

Rituxan[®] Anniversary: 10 Years of Progress



by Candice J. Bruce, PhD

We celebrate the 10 year anniversary of the first FDA approved targeted therapy by tracking its advances and speaking to physicians about how Rituxan[®] has changed the treatment of NHL.

The 10 year anniversary of the FDA approval of Rituxan[®] [rituximab; Genentech, Biogen Idec], the first monoclonal antibody (MAb) therapy for cancer, represents an exciting decade during which MAb therapies have revolutionized cancer treatment. Rituxan targets the CD20 protein which is expressed on over 95% of B cell lymphomas. It was the first MAb therapy to show a clinically significant anti-tumor response, which after decades of research into the use of MAbs for cancer treatment, finally provided proof of principle that MAbs could be an efficacious as well as less toxic treatment approach.

Before Rituxan there was little known about the use of therapeutic MAbs for any indication, and other monoclonal antibodies had failed in clinical trials, including clinical trials in oncology. According to Dr. Nancy Valente,

Group Medical Director of Hematology and Oncology at Genentech, “The success of Rituxan has dramatically changed cancer treatment paradigms because it demonstrated that biologics could be active on their own and in combination with chemotherapy.”

The development of Rituxan began in the early 1990s at IDEC (see Table 1). In Phase 1 and 2 clinical trials of patients with NHL who had relapsed or not responded to standard chemotherapeutic regimens, half of these patients responded to Rituxan therapy which was a significant improvement over other therapies available for relapsed disease. In 1995, IDEC partnered with Genentech to co-develop Rituxan. As to what attracted Genentech to Rituxan, Dr. Mark Benyunes, Senior Group Medical Director of Hematology and Oncology at Genentech, stated, “At the time, Genentech had several years of experience in biologics and was interested in MAb therapeutics, which was a totally new and exciting area.”

The approval of Rituxan launched Genentech into the field of MAb cancer therapeutics, which resulted in the bio-

Table 1. Rituxan Milestones



Rituxan Packaging

Year	Newly Diagnosed
1991	First anti-CD20 antibodies produced at Biogen Idec
1992	Rituxan IND filed
1995	Biogen Idec and Genentech sign co-development agreement for Rituxan
1997	FDA approves Rituxan for relapsed or refractory, CD20+, B cell low-grade non-Hodgkin's lymphoma (NHL)
1998	Rituxan is approved in the European Union under the trade name mAbThera [®]
2001	New uses for Rituxan approved including retreatment with Rituxan for patients who relapsed after initial Rituxan treatment and treatment of patients with bulky NHL
2002	<ul style="list-style-type: none"> Phase 3 GELA study demonstrates Rituxan plus chemotherapy may significantly improve event-free and overall survival compared to chemotherapy alone—first improvement in NHL patient survival in over 25 years Rituxan becomes a billion dollar/year drug
2004	DANCER, a Phase 2b study of Rituxan in rheumatoid arthritis, met its primary endpoint

tech company becoming a major player in the field with the introduction of three additional MAb therapies approved by the FDA. These include Herceptin, (trastuzumab) for the treatment of breast cancer, Campath, (alemtuzumab) for the treatment of chronic lymphocytic leukemia (CLL), and Avastin, (bevacizumab) for the treatment of colorectal cancer.

Rituxan was initially approved by the FDA to only treat a specific subset of patients with NHL. Over the years, Rituxan has gained approval to treat additional types of NHL and has become a front-line therapy when used in combination with chemotherapeutic regimens.

Ongoing clinical trials are investigating long-term use of Rituxan as a maintenance therapy to prevent relapse in patients with follicular lymphoma. These studies have demonstrated that maintenance therapy with Rituxan prolongs the duration of remission and that Rituxan can be safely administered for up to two years. In addition, clinical trials investigating the use of Rituxan in combination with chemotherapeutic agents for CLL have shown improved clinical outcomes in these patients.

Rituxan has expanded into treatment areas beyond cancer. Because it depletes CD20 B cells which are an integral part of the immune system, clinicians began investigating the use of Rituxan in indications in which the immune system is dysregulated. In 2006, Rituxan was approved for the treatment of rheumatoid arthritis (RA) in adults when used in combination with methotrexate. This combination reduces the signs and symptoms of RA in adults who have an inadequate response to the standard tumor necrosis factor antagonist therapy. Ongoing clinical trials are investigating Rituxan for the treatment of lupus, multiple sclerosis, and platelet disorders.

The clinical and financial success of Rituxan has paved the way for the entry of additional MAb therapies for cancer. In the 10 years since its approval, sales of Rituxan have totaled over \$10 billion worldwide (see Fig.1).

Dr. John P. Leonard, a leading clinician and professor in hematology and oncology at Cornell University, stated that Rituxan “provided proof of principle that antibodies could work to treat cancer. The fact that it had an initial small niche that then became much larger has encouraged drug developers/biotech companies that this was an area warranting investigation and investment.”

Currently, there are eight other approved MAb cancer therapies on the market for several indications including leukemia, colon, breast, lung, and head and neck cancer.

Rituxan has not only changed the natural history of NHL, it has significantly changed the way cancer is treated and how cancer research is approached. MAb therapies are now an indispensable component of cancer treatment with over 300 clinical trials involving antibody-based therapies. The challenge for the future will be to integrate new MAb therapies with the current MAb therapies and chemotherapeutic regimens. **CJB**

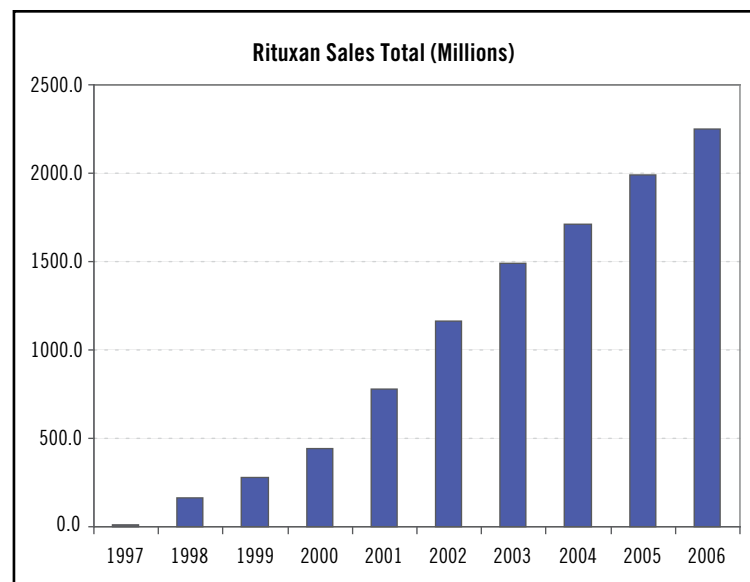


Figure 1. Rituxan Annual Worldwide Sales. Source: Genentech



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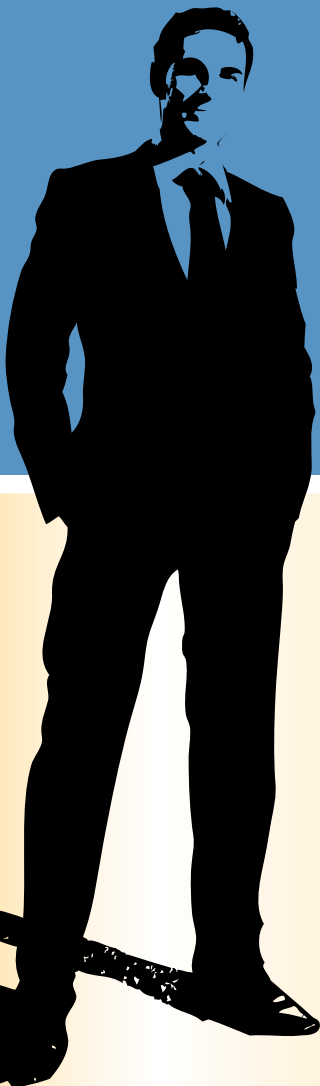
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