

Global perspectives:

HAEi MAGAZINE · ISSUE 4/2018



“My life has changed. Getting the right medication has changed everything, really. Today I handle my disease, and I am not a victim of HAE anymore.”

– Tad Rockwell, USA



Dear HAEi Friends,

On behalf of the HAEi Executive Committee, I wish all HAEi friends and their families a joyous holiday season and sincerest best wishes for a healthy New Year!

We are very excited to present this final 2018 edition of the HAEi magazine, and can confidently look to the events that took place last year when we witnessed the HAE Global Patient Movement firmly establish its roots. Something special was in the air this May as 736 highly energetic and motivated patient advocates, caregivers, physician/scientists, and representatives from industry gathered at the HAE Global Conference in Vienna, Austria to spend a weekend sharing ideas on how to “Take Control of HAE.” The positive experience and learning that patient advocates took away from the Global Conference has fueled sustained efforts to increase home organization membership and expand HAE awareness, diagnosis, and access to modern HAE therapies. Looking to the future, we ask you to save the date for our next HAE Global Conference that will take place in Frankfurt, Germany 14-17 May 2020.

In 2018 we proudly welcomed eight new countries into the HAEi family, which now includes 69 member countries. Our consistent growth keeps us mindful that we must constantly evolve to ensure that every member organization receives the support and attention they need to fulfill their goals. With that idea in mind, we reorganized and expanded our Regional Patient Advocate (RPA) Program. As you will read in the pages that follow, we now have eight people fulfilling the RPA role. These skilled, experienced, and compassionate advocates are the backbone of HAEi and stand ready to help you and your organization succeed by providing advice and facilitating access to HAEi’s knowledge, contacts, and membership management/web site hosting tools.

Global perspectives:

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Cover photo

Tad Rockwell – HAE patient.
Read his story on page 36 in this
issue of Global Perspectives

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In many ways, 2018 was the year of HAEi youth. The youngsters program at the HAE Global Conference has empowered our younger members to change the current “frame” of global HAE treatment patterns through actions that break down barriers preventing access to modern HAE medicines. Recognizing the power of our HAEi youth, we have decided to offer a special 2019 Youngsters’ Advocacy Workshop that will take place 25-28 July 2019 in Atlanta, Georgia, USA – in conjunction with the US HAEA National Patient Summit. The workshop will be a fun, but intensive lecture and project-based course that will train HAE youth in the art of HAE advocacy. HAEi will provide financial support for 40 youngsters who reside outside of the US and wish to attend the workshop.

Finally, while we should all be encouraged by the development of new and better HAE medicines, we must also recognize the plight of patients in countries that have either limited or no access to modern HAE therapy. The solution to this situation is not easy, but there is one key step that dramatically increases the odds for success in getting access to modern medicine – forming a local HAE patient advocacy organization! HAEi and its RPAs are committed to helping anyone interested in starting a local

HAE group. We are likewise enthusiastic about helping existing member organizations overcome obstacles to grow and broaden access to modern HAE therapy.

As always, *Global Perspectives* provides a comprehensive global overview of just about everything that is going on in HAE – we wish you pleasant reading.

Warmest holiday regards,



Anthony J. Castaldo
President, HAEi



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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**HAE
GLOBAL
CONFERENCE
FRANKFURT
14-17 MAY
2020**



Welcome to the 5th HAE Global Conference

“2012 Copenhagen, 2014 Washington D.C., 2016 Madrid, 2018 Vienna. And now we are ready to present the venue for the 5th HAE Global Conference as it will be taking place in Frankfurt am Main, Germany from 14 to 17 May 2020”, says HAEi President Anthony J. Castaldo.

“Frankfurt was an obvious choice as its airport serves as a hub for many destinations worldwide. We have also chosen the Sheraton Frankfurt Airport Hotel as our venue. This hotel is located directly at Terminal 1 at Frankfurt International Airport. More information about the 2020 HAE Global Conference will follow during 2019,” says, HAEi Executive Director Henrik Balle Boysen.





2019 HAE YOUNGSTERS' ADVOCACY WORKSHOP

The 2019 HAE Youngsters' Advocacy Workshop will take place 25 to 28 July 2019 in Atlanta, Georgia, USA – in conjunction with the US HAEA Patient Summit.

"The Youngster Track at the 2018 HAE Global Conference in Vienna, Austria was our first dedicated two-day youngster track and was a great success. At the end of the conference, we proudly introduced the official HAEi Youngsters Community. It is wonderful to see how the youngsters appreciate and make the most of the opportunity of having a truly global network of fellow HAE patients, with whom they can share experiences and ideas. We are truly moved by the passion and dedication of the youngsters, and the HAEi Executive Committee has unanimously agreed to keep supporting their future initiatives. Furthermore, HAEi is making a significant investment in helping the Youngsters Community develop the knowledge and skills to become global advocates", says HAEi Executive Director Henrik Balle Boysen.

The 2019 HAE Youngsters' Advocacy Workshop will be a fun, but intensive lecture and project-based course that will train the HAE youth in the art of HAE advocacy.

HAEi Project Manager, Nevena Tsutsumanova says: "We are asking our Member Organizations to select youngsters from their countries who will most benefit from taking part in the workshop. We are looking for dedicated and determined youngsters, who can both write and communicate in English, who are motivated to learn new skills, be part of a team, and have a passion for getting more involved in their local member organization."

HAEi will provide financial support for 40 international youngsters who are selected to attend the workshop in Atlanta.

"Places are limited, and we anticipate that demand will exceed the places available. As a result, we will need to look at an allocation process, which will take date and time of preliminary application, as well as global representation into account", says Henrik Balle Boysen.

QUESTIONS?

See www.haei.org for further information
 – and please do not hesitate in contacting
Nevena Tsutsumanova at n.tsutsumanova@haei.org
 should you have any questions regarding the
 2019 HAE Youngsters' Advocacy Workshop.

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:

- **Michał Rutkowski** – Central and Eastern Europe
- **Natasa Angeleska** – South East Europe
- **Maria Ferron** – Mediterranean
- **Rashad Matraji** – Gulf Region and Middle East
- **Javier Santana** – Central America
- **Patricia Karani** – Sub-Saharan 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.

Javier Santana

Central America and the Caribbean

GENERAL

Over the recent months, Javier has been adapting to his new role as RPA for Central America and the Caribbean. He has been reaching out to and enlisting the help of patients and doctors in many countries throughout the region to establish patient groups and to find other individuals who would be interested in joining their respective groups. Furthermore, Javier has been working closely with the member organization in Peru and specifically Suzet Lam Torres to support them with a number of media activities to raise awareness of HAE.



PANAMA

In September Javier helped to organize the first meeting for members of the Panama patient group. He introduced them to HAEi and showed them how the global organization can support their group. He also informed them of the alternative medicines which are available in other countries and encouraged them to try to gain access in their own country. Most recently Javier has been assisting the Panama patient group to become officially recognized by the government, as well as creating an HAEi-hosted website and helping to organize local meetings.



EL SALVADOR

Following the Association of Latin American Physicians Conference in Chile, Javier has been speaking to a physician from El Salvador, Dr Marlo Ochoa, who has connected Javier with some of his patients. After discussions regarding HAEi and what it can offer HAE patients around the world, the patients agreed to lead the set-up of a patient organization in El Salvador and Javier is happy to support them.

Fiona Wardman

Asia Pacific

GENERAL

Fiona has been busy establishing contacts to help her in countries throughout the Asia Pacific region. She attended the Asia Pacific Alliance of Rare Disease Organizations (APARDO) workshop in Singapore and the Asia Pacific Association of Allergy, Asthma and Clinical Immunology (APAAACI) meeting in Bangkok which helped her meet a host of new contacts. Fiona was elected onto the board of APARDO at the workshop in Singapore, and along with HAEi President Anthony J. Castaldo and HAEi Executive Director Henrik Balle Boysen, she presented at the APAAACI meeting.



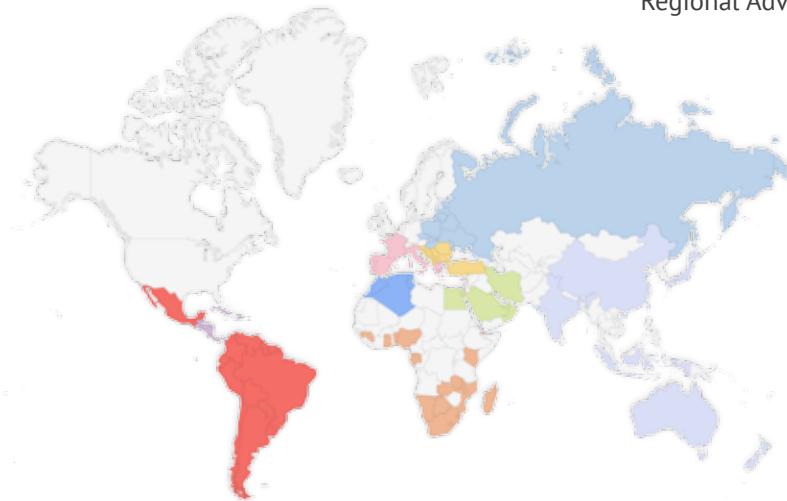
JAPAN

Fiona was delighted to hear that Firazyr is now available to HAE patients in Japan, thanks to HAEi President Beverley Yamamoto and the rest of the Japanese HAE organization for all their hard work to get the approval. Fiona has met with Yukiko Nishimura, the President of Advocacy Service for Rare and Intractable Diseases in Japan, during the APARDO meeting in Singapore. They discussed the overall situation in Japan and current activities which are underway.



AUSTRALIA

HAEi Connect has been set up and is working successfully for the member organization in Australia and patients are being encouraged to check and update their information as appropriate. Fiona has helped to organize and hold an HAE Healthy Minds workshop and Meet Up in Melbourne – and she has attended the Australian Society of Clinical Immunology and Allergy, where she spoke to physicians and other non-profit organizations about the treatments which are available in Australia.



Rashad Matraji

Gulf region and Middle East

GENERAL

Rashad's primary focus over the last few months has been the HAEi Gulf and Middle East Regional Workshop for HAE physicians, held in Beirut, Lebanon. The main topics discussed at the meeting were the importance of identifying patients, the benefits of national registries, and raising awareness of HAE amongst public authorities. The regional meeting was a single day event and was attended by 25 doctors from 15 countries throughout the region. Doctors

attending the workshop agreed to work together and to lead the initiatives, which were decided on at the meeting. Members of the Board of Directors of The World Allergy Organization (WAO) also attended the meeting and agreed to support future activities. The national workshop for HAE physicians from Lebanon then took place on the following day. A number of HAE related topics were discussed including advances in HAE therapy and HAE Diagnoses.



SYRIA

Dr Lubna Hwejeh attended the HAEi Gulf and Middle East Regional Workshop in Beirut, Lebanon and agreed to be a contact for people in Syria wanting to find out more about HAE. Dr Hwejeh has also decided to reach out to patients to establish an active patient group in Syria. For contact details, please see www.haei.org/location/physician-syria.

JORDAN

Dr Hani Ababneh has agreed to be a point of contact for HAE patients in Jordan. For contact details, please see www.haei.org/location/physician-jordan.

Maria Ferron

Mediterranean

GENERAL

Maria joined the HAEi Gulf and Middle East Regional Workshop for HAE physicians, held in Beirut, Lebanon as some Northern African countries in her region also attended which allowed her to build strong connections within these countries. Maria has been starting to contact pharmaceutical companies to establish if there are dedicated relationship managers that cover the Northern African countries, to provide access to medication for HAE patients.

MOROCCO

At the meeting in Beirut, Lebanon Maria met Dr Moussayer, and they discussed the approximate number of patients in Morocco and the treatments currently available. Dr Moussayer later made an appearance on national TV to talk about HAE and raise awareness within the country. The Moroccan member organization attended a forum on rare diseases and the President, Imad Elaouni, gave a presentation about HAE, how it affects patients and the lack of available medication to treat it. Ayoub Chajer, a patient and Deputy Secretary General of the association, supported Imad by sharing his personal experiences of HAE.

The first meeting of the Moroccan HAE Association will take place on 19 January 2019. If you are interested in attending, please contact Maria at m.ferron@haei.org or Dr Moussayer – see his details at www.haei.org/location/hae-in-morocco.

TUNISIA

Maria talked to Dr Habib Ghedira at the meeting in Beirut, Lebanon and he was keen to be further involved with patient advocacy initiatives. Maria then connected Dr Ghedira with a Tunisian patient, and they are going to work together to set up a patient organization. Maria continues to support both of them in this endeavour.





Patricia Karani
Sub-Saharan Africa



UGANDA AND TANZANIA

Patricia has been reaching out to people in Uganda and Tanzania to establish contacts who are willing to help raise awareness and set up organizations within these countries.



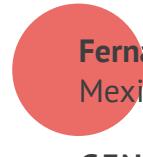
RWANDA

Patricia contacted a paediatric pulmonologist who is a member of the Rwanda Allergy Society, and they arranged an introductory meeting at the end of October to discuss the current situation in Rwanda. The Doctor highlighted the high likelihood that he might have a child as well as an adult HAE patient. Arrangements are underway to follow up with the patients to organize comprehensive diagnostic tests. The Doctor hopes the adult patient would be interested in establishing a patient organization in the country.



KENYA

Patricia had a successful meeting with an official from the Ministry of Health's Non-communicable Disease Department. Also, she attended the 2018 Biennial Allergy Conference organized by the WAO and ASOK, to raise awareness of HAE. At the conference, Patricia received some information about possible HAE patients in Nigeria and Rwanda, who she plans to follow up with.

Fernanda de Oliveira Martins
Mexico and South America

GENERAL

Since starting her role as an RPA Fernanda has been busy familiarising herself with the member organizations in her region and their needs. She has also been exploring how HAEi resources might benefit the countries in her region.



BRAZIL

Fernanda met with Dr Anete Grumach to discuss gaining access to medicines. They have identified processes to make medications available through reference centers or clinical trials and are enthusiastic about moving forward with their plan. Fernanda has supported Abranghe, the member organization in Brazil, with a successful exhibit at the ASBAI (Brazilian Association of Allergy and Immunology) Conference. Furthermore, she was delighted to learn that Mara Gabrilli was recently elected as a Senator in Brazil as she is a public supporter of rare diseases and has talked about HAE in the past. Abranghe has already reached out to Mrs Gabrilli to include her in future activities.



PERU

In September AEH Peru had elections to decide who would hold positions on the Board for the next two years. Suzet Lam Torres was elected President, while Claudia Raffael Hermoza is Secretary, and Bresia Terrazas Cossio is Treasurer. Following the election, Suzet Lam Torres appeared on national TV, alongside Dr Leslie Soto and Dr Oscar Calderón to discuss HAE generally and raise awareness of the disease.

HAEi South Eastern Europe Workshop 2018

*“When you fight something, you’re tied to it forever.
As long as you are fighting it, you’re giving it power.”*

– Anthony de Melo



By Natasa Angeleska, HAEi Regional Patient Advocate
South Eastern Europe

Before being nominated as HAEi Regional Patient Advocate for the South Eastern Europe countries (SEE), I established communications through my colleagues from HAE Macedonia with some of the HAE patients in this region. We were motivated by the will to meet with patients from neighboring countries, and to share mutual life challenges, sympathize with each other, and share ideas for assistance.

At our first Balkan meeting of patients and doctors held in June 2016 in Skopje, Macedonia we gathered together patients and physicians from 10 countries and started more organized communications afterwards, as well as some joint activities that helped us stay motivated for the second SEE meeting held in September 2017 in Skopje. Once more we shared successes from some of the countries as well as discussed what worries us most.

This year we were proud to host another great workshop taking part in Skopje, Macedonia 28-30 September 2018. We had 70 participants out of whom 44 were patients/caregivers and 20 physicians from 11 countries in SEE, as well as six pharma representatives. The SEE region covers six countries with registered patient organizations: Bulgaria, Macedonia, Romania, Serbia, Turkey – and we were excited to welcome the newest member organization, Montenegro. Furthermore, we have very active patient groups in Albania, Croatia, and Slovenia – with the potential to have another member organization soon in Croatia. It was so exciting to have patients’ representatives from Bosnia and Herzegovina at the regional meeting this year. A couple from Tuzla, together with Dr Mensuda Hasanhodzic seemed very

enthusiastic and started planning patient activities in this country, and they hope to identify and gather more patients. We were also happy to have physician representatives from Kosovo at our meeting this year and already discussed how we can assist in identifying patients in this country as well.

Our guest speakers for the regional workshop were Dr Bruce Zuraw and Dr Sandra Christiansen who delivered very motivational presentations and lectures divided into three sub-sessions:

- 1. HAE Fundamentals**, covering basic information about HAE – What should every patient know about the science underlying HAE? How do you make the HAE diagnosis? Who in the family should be tested for HAE and what tests do you recommend? What if I have HAE symptoms, but my C1-inhibitor is normal? What facts or data could be used if we have to visit the emergency room? What, from the physician perspective, can a patient do to make appointments more effective and efficient?
- 2. Currently Available Treatments** – An overview of HAE treatments that are currently available – What are the risks/benefits of anabolic steroids for prevention in countries with no HAE therapies; and what is the professional opinion regarding the use of these medicines when nothing else is available?
- 3. Looking to the future** – An overview of HAE-related scientific breakthroughs in the past 5 to 10 years from academia as well as industry, Current and planned clinical trials – mechanism of action for planned or new therapies.

The doctors were available throughout the whole two-day workshop for questions from participants.

Dr Vesna Grivcheva Panovska, a dedicated physician for the HAE adult patients in Macedonia, presented about the newest treatment options for HAE patients and shared the latest data published about the Oral Plasma Kallikrein Inhibitor for Prophylaxis in Hereditary Angioedema – or about the effects of BCX7353. She co-authored the article about this new therapy that is going to be the very first oral treatment for HAE patients, and we were happy to hear about the positive outcomes from the clinical trials in which patients from our region are also part.

Patient involvement in advocacy is the key to improve conditions and access to therapies worldwide. This



Dr Bruce Zuraw and Dr Sandra Christiansen gave very motivational presentations and lectures about HAE

is why the president of HAEi, Anthony J. Castaldo and myself held an interactive session with participants to hear and discuss successful activities in some of the countries so that we can learn from each other. For instance, representatives from Serbia secured funding and access to novel therapies after a long year of “wrestling” and advocacy with health officials. We heard about the long period of advocacy from representatives from Turkey and the constant obstacles that are faced in reimbursement procedures. We learned about the challenges Romanian patients face and about the extremely important joint activities with physicians, and alliances with other rare disease associations, as in the case of Macedonia.

This year our participants had the opportunity to hear about HAEi resources available for the member organizations and patient groups, especially HAEi web hosting and HAE Connect. HAEi Executive Director Henrik Balle Boysen and HAEi Project Manager Ole Frölich met with the country representatives to have a practical presentation of these tools that patient groups and organizations can get access to free of charge. Already at the workshop, several countries expressed that they will join HAE Connect and many were interested in having their web page hosted at www.haei.org.



Also, we had the opportunity to hear the current state with patients, physicians, care centres, available medications, and challenges and successes from each of the countries present at the meeting. Among them were the workshop's youngest presenter coming from Romania, who took the challenge to speak in front of the audience and received huge applause.

The meeting was very motivational and emotional, and it is of huge importance to have these opportunities to meet and share among representatives in our region. We live in the same geographical territory; we share a lot from our history, food, folklore, culture and habits. These things sometimes unite us, while other times divide us, but now we have a higher unifying goal: to join together in the care and fight for an improved life for HAE patients in each country in the SEE region.

Several tasks for the coming period are set: to reach more patients so that no-one is left alone, in struggle and/or isolated; fight for awareness about the seriousness of the condition; seek improved diagnosis; demand access to treatments; work for individualized care for patients; seek for friendly and expert physicians respected for their knowledge and expertise by the public and authorities; establish cooperation with authorities; network and collaborate with other patient groups and associations.

Some of these tasks may be easily accomplished in some of the countries, while there may be obstacles in others. Nevertheless, we must not be discouraged. On the contrary, we should always think that “Winners are not those who didn’t experience defeat, winners are those who never quit!!!” – as said by the Macedonian bestseller writer and inspirational speaker Kosta Petrov.



Status in South Eastern Europe

In the introduction leading up to the national presentations at the HAEi South Eastern Europe Workshop 2018 the HAEi Regional Patient Advocate Natasa Angjeleska summarized: Of the 11 countries in the region six have a member organization – that is Bulgaria, Macedonia, Romania, Serbia, Turkey – while Montenegro was added to the list during the workshop in Skopje, Macedonia. Then there are three countries with patient groups – that is Albania, Croatia, and Slovenia. Finally, Bosnia & Herzegovina and Kosovo have not yet set up a formal group or organization.

Altogether these 11 countries have approximately 130 million inhabitants. Two years ago 888 patients were diagnosed with HAE while this number by 2017 had grown to 1,050.

The following is a short status for each of the 11 countries mainly based on the presentations made at the workshop.



BULGARIA

Organization: HAEA Bulgaria (2016)

Number of patients: 95 estimated

Members of organization: 52

Specialist physicians: 12

Treatment centers: 1

Diagnosis: Laboratory analysis of blood samples for type I and type II; genetic samples for type III

Available treatment: Berinert and Ruconest for home administration; prophylactic treatment is also available

Knowledge: The level among most physicians is still unsatisfactory and inadequate

Challenges: Health care specialist awareness; long period of struggling without a proper diagnosis and a lot of difficulties even when patients have medicine

Successes: Change in Bulgarian laws to give a wide range of medical professionals the right to treat HAE in hospitals and to be paid by the National Health Fund



MACEDONIA

Organization: HAE Macedonia (2009)

Number of patients: 22 diagnosed; 50-100 estimated

Members of organization: 16

Specialist physicians: 2

Treatment centers: 1

Diagnosis: Performed by testing C1 and C4 in blood samples

Available treatment: Ruconest; Berinert; androgens are not available

Knowledge: HAE Macedonia has been involved in raising awareness, but a lot of challenges are still ahead

Challenges: Receiving enough treatment; raising awareness for the public but also medical personnel; motivating young doctors to learn about HAE

Successes: Constant communication with the Ministry of Health; educational caravan; public appearances and activities; involvement of Prof. Vesna Grivceva in rare disease committee; huge effort and activities of our RPA in defining laws in Macedonia; much media appearance of all active HAE members; workshop for youngest ones; participation in a marathon for support of all rare disease patients



MONTENEGRO

Organization: HAE Crna Gora (2017)

Number of patients: 50 estimated

Members of organization: 15

Specialist physicians: 1

Treatment centers: 1

Diagnosis: There is no ability to determine C1-INH qualitatively

Available treatment: Firazyr (provided by the health fund)

Knowledge: Low among both medical staff and in general

Challenges: Insufficient therapy; pregnant women and children the most vulnerable; no significant activities

Successes: Cooperation with the HAE organizations in Serbia, Croatia, Macedonia, and Bulgaria



ROMANIA

Organization: Asociația Pacienților cu Angloedem Ereditar din România (2012)

Number of patients: 109

Members of organization: 47

Specialist physicians: 1

Treatment centers: 3

Available treatment: Icatibant (covered by the National Insurance Company for all patients); Recombinant human C1-INH and plasma derived C1-INH available in some ERs; no prophylaxis available; Danasol brought from abroad

Knowledge: Improving thanks to publications and workshops

Challenges: Attenuated androgens are not available (e.g., for the selected cases with >4 attacks per month and poor response to attack treatment); SC C1-INH concentrate for prophylaxis still a dream; IV C1-INH concentrate is not available for pregnant HAE patients

Successes: From 2018 Icatibant is available for home treatment for adults; children will also be treated for their attacks soon; media coverage; improved education of patients and physicians; no patient with confirmed C1-INH deficiency has died since 2013



SERBIA

Organization: HAE Serbia (2016)

Number of patients: Diagnosed 90; estimated 140

Specialist physicians: 10

Treatment centers: 5

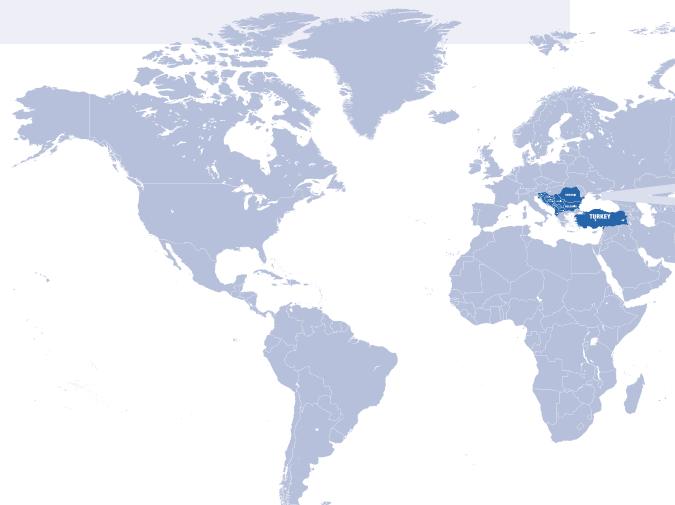
Diagnosis: C4, C1-INH, state funded genetic testing available abroad

Available treatment: Berinert; Ruconest; Firazyr; Tranexamic acid

Knowledge: Poor to average

Challenges: Time to diagnosis; time to treatment; dosing of C1-INH products off-label

Successes: Securing access to modern treatments; increased public awareness of HAE





TURKEY

Organization: HAÖDER – Herediter Anjiyoödem Hastaları Dayanışma ve Yardımlaşma Derneği (2015)

Number of patients: 760 diagnosed

Members of organization: 82

Specialist physicians: No specific number but most immunologists and 10 per cent of general practitioners are able to diagnose and treat HAE

Treatment centers: Approx. 60

Available treatment: Cinryze and Danazol (licensed and used widely except C1 for home treatment); Firazyr (quite commonly used but imported); all HAE medications are reimbursed

Knowledge: It improves among physicians and patients but more is required

Challenges: We have modern therapy but cannot use it effectively/successfully; getting the government to admit that home therapy is the only solution

Successes: Gathering all patients and some qualified professors for brunch; better engagement among patients broadening their perspective of HAE; physicians and patients communicating well and sharing experiences; more activity on Facebook page



ALBANIA

Organization: Patient group

Number of patients: 15 diagnosed since 2017; totally approx. 50

Available treatment: Fresh frozen plasma; Ruconest for ER's

Challenges: Working on government approval of reimbursement



CROATIA

Organization: Patient group

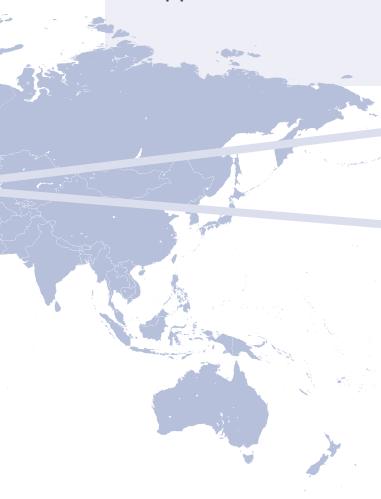
Number of patients: 100 estimated

Specialist physicians: 13

Treatment centers: 8

Available treatment: Firazyr; Ruconest; Berinert; Danazol; C1-INH concentrate

Successes: Patient ID card; HAE poster at ER's; informal Facebook group of patients and doctors helping to identify patients and available medications; easier approach to medications approved by Hospitals' Boards





SLOVENIA

Organization: Patient group

Number of patients: 27 diagnosed

Specialist physicians: 2

Treatment centers: 1

Diagnosis: Screening for C4; confirmation with C1-INH level and function; genetic testing available

Available treatment: C1-INH concentrate, recombinant C1-INH and Icatibant for acute treatment; Danazol is not registered but available at the clinic for recognized patients for prophylactic treatment

Knowledge: The curriculum at the medical faculty mentions HAE; sessions about HAE have been organized at meetings for primary care physicians and allergy/pulmonology specialists

Challenges: Constant availability of treatment for acute episodes at all emergency units

Successes: Local meeting of patients and interested health care providers September 2018; HAE card in Slovenian and English; information for health care providers that patients can present in the case of acute attack



BOSNIA & HERZEGOVINA

Organization: Patient group

Number of patients: 3 diagnosed

Specialist physicians: 1?

Treatment centers: None

Diagnosis: Mostly public institutions do not have tests to prove C1-INH, so they have to be conducted in private laboratories; genetic tests are done abroad

Available treatment: None

Knowledge: General physicians are sufficiently informed about angioedema, but they mainly think about idiopathic or allergic angioedema; patients also do not know enough about their illness and the possibilities of treatment

Challenges: No organization yet; no common umbrella organization of patients with rare diseases; specific drugs for HAE are not available, pharmaceutical companies have no interest in the registration of their drugs in the country

Successes: Lectures on HAE; introduction of diagnostic and therapeutic methods to public institutions in major cities; addressing the media; establishing a register of HAE patients; co-operation with other organizations in order to change the administrative regulations on rare diseases



KOSOVO

Organization: None yet

Number of patients: None registered yet

Specialist physicians: 2

Treatment centers: None

Diagnosis: Unknown

Available treatment: None



Let HAEi host your website

A growing number of national HAE organizations have decided to let HAEi host their website. Some had a national site already while others now have one as part of the hosting service through the global organization.

"We have established an advanced 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 Project Manager Ole Frölich.

"At this point national websites have been launched for the 16 countries and we are also talking to Albania, Belarus, Brazil, Bulgaria, Czech Republic, Montenegro, Slovenia, and Ukraine", says Ole Frölich.

Current websites hosted by HAEi:

- **Australia:** www.haeaustralasia.org.au
- **Ecuador:** http://haei.org/aeh_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/>

At www.haei.org/haei_countries

you'll find an overview of all 69 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.).





HAEi Central Eastern Europe Conference and Workshop 2018

The HAEi Central Eastern European region is a massive one consisting of 12 countries with a population close to 300 million people – and with only around 15 per cent of all HAE patients diagnosed. Therefore, this region requires an individual approach and hands-on assistance in activities related to advocacy, gaining access to and reimbursement of modern therapies.

“It all starts and finishes with motivated HAE patients, caregivers, and physicians who desire to improve quality of life”, says Michal Rutkowski, Vice President of HAEi and President of the Polish HAE organization Pięknie Puchnę.

27-28 October 2018 HAEi and Pięknie Puchnę once more teamed up for the Central Eastern Europe Conference and Workshop in Warsaw, Poland. This third event of its kind in this region brought comprehensive assistance, guidance, education, and awareness programs to HAE patients as well as support and motivation to physicians to serve as expert medical advisors.

Among many other things the 221 delegates heard Professor Marc Riedl from the US HAEA Angioedema Center at UCSD in USA talk about “HAE background and Treatment Landscape (now and the future)”. Based on the acute treatment recommendations from the most recent World Allergy Organization/International Association of Allergy and Clinical Immunology guidelines (2017) Professor Riedl said that all attacks should be considered for on-demand treatment and any attack affecting or potentially affecting the upper airway should be treated. Furthermore, HAE attacks should be treated as early as possible – either with C1-INH, ecallantide, or icatibant. Also, he said that all patients should have sufficient medication for on-demand treatment of two attacks and carry on-demand medicines at all times and that any patient who is provided with on-demand treatment licensed to self-administer should be taught to self-administer.

Regarding prophylactic treatment recommendations, Professor Riedl said that patients should be evaluated





for long-term prophylaxis at every visit and that disease burden, as well as patient preference, should be taken into consideration. Regarding medication, he suggested the use of C1-INH for first-line long-term prophylaxis and androgens as second-line long-term prophylaxis. Also, he suggested the adaptation of long-term prophylaxis in terms of dosage and/or treatment interval as needed to minimize the burden of the disease.

On the topic of progress in HAE the Professor spoke about the educational and diagnostic efforts, not least improved recognition and testing for HAE, family testing, and development of specialized centers for HAE care. Regarding treatment advances, he said that there is improved global access to effective HAE medications and that he sees a shift towards increased use of preventative strategies.

The program also included an orientation on “HAE during pregnancy”, delivered by Professor Henriette Farkas from the Hungarian HAE Center at Semmelweis University in Budapest. The Professor asked why women with C1-INH-HAE are unique – and answered the question herself: Women have more frequent attacks than men, women have more severe attacks than men, hormonal factors play a significant role in the worsening of the condition, and female sex hormones affect the synthesis of many proteins.

Both HAEi President Anthony J. Castaldo and HAEi Executive Director Henrik Balle Boysen spoke at the conference. While Mr Balle Boysen gave an orientation on HAEi advocacy tools one of the topics for Mr Castaldo was “Advancing HAE Advocacy”. Among other things he said that the advocacy key to success is always to be ready to demonstrate how modern treatments result in dramatic improvements in patient quality of life, never take no for an answer, and to stay vigilant, patient, and creative even though the path to success is a long one with unexpected turns. Most importantly, Mr Castaldo urged the delegates to call upon HAEi Regional Patient Advocate Michal Rutkowski to bring his experience and resources. Furthermore, the HAEi President said:

“You must build your national HAE organization as there is strength in numbers. And you must forge partnerships to sharpen advocacy effects – not least by finding and working with healthcare professionals, seeking out industry representatives and exploring ways to collaborate on raising awareness and broadening access to life-saving medicines, and working with government at all levels.”

Mr Castaldo also gave an overview of the extensive ongoing research for new HAE treatments:

- Ongoing trials on an oral treatment for prophylaxis and acute attacks (BioCryst)
- Ruconest recombinant C1-INH for prophylaxis (Pharming)
- Long-acting subcutaneous humanized monoclonal antibody against factor XIIa (CSL Behring)
- Developing oral treatment (KalVista)
- Adeno virus assisted gene therapy (Adverum)
- A number of companies with compounds in early stage development

Among many other items, the program included a talk on "How Patients' Organization can help Stakeholders (Physicians and Pharmaceuticals Companies) improve patients' quality of life" by Paweł Przewięźlikowski, CEO of Selvita SA. Furthermore, at the welcome evening on the first conference day, the organizers premiered a film on living with HAE from the Polish patients' perspective. As previously the program included a Q&A session as well as presentations from the majority of the countries in the HAEi Central Eastern European region.



Status in Central Eastern Europe

At the HAEi Central Eastern Europe Conference and Workshop 2018 eight of the 12 countries in the region gave an orientation on the present state. The following is a short summary mainly based on the presentations.



BELARUS

Organization: Рэспубліканскае грамадскае аб'яднанне “Дапамога пацыентам з спадчынным ангіацёкам” (patient group 2011; organization 2017)

Number of patients: 41 diagnosed; 250 estimated

Members of organization: 53

Specialist physicians: 10

Treatment centers: 2

Diagnosis: Diagnosis is free but waiting for lab tests may take a few months

Available treatment: Fresh frozen plasma for acute treatment; androgens for prophylactic treatment

Knowledge: Only specialists and intensive care physicians know about HAE

Challenges: 80 per cent of the HAE patients are undiagnosed; in average it takes 12.4 years to get the right diagnosis; there are patients that have been seeking for their diagnosis for more than 40 years and one patient for almost 50 years; access to effective HAE medication; a massive corruption scandal has rocked Belarus healthcare

Successes: Official registration of the organization; an HAE-related session during the 5th International Conference of Immunology Diseases in Minsk in April 2018; press conferences; educational materials; publications in media; participation in HAE Global Conference in Vienna, Austria in May 2018



CZECH REPUBLIC

Organization: Občanské sdružení na ochranu pacientů s hereditárním angioedémem

Number of patients: 162 diagnosed

Members of organization: 150

Specialist physicians: 8-10

Treatment centers: 4

Diagnosis: Tests are available and encouraged in families with HAE, even if symptom free

Available treatment: Androgens and tranexamic acid/Exacyl for prophylactic treatment; Berinert, Firazyr, and Ruconest for acute treatment; fully reimbursed and accessible via the HAE treatment centres

Knowledge: The general level of HAE awareness remains limited

Challenges: Current approach is focused on saving lives only with no focus on quality of life; no LT C1-INH prophylactic treatment is approved leading to extra burdens on pediatric and special adult patient groups (pregnancy; breastfeeding mothers; androgen side-effects); there is a low number of rare disease patients in clinical trials

Successes: First educational seminar for HAE and primary immunodeficiencies patients in the country in June 2018; Czech Ministry of Health plans to improve access to medication for rare diseases, to speed up the new medication approval process, and to work closely with patient organizations



ESTONIA

Organization: None

Number of patients: 17 registered; 40-50 expected

Treatment centers: 2

Available treatment: Berinert, Cinryze, Firazyr, and Ruconest

Successes: Reimbursement in place



HUNGARY

Organization: Magyarországi Angio-Ödémás Betegek Egyesülete (patient group 1996; organization 2006)

Number of patients: 185 registered; 200 expected

Members of organization: 185

Treatment centers: 1

Available treatment: Berinert, Danazol, and tranexamic acid for prophylactic treatment; Berinert, Firazyr, and Ruconest for acute treatment; reimbursement depending on medicine and/or individual entitlement; all acute treatments can be self-administered

Knowledge: Knowledge among general physicians is improving

Challenges: Patients need to do yearly checkups and attend patient meetings; family members should be persuaded to come up for screening; doctors need to communicate easier and more direct; more physicians must be provided with training and knowledge; access to medicines

Successes: Self-administration trainings





KAZAKHSTAN

Organization: Организация пациентов НАО Казахстан (2018)

Number of patients: 300 estimated

Members of organization: 10

Specialist physicians: 1

Treatment centers: None

Diagnosis: Only outside the country

Available treatment: None

Knowledge: Very low

Challenges: Extremely low level of HAE recognition among physicians; no treatment available

Successes: Two hour HAE session as a part of PID conference among immunologist/allergists in Astana in October 2017; protocol of treatment is issued – next step is registration in the list of rare diseases; a few posts about HAE in social media; article in the press



POLAND

Organization: Pięknie Puchnę (2005)

Number of patients: 400

Members of organization: 290

Specialist physicians: 19-24

Treatment centers: 1

Available treatment: Berinert, Firazyr, and Ruconest for on-demand treatment (limited access); androgens (Danazol), tranexamic acid, and fresh frozen plasma for off-label treatment

Knowledge: Poor or very poor among society, patients, caregivers, and healthcare professionals

Challenges: The biggest challenge is awareness

Successes: Conferences and regional workshops with self-administration courses



RUSSIA

Organization: Межрегиональная общественная организация Общество пациентов с Наследственным Ангионевротическим Отеком (МОО ОПНАО)

Number of patients: 130 diagnosed (2015)

Specialist physicians and treatment centers: It is difficult to determine the exact number of care centers, hospitals and doctors capable of HAE diagnostic and treatment; often it is particular physicians taking care of HAE patients in their region (2015)

Available treatment: Berinert and Firazyr

Challenges: Medicine supply; low awareness among the medical community; threat to patients' lives; problems with diagnosis; interaction with government agencies; scientific and practical conferences



UKRAINE

Organization: Громадська Організація "Українська Асоціація Пацієнтів на Спадковий Ангіоневротичний Набряк" (2017)

Number of patients: 860 estimated

Members of organization: 37

Specialist physicians: 4

Treatment centers: 1

Diagnosis: Lab tests are expensive as no pharmaceutical company finances it

Available treatment: Aminocapronic and tranexamic acid; Danazol; fresh frozen plasma (only for adults)

Challenges: Awareness – including among patients; active involvement of patients; getting non-registered drugs to be purchased by the state and the process of distribution among the regions; drug producers are not willing to come to Ukraine

Successes: Budget for the medication in 2019 (kids confirmed); demonstration in front of the Ministry of Finance; joint efforts of patients and doctors is the key to success



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 straightforward information about HAE and treatment required during an attack. It also includes 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 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 has 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 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 an 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:

Albanian, Arabic, Bulgarian, Chinese, Croatian, English, French, Greek, Hebrew, Italian, Macedonian, Portuguese, Romanian, Slovenian, Spanish, and Turkish.

If you are looking for further information on Emergency Cards, please contact:

Project Manager Deborah Corcoran:

 d.corcoran@haei.org

HAEi Regional Patient Advocates' contact:

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



Status per
21 December 2018

17 have pre-registered
- representing HAE patients from
**Chile, Denmark, France, Germany,
Norway, Panama and United Kingdom**

Are you ready for the 2019 Camino Walk?

After the very successful HAEi/AEDAF Camino Walk on the legendary Camino de Santiago in northwestern Spain in May 2016 and 2017 as well as the Jakobsweg Walk in Vienna, Austria in 2018, quite a number of people have expressed an interest in repeating the experience in May 2019.

Consequently, HAEi has once more teamed up with the Spanish HAE organization AEDAF to organize a Camino Walk to commemorate the global HAE awareness day **hae day :-)** in 2019.

The 2019 HAEi/AEDAF Camino Walk team – that is the President of HAE Spain (AEDAF) Sarah Smith, the AEDAF Vice President Concepción Lopez Serrano, the HAEi Regional Patient Advocate Maria Ferron, the HAEi Communications Manager Steen Bjerre, and the excellent organizer and guide of the 2016 and 2017 Camino Walk Rafael Moreno – has gladly agreed to organize and support another walk.

Provided that a sufficient number of people sign up to fill a bus the organizers will follow this well-known format:

- *15 May 2019:* Exit by bus from Madrid to El Ferrol – hotel in El Ferrol
- *16 May 2019:* First stage appropriately coinciding with **hae day :-)** going from El Ferrol to Puentedeume (approx. 15 km) – hotel in El Ferrol
- *17 May 2019:* Second stage from Puentedeume to Betanzos (approx. 18 km) – hotel in A Coruña
- *18 May 2019:* Third stage from Sigüeiro to Santiago de Compostela (approx. 14 km) – hotel in Santiago de Compostela
- *19 May 2019:* Pilgrim's mass at the cathedral in Santiago de Compostela – bus back to Madrid

"To organize another successful Camino Walk, we need to have a reliable estimate of the number of people who would be participating. Therefore, we kindly ask anyone interested in doing the HAEi/AEDAF Camino Walk 2019 to pre-register. I would like to stress that it is not a formal commitment or final registration, but it gives us a good indication of how many people are reliably serious about taking part in this event", says Sarah Smith.

PLEASE CONSIDER

When considering taking part in the 2019 Camino Walk please bear in mind that:

- Included in the price is bus from Madrid Airport to the Camino Walk // bus during the days of walking // bus from the Camino Walk back to Madrid Airport // fours days of hotel accommodation (incl. breakfast) in shared double room (unless you want a single room and pay a bit more)
- The price may be a little more expensive than in 2017 (225 EUR per person in shared double room/310 EUR per person in single room); it will depend on the number of people taking part and hotel availability.
- There will be **no** HAEi travel grants to/from Spain (as was the case with the Camino Walk in 2016)
- There will not be as much leeway as in 2016 to accommodate people who cannot or do not want to do all the walking, i.e. most likely there will be no "Plan B" except for emergencies.

18:
 registered
 Brazil,
 Mexico,
 Spain,
 gdom

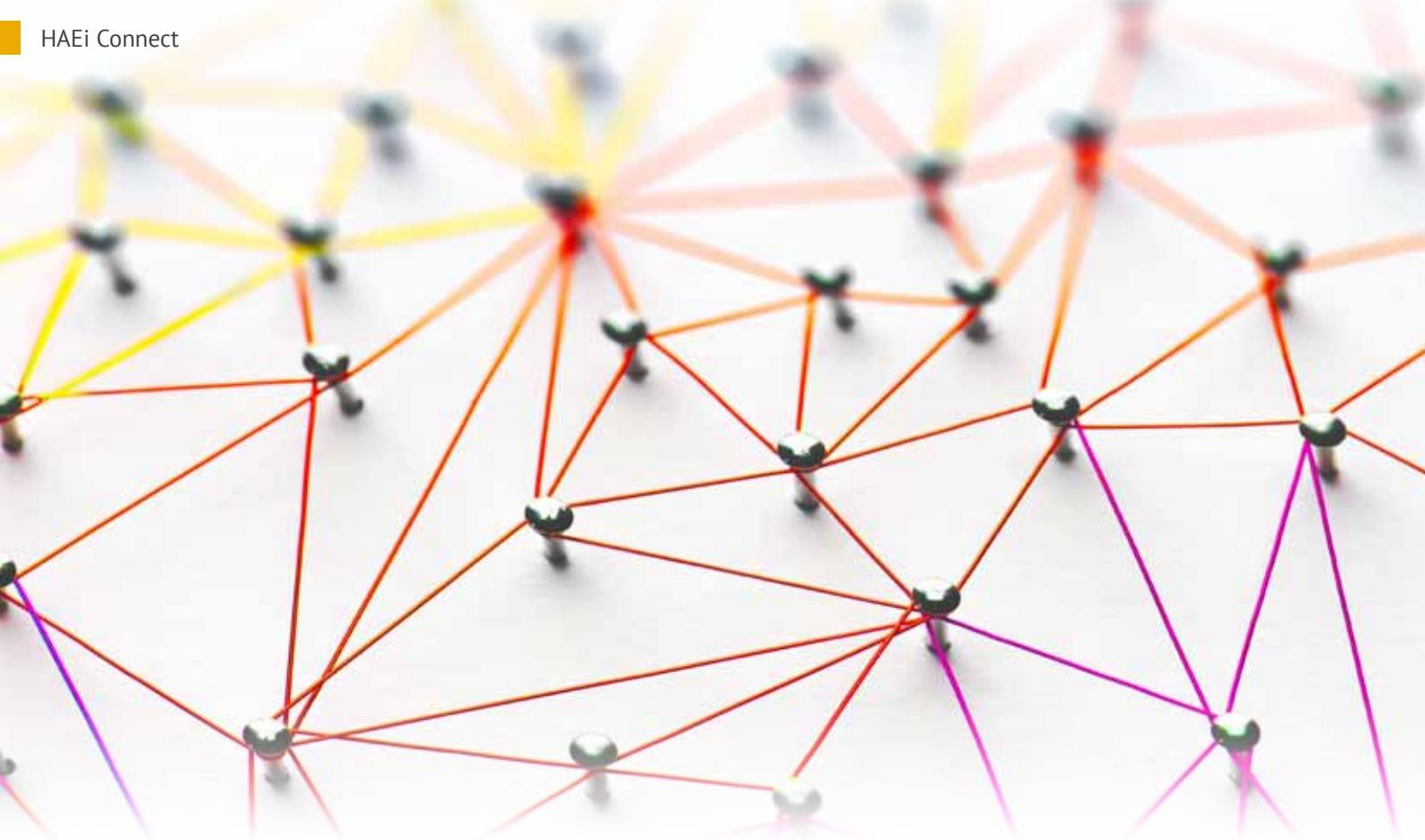


INTERESTED IN TAKING PART?

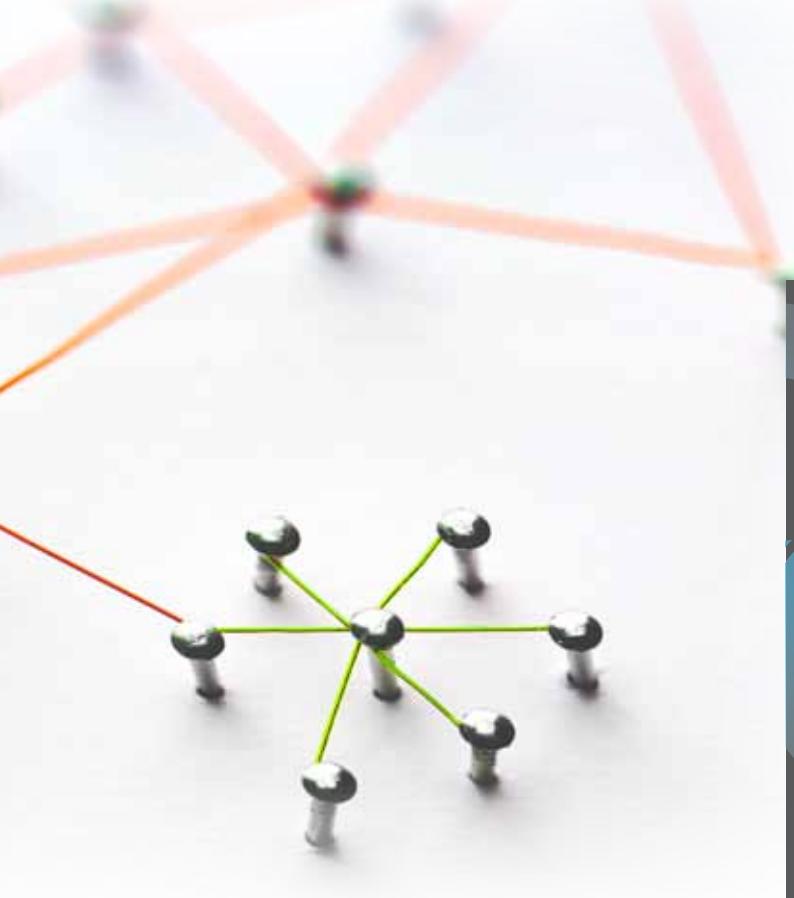
Please pre-register at www.haei.org/cw19. It is **not** a formal commitment or final registration but it gives HAEi/AEDAF a good indication of how many people are reliably serious about taking part in the HAEi/AEDAF Camino Walk 2019.

Questions?

Don't hesitate to contact Steen Bjerre at s.bjerre@haei.org or Sarah Smith at s.smith.foltz@haei.org.



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.



Still more countries on HAEi Connect

A while back HAEi presented HAEi Connect – a cloud-based member database for national organizations to manage their members.

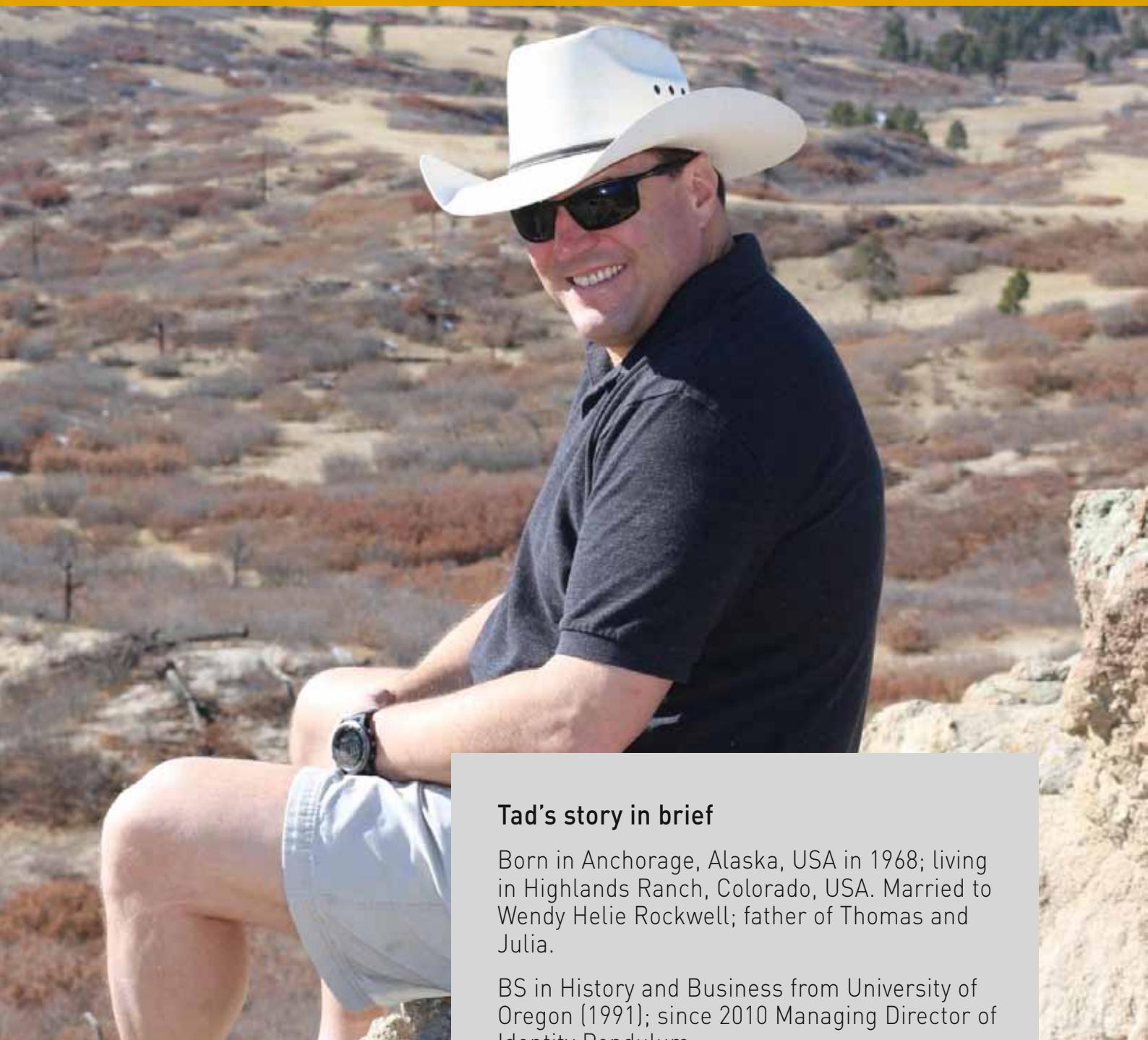
“In our close collaboration with the national member organizations, we have learned that management of members is handled in many different ways – ranging from simple Word files and small local databases to excel spreadsheets and more complex systems. In order to make management of the member database 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. It secures a uniform and secure member management worldwide – and it is being developed based on ideas and requests from the member organizations.

“HAEi Connect has had a great start and is already rolled out in number of countries. We continue to introduce the membership database and communication tool to member organizations around the world – primarily through our Regional Patient Advocates. It is important for us to have all member organizations sign up for HAEi Connect as this will help us have a better understanding of our global membership volume”, says Henrik Balle Boysen.

At the moment HAEi Connect is rolled out to Australia, Bulgaria, Denmark, India, Israel, Kenya, Macedonia, Mexico, New Zealand, Norway, Peru, Poland, Slovenia, South Africa, Spain, Sweden, and Turkey.

“Furthermore, we are presently talking to the national organizations in Belarus, Brazil, Canada, Czech Republic, Greece, Hungary, India, Montenegro, Romania, Ukraine, United Kingdom, and the USA”, says HAEi Project Manager Ole Frölich.



Tad's story in brief

Born in Anchorage, Alaska, USA in 1968; living in Highlands Ranch, Colorado, USA. Married to Wendy Helie Rockwell; father of Thomas and Julia.

BS in History and Business from University of Oregon (1991); since 2010 Managing Director of Identity Pendulum.

HAE symptoms started at five; diagnosed at 23.
Other HAE patients in his family: None.

HAE patient Tad Rockwell was born in Anchorage, Alaska, USA in 1968. He now lives in Highlands Ranch, Colorado, USA with his wife Wendy and their children Thomas and Julia. Tad is a BS in History and Business from University of Oregon and since 2010 he has been Managing Director of Identity Pendulum. This is Tad Rockwell's HAE story.

Patient story: Tad Rockwell

I am not a victim of HAE anymore

When you were five years old you had your first HAE attack – the first of hundreds. What do you remember about that experience?

I woke in the middle of the night, my face swollen. My tongue was three inches thick, poking out of my mouth, and the swelling in my throat nearly suffocated me. I shook my parents awake, and they rushed me to the emergency room. The doctors decided the cause must have been a spider bite, but this made no sense to my mom. A spider bite? It's November in Alaska. The spiders are all frozen, and there wasn't a mark on my body. I was treated with antihistamines and stayed in the hospital until the swelling subsided but other than that there was no treatment – or research into what had caused the swelling.

That attack happened more than 40 years ago, but I remember it like it was yesterday, because it was really scary. You have got to understand, I was not your normal kid. By the time I was five I was an advanced skier; by my teens, I was an extreme skier before there was such a thing as extreme skiing. I was dropping down avalanche chutes and jumping off 70-foot cliffs.

Altogether you have been doing quite a number of things one wouldn't expect of a HAE patient.

Well, to mention just one I was a commercial fisherman, working 70 hours a stretch on rough seas and chasing bears away from our fishing nets. Throw in the fact that I also played football for 11 years. In my mind, nothing on this planet could knock me down. This was my mindset despite the fact I suffered scattered abdominal attacks throughout my childhood and teen years. Attacks so painful it felt like someone scraping a broken bottle through my intestines.

When were you diagnosed?

It was kind of a fluke. When I was 23 my hand was swelling pretty bad, and I went to a local walk-in clinic. Once again it was suggested that it could be a spider bite and as it went away after a few days nothing more was done about it. However, 30 days later it came back in the exact same place and in the exact same way, so I went to the same walk-in. By chance, I ran into the same doctor, and he suggested we do a blood test – and

that led to the diagnosis HAE type 1. The doctor simply explained there was no treatment and prescribed me antihistamines as he told me he really didn't know what else to give me. Then, he sent me on my way with this advice: "If your throat swells, go to a hospital." To me, that was common sense, so I dismissed the whole thing. There was nothing to be done! At the time, the swelling was occurring only in my hands, and the pain was inconvenient, not incapacitating. So my reaction to the diagnosis was: "Who cares? There is nothing on this planet that can knock me down". So, I continued with my nothing-can-stop-me attitude and lived my life in denial of the true nature of my disease.

But then the attacks got more severe.

Yes. Fresh out of college I moved to California to start a career in business, and it was there I met my soul mate and soon-to-be wife, Wendy. As the years went on, I advanced in my career and started a family. It was during this time that the attacks became more frequent and more severe. In the 10 years following my diagnosis, I suffered hundreds and hundreds of attacks in my hands, arms, feet, legs, and scrotum. During this period, I tried steroids. This slightly reduced my number of attacks, but I also developed a personality that almost caused an end to the most important relationship in my life. I decided the side effects weren't worth it, and I stopped taking steroids. I told myself: "I'll be fine. It's no big deal. And there's nothing to be done anyway." Denial becomes a useful tool in dealing with a disease when there is no treatment available.

Along the way, you found out that you might be triggering the attacks yourself?

Well, as my job responsibilities grew and two kids came along, my stress level went through the roof. It turned out that for me stress was the main trigger for HAE attacks. And this time around, the attacks turned to my abdomen. Over the next three years, I experienced more than 70 abdominal attacks, and I gained an entirely new definition of pain. In my life, I've dislocated my shoulder more than 30 times, shattered my hand, smashed my face, surfed with a fractured collarbone, and skied on a broken leg. On a pain scale from one to 10, I'd say a broken bone feels

like a two. At my seven, I'm hyperventilating and on the ground not able to speak or communicate. At eight, I'm screaming uncontrollably, vomiting and gagging. At nine, I'm not a human anymore. I experienced a nine many times during these three years, and I wound up in the emergency room more than 40 times.

They must have gotten used to treating you there?

Not really, no. In most of the emergency rooms I walked into, the staff saw my HAE symptoms and thought I was a drug seeker. In the best cases, I endured countless tests and CT scans and was given antihistamines or steroids. But more often than not, I experienced neglect and even outright abuse. The attacks could last anywhere from six to eight hours, and I would spend most of that time in the waiting room, screaming and vomiting. Sometimes, I'd crawl into the restroom and lie in god-knows-what for hours, crying and vomiting – but at least then I could escape the stares. I have even been thrown out of emergency rooms to work through my attacks alone in the grass or bushes in front of the building. Eventually, I couldn't take it anymore, and I just stopped going to the hospital.

Obviously, that didn't mean the HAE attacks stopped. They were relentless. If they happened in the car, I would have to pull over on the side of the road or freeway for hours, and pray no one would find me. They would strike at my kids' soccer games. Anywhere I happened to be, as soon as I sensed an attack, I would search frantically for a dark place to lie on the ground so I wouldn't injure myself or scare others. Twice, the police and paramedics came to my house because the neighbors heard my screaming, and they literally dragged me gagging and writhing out of the house while I was having an attack. My kids got to watch all this happen. My wife got to watch all this happen.

Have your experiences with hospitals been all lousy up until you found the right medication?

A vast majority have been. However there were some exceptions, there was one time I was in New York City for a few days of meetings, and my throat closed at the airport as I was boarding a plane. At that time I had gotten in contact with the US HAEA via the hotline.

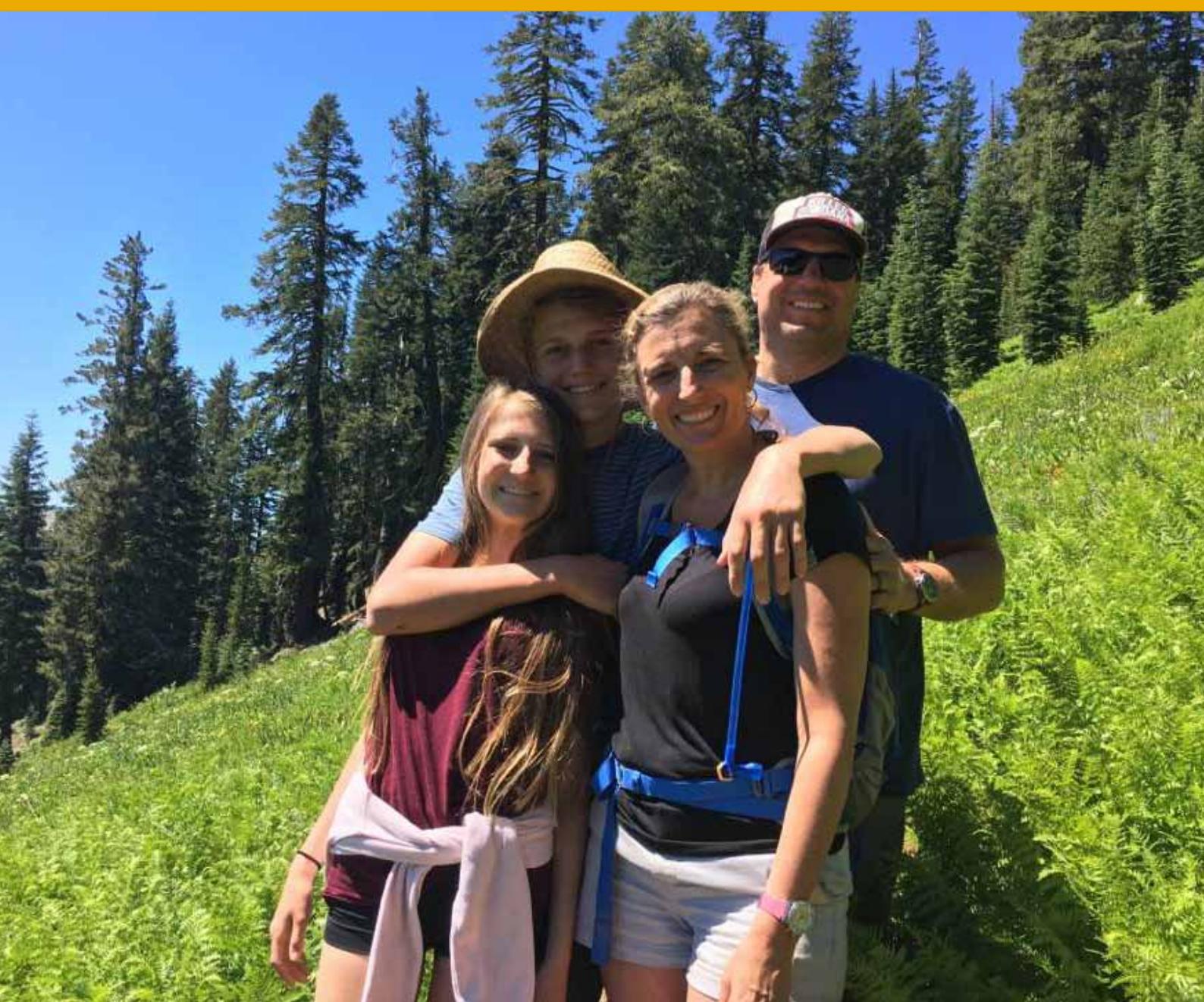


I was told to go to Mount Sinai Hospital. I called them, went there, and the doctor came and met me in the emergency room. That is probably the busiest emergency room you can imagine right in the middle of Manhattan but never the less they knew my name when I walked through the door. Within 10 minutes I was getting an effective treatment that stopped my attack quickly. That was the first time I experienced knowledge about HAE in an emergency room. That was a positive experience and one that probably saved my life.

How have you been coping with HAE when it comes to working?

I worked for many years in the automotive industry helping companies re-build their businesses, streamline operations, and make them more profitable. I have

done this with many companies over the last 20 years. However, back in 2010, I realized that my career kept me so busy that I didn't have time to spend with my children, wife, friends, and family, and that travel had become pretty much just for business. So while in the past, I was making good money my home/work balance wasn't what I wanted it to be. Today I work from home with good people who are like-minded, thus achieving my goal of balance, fun, and healthy passive income. I help people build greatness in their organizations, and in themselves. Without this flexibility in my job I am pretty sure I would have been unemployed, and before the right medication, unemployable with a wife and two children. I chose to change my lifestyle and profession to fit my needs, my health being a major component of that.



Talking about family: You had your wife and kids, but from a HAE perspective you were pretty much alone in the world?

Yes. From the time I was finally diagnosed at 23 until I was 44 – that is a little more than 20 years – I visited more than 20 different doctors, none of whom specialized in HAE and none who could help me. I didn't know a single person on the planet who had HAE. I was truly alone and completely overwhelmed by the disease, and the thought that “nothing can be done” ruled my life and kept me from doing anything about it. From attack to attack, HAE owned me. I didn't own it.

In my late 30s, the abdominal attacks eventually subsided to the point where I could get back on my mountain bike. One day, one of my mountain-biking buddies mentioned he had heard about a new drug on the market that might be able to help me with my attacks. I remember exactly what I said to him: “There's nothing on this planet that can help me except me.” To me, this meant watching my diet and exercising more – doing all the things that helped my body cope with stress. This was the only solution I could see even though there were actually new and effective solutions around me. I just didn't think they would be able to help me.

And then came what you describe as your wake-up call. How come?

During a vacation to my in-laws, two hours away from my house, my face swelled uncontrollably and then dropped into my throat, and it became clear that I needed help. I didn't want to go to a hospital I had never been to. I wanted to go to the hospital by my house, so Wendy and I quickly packed our bags and we left for the two-hour drive home. We stopped for gas, and while there, my throat started closing like a vise and all I could think was: “Oh my god, I'm going to die at a gas station. I'm going to die and my wife and children are going to watch it happen. All because I didn't handle this disease responsibly.” It was truly frightening. Those dark days and years of not respecting this disease had finally come to a head. It was pretty obvious that I had to my change. Like right now. Or never.

Wendy immediately drove me to the emergency room of the nearest hospital, where a doctor actually listened and moved on what she heard. She had drugs brought

in, and I was immediately moved to the intensive care unit. At this point, Wendy had had enough. For years I had been telling her that there was nothing anyone could do for me and that even the US HAEA couldn't tell me anything I didn't already know. She was tired of hearing it, and she took a stand and called the US HAEA hotline. Lois Perry from the US patient organization immediately connected with the hospital and provided critical instructions for treatment.

And after that, you kept in contact with US HAEA?

I did. After I got out of the hospital, Lois really fought for me. Over the following weeks, US HAEA helped me find the right doctor and get to the right medication. Lois connected me with an HAE specialist 20 minutes from my house. This blew my mind! I had felt so alone for decades, and all along there was an HAE specialist treating HAE patients 20 minutes from my house?! A couple of days later, when Wendy and I visited Dr. Levy, he told us there were at that point four treatments available. So kindly but firmly, he told me I was in denial and that I was going to leave my kids without a dad if I didn't get responsible with this disease. As soon as the words, “No, I'm not,” slipped from my mouth, I knew. I had been in denial all along. I would have continued down that path if not for the people who made a stand for me when I wasn't willing or ready to make a stand for myself: my wife, my US HAEA advocate, and now, Dr. Levy. He is the one who started me on the path to effective treatment immediately and aggressively.

I know that you did quite a lot of research regarding HAE – among other things on the Internet – but you never came across US HAEA back then?

Well, as a matter of fact, I did. The US HAEA had a pretty static website back in the 90's. I guess I thought that it was good to know that there was some sort of organization but as there was no medication available at that time I didn't join. And when Wendy finally contacted US HAEA, I hadn't looked at the website for 10 years as I had already decided that there was nothing that they could do for me.

And now your use of US HAEA is different from before?

Absolutely. Following the eye-opener, I got to know a few people from the US HAEA staff, and since then my HAE family has grown quite a bit. Among other things, I have attended the national summits arranged by US HAEA. I also took part in the HAE Global Conferences in Madrid in 2016 and in Vienna in 2018 – and together with Wendy I participated in the first HAEi Camino Walk in northwestern Spain to promote hae day :-) in May 2016. Today there is no doubt in my mind: US HAEA and HAEi are the best ways to connect.

And how is your situation now – do you still have frequent attacks?

Since I started participating in the clinical trial for a plasma-derived C1 Esterase Inhibitor for subcutaneous injection things have been very different. Today it is one of the six medications available to HAE patients in the United States, and I am grateful for the treatment that

I have today. I can't tell you how it makes me feel to have a therapy like this helping to manage my disease – and even to have it for self-administration. Everyone is different, but for me, I haven't had a severe attack in – well, years now. Some people have experienced injection site reactions, hypersensitivity, and dizziness but for me, there have been no side effects. However, there could very well be side effects for other HAE patients, so naturally, it is very important to talk to your doctor and make your own plan for treating your HAE before you start on a new medication.

Based on your experiences what are your recommendations to other HAE patients?

First and foremost, it would be not to let HAE rule your life as it did mine for decades. Don't live in denial about what's going on – get diagnosed and get treated. No one has to suffer. No one ever again has to have this kind of story about HAE. Don't let this disease limit you. Don't ever settle for normal when it's possible to choose



extraordinary. Most people with a rare disease simply want to live what they call a normal life. For decades, I lived in denial of my HAE, and because of that, I lived a nightmare. I endured hundreds of painful attacks, many of which threatened my life, before choosing to find a way out. Now, I am here to say: You don't even have to settle for a normal life. You can choose the life you want.

So to summarize: How is your life now compared to the one you lived for years?

My life has changed. Getting the right medication has changed everything, really. Today I handle my disease, and I am not a victim of HAE anymore.

I know now that, along with my healthcare team, I'm 100 percent responsible for managing my disease and managing my mindset. It took me nearly 40 agonizing years to come to this realization. Eighteen years passed from my first attack at age five to my diagnosis, and nearly 20 more years of denial passed between diagnosis and effective treatment.

Now that I've taken a stand for myself, for the first time ever I love my life, and I love the person I've become. I'm living my life on my terms, focused on doing the things I love with the people I love. Like skiing with my daughter, Julia, and my son, Thomas, or hiking with my wife. And I seriously feel like I'm just getting started. There's still a lot I want to do and a lot of places in the world I want to explore.

You mentioned that throughout the years you have dislocated your shoulder, shattered your hand, smashed your face, and surfed with a fractured collarbone. There is a more recent incident.

Certainly! In March 2018 I had a ski crash that resulted in a severe injury to my right knee. However, the experience was entirely different than the previous ones: For the first time ever an HAE attack was not the first thing on my mind after the incident. It only occurred to me days later that due to the medication I have now there was no attack. This is extraordinary in my mind! I can ski 500,000 vertical feet in one winter season, have a horrible crash, and not think about HAE or worry about an attack? Game on!

HAE in the United States

- *Member Organization*
HAEA established 1999.
www.haea.org.
- *Patients*
Estimated 6-10,000.
- *Care center and hospitals*
For assistance in finding an HAE knowledgeable physician or treatment center in the United States, please contact the US HAEA's Patient Services Representative assigned to the state(s) of your inquiry. You'll find the representative at www.haea.org.
- *Physicians*
Many from a wide array of disciplines but only a small number of truly specialist HAE physicians.
- *Available medication*
Berinert, Cinryze, Firazyr,
HAEGARDA, Kalbitor, Ruconest.

News from around the Globe



AUSTRALASIA www.haeaustralasia.org.au

From Fiona Wardman, CEO HAE Australasia:

HAE Australasia recently held their strategy meeting to discuss the focus, tasks, and objectives for the next 12 months and beyond. The Board is excited for the year ahead with a few new initiatives to be rolled out for both Australia and New Zealand such as an HAE nurse forum and a new resource. HAE Australasia is also looking forward to continuing with some of the programs that have been running for a while such as the Meet Ups, and the next Patient & Carers Conference which is being held 13-14 April 2019 on the Gold Coast, Queensland. It would seem that Aussie and Kiwi patients and carers are excited too as there have been so many RSVPs come through in a short amount of time.

If any patients and/or carers have any questions about the conference or have not received information, please email fiona@haeaustralasia.org.au.

HAE Australasia took part in the recent Rare Voices Australia (RVA) 2018 National Rare Disease Summit in Melbourne where the Honorable Greg Hunt MP, Minister for Health announced the governments support for the National Disease Framework by providing a grant. RVA represents nearly 2 million Australians living with rare diseases.

A quick reminder about our Facebook pages 'HAE Australasia Support & Awareness' (open to all), and 'HAE Australasia' (closed page for Australasian patients and carers), and to make sure you are receiving all relevant information become a member of HAE Australasia via haeaustralasia.org.au/stay-in-touch/become-a-member.



MONTENEGRO www.haei.org/location/hae-in-montenegro

Thanks to the good work of HAEi Regional Patient Advocate Natasa Angeleska HAEi can welcome HAE Montenegro as a new member to the global family.

The President of the organization is Mrs Marija Kaludjerovic Nikolic, and she can be contacted at hae.montenegro@gmail.com. She writes: "We are proud that we are part of the HAEi family. The workshop in Macedonia was a great experience for me, thank you all for the support!"



TAIWAN www.haei.org

Taiwan now has an HAE doctor as well as an HAE knowledgeable hospital. See more at:

www.haei.org/location/physician-taiwan and
www.haei.org/location/hospital-taiwan.



SERBIA www.haei.org/rs

Please help HAEi in welcoming the new patient contact in Croatia, Ms Maja Kalebic Marusic. She lives in Split and can be contacted via majakabelic@hotmail.com and +385 95 516 1038.



BULGARIA

www.haebg.org

From Danail Dimov, Chairman of HAE Bulgaria:

The VII National Congress of Allergology with international participation was held in Sofia, Bulgaria 16 to 18 November 2018. The main focus of the congress was to raise the awareness of allergy professionals and the general public about the rare forms of angioedema.

A lecturer on HAE was Professor Marco Cicardi, a world-renowned scientist at the University of Milan, a visionary who has changed medical knowledge about HAE and who is extremely committed to the cause of patients with this disease worldwide. The Congress was visited by allergic physicians from around the country who listened with great interest to Professor Cicardi's lecture on HAE.

The Hereditary Angioedema Association Bulgaria, in partnership with the Bulgarian Society of Allergology and the specialists of the Allergy Clinic of Alexandrovska University Hospital, developed and provided for each participant in the congress a special information leaflet on HAE in order to raise awareness among allergology specialists and to facilitate diagnosis and proper treatment of HAE. The information leaflet contains the basic information about the disease – symptoms and signs, ways to diagnose, treatment options, possible crises complications, and information on specialized treatment centers. The prospectus also provides a link to the website of the Hereditary Angioedema Association Bulgaria, which in turn contains detailed information on the illness that could benefit all doctors and patients.

The interest of the specialists in HAE provoked by Professor Cicardi's lecture was followed by a spontaneous discussion between allergic physicians



and representatives of the Hereditary Angioedema Association Bulgaria on the problems and difficulties of patients in the diagnosis and treatment of the disease in the various hospitals in the country.

As a continuation of the campaign to raise awareness of HAE across Bulgaria on 17 November, the National Palace of Culture in Sofia was illuminated in purple to support all patients suffering from HAE.

The Congress and all of its accompanying information campaign on HAE were widely reported in a number of central and specialized print and electronic media in Bulgaria.





From Paige Gunderson, HAE Canada youth member:

The HAE Canada Team has been busy these past few months. In May, some HAE Canada members participated in the HAEi Global Walk where many Canadians put their best foot forward into walking for a cause. Canada came out on top with over 9,000,000 steps. Congratulations Canada!

At the HAE Global Conference in Vienna, Austria we launched our own HAE Canada Youngsters Program helping more youth like me feel at home and empowered with their diagnosis. We are grateful that HAEi Youngsters launched their website and magazine where any HAE youth wishing to submit something to either platform can now do so. Here is the link for the site and more information about the magazine is found on its amazingly inspiring pages: www.haei.org/youngsters.

In addition to attending the Global Conference, some HAE Canada Board of Director members were lucky enough to have a tour of the CSL Marburg Plant, and a tour of the Shire Vienna Manufacturing Facility. The visit helped the board members get a look into the other side of the needle, you could say.

We are also very proud to announce that Health Canada has approved Takhzyro™ (lanadelumab injection), a first-of-its-kind monoclonal antibody treatment for the prevention of HAE attacks. This is the first step in the approval process for new drugs in Canada.

HAE Canada had the privilege of being involved in the Canadian Society of Allergy and Clinical Immunology (CSACI) Conference held in Halifax 12-16 September 2018. Many specialists representing all regions of Canada who treat HAE patients were in attendance. Others included allied health professionals, medical students, Immunology Fellows and pharma representatives. Dr Jonathan Bernstein, an Allergist and Immunologist from the United States, delivered a presentation on the different types of HAE and the current research on new treatments carried out in the US and on genetics. Dr Gina Lacuesta, Allergist and Immunologist in Halifax, spoke about the pathophysiology of HAE, the various blood components that play a role in the condition and the current treatments available in Canada. The change they are promoting within their local medical communities is encouraging to HAE patients and their families.

Their presentations increased awareness of advances in ongoing drug trials. It is hoped these drugs will be available for the HAE Canada community. It was amazing to get to meet many physicians and the pharma representatives who visited the booth and appreciate their keen interest in the HAE condition that my family and I struggle through daily.

HAE Canada, CSL Bering, Shire and other companies held booths alongside one another during this conference. We were lucky to have our President, two other Board



News from around the Globe

members, and helpful HAE Canada volunteers support the booth. HAE Canada's main goal for supporting a booth was to spread the message to physicians about our organization and ask them to help spread the word about HAE Canada and to encourage any patients with HAE to join our organization.

Four HAE Canada posters were presented at the conference that were based on data of the HAE Canada National Report Card Survey issued by HAE Canada to our membership in 2017-2018. Several conference participants viewed the HAE Canada posters, and those who developed the posters answered questions.

By offering information at the booth, it gave me the chance to meet face to face with specialists or other medical personnel who may or may not have HAE patients. This allowed me as a patient to share information brochures as well as my personal experience of living with HAE. I was also able to provide them with direction on how to get more HAE information to further their understanding for themselves and or their patients.

I visited a couple of pharma booths and reviewed a few very informative audiovisual tools for patients. These audiovisual programs show how important it is for others to learn more about treating HAE and how the quality of life for myself and my fellow HAE patients are impacted by our condition.

In addition to attending the CSACI Scientific Meeting, two board members and an HAE Canada member participated at the recent Science for Rare Warriors: Rare Disease Knowledge Translation Conference in October in Toronto. The Rare Disease Review, which is a medical and health policy journal that translates current rare disease research into informative reports that anyone can understand, hosted the conference. Those who attended found the conference helpful as it taught the basics of medical science, and how to break down complex medical information.

One final, but essential, item we would like to share is that in the fall, HAE Canada President, Jacquie Badiou, traveled to St. John's to meet with Deputy Minister of Health and Community Services, John Abbott and Ms Jamie O'Dea, Director of Pharmaceutical Services to discuss treatments for HAE patients in Newfoundland & Labrador. During their meeting, they discussed the importance of providing all available treatments to HAE patients across Canada. We have been informed of the wonderful news that Newfoundland & Labrador has added Icatibant (Firazyr 10mg/ml solution) to the province's benefit list. We would like to thank Deputy Minister Abbott for the attention he and his government gave to this very important step towards equal access for all Canadians with Type 1 and 2 HAE. We are pleased to announce that Firazyr is now available from coast to coast – a fantastic way to end 2018.



CHINA

www.haei.org/location/hae-in-china

HAEi has recently registered the first HAE knowledgeable physician and hospital in China: Prof. Yuxiang Zhi, Peking Union Medical College Hospital in Beijing. The professor can be contacted via telephone 0086 13426303007 and email yuxiang_zhi@126.com.



EL SALVADOR

www.haei.org/location/el-salvador

From the HAEi Regional Patient Advocate Javier Santana, we have learned that there is a patient in El Salvador who is supporting him to develop the first group of patients in the country. Raquel Fuentes is willing to act as HAE point-of-contact in El Salvador – here are her contact information: raquellfuentess27@gmail.com; phone +503 7615 9368.



From Elena Bezbozhnaya, Chairman of OP-NAO:

It has been a quite busy autumn as we have organized and participated in several significant events.

19 September 2018 the Medical Genetics Center of Tomsk held a scientific-practical conference titled "Orphan diseases in the practice of doctors of various specialities" and organized by the Society of Patients with Hereditary Angioedema (OP-NAO) in collaboration with health care institutions and the medical-scientific community. The conference gathered general practitioners and specialists from Siberian medical institutions and the members of the Society of Patients. The conference focused on the problems of diagnosis and treatment of HAE. Denis Bezbozhny, Deputy Chairman of the Board of OP-NAO, presented the patient organization and its activities, while Ilya Ushankov, lawyer, Ph.D., concentrated on medicine supply for people diagnosed with HAE in different regions of the country and the existing forms of patient legal support. Yulia Faykova introduced her patient history and answered questions regarding the manifestations of the disease, the treatment regimen, and methods of relieving seizures.

24 October 2018 a webinar was held for the members of OP-NAO on the routing patients with HAE. The participants were introduced with diagnosis rules

News from around the

and medical care for patients with HAE. The proposed scheme included:

- Preliminary diagnosis at the place of residence;
- Directions for further examination;
- Consultation of an allergist-immunologist;
- Laboratory-based diagnostics to confirm the diagnosis.

Besides, the project provided methods for further medical support and the patient's hospitalization in emergency and scheduled cases; proposals for introducing patient self-control diaries into practice – based on these diaries doctors will specify a treatment regimen and the required amount of medicines. The participants approved the proposed routing scheme. Then the project was sent to the federal health authorities for further discussion. In mid-November, I received a response from the representatives of the Ministry of Health of Russia with prior approval. The project will be submitted to the legislative level for the final approval.

27-28 October 2018 representatives of OP-NAO took part in the 3rd International Conference of Patients with HAE from the countries of Central and Eastern Europe in Warsaw, Poland. The Russian delegation



BOSNIA AND HERCEGOVINA

haei.org/location/hae-in-bosnia-herzegovina

Mr Miroslav Dragnic has agreed to be the HAEi patient representative in Bosnia and Herzegovina, adding yet another member to the steadily growing HAEi family.

You can contact him via
e-mail: miroslavdragnic@yahoo.com and
phone: +38761727477



JORDAN

[www.haei.org/location/physician-jordan](http://haei.org/location/physician-jordan)

Dr Hani Ababneh at the Dar Al-Salam Hospital in Amman is the first HAE physician in Jordan. His contact information is at haei.org/location/physician-jordan.



SWITZERLAND

www.hae-vereinigung.ch

From Helene Saam, HAE Switzerland President:

The 17th General Assembly of HAE Switzerland took place 9 November 2018, and I could welcome 18 members. We are pleased that Ernst Greber was unanimously elected as an associate to the board. We look forward to the cooperation. All other agenda items were also decided unanimously.

The 20th patient meeting of the Swiss HAE organization will take place 18 May 2019 in Bern. Participants will be members of the national organization, HAE experts, pharma representatives as well as HAEi Executive Director Henrik Balle Boysen. The agenda includes lectures from HAE experts and a visit to the CSL Behring facilities. Registrations will be sent in March 2019.



Globe

included eight people headed by myself. Together with the medical lawyer Ilya Ushankov we presented the organization, talked about the problems of the Russian patients with HAE and the methods of OP-NAO working to change the situation. Also, I shared the data of the statistical study conducted by OP-NAO in 2018 based on a sociological survey of the organization's members. Representatives of the Russian delegation completed their presentation with a cartoon film created by OP-NAO for the smallest patients diagnosed with HAE, about the illness in accessible language, how to learn to live with it without fear.

8 November 2018, the Moscow School No. 843 hosted an informational and educational seminar for teachers titled "Implementation of an educational program for children with rare diseases". The event was initiated and organized by OP-NAO. The conversation with teachers focused on creating equal educational opportunities for all students as well as a comfortable and safe environment for children with special needs. Professor Andrey Prodeus, pediatrician-immunologist and doctor of medical sciences, as the main speaker introduced the teachers with the orphan diseases associated with impaired immune systems. In more detail, the doctor focused on the HAE diagnosis, mechanism of the disease, existing risk zones and actions required in extreme

situations. The psychologist Ekaterina Shutkova accentuated the problem of school adaptation for a child diagnosed with HAE. Teachers had the opportunity to ask questions regarding work with children with rare diseases.

27 November 2018 OP-NAO held a Regional School of Patients with HAE for residents of the southern regions of Russia in Krasnodar. Andrei Prodeus, pediatric immunologist, MD, professor, Ilya Ushankov, medical lawyer, and Yulia Faykova, psychologist, chaired the meeting. The event discussed the problems faced by patients in southern Russia, modern methods of treating the disease, and issues of preferential drug supply in the southern regions of the country. Yulya Faykova conducted an art therapy lesson for the school participants.

In addition to organizing events and participating in conferences, the OP-NAO management conducts its regular work: legal and psychological support to members of the organization, assistance in medicine supply for patients with HAE, and individual routing schemes for residents of different regions of the country, if required, so the daily life challenges for the members of the organization.





News from around the globe

Alvaro Cieza Macedo third from left



PERU
www.haei.org/peru

Suzet Lam Torres, President of AEH Peru, has sent this story from Alvaro Cieza Macedo:

My name is Alvaro Cieza. I am 23 years old, a 7th-year medical student and an HAE patient. I don't remember well when I had my first crisis, but my parents say it was at the age of two. In the beginning, I had edema in the hands, feet and abdominal viscera (even the time I underwent surgery for an abdominal pain misdiagnosed as appendicitis). During this period I had around six crises per year, visited many doctors – and some curanderos for sure – but they tended to consider it "an allergy" or "a rare disease".

It took about ten years for the physicians to diagnose me with HAE, so I started receiving prophylactic treatment with tranexamic acid when I was 13 years old. Some years later I had one or two episodes per year, whereby I believed that the disease was under control. As my college studies progressed, I understood my illness better and realized that very few doctors knew about HAE. But something happened when I was finishing my career as the crises (mostly as acute abdominal pain, nausea, and vomiting) suddenly became more frequent, resulting in approximately 40 visits to the emergency room just in 2017.

Despite this development I tried to finish my career; however, when I was in the medical internship, I had more than eight episodes of viscera edema during the

first month. I explained to the doctors in charge of the internship about this rare disease and how I was suffering, but they completely ignored it and even tried to disqualify the diagnosis. Only once, when I had an intense crisis, they were afraid of the possibility of laryngeal edema. They suggested that it was better for me to retire from the medical internship. During that time I felt too lost, alone and desperate since my co-workers and mentors couldn't understand the whole situation. I tried to continue the internship, but it was impossible; there were doctors who supported me during the crises and others thought that it was just an excuse for not working.

Here in Peru, in the case of HAE and other rare diseases, adding to the problem of the poor understanding of the disease is the scarcity/non-existence of specific drugs to treat them.

This year through Ms Suzet Lam Torres I met AEH Peru, and I am now a member of this organization as well as of the Federation of Rare Diseases in Peru (FEPER). Thanks to that I understood that many people in Peru have the same problems as me. Finally, I hope – as a patient and future doctor – more people will learn about this disease in my country, and we will all have access to the current treatments, all this supported by better health policies.

nd the Globe



SPAIN

www.angioedema-aedaf.org

From Sarah Smith Foltz, President of AEDAF:

Patient Workshop: AEDAF held its 14th regional patient workshop on 4 October 2018 in Almeria (Andalusia), in Hotel Catedral. Twenty-one people, including patients, family members and physicians, attended the workshop. Dr Concepción Lopez Serrano, who is Vice President of AEDAF, and myself as well as Dr M. Carmen Moya Quesada of the Allergy Department of Almeria's Torrecardenas Hospital presented the activities of AEDAF and HAEi, an update of HAE and current treatment options, and the situation of HAE in the region of Andalusia and the province of Almeria.



Next Patient Workshop: AEDAF's 15th regional patient workshop is scheduled to be held in Valencia 15 February 2019.

Annual Meeting: AEDAF will be holding its 21st General Assembly and Annual Meeting 9 March 2019 at La Paz University Hospital in Madrid. In addition to the regular program, we are planning to organize a session for our AEDAF youngsters, as well as a self-administration workshop.

3rd HAEi-AEDAF Camino Walk: AEDAF is again supporting HAEi and HAEi Communications Manager Steen Bjerre to help turn the idea of a 3rd Camino Walk in Spain into reality. If all turns out as planned, we will be meeting again in Galicia in northwestern Spain around **hae day :-)** 2019 to walk several stages of the Camino de Santiago in order to raise awareness of HAE. We hope to see you there!

From Spain, AEDAF wishes everyone in the Global HAE Community: Feliz Navidad, Happy Holidays and a Happy and Healthy New Year!



MACEDONIA

www.haei.org/haemacedonia

HAE Macedonia physician representatives have been quite active during the most recent months. Dr Katarina Stavric, pediatrician, who is head of the Children's hospital in Skopje, delivered a presentation about a case study of a child with HAE at the International Alergology and Immunology Conference held in Ohrid, Macedonia on 29-30 September 2018.

Dr Stavric also agreed to assist HAE Macedonia in the efforts to identify reliable physicians and help in expert advice to identify patients in Macedonia. Furthermore, she was a speaker and facilitator at a congress organized by the Pediatric Associates of the Republic of Kosova for the Primary Immunodeficiency on 10 November 2018. She gave a presentation about the Macedonian experiences in treating children with HAE, and she assisted Dr Shendvere Hassani to present about HAE to the audience.

HAE Macedonia hopes that the start of this cooperation will help in identifying HAE patients in the country and that the organization can assist them in the near future in other educational and advocacy activities as well.



News from around the Globe

From Michelle Cuevas, Managing Director:

It has been a hectic and productive year for the US HAEA community, as many of our patients, family members, and industry partners took the time to participate in our HAEA sponsored events. We had record-setting participation in: HAE IN-MOTION® 5K run/walk events hosted across the country; HAEA Treatment Education series webinars; Capitol Hill Day; Youth Advocacy and learning activities; **hae day :-)** events; the HAE Global Conference in Vienna, Austria, and the Advance HAE Scientific Registry.

Together, we have made great strides in the quest for improved HAE treatments and supporting groundbreaking research to continue to solve the remaining scientific mysteries of HAE. This year, the US HAEA patient community welcomed another important FDA-approved HAE therapy, and the US HAEA Angioedema Center announced the discovery of a promising new blood test that will facilitate treatment by clarifying the cause of swelling in the many patients who have an uncertain diagnosis. 2018 was also a



record-breaking year for the Scholarship Program that we recently named after our Chief Operating Officer Pam King – a true advocate for our HAE youth – who passed away in June. We are happy to announce that the Pam King HAEA Scholarship Fund provided financial aid to help 42 college students achieve their lifelong educational goals and life aspirations.

As we get ready to celebrate the 20th anniversary of US HAEA's creation, we find ourselves more motivated and fiercely committed than ever to lead a nationwide HAE advocacy movement dedicated to increasing awareness and education, empowering patient access to a suitable therapy, and fostering groundbreaking research that includes searching for a cure. US HAEA friends can always count on us for authoritative, unbiased information, and highly personalized services that are delivered with the kindness and compassion one would expect from our staff of fellow HAE patients/caregivers.

The US HAEA plans to expand its core services in 2019 with a particular focus on making sure our patient community has adequate access to and reimbursement for HAE therapies. US HAEA friends can count on us to continue offering patient-centric programs and activities geared toward our longstanding goal – improving the quality of life for everyone in the HAEA community. We also look forward to celebrating the 2019 HAEA National Patient Summit next summer in Atlanta.

From Lois Perry, HAEA Director of Health:

Tribute to Pam King: Scholarship recipients, patients, industry partners, HAEA staff, and guests came together in Providence in October 2018 to pay tribute to Pam King and the realization of her dream to establish a Scholarship Program for HAE patients. Throughout her career in the worlds of pharmaceutical industry and patient advocacy, Pam inspired many with her heartfelt dedication to helping people with serious medical conditions lead a better life, and provided young patients with the opportunity to overcome obstacles and fulfill their educational goals and aspirations. Guests and members of Pam's family, among the attendees, heard scholarship recipients share their powerful stories

of how they are overcoming personal challenges and focusing on their future, thanks to Pam's lasting belief in their potential.

To support the Pam King HAEA Scholarship Program and transform the lives of HAE patients, visit www.haeascholarship.org/support.php.

Youth Stand Up Strong: Congratulations to all the kids and teens who participated in the first annual HAE Youth Advocacy Month. Their willingness to help raise HAE awareness and educate others in their community made an important impact on the care of patients everywhere. The HAEA is proud of the contributions of all of our youth! So many of you planned and held events, ordered ER Tool Kits to distribute in your community, joined us for an HAE IN-MOTION® 5k, and raised awareness in your schools.



SYRIA

www.haei.org/location/physician-syria

Thanks to HAEi Regional Patient Advocate Rashad Matraji another HAE physician has been added to the HAEi world map. That is Dr Lubna Hwejeh, a Specialist in Pulmonary Diseases at the Al Assad University Hospital in Damascus, Syria. Contact information can be found at www.haei.org/location/physician-syria.



CYPRUS

www.haei.org/location/cyprus

Country number 69 has joined the global HAEi family as there is now an official point-of-contact on Cyprus:

Evangelia Englezaki can be contacted via

phone: +35799338953 and
e-mail: evaggelin@hotmail.com.



From Ersan Sevinc, International Communications Manager, HAE Turkey (HAÖDER):

It has been hectic days since the beginning of September. After a long and a beautiful summer, HAE Turkey took off to attend the HAEi SEE Workshop annually held in Skopje, Macedonia. We presented the improvements and our goals for the next year. We are now focused on how we can prevail the current home treatment approach of the government. What we believe is that home treatment should not be an option, rather it should be accessible for all the patients all around the world.

Another respectable event that HAE Turkey has attended is the National Allergy, and Clinical Immunology Congress held 17-21 November in Antalya, Turkey. We are proud to be the first patient organization invited for the second time to such a significant congress in our country. The audience of the congress is all the specialists who are meeting many possible HAE patients, and this year 650 attendants were there to expand their knowledge and expertise on a number of diseases. HAE was referred to many times in various sessions by the HAE professors of Turkey. A special course named "Angioedema School" was organized during the congress, and HAE was almost the main subject of the whole event. We truly believe this congress and the efforts of many HAE physicians serve a great purpose since it is always followed by a significant increase in diagnosed patients after such events.



News

Now we have the Rare Diseases Day, which is another event and chance to gather and raise our voices. Next time, we plan to meet with other rare disease associations and organize a joint event. Although we have now some connections with the other rare disease organizations, it is disappointing that Turkey still doesn't have an umbrella organization or network for the rare diseases associations. We hope to build one and take our place in that organization soon.

HAE Turkey will have its national assembly in February 2019. This assembly will mainly focus on the organization and its future agenda. Patients will also be invited, and a patient-oriented session will be organized to share and discuss the latest HAE news from around the world.



KOSOVO

Natasa Angeleska, the HAEi Regional Patient Advocate for South Eastern Europe, informs that Kosovo now has two HAE physicians:

The first one is Lidvana Spahiu – a pediatrician nephrologist – at KBC in Pristina. The specialist can be contacted via phone +38344160738 and lidvanaspahiu@gmail.com.

The second is Shendvera Hasani – pediatrician – at Children's Clinic (Pediatrijska Klinika), also in Pristina. This doctor can be contacted via phone +38344225769 and shendverehasani@gmail.com.



HUNGARY

www.haei.org/hungary

The 11th C1-inhibitor Deficiency & Angioedema Workshop will take place 23-26 May 2019 in Budapest. The conferences organized every second year are devoted to the presentation and discussion of the latest scientific findings related to bradykinin-mediated angioedemas. It has long been known that in addition to C1-inhibitor deficiency, the background of these angioedematous disorders might also include further – genetic and other – factors. Therefore, the title of the conference has been supplemented with the word 'Angioedema', in order to harmonize it with its agenda.

from around the Globe



KAZAKHSTAN

www.haei.org/location/hae-in-kazakhstan

Coming back from the HAE Global Conference 2018 the national organization in Kazakhstan posted a review on the social media. Also, this information was distributed in a closed physician group and promoted to social media pages of government as well as private clinics and hospital with immunologists and allergologists. Furthermore, HAE Kazakhstan has started collecting information on independent physicians for upcoming communication.



KOREA

Another country can be added to the HAEi world map: In Korea, there are now two hospitals as well as two physicians with knowledge of HAE. Type "Korea" and see more at www.haei.org/resources/world_map.



TUNESIA

www.haei.org/location/care-center-tunisia

The Department of Respiratory Diseases and Allergology I at the Abderrahman Mami Hospital in Ariana, Tunisia has been added as an HAE care center. See more at www.haei.org/location/care-center-tunisia.



PUERTO RICO

www.haea.org

From Regional Patient Advocate Javier Santana:

15 December 2018 the Puerto Rican HAE group had a Christmas meeting with the special participation of HAEi President Anthony J. Castaldo, who gave an excellent presentation about the updates of new treatments and important data for patients. After Hurricane Maria in Puerto Rico last year, this was the first meeting to bring the HAE group together and share their experiences and establish the new plans for 2019. Representatives of pharmaceutical companies and the President of the Association of Allergists and Immunologists in Puerto Rico, Dr Rafael Zaragoza, gave a warm welcome to all patients and wishing that all were well after the hurricane. Ianice Viel, who is the new leader of the HAE group, as well as Janet Long of the US HAEA also participated in the event.



News from around the Globe



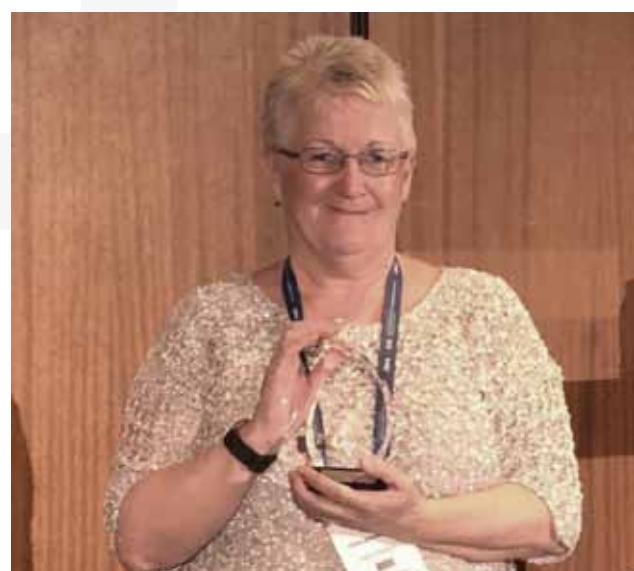
From CEO Laura Szutowicz, HAE UK:

The end of the year sees our two Patient Days, one in Scotland and one for England, so that keeps us busy from the end of summer. We still managed to squeeze in a few events before that. One of these was organized by June Cole, who is absolutely passionate about raising awareness of HAE and educating both the public and clinicians. She has successfully presented to both her A&E department and her local general practice doctors about HAE, treatment, and living with the condition. Her latest brainchild was to combine her love of music with awareness raising: She sings with her local Rock Choir and organized a flash mob at the huge Westwood Cross Shopping Centre in Broadstairs. A flash mob begins with one or two people casually starting to sing – then all the choir who are pretending just to be shopping join in to end up with a fantastic event.

Several of the Immunology Centres have run their own Patient Days this year; Leeds, Birmingham, Salford, and Addenbrookes. These have all been well attended and a variety of interesting topics covered during the days. It is very good to know that the consultants and nurses are really involved with treating HAE and are trying to make as much progress as possible with treating all patients as individuals rather than a 'one size fits all' approach.

We have also had success over the summer with the devolved governments, Scotland accepting an application for Ruconest to be available to Scottish patients, and Wales allowing Icatibant and Ruconest to be available. This means they are automatically funded by NHS Scotland/NHS Wales and are freely available for prescription.

We spent a wonderful weekend in Edinburgh for the 3rd Scottish Patient Day. Again, we had about 50 attendees; mostly patients but some of the specialist nurses also took part. Miss Darcy Annals aged 5, Rachel's daughter,



attended and kept us all in order. We are particularly grateful to Dr Moira Thomas and Dr Charu Chopra for giving up their Saturday to attend and to make such a successful day. Goodness, Scotland is so lucky to have such expert and sympathetic clinicians looking after our HAE patients. Of course, there are always problems, one of which is getting a level provision of home delivery to patients but with people like these looking after our patients I can sleep more peacefully. Paediatric specialist nurse Charlotte Vost gave us a presentation on dealing with younger patients and Rachel Annals told us her patient story. The day finished with a lively question-and-answer session.

The next big event in the calendar was the annual Patient Day. This year we held it in Farnham, a very historic town, site of a battle in the 9th century where the Anglo Saxons had a decisive victory over the invading Danes (don't tell Henrik!), and we were very fortunate to hold the meeting in the Mercure Hotel right in the middle of Farnham. Our only sadness was that Furkhanada Haxton who has been at every HAE Patient Day since they started and is our 'front of house' when people arrive giving them delegate packs, badges etc. could not be with us due to having injured her neck. I am glad to say she has recovered and is back to her usual self.

Dr Patrick Yong who is Consultant Immunologist at Frimley Park led the meeting. He is also the lead on the HAE Consultant Network, which is now functioning as a division of the UKPIN, which is the UK association of immunology doctors and nurses. The idea of the network is to have an HAE expert in each region who can be called upon to give advice where needed, also for the network to develop research projects, surveys and so on.

Our meeting had a truly international flavor as Michal Rutkowski, the HAEi Vice President and leader of the Polish affiliate as well as Katie O'Sullivan who heads up the Eire affiliate were able to attend. The first presentation was Dr Scott Hackett, one of our medical advisory panel members, who gave us an overview of treatment for children. This was followed by a presentation from Alex Graham, and Jack Cope, our Youth Ambassadors, two of the most inspirational young people anyone would care to meet and both of whom are going to Georgia next summer. They gave us a taste of what young people can achieve and then went off to lead the Young Peoples' track with 14 delegates.

We were so thrilled to have such a good response from younger people, and it included the Carthy boys from Ireland. We then didn't see much of any of them for the rest of the day, but they all seemed to enjoy themselves, and we have some great ideas come out of this group.

Next up for the adults was Dr Sorena Kiani giving a taste of the recent products undergoing clinical trials. He was lead investigator for Lanadelumab in the UK and gave us a fascinating insight into how each product works and where and why one product may suit a patient more than another. Reinforcing the 'one size does not fit all' theme from our Scottish day. Dr Kiani's session concluded with his clinical nurse specialist John Dempster giving some case histories of patients who have been involved in various clinical trials. Ed Price, our Chair of Trustees, gave us his patient experience and reinforced how vigilant one must be and not just dismiss an increase in attacks as 'oh, it's just my HAE', when so often there is an underlying cause that is nothing to do with HAE. Just because you have HAE does not mean you cannot have other medical issues.

The afternoon kicked off with a double act of Christine Symons and Fran Ashworth, two of the most experienced nurses one would ever meet. Indeed, Fran had just come home from the European Congress on Immunodeficiencies having been awarded a Lifetime Achievement by the International Nursing Group for Immunodeficiencies.

Michal Rutkowski then gave us a worldwide perspective on HAE around the globe. He is one of our most popular speakers, as people love hearing about what is going on and the various activities of HAEi.

The rest of our afternoon was filled by John Bell, a motivational speaker, who gave us all some ways of turning our lives around to make them more fulfilling. He also put great importance on the benefits of a family – which is what we have. We have our HAE family – an invaluable support.

We did have a film crew filming during the Farnham Patient Day, so when that is available, we will share it with our International HAE Family.

We wish you all a very Happy Christmas ... Joyeux Noel ... Frohe Weihnachten ... Glædelig jul ... Wesołych Świąt ... Feliz Navidad ... Fijne kerstdagen and many, many more languages of HAEi!

**BRAZIL**

www.abranghe.org.br

20-23 October Abranghe participated in the XLV Brazilian Congress of Allergy and Immunology in Recife. The organization had an information booth and managed to register 22 new doctors with knowledge of HAE. Furthermore, an HAE session was moderated by Dr Regis Campos and had lectures from Dr Anete Grumach, Dr Eliana de Toledo, and Dr Maria Luisa Alonso.



News from around the Globe

In September 2018 Abranghe was among the participants – from 14 Latin American countries – meeting in Chile for a gathering organized by the Latin American Association of HAE (ALAeh). The purpose of the meeting was to launch the implementation of the Global Registry of Patients with HAE of Latin America. Part of the event was a panel discussion between José Fabiani (Argentina), Sandra Nieto (Mexico), Margarita Olivares (Colombia), Solange do Valle (Brazil), Ana María Gallardo (Chile), Raquel Martins (Brazil), and the HAE Regional Patient advocate Fernanda Martins.



Recently the Brazilian HAE organization has also held a lecture on HAE in the city of Serro for patients, the Secretary of Municipal Health Ronam Sales, and health care professionals such as doctors, dentists, and nurses.





National Institutes of Health
Turning Discovery Into Health

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 the moment:

A Study to Investigate CSL312 in Subjects with HAE – recruiting in USA.

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.

Study to Assess the Tolerability and Safety of Ecallantide in Children and Adolescents with HAE – recruiting in USA.

Patient Registry to Evaluate the Real-world Safety of Ruconest – recruiting in USA.

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, Serbia, Slovakia, South Africa, Spain, Switzerland, and United Kingdom.

C1 Inhibitor Registry in the Treatment of HAE Attacks – recruiting in Bulgaria, Czech Republic, France, Germany, Hungary, Italy, Macedonia, Norway, Poland, Slovakia, and Sweden.

Biomarker for HAE Disease Type 1 (BioHAE) – recruiting in Germany.

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.

Determination of Specific Biomarkers of Acute Attack of Angioedema Within Pediatric Population (BRADYKID) – recruiting in France.

The Role of the Coagulation Pathways in Recurrent Angioedema (Angiocoag) – recruiting in France.

A clinical trial to assess 2 different doses of BCX7353 compared to placebo as an oral treatment for the prevention of attacks in people with HAE – recruiting in Austria, Canada, Czech Republic, Denmark, Germany, Ireland, Macedonia, Netherlands, and USA.

BCX7353 for the prevention of HAE attacks – recruiting in Australia, Austria, Canada, Denmark, Germany, Hungary, Macedonia, Spain, Switzerland, and United Kingdom.

A placebo controlled trial of three doses of BCX7353 to evaluate the safety and efficacy in the prevention of attacks in patients with HAE – recruiting in Canada, Germany, Hungary, and United Kingdom.

A Phase 3, Multicenter, Randomized, Single-Blind, Dose-Ranging, Crossover Study to Evaluate the Safety and Efficacy of Intravenous Administration of Cinryze (C1 Esterase Inhibitor [Human]) for the Prevention of Angioedema Attacks in Children 6 to 11 Years of age with HAE – recruiting in Argentina, Germany, Italy, Mexico, Romania, United Kingdom, and USA.

Pathophysiological study for autoimmune dysregulation of HAE – recruiting in Japan.

Epidemiological Analysis for HAE Disease (EHA) – will be recruiting in 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:

Chemotherapy in Patients with HAE – by C. Morelli, Tor Vergata University Hospital, Italy, et al.:

The stress induced by chemotherapy such as standard oxaliplatin/fluorouracil increases the risk of attacks in patients with HAE. However, circulating biomarkers such as D-dimers, C3 and C1-INH functional may serve as early predictors of acute HAE crisis. (*Anticancer Res., December 2018*)

Effect of Lanadelumab Compared with Placebo on Prevention of HAE Attacks: A Randomized Clinical Trial – by A. Banerji, Harvard Medical School, USA, et al.:

Among patients with HAE type I or II, treatment with subcutaneous Lanadelumab for 26 weeks significantly reduced the attack rate compared with placebo. These findings support the use of Lanadelumab as a prophylactic therapy for HAE. Further research is needed to determine long-term safety and efficacy. (*JAMA, November 2018*)

An Investigational RNAi Therapeutic Targeting Factor XII (ALN-F12) for the Treatment of HAE – by J. Liu et al., Alnylam Pharmaceuticals:

RNA interference (RNAi) mediated knockdown of plasma factor FXII by ALN-F12 is a potentially promising approach for the prophylactic treatment of HAE. (*RNA, November 2018*)

Practicalities of a reduced volume formulation of a C1-INH concentrate for the treatment of HAE: real-life experience – by J. Dempster, The Royal London Hospital, United Kingdom:

The volume-reduced C1-INH concentrate (Berinert) 1500 IU is a practical and convenient alternative to multiple 500 IU vials for the treatment of HAE, which provides patients with more control and independence over their disease owing to a simpler to administer treatment. (*Allergy Asthma Clin Immunol., October 2018*)

The diagnosis of HAE with C1-INH deficiency: a survey of Canadian physicians and laboratories – by X. Charest-Morin, Laval University, Canada, et al.:

C1-INH functional assay was widely available in Canada (93%), but was only offered by a small number of hospitals meaning that there could be longer delays in the analysis of these samples that may explain why the physicians expressed a lower level of confidence in this assay (59%). Antigenic C1-INH was available to the vast majority of the physicians treating C1-INH-HAE (93%) and was considered reliable by 96% of the respondents. Antigenic C4 was found available to all Canadian physicians and, although with limited specificity, was considered very reliable by all the participants. This study revealed that 81% of physicians were able to order the antigenic C1q and the confidence in this assay was moderate (70%). Concerning genetic testing, the survey revealed that most of the CHAEN members never had to or couldn't order this test. The study highlights the need for improved education and knowledge exchange about biological assays available to Canadian physicians and their performance in proper diagnosis of C1-INH-HAE to improve confidence and access to relevant tests. (*Allergy Asthma Clin Immunol., November 2018*)

Gene mapping strategy for Alu elements rearrangements: Detection of new large deletions in the SERPING1 gene causing HAE in Brazilian families – by P. Nicolicht, Federal University of São Paulo, Brazil, et al.:

Exon Quantification Technique (EQT) – a molecular diagnostic test for the detection of large genetic rearrangements in SERPING1, mapping the exact size and location of the deletion caused by the recombination of Alu elements – could be used as a simple, rapid, and efficient diagnosis test for analysis of large deletions and insertions involving SERPING1, otherwise not detected by Sanger sequencing, serving as a support technique for molecular diagnosis of HAE. (*Gene, October 2018*)



HAE: a mother diagnosing her child using Google as a diagnostic aid – by T. Srikantharajah, Zealand University Hospital, Denmark, et al.:

At times ‘Doctor Google’ may be an important tool in establishing the diagnosis. This case report would emphasize the importance of listening to patients and relatives and being humble to ‘Doctor Google’. Furthermore, the aim is to remind all healthcare personal of HAE and the importance of considering the rare differential diagnoses to common symptoms. (*BMJ Case Rep.*, October 2018)

Treatment of HAE Attacks with Icatibant and Recombinant C1 Inhibitor During Pregnancy – by R. Hakl, St. Anne’s University Hospital, Czech Republic, et al.:

The results show good C1-INH or icatibant treatment efficacy for HAE attacks in pregnancy. The treatment by the first drug used was effective in 93.7% of all attacks. In 6.3% of attacks, a second treatment had to be used. No adverse effects were observed. (*J Clin Immunol.*, October 2018)

Lanadelumab for the Prophylactic Treatment of HAE with C1-INH Deficiency: A Review of Preclinical and Phase I Studies – by P.J. Busse, Icahn School of Medicine at Mount Sinai, USA, et al.:

Despite improved availability of medications for on-demand treatment during attacks and prophylaxis of future attacks, unmet needs remain. Lanadelumab, a fully human monoclonal antibody, may help address some of the limitations of existing prophylactic options such as the need for intravenous administration or frequent dosing. Preclinical studies demonstrate that it is highly potent and specifically inhibits plasma kallikrein, and findings from phase Ia and Ib studies suggest this agent is well tolerated and provides sustained inhibition of plasma kallikrein, allowing for less frequent dosing. (*BioDrugs.*, December 2018)

Training patients for self-administration of a new subcutaneous C1-INH concentrate for HAE – by E. Murphy, CSL Behring, et al.:

International guidelines recommend that all patients with HAE be considered for self-administration if they are willing. Although some patients may initially be intimidated by the idea of self-administration of subcutaneous (SC) injections, the provision of appropriate education, training and counseling will allow most patients to feel comfortable with the process. There is a long history of patients with other chronic diseases mastering self-administered SC injections. Patient training needs to be individualized. Most patients are capable of learning self-injection. However, the amount of time required will vary from patient to patient. If applicable, parents and/or caregivers should be trained at the same time. Patients should be taught the value of planning ahead and getting into a routine, such as setting up a regular schedule that allows sufficient time from beginning to end. The patient/caregiver must learn to master reconstitution of C1-INH (SC), injection site and needle/syringe preparation (including aseptic technique), and injection of C1-INH (SC).

It is critical to keep in close contact with patients during the first few months of C1-INH (SC) use. The frequency will depend on the patient, their ability and skill level; weekly contact for the first month or two may be advisable. Patients should be encouraged to keep a diary or log book to document their injections and treatment compliance. It is also recommended that patients document and report any breakthrough HAE attacks, their treatment and unusual/lingering symptoms to ensure that all symptoms are being treated appropriately and to help assess the patient’s ability to manage their condition. (*Nurs Open.*, August 2018)

News from the Industry

22 October 2018

The University City Science Center in Philadelphia, USA and **CSL Behring** are partnering to identify and help commercialize potential new medicines at research and academic institutions across the Greater Philadelphia region.

Through the partnership agreement, the Science Center's framework for technology commercialization, services and support – which starts with the QED Proof-of-Concept Program that advances scientific breakthroughs – along with the Science Center's network of research and academic partners, will provide the support and infrastructure for CSL Behring to efficiently evaluate promising technologies from multiple institutions. Researchers at academic and research institutions through the region will be invited to submit proposals for projects with a focus on therapeutics that fit within CSL Behring's areas of expertise.

Projects selected for further review will be matched with CSL Behring advisors, who will work with the researchers to develop proof-of-concept plans for the technologies. Altogether, awarded projects will receive a total of up to 250,000 USD in research funding from CSL Behring, together with scientific and in-kind support including reagent generation and consultancy on drug development strategy. The partner institution will add up to another 50,000 USD.

"Innovation has been key to our success for more than 100 years and we are pleased to collaborate with the Science Center and academic partners to advance innovation in a region of strategic importance to CSL," says Andrew Nash, CSL's Senior Vice President of Research. "By working together to focus on novel targets that are supported in whole or in part by proof-of-concept data, we continue delivering on our promise of developing new medicines that save and protect the lives of people around the world."

"For the last 10 years, the Science Center's commercialization platform has been a unique and effective resource for sourcing new ideas, technologies and research," says Peter Melley, Director of New Ventures at the Science Center. "We're enthusiastic about the opportunity to work with an international leader like CSL Behring and connect them with the region's top research institutions to develop promising technologies that have real market potential."

The Science Center and CSL Behring intend to accelerate the innovation and advancement of research ideas that otherwise might not come to fruition into developed products. The partnership between the Science Center and CSL Behring is especially timely in light of the Greater Philadelphia Region's growing reputation as a biotechnology hub.

(Source: CSL Behring)

CSL Behring



25 October 2018

The European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion recommending the granting of marketing authorisation of Lanadelumab injection for routine prevention of recurrent attacks of HAE in patients aged 12 years and older. If approved, Lanadelumab will be a first-of-its-kind, fully human monoclonal antibody (mAb) available in the EU that inhibits the activity of plasma kallikrein, an enzyme that is uncontrolled in people with HAE, to help prevent attacks.

"This positive opinion marks an important step towards providing adults and adolescents living with HAE in Europe a first-of-its-kind monoclonal antibody treatment option to help prevent attacks," said Andreas Busch, Ph.D., Executive Vice President, Head of Research and Development at **Shire plc**. "We are excited about the future potential of Lanadelumab in helping to address the needs of those living with this chronic and unpredictable disease."

The positive opinion is supported by data from the Phase III HELP (Hereditary Angioedema Long-term Prophylaxis) Study, the largest randomized controlled prevention study conducted to date in HAE, which evaluated the efficacy and safety of subcutaneously administered Lanadelumab versus placebo over 26 weeks in 125 patients 12 years of age or older with HAE.

Lanadelumab was previously granted accelerated assessment by the EMA, reducing the number of evaluation days required from 210 to 150. The CHMP's positive opinion will be reviewed by the European Commission, which has the authority to grant marketing authorization in the EU.

Lanadelumab received approval for the prevention of HAE attacks in patient 12 years and older in the U.S. on 23 August 2018 and Canada on 19 September 2018, under the brand name TAKHZYRO.

The primary endpoint of the HELP Study was the number of investigator-confirmed HAE attacks over the entire 26-week study duration. Lanadelumab demonstrated that subcutaneous injections every two or four weeks reduced the mean monthly number of attacks across all three Lanadelumab treatment arms studied: 300 mg every two weeks, 300 mg every four weeks, and 150 mg of Lanadelumab every four weeks. At 300 mg every two weeks, Lanadelumab reduced the number of mean monthly HAE attacks by 87% vs. placebo (adjusted P<0.001).

Overall, each Lanadelumab treatment arm demonstrated statistically significant attack rate reductions compared with placebo for all secondary efficacy endpoints (adjusted P<0.001 for all comparisons). Patients taking Lanadelumab 300 mg every 2 weeks had 83% fewer moderate or severe attacks and 87% fewer attacks that needed on-demand treatment. A pre-specified, exploratory analysis showed that 44% of patients (n=27) receiving Lanadelumab 300 mg every two weeks had zero attacks compared to placebo (2%, n=41) for the 26-week treatment period. Additionally, in a post hoc sensitivity analysis of the steady state period from Day 70 to Day 182, 77% of patients (n=26) treated with Lanadelumab in the same dosage arm of the trial were attack-free compared to placebo (3%, n=37).

(Source: Shire)



6 November 2018

"With enrollment in APeX-2 complete, and the successful results from ZENITH-1, we are excited with the momentum that is building towards meeting the urgent demand of HAE patients for an oral therapy option to prevent and treat their attacks," said Jon Stonehouse, President and CEO of **BioCryst Pharmaceuticals, Inc.** at the presentation of the financial results for the third quarter ended 30 September 2018.

"We have many significant milestones lined up over the next several months and we are focused on delivering high quality APeX-2 data in the second quarter of 2019, filing our New Drug Application (NDA) for BCX7353 in the fourth quarter of 2019 and advancing at least one additional pipeline program into the clinic in the first half of the year," Stonehouse added.

Upcoming Key Milestones:

- Complete the 250 mg and 500 mg dose cohorts of the ZENITH-1 clinical trial for acute treatment of HAE attacks with BCX7353 (Q1 2019)
- Meet with U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) for input on the design of a Phase 3 clinical trial of BCX7353 for acute treatment of HAE attacks, and commence the Phase 3 trial (Summer 2019)
- Report results from the APeX-2 clinical trial (Q2 2019)
- Advance at least one preclinical program into the clinic and begin the Phase 1 clinical trial (1H 2019)
- File NDA for BCX7353 for prevention of HAE attacks with FDA (Q4 2019)

(Source: BioCryst)

**13 November 2018**

"Thanks to our recent equity financing and the exciting Phase 1 data from our HAE candidate KVD900, we are pleased to announce that we are building on these successes with a more aggressive development plan for KVD900, to potentially accelerate our time to market," says Andrew Crockett, CEO of **KalVista Pharmaceuticals, Inc.** "Our first step has been to design a larger Phase 2 clinical trial for KVD900 as on-demand treatment for HAE attacks in patients to generate more robust data that we intend to use as the basis for discussions with the FDA about a faster approval pathway. We still plan to initiate this trial before year-end, with data anticipated in late 2019. This Phase 2 trial will also benefit from our recently completed food effect study, which showed that dosing following a meal had no significant impact on the pharmacodynamic profile of KVD900. We do not expect food to impose any limitations as to when a patient can take the drug."

The food effect cohort of our Phase 1 study evaluated the impact of food on the pharmacokinetic profile of KVD900 in healthy volunteers. The Phase 1 study of KVD900 included a total of 68 subjects on active drug, of which 18 received the top dose of 600 mg, including the cross-over food effect cohort. Dosing following a standardized high calorie and high-fat meal had little impact on the pharmacodynamic profile of KVD900 tablets, which continued to result in 95% inhibition of plasma kallikrein within 30 minutes, a timeframe that we believe potentially compares favorably to approved injected therapies."

KalVista believes that KVD900 displays a profile well-suited for use as an on-demand therapy for HAE attacks, with a combination of rapid and high uptake into the plasma resulting in fast and strong inhibition of plasma kallikrein. To date, KVD900 has shown no dose-limiting safety signals.

16 November 2018

The enlarged Phase 2 trial evaluating the utility of KVD900 as an on-demand treatment for HAE attacks is expected to initiate before the end of 2018 and is expected to investigate efficacy in approximately 50 type 1 and 2 HAE patients. This two-part study will include an in-patient investigation of safety, pharmacokinetic and pharmacodynamic profile of KVD900 and an out-patient cross-over phase to investigate the efficacy of KVD900 versus placebo. KVD900 or placebo will be dosed within one hour of the start of an attack, with symptom severity monitored for at least 24 hours following administration. Patients will use their normal, on-demand treatment if the attacks worsen. Data is expected from this trial in late 2019, and KalVista will provide more information on the details of the trial design once the trial has initiated.

(Source: KalVista)



Shire plc has announced additional data from the Phase 3 HELP (Hereditary Angioedema Long-term Prophylaxis) Study, evaluating the efficacy and safety of subcutaneously administered Lanadelumab in HAE.

Data shows that patients treated with Lanadelumab 300 mg every two weeks experienced significantly fewer HAE attacks, were less likely to have moderate or severe attacks or use rescue medication (primary and secondary endpoints), and were more likely to be HAE attack-free than those treated with placebo. These results were noted during the entire 26-week treatment period and, according to a post hoc sensitivity analysis, were greatest for patients during the 16-week steady state period (days 70-182).

Andreas Busch, Ph.D., Executive Vice President, Head of Research and Development at Shire said, "For those living with this chronic and unpredictable disease, it is important that they can reduce the frequency of their HAE attacks. Additional analysis of the HELP Study continues to support the use of Lanadelumab as a preventive subcutaneous treatment option for HAE in appropriate patients 12 years of age and older."

Interim results from the HELP Study open-label extension found treatment with Lanadelumab was generally well-tolerated and consistent with the previously observed safety profile. At the time of interim analysis, patients had been exposed to Lanadelumab for a mean (SD) of 8.21 (2.17) months and continued to experience a reduction in HAE attacks.

"The data we have seen from the HELP open-label extension are very promising and we look forward to receiving the final results," said Dr. Busch.

(Source: Shire)



16 November 2018

BioCryst Pharmaceuticals, Inc. presents data showing that an oral formulation of BCX7353 was rapidly absorbed and exhibited a long half-life, two important characteristics of desired new acute treatments for HAE attacks.

In the trial, the pharmacokinetic (PK) and kallikrein inhibition profiles of BCX7353 were evaluated for 24 hours post-dose in six subjects with HAE Type I or II who were given a single 750 mg oral dose of BCX7353 in a period between HAE attacks.

The target concentration of BCX7353 that restores plasma kallikrein suppression to normal, or above-normal, levels is $\geq 8x$ EC50. In the trial, mean concentrations of BCX7353 were approximately 16x EC50 within 30 min, and remained at or above this level through at least 24 hours post-dose.

"Both rapid onset of action and sustained duration of activity are critical attributes that patients and physicians seek in an improved single-dose oral option for the acute treatment of HAE attacks," said Dr. William Sheridan, Chief Medical Officer of BioCryst.

"This PK profile supports the clinical benefits that we saw in the placebo-controlled ZENITH-1 clinical trial of a single 750 mg dose of BCX7353 to treat HAE attacks," Sheridan added.

In order to evaluate prevention of attack progression and symptom relief in the ZENITH-1 trial, study drug (BCX7353 or placebo) was administered early (mean time of administration was 35 minutes) after the onset of symptoms of angioedema, when baseline mean composite visual analog scale (VAS) scores were 14 to 15, on a scale of 0-100.

In ZENITH-1, the VAS scores of subjects receiving a single dose of BCX7353 750 mg were reduced by 6.98 points ($p=0.0024$) compared to placebo by four hours post-dose, and, through 24 hours, use of standard of care medication to treat HAE attacks was reduced by 31.6 percent after treatment with BCX7353 compared to treatment with placebo ($p=0.0029$). BCX7353 750 mg single doses were generally safe and well tolerated.

(Source: BioCryst)



27 November 2018

The Journal of the American Medical Association (JAMA) publishes the complete results from the Phase 3 HELP Study™, a randomized, placebo-controlled trial evaluating the efficacy and safety of subcutaneously administered Lanadelumab versus placebo over 26 weeks in 125 patients 12 years of age or older with HAE. The HELP Study™ is the largest randomized controlled prevention study ever conducted to date in HAE.

Lanadelumab, which is approved under the brand name TAKHZYRO™ in the U.S. and Canada, is a first-of-its-kind monoclonal antibody that inhibits the activity of plasma kallikrein, an enzyme that is uncontrolled in people with HAE, to help prevent attacks.

The study met all primary and secondary endpoints, with all three Lanadelumab treatment regimens demonstrating statistically significant reductions in the mean monthly HAE attack rate compared to placebo. At 300 mg every two weeks, Lanadelumab reduced the number of mean monthly HAE attacks by 87% relative to placebo (adjusted $P<0.001$). Patients receiving Lanadelumab 300 mg every two weeks had 83% fewer moderate to severe attacks (vs. placebo), 87% fewer attacks that needed on-demand treatment (vs. placebo) and an 89% attack rate reduction (vs. placebo) from day 14 to 182.

"HAE can be an unpredictable disease which requires an individualized approach to treatment," said Aleena Banerji, MD, Massachusetts General Hospital, Boston, Mass. and principal investigator of the clinical trial. "The findings from HELP support the use of Lanadelumab as a subcutaneous prophylactic therapy to prevent HAE attacks in appropriate patients, helping address the need for new treatment options."

A pre-specified, exploratory analysis showed that over the entire 26-week study period, 44% of patients receiving Lanadelumab 300 mg every two weeks ($n=12/27$) were attack-free vs. 2% of patients receiving placebo ($n=1/41$). Additionally, in a post-hoc sensitivity analysis of the steady-state period of the last 16 weeks of the study, 77% of patients ($n=20/26$) receiving Lanadelumab 300 mg every two weeks were attack-free vs. 3% of patients on placebo ($n=1/37$).

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"We are excited about the potential of Lanadelumab," said Donatello Crocetta, Head, Global Medical Affairs, Immunology at **Shire plc**. "Data from HELP demonstrate the efficacy of Lanadelumab in preventing HAE attacks over the entire duration of the study, with many patients remaining attack-free during the 16-week steady state period. We remain focused on our work to help make Lanadelumab available to patients living with HAE in additional countries around the world."

A clinically meaningful improvement was also observed in 81% of patients treated with Lanadelumab 300 mg every two weeks based on the Angioedema Quality of Life Questionnaire (AE-QoL) compared to 37% of patients in the placebo group. The AE-QoL measures the impact of angioedema over a four-week period across four domains: fear/shame, functioning, fatigue/mood, and nutrition.

The most commonly reported treatment-emergent adverse events (excluding HAE attacks) in patients treated with Lanadelumab during the entire treatment period were injection site pain (42.9%), viral upper respiratory tract infection (23.8%), headache (20.2%), injection site erythema (9.5%), injection site bruising (7.1%), and dizziness (6.0%). Most treatment-emergent adverse events (98.5%) were mild to moderate in severity. The most commonly reported treatment-emergent adverse events in patients treated with Lanadelumab that were considered related to treatment were injection site pain (41.7%), injection site erythema (9.5%), injection site bruising (6.0%), and headache (7.1%). There were no deaths or related serious treatment-emergent adverse events.

(Source: Shire)



The European Commission (EC) has granted **Shire plc** Marketing Authorisation for TAKHZYRO™ (as Lanadelumab) subcutaneous injection for routine prevention of recurrent attacks of HAE in patients aged 12 years and older. TAKHZYRO is a first-of-its-kind fully human monoclonal antibody (mAb) that inhibits the activity of plasma kallikrein, an enzyme which is uncontrolled in people with HAE, to help prevent attacks.

"We are delighted to receive today's European approval. For those with HAE, the burden of disease can significantly impact their day to day life," said Andreas Busch, Ph.D., Executive Vice President, Head of Research and Development at Shire. "With TAKHZYRO, we can now provide an innovative treatment that has potential to change the way HAE is currently treated."

The recommended starting dose is 300 mg Lanadelumab every two weeks. In patients who are stably attack free on treatment, a dose reduction of 300 mg Lanadelumab every four weeks may be considered, especially in patients with low weight.

The Phase III HELP (Hereditary Angioedema Long-term Prophylaxis) Study™ supporting the approval was recently published in JAMA. The primary endpoint was the number of investigator-confirmed HAE attacks over the entire 26-week study duration. TAKHZYRO reduced the mean number of monthly HAE attacks by 87% relative to placebo when administered at 300 mg every two weeks and 73% relative to placebo when administered at 300 mg every four weeks (adjusted P<0.001).

Overall, each TAKHZYRO treatment arm demonstrated statistically significant attack rate reductions compared with placebo for all secondary efficacy endpoints (adjusted P<0.001 for all comparisons). Patients taking TAKHZYRO 300 mg every two weeks had 83% fewer moderate to severe attacks (vs. placebo), 87% fewer attacks that needed on-demand treatment (vs. placebo) and an 89% attack rate reduction (vs. placebo) from day 14 to 182. A prespecified, exploratory analysis showed that over the entire 26-week study (Days 0-182), 44% (n=12/27) of patients taking TAKHZYRO 300 mg every

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two weeks were attack-free vs. 2% (n=1/41) of patients taking placebo. Additionally, it is anticipated that TAKHZYRO reaches steady-state after approximately 70 days. A post-hoc sensitivity analysis showed that 77% (n=20/26) of the patients receiving TAKHZYRO 300 mg every two weeks were attack-free during steady-state (day 70-182) vs. 3% of patients on placebo (n=1/37).

Based on an exploratory endpoint, a clinically meaningful improvement in quality of life was observed in 81% of patients treated with TAKHZYRO 300 mg every two weeks compared to 37% of patients in the placebo group [assessed by the Angloedema Quality of Life Questionnaire (AE-QoL)]. The AE-QoL measures the impact of angioedema over a four-week period across four domains: fear/shame, functioning, fatigue/mood, and nutrition.

Henrik Balle Boysen, Executive Director for HAEi said, "On behalf of the HAE community, we welcome today's news that provides a new option for the prevention of HAE attacks. We are grateful for the time and effort put forth by the patients and researchers who participated in the clinical program that enabled this important addition to the HAE treatment landscape."

TAKHZYRO has a half-life of approximately two weeks and may be self-administered as one subcutaneous injection every two weeks. In clinical trials, the majority of patients took within 10 to 60 seconds to administer the injection.

(Source: Shire)



A new study examines and compares re-dosing rates inter alia for human C1 esterase inhibitor in recombinant form (Ruconest®) and plasma-derived forms (Berinert®, Cinryze®) to icatibant (Firazyr®) in seven individual patients at risk of HAE attacks. A total of 69 attacks were recorded. The study was led by Professor Dr Marcus Magerl of the Department of Dermatology and Allergy at the Charité Universitätsmedizin Berlin, Berlin, Germany. The main outcome of the study was that treatment with recombinant therapy Ruconest® and plasma-derived C1 treatments requires significantly less re-dosing than icatibant (Firazyr®) to resolve HAE attacks.

There were 69 initial attacks in total across all seven patients. In this real-world study, the patients were able to choose the treatment for their attack. Following initial intervention, some patients needed to treat their attacks with a second dose or subsequent treatments to try to resolve the attack. The choice of the subsequent re-treatments was also decided by the patient. The majority of the attacks were classified as mild (67%), with 27% moderate and 6% severe.

Patients treated their attack initially with either Berinert® (five attacks) or Cinryze® (17 attacks), both plasma-derived C1 esterase inhibitors ("pdC1INH"), or Firazyr® (25 attacks) (icatibant, a small molecule bradykinin inhibitor, "Icatibant"), or Ruconest® (20 attacks), a recombinant human C1 esterase inhibitor ("rhC1INH").

In the study, Ruconest® showed 100% efficacy with first dose at appropriate clinical levels. In two cases, additional therapy was applied because of initial underdosing of the first treatment. Cinryze® and Berinert® also showed good results.

The main difference, however, was shown in those patients who selected Firazyr® as their first line therapy. These patients recorded re-dosing rates that were higher than controlled clinical studies have indicated before.

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Of the 25 attacks treated with Firazyr® as a first line therapy, 11 (44%) failed on the first dose. In eight of those 11 failed therapy situations (72%), the patient took a second dose of Firazyr® to try to end the attack. In the other three cases, the patients took a C1 esterase inhibitor (two taking Berlinert®, and one Ruconest®).

All of the patients who took a C1 esterase inhibitor reported the attack resolved, whereas in a further five of the eight Firazyr® treatments patients had to take a third dose of medication to try to resolve the attack. Where either Ruconest® (two) or Berlinert® (one) were used as the third treatment of the attack, it was again resolved, whereas one out of two attacks re-treated with Firazyr® required a fourth dose of Firazyr® for the attack to be resolved.

Further data regarding reasons for drug selection and subjective observations on the performance of the drugs in each attack are being analysed and the full results of the study will be published by the investigators in due course.

Dr Bruno Giannetti, Chief Operations Officer of **Pharming Group N.V.**, said:

“This was a well-run independent investigator-led comparative study under real world conditions, which gives a clear signal confirming reports from patients: Treatment with adequate doses of C1 esterase inhibitor is an excellent therapy to minimize and end an acute HAE attack. It also confirms that re-dosing with icatibant is often needed to successfully treat an attack. In fact, this study reports failure rates for treatment with icatibant of 44% for the first dose and 62% for the second dose, with one of the patients needing to take four doses to stop one attack.”

(Source: Pharming)



KalVista Pharmaceuticals, Inc. has provided an operational update and released financial results for the fiscal second quarter ended October 31, 2018. CEO Andrew Crockett says:

“We are still on track with our robust Phase 2 study for KVD900 as a potential acute therapy for patients with HAE. Our intention is to have an aggressive development plan for KVD900, and use this Phase 2 data set as a basis for discussions with regulators about a faster approval pathway.”

(Source: KalVista)





HAEi around the world

Currently there are HAE member organizations in **69** 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.

