

Basel, 31 January 2011

FDA approves Rituxan/MabThera for first-line maintenance use in follicular lymphoma

Approval provides option that improves the length of time people with incurable blood cancer live without the disease worsening

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the U.S. Food and Drug Administration (FDA) approved Rituxan/MabThera (rituximab) as a maintenance treatment for patients with advanced follicular lymphoma who responded to initial treatment with Rituxan/MabThera plus chemotherapy (induction treatment). This milestone follows the clearance of MabThera for this indication by the European Commission in October 2010.

“This approval is important because it shows that maintenance treatment with Rituxan/MabThera after initial therapy with Rituxan/MabThera and chemotherapy, further reduces the risk of relapse in people with follicular lymphoma,” said Hal Barron, M.D., Head of Global Development and Chief Medical Officer at Roche. “Maintenance use of Rituxan/MabThera offers people with this incurable disease the opportunity to live longer without their disease getting worse, a primary goal of treatment.”

Follicular lymphoma is considered incurable and is characterised by periods of relapse and remission over a number of years. This approval, based on the PRIMA study, showed continuing Rituxan/MabThera administration every two months for two years in patients who responded to initial treatment with Rituxan/MabThera plus chemotherapy, nearly doubled the likelihood of them living without their disease worsening (progression-free survival or PFS) compared to those who stopped treatment (based on a hazard ratio of 0.54, 95% CI, 0.42–0.70; $p \leq 0.0001$).

According to the American Cancer Society, an estimated 574,000 Americans are living with non-Hodgkin’s lymphoma (NHL). Approximately 65,540 Americans will have been newly diagnosed with NHL in the United States in 2010. Of those diagnosed with NHL, 1 in 5 patients will have follicular lymphoma.

About PRIMA

This approval was based on data from a Phase III study, PRIMA. Sponsored by the Groupe d'Etude des Lymphomes de l'Adulte (GELA), PRIMA is an international, multicenter, randomised, phase III clinical study that enrolled 1,217 patients with previously untreated advanced follicular lymphoma. The study evaluated the efficacy and safety profile of maintenance Rituxan/MabThera in patients who achieved a response (complete or partial) to Rituxan/MabThera in combination with chemotherapy.

In the study, eight cycles of Rituxan/MabThera plus either CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone), CVP (cyclophosphamide, vincristine and prednisone) or FCM (fludarabine, cyclophosphamide and mitoxantrone) chemotherapy was used as initial treatment. Patients who responded to this initial treatment and were eligible for maintenance treatment (1,018/1,217) were randomised to receive Rituxan/MabThera as a single-agent maintenance therapy, given once every two months for two years (maintenance), or to observation alone.

The safety profile was consistent with those previously reported in pivotal studies of Rituxan/MabThera alone or in combination with chemotherapy. Grade ≥ 2 infections were reported more frequently in patients who received Rituxan/MabThera maintenance compared to the observation arm (37% vs. 22%). Grade 3-4 adverse reactions occurring at a higher incidence ($\geq 2\%$) in the Rituxan/MabThera group were infections (4% vs. 1%) and neutropenia (4% vs. $<1\%$).

About Follicular Lymphoma

Follicular lymphoma (FL), a cancer of the blood, is a common type of non-Hodgkin's lymphoma (NHL). Approximately 286,000 people worldwide are diagnosed with NHL each yearⁱ, and FL accounts for about 1 in 5 of these cases. Follicular lymphoma unfortunately remains incurable and despite substantial progress, patients ultimately relapse and relapses require additional treatments and can lead to fatal outcomes.

Follicular lymphoma can occur at any time during adulthood, though people are typically diagnosed during their fifties and sixties, affecting both men and women.

About Rituxan/MabThera

Rituxan/MabThera is a therapeutic antibody that binds to a particular protein - the CD20 antigen - on the surface of normal and malignant B-cells. It then recruits 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 within several months.

Rituxan/MabThera, 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 EU under the trade name MabThera in June 1998. Over 2.1 million patient exposures with MabThera/Rituxan have been recorded worldwide since launch, 2.0 million in haematological malignancies.

MabThera is known as Rituxan in the United States, Japan and Canada. Genentech and Biogen Idec collaborate on Rituxan in the United States, and Roche markets MabThera in the rest of the world, except Japan, where MabThera is co-marketed by Chugai and Zenyaku Kogyo Co. Ltd.

In oncology, Rituxan (rituximab) is indicated in the US:

- For the treatment of NHL and chronic lymphocytic leukemia (CLL) as follows:
 - Relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL as a single agent;
 - Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and as a single-agent maintenance therapy after achieving a response to Rituxan in combination with 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).

In oncology, MabThera (rituximab) is indicated in the EU:

- For the treatment of patients with previously untreated or relapsed/refractory chronic lymphocytic leukemia (CLL) in combination with chemotherapy; only limited data are available on efficacy and safety for patients previously treated with monoclonal antibodies including MabThera or patients refractory to previous MabThera plus chemotherapy;
- For the treatment of previously untreated patients with stage III-IV follicular lymphoma in combination with chemotherapy;
- As maintenance treatment for patients with follicular lymphoma responding to induction therapy;

- For the treatment of patients with CD20 positive diffuse large B cell non-Hodgkin's lymphoma in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone) chemotherapy;
- As monotherapy for treatment of patients with stage III-IV follicular lymphoma who are chemoresistant or are in their second or subsequent relapse after chemotherapy.

Rituxan/MabThera in Rheumatology

In the US: Rituxan received FDA approval for rheumatoid arthritis in February 2006 and is currently indicated in combination with methotrexate (MTX) to reduce signs and symptoms and to slow the progression of structural damage in adult patients with moderately-to severely-active rheumatoid arthritis who have had inadequate response to one or more TNF antagonist therapies.

In the EU: MabThera in combination with methotrexate is indicated for the treatment of adult patients with severe active rheumatoid arthritis who have had an inadequate response to initial anti-TNF therapy. MabThera offers a superior clinical response over a second anti-TNF.

About Roche

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's largest biotech company with truly differentiated medicines in oncology, virology, inflammation, metabolism and CNS. Roche is also the world leader in in-vitro diagnostics, tissue-based cancer diagnostics and a pioneer in diabetes management. Roche's personalised healthcare strategy aims at providing medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2009, Roche had over 80'000 employees worldwide and invested almost 10 billion Swiss francs in R&D. The Group posted sales of 49.1 billion Swiss francs. Genentech, United States, is a wholly owned member of the Roche Group. Roche has a majority stake in Chugai Pharmaceutical, Japan. For more information: www.roche.com.

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Additional information

- Roche in Oncology: http://www.roche.com/media_backgroundunder/media_oncology.htm
- Cancer: www.health-kiosk.ch/start_krebs.htm

- World Health Organization: www.who.int
- Groupe d'Etude des Lymphomes de l'Adulte (GELA): www.gela.org

Roche Group Media Relations

Phone: +41 -61 688 8888 / e-mail: basel.mediaoffice@roche.com

- Alexander Klauser (Head)
- Silvia Dobry
- Daniel Grotzky
- Claudia Schmitt
- Annette Walz

References

ⁱ <http://www.lymphoalition.org/types-of-lymphomas/non-hodgkin-lymphoma.html> accessed November 2010