

# Global perspectives:

HAEi MAGAZINE · ISSUE 2/2018



The 2018 HAE Global Conference in Vienna, Austria – the fourth conference of its kind – was record-breaking in more than one way: The largest number of participants (736 from 57 countries), the largest scientific track as well as the most keynote speakers.

This issue of Global Perspectives is dedicated to the conference #haeGC18.



## Dear HAEi Friends,

This edition of Global Perspectives focuses on our incredibly successful 2018 HAE Global Conference (GC18). Vienna was a great setting for the 736 HAE patients, caregivers, physician/scientists, and pharmaceutical company representatives from 57 countries who gathered to share ideas and actions plans focused on helping the global HAE community "Take Control of HAE".

GC 2018 had a very special atmosphere created by an extraordinary sense of camaraderie, shared purpose, and positive energy that could be felt during every session and in every part of the meeting venue.

As you will read in the following pages, every session, activity, and event held during this highly successful conference represents a highlight!

The GC18 plenary sessions included: An overview what every patient and caregiver needs to know about HAE; roundtable discussions of advocacy strategies that worked in various countries; a lecture by expert physicians on current and future HAE therapies; and a highly informative Q and A session with the world-class HAE physician experts.

The Scientific Track brought together the world's foremost HAE researchers who discussed important issues such as a new genetic pathway for causing HAE, an animal model that could help test HAE drug candidates, diagnostic delays, and perspectives on the burden of illness.

Because our HAEi youth are so near and dear to all of our hearts and represent the future for HAE advocacy, GC18 offered a special and comprehensive Youth Program. Yujin Yamamoto, a college student from Japan, addressed the entire conference and gave an inspiring talk about his personal experience witnessing the positive impact of parents, physicians, and advocacy organizations working together on his behalf. During the conference, our HAEi Youth were very busy establishing a new Youngster's


community, creating their own website and HAEi Youth Magazine, and participating in talks from two expert physicians that focused on managing HAE. The entire HAEi Youth group got up on stage during the gala dinner and gave inspirational testimonials about taking control of HAE. They also mesmerized the crowd by presenting their beautiful HAEi Youth website and informative and handsomely designed HAEi Youth magazine.

The power of patient advocacy was on display at GC18 and the HAEi Team, especially our Regional Patient Advocates, look forward to maintaining the positive energy and momentum established in Vienna. We are fiercely committed to helping broaden access to medicine in existing patient groups and find ways to start new organizations in countries where one does not exist.

Finally, the HAEi Friends who participated in the HAEi Jakobsweg Walk through Vienna deserve a special "shout out!"

Organizing a successful meeting that involves such a large group coming in from all over the globe is a complex and daunting task! Please join me in thanking our talented Executive Director, Henrik Balle Boysen, and his extremely competent team including Debs Corcoran, Nevena Tsutsumanova, and Laura Bjørn Dahl from Conference Care. Their skill, expertise, and tireless efforts are a key reason why GC18 was a resounding success!

Warm regards to all HAEi friends,

  
Anthony J. Castaldo  
President, HAEi

Global perspectives:

Global Perspectives  
Issue 2/2018  
July 2018

**Layout and design**  
Mrs. Rikke Sørensen, Plus R

**Magazine staff**  
Mr. Steen Bjerre  
Communications Manager  
E-mail: s.bjerre@haei.org  
Phone: +45 22 20 46 01

Mr. Henrik Balle Boysen  
Executive Director  
E-mail: h.boysen@haei.org  
Phone: +45 31 591 591

**Subscription**  
If you would like to subscribe to our magazine please send an email to [info@haei.org](mailto:info@haei.org) or register directly on our website [www.haei.org](http://www.haei.org)

HAEi is registered as a non-profit organization in Switzerland



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 of Global Perspectives



10



23



32



45

**06** Highlights from the 2018 HAE Global Conference

**23** A website and a magazine is all in a day's work  
haeGC18 Youngster's Track

**24** What patients and family need to know about HAE

**26** Take control using advocacy tools

**27** Take control: A global HAE assessment

**28** Take control: A regional perspective

**32** HAEi Jakobsweg Walk 2018

**34** Record-breaking HAE Global Walk 2018

**38** News from around the Globe

**54** Working on a unified voice for HAE patients in South Korea

**56** Global advocacy work

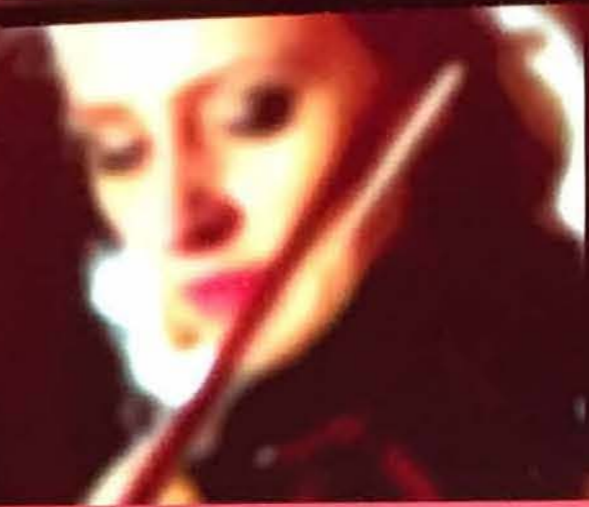
**58** Clinical trials

**60** News from the industry

**66** HAEi around the world

**736 participants  
57 countries**

**736 participants  
57 countries**



Highlights from the  
2018 HAE Global Conference



Biannually HAEi welcomes HAE patients, caregivers, healthcare professionals, and industry representatives to the HAE Global Conference – by far the most significant international gathering of its kind solely with focus on HAE topics. At these conferences, the participants learn much more about HAE as they share experiences and knowledge in a friendly atmosphere conducted and driven by HAEi.

The first HAE Global Conference took place in Copenhagen, Denmark in 2012, followed by Washington D.C., USA in 2014 and Madrid, Spain in 2016 – and most recently the record-breaking conference in Vienna, Austria in 2018.

Indeed, the fourth HAE Global Conference set new records in more than one way: The largest number of participants (736 from 57 countries), the largest scientific track as well as the most keynote speakers.

The conference took place at the Hilton Vienna hotel in the center of Vienna. While most of the conference attendees arrived in Vienna on Thursday 17 May 2018, the HAEi Executive Committee and the HAEi Scientific Program Committee met during the afternoon to make the final preparations. However, quite a number of the conference delegates started their Vienna experience already Wednesday morning with one or more stages of the HAEi Jakobsberg Walk through the Austrian capital.

Most of this issue of Global Perspective is dedicated to the 2018 HAE Global Conference.





*The 736 participants from 57 countries worldwide also had the opportunity to relax, enjoy, and network attending the 2018 HAE Global Conference in Vienna.*





## Friday 18 May 2018

After opening remarks from HAEi Project Manager **Deborah Corcoran**, the welcome address was delivered by HAEi President **Anthony J. Castaldo** and HAEi Executive Director **Henrik Balle Boysen**. Then the delegates split into three groups to follow the patients', the scientific or the youngsters' program.

Regarding the youngsters' program please see the article page 22-23.

### Scientific Program

Under the headline *"Insights in Clinical Practice"* the first part of the scientific program – chaired by **Prof. Bruce Zuraw** (US HAEA Angioedema Center at UC San Diego, USA) – opened with presentations by **Dr. Teresa Caballero** (Hospital Universitario La Paz in Madrid, Spain) and **Prof. Marc Riedl** (US HAEA Angioedema Center at UC San Diego, USA).



Marc Riedl

Then followed two abstracts sessions – firstly *"Take Control of HAE with Real-World Data"* chaired by **Prof. Marco Cicardi** (Milan University, Italy) and secondly *"Take Control of HAE – New Advances and Approaches"* chaired by **Prof. Konrad Bork** (University Medical Center in Mainz, Germany). In the first part, Professor Cicardi delivered the keynote speech, while **Prof. Allen Kaplan** (Medical University of South Carolina, USA) gave the second.

The title of the oral presentation by **Dr. Andrea Zanichelli** (University Hospital ASST Fatebenefratelli Sacco in Milan, Italy) was *"Improvement in Diagnostic Delays over time in Patients with HAE: Findings from the Icatibant Outcome Survey"*. He concluded that although delay in diagnosis of patients with C1-INH-HAE has improved over time, there is still a need to raise awareness of HAE.

In her presentation titled *"Burden of Illness in HAE: Findings From a US Patient Survey"*, Sr. Director of Research for the US HAEA **Janet Long** spoke about large differences in disease burden being observed according to HAE attack frequency. Patients with more attacks reported more physical difficulties and symptoms of depression and anxiety. Despite the availability of prophylactic treatment, many HAE patients in the United States continue to experience a high number of attacks. There is a need for improved therapy that may help more patients become attack-free.

**Dr. Kinga Viktória Köhalmi** (Semmelweis University in Budapest, Hungary) spoke about *"Genetic Biomarkers and Clinical Significance of Erythema Marginatum in Hungarian Patients with HAE due to C1-Inhibitor Deficiency"*: Erythema marginatum manifests later than the onset of HAE attacks and is characterized by female predominance. As 73 percent of erythema marginatums were followed by an HAE attack, early introduction of individual therapy should be considered. Genetic predisposition is likely in erythema marginatum, and therefore, a predictive genetic pattern could be created by the analysis of further genes.

Dr. Köhalmi was given the 1st Young Researcher's Award at the 2018 HAE Global Conference.

In her presentation *"Transgenic Rats Overexpressing the B2 Receptor as an Alternative Model for Bradykinin-Induced and HAE"* **Dr. Camilla Lopez Veronez** (Federal University of Sao Paulo, Brazil) concluded that kinin B2 receptor in endothelial cells is a promising model for the study of vascular permeability, spontaneous abdominal bradykinin-mediated angioedema and for the test of new drugs. Pancreatic lesions accompanying abdominal

angioedema corroborate sparse clinical reports of HAE patients developing pancreatitis, suggesting that acute pancreatitis can be underdiagnosed secondary event in HAE.

**Nathália Cagini** (Federal University of Sao Paulo, Brazil) spoke about *"Alterations in ANGPT1 Gene Supports a new Pathway Responsible to Mediate HAE in Brazilian Patients"*: In silico analysis provide pathogenic supporting evidence according to the American College of Medical Genetics and Genomics, opening a new range of studies to different pathophysiologies involved in HAE with unknown pathogenesis.

The title of the presentation by **Dr. Sandra Christiansen** (US HAEA Angioedema Center at UC San Diego, USA) was *"Long-term Treatment Experience with Subcutaneous C1-Esterase Inhibitor for the Prevention of HAE Attacks: 2-year Efficacy Results from the US COMPACT Open-Label Extension Study"*. She concluded that long-term replacement therapy with twice-weekly subcutaneous C1-INH at 60 IU/kg in patients with frequent HAE attacks provides a sustained and profound preventive effect with >80 percent of patients achieving symptom-free status.

**Prof. Vesna Grivcheva-Panovska** (University St. Cyril and Methodius in Skopje, Macedonia) talked about *"Taking Control of HAE: Lessons Learned from Assessing Anxiety and Depression in HAE Patients' Family Members and Caregivers"*. She concluded that the complex impact of HAE on family members and caregivers must not be overlooked and it is time for a more inclusive approach to achieve optimal control of HAE in a broader sense.



Yujin Yamamoto

### Patient Program

The Patient Program was opened by the Japanese HAE patient **Yujin Yamamoto** who gave a strong personal story under the headline "Take Control: Don't let HAE hold you back". HAEi is presently working on a patient story based on Mr. Yamamoto's speech, and hopefully, this will be available in the upcoming issue of this magazine.

Then followed a presentation named "Take Control: What Patients and Family need to know about HAE" and presented by the HAEi Executive Committee members Sarah Smith Foltz (Spain) and Fiona Wardman (Australia). You will find the highlights from the presentation in a separate article in this magazine.

The patient program of the first conference day ended with two presentations by Anthony J. Castaldo and Henrik Balle Boysen. First, they talked about "Take Control using advocacy tools" and then followed "Take Control: A global HAE assessment". Highlights from both presentations can be found in separate articles in this magazine.

### Poster session

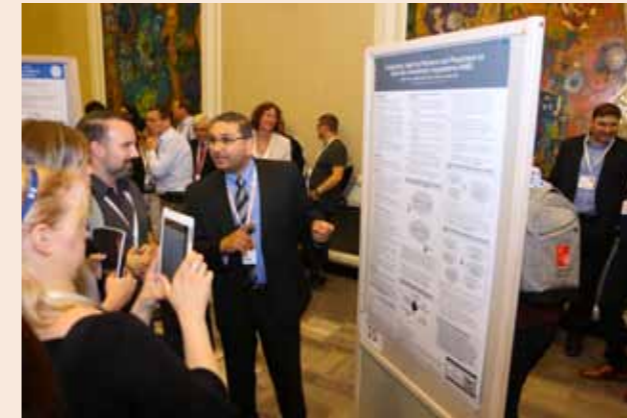
**The Lived Experience of Women who have HAE** – Pippa Adams and Stephanie Kilinc, Teesside University, United Kingdom

HAE restricts daily life, and future plans and women feel they have little control; however home therapy provides them with a sense of control leading to a fuller life. Although this is only possible when they receive a diagnosis, which can take years when they luckily find a professional who recognizes it, this can be overlooked even with a diagnosis. The psychosocial impact demonstrates women's well-being is in jeopardy due to attacks themselves isolating women and the conditioned being labeled as psychosomatic. Future directions for health psychology HAE awareness need to be promoted, so patients are diagnosed sooner.



**Efficacy and Safety of Recombinant Human C1 Esterase Inhibitor Treatment for HAE Attacks: Interim Analysis of a European Registry** – Roman Hakl, Masaryk University, Czech Republic, et al.

The rhC1-INH treatment registry provides real-world data on the treatment of 1608 HAE attacks. Data are consistent with previous reports on the safety and efficacy of rhC1-INH therapy.



**Real World Data of Canadian Adults Living with HAE: Part II – Attack Profile** – Linda Howlett, HAE Canada, et al.

The majority of patients are knowledgeable in identifying their triggers and managing their attacks. Improvements are necessary for proper diagnosis and awareness of the disease. Better communication between patients and physicians is necessary regarding symptom awareness and correct diagnosis.

**The Well Being of Patients who have HAE** – Pippa Adams, Anna van Wersch and Stephanie Kilinc, Teesside University, United Kingdom

There is psychological distress due to a lack of diagnosis and as to what is causing the attacks. The patient feels like a burden on the family, as they become their carers. A quicker diagnosis can relieve this and access to medication, which can stop attacks fully developing. There is also distress caused after diagnosis as it can be passed to patients' children so genetic counseling should be provided. Patients also need to create coping strategies to effectively use the medication, enabling them to make the adjustments necessary to live with HAE.

**HAE, Still a Fatal Illness Despite C1-INH Substitution** – Tamar Kinaciyani, Medical University of Vienna, Austria

In 2007, after hemodialysis a 35-year-old man developed fever, dyspnea, cough, hematemesis regardless of treatment with C1-INH and died of respiratory and heart failure while waiting for a second kidney transplantation. This was before the new treatments for HAE and the patient suffered from additional serious diseases but can we still be confident that we would have survived with today's possibilities?

**Treatment of Severe HAE During Pregnancy and Lactation Period** – Tamar Kinaciyani, Medical University of Vienna, Austria

There are only limited data for the use of human-plasma-derived, pasteurized, nanofiltered C1-INH concentrate during pregnancy. This case confirms the safety and efficacy of the named drug in HAE patients during pregnancy and lactation.

**Real World Data of Canadian Adults Living with HAE: Part I – Demographics** – Jacque Badiou, HAE Canada, et al.

This survey helps to better understand the current demographic profile for patients living with HAE and is the first national HAE survey done in Canada. Overall, our results demonstrate that HAE patients can be found across Canada and that the majority of patients in this survey are aware of their diagnosis.





#### **Defining HAE Severity and Activity: one year Ambulatory Survey** – Francesca Perego, Luigi Sacco Hospital, Italy, et al.

The severity score, even if independent by disease activity, is able to discriminate patients upon the disease activity evaluated over a long period of time and should be routinely used to improve the quality of patients' management.

#### **Treatment of HAE Attacks in Children: A Phase 2 Trial of Recombinant Human C1 Esterase Inhibitor** – Avner Reshef, Barzilai University Hospital, Israel, et al.

rhC1-INH is efficacious, safe, and well tolerated in treating HAE attacks in children. Most patients only require a single dose of rhC1-INH and it is efficacious and well tolerated across various age groups. Data support the use of the same dosing regimen for HAE attacks in children (50 IU/kg; up to 4200 IU, followed by an additional dose, in needed) as currently recommended for adults and adolescents.

#### **Safety, Effectiveness, and Impact on Quality of life in Self-Administration with Plasma-Derived Nanofiltered C1 Inhibitor in Patients with HAE** – Andrea Zanichelli, Luigi Sacco Hospital, Italy, et al.

Self-administration of plasma-derived nanofiltered C1-INH is safe and increases patients' confidence in the treatment, also showing a trend towards an improvement in the quality of life. It reduces the need for Emergency Room admission/healthcare professionals help for the acute attack, as well as the related costs.

#### **Simultaneous Determination of Human Plasma Serine Proteases Complexed with C1-Inhibitor** – Erika Kajdácsi, Semmelweis University, Hungary, et al.

We successfully developed a set of ELISAs for the sensitive determination of various enzyme-C1-inhibitor complexes. They could greatly contribute to a better understanding of the pathomechanism of C1-INH-HAE and to the exploration of attack kinetics. C1-INH dominantly forms complexes with C1s and C1r in vivo, suggesting that the activation of the classical and lectin pathways of the complement system significantly shifts the amount of accessible C1-INH. Therefore, infections might have greater contribution to the precipitation of edematous attacks than thought before.

#### **The Influence of Individualized Treatment on the Quality of life (QoL) in 100 Patients with HAE (HAE C1-INH)** – Inmaculada Martinez Sager, Haemophilia Centre Rhine Main, Germany, et al.

Our data indicate significant differences on quality of life between patients on on-demand treatment and patients on IRT treatment. Our results show a trend towards a better quality of life for patients on prophylactic therapy. 85 percent of the patients preferred modern communication channels to support individualized home treatment.

#### **First-ever Survey of the Prevalence, Epidemiology and Distribution of HAE Patients in Austria** – Clemens Schöffl, Medical University of Graz, Austria, et al.

There is a rising awareness of HAE in Austria. Due to the presence of an active local patient organization and its excellent collaboration with treating physicians, HAE has received significant attention, and increasing awareness among doctors has led to an early diagnosis. Nevertheless, the fact that very few or no patients are diagnosed in some parts of the country shows a still existing need for greater awareness.

#### **Vocabulary Used by Patients and Physicians to Describe HAE** – Gajan Jain, Shire, et al.

Differences in patient and physician vocabulary may cause misalignment in the assessment of the burden of HAE. Discussion between patients and physicians on how the disease and its management affect the daily life of patients was not observed. This may affect appropriate approaches to HAE management for patients.

#### **Self-infusion of Berinert® (Human C1-Esterase Inhibitor) in the home – Learnings from 27 Patients Within Berinert Nursecare Program** – David Tognarini, Aesir Health, Australia, et al.

The most surprising finding is that most patients were very willing to learn and were keen to take control of their condition. They all saw the opportunity as a significant addition to their treatment algorithm. This was especially true if the patient had a positive experience of C1-INH therapy resolving a swelling attack.

#### **Family Perspective on the Diagnosis of HAE** – Francisco Sánchez Hernández, University of Almería, Spain

HAE can be devastating for patients and their families, which is why we must find different methods to help family members know the diagnosis and improve the management of this phase of the disease in the context of the family.





## General Assembly

After the first two presentations, most of the participants in the patients' program gathered for the General Assembly of HAEi.

Following a short welcome from HAEi Executive Director **Henrik Balle Boysen**, the HAEi President **Anthony J. Castaldo** took the floor for his report for 2016 and 2017. For 2016 the President focused on the HAE Global Conference in Madrid, Spain and the fact that the organization managed to grow to a total of 55 countries. Throughout the year HAEi participated in 13 HAE-related conferences, conducted and hosted three HAEi Regional Workshops, and expanded communications with member organizations and other stakeholders. Furthermore, the year saw five issues of the HAEi Magazines, a great amount of social media

presence, the introduction of a new comprehensive toolkit for **hae day** :-)) as well as HAEi assisting in clinical trial recruitment.

As for 2017 the HAEi membership grew to 61, the organization presented the first HAEi Youngster's Summer Camp in Frankfurt, Germany – and not least HAEi expanded the network of Regional Patient Advocates, now covering Central Eastern Europe, South East Europe, Mediterranean, Middle East/Gulf Region, Sub Sahara Africa, and Latin America. During 2017 HAEi issued four magazines, advocated on behalf of patients at nine major international medical meetings – and naturally put a lot of energy into planning for the 2018 HAE Global Conference. Additionally, HAEi launched the HAEi Global Access Program, HAEi Connect, a new format for HAEi website hosting, and the HAE Global Registry.

Following approval of the President's report Treasurer **Fiona Wardman** presented the financial report for 2016 and 2017. As this too was approved the assembly could proceed to the election of candidates to the Executive Committee. This time present members **Michal Rutkowski** (Poland), **Fiona Wardman** (Australasia), **Jørn Schultz-Boysen** (Scandinavia), **Natasha Jovanovska Popovska** (Macedonia), and **Beverley Yamamoto** (Japan) were up for election – and new candidates were **Arianna Kitzinger** (Hungary), **Fernanda de Oliveira Martins** (Brazil), and **Ivana Golubovic** (Serbia).



All candidates presented themselves, and then the 40 full members of HAEi voted – either directly or by proxy. After thorough counting of the votes by the election controllers HAEi Communications Manager **Steen Bjerre**, US HAEA Director of Data & Automation **Leigh Farrar**, and Executive Committee member **Rachel Annals** the HAEi Executive Director declared that all five present Executive Committee members up for election had been reelected.

At the end of the General Assembly, the HAEi President stressed that everyone willing to work for HAE awareness is more than welcome to contribute. Naturally, that also goes for the three candidates that were not elected to the Executive Committee.

The General Assembly also voted on a resolution authorizing the Executive Committee to make changes to the HAEi Charter to fulfill these objectives:

- Broaden participation in HAEi Governance by establishing Regional Advisory Groups that correspond to areas covered by HAEi Regional Patient Advocates,
- Reduce taxes as HAEi currently pays income tax as well as VAT.

The General Assembly unanimously decided upon the resolution.

Shortly after the adjournment of the General Assembly the Executive Committee met and constituted itself with **Anthony J. Castaldo** as President, **Michal Rutkowski** as Vice President, **Alejandra Menendez** as Secretary, and **Fiona Wardman** as Treasurer.

## These countries were present at the General Assembly or voted by proxy:

- Argentina, Australia, Austria,
- Belarus, Belgium, Brazil, Bulgaria,
- Canada, Chile, Czech Republic,
- Denmark,
- Finland, France,
- Germany, Greece,
- Hungary,
- Iceland, Israel, Italy,
- Japan,
- Macedonia, Mexico,
- New Zealand, Norway,
- Peru, Poland, Portugal, Puerto Rico,
- Romania,
- Serbia, Slovakia, Spain, Sweden, Switzerland,
- The Netherlands, Turkey,
- Ukraine, United Kingdom, United States of America,
- Venezuela.



Venko Filipce

## Saturday 19 May 2018

### General Program

While the youngsters continued with their own program most of the day patients and scientists rejoined for a general program all Saturday.

First on the agenda was a keynote speech by the Macedonian Minister of Health **Venko Filipce** speaking about *"Take Control: Dealing with public authorities"*. Since taking office in December 2017, Mr. Filipce's priorities for the advancement of the health system have among others been the improvement of the condition and life of patients with rare diseases.

Previous years the program has included an insight into a number of HAEi member countries around the globe. However, as the organization has grown quite much since the conferences in 2014 and 2016, the organizers chose to give a status of the development via the HAEi Regional Patients Advocates. During Saturday's program, they presented a regional perspective on taking control as seen from South East Europe, the Mediterranean area, Central Eastern Europe, Middle East and Africa as well as Latin America. Highlights from these sessions can be found in a separate article in this magazine.

Next the program featured three keynote speeches under the mutual heading *"Take Control: the science of improving HAE care"*. Speakers were the conference co-chairs **Prof. Bruce Zuraw**, **Prof. Marco Cicardi**, and **Prof. Konrad Bork**.

Then followed the Danish motivational speaker **Mark Anthony** whose topic was *"Take Control: Stay motivated"*. Before giving the audience some tangible tools for their daily self-motivation, Mr. Anthony said that he was really the one that was very motivated by listening to previous speakers and talking to a number of the conference delegates before entering the stage. He did not do so while playing David Bowie's 'Heroes' but could very well have chosen to as he described the conference delegates as his new and true heroes.



Mark Anthony



In a Q&A session that has been a very popular part of previous conferences **Prof. Bruce Zuraw** distributed a large amount of questions among the HAE Experts of the panel: **Prof. Bruce Ritchie** (Canada), **Dr. Teresa Caballero** (Spain), **Prof. Anete S. Grumach** (Brazil), **Prof. Marco Cicardi** (Italy), **Prof. Konrad Bork** (Germany), **Prof. Henriette Farkas** (Hungary), **Dr. Hillary Longhurst** (United Kingdom), **Prof. Marc Riedl** (USA), **Prof. Markus Magerl** (Germany), and **Dr. Isao Ohsawa** (Japan).

Last to enter the stage were **Prof. Marc Riedl** and **Prof. Markus Magerl** speaking on the topic *"Take Control: Now and the future"*. Prof. Riedl concentrated on the development up until now, starting with the advice of Dr. Quincke and Dr. Dinkelacker (both from 1882). These physicians recommended regulation of way of life, resting, footbaths, purging of bowels, and activity of the vasomotoric nerves. Fortunately, things have developed a great deal over the last 136 years with testosterones and fresh frozen plasma (1960's), Danazol (1970's), pasteurized C1-INH (1980's), kallikrein inhibitor (2000's) as well as rhC1-INH and subcutaneous C1-INH (2010's) as some of the milestones.



Speaking about the possible future of HAE treatment Prof. Magerl among other things mentioned the BioCryst phase 3 study on an oral kallikrein inhibitor (BCX-7353), the Zenith study for an on-demand oral administration from the same company, CSL Behring's research into a subcutaneous, monoclonal antibody against FXIIa as well as Shire's subcutaneous, monoclonal antibody against kallikrein. Also, there is Shire's subcutaneous C1-INH (SHP616), an oral, small-molecule plasma kallikrein inhibitor (KVD 900) from KalVista, and Shire's Lanadelumab (SHP 643) under speedy review by the US regulators with an expected decision by August this year. Prof. Magerl also mentioned Ibio's attempts to produce C1-INH from plants.

Prof. Magerl concluded that given that new drugs are well tolerated and efficient this might mean a change in treatment paradigms with more treatment options and more room for individualization. From his perspective, the future will soon bring C1-INH for subcutaneous prophylaxis, kallikrein-antibody prophylaxis, and kallikrein tablet prophylaxis as well as kallikrein liquid for on-demand treatment, and FXII-antibody for prophylaxis.

After the closing remarks from **Anthony J. Castaldo** and **Henrik Balle Boysen**, the delegates had some time off to socialize before the conference dinner, also held at Hilton Vienna.

The official highlight video from the 2018 HAE Global Conference as well as videos from most of the presentations can be found at [www.haei.org/gc2018](http://www.haei.org/gc2018)

A great number of photos – official as well as those taken by delegates – can be found at [www.haei.org/gc2018](http://www.haei.org/gc2018)

## A website and a magazine is all in a day's work

Following the success of the first-ever youngsters' track at the 2016 HAE Global Conference in Madrid, Spain and not least the equally inaugurating Youngsters' Summer Camp in Frankfurt, Germany in August 2017 the 2018 HAE Global Conference introduced two full days of specific youngsters' activities.

After the opening of the conference, the youngsters' program started out Friday 18 May 2018 with the presentation "Creating a new Youngsters Community" by **Facundo Cabreros** (Argentina), **Natalie Galarrega** (Ecuador), and **Anna Bianchi** (Brazil). Following some time to get to know each other a little better HAEi Administrative and Marketing Assistant **Nevena Tsutsumanova**, Project Manager **Hannah Clarke**, Graphic Designer **Rikke Sørensen**, and HAEi Project Manager **Ole Frølich** introduced the weekend-long project of producing a website as well as a dedicated youngsters' magazine. In the afternoon HAEi President **Anthony J. Castaldo**, HAEi Regional Patient Advocate **Rashad Matraji**, and HAE patient **Yujin Yamamoto** visited the youngsters and spoke about "How I Took Control of HAE" – and the project work continued.

Saturday morning the 16+ participants started with a patient/physician talk lead by Prof. **Markus Margerl** and Prof. **Connie Kataris**, while the rest of the group went for a walk-and-talk with **Nevena Tsutsumanova** and **Hannah Clarke**. Afterwards, the youngsters up to 15 years met with the professors while the 16+ youngsters did the walk-and-talk. Later in the morning, the project work continued, and in the afternoon the program included topics like "Take Control of Your Game Plan" and "Taking Control: the HAEi Youngsters Community" before the youngsters joined the rest of the delegates for the official closing of the conference.

At the beginning of the conference dinner Saturday evening the youngsters presented the results of their hard work – a fully functional website as well as a youngsters' magazine.



You can see the youngsters' website at <http://haei.org/youngsters>  
Also, have a look at "Youngsters Voice" at <http://haei.org/youngsters/youngsters-voice>





Fiona Wardman



Sarah Smith Foltz

## What patients and family need to know about HAE

On the morning of the first day of the 2018 HAE Global Conference HAEi Executive Committee members, **Sarah Smith Foltz** (President of AEDAF in Spain) and **Fiona Wardman** (CEO of HAE Australasia) spoke about “*Take Control: What Patients and Family need to know about HAE*”.

These are the highlights from their presentation:

### (1)

- HAE types 1 and 2 are caused by a genetic defect that results in a deficiency of the blood protein C1 inhibitor.
- HAE with Normal C1 Inhibitor is being actively researched, and progress is being made to determine a biomarker for diagnosis and the cause of swelling for these patients.

### (2)

- HAE has an autosomal dominant inheritance pattern. It does not “skip” generations. One parent must have HAE to pass it along to a child.

### (3)

- In most cases, blood tests confirm the HAE diagnosis, and genetic testing is not required.
- HAE Expert Physicians recommend testing Complement Component 4 (C4) to screen for HAE.

### (4)

- HAE swellings are not caused by an allergic reaction.

### (5)

- That is why antihistamines, epinephrine, and corticosteroids such as prednisone do not stop or prevent HAE attacks.

### (6)

- HAE swelling is caused by the release of Bradykinin.

### (7)

- Swelling of the mouth, tongue, and throat are medical emergencies that require immediate attention.

### (8)

- Modern HAE therapies:
  1. **Cinryze™** brand of C1-INH (intravenous prophylaxis)
  2. **Beriner®** brand of C1-INH (intravenous acute attacks)
  3. **Firazyr®** brand of bradykinin receptor antagonist (subcutaneous acute attacks)
  4. **Kalbitor®** brand of plasma kallikrein inhibitor (subcutaneous acute attacks – only in USA)
  5. **Ruconest™** Recombinant Human C1-INH (intravenous acute attacks)
  6. **HAEGARDA®** C1-inhibitor (subcutaneous prophylaxis)

### (9)

- Extensive Ongoing Research:
  - **Shire** – long-acting subcutaneous treatment for prophylaxis (under FDA review)
  - **Pharming** – intravenous Ruconest for prophylaxis (under FDA review)
  - **BioCryst** – ongoing trials – oral treatments for prophylaxis and acute attacks
  - **CSL Behring** – long-acting subcutaneous humanized monoclonal antibody against Factor XIIa
  - **KalVista** – developing candidates for oral HAE treatments
  - **Adverum** – Adeno virus assisted gene therapy
  - At least five other companies working in the space.

### (10)

- Patient Organizations Create the Spark for Gaining Access to Therapies!
- Success is achieved by
  - Intelligent use of available resources – HAEi, physician advisors, local consultants, government officials, pharma companies.
  - Crafting a sound argument for HAE therapies by demonstrating the dramatic improvement in Quality of Life.
  - Sustained effort! You will lose some battles... stay in it and win the war

## Take control using advocacy tools

In their first mutual presentation on the first day of the 2018 HAE Global Conference HAEi President **Anthony J. Castaldo** and HAEi Executive Director **Henrik Balle Boysen** spoke about taking control of HAE through the use of advocacy tools. Stating the fact that patient empowerment and action through the national patient organizations is the key to a better future for patients and caregivers they focused mainly on these items in the HAEi Toolbox:

- HAE Global Patient Registry
- HAEi Global Access Program
- HAEi Connect
- HAEi Website Hosting
- [www.haeday.org](http://www.haeday.org)

As for the HAE Global Patient Registry Anthony J. Castaldo characterizes it as 'a unique and ambitious undertaking' that is based on a registry developed by Prof. Cicardi for patients in Italy:

"It is the first truly global rare disease registry that systematically collects on a global scale, highly accurate scientific data submitted by both physicians and patients."



Henrik Balle Boysen

Among the benefits of a global registry is that data from a large number of patients provides insights that are not seen in small sample sizes. At the same time, it provides evidence-based data on potential improvements in HAE standard of care as well as greater confidence in the validity of conclusions. Henrik Balle Boysen says:

"It enables robust analyses of treatment effectiveness and improvements in quality of life to support government and private insurance reimbursement decisions – and it can help in early detection of unexpected side effects or adverse events."

As for the HAEi Global Access Program, the speakers informed the delegates that the focus will initially be on markets served via Named Patient Programs in Eastern and Southern Europe, Asia, and Latin America.

HAEi Connect was described as a cloud-based free online membership database for HAEi's member organizations. It serves as a tool for the member organizations to build and grow their member database as well as handle and communicate with members. From the members' point of view, HAEi Connect can ensure them targeted information from their member organization and help them update their member information.

Supporting many languages both for administrators and for members HAEi Connect has a high level of data security. The system works with encrypted data communication, a two-factor login for administrators, and no storage of member passwords. Naturally, HAEi Connect is compliant with the EU General Data Protection Regulation (GDPR) introduced shortly after the end of the 2018 HAE Global Conference.

Anyone interested in the HAE Global Patient Registry, the HAEi Global Access Program, HAEi Connect or website hosting under the HAEi umbrella should reach out to their Regional Patient Advocate or send an email to [info@haei.org](mailto:info@haei.org).

## Take Control: A global HAE assessment

At the 2018 HAE Global Conference, HAEi President **Anthony J. Castaldo** and HAEi Executive Director **Henrik Balle Boysen** also presented a global HAE assessment.

Before the conference, a 13 question online survey was sent out to all member organizations, and 42 of them completed the survey, which addressed a variety of issues related to the management of HAE in their respective countries. In total, the study represents more than 15,000 patients around the globe.



Anthony J. Castaldo

"The most important challenges identified by our member organizations are access to – including reimbursement for – modern HAE medications, the impact on everyday life and education, work, social life, and lack of awareness of HAE", says Anthony J. Castaldo:

"In one-third of the countries, less than 50 percent of the patients have access to modern medication. In one-fourth of the countries only one out of 10 patients have access to modern medication, and in five countries patients have no access to modern medication. Furthermore, in six countries more than half of the patients are on a prophylactic therapy with attenuated androgens or tranexamic acid, while in 21 countries less than 20 percent of the patients are on a prophylactic therapy with attenuated androgens or tranexamic acid – and in only two countries attenuated androgens and tranexamic acid is not being used."

The survey shows that compliance with HAE guidelines has improved, but it remains a challenge.

- Only nine of the countries reported that 'almost all patients have two doses of acute HAE therapy available for on-demand use'
- 18 countries reported that 'more than 70 percent of the patients have two doses of acute HAE therapy available for on-demand use'
- Only 10 of the countries reported that 'almost all patients have a treatment plan in place' – and only seven said that 'almost all patients have an emergency plan in place'
- In 16 countries prophylactic therapy with one of the modern HAE medicines is not available.
- In 36 countries less than 20 percent of the patients are on prophylactic therapy with one of the modern HAE medicines.
- In 31 countries self-administration (home administration) is allowed based on product label and indication.

As for the need for awareness and education Anthony J. Castaldo says:

"69 percent of the countries rated the HAE knowledge physicians who treat HAE patients as 'Good' or 'Excellent', while 64 percent rated the HAE knowledge of the Emergency Room physicians as 'Poor' or 'Very Poor'. Furthermore, 76 percent of the countries rated the average physician's – including the family doctor – HAE knowledge as 'Poor' or 'Very Poor'."

### HAE impact on everyday life

On a scale of 0 to 5, how does HAE impact the everyday life of patients in your country?



On a scale from 0 to 5, to what extent does HAE limit patients in your country from fulfilling their life's potential (in school, at work, in social life)?



## Take Control: A regional perspective

Previous years the HAE Global Conference program has included an insight into a number of HAEi member countries. However, as the organization has become truly global the number of members has grown considerably, and for the 2018 conference, it made more sense to give a status of the development via the HAEi Regional Patients Advocates. In a couple of sessions Saturday, they presented a regional perspective on taking control as seen from selected countries in South East Europe, the Mediterranean area, Central Eastern Europe, Middle East and Africa as well as Latin America. Furthermore, members of the HAEi Executive Committee presented the situation in their countries. This is a quick rundown of the HAE status in the countries highlighted during the conference.



**Country:** Argentina

- **Organization:** Asociación Argentina de Angioedema Hereditario (AEH Argentina)
- **Number of patients:** Estimated 1,400 with 500+ diagnosed
- **Members of organization:** 448
- **Specialist physicians:** Expert specialists 2; good knowledge 8; acceptable knowledge 20-25
- **HAE centers:** None
- **Treatment:** Berinert, Firazyr, Danazol and tranexamic acid
- **Successes:** C1-INH treatment approved for more than 20 years; education and raising of awareness among the patient population
- **Challenges:** Optimum management of the disease (acute as well as home treatment); availability of other treatments; accessibility even with difficulties
- **Website:** [www.aehargentina.org](http://www.aehargentina.org)



**Countries:** Australia and New Zealand

- **Organization:** HAE Australasia
- **Number of patients:** Estimated 570 (Australia 480, New Zealand 90)
- **Members of organization:** 156 (Australia 139, New Zealand 17)
- **Specialist physicians:** 19 (Australia 15, New Zealand 4)
- **HAE centers:** 13 (Australia 11, New Zealand 2)
- **Treatment:** In Australia Berinert, Danazol, and tranexamic acid for prophylaxis and Berinert and Firazyr for acute attacks; in New Zealand Danazol

and tranexamic acid for prophylaxis and Berinert and Firazyr for acute treatment

- **Successes:** Good awareness of HAE but there is room for improvement
- **Website:** [www.haeaustralasia.org.au](http://www.haeaustralasia.org.au)



**Country:** Belarus

- **Organization:** HAO Беларусі (HAE Belarus)
- **Number of patients:** Estimated 250 with 41 diagnosed
- **Members of organization:** 53
- **Specialist physicians:** 10 specialist physicians (at least 1 in every state region)
- **HAE centers:** 2
- **Treatment:** Fresh frozen plasma for acute treatment; androgens for prophylactic treatment
- **Successes:** First national HAE patients summit; official registration of the national organization; a HAE-related session during the International Conference of Immunology Diseases in Minsk; HAE advocacy activities like press conferences, lectures, educational meetings, and publications
- **Challenges:** 80 percent of patients are still undiagnosed; access to the effective HAE medication



**Country:** Bulgaria

- **Organization:** HAEA Bulgaria
- **Number of patients:** Estimated 95
- **Members of organization:** 52
- **Specialist physicians:** 12
- **HAE centers:** 1
- **Treatment:** Berinert and Ruconest is approved for home administration – Firazyr is expected from 2019; prophylactic treatment is also available
- **Successes:** The changing of the laws regarding the list of professionals who have the right to treat HAE in hospitals and to be paid by the National Health Fund
- **Challenges:** The Level of HAE knowledge among most physicians is still unsatisfactory and inadequate; long periods of struggling as it usually takes 3 to 10 years to have a proper diagnosis
- **Website:** [www.hereditary-angioedema.org](http://www.hereditary-angioedema.org)



**Country:** Canada

- **Organization:** Hereditary Angioedema (HAE) Canada / Angioédème Héritaire (AEH) Canada
- **Number of patients:** 400 diagnosed of estimated 880
- **Specialist physicians:** 35
- **HAE centers:** 35
- **Treatment:** Berinert and Cinryze for acute attacks and prophylaxis, Firazyr for acute attacks, tranexamic acid for prophylaxis, and fresh frozen plasma for acute attacks
- **Successes:** Emergency Room physicians are aware of HAE (yet not always following HAE specialists' recommendations)
- **Challenges:** Other specialists (gastroenterologists, dermatologists, especially pediatrics) are lacking awareness
- **Website:** [www.haecanada.org](http://www.haecanada.org)



**Country:** Chile

- **Organization:** Fundación Angioedema Hereditario Chile
- **Number of patients:** Estimated 600
- **Members of organization:** 140 diagnosed
- **Specialist physicians:** Unknown
- **HAE centers:** Any emergency center will be able to assist patients throughout the country.
- **Treatment:** Berinert, tranexamic acid, and Danazol
- **Successes:** 85 tests carried out on hae day :-) 2016; 100 more tests carried out for free in 2017-2018; symposiums for immunological doctors in 2016 and 2017, round table discussion with representatives from the Ministry of Health; law on national funding for all patients with confirmed diagnosis of HAE type I and II
- **Challenges:** Confirmed diagnosis of patients; appropriate medication free of charge for all; patient's lack of interest
- **Website:** [www.aehchile.com](http://www.aehchile.com)



**Country:** Costa Rica

- **Organization:** AEH Costa Rica
- **Number of patients:** 15 diagnosed
- **Members of organization:** 30+
- **Specialist physicians:** 3
- **HAE centers:** None
- **Treatment:** Fresh frozen plasma as a treatment (at best) and Danazol as a prophylactic
- **Successes:** Increased public awareness; organizing a meeting on rare diseases with several associations; leading in the creation of national federation of rare diseases



**Countries:** Denmark, Norway, and Sweden

- **Organization:** HAE Scandinavia
- **Number of patients:** 440 diagnosed (Sweden 170, Denmark 140, Norway 130) of estimated 695 (Sweden 330, Denmark 190, Norway 170)
- **Members of organization:** 360
- **Specialist physicians:** Sweden 12, Norway 6-10, and Denmark 3-4 (but more a re treating)
- **HAE centers:** 8 (Norway 4, Sweden 3, Denmark 1)
- **Treatment:** Berinert, Cinryze, Firazyr, and Ruconest
- **Successes:** Knowledge is very good among specialists
- **Challenges:** Knowledge is low among general physicians
- **Website:** <http://haescan.org>



**Country:** Italy

- **Organization:** Associazione volontaria per l'angioedema ereditario ed altre forme rare di angioedema (A.A.E.E.)
- **Number of patients:** Estimated 1,000
- **Members of organization:** 708 (603 patients)
- **Specialist physicians:** Medical and Scientific committee made of 14 qualified physicians and many other researchers
- **HAE centers:** 14 certified centers but treatment is available in most emergency room hospitals
- **Treatment:** Berinert, Cinryze, Ruconest, and Firazyr for acute attacks; tranexamic acid, Danazol, and Cinryze for prophylaxes; not all regions allow all treatments
- **Successes:** The Italian HAE patient's registry and diary online; creation of a poster with main information on HAE, therapies in case of acute attack and a phone number for further information or in case of emergency
- **Challenges:** Spreading the knowledge about HAE
- **Website:** [www.angioedemaereditario.org](http://www.angioedemaereditario.org)



- **Country:** Japan
- **Organization:** HAE Japan
- **Number of patients:** 760 diagnosed of estimated 2,400
- **Members of organization:** 60
- **Specialist physicians:** 234
- **HAE centers:** 100
- **Treatment:** Berinert for acute attack and short-term prophylaxis; no modern long-term prophylactic treatments
- **Successes:** Media coverage has raised the level of awareness but it is still low
- **Challenges:** More awareness; access to modern medication
- **Website:** www.haej.org



- **Country:** Poland
- **Organization:** Pięknie puchnę
- **Number of patients:** 1,270 with 420 diagnosed
- **Members of organization:** 280
- **Specialist physicians:** 5 experts with 20 years of experience; 20+ experts with maximum 5 years of experience
- **HAE centers:** 1 national center and 15-18 medical sites on different levels, where HAE is recognized and patients would likely receive treatment
- **Treatment:** Berinert, Firazyr, and Ruconest for on-demand treatment (limited access); androgens (Danazol), tranexamic acid, and fresh frozen plasma for off-label treatment
- **Successes:** The national and Central Eastern Europe Conference has been the most successful activity so far
- **Challenges:** Correct diagnosis is difficult; patients will only be reimbursed if they experience severe abdominal and/or laryngeal attacks
- **Website:** http://haei.org/pl



- **Country:** Romania
- **Organization:** Asociația Pacienților cu Angioedem Ereditar din România (AEE Romania)
- **Number of patients:** Estimated 100
- **Members of organization:** 42
- **Specialist physicians:** 3
- **HAE centers:** 1
- **Treatment:** Danazol for prophylactic use; Ruconest/Berinert available in some Emergency Rooms but only for laryngeal and severe abdominal attacks

- **Successes:** Firazyr has been made available 100 percent reimbursed; creation and launch of AEE Romania web page allowing the association to connect to and inform more patients
- **Challenges:** Making Firazyr available for all patients as so far only association members have treatment
- **Website:** http://haei.org/romania



- **Country:** Spain
- **Organization:** Asociación Española de Angioedema Familiar (AEDAF)
- **Number of patients:** Estimated 1,000+
- **Members of organization:** 397 (323 patients)
- **Specialist physicians:** 18 allergists in the Spanish Study Group on Bradykinin-Induced Angioedema (GEAB)
- **HAE centers:** The allergists are divided among 12 major public hospitals; most major cities have at least one good treatment center
- **Treatment:** Specific HAE medicines are Berinert, Cinryze (for prophylaxis), and Firazyr while non-specific treatments are attenuated androgens (Danatrol) and tranexamic acid (Amchifibrin) for prophylaxis and acute attacks
- **Successes:** There is a high level of knowledge in the GEAB and a medium level among allergists in general; annual meeting and regional workshops; the HAEi/AEDAF Camino Walk in 2016 and 2017
- **Challenges:** No uniform standards and policies for diagnosis and treatment across regions; lack of patient involvement; Low level of knowledge especially in the Emergency Rooms
- **Website:** http://haei.org/angioedema-aedaf



- **Country:** Ukraine
- **Organization:** HAE Ukraine
- **Number of patients:** Estimated 860
- **Members of organization:** 36
- **Specialist physicians:** 4
- **HAE centers:** 1
- **Treatment:** Aminocaproic and tranexamic acid, Danazol, and fresh frozen plasma (only for adults)
- **Successes:** Patient meetings thanks to support from members and physicians;
- **Challenges:** Awareness of HAE including among patients; activity of patients; access to the medication
- **Website:** http://haei.org/location/hae-in-ukraine



- **Country:** United Kingdom
- **Organization:** HAE UK
- **Number of patients:** Estimated 1,500
- **Members of organization:** 470
- **Specialist physicians:** 36
- **HAE centers:** 33
- **Treatment:** Firazyr, Ruconest, Berinert, Cinryze, Danazol, Oxandrolone, and tranexamic acid
- **Successes:** Overall the UK has good knowledge of HAE
- **Website:** www.haeuk.org



- **Country:** USA
- **Organization:** US Hereditary Angioedema Association (HAEA)
- **Number of patients:** Estimated 6,000-6,500
- **Members of organization:** 5,900
- **Specialist physicians:** 14 HAEA Medical Advisory Board Members; 2,000 treating physicians
- **HAE centers:** US HAEA Angioedema Center at UCSD, various centers of the Medical Advisory Board Members, and treating physician practices
- **Treatment:** All modern therapies are approved in the US; prophylaxis and on-demand use considers the patient's life situation and treatment is decided in partnership with the treating physician
- **Successes:** The number of years to diagnosis has dropped from an average of 22 years to about 9 years
- **Website:** www.haea.org

- Furthermore, two of the HAEi Regional Patient Advocates – Patricia Karani (Sub Sahara Africa) and Rashad Matraji (Middle East, Gulf, and India) gave an insight into the overall situation in their regions:



- **Region:** Sub Sahara Africa – 49 countries (working in 5 presently)
- **Organizations:** 2 (HAE Kenya and HAE South Africa)
- **Number of patients:** Estimated 35,000 with 71 diagnosed
- **Specialist physicians:** 6 clinically trained medical doctors and 29 newly trained doctors
- **HAE centers:** 3 (South Africa 2, Kenya 1)
- **Treatment:** Danazol for prophylactic treatments; fresh frozen plasma, icabitan, and Ruconest (available in one country) for acute treatment

- **Successes:** 1st HAE African Doctors' Seminar in Kenya; 1st HAE patients' support group meeting in South Africa; participation in Kenya Pediatric Association Scientific Conference
- **Challenges:** Low levels of HAE awareness; no government priority for rare diseases; no modern HAE medications licensed; most patients are misdiagnosed leading to probable high mortality
- **Websites:** http://haei.org/haekenya and http://haei.org/southafrica



- **Region:** Middle East, Gulf, and India – 10 countries (working in all presently)
- **Organizations:** 1 (HAE United Arab Emirates)
- **Number of patients:** 240 diagnosed
- **Specialist physicians:** More than 10 clinically trained medical doctors that support HAEi
- **HAE centers:** None
- **Treatment:** Danazol for prophylactic treatments; fresh frozen plasma and C1 esterase inhibitor available in a few countries for acute treatment; medication is registered in Saudi Arabia and Qatar but not available recently due to shortage; some countries have no medication at all (not even Danazol)
- **Successes:** Meetings with physicians; raising awareness via the media
- **Challenges:** Low levels of HAE awareness; nationals and citizens have different access; little pharmaceutical support
- **Facebook:** www.facebook.com/groups/111656808988882 (Middle East)





## HAEi Jakobsweg Walk 2018

Following the two successful HAEi/AEDAF Camino Walks on the Camino de Santiago in northwestern Spain in May 2016 and May 2017, HAEi organized yet another walk – this time leading up to the HAE Global Conference in Vienna, Austria.

“Working on the preparation for the conference we found out that there is actually also a pilgrimage route – a ‘Camino’ if you will – going through the Austrian capital and connecting to the large system of routes leading to shrine of the apostle St. James the Great in the cathedral of Santiago de Compostela in Galicia in northwestern Spain. Furthermore, we found out that there is an organization in Vienna that would very much like to cooperate with us and this is how it all came together so the HAE pilgrims could walk the Jakobsweg in the days leading up to the conference”, says the HAEi Communications Manager **Steen Bjerre**.

Camino de Santiago, Way of St. James, and Jakobsweg are names in different languages for the same thing: A huge network of pilgrims’ ways leading to Santiago de Compostela, where tradition has it that the remains of Saint James are buried. Many follow its routes as a form of spiritual path or retreat for their spiritual growth. Traditionally, as with most pilgrimages, the Way of St. James began at one’s home and ended at the pilgrimage site, often following highly traveled routes through Europe. As it turns out one of these traditional routes goes right through Vienna – and that was the one the HAE pilgrims took.

“Some 70 HAE pilgrims set out for the first stage of 14.8 km from Jakobskirche near Vienna’s airport and to the Basilika in Kaisermühlen. Here some left the group while others joined and now approx. 85 pilgrims walked the 5.1 km to the Stephansdom in the center of Vienna. After a short ceremony and a blessing from Bishop Franz Scharl – in the middle of the enormous cathedral – there was a welcome break with drinks and finger food before some 90 people walked the last 5.5 km of the day leading to the Schönbrunn castle”, says Steen Bjerre.

The day after **hae day :-)** 2018 around 40 pilgrims walked the fourth and last stage from the Schönbrunn castle to Jakobskirche in Pukersdorf west of Vienna.

All in all the HAE pilgrims – patients, relatives, care-givers, doctors, nurses, industry representatives, and other HAE friends – took more than 3,000,000 steps for HAE awareness. In the words of HAEi Executive Committee member **Beverley Yamamoto**: “The walk is hugely valuable. Not only the publicity, but during the walk you get to talk to lots of people you would not usually have an opportunity to talk to. It helps to cement our HAEi family.”



The HAEi Jakobsweg Walk was organized in cooperation with the Austrian non-profit organization Verein Jakobsweg Wien. The President of the organization, **Stephan Aigner**, acted as guide during all four stages of the walk and he says:

“It was a great pleasure for us to be with the HAE people on the way of St. James in Vienna. Our bishop is still impressed about the organization and its people. Each of the group has a great character and a very personal story about to accept the fate.”



## Record-breaking HAE Global Walk 2018

In 2016 HAEi introduced the HAE Global Walk in order to raise awareness around the world. The first year some 12,000,000 steps were taken and in 2017 the number rose to 21,000,000+.

“The third edition of the HAE Global Walk took place from 1 April to 31 May 2018 and broke each and every record as 54,609,008 steps were taken by 4,262 people from 37 countries. That is 42,007 km or 26,102 miles – or more than one time around the globe. Well, if that isn’t truly global we don’t know what is. All the more we would like to thank everyone who walked for HAE awareness – in their home country or while traveling abroad. A short stroll around the block, a hike with friends and family or an actual HAE awareness event organized by themselves. HAE awareness comes in many forms – and this campaign proves to show that every step counts”, says HAEi Communications Manager **Steen Bjerre**.

“In total walkers from 37 countries were involved in the campaign. Some reported a few walks while others did a lot to organize local walks thus contributing significantly to the 2018 version of the HAE Global Walk. The ten countries with the most steps are Canada, Austria, Argentina, Peru, USA, Macedonia, Brazil, United Kingdom, Spain, and Denmark.”

With more than 9,000,000 steps the Canadians are very clear winners of this years HAE Global Walk when it

comes to contributing steps. As Canada has contributed approximately 3,000,000 steps more than number two Austria it is quite natural to ask how this was achieved. Here is the explanation from the HAE Canada Team:

“We are very proud of the many Canadians who put their best foot forward and participated in the HAE Global Walk. Thank you to everyone who contributed their time and energy to this global initiative. Canada came out on top boasting over 9,000,000 steps because of all the work that happened behind the scenes at HAE Canada.

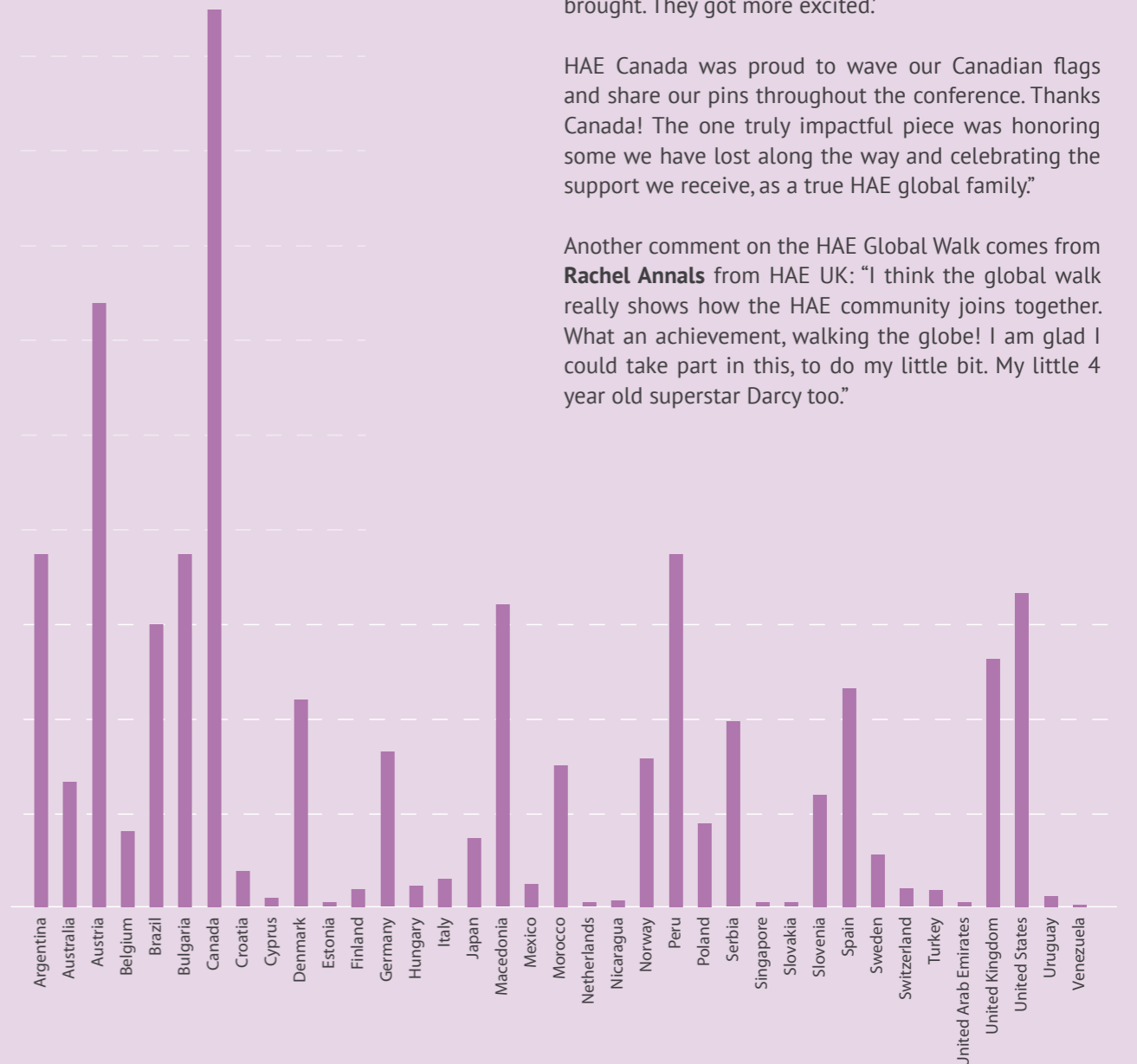
Firstly, our social media team, initiated by Jessica Howlett, repeatedly promoted the walk on Facebook, Twitter and Instagram, encouraging all Canadians to log their steps on [www.haeday.org](http://www.haeday.org). The HAE Canada Board of Directors also actively engaged different organizations who make a difference in the HAE community in Canada. Board members and staff emailed the HAE Global Walk’s link to the Canadian Hereditary Angioedema Network (CHAEN), who further sent to HAE specialists’ across the nation, Angio-oedème héréditaire du Québec/ HAE Quebec (AOHQ), our current and upcoming Canadian pharmaceutical sponsors, our staff, Daphne Dumbrille from the HAE Canada Office and Events Management Plus, along with allied partners, asking they log their steps to show support for HAE. HAE Canada is grateful that our requests were answered.

Some families, such as the Badiou and LeGras families, took things even further by involving their grandchildren and started family walking groups to clock their kilometers, making it truly a family effort. Having the Winnipeg Jets winning streak during the Stanley Cup finals helped them engage their Facebook friends. Challenging the Visser, Simon, Howlett, Feere/ Gunderson families brought out the Canadian pride and the race was on. The picture of Johnathan Howlett and his son tugged at everyone’s heart, as well as the Badiou sweethearts. When the HAE Canada Board posted their walking efforts on their Facebook sites, their Facebook friends took notice and walked along with them. Bob and Judy Simon shared how they helped with Canada’s steps: ‘Over the last few weeks we have been able to track approximately 5kms per day, with our thoughts going out to all that suffer, not only with the rare blood disorder of HAE but all disorders in this world and thoughts for a better day for all down the road.’

Jessica and Amanda Howlett walked the entire HAEi Jakobsweg Walk. Special thanks to Ken, Linda, Jacque, Richard, Charles St. Pierre, Tina Huk, Kari Feere and her daughter Paige Gunderson, Joseph Andolfatto & Lindsay Williams who also participated in the walk in Austria. Kari was particularly moved by her experience on her first conference walk: ‘My daughter Paige and I walked, sporting our Canada flags. It was my first conference and walk. We chose the first big leg of the walk, knowing it would be a huge challenge for us both as HAE patients, but we made it. It was a struggle, but worth it for all those who suffer with HAE around the world. Meeting other patients and even some local Vienna people along the way who were drawn to us from our flags and Canadian scarf I wore in my hair. They were so happy to know we came to their country. We also met a teacher with a group of young students. They were excited to see our flags so our group gave them the flags and some Canadian pins Ken and Linda brought. They got more excited.’

HAE Canada was proud to wave our Canadian flags and share our pins throughout the conference. Thanks Canada! The one truly impactful piece was honoring some we have lost along the way and celebrating the support we receive, as a true HAE global family.”

Another comment on the HAE Global Walk comes from **Rachel Annals** from HAE UK: “I think the global walk really shows how the HAE community joins together. What an achievement, walking the globe! I am glad I could take part in this, to do my little bit. My little 4 year old superstar Darcy too.”



## In memory of Pam King



*Pamala King, US HAEA*

Pamela Lee King, 51, died Saturday, June 16, 2018, from metastatic breast cancer, nearly 3 years after her initial diagnosis.

Pam served as a consultant and valued advisor to HAEi and the US HAEA for the past nine years.

Born in Syracuse, Pam grew up in Lewiston, NY. A gifted athlete in many sports, she attended Niagara University on a soccer scholarship. She finished her degree at the University of Buffalo, in marketing and communications. She began her career in pharmaceutical sales in Pittsburgh. She and her husband, Chris Pike, were married in 2001, and built their lives together in Jamestown.

An independent consultant in the medical field, Pam was a global strategic thinker, working with medical professionals, patient advocacy teams, pharmaceutical companies, and legislative lobbying groups to advance the development of better treatment options, insurance coverage and support for people living with an array of underrepresented diseases. She played an integral role in launching The US HAEA Angioedema Center at the University of California San Diego, helping to raise necessary funding and advising on their commitment to improve the lives of angioedema patients throughout the world.

Soon after being diagnosed with metastatic breast cancer, Pam reached out to METAvivor, an organization established to promote metastatic breast cancer awareness, research and support. Using her professional expertise for a very personal cause, Pam helped move the non-profit forward through her strategic planning in legislative efforts; in raising funds for research; and in securing grants from companies to continue the work of the volunteer-run organization.

Pam's life touched many. Friends from her childhood outside of Western New York; her early working career in Pittsburgh; the time spent in Toronto, where she met her husband; and from many cities in the United States and internationally where she travelled in her professional role, are experiencing the loss of this dynamic woman.

Knowing her life was coming to an end, Pam embarked on a cross-country road rally, with her husband, Chris and friends. Raising money for MBC research and awareness of the disease, Pam's last days were spent working for a cause she believed in. "I can sit at home and deteriorate," she said, preparing for the rally, "or I can go try to have fun. I choose to have fun!" Those who knew Pam King will appreciate knowing she did have fun.

Pam is survived by her much-loved husband, Chris Pike; her mother, Pat King; and her brother, Don King. Pam would also want her beloved dogs, Finn and Dodger, to be recognized. She was preceded in death by her father, Don King, with whom she had a very special connection.

A service will be held Saturday, August 4th, 1:00 PM, St. Mark Church, Jamestown, Rhode Island with a Celebration of Life to follow, 3:00 PM at the Conanicut Yacht Club.

Donations to METAvivor can be made on-line in Pam's honor here: <https://goo.gl/LPfPT4>.

If you prefer to make a donation by check, you can find the information you need here: <https://goo.gl/V2Rdwk>.



## HAEi Global Access Program

Helping to change the lives of patients with hereditary angioedema (HAE)

## News from around the Globe



### BELARUS [www.hereditary-angioedema.org](http://www.hereditary-angioedema.org)

19-21 April 2018 the Ministry of Health of the Republic of Belarus and Belarusian Research Center for Pediatric Oncology, Hematology and Immunology organized the International Immunology Conference in Minsk, the capital of Belarus. The two-day conference gathered approximately 150 attendees from Russian speaking countries of Eastern Europe. One of the most important issues for HAEi community was the separate session dedicated to HAE that took place during the second day of Conference.

HAEi Vice President and HAEi Regional Patient Advocate for Central and Eastern Europe Michal Rutkowski, together with Volha Puhach – the President of HAE

Belarus – gave a presentation on “The Importance of Patients Advocacy”. Michal Rutkowski was also involved in the presentation during the patients meeting, where HAE and PiD patients joined forces to enable improvement in the national advocacy efforts. Based on the recommendations of the HAEi Regional Patient Advocate, Prof. Henriette Farkas from the Medical University of Budapest, Hungary and Prof. Marcin Moniuszko from the Medical University of Bialystok, Poland were invited by the organizer to exchange, with the Belarusian Society of Immunologists, the international experience and approach to HAE.

### SERBIA <http://haei.org/rs>

On 21 April 2018, during the two-days National Preventative Pediatrics Conference, which gathered more than 250 pediatricians from the country and the region, HAE Serbia gave a presentation on the work of the organization and the current state of management of HAE in Serbia. Prof. Pasic, a world-renowned pediatric immunologist, and PID specialist moderated the session dedicated to HAE and gave a lecture on HAE in children. Dr. Dušanka Paskaš Marković spoke of laboratory diagnostics of HAE, and Dr. Andrejevic discussed HAE genetics and AE clinical characteristics. HAE Serbia wishes to thank Dr. Paskas Markovic who organized this important session and continues to support the organization's work to raise awareness of HAE among health care professionals in Serbia.



### CANADA [www.haecanada.org](http://www.haecanada.org)

From Paige Gunderson, HAE Canada youth member:

Greetings from HAE Canada! We are proud to say that our Board members have been very active advocating for HAE by attending many functions these last few months. In March, Jacquie, along with two members and staff attended the Canadian Organization for Rare Disorders (CORD)'s Rare Disease Day Conference and participated in Action Day on Parliament Hill to mark Rare Disease Day in Ottawa. A few weeks after the conference, Jacquie, along with fellow Board members, Richard, Ken, and Linda, traveled to Toronto to attend the Network of Rare Blood Disorder Organization (NRBDO)'s Spring Forum. Also in April, HAE Canada organized and hosted a successful and informative Patient Event in Hamilton, which was well attended. In Halifax, Board member Kari, along with a fellow HAE Canada member, participated at the Canadian Agency for Drugs and Technologies in Health (CADTH) Symposium: Supporting Appropriate, Affordable and Accessible Care. Across the country, HAE Canada member, Lorraine attended the Rare Disease Foundation “Feast for the Senses”, in Vancouver in April. Lorraine also traveled to Edmonton in May to attend a Patient Update Event that was hosted in conjunction with the Canadian Immunodeficiencies Patient Organization (CIPO). Also in May, Jacquie and Richard were fortunate to visit the newly renovated Manitoba Clinic and attend the Blue Skies Gala.



Furthermore, over 30 Canadians made their way to the 2018 HAE Global Conference in Vienna, Austria. We are pleased and proud that so many Canadians had the opportunity to attend this event.

We are recruiting for clinical trials for youth and adult HAE patients with Type 1 and Type 2, which is exciting news for future treatments in Canada. We are also in the process of preparing to offer a youth membership, which we have not had thus far.

### EGYPT [www.facebook.com/HAE-Egypt-374132739770843](http://www.facebook.com/HAE-Egypt-374132739770843)

Earlier this year HAE Egypt opened a page on Facebook – please have a look at:

[www.facebook.com/HAE-Egypt-374132739770843](http://www.facebook.com/HAE-Egypt-374132739770843)





## SWITZERLAND

[www.hae-vereinigung.ch](http://www.hae-vereinigung.ch)

The 19th HAE patient meeting of HAE Switzerland took place 9 June 2018 in the Swiss Museum of Transport in Lucerne. The meeting was attended by some 50 people listening to exciting lectures by HAE experts as well as a presentation by a company offering support in home therapy. After a fine lunch, the museum has arranged two interesting tours on the subject of cars and air. HAE Switzerland would like to thank the pharmaceutical companies for sponsoring the meeting.

Over the last half year, the board of HAE Switzerland has been working on the new member flyer, and it was presented at the meeting. The new flyer should serve the purpose of addressing new stakeholders and expanding the network of the association. This is to improve the exchange between members, disseminate information, and make HAE better known.



## SOUTH AFRICA

<http://haei.org/southafrica>

Right after the 2018 HAE Global Conference HAE South Africa added a Facebook page to the organization's communication – please have a look at

[www.facebook.com/hereditaryangioedemasouthafrica](http://www.facebook.com/hereditaryangioedemasouthafrica).



## KENYA

<http://haei.org/haekenya>

HAEi President Tony Castaldo and HAEi Regional Patient Advocate for Sub-Saharan Africa Patricia Karani were guest speakers at the Annual Meeting of the Kenya Paediatric Association in Mombasa, Kenya earlier this year. They took full advantage of this unique opportunity to raise HAE awareness and point out that pediatricians are the ones who can make an early diagnosis because most patients have swelling symptoms in childhood.



## UNITED KINGDOM

[www.haeuk.org](http://www.haeuk.org)

From Laura Szutowicz, CEO of HAE UK:

Some 30 members from the UK attended the 2018 HAE Global Conference in Vienna, which was a fantastic event! Many thanks to Tony, Henrik and all the team for organizing and facilitating the 'long weekend' meeting. We are all very grateful for the opportunity to meet so many people from so many countries, and I think some lasting friendships have been made.

Amongst the UK group were our two Youth Ambassadors, Alex and Jack, who came back from the youngsters' track positively buzzing with ideas for us to implement here in the UK.

As always, the presentations were inspiring and particularly interesting is the new research coming out almost continually to improve diagnosis, understanding and treatment of HAE.

Here in the UK, I have been busy this spring with various rounds of the commissioning process to ensure good supply and equal access to all available HAE medication across England, Scotland, and Wales. This hopefully means that there will be adequate supplies for all our patients for the next few years, although there is always the risk that a supplier will have a manufacturing problem with a batch of product, which then causes a shortage. This is one reason why I try to ensure that the complete range of products are available for clinicians to prescribe so that the risk of shortage is minimized. The commissioners are sometimes a little difficult to persuade on this, as they tend to try to reduce the number of products available to keep prices down, so some of my meetings become quite exciting! I am fortunate that I also have great back up from the clinicians in the UK with several also attending the meetings to put our case.

A new initiative this spring, kindly supported by Pharming, was the inaugural meeting of what we hope will become a UK-wide network of HAE experts. It was the brainchild of Dr. Patrick Yong from Frimley Park and Royal Surrey County Hospitals and is to eventually ensure that there is at least one HAE expert in each locality who can ask as an expert resource for other clinicians and will also head up research and clinical work. The first meeting was very well attended with nearly all the invited clinicians able to attend. I look forward to the next one now that the foundations have

News from around the Globe

Other activities HAE UK have been involved in included Rachel's idea of a video presentation. She has been developing this for some time, collecting stories and photographs and working with the production company to put it all together. She also found the soundtrack, which is by Moby who allows free use of his work for this type of project. We want to celebrate the courage and achievements of our members who will not let their HAE get in the way of the 'Perfect Life'. You can view the video at [www.youtube.com/watch?v=HMw89bG5lk8](http://www.youtube.com/watch?v=HMw89bG5lk8). I am sure you will agree that Rachel and our contributors have made a really inspirational film.

Some of you may have seen on Facebook that the HAE truck has been spotted several times.

Thanks to Ray for organizing this and to Ford for allowing the use of their vehicle.

Declan McComb cycled 55 miles around Essex on 9 June for HAE UK. We are so lucky to have people like him who will give up their time and muscle power to raise money and awareness for us. It really does pay off – every time someone does something like this we get increased inquiries for information by phone and on the website.

We now have a date and venue for our National Patient Day. This annual event will take place on 17 November 2018 with the evening before again being a social event for people to get to know one another. The venue is the Mercure Bush Hotel, Farnham, Surrey. Further details will be sent to all HAE UK members in the coming weeks. We look forward to seeing you there.

We are also returning to Scotland for a Patient Day, but have yet to confirm the date.

Another new entry to Facebook comes from HAE UK: 'Young HAE UK' is a social group for young people in the UK (up to the age of 22) who suffer from HAE. Alex Graham is the administrator of the new group. Please have a look at [www.facebook.com/groups/1581929458775712](http://www.facebook.com/groups/1581929458775712).

## News from around the Globe



### MACEDONIA

<http://haei.org/haemacedonia>

#### Natasa Angjeleska from HAE Macedonia writes:

HAE Macedonia is embarking on yet another exciting journey with the HAE Caravan. Beginning 24 March 2018 the HAE Caravan – a series of lectures on HAE for the general practitioners and emergency room staff – encompasses several cities in Macedonia.

“Patients and physicians should forge a strong bond, a type of a fortress to fight against all the administrative hurdles and obstacles”, Prof. Vesna Grivcheva Panovska, MD said in her address at the HAE lecture in Probishtip. This lecture was the first of several accredited lectures



within the HAE Caravan. “I knew most of the problems that Macedonian patients have been facing throughout years, but it is only recently that I became fully aware of just what they managed to overcome. Having been involved for several months in the Rare Disease Committee and into shaping Macedonian health policies about rare diseases, it has become clear to me that both patients and physicians need to stand together and face all the challenges together”, she added.

The first lecture was very engaging and motivating as Prof. Grivcheva Panovska provided solid information and stimulated doctors into asking interesting questions, which on the long run might be life-changing for some undiagnosed patients who might be struggling in smaller towns in Eastern Macedonia.

The purpose of the lectures in the following months is to raise awareness among the medical population on this disease and possibly find other HAE patients who might be struggling without proper diagnosis. The Medical Chamber of Macedonia accredits the lectures. Posters and brochures are distributed in hospitals and emergency rooms throughout Macedonia.

Natasha Jovanovska Popovska, the president of HAE Macedonia and Prof. Grivcheva Panovska were guests on several media such as the national Alfa TV. They explained this disease to the general public, talking about the symptoms and treatments as well as about the ongoing activities of HAE Macedonia. Furthermore, they emphasized the importance of educating primary health care physicians and other medical personnel.

In anticipation of **hae day :-)** 2018, HAE Macedonia organized a creative workshop for the youngest ones. We feel that children should be taught compassion and empathy from the earliest days. It can best be taught if they “experience” how their friends with HAE feel first hand. By using dough, they were trying to draw, write and play with a ball to try and get what it feels like to do all that with a swelling on their hand. They learned to rap a song about HAE, drew a swollen part to the body of their favorite animal or a superhero and learned to share something nice by making a friendship bracelet and giving it to their friend while receiving a friendship bracelet in return. The whole event happened in a friendly, exuberant and vibrant atmosphere and we can't wait to do something like this again next year, as many children requested!

On 16 May I was invited on one of the national TV stations in the prime news time to speak about patients with HAE, symptoms, and therapies, activities of HAE Macedonia and the HAE Global Conference in Vienna, Austria.

Six representatives from HAE Macedonia participated at the HAE Global Conference. We are thrilled that Natasha Jovanovska Popovska was re-elected as a member of the Executive Committee of HAEi and will thus be able to continue her dedicated work together with all members of the committee to work on improving conditions for all patients globally.

Also, it was our pleasure to invite and welcome the Minister of Health in Macedonia, Dr. Venko Filipce, who addressed the audience at the conference. In the six months that he has been a minister, HAE Macedonia has succeeded in having constructive collaboration, and as a result, we have increased the number of therapies available for our patients, although there are gaps and challenges for resolving in the future. However, with his inspirational speech at the conference, and his openness to cooperate with patients, doctors and pharmacies, he leaves a positive impression and gives hope that things might drastically improve in the legislation and care for rare disease patients, including HAE.

At the conference, Dr. Grivcheva Panovska had a presentation in the scientific track talking about lessons learned from assessing anxiety and depression in HAE patients' family members and caregivers.

The HAE Macedonia team participated at the 2nd edition of a very popular marathon in Ohrid, a popular tourist destination in Southwest Macedonia, called “Ohrid trchaT”. Four members, two of them HAE patients, ran a 5 km race in a group for rare disease patients, that at the end was announced to have the best result as a group. It was a special moment for the vice-president of HAE Macedonia, Verche Jovanovska Jankovska to receive a birthday cake just before the race and receive felicitations from the host organizer Gordana Loleska together with all others from the rare disease group runners, as her birthday was on the same day as the race.



**SCANDINAVIA**

[www.haescan.org](http://www.haescan.org)

In the fall HAE Scandinavia will be arranging three patient meetings. One in Norway (24 November in Ålesund) where Dr. Robert Brudevold will be the main speaker, and two in Sweden (6 October in Stockholm and 10 November in Malmö), where Dr. Patrik Nordenfelt will be the main speaker.

HAE Scandinavia will have its annual general assembly in Denmark on 3 November 2018.

HAE Scandinavia has recently completed a survey and report about the Quality of Life and Burden of Illness

living with HAE. This report will be published in the early fall.

Together with its Medical Advisory Panel, HAE Scandinavia is also preparing a "Principles of Care" document that is intended to secure Scandinavian patients with the best modern treatment options.

Other initiatives on securing patient access to medication will follow later in the year.

Finally, HAE Scandinavia has announced that its 2019 Scandinavian Conference will take place in Oslo, Norway 8-10 November 2019.



**BRAZIL**

[www.abranghe.org.br](http://www.abranghe.org.br)

The first six months of 2018 have been really busy for ABRANGHE (HAE Brazil). In March the organization attended a conference on rare diseases in Sao Paulo, followed by 'IV Caminhada de Doencas Raras' as well as a seminar on rare diseases in Rio de Janeiro. Then came another meeting on rare diseases in Cinelandia in March as well as a Shire workshop in Sao Paulo early May. A large group of patients, caregivers, and doctors

participated in the HAE Global Conference in Vienna, Austria – and in Brazil a number of patient meetings and other arrangement took place on and around hae day :) 2018: Brasilia 14 May, Carmo de Rio Claro, Campinas, Rio Preto, Salvador, Vitória, and Bacabal 16 May, Rio de Janeiro 17 May, Fortaleza 27 May, and Belo Horizonte 30 May. Also, a major meeting on rare diseases was arranged in Sao Paulo in the second half of May.



**CZECH REPUBLIC**

[www.hae-imuno.cz](http://www.hae-imuno.cz)

**From Camelia Isaic, HAE Czech Republic:**

Czech patients with HAE, their families, and physicians for the first time had an opportunity to participate in an educational seminar dedicated to HAE. This meeting took place as a part of the annual patients' meeting for patients with primary immunodeficiencies and was organized by MeDitorial agency with sponsorship provided by Shire. The event was held 9-10 June 2018 in Hotel Jezerka by the beautiful lake Sec. The HAE track agenda was prepared under the supervision of MU Dr. Marta Sobotkova from the HAE Center at the University Hospital Motol in Prague, with the participation of medical experts from all HAE centers in the Czech Republic (Brno, Plzen, Prague and Hradec Kralove). In addition to learning more about HAE diagnose and treatment from doctors, Czech patients and their families also had an opportunity to attend two patient-

led presentations: one introducing the Association of Patients with Immunodeficiency HAE/AAE (presented by Mrs. Iveta Maselli) and another one on "Living with HAE: Inputs from the 2018 HAE Global Conference in Vienna 2018" (presented by myself). The feedback from all attendees was overwhelmingly positive; patients greatly appreciated the opportunity to meet and learn more about HAE. Parents of HAE-diagnosed children showed great interest in the latest pediatric therapies and the new HAEi programs for youngsters. At the end of the event, all participants from both the Primary Immunodeficiencies and the HAE program tracks marked the moment by letting dozens of colorful balloons fly away: a beautiful and memorable group photo opportunity!



**CHILE**

<https://www.aehchile.com>

The Ministry of Health in Chile has issued a protocol regarding treatment with C1 Esterase Inhibitor for HAE type I and II, focusing on the granting of benefits for diagnoses with high-cost therapies. This means that soon patients throughout the country will have free medication for their crisis.

## News from around the Globe



USA

www.haea.org

### From Michelle Cuevas, HAEA Director of Communications:

May was an exciting month as our US patient community came together in so many different ways to raise awareness for **hae day** :-) 2018. Every event to raise HAE awareness, drive research, and raise funds to benefit HAEA programs for our community moves us closer to living healthier, happier, and normal lives. The following are just some of the amazing events that took place and that showcase how the HAEA continues to Stand Up Strong for HAE:

**HAE Global Conference:** Over 150 patients, family members, and caregivers from the US attended the 2018 HAE Global Conference in Vienna, Austria where they joined a total of 730+ delegates from 57 countries to learn more about how to "Take Control of HAE".

### Man Cave Show

*Participants:* 500+

*Organizers:* Abby & Ollie Mallory

*Event location:* Hamilton, Ohio

*Description:* A show dedicated to outdoor activities. Ollie & Abby set up a booth to create awareness and promote their golf outing.

### Elda Elementary Mom's Night Out

*Participants:* 400+

*Organizer:* Stephen Mallory

*Event location:* Elda Elementary, Ross, OH

*Description:* Movie night at an elementary school. Stephen set up a booth to spread HAE awareness and promote his upcoming golf outing.

### Cincinnati Reds Opening Day Parade

*Participants:* 45 participants on the float

*Organizer:* Mike Mallory

*Event location:* Cincinnati, OH

*Description:* 99th annual parade to celebrate the first Red's home game and the official kickoff to the baseball season. The parade float included several members of the HAE Youth Leadership Council as well as local HAE patients, caregivers, and friends.

### HAE Ribbon t-shirt sale

*Participants:* 200+

*Organizer:* Dakota Thompson

*Location:* Kernersville, NC

*Description:* Over 200 HAE T-shirts sold and shipped in time for hae day :-) 2018.

### HAE Awareness Race

*Participants:* 50

*Organizer:* Luci Toman

*Event location:* Strasburg, VA

*Description:* Electric Slot Car Drag Race event to fundraise and increase HAE awareness.

### HAE Abby Glow golf

*Participants:* 65+

*Organizer:* Mike & Missy Mallory

*Event location:* Cincinnati, OH

*Description:* Fun-filled night golf outing to fundraise and raise HAE awareness.

### Lyndon's Walk across America

*Participants:* 70+

*Organizer:* Lora Moore

*Event location:* Cullman, AL

*Description:* 7th annual event to raise HAE awareness and funding for research in memory of Lora Moore's daughter, Lyndon Brooke Stidham. Cullman was the first stop on Lyndon's Walk Across America for HAE.

### Show your swell 5k

*Participants:* 100+

*Organizer:* Chris Koepp

*Event location:* Liverpool, NY

*Description:* Annual 5k Organized by Chris Koepp in memory of his father, who passed away from HAE.

### Medical Group Presentation

*Participants:* 125 ICU Critical Care Nurses

*Organizer:* Crystal Lewis

*Event location:* Mobile, AL

*Description:* Presented a 60-minute talk on acute pharmacologic management of non-allergic angioedema at the American Association of Critical Care Nurses National Teaching Intensive Conference.



### Fundraising and Spreading Awareness for HAE

*Participants:* 50+

*Organizer:* Maude Devine

*Event Location:* Alpharetta, GA

*Description:* Created a personal fundraising page to share with family, friends, and co-workers to raise awareness and funds for HAE - see [www.haea.org/ci/page/event/34](http://www.haea.org/ci/page/event/34)

### Wear Jeans for Rare Genes

*Participants:* 200+

*Organizer:* Carlie Dalgo

*Event location:* Luling, LA

*Description:* Carlie Dalgo held an event at her school and a bake sale to raise awareness and funding for HAE.

### Wouldn't it be swell to find a cure

*Participants:* 100+

*Organizer:* Maddie F

*Event Location:* Pittsburgh, PA

*Description:* Tables set up during her school lunch break to spread HAE awareness.

### Brooks Life Sciences Services Town Hall Meeting

*Participants:* 200+

*Organizer:* Tina Agnew

*Event Location:* Indianapolis, IN

*Description:* HAE awareness event at her place of employment.

Over 200 emergency room kits and Advance HAE info kits have been sent out this year to be distributed at local emergency facilities. Kits are still available, so order at [www.haea.org/ERkit.php](http://www.haea.org/ERkit.php) or <https://www.haea.org/AdvanceHAEInfoKit.php>

You can help us raise awareness and funds for the HAEA's programs for those living with HAE. Creating and hosting an event is a fun way to build new relationships, educate others about HAE, and strengthen your HAEA community's voice.





## COSTA RICA

[www.haei.org/location/hae-in-costa-rica](http://www.haei.org/location/hae-in-costa-rica)

### From Lisa Layera, HAE Costa Rica:

Costa Rica's HAE Association proudly supported HAE patient Isabel Gonzalez in her fight to secure C1 inhibitor concentrate treatment for her 10-year-old daughter via a constitutional challenge. Mrs. Gonzalez' daughter was denied treatment twice by the Central Committee of Pharmacotherapy despite two separate unanimous votes by a dozen Costa Rican physicians in favor of her daughter receiving C1 inhibitor treatment.

Mrs. Gonzalez submitted an action of protection for her daughter's constitutional rights to the Constitutional Chamber of the Costa Rican Supreme Court. Part of the submission included a 35 entry long bibliography of key HAE research papers as well as making the case for efficacy and safety of the drug being requested. Costa Rica's Supreme Court was the first in the world to declare that they would make their rulings using evidence-based medicine. We are very grateful to HAE experts around the world who continue to publish to the highest of standards. If the challenge is won, it will be due to the evidence provided by HAE patients in clinical trials and compiled by HAE experts – we thank you.

One of our current projects includes working towards confirming new hospital protocols for HAE patient treatment at three major hospitals and requesting that a care center is designated for HAE patients.

This month Dr. Sergio Castro, specialist in oral pathology and maxillofacial medicine, will travel to Mexico to attend an HAE Symposium hosted by patient, physician and HAE advocate, Dra. Sandra Nieto. Dr. Castro was sponsored by the University of Costa Rica to receive this HAE training. Furthermore, Dr. Castro will be hosting an HAE track at the College of Dentistry's XIV National and International Congress for Dentistry in 2019 (CONGRESO NACIONAL E INTERNACIONAL DE ODONTOLOGÍA) hosted by the Faculty of Dental Surgeons of Costa Rica.



## RUSSIA

[www.fondpodsolnuh.ru](http://www.fondpodsolnuh.ru)

After the 2018 HAE Global Conference in Vienna, the HAEi family became larger due to the fact of enrolment of a new member organization in Russia called (in English translation) "Interregional public organization - Society of patients with Hereditary Angioedema", which consolidates patients with HAE, providing assistance in addressing the issues of treatment and prevention of the disease, as well as ensuring supply of modern therapies for patients. This is another important step forward for HAEi that brings new patients and member organizations from Eastern Europe.

Furthermore, the new society organized the Second All-Russian Conference of Patients with Hereditary Angioedema "The Right to Life" that took place in Moscow 18 June 2018. This event has gathered patients, scientists, physicians, lawyers, and psychologists dealing specifically with diagnosis and treatment of HAE. If you would like to know more about the conference and the patients' organization itself, please contact the organization at [79167260021@yandex.ru](mailto:79167260021@yandex.ru).



## AUSTRALASIA

[www.haeaustralasia.org.au](http://www.haeaustralasia.org.au)

### From HAE Australasia CEO Fiona Wardman:

It was great to be part of the HAE Global Conference in Vienna and have so many Australasians in attendance.



We had a great time walking the Jakobsweg, and we also captured some short videos of our attendees' impressions, which will be available on [www.haeaustralasia.org.au](http://www.haeaustralasia.org.au) very soon.

Over the last few months, we have held HAE Healthy Minds Workshops and Meet Ups in Auckland and Sydney. Facilitated by a clinical psychologist, the workshops are a great way for patients and carers to learn how to best cope with their HAE. We ran consecutive adolescent and adult workshops, and from the feedback, we received from everyone who attended felt they benefited in taking part. Both Meet Ups were in an informal setting over lunch after the workshops. Patients and carers were able to gain support, education, and resources. HAE Australasia would like to thank The Sisters of Charity Foundation, CSL Behring, and Shire for supporting these events.

After a slight delay, HAE Australasia will be going live with HAEi Connect. We look forward to patients being able to update their data and sending out information with ease. If any of our HAE Australasia members haven't received an email, please contact [fiona@haeaustralasia.org.au](mailto:fiona@haeaustralasia.org.au).

News from around the Globe

We have also been busy writing funding and grant proposals. Fundraising via community grants is continuing.

HAE Australasia has announced that our next conference will be on the Gold Coast, Queensland on 13-14 April 2019. The conference will focus on the genetic aspect of HAE and supporting kids and their families with HAE. Presenters (including world-renowned Australian and international HAE specialists) will provide education, research information, and treatment updates, and discuss how genes play a role in HAE, pre-implantation testing for HAE, provide HAE education to children and much more!

In our continued work to provide education, awareness and locate patients, HAE Australasia will be again taking part in the Australasian Society of Clinical Immunology and Allergy (ASCI) Conference, and we will also be advertising in a medical publication to gain access to a wider medical audience.

On 22 July, our CFO Louise will take part in a Stadium Stomp. Louise is raising awareness as well as raising funds for HAE Australasia. The event will be held at the Melbourne Cricket Ground, and she is already able to 'smash' 7,300 stairs in 1.5hrs! This is an incredible effort for someone with HAE. You can support Louise and HAE Australasia by following <https://stadiumstompmcg2018.gofundraise.com.au>. We would also like her to stay on top of the leaderboard of 'top individual fundraiser'! Good luck, Louise – we know you will continue to stomp it!

## News from around the Globe

### POLAND

<http://haei.org/pl>

#### From President Michal Rutkowski, HAE Poland:

The Polish HAE patients' organization (in English translation "Swelling Beautifully") continues its efforts of increasing the awareness of HAE among patients, caregivers, and healthcare professionals by organizing numerous different activities. The Regional Patients Workshops – the event where patients have an opportunity to extend their knowledge on the disease, as well as get to know how to self-administer – are already very successful, and since the beginning of 2018, we have been able to attract more than 90 patients to these significantly important reunions. The latest workshops were:

- 12 May 2018: Regional Patients' Meeting in Kraków (South Poland) with 18 patients, five healthcare professionals, two caregivers and three pharmaceuticals representatives;

- 16 June 2018: Regional Patients' Meeting in Wrocław (South-West Poland) with 11 patients, three healthcare professionals, and two caregivers.



Until the next edition of "Global Perspectives", another three Regional Patients Workshops are planned.

On 16 May 2018 we celebrated **hae day :-)** together with Shire. I gave an educational presentation on the "Importance of Patients' Advocacy" in front of approximately 50-60 Shire employees at Shire's CEE office in Warsaw. Also, Shire had encouraged their employees to take part in the HAE Global Walk by organizing a specific event in one of the leading fitness clubs in Warsaw. Furthermore, "Swelling Beautifully" and Shire agreed to collaborate on another awareness project in the area of HAE that is initially planned to launch in late July/early August 2018.



The most important event of 2018 so far has been the HAE Global Conference in Vienna. We are proud to announce that due to the enormous effort of many people "Swelling Beautifully" was represented by 18 patients and seven physicians. The importance of this meeting was significant, as the patients and invited physicians could experience and understand how meaningful it is with close teamwork and how powerful patients' organizations are in the area of HAE. Also, I am happy to say that the general assembly of HAEi decided to reelect me to the Executive Committee – and afterward I was reelected as HAEi Vice President. Finally, we would like to thank everyone who contributed and helped "Swelling Beautifully" in coming to Vienna in such a big number. Stronger together ...

"Swelling Beautifully" is privileged and honored to invite you to the 5th HAE National Conference that will take place 27-28 October 2018 in Warsaw. The two days of conference will gather approximately 170 participants from 12 CEE countries, including patients, caregivers, healthcare professionals, and as always world-class scientists and physicians. The program is expected to be full of the latest news regarding HAE and several projects that enable patients to live with a better quality of life, as well as enable physicians to provide better solutions for the patients. This year theme of the conference is "No Swelling". The official website of the conference will be launched at the beginning of July, and you can follow it and register for the event at [www.haeceec.org](http://www.haeceec.org).



## News from around the Globe

### JAPAN

<https://haej.org>

#### From President Beverley Yamamoto, HAE Japan:

HAE Japan (HAEJ) has completely renewed the website at <https://haej.org>. The new look for the website is attracting far more attention than the old one. At the moment the site is only in Japanese, but it is very visual, so please take a look.

A video recording that we made for **hae day :-)** has been uploaded on the website with English subtitles – you will find it at <https://haej.org/about-haeday>.

We have developed a small pamphlet to raise awareness about HAE in Japan and to help newly diagnosed patients access up-to-date information about their condition.

On 9 May 2018 Shire launched a new application for Japanese patients to record their attacks and family history among other things. This application was developed in close collaboration with HAEJ and our

medical advisory team. We assessed the needs of patients by taking an ethnographic approach to identify what was important to end-users. We expect that this application will help patients in Japan communicate better with doctors about the frequency and nature of attacks.

We are continuing to work with Osaka University and University of Oxford in the development of HAE related pages for the patient-centric initiative (PCI) RUDY, which aims to improve treatments for rare diseases through patient-driven research. More information at <https://rudypatient.info> and <https://research.ndorms.ox.ac.uk/rudy>.

Finally, 15 patients and caregivers, and two physicians from HAEJ attended the HAE Global Conference in Vienna.



## Delegates' evaluation of the 2018 HAE Global Conference

Following the 2018 HAE Global Conference in Vienna, Austria HAEi asked the participants to complete a conference evaluation survey. These are the first output from the survey:

**92% found the conference 'extremely useful' or 'useful'**

**95% of attendees would attend another global conference**

**95% would recommend the conference to others**

HAEi asked the conference delegates to put their impressions into words and here are just a few of the many comments:

- I loved my very first global conference, met some great people from other countries, learned some great information about the research of HAE and exploring Vienna was wonderful too.
- It was spectacular, informative, fun and life-changing.
- The conference was a great opportunity to interact with other patients, doctors, lab representatives and other people of the HAE world. It was an enriching and motivating experience that helps us really think of how much control we can have over HAE if we keep updated and connected with others.
- An extremely well organized and attended the event. It is so encouraging to see so many HAE patients and caregivers from all over the world gathering together to learn, share and support each other. Thank you HAEi for the opportunities you have given us.
- The global conference is a great opportunity to learn from physicians, caregivers, and patients in other countries and the successes and challenges of managing their HAE.
- This conference brought knowledge that is priceless to me as a caregiver for my daughter. My daughter gained an amazing support group from the youth program! I left the conference feeling like I wanted to be more involved! Amazing conference that we truly feel honored to have been part of!
- The global conference is for HAE patients, caregivers and providers who want to embrace the challenges of HAE and create a legacy of empowerment, connectedness, and fun.
- Attendance at the global conference not only helped open new doors for personal growth and coping skills but gave an opportunity to meet others from around the world and make new friendships

## Working on a unified voice for HAE patients in South Korea

### From Executive Committee member Fiona Wardman

With HAEi's continued work to help HAE patients around the globe, HAEi President Anthony J. Castaldo and I had the pleasure of visiting Seoul, South Korea, for a meet and greet to establish what can be done to help this country's patients receive earlier diagnosis, and gain access to funded treatments.



Most of Asia is "untapped" when it comes to diagnosis and available treatments for HAE patients, and along with this, there are language and cultural obstacles that need to be considered and overcome.

South Korea is a wealthy, vibrant, modern and traditional country, which has a population of around 50 million people, and Seoul alone has approximately 10 million. Based on these numbers we could expect there to be about 1,000 to 1,200 HAE patients living in South Korea.

Tony and I met with Mr. Hyun-Min Shin, Chairman of the Korean Organization for Rare Diseases. Mr. Shin was very generous with his time and shared his personal story of living with a rare disease. He understands how difficult it can be for patients, and how much better life would be for patients to be diagnosed earlier, and to have access to treatment to help them have a fulfilled life no matter what rare disease they may have. HAEi will continue to work with Mr. Shin in establishing a HAE patient organization to create a unified voice for HAE patients.

We also met with three very interested and passionate Allergists who care for HAE patients in Seoul. Prof. Chang, Prof. Kang, and Prof. Park see a small number of patients in separate hospitals in Seoul. They are all concerned for the welfare of their patients, and others in the country that have not yet been diagnosed.

Currently, patients have access to fresh frozen plasma in hospital, and androgens for prophylaxis. Although Firazyr (Icatibant) is registered, it is not yet funded, and therefore not accessible to (all) patients.

There is a lot of work to be done in South Korea, and HAEi will continue to collaborate with Mr. Shin, Prof. Chang, Prof. Kang and Prof. Park, along with our industry partners to ensure a better future as soon as possible for patients in South Korea.



## Global Advocacy Work

### Recent events

- 25 –26 March:** HAEi was in **Zürich, Switzerland** participating in Shire AdBoard Patient Journey.
- 12 – 14 April:** HAEi participated in the HAE Global Registry Foundation's Registry Meeting in **Bucharest, Romania**.
- 24 – 28 April:** HAEi was in **Nairobi, Kenya** working with Regional Patient Advocate Patricia Karani.
- 1 -2 May:** HAEi met with the financial auditors Ofico in **Lausanne, Switzerland** to finalize the 2017 fiscal year.
- 14 - 20 May:** HAEi was in **Vienna, Austria** for the 2018 HAE Global Conference and the HAEi Jakobsweg Walk.
- 27 - 30 May:** HAEi attended the 2018 European Academy of Allergy and Clinical Immunology (EAACI) meeting taking place in **Munich, Germany**.
- 1 – 5 June:** In **Manila, Philippines** HAEi met with patients and the Philippine Society for Orphan Disorders to discuss possible funding for a HAE patient group.

### Upcoming events

- 7-9 August:** HAEi will be in **Sao Paulo, Brazil** to discuss HAEi GAP with Dr. Anete Grumach and to meet with the member organization.
- 13-14 August:** HAEi is planning a visit to **Lisbon, Portugal** to work with the member organization on access for therapy as Portuguese patients are currently not allowed to have medication at home and are also not allowed to perform self-administration.
- 20 August:** HAEi will meet with Prof. Marco Cicardi in **Milan, Italy** to discuss elements of the HAE Global Registry Board and Foundation.
- 27-30 August:** HAEi will be in **Cape Town, South Africa** to participate in an allergy meeting and to discuss HAEi GAP with two dedicated physicians. Also, HAEi will use this opportunity to work with the local member organization.
- 5-7 September:** HAEi will be in **Berlin, Germany** for the Bradykinin Symposium arranged by Prof. Maurer and Prof. Magerl at Charité, Berlin.
- 27-29 September:** HAEi will present at and participate in the 2018 HAEi South Eastern Europe Workshop in **Skopje, Macedonia**.





## Clinical Trials

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

### Study of BCX7353 as a Treatment for Attacks of HAE

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

### Safety of Ruconest in 2-13 Year Old HAE Patients

– recruiting in Czech Republic, Germany, Hungary, Israel, Italy, Macedonia, Poland, Romania, and Slovakia.

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

– recruiting in United States.

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

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

### C1 Inhibitor Registry in the Treatment of HAE Attacks

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

### Biomarker for HAE Disease Type 1 (BioHAE)

– recruiting in Germany.

### Epidemiological Analysis for HAE Disease (EHA Study) (EHA)

– will be recruiting.

### Efficacy and Safety Study of BCX7353 as an Oral Treatment for the Prevention of Attacks in HAE (APeX-2)

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

### Firazyr® Patient Registry Protocol (Icatibant Outcome Survey - IOS)

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

### Determination of Specific Biomarkers of Acute Attack of Angioedema Within Pediatric Population (BRADYKID)

– recruiting in France.

### The Role of the Coagulation Pathways in Recurrent Angioedema (Angiocoag)

– recruiting in France.

### A Phase 3, Multicenter, Randomized, Single-Blind, Dose-Ranging, Crossover Study to Evaluate the Safety and Efficacy of Intravenous Administration of Cinryze® (C1 Esterase Inhibitor [Human]) for the Prevention of Angioedema Attacks in Children 6 to 11 Years of Age With HAE

– recruiting in Argentina, Germany, Italy, Mexico, Romania, United Kingdom, and United States.

### Pathophysiological study for autoimmune dysregulation of HAE

– recruiting in Japan.

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

# News from the Industry

30 March 2018

The European Medicines Agency (EMA) has validated its marketing authorization application (MAA) for Lanadelumab (SHP643) from **Shire plc** – and Health Canada has completed screening and accepted the New Drug Submission (NDS) under Priority Review for this investigational compound. Lanadelumab is an investigational treatment being evaluated for the prevention of angioedema attacks in patients 12 years and older with HAE.

Andreas Busch, Ph.D., Executive Vice President, Head of Research and Development at Shire: “Lanadelumab is the first monoclonal antibody under evaluation to prevent HAE attacks and has the potential to change the treatment paradigm for this rare disease, if approved. We look forward to working with regulatory bodies to bring a new treatment option to HAE patients.”

The EMA MAA validation confirms the submission for Lanadelumab is sufficiently complete and an accelerated assessment for the potential therapy will begin. In February 2018, the Committee for Medicinal Products for Human Use (CHMP) of the EMA granted an accelerated assessment for Lanadelumab reducing the number of evaluation days required, from 210 to 150. Similarly, Health Canada’s recent acceptance of the Lanadelumab NDS for Priority Review shortens the review timeline from 300 to 180 days.

Filings are supported by data from four clinical trials, including HELP, the pivotal Phase 3 efficacy and safety study, along with interim data from its extension study. HELP, the largest prevention study in HAE conducted to date, enrolled a total of 125 patients aged 12 years and over with type I/II HAE. The HELP study demonstrated that subcutaneous administration of 300 mg Lanadelumab once every two weeks resulted in an 87% reduction in the mean frequency of HAE attacks. In addition, an exploratory endpoint and post-hoc analysis showed that during the steady state stage of the trial (day 70-182) a 91% attack reduction was achieved and nearly 8 out of 10 patients reached an attack free state.

In this study, 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).

“As a physician treating patients with HAE, I would welcome new treatment options to help prevent attacks, as it is important to recognize the impact HAE can have on the quality of life of these individuals,” said Marcus Maurer, Prof. Dr. Med., Department of Dermatology and Allergy, Charité – Universitätsmedizin Berlin, Germany and clinical trial investigator. “I am pleased to see the progress in the review of Lanadelumab, that if approved, would offer a targeted mechanism of action inhibiting plasma kallikrein.”

Both the EMA MAA validation and Health Canada’s acceptance to review Lanadelumab reinforces Shire’s global leadership in rare disease innovation. In addition to receiving accelerated assessment from EMA and Priority Review from Health Canada, Lanadelumab has received priority review from the U.S. FDA and is expected to provide a decision by 26 August 2018, based on the Prescription Drug User Fee Act V action date. Lanadelumab has also received priority review and orphan drug designation from the Therapeutic Goods Administration in Australia. In 2017 alone, Shire received breakthrough therapy, orphan drug or fast track designations by the FDA for five of its rare disease therapies and anticipates continued progress of key regulatory milestones for late-stage programs.

(Source: Shire)



18 April 2018

The Swiss Agency for Therapeutic Products (Swissmedic) has validated the marketing authorization application (MAA) for Lanadelumab (SHP643). The validation of the MAA confirms that the Lanadelumab MAA submission is complete and that the formal review process will begin. Lanadelumab is an investigational treatment being evaluated for the prevention of angioedema attacks in patients 12 years and older with HAE. Lanadelumab was also designated orphan drug status by Swissmedic.

Andreas Busch, Ph.D., Executive Vice President, Head of Research and Development at **Shire plc** said, “Today’s announcement represents another important step forward as we continue our work to make Lanadelumab available to the global HAE community. For those living with HAE, the recurring attacks of swelling can be debilitating. Lanadelumab, if approved, has the potential to change the HAE treatment landscape by directly targeting plasma kallikrein to inhibit excessive bradykinin formation, which stops the blood vessel permeability that causes these swelling attacks.”

Lanadelumab Regulatory Status:

- U.S. Food and Drug Administration (FDA) accepted Shire’s biologics license application (BLA) and granted priority review for Lanadelumab in February 2018. The FDA is expected to provide a decision on Lanadelumab by 26 August 2018, based on the Prescription Drug User Fee Act V action date.
- European Medicines Agency (EMA) validated the marketing authorization application for Lanadelumab in March 2018. EMA had previously granted Lanadelumab an accelerated assessment reducing the number of evaluation days required, from 210 to 150.
- Health Canada accepted the New Drug Submission (NDS) for Lanadelumab under Priority Review in March 2018 shortening the review timeline from 300 to 180 days.
- Therapeutic Goods Administration in Australia granted Lanadelumab priority review and orphan drug designation in February 2018.

Regulatory filings are supported by data from four clinical trials, including HELP, the pivotal Phase 3 efficacy and safety study, along with interim data from its ongoing extension study. HELP, the largest prevention study in HAE conducted to date, enrolled a total of 125 patients aged 12 years and over with type I/II HAE. The HELP study demonstrated that subcutaneous administration of 300 mg Lanadelumab once every two weeks resulted in an 87% reduction in the mean frequency of HAE attacks versus placebo. In addition, an exploratory endpoint and post-hoc analysis which would require confirmatory studies, showed that during the steady state stage of the trial (day 70-182), a 91% attack reduction was achieved versus placebo, and nearly 8 out of 10 patients reached an attack free state. In this study, no treatment-related serious adverse events or deaths were reported. The most commonly reported treatment-related adverse events in patients treated with Lanadelumab during the entire treatment period were injection site pain (29.3% placebo vs. 42.9 % combined Lanadelumab arms), viral upper respiratory tract infection, headache, injection site erythema, injection site bruising, and dizziness. Most adverse events were mild to moderate in severity.

(Source: Shire)



## 8 May 2018

**CEVEC Pharmaceuticals GmbH** and **CSL Limited** have signed an exclusive licensing agreement for the development, manufacture, and commercialization of recombinant C1 Esterase Inhibitor (C1-INH) proteins for HAE and other potential indications using CEVEC's proprietary CAP®Go technology.

Under the terms of the agreement, CEVEC grants an exclusive license for the development, manufacture and commercialization of CAP®Go-derived C1-INH proteins to CSL. In addition, CEVEC will provide its expertise in the development and use of CAP®Go cell lines expressing C1-INH, and in optimizing the expression of highly glycosylated and difficult to produce proteins. The licensing agreement was the result of an ongoing collaboration between CSL and CEVEC, which yielded initial data on the significant potential of the CAP®Go technology to enable the development of a differentiated recombinant C1-INH product candidate.

Under the agreement, CSL aims to develop CAP®Go-derived C1-INH proteins with tailored glycosylation, leading to an improved half-life and more convenient application. CEVEC's proprietary CAP-technology may allow for the industrial manufacture of such a protein given the scalable production process established for CAP®Go cells.

"The agreement with CSL is a further endorsement of our unique human expression system with the intention to take our CAP®Go technology to the next level of implementation for the production of difficult to express recombinant proteins," said Dr. Nico Scheer, Chief Business Officer of CEVEC Pharmaceuticals GmbH. "Its outstanding characteristics in terms of authentic and tailor-made glycosylation capabilities, high yield production of complex proteins and scalability, combined with its IP protection and the complete documentation of the CAP® cells make the CAP®Go technology the ideal choice for industrial scale production of glyco-optimized proteins. We are looking forward to supporting CSL with this exciting project."

"At CSL, we are patient focused and we are driven by our promise to patients. CEVEC's CAP®Go technology provides us with the opportunity to develop an innovative and differentiated recombinant and glyco-optimized C1-INH protein for HAE and potential other indications. The potential increase in convenience and quality of life for patients will help us further expand our position in this very important market," Dr. Andrew Nash Senior Vice President Research, CSL added.

(Source: CEVEC)



## 25 May 2018

The European Medicines Agency's (EMA) Committee for Orphan Medicinal Products (COMP) has issued a positive opinion on **BioCryst Pharmaceuticals, Inc.**'s application for orphan designation of BCX7353 for the treatment of HAE. In addition, the United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) has granted a Promising Innovative Medicine (PIM) designation to BCX7353.

The positive opinion issued by COMP is expected to be adopted by the European Commission within 30 days. Orphan Drug Designation in Europe is available to companies developing products intended to treat a life-threatening or chronically debilitating condition that affects fewer than five in 10,000 persons in the European Union. This designation allows for financial and regulatory incentives that include a 10-year period of marketing exclusivity in the EU after product approval. BCX7353 has previously received Orphan Drug Designation in the United States from the Food and Drug Administration.

A PIM designation is an early indication that a medicinal product is a promising candidate for the Early Access to Medicines Scheme (EAMS) in the United Kingdom, which supports products intended for the treatment, diagnosis or prevention of a life-threatening or seriously debilitating condition, with the potential to address an unmet medical need.

"We are pleased to receive these important regulatory designations granted to BCX7353. These provide further support for the potential for BCX7353 to address a clear unmet medical need with an oral treatment for patients with HAE," said Jon P. Stonehouse, President & CEO.

(Source: BioCryst)



## 30 May 2018

**BioCryst Pharmaceuticals, Inc.** presented additional analyses of the APeX-1 trial of BCX7353 for the prevention of attacks in patients with HAE at the annual congress of the European Academy of Allergy and Clinical Immunology (EAACI) 26-30 May 2018 in Munich, Germany.

"These additional analyses of our Phase 2 APeX-1 trial of once-daily oral BCX7353 provide further details regarding pharmacokinetics, safety, and effects on target enzyme (plasma kallikrein) inhibition as well as measures of quality of life and symptoms of stress, anxiety, and depression in patients with HAE," said Dr. William Sheridan, SVP and Chief Medical Officer of BioCryst Pharmaceuticals. "The APeX-1 trial results formed the basis of our ongoing double-blind randomized Phase 3 trial, APeX-2, comparing 2 dose levels of daily BCX7353 to placebo. We remain on track to report the results of APeX-2 in the first half of 2019."

Copies of the four posters are available at [www.biocryst.com](http://www.biocryst.com).

(Source: BioCryst)





## 21 June 2018

The U.S. Food and Drug Administration (FDA) has approved a label expansion for Cinryze® (C1 esterase inhibitor [human]), making it available to help prevent angioedema attacks in children aged 6 years and older with HAE. Cinryze has been approved in the U.S. since October 2008 for routine prophylaxis against attacks in adolescents and adults living with HAE.

Andreas Busch, Ph.D., Executive Vice President, Head of Research and Development at **Shire plc** said: "Symptoms of HAE often present in childhood with the average child experiencing their first HAE attack around the age of 10. With the FDA label expansion of Cinryze, children as young as 6 years old living with HAE now have the first FDA approved treatment option available to help prevent attacks."

The approval was based on data from a dedicated Phase 3 multicenter single-blind study (0624-301) that evaluated the use of Cinryze in 12 patients living with HAE aged 7 to 11. Compared to the baseline observational period, the mean reduction in the normalized number of attacks for Cinryze 500 U and Cinryze 1,000 U was 71.1% and 84.5%, respectively. Both doses lessened the severity of attacks and reduced the use of acute treatment compared to baseline. The adverse reactions were headache, nausea, pyrexia (fever), and infusion site erythema (redness of the skin). None of these adverse reactions were severe, and none led to discontinuation (n=12, ages 7-11).

"This news is exciting for the HAE community because those living with HAE who are as young as 6 have a new option to help prevent attacks," said Anthony Castaldo, President of the U.S. Hereditary Angioedema Association.

In March 2017, Cinryze was granted European Commission (EC) approval for the label expansion granting three new indications, including routine prevention of angioedema attacks in children (ages 6 years and above) with severe and recurrent attacks of HAE.

Study 0624-301 was a Phase 3 multicenter, single-blind study that enrolled 12 patients aged 7 to 11 with HAE who were required to have an average of  $\geq 1.0$  angioedema attacks per month that were moderate, severe, or required acute treatment during the 12-week baseline observation period. Patients received 500 U and 1000 U of Cinryze every 3-4 days for 12 weeks. The primary efficacy endpoint was the monthly-normalized number of attacks.

Overall the safety and tolerability of Cinryze has been shown to be similar in clinical studies of pediatric, adolescent and adult patients with HAE.

(Source: Shire)



## 25 June 2018

**BioCryst Pharmaceuticals, Inc.** has reached agreement on the design of a Phase 3 trial and regulatory requirements for marketing authorization of BCX7353 for HAE with the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan.

The Phase 3 trial design agreed upon for Japan, APeX-J, is a randomized, placebo-controlled double-blind trial of 24 weeks duration with a 28-week safety extension. Approximately 24 Japanese subjects with HAE will be enrolled. The APeX-J trial design closely follows the design of APeX-2, a Phase 3 clinical trial being conducted in the U.S., Canada, and European countries. APeX-J tests the same dose levels of BCX7353 as in APeX-2, 110 mg daily and 150 mg daily, and the endpoints are identical to those in APeX-2. Data from the APeX-J and APeX-2 trials will be combined for regulatory submission in Japan.

"Japanese HAE patients would welcome an oral prophylactic drug as another treatment alternative, which provides HAE patients ease in daily life as well as relief from travelling outside their hometown for treatment to receive on-demand therapy of HAE attacks in a hospital," said Professor Michihiro Hide, M.D., Ph.D., Dean of the School of Medicine and Professor and Chairman, Department of Dermatology, Hiroshima University, and a leading expert in HAE in Japan.

BCX7353 was one of the first products granted Sakigake designation by the Japanese PMDA in October 2015. Sakigake designation is awarded to innovative products addressing an unmet medical need in Japan or providing improved efficacy compared to available treatment. Sakigake designation is associated with accelerated review of a Japanese NDA as well as pricing and other corporate benefits for the holder.

"Now that we have agreement on the regulatory requirements for marketing authorization of BCX7353 in Japan, we can move forward with executing APeX-J and selecting a commercialization partner for this region," said Jon P. Stonehouse, President & CEO. "A once-a-day oral treatment for this rare disease represents a high unmet medical need in Japan and an excellent partnering opportunity."

(Source: BioCryst)





# HAEi around the world

Currently there are HAE member organizations in 63 countries. You will find much more information on the HAE representations around the globe at [www.haei.org](http://www.haei.org) – and the world map will provide you with contact information for the member organizations as well as care centers, hospitals, physicians, and available medication.

The information on [www.haei.org](http://www.haei.org) is being updated as soon as HAEi receives fresh data from the national member organizations.

