

WHEN LIVING WITH EGFR MUTATION-POSITIVE METASTATIC NON-SMALL CELL LUNG CANCER (NSCLC)...

THE LITTLE THANGS FEEL EVEN BIGGER, SO I'LL MAKE EVERY MOMENT COUNT.

CYRAMZA is used in combination with erlotinib as an initial treatment for certain types of epidermal growth factor receptor (EGFR) mutation-positive metastatic non-small cell lung cancer (NSCLC).* CYRAMZA + erlotinib is for people who have not been previously treated for metastatic NSCLC.

*Metastatic cancer refers to cancer that has spread from the place where it started to other parts of the body.

SELECT SAFETY INFORMATION CYRAMZA may cause serious side effects, including:

Severe bleeding, including bleeding in the stomach or bowel, has happened with CYRAMZA. This can be life threatening. Tell your doctor right away if you have bleeding or symptoms of bleeding, including lightheadedness. If severe bleeding happens, you will have to stop receiving CYRAMZA.



Me? I always give <u>100</u> - no, <u>110%</u>. That's just who I am. And where, no doubt, this will be my to ugh est challenge yet. I think about what keeps me going - and I th in k about my grandson, all <u>sticky</u> hands and bubbling with energy. And now I know, the net's about three feet tall at best. But I can't help but s a v o r the moment when I see the ball sail through the air and his expression as he makes his first shot. Because to me, as I start my fight with EGFR mutation-positive metastatic <u>lung cancer</u>,

> these little things feel even bigger...

UNDERSTANDING YOUR CONDITION

Lung cancer is a cancer that starts in your lung. There are 2 main types of lung cancer: non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). NSCLC represents about 80% to 85% of all lung cancer cases.

WHAT IS METASTATIC CANCER?

When a cancer is referred to as "metastatic," it means that the cancer has spread from the place where it started (your lungs) to other parts of the body. If the cancer has spread to farther parts of the body (for example, from the lungs to the liver), the cancer is considered to have "metastasized."

WHAT IS BIOMARKER TESTING?

Biomarker testing may help your doctor better understand what is causing your lung cancer to grow. Your doctor may also refer to biomarkers as "mutations." Mutations that can contribute to cancer have been identified in NSCLC. Identified mutations include alterations in epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK), and other proteins.

UNDERSTANDING EGFR BIOMARKERS IN METASTATIC NSCLC What is EGFR?

One type of biomarker is the epidermal growth factor receptor, also known as EGFR. EGFR is a protein found on the surface of cells in the body.

Sometimes mutations cause changes in this protein, and it becomes unusually active, which can lead to the growth and spread of cancer cells.

What is EGFR mutation-positive metastatic NSCLC?

Some metastatic NSCLC tumors will have certain types of abnormal, or mutated, EGFR genes.

About 10% to 20% of Caucasian people and 40% to 60% of Asian people diagnosed with NSCLC test positive for an EGFR mutation.

SELECT SAFETY INFORMATION

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Tears in the stomach or bowel wall may happen with CYRAMZA. This can be life threatening. Tell your doctor if you have severe diarrhea, vomiting, or severe abdominal pain. If you have tears in the stomach or bowel wall, you will have to stop receiving CYRAMZA.



CYRAMZA MAY HELP YOU FIGHT FOR WHAT MATTERS TO YOU

You're not the type to settle for average. You're the type who pushes for more. But where individual results with CYRAMZA can vary, clinical studies have shown...



MORE TIME WITHOUT DISEASE PROGRESSION

In a clinical study, CYRAMZA + erlotinib provided more time without disease progression than placebo + erlotinib for people with metastatic NSCLC with certain types of EGFR mutations.

• On average, people taking CYRAMZA + erlotinib lived 19 months without disease progression compared with 12 months for those taking placebo + erlotinib

The clinical study is still ongoing to determine if CYRAMZA + erlotinib may help you live longer compared with placebo + erlotinib.



In a clinical study, tumors shrank* in 76% of people taking CYRAMZA + erlotinib compared with 75% of those taking placebo + erlotinib.

*The percentage of patients who experienced tumor shrinkage was similar between those taking CYRAMZA + erlotinib compared with those taking placebo + erlotinib. Tumor shrinkage is defined as a reduction of 30% or more in tumor size.

CYRAMZA + erlotinib was studied in a clinical trial for the initial treatment of people with metastatic NSCLC with certain EGFR mutations. Of the 449 people included in the trial, 224 people received CYRAMZA + erlotinib and 225 people received placebo + erlotinib.

The trial was designed to measure disease progression, which is the time that people lived without their cancer spreading or growing after taking treatment. The study also measured the proportion of patients who had a reduction in tumor size of 30% or more.

SELECT SAFETY INFORMATION

CYRAMZA may cause serious side effects, including:

Wounds may not heal quickly or completely. Tell your doctor if you have a wound that doesn't heal properly or have a surgery planned. If you are having surgery, CYRAMZA treatment should be stopped beforehand. Your doctor

may put you back on CYRAMZA after your surgical wound has healed.



CYRAMZA MAY HELP STARVE CANCEROUS TUMORS

CYRAMZA may work as a tumor-starving agent to attack your cancer. Tumors need nutrients to grow, which are mainly supplied through your blood vessels. CYRAMZA is thought to stop new blood vessels from forming, including those that feed your tumor. This may help starve the tumor of the nutrients it needs to keep growing. The process of how CYRAMZA is thought to work was shown in laboratory studies.

As an anti-angiogenic, CYRAMZA works differently from traditional chemotherapy or targeted therapy. Depending on what type of metastatic NSCLC you have, CYRAMZA may be used in combination with either your chemotherapy or the targeted therapy, erlotinib, to help fight your metastatic NSCLC.

If you're diagnosed with EGFR mutationpositive metastatic NSCLC, CYRAMZA may be an appropriate initial treatment option for you when used in combination with erlotinib. Talk to your doctor about whether CYRAMZA is right for you.

SELECT SAFETY INFORMATION

CYRAMZA may cause serious side effects, including: Strokes, mini-strokes, blood clots, and heart attacks have happened to people on CYRAMZA. These can be fatal. If you have one of these events, you will have to stop receiving CYRAMZA.









CYRAMZA is given by intravenous infusion, commonly referred to as an IV. A doctor or nurse will administer treatment at the doctor's office, a hospital, or an infusion center.

Your first infusion will take about 60 minutes. If you tolerate the first infusion of CYRAMZA well, then your next CYRAMZA infusions may take only 30 minutes.



Before you receive CYRAMZA, your doctor will give you different medicines to help prevent an allergic reaction that may occur during the infusion.

CYRAMZA is given in combination with erlotinib, a daily tablet.

CYRAMZA will be given to you once every 2 weeks, or as recommended by your doctor. Your doctor will determine the number of treatments you receive.

SELECT SAFETY INFORMATION

CYRAMZA may cause serious side effects, including:

Reactions related to infusing CYRAMZA have happened. These can be severe and life threatening. Most of these reactions happened during or after the first or second CYRAMZA infusion. Symptoms of infusion reactions include shaking or stiffness of the body, back pain or spasms, chest pain or tightness, chills, flushing (sudden warmth and/or reddened skin on the face, neck, or upper chest), difficulty breathing, wheezing (a whistling sound in the breath caused by narrowed breathing tubes), becoming blue due to lack of oxygen, and tingling or numbness of the skin. In severe reactions, rapid heartbeat, low blood pressure, and severe trouble breathing may happen. Your health care team will give you medicine before each CYRAMZA infusion and will watch you for these side effects. If a reaction happens, CYRAMZA treatment may be infused at a slower rate or may be permanently stopped, depending

or may be permanently stopped, depending on how severe the reaction is.



YOUR DOSING SCHEDULE



CYRAMZA will be given to you once every 2 weeks, or as recommended by your doctor.



SELECT SAFETY INFORMATION

CYRAMZA may cause serious side effects, including:

Severe high blood pressure has happened with CYRAMZA. Your doctor will take your blood pressure at least every two weeks while you are receiving CYRAMZA. Depending on your blood pressure, your doctor may pause or permanently stop CYRAMZA. Tell your doctor if you have high blood pressure or symptoms of high blood pressure, including severe headache or lightheadedness or confusion, changes in your vision, or seizure. TIPS FOR DAY OF TREATMENT

You may be nervous about your first treatment. Or maybe you're an old pro at this. But no matter where you're coming from, here are some important tips to help get you through each infusion with CYRAMZA:

BEFORE YOUR INFUSION

- GET PREPARED: Get a good night's sleep, hydrate, and eat a healthy, light meal before treatment. Make sure to ask your healthcare provider for their advice.
- DRESS DOWN: Everyone has their go-to outfit that makes them feel snug and safe. Whether it's a sweater with sweatpants or leggings, or an old hoodie, designate your comfy outfit ahead of time so you can just grab and go.
- BUDDY UP: Ask a friend or loved one to accompany you to your appointment for support. You'll need a ride home from treatment, so they can also serve as your driver.
- PACK A TOOLKIT: Pack a bag with plenty of distractions: books, magazines, music, games, entertainment on your laptop, tablet, or phone. While you're distracted, it's also important to keep comfy—a travel-size pillow and extra sweater or blanket can help you stay both cozy and warm.

If your doctor says it's okay, bring beverages, light snacks, and candy or mints. This can help you stay hydrated, keep your energy up, and combat any dry mouth or nausea that treatment might cause. Treatment may also cause cracked lips, so consider packing lip balm in your bag as well.

AFTER YOUR INFUSION



TAKE A MINUTE: First things first, take a deep breath.

TAKE TEN: How are you feeling? What went well? What would you change for next time? Consider keeping a journal with your notes, and if you're experiencing any side effects, make sure to mention these to your doctor.

TAKE A LOAD OFF: If you're up for it, make time to see your family and friends. Loved ones are a great way to restore strength.





You are encouraged to report negative side effects of prescription drugs to the FDA. Visit **www.fda.gov/safety/medwatch** or call 1-800-FDA-1088.

Please see Purpose and Safety Summary with Warnings on pages 8–9 for more safety information for CYRAMZA.

UNDERSTANDING COMMON SIDE EFFECTS

CYRAMZA in combination with erlotinib may cause side effects. If you experience symptoms while on treatment, it is important that you speak with your doctor.

The most common side effects were:

- Infections
- Increased levels of liver enzymes
- Diarrhea
- High blood pressure
- Low red blood cell count
- A sore or inflammation inside the mouth
- Low blood platelet count
- Loss of hair
- Nosebleeds

- Too much protein in the urine
- Decrease in a type of white blood cell
- Low potassium in the blood
- Swelling in the arms, legs, hands, and feet
- Headache
- Gastrointestinal bleeding events
- Gums bleeding
- Bleeding in the lungs or respiratory tract

The most common serious side effects were:

- Pneumonia (infection in one or both lungs)
- Skin infection (bacterial infection under the skin)
- Collapsed lung (air or other gas in the pleural cavity in the lungs)

Talk to your doctor about any questions, concerns, or side effects you might have with CYRAMZA. Your doctor may be able to make recommendations to help you feel more comfortable.



PURPOSE AND SAFETY SUMMARY

Important Facts About CYRAMZA® (sigh-RAM-zuh). It is also known as ramucirumab.

CYRAMZA is a prescription medicine used to treat certain types of cancer. It is given by intravenous (IV) infusion. An IV infusion is when a needle is placed into your vein and a medicine is given slowly. CYRAMZA is prescribed in these ways:

- By itself or with a chemotherapy medicine called paclitaxel to treat certain kinds
- of stomach cancer, or cancer of the area where the stomach and esophagus (food pipe) meet that is advanced or has spread to other parts of the body. The area where the stomach and esophagus meet is often called the gastroesophageal (GE) junction. CYRAMZA is for people whose stomach cancer got worse during or after certain other types of chemotherapy.
- With a chemotherapy medicine called docetaxel to treat non-small cell lung cancer (NSCLC) that has spread to other parts of the body and has gotten worse during or after another type of chemotherapy. People who have tumors with certain abnormal genes should not receive CYRAMZA unless they have already been treated with medicine that targets those changes and their cancer became worse during treatment.
- With a combination of chemotherapy medicines called FOLFIRI (irinotecan, folinic acid, and fluorouracil). This is given to treat colorectal cancer (CRC) that has spread to other parts of the body and has gotten worse during or after certain other types of chemotherapy.
- By itself to treat a type of liver cancer called hepatocellular carcinoma (HCC). CYRAMZA is for people who have levels of alpha-fetoprotein of at least 400 nanograms per milliliter (ng/mL) in their blood and have been treated with another type of chemotherapy medicine called sorafenib.
- In combination with another medicine called erlotinib as a first-line treatment for certain types of EGFR mutation positive non-small cell lung cancer (NSCLC) that has spread to other parts of the body.
- It is not known if CYRAMZA is safe and effective in children.

Warnings

CYRAMZA may cause serious side effects, including:

- Severe bleeding, including bleeding in the stomach or bowel, has happened with CYRAMZA. This can be life threatening. If severe bleeding happens, you will have to stop receiving CYRAMZA.
- Tears in the stomach or bowel wall may happen with CYRAMZA. This can be life threatening. If you have tears in the stomach or bowel wall, you will have to stop receiving CYRAMZA.
- Wounds may not heal quickly or completely. If you are having surgery, CYRAMZA treatment should be stopped beforehand. Your doctor may put you back on CYRAMZA after your surgical wound has healed.
- Strokes, mini-strokes, blood clots, and heart attacks have happened to people on CYRAMZA. These can be fatal. If you have one of these events, you will have to stop receiving CYRAMZA.
- Severe high blood pressure has happened with CYRAMZA. Your doctor will take your blood pressure at least every two weeks while you are receiving CYRAMZA. Depending on your blood pressure, your doctor may pause or permanently stop CYRAMZA.
- Reactions related to infusing CYRAMZA have happened. These can be severe and life threatening. Most of these reactions happened during or after the first or second CYRAMZA infusion. In severe reactions, rapid heartbeat, low blood pressure, and severe trouble breathing may happen. Your health care team will give you medicine before each CYRAMZA infusion and will watch you for these side effects. If a reaction happens, CYRAMZA treatment may be infused at a slower rate or may be permanently stopped, depending on how severe the reaction is.

- CYRAMZA may worsen certain types of liver disease.
- A very rare but serious brain disorder has been found in research trials with CYRAMZA The disorder is called PRES (posterior reversible encephalopathy syndrome). Signs of PRES may include seizure, headache, nausea, vomiting, blindness, and changes in your thinking. These symptoms may stop or improve within days. However, the changes in thinking can be ongoing, and PRES can be fatal. If you develop PRES, you will have to stop receiving CYRAMZA.
- Too much protein in the urine (called proteinuria) has been found in research trials with CYRAMZA. This may be a sign of kidney damage. Your doctor will watch your urine protein levels during treatment. If you develop protein in your urine, your doctor may pause your treatment and lower your dose of CYRAMZA. If you have severe proteinuria, you will have to stop receiving CYRAMZA permanently.
- Thyroid gland problems have been found in research trials with CYRAMZA. Your doctor will do blood tests to track how well your thyroid gland works during treatment.
- CYRAMZA can harm your unborn baby. You should avoid getting pregnant, and use effective birth control while receiving CYRAMZA and for 3 months after your last dose.
- CYRAMZA may harm a breastfeeding child. Do not breastfeed your child during treatment with CYRAMZA and for 2 months after your last dose.

Tell your doctor right away if you have:

- Bleeding or symptoms of bleeding, including lightheadedness.
- Severe diarrhea, vomiting, or severe abdominal pain.
- A wound that doesn't heal properly or have a surgery planned.
- High blood pressure or symptoms of high blood pressure, including severe headache or lightheadedness or confusion, changes in your vision, or seizure.
- Symptoms of infusion reactions, including:
- Shaking or stiffness of the body
- Back pain or spasms
- Chest pain or tightness
- o Chills
- Flushing (sudden warmth and/or reddened skin on the face, neck, or upper chest)
- Had liver disease or other liver problems.
- Symptoms of PRES, including seizure, headache, nausea or vomiting, or changes in vision or thinking.

• Difficulty breathing

• Wheezing (a whistling sound in the breath

caused by narrowed breathing tubes)

• Becoming blue due to lack of oxygen

• Tingling or numbness of the skin

Common side effects

The most common side effects of CYRAMZA when given by itself include:

- Low blood platelet count
- Feeling tired
- Low albumin (protein in the blood)
- Low sodium in the blood
- Swelling in the arms, legs, hands, or feet
- High blood pressure
- Stomach pain
- Low white blood cell count
- Not feeling hungry
- Too much protein in the urine
- Feeling like you want to throw up (vomit)



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- Unusual buildup of fluid in the belly
- Low calcium in the blood
- Headache
- Diarrhea
- Nose bleeds
- Trouble falling or staying asleep
- Fever Vomiting
- Back Pain

The most **common serious side effects** of CYRAMZA when given **by itself** include:

- Anemia (a decrease in red blood cells)
- Unusual buildup of fluid in the belly

• Blocked digestive tract

- Pneumonia (infection of one or both lungs)

Some people needed to have extra red blood cells put into their blood.

The most common side effects of CYRAMZA when given with certain chemotherapy medicines include:

- Low white blood cell count
- Diarrhea
- Tiredness
- Mouth sores with or without swelling in the lining of the mouth
- Decreased appetite
- Nose bleeds
- Low blood platelet count
- High blood pressure

• Too much protein in the urine • Low white blood cell count with a fever

• Swelling in the arms, legs, hands, or feet

- Swelling, redness, or pain in the palms or soles
- (hand-foot syndrome) • Increased production of tears
- Bleeding in the digestive tract
- Low albumin (a protein in the blood)

The most common serious side effects of CYRAMZA when given with certain chemotherapy medicines include:

- Low white blood cell count with a fever
- Pneumonia

- Diarrhea
- Blocked digestive tract
- Low white blood cell count Some people needed treatment to increase their white blood cell counts.

The most common side effects of CYRAMZA when given with erlotinib include:

- Infections
- Increased levels of liver enzymes
- Diarrhea
- High blood pressure
- Low red blood cell count
- A sore or inflammation inside the mouth
- Low blood platelet count
- Loss of hair
- Nosebleeds

- Too much protein in the urine
- Decrease in a type of white blood cell
- Low potassium in the blood
- Swelling in the arms, legs, hands, and feet
- Headache
 - Gastrointestinal bleeding
 - Gums bleeding
 - Bleeding in the lungs or respiratory tract
- The most common serious side effects of CYRAMZA when given with erlotinib include:
- Pneumonia (infection in one or both lungs)
- Skin infection (bacterial infection under the skin)
- Collapsed lung (air or other gas in the pleural cavity in the lungs)

Some people needed to have extra red blood cells put into their blood.

These are not all the possible side effects of CYRAMZA. Tell your doctor if you have any side effects. You can report side effects at 1-800-FDA-1088 or www.fda.gov/medwatch.

Before using

Before you receive CYRAMZA, tell your doctor if you:

- Have had or are at high risk for strokes or heart attack.
- Have high blood pressure or have blood pressure problems.
- Are planning to have surgery of any kind.
- Have ever had liver problems, including cirrhosis or other diseases of the liver.
- Are pregnant or may be pregnant: CYRAMZA can harm your unborn baby. You should avoid getting pregnant and use effective birth control during treatment with CYRAMZA and for 3 months after the last dose.
- Are breastfeeding: Your doctor will tell you to stop breastfeeding during treatment with CYRAMZA and for 2 months after the last dose.

Also tell your doctor about all the medicines and supplements you take, whether they have been prescribed for you or you buy them without a prescription.

How to take

- CYRAMZA is given by intravenous (IV) infusion. The infusion will last 60 minutes. If you handle the first infusion of CYRAMZA well, then your next infusions may only take 30 minutes. The schedule for receiving CYRAMZA depends on what type of cancer you are being treated for. These are typical schedules:
- Once every 2 weeks for stomach cancer or GE junction cancer that is advanced or has spread to other parts of the body, colorectal cancer that has spread to other parts of the body, hepatocellular carcinoma that has AFP levels of at least 400 ng/mL or higher, or when used with the targeted therapy, erlotinib, for certain types of EGFR mutation positive non-small cell lung cancer that has spread to other parts of the body.
- Once every 3 weeks, when used with the chemotherapy, docetaxel, non-small cell lung cancer that has spread to other parts of the body.

Your doctor will give you other medicines before your CYRAMZA infusion to help lower the chance of an infusion reaction

Learn more

For more information, call 1-800-545-5979 or go to CYRAMZA.com

This summary provides basic information about CYRAMZA. It does not include everything known about this medicine. This information does not take the place of talking with your doctor. Be sure to talk to your doctor or other health care provider about CYRAMZA and how it is given. Your doctor is the best person to help you decide if CYRAMZA is right for you.

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Lilly Oncology Support Center

The Lilly Oncology Support Center is committed to helping qualified patients when they're prescribed a Lilly Oncology product. We focus on financial and coverage issues, offering resources and individualized support for eligible patients, whether they're uninsured, underinsured, or insured. Services include help with benefit verification, prior authorization, paying for medicine, and specialty-pharmacy coordination.

Savings Card Program

- Supports eligible, commercially insured patients with Savings Card and coinsurance costs for prescribed Lilly Oncology products*
- No income eligibility requirement
- Provides an annual maximum patient benefit of \$25,000

*Offer good until 12/31/2021 for up to 12 months. Patients must use card by 12/31/2020. Patient must have coverage for the Lilly Oncology infused product through their commercial drug insurance to pay as little as \$25 per dose. Offer subject to a monthly cap of wholesale acquisition cost plus usual and customary fees and a separate annual cap of \$25,000. Patient is responsible for any applicable taxes, fees, or amounts exceeding monthly or annual caps. **This offer is invalid for patients without commercial drug insurance or whose prescription claims for the Lilly Oncology product are eligible to be reimbursed, in whole or in part, by any governmental program, including, without limitation, Medicaid, Medicare, Medicare Part D, Medigap, DoD, VA, TRICARE®/CHAMPUS, or any state patient or pharmaceutical assistance program.** Offer void where prohibited by law and subject to change or discontinue without notice. Card activation is required. Subject to additional terms and conditions, which can be found at LillyOncologySupportCenter.com.

Insurance Support

- Eligibility determination
- Benefits investigation
- Prior authorization assistance
- Appeals information
- Specialty-pharmacy coordination

Referrals to Other Assistance Programs

For patients who can't afford their co-pay or coinsurance, the Lilly Oncology Support Center can provide information on patient assistance programs offered through foundations, separate from Eli Lilly and Company.

These foundations may be able to assist eligible underinsured and uninsured patients through a variety of foundation-specific support options.

For more information about the Lilly Oncology Support Center, call **1-866-472-8663**, Monday–Friday, 8 AM–10 PM ET, or visit LillyOncologySupportCenter.com







Please see Purpose and Safety Summary with Warnings on pages 8-9.

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