JUNE 2017

Global perspectives:

HAEi MAGAZINE · ISSUE 3

HAE GLOBAL CONFERENCE
VIENNA
17-20 MAY 2018

Take control of your HAE

Patient story

Patricia Karani

I will not only fight for my own life

Highlights from the 10th C1-INH workshop in Budapest, Hungary

The 10th version of the biannual international C1-INH deficiency workshop was held in Budapest, Hungary 18-21 May 2017. The conference focused on bradykinin-mediated angioedemas, and the topics of this four-day long event covered a wide range of subjects.

Website hosting
– come to us!

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

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

At this point national websites have been launched for Iceland, Greece, Kenya, Macedonia, Serbia, Spain, and Turkey – and most recently Hungary.

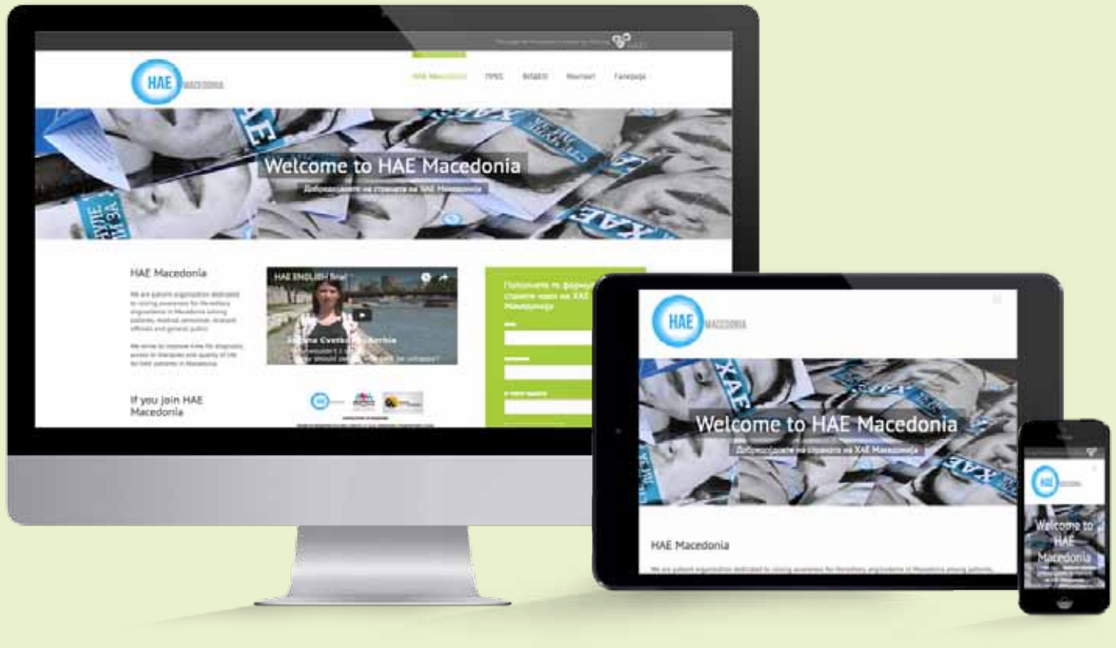
"We are preparing a few more at the moment and hopefully both Ireland and Poland will be launched later this year", says Henrik Balle Boysen.

At **www.haei.org/haei_countries** you'll find an overview of all 55 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.)



Dear HAEi Friends,

We cordially welcome you to the June 2017 edition of HAEi's *Global Perspectives*, a magazine that provides a comprehensive look at what's going on in the world of HAE.

The HAEi patient community is fortunate to have a group of scientists who spend countless hours searching for clues that will ultimately improve the lives of angioedema patients. Almost all of these dedicated professionals attended the 10th international C1-INH deficiency workshop held in Budapest, Hungary. The meeting attracted participants from 42 countries and featured 86 presentations related to the science of angioedema. Drs. Henrietta Farkas and Lillian Varga organized yet another highly successful gathering of the foremost angioedema scientists in the world including an impressive group of young researchers who represent the future of HAE research.

HAEi is very pleased to announce that Patricia Karani, the founder of HAE Kenya, has agreed to serve as the HAEi Patient Advocate for Sub-Sahara Africa. Those of us who attended the 2016 Global Conference in Madrid had the opportunity to hear her eloquent presentation on the challenges she faced as a rare disease patient in Africa. I will never forget how Patricia characterized her HAE path, "The journey of a thousand miles begins with one step." Patricia shares her gripping story in the pages that follow.

Our growing global community of HAEi member patient organizations and network of physicians who treat the condition provides a positive environment for attracting pharmaceutical industry investment in new treatments. HAEi congratulates CSL Behring, which in late June announced that the FDA has approved HAEGARDA—a subcutaneous C1 inhibitor product for preventing HAE attacks. There are two other attack prevention treatments designed to inhibit kalikrein that are currently undergoing clinical trials: Shire's Lanadelumab, a long acting subcutaneous preparation, and BioCryst's 7353, a once a day pill. Two other companies are making progress in developing oral kalikrein inhibitors and yet another is pursuing a gene therapy option.

Finally, HAEi is excited to announce that our next Global Conference will take place in Vienna, Austria 17 - 20 May 2018. We kindly ask HAEi friends to mark their calendars now so they can be sure to attend this exciting biannual event!

Warmest regards,

Anthony J. Castaldo
President, HAEi

Global perspectives:

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Cover photo
Meet us at the HAE Global Conference in Vienna 2018.
Read more on page 6

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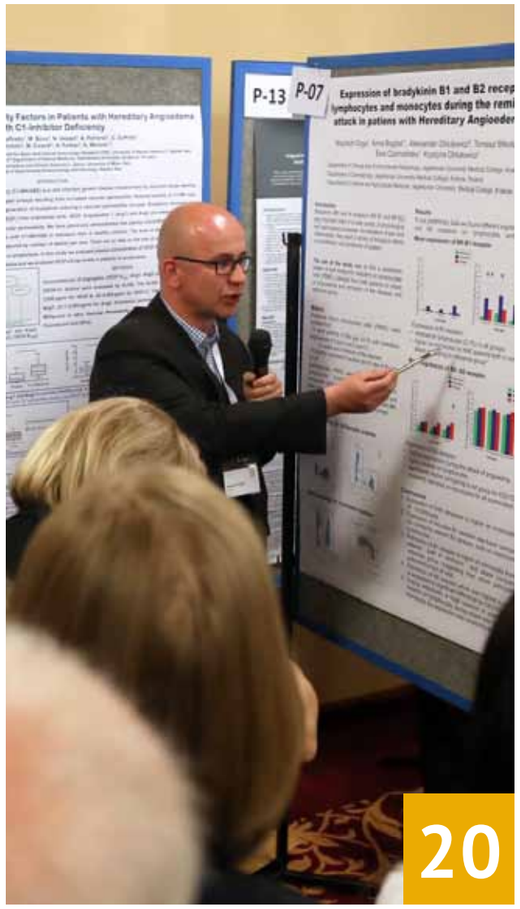
HAEi is registered as a non-profit organization in Switzerland

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

In this issue

In this issue of Global Perspectives



HAE GLOBAL CONFERENCE VIENNA 17-20 MAY 2018

HAE Global Conference

Vienna calling

Following the very successful HAE conferences in Copenhagen, Denmark in 2012, Washington D.C., USA in 2014, and Madrid, Spain in 2016, HAEi is delighted to announce that the fourth HAE Global Conference will be held in Vienna, Austria in May 2018.

"Once again, we welcome HAE patients, caregivers, healthcare professionals, and industry representatives to the largest international gathering of its kind solely with a focus on HAE. We hope to see you in Vienna in May 2018", says HAEi President, Anthony J. Castaldo.

HAE friends can expect plenty of time to interact with fellow attendees from throughout the world, as well as a wide variety of important information, and learning opportunities. These include what every patient and family must know about HAE; the most recent clinical advances and consensus treatment recommendations; and advocacy strategies/techniques for gaining or broadening access to HAE medicines. There will be a separate track for HAE youngsters that will enable peer group interaction and sharing of insights on how to cope with HAE.

"HAE physicians and researchers from literally all corners of the world will gather to present abstracts and discuss future research opportunities. In addition, we will offer an educational and networking session for all healthcare professionals interested in HAE", says HAEi Executive Director, Henrik Balle Boysen.

The agenda for the 2018 HAE Global Conference will be updated on www.haei.org as it evolves. Please make sure that you sign up for the e-mailed conference updates on www.haei.org.

HAEi Youngster's Summer Camp

2017
HAEi Youngster's
Summer Camp

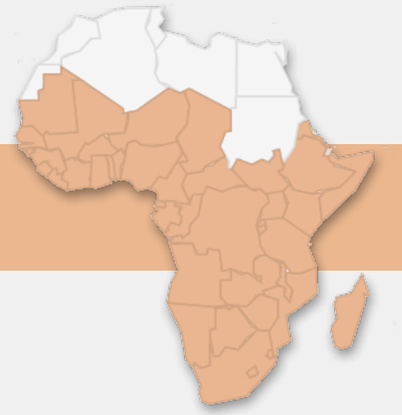
More than **70 youngsters** will meet in Germany

The Youngster Track at the 2016 HAE Global Conference in Madrid, Spain was a great success. Since then a large group of young HAE patients have kept in touch via social media.

"It is wonderful to see how the youngsters enjoy the opportunity of having a truly global network of fellow HAE patients, with whom they can share experiences and ideas. The HAEi Executive Committee has therefore unanimously decided to arrange a HAEi Youngster's Summer Camp to further support and encourage our young patients in the global HAE community. We are delighted to inform you that the first summer camp will take place 3 to 6 August 2017 in Frankfurt, Germany", says HAEi President, Anthony J. Castaldo.

HAEi has now reached more than 70 participants from 21 countries around the world and registration for the summer camp is closed.

New HAEi Regional Patient Advocate for Africa



Patricia Karani
Sub-Sahara Africa

Early 2016 HAEi appointed five Regional Patient Advocates, dividing a large portion of the world between them. As per 1 July 2017 they are joined by Patricia Karani who will be focusing on the Sub-Sahara part of the African continent.

Patricia was born in Nairobi, Kenya where she is currently residing. She holds a university degree in Sociology and Economics as well as a higher advanced diploma in Human Resource Management and she has a decade of experience in the HR field. Today she is working in the food and hospitality industry. Patricia, who was diagnosed when she was about 18 or 19 years old, is the founder of HAE Kenya.

You can read Patricia's story in this issue of Global Perspectives.

News from the Regional Patient Advocates

HAEi regularly receives progress updates from the Regional Patient Advocates and you can read more about their work in the following. However, it is only possible to feature a few countries each time, if possible different from issue to issue. You can find out more about the RPAs on the HAEi website and check which countries each RPA supports via the interactive map – have a look at www.haei.org.

Michal Rutkowski
Central and Eastern Europe

IN GENERAL

I have been working hard making contact with many physicians and patient representatives throughout my region, particularly surrounding the organisation and plans for the HAE Central and Eastern Europe Workshop and Conference in Warsaw, Poland later this year. The dates have been set for 7-8 October 2017.

POLAND

HAE Poland (Pięknie Puchnę or Swelling Beautifully) has been preparing a new website. This includes a review of all the content and an updated design and it is due to be launched very soon. The organization is also working on three more HAE regional patient's meetings, which will include self-administration courses.

KAZAKHSTAN

I have been working with two very motivated individuals – the HAE patient Yekaterina and the caregiver Sergey – to understand more about the HAE situation in the country. They are already in contact with two physicians and a number of other HAE patients and have been finding out more about the process of reimbursement for HAE medication with the Health Ministry. I am supporting them on awareness raising and how HAEi can also provide support and help.

BELARUS

Supporting HAE Belarus, I was able to guide the organization through the process of successfully securing a grant to enable a Belarusian physician to attend the C1-INH Deficiency Workshop in Budapest, Hungary. HAE Belarus is also working towards their national meeting and I hope to be able to share an update on this in the next edition of this magazine.

Javier Santana
Latin America

IN GENERAL

After introducing myself to the HAEi Member Organization representatives in the countries of my region when I began my role in February, I have established communication and collaboration with a number of countries, working together to raise awareness of HAE throughout the region. Many organisations are working with me to make the most of HAEi resources available and are looking to have their local website hosted via www.haei.org.

PERU

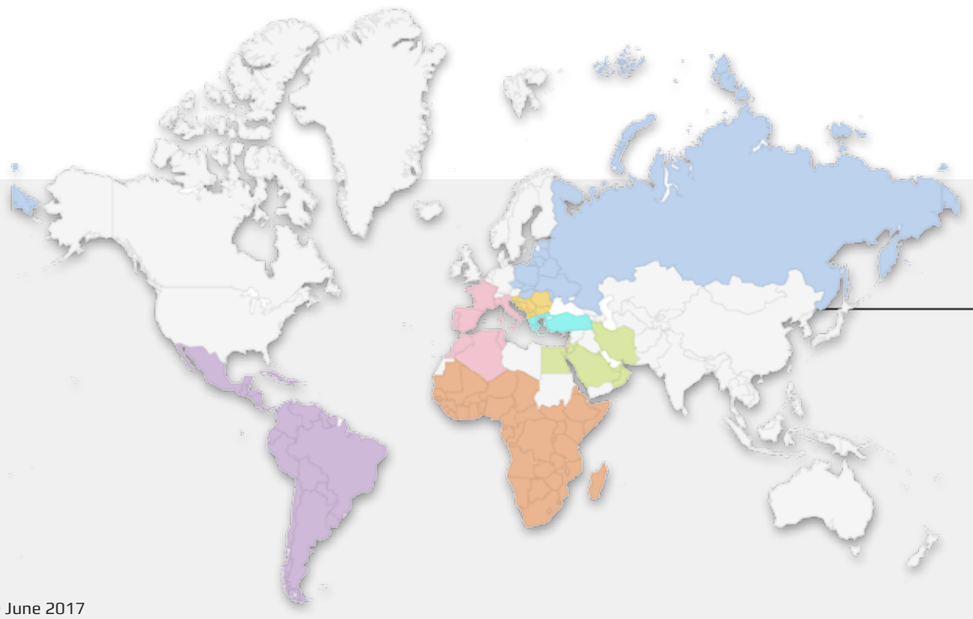
The HAE member organization representative in Peru, Suzet Lam Torres, has kindly put me in touch with Dr. Calderon to further the exchange of information about HAE management in Peru. Suzet and Dr. Calderon are working on a number of initiatives to add information to an HAE patient registry in the country. The organization is delighted to report that following an invitation from Suzet and Dr. Calderon, Dr. Javier Perez has agreed to serve as an honorary member of the HAE Association in Peru.

ARGENTINA

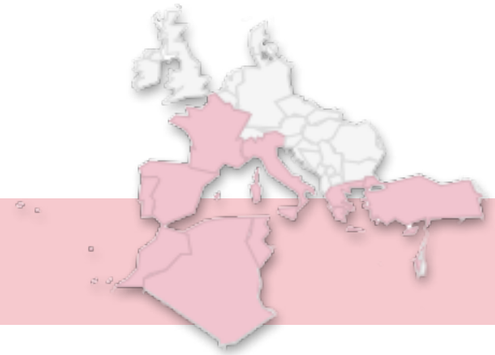
HAE Argentina (Asociación Argentina de Angioedema Hereditario) has announced that due to a number of recent successful awareness events, the organization now represents over 400 people. At the moment, the organization is coordinating a national meeting that will take place at the start of July.

BRAZIL

HAE Brazil (Abranghe) now represents over 1,300 patients in Brazil and the organization is very active in organizing patient evens and news programs. Although there are several therapies available in Brazil, access continues to be a major challenge as they are not available through the government healthcare program. The organization continues to work for broader access to medications for all patients.



Maria Ferron
Mediterranean



IN GENERAL

I continue to make the most of social media in order to connect with HAE associations and patients in my region, to share the latest news, for example the upcoming HAE Summer Camp, and raising awareness of **hae day :-)** 2017.

FRANCE

HAE France (AMSAO) held a meeting in Lyon that brought together patients, doctors and staff of the reference centre. Following this they held a meeting for the members of the association. The meeting was a great opportunity to discuss a number of topics including diagnosis and emergency treatments, along with the chance for patients to ask questions to the doctors. AMSAO would like to thank Dr. Bernard Floccard (CHU de Lyon) and Dr. Isabelle Boccon-Gibod (CHU Grenoble) for their support and participation in the meeting.

MALTA

We are pleased to report that for the first time, there has been an agreement between a hospital and an HAE patient to allow the patient to have two doses of medication at home and self-administer in case of an attack. This is a very positive step forward and will hopefully mean that other HAE patients in Malta will be able to have this opportunity in the future.

ISRAEL

I am delighted to share the news that HAE Israel (EDEMA) has confirmed that Berinert is now available to be administered for HAE patients having oral surgical procedures.

SPAIN

HAE Spain (AEDAF) held their 19th General Assembly & Annual Meeting at the La Paz Hospital in Madrid with 65 attendees. Discussion topics included AEDAF Activities Report, the HAEi/AEDAF Camino Walk, social media activities, and the economic report. At the meeting, AEDAF were very pleased to be able to screen the documentary “Special Blood” by Natalie Metzger with Spanish subtitles.

The Regional Patient Advocates

- **Michal Rutkowski;** Central and Eastern Europe
- **Maria Ferron Smith;** Mediterranean
- **Natasa Angjeleska;** South East Europe/Balkans
- **Patricia Karani;** Sub-Sahara Africa
- **Alejandra Menéndez;** Latin America
- **Rashad Matraji;** Gulf Region and Middle East
- **Maria Ferron and Natasa Angjeleska**

Rashad Matraji
Gulf Region and Middle East

IN GENERAL

I continue to contact and work with doctors and patients throughout the region as well as undertaking awareness raising activity directly.

UNITED ARAB EMIRATES

Contact has been made with a new doctor, Dr. Ravi, who looks after five patients in Dubai. All these patients now have insurance approval and I am working with Dr. Ravi on securing medicines for these patients including access through the HAEi Global Access Program. I have also taken part in several hikes, during which I had the opportunity to chat with patients and answer any questions they had about HAE.

EGYPT

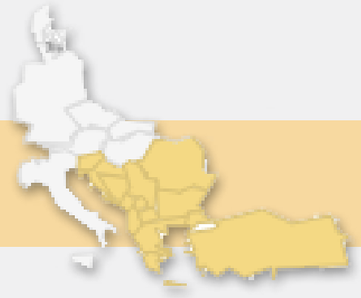
I have made contact with an HAE patient and will be discussing how HAEi can help support patients in this country.

IRAN

An HAE center in Teheran has been identified following the contact with a doctor from Iran and I am now working with the doctor to look for individuals who may be happy to work more on HAE awareness raising in the future.

Roles of the Regional Patient Advocates

- Supporting the member organizations already in place
- Assisting in setting up new groups in countries with no existing organization



Natasa Angjeleska
South East Europe/Balkans

IN GENERAL

There have been interesting initiatives within the region many of which focussed on **hae day :-)** 2017. A joint initiative was agreed and a short video created with messages from patients from the region answering two questions "What makes you smile, although you are an HAE patient?" and "What is your message for **hae day :-)**?" Participants from Macedonia, Turkey, Slovenia, Serbia, Romania, and Bulgaria spoke either in their native language or in English. The full video with English subtitles can be viewed at https://youtu.be/9V5K18PEEZI.

I am currently working hard towards the second HAEi workshop for the South Eastern Europe/Balkans region scheduled to take place at the end of September and invitations have been sent to representatives from all 11 countries in the region. To date acceptances have been received from Macedonia, Slovenia, Serbia, Croatia, Turkey, Kosovo, Bosnia & Herzegovina, Montenegro, and Bulgaria. Greece is hoping to confirm participation and communication has been established with physicians from Kosovo.

MACEDONIA

A group of runners (Skopje Night Running) agreed to run the Skopje Wizz Air marathon on 7 May 2017 under the motto: "I swell, but you cannot tell, I run like hell" as part of the activities for **hae day :-)** 2017. The organization continues to raise awareness of HAE through events and social media initiatives with a video story about a teenage patient gaining more than 22,000 views. In addition, meetings were held with official representatives from the Ministry of Health in regard to the delay in the procurement of medicines for rare diseases due to the political crisis.

SERBIA

Some fantastic news was received in Serbia: following the work of the HAE patient organization and with support from HAEi, the government decided to reimburse HAE medications for Serbian patients. This news was received around the time of the one-year anniversary for HAE Serbia and to mark the occasion a meeting of HAE patients and physicians was held, which also celebrated the approval of the funding for HAE medications.

SLOVENIA

Teja Iskra, the Slovenian HAE patient organization lead, gave a presentation around the challenges of living with HAE to a pulmonology section of nurses. She also participated in the SEE **hae day :-)** video project.

Step by Step

21,215,757
steps taken in total

16,320	10,141	2120	32
Kilometers	Miles	Participants	Countries

Thousands helped raise HAE awareness

Step by Step

On and around **hae day :-)** 2017 a group of HAE patients, caregivers, doctors and people from HAE organizations walked four stages of the Camino in northern Spain. Many more would have liked to take part in this walk but were not able to do so. Therefore HAEi arranged the HAE Global Walk 2017, allowing everyone to participate no matter where they were.

The HAE Global Walk was first launched in 2016 and from late April and all through May 2016 individuals and groups wanting to be part of the global HAE awareness movement took more than 12,000,000 steps.

The 2017 campaign reached even further as 2,120 people in 32 countries across the globe took steps for HAE awareness. From all geographical directions people walked for HAE, some on their own, others in larger groups – and in total they took 21,215,757 steps.

“We would like to thank each and everyone who took part in the campaign, thus emphasizing our message: Every step counts”, says HAEi Communications Manager, Steen Bjerre.

See more about the campaign at www.haeday.org.

Raising awareness on the Camino

30 people – many of them suffering from HAE – met mid-May in northern Spain in order to walk part of the legendary Camino de Santiago together.

The participants – this time coming from USA, Mexico, Argentina, Denmark, Spain, Malta, and South Africa – walked four selected stages of 20, 20, 20, and 5 kilometers, eventually leading them to the pilgrims' mass in the cathedral in Santiago de Compostela.

Just like the initial event in 2016 the walk was organized in close collaboration between the Spanish HAE organization AEDAF and HAEi, once more with very valuable help from the Spanish Camino guide, Rafael Moreno.

"Once again there was a dual purpose of the event. Firstly, for each and every patient to prove that the disease does not limit the ability to live life to the fullest. And secondly to raise the global awareness of the disease through every step taken on the Camino", says HAEi Communications Manager, Steen Bjerre.

10th C1-INH workshop

Highlights from the 10th C1-INH workshop in Budapest, Hungary

The 10th version of the biannual international C1-INH Deficiency Workshop was held in Budapest, Hungary 18-21 May 2017.

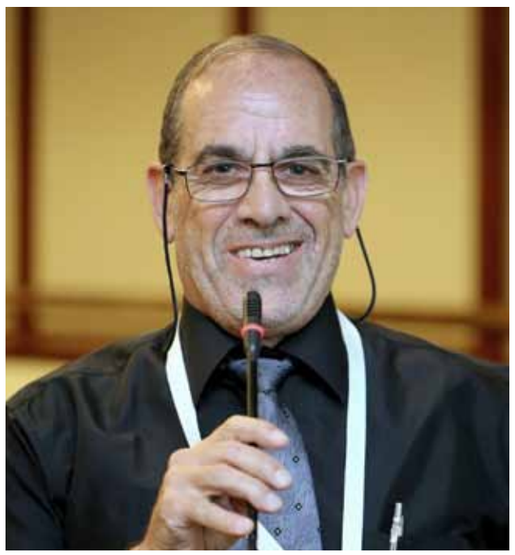
Once again the conference focused on bradykinin-mediated angioedemas, and particularly on the types resulting from C1-inhibitor deficiency. The topics of this four-day long event covered a wide range of subjects. These were, among others, the latest achievements in the diagnostics of the disease as well as the exploration of its hereditary, pathogenetic, and clinical background, and the management and follow up of the patients.

Attracting more than 300 participants from 42 countries worldwide the conference had 86 presentations – oral lectures as well as poster presentations. The following are but a few of the many data presented at the conference.

From the oral presentations

Alvin H. Schmaier, Case Western Reserve University, USA: The basic mechanism for initiation of plasma kallikrein activation in acute attacks of HAE is still as yet unknown. Only until we fully understand the pathogenesis of common and variant forms of this disease will we be able to institute complete and definite therapy for these deficiency states.

Avner Reshef, The Sheba Medical Center, Israel: Both histamine and bradykinin are attributable to vascular endothelial hyperpermeability in angioedema syndromes. Recent data indicate that there might be a 'cross-talk' between mast cell-mediated 'allergic' events, and activation of bradykinin-generating contact cascade.



Avner Reshef

Dumitru Moldovan, Romanian Network for HAE: There is still a lot to do to raise the awareness and expand the education of both physicians and patients. However, our aim is above all to address the challenge in finding an estimated 250 patients that are missing from our database.

Dumitru Moldovan

Anastasios E. Germenis, University of Thessaly, Greece: With every passing day, genotyping of subjects who may suffer from HAE becomes more indispensable in the clinical practice.

Anastasios E. Germenis

Maria Bova, University of Naples Federico II, Italy: Italian patients with FXII-HAE appear to come from the same common ancestor as those from other countries.

Anete S. Grumach, ABC School of Medicine, Brazil: Latin America doubled the number of HAE patients identified in the last four years. Moreover, most countries improved the diagnosis although on demand therapy is not accessible.

Anete S. Grumach

Marta L. Debreczeni, Semmelweis University, Hungary: We have successfully optimized a new, simple, high-troughput and cheap method for permeability measurement, which is based on the reaction of biotinylated gelatin and a streptavidin-conjugated fluorescent dye.

Ira Kalfus, Attune Pharmaceuticals, USA: There is a need for safe orally-administered therapies that control plasma kallikrein activity, prevent HAE attacks, and are well-tolerated.

Andrea Zanichelli, University of Milan, Italy: Despite the fact that C1-INH-HAE symptoms present in childhood or adolescence, paediatricians rarely diagnose patients. Raising disease awareness among paediatricians may reduce the diagnostic delay, possibly allowing for more efficient referral of symptomatic patients to appropriate specialists.

Andrea Zanichelli

Isabelle Boccon-Gibod, CHUGA, France: The EDUCREAK program set up the last four years has allowed a positive dynamic attitude for education of health care professional teams with a project focused on the HAE patients. It improved patients' quality of life, autonomy and safety.

10th C1-INH workshop

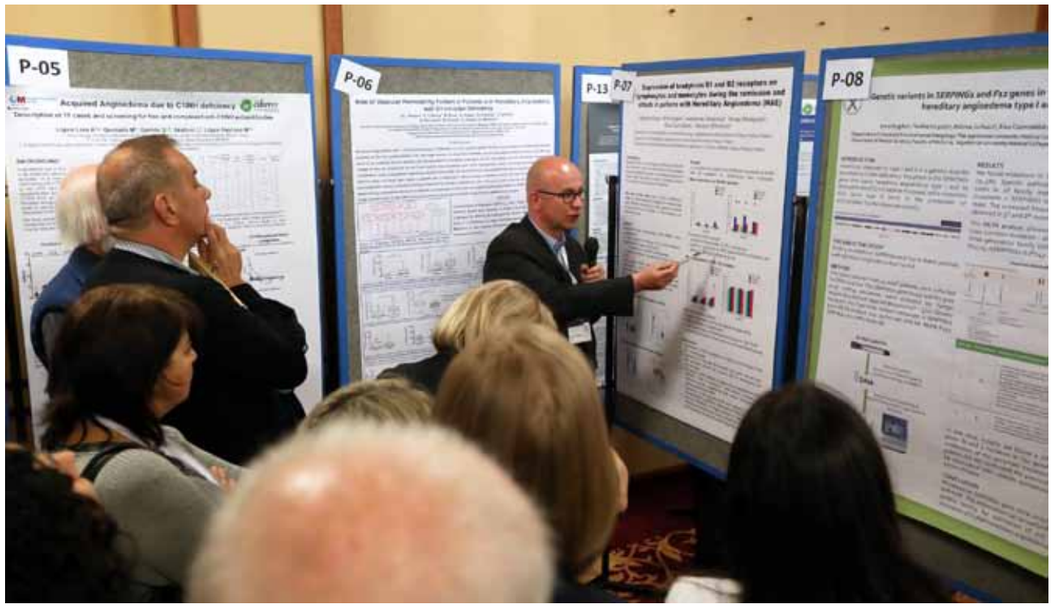
The +300 participants from 42 countries worldwide also had the oppertunity to relax, enjoy and network attending the 10th C1-Inhibitor Deficiency Workshop in Budapest, Hungary

From the poster sessions

Early versus late administration of icatibant in patients with HAE – Irmgard Andresen, Shire, et al.: Early treaters had significantly shorter time to resolution and attack duration compared with late treaters, which may indicate the importance of early access to icatibant in the face of an HAE attack.

The clinical appearance of idiomatic nonhistaminergic acquired angioedema and its comparison to other HAE forms – Noemi Andrasi, Hungarian Angioedema Center et al.: It appears that clinical symptoms in the InH-AAE group are diffent compared to the C1-INH-HAE group. It can be assumed that there are different mechanisms that contribute to the onset of the oedema. The clinical symptoms were similar which implies that the underlying pathomechanisms are also similar.

First kinetic follow-up of symptoms and complement parameters during a HAE attack – Nora Veszeli, Semmelweis University, Hungary, et al.: The concentration and activity of C1-INH decreased progressively before edematous attack. We could not find any increase in C1-INH after spontaneous resolution of the attack. Other factors than C1-INH itself may play a crucial role. Changes in the level of C4a suggest that elevated C4a level precedes the edema formation. It appears that the activation of the classical complement pathway is downregulated at the level of C3, and additional complement activities cannot be detected.



An investigation into the importance of body mass in the case of patients with HAE caused by C1-inhibitor deficiency – Tamas Szilagyi, Hungarian Angioedema Center et al.: BMI has no impact on the frequency of HAE attacks. Pediatric patients with lower bodyweight are less affected by the symptoms. Taking danazol on a regular basis results in significantly higher BMI values.

Results from an interim analysis of a Ruconest treatment registry in Europe – Roman Haki, St. Anne's University Hospital, Czech Republic, et al.: The registry provides real-world data on the treatment of 1351 HAE attacks that is consistent with previous reports on the safety and efficacy of Ruconest therapy.

Radiation as a trigger of attacks in a misdiagnosed patient with HAE and Hodgkin's disease – Maria Palasopoulou, University of Thessaly, Greece, et al.: The emergence of lymphoma in this patient cannot be considered unrelated to longstanding administration of corticosteroids. Radiation and nivolumab treatment are reported as triggering factors of angioedema attacks.

Role of vascular permeability factors in patients with HAE with C1-Inhibitor Deficiency – Anne Lisa Ferrara, University of Naples Federico II, Italy, et al.: Vascular Endothelial Growth Factors and Angiopoietins contribute to alter basal vascular permeability of angioedema patients. During acute attacks the increase of Angiopoietin 1 suggests that it may play an important role in restoring physiological vascular balance in patients.

Treatment administrated in attacks in HAE during pregnancy and breastfeeding – Marta Sanchez-Jareno, Hospital Universitario La Paz, Spain, et al.: There were no significant differences in percentage of treated attacks among periods T1 (number of attacks in the previous six months), T2 (pregnancy) and T3 (breastfeeding). Time to onset of improvement and percentage of improvement at four hours in pregnancy and breastfeeding was shorter compared to attacks treated in the six months prior to pregnancy. There were no differences in time to treatment, time to complete improvement and duration of attack in the three periods.

Ambigious symptoms of HAE may delay diagnosis of concomitant diseases: two case reports – Inmaculada Martinez Saguer, Haemophilia Centre Rhine Main, Germany, et al.: C1-INH-HAE symptoms such as abdominal swelling can easily disguise similar symptoms of not yet diagnosed concurrent conditions. It is important to pay attention to unexpected increases in attack frequency for which no triggers can be identified, especially when otherwise effective treatment with C1-INH-HAE fails to provide lasting relief.

HAE in Ukraine: a national survey – Liudmyla Zabrodska, National Academy of Medical Sciences of Ukraine: The Ministry of Healthcare has started paying attention to patients suffering from rare diseases. A major obstacle to the HAE treatment is absence of medical guidelines. The medical community along with the Ukrainian Association for HAE patients is closely working on the treatment guideline. Other problems such as HAE diagnosis and access to medication must also be solved in order to create a quality of life for HAE patients. There are 49 patients (30 families); around 811 patients are not diagnosed and may not be treated properly. The treatments available are tranexamic acid, hormones, and fresh frozen plasma.

Complex interplay between autonomic and contact/complement systems underlying attacks of HAE due to C1-inhibitor deficiency – Maddelena A. Wu, University of Milan, Italy, et al.: Sympathetic activation (as during tilt test orthostatic challenge) can lead to increased high molecular weight kininogen cleavage, bradykinin generation and eventually to angioedema attacks.

HAE: Report from the Czech registry – Roman Haki, St. Anne's University Hospital, Czech Republic, et al.: The fact that more than 15% of the attacks required repeated treatment of single attack shows that although various therapeutical approaches are available, it is still difficult to choose the best therapeutic approach for a concrete patient.

Genetic variants in SERPING1 and F12 genes in Polish patients with HAE type I and II – Anna Bogdali, Jagiellonian University Medical College, Poland, et al.: Mutations in the SERPING1 gene were unique for every family with HAE. This information can be useful for future targeted genetic testing for estimation of risk of familial reoccurrence of C1INH HAE.

Home treatment with conestat alfa in attacks of HAE due to C1-inhibitor deficiency – Nora Veszeli, Semmelweis University, Hungary, et al.: Home treatment with rhC1-INH was an effective and well-tolerated therapy for all types of HAE attacks. Early treatment of attacks resulted in better outcomes.

Expression of bradykinin B1 and B2 receptors on lymphocytes and monocytes during the remission and attack in patients with HAE – Wojciech Dyga, Jagiellonian University Medical College, Poland, et al.: Expression of both receptors is higher on monocytes than on lymphocytes. In both cases expression of inducible B1 receptor was lower comparing to the constantly present B2 receptor. Expression of B1 receptor is higher on monocytes from HAE patient both in remission and attack comparing to the reference group. Expression of B2 receptor, which was highest during attack of HAE. A huge variation in expression of B2 receptor on lymphocytes during attack was found, while on monocytes the expression was constantly elevated.

The conference had 86 oral lectures and poster presentations


Szívünk
hungarikumai

The challenging management of idiopathic systemic capillary leak syndrome – Maddelena A. Wu, University of Milan, Italy, et al.: Shock related to idiopathic systemic capillary leak syndrome may be differentiated from other forms of distributive shocks thanks to peculiar characteristics, namely clinical picture of hypovolemic shock, extreme hemoconcentration, and severe hypoproteinemia. Detection of IgG monoclonal band may serve for further confirmation. Fluid replacement and amines should be minimized. Careful surveillance of potential complications is warranted.

Quality of life in 41 patients with HAE: first report from Iranian National Registry of HAE – Maryam Ayazi, Teheran University of Medical Sciences, Iran, et al.: A low score of general health in Iranian HAE patients despite rather good scores in physical domains might indicate the strong impact of mental/emotional domains on quality of life. Female patients seem to be more affected by HAE. Patients are suffering a lower health related quality of life because of their medical condition. Improvement in the health condition of HAE patients within the last year might be influenced by the Iranian HAE registry's efforts to ameliorate awareness and facility for this disease.

Acquired angioedema due to C1INH deficiency – description of 12 cases and screening for free and complexed anti-C1INH autoantibodies – Albert Lopez-Lera, Hospital Universitario La Paz, Spain, et al.: The detection of plasma C1INH:lg complexes in autoantibody-negative patients is clinically relevant and indicates that anti-C1INH autoantibodies could be underestimated by conventional screening methods and represent an additional diagnostical tool.

Development of a sensitive assey for measuring C1-inhibitor protein – Dominik Gulyas, Semmelweis University, Hungary, et al.: We developed a high-sensitivity test, which can be readily implemented also in laboratories where radial immunediffusion is not in routine use.

The importance of C1q in diagnosis of acquired angioedema – Susanne Trainotti, Ulm University Medical Center, Germany, et al.: C1q is an important marker to discern between HAE and AAE, especially if the correlation between AAE and lymphoproliferative diseases is considered.

Off-label subcutaneous use of 1500 IE C1-INH for prophylaxis in HAE; a case report – Melanie Nordmann-Kleiner, Ulm University Medical Center, Germany, et al.: Subcutaneous use of 1500 IE C1-INH seems to be easy and safe. It shower similar effectiveness compared to the intravenous therapy. No adverse events could be noticed. The quality of life could be improved. By learning a self-application the patient gained independence.

SERPING1 gene typing in the era of Next-Generation Sequencing (NGS) – Gedeon Loules, CeMIA SE, Greece, et al.: Our NGS custom platform represents a time- and cost-efficient screening approach for SERPING1 typing that is valid for the detection of the vast majority of disease-associated single nucleotide varients. Given that conventional typing methods and workflows are highly dependent on the users' experience and knowledge, the NGS-HAE could be a useful initial approach for detecting HAE-causing SERPING1 variants.

Late onset of angioedema attacks due to C1-inhibitor deficiency; a diagnostic challenge – Marcin Stobiecki, Jagiellonian University, Poland, et al.: Late onset of angioedema attacks due to C1-INH deficiency may appear in patients with negative family history.

The KLKB1-Ser143Asn polymorphism; a new genetic biomarker predicting the age of disease onset in patients with HAE due to C1-INH deficiency – Panagiota Gianni, University of Thessaly, Greece, et al.: Functional alterations in genes encoding for proteins involved in bradykinin metabolism and function could affect the clinical phenotype of C1INH-HAE.

HAE in a Brazilian cohort: delay in diagnosis – Maria L. Oliva Alonso, Federal University of Rio de Janeiro, Brazil, et al.: There is a long time between the early manifestations and diagnosis of HAE, even in those patients with a positive familial history. Early diagnosis and successful treatment is critical to survival and to improve quality of life. Screening of family members, including asymptomatic individuals, improved the number of cases detected.

HAE in Mexican peadiatric population – Melissa I. Espinosa, Instituto Nacional de Pediatria, Mexico, et al.: Misdiagnosis is common in paediatric population, especially in those with initial gastrointestinal symptoms or atypical manifestation as asthmatic-like attack. Subcutaneously administered Nadroparin has been reported to be effective for symptoms resolution, not recommended in current guidelines, but have shown efficacy and safety in these patients.

New mutations in C1-inhibitor gene leading to HAE – Camila L. Veronez, Federal University of Sao Paulo, Brazil, et al.: Although most physicians do not appreciate the need of molecular sequencing in all cases of HAE, it is a special tool in difficult to diagnose HAE patients. It also allows genetic counseling and increases knowledge regarding the mutational spectrum of SEPRING1.

HAE in Bulgaria: clinical and therapeutic characteristics – Anna Valeriava, University Hospital Alexandrovska, Bulgaria, et al.: Bulgarian HAE patients do not show major differences from other populations. Frequency of attacks is reported to be rather high. The great majority of patients have access to C1inh concentrate.

Effect of menopause on HAE: a descriptive study on 53 postmenopausal French patients – Aurore Billebeau, Paris Descartes University, France: Menopause has a non-predictive effect on HAE course. A systematic study on the hormone imbalance in these patients could be helpful to improve their management in the post menopause.

Management of HAE: C1-inhibitor esterase and icatibant acetate self-administration for acute attacks – Ana Rodriguez, Hospital General Universitario Gregorio Maranon, Spain, et al.: Self-administration programs decrease disease burden and improves patient's quality of life.

HAE rapid triage (HAE-RT) tool: a Delphi study – Lisa Fu, University of Toronto, Canada, et al.: The HAE-RT tool will be used as a directive tool (ED setting) and will be applied to all patients presenting with angioedema (with absence of hives) and will include risk factors of recurrent episodes of angioedema and family history.

Off-label intramuscular administration of conestat alfa (rhC1inh) in HAE patient: a case study – Anna Valerieva, Medical University of Sofia, Bulgaria, et al.: Intramuscular administration of rhC1inh could be an alternative to the intravenous route of application, especially when intravenous administration is compromised or access to medical care facilities is difficult. Intramuscular application of rhC1inh seems to be safe and effective. Long-term prophylaxis with rhC1inh seems to be safe and effective in subjects with severe HAE.

Are we ready to propose a pharmacological approach for HAE with normal C1-inhibitor (HAEnlC1INH)? – Stephanie K.A. Almeida, Faculty of Medicine ABC, Brazil, et al.: We observed no symptomatology in 50% of HAE-nlC1INH women after contraceptive withdrawal during the observational period. Tranexamic acid was used with lower dosage and better response. Progrestins have been used before androgens for HAE-nlC1INH women and good response.

Emergency call number for angioedema without wheals: a 4 month experience in France – Isabelle Boccon-Gibod, CHU Grenoble, France, et al.: The diagnosis of bradykinin-induced angioedema represent more than one third of the calls and it was unexpected. The emergency number was helpful for the therapeutic care of the angioedema.

A global multicenter registry of patients with different forms of angioedema without urticaria – Francesca Perego, University of Milan, Italy, et al.: This is the starting point for the first global disease registry for angioedema patients. It is open globally, scalable, secure and it will provide prospective data to expand the understanding of the disease and to improve the standard of care.

HAE: analysis of 287 attacks treated with Berinert in the French cohort COBRA – Laurence Bouillet, Grenoble University Hospital, France, et al.: COBRA registry affords the opportunity to systematically describe type I-II bradykinin mediated AE patients treated with Berinert and to monitor its efficacy in attack treatment.

Delayed diagnosis of HAE in an adult patient; a case report – Erika J. Sifuentes, Instituto Nacional de Pediatria, Mexico, et al.: Abdominal pain attacks occurring in HAE are a diagnostic problem that may lead to laparotomy. We consider a simple test, as a determination of C4 levels should be performed during the initial approach to every patient presenting appropriate clinical manifestations of HAE.

Normal C1-INH angioedema in Israel: phenotyping and F12 gene sequencing – Avner Reshef, The Sheba Medical Center, Israel, et al.: The study shows that 16 of 38 patients could be classified as FXII-HAE. Genetic analysis of other patients and normal siblings is underway.

Clinical and analytical characteristics of children with HAE due to C1-inhibitor deficiency – Maria Pedrosa, Hospital Universitario La Paz, Spain, et al.: The majority of children with C1-INH-HAE are diagnosed before presenting symptoms. Less than half need long-term prophylaxis. There is no correlation between the age at onset of symptoms or the levels of complement with the severity of the disease.

A survey of HAE in Israel – Iris Leibovich-Nassi, Sheba Medical Center, Israel, et al.: Remarkable progress has been made over the last decade, due to a renewed interest in the disease, better diagnosis and new treatment modalities.

Improvement in diagnosis delays over time in patients with HAE: findings from the icatibant outcome survey – Andrea Zanichelli, University of Milan, Italy, et al.: The age at diagnosis and delay in diagnosis of C1-INH-HAE vary widely across countries. The findings are encouraging; however, an important need continues to exist for improved disease awareness and an earlier diagnosis.

Development of a set of sensitive assays for measuring enzyme/c1-inhibitor complexes – Anna Koncz, Semmelweis University, Hungary, et al.: We successfully developed a set of ELISAs for the sensitive determination of various enzyme-inhibitor complexes, which makes the simultaneous investigation of C1-INH-regulated activation systems possible in C1-INH-HAE.

Mutational spectrum of SERPING1 gene and determinants of disease phenotype in Turkish families with HAE: Identification of 15 novel mutations – Nihal Mete Gokmen, Ege University, Turkey, et al.: Earlier disease onset age, and lower level of C1 inhibitor function may have negative impact on the course of C1INH-HAE. The earlier onset age could be a sign of lower baseline C1 inhibitor function levels at the adult life.

Development of a sensitive assay for measuring C1-inhiobitor protein – Dominik Gulyas, Semmelweis University, Hungary, et al.: We have developed a high-sensitivity test, which can be readily implemented also in laboratories where radial immunodiffusion is not in routine use.

News from around the Globe

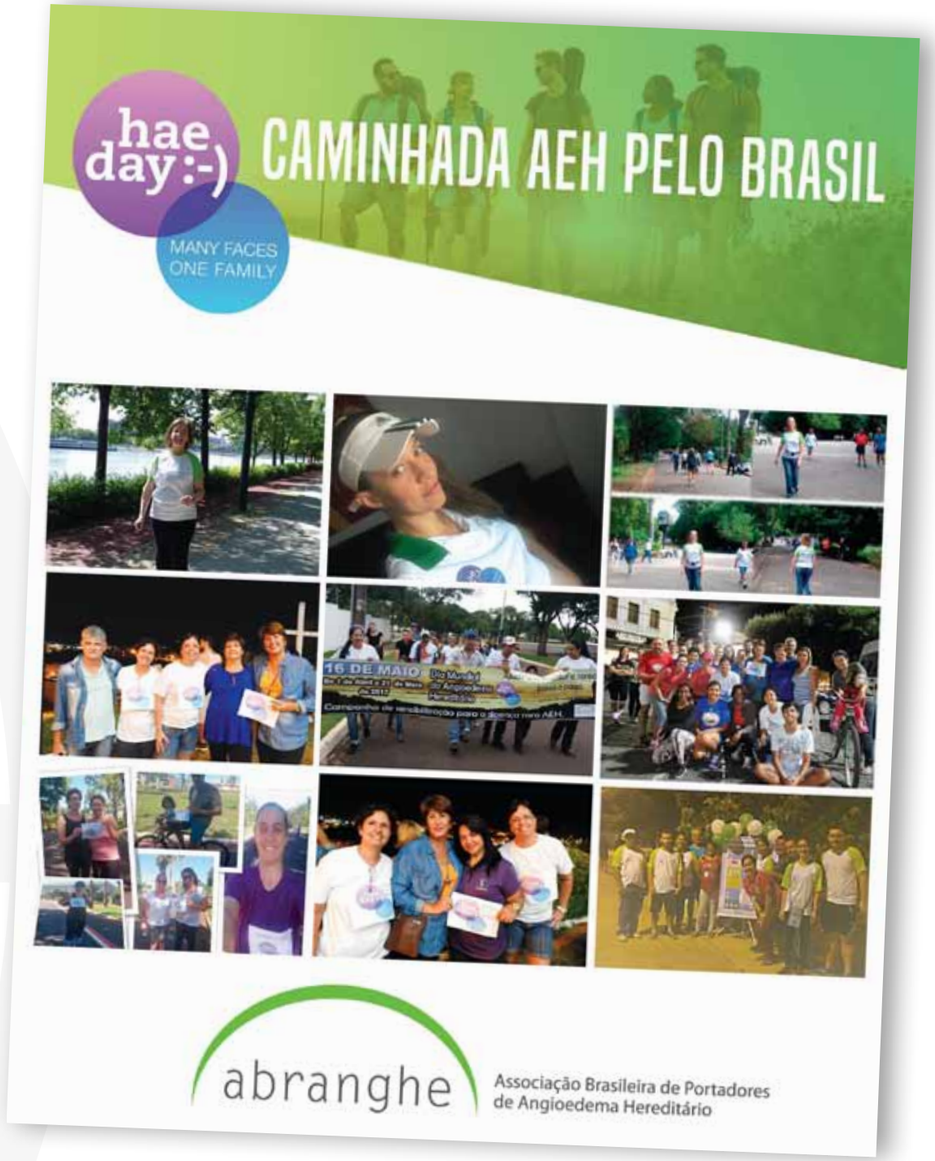
BELARUS
www.hereditary-angioedema.org

On 17 June 2017, 28 adults and 6 children accompanied by two dedicated physicians gathered for the statutory meeting of the HAE Belarusian Patients' Organization. The meeting took place in the National Research Center for Pediatric Oncology, Hematology and Immunology in Minsk, Belarus.

The meeting proved to be a great success, as Belarusian patients will transform from a patient group into a National Member Organization, thus trying to make significant steps forward in HAE awareness and access to medication. The registration process needs yet to be confirmed by the governing agency, and it is expected to happen within 45 working days.

The newly elected President Volha Puhach – the sister of the former HAEi Executive Committee member Viktar Lebedz – promised to step up and put all the efforts into the direction of permanent advocacy, so that the HAE patients' voice can finally be heard in the Ministry of Health.

The HAEi Regional Patients Advocate Michal Rutkowski was present at the meeting and gave a clear message full of motivation and encouragement.



BRAZIL
www.abranghe.org.br

A Patients' Meeting took place in Bom Despacho, MG, on 8 April 2017. Present were the Municipal Health Secretary Neide Aparecida Braga Lopes, Dr. Péricles Marcelo Gontijo, Welbert Matos who is an Advisor to Deputy Arantes, health professionals, patients, family and friends. Speakers were Dr. Gustavo Fusaro, who is an allergist and immunologist, as well as Raquel de Oliveira Martins from HAE Brazil (Abranghe).

Also, a lot of people in Brazil walked for HAE on or around **hae day :-)** 2017.

CHILE
www.facebook.com/angioedema.hereditariochile?fref=ts

To commemorate **hae day :-)** 2017 HAE Chile held a meeting of patients in the VIII Region of Chile in which 13% of HAE patients are found. Information was spread and the organization met new doctors who know this pathology. On 20 May a meeting took place in Santiago where many patients attended and heard about topics like disability and how to retire. Also Dr. Rolando Campillay spoke to the patients and their families about HAE and answered their questions. The magician Bersam made the audience laugh and there also was a beautiful presentation by the Ingrid tribal dancers.

Finally the participants were given the first guide for patients.

CANADA
www.haecanada.org

From Daphne Dumbrille, the HAE Canada Office Manager:

HAE Canada is pleased to report that our Regional Director from Ontario, Linda Howlett with her daughter Amanda Howlett, helped develop a Quick Reference Guide (QRG). This QRG was created in collaboration with Steve Baker (RN), the Performance Improvement Specialist, Clinical Educator, at her local health care facility, Woodstock Hospital. The QRG is to assist in the delivery of emergency care for identified HAE patients who present at their Emergency Department (ED).

The QRG was finalized in early 2017 and has been used successfully on a number of occasions for local, known HAE patients; but also for HAE patients unknown to the hospital who have presented at the ED who require immediate care. This QRG was approved by Dr. Stephen Betschel, the Chair of the Canadian Hereditary Angioedema Network (CHAEN), a network of Canadian specialists treating HAE patients. The QRG outlines the sequential steps to take when delivering emergency care to HAE patients in an acute attack. All three approved treatments for emergency care are outlined as options in the QRG since hospitals will not likely stock all three treatments. This QRG has been proven to decrease ED waiting times; one patient has reported that when using the QRG, her waiting time at the ED decreased from approximately four hours to 30 minutes. The intention is to share this QRG with other ED staff to assist them in developing their own QRG to treat known HAE patients in their community.

This QRG was being introduced at the Canadian Association of Emergency Physicians (CAEP) conference in June 2017 in Whistler. Five HAE Canada Board members were attending the conference.

The HAE Canada Medical Advisory Committee was involved in the development of an Angioedema Order Set for ED physicians also being introduced at the CAEP conference. The Angioedema Order Set will help to identify whether patients presenting in the ED with angioedema is caused by allergies or HAE. We are hoping this Angioedema Order Set will assist in more appropriate and timely diagnosis, treatments and referrals for HAE patients.

In other news, an HAE Canada member who is a Member of the Legislative Assembly in Manitoba, recognized **hae day :-)** 2017 in his local legislature. Please click on the link to hear Blair Yakimoski's presentation: https://www.youtube.com/watch?v=7WYl9FbWL-4&sns=em.

As well, Paula De Pauli, an HAE Canada member who is active in the HAE community, set up a fund in memory of her husband, who had HAE. The fund was established with the goal of furthering education on HAE to health care professionals in Northern Ontario. To read about her story, please visit http://www.nomj.ca/2017/03/10/fund-promotes-knowledge-of-rare-disease.html.

FINLAND
www.haefinland.org

HAE Finland is celebrating its 10th anniversary this year. During that time, the organization has influenced the availability of HAE medications in Finland both in hospitals and for home usage. Also, HAE Finland has had strong influence on the diagnostic and improvement of patient treatment. However, there is still a lot of work to be done for patients and their relatives.

News from around the Globe

GREECE

www.facebook.com/groups/HAE.GREECE

On 27 May 2017, a scientific HAE symposium, entitled "Current approaches in the management of patients with Hereditary Angioedema (HAE)", was held in Athens, Greece. Medical experts from the country's largest treatment centers welcomed numerous colleagues to discuss topics in the fields of diagnostics, therapy, and patient management. Of special interest were the presentations from the German HAE specialists Professor Konrad Bork (Department of Dermatology, University Hospital Mainz) and Dr. Inmaculada Martinez Saguer (Haemophilia Centre Rhine Main, Frankfurt Moerfelden) both with decades of experience in the treatment of HAE patients. CSL Behring sponsored the symposium.

JAPAN

www.facebook.com/NPO法人-HAEJ-715385295244492

From HAE Japan President Beverley Yamamoto:

On 25 February 2017 HAE Japan took charge of running a Rare Disease Day (RDD) event in Kobe. We have recently moved our head office to Hyogo Prefecture to aid smooth running of organization. We became aware that Hyogo Prefecture had not yet held a RDD event so we suggested to the organizers that we arrange something. The event was well attended not only by HAE patients and carers, but also other rare disease patients. Tada Yuka, a rare disease patient who is a well-known singer in Japan, generously attended our meeting and gave a performance. Some of her fans came from Tokyo and beyond to hear her sing. An article about the event appeared in the local Kobe newspaper. With the help of CSL Behring, we ran an advertisement about HAE Japan there as well prior to the meeting. We will also run the event in 2018.

In March this year, short-term prophylactic (pre-procedural) use of C1 INH was authorized. This is an important step forward as we lobby for effective long-term prophylactic treatment options as well as self-infusion and home use for acute attack treatment. At the moment we still only have access to Berinert and only for acute attack treatment in a designated clinical setting.

Last year we carried out the first survey of patients to gather data relating to clinical history (onset of symptoms, pathway to diagnosis, access to medication, specialism of treating physician etc.) as well as current attack and treatment baseline data. This survey was done with the cooperation of Shire and key doctors in our advisory team: Dr. Hide, Dr. Ohsawa and Dr. Iwamoto. We met in Tokyo in April to discuss the result with a variety of physicians who are leading the way in Japan with HAE treatment and research. We are planning a publication of the results that we hope will appear in 2018.

On 13 May, we held an **hae day :-)** event at Saiyu Soka Hospital in Saitama, Tokyo. Dr. Isao Ohsawa, who serves on our Executive Board, is Director of the Hospital and recently started up the first HAE outpatient clinic in Japan. We are hoping that in the future Saiyu Soka will become a center of excellence for HAE. Unfortunately the weather was bad that day and an outdoor Nordic walking event had to be held inside. Nevertheless, it was a fun event and participants asked for more activities that help them feel active and confident. Without home use or self-administration of treatment it was impossible for Japanese patients to attend the Camino walk in Spain, so this was our way of supporting the HAEi steps for **hae day :-)** 2017. In addition, Dr. Ohsawa gave a lecture on HAE and time was made for patient, carer and physician exchange over snacks and drinks. The participants ranged in age from under 1 to 70 years of age. The event received good media coverage.

21 May we held an Executive Board meeting in Tokyo to discuss our strategy for the next year and finalize accounts for the previous year. We are currently making a video from the **hae day :-)** event and interviews to raise awareness of HAE in Japan.

News from around the Globe

KENYA
http://haei.org/haekenya

Patricia Karani from HAE Kenya writes:

We held a successful Rare Disease Day in Nairobi, Kenya on 27 February 2017 at the Gertrude Children's Hospital. There were many in attendance and rare diseases represented where Muscular Dystrophy, Multiple Sclerosis, Albinism and HAE. Every year we normally have representative speakers from various groups who speak about their challenges and who also encourage us with their wonderful inspirations. We were glad to have for the first time a nominated Member of the Parliamentary Assembly present. He suffers from albinism and has been at the forefront in our Kenya parliament fighting for those with rare conditions. The aim of this day was to learn more about other rare disease organizations and how they conduct their advocacy work here in Kenya. Some groups had a short movie as well as a published book where they talk about their condition. They marketed their book to be able to raise funds for their group.

This day was televised on our local TV channel in a program called "Abled Differently" and I am glad that I got an opportunity to be a speaker on this program. They have a YouTube channel as well called "Abled Differently Season 14episode 12".

At the end of this day we agreed to form an umbrella group for rare diseases in Kenya where all rare disease organizations will be represented. I was honored to be part of the admin of this group. My task is mainly to put together the many people who have rare conditions in one online group so that we can air our views on how best our voices can be heard as a group. This was an awesome day and indeed all the groups present felt rejuvenated to continue with the fight to be heard so as to be able to access affordable medication and therapy as well as continue with the fight for a better future.

I am truly glad to be part of this large group. Indeed when I see children who have physically disabling conditions, I am touched by their strong will to live and their ability to afford a smile. It is my hope that as we struggle to look for more HAE patients in Kenya we may be able to reach all those who feel they are alone and be able to give them hope and get affordable medical therapy for them.

Rare Disease Day in Nairobi

MACEDONIA
http://haei.org/haemacedonia

From Natasa Angjeleska, HAE Macedonia:

In May 2017 HAE Macedonia together with "Life with Challenges" and "Skopje Night Running" had a group of runners to run the Skopje half marathon, They were running under the motto "I swell but you cannot tell – I run like hell!"

A student radio station initiated filming a documentary film of a teenage patient with HAE, his struggles with school, everyday activities, as well as his motivation and hope for future. The documentary finishes with his sentence: "This condition made me stronger and more mature… You shouldn't take life lightly, and we should live every moment of our life in the best way possible!" The film is available now with English subtitles on http://haei.org/haemacedonia.

In the light of celebrating **hae day :-)** 2017 regionally, on 16 May we initiated, translated and produced a short video with messages from patients from the region. Patients from Macedonia, Serbia, Bulgaria, Romania, Turkey and Slovenia took part, and that video is available on our Facebook page: https://www.facebook.com/470874113260295/videos/470904726590567/.

During May and June we have been preparing for a South Eastern European (SEE) regional conference for patients and doctors. The event will take place 29 September to 1 October 2017 in Skopje, Macedonia. The agenda is currently being defined but we plan to have three to five participants (patients and doctors) per country, similarly to the 2016 event. Among the speakers are prof. Marco Cicardi, prof. Henriette Farkas as well as the HAEi President Anthony J. Castaldo and the HAEi Executive Director Henrik Balle Boysen.

In May 2017 the political situation in Macedonia changed as a new government was introduced. HAE Macedonia initiated contact with the new Minister of Health and we hope soon to be able to arrange an initial meeting as part of the National Alliance of Rare Diseases in order to introduce him with our goals and problems.

This month several runners from HAE Macedonia ran the Ohrid marathon – "Ohrid trchaT" (Ohrid is running). Among the runners was an eight-year-old boy who ran a couple of hours after an abdominal attack and appropriate treatment administered. The information was spread in the media, showing the public that having HAE does not stop you, but life without treatment stops you from achieving your goals. It contributed to the fact that HAE is not an obstacle, but lack of treatment is.

MEXICO
www.facebook.com/AMAEH.AC

Sandra Agustina Nieto-Martínez, President of HAE Mexico, writes:

Veracruz is the first state of the Mexican Republic to implement a registry of patients with rare diseases as well as the policies necessary to provide patients with comprehensive diagnoses, medical care, and orphan drugs.

The initiative of Deputy Yazmin Copete Zapot was unanimously approved by the LXIV Legislature of the Congress of the State of Veracruz of Ignacio de la Llave and published in the Official Gazette on 17 February 2017.

According to the decision "The Secretary of Health of the state will implement the policies necessary to provide patients with rare diseases with comprehensive diagnoses, medical care, and orphan drugs necessary for each case" and "the Secretariat of Health of the state will integrate the State Registry of Rare Diseases to provide the patients the necessary and sufficient medical attention."

To make known such an important decree the Congress of the State of Veracruz convoked on 1 June 2017 to the Legislative Forum on Rare Diseases in Mexico, held at the Congress of the State of Veracruz of Ignacio de la Llave, in the City of Xalapa, Veracruz. The forum was represented by the President of the Mexican Organization of Rare Diseases Dr. Jesús Navarro, inviting the Mexican Association of Hereditary Angioedema (AMAEH) to present the problem of treatment presented by patients with HAE. Apart from myself testimony was given by the patient and founding President of the association Mr. Antonio López Huesca. Accompanying in this event were Ms. Alma Montero Palmeros, Vice President of AMAEH, and Dr. Esthela Hernández Landeros representing the Latin American Association of Hereditary Angioedema.

PERU
www.facebook.com/AngioedemaHereditarioPeru

HAE Peru has adopted Dr. Javier Perez as Honorary Member.
Dr. Perez attends HAE patients and he is the Chief Medical Officer at the Immunology and Allergy Unit of the Hospital Guillermo Almenara Irigoyen in Lima, Peru.

POLAND
www.hae.org.pl

The second Eastern European HAE Conference – and at the same time the fourth HAE conference of HAE Poland is expected to take place 7-8 October 2017 in Warsaw, Poland.

PUERTO RICO
www.facebook.com/haeapr

In only its second year, over 500 participants showed up at San Juan's Parque Central to support the local HAE patient community for the HAE IN-MOTION 5K event. Friends, families, professional runners, and enthusiastic cheerleaders enjoyed the beautiful Caribbean weather while sharing stories of overcoming challenges and celebrating personal triumphs.

The HAE IN-MOTION 5K is organized by the US HAEA. The events serve as the largest HAEA national fundraising platform. The name HAE IN-MOTION reflects the three fundamental components of the HAEA's overall commitment to improving the lives of HAE patients:

- The increasing momentum in research efforts,
- The mile markers crossed in realizing treatments to help HAE patients lead normal lives,
- The strides toward finding a cure.

SERBIA
http://haei.org/rs

In Serbia, PGD (pre-implantation genetic diagnosis) is state financed for people suffering from rare diseases or at risk of passing on a defected gene thanks to a special law regarding rare diseases, which was recently presented in the United Nations.

SWITZERLAND
www.hae-vereinigung.ch

Patients meeting: HAE Switzerland had its 18th HAE patients' meeting 24 June 2017 at the Triemli Spital Zürich. On the agenda were items such as an orientation of available HAE drugs and initial experience with the new C1 inhibitor drug Cinryze, results of the medication study BCX7353, and a talk on HAE drugs for children.

Annual General Meeting: The 16th Annual General Meeting of HAE Switzerland is scheduled for 10 November 2017.

News from around the Globe

SPAIN
www.angioedema-aedaf.org

From the AEDAF President Sarah Smith Foltz:

AEDAF would like to thank everyone who joined us for another memorable experience on the HAEi/AEDAF Camino Walk 2017.

AEDAF held its 19th General Assembly and Annual Meeting on 1 April 2017 in La Paz University Hospital in Madrid. We had around 65 people in attendance. We would like to thank Anthony J. Castaldo, President of HAEi, Henrik Balle Boysen, Executive Director, and Maria Ferron, Regional Patient Advocate for the Mediterranean countries, for joining us to give us an update of HAEi and its ongoing activities and programs.

AEDAF was back in Santiago de Compostela (Galicia) on 30 May 2017 for its 12th regional patient workshop. The vice president of AEDAF, Dr. Concepción Lopez Serrano, and myself were joined by Dr. Maria Angeles Rico Diaz, allergist in La Coruña and president of the Society of Allergology and Clinical Immunology of Galicia (SGAIC), and Dr. Carmen Marcos Bravo, head of the Allergology Department of the Hospital Complex of Vigo, to present the activities of AEDAF and HAEi and an update of HAE and the current treatment options, as well as the situation of HAE in the region of Galicia.

News from around the Globe

News from around the Globe

USA
www.haea.org

Fight for Patient Rights: Over 195 HAEA Members have signed up to actively participate in the various grassroots campaigns that are being coordinated by the US HAEA. The association has lead three letter-writing campaigns that have resulted in over 100 letters being sent to US congressional leaders. The campaigns have been highly successful in generating important legislative discussions for changes to the Affordable Healthcare Act that can impact the lives of rare and chronic disease patients. Through the HAEA's collaborative efforts, three patients have had their letters read by a Congressman on the House of Representatives floor. Additionally, one of our patients attended the Presidential State of the Union Address and participated in a CSPAN interview along with her Congressman. Two other patients have been interviewed by the press.

For Rare Disease Day, HAEA Patient Advocate, John Williamson joined members of NORD and the Rare Action Network Texas, at the Texas State Capitol to fight for legislation regarding Step Therapy, which requires failing androgen treatment before being allowed to take other medicines. This legislation would allow physicians in the state of Texas to request an exemption from step therapy on behalf of their rare and chronic disease patients. This legislation has been approved and will take effect in September 2017.

hae day :-) celebration: The US HAEA focused efforts on providing Emergency Room and/or hospital staff with HAE related educational materials. An HAE ER Tool Kit was created with important information that patients could share with their local emergency and/or medical facility. The Tool Kit contains an overview of HAE symptoms, diagnosis, and treatments along with links to a HAEA sponsored accredited Continuing Medical Education video designed for Emergency Room professionals. Over 1,200 HAE ER Tool Kits were ordered by patients and family members to help raise awareness.

By distributing the Tool Kit to local emergency rooms, the patient community provided important information that will (1) lead to better treatment of HAE patients in their community, and (2) help ER staff identify people who should be tested for HAE. Patients and staff members also encouraged others to order their free tool kits by posting their selfies on social media under #StandUpStrong4HAEedu.

US HAEA 2017
NATIONAL PATIENT SUMMIT
STAND UP STRONG

Summit registration now open: Registration for the National Patient Summit is now open. The summit will take place 15-17 September 2017 in Bloomington, Minnesota. This year's theme, "Stand Up Strong", is a unifying call to action for the HAE community and a celebration of work being done by HAE heroes who make a difference every day by raising HAE awareness within their communities.

The 2017 meeting is open to the US HAEA patient community and will feature programs for the entire family. Don't miss the opportunity to; learn about breakthrough therapies on the horizon, get your questions answered by our world-class HAE expert physician/researchers, hear first-hand from Washington insiders the latest on healthcare legislative issues; and be the first to gain insights into never previously disclosed data from the HAEA's Scientific Registry. You'll end the day with an incredibly fun evening that includes dinner and entertainment with the entire HAEA community. On Sunday morning, the summit will close out with another exciting HAE-IN-Motion 5K walk/run.

Also, this year's Youth Programs offer special events organized just for children and teens attending the conference. There will be a variety of engaging activities as well as plenty of time to get to know other kids and teens in the HAEA community. A super fun off-site TEEN trip for ages 12-17 is planned for Saturday 16 September, while KIDS 5-12 will enjoy their time together on-site at the SUMMIT venue.

Dr. Bruce Zuraw (middle) receiving the "For HAE Patients Award" 2017 – here with Dr. Lillian Varga, Dr. Sandra Christiansen, Dr. Henriette Farkas, and HAEi President Anthony J. Castaldo

"For HAE Patients Award": Dr. Bruce Zuraw, Chair of the US HAEA Medical Advisory Board and Director of the U.S. HAEA Angioedema Center at UC San Diego, and Division Chief of the Rheumatology, Allergy and Immunology in the Department of Medicine, UC San Diego received the prestigious "For HAE Patients Award" during the 10th C1 Inhibitor Deficiency Workshop that took place in Budapest, Hungary 18-21 May 2017.

Dr. Zuraw has dedicated his career to conducting groundbreaking research that has contributed to the life-saving medicines now available to the HAE community. His laboratory, which is part of the US HAEA Angioedema Center at UCSD, continues to vigorously pursue genetic and molecular level research on swelling disorders that provide progress toward a cure. During the workshop, Dr. Zuraw kicked off the Scientific Program with his presentation "Let the Treatment fit the Disease."

On the Hill: Patients from the US HAEA community joined President Anthony J. Castaldo, Executive Vice President Janet Long, and Senior Patient Advocate John Williamson 27 June 2017, during visits to multiple Senate offices in order to advocate on behalf of the protection of patient rights. The Senate was expected to present and vote on changes to the healthcare bill. However, after mounting objections from multiple patient organizations such as the HAEA, they announced late afternoon that it would postpone its vote until after the July 4th recess. The grassroots advocacy of patients and provider groups has been instrumental in slowing down this legislation, which as currently written, could severely compromise access to care for rare and chronic disease patients.

HAE Documentary: "Special Blood" is a poignant, heartfelt HAE documentary that chronicles the lives of four HAE patients. Due to the rarity of HAE, Ava, Noah, Kelsie, and Lora face misdiagnosis, improper treatment, and challenges in the emergency room all as they fight to live normal lives. They join their voices together to face challenges and encourage others with HAE. Look for the Digital Release of the HAE documentary at http://radi.al/SpecialBlood.

News from around the Globe

UNITED KINGDOM
www.haeuk.org

From Laura Szutowicz, CEO of HAE UK:

One of the time-consuming tasks so far this year has been to ensure that the new website on www.haeuk.org was up and running. As with all these things it sounded easier than it actually was and poor Rachel had to work incredibly hard to make it all come right. But it is now and for those of you who have not seen it take a look! It is much more user friendly, works on phones and tablets, has a breaking news ticker and much more.

I have been very involved, along with various other organizations, in bringing home the facts about Rare Diseases to the UK Government and National Health Service (NHS). It is a constant battle to ensure that funding is kept in place to ensure the best outcomes for our members, and one of the points I keep making is that keeping HAE patients well is a huge benefit to the country. Because of the stupid way things are, the NHS only counts the cost of treatment and does not rationalize the contributions a treated patient make to society.

The General Election has meant a hold has been put on some of the decisions that were going to make life possibly more difficult for people with a rare disease and hopefully, we have some excellent champions now in Parliament in Philip Dunne and Ben Howlett as well as some other politicians. Our Second Chamber, the House of Lords, scored a big success in modifying a bill, which hopefully will ultimately benefit patients.

Another thing I have been working on is that I now have a supply of various 'template' letters so that I can send in support of members who have to provide things like Education Plans for children at school; support in employment issues; or for members who are undergoing PIP (State Benefit) assessment.

We are very excited to be able to welcome four new Trustees who have joined the existing Trustee Board. They are all bringing different skills with them and will help to make us more active and efficient. Samantha Oxley and Rose Joseph many of you will have met at the HAE Global Conference last year in Madrid, Keven White is an HAE patient who is also a senior nurse, and Dana Shapiro who trained very hard to climb Mount Kilimajaro despite suffering severe HAE attacks. John Price has stood down as Chair of Trustees after many successful years guiding the organization and his son Ed has taken on this role.

We are encouraging members to get the word about HAE out there and one of the things we are offering is that we will visit GP surgeries or hospital departments and give an introduction to HAE, diagnosis and treatment. We have a template for presentations that can be tailored to suit the audience.

We ran a surveymonkey to see what members felt about their treatment. On the whole time to diagnosis is getting much shorter, and as per the 2014 Consensus Document most patients are seen by immunology. Some of the answers have raised more questions! So to drill down and get even better results the Medical Advisory Panel are advising on some further questions.

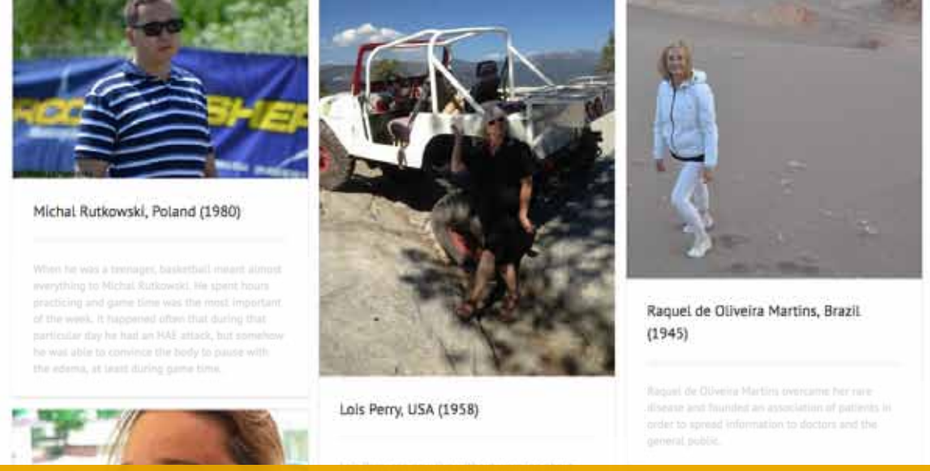
We are well forward with arranging the two Patients Days, one for Scotland in Glasgow 30 September, and 18 November in Sheffield for the National day.

HAEi GAP GLOBAL ACCESS PROGRAM

HAEi Global Access Program

With the launch of the HAEi Global Access Program (HAEi GAP) – a first-of-its-kind medication access program – thousands of patients suffering from HAE will have access to medicines for the first time.

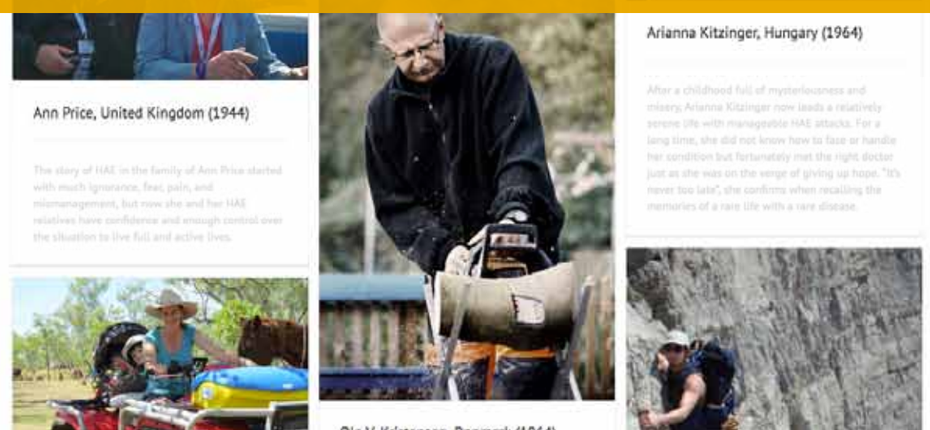
See the latest information about the program at www.haei.org.



Patient stories

At www.haei.org HAE patients from Australia, Belarus, Brazil, Denmark, Hungary, Kenya, Norway, Poland, Russia, the United Arab Emirates, the United Kingdom, and the United States tell their touching and motivating stories.

Here you can read about the HAE lives of a diverse group of patients that include a university lecturer, a truck driver, a retired nurse, an operations manager, an architect, and a cattle farmer.



Patient story

Patricia Karani (Kenya) will not only fight for her own life but the life of a child, a parent, a mother, a father or a friend who has lost hope.

Patient story: Patricia Karani

I will not only fight for my own life

My African childhood was nothing but bliss and fun; climbing trees looking for the ripest mango, competing in athletics and even beating the boys in relay games. I loved to run. Whatever game a boy could do, I felt I could do it better. I loved being young and vibrant. I could be squeezed in a small space with practically no air to breathe and I would still come out alive, smiling and well. I was energetic and strong.

But your body had other plans for you, I guess?

You can say that! I never realized then I had an invisible illness. At the age of about 10 years, I was hit by the edge of a window while being my normal boyish self, running around the compound while playing hide and seek. I developed a swelling that was larger than usual but I never thought of it as anything serious. Some years later, I visited our village with my family and the next day I was left there to do the manual work women were expected to do; cooking lunch for 50 farm workers using firewood and a big sufuria– that is a cooking pot – that was the size of a washing basin. I was okay until I got up the next morning and I couldn't hold anything because my hands were extremely swollen. When I tried doing something I felt excruciating pain. That day the boys had to cook for themselves since my mother had returned to the city. I suffered because I was still expected to do manual work regardless of my evident swelling.

But you didn't think that much about it at that point?

I was a bit bewildered but no, I didn't give it that much thought. However, several years later I went back to the village with my mother. There was a lot of walking involved and the house was full of dust as it was rarely occupied. Once we got there, the first job was to clean the house. Then my throat started to swell and we had to take public transport back to the city and head straight for the hospital because I could barely breathe.

This was your first throat attack?

Yes. I was extremely confused and scared and I wondered what was wrong with me. I remember that as the longest journey ever and it was the beginning of my quest to find out what I was really suffering from.

I flashed back on my childhood and the only health issue I could remember was when I had some sort of stomach discomfort, especially when the car windows were rolled up. I would get extremely nauseated if I was in a car where no fresh air was getting in and I

Patricia's story in brief

Born 1981 in Nairobi, Kenya – currently residing in Nairobi. Single, no children.

Holds a university degree in Sociology and Economics as well as a higher advanced diploma in Human Resource Management; has 10 years experience in the Human Resource Management field and is currently working in the food and hospitality industry.

Diagnosed when she was about 18 or 19 years old after her first facial swell almost 10 years earlier.

Other HAE patients in her family: Grandmother (died from an HAE-related swelling to her neck), father, and two brothers.

would throw up. Strong perfumes also affected me and made me extremely nauseated. I used to get swellings for no apparent reason. No one knew what ailed me but my mother helped me seek for private doctors who could assist me because all we knew was that I must be allergic to something.

Did you tell people – apart from your mother – about the swellings?

Well, when asked why I was so swollen, I preferred to lie and say that I sprained or injured my muscles, as I didn't want to start explaining something, which I myself was not sure about. If I did, in fact, dare try to explain, my long stories normally ended up with responses like "You need to visit your local pastor for prayers and deliverance" or "That looks infectious" or "This is a curse from your forefathers – you need to pray hard and repent".

Around 16 the swellings began to increase.

Yes, when I was in secondary school and heading to 16 years of age my swellings really increased and my normal day-to-day life got a lot of setbacks. My once playful nature had to be scaled down a big notch so as to avoid any instances of swelling. Therefore I was exempted from games and running – and ultimately I was put on a sick children's list in school.

A milliard of problems began; my body would really overheat even in cold weather. A lot of sweating was involved when I have an attack anywhere on my body. At times I would get really thirsty and at other times my body would crave for some types of foods. My energy levels would go down such that I couldn't even focus or think straight, let alone get out of bed. I would get very nauseated before and after my monthly periods and end up throwing up till I have nothing else to throw up but air. Frequently I had painful bowel movements that would cause me to pass out and I experienced terribly painful swellings to the face, hands, and legs. These could last five to six days. I would get extremely moody and annoyed due to feelings of helplessness with no hope for a solution.

So your life was basically on a downhill slide?

It was. Especially when I was feeling unwell and those around me still expecting me to do things, which I had no energy to do. Moreover, trying to explain how I felt was not easy because when my energy levels dropped due to internal swellings, I had no external swelling to justify what I was feeling. Due to this, I was labeled as "the lazy one". This really brought down my once confident and free-spirited nature. I became conservative – a closed human shell. I became very selective about whom to interact with when I was feeling unwell.

I had only one friend who took the time to fully understand me and bear with me when I was feeling sick. Feelings of despair and loneliness encompassed me as I got discriminated upon at work as well as in hospitals where doctors didn't want to take up my case. They said that I was "a walking time bomb" and obviously they didn't want any legal issues should I die when in their hands. I got discouraged, I felt cursed and abnormal and I would often cry when I had an attack. What ailed me did not have any explanation, no exact trigger nor did it seem to have any mercy on me.

With time I realized that when I strain my body like sitting down or standing up for too long, lifting heavy items, having pimples on my face, inhaling too much dust or receiving trauma on any part of my body, it would cause some serious swellings. At times taking extremely cold drinks would also start a throat swell as would emotional stress.

At this point, I wondered if I was going to reach the age of 30 without death rearing its ugly head upon me. I would swell practically anywhere; my face, throat, lips, neck, chest, stomach, feet, along my spine, and shockingly I discovered genital swellings too.

You began going to the hospital when you were in your teens. Why was that?

Well, the school nurse used to get scared that I might die in her little dispensary so I had no alternative but to start visiting hospitals and having numerous tests.

Naturally, this was affecting my education. And it led to my senior teachers and my headmistress asking many questions about the illness with no name. At that time we started looking for specialists because the headmistress suggested I should look for another school to enroll in. She wasn't exactly understanding of my situation.

At one time I changed hospitals to try and see if maybe the new place would better know what I was suffering from and maybe even how to treat me. However, I only got subjected to further tests and a hefty medical bill, which accrued within six hours as they tried to bring down enormous facial and throat swells with all sorts of medicines. I felt like a laboratory rat and I was truly upset because it wasn't fair towards my family as they were not very well off.

But then you made a decision to self-medicate.

Yes, at that point I chose to kiss the hospital doors goodbye. The medicines I was being injected never brought down my swellings and I would still reach the terrible choking stage but I really had had enough of hospitals. I self-medicated on antihistamines and chose to just overdose them so as to reduce the pace of the swellings. I would do so especially for my throat swellings. They devastated me and I knew that if I would not overdose and die, then my throat swellings would eventually take me to my Maker. I would buy 30 tablets of celestamine– a steroid that works by inhibiting the production of a compound in the body causing pain and inflammation. I would finish them in a period of just four days. This really frustrated me, you know, because I didn't want to overdose but at the same time I didn't want to die. I would sit on my bed for hours and pray that this was not my last day on earth.

Patient story

Patricia Karani loves nature and has revived her past hobbies of taking care of the wildlife in Kenya and going on mountain hikes

But then there was what one could call a turning point?

Indeed. I had a throat swell and once more I was taken into hospital emergency. The medicines did nothing much and I could barely see anyone because my eyes were swollen shut. I struggled to breathe and the doctors kept asking for my consent to cut my throat open so as to get some air into my lungs, but I wrote "NO" on a small piece of paper. So they kept a vigilant watch over me. The next thing I remember, I was seeing a white light and I thought, "Oh my goodness, is this Heaven?" – had I really passed to the other side? At that very moment I felt a strong message coming through that said, "No, you have not completed your purpose in life". Then I regained consciousness and my ears opened up just to hear the patient in the next bed snoring. I was still on my hospital bed and my throat had opened up a bit and now I wasn't struggling to breathe as much. My mom was by my side and I reached out to touch her and she touched me back. That to me was my first near-death experience. However, there were many more to come and many more to fight.

I guess it is almost needless to say that you were very misdiagnosed?

I was diagnosed with amoeba, stomach bacteria, typhoid, chronic duodenitis, hyperacidity, anemia, and allergies of all kinds. That kept on until one day I met a doctor who called it "angioneurotic edema". The next thing that came from his mouth was "There is no cure – you have to just learn to live with it". My heart sank!

So how did you get to know what it really is?

I chose to do research on my own and I discovered many things about angioneurotic edema. Along the way, I found out that I most likely had HAE as my dad had similar swellings. Furthermore, my paternal grandmother died from a throat swelling after she had come in from tilling the land on her farm. My two brothers had the same symptoms and through them, I first heard about research going on in the United States and how they had been enrolled in a clinical trial in order to come up with a cure for the condition. My brothers gave me an amount of hope when they told me that some medicines had been discovered which would reduce swellings in just 15 minutes. Based on what I had experienced at that point, I didn't really believe what they said. I was hopeful, for sure – but without hope, at the same time because these medicines were not within my reach in Kenya.

Up to this day, your country has no HAE medications for acute attacks?

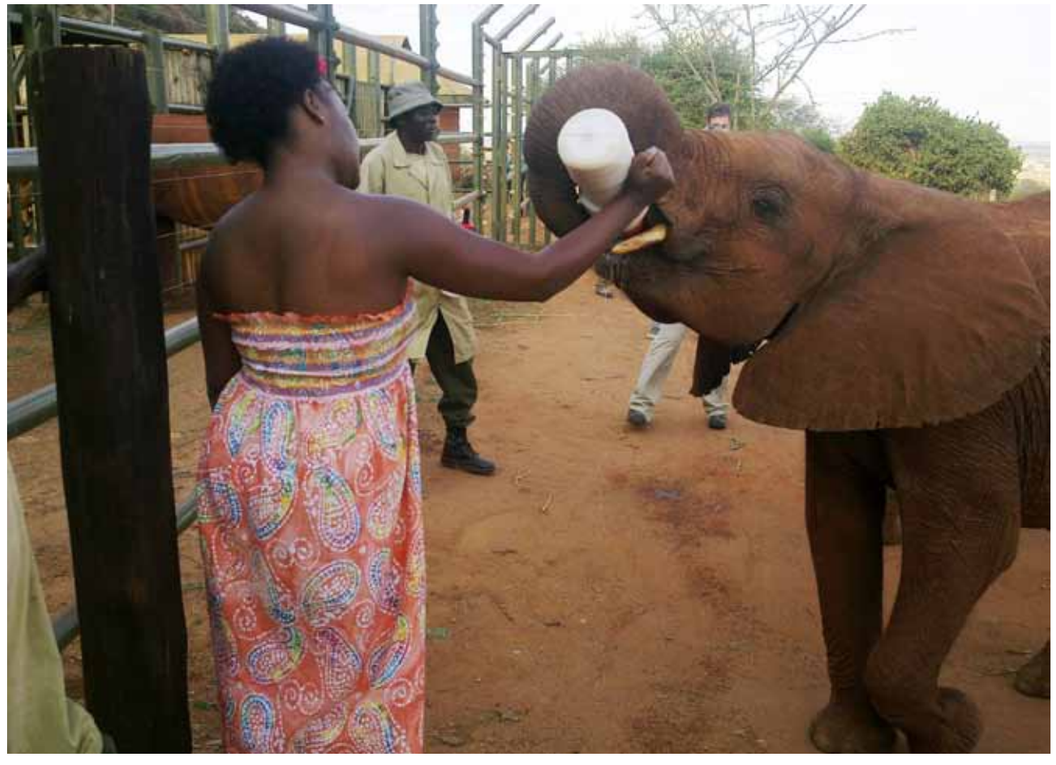
No, most rare diseases are neglected in Kenya since the emphasis is on infectious diseases such as TB and HIV and the growing pandemic of non-communicable diseases such as CVD and cancer. A condition with a prevalence rate of maybe one out of 5,000 is not given any priority in Kenya. Subsequently, treatments are not reimbursed by the national health insurance scheme or by private insurance. At the same time most modern HAE medications are not available in the hospitals other than androgens and for emergency treatments, there is only access to fresh frozen plasma.

So you were in the dark.

Well, they say that dawn comes after dusk, don't they? My whole productive life was indeed filled with dusk. I lost jobs because of my frequent swellings, which would often start on Monday mornings. One would think I was suffering from a hangover due to over-indulgence in alcohol during the weekend or maybe I was just plain lazy. I lost friends who did not understand why I refused to take long bus trips with them. I lost love relationships as men took to their heels and thought that I must be suffering from an infectious disease. I would sit and remember the days when I was active and how my life had changed to current inability and lack of energy.

When you made the national presentation on behalf of Hereditary Angio Edema-Kenya at the HAE Global Conference in Madrid in May 2016, you said, "The journey of a thousand miles begins with one step".

That's just the way it is, isn't it? And you know, one day a ray of light did actually shine on my dark path and I decided to move a step forward and fight even harder. The change came when my brother – who was still in the United States – told me that he would send me a lovely lady who had children with HAE to come and help me and be there for me. She – Karen Baird, that is – did, in fact, come to Kenya and she advised me to look for danazol. It is a synthetic steroid that works by decreasing the level of certain hormones, which reduces the symptoms and severity of a disease. I was, however, pretty scared of danazol then because I heard it had bad side effects such as growing a beard. Now, that would not have been a pretty sight to behold considering the fact that I am a lady. Danazol is not readily available in Kenya, so I had to really search from one pharmacy to another for six months and it is also not a cheap drug. It took me a while to realize that generic danazol does not help much. Original danazol, which I got finally, would prevent frequent swelling. However, there were still some rare breakthrough swellings.



My newfound friend encouraged me and held my hand and we would cry together. She truly felt my pain and would understand everything I tried to tell her. She was heaven sent. For the first time ever I would talk to someone who knew and understood what I felt and what I had gone through. I would not even need to explain much. Karen never judged or criticized me. Indeed, she has encouraged me up to this day and I hold her very dearly to my heart.

The medication did, in fact, help you?

Yes, since I began taking danazol, I have been able to work without fear of swellings and I can take a long swim, my favorite sport. This relief was brought not by any doctor but by my sheer will to live and complete my purpose on this earth. I realized that this illness requires one to be in control of one's own health and in charge of one's own happiness. Naturally, I still hope to have access to affordable HAE medicines one day so that my breakthrough attacks may not haunt me but I have already smelt freedom again. I feel I have another chance to live my free-spirited life. Now I am happy and I can manage my condition with a positive attitude. At times that's all an HAE patient requires – a helping and encouraging hand of someone who will not criticize you when you are down. Once again I can only say thank you so much, Karen.

HAE in Kenya

- *Member organization*
  Established in 2015
  www.haei.org/haekenya
- *Diagnosed patients*
  HAE Kenya anticipates around 940 HAE cases in the country but at this moment only a few patients have been confirmed.
- *Points of HAE interest*
  HAE currently has no government recognition and the knowledge among medical personnel is dangerously low. There is no specialist center for HAE in the whole country, nor are there HAE clinically trained medical personnel. In urban areas, physicians and general practitioners see patients while patients are seen by clinical officers and nurses in rural areas.
- *Available medication*
  Only androgens are licensed and treatment is not reimbursed by the national health insurance scheme or private insurance. There is no access to emergency treatments other than fresh frozen plasma.

How did your life in general change at that point?

I love nature, so I have revived my past hobbies of taking care of our wildlife and going on mountain hikes. Also, I have decided to be a dedicated advocate for this life threatening disease and I will not only fight for my own life but the life of a child, a parent, a mother, a father or a friend who has lost hope in dealing with the gruesome episodes of this unpredictable illness. Indeed, through my rough experiences, I feel I am a fighter. I fought for some sanity in my life in the midst of an illness that depressed my very spirit, and now I can fight for another's life. I am hopeful a cure will be found one day and those ailing from this illness will be able to live normal lives.

I am thankful for the gift of life and for the gift of breath that God gives me free of charge every morning. I am grateful to be alive. A new dawn surely comes after dusk!

What is your hope for Kenya?

I hope that our Kenyan medical fraternity will one day be able to see the severity of HAE and source proper equipment to test and diagnose this condition. That is not only a hope for HAE patients in my country but all over Africa and that is why Hereditary Angio Edema-Kenya is working on including patients in our neighboring countries Uganda and Tanzania where we know there are confirmed cases.

Other plans include incorporating Hereditary Angio Edema-Kenya as an organization with government recognition, expanding the Facebook page and our website, publishing a booklet on life with HAE, conducting interviews with the media, and establishing an 'Aid my HAE'-campaign program to seek medical funds for individual HAE patients who are in need of financial assistance for their HAE therapy. Also, we want to secure access to life-saving medications in both public and tertiary referral hospitals, create a fund that will facilitate HAE treatment and training of medical personnel, and naturally locate more HAE patients. Today, we know of five confirmed cases in Eastern Africa. Four are in Kenya – though one of them passed away a few months ago from lung cancer – and one is in Uganda. However, based on the population there must be close to 1,000 HAE patients in total in Kenya alone.

How is the knowledge level among medical personnel in Kenya?

There is no specialist center for HAE in the whole country, nor are there HAE clinically trained medical personnel. When it comes to HAE, the knowledge of our Kenyan doctors is dangerously low – around "1" on a scale from 1 to 10, I'd say. Furthermore, the access to medication is very limited and in case of an attack, patients are given antihistamines, hydrocortisone or adrenaline. However, Dr. Eric Njenga, who is a vital part of Hereditary Angio Edema-Kenya, is working hard to raise awareness though doctors and nurses in the emergency rooms of the hospitals in Kenya.

Most recently you have been appointed HAEi Regional Patient Advocate from Africa. Do you have any thoughts on that particular topic?

I never in my wildest dreams imagined that an illness that had plagued and tortured me for so long would one day make me have confidence enough to stand and speak in an international gathering as I did at the HAE Global Conference in Madrid, Spain in May 2016. I am glad that the HAEi community found me in my small African town and generously chose me to represent Africa in Spain. I love my newfound HAE family and I am more overwhelmed that I now have this great opportunity to advocate for the African patients. Indeed, the African continent poses great challenges from lack of clinically trained medical personnel to lack of adequate knowledge of HAE. Africa is an uphill task but I love my continent – and every step indeed does start with baby steps! I am more than hopeful that together with HAEi we will bring a change in HAE in Africa – and that there will be access to modern affordable life-saving HAE medicines. My life is more hopeful now that HAEi has taken me under its wing.

A closing remark, Patricia?

I would really like to be able to say "Hakuna Matata". Maybe you are familiar with it from the musical "The Lion King"? It is a phrase in Swahili meaning "no worries". It is in common use in Kenya – and I do hope that HAE patients in my country will be able to say that in a not too distant future.

Ask the Doctors

In 2015 the US HAE Association implemented a process for answering patients' questions about HAE. Physician/Scientists at the US HAEA Angioedema Center at the University of California San Diego field questions and the answers are posted on Facebook pages of the Angioedema Center and the US HAEA. Dr. Sandra Christiansen, Dr. Marc Riedl, and Dr. Bruce Zuraw answer a recently asked question.

"Urticaria and Prodromal Symptoms Including Erythema Marginatum in Danish Patients with Hereditary Angioedema"

Dr. Christiansen: I thought that it would be something of interest to discuss the article "Urticaria and Prodromal Symptoms Including Erythema Marginatum in Danish Patients with Hereditary Angioedema" by Rasmussen et al published in Acta Derm Venereol in 2016. This article addresses two important issues: (1) How often and what type of prodromal symptoms are experienced by HAE patients in advance of an attack of swelling and (2) How does this affect clinical care? The authors were interested in particular about erythema marginatum, or EM, which has been described as the most specific prodromal symptom for HAE. As many of you know this a reticular, seripiginous erythematous skin eruption (aka circular red rash), which is typically non pruritic (not itchy). It is unknown why HAE patients experience EM, but it has been suggested to be mediated by bradykinin due to the lack of response to antihistamines. The authors also wanted to investigate the long-standing belief that HAE patients do not have urticaria (hives). A history of urticaria has been used by clinicians to exclude the likelihood that a patient might be suffering from HAE.

The findings of the investigation were illuminating. 56% of patients had EM and 25% had a lifetime history of urticaria. More then 25% had both. Half of the patients participating had their EM rash misdiagnosed as urticaria on one or more occasions. In keeping with the belief that HAE patients 'don't have hives' the diagnostic delay in these patients was 2 years longer then in HAE patients without EM.

HAE patients overall had a 90% rate of reporting prodromal symptoms. This included malaise (27%), fatigue (21%), skin symptoms other then rash (38%), psychological changes (21%), and gastrointestinal symptoms (17%).

Dr. Zuraw: First let me make a comment about urticaria and HAE. As you point out, most of the so-called urticartia was actually EM and the diagnosis of urticaria represented a miss-diagnosis. That said, urticaria is very common in the general population and HAE patients are not protected from having urticaria. Indeed, there have been isolated reports of HAE patients suffering from urticaria. The point is that urticaria is not part of the HAE attack. Up to nearly 90% of HAE patients report having experienced prodromal symptoms, with about half of patients experiencing some prodromal symptoms before each attack. My best guess is that this does represent an early manifestation of bradykinin generation, perhaps when the level is quite low.

While HAE is indeed a systemic condition, we don't yet understand why the attacks of swelling are localized. It is certainly plausible that constitutional symptoms such as malaise and fatigue represent a systemic manifestation of contact system activation, but in truth we don't really know. Many patients and physicians have wondered if these prodromal symptoms could be used to determine when to treat with an on-demand drug in order to stop the attack before it can really get going. While there is good evidence that early treatment is more effective than treatment given once the attack is more severe, we have in general not recommended treating based on prodromal symptoms. The major reason for not treating is that many of the prodromal symptoms are non-specific and may occur at other times than just before an attack. The only possible exception would be EM, which in some patients is a reliable indicator of an impending attack.

Dr. Riedl: Pictures are incredibly helpful, as people often don't have the rash at the time of their office visit. It's also important to realize that people with HAE sometimes DO get other skin rashes, including hives, as a separate unrelated medical condition. Hives are pretty common in the general population (about 20% of people experience them at some point in life) and in this study 25% of individuals with HAE appear to have had true hives. So we also can't get tunnel-vision and blame all skin symptoms on HAE, since true hives frequently require allergy medications. In cases where HAE and chronic hives exist in the same person, the treatment plan can become more challenging and complex as we try to sort out what is due to bradykinin and what is due to histamine. Fortunately, these situations are pretty rare. But this study is a reminder that we must take a careful detailed medical history and exam of the skin (or photos) to ensure we gather important clues leading to the correct dermatologic and angioedema diagnosis.

Global Advocacy Work

Recent events

31 March – 2 April: HAEi participated in and present at the Spanish member organization AEDAF's Annual Meeting in **Madrid, Spain**. It was a very well organized meeting where many members showed up both for the general assembly and the more "informative" part, where patients were updated on developments in the world of HAE.

18 – 20 April: HAEi met in **Milan, Italy** with Professor Marco Cicardi and Cloud-R to discuss the framework for a global HAE patient registry. Establishing a global patient registry will be one of the most important tasks for HAEi over the coming year(s).

3 – 6 May: HAEi conducted meetings in **Manila, Philippines** with (1) the HAE family that has created the patient organization, (2) a physician who is interested in being the group's medical advisor, and (3) the Philippine Society for Rare Disorders which is assisting HAEi in the effort to raise HAE awareness and strategize for approaching the health ministry to discuss access to medicine.

9 - 10 May: HAEi had a strategic meeting with the coming partner of the HAEi Global Access Program.

18 – 21 May: HAEi participated in the C1-Inhibitor Workshop in **Budapest, Hungary**.

11 – 12 June: HAEi took part in the BioCryst investigator meeting in **Prague, Czech Republic**, for the upcoming clinical trial on BCX-7353 used for acute attacks.

18 – 21 June: HAEi participated in the European Academy of Asthma, Allergy and Clinical Immunology (EAACI) Annual Meeting in **Helsinki, Finland**.

Upcoming events

3 - 6 August: HAEi will host it's first Youngster's Summer Camp in **Frankfurt, Germany**. More than 70 youngsters and caregivers will attend.

2 - 4 September: HAEi will hold a Regional Patient Advocates gathering in **Malta**.

15 - 17 September: HAEi will participate in the 2017 US HAEA Patient Summit in **Bloomington, USA.**

29 - 30 September: HAEi will host the 2017 HAEi South Eastern Europe Workshop in **Skopje, Macedonia**.

6 - 8 October: HAEi will host the 2017 HAEi Central Eastern Europe Workshop in **Warsaw, Poland**.

10 - 12 November: HAEi will participate in the 2017 Scandinavian Conference by HAE Scandinavia in **Stockholm, Sweden**.

News from the Industry

24 March 2017

As of 24 March 2017, Japan's Ministry of Health, Labour and Welfare (MHLW) has approved an extended use of Berinert from **CSL Behring**, a C1-esterase inhibitor (C1-INH) concentrate, for pre-procedure prevention (short-term prophylaxis) of acute episodes of HAE.

Berinert is now indicated for the treatment of acute episodes and for pre-procedure prevention (short-term prophylaxis) of acute episodes of HAE. Berinert as the first and only C1-INH concentrate therapy in Japan has been used for acute episodes of HAE for many years.

This important approval supports further treatment options for the use of C1-INH concentrate as first-line therapy for the prevention of potentially life-threatening HAE attacks triggered by surgical or dental procedures.

Responding to reports of swelling of tongues or larynx triggered by surgical or dental procedures that may become fatal, the Japanese Society of Oral and Maxillofacial Surgeons and the Japanese Dermatological Association petitioned an extended use of C1-INH concentrate for short-term prophylaxis at pre-procedure prevention.

The petition has successfully been supported to apply Public Knowledge-based Application be submitted by "Review Committee on Unapproved Drugs and Indications with High Medical Needs" as to be an indication that can provide significant clinical benefits, and then concluded by the MHLW advisory committee as of November 2016 that efficacy and safety profiles of this product were already well-known medically pharmaceutically.

(Source: CSL Behring K.K.)

CSL Behring

13 April 2017

BioCryst Pharmaceuticals, Inc. plans to explore a new oral liquid formulation of BCX7353 for the treatment of acute attacks in patients with HAE. The company has received initial regulatory approvals in Europe to initiate the ZENITH-1 exploratory clinical trial this summer.

"To complement the attractive profile of our prophylactic treatment program, as evidenced by the interim results from our APeX-1 trial, we made a decision to explore an additional indication for the treatment of acute attacks with a new oral liquid formulation. The rapid absorption and long half-life of BCX7353 observed after single oral doses in healthy volunteers, and the strong encouragement from disease experts and patient advocates have motivated us to explore '7353 as an acute treatment," said Jon Stonehouse, CEO. "We believe this new formulation can fill an unmet need for patients with less frequent attacks who are looking for better ways to manage their illness. This initiative has the potential to provide patients with a more convenient option for the treatment of acute attacks, and if successful, the first oral acute therapy for HAE."

The purpose of ZENITH-1 is to explore whether single oral doses of a liquid formulation of BCX7353 could have utility in the treatment of acute angioedema attacks in patients with HAE. It is designed as a randomized, double-blind, placebo controlled, dose-ranging trial with BCX7353 self-administered at home to treat attacks. Additional information and clinical trial design will be provided upon completion of the regulatory process and trial initiation.

Discovered by BioCryst, BCX7353 is a novel, once-daily, selective inhibitor of plasma kallikrein currently in development for the prevention of angioedema attacks in patients diagnosed with HAE. With the initiation of the ZENITH-1 clinical trial, the oral liquid formulation of BCX7353 will be evaluated for treating acute angioedema attacks. BCX7353 has been generally safe and well tolerated in the ongoing Phase 2 ApeX-1 clinical trial and in clinical pharmacology studies in healthy volunteers.

(Source: BioCryst)

BioCryst Pharmaceuticals, Inc.

2 May 2017

Shire plc has announced the unaudited results for the three months ended March 31, 2017. Flemming Ornskov, Shire CEO, commented:

"In the first quarter we delivered strong top-line growth. (…) Our priorities for the rest of 2017 remain unchanged: launching new products while driving commercial excellence, generating operational efficiencies, and advancing our pipeline of novel therapies. Additionally, we continue to prioritize paying down debt, and we are on track to achieve our full-year financial guidance. Looking ahead, I see tremendous opportunity for further growth as we continue to build on our position as the global leader in treating patients with rare diseases."

From the Product and Pipeline Highlights:

- On March 16, 2017, the EC approved a label extension for Cinryze (C1 inhibitor [human]), broadening its use to children with HAE. Cinryze is now the first and only treatment indicated for routine prevention of angioedema attacks in children aged six years or older who have severe and recurrent attacks of HAE and cannot tolerate or are not adequately protected by oral preventative treatments, or who are inadequately managed with repeated acute treatment. Cinryze is also now approved for acute treatment and pre-procedure prevention of angioedema attacks in children aged two years or older with HAE.
- The SHP643 open-label extension study completed enrollment in March 2017. Topline pivotal Phase 3 study results are expected in Q2 2017.

(Source: Shire)

5 May 2017

BioCryst Pharmaceuticals, Inc. has announced the financial results for the first quarter ended March 31, 2017.

"We have completed enrollment in Part 1 and 2 of the APeX-1 Phase 2 clinical trial of BCX7353 for prevention of angioedema attacks and will report top-line data in the second quarter of 2017 as planned," said Jon P. Stonehouse, President & CEO. "Enrollment in Part 3 has begun, and at the current enrollment pace, we expect to report complete APeX-1 results in the third quarter of 2017."

From the Clinical Development Update & Outlook:

- On February 27, BioCryst announced positive results from an interim analysis of Part 1 of the APeX-1 trial for the prevention of attacks in HAE patients. Following 28 days of dosing with 350 mg once daily BCX7353 or placebo, an overall reduction of 0.57 attacks/week (63%, p = 0.006) was observed in BCX7353-treated subjects, with reductions of 88% and 24% respectively in peripheral and abdominal attacks. Based upon additional post-hoc analyses, it appeared that subjects may have recorded transient abdominal adverse events as HAE attack symptoms. Oral BCX7353 350 mg once-daily for 28 days was generally safe and well tolerated in subjects with HAE. Evaluation of lower dose cohorts is ongoing in Part 2 and 3 of the APeX-1 trial.
- On April 12, BioCryst announced plans to explore a new oral liquid formulation of BCX7353 for the treatment of acute attacks in patients with HAE. The Company has received initial regulatory approvals in Europe to initiate the ZENITH-1 exploratory clinical trial, anticipated to start this summer. The goal of the trial is to explore whether single oral doses of a liquid formulation of BCX7353 could have utility in the treatment of acute angioedema attacks in patients with HAE. ZENITH-1 is designed as a randomized, double-blind, placebo controlled, dose-ranging clinical trial with BCX7353 self-administered at home to treat attacks.

(Source: BioCryst)

11 May 2017

Adverum Biotechnologies, Inc. has reported the financial results for the first quarter ended March 31, 2017.

"Adverum is well positioned in the gene therapy space with a robust pipeline and a platform of industry-leading AAV vector technology, including novel vector development capabilities," said Amber Salzman, Ph.D., president and CEO of Adverum Biotechnologies. "Our strong cash position will help us execute our plans and is expected to fund our three lead gene therapy programs through the end of 2019 to generate meaningful clinical data for at least one of these programs. We are committed to transforming Adverum into a clinical-stage company by the end of this year."

From the 2017 Outlook:

- For ADVM-053, Adverum's gene therapy product candidate for treating HAE, the Company met with the FDA in the first quarter of 2017 and is preparing to file an IND.

(Source: Adverum)

16 May 2017

On 16 May HAE patient organizations from around the world, led by HAEi come together to support the global awareness day for HAE.

Dr. Sijmen de Vries, **Pharming**'s CEO commented:

"We are proud to provide the first and only recombinant (C1- esterase inhibitor) protein replacement therapy for the treatment of acute angioedema attacks in adults and adolescents with HAE. Pharming has been collaborating with the HAE community since 2000. We are delighted to support this year's **hae day :-)** and are dedicated to continue making a difference in patients' and their families' lives, working in close partnership with HAEi and its local affiliates."

As part of the awareness initiatives, HAEi introduces "Support Family Testing" tools on the organization's campaign website www.haeday.org.

"As HAE is an hereditary disorder, it is very important to have other family members tested. To help patients in this process we have developed two documents, one for patients and one for physicians", says Henrik Balle Boysen, Executive Director of HAEi. "Patients are frequently misdiagnosed because HAE symptoms often resemble those of more common conditions. Through 2017 **hae day :-)** we hope to spread the word about HAE, so patients can receive an accurate diagnosis and appropriate medical care. We are very excited by the level of participation from the HAE national organizations across the globe and hope that the awareness day will make a real difference to lives of HAE patients in the future."

(Source: Pharming Group)

19 May 2017

Shire plc announces positive topline Phase 3 results for the HELP study, a global, multi-center, randomized, double-blind placebo-controlled parallel group trial that evaluated the efficacy and safety of subcutaneously administered lanadelumab versus placebo over 26 weeks in patients 12 years of age or older with HAE. Lanadelumab is an investigational treatment being evaluated for the prevention of angioedema attacks in patients with HAE.

This study met its primary endpoint and all secondary endpoints with highly statistically significant and clinically meaningful results for all three lanadelumab treatment arms compared to placebo. The 300 mg dose administered once every two weeks resulted in a statistically significant reduction in mean HAE attack frequency of 87% compared to placebo ($p < 0.001$). Results were consistent regardless of baseline attack rate. Notably for each of the three lanadelumab regimens studied, whether administered biweekly or monthly, a significantly higher proportion of patients—compared to placebo—were attack free throughout the entire 26 week study period.

This study was representative of the full HAE disease spectrum. Overall, 52% of patients experienced three or more attacks per month at baseline, 65% of patients reported a history of laryngeal attacks and 56% were on long-term prophylaxis (LTP). Ninety percent of patients completed the study. Ninety-six percent of those who completed the study chose to roll-over into the ongoing long-term safety study (HELP Study Extension).

"In the U.S., available treatment options include either injections for acute attacks or short-acting intravenous infusions administered twice a week," said Aleena Banerji, M.D., Massachusetts General Hospital, Boston, MA and clinical trial investigator. "If approved, lanadelumab may offer patients a long-acting treatment option that significantly reduces HAE attacks when administered subcutaneously as infrequently as every four weeks."

"The possibility of a new way to address the underlying cause of HAE to prevent attacks could transform how we treat the disease in the future," said Professor Marcus Maurer, M.D., Charité –Universitätsmedizin Berlin, Germany and clinical trial investigator. "Patients with HAE want to live independently and without fear of an angioedema attack."

Lanadelumab was generally well tolerated over the 26-week treatment period. No treatment-related serious adverse events or deaths were reported. The most common adverse event was injection site pain (29.3% placebo vs. 42.9 % combined lanadelumab arms).

"We are extremely encouraged by these topline Phase 3 results," said Flemming Ornskov, M.D., M.P.H., Shire CEO, "We have nearly a decade of experience and a strong portfolio and pipeline in HAE and believe these data demonstrate high potential for transforming the way patients living with this condition are treated."

Shire plans to submit a biologics license application (BLA) for evaluation by the U.S. Food and Drug Administration (FDA) by late 2017 or early 2018. Lanadelumab has received both Orphan Drug Designation and Breakthrough Therapy Designation from the FDA and Orphan Drug Designation from the European Medicines Agency (EMA).

(Source: Shire)

23 May 2017

Attune Pharmaceuticals announces positive results from preclinical safety studies evaluating ATN-249, a novel orally administered plasma kallikrein inhibitor for the treatment of HAE. The strong safety, high potency, and high selectivity results suggest a wide therapeutic window with once-daily dosing potential of ATN-249.

In the preclinical toxicology and safety pharmacology studies, ATN-249 was generally safe and well tolerated. In addition, pharmacokinetic studies indicated high 24-hour exposure and comprehensive drug recovery after repeat oral doses of ATN-249.

"This encouraging data, along with prior published potency and efficacy results, reinforce our belief that our lead drug candidate, ATN-249, has a favorable safety profile and once-a- day dosing regimen to address the unmet need for well-tolerated and safe oral therapies with improved patient quality life and prophylactic efficacy," said Dr. Andrew McDonald, CEO of Attune Pharmaceuticals, "These IND-enabling study results support commencing the Phase 1 clinical development of ATN-249 this summer."

The oral presentation outlined the results of several well-established preclinical assays. Studies included evaluation of potency of ATN-249 compared to C1INH via inhibition of plasma kallikrein, selectivity of ATN-249 on biochemical inhibition of plasma kallikrein relative to other closely related serine proteases, and ATN-249's pharmacokinetics, general toxicity, safety pharmacology, and genotoxicity profiles.

(Source: Attune)

28 May 2017

BioCryst Pharmaceuticals, Inc. has announced results from a second interim analysis of its Phase 2 APeX-1 clinical trial in HAE. APeX-1 is a 3-part dose ranging trial designed to evaluate the efficacy, safety, tolerability, pharmacokinetics and pharmacodynamics of orally administered once-daily (QD) BCX7353 for 28 days, as a preventative treatment to reduce the frequency of attacks in HAE patients. This second interim analysis evaluated data from all patients in Parts 1 and 2 of the trial. The first interim analysis evaluated data from 28 of 36 patients in Part 1.

"These data support our hypothesis regarding the initial findings seen from the first interim analysis," said Jon Stonehouse, CEO & President of BioCryst. "We are delighted to see that a daily dose of 125 mg of BCX7353 results in a high level of efficacy with an improved tolerability profile compared to the 350 mg dose observed in the first interim analysis. We look forward to completing Part 3 of the trial to select appropriate doses for our pivotal program."

This second interim analysis of pooled data from Parts 1 and 2 evaluated doses of BCX7353 125 mg (n=7), 250 mg (n=6) and 350 mg (n=18) QD versus placebo (n=20) for 28 days. The baseline attack rate was approximately 1/week. Baseline characteristics were generally well balanced between the treatment groups. Compliance with study drug dosing was excellent (≥ 98%).

The pre-specified per-protocol (PP) interim analysis included data on a total of 44 subjects with confirmed Type 1 or Type 2 HAE completing 28 days of treatment. The percentage reductions by treatment group in the mean rate of independently- adjudicated angioedema attacks for the pre-defined effective dosing period (weeks 2 through 4) in BCX7353 treated subjects were: 125 mg QD, 73% (p=0.002); 250 mg QD, 37% (p=0.128) and 350 mg QD, 58% (p=0.001) compared to placebo. In the intent-to-treat (ITT) population, corresponding reductions by treatment group were: 125 mg QD, 73% (p=0.004); 250 mg QD, 44% (p=0.090) and 350 mg QD, 45% (p=0.014) compared to placebo.

Continued on next page ....

10 March 2017

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A pre-planned analysis of peripheral and abdominal attacks showed reductions in peripheral attacks of 74% (125 mg QD), 54% (250 mg QD) and 90% (350 mg QD) compared with placebo (PP analysis, weeks 2 through 4) and reductions in abdominal attacks of 72% (125 mg QD), 10% (250 mg QD) and 8% (350 mg QD) compared with placebo (PP analysis, weeks 2 through 4). Based on this distribution, it is likely that subjects in the 250 mg and 350 mg arms recorded transient abdominal adverse events (AEs) as HAE attack symptoms in their diary. In contrast, a consistent reduction in attacks regardless of anatomical location was observed in the 125 mg arm.

Oral BCX7353 once-daily for 28 days was generally safe and well tolerated in subjects with HAE. There were no serious AEs and no severe AEs. Three subjects in the BCX7353 350 mg treatment arm, two of which were previously reported, discontinued study drug before day 28. A third subject in this arm discontinued study drug due to vomiting and abdominal cramps concurrent with menses. The most common treatment-emergent adverse events were the common cold and diarrhea. The gastrointestinal AEs previously observed in the 350 mg arm were not seen at the 125 mg dose. Additionally, no significant laboratory abnormalities were observed in the two lower dose groups.

Steady state BCX7353 plasma levels and kallikrein inhibition levels in HAE subjects were similar to those seen in healthy subjects administered the same doses in a previously completed Phase 1 trial. Steady state trough drug levels (24 hours after dosing) greatly exceeded the target therapeutic range at the 250 mg and 350 mg dose levels. Trough levels for the 125 mg dose were generally within the target range.

The efficacy, safety and tolerability profile of BCX7353 observed in this interim analysis strongly supports its continued investigation as a prophylactic treatment for HAE. Enrollment into Part 3 of the trial is progressing well. Completion of Part 3 will enable a full evaluation of the dose response necessary to select doses for a pivotal program.

(Source: BioCryst)

BioCryst Pharmaceuticals, Inc.

23 June 2017

The U.S. Food and Drug Administration has approved Haegarda, the first C1 Esterase Inhibitor (Human) for subcutaneous (under the skin) administration to prevent HAE attacks in adolescent and adult patients. The subcutaneous route of administration allows for easier at-home self-injection by the patient or caregiver, once proper training is received.

"The approval of Haegarda provides a new treatment option for adolescents and adults with HAE," said Peter Marks, M.D., Ph.D., director of FDA's Center for Biologics Evaluation and Research. "The subcutaneous formulation allows patients to administer the product at home to help prevent attacks."

Haegarda is a human plasma-derived, purified, pasteurized, lyophilized (freeze-dried) concentrate prepared from large pools of human plasma from U.S. donors. Haegarda is indicated for routine prophylaxis to prevent HAE attacks, but is not indicated for treatment of acute HAE attacks.

The efficacy of Haegarda was demonstrated in a multicenter controlled clinical trial. The study included 90 subjects ranging in age from 12 to 72 years old with symptomatic HAE. Subjects were randomized to receive twice per week subcutaneous doses of either 40 IU/kg or 60 IU/kg, and the treatment effect was compared to a placebo treatment period. During the 16 week treatment period, patients in both treatment groups experienced a significantly reduced number of HAE attacks compared to their placebo treatment period.

The most common side effects included injection site reactions, hypersensitivity (allergic) reactions, nasopharyngitis (swelling of the nasal passages and throat) and dizziness. Haegarda should not be used in individuals who have experienced life-threatening hypersensitivity reactions, including anaphylaxis, to a C1-INH preparation or its inactive ingredients.

Haegarda received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs to treat rare diseases or conditions.

The FDA granted approval of Haegarda to **CSL Behring LLC**.

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines, and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

(Source: FDA)

CSL Behring

HAEi around the world

Currently there are HAE member organizations in 55 countries. You will find much more information on the HAE representations around the globe at **www.haei.org** as the world map will provide you with contact information for the member organizations as well as care centers, hospitals, physicians, available medication, and clinical trials.

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