Fact Sheet

Gazyva® (obinutuzumab) Injection

in Previously Untreated Chronic Lymphocytic Leukemia

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GAZYVA®
obinutuzumab injection

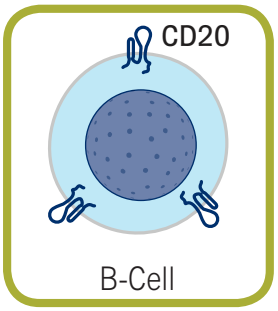
Gazyva is a medicine that works with the body's own immune system to attack blood cells called B-cells that have a certain marker on their surface (CD20). Abnormal B-cells are the most common cause of chronic lymphocytic leukemia (CLL), which is one of the most common blood cancers.[1,2]

Gazyva is FDA-approved for the treatment of people with previously untreated CLL in combination with chlorambucil chemotherapy.[3] This approval was based on a Phase III clinical trial that compared Gazyva plus chlorambucil chemotherapy to rituximab plus chlorambucil chemotherapy or chlorambucil alone.[3]

What is CLL?

CLL is a slow-growing cancer of the blood and bone marrow that is generally considered incurable. In the United States, there are approximately 14,600 new cases each year and 4,650 deaths expected in 2015.[2,4]

Most cases of CLL start in B-cells which express the marker **CD20** on their surface.[2]



Important Safety Information

Patients must tell their doctor right away about any side effects they experience. Gazyva can cause side effects that can become serious or life threatening, including:

Hepatitis B Virus (HBV): Hepatitis B can cause liver failure and death. If a patient has had history of hepatitis B infection, Gazyva could cause it to return. Patients should not receive Gazyva if they have active hepatitis B liver disease. The patient's doctor or healthcare team will need to screen for hepatitis B before, and monitor the patient for hepatitis during and after, treatment with Gazyva. Sometimes this will require treatment for hepatitis B. Symptoms of hepatitis include: worsening of fatigue and yellow discoloration of skin or eyes.

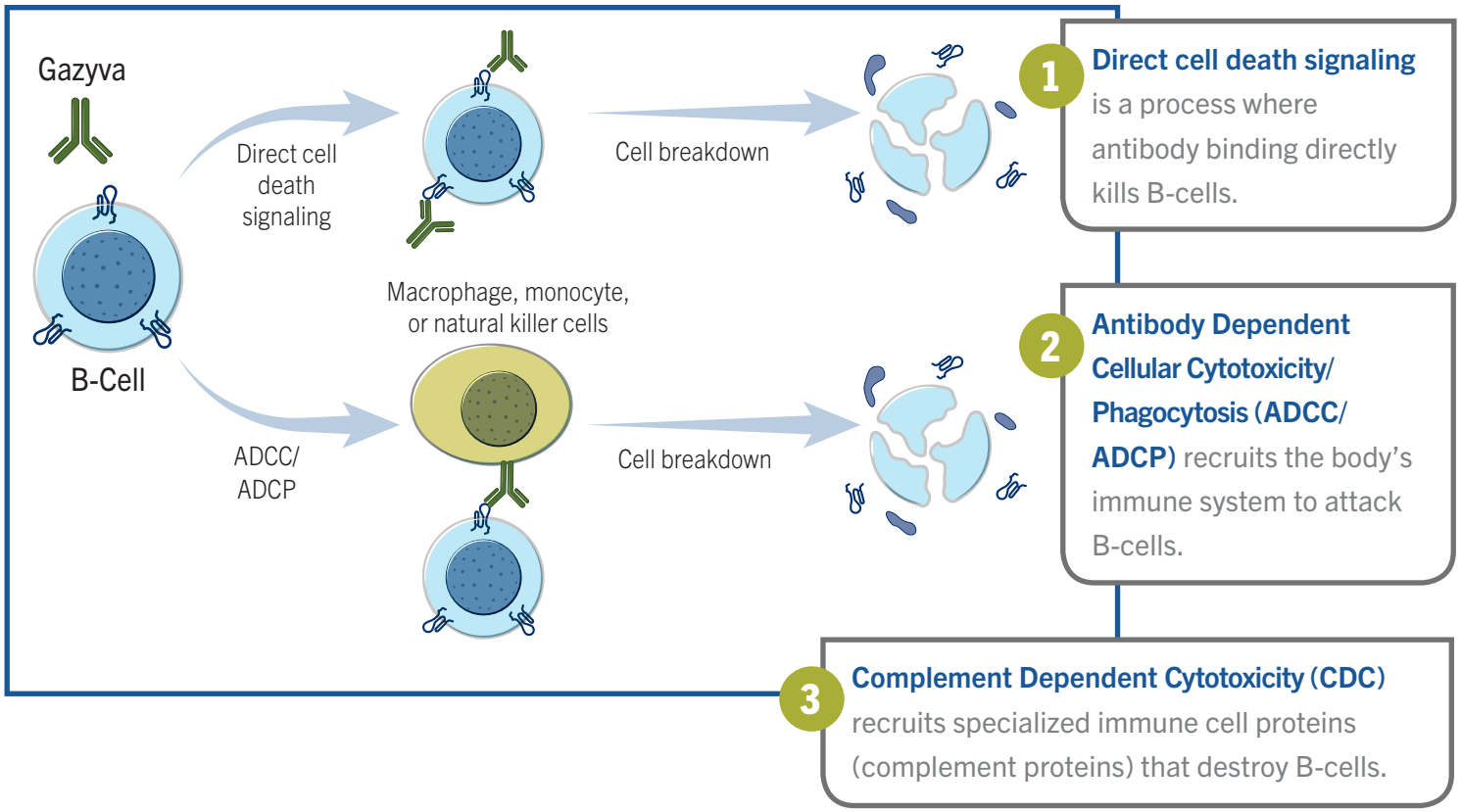
Progressive Multifocal Leukoencephalopathy (PML): PML is a rare and serious brain infection caused by a virus. PML can be fatal. A patient's weakened immune system could put the patient at risk. The patient's doctor will watch for symptoms. Symptoms of PML include: confusion, difficulty talking or walking, dizziness or loss of balance, and vision problems.

Please see the following pages and Gazyva full Prescribing Information for Important Safety Information including Most Serious Side Effects.

What is Gazyva® (obinutuzumab)?

Gazyva is a type of antibody that targets the CD20 molecule found on B-cells. It is designed to help the immune system destroy B-cells in the body.[1,2]

How Gazyva is believed to work (mechanism of action):[1,3]



Additional Possible Serious Side Effects of Gazyva:

Patients must tell their doctor right away about any side effects they experience. Gazyva can cause side effects that can become serious or life threatening, including:

Infusion Reactions: These side effects may occur during or within 24 hours of any Gazyva infusion. Some infusion reactions can be serious, including, but not limited to, severe allergic reactions (anaphylaxis), acute life-threatening breathing problems, or other life-threatening infusion reactions. If a patient has a reaction, the infusion is either slowed or stopped until the patient's symptoms are resolved. Most patients are able to complete infusions and receive medication again. However, if the infusion reaction is serious, the infusion of Gazyva will be permanently stopped. The patient's healthcare team will take a few steps to help lessen any side effects the patient may have to the infusion process. The patient may be given medicines to take before each Gazyva treatment. Signs of infusion reactions may include: dizziness, nausea, chills, fever, vomiting, diarrhea, breathing problems, and chest pain

Tumor Lysis Syndrome (TLS): Gazyva works to break down cancer cells quickly. As cancer cells break apart, their contents are released into the blood. These contents may cause damage to organs and the heart, and may lead to kidney failure requiring the need for dialysis treatment. The patient's doctor may prescribe medication to help prevent TLS. The patient's doctor will also conduct regular blood tests to check for TLS. Symptoms of TLS may include nausea, vomiting, diarrhea, and tiredness

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Gazyva® (obinutuzumab) Efficacy Profile in First-Line CLL[3]

CLL11 Study

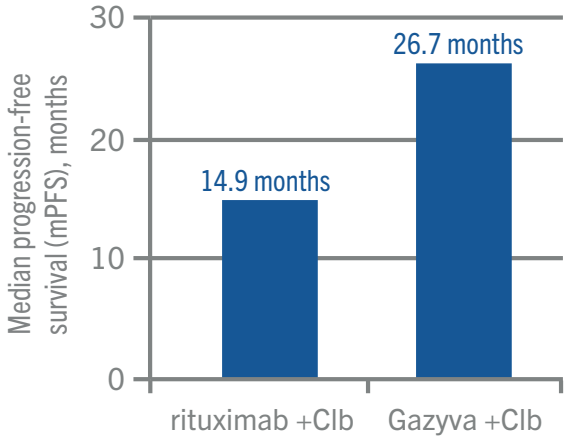
The FDA approval of Gazyva plus chlorambucil (Clb) for previously untreated CLL was based on data from the pivotal Phase III CLL11 study, which investigated Gazyva plus Clb compared to Clb alone, and Gazyva plus Clb compared head-to-head against rituximab plus Clb, in previously untreated people with CLL.

The first stage of the study showed that compared to Clb alone, Gazyva plus Clb significantly reduced the risk of disease progression or death by 81 percent (mPFS 27.2 months vs. 11.2 months; HR=0.19; p<0.0001) and **reduced the risk of death** by 59 percent (overall survival; HR=0.41; 95% CI 0.23-0.74).

The head-to-head stage of the study showed that Gazyva plus Clb significantly reduced the risk of disease progression or death by 58 percent compared to rituximab plus Clb (HR=0.42; p<0.0001).

Median Progression-Free Survival (PFS)

In the CLL11 study, people who received Gazyva plus Clb **lived almost a year longer without the disease getting worse** than people who received rituximab plus Clb.



Additional Possible Serious Side Effects of Gazyva:

Patients must tell their doctor right away about any side effects they experience. Gazyva can cause side effects that can become serious or life threatening, including:

Infections: While a patient is taking Gazyva, the patient may develop infections. Some of these infections may be severe. Fatal infections have been reported, so the patient should be sure to talk to the doctor if the patient thinks the patient has one. Patients with active infection should not be treated with Gazyva. Infections may continue even after the patient stops taking Gazyva. The patient's doctor may prescribe medications to help prevent infections. Symptoms of infection include fever and cough

Low White Blood Cell Count: When a patient has an abnormally low count of infection-fighting white blood cells, it is called neutropenia. While the patient is taking Gazyva, the patient's doctor will do blood work to check the patient's white blood cell counts. Neutropenia can develop during or after treatment with Gazyva. It may also last for more than one month. If a patient's white blood cell count is low, the patient's doctor may prescribe medication to help prevent infections

Low Platelet Count: Platelets help stop bleeding or blood loss. Gazyva may reduce the number of platelets the patient has in the blood. This may affect the clotting process. While the patient is taking Gazyva, the patient's doctor will do blood work to check the patient's platelet count

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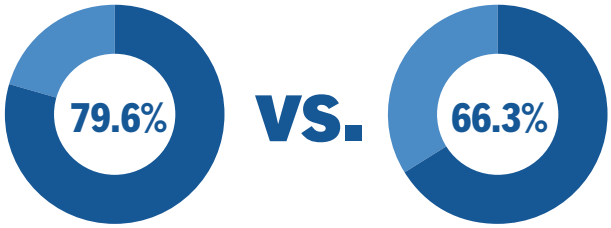
Gazyva® (obinutuzumab) Efficacy Profile in First-Line CLL[3]

CLL11 Study

Additional data from the head-to-head stage of the CLL11 study showed the following:

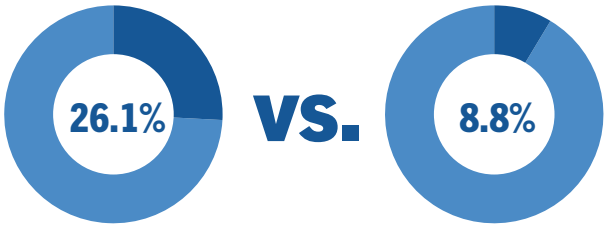
Overall Response Rate (ORR)



79.6% of people responded to Gazyva + Clb

66.3% of people responded to rituximab + Clb

Complete Response (CR) Rate



26.1% of people had a complete response to Gazyva + Clb

8.8% of people had a complete response to rituximab + Clb

A **complete response** means no evidence of the cancer can be detected for a period of time.

Minimal Residual Disease (MRD)

Of the people who achieved a complete response with or without complete recovery from abnormal blood cell counts (CR, CRi):

- **19 percent** (18/94) of people in the Gazyva plus Clb arm compared to **6 percent** (2/34) of people in the rituximab plus Clb arm were **MRD negative in the bone marrow**.
- **41 percent** (39/94) of people in the Gazyva plus Clb arm compared to **12 percent** (4/34) of people in the rituximab plus Clb arm were **MRD negative in the peripheral blood**.

MRD negative means **no residual traces of the cancer were found** using a specific test.

Before receiving Gazyva, patients should talk to their doctor about:

IMMUNIZATIONS: Before receiving Gazyva therapy, the patient should tell the patient's healthcare provider if the patient has recently received or is scheduled to receive a vaccine. Patients who are treated with Gazyva should not receive live vaccines.

PREGNANCY: A patient should tell the doctor if the patient is pregnant, plans to become pregnant, or is breastfeeding. It is not known if Gazyva may harm the patient's unborn baby or pass into the patient's breast milk. The patient should use birth control while using Gazyva and for 12 months after treatment. Mothers who have been exposed to Gazyva during pregnancy should discuss the safety and timing of live virus vaccinations for their infants with their child's healthcare providers. The patient should speak to the doctor about discontinuing Gazyva if the patient is breastfeeding.

Please see the next page and Gazyva full Prescribing Information for Important Safety Information including Most Serious Side Effects.

Additional Safety Information[3]

Most Common Side Effects of Gazyva® (obinutuzumab)

- Infusion reactions
- Low white blood cell counts
- Low platelet counts
- Low red blood cell counts
- Fever
- Cough
- Nausea
- Diarrhea

Patients must tell their doctor about any side effect that bothers them or that does not go away.

These are not all of the possible side effects of Gazyva. For more information, patients should ask their doctor or pharmacist.

Gazyva is available by prescription only.

Study-Specific Safety Profile of Gazyva in First-Line CLL[3]

In the head-to-head stage of the CLL11 study, the most common severe to life-threatening side effects (Grade 3-4) that occurred in at least 2 percent more people in the Gazyva plus Clb arm compared to the rituximab plus Clb arm were low white blood cell counts (neutropenia, 33% vs. 28%; leukopenia, 4% vs. <1%), infusion reactions (20% vs. 4%), and low platelet counts (thrombocytopenia, 10% vs. 3%).

In the first stage of the CLL11 study, the most common severe to life-threatening side effects (Grade 3-4) that occurred in at least 2 percent more people in the Gazyva plus Clb arm compared to the Clb alone arm were low white blood cell counts (neutropenia, 35% vs. 16%; leukopenia, 5% vs. 0%), infusion reactions (21% vs. 0%), and low platelet counts (thrombocytopenia, 11% vs. 4%).

Additional Information

Report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch.
Report side effects to Genentech at (888) 835-2555.

Please visit www.Gazyva.com for the full Prescribing Information, including Boxed WARNINGS, for additional Important Safety Information.

Visit Genentech Access Solutions (www.GenentechAccessSolutions.com) for coverage and reimbursement support, patient assistance and information resources.

References

1. Goede V., Fischer K., Busch R., Engelke A., Eichhorst B., Wendtner C.M., … Hallek M. Obinutuzumab plus chlorambucil in patients with CLL and coexisting conditions. *N Engl J Med*. January 8 2014; DOI: 10.1056/NEJMoa1313984.
2. Leukemia & Lymphoma Society. Chronic Lymphocytic Leukemia. http://www.lls.org/content/nationalcontent/resourcecenter/freeeducationmaterials/leukemia/pdf/cll.pdf. Accessed September 22, 2014.
3. Gazyva (obinutuzumab) Injection Prescribing Information. Genentech, Inc. December 2014.
4. American Cancer Society. *Cancer Facts & Figures 2015*. Atlanta: American Cancer Society; 2015.