Qu Biologics Seeking **Crohn's Disease Patients** for Promising Clinical Trial

Qu Biologics Inc., a biotechnology company based in British Columbia, is conducting a randomized placebo-controlled trial for one of its experimental site-specific immunomodulator (SSI) treatments, called QBECO SSI, which showed promise during a compassionate use program in the treatment of inflammatory bowel disease (IBD).

Inflammatory Bowel Disease

IBD mainly includes Crohn's disease and ulcerative colitis and involves chronic inflammation and associated symptoms, such as severe abdominal pain, diarrhea, and bleeding.

In ulcerative colitis, the inflammation only involves the colon and always begins at the anus, with the disease continuously progressing upward. In Crohn's disease, the inflammation can be in multiple patches or one large patch, and may involve any area throughout the entire digestive tract. In ulcerative colitis, inflammation only involves the inner mucosal lining, while in Crohn's disease, inflammation can extend right through the entire thickness of the bowel wall. Extraintestinal complications of IBD can involve the skin, joints, and eyes.

Immune System Dysbiosis

While the exact cause remains unknown, most researchers agree that IBD is associated with microbial imbalance in the gut (dysbiosis), affecting the immune system. Many types of pathogens can enter our bodies. Our immune system reacts by producing inflammation in affected areas, usually eradicating the potentially harmful intruder. An **innate immune response** involves specific cells that fight foreign pathogens, which enter the body as a first defense. In the GI tract these include, for example, some of the cells in the lining of the intestines. An **adaptive immune response** is more complicated and involves the body's ability to produce new, specialized cells and antibodies in order to fight specific antigens that somehow evade the innate immune response, as well as specific pathogens fought previously.[1]

One hypothesis, which is the basis of SSI treatment, is that the innate immune response in the GI tracts of IBD patients is suppressed.[2] Specifically, some research suggests that a certain type of immune cell called a macrophage, which is responsible for clearing bacteria and infected and damaged cells, does not work well in IBD patients. Due to this macrophage suppression, the dysbiosis and chronic infection with multiple pathogens remain in the GI tract. This stimulates the adaptive immune response to produce cells that attack and create inflammation in tissues affected by these pathogenic bacteria. The result is chronic inflammation that produces recurring IBD flares and associated symptoms.

What is different about SSI treatment is that it is designed to clear the underlying trigger of dysbiosis and bacterial infection, with the goal of achieving sustained remission after a course of treatment so that the person only needs to take the medication for a short course and then the correction to the innate immune system has a long-lasting effect.

Targeting the Innate Immune Response

Many existing treatments for IBD, such as corticosteroids (e.g., prednisone) or anti-TNFα biologic medications (e.g., infliximab, adalimumab,

golimumab) work differently from each other but all aim to decrease an over-reactive adaptive immune response. In contrast, QBECO SSI stimulates the innate immune response in the GI tract..

Similar to a vaccine, QBECO SSI is derived from inactivated pathogenic bacteria. The Qu Biologics researchers chose *E.coli* because it is a pathogen specific to the gastrointestinal tract. Researchers think that the innate immune response might react by harnessing new, more effective activated macrophage cells in the area, which will correct the overall innate immune response of the GI tract. With the innate immune response working properly, the adaptive immune response no longer has any reason to overreact, resulting in a resolution of the inflammation and IBD clinical symptoms.

Tyler's Story

The GI Society spoke with 31-year-old Tyler, an electrician in Ontario, who was the first Crohn's disease patient in the world to try Qu Biologic's SSI treatment. He was part of the original compassionate use program in 2010, which eventually included ten Crohn's disease patients and two ulcerative colitis patients, who administered the SSI treatment themselves with a subcutaneous injection.

During that program, all Crohn's disease patients reported an improvement of symptoms, and seven of those experienced a sustained resolution of clinical symptoms after taking the SSI for at least three months. Four of those seven, including Tyler, experienced sustained clinical remission after discontinuing all IBD medication, including the SSI.

Diagnosed with Crohn's disease in 2006, for about three years Tyler took prednisone, a type of corticosteroid. While this medication helped to manage his disease flares to a degree, it came with side effects. Tyler said he experienced regular insomnia and 'felt like a robot'. While his health care team tried to gradually decrease his dose of prednisone, they could not do so without losing effectiveness. His treatment with prednisone continued, but with the addition of azathioprine (Imuran®), a medication that helps some patients lessen or eliminate the need for prednisone. However, these medications didn't work for Tyler and he languished with painful disease flares along with miserable side effects from the treatment.

Tyler learned about Qu Biologics' early research into SSIs through his uncle, who was participating in Qu Biologics' compassionate care program for cancer treatment. At the time, Tyler's health care team recommended he try infliximab (Remicade®), a biologic medication that helps many IBD patients when earlier treatments fail to relieve clinical symptoms. However, Tyler chose to participate in the new research using SSI treatment instead.

Tyler told us that he started to notice improvements just one week after starting the SSI treatment. The bleeding stopped, his pain subsided, and his stools started to become normal. "I had energy!" he told us. Previously, his symptoms were so severe that he was unable to work and almost never participated in social events. "Before this treatment, I didn't go out with friends at all for two years," he said. After about two months of SSI treatment, Tyler no longer required prednisone and, a month after that, he was also able to stop taking Imuran®. He told us he was amazed that, in addition to resolving his IBD symptoms, he experienced no side effects from the SSI treatment. After nine months of only the SSI treatment, Tyler stopped that as well. As of our recent interview, more than 3 years after stopping SSI treatment, he remains in sustained remission. "It gave me my life back," he told us, of his participation in the study. While every patient is unique and QBECO SSI is in the early testing stages, Tyler is optimistic about the treatment based on his own remarkable experience. He hopes that one day it could help tens of thousands more IBD patients just like him.

Qu's Clinical Trial Currently Recruiting

The GI Society also spoke with Hal Gunn, Qu Biologics founder and CEO. He, too, is optimistic, but he stressed that this research is early and many more studies are required to determine this treatment's safety and effectiveness.

For the current clinical trial, which is for Crohn's disease patients only, the researchers are looking for a maximum of 60 participants. Dr. Gunn told us that they currently have about 24 slots remaining. "The primary eligibility criteria are that patients are the age of majority in their province, diagnosed no less than six months previous, and experiencing active, moderate to severe Crohn's disease." Dr. Gunn advised that participants can live anywhere, even outside Canada, but participation requires three short visits to British Columbia over a 16-week period. Qu Biologics provides a stipend to cover flights and accommodation.

During the first eight weeks, study subjects will take either the SSI treatment or placebo every second day by self-administered injection just under the skin. This type of randomized, placebo-controlled study yields the highest quality results compared to other types of studies. Dr. Gunn stressed that if trial participants taking the placebo experience no improvement in symptoms during the first 8-week period, then they will automatically receive the SSI treatment for the remaining eight weeks. To find out more or to take the online screening test for eligibility in the study, visit www.QuCrohnsTrial.com.

Top: Tyler, Bottom: Dr. Hal Gunn

1 Janeway CA *et al.* Principles of innate and adaptive immunity. *Immunobiology: The Immune System in Health and Disease.* 5th edition. New York: Garland Science;2001. Available at: http://www.ncbi.nlm.nih.gov/books/NBK27090/. Accessed 2014-10-15.

2 How It Works page. *Qu Biologics website.* Available at http://www.qubiologics.com/technology/how-it-works/. Accessed 2014-10-16.