



Phase III Study Showed Rituxan® for Initial Use Followed by Continued Use Delayed the Need for Additional Therapy in People with Asymptomatic Follicular Lymphoma, a Common Type of Blood Cancer

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Rituxan Decreased the Risk of Needing Later Treatment with Chemotherapy or Radiotherapy by 80 Percent

SOUTH SAN FRANCISCO, Calif. & WESTON, Mass.--([BUSINESS WIRE](#))--[Genentech](#), Inc., a member of the Roche Group (SIX: RO, ROG; OTCQX: RHHBY), and Biogen Idec (Nasdaq: BIIB) announced today positive data from a Phase III study of [Rituxan](#) (rituximab) in patients with advanced follicular lymphoma who did not have symptoms of disease (asymptomatic disease).

Based on results from previous studies that showed no benefit of immediate chemotherapy after diagnosis, asymptomatic patients are managed by a "watchful waiting" approach and treatment for these patients usually does not begin until specific symptoms occur or their disease worsens. This study showed that immediate administration of single-agent Rituxan (induction), followed by continued use of Rituxan (maintenance) delayed the need for chemotherapy or radiotherapy and decreased the risk of the disease worsening (progression-free survival or PFS), compared to watchful waiting. The safety profile was consistent with previous experience with Rituxan.

The data were featured today during a press briefing at the 52nd Annual Meeting of the American Society of Hematology (ASH) in Orlando, Fla. Full study results will be presented by Kirit Ardeshtna, M.D., today at 3:15 p.m. EST.

"These are the first Phase III data to have shown that initial use of Rituxan monotherapy as induction followed by maintenance had an impact in patients with asymptomatic follicular lymphoma, a disease that is commonly treated only after symptoms appear," said Hal Barron, M.D., executive vice president, Product Development and chief medical officer. "Early treatment interventions in prior studies in this population were not considered to provide meaningful clinical benefit. In this study, the use of Rituxan delayed the need for additional treatment."

The Phase III results showed that immediate use of Rituxan monotherapy as induction followed by maintenance when compared to watchful waiting, decreased the risk of needing additional therapy by 80 percent (hazard ratio of 0.20, 95 percent CI, 0.13-0.29, $p < 0.001$) and decreased the risk of their disease worsening (PFS) by 79 percent (based on a hazard ratio of 0.21, 95 percent CI, 0.15-0.29, $p < 0.001$). The median time to initiation of new therapy (chemotherapy or radiotherapy) for patients managed by watchful waiting was 34 months and the median PFS was 23 months. However, in patients given immediate Rituxan followed by maintenance, the median of these parameters was significantly longer ($p < 0.0001$) and has not been reached after four years. Serious adverse events Grade 3 or higher in patients treated with Rituxan in this study included infection (4 percent), allergy (3 percent), neutropenia (3 percent) and neutropenic sepsis (1 percent).

About the "Watch and Wait" Study

Sponsored by University College London Hospitals, this Phase III study was an international, multicenter, randomized, trial that enrolled 462 patients with previously untreated asymptomatic Stage II-IV follicular lymphoma. The trial compared the safety and efficacy profile of first-line induction followed by maintenance use of Rituxan alone (four weekly doses followed by maintenance doses once every two months for two years) compared to careful observation (i.e., watchful waiting). Patients were randomized to receive one of the following:

- Arm A: No therapy/watchful waiting
- Arm B: Rituxan alone (375mg/m² weekly) for four cycles only (without maintenance Rituxan)
- Arm C: Rituxan alone (375mg/m² weekly) for four cycles followed by Rituxan maintenance, given once every two months for two years

Three years after the enrollment of the first patient, the Rituxan arm that did not include maintenance (Arm B) was closed because of emerging evidence of Rituxan efficacy in the maintenance setting. The trial was then amended to compare Rituxan maintenance following initial use of Rituxan alone to watchful waiting (Arm C compared to Arm A).

About Follicular Lymphoma

Follicular lymphoma, a cancer of the blood, is a common type of [non-Hodgkin's lymphoma](#) (NHL), which is slow-growing and characterized by periods of relapse and remission. Follicular lymphoma unfortunately remains incurable and despite substantial progress, patients ultimately relapse and require additional treatment. An estimated 65,540 people in the US were diagnosed with NHL in 2010, and follicular lymphoma accounts for between 15 and 20 percent of these cases. The disease can occur at any time during adulthood, though people are typically diagnosed during their 50s and 60s, affecting both men and women.

About Rituxan

Rituxan is a therapeutic antibody that binds to a specific protein called CD20 found on the surface of cancerous and normal B-cells. In NHL and rheumatoid arthritis (RA), Rituxan works with the body's own immune system to eliminate marked CD20-positive B-cells. Stem cells (B-cell progenitors, those cells that give rise to B-cells) in bone marrow do not have the CD20 protein. B-cells usually regenerate after Rituxan treatment and return to normal levels in about 12 months for most patients.

Rituxan, discovered by Biogen Idec, first received FDA approval in November 1997 for the treatment of relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL as a single agent. It was approved in the European Union under the trade name MabThera in June 1998. Rituxan is also approved for the treatment of NHL and chronic lymphocytic leukemia (CLL) as follows:

- Previously untreated follicular, CD20-positive, B-cell NHL in combination with first-line chemotherapy.
- 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 or other anthracycline-based chemotherapy regimens.
- Previously untreated and previously treated CD20-positive CLL in combination with fludarabine and cyclophosphamide (FC).

Rituxan received FDA approval for RA in February 2006 and is currently indicated in combination with methotrexate (MTX) in adult patients with moderately-to-severely active RA who have had inadequate response to one or more TNF antagonist therapies.

People with serious infections should not receive Rituxan.

Genentech and Biogen Idec collaborate on Rituxan in the United States 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 can cause serious side effects that can lead to death, including: **infusion reactions, tumor lysis syndrome (kidney failure due to fast breakdown of cancer cells), severe skin and mouth reactions, and progressive multifocal leukoencephalopathy (a rare, serious brain infection).**

Rituxan has also been associated with serious and life-threatening side effects, including: the return of active hepatitis B virus infection with sudden and serious liver problems including liver failure, and death, other serious infections that can lead to death, heart problems, kidney problems, and stomach and serious bowel problems including blockage and tears in the bowel, that can sometimes lead to death.

Other serious, potentially life-threatening side effects seen in RA patients are: hepatitis B infection that may become active again, other infections, heart problems, and low blood cell counts. The most common side effects of Rituxan seen in patients with NHL were infusion reactions, fever, chills, low white blood cells, infections, body aches, and tiredness. The most common side effects of Rituxan in patients with CLL were infusion reactions and low white blood cells. Common side effects in patients with RA include infections and infusion reactions. Patients should talk to their doctor about their medical history before starting treatment with Rituxan.

Patients should 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 with Rituxan.

Patients should read the Rituxan Full Prescribing Information including Boxed WARNINGS, and the Medication Guide at <http://www.rituxan.com>.

About Genentech

Founded more than 30 years ago, Genentech is a leading biotechnology company that discovers, develops, manufactures and commercializes medicines to treat patients with serious or life-threatening medical conditions. The company, a member of the Roche Group, has headquarters in South San Francisco, California. For additional information about the company, please visit <http://www.gene.com>.

About Biogen Idec

Biogen Idec uses cutting edge science to discover, develop, manufacture and market biological products for the treatment of serious diseases with a focus on neurological disorders. Founded in 1978, Biogen Idec is the world's oldest independent biotechnology company. Patients worldwide benefit from its leading multiple sclerosis therapies, and the company generates more than \$4 billion in annual revenues. For product labeling, press releases and additional information about the company, please visit <http://www.biogenidec.com>.

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