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 a therapeutically 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 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

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

(b) the patent is to be subjected to monotherapy adjuvant therapy with a therapeutically effective amount of 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 emtansine (T-DM1) is to be administered to the patient in a therapeutically 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.

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 a therapeutically 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.

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

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 a therapeutically 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.

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

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

3. 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

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

(b) the patent is to be subjected to monotherapy adjuvant therapy with a therapeutically effective amount of trastuzumab emtansine (T-DM1).

4. The use of claim 3, wherein the patient has residual disease in the breast or axillary lymph nodes after neoadjuvant therapy with a taxane and HER2 targeted therapy.

5. The use of claim 3, 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;

(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 dose of 3.6 mg/kg every 3 weeks.

6. The use of claim 3, 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 trastuzumab.

7. 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 a therapeutically 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.

8. The use of claim 7, wherein the use does not comprise prior or concurrent adjuvant treatment with chemotherapy.

9. The use of claim 7, wherein the neoadjuvant therapy comprises a taxane and HER2 targeted therapy, optionally wherein the HER2 targeted therapy comprises trastuzumab.

10. The use of claim 7, 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;

(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.

11. 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 trastuzumab.

12. 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 in a therapeutically 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.

13. The use of claim 12, wherein the use does not comprise prior or concurrent adjuvant treatment with chemotherapy.

14. The use of claim 12, wherein the neoadjuvant therapy comprises a taxane and HER2 targeted therapy, optionally wherein the HER2 targeted therapy comprises trastuzumab.

15. The use of claim 12, 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;

(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.

16. The use of claim 12, 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;

(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.