

## Campath: Collaborations Across Continents Prove Successful

University of Cambridge



It is fitting that the promising cancer therapy called Campath® begins with the letter “C” — the same letter that starts the word “collaboration” (not to mention “continents” and “commitment.”) For the story behind Campath is characterized by collaborative efforts that span several countries and involve hundreds of committed individuals.

Backed by several decades of research and development and then subjected to a dizzying series of mergers and acquisitions during its commercialization, Campath’s history is both long and winding. Yet in the end, the personal stories like those of Juliana Oliveri, a chronic lymphocytic leukemia (CLL) patient successfully treated with Campath, are what matter the most.

### **One Grateful Patient’s Story**

The last thing a busy professional like Oliveri had time for in her life was a chronic disease. A former society singer and performer in major cities across the U.S., she had since switched the focus of her career and was working 16-hour days

for the luxury goods industry in New York City. When a routine physical by her internist revealed an alarmingly high white blood cell count five years ago, Oliveri had no intention of slowing down, especially since she felt physically fine. Additional tests indicated that although asymptomatic, Oliveri had CLL, the most common form of adult leukemia.

Her doctors adopted a “watch and monitor” approach, and for the next three years Oliveri continued to work long hours, travel, and cater to demanding celebrity clients. The symptoms struck quite suddenly on her 49th birthday in July 2005, and they were serious enough to warrant admission to the hospital and the initiation of therapy. At the time she was first diagnosed, Oliveri had learned about a promising CLL therapy called Campath, and she took a proactive approach in helping her physicians formulate a treatment plan. Campath was the therapy she felt she needed, and fortunately that is what she received.

For six months Oliveri checked into the hospital three mornings a week as an outpatient. There she would endure routine blood work, followed by intravenous administration of Campath, and after an hour of close monitoring, she would leave the hospital to begin a full day of work “tending to the rich and famous.” Recalls Oliveri, “I had no side effects during treatment — it was amazing.” She has remained in full remission since completing Campath therapy in January 2006 and continues to lead a life as busy and demanding as ever.

Oliveri’s experience with CLL has taught her many valuable lessons such as the importance of teaming up with health care specialists who understand cutting edge treatments. But overall, she credits her health to the availability of Campath.

“*Knowing I had Campath to go to when the time came for treatment was the best thing that could have happened to me.*”

Juliana Oliver

### **A Long and Winding History**

The discovery of Campath, a monoclonal antibody that targets cancerous blood cells, began in the 1970s in the laboratory of Herman Waldmann, Ph.D., at the University of Cambridge in Cambridge, England. Waldmann, a pioneer in the field of monoclonal antibody production, first sought to develop the proteins to treat problems associated with bone marrow transplantation. Through Britain’s Medical Research Council (MRC), money was raised to establish research projects along these lines. Joining him in those efforts in the early 1980s were two ambitious researchers in Cambridge’s department of pathology — Mike Clark, Ph.D., and Geoff Hale, Ph.D.

The team of scientists spent years searching for monoclonal antibodies effective in targeting human immune cells. Eventually, they successfully discovered several. One of the next critical steps involved gaining the technical expertise to use the antibodies in human patients. With the help of colleague Greg Winter, Ph.D., they learned how to humanize antibodies, and in 1988, they successfully treated their very first lymphoma patient using the humanized antibody. The promising molecule, which binds to a specific target called CD52 on cell surfaces and directs the body’s immune system to destroy those CD52-bearing cells, was named Campath, for Cambridge University Department of Pathology.

The commercialization potential of Campath had meanwhile generated discussion between Cambridge and the British government’s technology transfer arm, the National Research and Development Corporation (now renamed the British Technology Group, or BTG). Richard Jennings, Ph.D., director of technology transfer and consultancy at the University of Cambridge, was involved in the negotiations at that stage and recalls that they represented a rather complex nexus of interest between different people and different organizations.

“It was a really fascinating project to work on, and it was driven by fantastic enthusiasm on the part of the academic inventors who showed a long-standing motivation to get new types of therapies to market for patients,” says Jennings. “They remained driven, and this impressed us.”

When Clark recounts the early phases in Campath’s development, the power of collaboration is what stands out above and beyond everything else. “We had already established that the antibody worked clinically, but we now needed to convince those involved that it was a commercially viable product,” he says. “That initial direct collaboration between researchers and clinicians has been the key to the success of this entire project.”

Through the work of Jennings’ office and the BTG the Campath team connected with The Wellcome Foundation (which became Glaxo- Wellcome and is now part of GlaxoSmithKline). Campath was licensed to the company in 1985 and efforts to commercialize it for use in the treatment of lymphoma and leukemia, as well as an immunosuppressive agent in rheumatoid arthritis patients, began in earnest. By the mid-1990s Phase II trial results were demonstrating that Campath showed potential for treatment of lymphoma and CLL patients.

The results of rheumatoid arthritis clinical trials however were unimpressive. Thus began the rollercoaster ride for Campath and its inventors. In 1995, around the time that Wellcome was considering a merger with pharmaceutical company Glaxo, it announced it was abandoning the project.

Yet the strength of scientific connections served to rescue the faltering project. Waldmann contacted Harvard University pathologist Timothy Springer, Ph.D., a colleague whose path he had first crossed when the two were learning monoclonal antibody technology in the MRC laboratory of Nobel Laureate scientist César Milstein, Ph.D. Springer had since returned to the U.S. and had founded a startup company, LeukoSite, in the Boston area. LeukoSite, it turned out, was in a position to license the rights to Campath from BTG.

By 1997 LeukoSite had negotiated a new licensing deal for Campath and clinical trials designed to test the therapy in CLL patients were back on track. Yet again the route of Campath was altered by a series of commercial mergers and acquisitions. Within two years LeukoSite announced its merger with another Boston area company, Millennium Pharmaceuticals, Inc. While the company quickly gained Food and Drug Administration (FDA) approval of Campath for the treatment of B-cell CLL patients who fail conventional chemotherapy, Millennium eventually transferred the rights to ILEX Oncology, Inc. In 2004 Genzyme Oncology, Inc. acquired ILEX and gained the production rights to Campath. While Campath’s history with ILEX was short-lived, it was beneficial, as Genzyme investors recognized the therapy’s potential at a time when it was looking to expand its prognostic and diagnostic portfolio in the treatment of hematological cancers.

According to Terry Murdock, Genzyme senior vice president and general product manager of Campath, the gain of Campath as a therapy in the treatment of CLL was the perfect platform for the company in which to leverage a diagnostic tool and a targeted therapy. “In hematological malignancies like CLL, the need to eradicate residual disease in patients is important as relapses are often related to the residual nature of the disease,” says Murdock.

The merging of ILEX and Genzyme was ideal as the strengths and directions of the two companies complemented one another. “ILEX had a strong clinical operating route University of Cambridge and a strong base of experience in getting clinical trials completed. It also had a solid track record of getting drugs developed,” says Murdock. “Genzyme has a strong academic and clinical physician base, as well as experience with regulatory approval and manufacturing. Putting those two things together, we provide a solid base to move forward with Campath.”

## **A Bright Future Ahead**

Under the protection of Genzyme, Campath remains the first and only monoclonal antibody approved by the FDA for the treatment of patients with B-cell CLL. In the fall of 2007 the FDA granted a label expansion and approved Campath as a first-line treatment for the disease. Along with Bayer Healthcare Pharmaceuticals, which markets Campath, Genzyme is also developing the therapy as a treatment for multiple sclerosis. The latest news reports successful results in Phase II trials of Campath for multiple sclerosis patients; Phase III trials are now underway.

Reflecting on the long history and sometimes uncertain future of the therapeutic protein to which Clark has devoted much of his life, he recognizes certain recurrent themes. Most significant he claims were the collaborations that existed between clinicians and university research groups that provided the dedicated Campath researchers with the confidence necessary to push for its commercialization.

Hale echoes those sentiments and points to the unusually strong tie between himself, Clark and Waldmann — the original three behind the discovery of Campath.

“One of the greatest things about this project is that while the three of us have been working on it going back to the early 1980s, we’ve all remained very close,” says Hale. “And there have been hundreds of other scientists, clinicians and patients who have helped along the way and made this project successful. Everyone has been very loyal every step of the way.”

This story was originally published in 2008.

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