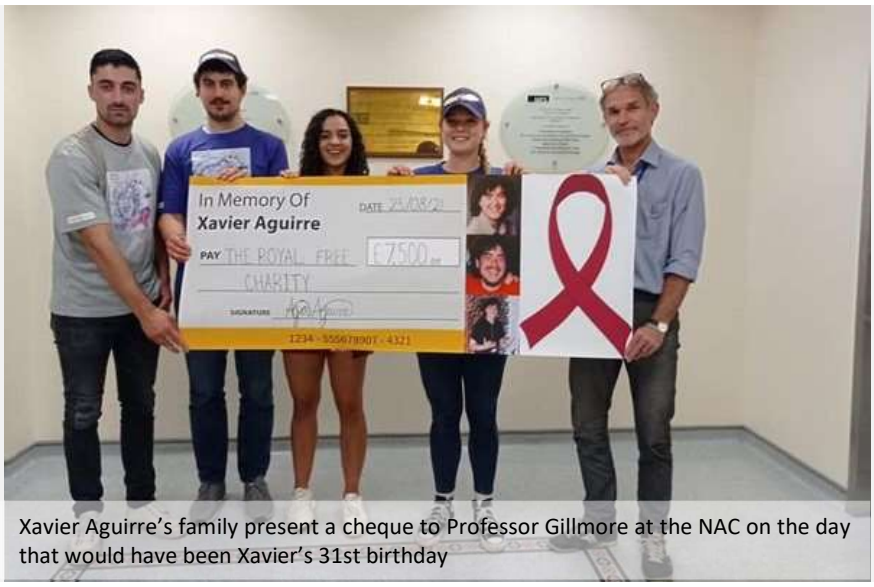

Xavier Aguirre's family present a cheque to Professor Gillmore at the NAC on the day that would have been Xavier's 31st birthday

National Amyloidosis Centre News

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"Bridging the Gap" - How Technology is Extending our Reach & Support for Amyloidosis Patients

The Scottish Amyloidosis Patient Support Group - News Round-Up

By Mark McConway

We call ourselves "The Scottish Amyloidosis Patient Support Group" but, since the start of the Covid pandemic lockdowns in March 2020, our reach has become much wider than any of us ever thought possible. We are no longer a 'lunch club' for Amyloidosis patients who live in the Central Belt of Scotland. In many respects, that decision was imposed upon us by Covid. We simply could not meet up for a face-to-face chat in the way that we had been doing since we started the group in 2014.

Instead, we decided to experiment with the new communications technologies that were emerging – 'Zoom' to be specific – that would allow us to connect with people from the comfort of their own homes. When we started, none of us knew if anyone would show up online. The lunchtime meetings had been so good, so personal, so supportive, that it was difficult to see how a meeting on a screen could take its place.

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But take its place, it has and, for many of us, the online version has proved itself to be even more effective than the original in-person meetings. "How so?", you might ask. Well, think about this. Under normal circumstances, we would meet four times a year for our lunchtime chat with patients and carers. In the year between April 2020 and April 2021, we held over fifty online sessions over Zoom, bringing support and sharing stories with people from around the world.

Journey for X: In July 2021, Aja, her boyfriend (Luke), Mum (Fionna), Dad (Tony), cousin (Jake) and Brian McHattie from the Scottish Amyloidosis Support Group set off from Parkhead Stadium in Glasgow, to the skirl of the bagpipes.

To give you an example –\ and it's not the only one – of the sheer power of the Internet to connect people - and then allow them to communicate over platforms like Zoom – you need to hear the story of Aja Aguirre and her family.

With Aja's permission, I've included an extract from her very first email to me in September 2020, an email which set in tow an amazing chain of events…

"Hi Mark,
Apologies for the unsolicited email. I was on the Amyloidosis website discussion forums and I came across your name several times in different posts. You seem to be a very active member of the community, and I was hoping you might be able to offer some insight to me. Up until about two months ago I had never even heard of Amyloidosis. My brother got very ill very fast this year, starting in around March or so (although in hindsight and looking at photos we suspect he had been getting ill for at least a year or two before this). He was hospitalised due to retaining fluid and not being able to eat without bloating etc. He had 4 litres of fluid drained from him, and yet the hospital for some reason sent him home. He got many tests done and he just wasn't getting better, but the doctors did not know what was wrong with him. My parents finally called me at the end of June - four days after he was hospitalized again - to tell me that there was something very wrong with him. Being from Canada but living abroad here in Nottingham, I was 7000km away while all of this was happening in Burnaby, British Columbia.

He went from bad to worse rapidly and his organs were failing him while they still didn't know the problem. They put him on dialysis and said his kidneys and liver were failing and that he could end up needing a transplant. On July 9th, 2020, after weeks of testing, he was diagnosed with Amyloidosis and moved to Vancouver General Hospital to be seen by specialists. They did a bone marrow biopsy and found out it was AL Amyloidosis. Six days later I got a frantic video call from my parents while I was at work, saying that he had had a heart attack and wasn't expected to make it through the night. I booked the next flight home to Canada, which was the next morning. I arrived on July 15th, just in time to see him one more time. He passed away on July 16th at 8pm, surrounded by family and friends. My brother was only 30 years old. The doctors said that while it is so rare to have this disease, it is even more rare for someone his age, and to have such an aggressive kind (1 in 8 million they told us)."

Aja (pronounced 'Asia', by the way) went on to say that, in honour of her brother, Xavier, she would like to do a fundraising bike-ride from Glasgow (where part of her family came from originally) and Nottingham, where she lives and plays football professionally for Nottingham Forest's women's team. Aja is not a cyclist and had never done anything like this before. The route would be approximately 500km.

Aja joined the group's online Zoom chats and, having found them helpful, encouraged Mum, Fionna and Dad, Tony, to join in from Canada too. The group has members who have been bereaved as well as those who have experienced similar symptoms to those that Xavier had endured. Successful treatment in the UK had kept these people alive.

Throughout the remainder of 2020 and into 2021, Aja and her family got to know the group much better and her plans for the bike ride were assisted by practical support from some of the members. Mark McConway (an AL survivor from first diagnosis in 2011) and Brian McHattie (who had lost his wife to Amyloidosis) said that they would like to accompany the family on Day 1 of their adventure. Mark had to pull out of the ride on relapsing after ten years in remission.

Journey for X

Amazingly, in July 2021, Aja, her boyfriend (Luke), Mum (Fionna), Dad (Tony), cousin (Jake) and Brian McHattie from the Scottish Amyloidosis Support Group took off from Parkhead Stadium in Glasgow, to the skirl of the bagpipes and the sound of clapping from a small crowd of well-wishers, as they headed South on their way to Nottingham. It was a poignant send-off, with words of tribute offered up to Xavier by his father, Tony. With the exception of Brian – who left the family after cycling with them on Day 1 – the remainder of the group cycled into Nottingham on July 16th 2021, to coincide with the first anniversary of Xavier's death. As well as increasing awareness, Aja and her family raised the massive sum of £11,000 for Amyloidosis research, split between the National Amyloidosis Centre in London, the Mayo Clinic and the Amyloidosis Unit at The University of Calgary.

We've highlighted Aja's journey here to demonstrate what can be achieved when like-minded people are given the space and security to talk openly about the way in which Amyloidosis is affecting their daily lives. This has to include the mental health toll that this disease can take on people. Face-to-face meetings will always have the benefit of the parting 'hug' but, until that becomes the norm once more, we would argue that the online world offers huge benefits for communication, if used with sensitivity.

Anyone wishing to join the Scottish Amyloidosis Patient Support Group should email Mark at mcconway.mark@gmail.com

Loch Lomond swim raises over £12,000 for the Amyloidosis Research Fund!

By John McKelvey

My dad's family have suffered with familial Amyloidosis for years before it was diagnosed. Having lost a number of family members to this disease, I wanted to raise funds to support the research and treatment of Amyloidosis.

My dad's siblings are all from Co. Donegal on the west coast of Ireland and are now spread across the UK and Donegal. One of my uncles passed away in 2015, after suffering for a number of years with Amyloidosis and receiving treatment at National Amyloidosis Centre at The Royal Free Hospital in London.

After my uncle's death in 2015, I decided to raise funds for the National Amyloidosis Centre to help them continue researching and treating this awful disease. I decided to use my hobby of open water swimming and do a one mile sponsored swim of Loch Lomond. Having never fundraised before, I set up a JustGiving page not knowing what to expect in terms of funds but was absolutely bowled over when I raised £5970 + £1,140 in gift aid, which was amazing.

Following on from this, I was fortunate to be asked to the opening of the new scanner in 2016 where Princess Anne was present. We had a tour of the unit and saw

the amazing work that was being undertaken and met some of the medical team that had treated my uncle.

Unfortunately, as the years have passed, I have lost more family members to the disease and a number have since been diagnosed and are undergoing treatment for Amyloidosis, both in London and in Ireland. So I decided to have another go at raising funds for this amazing research center. I signed up for another swim in Loch Lomond but decided to double my distance and do a two mile swim and I began my fundraising, determined to beat my previous total. I shared it with friends, family and colleagues and as people heard more about the story, donations started to flood in, even reaching as far afield as Australia! To my amazement I raised £12,700 + £1088 in gift aid.

Having been a bit out of practice thanks to the pandemic, I knew I had to throw everything in to my training to make sure I could finish the swim! I trained at my local pool, Salford Quays and Sale Water park in the early mornings and evenings before and after work in all types of weather!

Thankfully, on the 28th August last year, the weather was a warm 15 degrees in Loch Lomond and the swim was amazing. I beat my best time and it was made all the better knowing that I had not only raised funds but awareness for the National Amyloidosis Centre at The Royal Free Hospital in London.

NAC Research

NAC at the Forefront – Gene Therapy in ATTR Amyloidosis

Gene therapy has been an exciting prospect on the scientific horizon for decades, with researchers around the world working to develop therapies to treat illnesses by altering faulty genes. For many years technical difficulties and the complexity of the human genome have hampered these efforts and progress has been frustratingly slow. But in recent years, the NAC has been at the forefront of this field, with trials of three different genetic therapies showing tremendous promise in treating ATTR amyloidosis.

The recent advent of two genetic therapies, patisiran and inotersen, has transformed the outlook for patients with ATTR amyloidosis. In 2019 these drugs were approved by regulatory authorities on the basis of clinical trials at the NAC. Both these approaches aim to temporarily 'switch off' the gene for the TTR protein which misfolds to form ATTR amyloid deposits. NAC patients with hereditary ATTR amyloidosis receiving these drugs are now experiencing very real improvement in symptoms. In addition, ongoing clinical trials at the NAC are testing patisiran, inotersen and other new drugs from their classes in a wider variety of patients, including those with wild type ATTR amyloidosis who were not included in the original trials.

Professor Julian Gillmore: "This is wonderful news for patients with this condition. If this trial continues to be successful, the treatment may permit patients who are diagnosed early in the course of the disease to lead completely normal lives without the need for ongoing therapy"

Experience with patisiran and inotersen has provided 'proof of concept' that blocking TTR production is effective and safe in treating ATTR amyloidosis. In a recent ground-breaking paper in the prestigious New England Journal of Medicine, the NAC doctors reported results of a landmark trial of a new type of genetic therapy for ATTR amyloidosis called NTLA-2001. This therapy uses CRISPR/cas9 technology and could potentially be the first curative treatment for ATTR amyloidosis. This paper has caused widespread interest in both medical publications and the popular press, because it was the first time that a novel therapy using CRISPR/cas9 technology had been successfully given to patients.

CRISPR/cas9 technology allows scientists to alter genes very precisely and efficiently. It is rather like a 'cut and paste' system for the genetic code. The protein Cas9 (or CRISPR-associated) is an enzyme that functions like a pair of molecular scissors, so that specific sections of the DNA can be removed, altered or added. It has been suggested that this type of 'gene editing' holds the potential to transform treatment for a wide variety of diseases. In 2020 the scientists who developed CRISPR/cas9 technology received the Nobel prize for their work. Until recently this type of therapy had only been used on cells taken out of the body then reinfused back into patients. But gene editing directly inside patients' bodies holds extensive potential to treating a wide range of illnesses.

The NAC trial was the first study in the world to show that CRISPR/cas9 therapy can be safely and effectively administered systemically (intravenously) to edit genes inside the body. The novel CRISPR/cas9 drug in the NAC trial uses a lipid nanoparticle delivery system to deliver the gene editing CRISPR protein to the liver where almost all the TTR protein is made. The goal is to permanently delete the gene for TTR in a single course of treatment. In the initial NAC trial, six patients with hereditary ATTR amyloidosis with polyneuropathy received a single infusion of NTLA-2001, with no significant ill effects. One month after receiving the treatment, all six participants experienced a significant drop in TTR levels with an average decline of 87% in those who received the higher of the two doses tested. Following these promising results, the trial is continuing, with a plan to recruit up to 38 patients with hereditary ATTR amyloidosis and approximately 20 patients with wild-type ATTR amyloidosis who will receive the higher dose of NTLA-2001 and then be followed for up to two years.

Professor Julian Gillmore, the Centre Head, said: "This is wonderful news for patients with this condition. If this trial continues to be successful, the treatment may permit patients who are diagnosed early in the course of the disease to lead completely normal lives without the need for ongoing therapy. Until very recently, the majority of treatments we have been able to offer patients with ATTR amyloidosis have had limited success. If this trial continues to go well, it will mean we can offer real hope and the prospect of meaningful clinical improvement to patients who suffer from this condition."

Long term outcomes of bortezomib (velcade) for AL amyloidosis

The NAC doctors recently published a report mapping the treatment journey of all 1276 patients seen at the NAC between 2010 and 2019 and treated with up-front bortezomib (velcade). The results were encouraging, with nearly 40% of patients achieving a deep, lasting response and not requiring subsequent treatment after more than two years follow up. When further treatment was needed, in many cases this was because of inadequate response rather than a true relapse. Patients who started treatment with less organ progression tended to have better outcomes, emphasizing the importance of early diagnosis and treatment.

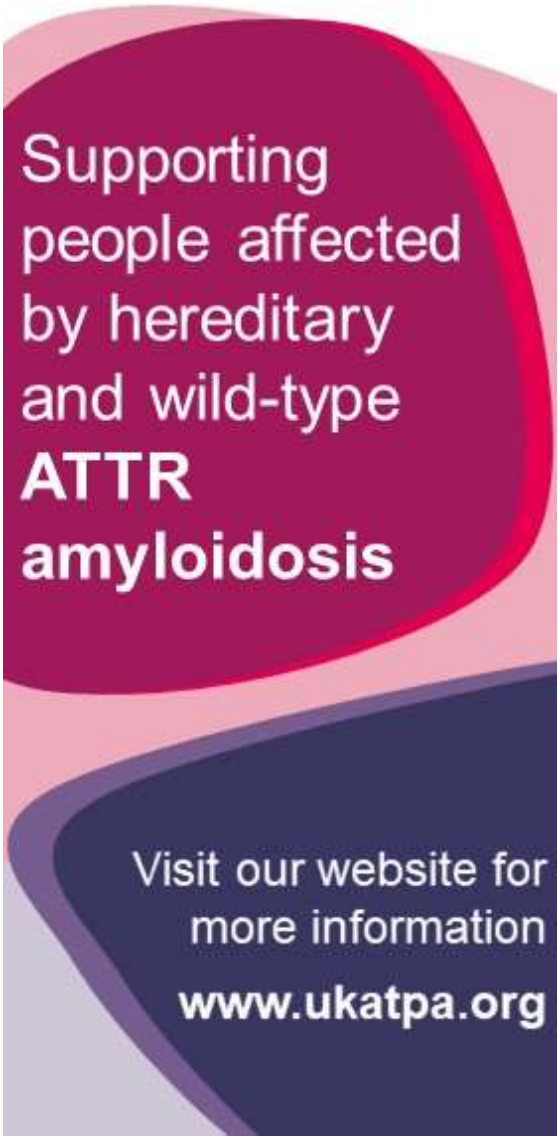
Patients who experience relapse after treatment can take heart from the observation that most patients in this study had no significant difference in outcomes from the first, second, third or fourth lines of therapy. Following each line of treatment, the deeper the response, the better the outcome. The authors concluded that achieving deep responses should be a focus in development of novel drugs for AL amyloidosis. Also, that although relapses occur in AL amyloidosis, outcomes and responses do not worsen with each relapse, making it attractive to design therapeutics with curative intent.

3rd European ATTR Amyloidosis meeting for Patients and Doctors

By David Gregory Trustee, UKATPA

The Amyloidosis Alliance, National Amyloidosis Centre and UK ATTR Amyloidosis Patient Association (UKATPA) organized a virtual conference. It was supposed to be a live event which was going to be held in London but due to Covid it was decided to move it to online. The 3rd European ATTR Amyloidosis meeting for Patients and Doctors was held over 3 days from the 6th to the 9th of September 2021.

We are proud to say that these three days were a huge success with over 700 attendees from all over the world taking part in the sessions. There were high quality presentations both on the channel dedicated to patients and doctors. The presenters delivered a packed and high-quality scientific programme with partnering companies, poster sessions and much more. The patient channel on day one focussed on the benefits of having a positive lifestyle with talks including Nutrition, Physical Activities and Mindfulness. Day two gave presentations from the leading doctors from around the world which talked about the treatments available now and what may be coming in the future. The final day discussed symptomatic management including neuropathy, cardiac and autonomic symptoms. Every presentation were followed by questions and answers from those presenters. It proved to be the perfect place to keep updated about amyloidosis. The organising committee is delighted with the success of this third congress and would like to thank everyone who attended for coming from all over the world to be there. The event is held every two years and the next will be held in Madrid. It will also be recorded to be online for those who cannot attend.



Patient story

By Paul Pozzo

My name is Paul Pozzo, I am seventy-one years old, a retired M.D. of a hydraulic engineering company. I have had wild type Amyloidosis for seven years.

I was diagnosed in March 2015, after being taken into hospital in January of the same year, after returning from the USA, where we had spent Christmas with my sister. I could not breathe. I was taken to A and E where I was kept in

overnight, the cardiologist who saw me arranged for fluid to be drained from around my heart and lungs, she also thought there was a strong possibility that I had amyloidosis. She sent me to the NAC, National Amyloidosis Centre, I had my appointment in March 2015. After a series of tests, it was confirmed that I did indeed have wild type amyloidosis.

I had been a keen cyclist, completing the London to Paris bike ride in 2012, but I felt I was getting breathless, I put this down to old age. I also had Carpal Tunnel Syndrome 10 years previous, this can be an indicator to Amyloidosis.

My initial feeling when diagnosed was one of fright. My friends and family, especially my wife, were fantastic, giving unwavering support. I started reading the internet about ATTR, this left me feeling depressed as I didn't know anything about the condition. Looking back, I would have liked to talk to other people with the same disease. Although I had an early diagnosis I don't think I benefitted as there was no medication available and still isn't.

My limitations living with ATTR are varied, I can still cut the grass or walk a couple of miles on a level path but can't do any heavy work or walk uphill. The most challenging symptoms for me are breathlessness and limited heavy work. I talk to people about my condition, I have always been outgoing. I heard about the ATTR charity prior to the Amyloidosis conference in Berlin. It was very informative; I met trustees of the charity and offered my help. I became a trustee last year of UK Amyloidosis Patients Association and I have been involved in helping set up the new website which is well worth a visit at UKATPA.org.

My most positive experiences since diagnosis were attending the Berlin conference and starting on a new drug trial. Until the pandemic we went on holiday with friends who appreciated my limitations but took to pushing me, uphill sometimes, as much as they could see I could manage. I was pleased with myself for riding my new electric bike about ten miles and digging a flower bed which should have taken about three hours, but it took me a couple days!!!

I do feel more confident about living with the illness and I am determined to live life to the full. I am hopeful about current drug trials and a cure for Amyloidosis in the future. My message to others who have recently been diagnosed is; don't give up you are not alone there is a support network out there for you. You must learn to change with the disease and find different things to do. I am looking forward to finishing the drug trial there is definitely hope on the horizon.

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from

Laura Lock

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