FDA-approved biosimilars such as trastuzumab-qyyp (TRAZIMERA™) are recommended as treatment options in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)[1,2*†]

TRAZIMERA®
(trastuzumab-qyyp)

Product Monograph Supporting Biosimilarity

INJECTION
Trazimera®
trastuzumab-qyyp
Pfizer

*Biosimilar means that the biological product is approved based on data demonstrating that it is highly similar to an FDA-approved biological product, known as a reference product, and that there are no clinically meaningful differences between the biosimilar and the reference product.

†NCCN Guidelines® recommend the use of an FDA-approved biosimilar as an appropriate substitute for trastuzumab. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

SELECTED SAFETY INFORMATION

BOXED WARNINGS

Cardiomyopathy

- Administration of trastuzumab products can result in sub-clinical and clinical cardiac failure. The incidence and severity was highest in patients receiving trastuzumab with anthracycline-containing chemotherapy regimens
- Evaluate left ventricular function in all patients prior to and during treatment with TRAZIMERA. Discontinue TRAZIMERA treatment in patients receiving adjuvant therapy and withhold TRAZIMERA in patients with metastatic disease for clinically significant decrease in left ventricular function

Infusion Reactions; Pulmonary Toxicity

- Administration of trastuzumab products can result in serious and fatal infusion reactions and pulmonary toxicity. Symptoms usually occur during or within 24 hours of administration. Interrupt TRAZIMERA infusion for dyspnea or clinically significant hypotension. Monitor patients until symptoms completely resolve. Discontinue TRAZIMERA for anaphylaxis, angioedema, interstitial pneumonitis, or acute respiratory distress syndrome

Embryo-Fetal Toxicity

- Exposure to trastuzumab products during pregnancy can result in oligohydramnios and oligohydramnios sequence manifesting as pulmonary hypoplasia, skeletal abnormalities, and neonatal death. Advise patients of these risks and the need for effective contraception

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

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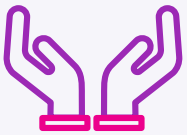
FDA-approved biosimilars such as trastuzumab-qyyp (TRAZIMERA™) are recommended as treatment options in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)[1,2*]

With the largest portfolio of biosimilars—including TRAZIMERA—Pfizer is committed to expanding options for patient care[3]

Favorable coverage[4]

Potential savings[4]



Support for you and your patients

Pfizer has 30 years of biologic experience, and more than 11 years in the global biosimilars market.[4]

*NCCN Guidelines® recommend the use of an FDA-approved biosimilar as an appropriate substitute for trastuzumab. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

SELECTED SAFETY INFORMATION

Cardiomyopathy

- **Administration of trastuzumab products can result in sub-clinical and clinical cardiac failure. The incidence and severity was highest in patients receiving trastuzumab with anthracycline-containing chemotherapy regimens. In a pivotal adjuvant breast cancer trial, one patient who developed CHF died of cardiomyopathy**
- Trastuzumab products can cause left ventricular cardiac dysfunction, arrhythmias, hypertension, disabling cardiac failure, cardiomyopathy, and cardiac death
- Trastuzumab products can also cause asymptomatic decline in LVEF
- **Discontinue TRAZIMERA treatment in patients receiving adjuvant breast cancer therapy and withhold TRAZIMERA in patients with metastatic disease for clinically significant decrease in left ventricular function**

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

1.1: *Coverage*

TRAZIMERA coverage

- 93% of Medicare lives covered, including managed Medicare[4]*

*Medical policy data are current as of February 2021. Please verify individual patient benefits to confirm coverage.

SELECTED SAFETY INFORMATION

Cardiac Monitoring

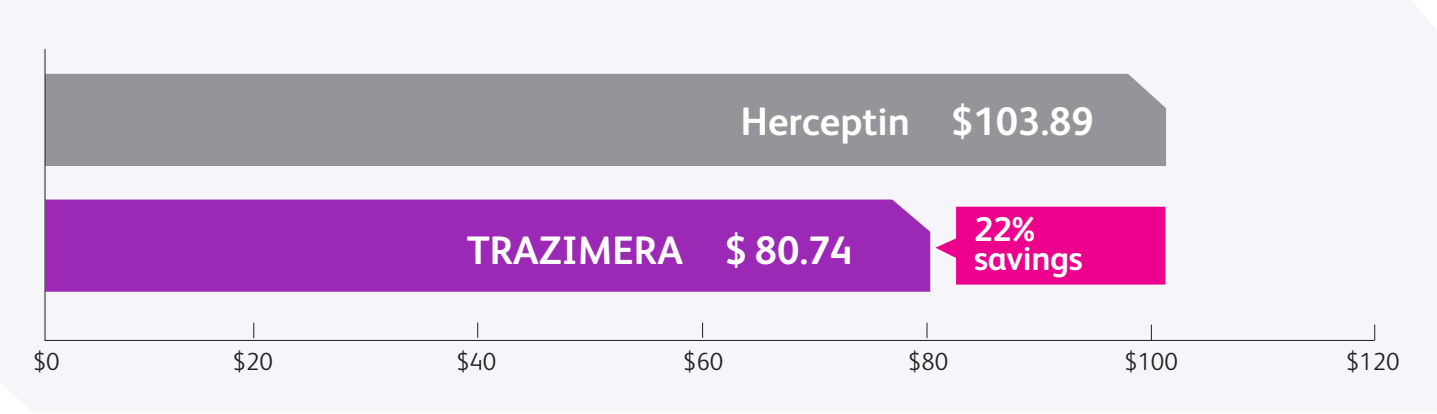
- **Evaluate cardiac function prior to and during treatment. For adjuvant breast cancer therapy, also evaluate cardiac function after completion of TRAZIMERA**
- Conduct thorough cardiac assessment, including history, physical examination, and determination of LVEF by echocardiogram or MUGA scan
- Monitor frequently for decreased left ventricular function during and after TRAZIMERA treatment
- Monitor more frequently if TRAZIMERA is withheld for significant left ventricular cardiac dysfunction

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

1.2: *Potential savings*

Potential cost savings with TRAZIMERA

Wholesale acquisition cost (WAC)* represents a 22% discount vs Herceptin® (trastuzumab) per 10 mg[4]



*WAC is a manufacturer's undiscounted or list price to wholesalers/direct purchasers and, therefore, is not inclusive of discounts to payers, providers, distributors, and other purchasing organizations. Data as of February 2020.

An estimated cumulative maximum potential savings over 10 years from implementation of all available biosimilars could reach as much as $150 billion[5†]

†Estimated reduction in direct spending on biologic drugs between 2017 and 2026 (RAND Corporation). Based on an assumption of a biosimilar market share of 50% and biosimilar prices at 50% of the reference product.

SELECTED SAFETY INFORMATION

Infusion Reactions

- Administration of trastuzumab products can result in serious and fatal infusion reactions
- Symptoms usually occur during or within 24 hours of administration of trastuzumab products
- Interrupt TRAZIMERA infusion for dyspnea or clinically significant hypotension
- Monitor patients until symptoms completely resolve

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

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1.3: *Co-Pay Savings Program for Injectables*

Pfizer Oncology Together™ Co-Pay Savings Program for Injectables

Eligible patients may pay as little as **$0** per Tx

Eligible,* commercially insured patients† may pay as little as $0 per TRAZIMERA treatment.‡ Limits, terms, and conditions apply.

- This program covers up to **$25,000 per calendar year**§
- There are **no income requirements** for patients to qualify
- For information on enrollment, claims submissions, and reimbursement, visit **PfizerOncologyTogether.com** to download the Co-Pay Savings Program Brochure

***Terms and Conditions:** By using this program, you acknowledge that you currently meet the eligibility criteria and will comply with the terms and conditions below:

- The Pfizer Oncology Together Co-Pay Savings Program for Injectables for TRAZIMERA® is not valid for patients who are enrolled in a state or federally funded insurance program, including but not limited to Medicare, Medicaid, TRICARE, Veterans Affairs health care, a state prescription drug assistance program, or the Government Health Insurance Plan available in Puerto Rico (formerly known as "La Reforma de Salud").
- Program offer is not valid for cash-paying patients.
- With this program, eligible patients may pay as little as $0 co-pay per TRAZIMERA treatment, subject to a maximum benefit of $25,000 per calendar year for out-of-pocket expenses for TRAZIMERA including co-pays or coinsurances.
- The amount of any benefit is the difference between your co-pay and $0.
- After the maximum of $25,000 you will be responsible for the remaining monthly out-of-pocket costs.
- Patient must have private insurance with coverage of TRAZIMERA.
- This offer is not valid when the entire cost of your prescription drug is eligible to be reimbursed by your private insurance plans or other private health or pharmacy benefit programs.
- You must deduct the value of this assistance from any reimbursement request submitted to your private insurance plan, either directly by you or on your behalf.
- You are responsible for reporting use of the program to any private insurer, health plan, or other third party who pays for or reimburses any part of the prescription filled using the program, as may be required.
- You should not use the program if your insurer or health plan prohibits use of manufacturer co-pay assistance programs.
- This program is not valid where prohibited by law.
- This program cannot be combined with any other savings, free trial or similar offer for the specified prescription.
- **Co-pay card will be accepted only at participating pharmacies.**
- **This program is not health insurance.**
- This program is good only in the U.S. and Puerto Rico.
- This program is limited to 1 per person during this offering period and is not transferable.
- No other purchase is necessary.
- Data related to your redemption of the program assistance may be collected, analyzed, and shared with Pfizer, for market research and other purposes related to assessing Pfizer's programs. Data shared with Pfizer will be aggregated and de-identified; it will be combined with data related to other assistance redemptions and will not identify you.
- Pfizer reserves the right to rescind, revoke or amend this program without notice.
- This program may not be available to patients in all states.
- For more information about Pfizer, visit www.pfizer.com.
- For more information about the Pfizer Oncology Together Co-Pay Savings Program for Injectables, visit pfizeroncologytogether.com, call 1-877-744-5675, or write to
  Pfizer Oncology Together Co-Pay Savings Program for Injectables
  P.O. Box 220366
  Charlotte, NC 2822
- Program terms and offer will expire at the end of each calendar year. Before the calendar year ends, you will receive information and eligibility requirements for continued participation.

†For patients to be eligible for the Injectables Co-Pay Program for TRAZIMERA, they must have commercial insurance that covers TRAZIMERA and they cannot be enrolled in a state or federally funded insurance program. Whether a co-pay expense is eligible for the Injectables Co-Pay Program for TRAZIMERA benefit will be determined at the time the benefit is paid. Co-pay expenses must be in connection with a separately paid claim for TRAZIMERA administered in the outpatient setting.

‡The Injectables Co-Pay Program for TRAZIMERA will pay the co-pay for TRAZIMERA up to the annual assistance limit of $25,000 per calendar year per patient.

§The Injectables Co-Pay Program for TRAZIMERA provides assistance for eligible, commercially insured patients prescribed TRAZIMERA for co-pays or coinsurance incurred for TRAZIMERA up to $25,000 per calendar year. It does not cover or provide support for supplies, services, procedures, or any other physician-related services associated with TRAZIMERA treatment.

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

1.4: *Access and reimbursement*

Pfizer Oncology together™
Patient Support. Financial Assistance. Together.

Navigating access and reimbursement. Together.

If patients need access or reimbursement support, Pfizer Oncology Together is here to help.

Benefits Verification

We can help determine a patient's coverage and out-of-pocket costs.

Prior Authorization (PA) Assistance

We can coordinate with a patient's insurer to determine the PA requirements. After a PA request is submitted, we can follow up with the payer until a final outcome is determined.

Appeals Assistance

We can review the reasons for a denied claim and provide information on payer requirements. After an appeal is submitted, we can follow up with the payer until a final outcome is determined.

Product Distribution

TRAZIMERA is available through most major wholesalers.

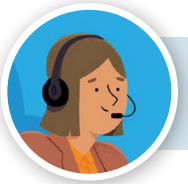
Billing and Coding Assistance for IV Products

For your patient claim submissions, we provide easy access to sample forms and template letters, along with billing and coding information for physician's office and hospital outpatient settings of care.

Dedicated Local Support

A Pfizer Oncology Account Specialist can provide detailed information on Pfizer Oncology medications and access resources. In addition, they can help you and your office staff contact a Pfizer Field Reimbursement Manager (FRM) in your area.

FRMs are trained to help address specific access issues—in person or over the phone. They can help educate your staff on our access and reimbursement resources and help address challenging or urgent Pfizer Oncology patient cases you have sent to Pfizer Oncology Together.



FOR LIVE, PERSONALIZED SUPPORT
Call **1-877-744-5675** (Monday–Friday 8 AM–8 PM ET)

VISIT PfizerOncologyTogether.com

SELECTED SAFETY INFORMATION

Infusion Reactions (continued)

- **Discontinue TRAZIMERA for infusion reactions manifesting as anaphylaxis, angioedema, interstitial pneumonitis, or acute respiratory distress syndrome. Strongly consider permanent discontinuation in all patients with severe infusion reactions**
- Infusion reactions consist of a symptom complex characterized by fever and chills, and on occasion include nausea, vomiting, pain (in some cases at tumor sites), headache, dizziness, dyspnea, hypotension, rash, and asthenia

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

1.5: *Tools and resources*

Pfizer is committed to supporting you and your patients

For commercially insured patients

Co-Pay Savings Program for Injectables

Finding financial support options. Together.

Limits, terms, and conditions apply.
Please see page 6 for terms and conditions.

Eligible patients may pay as little as **$0** per Tx

Pfizer Oncology together™

FOR LIVE, PERSONALIZED SUPPORT
Call **1-877-744-5675** (Monday–Friday 8 AM–8 PM ET) or
Visit **PfizerOncologyTogether.com**

PfizerBiosimilarsResource.com

Downloadable tools are available to help support you when implementing Pfizer biosimilars into your practice.

ThisIsLivingWithCancer.com

A free app designed to help manage life with cancer

Help your patients and their caregivers stay connected and get organized by telling them about **LivingWith™**.

The LivingWith app is available to anyone living with cancer and their loved ones, and is not specific to TRAZIMERA.

SELECTED SAFETY INFORMATION

Embryo-Fetal Toxicity

- **Exposure to trastuzumab products during pregnancy can result in oligohydramnios and oligohydramnios sequence manifesting as pulmonary hypoplasia, skeletal abnormalities, and neonatal death. Advise patients of these risks and the need for effective contraception**
- Verify the pregnancy status of females of reproductive potential prior to the initiation of TRAZIMERA

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

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FDA-approved biosimilars such as trastuzumab-qyyp (TRAZIMERA™) are recommended as treatment options in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)[1,2*]

TRAZIMERA is a biosimilar† to Herceptin® (trastuzumab)[6]

Approved across all indications of Herceptin[6]

Same dosing and administration schedule as Herceptin[6]

Useful ordering and coding information

*NCCN Guidelines® recommend the use of an FDA-approved biosimilar as an appropriate substitute for trastuzumab. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

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SELECTED SAFETY INFORMATION

Embryo-Fetal Toxicity (continued)

- Advise pregnant women and females of reproductive potential that exposure to TRAZIMERA during pregnancy or within 7 months prior to conception can result in fetal harm
- Advise females of reproductive potential to use effective contraception during treatment and for at least 7 months following the last dose of TRAZIMERA
- Consider the developmental and health benefits of breastfeeding along with the mother's clinical need for TRAZIMERA treatment and any potential adverse effects on the breastfed child from TRAZIMERA or from the underlying maternal condition

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

2.1: *Indications*

TRAZIMERA is FDA approved across all indications of Herceptin® (trastuzumab)[6]

Adjuvant Breast Cancer

For adjuvant treatment of HER2-overexpressing node-positive or node-negative (ER/PR-negative or with one high-risk feature*) breast cancer:

- As part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel
- As part of a treatment regimen with docetaxel and carboplatin
- As a single agent following multimodality anthracycline-based therapy

Select patients for therapy based on an FDA-approved companion diagnostic for a trastuzumab product.

Metastatic Breast Cancer

- In combination with paclitaxel for first-line treatment of HER2-overexpressing metastatic breast cancer
- As a single agent for treatment of HER2-overexpressing breast cancer in patients who have received one or more chemotherapy regimens for metastatic disease

Select patients for therapy based on an FDA-approved companion diagnostic for a trastuzumab product.

Metastatic Gastric Cancer

- In combination with cisplatin and capecitabine or 5-fluorouracil, for the treatment of patients with HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma who have not received prior treatment for metastatic disease

Select patients for therapy based on an FDA-approved companion diagnostic for a trastuzumab product.

ER=estrogen receptor; HER=human epidermal growth factor receptor; PR=progesterone receptor.

*High risk is defined as ER/PR positive with one of the following features: pathological tumor size >2 cm, tumor grade 2 to 3, or age <35 years.

SELECTED SAFETY INFORMATION

Pulmonary Toxicity

- **Administration of trastuzumab products can result in serious and fatal pulmonary toxicity**, which includes dyspnea, interstitial pneumonitis, pulmonary infiltrates, pleural effusions, noncardiogenic pulmonary edema, pulmonary insufficiency and hypoxia, acute respiratory distress syndrome, and pulmonary fibrosis. Such events can occur as sequelae of infusion reactions
- Patients with symptomatic intrinsic lung disease or with extensive tumor involvement of the lungs, resulting in dyspnea at rest, appear to have more severe toxicity
- Discontinue TRAZIMERA in patients experiencing pulmonary toxicity

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

2.2: *Dosing and administration*

TRAZIMERA has the same dosing and administration schedule as Herceptin® (trastuzumab)[6]

- **Do not administer as an intravenous push or bolus. Do not mix TRAZIMERA with other drugs**
- **Do not substitute TRAZIMERA (trastuzumab-qyyp) for or with ado-trastuzumab emtansine**

INDICATION	DOSING
Adjuvant Treatment, Breast Cancer Administer according to one of the following doses and schedules for a total of 52 weeks of TRAZIMERA therapy:	
• During and following paclitaxel, docetaxel, or docetaxel and carboplatin	• Initial dose of 4 mg/kg as an intravenous infusion over 90 minutes, then at 2 mg/kg as an intravenous infusion over 30 minutes weekly during chemotherapy for the first 12 weeks (paclitaxel or docetaxel) or 18 weeks (docetaxel and carboplatin) • One week following the last weekly dose of TRAZIMERA, administer TRAZIMERA at 6 mg/kg as an intravenous infusion over 30 to 90 minutes every 3 weeks
• As a single agent within 3 weeks following completion of multimodality, anthracycline-based chemotherapy regimens	• Initial dose at 8 mg/kg as an intravenous infusion over 90 minutes • Subsequent doses at 6 mg/kg as an intravenous infusion over 30 to 90 minutes every 3 weeks • Extending adjuvant treatment beyond one year is not recommended
Metastatic Breast Cancer • Alone or in combination with paclitaxel	• Initial dose of 4 mg/kg as a 90-minute intravenous infusion followed by subsequent once-weekly doses of 2 mg/kg as 30-minute intravenous infusions, until disease progression
Metastatic Gastric Cancer • In combination with cisplatin and capecitabine or 5-fluorouracil	• Initial dose of 8 mg/kg as a 90-minute intravenous infusion followed by subsequent doses of 6 mg/kg as an intravenous infusion over 30 to 90 minutes every 3 weeks, until disease progression

Please see the full Prescribing Information for Important Dosing Considerations.

SELECTED SAFETY INFORMATION

Exacerbation of Chemotherapy-Induced Neutropenia

- In randomized, controlled clinical trials, the numbers of per-patient incidences of NCI-CTC Grade 3-4 neutropenia and of febrile neutropenia were higher in patients receiving trastuzumab in combination with myelosuppressive chemotherapy as compared to those who received chemotherapy alone. The incidence of septic death was similar among patients who received trastuzumab and those who did not

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2.3: *Ordering information*

TRAZIMERA is available in single- and multiple-dose options[6]

Ordering TRAZIMERA–What you need to know

Unit of Sale	150 mg SDV	420 mg MDV*
Unit of Sale NDC	0069-0308-01	0069-0305-01
Unit of Sale Quantity	1 vial per carton	1 vial per carton
Unit of Sale List Price	$1,211.10	$3,391.08
HCPCS Code	Q5116[7]	
OPPS Status	G: Pass-through payment[7]	

MDV=multiple-dose vial; OPPS=Outpatient Prospective Payment System; SDV=single-dose vial.

- **Single- and multiple-dose options** for your individual practice needs
- **Diluent included** for multiple-dose vial
- **Efficiency** in preparation and reduced waste†
- **Enhanced electronic record keeping** with 2-D barcode vial label
- **Flexible storage** (can be stored in or out of the refrigerator)‡

*For multiple-dose vial unused product can be stored for future use. Store reconstituted TRAZIMERA MDV in the refrigerator at 2° to 8° C (36° to 46° F); discard unused TRAZIMERA after 28 days. If TRAZIMERA is reconstituted with Sterile Water for Injection without preservative, use immediately and discard any unused portion. Do not freeze.

†Multiple-dose feature of vials may support efficiency and reduce waste, as it allows fewer vials to be used and disposed of.

‡Store TRAZIMERA vials in the refrigerator at 2° to 8° C (36° to 46° F) in the original carton to protect from light. If needed, unopened TRAZIMERA vials may be removed from the refrigerator and stored at room temperature up to 30° C (86° F) for a single period of up to 3 months in the original carton to protect from light. Once removed from the refrigerator, do not return to the refrigerator and discard after 3 months or by the expiration date stamped on the vial, whichever occurs first. Write the revised expiration date in the space provided on the carton labeling.

SELECTED SAFETY INFORMATION

Most Common Adverse Reactions

- The most common adverse reactions associated with trastuzumab products in breast cancer were fever, nausea, vomiting, infusion reactions, diarrhea, infections, increased cough, headache, fatigue, dyspnea, rash, neutropenia, anemia, and myalgia

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

FDA-approved biosimilars such as trastuzumab-qyyp (TRAZIMERA™) are recommended as treatment options in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)[1,2*]

A totality of evidence supports biosimilarity to Herceptin® (trastuzumab)[6,8]

Biosimilarity established based on a totality of evidence[6,8]

Extrapolation allows potential approval for nonstudied indications[8]

No clinically meaningful differences in terms of efficacy or safety[4,6,9]

*NCCN Guidelines® recommend the use of an FDA-approved biosimilar as an appropriate substitute for trastuzumab. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

SELECTED SAFETY INFORMATION

Most Common Adverse Reactions (continued)

- The most common adverse reactions associated with trastuzumab products in metastatic gastric cancer were neutropenia, diarrhea, fatigue, anemia, stomatitis, weight loss, upper respiratory tract infections, fever, thrombocytopenia, mucosal inflammation, nasopharyngitis, and dysgeusia

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

3.1: *Data summary*

TRAZIMERA was approved by the FDA based on the totality of evidence demonstrating it is highly similar to Herceptin® (trastuzumab)[6,8]

CLINICAL STUDY	**TRAZIMERA showed no clinically meaningful differences to Herceptin-EU**[4,9*] • In a study of patients with HER2+ metastatic breast cancer, TRAZIMERA and Herceptin-EU had comparable ORRs (62.5% vs 66.5%, respectively) • Similarity between TRAZIMERA and Herceptin-EU is indicated by the 95% CI for the risk ratio (RR=0.940, TRAZIMERA over Herceptin-EU), which fell within the prespecified equivalence margin of 80%-125%
CLINICAL PHARMACOLOGY (PK/PD)	**TRAZIMERA demonstrated PK similarity to Herceptin in healthy male volunteers**[4] • In this study, all PK parameters were within the bioequivalence window of 80%-125%
NONCLINICAL	**TRAZIMERA is similar to Herceptin based on TK and toxicity**[10] • Nonclinical toxicology/TK studies compared TRAZIMERA vs Herceptin and supported their biosimilarity
ANALYTICAL	**TRAZIMERA is highly similar to Herceptin in terms of structure and function**[11] • Structural similarity: Identical primary amino acid sequence – Peptide mapping data supported identical primary amino acid sequence for TRAZIMERA and Herceptin • Functional similarity: Highly similar HER2 binding activity for TRAZIMERA and Herceptin

CI=confidence interval; HER=human epidermal growth factor receptor; ORR=objective response rate; PD=pharmacodynamics; PK=pharmacokinetics; TK=toxicokinetics.

*Product sourced from the EU is often used as a comparator in trials to demonstrate biosimilarity.

SELECTED SAFETY INFORMATION

BOXED WARNINGS

Cardiomyopathy

- **Administration of trastuzumab products can result in sub-clinical and clinical cardiac failure. The incidence and severity was highest in patients receiving trastuzumab with anthracycline-containing chemotherapy regimens**
- **Evaluate left ventricular function in all patients prior to and during treatment with TRAZIMERA. Discontinue TRAZIMERA treatment in patients receiving adjuvant therapy and withhold TRAZIMERA in patients with metastatic disease for clinically significant decrease in left ventricular function**

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

3.2: *FDA evaluation*

Biosimilars: Highly similar versions of existing biologic medicines[8]

- According to the FDA, a biosimilar is a medicine highly similar to another biological medicine or reference product already marketed in the United States
  - Biosimilars have no clinically meaningful differences in terms of safety, purity, and potency from their reference products

The FDA evaluates biosimilars based on a totality of evidence approach[8,12]

Development pathways

- The goal of biosimilar development is to demonstrate that there are no clinically meaningful differences based on the totality of evidence[8,12]
- Analytical studies are the foundation of biosimilar development and provide the greatest sensitivity for detecting differences between a biosimilar and its reference product[8,12]

PD=pharmacodynamics; PK=pharmacokinetics.

SELECTED SAFETY INFORMATION

BOXED WARNINGS (CONTINUED)

Infusion Reactions; Pulmonary Toxicity

- **Administration of trastuzumab products can result in serious and fatal infusion reactions and pulmonary toxicity. Symptoms usually occur during or within 24 hours of administration. Interrupt TRAZIMERA infusion for dyspnea or clinically significant hypotension. Monitor patients until symptoms completely resolve. Discontinue TRAZIMERA for anaphylaxis, angioedema, interstitial pneumonitis, or acute respiratory distress syndrome**

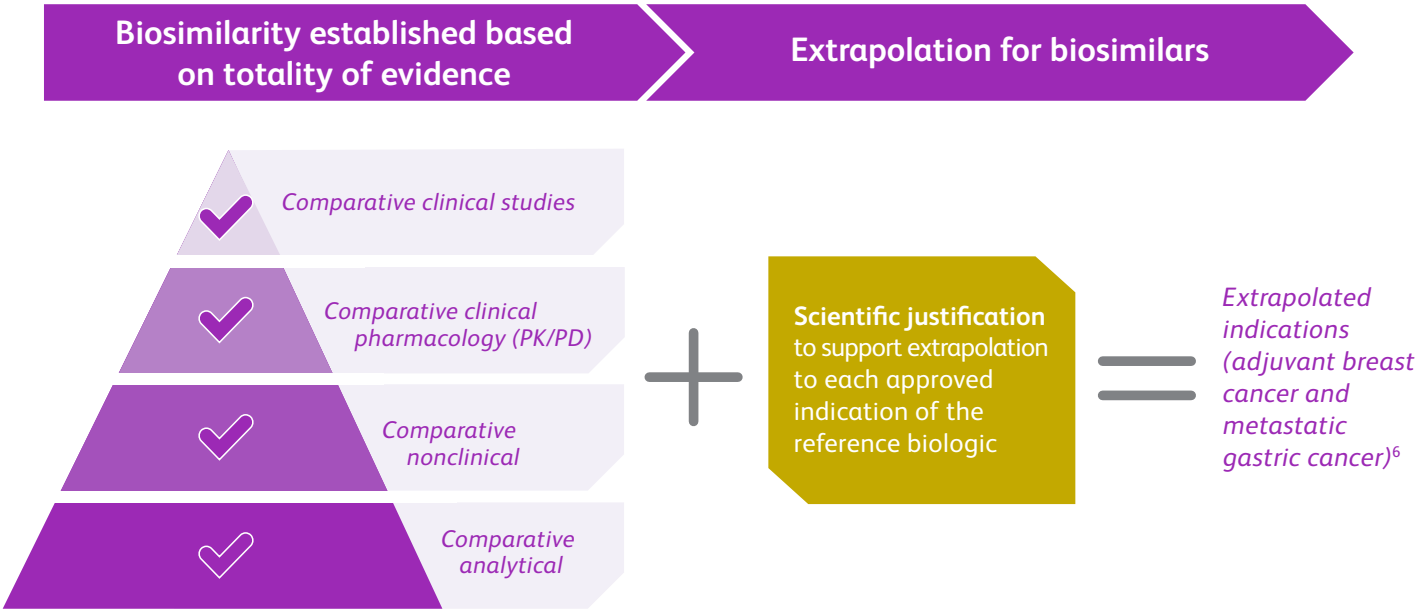
Embryo-Fetal Toxicity

- **Exposure to trastuzumab products during pregnancy can result in oligohydramnios and oligohydramnios sequence manifesting as pulmonary hypoplasia, skeletal abnormalities, and neonatal death. Advise patients of these risks and the need for effective contraception**

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

3.3: *Extrapolation*

Extrapolation: After biosimilarity is established, allows potential approval for nonstudied indications[8]



PD=pharmacodynamics; PK=pharmacokinetics.

Extrapolation builds on the thorough analysis of similarity between the biosimilar and reference biologic supported by the scientific evidence generated in robust analytical, nonclinical, and clinical comparability studies. Together with the well-known understanding of the reference biologic, this evidence is carefully analyzed to support scientific justification of extrapolated indications[8]

SELECTED SAFETY INFORMATION

Cardiomyopathy

- **Administration of trastuzumab products can result in sub-clinical and clinical cardiac failure. The incidence and severity was highest in patients receiving trastuzumab with anthracycline-containing chemotherapy regimens. In a pivotal adjuvant breast cancer trial, one patient who developed CHF died of cardiomyopathy**
- Trastuzumab products can cause left ventricular cardiac dysfunction, arrhythmias, hypertension, disabling cardiac failure, cardiomyopathy, and cardiac death

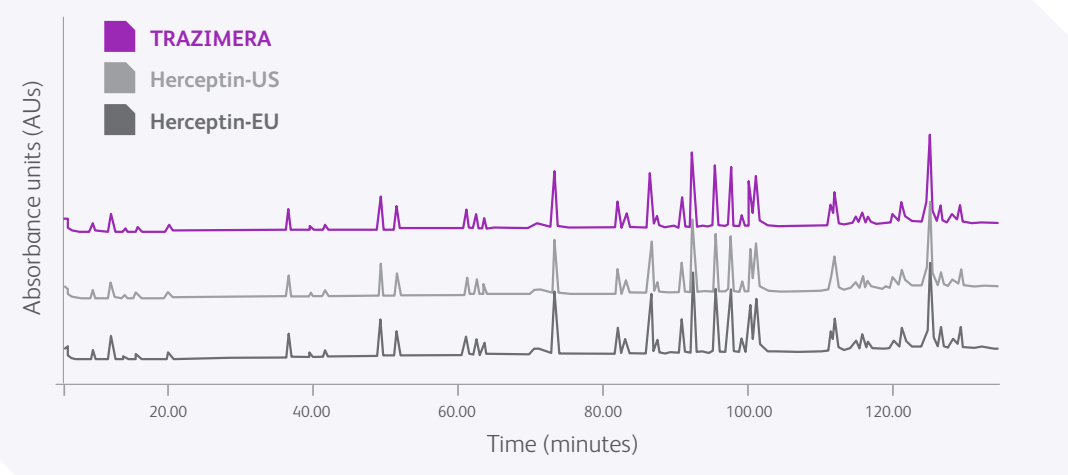
Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

3.4: *Similar structure and function*

TRAZIMERA is highly similar in structure and function to Herceptin® (trastuzumab)[11]*

Structural similarity: Identical primary amino acid sequence

Peptide mapping data supported identical primary amino acid sequence for TRAZIMERA and Herceptin



Functional similarity: Comparable statistical quality range to that of Herceptin for HER2 binding†

HER=human epidermal growth factor receptor; SD=standard deviation; SPR=surface plasmon resonance.

*TRAZIMERA was evaluated and compared to Herceptin using a battery of biochemical, biophysical, and functional assays, including assays that addressed each major potential mechanism of action. The amino acid sequences of TRAZIMERA and Herceptin are identical, and a comparison of the secondary and tertiary structures and the impurity profiles of TRAZIMERA and Herceptin support the conclusion that the 2 products are highly similar.[10]

†The solid circles represent the lots used in the clinical studies. The quality range of 82%-124% was established based on mean ±3 SD from Herceptin-US lots.[11]

SELECTED SAFETY INFORMATION

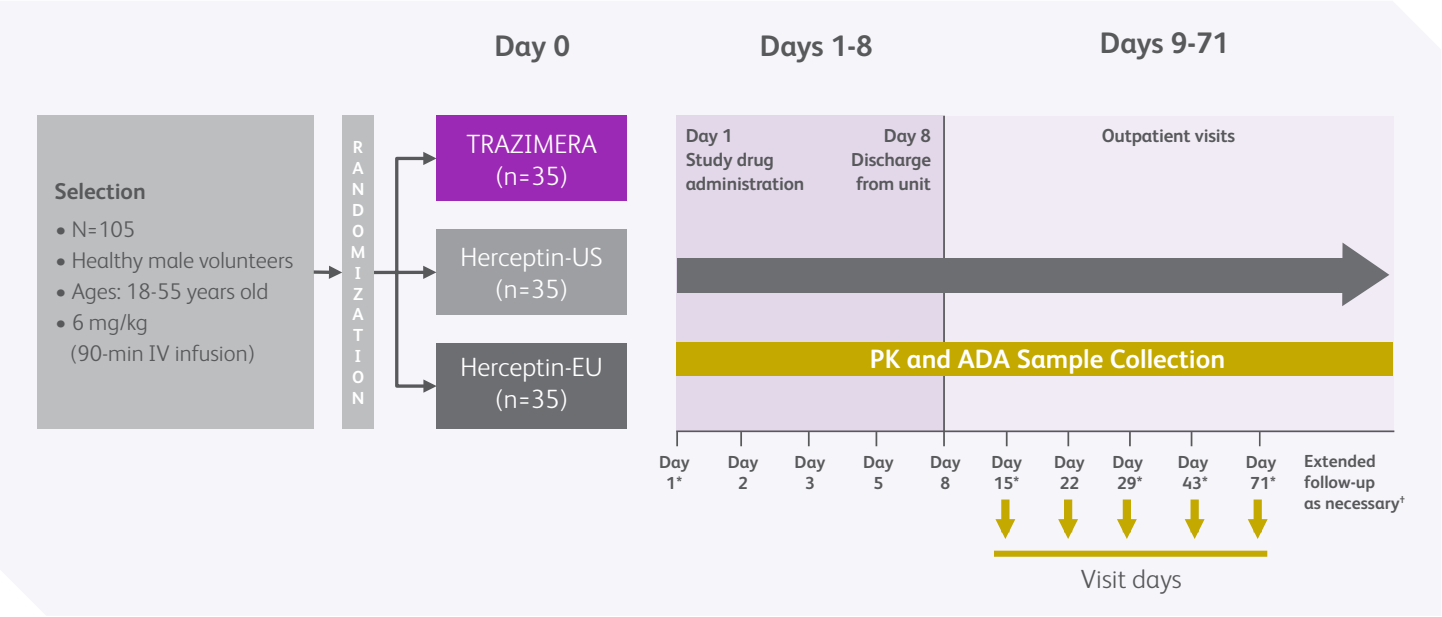
Cardiomyopathy (continued)

- Trastuzumab products can also cause asymptomatic decline in LVEF
- **Discontinue TRAZIMERA treatment in patients receiving adjuvant breast cancer therapy and withhold TRAZIMERA in patients with metastatic disease for clinically significant decrease in left ventricular function**

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

3.5: *Pharmacokinetics study*

Double-blind, single-dose comparative clinical pharmacology study[4]



Study objectives

- Evaluate PK similarity, safety, tolerability, and immunogenicity

Primary endpoints

- C_{max}
- $AUC_{0\text{-}t}$

ADA=antidrug antibody; $AUC_{0\text{-}t}$=area under the concentration-time profile from time zero to the time of the last quantifiable concentration; C_{max}=maximum concentration; IV=intravenous; PK=pharmacokinetics.

*Day on which samples were collected for ADA; samples for PK were collected at all times shown.

†ADA and PK samples were collected during follow-up.

SELECTED SAFETY INFORMATION

Cardiac Monitoring

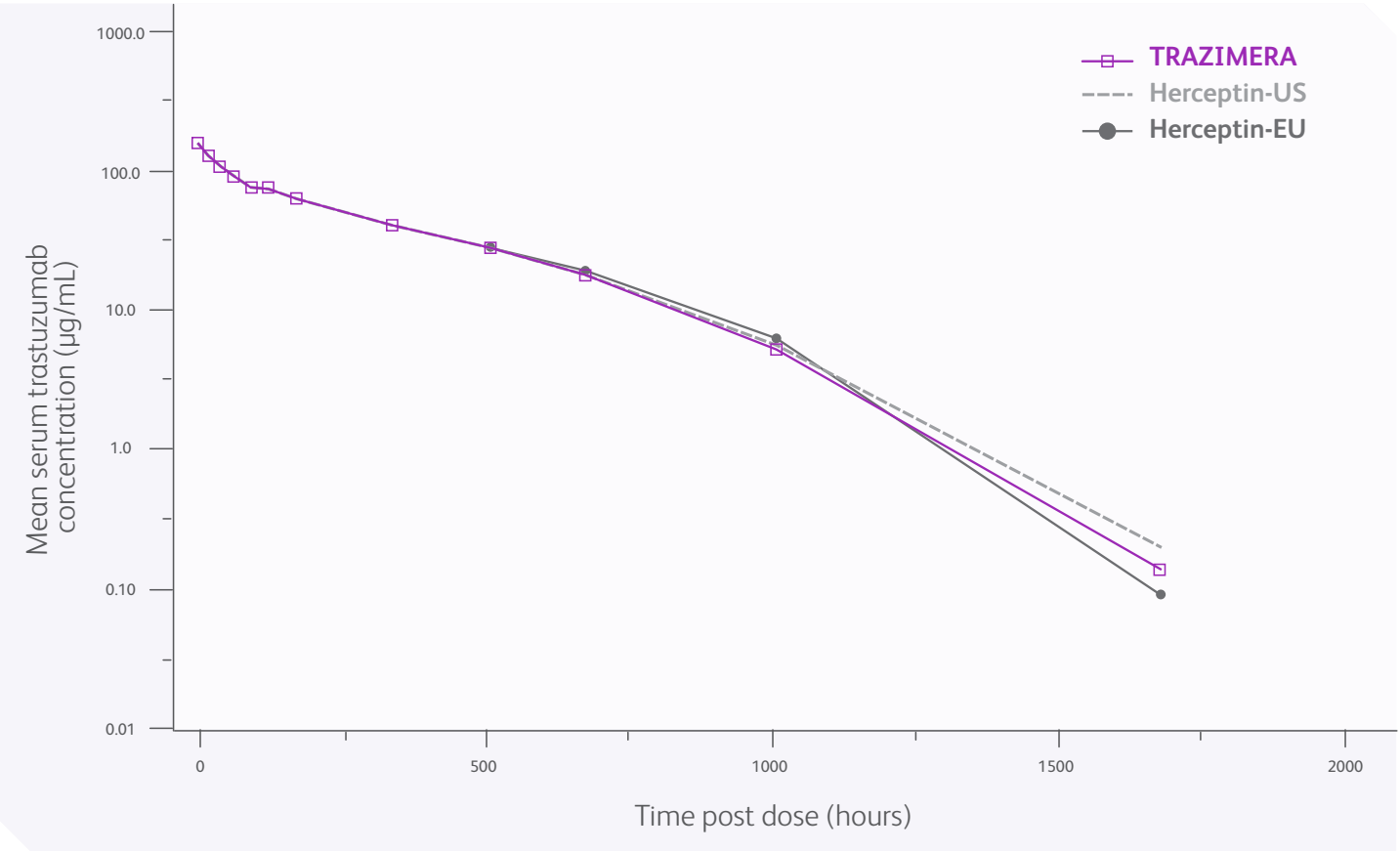
- **Evaluate cardiac function prior to and during treatment. For adjuvant breast cancer therapy, also evaluate cardiac function after completion of TRAZIMERA**
- Conduct thorough cardiac assessment, including history, physical examination, and determination of LVEF by echocardiogram or MUGA scan

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

3.5: *Pharmacokinetics study (continued)*

Similar PK profile to Herceptin® (trastuzumab) in healthy subjects in a 3-arm study[4]

Mean serum concentration-time profiles following a single dose of 6 mg/kg



- The primary PK endpoints of C_{max} and $AUC_{0\text{-}t}$ were within the bioequivalence window of 80% to 125% for the 90% CIs of the geometric mean ratios expressed as a percentage for all comparisons
  - 90% CIs of geometric mean ratios for C_{max}: TRAZIMERA vs Herceptin-EU, 85.32-98.09; TRAZIMERA vs Herceptin-US, 90.71-104.62; Herceptin-EU vs Herceptin-US, 99.20-114.30
  - 90% CIs of geometric mean ratios for $AUC_{0\text{-}t}$: TRAZIMERA vs Herceptin-EU, 86.44-99.34; TRAZIMERA vs Herceptin-US, 93.08-107.31; Herceptin-EU vs Herceptin-US, 100.50-115.75

$AUC_{0\text{-}t}$=area under the concentration-time profile from time zero to the time of the last quantifiable concentration; CI=confidence interval; C_{max}=maximum concentration; PK=pharmacokinetics.

SELECTED SAFETY INFORMATION

Cardiac Monitoring (continued)

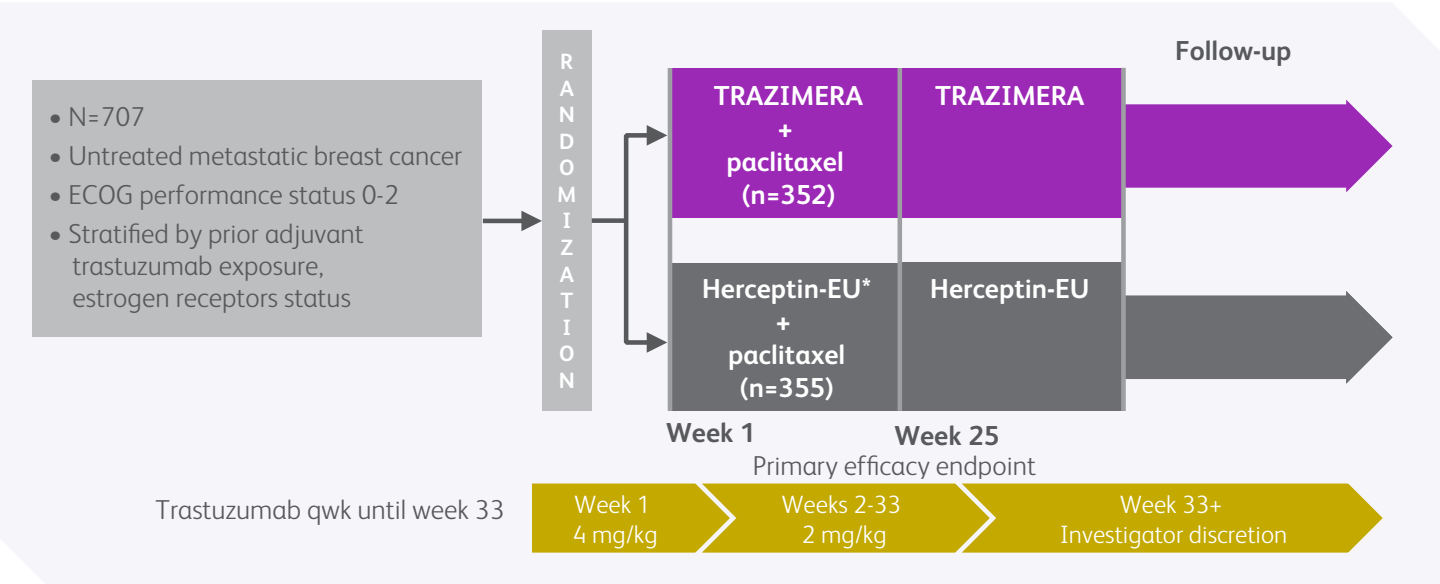
- Monitor frequently for decreased left ventricular function during and after TRAZIMERA treatment
- Monitor more frequently if TRAZIMERA is withheld for significant left ventricular cardiac dysfunction

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

INJECTION Trazimera® trastuzumab-qyyp Pfizer

3.6: *Clinical study design*

Comparative clinical study: Randomized, double-blind study in HER2+ metastatic breast cancer[4]



NOTE: The study was not designed to demonstrate equivalence in secondary efficacy endpoints.

*Product sourced from the EU is often used as a comparator in trials to demonstrate biosimilarity.

Study description[4]

A phase 3, randomized, double-blind study in patients with previously untreated HER2+ metastatic breast cancer. This study was part of a stepwise comparison exercise for demonstrating biosimilarity. TRAZIMERA or Herceptin-EU was administered weekly (4 mg/kg loading dose on cycle 1, day 1; subsequent doses 2 mg/kg) on days 1, 8, 15, and 22 of each 28-day cycle during the paclitaxel administration period and until at least week 33. Following completion of the paclitaxel administration period and beginning no earlier than week 33, TRAZIMERA or Herceptin-EU was continued as monotherapy, and the weekly regimen could be changed to 6 mg/kg every 3 weeks. Treatment with TRAZIMERA or Herceptin-EU could continue until disease progression. Primary endpoint: ORR, defined as the percentage of patients in each group with complete or partial response according to RECIST 1.1 by week 25 and confirmed by week 33, based on blinded central radiology review.

Primary endpoint[4]

- ORR at week 25 (confirmed by week 33); prespecified margin of risk ratio (0.80-1.25)

Secondary endpoints[4,9]

- 1-year PFS rate
- DOR
- 1-year survival rate
- Peak and trough concentrations
- Immunogenicity
- Safety (cardiotoxicity, infusion-related reactions, and lab abnormalities)

DOR=duration of response; ECOG=Eastern Cooperative Oncology Group; HER=human epidermal growth factor receptor; ORR=objective response rate; PFS=progression-free survival; qwk=once every week; RECIST=Response Evaluation Criteria in Solid Tumors.

SELECTED SAFETY INFORMATION

Infusion Reactions

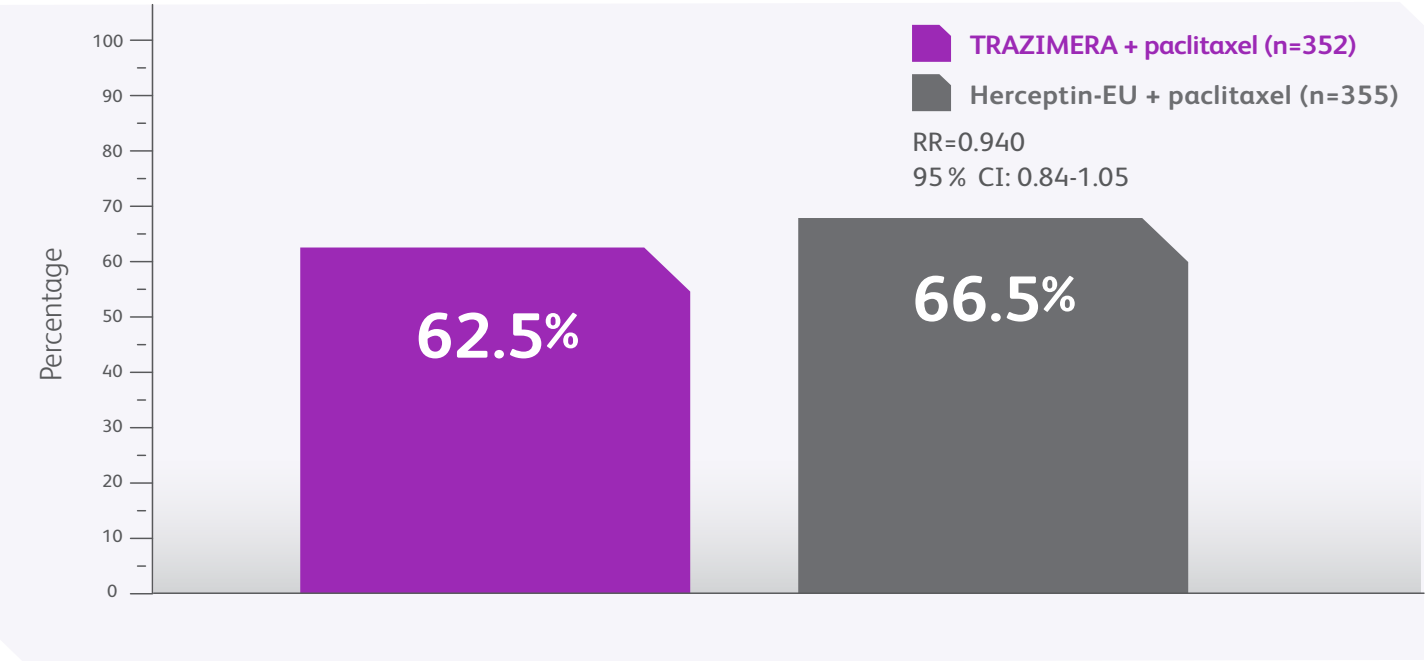
- **Administration of trastuzumab products can result in serious and fatal infusion reactions**
- **Symptoms usually occur during or within 24 hours of administration of trastuzumab products**
- **Interrupt TRAZIMERA infusion for dyspnea or clinically significant hypotension**

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

3.7: *Clinical study primary endpoint*

ORRs between the TRAZIMERA and Herceptin® (trastuzumab) treatment groups were equivalent[4]

TRAZIMERA and Herceptin-EU had comparable ORRs in the ITT population[9]



- Similarity between TRAZIMERA and Herceptin is indicated by the 95% CI for the risk ratio, which fell within the prespecified equivalence margin of 80%-125% (TRAZIMERA over Herceptin-EU)[4]
- ORR is an adequately sensitive endpoint for detecting between-product differences vs those that measure disease progression[13]

CI=confidence interval; ITT=intent to treat; ORR=objective response rate; RR=risk ratio.

SELECTED SAFETY INFORMATION

Infusion Reactions (continued)

- **Monitor patients until symptoms completely resolve**
- **Discontinue TRAZIMERA for infusion reactions manifesting as anaphylaxis, angioedema, interstitial pneumonitis, or acute respiratory distress syndrome. Strongly consider permanent discontinuation in all patients with severe infusion reactions**
- Infusion reactions consist of a symptom complex characterized by fever and chills, and on occasion include nausea, vomiting, pain (in some cases at tumor sites), headache, dizziness, dyspnea, hypotension, rash, and asthenia

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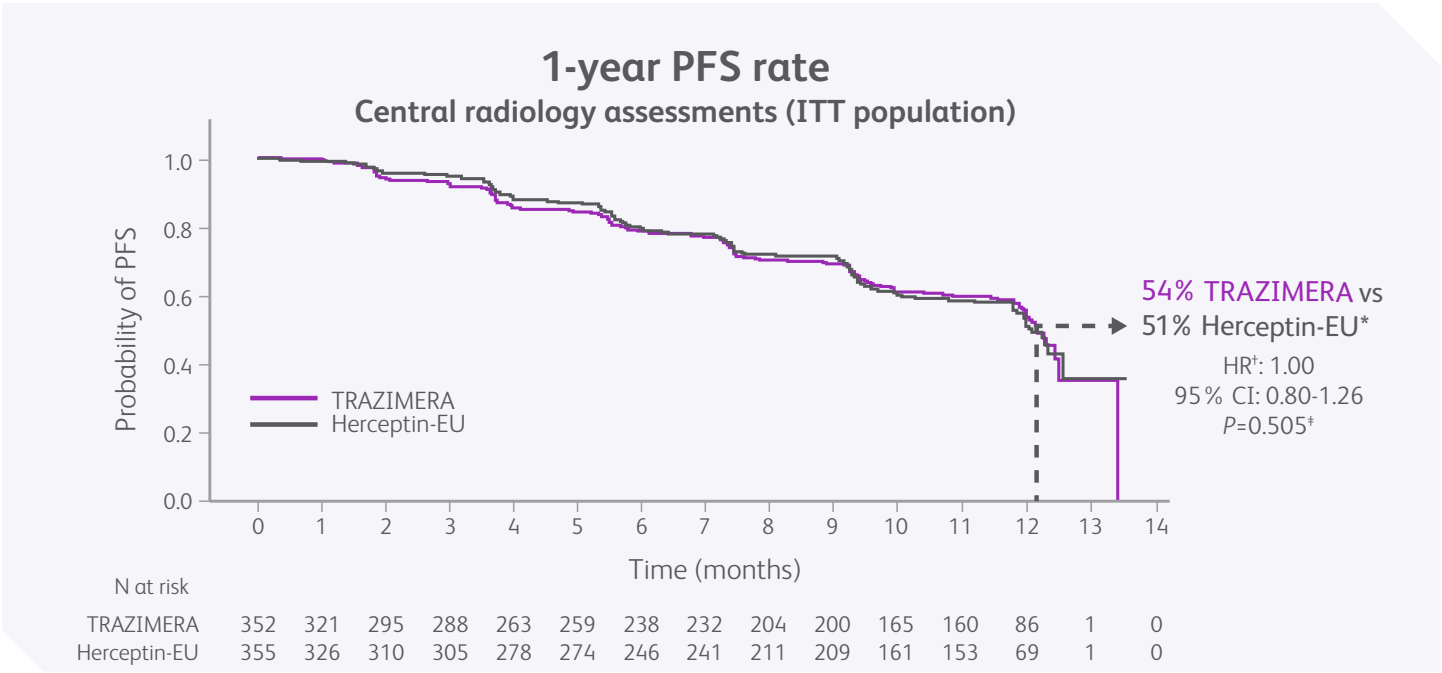
INJECTION Trazimera® trastuzumab-qyyp Pfizer

3.8: *Clinical study secondary endpoint*

No significant differences in 1-year PFS rate[4,9]



- Overall survival data were not mature at the time of analysis and are not shown[9]

CI=confidence interval; HR=hazard ratio; ITT=intent to treat; PFS=progression-free survival.

*Product sourced from the EU is often used as a comparator in trials to demonstrate biosimilarity.

†Hazard ratio from a Cox Proportional Hazards model with prior trastuzumab exposure and estrogen receptor status as strata. Hazard ratio >1 indicated an increase in progressive disease or death in the TRAZIMERA group.[4,9]

‡One-sided *P* value from stratified log-rank test.[4,9]

Data on secondary endpoint were generated in support of biosimilarity. There were no observed differences between treatment groups in PFS, however the study wasn't powered to test for equivalency

SELECTED SAFETY INFORMATION

Embryo-Fetal Toxicity

- **Exposure to trastuzumab products during pregnancy can result in oligohydramnios and oligohydramnios sequence manifesting as pulmonary hypoplasia, skeletal abnormalities, and neonatal death. Advise patients of these risks and the need for effective contraception**
- Verify the pregnancy status of females of reproductive potential prior to the initiation of TRAZIMERA

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

3.9: *Safety*

TRAZIMERA demonstrated a similar safety profile to Herceptin® (trastuzumab) in the comparative clinical trial[4,9]

Summary of treatment-emergent adverse events (TEAEs) for all categories[9]

	TRAZIMERA + paclitaxel (n=349)	Herceptin-EU + paclitaxel (n=353)
Patients with all grade treatment-related TEAEs	315 (90.3%)	313 (88.7%)
Patients with grade ≥3 treatment-related TEAEs	73 (20.9%)	91 (25.8%)
Patients with serious treatment-related TEAEs	17 (4.9%)	15 (4.2%)
Patients with treatment-related TEAEs leading to withdrawal from study	39 (11.2%)	38 (10.8%)

- The most frequently reported TEAEs (incidence of ≥5%) in the TRAZIMERA + paclitaxel arm and the Herceptin-EU + paclitaxel arm were alopecia (54% vs 52%, respectively) and neutropenia (28% vs 26%, respectively)[9]
- No significant differences in AEs of special interest, including cardiac disorders and infusion-related reactions[4]
- No new safety signals were identified with TRAZIMERA compared with the known AE profile of Herceptin[9]

AE=adverse event.

SELECTED SAFETY INFORMATION

Embryo-Fetal Toxicity (continued)

- Advise pregnant women and females of reproductive potential that exposure to TRAZIMERA during pregnancy or within 7 months prior to conception can result in fetal harm
- Advise females of reproductive potential to use effective contraception during treatment and for at least 7 months following the last dose of TRAZIMERA
- Consider the developmental and health benefits of breastfeeding along with the mother's clinical need for TRAZIMERA treatment and any potential adverse effects on the breastfed child from TRAZIMERA or from the underlying maternal condition

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

3.10: *Supplemental comparative clinical study*

Supplemental comparative clinical evidence[4]

- Included 226 patients with early-stage HER2+ breast cancer with planned definitive surgical resection of breast tumor and neoadjuvant chemotherapy
- This study was not required to establish biosimilarity

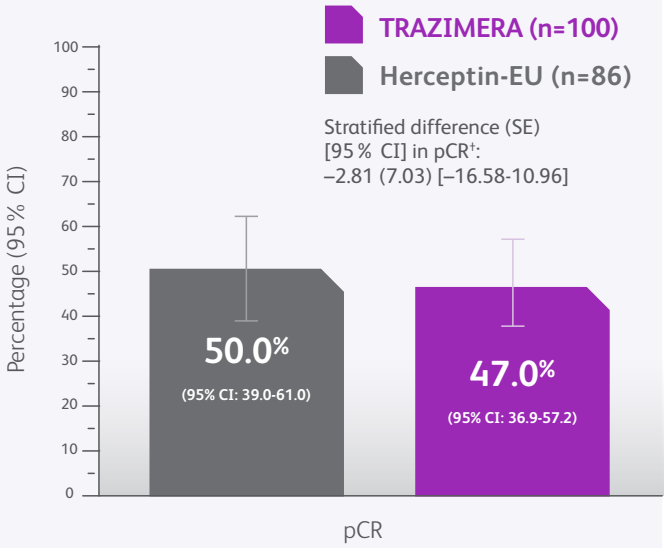
Primary endpoint

- In the primary PK analysis (per-protocol population), the percentage of patients who exhibited cycle 5 C_{trough} (cycle 6 predose) >20 µg/mL in the TRAZIMERA group was noninferior to that in the Herceptin® (trastuzumab) group

Secondary endpoint

- TRAZIMERA and Herceptin had comparable pCR rates and ORRs
- ORRs were comparable between TRAZIMERA and Herceptin-EU
  - 88% for TRAZIMERA (95% CI: 80.2-93.7) vs 82% for Herceptin-EU (95% CI: 72.5-89.4)

Secondary endpoint: pCR assessments (per-protocol population)[4]*



Study description

A phase 3, randomized, double-blind study for the neoadjuvant treatment of patients with HER2+ early breast cancer with planned definitive surgical resection of breast tumor and neoadjuvant chemotherapy. Patients received either TRAZIMERA + docetaxel and carboplatin or Herceptin-EU + docetaxel and carboplatin every 3 weeks through 6 cycles of treatment. TRAZIMERA or Herceptin-EU was given at a dose of 8 mg/kg over a 90-minute infusion at cycle 1; 6 mg/kg over a 30- to 90-minute infusion thereafter, each with docetaxel (75 mg/m^2; 60-minute infusion) and carboplatin (target AUC 6). Primary endpoint: the percentage of patients with cycle 5 C_{trough} (cycle 6 predose) >20 µg/mL.

*Pathology data were not recorded or response was not assessed for patients who completed the study but had no surgery (TRAZIMERA, n=1; Herceptin-EU, n=1) and for those who completed treatment but were lost to follow-up prior to surgery (Herceptin-EU, n=2).

†Stratified analysis was based on the normal approximation to the binomial distribution, adjusting for randomization strata (primary tumor size <5 cm vs ≥5 cm; estrogen receptor-positive vs estrogen receptor-negative; and progesterone receptor-positive vs progesterone receptor-negative).

AUC=area under the concentration vs time curve; CI=confidence interval; C_{trough}=steady state trough plasma concentration; HER=human epidermal growth factor receptor; ORR=objective response rate; pCR=pathological complete response; PK=pharmacokinetics; SE=standard error.

NOTE: The study was not designed to demonstrate equivalence in secondary efficacy endpoints.

Pfizer conducted an additional comparative study in patients with early-stage HER2+ breast cancer that was not required to establish biosimilarity. Neither the Herceptin nor TRAZIMERA US Prescribing Information include indications for use in neoadjuvant early breast cancer treatment

SELECTED SAFETY INFORMATION

Pulmonary Toxicity

- **Administration of trastuzumab products can result in serious and fatal pulmonary toxicity**, which includes dyspnea, interstitial pneumonitis, pulmonary infiltrates, pleural effusions, noncardiogenic pulmonary edema, pulmonary insufficiency and hypoxia, acute respiratory distress syndrome, and pulmonary fibrosis. Such events can occur as sequelae of infusion reactions

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

3.10: *Supplemental comparative clinical study (continued)*

TRAZIMERA had a similar safety profile to that of Herceptin® (trastuzumab) in the clinical study of patients with early-stage breast cancer[4]

All-causality TEAEs (safety population)*

	TRAZIMERA (n=113)	Herceptin-EU (n=112)
Number of AEs	569	511
Patients with event, n (%)		
AEs	109 (96.5)	106 (94.6)
SAEs†	7 (6.2)	6 (5.4)
Grade 3-4 AEs	43 (38.1)	51 (45.5)
Grade 5 AEs	1 (0.9)	0
Discontinued from the study due to AEs	1 (0.9)	3 (2.7)
Discontinued from any treatment‡ due to AEs	4 (3.5)	3 (2.7)
Dose reduced or temporary discontinuation for any treatment‡ due to AEs	37 (32.7)	30 (26.8)

- The incidence of AEs was comparable between treatment groups
- No TEAEs of congestive heart failure or clinically significant left ventricular ejection fraction abnormalities were observed for TRAZIMERA or Herceptin-EU
- No TEAEs indicative of infusion-related reactions were reported in the TRAZIMERA group; 2 (1.8%) patients in the Herceptin-EU group reported nonserious events of pyrexia and tachypnea

AE=adverse event; SAE=serious adverse event; TEAE=treatment-emergent adverse event.

*Includes data up to 50 days after the last dose of study drug. Patients were counted only once per treatment in each row, except for number of AEs.

†As determined by investigator. TRAZIMERA-treated patients reported 7 SAEs: febrile neutropenia, neutropenia, pancytopenia, proctitis, device-related sepsis, injection site abscess, and increased blood creatinine. Herceptin-treated patients reported 10 SAEs: anemia, febrile neutropenia (n=2 patients), neutropenia (2 SAEs in 1 patient), gastrointestinal infection, tooth infection, hip fracture, dehydration, and hypokalemia.

‡Trastuzumab (TRAZIMERA or Herceptin), docetaxel, or carboplatin.

SELECTED SAFETY INFORMATION

Pulmonary Toxicity (continued)

- Patients with symptomatic intrinsic lung disease or with extensive tumor involvement of the lungs, resulting in dyspnea at rest, appear to have more severe toxicity
- Discontinue TRAZIMERA in patients experiencing pulmonary toxicity

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

BOXED WARNINGS AND ADDITIONAL IMPORTANT SAFETY INFORMATION

Cardiomyopathy

- **Administration of trastuzumab products can result in sub-clinical and clinical cardiac failure. The incidence and severity was highest in patients receiving trastuzumab with anthracycline-containing chemotherapy regimens**
- **Evaluate left ventricular function in all patients prior to and during treatment with TRAZIMERA. Discontinue TRAZIMERA treatment in patients receiving adjuvant therapy and withhold TRAZIMERA in patients with metastatic disease for clinically significant decrease in left ventricular function**

Infusion Reactions; Pulmonary Toxicity

- **Administration of trastuzumab products can result in serious and fatal infusion reactions and pulmonary toxicity. Symptoms usually occur during or within 24 hours of administration. Interrupt TRAZIMERA infusion for dyspnea or clinically significant hypotension. Monitor patients until symptoms completely resolve. Discontinue TRAZIMERA for anaphylaxis, angioedema, interstitial pneumonitis, or acute respiratory distress syndrome**

Embryo-Fetal Toxicity

- **Exposure to trastuzumab products during pregnancy can result in oligohydramnios and oligohydramnios sequence manifesting as pulmonary hypoplasia, skeletal abnormalities, and neonatal death. Advise patients of these risks and the need for effective contraception**

Cardiomyopathy

- **Administration of trastuzumab products can result in sub-clinical and clinical cardiac failure. The incidence and severity was highest in patients receiving trastuzumab with anthracycline-containing chemotherapy regimens. In a pivotal adjuvant breast cancer trial, one patient who developed CHF died of cardiomyopathy**
- Trastuzumab products can cause left ventricular cardiac dysfunction, arrhythmias, hypertension, disabling cardiac failure, cardiomyopathy, and cardiac death
- Trastuzumab products can also cause asymptomatic decline in LVEF
- **Discontinue TRAZIMERA treatment in patients receiving adjuvant breast cancer therapy and withhold TRAZIMERA in patients with metastatic disease for clinically significant decrease in left ventricular function**

Cardiac Monitoring

- **Evaluate cardiac function prior to and during treatment. For adjuvant breast cancer therapy, also evaluate cardiac function after completion of TRAZIMERA**
- Conduct thorough cardiac assessment, including history, physical examination, and determination of LVEF by echocardiogram or MUGA scan
- Monitor frequently for decreased left ventricular function during and after TRAZIMERA treatment
- Monitor more frequently if TRAZIMERA is withheld for significant left ventricular cardiac dysfunction

Infusion Reactions

- **Administration of trastuzumab products can result in serious and fatal infusion reactions**
- **Symptoms usually occur during or within 24 hours of administration of trastuzumab products**
- **Interrupt TRAZIMERA infusion for dyspnea or clinically significant hypotension**
- **Monitor patients until symptoms completely resolve**
- **Discontinue TRAZIMERA for infusion reactions manifesting as anaphylaxis, angioedema, interstitial pneumonitis, or acute respiratory distress syndrome. Strongly consider permanent discontinuation in all patients with severe infusion reactions**
- Infusion reactions consist of a symptom complex characterized by fever and chills, and on occasion include nausea, vomiting, pain (in some cases at tumor sites), headache, dizziness, dyspnea, hypotension, rash, and asthenia

Embryo-Fetal Toxicity

- **Exposure to trastuzumab products during pregnancy can result in oligohydramnios and oligohydramnios sequence manifesting as pulmonary hypoplasia, skeletal abnormalities, and neonatal death. Advise patients of these risks and the need for effective contraception**
- Verify the pregnancy status of females of reproductive potential prior to the initiation of TRAZIMERA
- Advise pregnant women and females of reproductive potential that exposure to TRAZIMERA during pregnancy or within 7 months prior to conception can result in fetal harm
- Advise females of reproductive potential to use effective contraception during treatment and for at least 7 months following the last dose of TRAZIMERA

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

Embryo-Fetal Toxicity (continued)

- Consider the developmental and health benefits of breastfeeding along with the mother's clinical need for TRAZIMERA treatment and any potential adverse effects on the breastfed child from TRAZIMERA or from the underlying maternal condition

Pulmonary Toxicity

- **Administration of trastuzumab products can result in serious and fatal pulmonary toxicity,** which includes dyspnea, interstitial pneumonitis, pulmonary infiltrates, pleural effusions, noncardiogenic pulmonary edema, pulmonary insufficiency and hypoxia, acute respiratory distress syndrome, and pulmonary fibrosis. Such events can occur as sequelae of infusion reactions
- Patients with symptomatic intrinsic lung disease or with extensive tumor involvement of the lungs, resulting in dyspnea at rest, appear to have more severe toxicity
- Discontinue TRAZIMERA in patients experiencing pulmonary toxicity

Exacerbation of Chemotherapy-Induced Neutropenia

- In randomized, controlled clinical trials, the numbers of per-patient incidences of NCI-CTC Grade 3-4 neutropenia and of febrile neutropenia were higher in patients receiving trastuzumab in combination with myelosuppressive chemotherapy as compared to those who received chemotherapy alone. The incidence of septic death was similar among patients who received trastuzumab and those who did not

Most Common Adverse Reactions

- The most common adverse reactions associated with trastuzumab products in breast cancer were fever, nausea, vomiting, infusion reactions, diarrhea, infections, increased cough, headache, fatigue, dyspnea, rash, neutropenia, anemia, and myalgia
- The most common adverse reactions associated with trastuzumab products in metastatic gastric cancer were neutropenia, diarrhea, fatigue, anemia, stomatitis, weight loss, upper respiratory tract infections, fever, thrombocytopenia, mucosal inflammation, nasopharyngitis, and dysgeusia

INDICATIONS

Adjuvant Breast Cancer

TRAZIMERA is indicated for adjuvant treatment of HER2-overexpressing node positive or node negative (ER/PR negative or with one high risk feature*) breast cancer:

- As part of a treatment regimen containing doxorubicin, cyclophosphamide and either paclitaxel or docetaxel
- As part of a treatment regimen with docetaxel and carboplatin
- As a single agent following multi-modality anthracycline based therapy

Select patients for therapy based on an FDA-approved companion diagnostic for a trastuzumab product.

*High risk is defined as ER/PR positive with one of the following features: tumor size >2 cm, age <35 years, or tumor grade 2 or 3.

Metastatic Breast Cancer

TRAZIMERA is indicated:

- In combination with paclitaxel for the first-line treatment of HER2-overexpressing metastatic breast cancer
- As a single agent for treatment of HER2-overexpressing breast cancer in patients who have received one or more chemotherapy regimens for metastatic disease

Select patients for therapy based on an FDA-approved companion diagnostic for a trastuzumab product.

Metastatic Gastric Cancer

TRAZIMERA is indicated, in combination with cisplatin and capecitabine or 5-fluorouracil, for the treatment of patients with HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma, who have not received prior treatment for metastatic disease.

Select patients for therapy based on an FDA-approved companion diagnostic for a trastuzumab product.

Please see Important Safety Information on pages 26 and 27 and full Prescribing Information, including BOXED WARNINGS, at TrazimeraHCP.com.

TRAZIMERA: Pfizer Oncology's commitment to building onto the clinical experience of trastuzumab

With the largest portfolio of biosimilars—including TRAZIMERA—Pfizer is committed to expanding options for patient care[3]

Favorable coverage[4]

Potential savings[4]

Support for you and your patients

Approved across all indications of Herceptin® (trastuzumab), with an identical dosing and administration schedule[6]

Realize the full potential of biosimilars. Ask about the Pfizer Biosimilar portfolio.

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V.6.2020. © 2020 National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the guideline, go online to NCCN.org. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Gastric Cancer V.2.2020. © 2020 National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the guideline, go online to NCCN.org. **3.** McGowan S, Jesse M. *Biosimilars Pipeline Report*. AmerisourceBergen. July 27, 2020. Accessed March 1, 2021. https://www.amerisourcebergen.com/-/media/assets/amerisourcebergen/biosimilars-page/biosimilar-us-market-landscape_010421.pdf. **4.** Data on file. Pfizer Inc.; New York, NY. **5.** Mulcahy AW, Hlavka JP, Case SR. Biosimilar cost savings in the United States: initial experience and future potential. *RAND Health Quarterly.* 2018;7(4):3. **6.** TRAZIMERA [prescribing information]. New York, NY: Pfizer Inc.; November 2020. **7.** Centers for Medicare & Medicaid Services. July 2020 Update of the Hospital Outpatient Prospective Payment System (OPPS). Updated July 1, 2020. **8.** US Food and Drug Administration. Guidance for Industry: Scientific Considerations in Demonstrating Biosimilarity to a Reference Product. Silver Spring, MD: FDA, US Dept of Health and Human Services; April 2015. https://www.fda.gov/downloads/drugs/guidances/ucm291128.pdf. Accessed March 1, 2021. **9.** US Food and Drug Administration. Center for Drug Evaluation and Research. Application Number: 761081Orig1s000 Trazimera Clinical Review(s). https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/761081Orig1s000MedR.pdf. February 26, 2019. Accessed March 1, 2021. **10.** US Food and Drug Administration. Center for Drug Evaluation and Research. Application Number: 761081Orig1s000 Trazimera Summary Review. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/761081Orig1s000SumR.pdf. February 26, 2019. Accessed March 1, 2021. **11.** US Food and Drug Administration. Center for Drug Evaluation and Research. Application Number: 761081Orig1s000 Trazimera Product Quality Review(s). https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/761081Orig1s000ChemR.pdf. January 11, 2019. Accessed March 1, 2021. **12.** Melosky B, Reardon DA, Nixon AB, Subramanian J, Bair AH, Jacobs I. Bevacizumab biosimilars: scientific justification for extrapolation of indications. *Future Oncol.* 2018;14(24):2507-2520. **13.** He K, Chen H, Gwise T, et al. Statistical considerations in evaluating a biosimilar product in an oncology clinical study. *Clin Cancer Res.* 2016;22(21);5167-5170.

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