In August 2014, Health Canada gave regulatory approval to Eloctate®, an extended half-life factor VIII manufactured by Biogen. Since then, the Ministère de la Santé et des Services Sociaux in Quebec has approved Eloctate for distribution by Héma-Québec for those hemophilia A patients with difficulties of venous access and/or a shorter-than-normal half-life; it is now available. In the other provinces and territories, Eloctate is still under review. A decision on its reimbursement and distribution through Canadian Blood Services is anticipated in the coming months. With individuals with hemophilia A potentially facing a decision on whether or not to switch from their current FVIII concentrate, Hemophilia Today interviewed two physician/scientists having experience with Eloctate.

**HT:** Dr. Wong, can you describe the technology behind Eloctate?

**Dr. Wong:** The technology is based on a Fc fusion molecule linked to FVIII. When you infuse FVIII, it goes into cells and is then destroyed by liposomes. These are little pockets of enzymes that degrade the FVIII protein. So one way to slow down the degradation is by combining the Fc molecule to a receptor called the neo-natal Fc receptor. The word neo-natal is misleading as it is a natural component we all have, even adults. The Fc itself is a natural product that comes from immunoglobulin. So these are all naturally occurring substances. With Eloctate we link the Fc fusion molecule to the FVIII molecule so that when it goes into the circulation and into the cell, it isn’t degraded. It is protected and re-circulated back into the bloodstream several times.

**HT:** Has this technology been used in other medications?

**Dr. Wong:** We have about 17 years experience with Fc fusion going back to its use in rheumatoid arthritis. It has also been used in chronic immune thrombocytopenia, kidney transplant medicines and type 2 diabetes. These applications have been safe and efficacious.

**HT:** What other innovations do we see with Eloctate?

**Dr. Wong:** The Fc portion is a recombinant Fc molecule and not a foreign substance that we’re introducing into the body. We also use a humanized cell line in the manufacturing process to make the FVIII. Instead of a Chinese Hamster Ovary (CHO) or a Baby Hamster Kidney (BHK) cell line, as are used in the traditional products, we use a Human Embryonic Kidney (HEK) cell line. We have no long-term data on whether or not this makes a difference but having a more natural human cell line cannot be a negative.

**HT:** Some people might be worried by a human cell line. There has been such an effort to get away from plasma-derived elements, including albumin, in factor concentrates. Should that be a concern?

**Dr. Wong:** I encourage people to read up on human cell lines. There are many different types of human cell lines. The HEK cell line has many different strains. We, as in the medical world, have almost 30 years experience using them. The one we use for Eloctate has been used over many years in the manufacture of many drugs and has never shown any tendency to cause complications. It has a very stable safety profile. And Biogen uses all the standard purification steps.
processes to guarantee safety, including solvent detergent treatment, affinity chromatography and nanofiltration.

**HT:** How much is the half-life of Eloctate extended compared to the traditional FVIII concentrates?

**Dr. Wong:** The data shows that the half-life of Eloctate is about 19 hours, on average. This compares to other recombinant FVIIIs that are about 12 hours. So this represents a 50 percent extension in half-life, or 1.5 times that of traditional FVIIIs.

**HT:** Physicians and patients often think of concepts like time to one percent or time to three percent to estimate how long and well a person is protected from breakthrough bleeding while on a prophylactic protocol. How does Eloctate change how long it takes to fall to that critical level?

**Dr. Wong:** Of course, it's up for debate what that magic level of protection really is but from our studies, at doses of 50 IUs per kilogram, the time to one percent is 4.9 days (a range of 4.4 to 5.5 days with a 95% confidence interval) for Eloctate. This compares to 3.3 days (a range of 3.0 to 3.7 days with a 95% confidence interval) for the traditional products.

**HT:** What does this mean with regards to changes in treatment protocols?

**Dr. Wong:** The nice thing about Eloctate is that you can use it with a range of intervals, depending on the patient, as half-life varies from person to person. The label says to infuse 50 IUs/kg every three to five days.

**HT:** Dr. Mahlangu, you were very involved in the Phase III clinical trial. What was, in your opinion, your patients’ principal benefit?

**Dr. Mahlangu:** Twenty of my patients were enrolled in the Phase III clinical trial and extension study over four years. The principal benefit that I observed was safety. None of my patients, many of whom were Black, developed an inhibitor. It is well known that inhibitor rates tend to be higher in Black patients compared to other racial groups. This study was with previously treated patients. In fact, none of the 165 patients in the worldwide Phase III trial developed an inhibitor. The study with previously untreated patients is ongoing and it will be very interesting to see what the inhibitor rates are with these patients.

In the clinical trial, my patients used a number of prophylactic protocols, ranging from once a week to twice a week. On-demand therapy was ruled out as unethical. There was a huge difference in quality of life for those moving from on-demand therapy before the trial to prophylaxis. When I asked, “When did you last bleed?” many said, “I don’t remember.” While quality-of-life data is difficult to gather, there is no doubt there was significant improvement.

**HT:** Dr. Mahlangu was at one site. Did you have any other feedback about the trial?

**Dr. Mahlangu:** Adherence to the trial protocols while on study was excellent. It remains to be seen how that works out in real-world use; however, I would predict greater adherence with reduced frequency.

**HT:** Some have suggested that adherence to treatment protocols may be better with lower frequency therapies. Was that your experience?

**Dr. Mahlangu:** I applaud the development of all these new therapies with extended half-lives. The more, the better. I think they will lead to economies of scale. That and increased competition will lead to more affordable pricing and better access for patients, especially in the developing world. I also encourage differential pricing whereby products are priced more affordably in countries with limited health care budgets.

**HT:** Dr. Wong, what is the American experience since Eloctate was approved and marketed almost a year ago?

**Dr. Wong:** We have had a great safety profile. We have now had over 400 patients exposed to the product over the last year and there have been no undue safety problems identified. We continue to collect data so we can show how this product is working in the real world. We’re committed to sharing that data and learning from experience. And we want to say thank you to the community for getting involved in the research and allowing us to continue to elevate the standard of care.

**HT:** Do you have any final thoughts for our readers?

**Dr. Wong:** I think that your readers should know that, while Biogen is a relative newcomer to hemophilia, we are fully committed to the community. Our motto is Patients First. We also are not afraid to take up difficult challenges. We want to enhance patient care. We want to listen and take feedback to heart. We are here to make a difference.