



Rituxan in Combination with Chemotherapy Improves Progression-Free Survival in Difficult-to-Treat Form of Blood Cancer

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Results of Two Large Phase III Trials (CLL8 and REACH) Show Rituxan plus Chemotherapy Delayed Disease Progression in First- and Second-line Chronic Lymphocytic Leukemia

SOUTH SAN FRANCISCO, Calif. & CAMBRIDGE, Mass.--([BUSINESS WIRE](#))--Genentech, Inc. (NYSE:DNA) and Biogen Idec (Nasdaq:BIIB) today announced that two global Phase III studies in chronic lymphocytic leukemia (CLL), CLL8 and REACH, showed Rituxan® (rituximab) plus chemotherapy significantly increased the time patients lived without their disease advancing, as defined by the primary endpoint of progression-free survival (PFS), when compared to chemotherapy alone. No new safety signals were observed in either of these studies and the safety profile was consistent with previous experience with Rituxan. Results from both studies were featured today during a press briefing at the 50th Annual Meeting of the American Society of Hematology (ASH) in San Francisco.

"These are among the largest studies ever conducted in chronic lymphocytic leukemia and are significant for patients with newly diagnosed or relapsed disease," said David Schenkein, M.D., Genentech's senior vice president, Clinical Oncology and Hematology. "These data show that adding Rituxan to chemotherapy improved both progression-free survival and reduced patients' tumor burden."

In CLL8, patients who received Rituxan plus chemotherapy first-line had a 69 percent improvement in PFS compared to patients receiving chemotherapy alone (based on a hazard ratio of 0.59; $p < 0.0001$). The improvement in PFS can also be referred to as a 41 percent reduction in the risk of cancer progression or death. Patients who received Rituxan plus chemotherapy had a median PFS of 42.8 months compared to 32.3 months for those who received chemotherapy alone.

In REACH, patients who received Rituxan plus chemotherapy second-line experienced a 54 percent improvement in PFS compared to patients receiving chemotherapy alone (based on a hazard ratio of 0.65; $p = 0.0002$) as assessed by the treating physicians in the study (investigator-assessed). The improvement in PFS can also be referred to as a 35 percent reduction in the risk of cancer progression or death. Patients who received Rituxan plus chemotherapy had a median PFS of 30.6 months compared to 20.6 months for those who received chemotherapy alone.

An independent review of the PFS primary endpoint for REACH is expected to be complete early next year for U.S. regulatory purposes.

"Adding Rituxan to chemotherapy may be an additional option beyond chemotherapy alone for the more than 90,000 patients living with this incurable disease," said Cecil Pickett, Ph.D., Biogen Idec's president of Research and Development. "We plan to work with Genentech to submit the data from both CLL8 and REACH to the FDA for potential new indications for Rituxan in first- and second-line CLL."

Additional CLL8 Results

Immunotherapy with Fludarabine, Cyclophosphamide and Rituximab (FCR) Versus Fludarabine and Cyclophosphamide (FC) Improves Response Rates and Progression-Free Survival (PFS) of Previously Untreated Patients with Advanced Chronic Lymphocytic Leukemia (CLL) (Abstract #325) Michael Hallek, M.D., University of Cologne, Cologne, Germany; Monday, December 8, 2008, 11:00 a.m.; Halls B & C (Moscone Center).

The overall response rate in patients receiving Rituxan plus chemotherapy first-line was 93 percent compared to 85 percent in those receiving chemotherapy alone. Complete response was achieved in 45 percent of patients compared to 23 percent, respectively.

The most common adverse events that occurred more often in the Rituxan plus chemotherapy arm included blood and lymphatic system disorders, infections and neoplasms. Severe Grade 3 or greater events that occurred more often in the Rituxan plus chemotherapy arm included hematologic toxicity (56 percent vs. 39 percent), neutropenia (34 percent vs. 21 percent) and leukocytopenia (24 percent vs. 12 percent).

Additional REACH Results

Rituximab, Fludarabine, and Cyclophosphamide (R-FC) Prolongs Progression-Free Survival in Relapsed or Refractory Chronic Lymphocytic Leukemia (CLL) Compared with FC Alone: Final Results from the International Randomized Phase III REACH Trial (Abstract #15742) Tadeusz Robak, M.D., Dept. of Hematology, Medical University, Lodz, Poland; Tuesday, December 9, 2008, 7:30 a.m.; Halls B & C (Moscone Center).

The overall response rate in patients receiving Rituxan plus chemotherapy second-line was 70 percent compared to 58 percent in those receiving chemotherapy alone. Complete response was achieved in 24 percent of patients compared to 13 percent, respectively.

The most common adverse events that occurred more often in the Rituxan plus chemotherapy arm included blood and lymphatic system disorders, infections and neoplasms. Grade 3 or greater events such as neutropenia (42 percent vs. 40 percent), febrile neutropenia (15 percent vs. 12 percent) and neoplasms (7 percent vs. 3 percent) occurred more often in the Rituxan plus chemotherapy arm.

About the CLL8 and REACH Studies

Sponsored by Roche and conducted by the German CLL Study Group, CLL8 is a global, multi-center, randomized, open-label, Phase III study that enrolled 817 patients with previously untreated (first-line) CD20-positive CLL. REACH is a global, multi-center, randomized, open-label, Phase III study that enrolled 552 patients with previously treated (second-line) CD20-positive CLL sponsored by Genentech, Biogen Idec and Roche. Both studies evaluated Rituxan plus fludarabine and cyclophosphamide chemotherapy compared with fludarabine and cyclophosphamide alone. The primary endpoint of both studies was progression-free survival. Secondary endpoints for both studies included overall survival, event-free survival, duration of response, response rate and complete response.

About Chronic Lymphocytic Leukemia

CLL is a chronic disease that affects adults over the age of 60 and is a slow-growing type of leukemia where excess mature B-cells are found in the bone marrow. According to the American Cancer Society (ACS), CLL is the most common form of leukemia in adults, accounting for one-third of all leukemias in the U.S. More than 90,000 people are currently living with CLL. The ACS estimates that 15,000 new cases will be diagnosed and approximately 4,400 people will die from CLL this year.

About Rituxan

Rituxan is a therapeutic antibody that binds to a particular protein, the CD20 antigen found on the surface of malignant cells as well as normal B-cells. In cancer and autoimmune disorders such as rheumatoid arthritis (RA), Rituxan works with the body's natural defenses to attack and kill the marked B-cells. Stem cells (B-cell progenitors) in bone marrow lack the CD20 antigen, allowing healthy B-cells to regenerate after treatment and return to normal levels in about 12 months for most patients.

Rituxan first received FDA approval in November 1997 for the treatment of relapsed or refractory, low-grade or follicular, CD20-positive, B-cell non-Hodgkin's lymphoma (NHL) as a single agent. It was also approved in the European Union under the trade name MabThera® in June 1998. Rituxan is also approved for the treatment of NHL for the following:

- Previously untreated patients with follicular, CD20-positive, B-cell NHL in combination with CVP (cyclophosphamide, vincristine and prednisolone) chemotherapy.
- The treatment of non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single agent, after first-line CVP chemotherapy.
- Previously untreated diffuse large B-cell, CD20-positive, NHL in combination with CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) or other anthracycline-based chemotherapy regimens.

Rituxan received FDA approval for rheumatoid arthritis in February 2006 and is currently indicated:

- In combination with methotrexate (MTX) to reduce signs and symptoms in adult patients with moderately-to-severely active RA who have had an inadequate response to one or more tumor necrosis factor (TNF)-antagonist therapies.
- In combination with MTX to slow the progression of structural damage in adult patients with moderately-to-severely active RA who have had an inadequate response to one or more TNF-antagonist therapies.

Genentech and Biogen Idec co-market Rituxan in the U.S., and Roche markets MabThera in the rest of the world, except Japan, where Rituxan is co-marketed by Chugai and Zenyaku Kogyo Co. Ltd.

Rituxan Safety

Rituxan has been associated with **fatal infusion reactions, tumor lysis syndrome (TLS), severe mucocutaneous reactions and progressive multifocal leukoencephalopathy (PML).**

Hepatitis B reactivation with fulminant hepatitis, other viral infections, cardiovascular events, renal toxicity, and bowel obstruction and perforation have also been observed. Patients should be closely observed for signs of infection if biologic agents and/or disease-modifying anti-rheumatic drugs (DMARDs) other than MTX are used concomitantly.

The most common adverse reactions observed in Rituxan-treated RA patients are hypertension, nausea, upper respiratory tract infection, arthralgia, pruritus and pyrexia.

The most common adverse reactions observed in Rituxan-treated NHL patients (incidence greater than or equal to 25 percent) are infusion reactions, fever, chills, infection, asthenia and lymphopenia.

For additional safety information, please see the full prescribing information, including Boxed Warnings and Medication Guide, at 1-800-821-8590 or visit <http://www.gene.com>.

About Genentech

Founded more than 30 years ago, Genentech is a leading biotechnology company that discovers, develops, manufactures and commercializes medicines for patients with significant unmet medical needs. The company has headquarters in South San Francisco, California, and is listed on the New York Stock Exchange under the symbol DNA. For additional information about the company, please visit <http://www.gene.com>.

About Biogen Idec

Biogen Idec creates new standards of care in oncology, neurology and immunology. As a global leader in the development, manufacturing and commercialization of novel therapies, Biogen Idec transforms scientific discoveries into advances in human healthcare. For product labeling, press releases and additional information about the company, please visit <http://www.biogenidec.com>.

This press release contains a forward-looking statement regarding Rituxan as a treatment option for CLL patients. Such statement is forward looking and involves risks and uncertainties such that actual results may differ materially. Actual results may be affected by a number of factors including, but not limited to, unexpected safety, efficacy or manufacturing issues, the need for additional data, data analysis or clinical studies, FDA actions or delays, failure to obtain or maintain FDA approval, competition, pricing, reimbursement, the ability to supply product, product withdrawals and new product approvals and launches, and intellectual property or contract rights. Please also refer to the risk factors described in Genentech and Biogen Idec's periodic reports filed with the Securities and Exchange Commission. Genentech and Biogen Idec disclaim, and do not undertake, any obligation to update or revise any forward-looking statements in this press release.

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