

Global perspectives:

HAEI MAGAZINE · ISSUE 3/2018



The youngsters jumped out of the frame at the 2018 HAE Global Conference in Vienna, Austria – and they keep doing so in this edition of Global Perspectives



Dear HAEi Friends,

I am struck by the symbolism brought to mind by the cover picture of this *Global Perspectives* edition. The youngsters in the photo—HAEi Youth Leaders Natali and Anna—represent a growing and empowered youth movement that is pushing through the current “frame” of global HAE treatment patterns and breaking down barriers that prevent access to modern HAE medicines. Our HAEi Youth are prominently featured throughout the magazine. The following pages chronicle Yujin Yamamoto’s struggle to never let his severe HAE get in the way of playing at the highest level of scholastic and collegiate basketball while also maintaining academic excellence. Readers will also be treated to four very interesting and highly informative pages prepared by our HAEi Youth.

The Global HAE movement continues to build momentum. We are very pleased that HAEi’s advocacy work in South Korea served as a tipping point for the government’s decision to reimburse an acute attack HAE therapy. In addition, HAEi, working with our Brazilian patient organization, has discovered a process that could expedite the availability of acute attack medicine for Brazilian patients, first in the State of Sao Paulo, and, hopefully the entire country thereafter. We are encouraging pharmaceutical companies to take advantage of this exciting and most interesting opportunity. Great things are also starting to happen in South Africa where HAEi has worked with our local patient leaders to provide treatment through the Global Access Program. In addition, we are very pleased to announce that South African patients are also getting full access to medicine through the “open label” component of an ongoing international clinical trial.

HAEi’s Regional Patient Advocates (RPAs) are the backbone of our Global Patient Advocacy movement and these experienced leaders are having a huge impact in the countries they cover. As you will read in this magazine, HAEi is very pleased to announce the appointment of two new RPAs – Fernanda de Oliveira Martins from Brazil who will work with our South American and Mexican member organizations – and Fiona Wardman from Australia who will cover the Asia Pacific. These accomplished and highly energetic advocates are ready to help member organizations in the ongoing quest of raising HAE awareness, improving diagnosis, and winning access to and reimbursement for modern HAE medicines.

Global Perspectives provides comprehensive overview of just about everything that is going on in HAE – we wish you pleasant reading.

Warmest regards to all!

Anthony J. Castaldo
President, HAEi

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Youngsters at the 2018 HAE Global Conference in Vienna, Austria

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HAEi is a global non-profit umbrella organization dedicated to working with a network of national HAE member organizations to raise awareness of HAE

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Meet the two new Regional Patient Advocates



Fernanda de Oliveira Martins
Mexico and South America

“We are excited that Fernanda de Oliveira Martins has accepted the role as the HAEi Regional Patient Advocate for South America and Mexico. Besides being a care giver for two HAE patients (her mother and sister), she also brings a wealth of experience from her day time job. We look forward to working with Fernanda in the region. She is covering Argentina, Bolivia, her native country Brazil, Chile, Colombia, Ecuador, French Guiana, Guyana, Mexico, Paraguay, Peru, Suriname, Uruguay, and Venezuela”, says HAEi executive Director Henrik Balle Boysen.

Latin America remains a very high priority for HAEi. Having two RPA's in the region significantly increases the ability to help the talented and motivated patients in this region achieve their very important goals.

Fernanda de Oliveira Martins is a Biologist, Nutritionist, and has a Master's degree in Public Health with specializations in business administration and in food marketing. Fernanda currently resides in São Paulo, Brazil and has also lived and worked in Canada, Spain, and The Netherlands. Her mother and sister both have HAE, and Fernanda has supported the activities of the Brazilian HAE patient organization ABRANGHE since 2005.

“My region is very diverse. Not only related to culture, typical foods, climate; but also the economic and political situation. This, of course, reflects on the health

care assistance and availability of medicine. For instance, in Mexico treatment is available with Berinert, Firazyr, Kalbitor, HBPM, Tranexamic acid, and fresh plasma. On the other hand, no treatment is available in Venezuela. This diverse condition can be seen as a weakness, due to the lack of alignment; but we can also try to see the positive side and learn from countries that are more developed in the medical area to improve the others”, says Fernanda de Oliveira Martins.

First of all the new Regional Patient Advocate will immerse into the situation of each country and establish good connections with the representatives of the national organizations.

“Together we will then define the priorities for each country. I think that implementing the HAEi Connect tool might be a good way to start my work with the countries, since this will not only facilitate contact with members, but provide a good figure of the situation in the country, for instance regarding the number of patients. This information will be useful to any other activity”, says Fernanda de Oliveira Martins.

“My main goal now is to have a good connection with the national representatives and learn from them since most of them have run their organizations for a long time – and naturally support them to further develop the great work that is already being done by them.”



Fiona Wardman
Asia Pacific

Considering the increased activities in the Asia Pacific region, most recently with China and South Korea, HAEi has appointed Fiona Wardman as the Regional Patient Advocate for this region.

“Fiona is an incredibly effective patient advocate who has already been heavily involved in helping patients in the region. Patients in Asia Pacific now have an experienced and energetic ‘partner’ to help them get organized, raise HAE awareness, and win access to modern HAE therapies”, says Anthony J. Castaldo.

Fiona Wardman is Chief Executive Officer of the Australasian HAE organization, which she co-founded in 2011. She is also the Treasurer for HAEi. Fiona is passionate about making a difference to HAE patients in her own region as well as globally. A patient herself Fiona lives in Glossodia, NSW, Australia.

“The Asia Pacific region and the countries I will be looking after are diverse, they are rich in history and culture, and some are underdeveloped which is quite different to what I know from living in Australia as a patient and advocate. Within these countries, the population is high, the social status or standing amongst the population diverse, and the economy and government within some of the countries is so varied. Access to treatment can be difficult, and finding information isn't as easy as some patients don't have access to a computer or service. Another challenge is the stigma attached to having a rare disease. For some patients having HAE can play a major role in a family or individuals prospects in marriage and their careers. All of this needs to be carefully navigated while

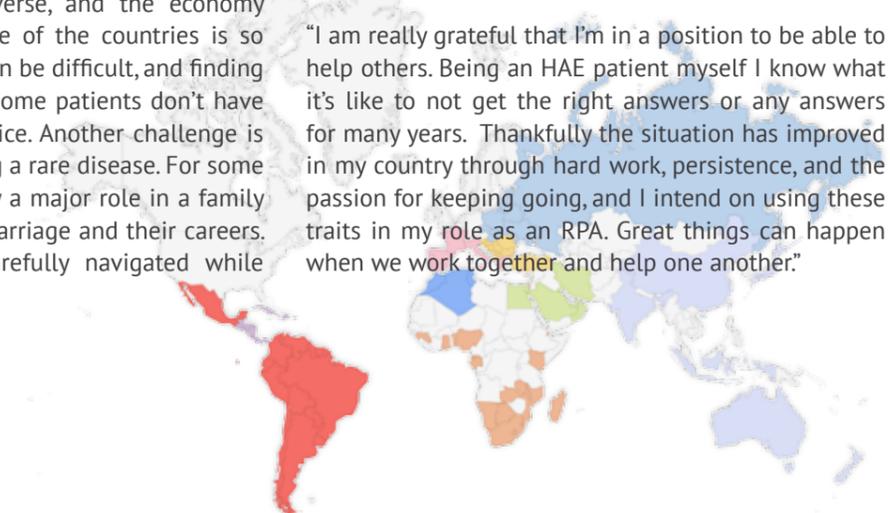
creating awareness, educating, and gaining access to treatments”, says Fiona Wardman.

In the Asia Pacific region, modern treatments are either not available, or not funded and therefore out of reach for patients; even common everyday medications can be out of reach for some of the population as they are expensive. Apart from a small handful of champion doctors, HAE knowledge amongst the medical professionals is fairly low which makes HAE underdiagnosed and misdiagnosed. Creating the awareness amongst the medical professionals is the key to turning this situation around. Fiona Wardman continues:

“I, fortunately, have a great network of contacts that I have accumulated over the last few years ranging from patients, rare disease groups, and industry partners, to someone I met once. I will be contacting each of them, speaking to them about the situation in each country, gather all information, and any other contacts, find out what the biggest challenges are and the best way to work together on a feasible plan.”

Regarding her new role as RPA Fiona Wardman says:

“I am really grateful that I'm in a position to be able to help others. Being an HAE patient myself I know what it's like to not get the right answers or any answers for many years. Thankfully the situation has improved in my country through hard work, persistence, and the passion for keeping going, and I intend on using these traits in my role as an RPA. Great things can happen when we work together and help one another.”



Regional Patient Advocates now covering most of the world

The HAEi Regional Patient Advocates (RPAs) have two roles: Supporting the member organizations already in place and assisting in setting up new groups in countries with no organization yet. Here are the eight RPAs and the regions they cover:

- **Michal Rutkowski** – Central and Eastern Europe
- **Natasa Angjeleska** – South East Europe
- **Maria Ferron** – Mediterranean
- **Rashad Matraji** – Gulf Region and Middle East
- **Javier Santana** – Central America
- **Patricia Karani** – Sub-Sahara Africa
- **Fernanda Martins** – South America and Mexico
- **Fiona Wardman** – Asia Pacific
- **Maria Ferron and Rashad Matraji**



News from the Regional Patient Advocates

There is so much going on in the regions that the HAEi Regional Patient Advocates are covering that it is only possible to update you on the activities of a select number of countries in this magazine. More information about the RPAs is available on www.haei.org.

Michal Rutkowski
Central and Eastern Europe

GENERAL

Over the last few months most of Michal's time has been taken up with preparations for the CEE Workshop taking place in Warsaw, Poland end October. During this work he has been in touch with all of the countries in his region.

As this is the biggest HAE conference in the CEE region – currently with around 150 delegates from 10 countries – conference preparations have been and are still quite intense. At this point the conference is almost full and most likely not everyone interested will be able to secure a place. Therefore we will bring you details from the conference in our next magazine – and you can read more about the plans for the conference at www.haeceec.org.

Maria Ferron
Mediterranean

GENERAL

Maria has been trying to set up meetings with national organizations to be able to share information on the HAEi resources. However, it is challenging in this region over the summer due to holidays – hopefully, dates will be set for the coming months.

ISRAEL

Maria has introduced Israel to HAEi Connect, and after a training session, the Israeli organization would like to join. The documentation process and the translation of the joining information have been started, and hopefully, things will be up and running shortly.

POLAND

HAE Poland is presently working with HAEi to join HAEi Connect. The process is well underway and it is hoped this will be successfully completed before the end of the year.

KAZAKHSTAN

Michal is supporting Sergey Morozov from HAE Kazakhstan to officially register the organization as a patient group. If everything goes according to plan the work should be completed over the coming months.

ALGERIA

Together with Michel Raguet from HAE France Maria has been able to put an Algerian doctor in touch with an Algerian patient hoping to establish a national HAE patient association. They will continue to support the patient as much as possible to develop a network of patients and doctors in Algeria.

Patricia Karani
Sub-Saharan Africa

GENERAL

Patricia has created the Hereditary Angio Edema Africa Facebook page to reach a wider HAE audience through social media hopefully – have a look at www.facebook.com/HAEInAfrica. She is also developing a survey to understand more about HAE knowledge and access to treatment amongst healthcare professionals in her region.

SOUTH AFRICA

There has been a status meeting in Cape Town for HAE patients and physicians regarding Ruconest in South Africa and the clinical trial currently underway. Patricia has been in contact with a youngster who is interested in creating a national youngsters' group. Furthermore, a Youth Program tab has been included on the HAE South Africa website – have a look at www.haei.org/southafrica. Training has also been scheduled on various schools to raise awareness of HAE.

KENYA

Patricia has been introduced to a Programs Officer from the Ministry of Health for Non-communicable Diseases in Kenya, who is interested in helping her in the process of how to work with the Ministry of Health. Future initiatives for HAE Kenya include an HAE training program being developed by doctors in Kenya for other healthcare professionals, as well as the first case study in HAE being written up for publication. A data management tool is also being developed for Kenya.

Fernanda de Oliveira Martins
South America and Mexico

GENERAL

Fernanda's key activities have been ensuring that she is up-to-date with HAEi materials and resources and introducing herself as the new Regional Patient Advocate to the member organizations in her region.

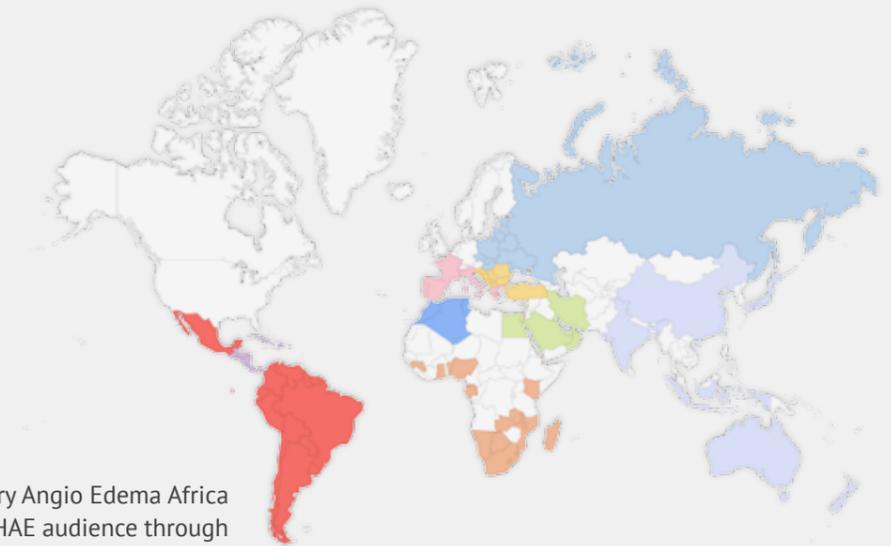
BRAZIL

Together with HAEi President Anthony J. Castaldo, HAEi Executive Director Henrik Balle Boysen and Dr. Anette Grumach, Fernanda has met with the Secretary of Health of the State of São Paulo to discuss access to modern medications in the state. Fernanda is now working on the next steps.

CHILE

1 September 2018 Fernanda attended the Association of Latin American Physicians Experts in Hereditary Angioedema Conference in Chile, where the HAE Global Registry was discussed.

The last session of the meeting was given to the patients – here Fernanda presented information on HAEi Connect, while Raquel Martins presented the work being done by HAE Brazil (ABRANGHE). Patients and patient associations were also represented by Lorena Merino from AEH Chile, Sandra Nieto from AMAEH Mexico, and the HAEi Regional Patient Advocate for Central America and Caribbean Javier Santana.



Javier Santana
Central America and Caribbean

GENERAL

1 September 2018 Javier attended the Association of Latin American Physicians Experts in Hereditary Angioedema Conference in Chile. This provided Javier with the opportunity to meet doctors who treat HAE patients within the countries that he represents and to find a way to work together to achieve the creation of new patient groups across Central America. While at the meeting, Javier introduced some of the physicians from Central America and the Caribbean to Dr. Rafael Zaragoza, the President of the Puerto Rico Allergists Association, to establish a collaborative effort so that physicians and patients can receive support from Dr. Zaragoza's clinic in Puerto Rico.

 **DOMINICAN REPUBLIC**

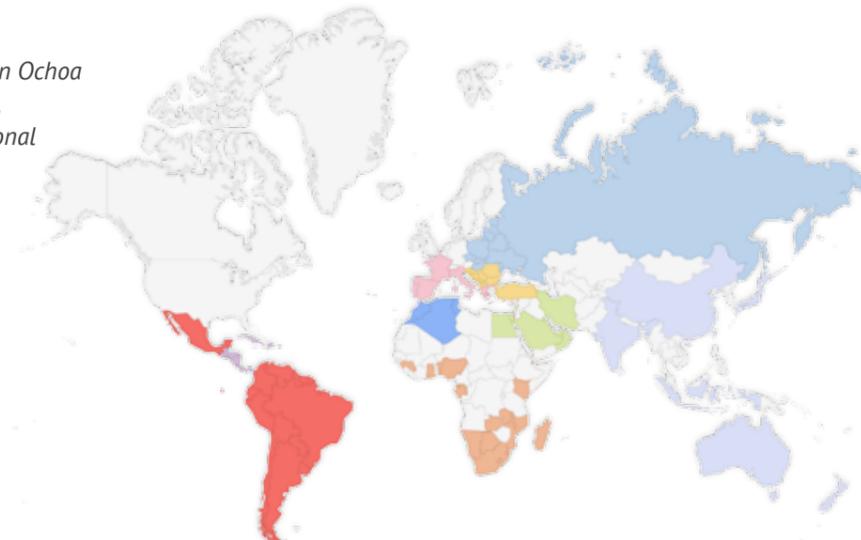
Javier has continued conversations with the Association of Allergists and Immunologists of the Dominican Republic. They have expressed a willingness to help organize a group of patients locally.

 **PANAMA**

Javier has been in frequent contact with Dr. Olga Melcina who looks after the majority of HAE patients. They have been discussing how to best help HAE patients in Panama.



From left: Dr. Emilia Morales (Guatemala), Dr. Rafael Zaragoza (Puerto Rico), Dr. Marlon Ochoa (El Salvador), Dr. Sergio Castro (Costa Rica), Dr. Olga Melcina (Panama), and HAEi Regional Patient Advocate Javier Santana.



Rashad Matraji
Gulf region and Middle East

GENERAL

Much time has gone into the preparations for the Middle East and Gulf HAEi Regional Summit 5 October 2018 in Beirut, Lebanon. Currently, 25 doctors from 14 countries throughout the region have confirmed they will attend.

 **INDIA**

Rashad has established contact with an Indian doctor currently in Dubai. This has led to contact with Dr. Murthy in India, who has experience in treating HAE patients. It is hoped that Dr. Murthy will be able to attend the Middle East and Gulf HAEi Regional Summit in Lebanon in October.

 **IRAN**

Rashad is supporting the Iran HAE group with the creation of a website that will be hosted by HAEi. The templates are currently being translated into Persian.

Natasa Angjeleska
South East Europe

GENERAL

Preparations continue for the SEE Workshop in Skopje, Macedonia at the end of September. Currently, 65 delegates from 11 countries throughout the region have confirmed they will attend, with more registrations expected.

 **SERBIA**

According to CSL Behring's Global Vice-President Berinert will be available in Serbia by the end of the year. Ivana Golubović from HAE Serbia sends her thanks to the HAEi President, Executive Director, and Regional Patient Advocate for their support in the matter.

 **CROATIA**

Natasa has met with a patient representative who had attended the HAE Global Conference 2018. They explored the potential for activity in Croatia, hopefully including the setup of a patient group. They are looking for other HAE patients in Croatia to help organize things. If you are interested in joining a patient group in Croatia, please contact Natasa at n.angjeleska@haei.org. The patient will attend the SEE Workshop in Skopje and can meet other HAE patients from Croatia there.

Fiona Wardman
Asia-Pacific

GENERAL

Fiona has been busy getting up to speed with the current HAE management in the countries in her region as well as research on names, contacts, rare disease groups, etc. as well as following up with quite a number of people to introduce herself and grow her network.

 **KOREA**

Fiona has made contact with doctors, the Korean Organization for Rare Disorders and pharmaceutical companies in the country. She coordinated a letter from HAEi to support Shire's application for funding Firazyf to the President of National Health Insurance Scheme in Korea – the approval came 22 August 2018.

 **INDONESIA**

Rudy Purwono, an HAE patient who Fiona met a few years ago, has agreed to lead HAE Indonesia. They are now working closely to distribute and utilize HAEi resources in the country. Furthermore, Rudy is working with his doctor to try and make contact with other doctors in the country who might see HAE patients.

 **INDIA**

Presently Fiona shares the responsibility for India with her RPA colleague Rashad Matraji. Fiona has been in contact with Dr. Shaibal Guha and an HAE Patient to discuss what the challenges are for HAE in India, and how HAEi can help. Fiona is supporting the patient with the process of developing an HAE India website to be hosted on www.haei.org. They also hope to translate the HAEi emergency card into Hindi and have this available soon.

HAEi Connect

– online membership database free for all member organizations



HAEi is proud to present a new initiative for the member organizations: HAEi Connect – a cloud-based member database for national organizations to manage their members.

“In our close collaboration with the national member organizations, we have learned that management of members is handled in many different ways – ranging from simple Word files and small local databases to Excel spreadsheets and more complex systems. In order to make management of the member database a lot easier for the national organizations under the HAEi umbrella we now offer a cloud-based platform for member management”, says HAEi Executive Director Henrik Balle Boysen.

HAEi Connect – a user-friendly interface with instant member e-mail communication – is a platform created and maintained by HAEi. Project Manager Ole Frølich explains:

“HAEi Connect will secure a uniform and secure member management worldwide. In addition to this, we will further develop the system based on ideas and requests from the member organizations”.

Among the key features of HAEi Connect are:

- Secure management of member information
- EU GDPR compliant system
- User-friendly interface
- The interface in the language(s) of the national member organization
- Dashboard with member data status
- Access to news from HAEi, download area and webinars
- Advanced function to search groups/segments of the members based on for instance age, gender, HAE type, member type, and type of treatment
- Send instant e-mails to members – single or searched segments
- Send profile update e-mail reminders to members – single or segments
- Customize e-mails and profile page identity with the national member organization name and logo
- Customize welcome e-mail and profile reminder e-mail
- Fields in the directory can be suited to national needs

“We have a very strong focus on securing the data of the members when entered into HAEi Connect as we want both the national organizations and every single member to feel safe using the tool. Many precautions have been made to secure the data as well as the server. Just to mention a few: All data traffic is handled in encrypted SSL protocol, the domain www.haei-connect.org is privately registered, and admin access is a two-factor login with username, password and text code. Furthermore, HAEi Connect is EU GDPR compliant with staff training, consent, privacy and all needed documents for non-disclosure agreement and code of conduct”, says Ole Frølich.



Learnings from Spain

“The Spanish HAE Association AEDAF approved the adoption of HAEi Connect in its 20th General Assembly, held in March 2018, and started using it in early June, when the first update reminder was sent out to all the members. The experience has been very positive. HAEi Connect is user-friendly and very secure, and it makes database management so much easier”, says AEDAF President Sarah L. Smith.

“AEDAF’s members have also responded very well. Approximately 50 percent of them reviewed and/or updated their data after the first update reminder was sent and, following the expiration of the 72-hour link to personal data in that first email, there were many individual requests for a new link to their personal data. In spite of this, we would like to keep on improving the member data in our database, and for this reason, we recently sent out a second update reminder to all members. We hope, with the use of this very helpful tool, to gradually update and refresh almost 100 percent of our 20-year-old database”, says AEDAF Secretary Maria Ferron.

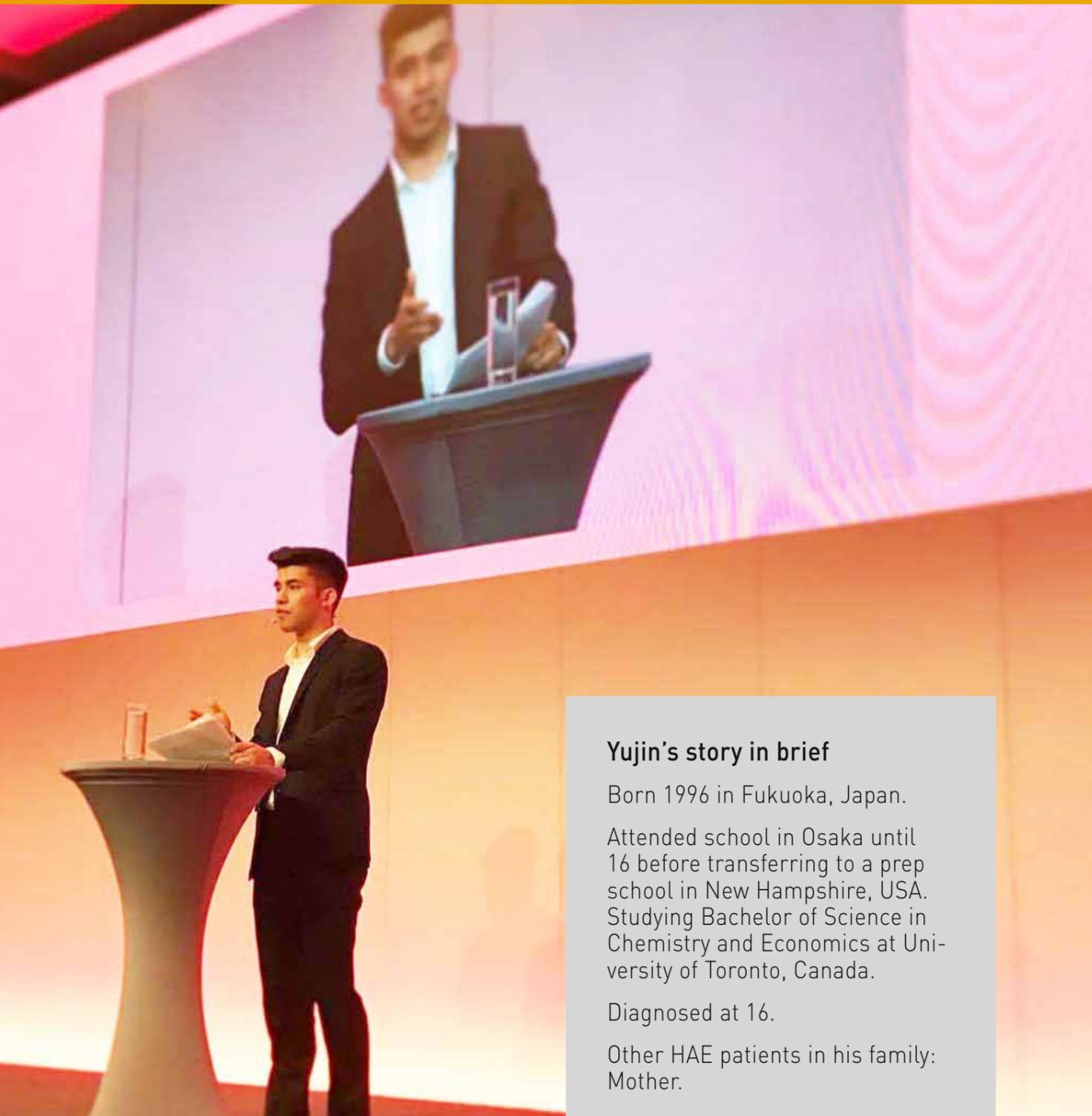
According to the HAEi Connect administrators in Spain, HAEi Connect is also what they characterize as a fantastic tool for fast, easy communication with all or a segment of members.



Currently, HAEi Connect is used by HAE Scandinavia, HAE Kenya, HAE Australasia, HAE Mexico, and HAE Spain (AEDAF), while the organizations in Argentina, Israel, Peru, Poland, Turkey, and United Kingdom have applied.

Please visit www.haei.org/connect if you want to know more about how to have your national member organization move its database to HAEi Connect.

This is Yujin Yamamoto's HAE story – based on the keynote speech he gave at the 2018 HAE Global Conference in Vienna, Austria.



Yujin's story in brief

Born 1996 in Fukuoka, Japan.

Attended school in Osaka until 16 before transferring to a prep school in New Hampshire, USA. Studying Bachelor of Science in Chemistry and Economics at University of Toronto, Canada.

Diagnosed at 16.

Other HAE patients in his family:
Mother.

Patient story: Yujin Yamamoto

Drawing upon our inner strength can empower us

HAE patient Yujin Yamamoto was born 1996 in Fukuoka, Japan. He attended school in Osaka until 16 before transferring to a prep school in New Hampshire, USA. He is now studying Bachelor of Science in Chemistry and Economics at University of Toronto, Canada.

You weren't diagnosed before the age of 16?

That's right. Even though it continued to worsen for both my Mum and myself, I wasn't diagnosed before my mid-teens. Around the time I turned 16, there were frequent visits to doctors and many hospitalizations all ending in an inaccurate diagnosis. This is the phase of my life where I began to realize that what might first appear as an impossible situation can result in something very positive. Our family faced something genuinely horrible when my Mum had a laryngeal attack that put her in the Intensive Care Unit where doctors worked to keep her alive while grappling with what they viewed as 'medically confusing' symptoms. This awful and dangerous experience, however, motivated doctors to figure out the puzzle finally and diagnose my Mum as having HAE type 1. Subsequently, the doctors had my sister and me tested, and that is when I found out that I also had HAE. On the one hand, it was great to finally know the cause of the problems I had been experiencing all my life. But after the doctor confirmed the HAE diagnosis, he added a chilling warning and said it would be dangerous and inadvisable for me to ever travel outside of Japan.

You say that drawing upon our inner strength can empower us. How is that?

There is no denying that HAE is a rare and serious orphan disease. Yet, by drawing upon our inner strength and accepting support from families, expert doctors, and HAE advocates the lessons we learn from having HAE can empower us to achieve whatever we strive for in our lives.

Starting at a young age, there were times when I would throw up for a day or more. My Mum experienced these symptoms as well so I figured that it was just something everybody had to deal with. I simply labeled my problem as an 'upset tummy' and blamed it on overeating a certain food or not getting enough sleep. It never occurred to me that something unusual was going on.

And that wasn't exactly the message you were looking for at that specific time?

Well, from a young age I had been obsessed with basketball. I ate, slept and dreamed about basketball. All I ever thought about was how to improve my game, and early on I set a goal of being recruited to play basketball at a prep school in the United States. Therefore the timing of my HAE diagnosis and the doctor's warning could not have come at a worse time.

How is that?

Just a few days prior to the diagnosis, I had been accepted to attend an elite month-long summer basketball camp in the United States. This camp meant everything to me because prep school coaches from around the US attend to watch international students showcase their basketball skills. I was determined to make a big enough impression to attract an offer to attend and play basketball at a prep school in the United States. At that moment, it looked like everything that I had thought about constantly and worked so hard to achieve would be completely taken away.

But after all it wasn't?

No, at this point in my life I came to understand the power of family, expert doctors who treat HAE, and people who advocate for HAE patients. I am fortunate to have a very smart and dedicated Mum who would do everything in her power to make sure HAE did not prevent me from pursuing my goals and aspirations. That was the case with my desire to attend basketball camp in the USA. My Mum is not someone who will take 'no' for an answer. She used her drive and ingenuity to figure out what would have to be done to ensure that I could fulfill my goal and safely travel to the USA. She made contact with a variety of expert HAE doctors including a very prominent one in London who believes in a 'no limits' approach for children with HAE. The doctor advised my Mum to develop a strategy that would keep me safe while traveling to the USA – and

that is precisely what she did. As part of this effort, my Mum contacted HAEi President Anthony J. Castaldo, and together they worked out a detailed travel logistics plan and devised a way to ensure that HAE treatment would be available if I needed it.

So in the end you did in fact go the camp in the USA?

Not only did I attend the basketball camp, I also managed to attract recruiting offers from a couple of top US prep school basketball programs. Not long after attending the camp, I received and accepted an offer to attend the New Hampton School in New Hampshire and be part of the school's basketball program. Throughout the summer months, we took care of the required paperwork that included obtaining a US Student Visa and registering for classes. Things were proceeding smoothly until three days before my flight was set to leave Japan for the USA. That was when we received an unexpected and disturbing email from the school's physician saying that I would not be allowed to attend New Hampton because I had HAE and the school was not equipped to handle my condition.

I guess you didn't just give up fighting at that point?

Definitely not, my Mum once again started to work tirelessly to overturn the doctor's decision. I admit this was the only time in my life when I thought to myself that maybe HAE really is a disability but the swift and positive action of the people around me quickly eliminated that thought from my mind.

True to form, my Mum spent hours explaining HAE to the school's doctor. She once again put the power of patient advocacy to work and asked the HAEi President to also call the doctor. Anthony J. Castaldo corroborated the information that my Mum provided, emailed a few relevant HAE medical journal articles, and arranged for a physician from the US HAEA Medical Advisory Board to consult with the New Hampton School doctor and nurses. Thankfully, the doctor reversed his decision in



From a young age Yujin has been obsessed with basketball.



All Yujin ever thought about as a young boy was how to improve his game, and early on he set a goal of being recruited to play basketball at a prep school in the United States.



time for me to make my flight and attend prep school in the USA. Once again, the power of family, expert doctors, and HAE advocates empowered a change that enabled me to fulfill a longstanding dream.

Finally arrived at your new school I guess you might for a moment have had a feeling that all of your HAE problems were now behind you?

I did, but that thought turned out to be false. Part of the 'deal' that changed the doctor's mind was that I would be proficient at self-administering intravenous HAE

medicine. While this is something I fully endorse as a best practice in HAE patient care, I had little experience with self-administration. You see, in Japan, patients must go to a hospital or a doctor's office to get an attack treated. Maybe it was the stress of living abroad by myself or the pressure of keeping good grades while spending countless hours practicing basketball, but at prep school, I experienced an increase in the frequency of my HAE attacks. I must say, learning to self-infuse proved to be a bit more challenging than I anticipated. But like with the other HAE circumstances this situation demonstrated something very important: the value of healthcare professionals who take care of us, and how we can rely upon them for help.

So initially you had difficulties self-administering your HAE medications?

Yes, sometimes I would get it on the first try, other times I would run out of veins to stick. I remember many failed attempts to treat abdominal attacks that created a bloody mess. There were multiple middle of the night calls to the nurse on duty followed by slow, painful treks over to the health center often through thick New Hampshire snow. The kind nurses were always there for me and patiently guided me to self-infuse successfully. These wonderful healthcare professionals made sure that I left prep school with the confidence to self-infuse. This experience once again illustrates that there are many people out there who will gladly help empower us to deal with HAE.

Having the ability to treat your attacks allowed you to continue your studies and basketball career abroad?

Indeed so. After graduating from the New Hampton School, I decided to attend the University of Toronto in Canada and most recently spent a year as an exchange student at the University of Nottingham in the United Kingdom.

What would you say that your experience as an HAE patient has taught you?

Most of all that I cannot change the fact that I have HAE – but more importantly that I can choose not to let HAE control my life. I now know that I can transform the disadvantage of having HAE into a personally empowering advantage. In his book 'David and Goliath' author Malcolm Gladwell chronicles the life of a young man with a devastating disorder called dyslexia that, among other things, impairs people's ability to read. Gladwell shows how the young man developed skills to compensate for his dyslexia and went on to find extraordinary success and fame as a lawyer – a profession that requires a keen ability to process and comprehend the written word. This story

resonated with me because it demonstrated that what I previously considered completely negative experiences brought on by HAE could actually be the source of great empowerment.

What I have come to realize is that enduring the intense abdominal cramps for all those years led me to develop a very high tolerance for pain. Turning the disadvantage of experiencing pain into the advantage of high pain tolerance turns out to be extremely useful in my athletic endeavors. My coaches take notice because I can sustain tough workouts for hours on end without showing any signs of weakening. Although I might not always have the height or other physical characteristics possessed by others I compete with on the basketball court, my high pain threshold allows me to push myself harder than any of my competition.

Your diagnosis and experiences with HAE have led to other things too.

Yes, as a result of my diagnosis I became interested in the science of HAE and decided to take courses in biology and chemistry so I could understand the biochemical mechanisms that cause swelling. This interest motivated me to seek an internship with a pharmaceutical company. Last summer, I was privileged to spend two weeks as an intern at BioCryst's Alabama research facility where I had a front-row seat observing hardworking and dedicated researchers as they navigated the complex and high-risk world of drug development.

It seems that your mother – who is Beverley Yamamoto – has played a central role in the way you are dealing with the condition that the two of you have in common.

Well, I have already alluded to the strength, courage, drive, and intelligence of my Mum and I have mentioned the things she has done to help me take control of HAE, but that is only part of the story. After getting diagnosed, my Mum quickly realized that Japan – despite its wealth and excellent medical infrastructure – was way behind the modern world when it came

to taking care of HAE patients. Not one to let this unfortunate situation continue, my Mum realized that Japan sorely needed an advocacy organization that would bring greater focus on improving HAE diagnosis, education, and treatment. She spent countless hours reaching out and gaining support from the Japanese and international HAE community of physicians, researchers, and pharmaceutical companies. She also began working with HAEi, which sponsored and supported her efforts to organize patient meetings in Tokyo and Osaka. Building on the success of the initial patient meetings, my Mum led a successful effort to create the formal organization HAE Japan. Never one to be satisfied with the status quo, she is now working to get the Japanese government to pass a policy permitting self-administration of HAE medicines. My Mum continues to build HAE Japan while pursuing her professional life as a full professor at the prestigious Osaka University. Her research interests have evolved and now include bioethics and the impact of patient advocacy. We can look forward to some interesting and important scholarly work that will inform future patient advocacy strategies.

Any thoughts on the work of HAEi?

As a young HAE patient, I wholeheartedly endorse HAEi's Youngsters' Summer Camp program and efforts to have special youth activities during the global conferences like the most recent one in Vienna, Austria. I also find it impressive that HAEi has presently six Regional Patient Advocates who are responsible for helping interested patients form national organizations and providing technical and other assistance to existing groups looking to expand their membership or broaden access to modern HAE medicines. I strongly recommend that member organizations make full use of HAEi's free web hosting services and HAEi Connect

– a secure, custom-built relational database that will help member organizations manage their membership and communications. HAEi's presence in China, India, Sub-Saharan Africa, Latin America, Eastern Europe, the Philippines, and Southeast Asia shows that HAEi is making smart, forward-looking strategic investments in the power of patient advocacy.

A closing remark, Yujin?

That would be that HAE patients – and their families – should always keep in mind that what might first appear as an impossible situation can result in something very positive. I hope that they can find the inspiration to look at their HAE experiences as a source of empowerment that puts them on the path to achieving their goals and aspirations.

HAE in Japan

- *Member Organization*
HAE Japan was established in 2013 – www.heaj.org
- *Patients*
760 patients are diagnosed (as per May 2018) – there are an estimated 2,400 patients in Japan
- *Specialist outpatient clinics*
2 (Tokyo area and Osaka area)
- *Physicians*
Many from a wide array of disciplines but only a small number of truly specialist HAE physicians
- *Available medication*
Berinert for acute attack and short-term prophylaxis; no modern long-term prophylactic treatments

In May 2016 Yujin took part in the first HAEi/AEDAF Camino Walk in northwestern Spain – here he is with his sister Shia and their mother Beverley





3 TEASERS FOR HAE YOUNGSTERS

1 FREEDOM THROUGH SELF-ADMINISTRATION

HAE patient Nanna, Denmark shares her story on how she has gained freedom through self-administration:



“Being a HAE patient through your childhood years comes with a lot of responsibility! You learn how your body reacts to an attack, how to decide when to have your medication and most of all know how to tackle the disorder. Some attacks are easier to react to, but some of them are hard to recognize. HAE for me was a fear throughout my childhood. It was through learning self-administration that I managed to turn my HAE into something I am not afraid of.”

To read all of Nanna’s story please go to <https://haei.org/youngsters/self-administration/>



2 RUNNING FOR HAE AWARENESS

After being diagnosed only two years ago, US patient Luke Granat and his family found strength and a sense of community through their participation in the HAE IN-MOTION event in their area.

“Team Luke and his Puffy Posse had an amazing show of support at the HAE IN-MOTION 5k in Wheaton Illinois! Our main goal was to raise awareness in our community for this rare disease, in which we succeeded. We had many friends and family join us in this great event. This 5k holds a special place in my heart because it is where we got our start in the HAE community.”

Want to read more? Then run over to https://haei.org/youngsters/haea_5k_wheaton/

REFLECTION ON THE HAEA 2018 CAPITOL HILL DAY 3

The US HAEA Advocacy Program leads a nationwide movement focused on maintaining a strong advocacy presence in health-related legislative and regulatory policy. The HAEA Youth Leadership Council and youth members joined the advocacy efforts during this summer’s Capitol Hill Day and demonstrated how they too, Stand Up Strong. Courtney Olson writes:

“If I could emphasize one thing from my experience at Capitol Hill Day, it would be that no matter how young, old, introverted,

extroverted, experienced, or inexperienced you are, be an advocate for what you believe in, those you care about, and yourself. I learned this valuable lesson at Capitol Hill Day, which I will always appreciate and set as my life mission. I also learned that youngsters in the United States and around the globe are making the world aware of HAE. HAE youngsters are tough, passionate, engaged, and truly remarkable young advocates ready to stir the world with change.”

Read the full story at https://haei.org/youngsters/haea_capitol_hill/



HAEI YOUNGSTERS COMMUNITY CREATING GAME PLANS

During the 2018 HAE Global Conference (GC 2018) the HAEi Youngsters community created a magazine and a website. They also spent time discussing their personal experiences and thinking of how these could be used to help other youngsters who may be facing some of the same challenges.

It is important for an HAE patient to have a clear action plan for when they have an attack that has been discussed and agreed with their doctor. However, there are some situations where it can be more difficult to carry out the plan, and it can be helpful to have a specific strategy for these times.

The Youngsters community developed game plans during the conference to help HAE patients think ahead and prepare for certain situations. HAEi has used these to create a list of hints and tips based on the youngster's personal experiences, which hopefully can help people with and without treatment. The template can be downloaded from www.haei.org/youngsters, and you can use the advice shared here to create your own game plan. This isn't medical advice, but it can support the plans that have been discussed with a healthcare professional.

1 GAME PLAN

When could a game plan be useful?

- Starting a new school or job
- Traveling in a vehicle e.g. a boat or plane
- Going traveling or on holiday
- Going to a sleepover

- Going on a field trip
- Going to university or college
- Taking your exams
- Starting a new sport or activity

2 WHO IS ON YOUR TEAM?

Think who could be able to help you and take note of their name and contact details.

- HAEi and the HAEi Youngsters Community!
- Doctors or HCPs
- HAEi Regional Patient Advocates
- National HAE organizations

- Family
- Friends
- Colleagues
- Teachers

5 TAKE CONTROL!

You can't predict when you might experience an attack. By preparing for the situation the best that you can, you can take control of your HAE and keep yourself as safe as possible.

The Youngsters Community has created lots of other materials and resources, which are available at www.haei.org/youngsters. You can also connect with the Youngsters Community for help, support and fun using social media.

3 HOW CAN YOU PREPARE?

These are some tips from the youngsters – some will be applicable to every situation and some only to a few. You can tailor your game plan appropriately so it suits you.

- Always carry an emergency card or information bracelet (Download the HAEi emergency card www.haei.org/resources/emergency-cards)
- Consider who is on your team and can help you
- Have a process ready to help you relax
- Understand what causes you to have an attack
- Always carry your medication
- Learn how to self-infuse
- Call ahead and make sure people are aware of your needs
- Research the local area and HAE resources, e.g. member organizations, hospitals and HAEi Regional Patient Advocates
- Discuss HAE with the appropriate people to help you plan ahead and make them aware of your triggers
- If travelling take an additional emergency card in the local language
- Carry an icepack for long journeys or long stopovers
- Make sure your mobile phone is charged and you have the means to charge it
- Wear loose or comfy clothing for long journeys
- Ensure there is a quiet place where you feel comfortable taking medication
- Divide your supply of medication between bags in case one gets lost

4 WHAT TO DO IF YOU HAVE AN ATTACK?

1. Remember to try and remain calm. This is especially important with HAE as stress can act as a trigger and increase the severity of the attack. That is why having a process to help you remain calm is a fantastic strategy to have in place before the attack takes place.
2. Work through the treatment plan you have developed with your doctor.
3. Other things to remember include:
 - **Take control** as quickly as possible, as the sooner you act the more effective you can be
 - Let the people with you or around you know what is happening
 - Try to be open and clear with your communication
 - Have someone else call for medical assistance
 - Take your treatment as soon as you feel an attack coming on, do not wait



Follow us on Instagram:
[@haeiyoungsters](https://www.instagram.com/haeiyoungsters)



Join our group on Facebook:
HAEi Youngsters Community

Visit our website:
haei.org/youngsters





HAE Emergency Cards

An emergency card can be a quick and effective way to let healthcare professionals know that you have a diagnosis of HAE when you arrive at a hospital or care center, and the treatment that should be considered.

The HAEi Regional Patient Advocates have developed a template Emergency Card, which contains clear and simple information about HAE and treatment required during an attack. It also contains space for patients to add personal information such as emergency contact details and their specialist treatment center.

The Emergency Card has been translated into a number of languages and is already being used by HAE advocacy organizations around the world.

On the HAEi website you can find examples of these cards for you to download and use. Each card has been designed to be printed at home, cut out and folded in half to create a format that can fit within a wallet/purse.

“The Emergency Card have been designed to be used by HAE patients from all countries and can be adapted by any HAEi member organization. If you are a member organization and have designed your own emergency card that could be displayed on the HAEi website, or if you would like help from HAEi in adapting a card, please contact me”, says Project Manager Deborah Corcoran. “If you are not a patient or part of a HAEi member organization and would like to use one of the cards, please contact the HAEi Regional Patient Advocate for your area and inform him or her that you plan to use the card.”

Currently the Emergency Card exists in these languages – and more are to be added:

Bulgarian, English, Farsi, French, Greek, Hebrew, Italian, Macedonian, Portuguese, Romanian, Spanish, and Turkish.

Project Manager Deborah Corcoran:

d.corcoran@haei.org

HAEi Regional Patient Advocates' contact:

www.haei.org/organization/meet-the-rpas

Get your website hosted at haei.org

A growing number of national HAE organizations have their own websites with their own individual hosting solution. However, some of them would like to change hosting or altogether change the look and content of their websites. And others would like to just have a website at all.

“In order to accommodate any such national HAE organization we have established a system under the HAEi website allowing us to host national websites as well as provide them with templates for an individualized website – naturally all in their native language”, says HAEi Executive Director, Henrik Balle Boysen.

At this point national websites have been launched for these 16 countries:

- **Australia:** www.haeaustralasia.org.au
- **Ecuador:** http://haei.org/ae_h_ecuador/
- **Greece:** <http://haei.org/greece/>
- **Hungary:** <http://haei.org/hungary/>
- **Iceland:** <http://haei.org/iceland/>
- **Kenya:** <http://haei.org/haekenya/>
- **Macedonia:** <http://haei.org/haemacedonia/>
- **New Zealand:** www.haeaustralasia.org.au
- **Peru:** <http://haei.org/peru/>
- **Poland:** <http://haei.org/pl/>
- **Romania:** <http://haei.org/romania/>
- **Serbia:** <http://haei.org/rs/>
- **South Africa:** <http://haei.org/southafrica/>
- **Spain:** www.angioedema-aedaf.org
- **Turkey:** <http://haei.org/turkey/>
- **Uruguay:** <http://haei.org/uruguay/>

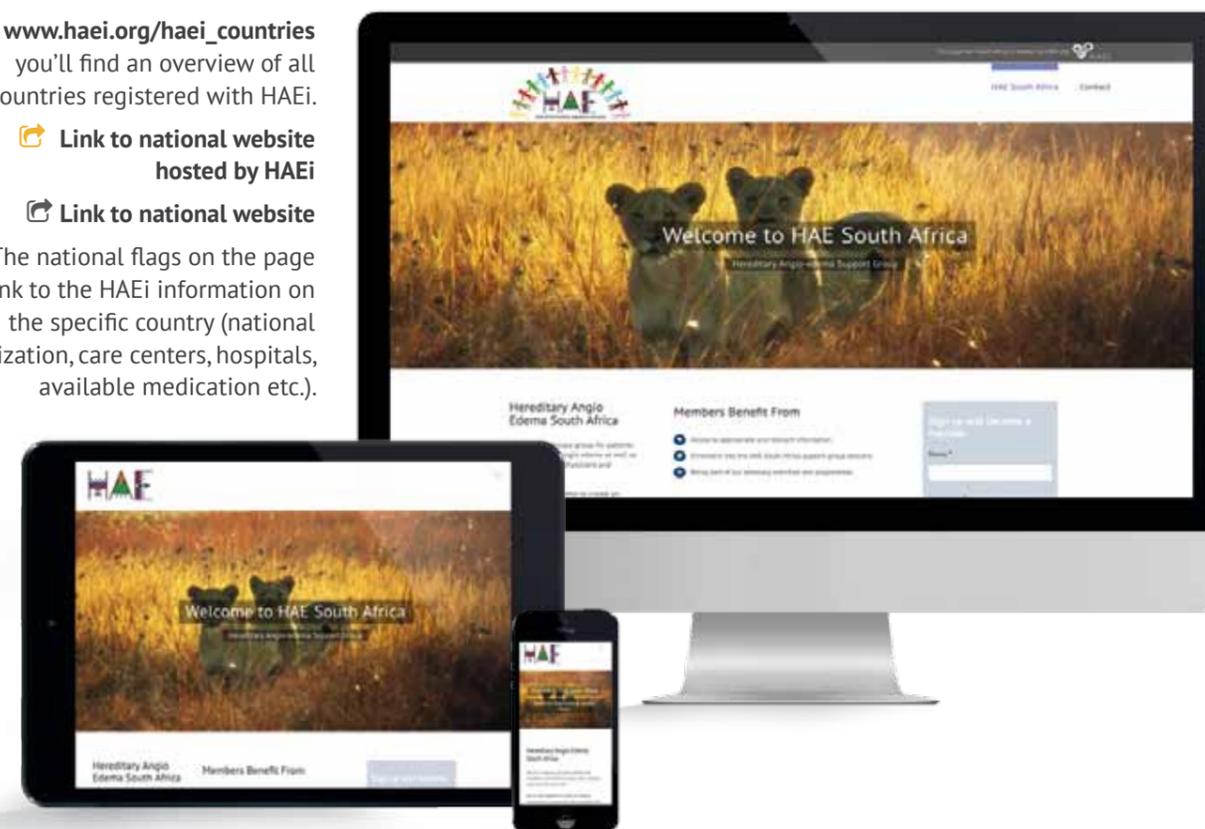
“We are preparing one or two at the moment and many more are welcome to join us”, says Henrik Balle Boysen.

At www.haei.org/haei_countries you'll find an overview of all 63 countries registered with HAEi.

[Link to national website hosted by HAEi](#)

[Link to national website](#)

The national flags on the page link to the HAEi information on the specific country (national organization, care centers, hospitals, available medication etc.).



News from around the Globe

POLAND www.haei.org/pl

The 5th HAE National Conference and the 3rd HAE CEE Conference will be taking place at the Double Tree By Hilton Hotel & Conference Centre in Warsaw 27-28 October 2018.

Among the speakers on the first day are Prof. Marc Riedl (*HAE background and treatment landscape – now and the future*), Dr. Anders Minken (*A mental approach to HAE*), Prof. Henriette Farkas (*HAE during pregnancy*), Dr. med. Marcin Stobiecki and Prof. Krystyna Obtutowicz (*HAE in Poland – an overview*), and HAEi President Anthony J. Castaldo (*Advancing HAE Advocacy*). On the second day the program includes presentations by HAEi

Executive Director Henrik Balle Boysen (*HAEi Advocacy tools*), Prof. Marc Riedl (*Implementing best practices*), HAEi Regional Patient Advocate Michał Rutkowski (*A regional perspective of CEE*), and CEO of Selvita SA Paweł Przewięźlikowski (*How Patients' Organization can help stakeholders improve patients' quality of life*).

The two conference days also include a Healthcare Professional Session, a Physician Session, a Scientific Session, country presentations, and the premiere of a documentary on living with HAE from the Polish patients' perspective. See the full conference program at www.haenk.org/en.



HAE Scandinavia will be arranging three patient meetings this fall: 6 October 2018 in Stockholm, Sweden and 10 November 2018 in Malmö, Sweden – both with Dr. Patrik Nordenfelt as the main speaker – and 24 November in Ålesund, Norway where Dr. Robert Brudevold will be the main speaker. Furthermore, HAE Scandinavia will have its annual general assembly in Denmark on 3 November 2018.

HAE Scandinavia will be publishing a survey completed amongst the Scandinavian patients and caregivers. The purpose of the survey was to improve the understanding of patients with HAE. The survey will be available in Danish, Norwegian and Swedish from the Scandinavian website.

HAE Scandinavia has just started an Instagram account – please have a look at [#haescandinavia](https://www.instagram.com/haescandinavia).



HAEi has added Indonesia as country no. 64 to the global family. The HAEi point of contact is Mr. Rudy Purwono who can be reached at purwonor_r@icloud.com and +62 812 3032006.



CEO Laura Szutowicz of HAE UK writes:

This very hot summer seems to have flown past and it seems like no time since I was writing about the HAE Global Conference in Vienna.

I was invited to speak at an Immunology Nurse meeting earlier this year with the theme of encouraging centers to run their own Patient Days as a way of getting patients to know one another as well as introducing them to all members of the Immunology team. Often patients only see one doctor or one nurse in clinic and most of our centers have several of each, several of whom have an interest in HAE so it is good for everyone to get to know who may see them if a doctor is off on holiday, for example. We are fortunate that so many nurses and doctors are keen to learn more about HAE.

The first of these patient meetings was hosted by the West Midlands Immunology Centre at the Crowne Plaza Hotel, Birmingham on 15 September followed by St James, Leeds 22 September, and then Salford Royal Hospital, 3 October 2018. The last one this year is Addenbrookes, Cambridge on 1 December. Anyone interested in attending should contact the Immunology Centre directly for more information.

Our own Patient Days start with our third Scottish meeting being held at the Novotel Edinburgh Centre on Saturday 6 October 2018. This day runs from 10.00am until 3.00pm and is open to all patients and families although we do request that under 16s are accompanied by an adult. Our theme for this year's meetings is "A Bright Future with HAE" as we do feel that the various treatments in development will make living with HAE so much easier.

I have been involved over the summer in various rounds of contracting and approval of products that will be reimbursed. This now means that there are three C1-INH products available for clinicians to prescribe (two plasma derived and one recombinant) in England and Scotland. Wales is currently assessing the recombinant but already has plasma derived C1-INH. There is also Icatibant available throughout the UK as well as Tranexamic acid and attenuated androgens, so we are very fortunate to have so much choice for clinicians and patients.

Our other Patient Day is our big national one and this year is being held in the south of England at the Mercure Farnham Bush Hotel on 17 November 2018. This has got an excellent program with a few new twists to make sure it remains relevant and interesting for attendees. The meeting will also have the welcome/social event on the Friday evening before and we hope as many people as possible will attend this. The same theme of "A Bright Future" will cover this day and we look forward to seeing as many people as possible. Vice President Michał Rutkowski, who is President of the Polish HAE organization, will represent HAEi. Michał has attended our patient days before and is a very popular speaker!

I look forward to reporting the Patient Days in the next edition of this newsletter!



AEDAF's next regional Workshop for Patients with HAE will be held on Thursday 4 October 2018 in Almeria (Andalusia), from 5:00 to 8:00 pm, in Hotel Catedral, Plaza de la Catedral, 8 – 04002 Almeria. This will be the 14th patient workshop organized by AEDAF. The agenda will be announced soon.

News from around the Globe



From Michelle Cuevas, HAEA Director of Communications:

U.S. HAEA Volunteer Advocates travel to Washington D.C. to request support for patients: The HAEA's 2018 Capitol Hill Day was a great success as 100 of HAEA's committed volunteers visited over 75 Senate and House offices to advocate on behalf of all HAE patients. Volunteer advocates delivered a vitally important message, requesting the continued support for HAE patients that includes expanded research, access to charitable assistance programs, and research funding.



Furthermore, this Capitol Hill Day included members of the HAEA Youth program, who participated in a specialized advocacy training session to learn about the importance of legislative policies, how they can get involved, and have an impact on these policies. Their training gave HAEA youth an overall better understanding of how the legislative process works.

Our HAEA representatives were strong, inspirational, and well informed. Due to their collective efforts on Capitol Hill, HAEA patients and family members were successful in adding six additional co-sponsors to H.R. 3976, a bill that supports charitable patient assistance programs. Together, we were also able to spread HAE awareness and educate lawmakers on the issues that impact all rare disease patients. Legislators heard from us how legislative decisions will affect access to life sustaining therapies and care for those in our HAEA community.

Youth Advocacy Month: The HAEA is proud to announce that the first annual HAE Youth Advocacy Month will be celebrated this October, spotlighting young HAE patients and their family members who are making a difference by raising awareness about HAE.

Scientist from the U.S. HAEA Angioedema Center at UCSD develop blood test to help physicians more accurately diagnose the cause of recurrent swelling in patients who do not have a deficiency of C1 Inhibitor: The HAEA has made significant investments in clinical research to advance our knowledge of HAE with Normal C1 inhibitor and to help improve the quality of life for members of the HAEA community living with this disease.

These investments are paying off and we are pleased to announce that the physician/scientists at the US HAEA Angioedema Center at University of California San Diego have published a medical journal article regarding a blood test they developed that will help physicians more accurately diagnose the cause of recurrent swelling in patients who do not have a deficiency of C1 Inhibitor. The test can determine if swelling is related to histamine or bradykinin, which is the cause of swelling in HAE types I and II. The results of this blood test could lead to more informed treatment decisions.

The article is entitled "Threshold-Stimulated Kallikrein Activity Distinguishes Bradykinin from Histamine-Mediated Angioedema" and appears in the Journal of Clinical & Experimental Allergy. For more information, please contact any member of the HAEA Health Team at <https://www.haea.org/ClinicalTeam.php>.

It is important to stress that like any new scientific discovery, this blood test is still experimental, and must be further evaluated before it can be approved by the FDA and used as a diagnostic tool.

HAEA is committed to moving forward with this and future scientific advances in the diagnosis and treatment of HAE with Normal C1 Inhibitor.

(continues on next page)

News from around the Globe

Scholarships are especially important for young people in our community because families with HAE often face financial challenges caused by the many burdens that result from dealing with HAE.



USA – cont.

From Lois Perry, HAEA Director of Health:

Pam King HAEA Scholarship Program: The HAEA is saddened about the recent passing of our Acting CEO, Pam King. Throughout her career in the pharmaceutical industry and the patient advocacy realm, Pam continuously inspired us with her relentless dedication to helping patients battling serious medical conditions lead a productive life. She had a special place in her heart for providing young HAE patients with opportunities for overcoming obstacles and fulfilling their goals and aspirations. Pam launched the HAEA Scholarship program in 2015, which has helped over 50 HAE patients pursue higher education even while facing enormous health challenges.

To honor Pam and her devotion to young HAE patients, we are memorializing the scholarship program in her name - the Pam King HAEA Scholarship Program. Scholarships will continue to be awarded to recipients who demonstrate the characteristics that Pam brought to the HAE community: relentless hard work, resilience, courage, and a passion for giving back.

Scholarships are especially important for young people in our community because families with HAE often face financial challenges caused by the many burdens that result from dealing with HAE.

We invite you to celebrate Pam's legacy by contributing to this worthy cause – please see www.haeascholarship.org/support.php. Your financial support will fulfill Pam's goal of empowering young patients to break free of the impediments caused by a rare, chronic disease and establish a path for a better future by pursuing a college degree. All gifts are immensely appreciated. Our average scholarship recipient receives 2,500 USD. How many lives can you help us change?

Spring scholarship applications are now open: Students can now fill out an online application for the Pam King HAEA Scholarship Program for Spring 2019. The scholarship program is available to US citizens with a confirmed HAE diagnosis. The deadline for applications is 30 September 2018 – see more at www.haeascholarship.org/applicationstart.php.



New features of the Brady Club: HAEA is launching some exciting new features of the Brady Club and we would like to invite kids and their families to participate. The club is now available for download on mobile devices: Find it on the Android and IOS app store, under the Brady Club (look for Brady the Bear on the app icon). Once you download the app, register on our secure platform to gain access to all the features. Once you download the app and register, kids can be signed up to receive a quarterly Activity Book in the mail. The Brady Club Activity Book is filled with fun games, information, photos and stories from other kids with HAE, and a special kids corner where an HAE specialist will answer questions about HAE.



1st annual HAE Youth Advocacy Month: Join us this October as we spotlight young HAE patients and their family members who are making a difference by raising awareness about HAE. We challenge you to think of a way to raise awareness in your community in October and share your efforts with us. For instance you can order a ER Tool Kit here: www.haea.org/ERkit.php.



News from around the Globe



RUSSIA

www.op-nao.ru

Elena Bezbozhnaia, Chairman of the interregional public organization "Society of patients with Hereditary Angioedema", has sent this report:

According to widely accepted figures (1 patient per 50,000 population), the prevalence in Russia should be estimated at 3,000 patients with diagnosed HAE. Officially, 282 patients with HAE, including 43 children, were inscribed in a public register during 2017. Of these 64 live in the capital of the Russian Federation, Moscow. The low screening rate suggests missed opportunities to identify the individuals with HAE. Highly qualified and experienced doctors, medical diagnostic centers are available in large cities. However, in many regional medical institutions, doctors are even not always aware of such a disease as HAE. Prior to the final diagnosis, doctors most often determine asthma, allergy, rheumatological diseases, Quincke's edema and other diseases. Proper diagnosis takes, on average, about 8.5 years. Inadequate therapy increases the risk of mortality among patients with HAE. About 25% of patients in the Russian Federation die from laryngeal edema under the age of 30.

In Russia, two pathogenetic preparations are recommended for use today: Icatibant syringe pen for patients able to self-administer subcutaneously (after special training) in an extreme situation, and Berinert, which is administered intravenously in a hospital (without special training).

The federal law "On the fundamentals of health protection of citizen in the Russian Federation" grants people with HAE the right to receive their medication for free. Patients shall be provided with proper medication under special regulations and orders. In reality, the law is not implemented in all regions of the federation. Patients need to seek the prescribed medicines on their own. Unfortunately, in many regions, people still do not get the appropriate medicines.

Until 2016, there was no official association of patients with HAE in Russia. Patients had to look for like-minded people on websites due to limited relevant information about the disease. However, that year an initiative group in Moscow created the interregional public organization "Society of patients with Hereditary Angioedema" (SPHA OPHAE), aiming at ensuring focused attention to HAE diagnosing and patient support. The Society focuses on three main areas: educational, legal, and psychological – to support patients and raise awareness of the medical community. Lawyers, who cooperate with SPHA OPHAE, provide members of the organization with legal support, represent their interests in regional courts when considering claims of patients to medical institutions about the failure to comply with legislation on the appropriate medical

provision. With this support, many patients have proved their right to access to essential lifesaving drugs. In 2017, SPHA OPHAE launched the project "The Right to Live". Within the project, the society organizes mobile schools for patients and interregional online webinars in different regions of the country. Leading specialists – doctors, lawyers, psychologists – are invited for participation. Patients learn about advanced methods of diagnosis and treatment of the disease in Russia and other countries, receive legal advice, participate in psychological training, and exchange personal experience.

SPHA OPHAE actively interacts with the Ministry of Health of the Russian Federation, regional ministries, and health departments. The society organizes scientific conferences and training seminars for doctors and patients, and SPHS OPHAE representatives are involved in significant events for the medical community and patients.

In May 2018, a delegation from Russia participated in the HAE Global Conference in Vienna, Austria. I had the pleasure of heading the group in my capacity as Chairman of the Moscow Society of Patients with HAE. The conference was a great experience and unique occasion to meet and share with highly regarded colleagues.



In June 2018, Moscow hosted the 2nd Scientific and Practical Conference "Hereditary Angioedema. Life without fear", where SPHA OPHAE presented a cartoon for children with HAE and an information video "Hereditary Angioedema. Life without Borders". The event also introduced a new project for children and adolescents: a special online platform for children to communicate and receive the necessary information and psychological support.

This month representatives of SPHA OPHAE will participate in the Scientific-Practical Conference "Orphan diseases in the practice of doctors of various specialties" in Tomsk, Russia. General practitioners and specialized experts from Siberian medical institutions are invited to the conference.

At the moment, both in Russia and abroad, there is a lack of information on the impact of HAE on the psychological state and quality of life of both the patient himself and his relatives. Therefore SPHA OPHAE has initiated psychological research for patients with HAE and their families. The study is based at the Dmitry Rogachev National Research Center of Pediatric Hematology, Oncology, and Immunology. Specially developed tests enable the experts to assess the current psychological state and the impact of the disease on the quality of life (emotional, social, physical aspects) of the study participants. The study will result in new data on the impact of the disease on the psycho-emotional state and quality of life of the patients with HAE and their relatives, and will also improve existing programs and develop new methods of psychological assistance for the rehabilitation of patients diagnosed with HAE and their families. Participation in this study is voluntary.

I consider the educational mission of SPHA OPHAE very essential. We want people in our country to know that such a disease exists, that edemas of unknown etiology require passing tests to exclude or confirm such a rare but very dangerous disease. Another reason why we created SPHA OPHAE – perhaps the most significant and highly important for us – for people not to face the condition alone, without adequate support. We try to help them in a variety of ways and are always ready to assist those who need it."

News from around the Globe

SOUTH AFRICA www.haei.org/southafrica

Adrienne de Jongh from HAE South Africa writes:

Since the HAE Global Conference in May we have concentrated on the HAEi Connect program which is up and running. We still have some work to do in tracking down patient details but we are very happy that many of our patients have updated themselves recently. We have used it for sending out memos etc. and are quite happy with the professional look and ease of use.

Our website is still pretty basic but Hana and Tamsin are working on that too. We are hoping to include details of our youth approach which is aimed at increasing awareness of HAE and Hana will be giving talks at schools in her area. Prof. Peter has formulated an acute treatment plan which is on our website, so that medical personnel anywhere in the country can access it at any time. This lack of guidance has been a problem in the past as medical staff unaware of HAE have tended not to listen to patients, who of course should know best!

We recently hosted a screening of the documentary "Special Blood" which we will repeat later in the year as many were not able to attend.

HAEi President Anthony J. Castaldo, Executive Director Henrik Balle Boysen, and Regional Patient Advocate Patricia Karani visited Cape Town in August and we met up Professors Peter and Levin and had some fruitful meetings.

We are presently hosting a clinical trial including over 20 patients from all over the country and we are also importing Ruconest for those patients who want it under the HAEi Global Access program.

All in all we are very happy that we have been able to come so far in less than 10 months from the date of our first meeting ever. We are fortunate that we have the medical infrastructure and highly qualified medical staff to drive this.

SOUTH KOREA www.haei.org/location/hae-treatment-in-south-korea

HAEi visited Seoul, South Korea in June 2018 to meet with Shire Korea representatives, the President of the Korean Organization of Rare Diseases (KORD), and three allergists from Seoul. We discussed the landscape of HAE in Korea, and the next steps to creating a dedicated HAE advocacy group. HAEi was encouraged by the meetings as everyone we met with were very motivated.

Shire Korea reached out to HAEi in August to write a letter of support for their submission for reimbursement to the National Health Insurance Scheme, which was sent to the President. We are delighted to have received notification that the submission was successful, and patients in Korea have had access to funded treatment Firazyr (Icatibant) from 1 September 2018.

AUSTRALASIA www.haeaustralasia.org.au

From the HAE Australasia CEO Fiona Wardman:

HAE Australasia are continuing to welcome new members from around Australia and New Zealand, and this is due to patients and carers finding our Facebook pages and website, along with patients being directed to us via their physicians. It's great to see our numbers growing, and we'd like to see that continue. For any patients and carers who have family members that have not yet signed up for our membership, we would appreciate you completing the online form through the 'Stay in Touch' page on www.haeaustralasia.org.au. With new treatments heading our way, it's essential for us to be able to represent as many Aussies and Kiwis as possible.

In the last month or so we went 'live' with HAEi Connect, we had a good response with members checking, updating and confirming their information. Patients and carers who weren't able to update their data within the timeframe can still do so by clicking on the expired link, or email fiona@haeuaustralasia.org.au and a new link will be sent out.

HAE Australasia are excited about the agenda for our 2019 Australasian Patient and Carers Conference, which will be held on the Gold Coast on 13-14 April next year. We have a few 'big names' coming to present during our two-day conference. The invitations will be sent out to our members very soon.

Melbourne was the latest city to host a 'Healthy Minds Workshop' for adults and adolescents, and a 'Meet Up'. Feedback received from the day has been positive, and both patients and carers were grateful for the opportunity to come along, meet others and share information.

HAE Australasia was represented at the recent Australasian Society of Clinical Immunology and Allergy (ASCI) conference, which was held in Canberra, Australia's capital city. The conference is always a great opportunity to meet and speak with clinical immunologists, nurses and other health professionals from around Australia and New Zealand about HAE, and to remind them about our organization. This event attracts international speakers, and it was a privilege to see Dr. Marc Reidl from the US HAEA Angioedema Centre at UC San Diego present on HAE and information on current and new treatments.

PANAMA www.haei.org/location/hae-in-panama

Earlier this month a group of HAE patients met at the San Fernando Hospital in Panama City to form a national HAE organization. With the help of Dr. Olga Melcina, medical specialists, and family members the group coordinated the meeting to legally establish the organization and work towards expanding HAE education and access to therapies in their country.



The HAE contacts in Panama are:

Mr. Muhammad Rawat:

rawatmuhammad@hotmail.com

Mr. Gilberto Price: price_@hotmail.com

Mr. and Mrs. Rodrigo and Aleyda Milord:
rooy131525@gmail.com

HAEi is excited to have another patient group in Latin America – and now a total of 65 countries around the globe.

News from around the Globe



ITALY

www.angioedemaereditario.org

Marco Castiglioni from HAE Italy gives a perspective of the first year with the HAE Global Registry:

All patients affected by HAE and enrolled in the Italian voluntary association for HAE and other rare forms (A.A.E.E – onlus) have access to their own online diary and to the global registry for HAE patients. To have this access, the patients must contact their referring physicians and fill in informed consent.

This project started in Italy in the middle of February 2018 thanks to all doctors and supported by the voluntary association of patients. From the start, 245 diaries have been activated, and for these patients, 896 attacks have been added by app and web.

The feedback from the patients is very good. The most important points that we found out are:

- Fast insertion of the attacks
- App on smartphone or by web
- Automatically saved in an “i-tech cloud”
- Quality of data (all the new attacks must be approved by the referring physician to conserve a high quality of system)
- Quick knowledge how to use the app
- It allows an own evaluation of the course of the disease during the time

All of these points can help the patient to control herself or himself and also these data can be very useful for research for new medications, for a better evaluation of the current medication and profilaxys.

It is not easy to get people involved on this project. Not all the patients in Italy known about the registry, because it is not easy to reach everyone. For this reason, we are trying to increase the communication, organizing meetings, sponsoring in the webpage and the social media.

As I heard a few times during conferences and meetings, this registry works best if there are a lot of data inside – like a million with a swollen river. But who can give this data? That is us – all the patients! We are the power, and we have to help because it is our cause. If a lot of people join we can have more data to work with – and that will help us all.



Clinical Trials

According to the International Clinical Trials Registry Platform under World Health Organization (WHO) and clinicaltrials.gov under the U.S. National Institutes of Health the following trials should be recruiting at this moment:

Efficacy and Safety Study of BCX7353 as an Oral Treatment for the Prevention of Attacks in HAE

– recruiting in Austria, Canada, Czech Republic, France, Germany, Hungary, Macedonia, Romania, Spain, United Kingdom, and the United States.

Study of BCX7353 as a Treatment for Attacks of HAE

– recruiting in Austria, Denmark, France, Germany, Hungary, Israel, Italy, Macedonia, Poland, Romania, Switzerland, and United Kingdom.

C1 Inhibitor Registry in the Treatment of HAE

– recruiting in Bulgaria, Czech Republic, France, Germany, Hungary, Italy, Macedonia, Norway, Poland, Slovakia, and Sweden.

A Long Term Safety Study of BCX7353 in HAE (APeX-S)

– recruiting in Australia, Austria, Denmark, France, Germany, Hong Kong, Hungary, Israel, Italy, Korea, Macedonia, New Zealand, Poland, Slovakia, South Africa, Spain, Switzerland, and United Kingdom.

Firazyr® Patient Registry (Icatibant Outcome Survey - IOS)

– recruiting in Australia, Austria, Brazil, Czech Republic, Denmark, France, Germany, Greece, Israel, Italy, Spain, Sweden, and United Kingdom

Study to Assess the Tolerability and Safety of Ecallantide in Children and Adolescents With HAE

– recruiting in the United States.

Biomarker for HAE Disease Type 1 (BioHAE)

– recruiting in Germany.

The Role of the Coagulation Pathways in Recurrent Angioedema

– recruiting in France.

Determination of Specific Biomarkers of Acute Attack of Angioedema Within Pediatric Population

– recruiting in France.

Epidemiological Analysis for HAE Disease (EHA)

– will be recruiting Germany.

Read more about these and other clinical trials at <https://clinicaltrials.gov> and <http://apps.who.int/trialsearch>.



Medical Papers

Here are summaries of some of the recently published HAE related scientific papers:

Management of patients with HAE in Germany: comparison to other countries in the Icatibant Outcome Survey – by M. Maurer, Charité -Universitätsmedizin Berlin, Germany, et al.:

German Icatibant Outcome Survey patients share similar demographic characteristics to patients from other Icatibant Outcome Survey countries. However, they treat their attacks with icatibant significantly earlier and have markedly fewer severe or very severe attacks. (*J Eur Acad Dermatol Venereol.*, September 2018)

Economic burden limiting proper healthcare delivery, management, and improvement of patient outcomes – by W.J. Cardarelli, Atrius Health, USA:

HAE has a significant economic impact with high direct and indirect costs, and high charges related to the new therapies developed for patients to reduce symptoms and attack recurrence. Effective management of HAE is often complicated by clinical and economic barriers to optimal patient outcomes that must be overcome to provide the best care possible and prevent future attacks and complications. (*Am J Manag Care.*, August 2018)

A HAE screening on an index case: Turkey – by M.Y. Ozkars, Kahramanmaraş Sutcu Imam University Faculty of Medicine, Turkey, et al.:

If there is an index case, the screening of family members is very important and can be life-saving. Therefore, all physicians, especially those working in emergency rooms, should be well aware of the clinical findings of HAE. Patients with recurrent edema should be asked to take a C4 test. In patients with low C4 levels, the C1 esterase inhibitor protein level and activity test should be requested. It may also be useful to require a gene test to confirm the diagnosis. Once diagnosed, asymptomatic patients need to be identified early and family screened to protect their lives. (*Asian Pac J Allergy Immunol.*, August 2018)

Costs and effects of on-demand treatment of HA in Italy: a prospective cohort study of 167 patients – by C. Federici, SDA Bocconi University, Milan, Italy, et al.:

Icatibant and pdC1-INH significantly reduced attack duration compared with no treatment. However, icatibant was more effective but also more expensive. (*BMJ Open.*, July 2018)

Gene Therapy for C1 Esterase Inhibitor Deficiency in a Murine Model of HAE – by T. Qiu, Weill Cornell Medical College, New York, USA, et al.:

As an approach to effectively treat HAE with a single treatment, we hypothesized that a one-time intravenous administration of an adeno-associated virus gene transfer vector expressing the genetic sequence of the normal human C1 esterase-inhibitor would provide sustained circulating C1EI levels sufficient to prevent angioedema episodes. Indeed, a single treatment has the potential to provide long-term protection from angioedema attacks in affected individuals. (*Allergy*, July 2018)

Oral Plasma Kallikrein Inhibitor for Prophylaxis in HAE – by E. Ayyören-Pürsün, University Hospital Frankfurt, Germany, et al.:

Once-daily oral administration of BCX7353 at a dose of 125 mg or more resulted in a significantly lower rate of attacks of HAE than placebo. Mild gastrointestinal symptoms were the principal side effect. (*N Engl J Med.*, July 2018)

Value co-creation in healthcare: evidence from innovative therapeutic alternatives for HAE – by R. Spanò, University of Naples Federico II, Italy, et al.:

Home-based therapies represent a feasible strategy for managing C1-INH-HAE and may result in lower costs and increased value for patients and the healthcare systems. (*BMC Health Serv Res.*, July 2018)

Emotional processes and stress in children affected by HAE with C1-inhibitor deficiency: a multicenter, prospective study – by L. Savarese, University Federico II, Milan, Italy, et al.:

Impaired regulation and processing of emotions, also known as alexithymia, is common in children with chronic diseases. In C1-INH-HAE, it may result in increased perceived stress and act as a trigger of edema attacks. (*Orphanet J Rare Dis.*, July 2018)

Efficacy of recombinant human C1 esterase inhibitor across anatomic locations in acute HAE attacks – by J.W. Baker, Baker Allergy Asthma Dermatology Research Center, USA, et al.:

HAE may occur at or spread to multiple anatomic locations during an acute attack. In shortening the median time to the beginning of symptom relief of acute HAE attacks, Recombinant human C1 esterase inhibitor 50 IU/kg was efficacious, regardless of attack location. (*Allergy Asthma Proc.*, September 2018)

Food as a trigger for abdominal angioedema attacks in patients with HAE – by U.C. Steiner, University Hospital Zurich, Switzerland, et al.:

Food seems to be a relevant trigger factor, causing angioedema in HAE affected patients. The reason, however, is not IgE-mediated hypersensitivity, but most probably an intolerance reaction to food products. (*Orphanet J Rare Dis.*, June 2018)

Icatibant for the treatment of HAE with C1-inhibitor deficiency in adolescents and in children aged over 2 years – by H. Farkas, Semmelweis University, Budapest, Hungary, et al.:

Icatibant undergoes rapid absorption, reaches a therapeutic level, and promptly relieves the symptoms. It is well tolerated, and the subcutaneous preparation, presented in a pre-filled syringe, ensures ease of use. It can be administered anytime, anywhere, and instantly – even by the patients themselves, or – in the case of children and adolescents – by a caregiver. Icatibant may greatly contribute to the improvement of the quality of life of pediatric patients. (*Expert Rev Clin Immunol.*, June 2018)

A transcriptomics study of HAE attacks – by G. Castellano, University “Aldo Moro”, et al.:

The study demonstrates the increase in levels of adrenomedullin and urokinase plasminogen activator in peripheral blood mononuclear cells during an acute HAE attack. Activation of these genes usually involved in regulation of vascular tone and in inflammatory response might have a pathogenic role by amplifying bradykinin production and edema formation in patients with HAE. (*J Allergy Clin Immunol.*, September 2018)

Idiopathic Nonhistaminergic Acquired Angioedema Versus HAE – by N. András, Semmelweis University, Budapest, Hungary, et al.:

The clinical manifestations of patients with idiopathic nonhistaminergic acquired angioedema were different from those of patients with HAE with C1-inhibitor deficiency. This may indicate different processes underlying edema formation in these disease forms. The close resemblance of the clinical manifestations might suggest a similarity between the pathophysiology of these conditions. (*J Allergy Clin Immunol Pract.*, July-August 2018)

Clinical Features of HAE in Korean Patients: A Nationwide Multicenter Study – by J.W. Jung, Seoul National University Medical Research Center, Republic of Korea, et al.:

The clinical manifestation and severity of HAE may vary according to ethnicity. HAE is more infrequent and gastrointestinal involvement is less likely in Korea compared with Western countries. (*Int Arch Allergy Immunol.*, 2018)

More papers can be found at for instance the National Center for Biotechnology Information, U.S. National Library of Medicine at www.ncbi.nlm.nih.gov/pubmed.

Global Advocacy Work

Recent events

- 21-23 June:** HAEi visited **Seoul, South Korea** to meet with Shire Korea representatives, the President of the Korean Organization of Rare Diseases (KORD), and three allergists from Seoul to discuss the landscape of HAE in Korea, and the next steps to creating a dedicated HAE advocacy group. HAEi was encouraged by the meetings as everyone we met with were very motivated.
- 7-9 August:** HAEi was in **Sao Paulo, Brazil** to discuss HAEi GAP with Dr. Anete Grumach and to meet with the member organization.
- 20 August:** HAEi met with Prof. Marco Cicardi in **Milan, Italy** to discuss elements of the HAE Global Registry Board and Foundation.
- 27-30 August:** HAEi was in **Cape Town, South Africa** to participate in an allergy meeting and to discuss HAEi GAP with two dedicated physicians. Also, HAEi used this opportunity to work with the local member organization.
- 5-7 September:** HAEi was in **Berlin, Germany** for the Bradykinin symposium arranged by Prof. Maurer and Prof. Magerl at Charité.

Upcoming events

- 27-29 September:** HAEi will present at and participate in the 2018 HAEi South Eastern Europe Workshop in **Skopje, Macedonia**.
- 4-5 October:** HAEi is hosting and will attend and present at the HAEi GCC & Middle East C1-Inhibitor Deficiencies Summit in **Beirut, Lebanon**.
- 6 October:** HAEi will attend and present at the HAE Scandinavia patients' meeting in **Stockholm, Sweden**.
- 11-13 October:** HAEi will be at the 2018 Asia Pacific Association of Allergy, Asthma and Clinical Immunology (APAAACI) and Asia Pacific Association of Pediatric Allergy, Respiratory and Immunology (APAPARI) meeting in **Bangkok, Thailand**. Here HAEi will also host a dedicated HAE symposium featuring Prof. Marc Riedl (USA) and Dr. Connie Katelaris (Australia).
- 27-28 October:** HAEi will present at and participate in the 2018 HAEi Central and Eastern European Workshop in **Warsaw, Poland**.
- 10 November:** HAEi will participate in and present at the 2018 Shire Global Forum in **Berlin, Germany**.
- 17 November:** HAEi will participate in and present at the 2018 HAE UK Patient Day in **Farnham, United Kingdom**.
- 21 November:** HAEi will participate in and present at the German Dermatology Angioedema Society's annual meeting in **Mainz, Germany**.
- 24 November:** HAEi will present at and participate in HAE Scandinavia's patients' meeting in **Aalesund, Norway**.
- 30 Nov-2 Dec:** HAEi will participate in the board meeting of the HAE Global Registry Foundation and the Canadian Guideline meeting in **Toronto, Canada**.

News from the Industry

26 July 2018

Results from the Phase 2, APeX-1 clinical trial of BCX7353 for the prevention of attacks in patients with HAE are published online in the July 26th issue of The New England Journal of Medicine.

The APeX-1 trial was a double blind, randomized, parallel group, placebo-controlled Phase 2 dose ranging trial comparing the safety and efficacy of 28 days of once-daily BCX7353 treatment, at doses of 62.5 mg, 125 mg, 250 mg, and 350 mg, with placebo. The trial demonstrated that oral administration of BCX7353 at a dose of 125 mg or more resulted in a significantly lower rate of attacks compared with placebo. Significant benefits with respect to quality of life were observed in the 125 mg and 250 mg dose groups. Mild gastrointestinal symptoms were the principal side effect, particularly in the 250 mg and 350 mg BCX7353 dose groups.

“For patients with HAE, the results of this trial suggest potential for the future to manage their disease with a prophylactic therapy that would combine efficacy and safety with the advantage of oral administration,” said Emel Aygören-Pürsün, M.D., principal investigator for the APeX-1 trial and Head of Interdisciplinary Competence Center for Hereditary Angioedema, and Specialist in Internal Medicine and Hemostaseology Department for Children and Adolescents, Goethe University Hospital Frankfurt.

“We are extremely pleased to have these important results published in The New England Journal of Medicine,” said Jon P Stonehouse, President and Chief Executive Officer of **BioCryst Pharmaceuticals, Inc.** “We look forward to confirming the results from APeX-1 in our pivotal Phase 3 trial, APeX-2, which we expect to report out in the first half of 2019.”

(Source: BioCryst)



27 July 2018

On the presentation of the **Pharming Group N.V.** financial report for the six months ended 30 June 2018 CEO Sijmen de Vries said:

“We are delighted with the further progress we have made expanding the reach of Ruconest, allowing more patients to access the clinical benefits of our product. We have continued net profitability in the second quarter of the year, which gives us the confidence and the financial resources to move forward with our new programs. With five studies underway or expected to initiate over the next six months, we anticipate significant strengthening of our pipeline.”

From the CEO's comments:

During the first half of the year, we continued to invest in the development of our commercial infrastructure in North America and Europe to drive the growth of new patients using our lead product Ruconest for the treatment of HAE, as well as to manage the increased demand for the product.

The positive sales momentum in the USA continued in Q2, following higher than expected sales in Q1 as a result of the shortage of a competitor product. As the clearest measure of the success of Ruconest, the number of patients using the product regularly in the USA has been increasing steadily since we reacquired the commercial rights.

In January, we announced that the U.S. Food and Drug Administration (FDA) had accepted for review Pharming's supplemental Biologics License Application (sBLA) for Ruconest for routine prophylaxis to prevent attacks in adult and adolescent patients with HAE. The FDA indicated that the sBLA was sufficiently complete to permit a substantive review and has set an action date of 21 September 2018.

The highlights of these announcements were:

- An ongoing investigator-sponsored study of Ruconest in Basel, Switzerland a double-blind, placebo-controlled trial of contrast-induced nephropathy which was initiated last year and is expected to report top-line data in Q3 2018.
- An ongoing investigator-sponsored head-to-head study of Ruconest in an open label clinical trial testing therapy failure rates (i.e. the need for re-dosing under either therapy) to treat an attack of HAE, which is expected to be fully recruited in Q3, with top-line data expected in Q4 2018.
- Pharming has developed new versions of small vial liquid and fast-dissolving dosage forms for Ruconest, for use in subcutaneous and intramuscular versions and in an entirely new, intradermal version expected to be painless, starting with subcutaneous studies later in 2018/ early 2019.
- Based on the continued momentum in sales volumes, underpinned by improving trends in identifying and diagnosing HAE patients, combined with better patient care and management practices, a focus on specialty pharmacy customers and subject to an FDA approval for prophylaxis of HAE, we expect to continue to increase sales of Ruconest further. If that approval is granted, we expect the efficacy of Ruconest to be appealing to healthcare professionals and the patients they manage for complete management of their HAE condition. It will also be the only approved product for both prophylaxis and treatment of breakthrough HAE attacks.

(Source: Pharming)



3 August 2018

Adverum Biotechnologies, Inc. updates its next-generation ADVM-053 targeting HAE.

“We are excited to be able to share positive progress in our lead gene therapy program and to share our continued commitment to improving the quality of life for patients with unmet medical needs,” said Leone Patterson, interim president and CEO of Adverum Biotechnologies. “We are planning to submit our IND for ADVM-053 in HAE in the fourth quarter of this year.”

ADVM-053 (AAVrh.10-C1EI) is designed as a potential single-administration treatment to provide sustained release of the C1 esterase inhibitor (“C1EI”) protein to eliminate protein level variability and prevent breakthrough angioedema attacks. In preclinical studies, a single intravenous administration of ADVM-053 increased C1EI protein expression above therapeutic levels.

(Source: Adverum)



7 August 2018

The U.S. Food and Drug Administration (FDA) has granted Fast Track Designation for **BioCryst Pharmaceuticals, Inc.’s** BCX7353 for the prevention of angioedema attacks in patients with HAE.

Fast Track Designation provides opportunities for frequent interactions with the FDA during development of a product candidate and provides the opportunity for priority review if supported by clinical data at the time of the new drug application (NDA) submission.

“Fast Track Designation from the FDA serves as another indicator of the importance of BCX7353 to meet an unmet medical need for HAE patients in the U.S.,” said Jon P. Stonehouse, President & CEO. “We remain focused on completing the Phase 3 program and preparing for an NDA filing in the second half of 2019.”

(Source: BioCryst)



24 August 2018

Following priority review, the U.S. Food and Drug Administration (FDA) has approved TAKHZYRO (lanadelumab-flyo) injection, for prophylaxis to prevent attacks of HAE in patients 12 years of age and older.

“TAKHZYRO provides the HAE community with a new option for the prevention of HAE attacks,” said Anthony J. Castaldo, President, U.S. HAEA. “We are grateful for the time and effort put forth by the patients and researchers who participated in the clinical trial program that enabled this important addition to the HAE treatment landscape.”

TAKHZYRO from **Shire plc.** is the only monoclonal antibody (mAb) that provides targeted inhibition of plasma kallikrein, an enzyme which is chronically uncontrolled in people with HAE, to help prevent attacks. The recommended starting dose of TAKHZYRO is 300 mg every two weeks. A dosing interval of 300 mg every four weeks is also effective and may be considered if the patient is well-controlled (e.g., attack free) for more than six months.

In the Phase III HELP (Hereditary Angioedema Long-term Prophylaxis) Study supporting FDA approval, TAKHZYRO reduced the number of monthly HAE attacks an average of 87% (n=27) vs. placebo (n=41) when administered at 300 mg every two weeks and 73% (n=29) vs placebo (n=41) when administered at 300 mg every four weeks (Adjusted P<0.001).⁵

In the 26-week clinical study, which included 125 people with HAE, patients taking TAKHZYRO 300 mg every 2 weeks also had 83% fewer moderate to severe attacks, and 87% fewer attacks that needed on-demand treatment. A pre-specified, exploratory analysis showed that 44% of patients (n=27) receiving TAKHZYRO 300 mg every two weeks had zero attacks compared to placebo (2%, n=41) for the 26-week treatment period from Day 0 to Day 182. Additionally, in a post hoc analysis of the 16-week period from Day 70 to Day 182, 77% of patients (n=26) treated with TAKHZYRO in the same dosage arm of the trial were attack-free compared to placebo (3%, n=37).

TAKHZYRO has a half-life of approximately two weeks and is administered as one subcutaneous self-injection every two weeks at the recommended starting dose. In clinical trials, the majority of patients took one minute or less to complete the injection.⁵ The most commonly observed adverse reactions ($\geq 10\%$ and higher than placebo) associated with TAKHZYRO were injection site reactions consisting mainly of pain, erythema, and bruising at the injection site; upper respiratory infection; headache; rash; myalgia; dizziness; and diarrhea.

Andreas Busch, Ph.D., Executive Vice President, Head of Research and Development at Shire said: “With the approval of TAKHZYRO, HAE patients have an innovative treatment that works differently than current options to help prevent attacks. Based on an exploratory and post hoc analysis, after six doses of TAKHZYRO 300 mg every two weeks, 77% or nearly 8 of 10 patients had zero attacks. This approval reinforces our ongoing commitment to developing novel therapies that have a meaningful impact on patients. Looking to the future, we continue to work towards our goal of a world in which those living with HAE can aim for zero attacks.”

The FDA approval of TAKHZYRO was based on data from four clinical trials, including the HELP Study, the largest prevention study conducted to date in HAE. Of the patients who completed the HELP Study who received TAKHZYRO, 97% opted in to an ongoing open-label extension study designed to evaluate the long-term safety and efficacy of TAKHZYRO.

Shire added TAKHZYRO to its HAE portfolio with the acquisition of Dyax Corp.

(Source: Shire)



26 August 2018

The US Food and Drug Administration (FDA) has granted Orphan Drug Designation (ODD) to ADVM-053, a preclinical gene therapy candidate being investigated as a potential single-administration treatment which has the potential to provide sustained levels of the C1 esterase inhibitor (“C1EI”) protein.

“We are pleased to receive the Orphan Drug Designation for ADVM-053 from the FDA,” said Leone Patterson, interim President and CEO of **Adverum Biotechnologies, Inc.** “We are committed to developing effective treatments for patients living with HAE and the support from the FDA will be invaluable towards this goal. We look forward to submitting our IND application in the fourth quarter.”

Orphan drug designation is granted by the FDA to novel drugs and biologics, which are defined as those intended for the safe and effective treatment, diagnosis or prevention of rare diseases/disorders that affect fewer than 200,000 people in the U.S. The designation provides incentives for sponsors to develop products for rare diseases, which may include tax credits towards the cost of clinical trials and prescription drug user fee waivers. The orphan drug designation also could entitle Adverum Biotechnologies to a seven-year period of marketing exclusivity in the United States for ADVM-053 should the company receive FDA approval for the treatment of HAE for this product candidate.

ADVM-053 (AAVrh.10-C1EI) is designed as a single-administration treatment with the potential to provide sustained expression of the C1 esterase inhibitor protein to eliminate protein level variability and to prevent breakthrough angioedema attacks. In preclinical studies, a single intravenous administration of ADVM-053 increased C1EI protein expression above therapeutic levels and decreased vascular permeability in a mouse model of HAE.

(Source: Adverum)



6 September 2018

Shire plc has acquired sanaplasma AG, a source plasma collection company headquartered in Switzerland. The acquisition is expected to increase Shire's access to plasma in the longer term and add to its European plasma collection network, complementing existing core capabilities in plasma supply and manufacturing.

Plasma is essential to the manufacture of immunoglobulin therapies that help treat patients living with certain rare immunological diseases. Immunology is Shire's largest franchise, with 18% growth on a pro-forma basis in 2017 to \$4.4 billion in product sales, primarily driven by increased global demand for subcutaneous and intravenous immunoglobulin brands. This acquisition is expected to support the growth of the Immunology business and help meet the needs of patients around the world.

Sue Brown, VP Global Operations for Shire BioLife Plasma Services, said: "The acquisition of sanaplasma AG demonstrates Shire's commitment to its rapidly growing and leading Immunology business. The combination of sanaplasma AG's 14 plasma centers in the Czech Republic and Hungary with our more than 100 BioLife centers in the US and Austria will help us to meet the continuously growing demand for plasma-derived medicines."

Dr. Martin Lukas, co-owner of sanaplasma AG said: "I look forward to working with the team at Shire during the transition to help ensure continuity of supply, know-how transfer, and a smooth handover to position the business for future success as it continues to meet patient needs."

sanaplasma AG is a privately-owned company focused on source plasma collection through its operation of 14 European plasmapheresis centers; 11 in the Czech Republic and three in Hungary.

Shire's immunology franchise has a strong legacy in developing therapies for people living with HAE, primary and secondary immunodeficiency, and rare autoimmune and neurological conditions. Shire is committed to serial innovation, and the company's broad portfolio includes a number of therapy options that can be tailored to meet personal patient needs. Beyond Shire's focus on developing novel treatments, the company provides specialized services and support offerings that help meet the needs of patients.

(Source: Shire)



6 September 2018

BioCryst Pharmaceuticals, Inc. announces the initial results from the ZENITH-1 trial showing that a single 750 mg oral dose of BCX7353 was well tolerated and superior to placebo ($p < 0.05$) against the majority of efficacy endpoints evaluated in HAE patients suffering an acute attack. BCX7353 is a novel oral plasma kallikrein inhibitor being developed for both prophylactic and acute treatment of HAE attacks.

In order to guide selection of dose and endpoints for a potential future registration trial for the acute treatment of HAE attacks, ZENITH-1 was designed as an exploratory trial to determine if BCX7353 showed a clinically meaningful benefit on any of several different efficacy endpoints evaluating HAE attack symptom severity.

In the 750 mg dose cohort of the trial, which has completed, 33 patients treated a total of 95 attacks (64 with BCX7353, 31 with placebo). Patients self-treated their HAE attacks on a blinded basis with oral BCX7353 or oral placebo and recorded their symptoms and attack severity using both a Visual Analog Scale (VAS) and a standardized questionnaire. Patients also recorded the time they used any standard-of-care (SOC) acute treatment medicine. BCX7353 was superior to placebo for multiple clinical outcomes.

Importantly, compared to placebo, improvement in symptoms and VAS scores was seen as early as one hour after oral BCX7353 dosing, and was sustained through 24 hours. Through 24 hours, SOC medication use was reduced by 31.6 percent after BCX7353 compared with placebo ($p = 0.0029$), and no or mild symptoms were reported in 64.1 percent of attacks treated with BCX7353 compared with 32.3 percent of attacks treated with placebo ($p = 0.0038$).

These and the other clinically meaningful results from ZENITH-1 highlight an attractive profile for patients seeking an oral treatment for acute HAE attacks.

In the ZENITH-1 trial, oral BCX7353 750 mg was generally safe and well tolerated. No serious adverse events were reported in patients receiving BCX7353. There were no grade 3 or 4 adverse events, and no grade 2, 3 or 4 laboratory abnormalities. The most commonly reported adverse events were nasopharyngitis (4/64 attacks treated with BCX7353 vs 1/31 for placebo), diarrhea (3/64 with BCX7353 vs 0/31 for placebo) and headache (3/64 with BCX7353 vs 0/31 for placebo). There were two discontinuations in the trial. One

patient discontinued following a BCX7353 dose due to a transient, localized rash and one patient discontinued following a placebo dose due to abdominal pain.

"ZENITH-1 represents a groundbreaking study, as the first clinical trial to demonstrate effective treatment of acute HAE attacks with an oral therapy. The observed effect of BCX7353 within one hour of dosing and the substantial reduction in rescue medication use compared to placebo suggest that BCX7353 has outstanding potential to offer physicians and patients an urgently needed new oral therapy option," said Dr. Hilary Longhurst, honorary consultant immunologist, Addenbrookes Hospital, Cambridge, UK, and principal investigator of the ZENITH-1 trial.

Results from the ongoing evaluation of the 250 mg and 500 mg dose levels of oral BCX7353 in ZENITH-1 are expected in the first quarter of 2019.

"These results from ZENITH-1, combined with the results we saw in APeX-1, are evidence that BCX7353 would be the first safe and effective oral drug for both treating and preventing HAE attacks. We know the HAE community is waiting for an oral option and we look forward to completing APeX-2 and to submitting our applications for product approval to regulatory authorities," said Jon Stonehouse, CEO of BioCryst.

Registration trials for previously approved injectable acute therapies for HAE were conducted in the clinic setting. In these studies, investigational treatment was administered in medical facilities by investigators at least four hours following onset of symptoms. ZENITH-1 is the first controlled clinical trial in the HAE acute therapy setting to assess patient-administered treatment at home, enabling treatment to be given quickly after the onset of symptoms.

"We are thrilled to see such a robust treatment effect with BCX7353 in ZENITH-1, using a modern approach with self-administered therapy. We were able to demonstrate clinically important treatment effects very early after oral dosing, which lasted through 24 hours," said Dr. William Sheridan, chief medical officer of BioCryst.

(Source: BioCryst)



14 September 2018

From the **KalVista Pharmaceuticals, Inc.** financial results for the fiscal first quarter ended July 31, 2018:

"Our recent financings provide significant additional capital for late-stage development of KVD900, our oral plasma kallikrein inhibitor for potential treatment of on-demand acute attacks in patients with HAE," said Andrew Crockett, CEO. Additionally, we remain committed to our work in discovering and developing oral plasma kallikrein inhibitors for prophylactic treatment of HAE. We recently moved to our new facility in Porton Down, England, which is intended to support our scientific team as they continue to work on discovery and development of additional drug programs."

(Source: KalVista)



19 September 2018

Pharming Group N.V. has received a Complete Response Letter (CRL) from the U.S. Food and Drug Administration (FDA) regarding the supplemental Biologics License Application (sBLA) for Ruconest [C1 Esterase Inhibitor (recombinant)] to expand the current indication to include prophylaxis in patients with HAE.

In November 2017, following feedback from FDA on two completed trials of Ruconest for prophylaxis of HAE attacks, Pharming filed a sBLA to expand the approved indication. The Phase 2 studies, an open-label study and a randomized, double-blind, placebo-controlled trial with 4-8 week treatment periods, showed consistent efficacy and safety results.

In January 2018, FDA deemed the application as sufficiently complete to permit a substantive review of the Phase 2 data. Based on their review, the FDA has requested an additional clinical trial to further evaluate the effectiveness of Ruconest in HAE prophylaxis.

“While today’s FDA decision is not what we were anticipating, we look forward to working with the FDA to generate additional clinical data required to enable access for patients to use Ruconest for HAE prophylaxis,” said Dr. Bruno Giannetti, MD PhD, Chief Operations Officer of Pharming.

“We see this as a minor setback. Pharming remains committed to serving the HAE community. We will continue and have the resources to develop new innovative and more convenient administration options of Ruconest for acute treatment and prophylaxis of HAE to improve patient care as outlined in our recent capital market briefing in June,” said Sijmen de Vries, MD, CEO of Pharming.

(Source: Pharming)



20 September 2018

Shire plc and **Shire Pharma Canada ULC (Shire Canada)** announces that following priority review, Health Canada has authorized TAKHZYRO (lanadelumab injection) for routine prevention of attacks of HAE in adolescents and adults (12 years of age and older).

“The burden HAE patients and their families face every day can’t be ignored,” said Jacquie Badiou, President, HAE Canada. “Our National Report Card shows that the unpredictable nature of this life-threatening disorder, not knowing when the next attack will come, has a negative impact on their lives and the lives of their loved ones. This new treatment option is great news as it was shown to significantly reduce the frequency of attacks.”

TAKHZYRO is a fully human monoclonal antibody that inhibits the activity of plasma kallikrein, an enzyme which is uncontrolled in people with HAE, to prevent attacks. The recommended dose of TAKHZYRO is 300 mg every 2 weeks. A dosing interval of 300 mg every 4 weeks may be considered if the patient is well-controlled (e.g., attack free) for more than 6 months.

Health Canada’s authorization of TAKHZYRO for the routine prevention of HAE attacks in adolescents and adults is supported by results of the Phase III HELP (Hereditary Angioedema Long-term Prophylaxis) Study, in which the primary efficacy endpoint was the number of investigator-confirmed HAE attacks during the 26-week study duration. The HELP study demonstrated that TAKHZYRO reduced the number of monthly HAE attacks by an average of 87 percent (n=27) vs. placebo (n=41) when administered at 300 mg every two weeks and 73 per cent (n=29) vs. placebo (n=41) when administered at 300 mg every four weeks (P<0.001).

In the 26-week clinical study, which enrolled 125 patients with HAE with C1 inhibitor deficiency, secondary endpoints included: the number of attacks requiring acute treatment and the number of attacks assessed as moderate or severe. Patients taking TAKHZYRO 300 mg every two weeks had 87 percent fewer attacks that required on-demand treatment and 83 percent fewer moderate to severe attacks. A pre-specified, exploratory analysis showed that 44 percent of patients (n=27) receiving TAKHZYRO 300 mg every two weeks had zero attacks compared to placebo (2 percent, n=41) for the 26-week treatment period.

Of the patients who received TAKHZYRO and completed the HELP Study, the largest prevention study conducted to date in HAE, 97 percent enrolled in an ongoing open-label extension study designed to evaluate the long-term safety and efficacy of TAKHZYRO. In the extension study, after receiving a single dose of TAKHZYRO 300 mg at study entry, 80 percent of patients who had been in the 300 mg every two weeks treatment group (n=25) in the HELP Study remained attack-free at week 4 post-dose.

The most common side effects seen with TAKHZYRO were injection site reactions including pain, redness, and bruising.

“As a physician who treats patients with HAE, I am pleased to have a treatment like TAKHZYRO available for the prevention of HAE attacks,” said Dr. Stephen D. Betschel. “The HAE community has a new option that can help prevent attacks.”

TAKHZYRO has a half-life of approximately 14 days and can be self-administered every two or four weeks as one subcutaneous injection. In the HELP Study extension the majority of self-injections took one minute or less to complete.

“This authorization reinforces our ongoing commitment to develop innovative therapies that can help make a positive impact on patients,” said Eric Tse, General Manager, Shire Canada. “We will continue to work towards our goal of improving the lives of those living with rare diseases, including HAE.”

(Source: Shire)



21 September 2018

The Ministry of Health, Labour and Welfare (MHLW) in Japan has granted manufacturing and marketing authorization for Firazyr for the acute treatment of HAE attacks in adult patients.

“As a long-term partner to the HAE community, we continually strive to bring treatments to those living with HAE around the world,” said Andreas Busch, Ph.D., Executive Vice President, Head of Research and Development at **Shire plc**. “HAE attacks can be unpredictable and debilitating and we are delighted that, subject to price listing, we will be able to provide the Japanese HAE community with the first subcutaneous on-demand therapy to treat acute HAE attacks.”

The use of Firazyr in Japanese patients was examined in an open-label, single-arm, Phase 3 study of 8 adult patients with a confirmed diagnosis of HAE who experienced angioedema attacks. During the study, 3 patients self-administered Firazyr and 5 patients had Firazyr administered by a physician. The primary efficacy endpoint was time to onset of symptom relief (TOSR), defined as a 50% reduction from baseline in patient Visual Analog Scale (VAS) score.

The study showed that Firazyr was well tolerated and demonstrated symptom relief during an acute HAE attack through a single injection. Overall, median TOSR was 1.75 hours, and TOSR was similar for patients who self-administered Firazyr or who had Firazyr administered by a physician. Symptom relief was attained as early as 1 hour after Firazyr injection and all patients had symptom relief within 5 hours.

The most common adverse events in patients treated with Firazyr were injection site reactions such as erythema, or swelling, which were found to be mild to moderate in severity.

(Source: Shire)





HAEi around the world

Currently there are HAE member organizations in 65 countries. You will find much more information on the HAE representations around the globe at www.haei.org – and the world map will provide you with contact information for the member organizations as well as care centers, hospitals, physicians, and available medication.

The information on www.haei.org is being updated as soon as HAEi receives fresh data from the national member organizations.

