Investor Update

Thursday, June 17, 2004 8:03 AM

Study in New England Journal of Medicine shows MabThera (rituximab) to be effective in the treatment of rheumatoid arthritis

The New England Journal of Medicine (NEJM) today published a study sponsored by Roche, Genentech and Biogen Idec, which offers hope for the thousands of rheumatoid arthritis (RA) patients who have an inadequate response to currently available Disease Modifying Anti-Rheumatic Drugs (DMARDs).

The multicentre study demonstrated that a single course of just two doses of MabThera/Rituxan (rituximab) two weeks apart, in combination with methotrexate (MTX), significantly improved symptoms in patients with severe RA by up to 70%, with response rates sustained for up to one year. Unlike other RA treatments, MabThera is a therapeutic monoclonal antibody that selectively depletes B cells, which are believed to play a key role in the inflammatory cascade of the disease.

"The study provides strong support for the idea that B lymphocytes play a central role in rheumatoid arthritis and suggests that B lymphocyte targeted therapy has significant potential", said Professor Jonathan Edwards, University College of London, UK, lead investigator for the study.

In the study, investigators followed patients for 6 months, with a further observation at 12 months assessing the response with MabThera alone or in combination with cyclophosphamide or MTX, compared to MTX alone (control arm). The results at 24 weeks showed that the proportion of patients reaching at least a 50% improvement in disease scores (ACR 50 - the primary endpoint) was significantly greater in the MabThera-treated groups compared with the control. Moreover, a significantly higher percentage of patients treated with MabThera plus MTX achieved a 70% improvement in symptoms (ACR 70).

Response rates at 24 weeks, when using MabThera in combination with MTX included:
- 73% of patients showed at least a 20% improvement in symptoms (ACR 20, p=0.003 vs. MTX alone)
- 43% showed at least a 50% improvement in symptoms (ACR 50 p=0.005 vs MTX alone)
- 23% showed at least a 70% improvement in symptoms (ACR 70 p=0.048 vs MTX alone)
- Peripheral blood immunoglobulin levels remained within the normal range throughout and MabThera was well tolerated with a favorable safety profile

In a further analysis, similar response rates were maintained up to at least 48 weeks without further MabThera treatment, in the MabThera plus MTX group, with ACR 20 in 65%, ACR 50 in 35% and ACR 70 in 15%.

About the study
The multicentre, randomized, double-blind, controlled study included 161 patients from 11 countries with severe, active, long-standing RA (mean duration 10.4 years) who had not responded or responded inadequately to multiple other therapies. Patients were randomized into one of four treatment groups. The first group continued receiving methotrexate (MTX) alone (10 mg weekly), the second group received MabThera alone (2 infusions of 1g two weeks apart), the third group received MabThera (2 infusions of 1g) in combination with cyclophosphamide (2 infusions of 750 mg) and the fourth group received MabThera (2 infusions of 1g) in combination with MTX (10 mg weekly). Each group also received a 17-day course of corticosteroids (total dose of 910 mg). MabThera was infused intravenously on days 1 and 15 of the study -

dlw 6/21

no further treatment with MabThera was given. The patients were assessed using the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) criteria.

Results from the other three arms of the study at 48 weeks include:
- MTX alone: 20% of patients experienced a 20% improvement in symptoms and 5% experienced a 50% improvement; none experienced 70% improvement
- MabThera alone: 33% experienced a 20% improvement, 15% experienced a 50% improvement and 10% experienced a 70% improvement
- MabThera and cyclophosphamide: 49% experienced a 20% improvement, 27% experienced a 50% improvement and 10% experienced a 70% improvement

According to the investigators, the study's safety profile indicates that all three MabThera regimens were well tolerated with similar levels and type of adverse events compared to MTX alone. Most adverse events were reported during the initial 15 days, with many associated with the first infusion of MabThera. The majority of events were of mild to moderate intensity. At week 48, the incidence and types of events, including infections, were evenly balanced across all groups.

About MabThera
MabThera (rituximab) is a genetically engineered, therapeutic monoclonal antibody that binds specifically to the CD20 protein found on the surface of B cells. By selectively targeting B cells, MabThera aims to break the inflammatory cascade of RA - a series of reactions inflaming the synovia and leading to the cartilage loss and bone erosion that is characteristic of the disease in which B cells are thought to play a key role.

MabThera (Rituxan in US, Japan & Canada) has been used in clinical practice for over 7 years for treatment of a form of lymphatic cancer called non-Hodgkin's lymphoma (NHL). More than 370,000 patients worldwide have been treated with MabThera to date.

About Rheumatoid Arthritis
Rheumatoid arthritis (RA) is a progressive, systemic autoimmune disease characterized by inflammation of the membrane lining in joints. This inflammation causes a loss of joint shape and function, resulting in pain, stiffness and swelling, ultimately leading to irreversible joint destruction and disability. Characteristics of RA include redness, swelling, pain, and movement limitation around joints of the hands, feet, elbows, knees and neck. In more severe cases of RA the eyes, lungs or blood vessels may be involved. RA may also shorten life expectancy by affecting major organ systems and after ten years, less than 50% of patients can continue to work or function normally on a day to day basis.

RA is one of the most common forms of autoimmune disease and affects more than 6 million people worldwide, up to 2 million of whom are in Europe.

About Roche
Headquartered in Basel, Switzerland, Roche is one of the world's leading innovation-driven healthcare groups. Its core businesses are pharmaceuticals and diagnostics. Roche is number one in the global diagnostics market, the leading supplier of pharmaceuticals for cancer and a leader in virology and transplantation. As a supplier of products and services for the prevention, diagnosis and treatment of disease, the Group contributes on a broad range of fronts to improving people's health and quality of life. Roche employs roughly 65,000 people in 150 countries. The Group has alliances and R&D agreements with numerous partners, including majority ownership interests in Genentech and Chugai.

About Genentech
Genentech is a leading biotechnology company that discovers, develops, manufactures and commercializes biotherapeutics for significant unmet medical needs. Eighteen of the currently approved biotechnology products originated from or are based on Genentech science. Genentech manufactures and commercializes 13 biotechnology products in the United States. The company has headquarters in South San Francisco, California and is traded 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 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 labelling, press releases and additional information about the company, please visit www.biogenidec.com.

Roche IR contacts:

Dr. Karl Mahler
Phone: +41 (61) 687 85 03
e-mail: karl.mahler@roche.com

Eva-Maria Schäfer
Phone: +41 (61) 688 66 36
e-mail: eva-maria.schaefer@roche.com

Dianne Young
Phone: +41 (61) 688 93 56
e-mail: dianne.young@roche.com

Dr. Zuzana Dobbie
Phone: +41 (0)61 688 80 27
e-mail: zuzana.dobbie@roche.com

North American investors please contact:
Richard Simpson
Tel: +1 (973) 235 36 55
email: richard.simpson@roche.com

With best regards,
Your Roche Investor Relations Team

F. Hoffmann-La Roche Ltd
Investor Relations
Grenzacherstrasse 68 / Postfach
4070 Basel
http://ir.roche.com/
email: investor.relations@roche.com
phone: ++41 61 688 88 80
fax: ++41 61 691 00 14