Nuwiq, another recombinant factor VIII option

by David Page, CHS national executive director

With the approval of Nuwiq by Health Canada and its success in obtaining a share of the factor VIII market in provinces served by Canadian Blood Services, Hemophilia Today sat down with Lidia Cosentino, Ph.D., director of medical and scientific affairs at Octapharma Canada, and Dr. Anthony K. C. Chan, pediatrician and co-director of the hemophilia program at Hamilton Health Sciences Centre, to learn more about this coagulation therapy.

Hemophilia Today (HT): Octapharma has called Nuwiq a novel recombinant factor VIII. In what way is Nuwiq different from other factor VIII products?

Dr. Cosentino: Inhibitor development is a devastating treatment complication of hemophilia care. Octapharma developed Nuwiq with the goal of reducing inhibitor development. A second goal was to try to reduce the number of infusions needed for prophylaxis without compromising bleed control. The post-translation modifications for Nuwiq, being derived from a human cell line, are very similar to naturally occurring factor VIII found in healthy individuals. Our clinical program demonstrated the half-life of Nuwiq to be 17.1 hours in adults and about 12.5 hours in children.

HT: That’s surprising. It’s not a fusion molecule and there’s no glycopeoylation as we see in some other products. How do you explain that the half-life appears to be even longer than native plasma-derived factor VIII?

Dr. Cosentino: The half-life of plasma-derived factor VIII is about 15 hours. We’ve demonstrated that Nuwiq has a very, very strong binding affinity to Von Willebrand factor. We believe that this binding affinity protects factor VIII from clearance, which accounts for the prolonged half-life.

Dr. Chan: I think it’s very important to recognize the half-life that is reported is actually a point estimate and there is individual variability. Just like people are taller and shorter, the half-life of a product in different individuals will vary. Some people are going to have a shorter half-life compared to what is being reported and some longer. We can speculate that the binding to von Willebrand factor is the reason why Nuwiq might have a longer half-life and warrant further study.
HT: Are you satisfied with the robustness of the data that show, at least looking at a median calculation, that half-life really truly is longer than some of the other products?

Dr. Chan: Yes, but the question comes down to whether there are any clinical implications. Will this actually lead to less frequent infusions? I think this is especially demonstrated in the adult study that showed, with the individually tailored pharmacokinetic (PK) dosing, that the interval could be extended. And when it comes to children, often the younger they are, the shorter the half-life. So I think it’s very worthwhile to perform a PK study in those individuals to take advantage of the potential longer half-life.

HT: What could this mean for some patients in terms of clinical use?

Dr. Chan: For patients it could mean two things. If the half-life is indeed longer in an individual patient, one could potentially keep the same frequency of prophylaxis and the same dose and end up with increased protection through a higher trough. For example, in the Canadian Hemophilia Prophylaxis Study, we have already showed that 9% of the patients can be kept on once a week prophylaxis. If the product you use has a longer half-life, you could give it once a week and the protection at the end of the seven days may actually be better. In other individuals, one may be able to reduce infusions from every second day or three times a week to only twice a week. This needs to be verified for each individual patient. How frequently this will be possible remains to be seen.

HT: The most serious complication of hemophilia treatment is inhibitor development. What have you learned so far from clinical trials and even real world use with regard to the risk of inhibitor development, first of all with previously treated patients?

Dr. Cosentino: In the clinical trial, over 200 previously treated patients were treated with Nuwiq and there have been no inhibitors detected. And, since Nuwiq was approved in Europe, the U.S. and Canada and used in real world settings, there have been no reports of inhibitor development in previously treated patients.

HT: That’s reassuring. What have you learned so far about the risk of inhibitors in previously untreated patients, the ones who are most at risk for development of inhibitors?

Dr. Cosentino: Our Phase III study in previously untreated patients (PUPs) is ongoing. Our interim analysis of 66 patients with more than 20 exposure days showed 8 high-titer inhibitors, an incidence of 12.8%. This is very promising. it compares quite favourably to what the SIPPET study data has shown as the incidence with plasma-derived factor VIII concentrates.

Dr. Chan: I think this is promising. Of course, everyone is a bit cautious and not wanting to make too firm of a conclusion until the study is finished and all the patients are reported up to 100 exposure days. I think that’s the end point. The interim data analysis looks fairly good. We’re are waiting for the study to be complete.

HT: Is the PUP study big enough that, if the trend continues and numbers are lower than with recombinant products and similar to other plasma-derived studies, you’ll be able to draw conclusions?

Dr. Cosentino: I believe so. Initially we were planning to recruit 100 patients but we’re now at 110. In the SIPPET study, I believe there were about 125 patients per therapeutic arm: recombinant factor VIII and plasma-derived factor VIII. So this is very similar to the SIPPET study and SIPPET is the largest randomized control study for PUPs that we have.
HT: When do you hope to publish that data?
Dr. Cosentino: The study will probably have final analysis by the end of 2018.

HT: Nuwiq is now available in provinces served by Canadian Blood Services. What programs does Octapharma have available for patients and for the treatment centres in case of a switch to Nuwiq?
Dr. Cosentino: We have patient brochures and a lot of web-based information. We have developed what we’re calling our ProCare program which includes two services. The first service that’s being offered is a home infusion service whereby a third party, highly trained nurse will go to the patient’s home to assist with the infusions, if assistance is required in the home. And the second is the personalized prophylaxis program, based on individual PK analysis. And to help facilitate this, we have a PK home service whereby, working with the hemophilia treatment centre (HTC), a third-party nurse will go to the patient’s home to collect the blood samples in order to do the PK at specific time points as instructed by the HTC. This program will facilitate personalizing prophylaxis, and all the blood draws can be done in the comfort of the patient’s home.

HT: Do you know how many draws that entails?
Dr. Cosentino: That is totally at the discretion of the HTC. We’ve partnered with Dr. Iorio so the analysis could be done through WAPPS (Web Accessible Population Pharmacokinetics Program, developed at McMaster University). I believe you need anywhere between 1 and 3 blood draws.

HT: Can you provide some information about Nuwiq in terms of administration?
Dr. Cosentino: Nuwiq is available in 250, 500, 1000 and 2000 IU vials, all with a prefilled syringe of 2.5 mL. Storage is refrigeration for 24 months and room temperature for one month.

HT: Who do you think would most benefit from using Nuwiq?
Dr. Cosentino: Patients who are at risk of inhibitors or with inhibitor management issues would be the first group. The second would be those who are looking to reduce the number of infusions without increasing their bleeding tendency while maintaining a trough over 1%.

Dr. Chan: Yes, with regard to the inhibitor risk, I think that is at least one of the potential groups. This needs to be discussed with the patients or parents. If I have a PUP, my first preference is for him to be on a PUP study. But lacking a PUP study, I think Nuwiq becomes an option. And then in terms of the slightly longer half-life, it becomes a potential option to try to decrease the frequency of the infusions. But I want to stress, in those situations it’s always important to check the pharmacokinetics of the product in the patient.