IMAGINE THIS: FROM RITUXAN PROJECT TEAM TO PATIENT

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During the many years that I worked on the product Rituxan, I can honestly say the thought never crossed my mind that I would actually become a blood cancer patient on a Rituxan regimen.

Work on the Rituximab Core Team

It all began in 1971 when, armed with a BS in Chemistry and an MBA, I began my career at Cutter Laboratories (soon to be acquired by the Bayer pharmaceutical company) which produced IV solutions and the products of blood fractionation. At Cutter I gained my grounding in finance and operations management, as well as in the healthcare industry itself. Ten years later, in 1981, I decided to leave the pharmaceutical industry and take a gamble with a small fledgling startup named Genentech and the new promise of biotechnology.

Biotechnology differs from the pharmaceutical industry. Pharmaceutical companies create chemical compounds to fight disease, and they harvest proteins and other natural compounds from the human body and package them for use in patients who are deficient. Biotechnology focuses on cloning and mass-producing these and other naturally occurring compounds with the aim of using the body’s own defense mechanisms to fight disease. Manufacturing such products avoids the potential shortages and contaminants or mutations that can occur when production is dependent exclusively on human sources.

At Genentech, after several years in finance, production planning, and logistics, I moved into the area of collaborations. In this role I was responsible for establishing relationships with companies that would either help Genentech manufacture products or that would be responsible for marketing Genentech’s products outside the United States. In 1997 I was appointed to a new senior team, the Rituximab Core Team.

The development of Rituxan was a joint collaboration between Biogen-Idec and Genentech. Biogen-Idec discovered the antibody protein rituximab and Genentech was responsible for its manufacture and commercialization as Rituxan. The Rituximab Core Team’s prime responsibility was to gain FDA approval for Rituxan and determine the focus of future clinical trials, patient needs, and, ultimately, manufacturing needs. I represented manufacturing and process development and negotiated with our foreign partners who would provide Rituxan outside the United States. My primary focus following initial FDA approval of Rituxan (and for the next eight or so years) was to help gain approval for Rituxan in countries around the world and to ensure that we could make adequate amounts of Rituxan to meet all worldwide needs.

To understand the huge quantity of Rituxan antibody required to meet these worldwide needs, consider, for example, how Rituxan works in the case of WM. As a monoclonal antibody to CD20, rituximab binds to the protein CD20 that is present on the cell surface of B-lymphocytes, including the malignant WM lymphocytes. Once bound, the Rituxan antibody can then kill the lymphocyte directly or enlist the body’s own immune system to do the job. However, because there are so many B-lymphocytes and because they are produced continuously, vast amounts of the Rituxan antibody must be infused to bind each of these CD20 sites. Because of the need for significant supply, the manufacturing process at Genentech had to be scaled up, and a new manufacturing facility had to be built and FDA approved.

Once the worldwide approvals were in place, the need for Rituxan exceeded original plans, and as a result much time was spent negotiating with Idec and international partners and carefully
allocating inventories to ensure no patient went without needed product. New production facilities were next planned and constructed. In addition, much effort had to be spent on developing a more productive cell line which could produce considerably more Rituxan per batch. Further FDA and worldwide approvals were required as we went forward.

**Exposure to patients**

As the going gets rough with the complexities of dealing with partners and meeting tight deadlines for plant construction and FDA approvals, nothing is more inspirational in spurring your job efforts than hearing a patient’s testimonial. On the Genentech campus many banners bearing the faces of our patients hang from buildings to remind us of our mission. In addition, our project team would invite patients with non-Hodgkin’s and other lymphomas to general campus meetings to recount how Rituxan helped prolong their lives.

But my first very personal exposure came from Toni, one of my Swiss collaborators with whom I was working on another drug launch in 1997. Toni confided in me that he was diagnosed with non-Hodgkin’s lymphoma. Despite various treatments in Switzerland his condition deteriorated. I relayed to him the promising results from Rituxan, and he was able to begin treatment. Many a time Toni would call me in the middle of the night, Swiss time, as he claimed the steroids he was getting made sleeping difficult. During one of these sessions Toni related his strong reaction to his first Rituxan infusion which entailed tremors, profuse sweating, shortness of breath, low blood pressure—so much so that the infusion was stopped until he was stable. Apparently Rituxan is so efficient at causing death to the cancer cells that the body has a hard time handling the cell debris. It was the first time I actually spoke directly with someone who had experienced the “potential” reactions patients could get with their first infusion. Subsequent infusions, however, went well for Toni. Unfortunately, possibly due to the fact that the disease had progressed so far already, Toni lost his battle.

Several years later, however, I had my second (and more emotionally satisfying) Rituxan encounter. My wife and I were on sabbatical in New Zealand where we met another couple while at a mountain lodge. They mentioned that they were there to celebrate the fact that the husband had just escaped death. He was failing treatment for non-Hodgkin’s lymphoma when his doctor put him on a “miracle drug” and now he was in remission. I asked if by any chance the drug was called Rituxan. And as he responded “How did you know?” I slipped on my “Rituxan Team” fleece vest, which I just happened to have on my chair. The profuse thanks I received was embarrassing, but I was immensely proud to have played even a small part in providing a drug which could affect lives so dramatically.

**How personal can you get?**

Then came my physical in early 2008: a high protein level required further investigation. Initial suspicion: multiple myeloma. I’m sure my initial response was that of all cancer patients. “This must be a mistake. I feel great. I can’t have cancer.” Then the fear jumps in and you start imagining the worst.

Fortunately for me, subsequent tests determined that the diagnosis was Waldenstrom’s macroglobulinemia. (I never thought I’d be happy to say I had this rare cancer, but I was when I learned that the prognosis was so much better). And, after online research, I discovered that one of the options for treatment was Rituxan! I couldn’t believe it. How, after all these years working on the Rituxan project team, had I never heard of this disease as a usage of the product? Such is the fate of “orphans”—such a small patient population that no drugs are approved specifically for the disease.
At that point I did a life evaluation and allowed diagnosis to be the final motivation for something I had been considering for a year. Time to retire! Who knows how much time we have left, so let’s do all the things that are most enjoyable. Hiking, biking, tennis, a little golf, watching the grandkids grow, traveling, lots of time with family and friends. And as for WM: watch and wait.

I went to my first Lymphoma Research Foundation meeting in San Francisco and was impressed with the turnout and the scientific presentations. There in a hall full of all sorts of blood cancer patients I got my first overwhelming feeling of how important Rituxan is as a base treatment for blood cancers and the significant results it has achieved in prolonging life and improving its quality. But most impressive that day was the breakout session devoted exclusively to a very small group of Waldenstrom’s patients. And the bonus of the day was Dr. Morie Gertz giving his “Garden Talk” to this small group. This was my introduction to the IWMF, and I can’t believe how fortunate we all are to have this forum for patients to compare notes and have a solid cadre of top-notch physicians and researchers devoted to not only making this a chronic disease but ultimately curing it. I was hooked. The next stop was the 2010 Las Vegas IWMF Educational Forum. Again I was blown away. I’ve never met a group of people so involved with the science of their disease and with such interesting backgrounds. Who would have guessed this healthy-looking group of people had cancer!

Armed with a new understanding of my disease and all the latest options for treatment, I met with my own oncologist at UCSF to determine the regimen I should embark on. Although I had no nagging symptoms, I did have the occasional night sweats and was getting more and more tired due to low hemoglobin levels. We decided on the regimen of Rituxan, Velcade, and dexamethasone recommended by Dr. Steven Treon. Based on high IgM levels we decided to forego Rituxan on the first round in acknowledgment of the potential IgM spike effect at initial infusion.

The first round was no problem, just some sleeplessness the first night or so. The second round was to end with my first Rituxan infusion. I got to the infusion center wearing my Genentech Rituxan T-shirt and fleece for good luck. To the nurses—I had worked with the spouses of several of them at Genentech—I remarked, “With all the hours I devoted to Rituxan over many years, it’s payback time for me.” With trepidation I recalled Toni’s account of his first infusion and hoped for the best. To my relief, I handled it well and the subsequent rounds of treatment were infused rapidly.

There was no peripheral neuropathy from the Velcade or adverse reactions from the four rounds of treatment. After two rounds of maintenance in early 2011 all treatment was stopped. But, alas, although I had a good response, it was not long-lived. My numbers continue to approach those of 2010 when treatment was required.

I went to the annual IWMF Ed Forum in Philadelphia again in June of this year, and once again I was struck by how lucky all of us Waldenstrom’s patients are to have such a dedicated group looking out for orphans like us. I strongly encourage anyone who has not yet gone to one of these meetings to make a point of it. The time and money expended are more than compensated for with the information you will garner, the camaraderie you will develop with other patients, and the hope you take away that this disease can be managed and potentially cured. It also prepared me to consult with my own oncologist upon my return to begin planning for my next course of treatment, which may begin late this year or early next year. Most likely this will be bendamustine and Rituxan.
How lucky can you get?

So 4 ½ years following diagnosis, I look back and consider myself triply blessed. Number 1: to have taken a risk back in 1981 to join a company that was based on cloning the body’s own defense mechanisms to fight diseases as opposed to manufacturing chemical compounds to poison them. Number 2: to have directly benefited from one of the products I was intimately involved with during that career. Number 3: to have outstanding physicians and researchers dedicated to better control and find a cure for WM. The benefits derived from Rituxan and other drugs could not have happened without the physicians and researchers we have all grown to love, respect, and congratulate for taking our orphan cause under their wings and making it their own personal crusade. Their ongoing clinical efforts with already approved lymphoma drugs and their research into the underlying causes and mechanisms activating our rare condition give us reason to plan for our own promising futures.