

MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG**Novartis drug Arzerra[®] improved median progression-free survival by 54% in patients with relapsed chronic lymphocytic leukemia**

- *Arzerra significantly improved PFS when added to fludarabine + cyclophosphamide (median 28.9 mos vs 18.8 mos) after initial treatment stopped working*
- *Patients receiving Arzerra plus existing CLL treatments also had a higher overall response rate (84% vs 68%) compared to fludarabine and cyclophosphamide alone*
- *Chronic lymphocytic leukemia (CLL) is the most commonly diagnosed adult leukemia in Western countries, accounting for approximately 1 in 4 cases of all leukemia^{1,2}*

Basel, June 12, 2015 – Novartis today announced data from the Phase III COMPLEMENT 2 study showing that treatment with Arzerra[®] (ofatumumab) plus fludarabine and cyclophosphamide significantly improved median progression-free survival (PFS) by 54% compared to treatment with fludarabine and cyclophosphamide alone (28.9 months vs 18.8 months, respectively; $p=0.0032$) in patients with relapsed chronic lymphocytic leukemia (CLL). Results are being presented at the 20th Congress of the European Hematology Association (EHA) in Vienna.

“There are limited treatment options for patients who have stopped responding to current CLL treatments, which happens in many patients with this disease over time,” said Tadeusz Robak, Professor of Hematology, Department of Hematology, Medical University of Lodz and Copernicus Memorial Hospital, Lodz, Poland. “These data showed that the addition of ofatumumab to fludarabine and cyclophosphamide extended the amount of time before a patient’s CLL progressed, and further add to the body of evidence supporting the potential use of ofatumumab for these patients.”

The most commonly diagnosed adult leukemia in Western countries, CLL accounts for approximately 1 in 4 cases of leukemia^{1,2}. Most CLL patients experience disease progression despite initial response to therapy and may require additional treatment³.

In this clinical study, median PFS was improved by 54% in patients receiving Arzerra[®] (ofatumumab) in combination with fludarabine and cyclophosphamide ($n=183$) compared to those receiving fludarabine and cyclophosphamide alone (28.9 months vs 18.8 months, respectively; HR 0.67 [95% CI: 0.51, 0.88]; $p=0.0032$). Additionally, patients receiving ofatumumab in combination with fludarabine and cyclophosphamide had a higher overall response rate (ORR) compared to those receiving fludarabine and cyclophosphamide alone (84% vs 68% of patients, respectively; $p=0.0003$), with a better complete response (CR) rate (27% vs 7% of patients, respectively), compared to those receiving fludarabine and cyclophosphamide alone ($n=182$). Median overall survival (OS) was 56.4 months for patients receiving ofatumumab in combination compared to 45.8 months for patients receiving fludarabine and cyclophosphamide alone (HR 0.78 [95% CI: 0.56, 1.09]; $p=0.1410$). The safety profile observed in this trial was consistent with other trials of ofatumumab and no new safety signals were observed. The most common AEs ($\geq 5\%$) reported were neutropenia, thrombocytopenia, anemia, nausea, leukopenia, vomiting, pyrexia, rash, fatigue, and pneumonia.

“The results from the COMPLEMENT 2 study validate the benefit of Arzerra treatment in combination with fludarabine and cyclophosphamide in certain patients with CLL,” said Alessandro Riva, MD, Global Head, Novartis Oncology Development and Medical Affairs. “We look forward to sharing the data with regulatory authorities.”

About COMPLEMENT 2

COMPLEMENT 2 ([NCT00824265](https://clinicaltrials.gov/ct2/show/study/NCT00824265)) is an open-label, two-arm, randomized, Phase III study, which included 365 patients with relapsed CLL in 18 countries. Patients in the study were randomized 1:1 to receive treatment with up to six cycles of Arzerra® (ofatumumab) in combination with fludarabine and cyclophosphamide or up to six cycles with fludarabine and cyclophosphamide alone.

The primary endpoint of the study was PFS as assessed by an Independent Review Committee (IRC) according to the International Workshop for Chronic Lymphocytic Leukaemia (iwCLL) updated 2008 National Cancer Institute-sponsored Working Group (NCIWG) guidelines⁴. Secondary endpoints included ORR, CR, OS, patient reported outcomes, time to response, duration of response (DoR), time to progression, time to next therapy (TTNT), safety assessments, and quality of life.

Results from additional secondary endpoints showed that DoR was 29.6 months vs 24.9 months, respectively (HR 0.77 [95% CI: 0.56, 1.05]; p=0.0878) for the patients receiving ofatumumab in combination compared to those receiving fludarabine and cyclophosphamide alone. Time to progression was 42.1 months in those receiving ofatumumab in combination compared to 26.8 months in those receiving fludarabine and cyclophosphamide alone (HR 0.63 [95% CI: 0.45, 0.87]; p=0.0036).

More patients receiving ofatumumab in combination (74%) experienced grade 3 or greater adverse events (AEs) compared to those receiving fludarabine and cyclophosphamide alone (69%). A higher incidence of Grade ≥3 neutropenia was observed in patients receiving ofatumumab with fludarabine and cyclophosphamide compared with those receiving fludarabine and cyclophosphamide alone (53% vs 39%, respectively) but a substantially higher rate of infection was not reported. Grade 3/4 infusion-related reactions (IRRs) were reported in 4% of patients receiving ofatumumab in combination with fludarabine and cyclophosphamide. IRRs led to discontinuation of study treatment in <1% of patients receiving ofatumumab in combination with fludarabine and cyclophosphamide. No fatal IRRs were reported.

Arzerra is not approved in combination with fludarabine and cyclophosphamide for relapsed CLL. Novartis will further analyze data from the COMPLEMENT 2 study and plans to share the results with regulatory agencies to evaluate the potential for future regulatory filings.

About Arzerra

Arzerra® (ofatumumab) is a human monoclonal antibody that is designed to target the CD20 molecule found on the surface of chronic lymphocytic leukemia (CLL) cells and normal B lymphocytes.

In the United States, Arzerra is approved for use in combination with chlorambucil for the treatment of previously untreated patients with CLL for whom fludarabine-based therapy is considered inappropriate. In the European Union, Arzerra is approved for use in combination with chlorambucil or bendamustine for the treatment of patients with CLL who have not received prior therapy and who are not eligible for fludarabine-based therapy. Arzerra is also approved for first-line use in Russia, Iceland, Norway, Luxembourg and Brazil.

In more than 50 countries worldwide, Arzerra is also indicated as monotherapy for the treatment of patients with CLL who are refractory after prior treatment with fludarabine and alemtuzumab.

Arzerra is marketed under a co-development and collaboration agreement between Genmab and Novartis, as successor in interest to GSK.

Important Safety Information for Arzerra (ofatumumab)

Treatment with Arzerra may cause side effects, some of which are serious and life-threatening.

Treatment with Arzerra may cause a side effect called an infusion reaction, which may be serious. Before treatment with Arzerra, doctors will prescribe 3 types of medicine to their patients to help reduce the risk of an infusion reaction, including a steroid (to reduce swelling and other symptoms of inflammation), a pain reliever, and an antihistamine (to reduce allergic reactions). Even though patients receive these medicines, they may still have an infusion reaction. If an infusion reaction occurs, the doctor will stop their patient's treatment with Arzerra so the infusion reaction can be treated. Patients should tell their doctor or seek medical treatment right away if they have any of these symptoms while receiving Arzerra or within 24 hours after receiving Arzerra: fever, chills, rash, hives, chest pain, back pain, stomach pain, swelling, dizziness, blurred vision, drowsiness, headache, cough, wheezing, or trouble breathing.

Treatment with Arzerra may cause hepatitis B virus (HBV) infection to reoccur, which may cause serious liver problems and death. Patients who are newly exposed to HBV during or following treatment with Arzerra may experience serious liver problems and death. Patients should tell their doctor if they have had HBV infection or are a carrier of HBV. Before starting Arzerra, doctors will do a blood test to check for HBV infection. In some patients, additional blood tests may be done during and several months after treatment. Patients should call their doctor right away if they feel more tired than usual or notice a yellowing of the skin or eyes. These may be symptoms of hepatitis.

Progressive multifocal leukoencephalopathy (PML) is a rare brain infection that can occur with treatment with Arzerra. PML causes severe disability and can lead to death. Patients should call their doctor right away if they notice new medical problems or problems that are getting worse, such as confusion, dizziness or loss of balance, difficulty talking or walking, or strength, vision or other problems that have lasted over several days.

Tumor lysis syndrome (TLS), including the need for a hospital stay, can occur with treatment with Arzerra. TLS is caused by the fast breakdown of cancer cells, which then release their contents into the blood. This may lead to serious problems, including kidney failure or an abnormal heartbeat. Doctors may do a blood test to check their patients for TLS and may give medicines before starting treatment with Arzerra to help prevent TLS.

Arzerra can cause low blood cell counts (white blood cells, platelets, and red blood cells). These low blood cell counts can be severe and, in some cases, lead to death. Low white blood cells counts (neutropenia), can happen during treatment. Neutropenia can occur 42 days or longer after the end of treatment with Arzerra and may also last between 24 and 42 days after the last treatment dose. Doctors should regularly check their patient's blood to see if they have low blood cell counts. Patients should call their doctor right away if they have any bleeding, bruising, red or purple spots on their skin, paleness, worsening weakness, tiredness, cough that will not go away, fever, chills, congestion, or any flu-like symptoms while receiving Arzerra.

After a patient receives Arzerra, they should not receive live vaccines until the doctor who prescribed Arzerra has told them that they may do so.

The most common side effects with Arzerra include infusion reactions, feeling tired, low white blood cell count, shortness of breath, pneumonia, rash, fever, nausea, cough, bronchitis, diarrhea, upper respiratory tract infection, and low red blood cell count.

Treatment with Arzerra can increase patients' chances for getting infections. Some infections, such as pneumonia, bronchitis, and sepsis (a blood infection), can be serious, and in some cases, life-threatening. Patients should call their doctor right away if they have a cough that will not go away, fever, chills, congestion, or any flu-like symptoms while receiving Arzerra. These symptoms may be signs of a serious infection.

Please see full [US Prescribing Information](#), including Boxed WARNING, for Arzerra (ofatumumab).

Please see full [EU Summary of Product Characteristics](#) for Arzerra.

Disclaimer

The foregoing release contains forward-looking statements that can be identified by words such as "potential," "may," "look forward," "will," "plans," "future," or similar terms, or by express or implied discussions regarding potential new indications or labeling for Arzerra, or regarding potential future revenues from Arzerra. You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that Arzerra will be submitted or approved for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that Arzerra will be commercially successful in the future. In particular, management's expectations regarding Arzerra could be affected by, among other things, the uncertainties inherent in research and development, including unexpected clinical trial results and additional analysis of existing clinical data; unexpected regulatory actions or delays or government regulation generally; the company's ability to obtain or maintain proprietary intellectual property protection; general economic and industry conditions; global trends toward health care cost containment, including ongoing pricing pressures; unexpected manufacturing issues, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Novartis

Novartis provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care and cost-saving generic pharmaceuticals. Novartis is the only global company with leading positions in these areas. In 2014, the Group achieved net sales of USD 58.0 billion, while R&D throughout the Group amounted to approximately USD 9.9 billion (USD 9.6 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 120,000 full-time-equivalent associates. Novartis products are available in more than 180 countries around the world. For more information, please visit <http://www.novartis.com>.

Novartis is on Twitter. Sign up to follow @Novartis at <http://twitter.com/novartis>.

Arzerra is a trademark of Novartis Pharma AG.

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