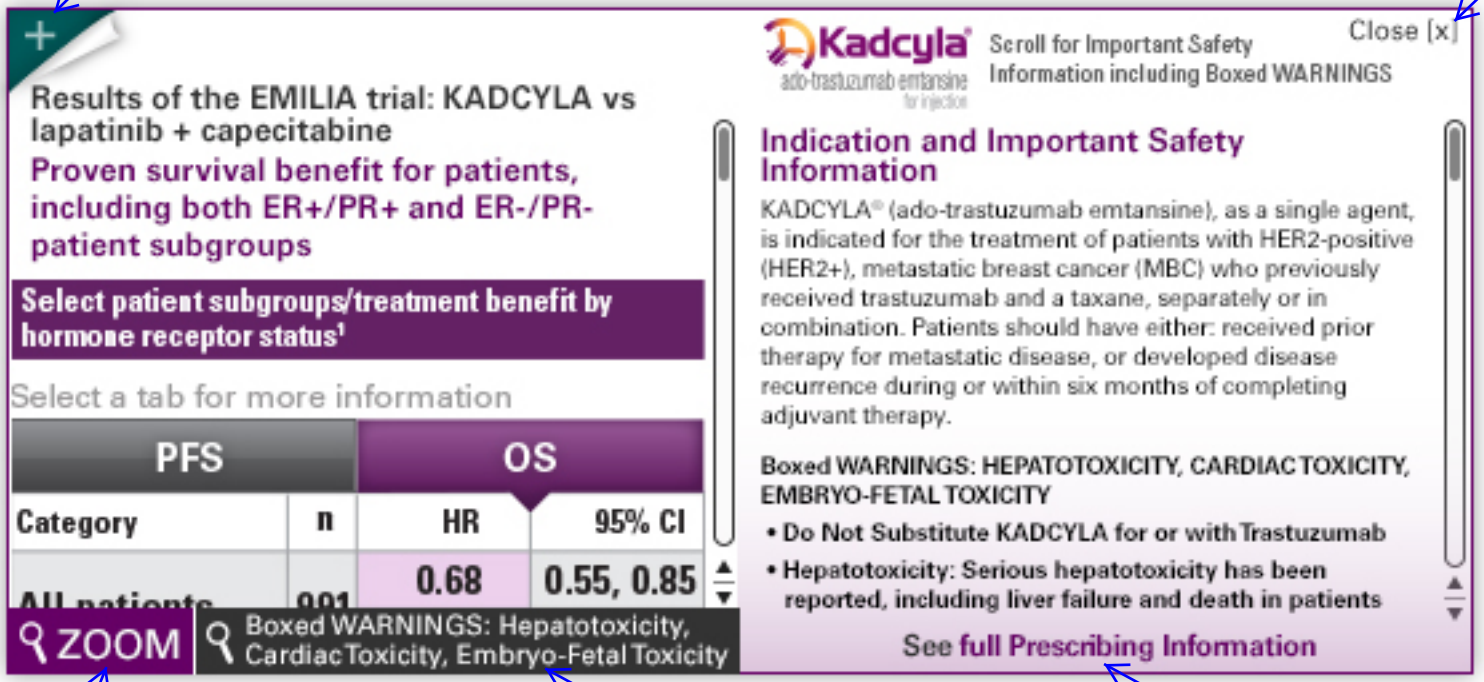
HPK0002464200

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.



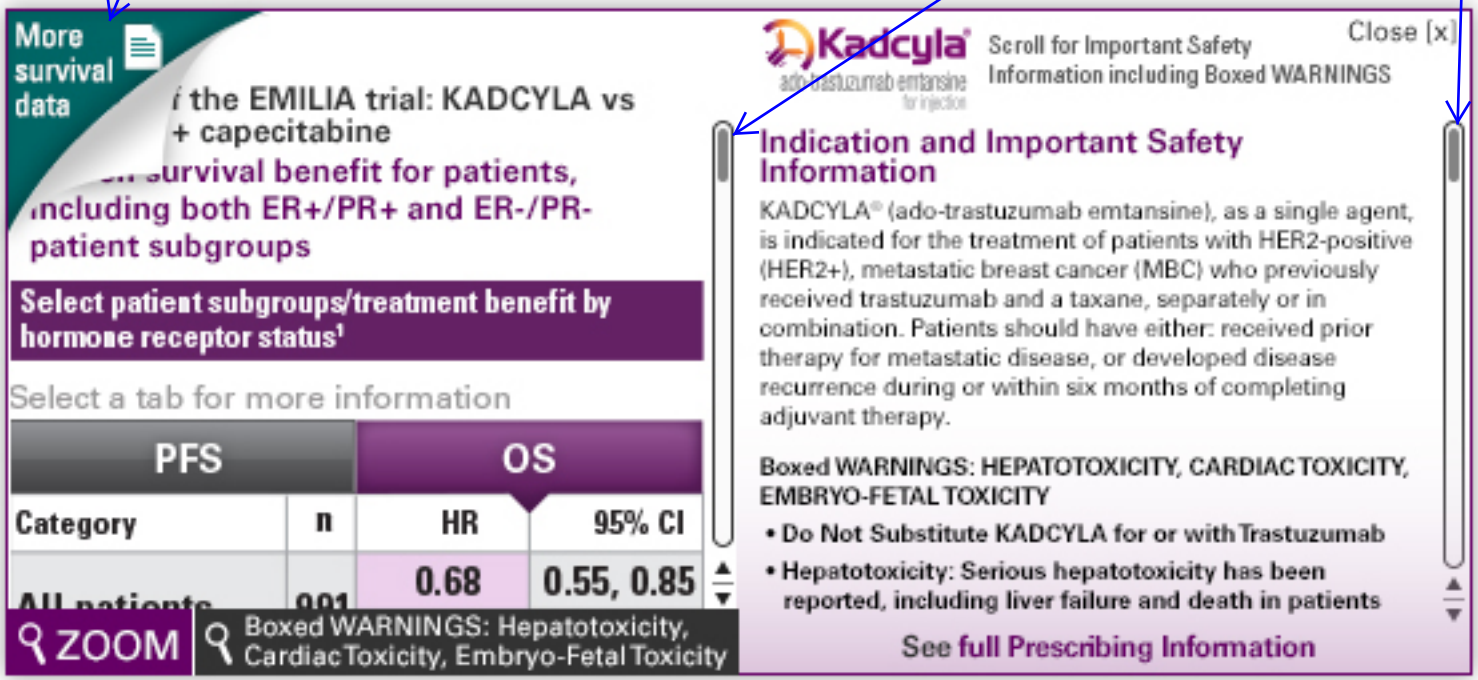
Clicking "Zoom" will enable users to see the content in in the full viewing space. See pp. 22-28 for example.

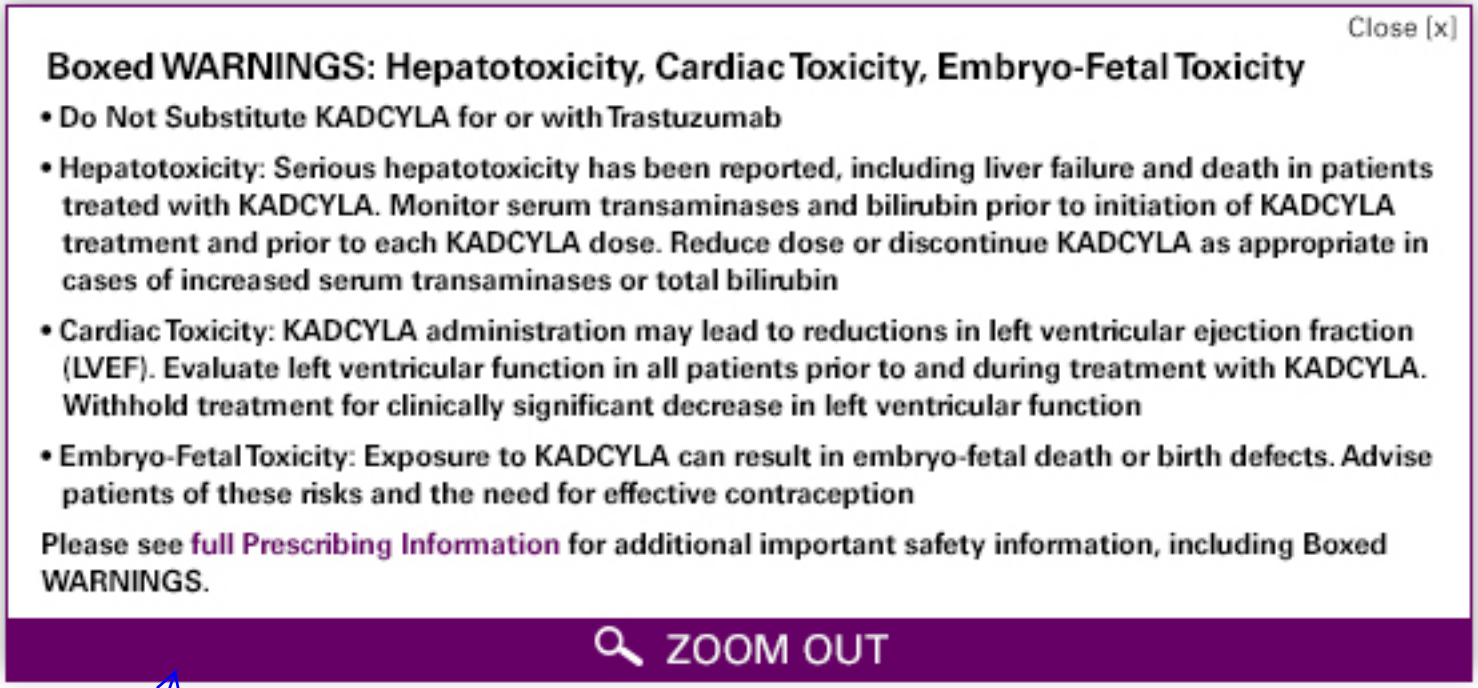
Clicking this space will present user with expanded Boxed WARNINGS view (see p. 4 for expanded view of KADCYLA warning text).

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).

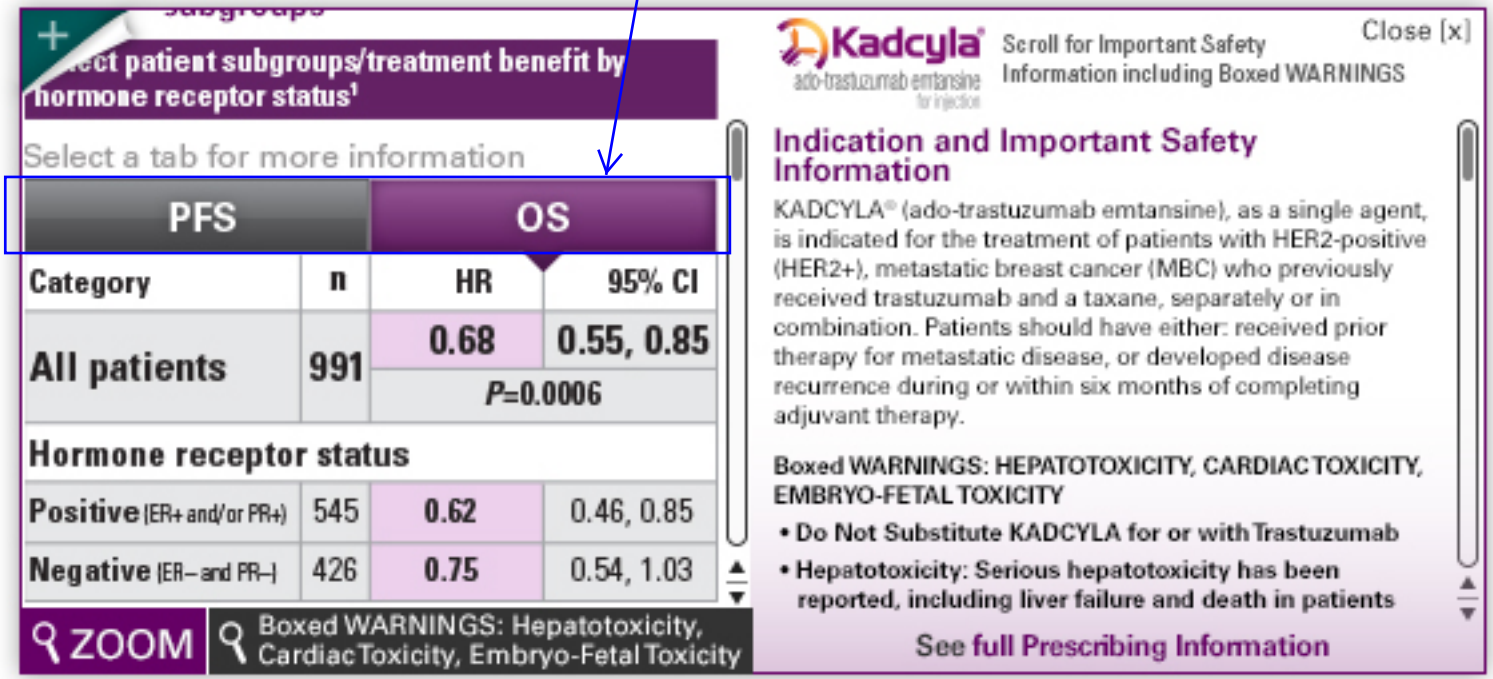
Global - users can use scroll bars in each section to navigate the content



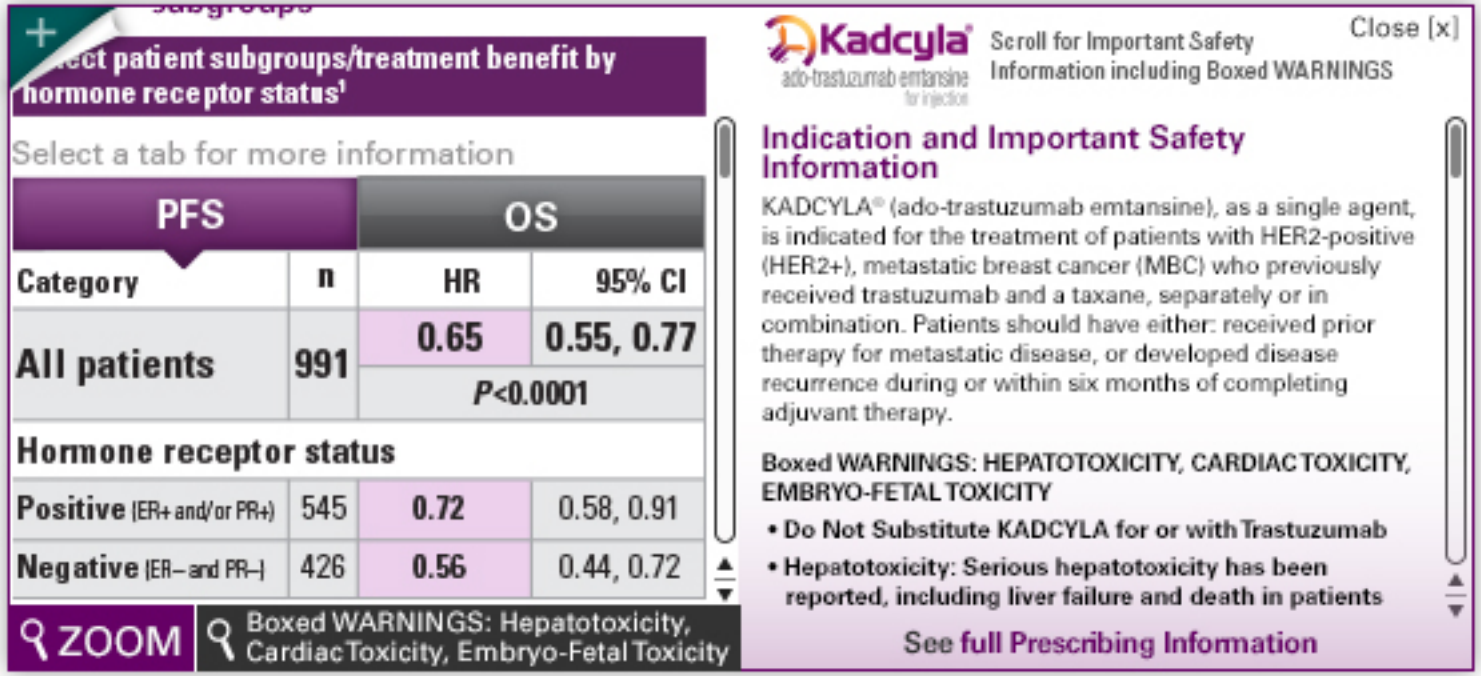


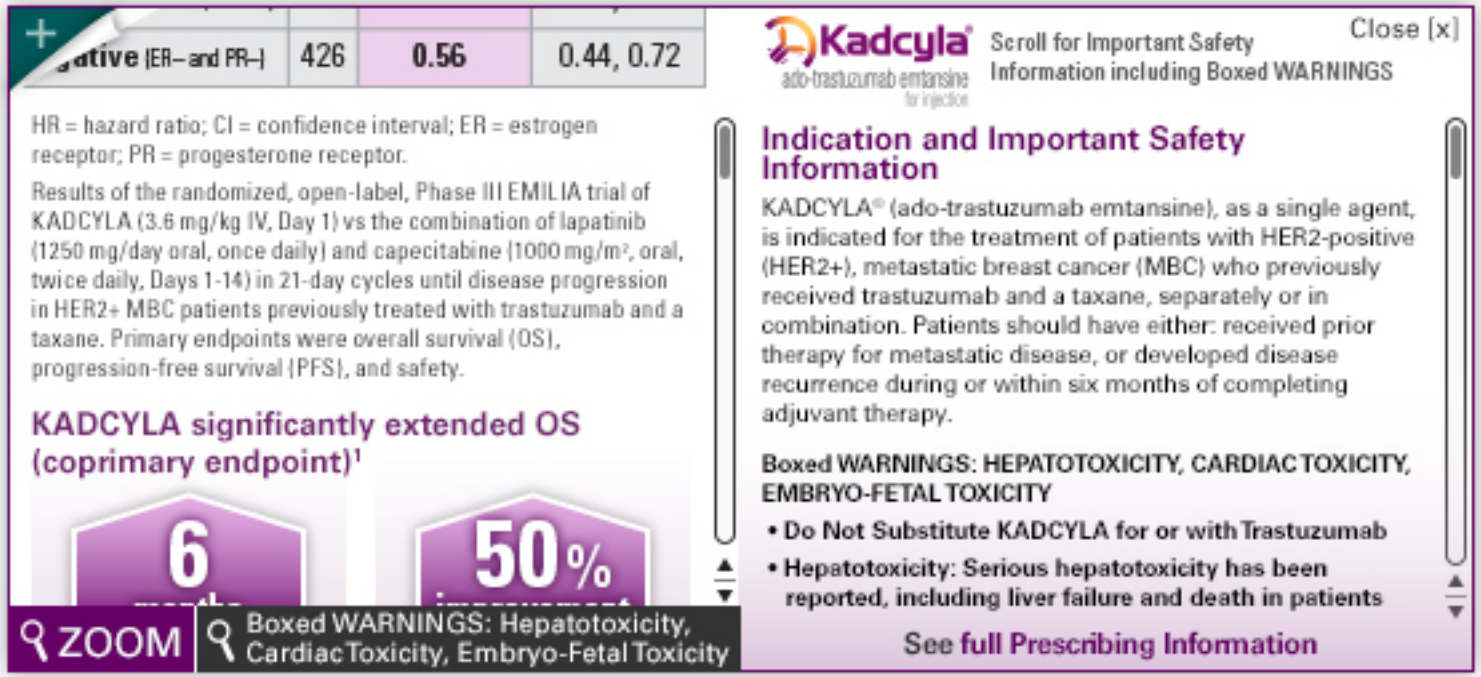
Clicking "zoom out" returns the user to the prior view.

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



PFS data


ect patient subgroups/treatment benefit by hormone receptor status[1]
Select a tab for more information
PFS
OS
Category
n
HR
95% CI
All patients
991
0.65
0.55, 0.77
P<0.0001
Hormone receptor status
Positive (ER+ and/or PR+)
545
0.72
0.58, 0.91
Negative (ER– and PR–)
426
0.56
0.44, 0.72
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


ative (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/m², 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)¹
6
50%
ZOOM
Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity
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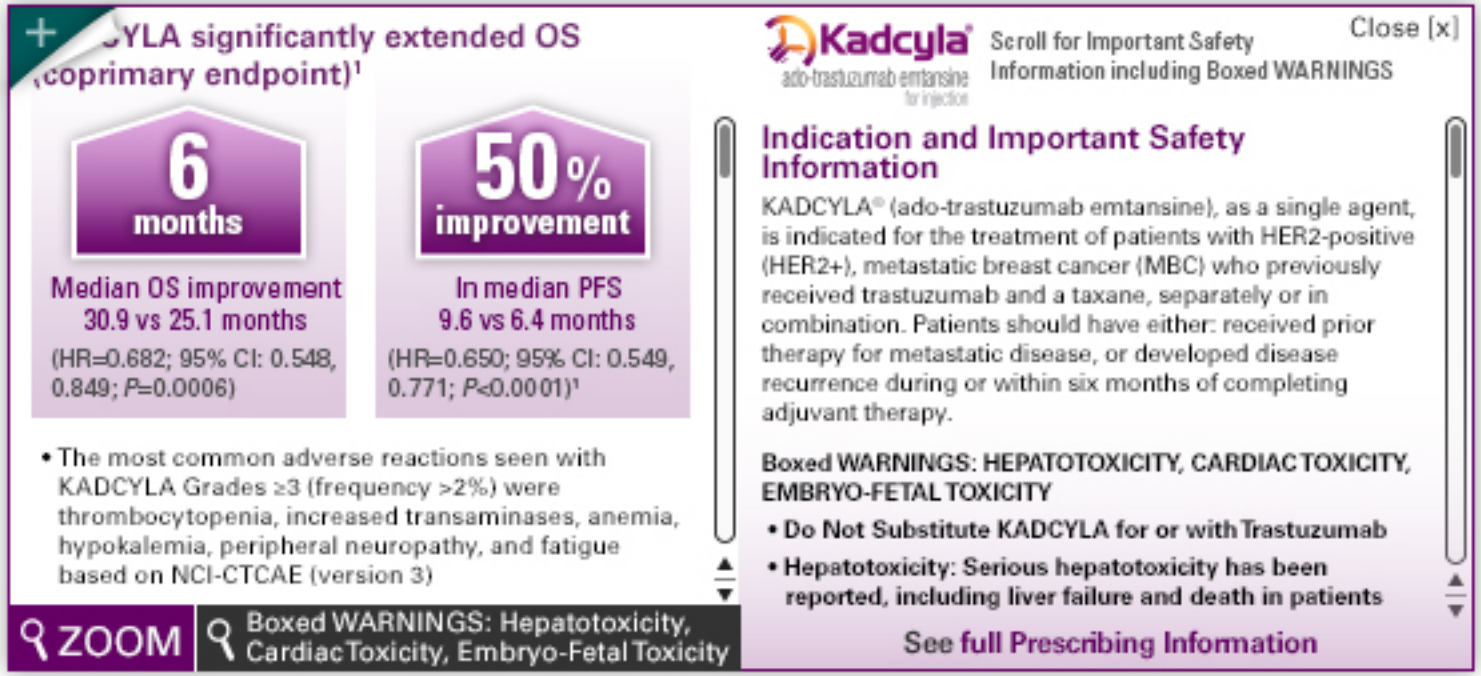
See full Prescribing Information


+ KADCYLA significantly extended OS (coprimary endpoint)¹
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)¹
• 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)
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]
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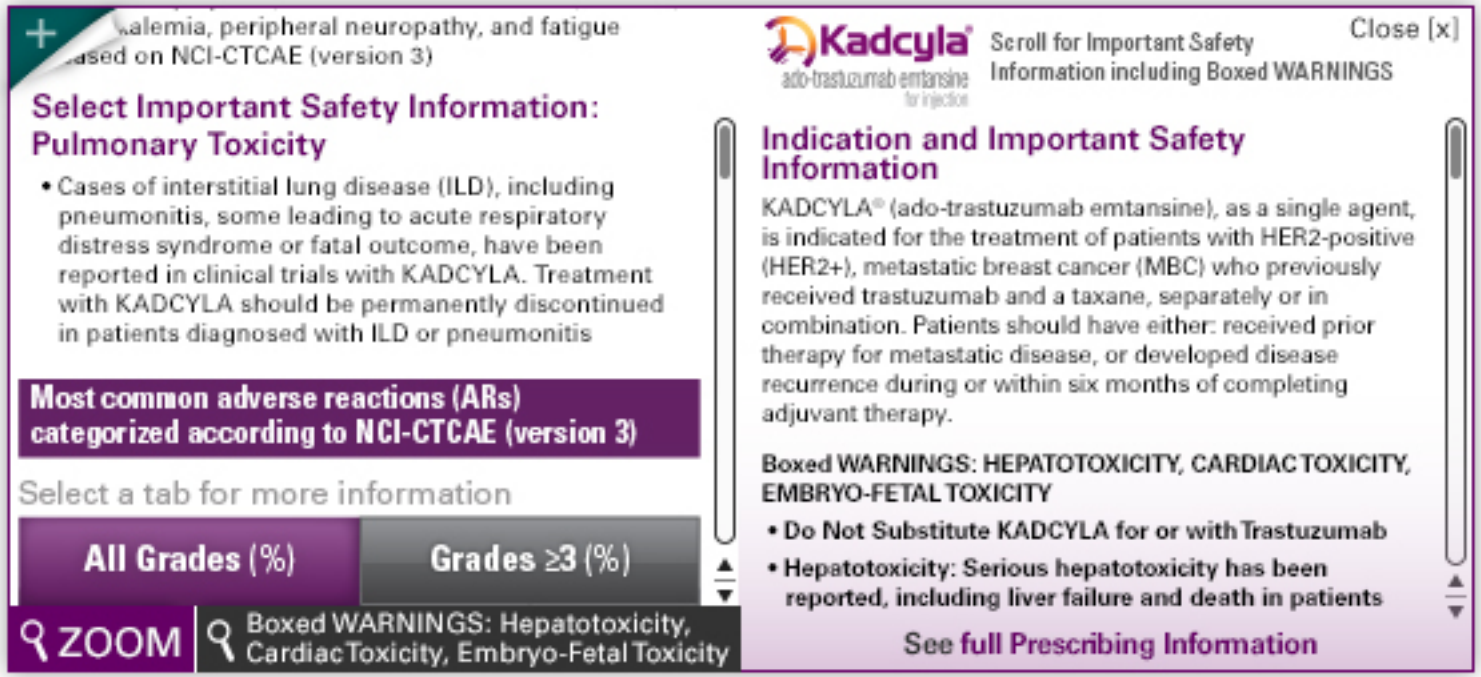
• Hepatotoxicity: Serious hepatotoxicity has been reported, including liver failure and death in patients
See full Prescribing Information


+
alemia, peripheral neuropathy, and fatigue
ased on NCI-CTCAE (version 3)
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
Kadcyla
ado-trastuzumab emtansine for injection
Scroll for Important Safety Information including Boxed WARNINGS
Close [x]
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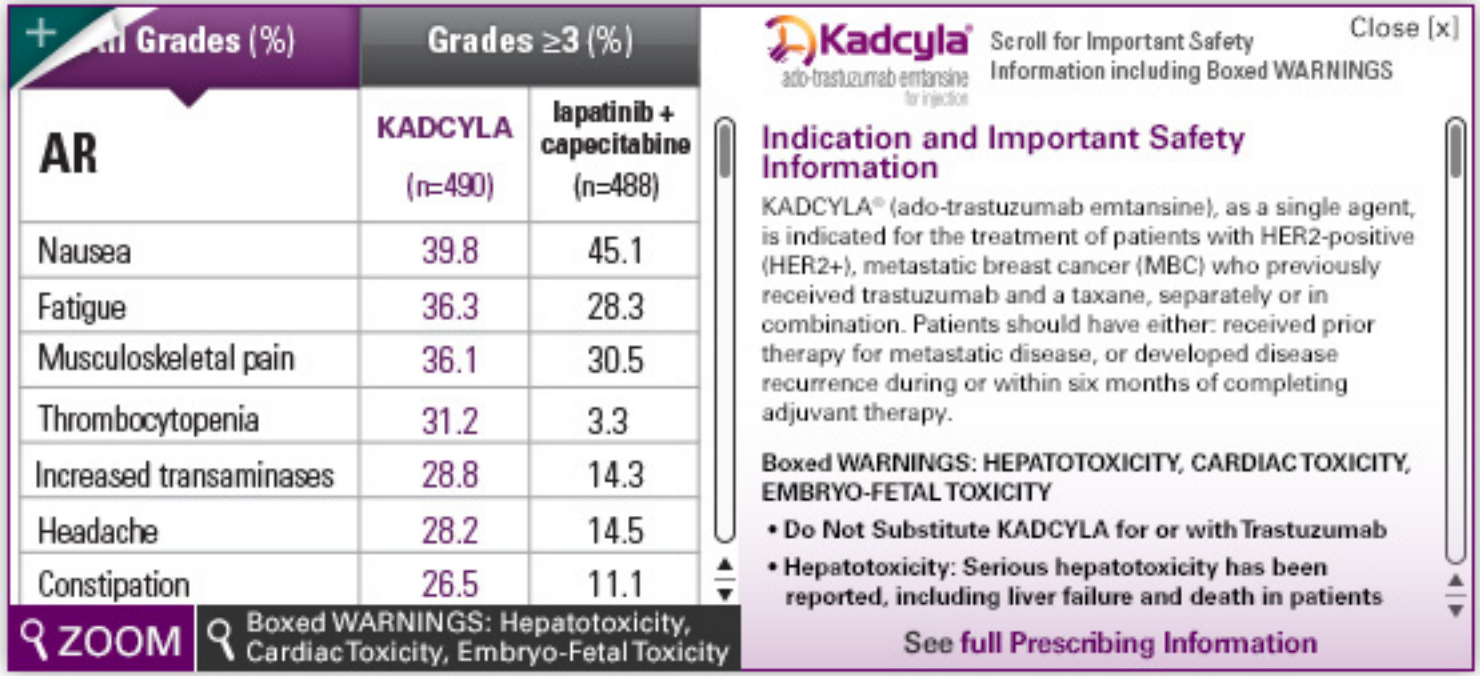
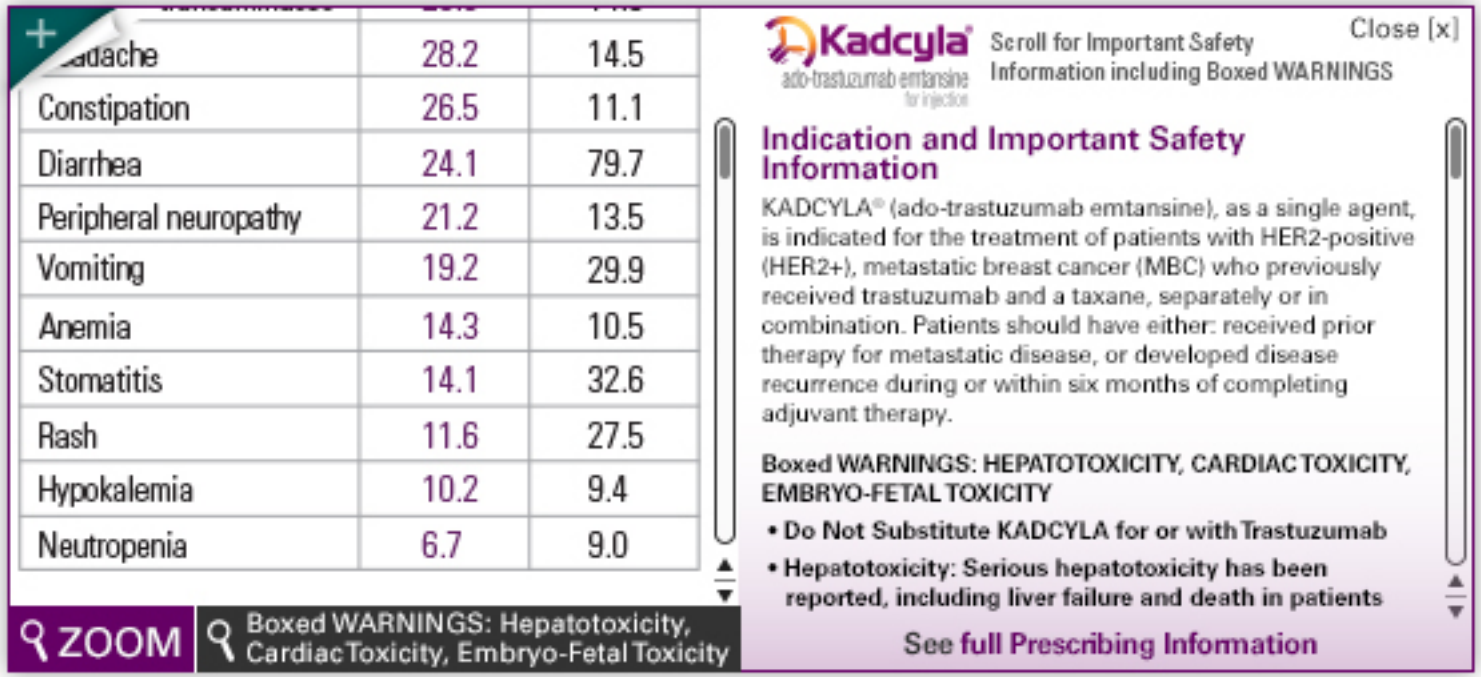
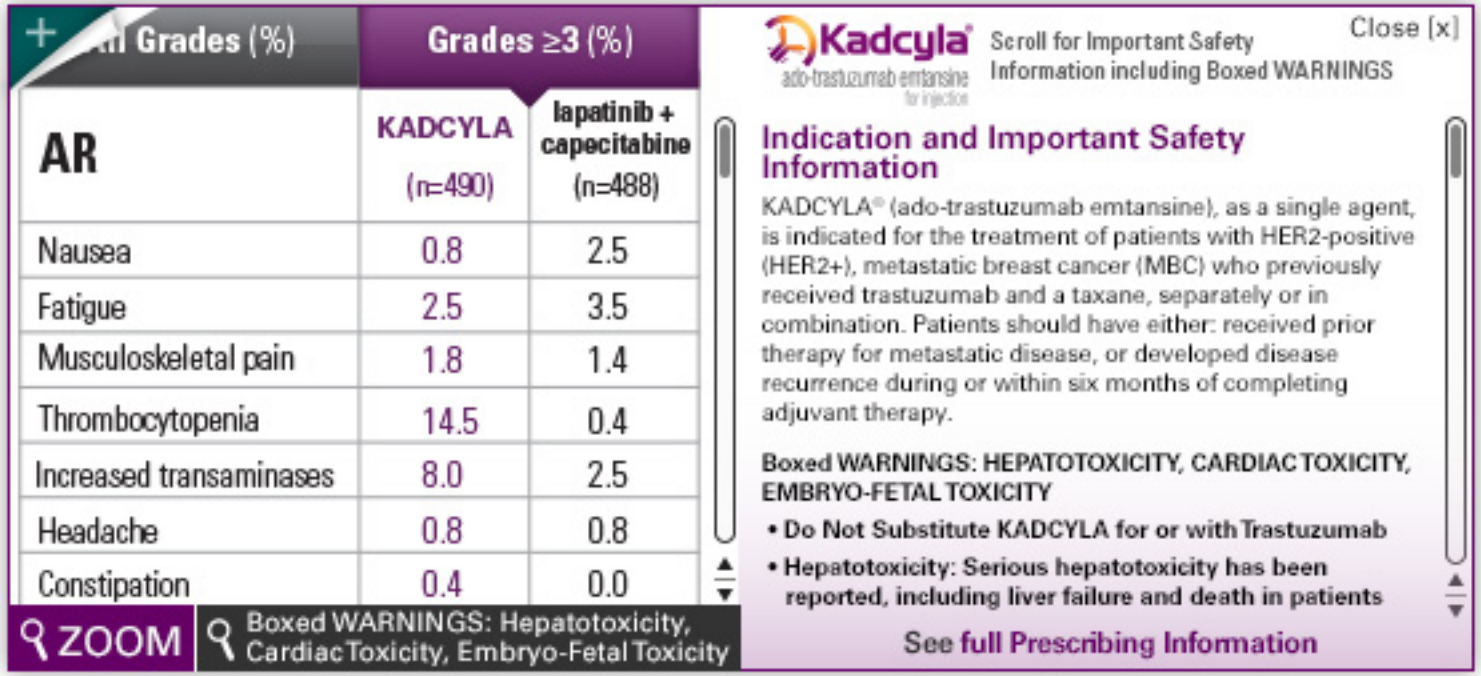
See full Prescribing Information



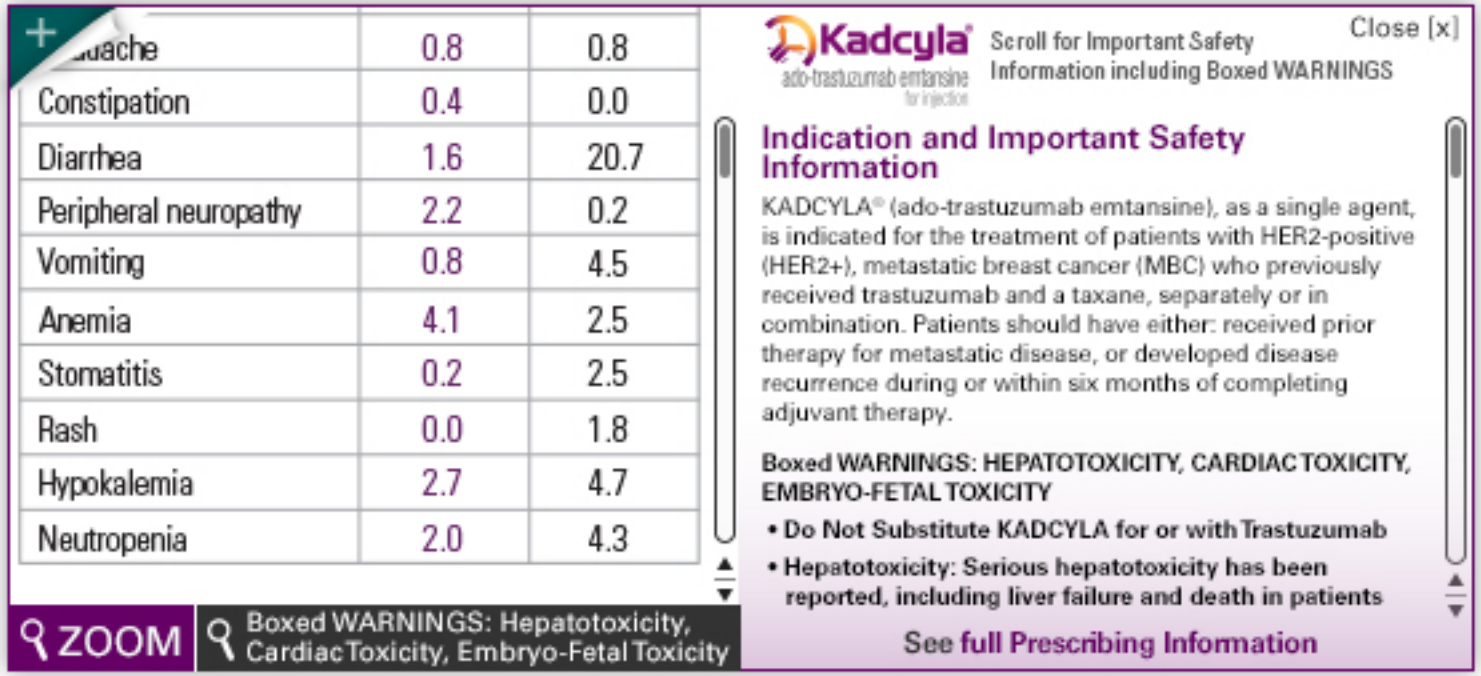
AR	KADCYLA (n=490)	lapatinib + capecitabine (n=488)
	All Grades (%)	Grades ≥3 (%)
Nausea	39.8	45.1
Fatigue	36.3	28.3
Musculoskeletal pain	36.1	30.5
Thrombocytopenia	31.2	3.3
Increased transaminases	28.8	14.3
Headache	28.2	14.5
Constipation	26.5	11.1



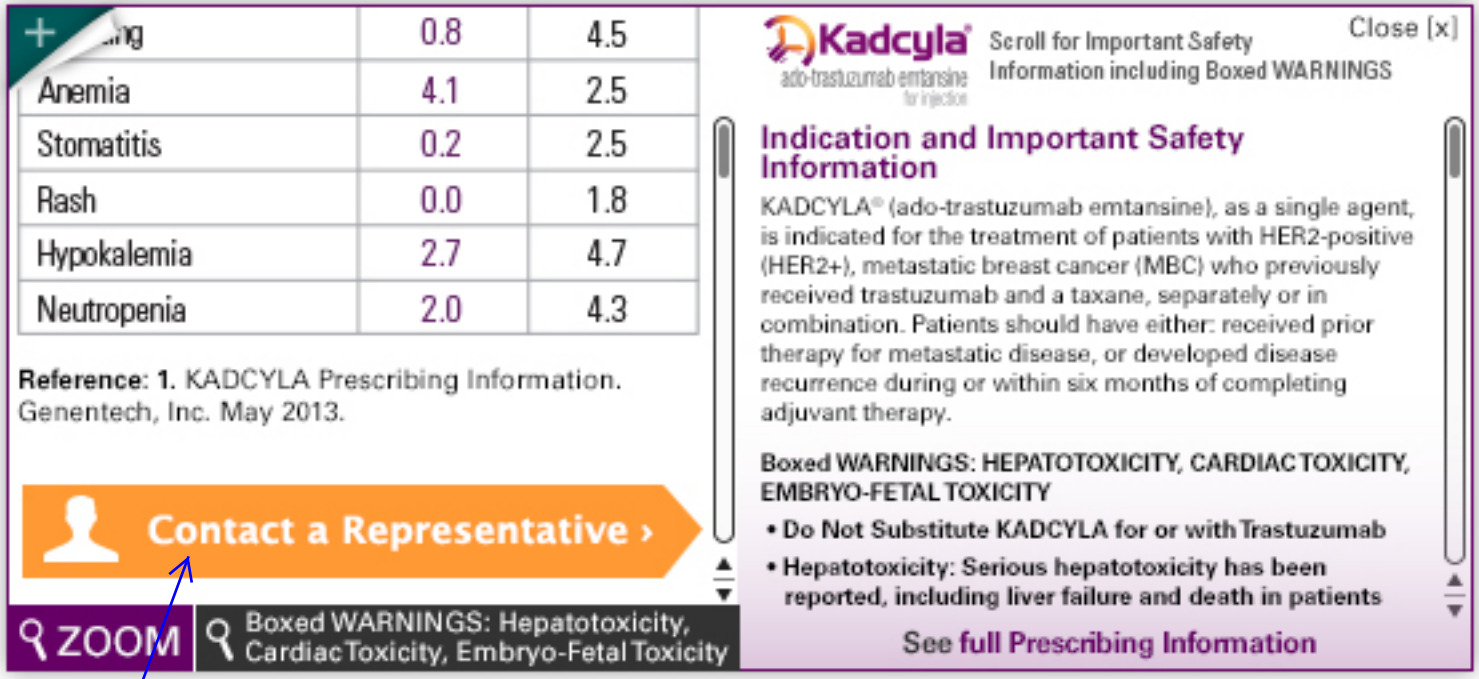
...adache	28.2	14.5
Constipation	26.5	11.1
Diarrhea	24.1	79.7
Peripheral neuropathy	21.2	13.5
Vomiting	19.2	29.9
Anemia	14.3	10.5
Stomatitis	14.1	32.6
Rash	11.6	27.5
Hypokalemia	10.2	9.4
Neutropenia	6.7	9.0



AR	All Grades (%) KADCYLA (n=490)	Grades ≥3 (%) KADCYLA (n=490)	Grades ≥3 (%) 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	

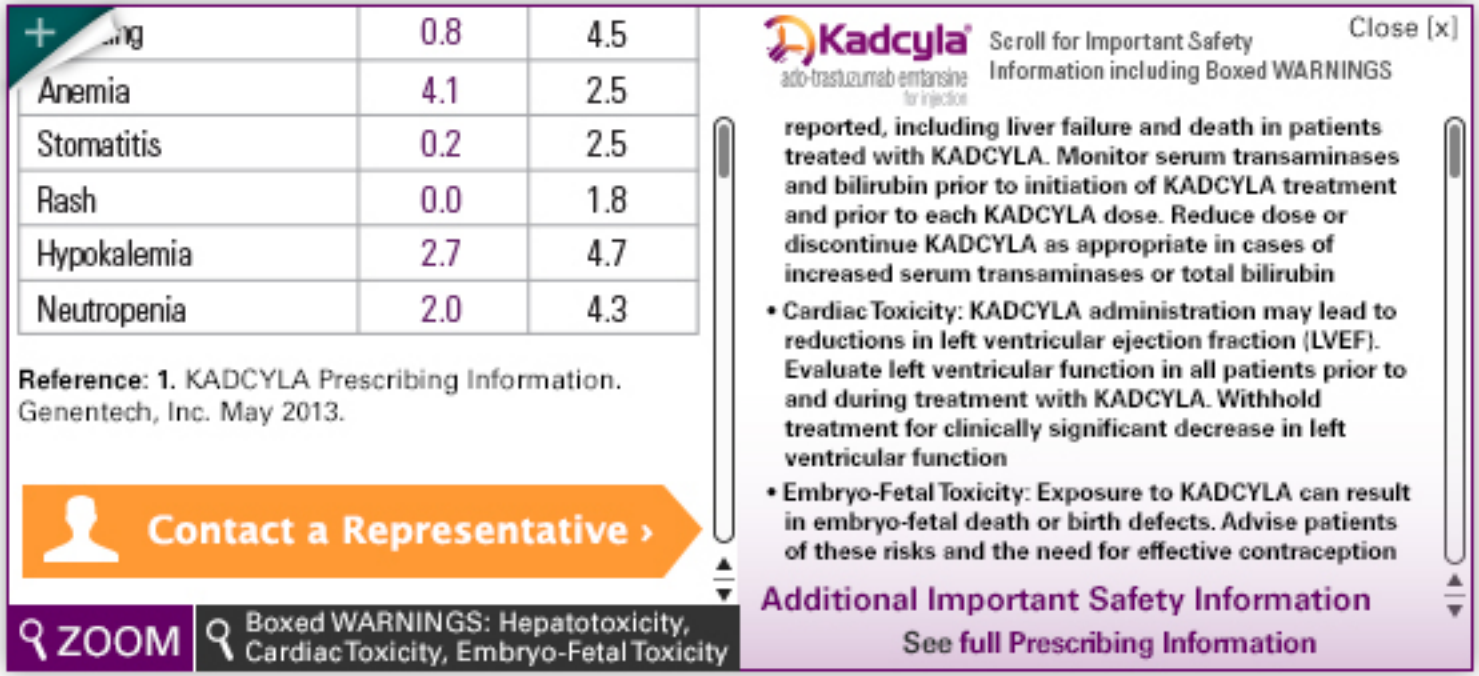


+uache	0.8	0.8
Constipation	0.4	0.0
Diarrhea	1.6	20.7
Peripheral neuropathy	2.2	0.2
Vomiting	0.8	4.5
Anemia	4.1	2.5
Stomatitis	0.2	2.5
Rash	0.0	1.8
Hypokalemia	2.7	4.7
Neutropenia	2.0	4.3



+ ...ng	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

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



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Anemia	4.1	2.5
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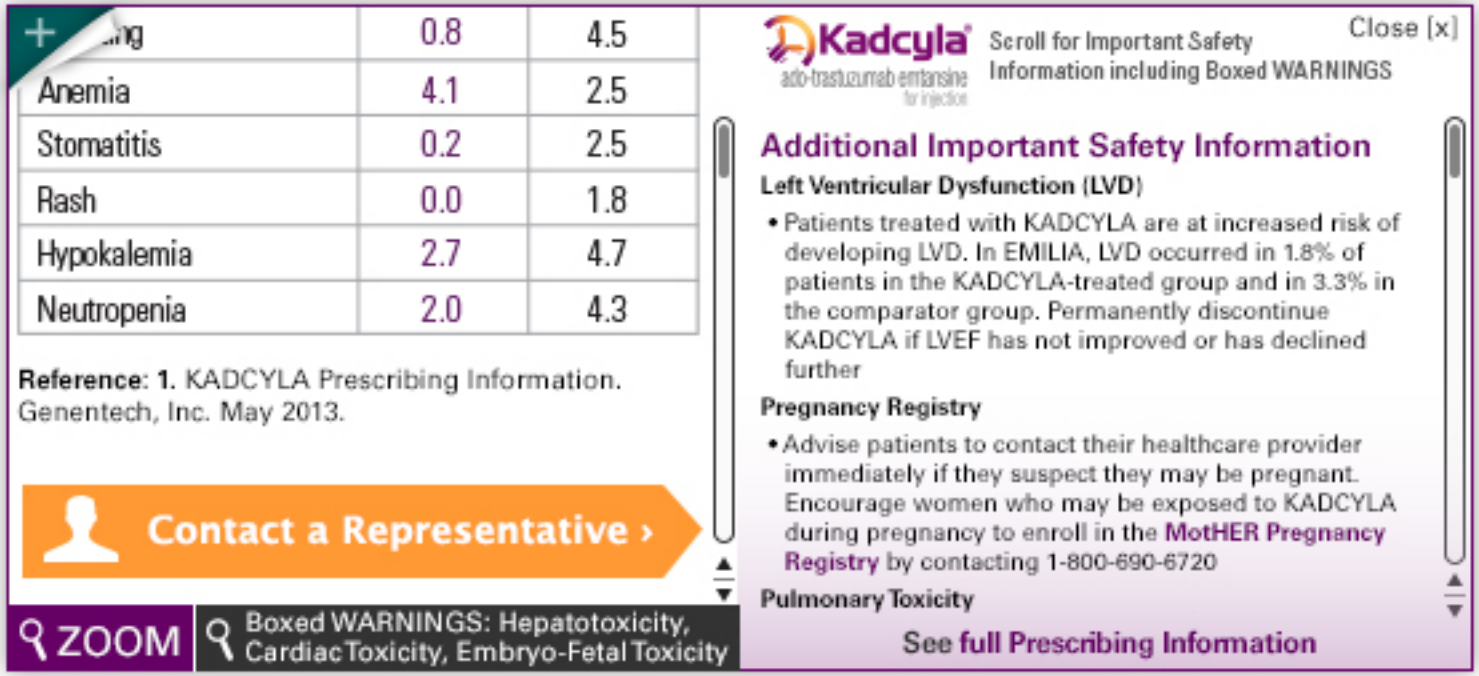

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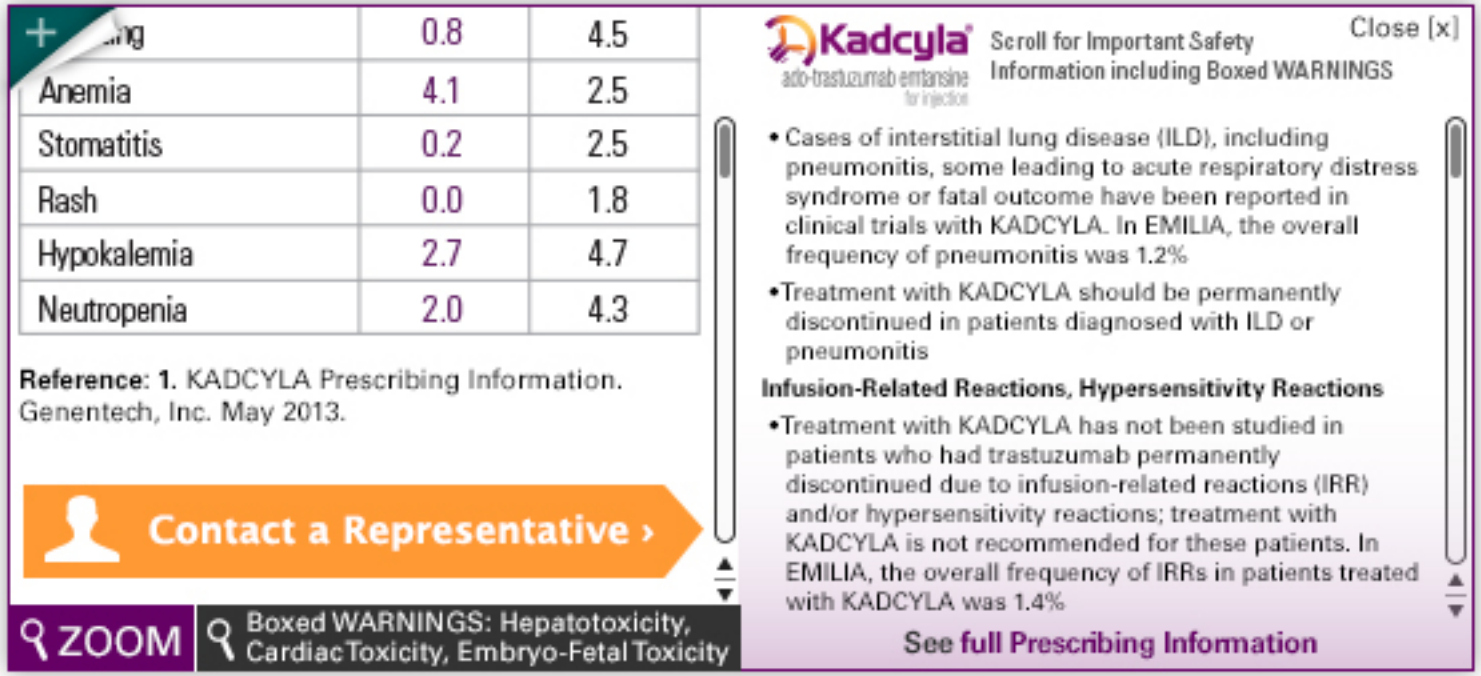

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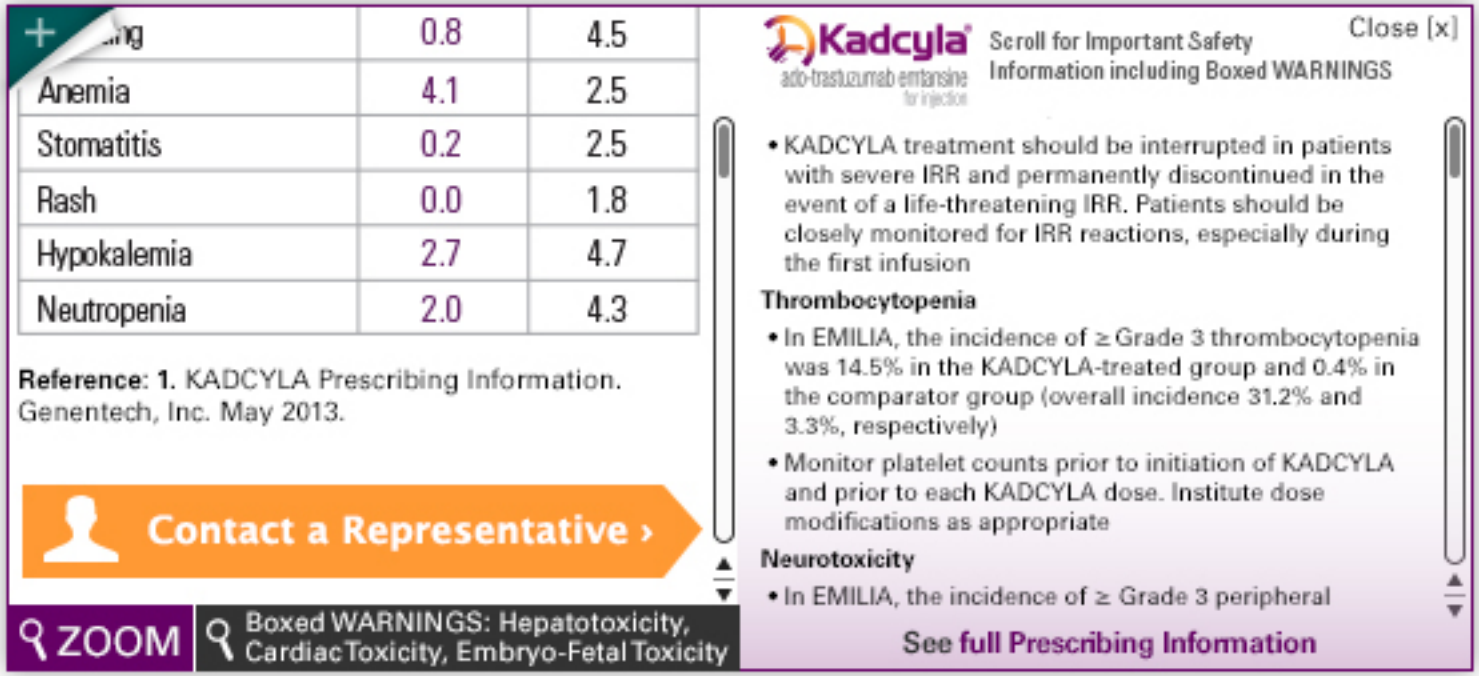

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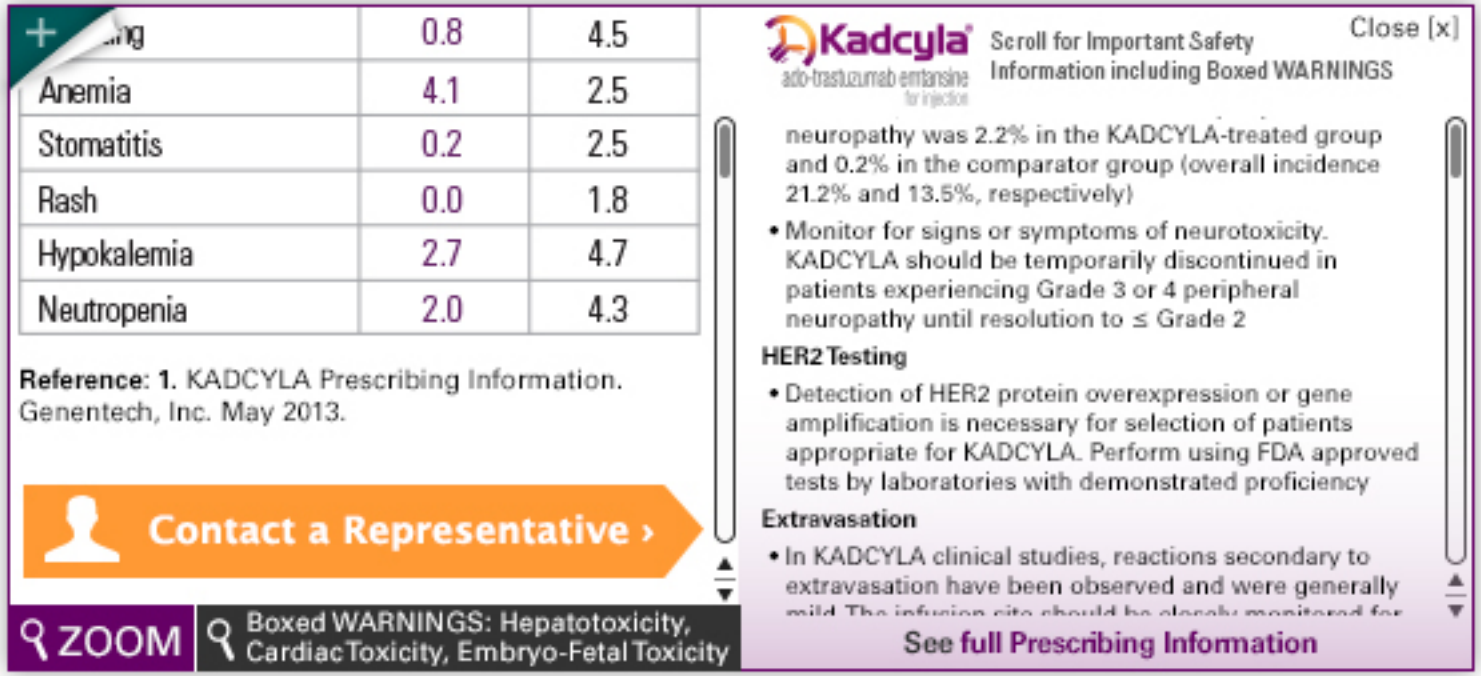

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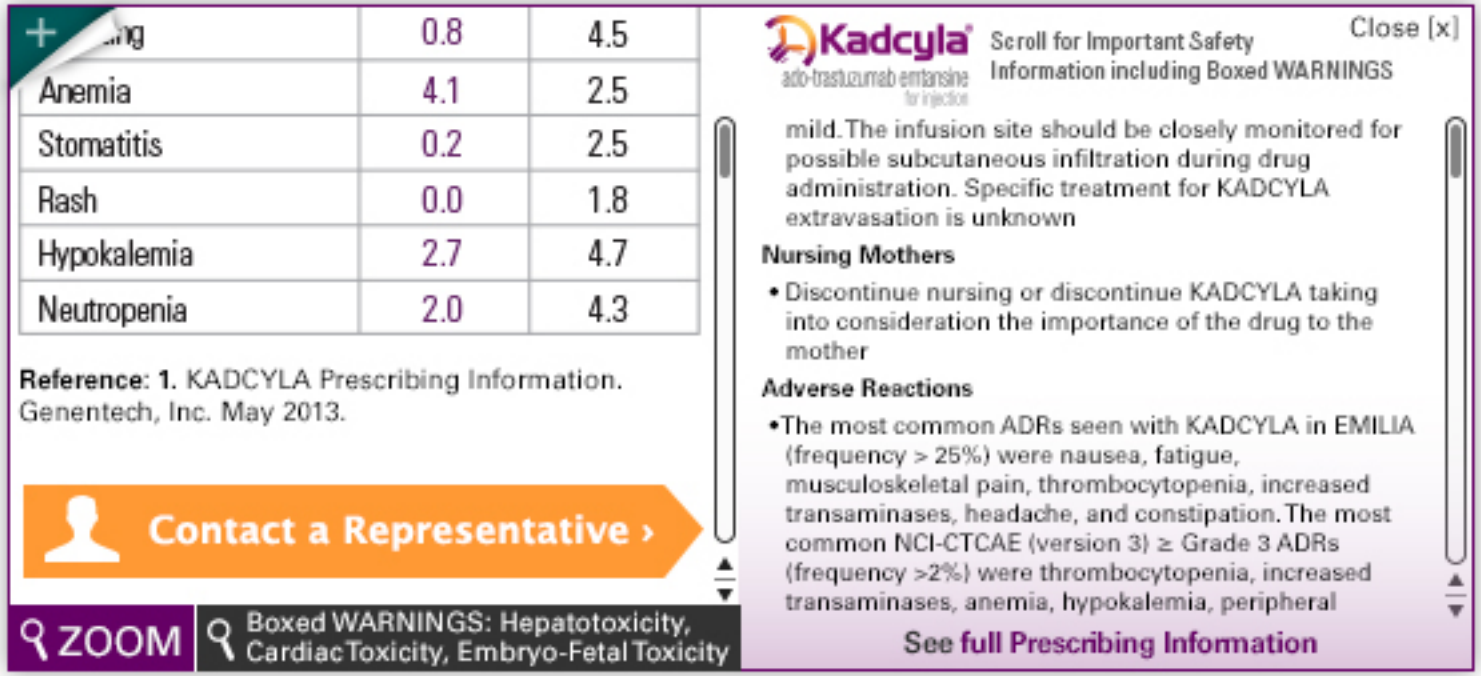
Neutropenia	2.0	4.3



+ing	0.8	4.5
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Stomatitis	0.2	2.5
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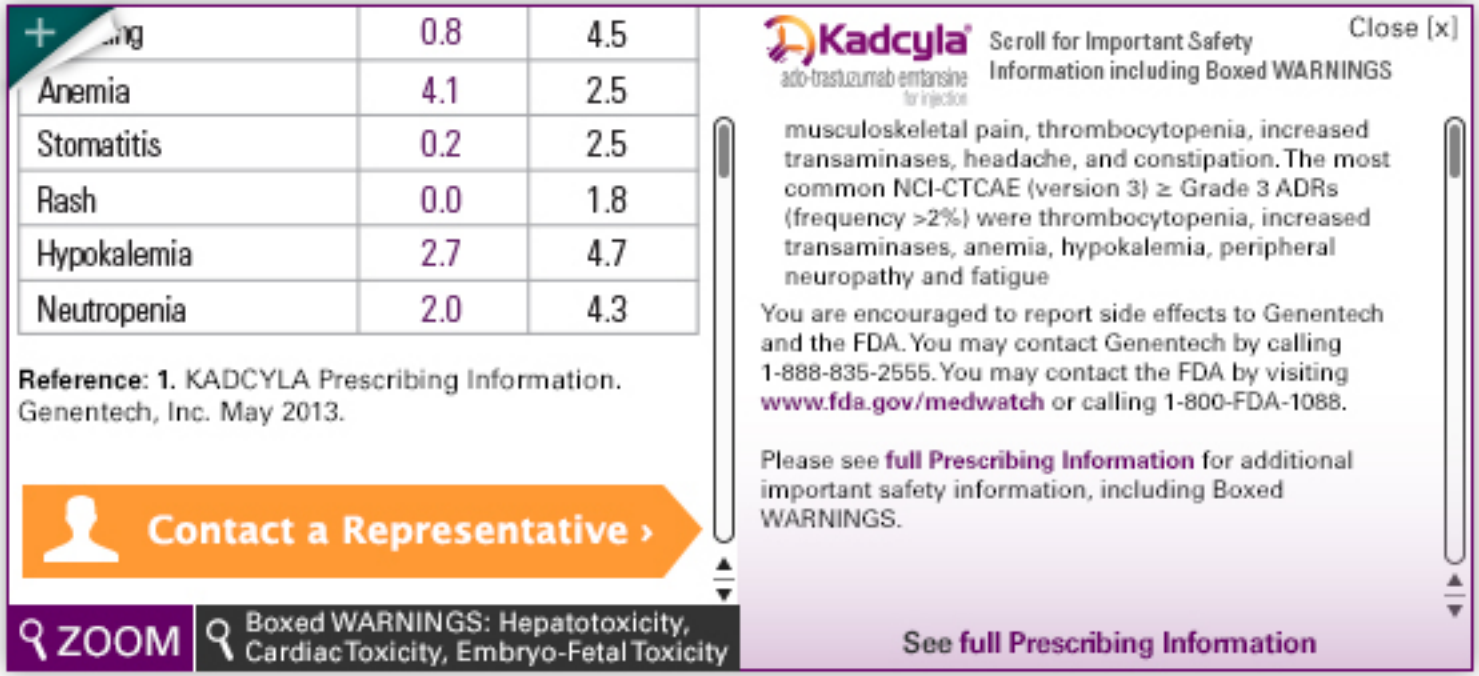

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Close [x]

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[1]

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**
		***P*<0.0001**		***P*=0.0006**	
Hormone receptor status					
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

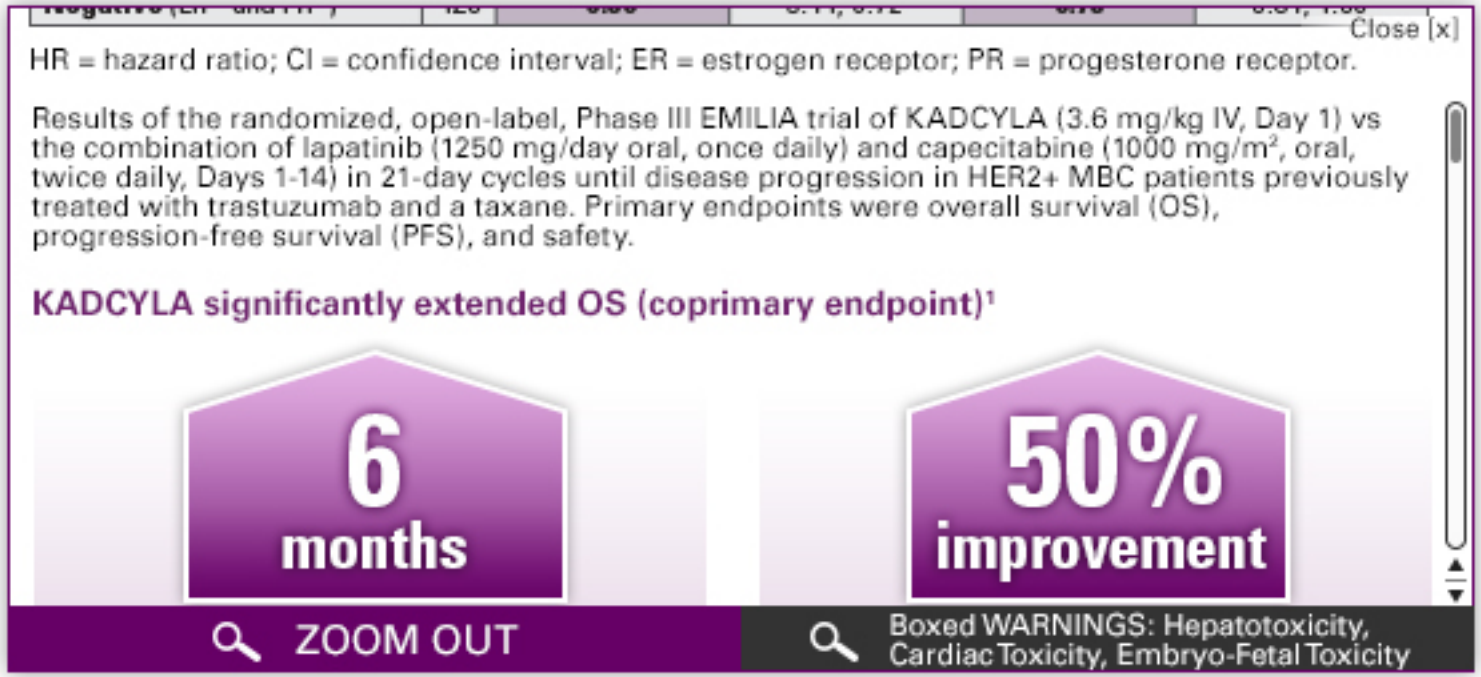
Close [x]

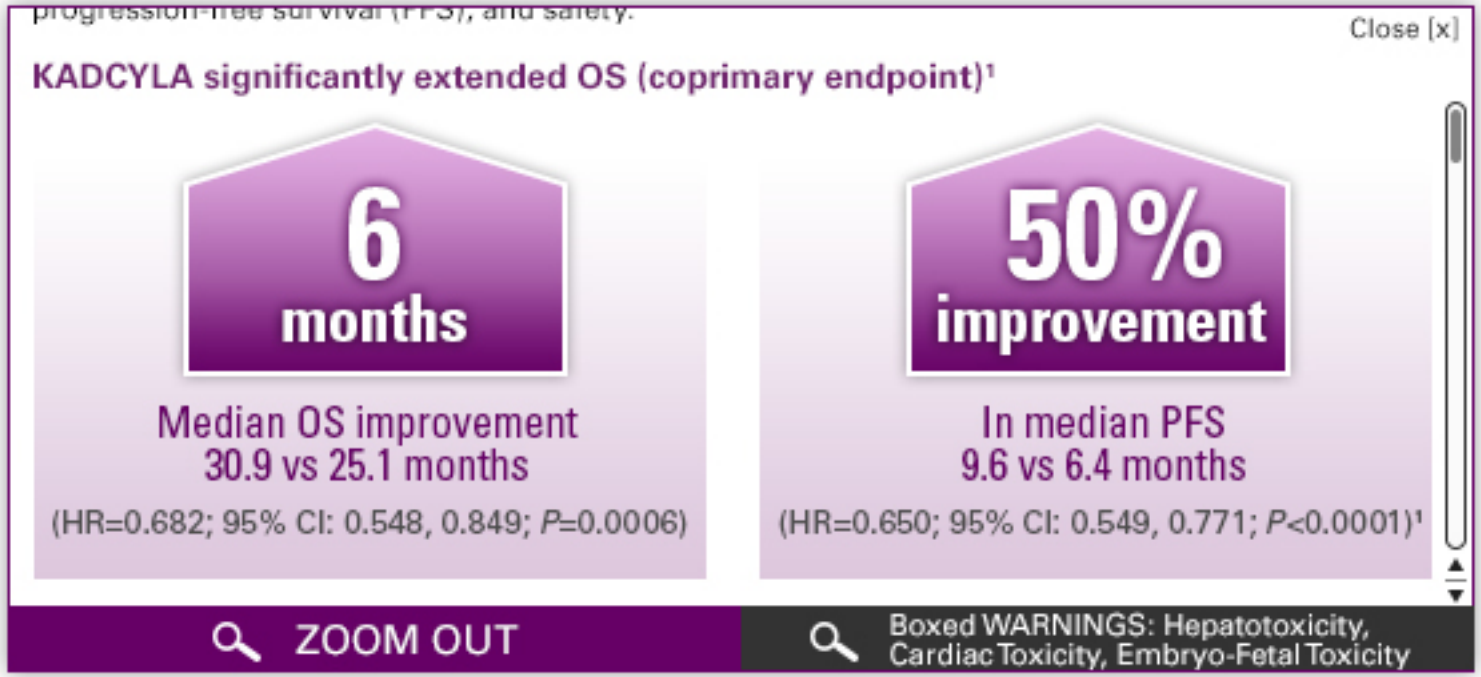
Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity

- 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


Close [x]
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/m², 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)¹
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)¹
6
months
Median OS improvement
30.9 vs 25.1 months
(HR=0.682; 95% CI: 0.548, 0.849; P=0.0006)
50%
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In median PFS
9.6 vs 6.4 months
(HR=0.650; 95% CI: 0.549, 0.771; P<0.0001)¹
ZOOM OUT
Boxed WARNINGS: Hepatotoxicity, Cardiac Toxicity, Embryo-Fetal Toxicity

Close [x]

- 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)

Select Important Safety Information: Pulmonary Toxicity

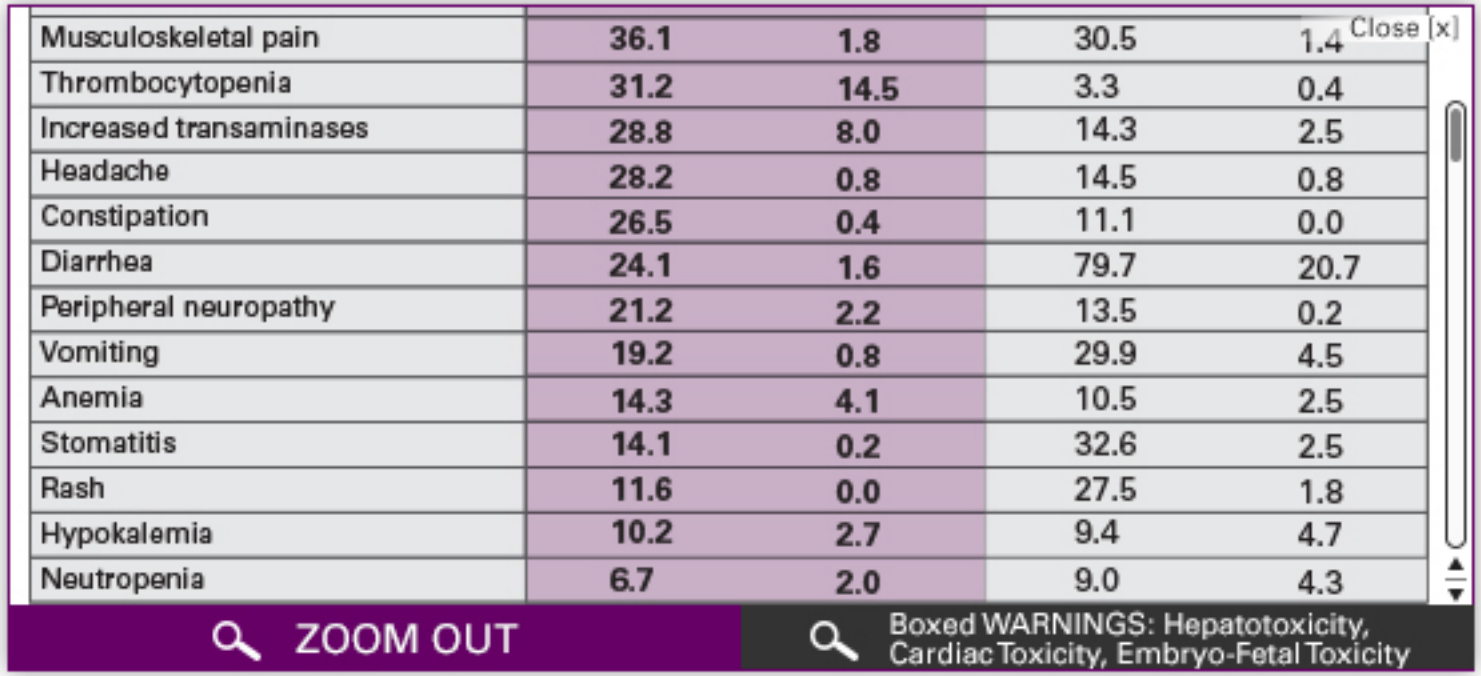
- Cases of interstitial lung disease (ILD), including pneumonitis, some leading to acute respiratory distress syndrome or fatal outcome, have been reported in clinical trials with KADCYLA. Treatment with KADCYLA should be permanently discontinued in patients diagnosed with ILD or pneumonitis

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

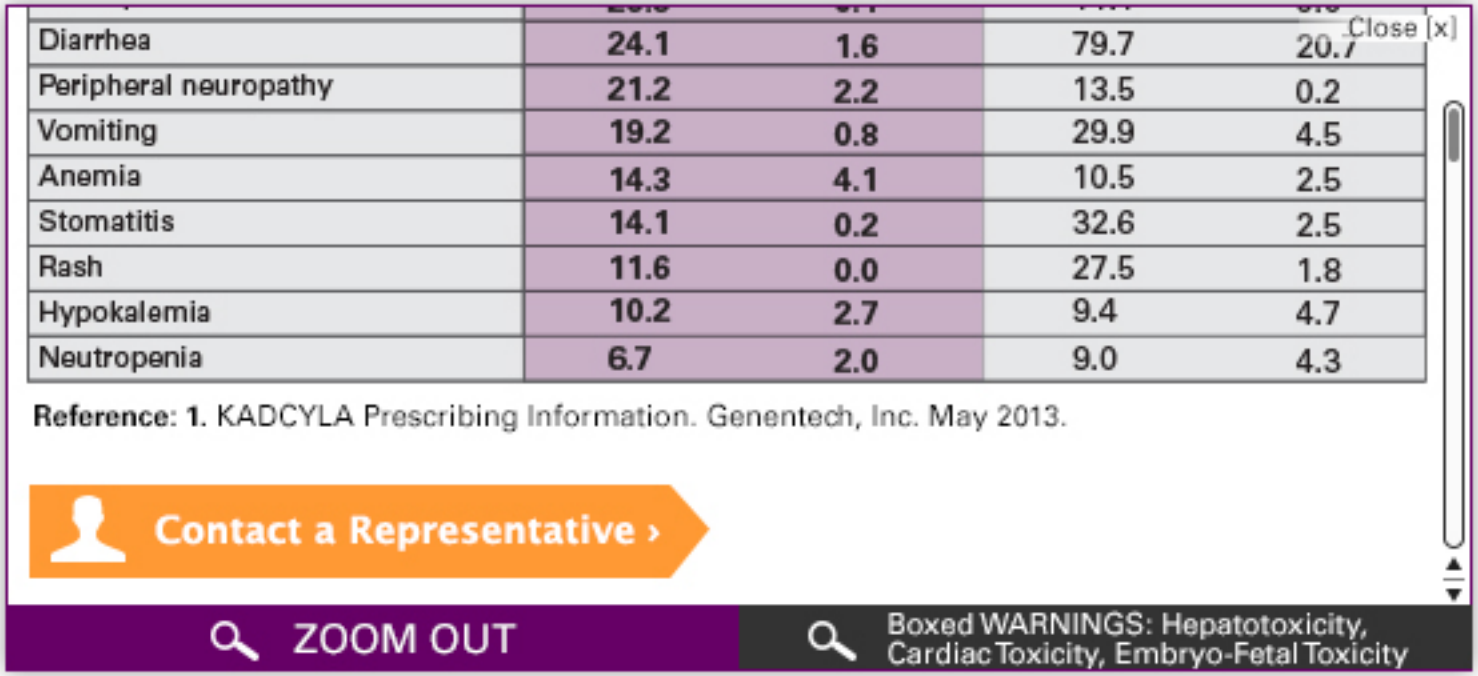
	KADCYLA (n=490)		lapatinib + capecitabine (n=488)	
ADVERSE REACTION	**All Grades, %**	**Grades≥3, %**	**All Grades, %**	**Grades≥3, %**
Nausea	39.8	0.8	45.1	2.5
Fatigue	36.3	2.5	28.3	3.5

ZOOM OUT

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



Musculoskeletal pain	36.1	1.8	30.5	1.4
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



Diarrhea	24.1	1.6	79.7	20.7
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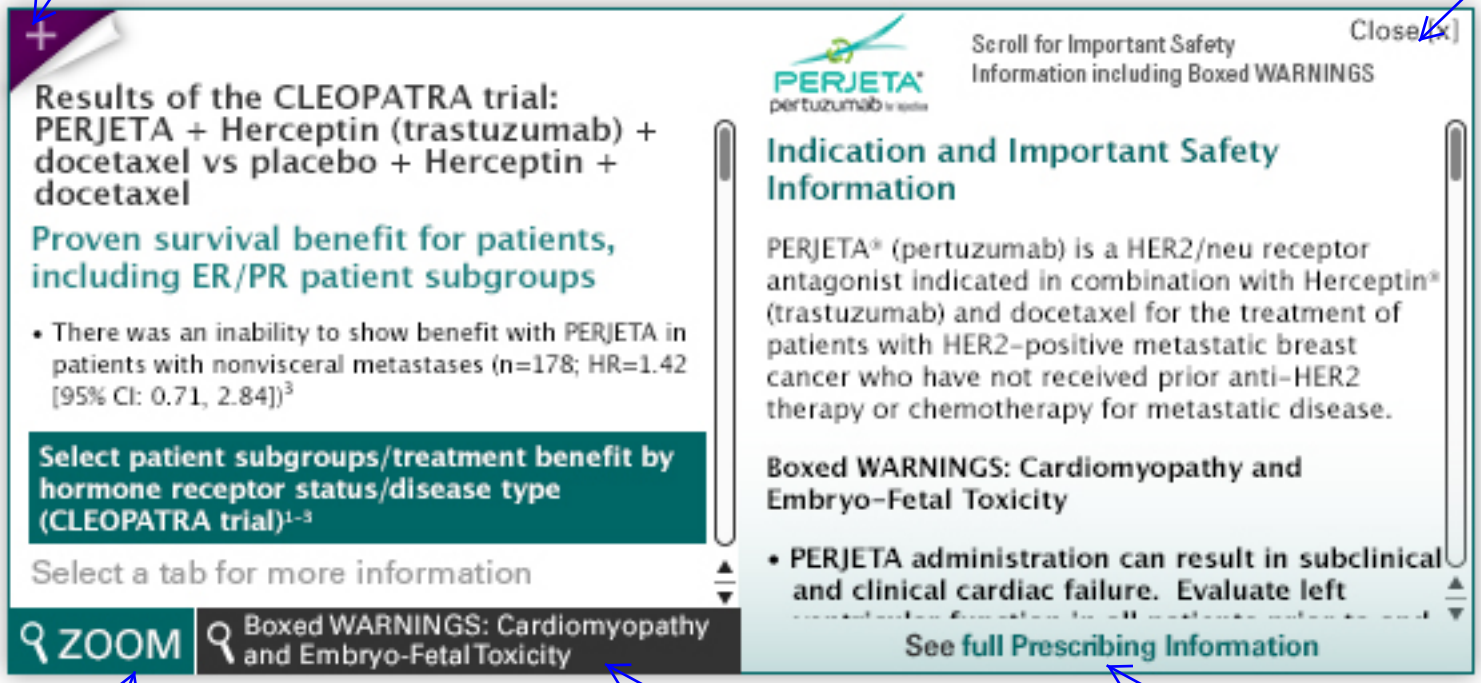
Clicking "Close" will collapse the banner to the initial state.



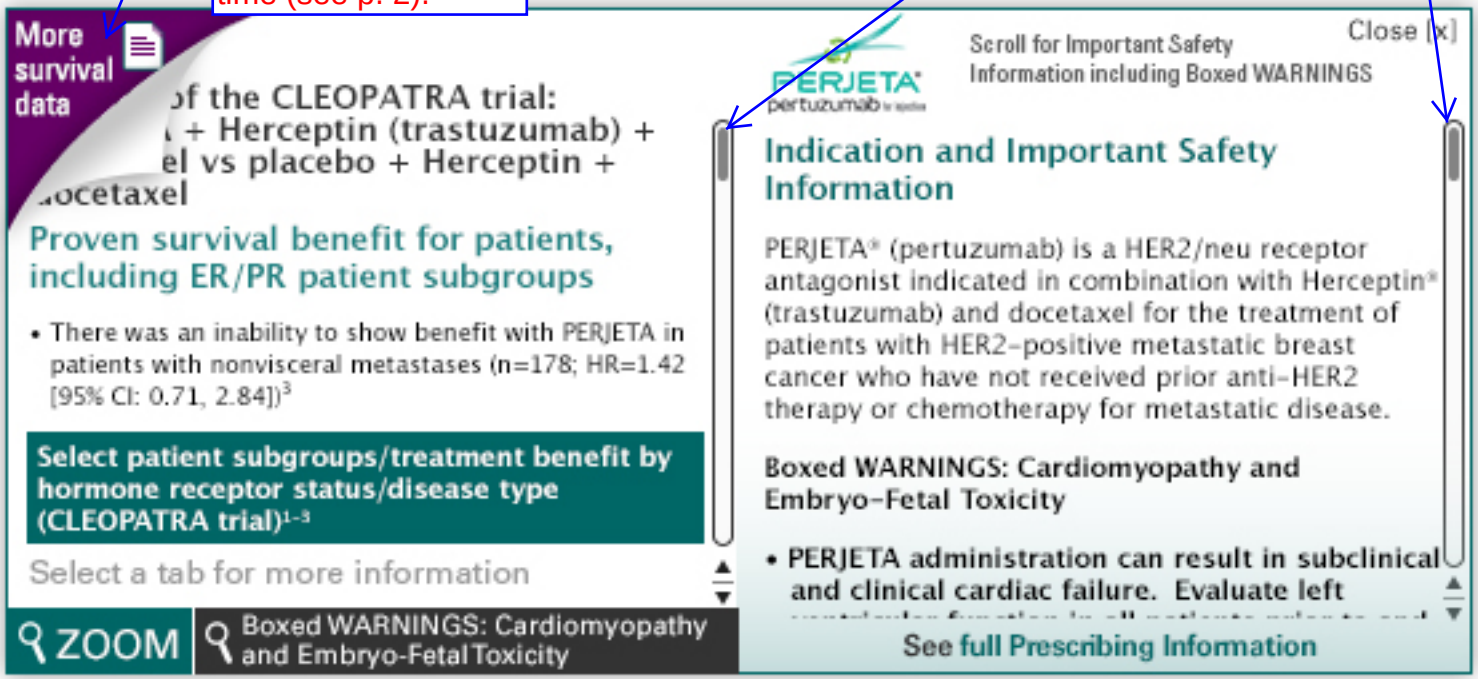
Clicking "Zoom" will enable users to see the content in in the full viewing space. See pp. 50-59 for example.

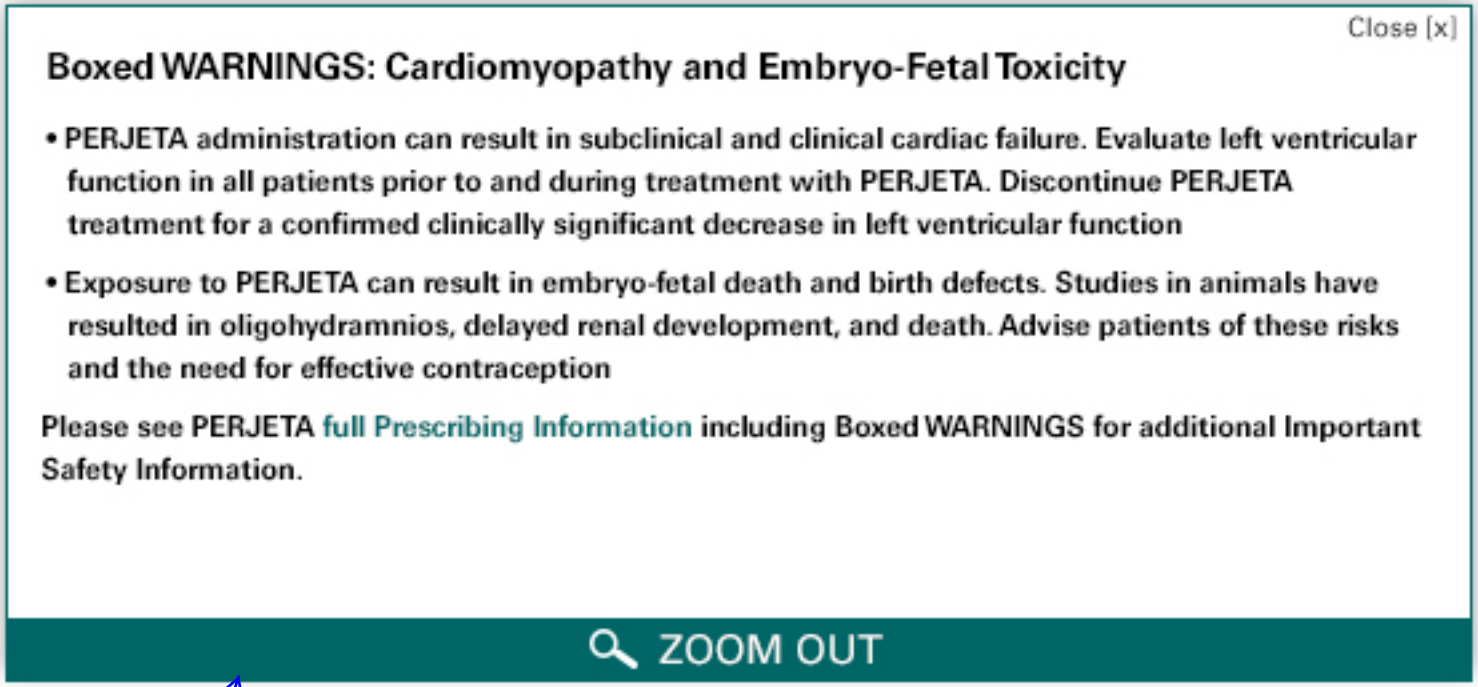
Clicking this space will present user with expanded Boxed WARNINGS view (see p. 31 for expanded view of PERJETA warning text).

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).

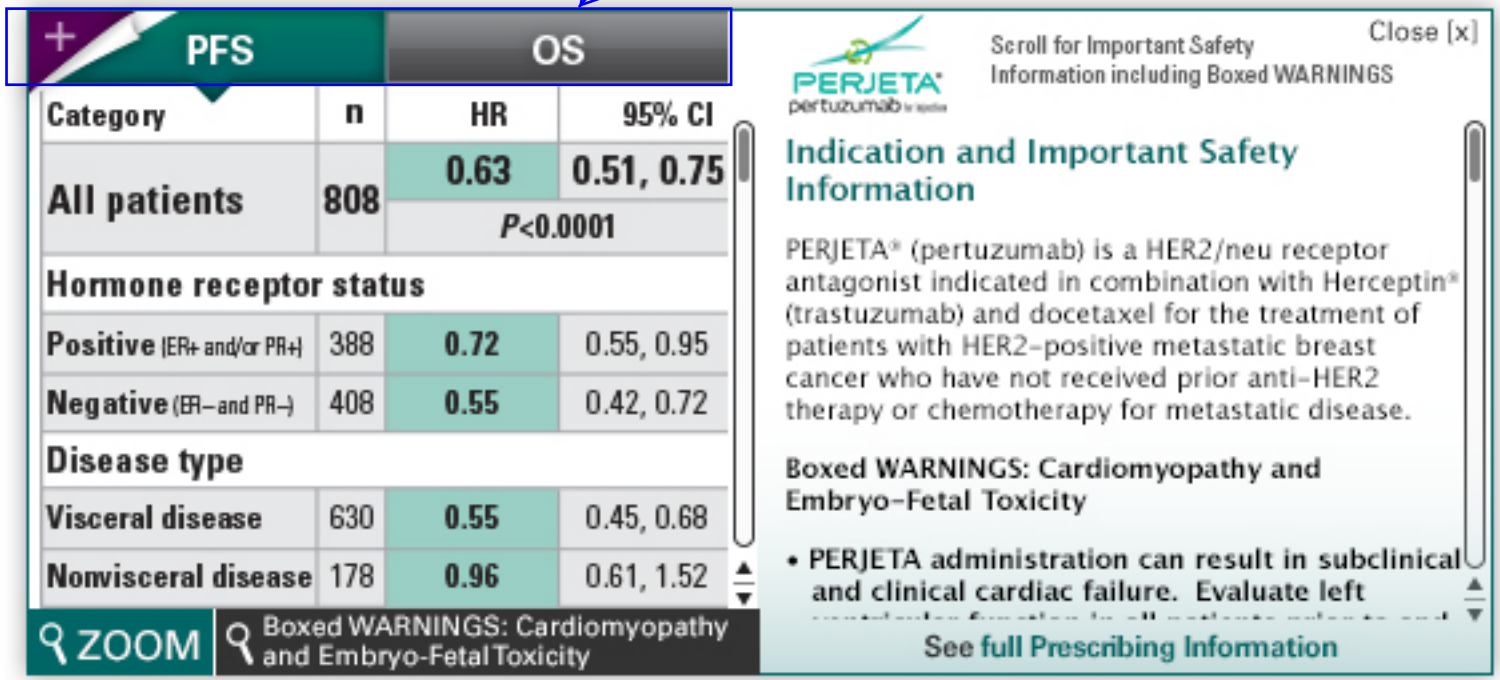
Global - users can use scroll bars in each section to navigate the content



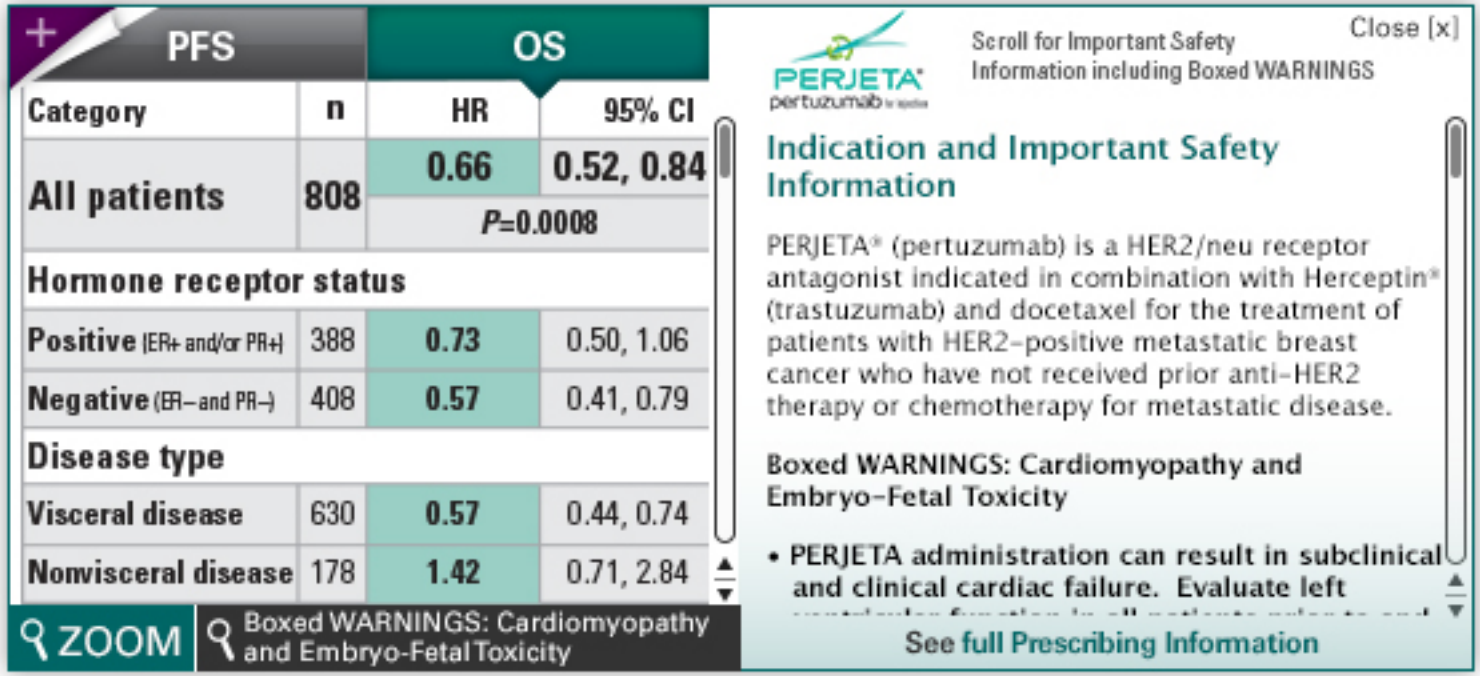


Clicking "zoom out" returns the user to the prior view.

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

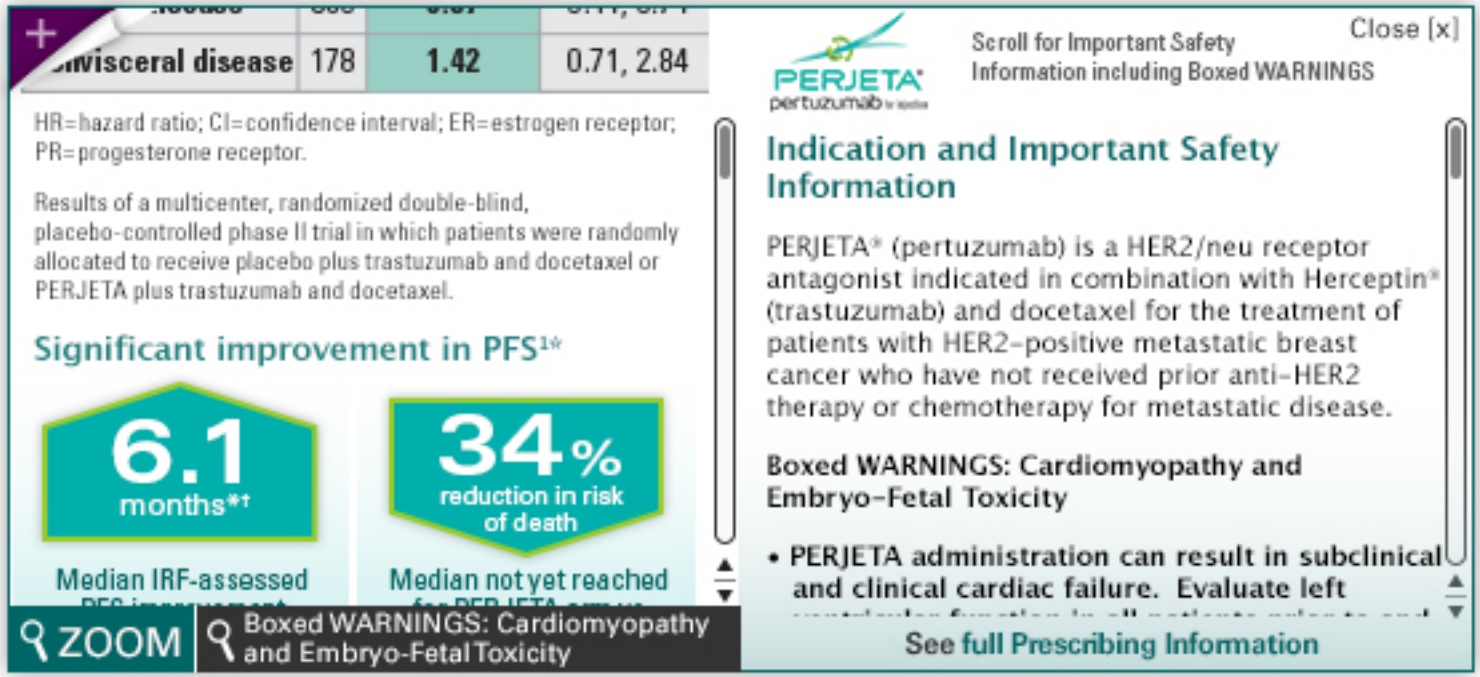


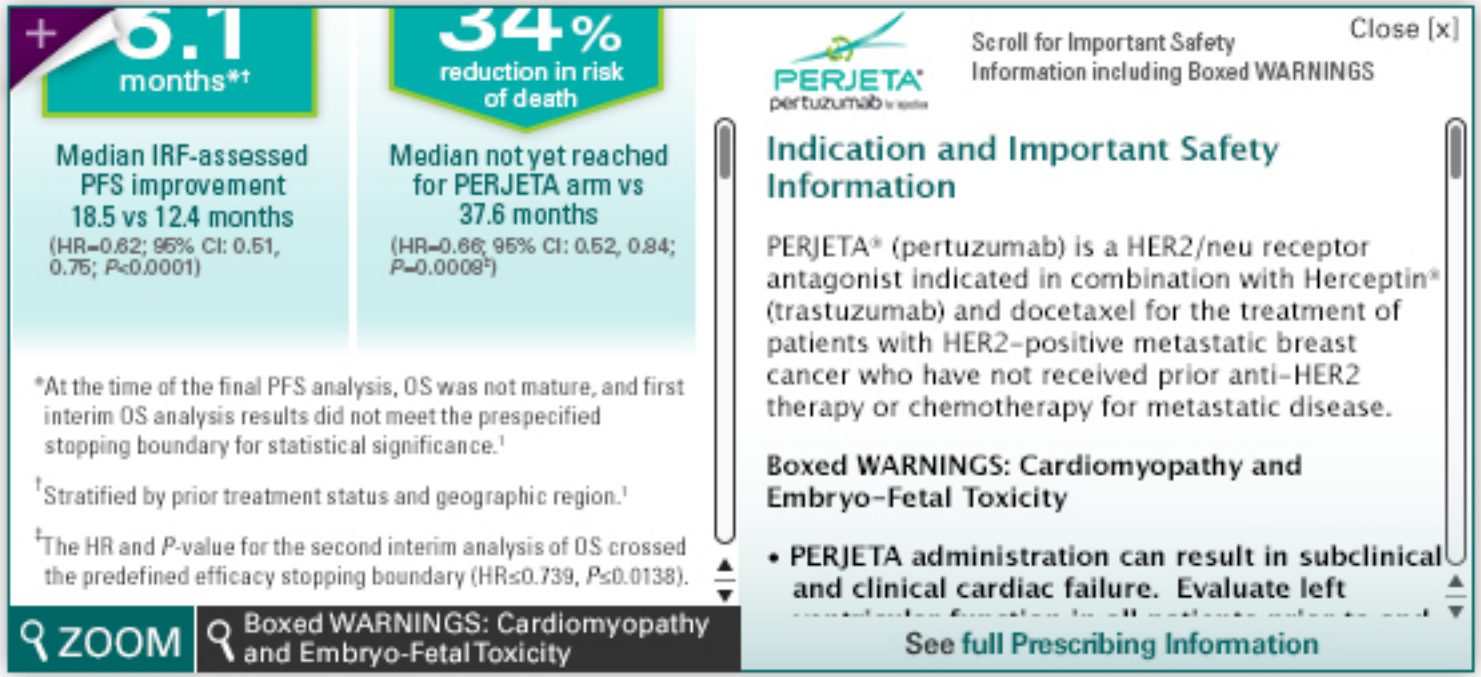
OS data

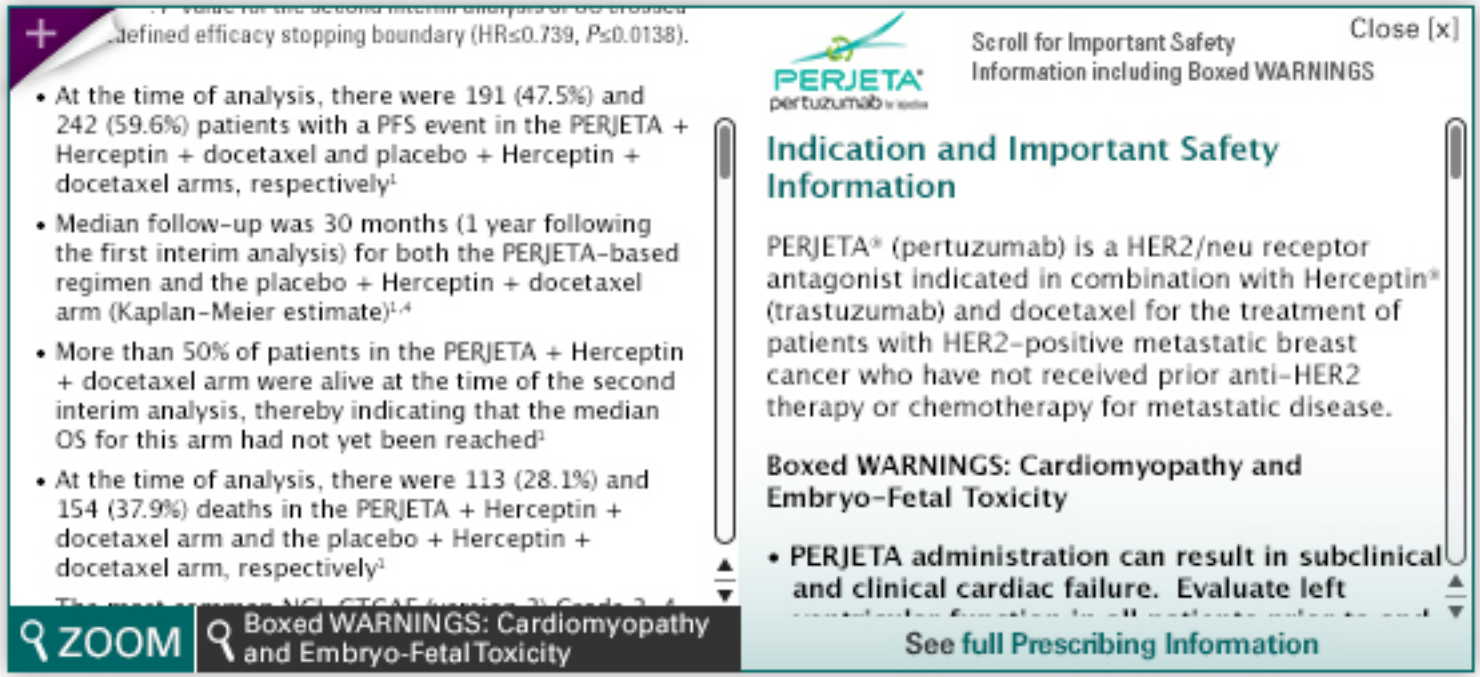


PFS | OS

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


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 PFS1*
6.1 months*†
Median IRF-assessed
34% reduction in risk of death
Median not yet reached
ZOOM
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




defined 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[1]
• 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)[1,4]
• 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[1]
• 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[1]
ZOOM
Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity
PERJETA
pertuzumab
Scroll for Important Safety Information including Boxed WARNINGS
Close [x]
Indication and Important Safety Information
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Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity
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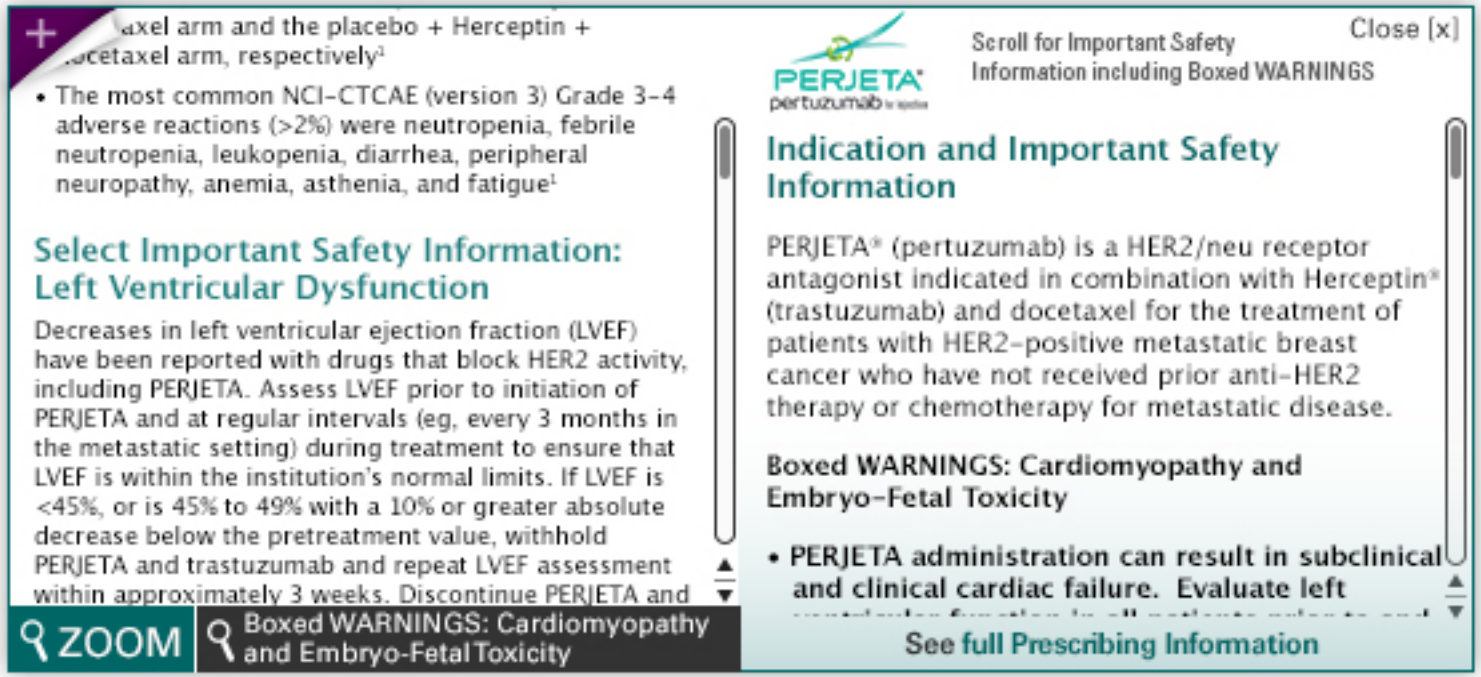
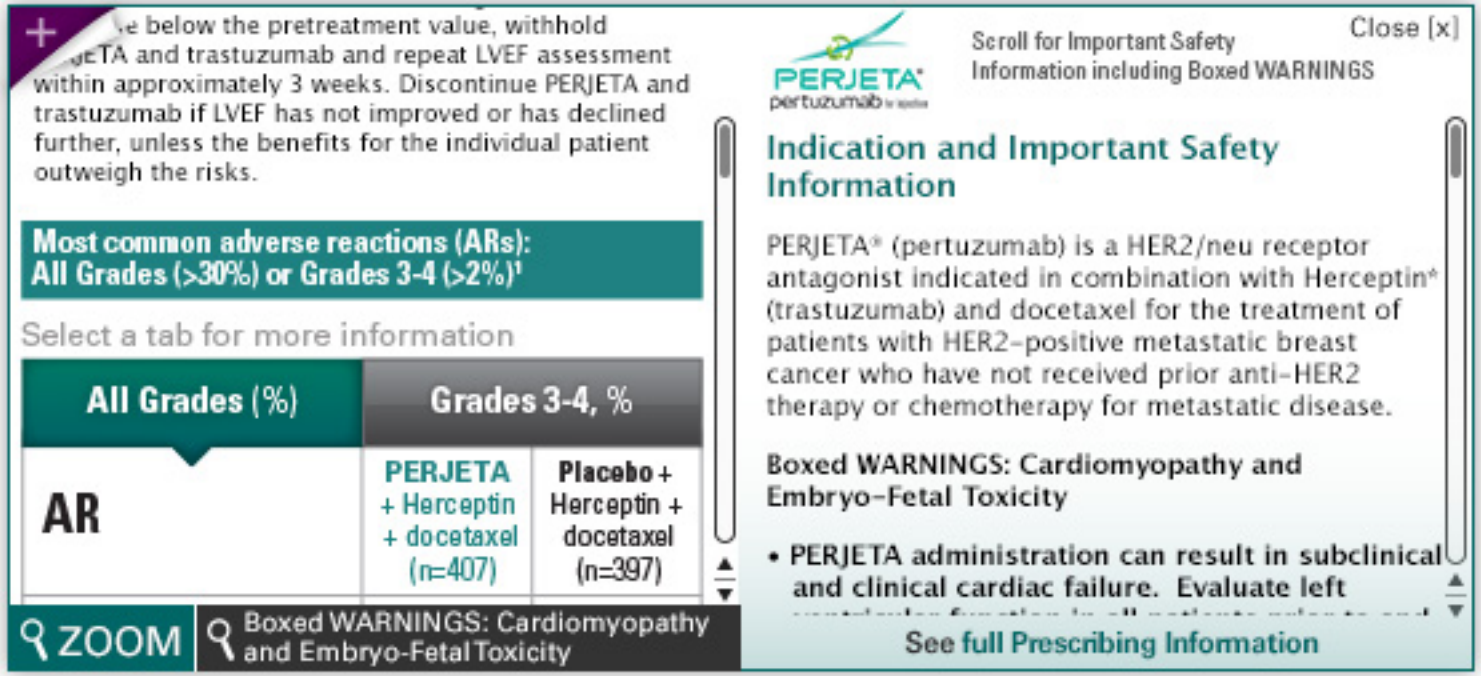
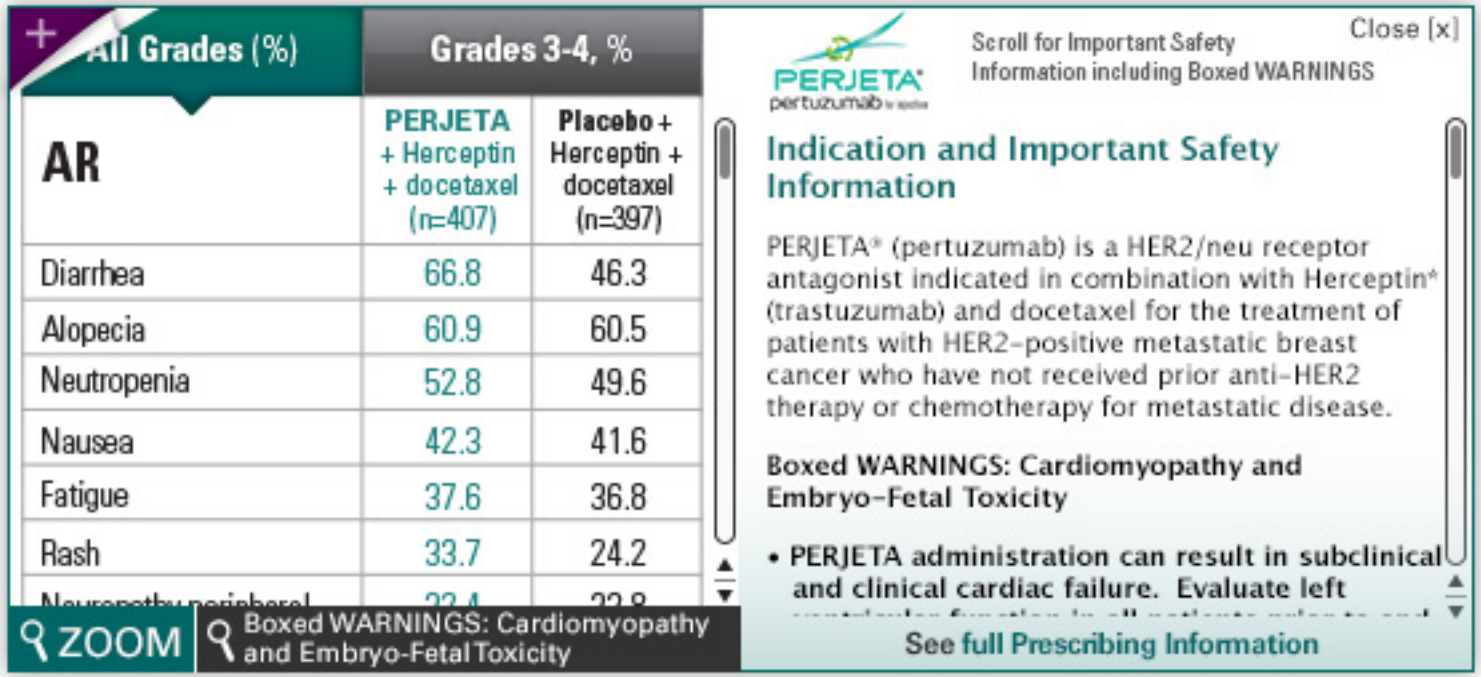
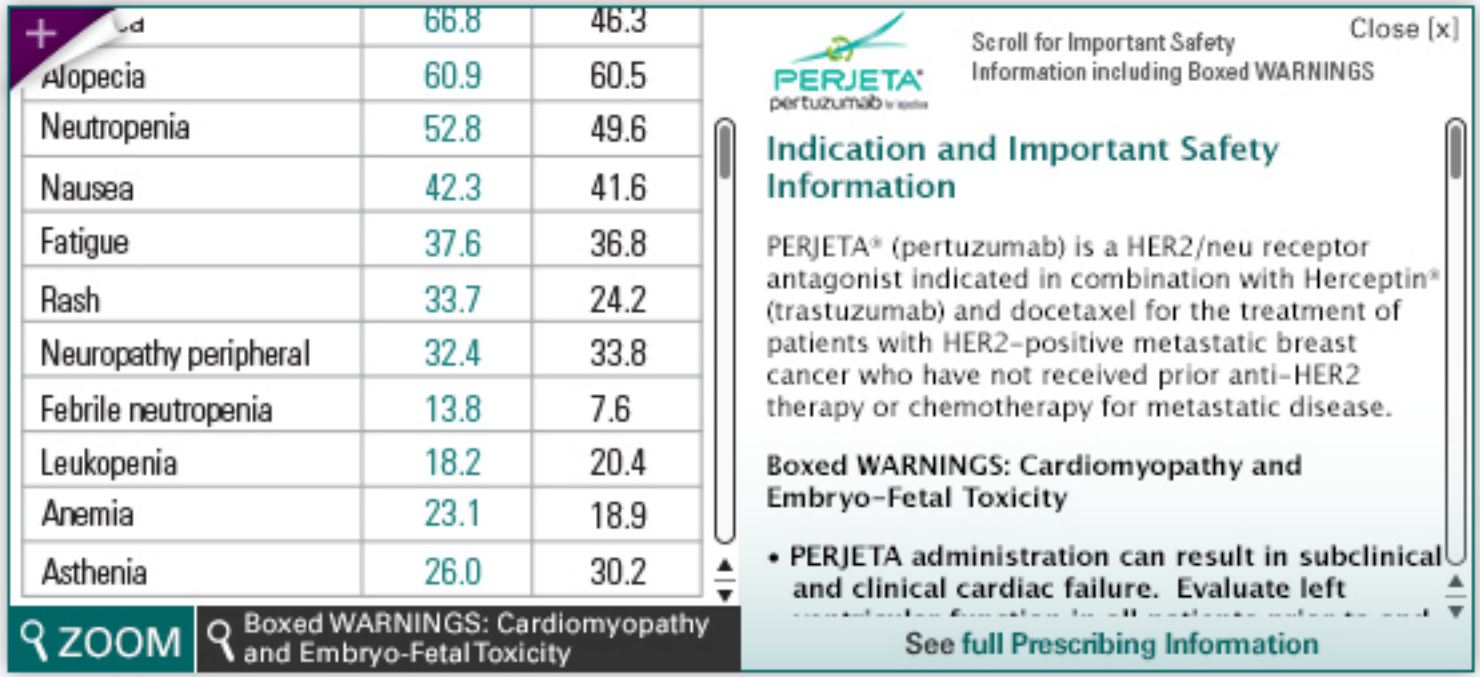
See full Prescribing Information


axel arm and the placebo + Herceptin +
cetaxel arm, respectively[1]
• 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[1]
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
ZOOM
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

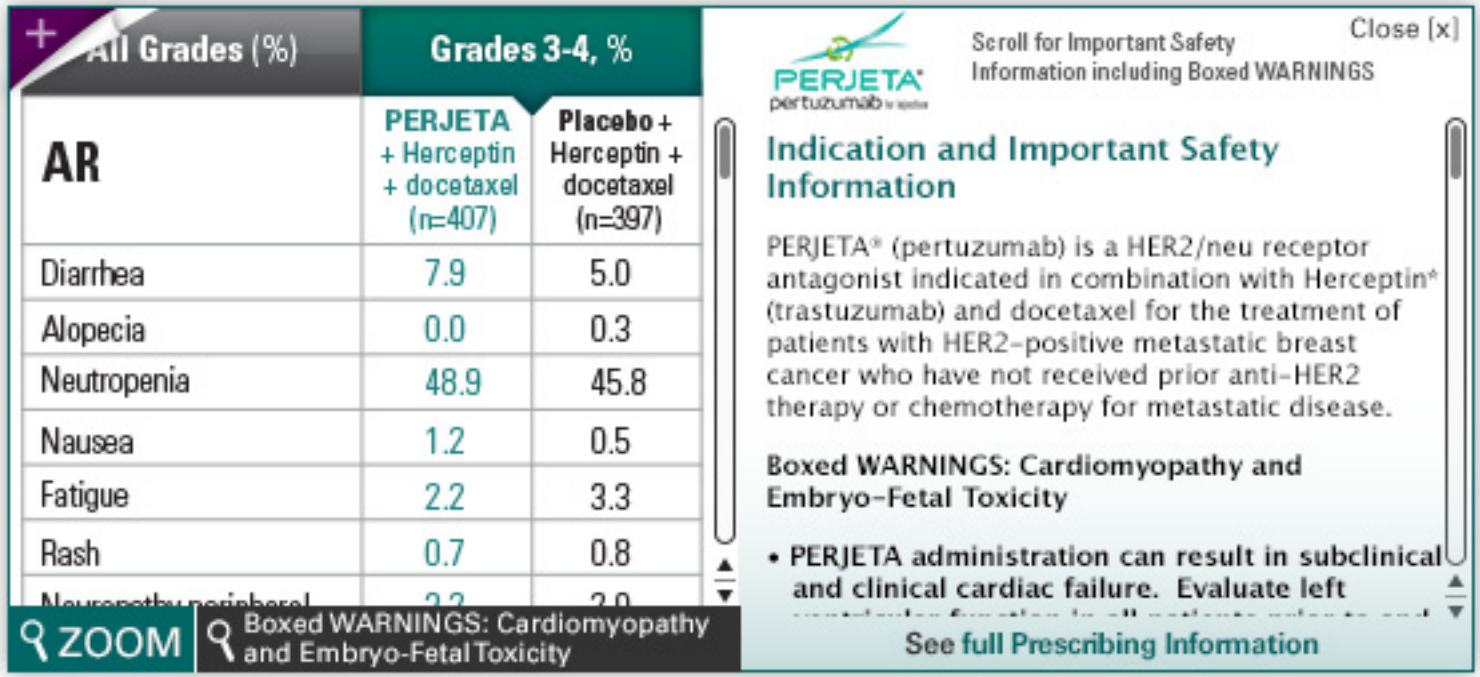

e below the pretreatment value, withhold
ETA and trastuzumab and repeat LVEF assessment within approximately 3 weeks. Discontinue PERJETA and trastuzumab if LVEF has not improved or has declined further, unless the benefits for the individual patient outweigh the risks.
Most common adverse reactions (ARs): All Grades (>30%) or Grades 3-4 (>2%)[1]
Select a tab for more information
All Grades (%)
Grades 3-4, %
AR
PERJETA + Herceptin + docetaxel (n=407)
Placebo + Herceptin + docetaxel (n=397)
ZOOM
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



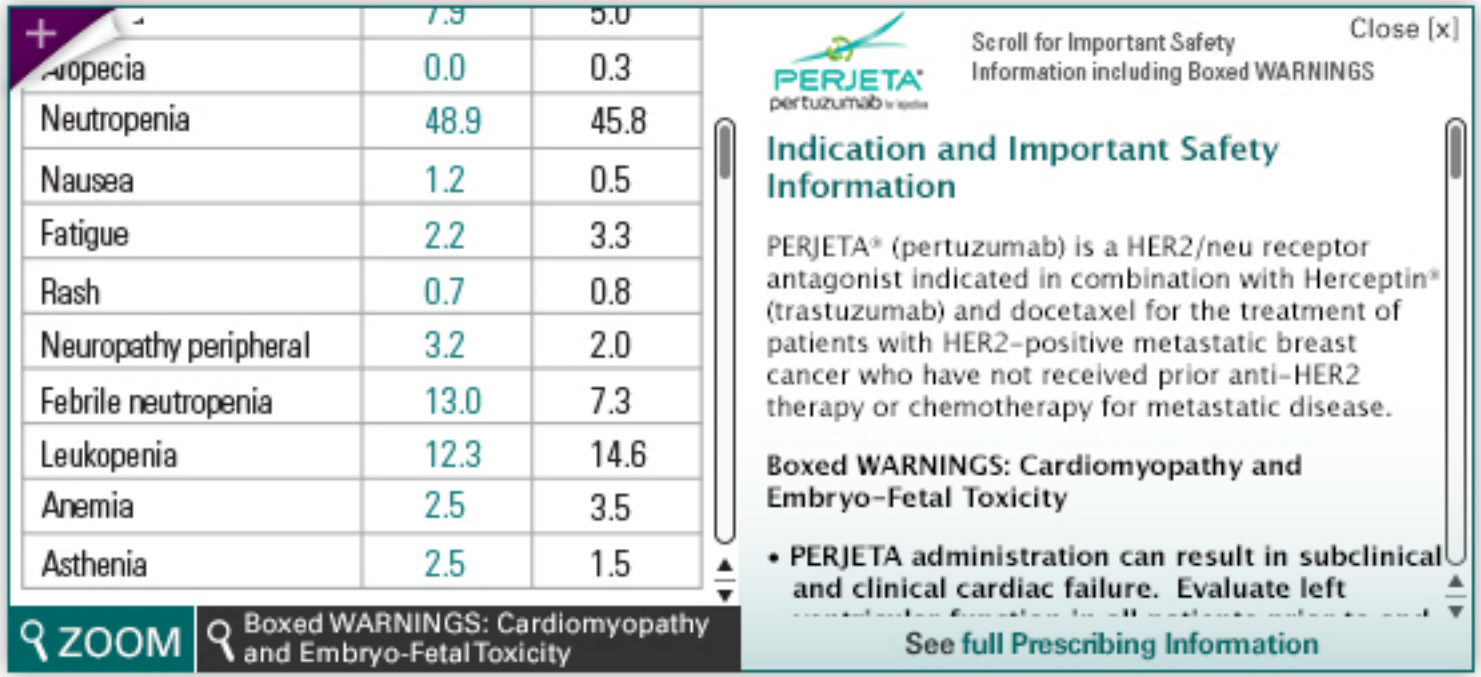
All Grades (%)	Grades 3-4, %	
AR	**PERJETA** + Herceptin + docetaxel (n=407)	**Placebo** + Herceptin + docetaxel (n=397)
Diarrhea	66.8	46.3
Alopecia	60.9	60.5
Neutropenia	52.8	49.6
Nausea	42.3	41.6
Fatigue	37.6	36.8
Rash	33.7	24.2
Neuropathy peripheral	22.4	22.8



[illegible]ed	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



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


7.9
5.0
Alopecia
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Nausea
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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
ZOOM
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
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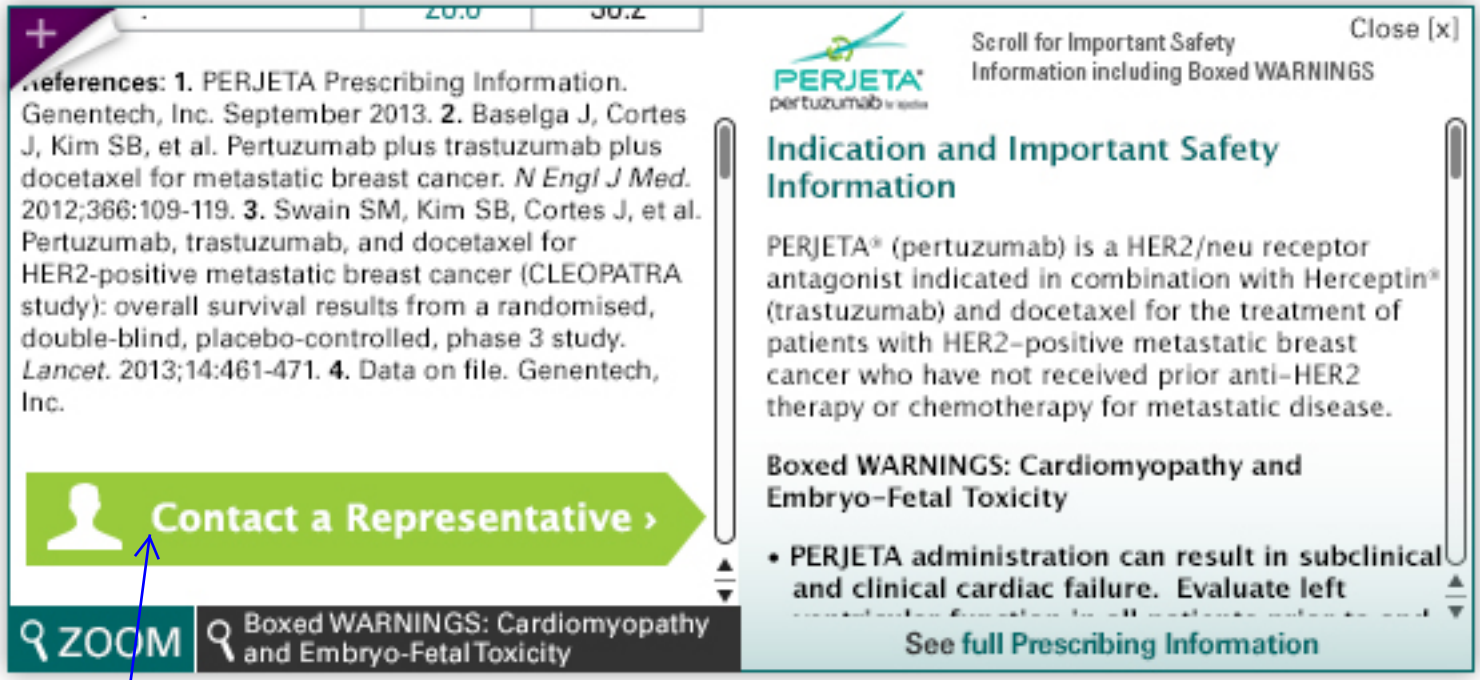
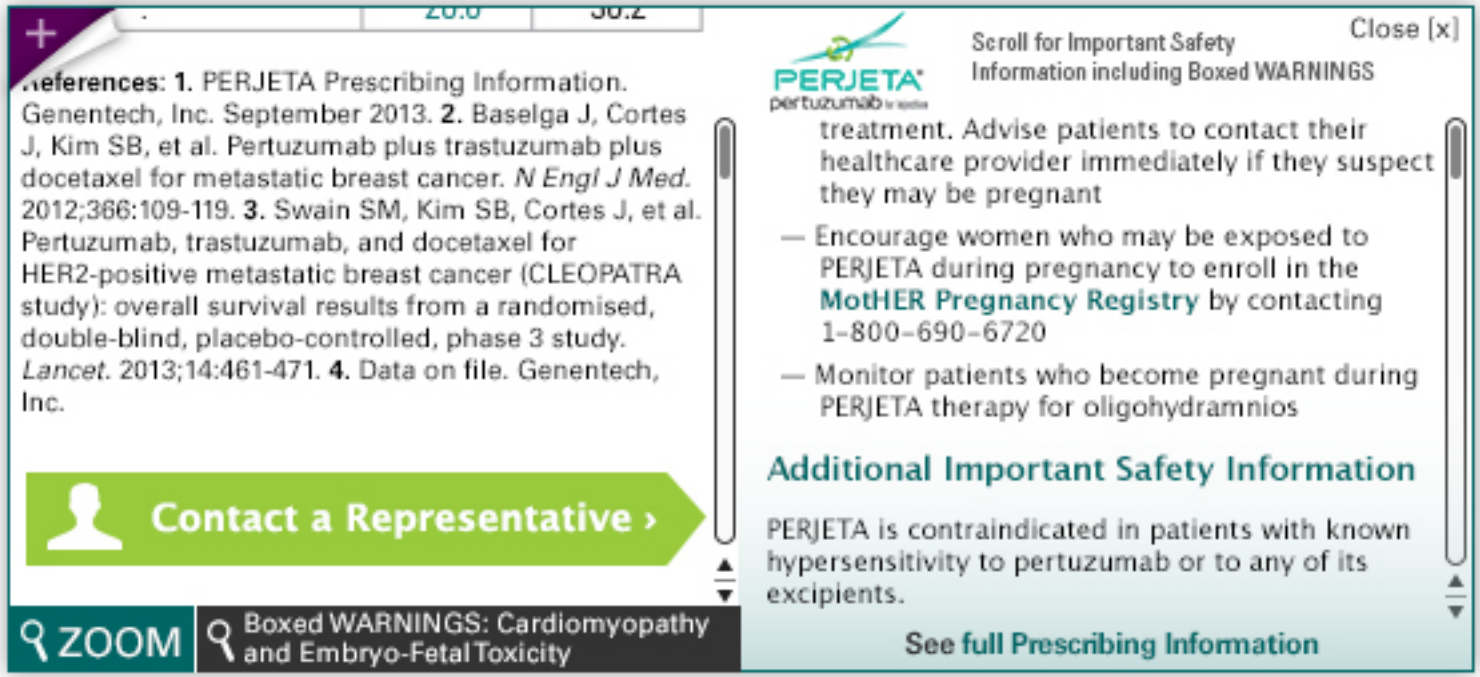
See full Prescribing Information



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


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
Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity
PERJETA pertuzumab
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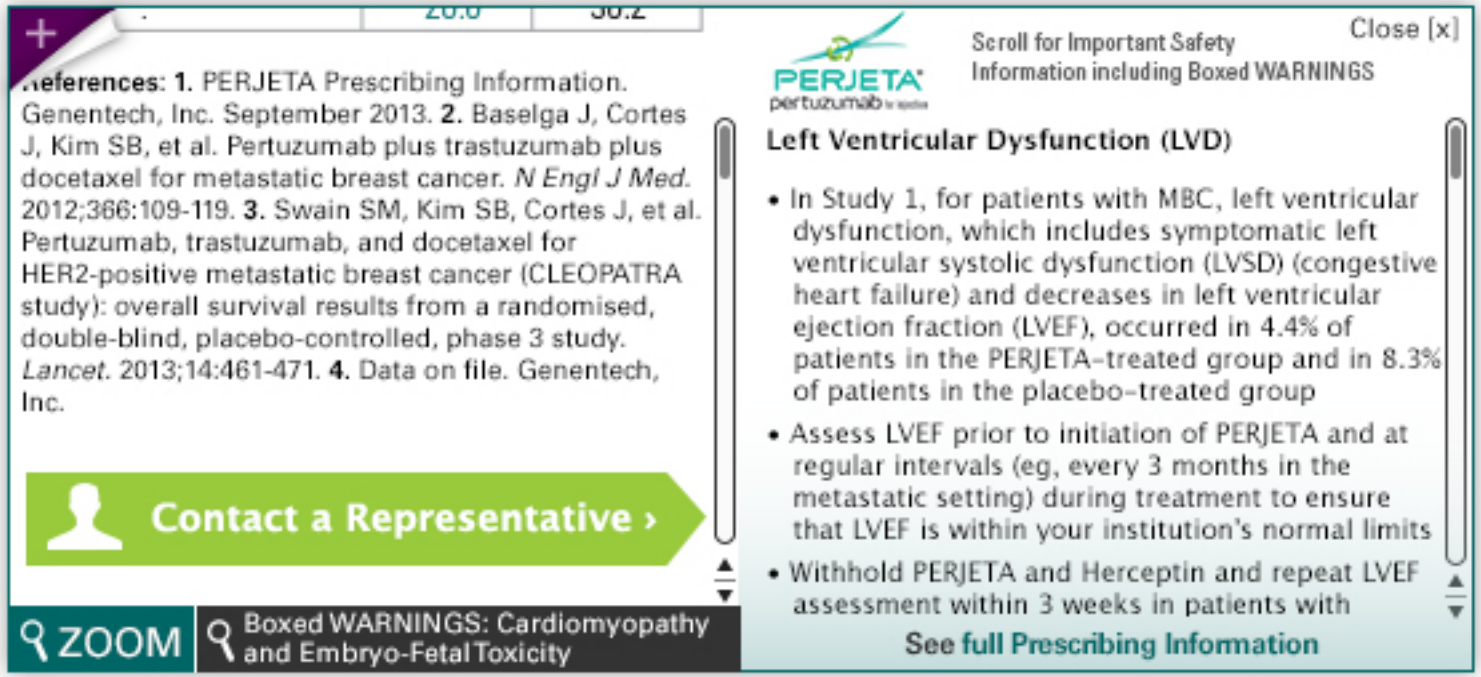
treatment. Advise patients to contact their healthcare provider immediately if they suspect they may be pregnant
— Encourage women who may be exposed to PERJETA during pregnancy to enroll in the MotHER Pregnancy Registry by contacting 1-800-690-6720
— Monitor patients who become pregnant during PERJETA 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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PERJETA pertuzumab
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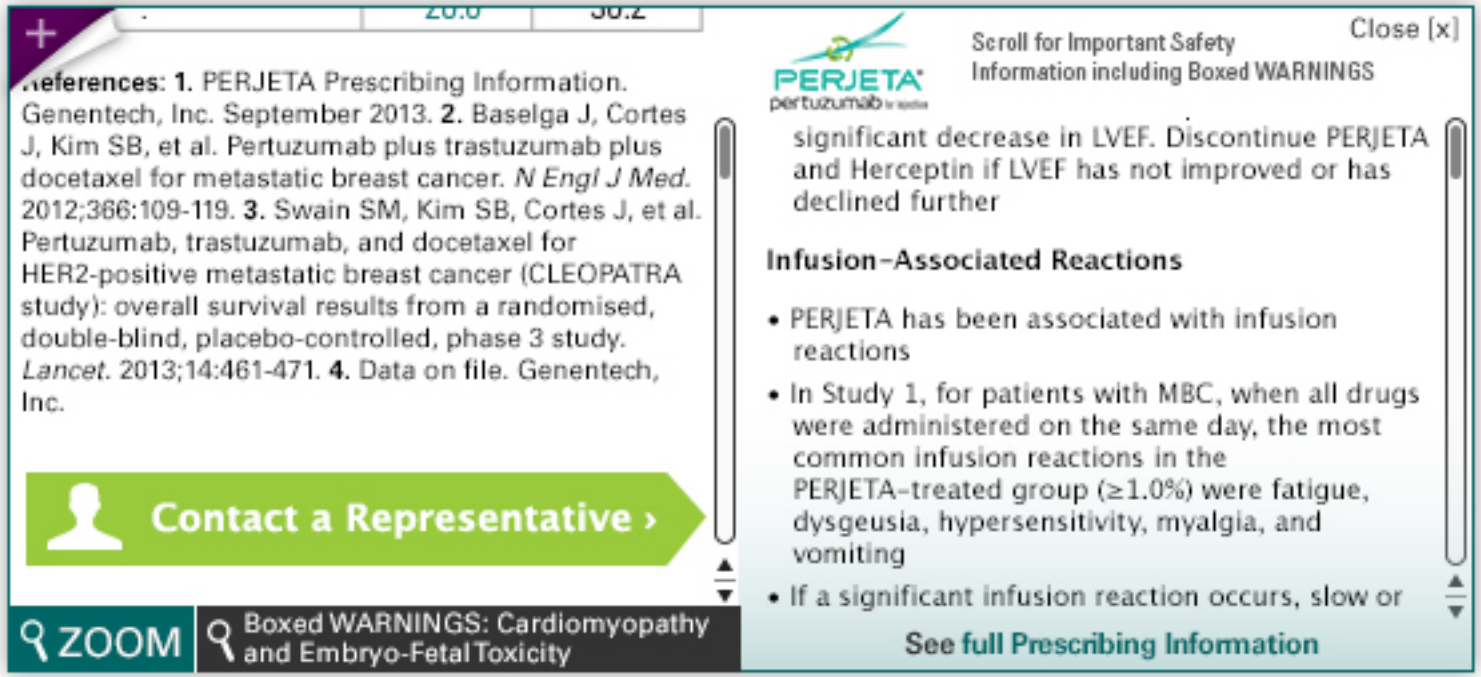
Left Ventricular Dysfunction (LVD)
• In Study 1, for patients with MBC, left ventricular dysfunction, which includes symptomatic left ventricular systolic dysfunction (LVSD) (congestive heart failure) and decreases in left ventricular ejection fraction (LVEF), occurred in 4.4% of patients in the PERJETA–treated 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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PERJETA pertuzumab
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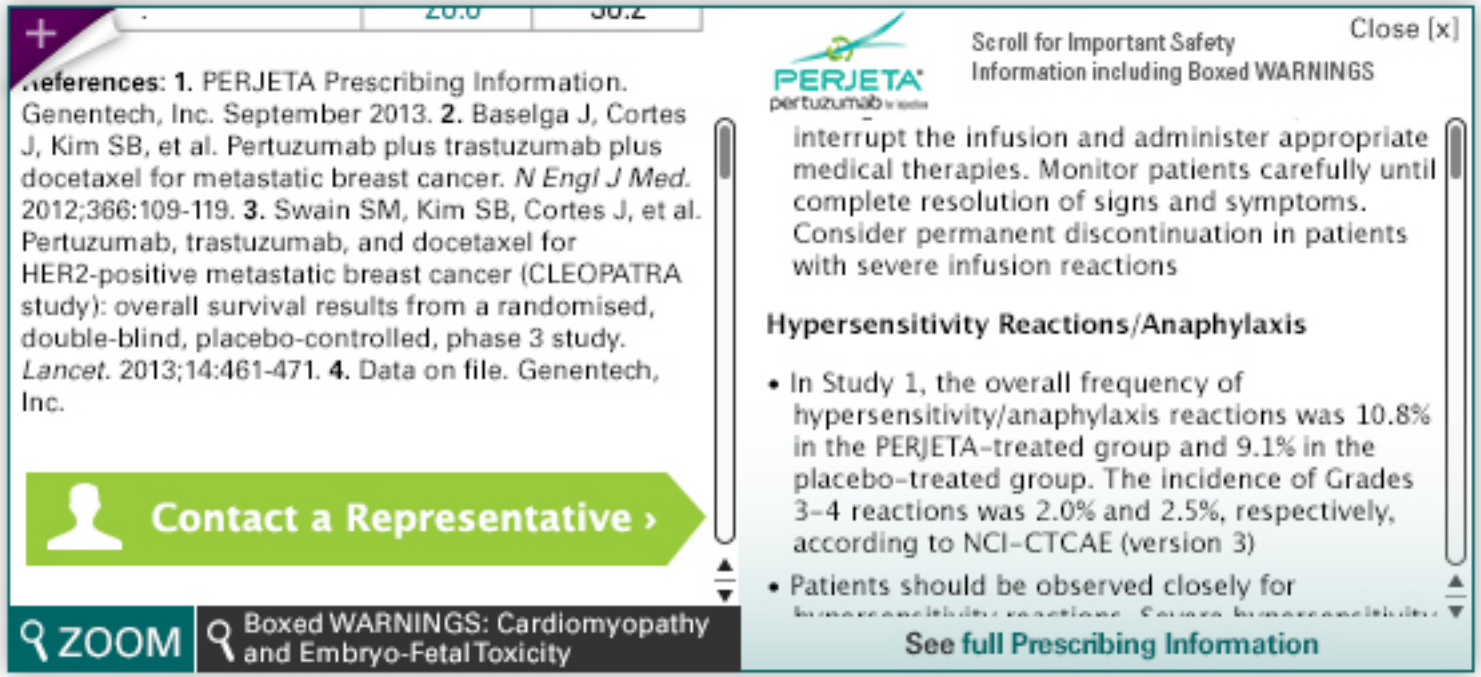
significant decrease in LVEF. Discontinue PERJETA and Herceptin if LVEF has not improved or has declined further
Infusion-Associated Reactions
• PERJETA has been associated with infusion reactions
• In Study 1, for patients with MBC, when all drugs were administered on the same day, the most common infusion reactions in the PERJETA-treated group (≥1.0%) were fatigue, dysgeusia, hypersensitivity, myalgia, and vomiting
• If a significant infusion reaction occurs, slow or
See full Prescribing Information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ZOOM
Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity
PERJETA pertuzumab
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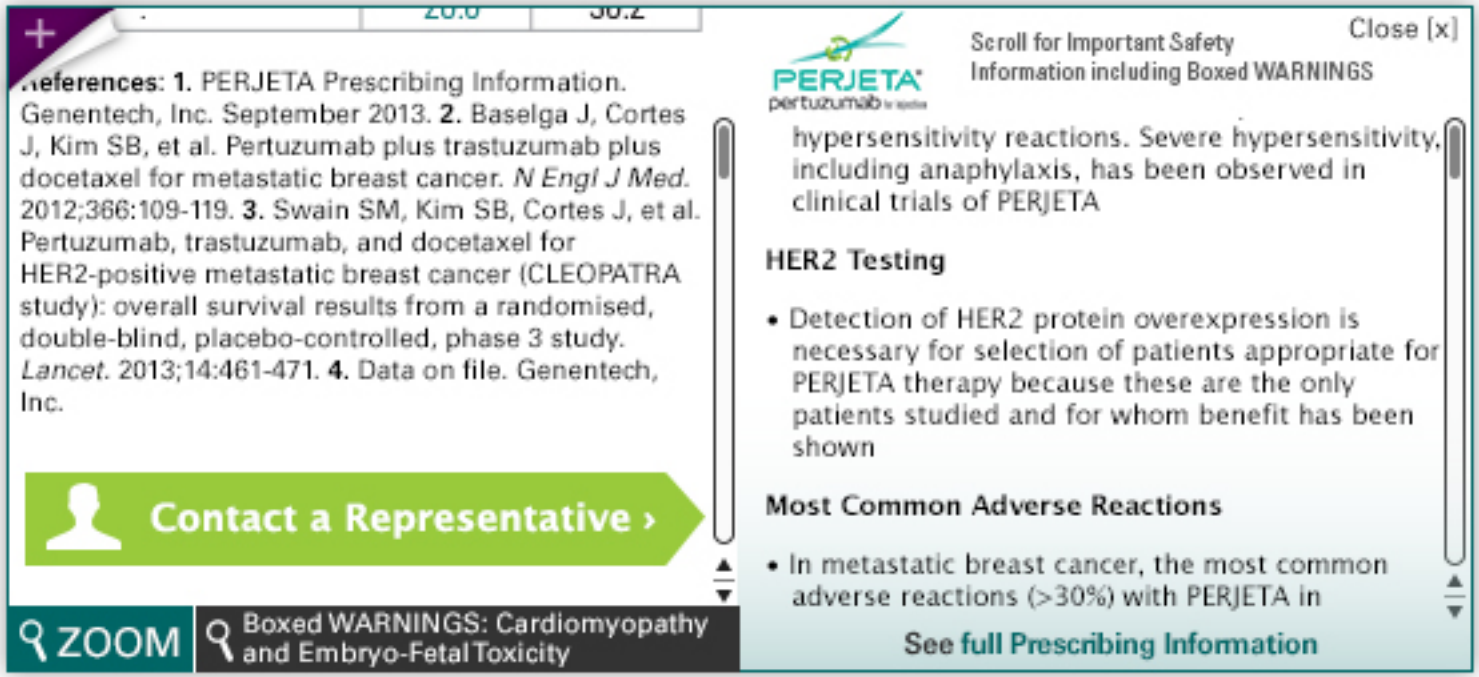
interrupt the infusion and administer appropriate medical therapies. Monitor patients carefully until complete resolution of signs and symptoms. Consider permanent discontinuation in patients with severe infusion reactions
Hypersensitivity Reactions/Anaphylaxis
• In Study 1, the overall frequency of 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
See full Prescribing Information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ZOOM
Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity
PERJETA pertuzumab
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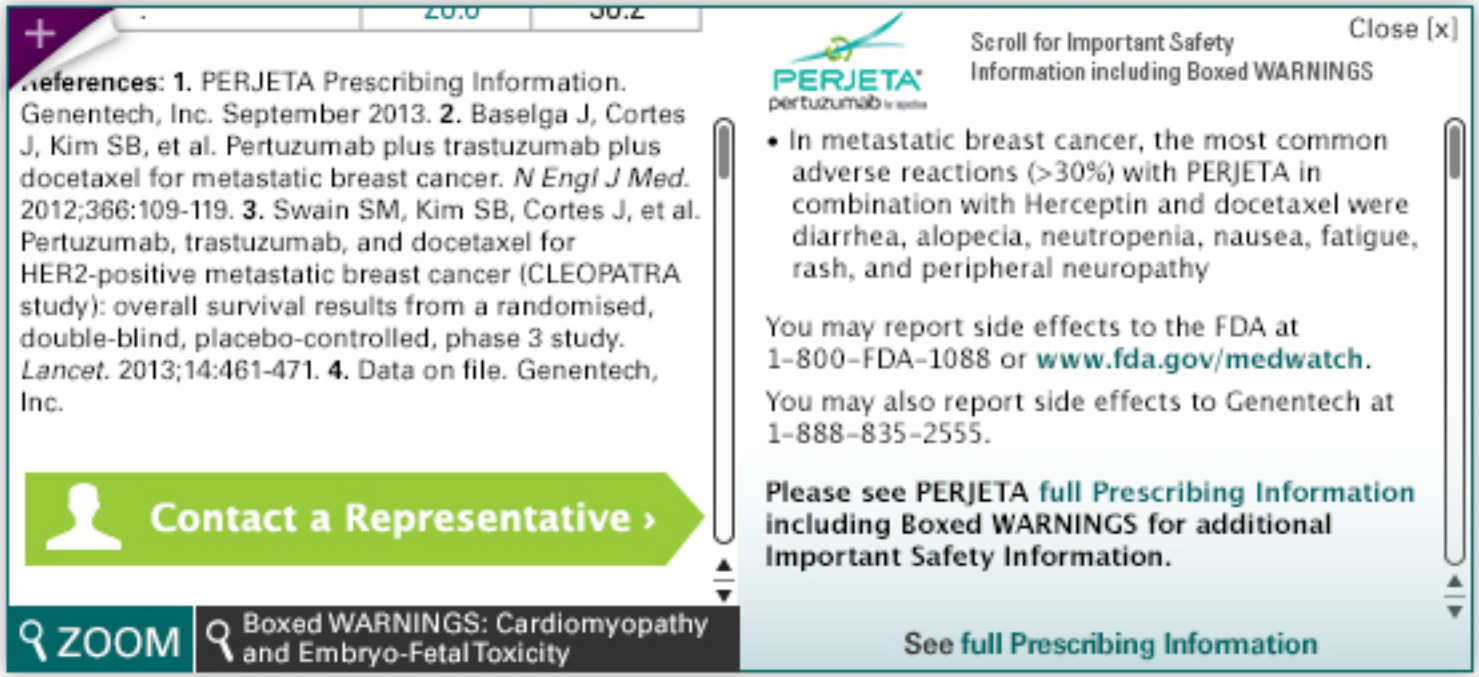
hypersensitivity reactions. Severe hypersensitivity, including anaphylaxis, has been observed in clinical trials of PERJETA
HER2 Testing
• Detection of HER2 protein overexpression is necessary for selection of patients appropriate for PERJETA therapy because these are the only patients studied and for 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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ZOOM
Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity
PERJETA pertuzumab
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• 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.
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.
See full Prescribing Information

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

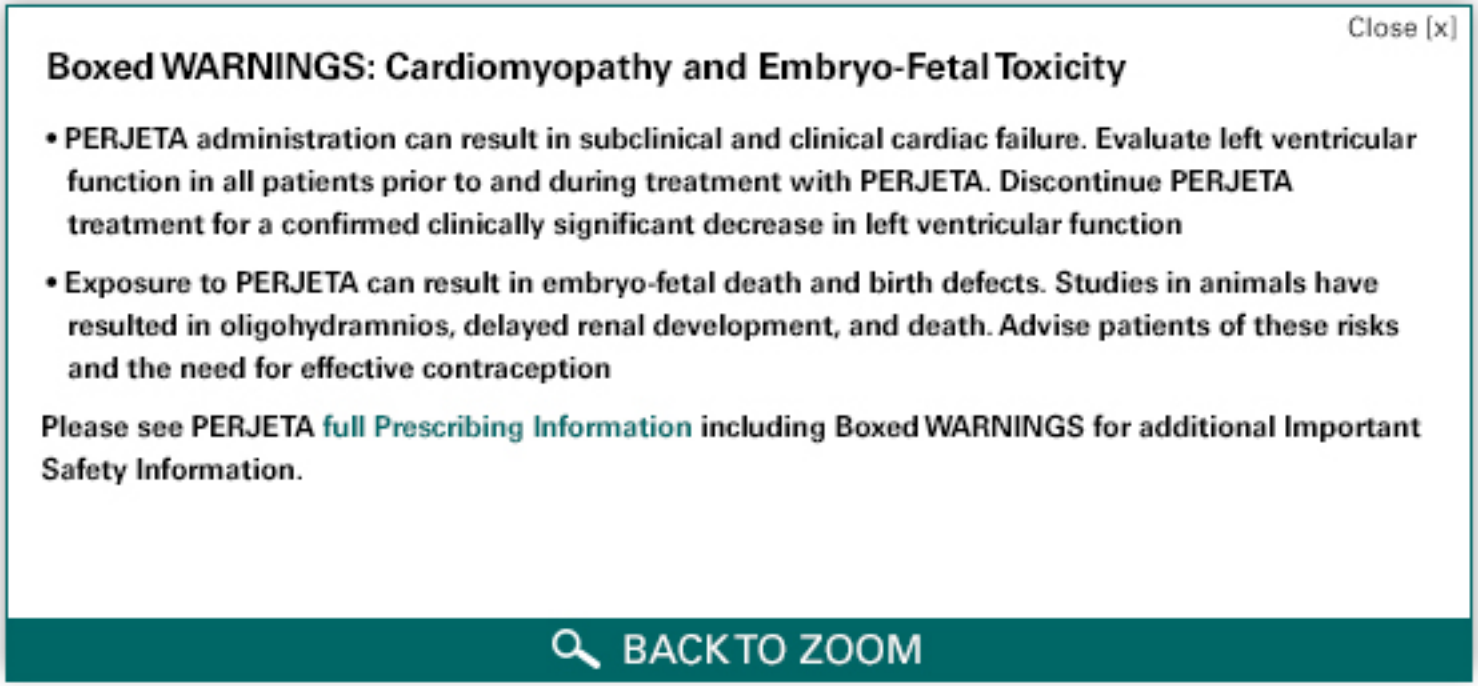
- There was an inability to show benefit with PERJETA in patients with nonvisceral metastases (n=178; HR=1.42 [95% CI: 0.71, 2.84])[3]

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

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]

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

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**
		***P*<0.0001**		***P*=0.0008**	
Hormone receptor status					
Positive (ER+ and/or PR+)	388	**0.72**	0.55, 0.95	**0.73**	0.50, 1.06
Negative (ER– and PR–)	408	**0.55**	0.42, 0.72	**0.57**	0.41, 0.79
Disease type					

ZOOM OUT

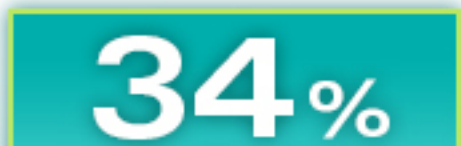
Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity

Disease type					Close [x]
Visceral disease	630	**0.55**	0.45, 0.68	**0.57**	0.44, 0.74
Nonvisceral disease	178	**0.96**	0.61, 1.52	**1.42**	0.71, 2.84

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

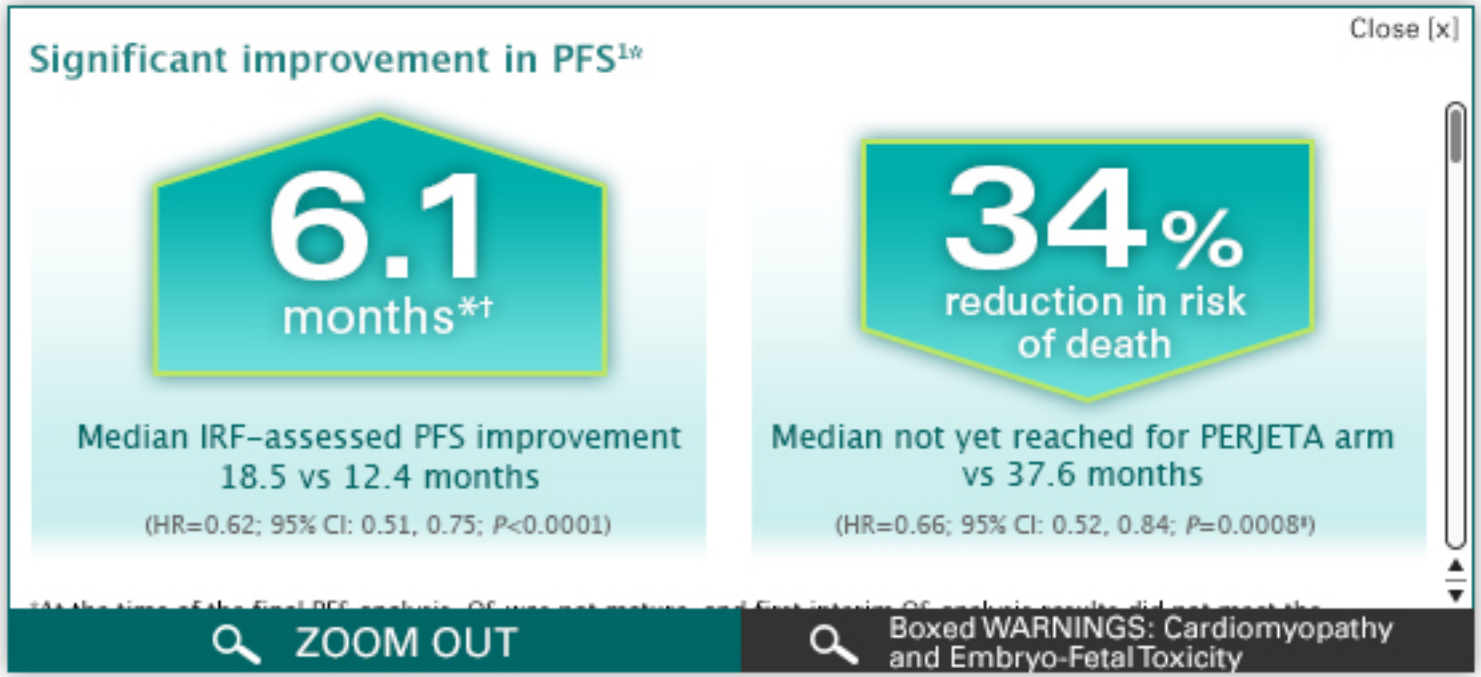
Results of a multicenter, randomized double-blind, placebo-controlled phase II trial in which patients were randomly allocated to receive placebo plus trastuzumab and docetaxel or PERJETA plus trastuzumab and docetaxel.

Significant improvement in PFS[1]*



ZOOM OUT

Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity


Close [x]
Significant improvement in PFS[1]*
6.1
months*†
Median IRF-assessed PFS improvement
18.5 vs 12.4 months
(HR=0.62; 95% CI: 0.51, 0.75; P<0.0001)
34%
reduction in risk
of death
Median not yet reached for PERJETA arm
vs 37.6 months
(HR=0.66; 95% CI: 0.52, 0.84; P=0.0008‡)
ZOOM OUT
Boxed WARNINGS: Cardiomyopathy
and Embryo-Fetal Toxicity

Close [x]

*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.[1]

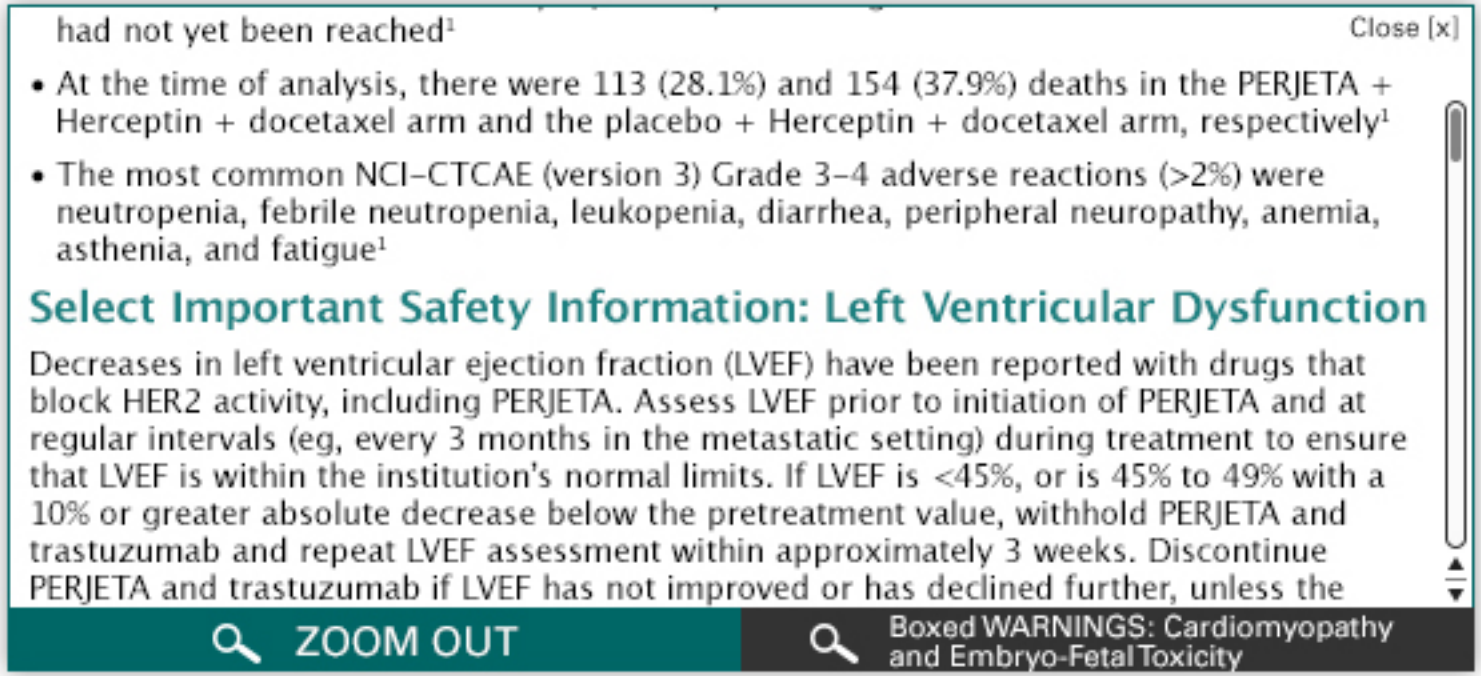
†Stratified by prior treatment status and geographic region.[1]

‡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[1]
- 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)[1,4]
- 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[1]

ZOOM OUT

Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity


had not yet been reached[1]
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[1]
• 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[1]
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.

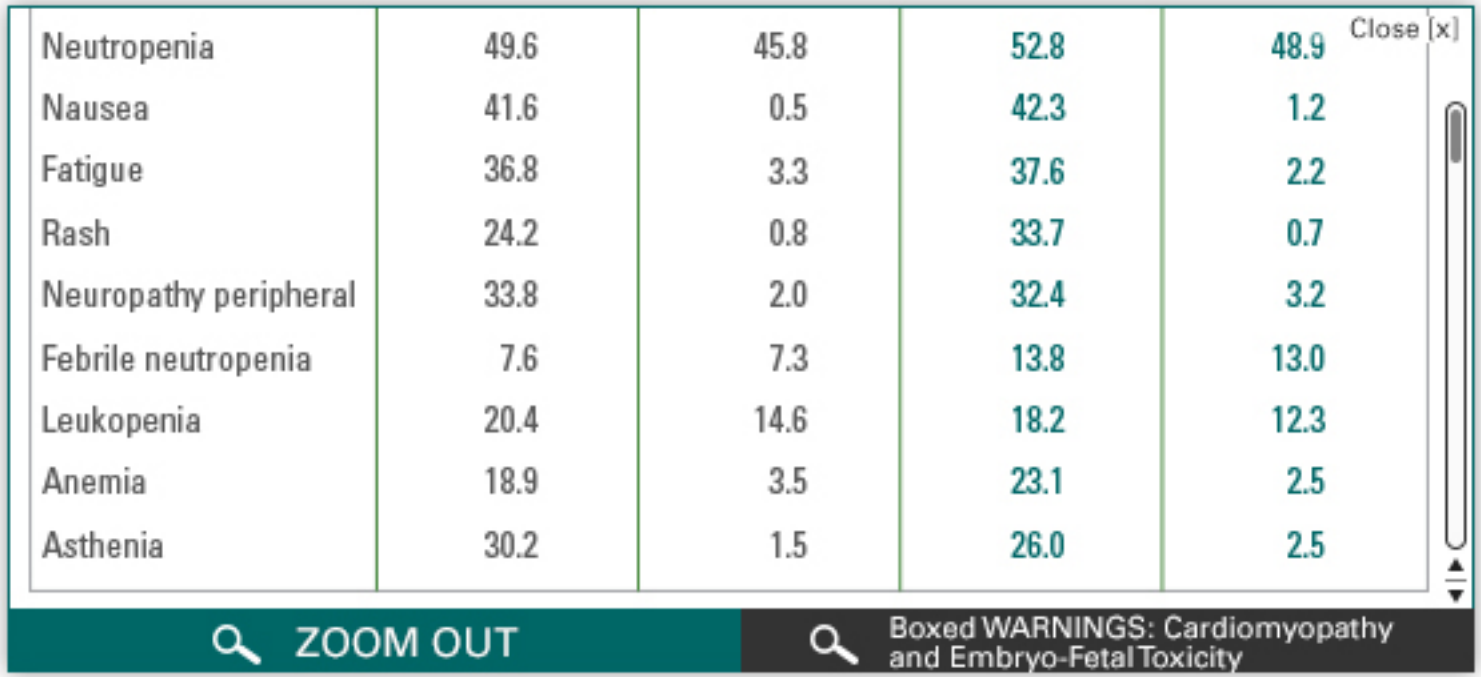
Close [x]

Most common adverse reactions: All Grades (>30%) or Grades 3-4 (>2%)[1]

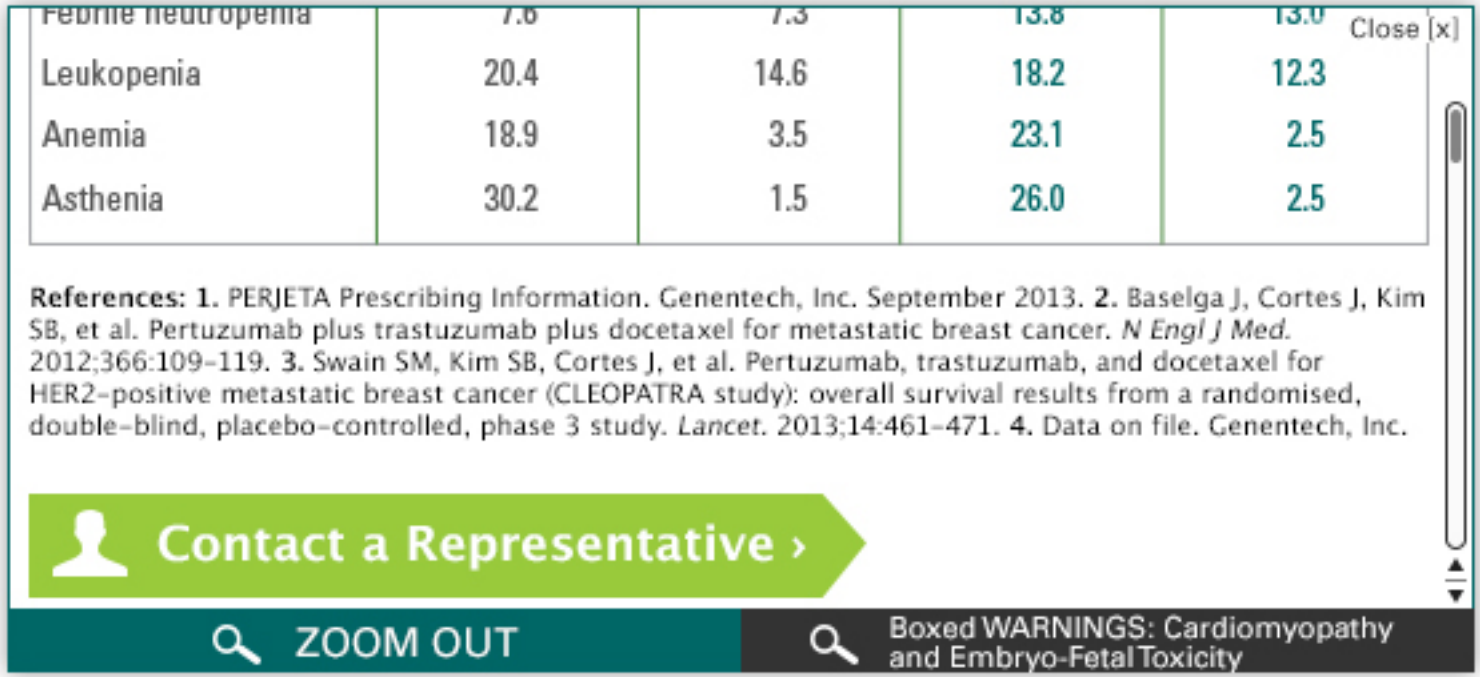
	Placebo+Herceptin+docetaxel (n=397)		PERJETA+Herceptin+docetaxel (n=407)	
	All Grades (%)	Grades 3-4 (%)	All Grades (%)	Grades 3-4 (%)
Diarrhea	46.3	5.0	66.8	7.9
Alopecia	60.5	0.3	60.9	0.0
Neutropenia	49.6	45.8	52.8	48.9
Nausea	41.6	0.5	42.3	1.2
Fatigue	36.8	3.3	37.6	2.2

ZOOM OUT

Boxed WARNINGS: Cardiomyopathy and Embryo-Fetal Toxicity



Neutropenia	49.6	45.8	52.8	48.9
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



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