TDM000211740

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Kadcyla® ado-trastuzumab emtansine for injection

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Safety first! Read below to see the Important Safety Information

Important Safety Information

Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY

- Do Not Substitute KADCYLA for or with Trastuzumab
- Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin
- Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA

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ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function

- Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception

Additional Important Safety Information

Left Ventricular Dysfunction (LVD)

- Patients treated with KADCYLA are at increased risk of developing LVD. In EMILIA, LVD occurred in 1.8% of patients in the KADCYLA-treated group and in 3.3% of patients in the comparator group. Permanently discontinue KADCYLA if LVEF has not improved or has declined further

Pregnancy Registry

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Safety first! Read below to see the Important Safety Information

- Advise patients to contact their healthcare provider immediately if they suspect they may be pregnant. Encourage women who may be exposed to KADCYLA during pregnancy to enroll in the **MotHER Pregnancy Registry** by contacting **1 (800) 690-6720**

Pulmonary Toxicity

- Cases of interstitial lung disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatal outcome have been reported in clinical trials with KADCYLA. In EMILIA, the overall frequency of pneumonitis was 1.2%
- Treatment with KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis

Infusion-Related Reactions, Hypersensitivity Reactions

- Treatment with KADCYLA has not been studied in patients who had trastuzumab permanently discontinued due to infusion-

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- KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR. Patients should be closely monitored for IRR reactions, especially during the first infusion

Thrombocytopenia

- In EMILIA, the incidence of ≥ Grade 3 thrombocytopenia was 14.5% in the KADCYLA-treated group and 0.4% in the comparator group (overall incidence 31.2% and 3.3%, respectively)
- Monitor platelet counts prior to initiation of KADCYLA and prior to each KADCYLA dose. Institute dose modifications as appropriate

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Institute dose modifications as appropriate

Neurotoxicity

- In EMILIA, the incidence of ≥ Grade 3 peripheral neuropathy was 2.2% in the KADCYLA-treated group and 0.2% in the comparator group (overall incidence 21.2% and 13.5%, respectively)
- Monitor for signs or symptoms of neurotoxicity. KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2

HER2 Testing

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA. Perform using FDA approved tests by laboratories with demonstrated proficiency

Extravasation

- In KADCYLA clinical studies, reactions

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Safety first! Read below to see the Important Safety Information

- In KADCYLA clinical studies, reactions secondary to extravasation have been observed and were generally mild. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Specific treatment for KADCYLA extravasation is unknown

Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

Adverse Reactions

- The most common ADRs seen with KADCYLA in EMILIA (frequency > 25%) were nausea, fatigue, musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency > 2%) were thrombocytopenia, increased

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importance of the drug to the mother

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You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling **1 (888) 835-2555**. You may contact the FDA by visiting **www.fda.gov/medwatch** or calling **1 (800) FDA-1088**.

Please see accompanying full Prescribing Information for additional important safety information, including Boxed WARNINGS.

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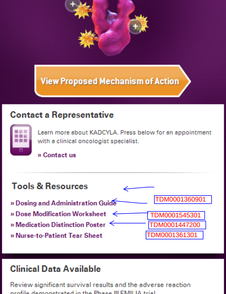
The first antibody-drug conjugate for the treatment of HER2-positive (HER2+) metastatic breast cancer (MBC)



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Tools & Resources

» Dosing and Administration Guide — TDM0001360901

» Dose Modification Worksheet — TDM0001545301

» Medication Distinction Poster — TDM0001447200

» Nurse-to-Patient Tear Sheet — TDM0001361301

Clinical Data Available

Review significant survival results and the adverse reaction profile demonstrated in the Phase III EMILIA trial.

» Learn more

Indication

KADCYLA® (ado-trastuzumab emtansine), as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:

- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy

Important Safety Information

Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY

- **Do Not Substitute KADCYLA for or with Trastuzumab**
- **Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin**
- **Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function**
- **Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception**

Additional Important Safety Information:

Left Ventricular Dysfunction (LVD)

- Patients treated with KADCYLA are at increased risk of developing LVD. In EMILIA, LVD occurred in 1.8% of patients in the KADCYLA-treated group and in 3.3% in the comparator group. Permanently discontinue KADCYLA if LVEF has not improved or has declined further

Pregnancy Registry

- Advise patients to contact their healthcare provider immediately if they suspect they may be pregnant. Encourage women who may be exposed to KADCYLA during pregnancy to enroll in the **MotHER Pregnancy Registry** by contacting **1 (800) 690-6720**

Pulmonary Toxicity

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HER2 Testing

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Extravasation

- In KADCYLA clinical studies, reactions secondary to extravasation have been observed and were generally mild. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Specific treatment for KADCYLA extravasation is unknown

Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

Adverse Reactions

- The most common ADRs seen with KADCYLA in EMILIA (frequency > 25%) were nausea, fatigue, musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency > 2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue

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Please see accompanying full Prescribing Information for additional important safety information, including Boxed WARNINGS.

KADCYLA Access Solutions

Kadcyla ado-trastuzumab emtansine for injection | Access Solutions

KADCYLA Access Solutions helps to resolve access and reimbursement issues for individual patients every day. Our dedicated Specialists help bring patient treatment and practice solutions together.

Our staff can:

- Help confirm **benefits and coverage** and resolve any related issues
- Refer underinsured patients for **co-pay assistance**
- **Provide free medicine to qualified uninsured patients** through the Genentech® Access to Care Foundation (GATCF)
- **Individualize services** to meet your patients' specific needs

New! Unique C-code is now available for KADCYLA reimbursement. **Click here** for more information.

To speak live with one of our Specialists, call **1 (888) 249-4918**. You can also visit **Genentech-Access.com/KADCYLA** for more information.

Additional resources

- **Get KADCYLA Access Solutions information**
- **See the latest list of distributors**
- **Download the KADCYLA Material Safety Data Sheet**

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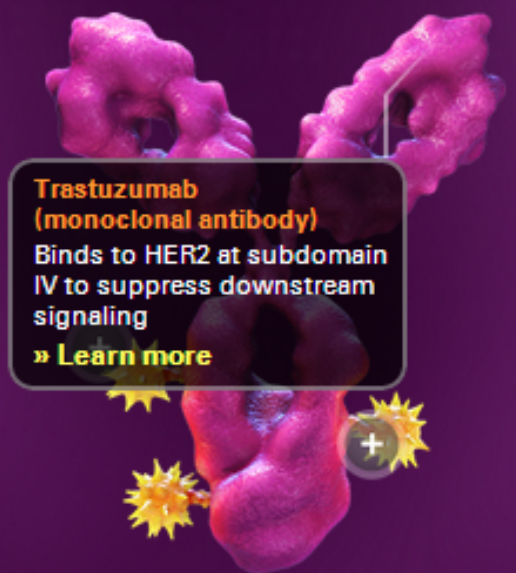
The first antibody-drug conjugate for the treatment of HER2-positive (HER2+) metastatic breast cancer (MBC)



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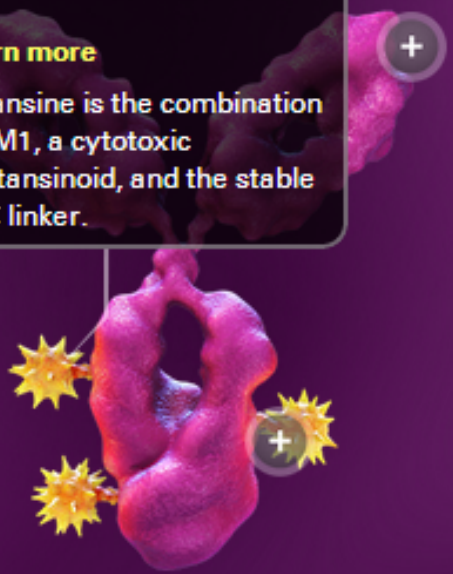
The first antibody-drug conjugate for the treatment of HER2-positive (HER2+) metastatic breast cancer (MBC)

DM1* (cytotoxic maytansinoid)
Inhibits tubulin polymerization to induce cell-cycle arrest and cell death

» Learn more

*Emtansine is the combination of DM1, a cytotoxic maytansinoid, and the stable MCC linker.



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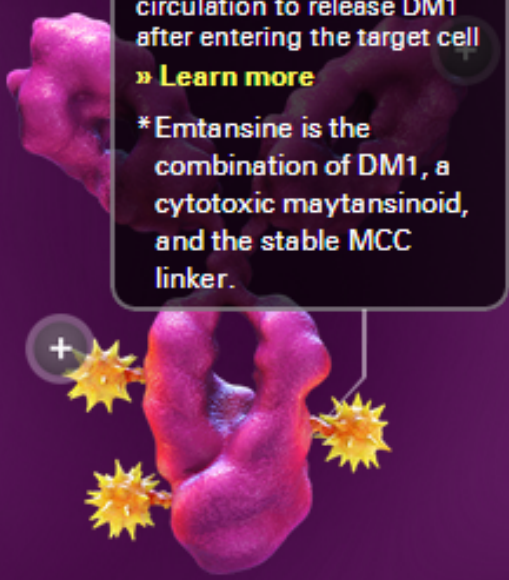

MCC* (stable linker)
Stabilizes KADCYLA in circulation to release DM1 after entering the target cell

» Learn more

*Emtansine is the combination of DM1, a cytotoxic maytansinoid, and the stable MCC linker.

View Proposed Mechanism of Action

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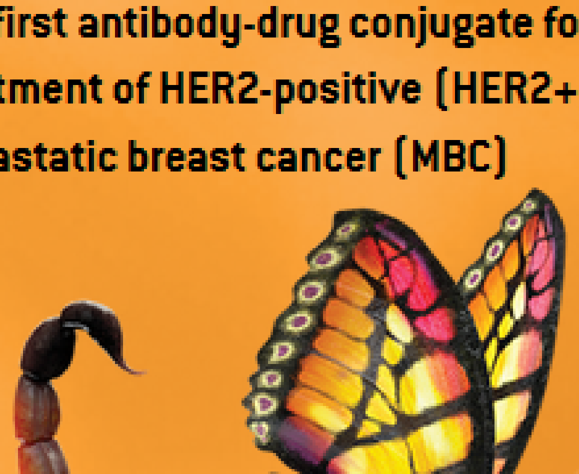

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Contact a Representative

Learn more about KADCYLA. Press below for an appointment with a clinical oncologist specialist.

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Tools & Resources

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- » Dose Modification Worksheet
- » Medication Distinction Poster
- » Nurse-to-Patient Tear Sheet

Clinical Data Available

Review significant survival results and the adverse reaction profile demonstrated in the Phase III EMILIA trial.

» Learn more

Indication

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Important Safety Information

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HER2 Testing

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA. Perform using FDA approved tests by laboratories with demonstrated proficiency

Extravasation

- In KADCYLA clinical studies, reactions secondary to extravasation have been observed and were generally mild. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Specific treatment for KADCYLA extravasation is unknown

Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

Adverse Reactions

- The most common ADRs seen with KADCYLA in EMILIA (frequency > 25%) were nausea, fatigue, musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency > 2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue

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KADCYLA Access Solutions

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Additional resources

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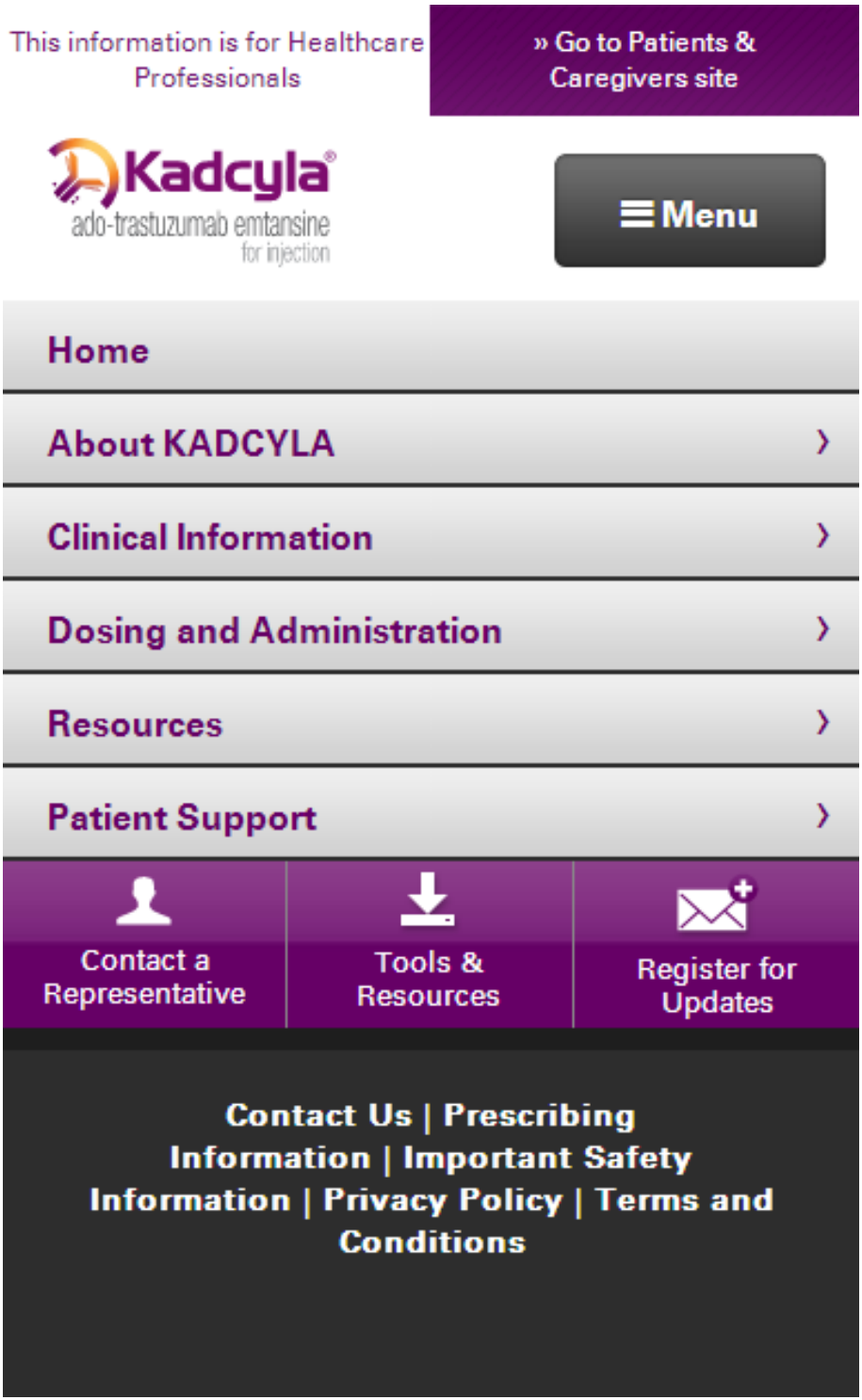
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Review significant survival results and the adverse reaction profile demonstrated in the Phase III EMILIA trial.

» Learn more

Indication

KADCYLA® (ado-trastuzumab emtansine), as a single a[illegible]s with HER2-p[illegible]C) who p[illegible], separately or in[illegible]

Audio Glossary ×

KADCYLA (ado-trastuzumab emtansine)

Hear it pronounced

[illegible]ease, or [illegible]within six months of completing adjuvant therapy

Important Safety Information

Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY

- **Do Not Substitute KADCYLA for or with Trastuzumab**
- **Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases**

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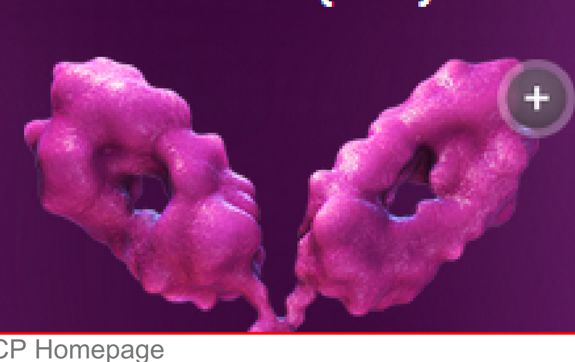
The first antibody-drug conjugate for the treatment of HER2-positive (HER2+) metastatic breast cancer (MBC)



Page Name: HCP Homepage
Page Title: KADCYLA® (ado-trastuzumab emtansine) Information for Healthcare Professionals
Meta Description: Find information for healthcare professionals about KADCYLA® (ado-trastuzumab emtansine), a treatment for HER2-positive metastatic breast cancer patients.
KADCYLA® (ado-trastuzumab emtansine), injection for intravenous use, as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either: Received prior therapy for metastatic disease, or Developed disease recurrence during or within six months of completing adjuvant therapy. Important Safety Information: Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYOFETAL TOXICITY: Do Not Substitute KADCYLA for or with Trastuzumab, Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each. KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin, Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function, Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception. The following additional serious adverse reactions have been reported in clinical trials with KADCYLA: Interstitial Lung Disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatality: KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis, Infusion-related reactions (IRR), Hypersensitivity: KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR, Thrombocytopenia: Monitor platelet counts prior to initiation of KADCYLA and prior to each dose. Institute dose modifications as appropriate, Peripheral neuropathy: KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2, Reactions secondary to extravasation: The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Additional Important Safety Information: Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA therapy, Nursing mothers: Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother, The most common adverse drug reactions (frequency > 25%) across clinical trials with KADCYLA were fatigue, nausea, musculoskeletal pain, thrombocytopenia, headache, increased transaminases, and constipation. You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling 1-888-835-2555. You may contact

Review significant survival results and the adverse reaction profile demonstrated in the Phase III EMILIA trial.

» Learn more

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- **Do Not Substitute KADCYLA for or with Trastuzumab**
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- **Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function**
- **Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception**

Additional Important Safety Information:

Left Ventricular Dysfunction (LVD)

- Patients treated with KADCYLA are at increased risk of developing LVD. In EMILIA, LVD occurred in 1.8% of patients in the KADCYLA-treated group and in 3.3% in the comparator group. Permanently discontinue KADCYLA if LVEF has not improved or has declined further

Pregnancy Registry

- Advise patients to contact their healthcare provider immediately if they suspect they may be pregnant. Encourage women who may be exposed to KADCYLA during pregnancy to enroll in the **MotHER Pregnancy Registry** by contacting **1 (800) 690-6720**

Pulmonary Toxicity

- Cases of interstitial lung disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatal outcome have been reported in clinical trials with KADCYLA. In EMILIA, the overall frequency of pneumonitis was 1.2%
- Treatment with KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis

Infusion-Related Reactions, Hypersensitivity Reactions

- Treatment with KADCYLA has not been studied in patients who had trastuzumab permanently discontinued due to infusion-related reactions (IRR) and/or hypersensitivity reactions; treatment with KADCYLA is not recommended for these patients. In EMILIA, the overall frequency of IRRs in patients treated with KADCYLA was 1.4%
- KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR. Patients should be closely monitored for IRR reactions, especially during the first infusion

Thrombocytopenia

- In EMILIA, the incidence of ≥ Grade 3 thrombocytopenia was 14.5% in the KADCYLA-treated group and 0.4% in the comparator group (overall incidence 31.2% and 3.3%, respectively)
- Monitor platelet counts prior to initiation of KADCYLA and prior to each KADCYLA dose. Institute dose modifications as appropriate

Neurotoxicity

- In EMILIA, the incidence of ≥ Grade 3 peripheral neuropathy was 2.2% in the KADCYLA-treated group and 0.2% in the comparator group (overall incidence 21.2% and 13.5%, respectively)
- Monitor for signs or symptoms of neurotoxicity. KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2

HER2 Testing

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA. Perform using FDA approved tests by laboratories with demonstrated proficiency

Extravasation

- In KADCYLA clinical studies, reactions secondary to extravasation have been observed and were generally mild. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Specific treatment for KADCYLA extravasation is unknown

Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

Adverse Reactions

- The most common ADRs seen with KADCYLA in EMILIA (frequency > 25%) were nausea, fatigue, musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency > 2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue

You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling **1 (888) 835-2555**. You may contact the FDA by visiting **www.fda.gov/medwatch** or calling **1 (800) FDA-1088**.

Please see accompanying full Prescribing Information for additional important safety information, including Boxed WARNINGS.

KADCYLA Access Solutions

Kadcyla® ado-trastuzumab emtansine for injection | Access Solutions®

KADCYLA Access Solutions helps to resolve access and reimbursement issues for individual patients every day. Our dedicated Specialists help bring patient treatment and practice solutions together.

Our staff can:

- Help confirm **benefits and coverage** and resolve any related issues
- Refer underinsured patients for **co-pay assistance**
- **Provide free medicine to qualified uninsured patients** through the Genentech® Access to Care Foundation (GATCF)
- **Individualize services** to meet your patients' specific needs

New! Unique C-code is now available for KADCYLA reimbursement. **Click here** for more information.

To speak live with one of our Specialists, call **1 (888) 249-4918**. You can also visit **Genentech-Access.com/KADCYLA** for more information.

Additional resources

- **Get KADCYLA Access Solutions information**
- **See the latest list of distributors**
- **Download the KADCYLA Material Safety Data Sheet**

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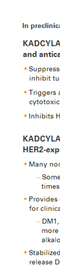
About KADCYLA

IN THIS SECTION
» KADCYLA Structure
» Proposed MOA

The first HER2-targeted ADC

KADCYLA: A single agent with 3 components[1-3]



In preclinical studies

KADCYLA maintains the HER2 suppression and anticancer activities of trastuzumab[1]

- Suppresses downstream signaling pathways to inhibit tumor cell proliferation and survival[1,4]
- Triggers antibody-dependent cell-mediated cytotoxicity (ADCC)[1]
- Inhibits HER2 shedding[1]

KADCYLA delivers cytotoxic DM1 to target HER2-expressing cells

- Many normal cells express HER2[5]
  - Some cancer cells overexpress up to 200 times more HER2 than normal cells
- Provides cytotoxicity previously unavailable for clinical use[1,2]
  - DM1, a maytansinoid, is 20 to 200 times more potent than taxanes and vinca alkaloids[2]
- Stabilized in circulation by the MCC linker to release DM1 inside the target cell[1]

ADC=antibody-drug conjugate.

Next: See Proposed MOA

Indication

KADCYLA® (ado-trastuzumab emtansine), as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:

- Received prior therapy for metastatic disease, or
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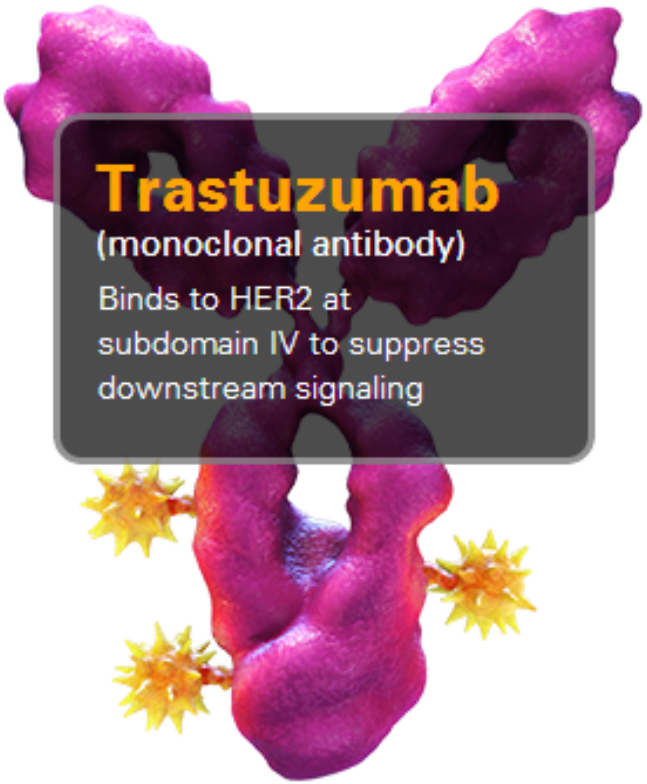
» Proposed MOA

The first HER2-targeted ADC

KADCYLA: A single agent with 3 components[1-3]



In preclinical studies

KADCYLA maintains the HER2 suppression

IN THIS SECTION

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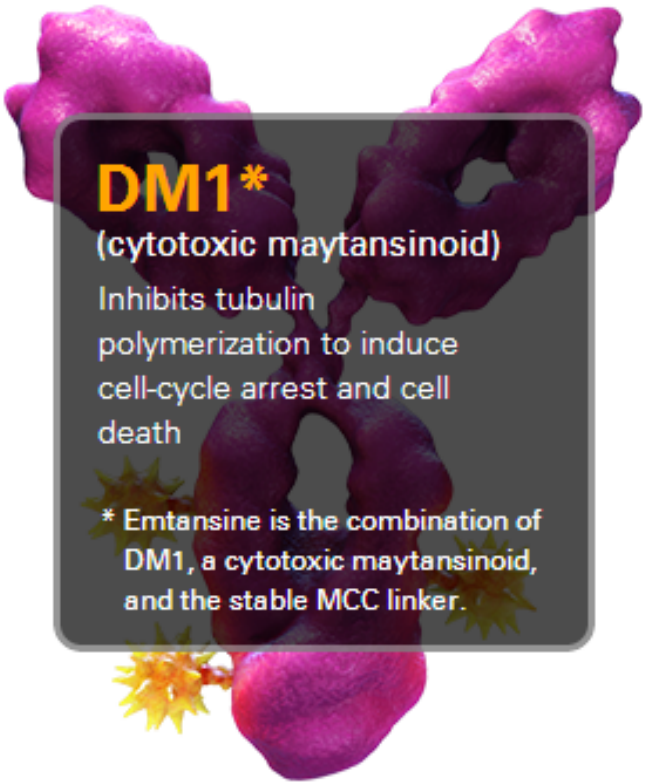
» Proposed MOA

The first HER2-targeted ADC

KADCYLA: A single agent with 3 components[1-3]



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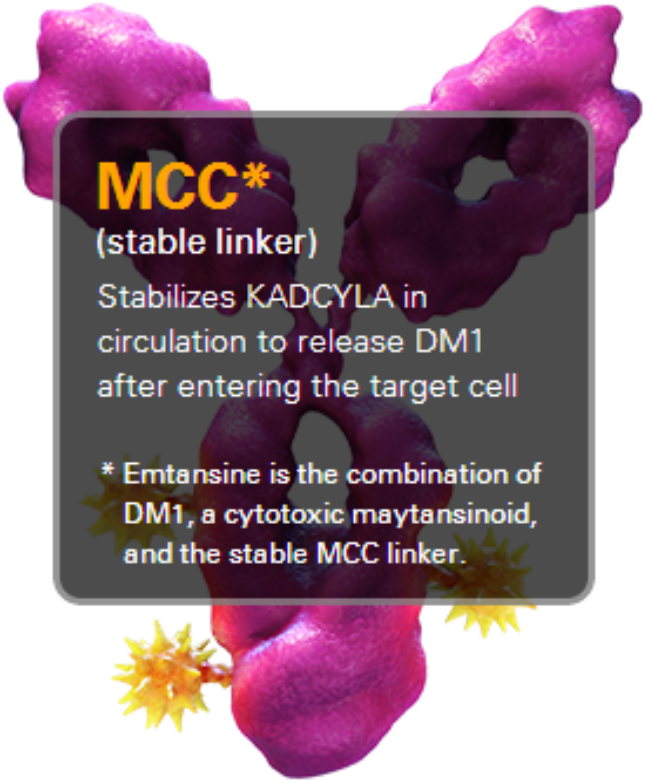

In preclinical studies

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About KADCYLA

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The first HER2-targeted ADC

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Page Name: KADCYLA Structure
Page Title: HER2-Targeted ADC Structure | KADCYLA® (ado-trastuzumab emtansine)
Meta Description: Learn more about the components of KADCYLA® (ado-trastuzumab emtansine) as the first HER2-targeted anti-drug conjugate.
KADCYLA® (ado-trastuzumab emtansine), injection for intravenous use, as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either: Received prior therapy for metastatic disease, or Developed disease recurrence during or within six months of completing adjuvant therapy. Important Safety Information: Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYOFETAL TOXICITY: Do Not Substitute KADCYLA for or with Trastuzumab, Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each. KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin, Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function, Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception. The following additional serious adverse reactions have been reported in clinical trials with KADCYLA: Interstitial Lung Disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatality: KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis, Infusion-related reactions (IRR), Hypersensitivity: KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR, Thrombocytopenia: Monitor platelet counts prior to initiation of KADCYLA and prior to each dose. Institute dose modifications as appropriate, Peripheral neuropathy: KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2, Reactions secondary to extravasation: The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Additional Important Safety Information: Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA therapy, Nursing mothers: Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother, The most common adverse drug reactions (frequency > 25%) across clinical trials with KADCYLA were fatigue, nausea, musculoskeletal pain, thrombocytopenia, headache, increased transaminases, and constipation. You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling 1-888-835-2555. You may contact the FDA by visiting www.fda.gov/medwatch or calling 1-800-FDA-1088.

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- Many normal cells express HER2[5]
  - Some cancer cells overexpress up to 200 times more HER2 than normal cells
- Provides cytotoxicity previously unavailable for clinical use[1,2]
  - DM1, a maytansinoid, is 20 to 200 times more potent than taxanes and vinca alkaloids[2]
- Stabilized in circulation by the MCC linker to release DM1 inside the target cell[1]

ADC=antibody-drug conjugate.

Next: See Proposed MOA

Indication

KADCYLA® (ado-trastuzumab emtansine), as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:

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Important Safety Information

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Additional Important Safety Information:

Left Ventricular Dysfunction (LVD)

- Patients treated with KADCYLA are at increased risk of developing LVD. In EMILIA, LVD occurred in 1.8% of patients in the KADCYLA-treated group and in 3.3% in the comparator group. Permanently discontinue KADCYLA if LVEF has not improved or has declined further

Pregnancy Registry

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Pulmonary Toxicity

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- KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR. Patients should be closely monitored for IRR reactions, especially during the first infusion

Thrombocytopenia

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Extravasation

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Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

Adverse Reactions

- The most common ADRs seen with KADCYLA in EMILIA (frequency > 25%) were nausea, fatigue, musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency > 2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue

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Safety first! Press here to read the Important Safety Information

About KADCYLA

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» KADCYLA Structure

» Proposed MOA

Multiple antitumor activities from a single agent

Proposed mechanism of action for KADCYLA, based on preclinical models[1,2]

» VIEW THE FULL ANIMATION BELOW

Proposed MOA

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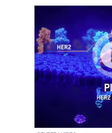

SELECT A VIDEO

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Animated MOA

MOA Video with Audio

Next: See Clinical Information

Contact a Representative

Want to discuss the KADCYLA proposed MOA?

Talk to a representative about getting the KADCYLA MOA Brochure

› Contact Us

Indication

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Multiple antitumor activities from a single agent

Proposed mechanism of action for KADCYLA, based on preclinical models[1,2]

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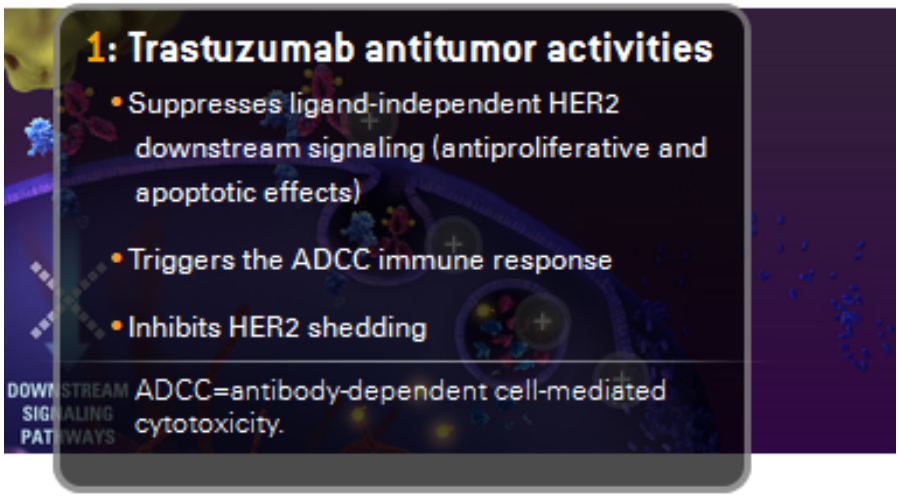

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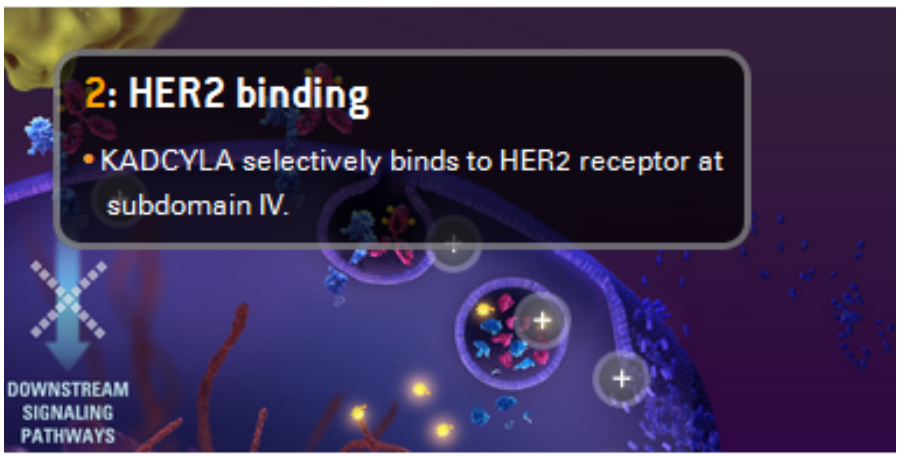
Proposed mechanism of action for KADCYLA, based on preclinical models[1,2]

›› VIEW THE FULL ANIMATION BELOW



Proposed MOA

Multiple antitumor activities from a single agent

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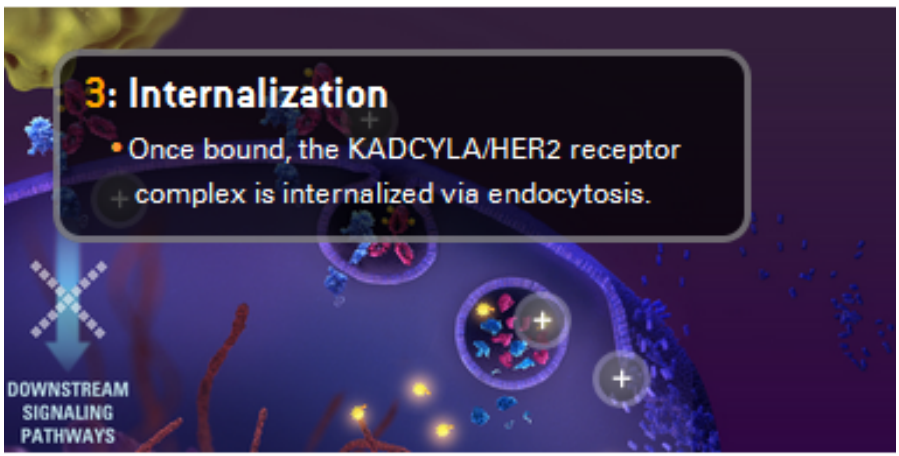

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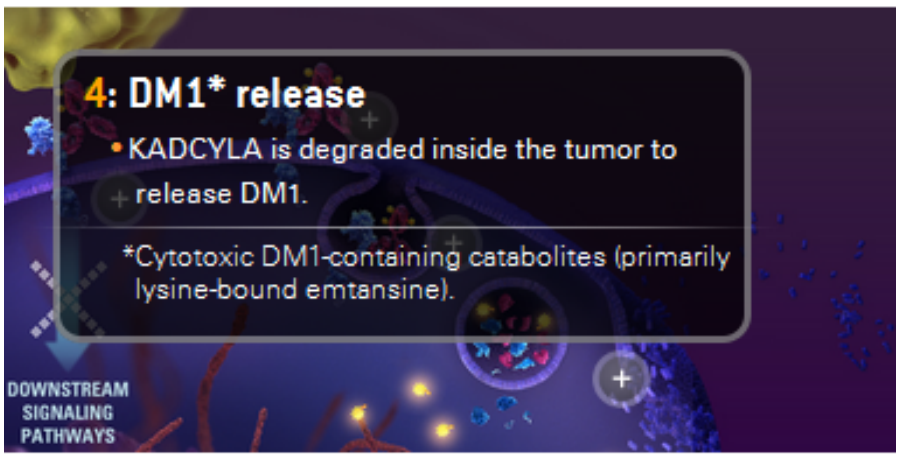

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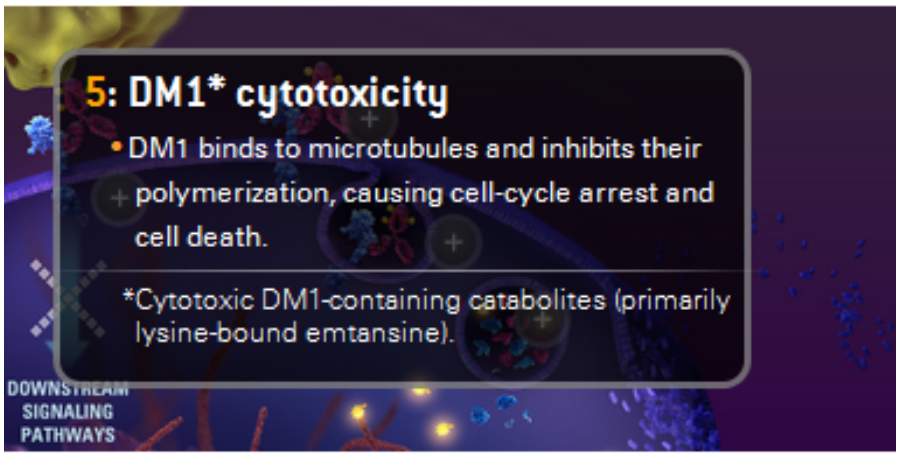

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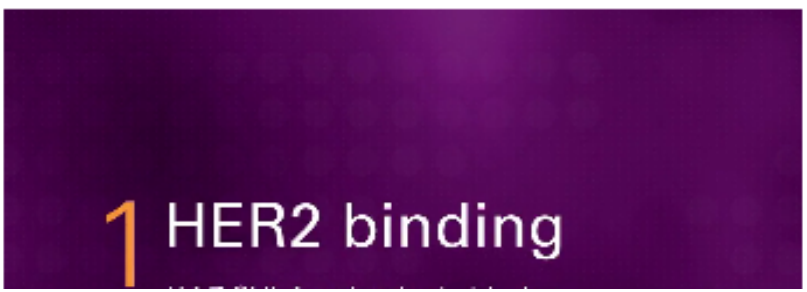

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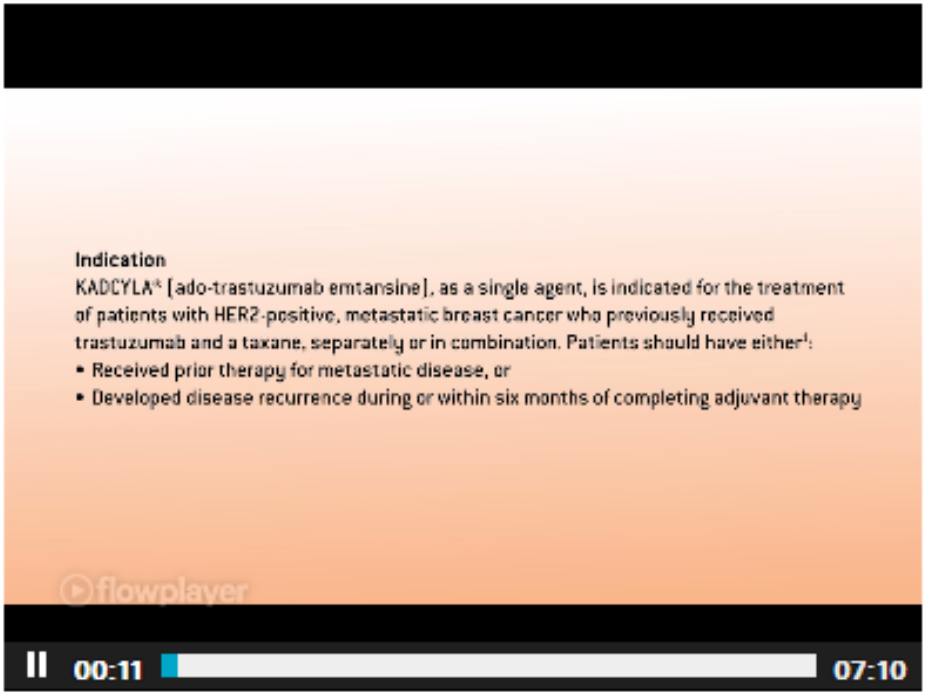
Proposed MOA



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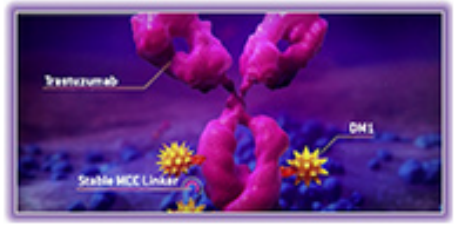
MOA Video with Audio



About KADCYLA

IN THIS SECTION

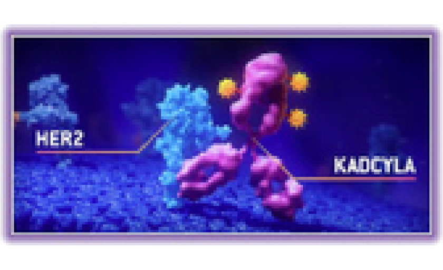
» KADCYLA Structure

» Proposed MOA

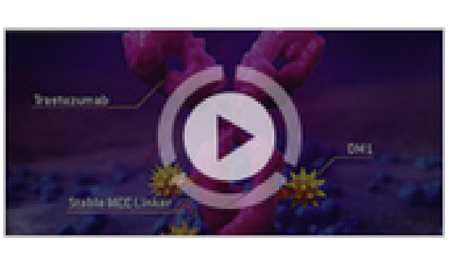
Multiple antitumor activities from a single agent

Page Name: Proposed MOA
Page Title: Mechanism of Action | KADCYLA® (ado-trastuzumab emtansine)
Meta Description: Learn more about the proposed mechanism of action for KADCYLA® (ado-trastuzumab emtansine) based on preclinical models.
KADCYLA® (ado-trastuzumab emtansine), injection for intravenous use, as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either: Received prior therapy for metastatic disease, or Developed disease recurrence during or within six months of completing adjuvant therapy. Important Safety Information: Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYOFETAL TOXICITY: Do Not Substitute KADCYLA for or with Trastuzumab, Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each. KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin, Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function, Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception. The following additional serious adverse reactions have been reported in clinical trials with KADCYLA: Interstitial Lung Disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatality: KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis, Infusion-related reactions (IRR), Hypersensitivity: KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR, Thrombocytopenia: Monitor platelet counts prior to initiation of KADCYLA and prior to each dose. Institute dose modifications as appropriate, Peripheral neuropathy: KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2, Reactions secondary to extravasation: The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Additional Important Safety Information: Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA therapy, Nursing mothers: Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother, The most common adverse drug reactions (frequency > 25%) across clinical trials with KADCYLA were fatigue, nausea, musculoskeletal pain, thrombocytopenia, headache, increased transaminases, and constipation. You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling 1-888-835-2555. You may contact the FDA by visiting www.fda.gov/medwatch or calling

Animated MOA



MOA Video with Audio



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Contact a Representative

Want to discuss the KADCYLA proposed MOA?

Talk to a representative about getting the KADCYLA MOA Brochure

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Indication

KADCYLA® (ado-trastuzumab emtansine), as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:

- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy

Important Safety Information

Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY

- **Do Not Substitute KADCYLA for or with Trastuzumab**
- **Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin**
- **Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function**
- **Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception**

Additional Important Safety Information:

Left Ventricular Dysfunction (LVD)

- Patients treated with KADCYLA are at increased risk of developing LVD. In EMILIA, LVD occurred in 1.8% of patients in the KADCYLA-treated group and in 3.3% in the comparator group. Permanently discontinue KADCYLA if LVEF has not improved or has declined further

Pregnancy Registry

- Advise patients to contact their healthcare provider immediately if they suspect they may be pregnant. Encourage women who may be exposed to KADCYLA during pregnancy to enroll in the **MotHER Pregnancy Registry** by contacting **1 (800) 690-6720**

Pulmonary Toxicity

- Cases of interstitial lung disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatal outcome have been reported in clinical trials with KADCYLA. In EMILIA, the overall frequency of pneumonitis was 1.2%
- Treatment with KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis

Infusion-Related Reactions, Hypersensitivity Reactions

- Treatment with KADCYLA has not been studied in patients who had trastuzumab permanently discontinued due to infusion-related reactions (IRR) and/or hypersensitivity reactions; treatment with KADCYLA is not recommended for these patients. In EMILIA, the overall frequency of IRRs in patients treated with KADCYLA was 1.4%
- KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR. Patients should be closely monitored for IRR reactions, especially during the first infusion

Thrombocytopenia

- In EMILIA, the incidence of ≥ Grade 3 thrombocytopenia was 14.5% in the KADCYLA-treated group and 0.4% in the comparator group (overall incidence 31.2% and 3.3%, respectively)
- Monitor platelet counts prior to initiation of KADCYLA and prior to each KADCYLA dose. Institute dose modifications as appropriate

Neurotoxicity

- In EMILIA, the incidence of ≥ Grade 3 peripheral neuropathy was 2.2% in the KADCYLA-treated group and 0.2% in the comparator group (overall incidence 21.2% and 13.5%, respectively)
- Monitor for signs or symptoms of neurotoxicity. KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2

HER2 Testing

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA. Perform using FDA approved tests by laboratories with demonstrated proficiency

Extravasation

- In KADCYLA clinical studies, reactions secondary to extravasation have been observed and were generally mild. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Specific treatment for KADCYLA extravasation is unknown

Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

Adverse Reactions

- The most common ADRs seen with KADCYLA in EMILIA (frequency > 25%) were nausea, fatigue, musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency > 2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue

You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling **1 (888) 835-2555**. You may contact the FDA by visiting **www.fda.gov/medwatch** or calling **1 (800) FDA-1088**.

Please see accompanying full Prescribing Information for additional important safety information, including Boxed WARNINGS.

References: 1. KADCYLA Prescribing Information. Genentech, Inc. May 2013. **2.** Scheuer W, Friess T, Burtscher H, Bossenmaier B, Endl J, Hassmann M. Strongly enhanced antitumor activity of trastuzumab and pertuzumab combination treatment on HER2-positive human xenograft tumor models. *Cancer Res.* 2009;69:9330-9336.

This information is for Healthcare Professionals

» Go to Patients & Caregivers site

Kadcyla® ado-trastuzumab emtansine for injection

Menu

Safety first! Press here to read the Important Safety Information

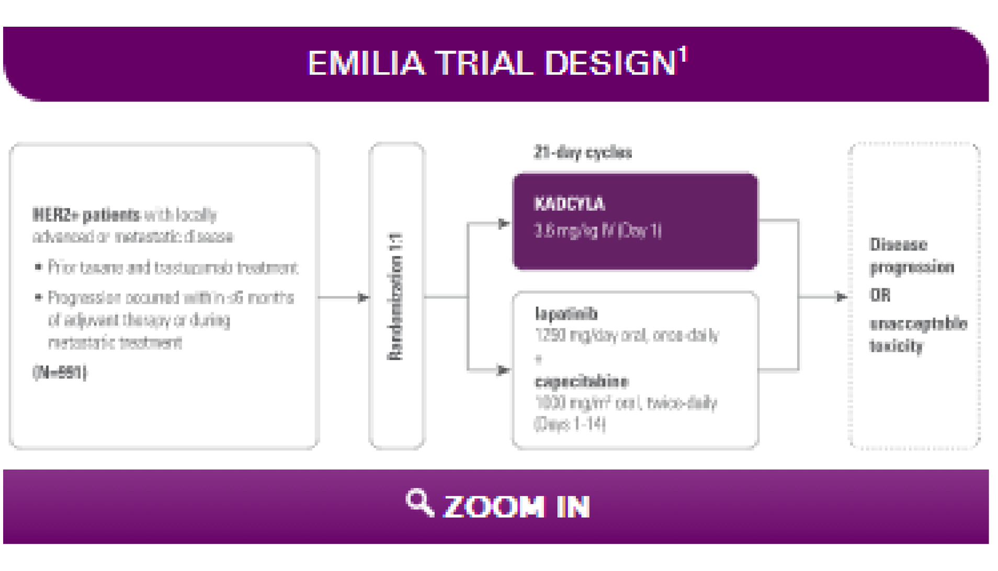
Clinical Information

Demonstrated benefit in a well-designed clinical trial

Efficacy and safety were demonstrated in HER2-positive (HER2+) metastatic breast cancer (MBC) patients previously treated with trastuzumab and a taxane[1]

- The EMILIA trial was a large (N=991), Phase III, multi-institutional, randomized trial in patients with HER2+ unresectable locally advanced or MBC

EMILIA TRIAL DESIGN[1]



ZOOM IN

Trial endpoints

- **Primary endpoints:** Progression-free survival (PFS) by independent review committee (IRC), overall survival (OS), safety[2]
- **Key secondary endpoints:** PFS by investigator review, objective response rate (ORR), duration of response (DoR), and time to symptom progression (TTP)[1]

The *National Comprehensive Cancer Network Guidelines (NCCN Guidelines)®—Breast Cancer* recommend KADCYLA as a preferred agent for HER2+ recurrent or metastatic trastuzumab-exposed disease (Category 2A)[3]*

Patient baseline characteristics were well balanced between treatment arms

Most patients (88%) had received one or more lines of systemic therapy in the metastatic setting[1]

- 12% of patients received only neoadjuvant or adjuvant therapy and had disease relapse during or within 6 months of completing treatment

SELECTED BASELINE PATIENT CHARACTERISTICS[1,2,4,5]

	KADCYLA (n=495)	lapatinib + capecitabine (n=496)
Median age, years (range)	**53** (25-84)	53 (24-83)
Race, % (n)		
White	**72** (358)	75 (374)
Asian	**19** (94)	17 (86)
Black/African American	**6** (29)	4 (21)
Other	**1** (7)	2 (10)
Not available	**1** (7)	1 (5)
ECOG PS, % (n)		
0	**60** (299)	63 (312)
1	**39** (194)	36 (176)
Measurable disease by IRC, % (n)		
Yes	**80** (397)	78 (389)
Metastatic sites, % (n)		
<3	**61** (298)	62 (307)
≥3	**37** (189)	35 (175)
Unknown	**2** (8)	3 (14)
Hormonal status, % (n)		
ER+ and/or PR+	**57** (282)	53 (263)
ER- and PR-	**41** (202)	45 (224)
Unknown	**2** (11)	2 (9)
Prior treatment type, % (n)		
Chemotherapy (anthracycline)	**61** (303)	61 (302)
Chemotherapy (other)	**78** (385)	77 (382)
Hormonal therapy	**41** (205)	41 (204)
Trastuzumab	**100** (495)	100 (496)
Prior trastuzumab treatment, % (n)		
MBC (±EBC)	**100** (495)	100 (496)
EBC only	**16** (78)	16 (77)
Duration of prior trastuzumab treatment, % (n)		
<1 year	**42** (210)	43 (212)
≥1 year	**58** (285)	57 (284)

ZOOM IN

ECOG PS=Eastern Cooperative Oncology Group performance status; IRC=independent review committee; ER=estrogen receptor; PR=progesterone receptor; EBC=early breast cancer.

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Next: See Clinical Efficacy Results

Indication

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Important Safety Information

Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY

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The following additional serious adverse reactions have been reported in clinical trials with KADCYLA:

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- Infusion-related reactions (IRR), Hypersensitivity: KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR
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- Peripheral neuropathy: KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2
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Additional Important Safety Information:

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA therapy
- Nursing mothers: Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother
- The most common adverse drug reactions (frequency > 25%) across clinical trials with KADCYLA were fatigue, nausea, musculoskeletal pain, thrombocytopenia, headache, increased transaminases, and constipation

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Clinical Information

Demonstrated benefit in a well-designed clinical trial

Page Name: EMILIA Overview
Page Title: EMILIA Clinical Trial Design | KADCYLA® (ado-trastuzumab emtansine)
Meta Description: Learn about the efficacy of KADCYLA® (ado-trastuzumab emtansine) and safety in HER2+ metastatic breast cancer patients previously treated with trastuzumab and a taxane from the EMILIA Trial.
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References: 1. KADCYLA Prescribing Information. Genentech, Inc. May 2013. **2.** Verma S, Miles D, Gianni L, et al; EMILIA Study Group. Trastuzumab emtansine for HER2-positive advanced breast cancer [published correction appears in *N Engl J Med.* 2013;368:2442]. *N Engl J Med.* 2012;367:1783-1791 and Supplementary Appendix. **3.** National Comprehensive Cancer Network. *National Clinical Practice Guidelines in Oncology (NCCN Guidelines)® Breast Cancer.* Version 3.2013. **http://www.nccn.org/professionals/physician_gls/pdf/b** Accessed June 26, 2013. **4.** Verma S, Miles D, Gianni L, et al. Updated overall survival results from EMILIA, a phase 3 study of trastuzumab emtansine (T-DM1) vs capecitabine and lapatinib in HER2-positive locally advanced or metastatic breast cancer. Presented at: European Society of Medical Oncology (ESMO) Congress; September 28-October 2, 2012; Vienna, Austria. **5.** Data on file. Genentech, Inc.

Safety first! Press here to read the Important Safety Information

Clinical Information

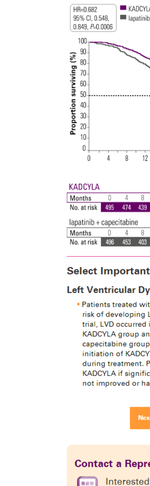
Results from the Phase III EMILIA trial comparing KADCYLA to lapatinib + capecitabine

Proven survival benefit

KADCYLA extended median OS by nearly 6 months[1]

- 30.9 months with KADCYLA vs 25.1 months with lapatinib + capecitabine; *P*=0.0006

PRIMARY ENDPOINT: OVERALL SURVIVAL (OS)[1]



KADCYLA											
Months	0	4	8	12	16	20	24	28	32	36	
No. at risk	495	474	428	349	242	164	111	62	28	5	

lapatinib + capecitabine											
Months	0	4	8	12	16	20	24	28	32	36	
No. at risk	496	453	403	297	204	133	86	45	17	4	

Select Important Safety Information:

Left Ventricular Dysfunction (LVD)

- Patients treated with KADCYLA are at increased risk of developing LVD. In the Phase III EMILIA trial, LVD occurred in 1.8% of patients in the KADCYLA group and in 3.3% in the lapatinib + capecitabine group. Assess LVEF prior to initiation of KADCYLA and at regular intervals during treatment. Permanently discontinue KADCYLA if significant decreases in LVEF have not improved or have declined further

Next: See Progression-Free Survival

Contact a Representative

Interested in additional information about EMILIA endpoints?

Talk to a representative about getting the Verma paper in *The New England Journal of Medicine*

› Contact Us

Indication

KADCYLA® (ado-trastuzumab emtansine), as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:

- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy

Important Safety Information

Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY

- **Do Not Substitute KADCYLA for or with Trastuzumab**
- **Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin**
- **Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function**
- **Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception**

Additional Important Safety Information:

Left Ventricular Dysfunction (LVD)

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Pregnancy Registry

- Advise patients to contact their healthcare provider immediately if they suspect they may be pregnant. Encourage women who may be exposed to KADCYLA during pregnancy to enroll in the **MotHER Pregnancy Registry** by contacting **1 (800) 690-6720**

Pulmonary Toxicity

- Cases of interstitial lung disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatal outcome have been reported in clinical trials with KADCYLA. In EMILIA, the overall frequency of pneumonitis was 1.2%
- Treatment with KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis

Infusion-Related Reactions, Hypersensitivity Reactions

- Treatment with KADCYLA has not been studied in patients who had trastuzumab permanently discontinued due to infusion-related reactions (IRR) and/or hypersensitivity reactions; treatment with KADCYLA is not recommended for these patients. In EMILIA, the overall frequency of IRRs in patients treated with KADCYLA was 1.4%
- KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR. Patients should be closely monitored for IRR reactions, especially during the first infusion

Thrombocytopenia

- In EMILIA, the incidence of ≥ Grade 3 thrombocytopenia was 14.5% in the KADCYLA-treated group and 0.4% in the comparator group (overall incidence 31.2% and 3.3%, respectively)
- Monitor platelet counts prior to initiation of KADCYLA and prior to each KADCYLA dose. Institute dose modifications as appropriate

Neurotoxicity

- In EMILIA, the incidence of ≥ Grade 3 peripheral neuropathy was 2.2% in the KADCYLA-treated group and 0.2% in the comparator group (overall incidence 21.2% and 13.5%, respectively)
- Monitor for signs or symptoms of neurotoxicity. KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2

HER2 Testing

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA. Perform using FDA approved tests by laboratories with demonstrated proficiency

Extravasation

- In KADCYLA clinical studies, reactions secondary to extravasation have been observed and were generally mild. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Specific treatment for KADCYLA extravasation is unknown

Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

Adverse Reactions

- The most common ADRs seen with KADCYLA in EMILIA (frequency > 25%) were nausea, fatigue, musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency > 2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue

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Progenix v. Immunogen
IPR2014-00976

Safety first! Press here to read the Important Safety Information

Clinical Information

Results from the Phase III EMILIA trial comparing KADCYLA® to lapatinib + capecitabine

Select Important Safety Information:

Left Ventricular Dysfunction (LVD)

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Important Safety Information

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Pregnancy Registry

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Pulmonary Toxicity

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HER2 Testing

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Extravasation

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Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

Adverse Reactions

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Clinical Information

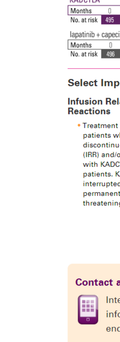
Results from the Phase III EMILIA trial comparing KADCYLA to lapatinib + capecitabine

Significantly improved median PFS

50% improvement in median PFS by independent review[1]

- 9.6 months median PFS with KADCYLA vs 6.4 months with lapatinib + capecitabine; P<0.0001

PRIMARY ENDPOINT: PROGRESSION-FREE SURVIVAL (PFS)[1]



KADCYLA										
Months	0	4	8	12	16	20	24	28	30	
No. at risk	495	341	183	101	54	30	9	1	0	
lapatinib + capecitabine										
Months	0	4	8	12	16	20	24	28	30	
No. at risk	496	310	129	53	25	9	5	0	0	

Select Important Safety Information:

Infusion Related/Hypersensitivity Reactions

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Next: See Objective Response Rate

Indication

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- **Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception**

Additional Important Safety Information:

Left Ventricular Dysfunction (LVD)

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Pregnancy Registry

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Pulmonary Toxicity

- Cases of interstitial lung disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatal outcome have been reported in clinical trials with KADCYLA. In EMILIA, the overall frequency of pneumonitis was 1.2%
- Treatment with KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis

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Neurotoxicity

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Safety first! Press here to read the Important Safety Information

Clinical Information

Results

KADCYLA									
Months	0	4	8	12	16	20	24	28	30
No. at risk	495	341	183	101	54	30	9	3	0

lapatinib + capecitabine									
Months	0	4	8	12	16	20	24	28	30
No. at risk	496	310	129	53	25	9	5	0	0

Select Important Safety Information:

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Next: See Objective Response Rate

Contact a Representative

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› Contact Us

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Pregnancy Registry

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Pulmonary Toxicity

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- Treatment with KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis

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Thrombocytopenia

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IMMUNOGEN 2226, pg. 35
Progenx v. Immunogen
IPR2014-00978

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Clinical Information

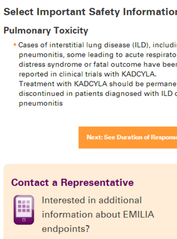
Results from the Phase III EMILIA trial comparing KADCYLA to lapatinib + capecitabine

Achieved superior tumor response rates

KADCYLA was shown to shrink tumors in more patients[1,2]

- More patients had a complete response (1.0% vs 0.5%) or partial response (42.6% vs 30.3%) with KADCYLA than with lapatinib + capecitabine

OBJECTIVE RESPONSE RATE (ORR)[1]



ZOOM IN

ORR defined as the proportion of patients who achieved a complete response (disappearance of all target tumors) or a partial response (≥30% decrease in the sum of the longest diameters of target tumors) based on Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1.[1,4]

Select Important Safety Information:

Pulmonary Toxicity

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Next: See Duration of Response

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Thrombocytopenia

- In EMILIA, the incidence of ≥ Grade 3 thrombocytopenia was 14.5% in the KADCYLA-treated group and 0.4% in the comparator group (overall incidence 31.2% and 3.3%, respectively)
- Monitor platelet counts prior to initiation of KADCYLA and prior to each KADCYLA dose. Institute dose modifications as appropriate

Neurotoxicity

- In EMILIA, the incidence of ≥ Grade 3 peripheral neuropathy was 2.2% in the KADCYLA-treated group and 0.2% in the comparator group (overall incidence 21.2% and 13.5%, respectively)
- Monitor for signs or symptoms of neurotoxicity. KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2

HER2 Testing

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA. Perform using FDA approved tests by laboratories with demonstrated proficiency

Extravasation

- In KADCYLA clinical studies, reactions secondary to extravasation have been observed and were generally mild. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Specific treatment for KADCYLA extravasation is unknown

Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

Adverse Reactions

- The most common ADRs seen with KADCYLA in EMILIA (frequency > 25%) were nausea, fatigue, musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency > 2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue

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This information is for Healthcare Professionals

» Go to Patients & Caregivers site

Kadcyla®
ado-trastuzumab emtansine
for injection

Menu

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Clinical Information

Results from the Phase III EMILIA trial comparing KADCYLA to lapatinib + capecitabine

Achieved superior tumor response rates

Page Name: Objective Response Rate
Page Title: Objective Response Rate | KADCYLA® (ado-trastuzumab emtansine)
Meta Description: Learn more about response rates (ORR) for patients treated with KADCYLA® (ado-trastuzumab emtansine) compared to lapatinib+capecitabine.
KADCYLA® (ado-trastuzumab emtansine), injection for intravenous use, as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either: Received prior therapy for metastatic disease, or Developed disease recurrence during or within six months of completing adjuvant therapy. Important Safety Information: Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYOFETAL TOXICITY: Do Not Substitute KADCYLA for or with Trastuzumab, Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each. KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin, Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function, Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception. The following additional serious adverse reactions have been reported in clinical trials with KADCYLA:

Interstitial Lung Disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatality: KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis, Infusion-related reactions (IRR), Hypersensitivity: KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR, Thrombocytopenia: Monitor platelet counts prior to initiation of KADCYLA and prior to each dose. Institute dose modifications as appropriate, Peripheral neuropathy: KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2, Reactions secondary to extravasation: The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Additional Important Safety Information: Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA therapy, Nursing mothers: Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother, The most common adverse drug reactions (frequency > 25%) across clinical trials with KADCYLA were fatigue, nausea, musculoskeletal pain, thrombocytopenia, headache, increased transaminases, and constipation. You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling 1-888-835-2555. You may contact the FDA by visiting www.fda.gov/medwatch or calling 1-800-FDA-1088.

Pulmonary Toxicity

- Cases of interstitial lung disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatal outcome have been reported in clinical trials with KADCYLA. Treatment with KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis

Next: See Duration of Response

Contact a Representative

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› Contact Us

Indication

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- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy

Important Safety Information

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Additional Important Safety Information:

Left Ventricular Dysfunction (LVD)

- Patients treated with KADCYLA are at increased risk of developing LVD. In EMILIA, LVD occurred in 1.8% of patients in the KADCYLA-treated group and in 3.3% in the comparator group. Permanently discontinue KADCYLA if LVEF has not improved or has declined further

Pregnancy Registry

- Advise patients to contact their healthcare provider immediately if they suspect they may be pregnant. Encourage women who may be exposed to KADCYLA during pregnancy to enroll in the **MotHER Pregnancy Registry** by contacting **1 (800) 690-6720**

Pulmonary Toxicity

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Infusion-Related Reactions, Hypersensitivity Reactions

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HER2 Testing

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Extravasation

- In KADCYLA clinical studies, reactions secondary to extravasation have been observed and were generally mild. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Specific treatment for KADCYLA extravasation is unknown

Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

Adverse Reactions

- The most common ADRs seen with KADCYLA in

EMILIA (frequency > 25%) were nausea, fatigue, musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency > 2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue

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Clinical Information

Results from the Phase III EMILIA trial comparing KADCYLA to lapatinib + capecitabine

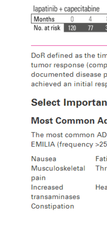
Sustained duration of response (DoR) beyond 1 year

Nearly doubled median DoR[1]

- 6.1 months improvement in median DoR was demonstrated (12.6 months vs 6.5 months with lapatinib + capecitabine)

DURATION OF RESPONSE (DoR)[2]

KADCYLA (n=173) 95% CI, 8.4-20.8
lapatinib + capecitabine (n=120) 95% CI, 5.5-7.2



KADCYLA

Months	0	4	8	12	16	20	24	28	30
No. at risk	173	126	65	42	27	12	2	0	0

lapatinib + capecitabine

Months	0	4	8	12	16	20	24	28	30
No. at risk	120	77	32	9	3	1	0	0	0

DoR defined as the time from initially documented tumor response (complete or partial) until documented disease progression. Only patients who achieved an initial response were evaluated for DoR.[2]

Select Important Safety Information:

Most Common Adverse Reactions

The most common ADRs seen with KADCYLA in EMILIA (frequency >25%) were:

- Nausea
- Musculoskeletal pain
- Increased transaminases
- Constipation
- Fatigue
- Thrombocytopenia
- Headache

Next: See Safety Information

Contact a Representative

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› Contact Us

Indication

KADCYLA® (ado-trastuzumab emtansine), as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:

- Received prior therapy for metastatic disease, or
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Important Safety Information

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- **Do Not Substitute KADCYLA for or with Trastuzumab**
- **Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin**
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Additional Important Safety Information:

Left Ventricular Dysfunction (LVD)

- Patients treated with KADCYLA are at increased risk of developing LVD. In EMILIA, LVD occurred in 1.8% of patients in the KADCYLA-treated group and in 3.3% in the comparator group. Permanently discontinue KADCYLA if LVEF has not improved or has declined further

Pregnancy Registry

- Advise patients to contact their healthcare provider immediately if they suspect they may be pregnant. Encourage women who may be exposed to KADCYLA during pregnancy to enroll in the **MotHER Pregnancy Registry** by contacting **1 (800) 690-6720**

Pulmonary Toxicity

- Cases of interstitial lung disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatal outcome have been reported in clinical trials with KADCYLA. In EMILIA, the overall frequency of pneumonitis was 1.2%
- Treatment with KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis

Infusion-Related Reactions, Hypersensitivity Reactions

- Treatment with KADCYLA has not been studied in patients who had trastuzumab permanently discontinued due to infusion-related reactions (IRR) and/or hypersensitivity reactions; treatment with KADCYLA is not recommended for these patients. In EMILIA, the overall frequency of IRRs in patients treated with KADCYLA was 1.4%
- KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR. Patients should be closely monitored for IRR reactions, especially during the first infusion

Thrombocytopenia

- In EMILIA, the incidence of ≥ Grade 3 thrombocytopenia was 14.5% in the KADCYLA-treated group and 0.4% in the comparator group (overall incidence 31.2% and 3.3%, respectively)
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- In EMILIA, the incidence of ≥ Grade 3 peripheral neuropathy was 2.2% in the KADCYLA-treated group and 0.2% in the comparator group (overall incidence 21.2% and 13.5%, respectively)
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HER2 Testing

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA. Perform using FDA approved tests by laboratories with demonstrated proficiency

Extravasation

- In KADCYLA clinical studies, reactions secondary to extravasation have been observed and were generally mild. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Specific treatment for KADCYLA extravasation is unknown

Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

Adverse Reactions

- The most common ADRs seen with KADCYLA in EMILIA (frequency > 25%) were nausea, fatigue, musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency > 2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue

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Clinical Information

Results from the Phase III EMILIA trial comparing KADCYLA to lapatinib + capecitabine

Sustained duration of

Page Name: Duration of Response
Page Title: Duration of Response | KADCYLA® (ado-trastuzumab emtansine)
Meta Description: Learn more about the duration of response (DoR) with KADCYLA® (ado-trastuzumab emtansine) compared to lapatinib +capecitabine.
KADCYLA® (ado-trastuzumab emtansine), injection for intravenous use, as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either: Received prior therapy for metastatic disease, or Developed disease recurrence during or within six months of completing adjuvant therapy. Important Safety Information: Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYOFETAL TOXICITY: Do Not Substitute KADCYLA for or with Trastuzumab, Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each. KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin, Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function, Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception. The following additional serious adverse reactions have been reported in clinical trials with KADCYLA: Interstitial Lung Disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatality: KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis, Infusion-related reactions (IRR), Hypersensitivity: KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR, Thrombocytopenia: Monitor platelet counts prior to initiation of KADCYLA and prior to each dose. Institute dose modifications as appropriate, Peripheral neuropathy: KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2, Reactions secondary to extravasation: The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Additional Important Safety Information: Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA therapy, Nursing mothers: Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother, The most common adverse drug reactions (frequency > 25%) across clinical trials with KADCYLA were fatigue, nausea, musculoskeletal pain, thrombocytopenia, headache, increased transaminases, and constipation. You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling 1-888-835-2555. You may contact the FDA by visiting

No. at risk	120	77	32	9	3	1	0	0	0

DoR defined as the time from initial documented tumor response (complete or partial) until documented disease progression. Only patients who achieved an initial response were evaluated for DoR.[3]

Select Important Safety Information:

Most Common Adverse Reactions

The most common ADRs seen with KADCYLA in EMILIA (frequency >25%) were:

Nausea	Fatigue
Musculoskeletal pain	Thrombocytopenia
Increased transaminases	Headache
Constipation	

Next: See Safety Information

Contact a Representative

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- The most common ADRs seen with KADCYLA in EMILIA (frequency > 25%) were nausea, fatigue, musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency > 2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue

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Clinical Information

Results from the Phase III EMILIA trial comparing KADCYLA to lapatinib + capecitabine

Adverse reaction (AR) profile

*Most common ARs (≥25% [all grades] or ≥2% [Grades ≥3] in either study arm) are included. ARs categorized according to NCI-CTCAE (version 3).

PPES=palmar-plantar erythrodysesthesia syndrome.

MOST COMMON ADVERSE REACTIONS (ARs)[1,2]

Select a tab for more information

All Grades (%) | Grades ≥3 (%)

AR*	KADCYLA (n=490)	lapatinib + capecitabine (n=488)
Nausea	39.8	45.1
Fatigue	36.3	28.3
Musculoskeletal pain	36.1	30.5
Thrombocytopenia	31.2	3.3
Increased transaminases	28.8	14.3
Headache	28.2	14.5
Constipation	26.5	11.1
Diarrhea	24.1	79.7
Peripheral neuropathy	21.2	13.5
Vomiting	19.2	29.9
Anemia	14.3	10.5
Stomatitis	14.1	32.6
Rash	11.6	27.5
Hypokalemia	10.2	9.4
Neutropenia	6.7	9.0
PPES	1.4	59.0

PPES=palmar-plantar erythrodysesthesia syndrome.

Lower overall incidence of severe (Grades ≥3) ARs[1]

- Overall incidence of ARs Grades ≥3 was 43.1% vs 59.2% with lapatinib + capecitabine[1]
- Most common ARs (Grades ≥3) more frequently associated with KADCYLA than with lapatinib + capecitabine were thrombocytopenia, peripheral neuropathy, anemia, increased transaminases, musculoskeletal pain, and constipation[1]
  - Incidence of alopecia was low (<5%) in both treatment arms[2]
- Diarrhea, PPES, hypokalemia, vomiting, neutropenia, fatigue, nausea, stomatitis, and rash (Grades ≥3) were the most common ARs more frequently associated with lapatinib + capecitabine than with KADCYLA[1]
  - Incidence of PPES (Grades ≥3) was 0.0% with KADCYLA vs 17.6% with lapatinib + capecitabine[2]

>> See here for full adverse reactions profile from the EMILIA trial

Next: See Dose Reductions/Treatment Discontinuations

Contact a Representative

Interested in a more detailed discussion of KADCYLA safety?

Review the KADCYLA safety profile with a KADCYLA representative

› **Contact Us**

Indication

KADCYLA® (ado-trastuzumab emtansine), as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:

- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy

Important Safety Information

Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY

- **Do Not Substitute KADCYLA for or with Trastuzumab**
- **Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin**
- **Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function**
- **Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception**

Additional Important Safety Information:

Left Ventricular Dysfunction (LVD)

- Patients treated with KADCYLA are at increased risk of developing LVD. In EMILIA, LVD occurred in 1.8% of patients in the KADCYLA-treated group and in 3.3% in the comparator group. Permanently discontinue KADCYLA if LVEF has not improved or has declined further

Pregnancy Registry

- Advise patients to contact their healthcare provider immediately if they suspect they may be pregnant. Encourage women who may be exposed to KADCYLA during pregnancy to enroll in the **MotHER Pregnancy Registry** by contacting **1 (800) 690-6720**

Pulmonary Toxicity

- Cases of interstitial lung disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatal outcome have been reported in clinical trials with KADCYLA. In EMILIA, the overall frequency of pneumonitis was 1.2%
- Treatment with KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis

Infusion-Related Reactions, Hypersensitivity Reactions

- Treatment with KADCYLA has not been studied in patients who had trastuzumab permanently discontinued due to infusion-related reactions (IRR) and/or hypersensitivity reactions; treatment with KADCYLA is not recommended for these patients. In EMILIA, the overall frequency of IRRs in patients treated with KADCYLA was 1.4%
- KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR. Patients should be closely monitored for IRR reactions, especially during the first infusion

Thrombocytopenia

- In EMILIA, the incidence of ≥ Grade 3 thrombocytopenia was 14.5% in the KADCYLA-treated group and 0.4% in the comparator group (overall incidence 31.2% and 3.3%, respectively)
- Monitor platelet counts prior to initiation of KADCYLA and prior to each KADCYLA dose. Institute dose modifications as appropriate

Neurotoxicity

- In EMILIA, the incidence of ≥ Grade 3 peripheral neuropathy was 2.2% in the KADCYLA-treated group and 0.2% in the comparator group (overall incidence 21.2% and 13.5%, respectively)
- Monitor for signs or symptoms of neurotoxicity. KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2

HER2 Testing

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA. Perform using FDA-approved tests by laboratories with demonstrated proficiency

Extravasation

- In KADCYLA clinical studies, reactions secondary to extravasation have been observed and were generally mild. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Specific treatment for KADCYLA extravasation is unknown

Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

Adverse Reactions

- The most common ADRs seen with KADCYLA in EMILIA (frequency > 25%) were nausea, fatigue, musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency > 2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue

You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling **1 (888) 835-2555.** You may contact the FDA by visiting **www.fda.gov/medwatch** or calling **1 (800) FDA-1088.**

Please see accompanying full Prescribing Information for additional important safety information, including Boxed WARNINGS.

References: 1. KADCYLA Prescribing Information. Genentech, Inc. May 2013. **2.** Data on file. Genentech, Inc.

Safety first! Press here to read the Important Safety Information

Clinical Information

Results from the Phase III EMILIA trial comparing KADCYLA to lapatinib + capecitabine

Adverse reaction (AR) profile

*Most common ARs (>25% [all grades] or >2% [Grades ≥3] in either study arm) are included. ARs categorized according to NCI-CTCAE (version 3).

PPES=palmar-plantar erythrodysesthesia syndrome.

MOST COMMON ADVERSE REACTIONS (ARs)[1,2]

Select a tab for more information

All Grades (%)		Grades ≥3 (%)	
AR*	KADCYLA (n=490)	lapatinib + capecitabine (n=488)	
Nausea	0.8	2.5	
Fatigue	2.5	3.5	
Musculoskeletal pain	1.8	1.4	
Thrombocytopenia	14.5	0.4	
Increased transaminases	8.0	2.5	
Headache	0.8	0.8	
Constipation	0.4	0.0	
Diarrhea	1.6	20.7	
Peripheral neuropathy	2.2	0.2	
Vomiting	0.8	4.5	
Anemia	4.1	2.5	
Stomatitis	0.2	2.5	
Rash	0.0	1.8	
Hypokalemia	2.7	4.7	
Neutropenia	2.0	4.3	
PPES	0.0	17.6	

PPES=palmar-plantar erythrodysesthesia syndrome.

Lower overall incidence of severe (Grades ≥3) ARs[1]

- Overall incidence of ARs Grades ≥3 was 43.1% vs 59.2% with lapatinib + capecitabine[1]
- Most common ARs (Grades ≥3) more frequently associated with KADCYLA than with lapatinib + capecitabine were thrombocytopenia, peripheral neuropathy, anemia, increased transaminases, musculoskeletal pain, and constipation[1]
  - Incidence of alopecia was low (<5%) in both treatment arms[2]
- Diarrhea, PPES, hypokalemia, vomiting, neutropenia, fatigue, nausea, stomatitis, and rash (Grades ≥3) were the most common ARs more frequently associated with lapatinib + capecitabine than with KADCYLA[1]
  - Incidence of PPES (Grades ≥3) was 0.0% with KADCYLA vs 17.6% with lapatinib + capecitabine[1]

>> See here for full adverse reactions profile from the EMILIA trial

Next: See Dose Reductions/Treatment Discontinuations

Contact a Representative

Interested in a more detailed discussion of KADCYLA safety?

Review the KADCYLA safety profile with a KADCYLA representative

› **Contact Us**

Indication

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- Received prior therapy for metastatic disease, or
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Important Safety Information

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Additional Important Safety Information:

Left Ventricular Dysfunction (LVD)

- Patients treated with KADCYLA are at increased risk of developing LVD. In EMILIA, LVD occurred in 1.8% of patients in the KADCYLA-treated group and in 3.3% in the comparator group. Permanently discontinue KADCYLA if LVEF has not improved or has declined further

Pregnancy Registry

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- In EMILIA, the incidence of ≥ Grade 3 thrombocytopenia was 14.5% in the KADCYLA-treated group and 0.4% in the comparator group (overall incidence 31.2% and 3.3%, respectively)
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- In EMILIA, the incidence of ≥ Grade 3 peripheral neuropathy was 2.2% in the KADCYLA-treated group and 0.2% in the comparator group (overall incidence 21.2% and 13.5%, respectively)
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HER2 Testing

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Extravasation

- In KADCYLA clinical studies, reactions secondary to extravasation have been observed and were generally mild. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Specific treatment for KADCYLA extravasation is unknown

Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

Adverse Reactions

- The most common ADRs seen with KADCYLA in EMILIA (frequency > 25%) were nausea, fatigue, musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency > 2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue

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Results from the Phase III EMILIA trial comparing KADCYLA to lapatinib + capecitabine

Adverse reaction (AR) profile

*Most common ARs (>25% [all grades] or >2% [Grades ≥3] in either study arm) are included. ARs categorized according to NCI-CTCAE (version 3).

Lower overall incidence of severe (Grades ≥3) ARs[1]

- Overall incidence of ARs Grades ≥3 was 43.1% vs 59.2% with lapatinib + capecitabine[1]
- Most common ARs (Grades ≥3) more frequently associated with KADCYLA than with lapatinib + capecitabine were thrombocytopenia, peripheral neuropathy, anemia, increased transaminases, musculoskeletal pain, and constipation[1]
  - Incidence of alopecia was low (<5%) in both treatment arms[2]
- Diarrhea, PPES, hypokalemia, vomiting, neutropenia, fatigue, nausea, stomatitis, and rash (Grades ≥3) were the most common ARs more frequently associated with lapatinib + capecitabine than with KADCYLA[1]
  - Incidence of PPES (Grades ≥3) was 0.0% with KADCYLA vs 17.6% with lapatinib + capecitabine[2]

>> See here for full adverse reactions profile from the EMILIA trial

Next: See Dose Reductions/Treatment Discontinuations

Indication

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Important Safety Information

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- **Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function**
- **Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception**

Additional Important Safety Information:

Left Ventricular Dysfunction (LVD)

- Patients treated with KADCYLA had an increased risk of developing LVD. In EMILIA, LVD occurred in 1.8% of patients in the KADCYLA-treated group and in 2.3% in the comparator group. Permanently discontinue KADCYLA if LVEF has not improved or has declined further

Pregnancy Registry

- Advise patients to contact their healthcare provider immediately if they suspect they may be pregnant. Encourage women who may be exposed to KADCYLA during pregnancy to enroll in the **MotHER Pregnancy Registry** by contacting **1 (800) 690-6720**

Pulmonary Toxicity

- Cases of interstitial lung disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatal outcome have been reported in clinical trials with KADCYLA. In EMILIA, the overall frequency of pneumonitis was 1.2%
- Treatment with KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis

Infusion-Related Reactions, Hypersensitivity Reactions

- Treatment with KADCYLA has not been studied in patients who had trastuzumab permanently discontinued due to infusion-related reactions (IRR) and/or hypersensitivity reactions; treatment with KADCYLA is not recommended for these patients. In EMILIA, the overall frequency of IRRs in patients treated with KADCYLA was 1.4%
- KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR. Patients should be closely monitored for IRR reactions, especially during the first infusion

Thrombocytopenia

- In EMILIA, the incidence of ≥ Grade 3 thrombocytopenia was 14.5% in the KADCYLA-treated group and 0.4% in the comparator group (overall incidence 31.2% and 3.3%, respectively)
- Monitor platelet counts prior to initiation of KADCYLA and prior to each KADCYLA dose. Institute dose modifications as appropriate

Neurotoxicity

- In EMILIA, the incidence of ≥ Grade 3 peripheral neuropathy was 2.2% in the KADCYLA-treated group and 0.2% in the comparator group (overall incidence 21.2% and 13.5%, respectively)
- Monitor for signs or symptoms of neurotoxicity. KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2

HER2 Testing

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA. Perform using FDA-approved tests by laboratories with demonstrated proficiency

Extravasation

- In KADCYLA clinical studies, reactions secondary to extravasation have been observed and were generally mild. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Specific treatment for KADCYLA extravasation is unknown

Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

Adverse Reactions

- The most common ADRs seen with KADCYLA in EMILIA (frequency > 25%) were nausea, fatigue, musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency > 2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue

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Clinical Information

Results from the Phase III EMILIA trial comparing KADCYLA to lapatinib + capecitabine

Fewer dose reductions and treatment discontinuations

ADVERSE REACTION (AR) MANAGEMENT OUTCOMES[1,2]

Dose reduction	
KADCYLA	**16.3%**
lapatinib	27.3%
capecitabine	53.4%
Treatment discontinuation	
KADCYLA	**6.5%**
lapatinib	8.4%
capecitabine	10.5%

- The most common ARs leading to dose reduction of KADCYLA (in ≥1% of patients) included thrombocytopenia, increased transaminases, and peripheral neuropathy[1]
- The most common ARs leading to discontinuation of KADCYLA were thrombocytopenia and increased AST[1]
- Incidence of dose delays was lower for KADCYLA (23.7%) compared with lapatinib (36.9%) or capecitabine (43.9%)[1,3]
  - ARs most frequently associated with a KADCYLA dose delay (in ≥1% of patients) were neutropenia, thrombocytopenia, leukopenia, fatigue, increased transaminases, and pyrexia[1]

Additional safety information

- Incidence of Grades ≥3 bleeding events was low in both treatment arms (1.4% with KADCYLA vs 0.8% with lapatinib + capecitabine)[2]
- Transaminase elevations were predominantly asymptomatic and transient[1]

Select Important Safety Information:

Thrombocytopenia

- Thrombocytopenia was reported in clinical trials of KADCYLA. The incidence and severity was higher in Asian patients. Independent of race, the incidence and severity of severe hemorrhagic events was low. Monitor platelet counts prior to initiation of KADCYLA and prior to each dose. Institute dose modifications as appropriate

Hepatotoxicity

- Hepatotoxicity, predominantly in the form of asymptomatic increases in the concentrations of serum transaminases, has been observed in clinical trials with KADCYLA. Serious hepatobiliary disorders, including at least 2 fatal cases of severe drug-induced liver injury and associated hepatic encephalopathy, have also been reported in clinical trials with KADCYLA. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin

Next: See Summary of Adverse Reactions

Indication

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Important Safety Information

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Additional Important Safety Information:

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Extravasation

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Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

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References: 1. KADCYLA Prescribing Information. Genentech, Inc. May 2013. **2.** Verma S, Miles D, Gianni L, et al; EMILIA Study Group. Trastuzumab emtansine for HER2-positive advanced breast cancer [published correction appears in *N Engl J Med.* 2013;368:2442]. *N Engl J Med.* 2012;367:1783-1791 and Supplementary Appendix. **3.** Center for Drug Evaluation and Research. Clinical review—BLA 125427: Kadcyla (ado-trastuzumab emtansine) for the treatment of patients with HER2-positive, metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. **Accessdata.fda.gov** Web site. **http://www.accessdata.fda.gov/drugsatfda_docs/nda/2** Completed: January 25, 2013. Accessed July 30, 2013.

This information is for Healthcare Professionals

» Go to Patients & Caregivers site

Kadcyla® ado-trastuzumab emtansine for injection

≡ Menu

Safety first! Press here to read the Important Safety Information

Clinical Information

Results from the Phase III EMILIA trial comparing KADCYLA to lapatinib + capecitabine

Page Name: Dose Reductions & Treatment Discontinuations
Page Title: Dose Reductions | KADCYLA® (ado-trastuzumab emtansine)
Meta Description: Find out which adverse reactions lead to dose reductions and treatment discontinuations for KADCYLA® (ado-trastuzumab emtansine).
KADCYLA® (ado-trastuzumab emtansine), injection for intravenous use, as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either: Received prior therapy for metastatic disease, or Developed disease recurrence during or within six months of completing adjuvant therapy. Important Safety Information: Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYOFETAL TOXICITY: Do Not Substitute KADCYLA for or with Trastuzumab, Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each. KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin, Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function, Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception. The following additional serious adverse reactions have been reported in clinical trials with KADCYLA: Interstitial Lung Disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatality: KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis, Infusion-related reactions (IRR), Hypersensitivity: KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR, Thrombocytopenia: Monitor platelet counts prior to initiation of KADCYLA and prior to each dose. Institute dose modifications as appropriate, Peripheral neuropathy: KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to <= Grade 2, Reactions secondary to extravasation: The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Additional Important Safety Information: Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA therapy, Nursing mothers: Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother, The most common adverse drug reactions (frequency > 25%) across clinical trials with KADCYLA were fatigue, nausea, musculoskeletal pain, thrombocytopenia, headache, increased transaminases, and constipation. You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling 1-888-835-2555. You may contact the FDA by visiting www.fda.gov/

KADCYLA dose delay (in ≥1% of patients) were neutropenia, thrombocytopenia, leukopenia, fatigue, increased transaminases, and pyrexia[1]

Additional safety information

- Incidence of Grades ≥3 bleeding events was low in both treatment arms (1.4% with KADCYLA vs 0.8% with lapatinib + capecitabine)[2]
- Transaminase elevations were predominantly asymptomatic and transient[1]

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- Developed disease recurrence during or within six months of completing adjuvant therapy

Important Safety Information

Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY

- **Do Not Substitute KADCYLA for or with Trastuzumab**
- **Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin**
- **Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function**
- **Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception**

Additional Important Safety Information:

Left Ventricular Dysfunction (LVD)

- Patients treated with KADCYLA are at increased risk of developing LVD. In EMILIA, LVD occurred in 1.8% of patients in the KADCYLA-treated group and in 3.3% in the comparator group. Permanently discontinue KADCYLA if LVEF has not improved or has declined further

Pregnancy Registry

- Advise patients to contact their healthcare provider immediately if they suspect they may be pregnant. Encourage women who may be exposed to KADCYLA during pregnancy to enroll in the **MotHER Pregnancy Registry** by contacting **1 (800) 690-6720**

Pulmonary Toxicity

- Cases of interstitial lung disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatal outcome have been reported in clinical trials with KADCYLA. In EMILIA, the overall frequency of pneumonitis was 1.2%
- Treatment with KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis

Infusion-Related Reactions, Hypersensitivity Reactions

- Treatment with KADCYLA has not been studied in patients who had trastuzumab permanently discontinued due to infusion-related reactions (IRR) and/or hypersensitivity reactions; treatment with KADCYLA is not recommended for these patients. In EMILIA, the overall frequency of IRRs in patients treated with KADCYLA was 1.4%
- KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR. Patients should be closely monitored for IRR reactions, especially during the first infusion

Thrombocytopenia

- In EMILIA, the incidence of ≥ Grade 3 thrombocytopenia was 14.5% in the KADCYLA-treated group and 0.4% in the comparator group (overall incidence 31.2% and 3.3%, respectively)
- Monitor platelet counts prior to initiation of KADCYLA and prior to each KADCYLA dose. Institute dose modifications as appropriate

Neurotoxicity

- In EMILIA, the incidence of ≥ Grade 3 peripheral neuropathy was 2.2% in the KADCYLA-treated group and 0.2% in the comparator group (overall incidence 21.2% and 13.5%, respectively)
- Monitor for signs or symptoms of neurotoxicity. KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2

HER2 Testing

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA. Perform using FDA approved tests by laboratories with demonstrated proficiency

Extravasation

- In KADCYLA clinical studies, reactions secondary to extravasation have been observed and were generally mild. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Specific treatment for KADCYLA extravasation is unknown

Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

Adverse Reactions

- The most common ADRs seen with KADCYLA in EMILIA (frequency > 25%) were nausea, fatigue, musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency > 2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue

You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling **1 (888) 835-2555**. You may contact the FDA by visiting **www.fda.gov/medwatch** or calling **1 (800) FDA-1088.**

Please see accompanying full Prescribing Information for additional important safety information, including Boxed WARNINGS.

References: 1. KADCYLA Prescribing Information. Genentech, Inc. May 2013. **2.** Verma S, Miles D, Gianni L, et al; EMILIA Study Group. Trastuzumab emtansine for HER2-positive advanced breast cancer [published correction appears in *N Engl J Med.* 2013;368:2442]. *N Engl J Med.* 2012;367:1783-1791 and Supplementary Appendix. **3.** Center for Drug Evaluation and Research. Clinical review—BLA 125427: Kadcyla (ado-trastuzumab emtansine) for the treatment of patients with HER2-positive, metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. **Accessdata.fda.gov** Web site. **http://www.accessdata.fda.gov/drugsatfda_docs/nda/2** Completed: January 25, 2013. Accessed July 30, 2013.

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Clinical Information

Results from the Phase III EMILIA trial comparing KADCYLA to lapatinib + capecitabine

Summary of adverse reactions

SUMMARY OF ADVERSE REACTIONS (ARs)[1]

Select a tab for more information

All Grades (%) | Grades ≥3 (%)

AR	KADCYLA (n=490)	lapatinib + capecitabine (n=488)
Blood and lymphatic system disorders		
Neutropenia	6.7	9.0
Anemia	14.3	10.5
Thrombocytopenia	31.2	3.3
Cardiac disorders		
Left ventricular dysfunction	1.8	3.3
Eye disorders		
Lacrimation increased	3.3	2.5
Dry eye	3.9	3.1
Vision blurred	4.5	0.8
Conjunctivitis	3.9	2.3
Gastrointestinal disorders		
Dyspepsia	9.2	11.5
Stomatitis	14.1	32.6
Dry mouth	16.7	4.9
Abdominal pain	18.6	17.6
Vomiting	19.2	29.9
Diarrhea	24.1	79.7
Constipation	26.5	11.1
Nausea	39.8	45.1
General disorders and administration		
Peripheral edema	7.1	8.2
Chills	7.6	3.1
Pyrexia	18.6	8.4
Asthenia	17.8	17.6
Fatigue	36.3	28.3
Hepatobiliary disorders		
Nodular regenerative hyperplasia*	0.4	0.0
Portal hypertension*	0.4	0.0
Immune system disorders		
Drug hypersensitivity	2.2	0.8
Injury, poisoning, and procedural		
Infusion-related reaction	1.4	0.2
Infections and infestations		
Urinary tract infection	9.4	3.9
Investigations		
Blood alkaline phosphatase increased	4.7	3.7
Transaminases increased	28.8	14.3
Metabolism and nutrition disorders		
Hypokalemia	10.2	9.4
Musculoskeletal and connective tissue disorders		
Myalgia	14.1	3.7
Arthalgia	19.2	8.4
Musculoskeletal pain	36.1	30.5
Nervous system disorders		
Dysgeusia	8.0	4.1
Dizziness	10.2	10.7
Peripheral neuropathy	21.2	13.5
Headache	28.2	14.5
Psychiatric disorders		
Insomnia	12.0	8.6
Respiratory, thoracic, and mediastinal disorders		
Pneumonitis	1.2	0.0
Dyspnea	12.0	8.0
Cough	18.2	13.1
Epistaxis	22.5	8.4
Skin and subcutaneous tissue disorders		
Pruritus	5.5	9.2
Rash	11.6	27.5
Vascular disorders		
Hypertension	5.1	2.3

ND=not determined.

*Nodular regenerative hyperplasia and portal hypertension occurred in the same patient.

Next: See Dosing and Administration

Indication

KADCYLA® (ado-trastuzumab emtansine), as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:

- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy

Important Safety Information

Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY

- **Do Not Substitute KADCYLA for or with Trastuzumab**
- **Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin**
- **Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function**
- **Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception**

Additional Important Safety Information:

Left Ventricular Dysfunction (LVD)

- Patients treated with KADCYLA are at increased risk of developing LVD. In EMILIA, LVD occurred in 1.8% of patients in the KADCYLA-treated group and in 3.3% in the comparator group. Permanently discontinue KADCYLA if LVEF has not improved or has declined further

Pregnancy Registry

- Advise patients to contact their healthcare provider immediately if they suspect they may be pregnant. Encourage women who may be exposed to KADCYLA during pregnancy to enroll in the **MotHER Pregnancy Registry** by contacting **1 (800) 690-6720**

Pulmonary Toxicity

- Cases of interstitial lung disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatal outcome have been reported in clinical trials with KADCYLA. In EMILIA, the overall frequency of pneumonitis was 1.2%
- Treatment with KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis

Infusion-Related Reactions, Hypersensitivity Reactions

- Treatment with KADCYLA has not been studied in patients who had trastuzumab permanently discontinued due to infusion-related reactions (IRR) and/or hypersensitivity reactions; treatment with KADCYLA is not recommended for these patients. In EMILIA, the overall frequency of IRRs in patients treated with KADCYLA was 1.4%
- KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR. Patients should be closely monitored for IRR reactions, especially during the first infusion

Thrombocytopenia

- In EMILIA, the incidence of ≥ Grade 3 thrombocytopenia was 14.5% in the KADCYLA-treated group and 0.4% in the comparator group (overall incidence 31.2% and 3.3%, respectively)
- Monitor platelet counts prior to initiation of KADCYLA and prior to each KADCYLA dose. Institute dose modifications as appropriate

Neurotoxicity

- In EMILIA, the incidence of ≥ Grade 3 peripheral neuropathy was 2.2% in the KADCYLA-treated group and 0.2% in the comparator group (overall incidence 21.2% and 13.5%, respectively)
- Monitor for signs or symptoms of neurotoxicity. KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2

HER2 Testing

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA. Perform using FDA approved tests by laboratories with demonstrated proficiency

Extravasation

- In KADCYLA clinical studies, reactions secondary to extravasation have been observed and were generally mild. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Specific treatment for KADCYLA extravasation is unknown

Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

Adverse Reactions

- The most common ADRs seen with KADCYLA in EMILIA (frequency > 25%) were nausea, fatigue, musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency > 2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue

You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling **1 (888) 835-2555**. You may contact the FDA by visiting **www.fda.gov/medwatch** or calling **1 (800) FDA-1088**.

Please see accompanying full Prescribing Information for additional important safety information, including Boxed WARNINGS.

Reference: 1. KADCYLA Prescribing Information. Genentech, Inc. May 2013.

Clinical Information

Results from the Phase III EMILIA trial comparing KADCYLA to lapatinib + capecitabine

Summary of adverse reactions

SUMMARY OF ADVERSE REACTIONS (ARs)[1]

Select a tab for more information

All Grades (%)	Grades ≥3 (%)	
AR	**KADCYLA** (n=490)	**lapatinib + capecitabine** (n=488)
Blood and lymphatic system disorders		
Neutropenia	2.0	4.3
Anemia	4.1	2.5
Thrombocytopenia	14.5	0.4
Cardiac disorders		
Left ventricular dysfunction	0.2	0.4
Eye disorders		
Lacrimation increased	0.0	0.0
Dry eye	0.0	0.0
Vision blurred	0.0	0.0
Conjunctivitis	0.0	0.0
Gastrointestinal disorders		
Dyspepsia	0.0	0.4

Stomatitis	0.2	2.5
Dry mouth	0.0	0.2
Abdominal pain	0.8	1.6
Vomiting	0.8	4.5
Diarrhea	1.6	20.7
Constipation	0.4	0.0
Nausea	0.8	2.5
General disorders and administration		
Peripheral edema	0.0	0.2
Chills	0.0	0.0
Pyrexia	0.2	0.4
Asthenia	0.4	1.6
Fatigue	2.5	3.5
Hepatobiliary disorders		
Nodular regenerative hyperplasia*	ND	0.0
Portal hypertension*	0.2	0.0
Immune system disorders		
Drug hypersensitivity	0.0	0.0
Injury, poisoning, and procedural		
Infusion-related reaction	0.0	0.0
Infections and infestations		
Urinary tract infection	0.6	0.0
Investigations		
Blood alkaline phosphatase increased	0.4	0.4
Transaminases increased	8.0	2.5
Metabolism and nutrition disorders		
Hypokalemia	2.7	4.7
Musculoskeletal and connective tissue disorders		
Myalgia	0.6	0.0
Arthalgia	0.6	0.0
Musculoskeletal pain	1.8	1.4
Nervous system disorders		
Dysgeusia	0.0	0.2
Dizziness	0.4	0.2

Peripheral neuropathy	2.2	0.2
Headache	0.8	0.8
Psychiatric disorders		
Insomnia	0.4	0.2
Respiratory, thoracic, and mediastinal disorders		
Pneumonitis	0.0	0.0
Dyspnea	0.8	0.4
Cough	0.2	0.2
Epistaxis	0.2	0.0
Skin and subcutaneous tissue disorders		
Pruritus	0.2	0.0
Rash	0.0	1.8
Vascular disorders		
Hypertension	1.2	0.4

ND=not determined.

*Nodular regenerative hyperplasia and portal hypertension occurred in the same patient.

Next: See Dosing and Administration

Contact a Representative

Interested in a more detailed discussion of KADCYLA safety?

Review the KADCYLA safety profile with a KADCYLA representative

› Contact Us

Indication

KADCYLA® (ado-trastuzumab emtansine), as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:

- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy

Important Safety Information

Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY

- **Do Not Substitute KADCYLA for or with Trastuzumab**
- **Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin**
- **Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function**
- **Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception**

Additional Important Safety Information:

Left Ventricular Dysfunction (LVD)

- Patients treated with KADCYLA are at increased risk of developing LVD. In EMILIA, LVD occurred in 1.8% of patients in the KADCYLA-treated group and in 3.3% in the comparator group. Permanently discontinue KADCYLA if LVEF has not improved or has declined further

Pregnancy Registry

- Advise patients to contact their healthcare provider immediately if they suspect they may be pregnant. Encourage women who may be exposed to KADCYLA during pregnancy to enroll in the **MotHER Pregnancy Registry** by contacting **1 (800) 690-6720**

Pulmonary Toxicity

- Cases of interstitial lung disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatal outcome have been reported in clinical trials with KADCYLA. In EMILIA, the overall frequency of pneumonitis was 1.2%
- Treatment with KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis

Infusion-Related Reactions, Hypersensitivity Reactions

- Treatment with KADCYLA has not been studied in patients who had trastuzumab permanently discontinued due to infusion-related reactions (IRR) and/or hypersensitivity reactions; treatment with KADCYLA is not recommended for these patients. In EMILIA, the overall frequency of IRRs in patients treated with KADCYLA was 1.4%
- KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR. Patients should be closely monitored for IRR reactions, especially during the first infusion

Thrombocytopenia

- In EMILIA, the incidence of ≥ Grade 3

thrombocytopenia was 14.5% in the KADCYLA-treated group and 0.4% in the comparator group (overall incidence 31.2% and 3.3%, respectively)

- Monitor platelet counts prior to initiation of KADCYLA and prior to each KADCYLA dose. Institute dose modifications as appropriate

Neurotoxicity

- In EMILIA, the incidence of ≥ Grade 3 peripheral neuropathy was 2.2% in the KADCYLA-treated group and 0.2% in the comparator group (overall incidence 21.2% and 13.5%, respectively)
- Monitor for signs or symptoms of neurotoxicity. KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2

HER2 Testing

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA. Perform using FDA approved tests by laboratories with demonstrated proficiency

Extravasation

- In KADCYLA clinical studies, reactions secondary to extravasation have been observed and were generally mild. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Specific treatment for KADCYLA extravasation is unknown

Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

Adverse Reactions

- The most common ADRs seen with KADCYLA in EMILIA (frequency > 25%) were nausea, fatigue, musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency > 2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue

You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling **1 (888) 835-2555**. You may contact the FDA by visiting **www.fda.gov/medwatch** or calling **1 (800) FDA-1088**.

Please see accompanying full Prescribing Information for additional important safety information, including Boxed WARNINGS.

Reference: 1. KADCYLA Prescribing Information. Genentech, Inc. May 2013.

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Clinical Information

Results from the Phase III EMILIA trial comparing KADCYLA to lapatinib + capecitabine

Summary of adverse reactions

SUMMARY OF ADVERSE REACTIONS (ARs)[1]

Select a tab for more information

All Grades (%) | Grades ≥3 (%)

Page Name: Summary of Adverse Reactions
Page Title: Adverse Reactions Summary | KADCYLA® (ado-trastuzumab emtansine)
Meta Description: Read a summary of adverse reactions for KADCYLA® (ado-trastuzumab emtansine) compared to lapatinib+capecitabine. KADCYLA® (ado-trastuzumab emtansine), injection for intravenous use, as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either: Received prior therapy for metastatic disease, or Developed disease recurrence during or within six months of completing adjuvant therapy. Important Safety Information: Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYOFETAL TOXICITY: Do Not Substitute KADCYLA for or with Trastuzumab, Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each. KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin, Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function, Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception. The following additional serious adverse reactions have been reported in clinical trials with KADCYLA: Interstitial Lung Disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatality: KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis, Infusion-related reactions (IRR), Hypersensitivity: KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR, Thrombocytopenia: Monitor platelet counts prior to initiation of KADCYLA and prior to each dose. Institute dose modifications as appropriate, Peripheral neuropathy: KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2, Reactions secondary to extravasation: The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Additional Important Safety Information: Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA therapy, Nursing mothers: Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother, The most common adverse drug reactions (frequency > 25%) across clinical trials with KADCYLA were fatigue, nausea, musculoskeletal pain, thrombocytopenia, headache, increased transaminases, and constipation. You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling 1-888-835-2555. You may contact

	KADCYLA	Lapatinib + capecitabine
Peripheral edema	7.1	8.2
Chills	7.6	3.1
Pyrexia	18.6	8.4
Asthenia	17.8	17.6
Fatigue	36.3	28.3
Hepatobiliary disorders		
Nodular regenerative hyperplasia*	0.4	0.0
Portal hypertension*	0.4	0.0
Immune system disorders		
Drug hypersensitivity	2.2	0.8
Injury, poisoning, and procedural		
Infusion-related reaction	1.4	0.2
Infections and infestations		
Urinary tract infection	9.4	3.9
Investigations		
Blood alkaline phosphatase increased	4.7	3.7
Transaminases increased	28.8	14.3
Metabolism and nutrition disorders		
Hypokalemia	10.2	9.4
Musculoskeletal and connective tissue disorders		
Myalgia	14.1	3.7
Arthalgia	19.2	8.4
Musculoskeletal pain	36.1	30.5
Nervous system disorders		
Dysgeusia	8.0	4.1
Dizziness	10.2	10.7
Peripheral neuropathy	21.2	13.5
Headache	28.2	14.5
Psychiatric disorders		
Insomnia	12.0	8.6
Respiratory, thoracic, and mediastinal disorders		
Pneumonitis	1.2	0.0
Dyspnea	12.0	8.0
Cough	18.2	13.1
Epistaxis	22.5	8.4
Skin and subcutaneous tissue disorders		
Pruritus	5.5	9.2
Rash	11.6	27.5
Vascular disorders		
Hypertension	5.1	2.3

ND=not determined.

*Nodular regenerative hyperplasia and portal hypertension occurred in the same patient.

Next: See Dosing and Administration

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› Contact Us

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Additional Important Safety Information:

Left Ventricular Dysfunction (LVD)

- Patients treated with KADCYLA are at increased risk of developing LVD. In EMILIA, LVD occurred in 1.8% of patients in the KADCYLA-treated group and in 3.3% in the comparator group. Permanently discontinue KADCYLA if LVEF has not improved or has declined further

Pregnancy Registry

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Pulmonary Toxicity

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Infusion-Related Reactions, Hypersensitivity Reactions

- Treatment with KADCYLA has not been studied in patients who had trastuzumab permanently discontinued due to infusion-related reactions (IRR) and/or hypersensitivity reactions; treatment with KADCYLA is not recommended for these patients. In EMILIA, the overall frequency of IRRs in patients treated with KADCYLA was 1.4%
- KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR. Patients should be closely monitored for IRR reactions, especially during the first infusion

Thrombocytopenia

- In EMILIA, the incidence of ≥ Grade 3 thrombocytopenia was 14.5% in the KADCYLA-treated group and 0.4% in the comparator group (overall incidence 31.2% and 3.3%, respectively)
- Monitor platelet counts prior to initiation of KADCYLA and prior to each KADCYLA dose. Institute dose modifications as appropriate

Neurotoxicity

- In EMILIA, the incidence of ≥ Grade 3 peripheral neuropathy was 2.2% in the KADCYLA-treated group and 0.2% in the comparator group (overall incidence 21.2% and 13.5%, respectively)
- Monitor for signs or symptoms of neurotoxicity. KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2

HER2 Testing

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA. Perform using FDA approved tests by laboratories with demonstrated proficiency

Extravasation

- In KADCYLA clinical studies, reactions secondary to extravasation have been observed and were generally mild. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Specific treatment for KADCYLA extravasation is unknown

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Adverse Reactions

- The most common ADRs seen with KADCYLA in EMILIA (frequency > 25%) were nausea, fatigue, musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency > 2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue

You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling **1 (888) 835-2555**. You may contact the FDA by visiting **www.fda.gov/medwatch** or calling **1 (800) FDA-1088**.

Please see accompanying full Prescribing Information for additional important safety information, including Boxed WARNINGS.

Reference: 1. KADCYLA Prescribing Information. Genentech, Inc. May 2013.

Dosing and Administration

Preparing and storing KADCYLA[1]

Calculating the correct dose

Dosing for KADCYLA is weight based (3.6 mg/kg; actual body weight).

1. Calculate dose (mg)

Patient Weight ____ kg x Drug Dose 3.6 mg/kg = KADCYLA ___ mg

2. Calculate volume (reconstituted mL)

KADCYLA ____ mg ÷ Vial Concentration 20 mg/mL = KADCYLA ___ mL

Example

For a patient who weighs 70 kg (154 lb)

Patient Weight *70 kg* x Drug Dose *3.6 mg/kg* = KADCYLA *252 mg*

KADCYLA *252 mg* ÷ Vial Concentration *20 mg/mL* = KADCYLA *12.6 mL*

Selecting the appropriate vial

KADCYLA is supplied as a sterile powder for concentrate and comes in 2 vial types. Vials will reconstitute to 20 mg/mL.

160 mg single-use vial yields 8 mL of reconstituted KADCYLA

100 mg single-use vial yields 5 mL of reconstituted KADCYLA

Look-Alike/Sound-Alike Medication[1]

Confirm vial label. KADCYLA (ado-trastuzumab EMTANSINE) and Herceptin® (trastuzumab) have similar generic names, but important differences, including dosing and indication.

- **Do not substitute KADCYLA for or with trastuzumab**
- **Do not administer KADCYLA at doses greater than 3.6 mg/kg**

Instructions for reconstitution

Use aseptic technique for reconstitution and preparation of dosing solution.

- Use appropriate procedures for the preparation of chemotherapeutic drugs

1. To yield a single-use **reconstituted solution of 20 mg/mL** of KADCYLA for IV infusion, using a sterile syringe, slowly inject:
   - 8 mL of sterile water for injection (SWFI) into the 160 mg vial
   - 5 mL of SWFI into the 100 mg vial
2. Gently swirl the vial until solution is completely dissolved. **DO NOT FREEZE OR SHAKE.**
   - Do not use if the reconstituted solution contains visible particulates or is cloudy or discolored

Instructions for dilution

1. Add reconstituted KADCYLA solution to an infusion bag containing 250 mL of 0.9% sodium chloride injection.
   - **Do not use Dextrose (5%) solution to dilute KADCYLA**
2. Mix diluted solution by gentle inversion to avoid foaming. **DO NOT FREEZE OR SHAKE.**
3. Administer the infusion immediately after preparation, using a 0.22 micron in-line PES* filter.
   - **Do not mix or dilute KADCYLA with other drugs during preparation**

Storing KADCYLA

- Store vials in a refrigerator at 2°C-8°C (36°F-46°F) until time of use
- Reconstituted vials with SWFI and diluted KADCYLA infusion solution should be used immediately or may be stored in a refrigerator at 2°C-8°C (36°F-46°F) for up to 24 hours prior to use. **DO NOT FREEZE OR SHAKE**
  - Storage time for KADCYLA infusion solution is additional to the time allowed for the reconstituted vials
  - Discard any unused solution after 24 hours

*PES=polyethersulfone.

Next: Administering KADCYLA

Indication

KADCYLA® (ado-trastuzumab emtansine), as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:

- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy

Important Safety Information

Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY

- **Do Not Substitute KADCYLA for or with Trastuzumab**
- **Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin**
- **Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function**
- **Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception**

Additional Important Safety Information:

Left Ventricular Dysfunction (LVD)

- Patients treated with KADCYLA are at increased risk of developing LVD. In EMILIA, LVD occurred in 1.8% of patients in the KADCYLA-treated group and in 3.3% in the comparator group. Permanently discontinue KADCYLA if LVEF has not improved or has declined further

Pregnancy Registry

- Advise patients to contact their healthcare provider immediately if they suspect they may be pregnant. Encourage women who may be exposed to KADCYLA during pregnancy to enroll in the **MotHER Pregnancy Registry** by contacting **1 (800) 690-6720**

Pulmonary Toxicity

- Cases of interstitial lung disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatal outcome have been reported in clinical trials with KADCYLA. In EMILIA, the overall frequency of pneumonitis was 1.2%
- Treatment with KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis

Infusion-Related Reactions, Hypersensitivity Reactions

- Treatment with KADCYLA has not been studied in patients who had trastuzumab permanently discontinued due to infusion-related reactions (IRR) and/or hypersensitivity reactions; treatment with KADCYLA is not recommended for these patients. In EMILIA, the overall frequency of IRRs in patients treated with KADCYLA was 1.4%
- KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR. Patients should be closely monitored for IRR reactions, especially during the first infusion

Thrombocytopenia

- In EMILIA, the incidence of ≥ Grade 3 thrombocytopenia was 14.5% in the KADCYLA-treated group and 0.4% in the comparator group (overall incidence 31.2% and 3.3%, respectively)
- Monitor platelet counts prior to initiation of KADCYLA and prior to each KADCYLA dose. Institute dose modifications as appropriate

Neurotoxicity

- In EMILIA, the incidence of ≥ Grade 3 peripheral neuropathy was 2.2% in the KADCYLA-treated group and 0.2% in the comparator group (overall incidence 21.2% and 13.5%, respectively)
- Monitor for signs or symptoms of neurotoxicity. KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2

HER2 Testing

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA. Perform using FDA approved tests by laboratories with demonstrated proficiency

Extravasation

- In KADCYLA clinical studies, reactions secondary to extravasation have been observed and were generally mild. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Specific treatment for KADCYLA extravasation is unknown

Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

Adverse Reactions

- The most common ADRs seen with KADCYLA in EMILIA (frequency > 25%) were nausea, fatigue, musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency > 2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue

You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling **1 (888) 835-2555**. You may contact the FDA by visiting **www.fda.gov/medwatch** or calling **1 (800) FDA-1088**.

Please see accompanying full Prescribing Information for additional important safety information, including Boxed WARNINGS.

Reference: 1. KADCYLA Prescribing Information. Genentech, Inc., May 2013.

Dosing and Administration

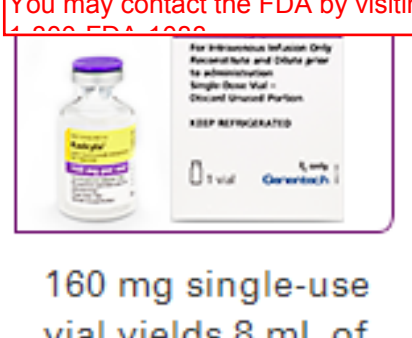
Preparing and storing KADCYLA[1]

Calculating the correct dose

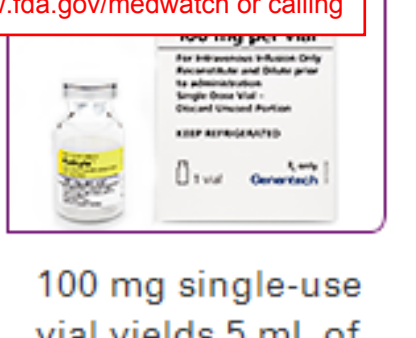
Dosing for KADCYLA is weight based (3.6 mg/kg; actual body weight).

1. **Calculate dose (mg)**

Page Name: Preparation & Storage
Page Title: Preparation & Storage | KADCYLA® (ado-trastuzumab emtansine)
Meta Description: Find out more about how to prepare and store KADCYLA® (ado-trastuzumab emtansine) for HER2-positive patients. KADCYLA® (ado-trastuzumab emtansine), injection for intravenous use, as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either: Received prior therapy for metastatic disease, or Developed disease recurrence during or within six months of completing adjuvant therapy. Important Safety Information: Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYOFETAL TOXICITY: Do Not Substitute KADCYLA for or with Trastuzumab, Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each. KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin, Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function, Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception. The following additional serious adverse reactions have been reported in clinical trials with KADCYLA: Interstitial Lung Disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatality: KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis, Infusion-related reactions (IRR), Hypersensitivity: KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR, Thrombocytopenia: Monitor platelet counts prior to initiation of KADCYLA and prior to each dose. Institute dose modifications as appropriate, Peripheral neuropathy: KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2, Reactions secondary to extravasation: The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Additional Important Safety Information: Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA therapy, Nursing mothers: Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother, The most common adverse drug reactions (frequency > 25%) across clinical trials with KADCYLA were fatigue, nausea, musculoskeletal pain, thrombocytopenia, headache, increased transaminases, and constipation. You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling 1-888-835-2555. You may contact the FDA by visiting www.fda.gov/medwatch or calling



160 mg single-use vial yields 8 mL of reconstituted KADCYLA



100 mg single-use vial yields 5 mL of reconstituted KADCYLA

Look-Alike/Sound-Alike Medication[1]

Confirm vial label. KADCYLA (ado-trastuzumab EMTANSINE) and Herceptin® (trastuzumab) have similar generic names, but important differences, including dosing and indication.

- **Do not substitute KADCYLA for or with trastuzumab**
- **Do not administer KADCYLA at doses greater than 3.6 mg/kg**

Instructions for reconstitution

Use aseptic technique for reconstitution and preparation of dosing solution.

- Use appropriate procedures for the preparation of chemotherapeutic drugs

1. To yield a single-use **reconstituted solution of 20 mg/mL** of KADCYLA for IV infusion, using a sterile syringe, slowly inject:
   - 8 mL of sterile water for injection (SWFI) into the 160 mg vial
   - 5 mL of SWFI into the 100 mg vial
2. Gently swirl the vial until solution is completely dissolved. **DO NOT FREEZE OR SHAKE.**
   - Do not use if the reconstituted solution contains visible particulates or is cloudy or discolored

Instructions for dilution

1. Add reconstituted KADCYLA solution to an infusion bag containing 250 mL of 0.9% sodium chloride injection.
   - **Do not use Dextrose (5%) solution to dilute KADCYLA**
2. Mix diluted solution by gentle inversion to avoid foaming. **DO NOT FREEZE OR SHAKE.**
3. Administer the infusion immediately after preparation, using a 0.22 micron in-line PES* filter.
   - **Do not mix or dilute KADCYLA with other drugs during preparation**

Storing KADCYLA

- Store vials in a refrigerator at 2°C-8°C (36°F-46°F) until time of use
- Reconstituted vials with SWFI and diluted KADCYLA infusion solution should be used immediately or may be stored in a refrigerator at 2°C-8°C (36°F-46°F) for up to 24 hours prior to use. **DO NOT FREEZE OR SHAKE**
  - Storage time for KADCYLA infusion solution is additional to the time allowed for the reconstituted vials
  - Discard any unused solution after 24 hours

*PES=polyethersulfone.

Next: Administering KADCYLA

Contact a Representative

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Get the Dosing and Administration Guide delivered by a KADCYLA representative

› Contact Us

Indication

KADCYLA® (ado-trastuzumab emtansine), as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:

- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy

Important Safety Information

Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY

- **Do Not Substitute KADCYLA for or with Trastuzumab**
- **Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin**
- **Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function**
- **Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception**

Additional Important Safety Information:

Left Ventricular Dysfunction (LVD)

- Patients treated with KADCYLA are at increased risk of developing LVD. In EMILIA, LVD occurred in 1.8% of patients in the KADCYLA-treated group and in 3.3% in the comparator group. Permanently discontinue KADCYLA if LVEF has not improved or has declined further

Pregnancy Registry

- Advise patients to contact their healthcare provider immediately if they suspect they may be pregnant. Encourage women who may be exposed to KADCYLA during pregnancy to enroll in the **MotHER Pregnancy Registry** by contacting **1 (800) 690-6720**

Pulmonary Toxicity

- Cases of interstitial lung disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatal outcome have been reported in clinical trials with KADCYLA. In EMILIA, the overall frequency of pneumonitis was 1.2%
- Treatment with KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis

Infusion-Related Reactions, Hypersensitivity Reactions

- Treatment with KADCYLA has not been studied in patients who had trastuzumab permanently discontinued due to infusion-related reactions (IRR) and/or hypersensitivity reactions; treatment with KADCYLA is not recommended for these patients. In EMILIA, the overall frequency of IRRs in patients treated with KADCYLA was 1.4%
- KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR. Patients should be closely monitored for IRR reactions, especially during the first infusion

Thrombocytopenia

- In EMILIA, the incidence of ≥ Grade 3 thrombocytopenia was 14.5% in the KADCYLA-treated group and 0.4% in the comparator group (overall incidence 31.2% and 3.3%, respectively)
- Monitor platelet counts prior to initiation of KADCYLA and prior to each KADCYLA dose. Institute dose modifications as appropriate

Neurotoxicity

- In EMILIA, the incidence of ≥ Grade 3 peripheral neuropathy was 2.2% in the KADCYLA-treated group and 0.2% in the comparator group (overall incidence 21.2% and 13.5%, respectively)
- Monitor for signs or symptoms of neurotoxicity. KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2

HER2 Testing

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA. Perform using FDA approved tests by laboratories with demonstrated proficiency

Extravasation

- In KADCYLA clinical studies, reactions secondary to extravasation have been observed and were generally mild. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Specific treatment for KADCYLA extravasation is unknown

Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

Adverse Reactions

- The most common ADRs seen with KADCYLA in EMILIA (frequency > 25%) were nausea, fatigue, musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency > 2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue

You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling **1 (888) 835-2555**. You may contact the FDA by visiting **www.fda.gov/medwatch** or calling **1 (800) FDA-1088**.

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Reference: 1. KADCYLA Prescribing Information. Genentech, Inc., May 2013.

Dosing and Administration

Administering KADCYLA[1]

Single IV infusion every 3 weeks

- Administer at a dose of 3.6 mg/kg via IV infusion. **Do not administer KADCYLA as an intravenous push or bolus**
- An in-line PES* filter (0.22 micron) is required
- No loading dose
- No recommended premedications

*PES=polyethersulfone.

Dosing schedule for KADCYLA[1]

Initial infusion **90 minutes** + Observation (90 minutes) → If first infusion is tolerated, subsequent infusions **30 minutes** + Observation (30 minutes) → **Treat until disease progression or unacceptable toxicity**

Monitoring for infusion-related reactions (IRRs)

IRRs have been reported in clinical trials with KADCYLA. In most patients, these reactions resolved over the course of several hours to a day after completing the infusion.

- Monitor patients for IRRs, especially during the first infusion
- Slow or interrupt the infusion and administer appropriate medical therapies if severe IRRs occur
- Permanently discontinue treatment in the event of life-threatening infusion reactions

Dose modifications and reductions[1]

Severe adverse reactions have been reported in clinical studies with KADCYLA. Before beginning treatment with KADCYLA, review the Preadministration Guidelines and the Dose Modifications and Reductions Guidelines, which can be found in the **Dosing and Administration Guide**. For more information, download the accompanying full **Prescribing Information**.

- When multiple dose-modification events occur, always use the most conservative guideline

Hepatotoxicity
Increased serum transaminases (AST/ALT)
>2.5 to ≤5x ULN (Grade 2)
1) Treat at same dose level
>5 to ≤20x ULN (Grade 3)
1) Hold until recovery to ≤5x ULN 2) Then reduce one dose level
>20x ULN (Grade 4)
1) Permanently discontinue KADCYLA
Hyperbilirubinemia
>1.5 to ≤3x ULN (Grade 2)
1) Hold until total bilirubin level recovers to ≤1.5x ULN 2) Then treat at same dose level
>3 to ≤10x ULN (Grade 3)
1) Hold until total bilirubin level recovers to ≤1.5x ULN 2) Then reduce one dose level
>10x ULN (Grade 4)
1) Permanently discontinue KADCYLA
Permanently discontinue KADCYLA treatment in patients: • **with serum transaminases >3 x ULN and concomitant total bilirubin >2 x ULN, OR** • **diagnosed with nodular regenerative hyperplasia (NRH)**

Left ventricular cardiac dysfunction
LVEF 40% to ≤45% AND <10% point decline from baseline
1) Continue KADCYLA 2) Repeat LVEF assessment within 3 weeks
LVEF 40% to ≤45% AND ≥10% point decline from baseline
1) Do not administer KADCYLA 2) Repeat LVEF assessment within 3 weeks 3) If LVEF has not recovered to within 10% points of absolute baseline, discontinue KADCYLA
LVEF <40%
1) Do not administer KADCYLA 2) Repeat LVEF assessment within 3 weeks 3) If LVEF <40% is confirmed, discontinue KADCYLA
Symptomatic CHF
1) Discontinue KADCYLA

Thrombocytopenia
25,000 to <50,000 cells/mm³ (Grade 3)
1) Hold until recovered to ≥75,000 cells/mm³ 2) Then treat at same dose level
<25,000 cells/mm³ (Grade 4)
1) Hold until recovered to ≥75,000 cells/mm³ 2) Then reduce one dose level

AST=aspartate aminotransferase; ALT=alanine aminotransferase; ULN=upper limit of normal; LVEF=left ventricular ejection fraction; CHF=congestive heart failure.

- **Pulmonary Toxicity:** Permanently discontinue in patients diagnosed with interstitial lung disease (ILD) or pneumonitis
- **Peripheral Neuropathy:** Hold treatment in patients with severe to life-threatening peripheral neuropathy (Grades ≥3) until resolution to Grades ≤2

Dose reduction guidelines for KADCYLA[1]

- Dose reductions should be made in decrements of 0.6 mg/kg
- A maximum of 2 dose reductions should occur before discontinuation
- **KADCYLA dose should not be re-escalated after a dose reduction has been made**

Dose levels

3.6 mg/kg
Starting dose

3 mg/kg

2.4 mg/kg

Discontinue KADCYLA

Missed doses[1]

If a planned dose is delayed or missed, administer as soon as possible at the most recently tolerated infusion rate. **Do not wait until the next planned cycle.**

Following a delayed or missed dose, adjust administration schedule to maintain a 3-week dosing interval.

Next: KADCYLA Professional Resources

Contact a Representative

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› Contact Us

Indication

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Neurotoxicity

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Extravasation

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Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

Adverse Reactions

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Dosing and Administration

Administering KADCYLA[1]

Page Name: Administering KADCYLA
Page Title: Dosing & Administration | KADCYLA® (ado-trastuzumab emtansine)
Meta Description: Learn more about administering KADCYLA® (ado-trastuzumab emtansine) and finding a proper dosing schedule. KADCYLA® (ado-trastuzumab emtansine), injection for intravenous use, as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either: Received prior therapy for metastatic disease, or Developed disease recurrence during or within six months of completing adjuvant therapy. Important Safety Information: Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYOFETAL TOXICITY: Do Not Substitute KADCYLA for or with Trastuzumab, Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each. KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin, Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function, Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception. The following additional serious adverse reactions have been reported in clinical trials with KADCYLA: Interstitial Lung Disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatality: KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis, Infusion-related reactions (IRR), Hypersensitivity: KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR, Thrombocytopenia: Monitor platelet counts prior to initiation of KADCYLA and prior to each dose. Institute dose modifications as appropriate, Peripheral neuropathy: KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2, Reactions secondary to extravasation: The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Additional Important Safety Information: Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA therapy, Nursing mothers: Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother, The most common adverse drug reactions (frequency > 25%) across clinical trials with KADCYLA were fatigue, nausea, musculoskeletal pain, thrombocytopenia, headache, increased transaminases, and constipation. You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling 1-888-835-2555. You may contact the FDA by visiting www.fda.gov/medwatch or calling 1-800-FDA-1088.

first infusion

- Slow or interrupt the infusion and administer appropriate medical therapies if severe IRRs occur
- Permanently discontinue treatment in the event of life-threatening infusion reactions

Dose modifications and reductions[1]

Severe adverse reactions have been reported in clinical studies with KADCYLA. Before beginning treatment with KADCYLA, review the Preadministration Guidelines and the Dose Modifications and Reductions Guidelines, which can be found in the **Dosing and Administration Guide**. For more information, download the accompanying full **Prescribing Information**.

- When multiple dose-modification events occur, always use the most conservative guideline

Hepatotoxicity
Increased serum transaminases (AST/ALT)
>2.5 to ≤5x ULN (Grade 2)
1) Treat at same dose level
>5 to ≤20x ULN (Grade 3)
1) Hold until recovery to ≤5x ULN 2) Then reduce one dose level
>20x ULN (Grade 4)
1) Permanently discontinue KADCYLA
Hyperbilirubinemia
>1.5 to ≤3x ULN (Grade 2)
1) Hold until total bilirubin level recovers to ≤1.5x ULN 2) Then treat at same dose level
>3 to ≤10x ULN (Grade 3)
1) Hold until total bilirubin level recovers to ≤1.5x ULN 2) Then reduce one dose level
>10x ULN (Grade 4)
1) Permanently discontinue KADCYLA
Permanently discontinue KADCYLA treatment in patients: • **with serum transaminases >3 x ULN and concomitant total bilirubin >2 x ULN, OR** • **diagnosed with nodular regenerative hyperplasia (NRH)**

Left ventricular cardiac dysfunction
LVEF 40% to ≤45% AND <10% point decline from baseline
1) Continue KADCYLA 2) Repeat LVEF assessment within 3 weeks
LVEF 40% to ≤45% AND ≥10% point decline from baseline
1) Do not administer KADCYLA 2) Repeat LVEF assessment within 3 weeks 3) If LVEF has not recovered to within 10% points of absolute baseline, discontinue KADCYLA
LVEF <40%
1) Do not administer KADCYLA 2) Repeat LVEF assessment within 3 weeks 3) If LVEF <40% is confirmed, discontinue KADCYLA
Symptomatic CHF
1) Discontinue KADCYLA

Thrombocytopenia
25,000 to <50,000 cells/mm³ (Grade 3)
1) Hold until recovered to ≥75,000 cells/mm³ 2) Then treat at same dose level
<25,000 cells/mm³ (Grade 4)
1) Hold until recovered to ≥75,000 cells/mm³ 2) Then reduce one dose level

AST=aspartate aminotransferase; ALT=alanine aminotransferase; ULN=upper limit of normal; LVEF=left ventricular ejection fraction; CHF=congestive heart failure.

- **Pulmonary Toxicity:** Permanently discontinue in patients diagnosed with interstitial lung disease (ILD) or pneumonitis
- **Peripheral Neuropathy:** Hold treatment in patients with severe to life-threatening peripheral neuropathy (Grades ≥3) until resolution to Grades ≤2

Dose reduction guidelines for KADCYLA[1]

- Dose reductions should be made in decrements of 0.6 mg/kg
- A maximum of 2 dose reductions should occur before discontinuation
- **KADCYLA dose should not be re-escalated after a dose reduction has been made**

Dose levels

3.6 mg/kg
Starting dose
3 mg/kg
2.4 mg/kg
Discontinue KADCYLA

Missed doses[1]

If a planned dose is delayed or missed, administer as soon as possible at the most recently tolerated infusion rate. **Do not wait until the next planned cycle.**

Following a delayed or missed dose, adjust administration schedule to maintain a 3-week dosing interval.

Next: KADCYLA Professional Resources

Contact a Representative

Need printed information on dosing and administration for your office staff?

Get the Dosing and Administration Guide delivered by a KADCYLA representative

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Indication

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- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy

Important Safety Information

Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY

- **Do Not Substitute KADCYLA for or with Trastuzumab**
- **Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin**
- **Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function**
- **Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception**

Additional Important Safety Information:

Left Ventricular Dysfunction (LVD)

- Patients treated with KADCYLA are at increased risk of developing LVD. In EMILIA, LVD occurred in 1.8% of patients in the KADCYLA-treated group and in 3.3% in the comparator group. Permanently discontinue KADCYLA if LVEF has not improved or has declined further

Pregnancy Registry

- Advise patients to contact their healthcare provider immediately if they suspect they may be pregnant. Encourage women who may be exposed to KADCYLA during pregnancy to enroll in the **MotHER Pregnancy Registry** by contacting **1 (800) 690-6720**

Pulmonary Toxicity

- Cases of interstitial lung disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatal outcome have been reported in clinical trials with KADCYLA. In EMILIA, the overall frequency of pneumonitis was 1.2%
- Treatment with KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis

Infusion-Related Reactions, Hypersensitivity Reactions

- Treatment with KADCYLA has not been studied in patients who had trastuzumab permanently discontinued due to infusion-related reactions (IRR) and/or hypersensitivity reactions; treatment with KADCYLA is not recommended for these patients. In EMILIA, the overall frequency of IRRs in patients treated with KADCYLA was 1.4%
- KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR. Patients should be closely monitored for IRR reactions, especially during the first infusion

Thrombocytopenia

- In EMILIA, the incidence of ≥ Grade 3 thrombocytopenia was 14.5% in the KADCYLA-treated group and 0.4% in the comparator group (overall incidence 31.2% and 3.3%, respectively)
- Monitor platelet counts prior to initiation of KADCYLA and prior to each KADCYLA dose. Institute dose modifications as appropriate

Neurotoxicity

- In EMILIA, the incidence of ≥ Grade 3 peripheral neuropathy was 2.2% in the KADCYLA-treated group and 0.2% in the comparator group (overall incidence 21.2% and 13.5%, respectively)
- Monitor for signs or symptoms of neurotoxicity. KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2

HER2 Testing

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA. Perform using FDA approved tests by laboratories with demonstrated proficiency

Extravasation

- In KADCYLA clinical studies, reactions secondary to extravasation have been observed and were generally mild. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Specific treatment for KADCYLA extravasation is unknown

Nursing Mothers

- Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother

Adverse Reactions

- The most common ADRs seen with KADCYLA in EMILIA (frequency > 25%) were nausea, fatigue, musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3) ≥ Grade 3 ADRs (frequency > 2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy and fatigue

You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling **1 (888) 835-2555**. You may contact the FDA by visiting **www.fda.gov/medwatch** or calling **1 (800) FDA-1088**.

Please see accompanying full Prescribing Information for additional important safety information, including Boxed WARNINGS.

Reference: 1. KADCYLA Prescribing Information. Genentech, Inc., May 2013.

This information is for Healthcare Professionals

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Kadcyla® ado-trastuzumab emtansine for injection

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Resources

Professional Resources and Downloads

Within this section, healthcare providers can find important supplemental information to help in the treatment of patients with HER2-positive (HER2+) metastatic breast cancer (MBC).

Clinical resources

Full Prescribing Information

Full Prescribing Information for KADCYLA

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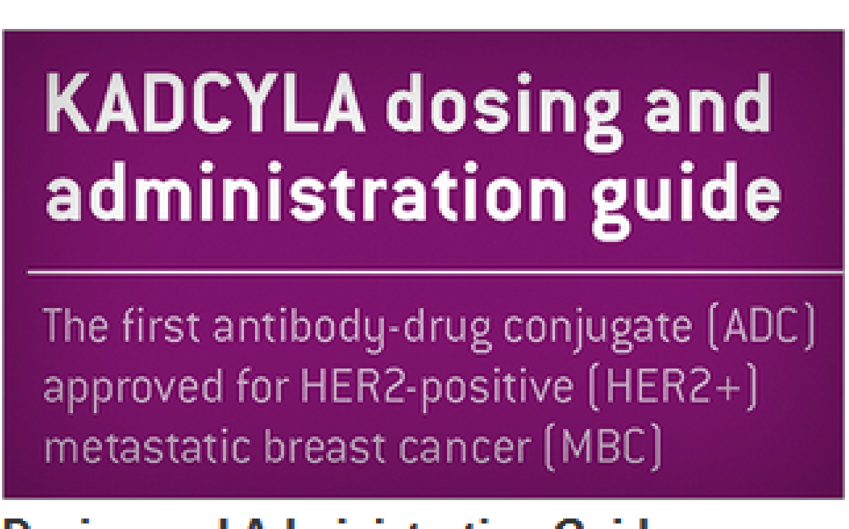
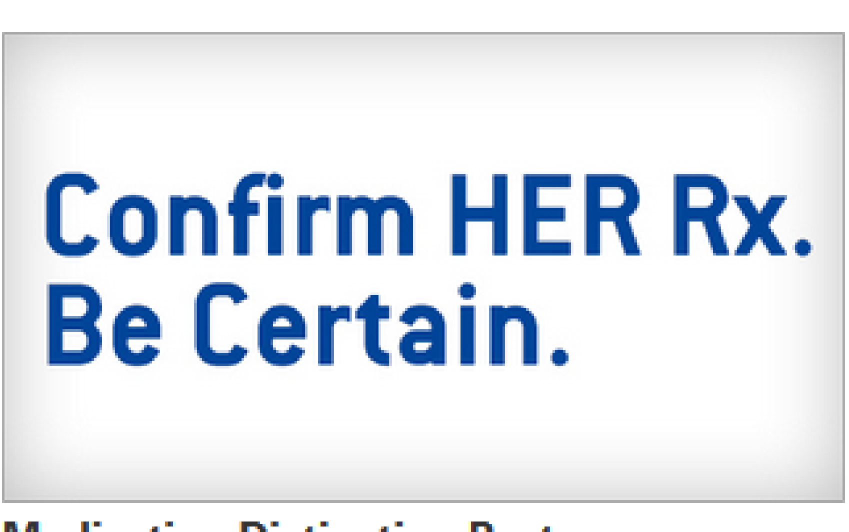


Dosing and Administration Guide

Dosing and administration guidelines to ensure patient receiv~~es accurate~~ dosing

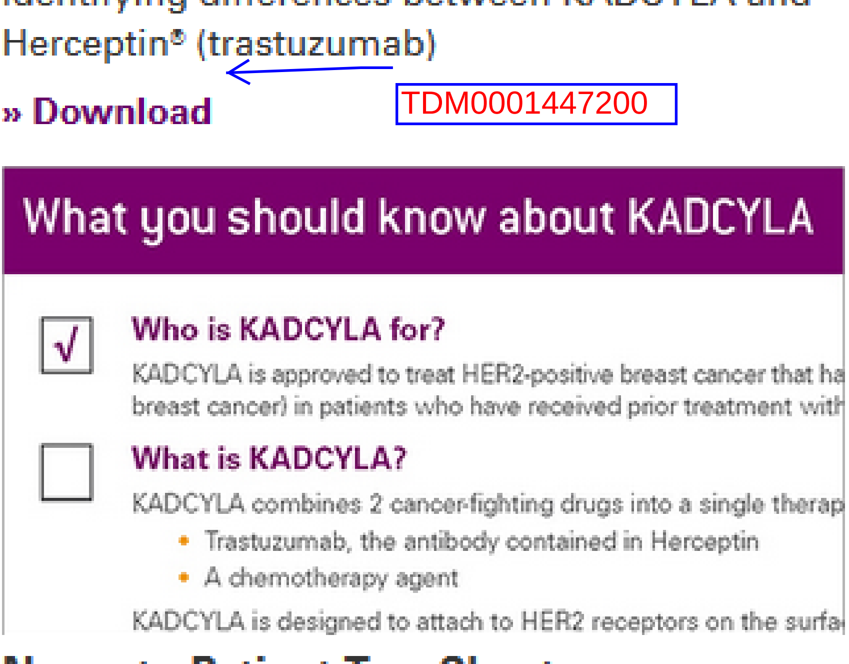
» Download TDM0001360901



Dose Modification Worksheet

Quick reference sheet for modifying the dose of KADCYLA

» Download TDM000154301



Medication Distinction Poster

Poster for HCPs, pharmacists, and office staff identifying differences between KADCYLA and Herceptin® (trastuzumab)

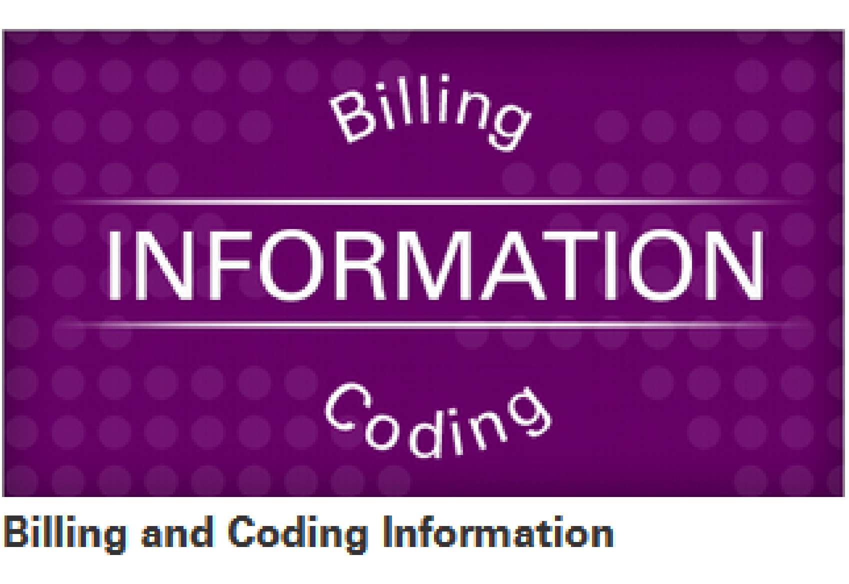
» Download TDM0001447200

Nurse-to-Patient Tear Sheet

A brief overview for patients, containing general information about KADCYLA

» Download TDM0001361301

Non-clinical resources



Authorized Distributors of KADCYLA

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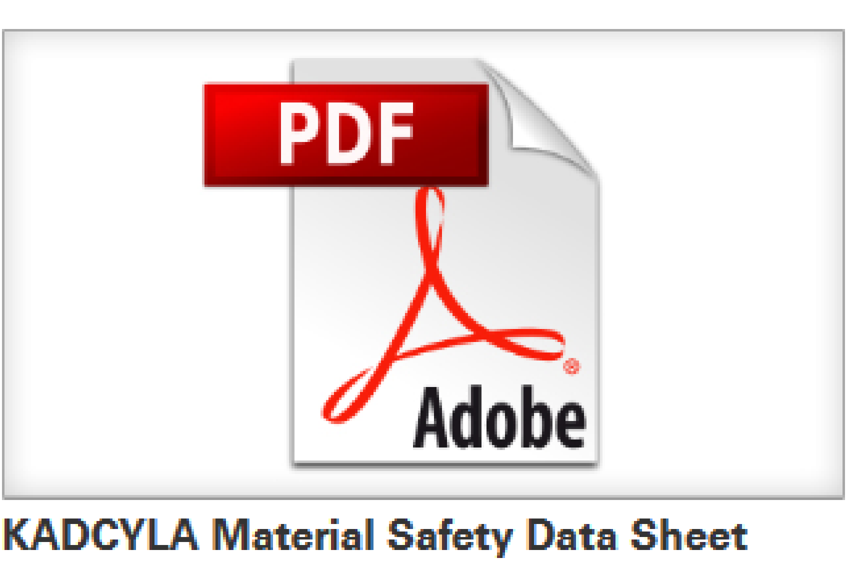

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KADCYLA Material Safety Data Sheet

Material Safety Data Sheet

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Access Solutions®

KADCYLA Access Solutions

Information for financial assistance to help support your patients

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Indication

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Important Safety Information

Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY

- **Do Not Substitute KADCYLA for or with Trastuzumab**
- **Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin**
- **Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function**
- **Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception**

The following additional serious adverse reactions have been reported in clinical trials with KADCYLA:

- Interstitial Lung Disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatality: KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis
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- Thrombocytopenia: Monitor platelet counts prior to initiation of KADCYLA and prior to each dose. Institute dose modifications as appropriate
- Peripheral neuropathy: KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2
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Additional Important Safety Information:

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA therapy
- Nursing mothers: Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother
- The most common adverse drug reactions (frequency > 25%) across clinical trials with KADCYLA were fatigue, nausea, musculoskeletal pain, thrombocytopenia, headache, increased transaminases, and constipation

You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling **1 (888) 835-2555**. You may contact the FDA by visiting **www.fda.gov/medwatch** or calling **1 (800) FDA-1088**.

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Menu

Page Name: Professional Resources & Downloads
Page Title: Professional Resources | KADCYLA® (ado-trastuzumab emtansine)
Meta Description: Find supplemental information to share with Kadcyla patients and to find KADCYLA® (ado-trastuzumab emtansine) patient materials.
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patient receives accurate dosing

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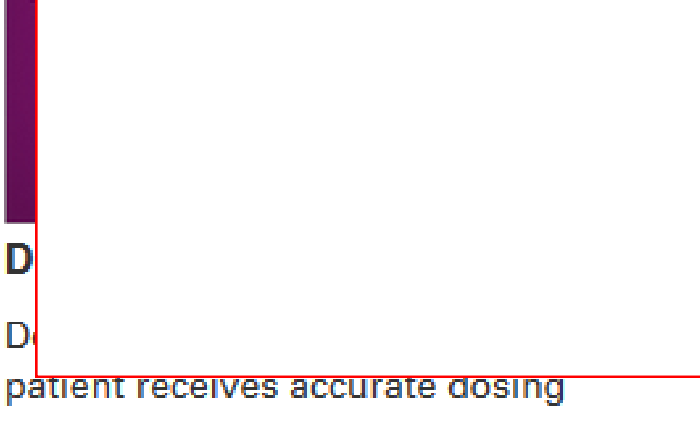

Dose Modification Worksheet

Quick reference sheet for modifying the dose of KADCYLA

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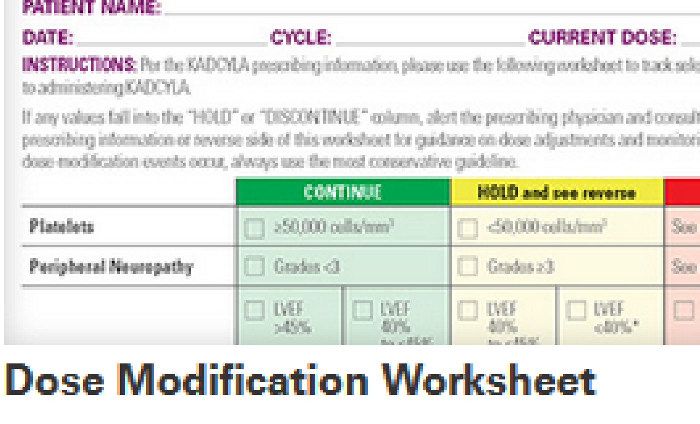

Medication Distinction Poster

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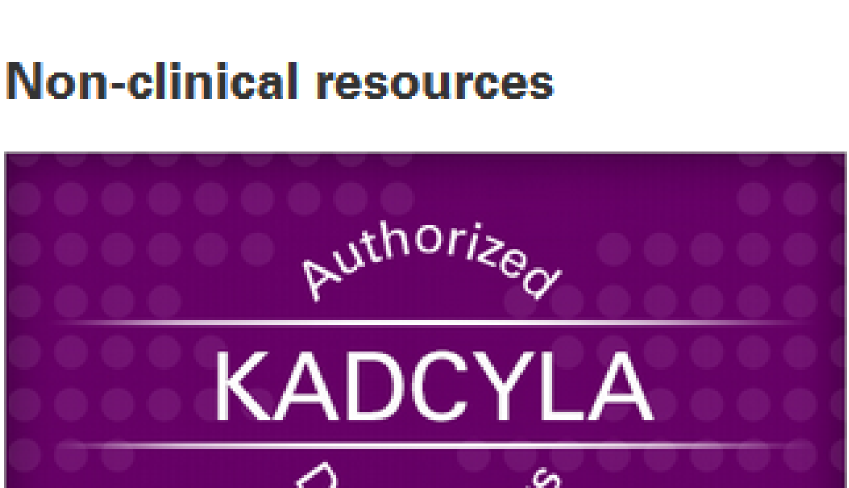

Nurse-to-Patient Tear Sheet

A brief overview for patients, containing general information about KADCYLA

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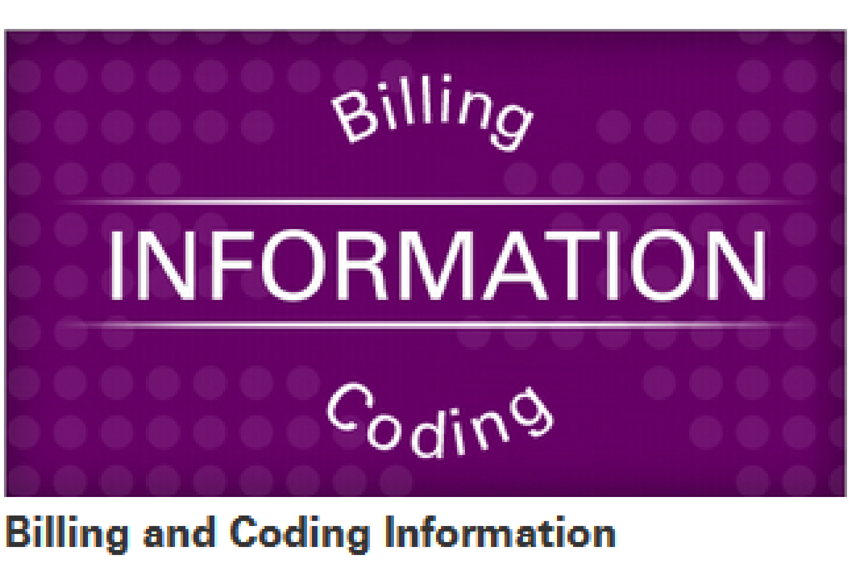

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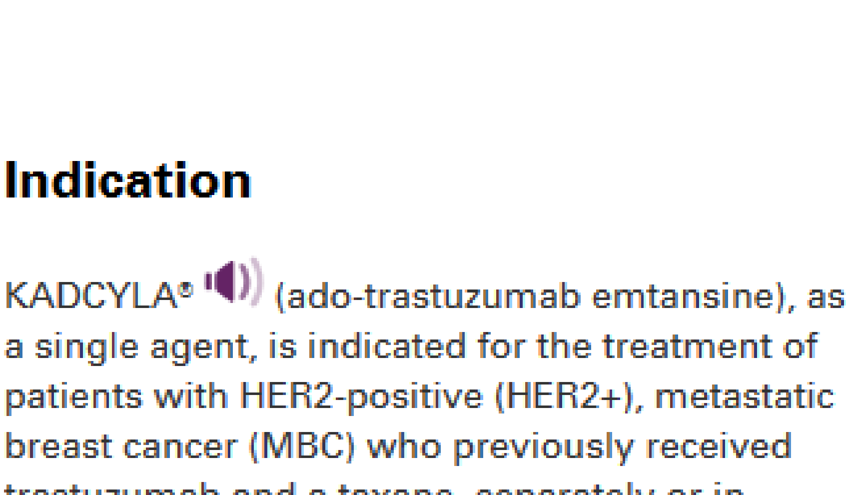

KADCYLA Access Solutions

Information for financial assistance to help support your patients

» KADCYLA Access Solutions

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Resources

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Please complete the form below if you would like a Genentech sales representative to contact you regarding your KADCYLA information request. You should receive a response within 2 business days.

Your contact information will not be used for any other purpose than for the representative to respond to your information request.

Your Contact Information (*indicates a required field)

Provider Type*

Select

Specialty*

Select

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Last Name*

Email Address*

Confirm Email Address*

Zip Code*

Practice/Organization

Topic

- Clinical Data
- Nurse Support
- Reimbursement Support
- General KADCYLA

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I would like to register for Genentech BioOncology updates

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Genentech will not sell, rent, or otherwise distribute your name and any personally identifiable information outside of Genentech and its agents. Genentech will only use your information in accordance with its **Privacy Policy**.

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Provider Type*

Select

- Select
- Resident/Fellow
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- Nurse Practitioner
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- Physician Assistant
- Other

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Select

- Select
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- Surgical Oncology

Resources

Contact a Representative

Reminder: This feature is intended for US healthcare professionals only.

Please complete the form below if you would like a Genentech sales representative to contact you regarding your KADCYLA information request. You should receive a response within 2 business days.

Your contact information will not be used for any other purpose than for the representative to respond to your information request.

Your Contact Information (*indicates a required field)

Provider Type*

Select

is missing and it is required

Specialty*

Select

is missing and it is required

First Name*

is missing and it is required

Last Name*

is missing and it is required

Email Address*

is missing and it is required

Confirm Email Address*

is missing and it is required

Zip Code*

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Practice/Organization

Topic

- Clinical Data
- Nurse Support
- Reimbursement Support
- General KADCYLA

For your security, please enter the codes below:

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Privacy & Terms

I would like to register for Genentech BioOncology updates

By checking the box above, you agree to allow Genentech and its agents to collect the information provided and to be contacted by Genentech and its agents in the future regarding BioOncology products, and related disease education.

By submitting this form, you agree to allow Genentech and its agents to collect the information provided and to be contacted directly by a Genentech sales representative. Your information will not be used for any other purpose than for a representative to respond to your information request, or for us to send you other Genentech BioOncology updates if you have registered to receive them.

Genentech will not sell, rent, or otherwise distribute your name and any personally identifiable information outside of Genentech and its agents. Genentech will only use your information in accordance with its **Privacy Policy**.

Submit

Indication

KADCYLA® (ado-trastuzumab emtansine), as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:

- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy

Important Safety Information

Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY

- **Do Not Substitute KADCYLA for or with Trastuzumab**
- **Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin**
- **Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function**
- **Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception**

The following additional serious adverse reactions have been reported in clinical trials with KADCYLA:

- Interstitial Lung Disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatality: KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis
- Infusion-related reactions (IRR), Hypersensitivity: KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR
- Thrombocytopenia: Monitor platelet counts prior to initiation of KADCYLA and prior to each dose. Institute dose modifications as appropriate
- Peripheral neuropathy: KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2
- Reactions secondary to extravasation: The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration

Additional Important Safety Information:

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA therapy
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You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling **1 (888) 835-2555**. You may contact the FDA by visiting **www.fda.gov/medwatch** or calling **1 (800) FDA-1088**.

Please see accompanying full Prescribing Information for additional important safety information, including Boxed WARNINGS.

Resources

Contact a Representative

Thank you

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Safety first! Press here to read the Important Safety Information

Resources

Contact a Representative

Page Name: Contact a Representative
Page Title: Contact Genentech Rep | KADCYLA® (ado-trastuzumab emtansine)
Meta Description: Sign up to have a Genentech representative contact you with KADCYLA® (ado-trastuzumab emtansine) information. KADCYLA® (ado-trastuzumab emtansine), injection for intravenous use, as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either: Received prior therapy for metastatic disease, or Developed disease recurrence during or within six months of completing adjuvant therapy. Important Safety Information: Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYOFETAL TOXICITY: Do Not Substitute KADCYLA for or with Trastuzumab. Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each. KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin. Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function. Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception. The following additional serious adverse reactions have been reported in clinical trials with KADCYLA: Interstitial Lung Disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatality: KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis. Infusion-related reactions (IRR), Hypersensitivity: KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR. Thrombocytopenia: Monitor platelet counts prior to initiation of KADCYLA and prior to each dose. Institute dose modifications as appropriate. Peripheral neuropathy: KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2. Reactions secondary to extravasation: The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Additional Important Safety Information: Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA therapy. Nursing mothers: Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother. The most common adverse drug reactions (frequency > 25%) across clinical trials with KADCYLA were fatigue, nausea, musculoskeletal pain, thrombocytopenia, headache, increased transaminases, and constipation. You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling 1-888-835-2555. You may contact the FDA by visiting www.fda.gov/medwatch or calling 1-800-FDA-1088.

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Confirm Email Address*

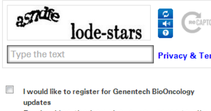
Zip Code*

Practice/Organization

Topic

- Clinical Data
- Nurse Support
- Reimbursement Support
- General KADCYLA

For your security, please enter the codes below:



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Submit

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Safety first! Press here to read the Important Safety Information

Patient Support

Financial Support for Your Patients

KADCYLA Access Solutions

KADCYLA Access Solutions helps to resolve access and reimbursement issues for individual patients every day. Our dedicated Specialists help bring patient treatment and practice solutions together.

»Learn more

BioOncology Co-pay Card

Genentech offers the Genentech BioOncology Co-pay Card to help qualified patients with the out-of-pocket costs associated with their KADCYLA prescription.

»Learn more

Genentech Access to Care Foundation (GATCF)

GATCF was established to help patients with unmet medical needs who are uninsured or rendered uninsured by payer denial and who meet specific financial and medical criteria to receive proper medical treatment.

»Learn more

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Patient Support

Financial Support for Your Patients

Page Name: Patient Financial Support
Page Title: Patient Financial Support | KADCYLA® (ado-trastuzumab emtansine)
Meta Description: Explore the financial resources that are available for KADCYLA® (ado-trastuzumab emtansine) patients. KADCYLA® (ado-trastuzumab emtansine), injection for intravenous use, as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either: Received prior therapy for metastatic disease, or Developed disease recurrence during or within six months of completing adjuvant therapy. Important Safety Information: Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYOFETAL TOXICITY: Do Not Substitute KADCYLA for or with Trastuzumab, Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin, Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function, Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception. The following additional serious adverse reactions have been reported in clinical trials with KADCYLA: Interstitial Lung Disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatality: KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis, Infusion-related reactions (IRR), Hypersensitivity: KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR, Thrombocytopenia: Monitor platelet counts prior to initiation of KADCYLA and prior to each dose. Institute dose modifications as appropriate, Peripheral neuropathy: KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2, Reactions secondary to extravasation: The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Additional Important Safety Information: Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA therapy, Nursing mothers: Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother, The most common adverse drug reactions (frequency > 25%) across clinical trials with KADCYLA were fatigue, nausea, musculoskeletal pain, thrombocytopenia, headache, increased transaminases, and constipation. You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling 1-888-835-2555. You may contact the FDA.

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Safety first! Press here to read the Important Safety Information

Patient Support

KADCYLA 24-hour Nurse Support Line

Expert advice any time your patients need it

When your patients have important questions about KADCYLA treatment, you want them to get information you can trust. With the KADCYLA Support Line, registered oncology nurses are always available to answer their questions and talk through any concerns.

Every nurse on our team:

- Specializes in oncology
- Has about 20 years of experience
- Is knowledgeable about KADCYLA treatment

We're here to help 24 hours a day—call the support line any time. Our nurses will be able to answer questions from patients about:

- How KADCYLA is designed to work
- The potential benefits of KADCYLA
- Side effects of KADCYLA
- What to expect from KADCYLA treatment
- Finding reimbursement help for KADCYLA

FOR 24-HOUR SUPPORT, CALL **1-855-KADCYLA (1-855-523-2952)**

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Safety first! Press here to read the

Page Name: Patient Clinical Support
Page Title: Patient Support | KADCYLA® (ado-trastuzumab emtansine)
Meta Description: Learn more about the 24-hour nurse support line for KADCYLA patients. KADCYLA® (ado-trastuzumab emtansine), injection for intravenous use, as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either: Received prior therapy for metastatic disease, or Developed disease recurrence during or within six months of completing adjuvant therapy. Important Safety Information: Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYOFETAL TOXICITY: Do Not Substitute KADCYLA for or with Trastuzumab, Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each. KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin, Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function, Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception. The following additional serious adverse reactions have been reported in clinical trials with KADCYLA: Interstitial Lung Disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatality: KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis, Infusion-related reactions (IRR), Hypersensitivity: KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR, Thrombocytopenia: Monitor platelet counts prior to initiation of KADCYLA and prior to each dose. Institute dose modifications as appropriate, Peripheral neuropathy: KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2, Reactions secondary to extravasation: The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Additional Important Safety Information: Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA therapy, Nursing mothers: Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother, The most common adverse drug reactions (frequency > 25%) across clinical trials with KADCYLA were fatigue, nausea, musculoskeletal pain, thrombocytopenia, headache, increased transaminases, and constipation. You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling 1-888-835-2555. You may contact the FDA by visiting

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FOR 24-HOUR SUPPORT, CALL 1-855-KADCYLA (1-855-523-2952)

Indication

KADCYLA® (ado-trastuzumab emtansine), as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:

- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy

Important Safety Information

Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY

- **Do Not Substitute KADCYLA for or with Trastuzumab**
- **Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin**
- **Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function**
- **Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception**

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- Interstitial Lung Disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatality: KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis
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- Peripheral neuropathy: KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2
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Additional Important Safety Information:

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Meta Description: Register for Updates | KADCYLA® (ado-trastuzumab emtansine)
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- Peripheral neuropathy: KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2
- Reactions secondary to extravasation: The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration

Additional Important Safety Information:

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA therapy
- Nursing mothers: Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother
- The most common adverse drug reactions (frequency > 25%) across clinical trials with KADCYLA were fatigue, nausea, musculoskeletal pain, thrombocytopenia, headache, increased transaminases, and constipation

You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling **1 (888) 835-2555**. You may contact the FDA by visiting **www.fda.gov/medwatch** or calling **1 (800) FDA-1088**.

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Safety first! Press here to read the Important Safety Information

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Indication

KADCYLA® (ado-trastuzumab emtansine), as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:

- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy

Important Safety Information

Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY

- **Do Not Substitute KADCYLA for or with Trastuzumab**
- **Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin**
- **Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function**
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The following additional serious adverse reactions have been reported in clinical trials with KADCYLA:

- Interstitial Lung Disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatality: KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis
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Important Safety Information
Warnings and Precautions

Hepatotoxicity (Boxed WARNING)

Hepatotoxicity, predominantly in the form of asymptomatic increases in the concentrations of serum transaminases, has been observed in clinical trials with KADCYLA.

Serious hepatobiliary disorders, including at least two fatal cases of severe drug-induced liver injury and associated hepatic encephalopathy, have been reported in clinical trials with KADCYLA. Some of the observed cases may have been confounded by comorbidities and concomitant medications with known hepatotoxic potential.

Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Patients with known active hepatitis B virus or hepatitis C virus were excluded from EMILIA. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases and/or total bilirubin. Permanently discontinue KADCYLA treatment in patients with serum transaminases > 3X ULN and concomitant total bilirubin > 2X ULN.

In clinical trials of KADCYLA, cases of nodular regenerative hyperplasia (NRH) of the liver have been identified from liver biopsies (3 cases out of 882 treated patients). NRH should be considered in all patients with clinical symptoms of portal hypertension but with normal transaminases and no manifestations of cirrhosis. Diagnosis can be confirmed only by histopathology. Upon diagnosis, KADCYLA treatment must be permanently discontinued.

Left Ventricular Dysfunction (Boxed WARNING)

Patients treated with KADCYLA are at increased risk of developing left ventricular dysfunction. A decrease of LVEF to < 40% has been observed in patients treated with KADCYLA. In EMILIA, left ventricular dysfunction occurred in 1.8% of patients in the KADCYLA-treated group and 3.3% of patients in the comparator group.

Assess LVEF prior to initiation of KADCYLA and at regular intervals (e.g. every 3 months) during treatment. Treatment with KADCYLA has not been studied in patients with LVEF < 50% prior to treatment. If, at routine monitoring, LVEF is < 40%, or is 40% to 45% with a 10% or greater absolute decrease below the pretreatment value, withhold KADCYLA and repeat LVE assessment within approximately 3 weeks. Permanently discontinue KADCYLA if the LVEF has not improved or has declined further.

Embryo-Fetal Toxicity (Boxed WARNING)

Pregnancy Category D. KADCYLA can cause fetal harm or death when administered to a pregnant woman. There are no adequate and well-controlled studies of KADCYLA in pregnant women and no reproductive and developmental toxicology studies have been conducted with ado-trastuzumab emtansine. Nevertheless, treatment with trastuzumab, the antibody component of KADCYLA, during pregnancy in the postmarketing setting has resulted in oligohydramnios, some associated with fatal pulmonary hypoplasia, skeletal abnormalities and neonatal death. DM1, the cytotoxic component, can be expected to cause embryo-fetal toxicity.

If KADCYLA is used during pregnancy, or if the patient becomes pregnant while receiving KADCYLA, apprise the patient of the potential hazard to the fetus.

Verify pregnancy status prior to the initiation of KADCYLA. Advise patients of the risks of embryo-fetal death and birth defects and the need for contraception during and for 6 months following treatment. Advise patients to contact their healthcare provider immediately if they suspect they may be pregnant.

If KADCYLA is administered during pregnancy or if a patient becomes pregnant while receiving KADCYLA, immediately report exposure to the Genentech Adverse Event Line at **1 (888) 835-2555**. Encourage women who may be exposed during pregnancy to enroll in the **MotHER Pregnancy Registry** by contacting **1 (800) 690-6720**.

Pulmonary Toxicity

Cases of interstitial lung disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatal outcome have been reported in clinical trials with KADCYLA. Signs and symptoms include dyspnea, cough, fatigue, and pulmonary infiltrates. In EMILIA, the overall frequency of pneumonitis was 1.2%.

Treatment with KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis.

Patients with dyspnea at rest due to complications of advanced malignancy and comorbidities may be at increased risk of pulmonary events.

Infusion-Related Reactions, Hypersensitivity Reactions

Treatment with KADCYLA has not been studied in patients who had trastuzumab permanently discontinued due to infusion-related reactions (IRR) and/or hypersensitivity; treatment with KADCYLA is not recommended for these patients.

Infusion-related reactions, characterized by one or more of the following symptoms – flushing, chills, pyrexia, dyspnea, hypotension, wheezing, bronchospasm, and tachycardia – have been reported in clinical trials of KADCYLA. In the randomized trial, the overall frequency of IRRs in patients treated with KADCYLA was 1.4%. In most patients, these reactions resolved over the course of several hours to a day after the infusion was terminated.

KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR. Patients should be observed closely for IRRs especially during the first infusion.

One case of a serious, allergic/anaphylactoid-like infusion reaction has been observed in clinical trials of single-agent KADCYLA. Medications to treat such reactions, as well as emergency equipment, should be available for immediate use.

Thrombocytopenia

Thrombocytopenia was reported in clinical trials of KADCYLA. The majority of these patients had Grade 1 or 2 events (< LLN to ≥ 50,000/mm³) with the nadir occurring by day 8 and generally improving to Grade 0 or 1 (≥ 75,000 /mm³) by the next scheduled dose. In clinical trials of KADCYLA, the incidence and severity of thrombocytopenia were higher in Asian patients. Independent of race, the incidence of severe hemorrhagic events in patients treated with KADCYLA was low.

In EMILIA, the incidence of ≥ Grade 3 thrombocytopenia was 14.5% in the KADCYLA-treated group and 0.4% in the comparator group. In Asian patients, the incidence of ≥ Grade 3 thrombocytopenia was 45.1% in the KADCYLA group and 1.3% in the comparator group.

Monitor platelet counts prior to initiation of KADCYLA and prior to each KADCYLA dose. KADCYLA has not been studied in patients with platelet counts ≤ 100,000/mm³ prior to initiation of treatment. In the event of decreased platelet count to Grade 3 or greater (< 50,000/mm³), do not administer KADCYLA until platelet counts recover to Grade 1 (≥ 75,000/mm³). Patients with thrombocytopenia (≤ 100,000/mm³) prior to initiation of KADCYLA and patients on anti-coagulant treatment should be closely monitored during treatment with KADCYLA.

Neurotoxicity

Peripheral neuropathy, mainly as Grade 1 and predominantly sensory, was reported in clinical trials of KADCYLA. In EMILIA, the incidence of ≥ Grade 3 peripheral neuropathy was 2.2% in the KADCYLA-treated group and 0.2% in the comparator group.

KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2. Patients should be clinically monitored on an ongoing basis for signs/symptoms of neurotoxicity.

HER2 Testing

Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA therapy because these are the only patients studied for whom benefit has been shown. Assessment of HER2 status should be done using an FDA-approved test performed by laboratories with demonstrated proficiency.

In the randomized study, patients with breast cancer were required to have evidence of HER2 overexpression defined as 3+ IHC and/or FISH amplification ratio ≥ 2.0 assessed by a validated test.

Extravasation

In KADCYLA clinical studies, reactions secondary to extravasation have been observed. These reactions, observed more frequently within 24 hours of infusion, were usually mild and comprised of erythema, tenderness, skin irritation, pain or swelling at the infusion site. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. Specific treatment for KADCYLA extravasation is unknown.

Use in Specific Populations

Nursing Mothers

It is not known whether KADCYLA specifically is excreted in human milk, but IgG is known to be excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or discontinue KADCYLA, taking into account the importance of the drug to the mother.

Adverse Events

Adverse Reactions

The most common NCI-CTCAE (version 3) ARs Grades ≥3 (frequency >2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy, and fatigue.

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Important Safety

Page Name: Important Safety Information
Page Title: Important Safety Information | KADCYLA® (ado-trastuzumab emtansine)
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Indication

KADCYLA® (ado-trastuzumab emtansine), as a single agent, is indicated for the treatment of patients with HER2-positive (HER2+), metastatic breast cancer (MBC) who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:

- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy

Important Safety Information

Boxed WARNINGS: HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY

- **Do Not Substitute KADCYLA for or with Trastuzumab**
- **Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients treated with KADCYLA. Monitor serum transaminases and bilirubin prior to initiation of KADCYLA treatment and prior to each KADCYLA dose. Reduce dose or discontinue KADCYLA as appropriate in cases of increased serum transaminases or total bilirubin**
- **Cardiac Toxicity: KADCYLA administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment with KADCYLA. Withhold treatment for clinically significant decrease in left ventricular function**
- **Embryo-Fetal Toxicity: Exposure to KADCYLA can result in embryo-fetal death or birth defects. Advise patients of these risks and the need for effective contraception**

The following additional serious adverse reactions have been reported in clinical trials with KADCYLA:

- Interstitial Lung Disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatality: KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis
- Infusion-related reactions (IRR), Hypersensitivity: KADCYLA treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life-threatening IRR
- Thrombocytopenia: Monitor platelet counts prior to initiation of KADCYLA and prior to each dose. Institute dose modifications as appropriate
- Peripheral neuropathy: KADCYLA should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2
- Reactions secondary to extravasation: The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration

Additional Important Safety Information:

- Detection of HER2 protein overexpression or gene amplification is necessary for selection of patients appropriate for KADCYLA therapy
- Nursing mothers: Discontinue nursing or discontinue KADCYLA taking into consideration the importance of the drug to the mother
- The most common adverse drug reactions (frequency > 25%) across clinical trials with KADCYLA were fatigue, nausea, musculoskeletal pain, thrombocytopenia, headache, increased transaminases, and constipation

You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling **1 (888) 835-2555**. You may contact the FDA by visiting **www.fda.gov/medwatch** or calling **1 (800) FDA-1088**.

Please see accompanying full Prescribing Information for additional important safety information, including Boxed WARNINGS.