# Living in the new world of novel haemophilia therapies

*Robyn Shoemark*

Discussion about the impact of novel therapies for haemophilia was a highlight at the WFH Congress. This included non-factor therapies such as emicizumab (Hemlibra®) and fitusiran and gene therapies for haemophilia A and B.

At the time of publication, fitusiran and gene therapy for haemophilia were not registered by the TGA in Australia as prescription medicines.

## CLINICIAN PERSPECTIVE

### Surgery in an era of novel therapies

*Chair ~ BJ Ramsay, Clinical Nurse Specialist, Blood and Cancer Centre, Wellington Regional Hospital, New Zealand*

I was fortunate to present in the nursing session on surgery when a patient is being treated with novel therapies, along with Jaime Chase from John Hunter Children's Hospital in Newcastle. In this session nurses from around the world discussed case studies of patients using new treatments and Jaime and I represented Australia with our patient case studies.

It was great to hear about the patients on emicizumab having surgery and the treatment regimens they used. When there is little information or limited use of the new treatments, seeing what someone else has tried can help clinicians make an informed decision when you are planning treatment or surgery for your patient.

### Changing treatment, changes diagnosis

*Chair ~ Kate Khair, Director of Research, Haemnet, London, UK*

### What PWH tell us about living in the new paradigm of hemophilia treatment

*~ Simon Fletcher, Lead Haemophilia Research Nurse, Oxford Haemophilia And Thrombosis Centre, UK*

### Non-factor therapy in persons with acquired hemophilia A and von Willebrand disease

*~ Ming Lim, Assoc Prof, Division of Hematology and Hematologic Malignancies, University of Utah Health, Salt Lake City, USA*

Patient panel:

### Life with hemophilia after gene therapy

*~ Luke Pembroke, Creative Director, Haemnet, London, UK*

### Life with hemophilia with fitusiran

*~ Louis Marlow, biotechnology researcher, University of Edinburgh, UK*

### Life with hemophilia on emicizumab

*~ Andrew Selvaggi, haemophilia advocate, Haemophilia Foundation Australia, Melbourne, Australia*

In the first session, Simon Fletcher presented his view on how changes in treatment have changed the lives of his patients. He was careful to start by saying that he did not have haemophilia and that he is a treater. His role was to undertake and review studies aiming to find out what it means to have haemophilia and then use that information to help patients.

He described current treatments available for patients as aiming to **Replace**, **Rebalance and Replicate**. He grouped the studies into two categories: one he called **Emi and Me** for patients on emicizumab and the other **Exigency** for patients undergoing/who have undergone gene therapy.

In these studies, people with haemophilia made the following comments about what changes/ improvements in treatment meant to them:

**Freedom** – patients gained freedom and felt they and carers were liberated with new treatment options.

**Control** – patients and carers being able to plan for the future. In some cases, this was the first time they had ever felt able to plan for the future.

**Reduction in pain** – many patients were experiencing less bleeds so in turn, less pain.

**Reduced burden** – newer treatments being quicker and easier to administer allowed more time for life.

**Side-effects** – for example, in gene therapy known side-effects include needing to take steroids but this is still better than having to do prophylaxis.


*Old Montreal* *Photo: Shauna Adams*

## ACQUIRED HAEMOPHILIA

Ming Lim then presented on non-factor therapy in people with acquired haemophilia A.

Acquired haemophilia is a rare autoimmune disease predominantly diagnosed in the elderly, where immunoglobulin (IgG) antibodies, also known as inhibitors, attack factor VIII (8). It presents often with severe bleeding and has a high morbidity and mortality often associated with gastrointestinal bleeds.

Past treatment was to control and prevent bleeding using bypassing agents or recombinant porcine factor VIII. The goal is to control bleeding and eradicate the inhibitor. Therapy includes the use of steroids and/or immunosuppressive therapies.

There have been several reports of off-label use of emicizumab. Ming Lim reported on a review of 24 patients using emicizumab to help control bleeding. Dosing varied from the same as that recommended for people with haemophilia A to a modified version of dosing. The duration of treatment ranged from 20 days to 10 months with 100% of patients reporting no further bleeds after commencing emicizumab. Clinical trials are ongoing.

## PATIENT PERSPECTIVE

In the patient panel, three men told us their story of their journey with changing treatment for their haemophilia.

**Luke from London** spoke to us from the jungle in Peru where he has been for the last month. He underwent gene therapy in February 2020. He now has factor levels around 20-25% and has not needed any factor in the past two years. He has taken emergency factor with him to Peru and the only time he touches it is when he changes out the ice packs to keep it cold.

The presentation made Luke reflect on the last two years and what it has meant for him. As he underwent the treatment one month prior to COVID lockdown in the UK, he not only had a change in his treatment but found himself moving to be close to the hospital so he could reduce his risk for getting COVID and continue his hospital visits as part of the trial he was on. This was difficult for both his physical and mental wellbeing. He felt unwell with the side-effects of the medications he needed to take post gene therapy. He thought his veins would get a rest but with all the blood tests, this was not an option for the first 12 months. Moving on, he now only has visits every 6 months and his veins are finally having a rest. >>

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He talked about how gene therapy has changed his life for the better. He is able to plan things for the future. He felt he was unable to do that prior to gene therapy as he never knew when he might bleed and need to be near the hospital. He no longer thinks about haemophilia every day. Going to Peru has been a road test for his therapy. He does still have ankle pain from previous joint bleeds, but he knows the difference between pain and bleeding and is able to rest, take his pain medication and keep going the next day.

In the Q & A, when asked if he would do it again, he replied absolutely yes. He felt the trial process outlined the risks versus benefits and he had a very good consenting process so he would strongly advocate for trials and collection of long-term data associated with trials. He is very positive and has no regrets but did say he would be very disappointed if the effects wore off and he had to return to having factor again.

**Louis from Scotland** talked about life with haemophilia on fitusiran. Louis was diagnosed with severe haemophilia B at 18 months and then went on to develop an inhibitor. He was then treated with the bypassing agent NovoSeven® (recombinant factor VIIa). When tolerisation was attempted, he had an anaphylactic reaction. He has undergone radiosynovectomies for his target joints.

In 2019 he joined a trial using fitusiran for his prophylaxis. Other than developing asthma, which is a known possible side-effect of the medication, Louis is very pleased with his new treatment. He has gone from having approximately 9 bleeds per year down to 1 bleed per year. He has been able to increase his activity levels and finds that his bleeds are now injury/trauma related rather than spontaneous. He has gone from regularly needing to use a wheelchair to now the wheelchair is taking up space in the garden shed. He is very happy to be on a new therapy.

**Andrew from Australia** talked about life with haemophilia on emicizumab. Andrew was diagnosed with severe haemophilia A at 15 months and by the age of 2 years had developed an inhibitor. By 2007 at age 20 years, he had had over 700 joint/muscle bleeds, had developed 7 target joints and was wheelchair bound from 5-18 years of age. He underwent a personal transformation and lost 30kg.

In 2016, he participated in the Haven clinical trial and had his first dose of emicizumab. The life changes for him have been immense. Since starting on the trial, he has not had any muscle or joint bleeds. Since commencing emicizumab he has undergone orthopaedic surgery again. In past surgeries, it had been difficult, 'full of bleeding' but this time it was controlled with less bleeding.

His described the challenges as both mental and psychosocial and that he needed to reset his expectations after starting the trial. He found he needed to build confidence and start trusting his body, something he had not been able to do pre-trial.

He did mention that while he strives to do his treatment as recommended, sometimes he forgets, likening it to putting out the bins. We all forget regular things sometimes. He is, after all, only human like the rest of us!

## CURRENT RESEARCH

**Late-breaking Clinical Research**

*Chair ~ Glenn Pierce, Vice President Medical, World Federation of Hemophilia, USA*

**A phase 1 sequential pharmacokinetic (PK) evaluation of octocog alfa, rurioctocog alfa pegol, and efanesoctocog alfa in severe hemophilia A**

*~ Annemieke Willemze, Senior Clinical Research Director, Sanofi Genzyme, Amsterdam, Netherlands*

I attended the Late Breaking Clinical Research session where Annemieke Willemze discussed the BIVV001 (efanesoctocog alfa) trial results. These are very promising for people with haemophilia A, with a 3-4-fold half-life increase to an average of 43.3 hrs and requiring a weekly treatment injection.

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