comprising administering to the patient an effective amount of T-DM1, wherein the patient did not achieve pathologic complete response with neoadjuvant therapy and the patient had definitive surgery prior to the administering of T-DM1. In certain examples, the method does not comprise prior or concurrent adjuvant treatment with chemotherapy. In certain examples, the neoadjuvant therapy comprises a taxane and HER2 targeted therapy. In certain examples, the neoadjuvant therapy comprises a taxane and trastuzumab. In certain examples, the patient has completed at least 16 weeks of neoadjuvant therapy. In certain

examples, the patient has completed at least 6 cycles of taxane-containing neoadjuvant therapy. In certain examples, the patient is subjected to treatment with T-DM1 no more than 12 weeks after definitive surgery. In certain examples, the definitive surgery is performed at least 14 days following the completion of neoadjuvant therapy. In certain examples, the definitive surgery is performed no later than 9 weeks following the completion of neoadjuvant therapy. In certain examples, the patient is subjected to treatment with an infusion of T-DM1 at a dose of 3.6 mg/kg every 3 weeks. In certain examples, the patient is subjected to treatment for fourteen cycles of an infusion of T-DM1 at a dose of 3.6 mg/kg every 3 weeks. In certain examples, the treatment substantially increases invasive disease-free survival (IDFS) as compared to adjuvant treatment with trastuzumab. In certain examples, the treatment leads to a decrease in distant recurrence as compared to adjuvant treatment with trastuzumab. In certain examples, the adjuvant therapy provides a 50% reduction in the risk of invasive disease recurrence as compared to adjuvant therapy with trastuzumab. In certain examples, the adjuvant therapy provides a 40% reduction in the risk of distant recurrence as compared to adjuvant trastuzumab.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a schematic of the KATHERINE study design.

Figures 2A-2C depict summaries of the baseline characteristics of KATHERINE trial treatment arms.

Figure 3 depicts a Kaplan-Meier plot of invasive-disease-free survival. Invasive-disease-free survival was defined as the time from randomization until the date of the first occurrence of ipsilateral invasive breast tumor recurrence, ipsilateral locoregional invasive disease recurrence, distant disease recurrence, contralateral invasive breast cancer, or death from any cause. CI, denotes confidence interval; HR denotes hazard ratio.

Figure 4A depicts a Kaplan-Meier plot of distant recurrence, defined as evidence of breast cancer in any anatomical site — other than ipsilateral invasive breast tumor or recurrence of locoregional invasive breast cancer — that was either histologically confirmed or clinically diagnosed as recurrent invasive breast cancer. No statistical adjustments were made for multiple comparisons.

Figure 4B provides a summary of the site of first invasive-disease event in patients.

Figure 5 provides a summary of secondary efficacy end points from the KATHERINE trial.

We claim:

1. Use of trastuzumab emtansine (T-DM1) in the manufacture of a medicament for the adjuvant treatment of HER2-positive early breast cancer, wherein the patient is to be administered an effective amount of trastuzumab emtansine (T-DM1) as a monotherapy,
5 wherein the patient has residual disease after a pre-operative systemic treatment;
 - (a) wherein the residual disease is present:
 - i) in a breast;
 - ii) a lymph node; or
 - iii) in a breast and lymph node;
 - 10 (b) wherein the pre-operative systemic treatment comprises a HER2 target therapy, optionally where the HER2 target therapy comprises:
 - i) trastuzumab;
 - ii) trastuzumab and pertuzumab;
 - iii) trastuzumab, pertuzumab, and an agent selected from the group consisting
15 of lapatinib, neratinib, dacomitinib, afatinib and combinations thereof; or
 - iv) a taxane in combination with: trastuzumab; trastuzumab and pertuzumab;
or trastuzumab, pertuzumab, and an agent selected from the group
consisting of lapatinib, neratinib, dacomitinib, afatinib and combinations
thereof; and/or
 - 20 (c) wherein the patient:
 - i) is an adult;
 - ii) is subjected to a definitive surgery prior to the administration of T-DM1;
 - iii) is administered T-DM1 no more than 12 weeks after the definitive surgery;
 - iv) has completed at least 16 weeks of pre-operative systemic treatment with a
25 taxane-containing chemotherapy regimen and HER2 targeted therapy;
 - v) has completed at least 6 cycles of taxane-containing chemotherapy;
 - vi) is administered T-DM1 at a dose of 3.6 mg/kg every 3 weeks; or
 - vii) is administered T-DM1 for fourteen cycles at a dose of 3.6 mg/kg every 3
weeks.
- 30 2. The use of claim 1, wherein the adjuvant therapy:
 - (a) substantially increases invasive disease-free survival (IDFS) as compared to adjuvant therapy with trastuzumab;

(b) provides a 50% reduction in the risk of invasive disease recurrence as compared to adjuvant therapy with trastuzumab;

(c) leads to a decrease in distant recurrence as compared to adjuvant therapy with trastuzumab; and/or

5 (d) provides a 40% reduction in the risk of distant recurrence as compared to adjuvant trastuzumab.

3. Trastuzumab emtansine (T-DM1) for use in an adjuvant therapy HER2-positive early breast cancer in a patient, wherein the adjuvant is a monotherapy and wherein the patient has residual disease after a pre-operative systemic treatment;

10 (a) wherein the residual disease is present:

i) in a breast;

ii) a lymph node; or

iii) in a breast and lymph node;

(b) wherein the pre-operative systemic treatment comprises a HER2 target therapy,
15 optionally where the HER2 target therapy comprises:

i) trastuzumab;

ii) trastuzumab and pertuzumab;

iii) trastuzumab, pertuzumab, and an agent selected from the group consisting
of lapatinib, neratinib, dacomitinib, afatinib and combinations thereof; or

20 iv) a taxane in combination with: trastuzumab; trastuzumab and pertuzumab;
or trastuzumab, pertuzumab, and an agent selected from the group
consisting of lapatinib, neratinib, dacomitinib, afatinib and combinations
thereof; and/or

(c) wherein the patient:

25 i) is an adult; and/or

ii) is subjected to a definitive surgery prior to the administration of T-DM1.

4. T-DM1 for the use of claim 3, wherein the adjuvant therapy:

(a) substantially increases invasive disease-free survival (IDFS) as compared to
30 adjuvant therapy with trastuzumab;

(b) provides a 50% reduction in the risk of invasive disease recurrence as compared to adjuvant therapy with trastuzumab;

(c) leads to a decrease in distant recurrence as compared to adjuvant therapy with trastuzumab; and/or

(d) provides a 40% reduction in the risk of distant recurrence as compared to adjuvant trastuzumab.

5. Use of trastuzumab emtansine (T-DM1) in the manufacture of a medicament for use in an adjuvant therapy HER2-positive early breast cancer in a patient, wherein the adjuvant is a monotherapy and wherein the patient has residual disease after a pre-operative systemic treatment;

(a) wherein the residual disease is present:

i) in a breast;

ii) a lymph node; or

iii) in a breast and lymph node;

(b) wherein the pre-operative systemic treatment comprises a HER2 target therapy, optionally where the HER2 target therapy comprises:

i) trastuzumab;

ii) trastuzumab and pertuzumab;

iii) trastuzumab, pertuzumab, and an agent selected from the group consisting of lapatinib, neratinib, dacomitinib, afatinib and combinations thereof; or

iv) a taxane in combination with: trastuzumab; trastuzumab and pertuzumab; or trastuzumab, pertuzumab, and an agent selected from the group consisting of lapatinib, neratinib, dacomitinib, afatinib and combinations thereof; and/or

(c) wherein the patient:

i) is an adult patient; and/or

ii) is subjected to a definitive surgery prior to the administration of T-DM1.

6. The use of claim 5, wherein the adjuvant therapy:

(a) substantially increases invasive disease-free survival (IDFS) as compared to adjuvant therapy with trastuzumab;

(b) provides a 50% reduction in the risk of invasive disease recurrence as compared to adjuvant therapy with trastuzumab;

(c) leads to a decrease in distant recurrence as compared to adjuvant therapy with trastuzumab; and/or

(d) provides a 40% reduction in the risk of distant recurrence as compared to adjuvant trastuzumab.

7. Use of trastuzumab emtansine (T-DM1) in the manufacture of a medicament for the treatment of breast cancer in a patient with HER2-positive early breast cancer who has residual disease in the breast or axillary lymph nodes after neoadjuvant therapy with chemotherapy and HER2 targeted therapy, wherein

5 (a) all clinically evident tumor cells in the breast and axillary lymph nodes are to be removed by definitive surgery; and

(b) the patient is to be subjected to monotherapy adjuvant therapy with trastuzumab emtansine (T-DM1).

8. The use of claim 7, wherein the patient has residual disease in the breast or axillary
10 lymph nodes after neoadjuvant therapy with a taxane and HER2 targeted therapy.

9. The use of claim 7, wherein the patient:

(a) has completed at least 16 weeks of neoadjuvant therapy with a taxane-containing chemotherapy;

(b) has completed at least 6 cycles of taxane-containing chemotherapy;

15 (c) is subjected to adjuvant treatment with T-DM1 no more than 12 weeks after definitive surgery;

(d) is subjected to adjuvant treatment with an infusion of T-DM1 at a dose of 3.6 mg/kg every 3 weeks; or

(e) is subjected to adjuvant treatment for fourteen cycles of an infusion of T-DM1 at a
20 dose of 3.6 mg/kg every 3 weeks.

10. The use of claim 7, wherein the use:

(a) substantially increases invasive disease-free survival (IDFS) as compared to adjuvant treatment with trastuzumab; and/or

(b) leads to a decrease in distant recurrence as compared to adjuvant treatment with
25 trastuzumab.

11. Use of trastuzumab emtansine (T-DM1) in the manufacture of a medicament for the treatment of HER2-positive early breast cancer in a patient with residual disease following neoadjuvant therapy, wherein trastuzumab emtansine (T-DM1) is to be administered to the patient an effective amount after the patient is subjected to definitive surgery, and wherein the
30 residual disease is a pathological residual invasive disease in:

(a) a lymph node; and/or

(b) in a breast.

12. The use of claim 11, wherein the use does not comprise prior or concurrent adjuvant treatment with chemotherapy.
13. The use of claim 11, wherein the neoadjuvant therapy comprises a taxane and HER2 targeted therapy, optionally wherein the HER2 targeted therapy comprises trastuzumab.
- 5 14. The use of claim 11, wherein the patient:
- (a) has completed at least 16 weeks of neoadjuvant therapy;
 - (b) has completed at least 6 cycles of taxane-containing neoadjuvant therapy;
 - (c) is subjected to treatment with T-DM1 no more than 12 weeks after definitive surgery;
- 10 (d) is subjected to treatment with an infusion of T-DM1 at a dose of 3.6 mg/kg every 3 weeks; or
- (e) is subjected to treatment for fourteen cycles of an infusion of T-DM1 at a dose of 3.6 mg/kg every 3 weeks.
15. The use of claim 11, wherein the use:
- 15 (a) substantially increases invasive disease-free survival (IDFS) as compared to adjuvant treatment with trastuzumab; and/or
- (b) leads to a decrease in distant recurrence as compared to adjuvant treatment with trastuzumab.
16. Use of trastuzumab emtansine (T-DM1) in the manufacture of a medicament for
- 20 reducing the risk of cancer recurrence in a patient with HER2-positive early breast cancer, wherein trastuzumab emtansine (T-DM1) is to be administered to the patient in an effective amount, wherein the patient did not achieve pathologic complete response with neoadjuvant therapy and the patient had definitive surgery prior to the administering of T-DM1.
17. The use of claim 16, wherein the use does not comprise prior or concurrent adjuvant
- 25 treatment with chemotherapy.
18. The use of claim 16, wherein the neoadjuvant therapy comprises a taxane and HER2 targeted therapy, optionally wherein the HER2 targeted therapy comprises trastuzumab.
19. The use of claim 16, wherein the patient:
- (a) has completed at least 16 weeks of neoadjuvant therapy;
 - (b) has completed at least 6 cycles of taxane-containing neoadjuvant therapy;
 - (c) is subjected to treatment with T-DM1 no more than 12 weeks after definitive surgery;
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(d) is subjected to treatment with an infusion of T-DM1 at a dose of 3.6 mg/kg every 3 weeks; or

(e) is subjected to treatment for fourteen cycles of an infusion of T-DM1 at a dose of 3.6 mg/kg every 3 weeks.

5 20. The use of claim 16, wherein the use:

(a) substantially increases invasive disease-free survival (IDFS) as compared to adjuvant treatment with trastuzumab; or

(b) leads to a decrease in distant recurrence as compared to adjuvant treatment with trastuzumab;

10 (c) provides a 50% reduction in the risk of invasive disease recurrence as compared to adjuvant therapy with trastuzumab; or

(d) provides a 40% reduction in the risk of distant recurrence as compared to adjuvant trastuzumab.