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Proven survival benefit for your HER2+ MBC patients

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alternate SL: Significant clinical benefit for your HER2+ mBC patients

Dear [Healthcare Provider Name]:

[Customize the text in this paragraph with your own message to the Healthcare Provider. Based on Regulatory requirements, you may only include a 500-character message with the preformatted HTML e-mail. This includes the signature.]

[Signature]
KADCYLA demonstrated clinical benefits in patients with HER2+ MBC

Proven survival benefit[1]

Kadcyla®
ado-trastuzumab emtansine
for injection

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:

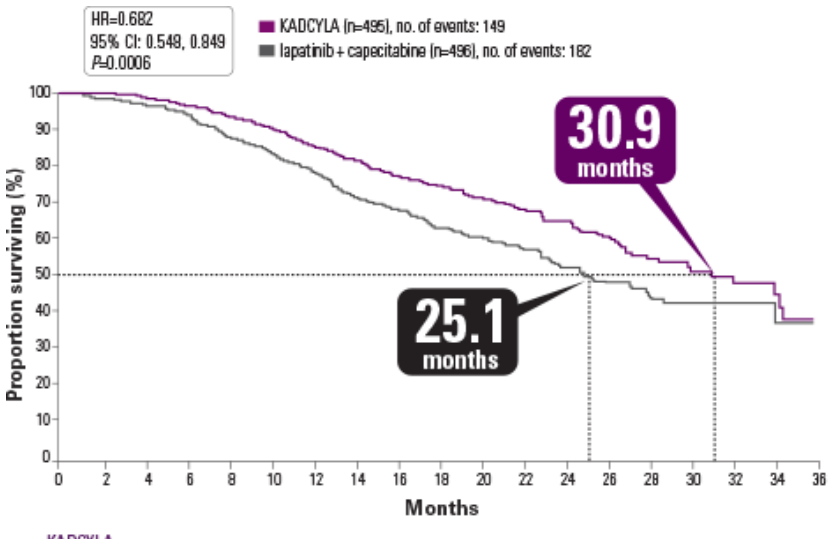
- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy

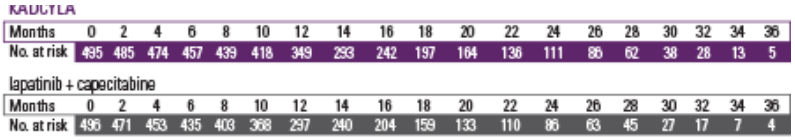
KADCYLA is the first HER2-targeted antibody-drug conjugate for HER2+ metastatic breast cancer.

In the Phase III EMILIA trial of KADCYLA vs the combination of lapatinib + capecitabine, KADCYLA extended median overall survival (OS) and significantly improved median progression-free survival (PFS).

KADCYLA extended median OS by nearly 6 months[1]

PRIMARY ENDPOINT: OVERALL SURVIVAL (OS)





Results of the randomized, open-label, Phase III EMILIA trial of KADCYLA (3.6 mg/kg IV, Day 1) vs the combination of lapatinib (1250 mg/day oral, once daily) and capecitabine (1000 mg/m^2, oral, twice daily, Days 1-14) in 21-day cycles until disease progression in HER2+ MBC patients previously treated with trastuzumab and a taxane. Primary endpoints were OS, progression-free survival (PFS), and safety.[1,2]

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

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**

For more information about these and other EMILIA trial endpoints, visit KADCYLA.com.

Important Safety Information

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 download the full Prescribing Information for additional important safety information, including Boxed WARNINGS.

For more information on KADCYLA, visit **KADCYLA.com**.

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.

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