

HPK0002464200

NOTE: Functional annotations apply to both the KADCYLA and the PERJETA sections of the banner.



Banner will be user-activated; the user hovers over the banner to expand it.

Upon initial expand, the page curl will animate to roll down briefly to reveal the option to view additional content (see p. 3 for rolled-down view).

Clicking "Close" will collapse the banner to the initial state.

**Kadcyla** ado-trastuzumab emtansine for injection Scroll for Important Safety Information including Boxed WARNINGS Close [x]

**Results of the EMILIA trial: KADCYLA vs lapatinib + capecitabine**  
**Proven survival benefit for patients, including both ER+/PR+ and ER-/PR- patient subgroups**

Select patient subgroups/treatment benefit by hormone receptor status<sup>1</sup>

Select a tab for more information

Category	n	OS	
		HR	95% CI
All patients	991	0.68	0.55, 0.85

**Indication and Important Safety Information**  
 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.

**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

**See full Prescribing Information**

**ZOOM** Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity

Clicking "Zoom" will enable users to see the content in in the full viewing space. See pp. 22-28 for example.

Clicking this space will present user with expanded Boxed WARNINGS view (see p. 4 for expanded view of KADCYLA warning text).

Link to PI is static so users can always see and click it.

Hovering over the page curl will cause the page to roll down to reveal the option for users to click to view the alternate brand content at any time (see p. 29).

Global - users can use scroll bars in each section to navigate the content

The screenshot displays a medical product page for Kadcyla. On the left, there is a section titled 'More survival data' with a document icon. Below it, text describes the EMILIA trial: 'KADCYLA vs + capecitabine' and mentions 'survival benefit for patients, including both ER+/PR+ and ER-/PR- patient subgroups'. A purple button reads 'Select patient subgroups/treatment benefit by hormone receptor status¹'. Below this is a tabbed interface with 'PFS' and 'OS' tabs. A table shows survival data for 'All patients' with a hazard ratio of 0.68 and a 95% CI of 0.55, 0.85. A 'ZOOM' icon is visible. On the right, the 'Kadcyla' logo is at the top, followed by the text 'Scroll for Important Safety Information including Boxed WARNINGS' and a 'Close [x]' button. The main content area is titled 'Indication and Important Safety Information' and contains text about the drug's use for HER2-positive metastatic breast cancer. Below this is a 'Boxed WARNINGS' section listing 'HEPATOTOXICITY, CARDIAC TOXICITY, EMBRYO-FETAL TOXICITY' and two bullet points: 'Do Not Substitute KADCYLA for or with Trastuzumab' and 'Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients'. A 'See full Prescribing Information' link is at the bottom. Vertical scroll bars are present on both the left and right sides of the main content area.

PFS		OS	
Category	n	HR	95% CI
All patients	901	0.68	0.55, 0.85

**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


[See full Prescribing Information](#)

Close [x]

### 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

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

 ZOOM OUT

Clicking "zoom out" returns the user to the prior view.



For all tabbed charts, users can click a tab to reveal which data they want to view

+

Kadcyla<sup>®</sup>

Scroll for Important Safety Information including Boxed WARNINGS

Close [x]

Select patient subgroups/treatment benefit by hormone receptor status<sup>1</sup>

Select a tab for more information

PFS

OS

Category	n	HR	95% CI
All patients	991	0.68	0.55, 0.85
P=0.0006			
Hormone receptor status			
Positive (ER+ and/or PR+)	545	0.62	0.46, 0.85
Negative (ER- and PR-)	426	0.75	0.54, 1.03

ZOOM

Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity

Indication and Important Safety Information

KADCYLA<sup>®</sup> (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.

**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

See full Prescribing Information

PFS data

**Select patient subgroups/treatment benefit by hormone receptor status<sup>1</sup>**

Select a tab for more information

PFS		OS	
Category	n	HR	95% CI
<b>All patients</b>	<b>991</b>	<b>0.65</b>	<b>0.55, 0.77</b>
<i>P</i> <0.0001			
Hormone receptor status			
<b>Positive</b> (ER+ and/or PR+)	545	<b>0.72</b>	0.58, 0.91
<b>Negative</b> (ER- and PR-)	426	<b>0.56</b>	0.44, 0.72

**Kadcyla**  
ado-trastuzumab emtansine  
for injection

Scroll for Important Safety Information including Boxed WARNINGS

Close [x]

**Indication and Important Safety Information**

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.

**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

[See full Prescribing Information](#)

**ZOOM**


**Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity**

+ HER2-positive (ER- and PR-)	426	0.56	0.44, 0.72
----------------------------------	-----	------	------------


HR = hazard ratio; CI = confidence interval; ER = estrogen receptor; PR = progesterone receptor.

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<sup>2</sup>, 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 overall survival (OS), progression-free survival (PFS), and safety.

**KADCYLA significantly extended OS (coprimary endpoint)<sup>1</sup>**



**6**



**50%**

**Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity**

**Kadcyla**  
ado-trastuzumab emtansine  
for injection

Scroll for Important Safety Information including Boxed WARNINGS

Close [x]

### Indication and Important Safety Information

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.

**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

**See full Prescribing Information**

**ZOOM**

**KADCYLA significantly extended OS (coprimary endpoint)<sup>1</sup>**

**6 months**  
Median OS improvement  
30.9 vs 25.1 months  
(HR=0.682; 95% CI: 0.548, 0.849; P=0.0006)

**50% improvement**  
In median PFS  
9.6 vs 6.4 months  
(HR=0.650; 95% CI: 0.549, 0.771; P<0.0001)<sup>1</sup>

• The most common adverse reactions seen with KADCYLA Grades ≥3 (frequency >2%) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy, and fatigue based on NCI-CTCAE (version 3)

**Kadcyla**  
ado-trastuzumab emtansine  
for injection

Scroll for Important Safety Information including Boxed WARNINGS

Close [x]

**Indication and Important Safety Information**

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.

**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


**ZOOM** Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity

**See full Prescribing Information**

+

anemia, peripheral neuropathy, and fatigue based on NCI-CTCAE (version 3)

Close [x]



Scroll for Important Safety Information including Boxed WARNINGS

**Select Important Safety Information: 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

**Most common adverse reactions (ARs) categorized according to NCI-CTCAE (version 3)**

Select a tab for more information

All Grades (%)

Grades ≥3 (%)

ZOOM

Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity

**Indication and Important Safety Information**

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.

**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

[See full Prescribing Information](#)

All Grades (%)	Grades ≥3 (%)	
	KADCYLA (n=490)	lapatinib + capecitabine (n=488)
<b>AR</b>		
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

**ZOOM**

Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity

Scroll for Important Safety Information including Boxed WARNINGS
 
Close [x]

### Indication and Important Safety Information

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.


**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

[See full Prescribing Information](#)



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



Scroll for Important Safety Information including Boxed WARNINGS Close [x]


### Indication and Important Safety Information


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.

**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

[See full Prescribing Information](#)




 Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity

+ All Grades (%)	Grades $\geq$ 3 (%)	
	KADCYLA (n=490)	lapatinib + capecitabine (n=488)
<b>AR</b>		
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

**ZOOM**

**Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity**

Scroll for Important Safety Information including Boxed WARNINGS

Close [x]

### Indication and Important Safety Information


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.

**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

See full Prescribing Information

+ Nausea	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



Close [x]

Scroll for Important Safety Information including Boxed WARNINGS

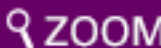
### Indication and Important Safety Information

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.

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



[See full Prescribing Information](#)


Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity

+ ...ing	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

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

 [Contact a Representative >](#)

 **ZOOM**  **Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity**

**Kadcyla**  
ado-trastuzumab emtansine  
for injection

Scroll for Important Safety Information including Boxed WARNINGS Close [x]

### Indication and Important Safety Information

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.

**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



[See full Prescribing Information](#)


This link takes users to brand site page to sign up to contact a representative

+ Anemia	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

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

 **Contact a Representative >**

 **ZOOM**  **Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity**

 **Kadcyla**  
ado-trastuzumab emtansine  
for injection

Scroll for Important Safety Information including Boxed WARNINGS Close [x]


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**  
See full Prescribing Information

+	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

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

 [Contact a Representative >](#)

 **ZOOM**  **Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity**

 **Kadcyla**  
ado-trastuzumab emtansine  
for injection

Scroll for Important Safety Information including Boxed WARNINGS Close [x]

### 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



[See full Prescribing Information](#)




+ ...ing	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

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

 **Contact a Representative >**

 **ZOOM**  **Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity**

 **Kadcyla**  
ado-trastuzumab emtansine  
for injection

Scroll for Important Safety Information including Boxed WARNINGS Close [x]

- 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%


**See full Prescribing Information**

+ Side Effect	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

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

 [Contact a Representative >](#)

 **ZOOM**  **Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity**

 **Kadcyla**  
ado-trastuzumab emtansine  
for injection

Scroll for Important Safety Information including Boxed WARNINGS Close [x]

- 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  $\geq$  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  $\geq$  Grade 3 peripheral


[See full Prescribing Information](#)

+ Anemia	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

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

 **Contact a Representative >**

 **Boxed WARNINGS:** Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity

 **Kadcyla**  
ado-trastuzumab emtansine  
for injection

Scroll for Important Safety Information including Boxed WARNINGS Close [x]

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


**See full Prescribing Information**

+ Anemia	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

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

 **Contact a Representative >**

 **Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity**

 **Kadcyla**  
ado-trastuzumab emtansine  
for injection

Scroll for Important Safety Information including Boxed WARNINGS Close [x]

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


**See full Prescribing Information**

+ Anemia	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

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

 **Contact a Representative >**

 **ZOOM**  **Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity**

 **Kadcyla**  
ado-trastuzumab emtansine  
for injection

Scroll for Important Safety Information including Boxed WARNINGS Close [x]

musculoskeletal pain, thrombocytopenia, increased transaminases, headache, and constipation. The most common NCI-CTCAE (version 3)  $\geq$  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](http://www.fda.gov/medwatch) or calling 1-800-FDA-1088.

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



**See full Prescribing Information**

Results of the EMILIA trial: KADCYLA vs lapatinib + capecitabine Close [x]

Proven survival benefit for patients, including both ER+/PR+ and ER-/PR- patient subgroups

Select patient subgroups/treatment benefit by hormone receptor status<sup>1</sup>

Category	n	PFS		OS	
		HR	95% CI	HR	95% CI
All patients	991	0.65	0.55, 0.77	0.68	0.55, 0.85
		<i>P</i> <0.0001		<i>P</i> =0.0006	
<b>Hormone receptor status</b>					
Positive (ER+ and/or PR+)	545	0.72	0.58, 0.91	0.62	0.46, 0.85
Negative (ER- and PR-)	426	0.56	0.44, 0.72	0.75	0.54, 1.03

 ZOOM OUT  Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity



Close [x]

**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

Please see [full Prescribing Information](#) for additional important safety information, including Boxed WARNINGS.

 **BACK TO ZOOM**

HR = hazard ratio; CI = confidence interval; ER = estrogen receptor; PR = progesterone receptor.

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<sup>2</sup>, 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 overall survival (OS), progression-free survival (PFS), and safety.

**KADCYLA significantly extended OS (coprimary endpoint)<sup>1</sup>**

**6 months**

**50% improvement**

ZOOM OUT

**Boxed WARNINGS:** Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity

progression-free survival (PFS), and safety.

Close [x]

**KADCYLA significantly extended OS (coprimary endpoint)<sup>1</sup>**

Metric	Value	HR	95% CI	P-value
Median OS improvement	6 months (30.9 vs 25.1 months)	0.682	0.548, 0.849	0.0006
In median PFS	50% improvement (9.6 vs 6.4 months)	0.650	0.549, 0.771	<0.0001

**6 months**  
Median OS improvement  
30.9 vs 25.1 months  
(HR=0.682; 95% CI: 0.548, 0.849; P=0.0006)

**50% improvement**  
In median PFS  
9.6 vs 6.4 months  
(HR=0.650; 95% CI: 0.549, 0.771; P<0.0001)<sup>1</sup>

**ZOOM OUT**

**Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity**


- The most common adverse reactions seen with KADCYLA Grades  $\geq 3$  (frequency  $>2\%$ ) were thrombocytopenia, increased transaminases, anemia, hypokalemia, peripheral neuropathy, and fatigue based on NCI-CTCAE (version 3) Close [x]

### Select Important Safety Information: 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


### Most common adverse reactions (ARs) categorized according to NCI-CTCAE (version 3)


ADVERSE REACTION	KADCYLA (n=490)		lapatinib + capecitabine (n=488)	
	All Grades, %	Grades $\geq 3$ , %	All Grades, %	Grades $\geq 3$ , %
Nausea	39.8	0.8	45.1	2.5
Fatigue	36.3	2.5	28.3	3.5

 ZOOM OUT

 Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity

Musculoskeletal pain	36.1	1.8	30.5	1.4 <span>Close [x]</span>
Thrombocytopenia	31.2	14.5	3.3	0.4
Increased transaminases	28.8	8.0	14.3	2.5
Headache	28.2	0.8	14.5	0.8
Constipation	26.5	0.4	11.1	0.0
Diarrhea	24.1	1.6	79.7	20.7
Peripheral neuropathy	21.2	2.2	13.5	0.2
Vomiting	19.2	0.8	29.9	4.5
Anemia	14.3	4.1	10.5	2.5
Stomatitis	14.1	0.2	32.6	2.5
Rash	11.6	0.0	27.5	1.8
Hypokalemia	10.2	2.7	9.4	4.7
Neutropenia	6.7	2.0	9.0	4.3

 ZOOM OUT

 **Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity**

	2010	2011	2012	2013
Diarrhea	24.1	1.6	79.7	20.7
Peripheral neuropathy	21.2	2.2	13.5	0.2
Vomiting	19.2	0.8	29.9	4.5
Anemia	14.3	4.1	10.5	2.5
Stomatitis	14.1	0.2	32.6	2.5
Rash	11.6	0.0	27.5	1.8
Hypokalemia	10.2	2.7	9.4	4.7
Neutropenia	6.7	2.0	9.0	4.3

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



Contact a Representative >



ZOOM OUT



Boxed WARNINGS: Hepatotoxicity,  
Cardiac Toxicity, Embryo-Fetal Toxicity



Upon initial expand, the page curl will animate to roll down briefly to reveal the option to view additional content (see p. 30 for rolled-down view).

Clicking "Close" will collapse the banner to the initial state.

PERJETA<sup>®</sup> pertuzumab

Scroll for Important Safety Information including Boxed WARNINGS

Close [x]

**Results of the CLEOPATRA trial: PERJETA + Herceptin (trastuzumab) + docetaxel vs placebo + Herceptin + docetaxel**

**Proven survival benefit for patients, including ER/PR patient subgroups**

- There was an inability to show benefit with PERJETA in patients with nonvisceral metastases (n=178; HR=1.42 [95% CI: 0.71, 2.84])<sup>3</sup>

Select patient subgroups/treatment benefit by hormone receptor status/disease type (CLEOPATRA trial)<sup>1-3</sup>

Select a tab for more information

**Indication and Important Safety Information**

PERJETA<sup>®</sup> (pertuzumab) is a HER2/neu receptor antagonist indicated in combination with Herceptin<sup>®</sup> (trastuzumab) and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

- PERJETA administration can result in subclinical and clinical cardiac failure. Evaluate left

See full Prescribing Information

**ZOOM** Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity

Clicking "Zoom" will enable users to see the content in in the full viewing space. See pp. 50-59 for example.

Clicking this space will present user with expanded Boxed WARNINGS view (see p. 31 for expanded view of PERJETA warning text).

Link to PI is static so users can always see and click it.

Hovering over the page curl will cause the page to roll down to reveal the option for users to click to view the alternate brand content at any time (see p. 2).

Global - users can use scroll bars in each section to navigate the content


The screenshot displays a medical product page for PERJETA (pertuzumab). On the left, a purple 'More survival data' section is partially unrolled, revealing text about the CLEOPATRA trial and a button to 'Select patient subgroups/treatment benefit by hormone receptor status/disease type (CLEOPATRA trial)<sup>1-3</sup>'. Below this is a 'ZOOM' section with a magnifying glass icon and the text 'Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity'. The main content area on the right is titled 'Indication and Important Safety Information' and includes a 'Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity' section. A 'See full Prescribing Information' link is at the bottom. The page has a 'Close [x]' button in the top right and a 'Scroll for Important Safety Information including Boxed WARNINGS' instruction. Two blue arrows point from external text boxes to the page curl and the scroll bars.

Close [x]

### Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity

- PERJETA administration can result in subclinical and clinical cardiac failure. Evaluate left ventricular function in all patients prior to and during treatment with PERJETA. Discontinue PERJETA treatment for a confirmed clinically significant decrease in left ventricular function
- Exposure to PERJETA can result in embryo-fetal death and birth defects. Studies in animals have resulted in oligohydramnios, delayed renal development, and death. Advise patients of these risks and the need for effective contraception

Please see PERJETA [full Prescribing Information](#) including Boxed WARNINGS for additional Important Safety Information.

 ZOOM OUT

Clicking "zoom out" returns the user to the prior view.

For all tabbed charts, users can click a tab to reveal which data they want to view

Category	n	HR	95% CI
<b>All patients</b>	<b>808</b>	<b>0.63</b>	<b>0.51, 0.75</b>
<i>P</i> <0.0001			
<b>Hormone receptor status</b>			
<b>Positive</b> (ER+ and/or PR+)	388	<b>0.72</b>	0.55, 0.95
<b>Negative</b> (ER- and PR-)	408	<b>0.55</b>	0.42, 0.72
<b>Disease type</b>			
<b>Visceral disease</b>	630	<b>0.55</b>	0.45, 0.68
<b>Nonvisceral disease</b>	178	<b>0.96</b>	0.61, 1.52

**PERJETA**  
pertuzumab

Scroll for Important Safety Information including Boxed WARNINGS

Close [x]

### Indication and Important Safety Information

PERJETA® (pertuzumab) is a HER2/neu receptor antagonist indicated in combination with Herceptin® (trastuzumab) and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

- PERJETA administration can result in subclinical and clinical cardiac failure. Evaluate left

[See full Prescribing Information](#)

**ZOOM** Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity

OS data

PFS		OS	
Category	n	HR	95% CI
<b>All patients</b>	<b>808</b>	<b>0.66</b>	<b>0.52, 0.84</b>
<i>P=0.0008</i>			
<b>Hormone receptor status</b>			
<b>Positive</b> (ER+ and/or PR+)	388	<b>0.73</b>	0.50, 1.06
<b>Negative</b> (ER- and PR-)	408	<b>0.57</b>	0.41, 0.79
<b>Disease type</b>			
<b>Visceral disease</b>	630	<b>0.57</b>	0.44, 0.74
<b>Nonvisceral disease</b>	178	<b>1.42</b>	0.71, 2.84

**PERJETA**  
pertuzumab

Scroll for Important Safety Information including Boxed WARNINGS Close [x]

### Indication and Important Safety Information

PERJETA® (pertuzumab) is a HER2/neu receptor antagonist indicated in combination with Herceptin® (trastuzumab) and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

- PERJETA administration can result in subclinical and clinical cardiac failure. Evaluate left

[See full Prescribing Information](#)

**ZOOM** Q **Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

+	visceral disease	178	1.42	0.71, 2.84
---	------------------	-----	------	------------

HR=hazard ratio; CI=confidence interval; ER=estrogen receptor; PR=progesterone receptor.

Results of a multicenter, randomized double-blind, placebo-controlled phase II trial in which patients were randomly allocated to receive placebo plus trastuzumab and docetaxel or PERJETA plus trastuzumab and docetaxel.

**Significant improvement in PFS<sup>1\*</sup>**

6.1  
months\*\*

Median IRF-assessed  
PFS improvement

34%  
reduction in risk  
of death

Median not yet reached  
for PFS-IPSA comparison

**PERJETA<sup>®</sup> (pertuzumab)**

Scroll for Important Safety Information including Boxed WARNINGS

**Indication and Important Safety Information**

PERJETA<sup>®</sup> (pertuzumab) is a HER2/neu receptor antagonist indicated in combination with Herceptin<sup>®</sup> (trastuzumab) and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

- PERJETA administration can result in subclinical and clinical cardiac failure. Evaluate left

**See full Prescribing Information**


**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**



+
6.1
months\*†
34%
reduction in risk  
of death
Scroll for Important Safety  
Information including Boxed WARNINGS
Close [x]

**Median IRF-assessed  
PFS improvement  
18.5 vs 12.4 months**  
(HR=0.62; 95% CI: 0.51,  
0.75; P<0.0001)

**Median not yet reached  
for PERJETA arm vs  
37.6 months**  
(HR=0.66; 95% CI: 0.52, 0.84;  
P=0.0008<sup>‡</sup>)



### Indication and Important Safety Information

PERJETA® (pertuzumab) is a HER2/neu receptor antagonist indicated in combination with Herceptin® (trastuzumab) and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

- PERJETA administration can result in subclinical and clinical cardiac failure. Evaluate left

[See full Prescribing Information](#)


\*At the time of the final PFS analysis, OS was not mature, and first interim OS analysis results did not meet the prespecified stopping boundary for statistical significance.<sup>1</sup>

†Stratified by prior treatment status and geographic region.<sup>1</sup>

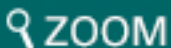

‡The HR and P-value for the second interim analysis of OS crossed the predefined efficacy stopping boundary (HR≤0.739, P≤0.0138).


ZOOM
Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity




 ...defined efficacy stopping boundary (HR $\leq$ 0.739, P $\leq$ 0.0138).

- At the time of analysis, there were 191 (47.5%) and 242 (59.6%) patients with a PFS event in the PERJETA + Herceptin + docetaxel and placebo + Herceptin + docetaxel arms, respectively<sup>1</sup>
- Median follow-up was 30 months (1 year following the first interim analysis) for both the PERJETA-based regimen and the placebo + Herceptin + docetaxel arm (Kaplan-Meier estimate)<sup>1-4</sup>
- More than 50% of patients in the PERJETA + Herceptin + docetaxel arm were alive at the time of the second interim analysis, thereby indicating that the median OS for this arm had not yet been reached<sup>2</sup>
- At the time of analysis, there were 113 (28.1%) and 154 (37.9%) deaths in the PERJETA + Herceptin + docetaxel arm and the placebo + Herceptin + docetaxel arm, respectively<sup>2</sup>


**ZOOM**

**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**


**PERJETA<sup>®</sup>**  
 pertuzumab

Scroll for Important Safety Information including Boxed WARNINGS
 Close [x]

### Indication and Important Safety Information

PERJETA<sup>®</sup> (pertuzumab) is a HER2/neu receptor antagonist indicated in combination with Herceptin<sup>®</sup> (trastuzumab) and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

#### Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity

- PERJETA administration can result in subclinical and clinical cardiac failure. Evaluate left

[See full Prescribing Information](#)

+ docetaxel arm and the placebo + Herceptin + docetaxel arm, respectively<sup>2</sup>

- The most common NCI-CTCAE (version 3) Grade 3-4 adverse reactions (>2%) were neutropenia, febrile neutropenia, leukopenia, diarrhea, peripheral neuropathy, anemia, asthenia, and fatigue<sup>1</sup>

**Select Important Safety Information:  
Left Ventricular Dysfunction**

Decreases in left ventricular ejection fraction (LVEF) have been reported with drugs that block HER2 activity, including PERJETA. Assess LVEF prior to initiation of PERJETA and at regular intervals (eg, every 3 months in the metastatic setting) during treatment to ensure that LVEF is within the institution's normal limits. If LVEF is <45%, or is 45% to 49% with a 10% or greater absolute decrease below the pretreatment value, withhold PERJETA and trastuzumab and repeat LVEF assessment within approximately 3 weeks. Discontinue PERJETA and

**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

**PERJETA® (pertuzumab)**

Scroll for Important Safety Information including Boxed WARNINGS

Close [x]

**Indication and Important Safety Information**

PERJETA® (pertuzumab) is a HER2/neu receptor antagonist indicated in combination with Herceptin® (trastuzumab) and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

- PERJETA administration can result in subclinical and clinical cardiac failure. Evaluate left

**See full Prescribing Information**

**ZOOM** **Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

+ ... below the pretreatment value, withhold PERJETA and trastuzumab and repeat LVEF assessment within approximately 3 weeks. Discontinue PERJETA and trastuzumab if LVEF has not improved or has declined further, unless the benefits for the individual patient outweigh the risks.

**Most common adverse reactions (ARs): All Grades (>30%) or Grades 3-4 (>2%)<sup>1</sup>**

Select a tab for more information

	All Grades (%)	Grades 3-4, %
<b>AR</b>	<b>PERJETA + Herceptin + docetaxel (n=407)</b>	<b>Placebo + Herceptin + docetaxel (n=397)</b>

**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

**PERJETA**  
pertuzumab

Scroll for Important Safety Information including Boxed WARNINGS

Close [x]

### Indication and Important Safety Information

PERJETA® (pertuzumab) is a HER2/neu receptor antagonist indicated in combination with Herceptin® (trastuzumab) and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.


**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

- PERJETA administration can result in subclinical and clinical cardiac failure. Evaluate left

[See full Prescribing Information](#)

**ZOOM**

+ All Grades (%)	Grades 3-4, %	
AR	PERJETA + Herceptin + docetaxel (n=407)	Placebo + Herceptin + docetaxel (n=397)
Diarrhea	66.8	46.3
Alopecia	60.9	60.5
Neutropenia	52.8	49.6
Nausea	42.3	41.6
Fatigue	37.6	36.8
Rash	33.7	24.2
Neuropathy peripheral	22.4	22.8


  
 Scroll for Important Safety Information including Boxed WARNINGS

Close [x]

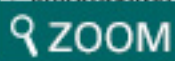
### Indication and Important Safety Information

PERJETA® (pertuzumab) is a HER2/neu receptor antagonist indicated in combination with Herceptin® (trastuzumab) and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**


- PERJETA administration can result in subclinical and clinical cardiac failure. Evaluate left

[See full Prescribing Information](#)


**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

+	66.8	46.3
Alopecia	60.9	60.5
Neutropenia	52.8	49.6
Nausea	42.3	41.6
Fatigue	37.6	36.8
Rash	33.7	24.2
Neuropathy peripheral	32.4	33.8
Febrile neutropenia	13.8	7.6
Leukopenia	18.2	20.4
Anemia	23.1	18.9
Asthenia	26.0	30.2

Close [x]


 Scroll for Important Safety Information including Boxed WARNINGS

### Indication and Important Safety Information

PERJETA® (pertuzumab) is a HER2/neu receptor antagonist indicated in combination with Herceptin® (trastuzumab) and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

- PERJETA administration can result in subclinical and clinical cardiac failure. Evaluate left

[See full Prescribing Information](#)

ZOOM

Q

Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity

All Grades (%)	Grades 3-4, %	
AR	PERJETA + Herceptin + docetaxel (n=407)	Placebo + Herceptin + docetaxel (n=397)
Diarrhea	7.9	5.0
Alopecia	0.0	0.3
Neutropenia	48.9	45.8
Nausea	1.2	0.5
Fatigue	2.2	3.3
Rash	0.7	0.8
Neuropathy peripheral	2.2	2.0

**PERJETA**  
pertuzumab

Scroll for Important Safety Information including Boxed WARNINGS Close [x]

### Indication and Important Safety Information

PERJETA® (pertuzumab) is a HER2/neu receptor antagonist indicated in combination with Herceptin® (trastuzumab) and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

- PERJETA administration can result in subclinical and clinical cardiac failure. Evaluate left

[See full Prescribing Information](#)

**ZOOM** **Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**



+	7.9	5.0
Diarrhea	0.0	0.3
Neutropenia	48.9	45.8
Nausea	1.2	0.5
Fatigue	2.2	3.3
Rash	0.7	0.8
Neuropathy peripheral	3.2	2.0
Febrile neutropenia	13.0	7.3
Leukopenia	12.3	14.6
Anemia	2.5	3.5
Asthenia	2.5	1.5

Close [x]

Scroll for Important Safety Information including Boxed WARNINGS

**PERJETA®**  
pertuzumab

### Indication and Important Safety Information

PERJETA® (pertuzumab) is a HER2/neu receptor antagonist indicated in combination with Herceptin® (trastuzumab) and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

- PERJETA administration can result in subclinical and clinical cardiac failure. Evaluate left

[See full Prescribing Information](#)

**ZOOM** Q **Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**



References: 1. PERJETA Prescribing Information. Genentech, Inc. September 2013. 2. Baselga J, Cortes J, Kim SB, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. *N Engl J Med.* 2012;366:109-119. 3. Swain SM, Kim SB, Cortes J, et al. Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA study): overall survival results from a randomised, double-blind, placebo-controlled, phase 3 study. *Lancet.* 2013;14:461-471. 4. Data on file. Genentech, Inc.

**Contact a Representative >**

**PERJETA®**  
pertuzumab

Scroll for Important Safety Information including Boxed WARNINGS

Close [x]

### Indication and Important Safety Information

PERJETA® (pertuzumab) is a HER2/neu receptor antagonist indicated in combination with Herceptin® (trastuzumab) and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

- PERJETA administration can result in subclinical and clinical cardiac failure. Evaluate left


**See full Prescribing Information**

**ZOOM** Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity

This link takes users to brand site page to sign up to contact a representative

+
20.0
30.2
Close [x]

**References:** **1.** PERJETA Prescribing Information. Genentech, Inc. September 2013. **2.** Baselga J, Cortes J, Kim SB, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. *N Engl J Med.* 2012;366:109-119. **3.** Swain SM, Kim SB, Cortes J, et al. Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA study): overall survival results from a randomised, double-blind, placebo-controlled, phase 3 study. *Lancet.* 2013;14:461-471. **4.** Data on file. Genentech, Inc.



Scroll for Important Safety Information including Boxed WARNINGS


treatment. Advise patients to contact their healthcare provider immediately if they suspect they may be pregnant


- Encourage women who may be exposed to PERJETA during pregnancy to enroll in the **Mother Pregnancy Registry** by contacting 1-800-690-6720
- Monitor patients who become pregnant during PERJETA therapy for oligohydramnios


**Additional Important Safety Information**

PERJETA is contraindicated in patients with known hypersensitivity to pertuzumab or to any of its excipients.

[See full Prescribing Information](#)


Contact a Representative >


**ZOOM**


**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

+
20.0 30.2
Close [x]

**References:** **1.** PERJETA Prescribing Information. Genentech, Inc. September 2013. **2.** Baselga J, Cortes J, Kim SB, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. *N Engl J Med.* 2012;366:109-119. **3.** Swain SM, Kim SB, Cortes J, et al. Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA study): overall survival results from a randomised, double-blind, placebo-controlled, phase 3 study. *Lancet.* 2013;14:461-471. **4.** Data on file. Genentech, Inc.


Scroll for Important Safety Information including Boxed WARNINGS

**PERJETA<sup>®</sup>**  
pertuzumab trastuzumab

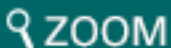
**Left Ventricular Dysfunction (LVD)**

- In Study 1, for patients with MBC, left ventricular dysfunction, which includes symptomatic left ventricular systolic dysfunction (LVSD) (congestive heart failure) and decreases in left ventricular ejection fraction (LVEF), occurred in 4.4% of patients in the PERJETA-treated group and in 8.3% of patients in the placebo-treated group
- Assess LVEF prior to initiation of PERJETA and at regular intervals (eg, every 3 months in the metastatic setting) during treatment to ensure that LVEF is within your institution's normal limits
- Withhold PERJETA and Herceptin and repeat LVEF assessment within 3 weeks in patients with

**See full Prescribing Information**




**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**



**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

+
20.0 30.2
Close [x]

**References:** **1.** PERJETA Prescribing Information. Genentech, Inc. September 2013. **2.** Baselga J, Cortes J, Kim SB, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. *N Engl J Med.* 2012;366:109-119. **3.** Swain SM, Kim SB, Cortes J, et al. Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA study): overall survival results from a randomised, double-blind, placebo-controlled, phase 3 study. *Lancet.* 2013;14:461-471. **4.** Data on file. Genentech, Inc.




Scroll for Important Safety Information including Boxed WARNINGS


significant decrease in LVEF. Discontinue PERJETA and Herceptin if LVEF has not improved or has declined further


**Infusion-Associated Reactions**

- PERJETA has been associated with infusion reactions
- In Study 1, for patients with MBC, when all drugs were administered on the same day, the most common infusion reactions in the PERJETA-treated group ( $\geq 1.0\%$ ) were fatigue, dysgeusia, hypersensitivity, myalgia, and vomiting
- If a significant infusion reaction occurs, slow or

[See full Prescribing Information](#)



Contact a Representative >


**ZOOM**


**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

+
20.0 30.2
Close [x]

**References:** **1.** PERJETA Prescribing Information. Genentech, Inc. September 2013. **2.** Baselga J, Cortes J, Kim SB, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. *N Engl J Med.* 2012;366:109-119. **3.** Swain SM, Kim SB, Cortes J, et al. Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA study): overall survival results from a randomised, double-blind, placebo-controlled, phase 3 study. *Lancet.* 2013;14:461-471. **4.** Data on file. Genentech, Inc.




Scroll for Important Safety Information including Boxed WARNINGS

interrupt the infusion and administer appropriate medical therapies. Monitor patients carefully until complete resolution of signs and symptoms. Consider permanent discontinuation in patients with severe infusion reactions

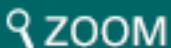

**Hypersensitivity Reactions/Anaphylaxis**

- In Study 1, the overall frequency of hypersensitivity/anaphylaxis reactions was 10.8% in the PERJETA-treated group and 9.1% in the placebo-treated group. The incidence of Grades 3-4 reactions was 2.0% and 2.5%, respectively, according to NCI-CTCAE (version 3)
- Patients should be observed closely for hypersensitivity reactions. Caution: hypersensitivity

[See full Prescribing Information](#)




**Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

+
20.0 30.2
Close [x]

**References:** **1.** PERJETA Prescribing Information. Genentech, Inc. September 2013. **2.** Baselga J, Cortes J, Kim SB, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. *N Engl J Med.* 2012;366:109-119. **3.** Swain SM, Kim SB, Cortes J, et al. Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA study): overall survival results from a randomised, double-blind, placebo-controlled, phase 3 study. *Lancet.* 2013;14:461-471. **4.** Data on file. Genentech, Inc.



Scroll for Important Safety Information including Boxed WARNINGS

hypersensitivity reactions. Severe hypersensitivity, including anaphylaxis, has been observed in clinical trials of PERJETA


**HER2 Testing**

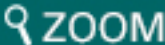
- Detection of HER2 protein overexpression is necessary for selection of patients appropriate for PERJETA therapy because these are the only patients studied and for whom benefit has been shown


**Most Common Adverse Reactions**

- In metastatic breast cancer, the most common adverse reactions (>30%) with PERJETA in

[See full Prescribing Information](#)





ZOOM


**Boxed WARNINGS:** Cardiomyopathy and Embryo-Fetal Toxicity



+
20.0 30.2
Close [x]

**References:** **1.** PERJETA Prescribing Information. Genentech, Inc. September 2013. **2.** Baselga J, Cortes J, Kim SB, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. *N Engl J Med.* 2012;366:109-119. **3.** Swain SM, Kim SB, Cortes J, et al. Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA study): overall survival results from a randomised, double-blind, placebo-controlled, phase 3 study. *Lancet.* 2013;14:461-471. **4.** Data on file. Genentech, Inc.




Scroll for Important Safety Information including Boxed WARNINGS


- In metastatic breast cancer, the most common adverse reactions (>30%) with PERJETA in combination with Herceptin and docetaxel were diarrhea, alopecia, neutropenia, nausea, fatigue, rash, and peripheral neuropathy


You may report side effects to the FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).  
You may also report side effects to Genentech at 1-888-835-2555.

Please see PERJETA **full Prescribing Information** including **Boxed WARNINGS** for additional Important Safety Information.


Contact a Representative >

**See full Prescribing Information**


ZOOM


Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity



Close [x]


## Results of the CLEOPATRA trial: PERJETA + Herceptin (trastuzumab) + docetaxel vs placebo + Herceptin + docetaxel


### Proven survival benefit for patients, including ER/PR patient subgroups

- There was an inability to show benefit with PERJETA in patients with nonvisceral metastases (n=178; HR=1.42 [95% CI: 0.71, 2.84])<sup>3</sup>

Select patient subgroups/treatment benefit by hormone receptor status/disease type (CLEOPATRA trial)<sup>1-3</sup>

Category	n	PFS		OS	
		HR	95% CI	HR	95% CI
All patients	808	0.63	0.51, 0.75	0.66	0.52, 0.84

 ZOOM OUT

 Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity

Close [x]

### **Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

- **PERJETA administration can result in subclinical and clinical cardiac failure. Evaluate left ventricular function in all patients prior to and during treatment with PERJETA. Discontinue PERJETA treatment for a confirmed clinically significant decrease in left ventricular function**
- **Exposure to PERJETA can result in embryo-fetal death and birth defects. Studies in animals have resulted in oligohydramnios, delayed renal development, and death. Advise patients of these risks and the need for effective contraception**

**Please see PERJETA [full Prescribing Information](#) including Boxed WARNINGS for additional Important Safety Information.**

 **BACK TO ZOOM**

Select patient subgroups/treatment benefit by hormone receptor status/disease type (CLEOPATRA trial)<sup>1-3</sup> Close [x]

Category	n	PFS		OS	
		HR	95% CI	HR	95% CI
<b>All patients</b>	<b>808</b>	<b>0.63</b>	<b>0.51, 0.75</b>	<b>0.66</b>	<b>0.52, 0.84</b>
		<i>P</i> <0.0001		<i>P</i> =0.0008	
<b>Hormone receptor status</b>					
<b>Positive</b> (ER+ and/or PR+)	388	<b>0.72</b>	0.55, 0.95	<b>0.73</b>	0.50, 1.06
<b>Negative</b> (ER- and PR-)	408	<b>0.55</b>	0.42, 0.72	<b>0.57</b>	0.41, 0.79
<b>Disease type</b>					

ZOOM OUT  Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity


**Disease type**
Close [x]

<b>Visceral disease</b>	630	<b>0.55</b>	0.45, 0.68	<b>0.57</b>	0.44, 0.74
<b>Nonvisceral disease</b>	178	<b>0.96</b>	0.61, 1.52	<b>1.42</b>	0.71, 2.84


HR=hazard ratio; CI=confidence interval; ER=estrogen receptor; PR=progesterone receptor.

Results of a multicenter, randomized double-blind, placebo-controlled phase II trial in which patients were randomly allocated to receive placebo plus trastuzumab and docetaxel or PERJETA plus trastuzumab and docetaxel.

**Significant improvement in PFS<sup>1w</sup>**



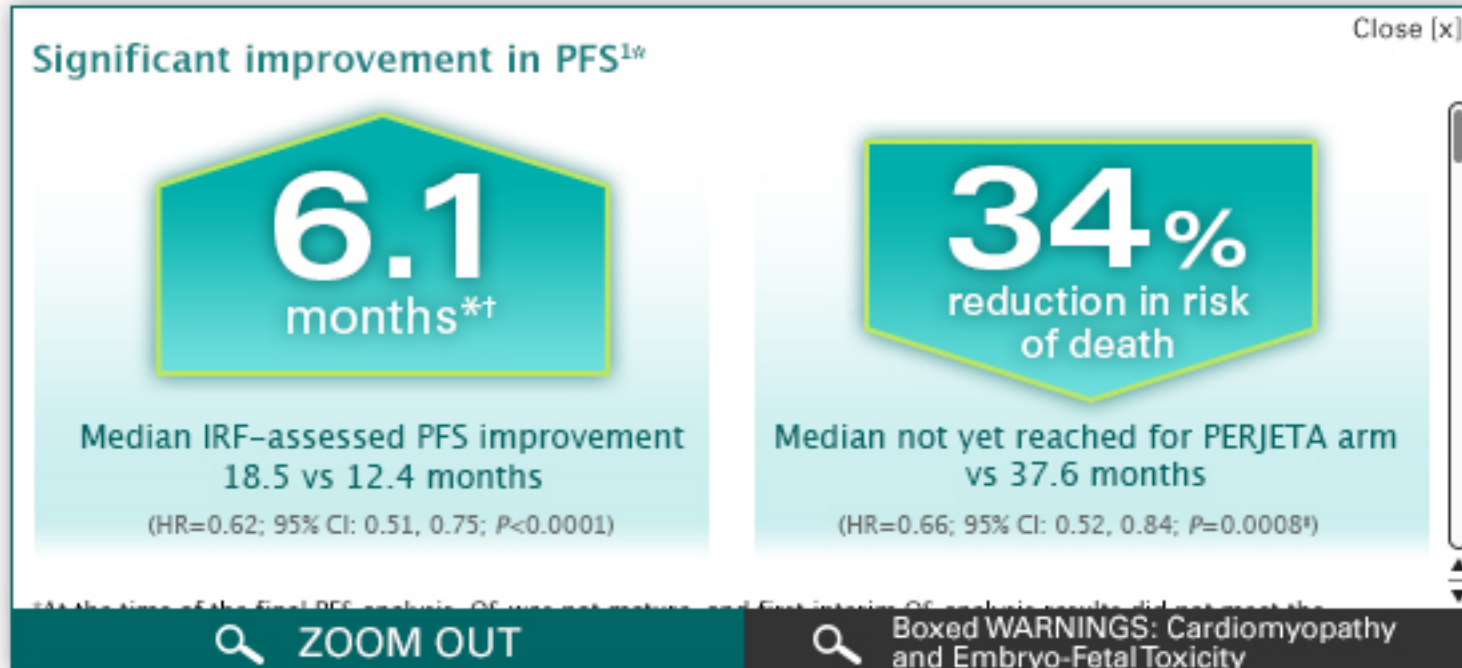
6.1



34%

🔍
ZOOM OUT

🔍
Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity





\*At the time of the final PFS analysis, OS was not mature, and first interim OS analysis results did not meet the prespecified stopping boundary for statistical significance.<sup>1</sup> Close [x]

<sup>†</sup>Stratified by prior treatment status and geographic region.<sup>1</sup>

<sup>‡</sup>The HR and *P*-value for the second interim analysis of OS crossed the predefined efficacy stopping boundary (HR≤0.739, *P*≤0.0138).

- At the time of analysis, there were 191 (47.5%) and 242 (59.6%) patients with a PFS event in the PERJETA + Herceptin + docetaxel and placebo + Herceptin + docetaxel arms, respectively<sup>1</sup>
- Median follow-up was 30 months (1 year following the first interim analysis) for both the PERJETA-based regimen and the placebo + Herceptin + docetaxel arm (Kaplan-Meier estimate)<sup>1,4</sup>
- More than 50% of patients in the PERJETA + Herceptin + docetaxel arm were alive at the time of the second interim analysis, thereby indicating that the median OS for this arm had not yet been reached<sup>1</sup>

 ZOOM OUT



 **Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

had not yet been reached<sup>1</sup> Close [x]

- At the time of analysis, there were 113 (28.1%) and 154 (37.9%) deaths in the PERJETA + Herceptin + docetaxel arm and the placebo + Herceptin + docetaxel arm, respectively<sup>1</sup>
- The most common NCI-CTCAE (version 3) Grade 3–4 adverse reactions (>2%) were neutropenia, febrile neutropenia, leukopenia, diarrhea, peripheral neuropathy, anemia, asthenia, and fatigue<sup>1</sup>

**Select Important Safety Information: Left Ventricular Dysfunction**

Decreases in left ventricular ejection fraction (LVEF) have been reported with drugs that block HER2 activity, including PERJETA. Assess LVEF prior to initiation of PERJETA and at regular intervals (eg, every 3 months in the metastatic setting) during treatment to ensure that LVEF is within the institution's normal limits. If LVEF is <45%, or is 45% to 49% with a 10% or greater absolute decrease below the pretreatment value, withhold PERJETA and trastuzumab and repeat LVEF assessment within approximately 3 weeks. Discontinue PERJETA and trastuzumab if LVEF has not improved or has declined further, unless the

 ZOOM OUT  **Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**



trastuzumab and repeat LVEF assessment within approximately 3 weeks. Discontinue PERJETA and trastuzumab if LVEF has not improved or has declined further, unless the benefits for the individual patient outweigh the risks. Close [x]

**Most common adverse reactions: All Grades (>30%) or Grades 3-4 (>2%)<sup>1</sup>**

	Placebo+Herceptin+docetaxel (n=397)		PERJETA+Herceptin+docetaxel (n=407)	
	All Grades (%)	Grades 3-4 (%)	All Grades (%)	Grades 3-4 (%)
Diarrhea	46.3	5.0	66.8	7.9
Alopecia	60.5	0.3	60.9	0.0
Neutropenia	49.6	45.8	52.8	48.9
Nausea	41.6	0.5	42.3	1.2
Fatigue	36.8	3.3	37.6	2.2

 ZOOM OUT

 **Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity**

Neutropenia	49.6	45.8	52.8	48.9	Close [x]
Nausea	41.6	0.5	42.3	1.2	
Fatigue	36.8	3.3	37.6	2.2	
Rash	24.2	0.8	33.7	0.7	
Neuropathy peripheral	33.8	2.0	32.4	3.2	
Febrile neutropenia	7.6	7.3	13.8	13.0	
Leukopenia	20.4	14.6	18.2	12.3	
Anemia	18.9	3.5	23.1	2.5	
Asthenia	30.2	1.5	26.0	2.5	

 ZOOM OUT

 Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity

Febrile neutropenia	7.6	7.3	13.8	13.0	Close [x]
Leukopenia	20.4	14.6	18.2	12.3	
Anemia	18.9	3.5	23.1	2.5	
Asthenia	30.2	1.5	26.0	2.5	

**References:** 1. PERJETA Prescribing Information. Genentech, Inc. September 2013. 2. Baselga J, Cortes J, Kim SB, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. *N Engl J Med.* 2012;366:109–119. 3. Swain SM, Kim SB, Cortes J, et al. Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA study): overall survival results from a randomised, double-blind, placebo-controlled, phase 3 study. *Lancet.* 2013;14:461–471. 4. Data on file. Genentech, Inc.



Contact a Representative >



ZOOM OUT



Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity