


Global perspectives:

HAEI MAGAZINE · ISSUE 2/2019

 **75** Member countries



LIFE-SAVING MEDICATION
to South African HAE patients

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ANOTHER SUCCESS
on the road to Santiago

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Global Perspectives
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Cover photo

Dr Teresa Caballero celebrating the 2019 "For HAE Patients" award presented to her at the 11th C1-INH Deficiency & Angioedema Workshop in Budapest, Hungary

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HAEi is registered as a non-profit organization in the United States of America



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



DEAR HAE INTERNATIONAL FRIENDS,

This edition of *Global Perspectives* is particularly exciting because it provides a comprehensive overview of the ever-growing number of events and activities that are fueling the rapidly growing Global Patient movement being led by HAE international. We congratulate all of our member organizations for the dedication, creativity, and energy exerted on behalf of the HAE advocacy.

As always, HAE international is ready to actively help make a difference in any country where there are fellow patients and/or caregivers ready to take on the inevitable challenges that come with advocating for a rare disease. As we pass the half year mark for 2019, we are pleased that our Regional Patient Advocates – the HAE international on-the-ground “force” that serves the global HAE community – have been busy and successful in blazing an “advocacy trail” and expanding our global footprint. Most recently, the Regional Patient Advocates have brought HAE international’s expertise and services to Rwanda, Senegal, Morocco, Tunisia, Algeria, China, Taiwan, India, Hong Kong, South Korea, Albania, Panama, Columbia, and Brazil – just to name a few. Also, HAE international continues to aggressively support existing member organizations’ efforts aimed at expanding access to currently available medicines, and/or winning approval for additional HAE therapies.

We are very happy to report that lifesaving HAE medicine is now being shipped to South Africa through the HAE international Global Access Program. For the first time ever, South African patients have the opportunity to gain access to modern HAE medicine outside of a clinical trial. We are working to establish the Global Access Program in many of the countries where the Regional Patient Advocates are educating physicians, raising awareness, and finding patients motivated to form a member organization.

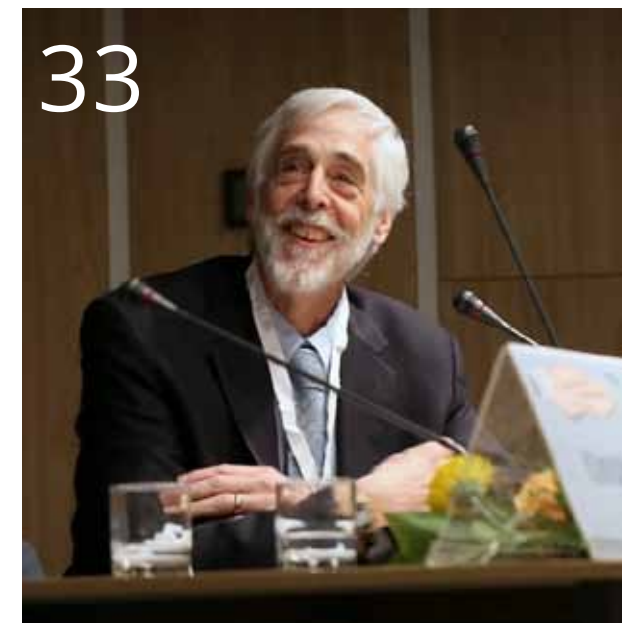
Finally, it is not too early for HAE international friends to start thinking about attending the next HAE Global Conference, which will take place 16-18 May 2020 in Frankfurt, Germany. As suggested by the conference theme – “*Creating the Path to Better Health*” – the 2020 HAE Global Conference will be an event nobody will want to miss.

I wish you pleasant reading, good health, continued fierce advocacy for the HAE cause, and overall happiness!

Warm regards,

Anthony J. Castaldo
President & CEO, HAE International

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NEWS FROM THE HAEI REGIONAL PATIENT ADVOCATES

As you will read in this section of Global Perspectives, and throughout the other pages in the magazine, the work that the HAEi Regional Patient Advocates (RPA's) have been doing is fantastic.

The **hae day** :-) 2019 activities have been inventive and have created the awareness of HAE on the broader community.

The work the RPAs do is essential in gaining access to treatments in countries where there are currently no modern options, and they help create the patient voice, which is an integral part of this process. The RPAs are also building relationships

and working with healthcare professionals, they attend and help educate with one on one meetings and by attending and taking part in medical conferences to help develop the awareness of HAE, especially in countries where HAE is not as well known.

I hope you enjoy reading about the great work that the RPA's have achieved since the last edition of this magazine.

Fiona Wardman
Chief Regional Patient Advocate

ROLES OF THE REGIONAL PATIENT ADVOCATES

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



PATRICIA KARANI
SUB-SAHARA AFRICA



SENEGAL

I got a chance to raise awareness at the 6th African Society of Immunodeficiencies (ASID) Congress that was held in Dakar, Senegal in April 2019. At the event Dr Priya Bowry from the Allergy Clinic in Nairobi, Kenya got to sensitize the doctors and nurses on what HAE is and how to carry about proper diagnosis and proper treatment in an African setup. I presented on my patient perspective to diagnosis in Kenya.

The conference was well attended by over 200 participants from the African region including doctors who are members of the African Society for Primary Immunodeficiency as well as nurses from the International Nursing Group for Immunodeficiencies (INGID) and the International Patient Organisation for Primary Immunodeficiencies (IPOPI) members. There were also students doing their masters in medicine present.

I had the pleasure of being honored with a gift for my work and participation in raising awareness and sharing the quest to save the lives of patients with Primary Immunodeficiencies.



RWANDA



Together with Dr Edgar Kalimba - the new HAE knowledgeable physician in Rwanda - I organized the 2nd HAE Doctors Symposium at Kigali, Rwanda to raise more awareness amongst African doctors. Hosted by the King Faisal Hospital in collaboration with HAE International it was a well attended event with pediatricians, doctors of internal medicine, and lead dermatologists among the attendants. We held fruitful discussions on ways of pioneering a steering committee in Rwanda. Our speakers included the HAE International President and Chief Executive Officer Anthony J. Castaldo, who shed more light on differentials in HAE, while Dr Priya Bowry - a well-known allergist from The Allergy Clinic in Nairobi, Kenya - gave an African perspective to diagnosis of HAE. I gave a patient perspective as well as a regional perspective to HAE and Dr Mugabo spoke on how to respond to a severe case of HAE in the emergency room.



MARIA FERRON
MEDITERRANEAN

★ MOROCCO

The national organization AMMAO is starting to work on their new website to be hosted under the HAE International umbrella. Also, HAE International is supporting AMMAO with a letter to be addressed to the Ministry of Health in Morocco. The scope is to introduce the disease to the Minister as well as to inform about the current situation the Moroccan patients are facing with no access to modern HAE medicines.

🇹🇵 TUNISIA

Dr Habid Ghedira has agreed with a patient (and a possible patient lead in the country) and their family to have a medical appointment in the next weeks to provide them with an official diagnose on HAE. Once this is done, we will start looking into the possibility of prescribing them with HAE modern medication and the set up of a local association.

🇩🇿 ALGERIA

On the celebration of **hae day :-)** 2019, the Algerian Society of Allergology and Clinical Immunology (organized by Doctor Habib Douagui) organized at Beni-Messous University Hospital a day of sensitization and information for general practitioners and patients about chronic and disabling diseases.

The 10th Euro-African Congress of Allergy and Clinical Immunology was held 12-13 June 2019n in Algeria. It had a full session entitled "HAE in the countries of the Maghreb – the current situation, problems and prospects" focusing on the creation of a national registry of HAE cases as well as the creation of the HAE patients' association in Algeria.



MICHAL RUTKOWSKI
CENTRAL & EASTERN EUROPE

GENERAL

As I was unfortunately unable to be in person in Switzerland, I recorded a special video that was presented at Takeda's offices in Zug and Zürich for **hae day :-)** 2019. Thus I had a chance to share with the audience the impact of living with HAE from the patient's perspective and understanding of physical, psychological, professional and personal aspects of the disease. I also introduced HAE International and the work we are doing to support the HAE community around the globe.

🇬🇪 GEORGIA

I have established contact with Professor Maia Gotua from the Allergy & Immunology Center in Tbilisi, who has been diagnosing HAE patients. There have been numerous patients already diagnosed in Georgia, however at this point no access to and reimbursement for modern HAE therapies are available. Currently, the Professor and I work on the implementation of the HAEi Global Access Program in Georgia that hopefully will secure patients with access to HAE medicines.

🇵🇱 🇧🇪 POLAND AND BELARUS

The HAE Regional Workshop organized by HAE Poland in the city of Bialystok, Poland became an international project with the attendance of patients from Belarus. Similarity of the language and mostly mutual respect and motivation shared among the patients is the key to the ultimate goal, which is the reimbursement for modern HAE therapies. HAE Poland and HAE Belarus have shared a long history of collaboration that hopefully will result in access to medication for the Belarusian HAE patients.

🇰🇿 KAZAKHSTAN

I plan to participate in the Immunology Conference in Astana on 5-6 October 2019 dedicated to health care professionals, where a separate HAE track will be organized. I work closely with Sergey Morozov from HAE Kazakhstan to enable organizing patients meeting during the conference dates.



FIONA WARDMAN
ASIA PACIFIC

TAIWAN

With the help of the very caring and knowledgeable Dr Shyur in Taipei, HAE International held the first ever HAE patient meet and greet in Taipei, Taiwan on 19 May 2019. Tony Castaldo and I had the pleasure of meeting patients and carers, listening to their very personal stories and how HAE has affected their lives.

We had the opportunity to share with patients and carers how HAE International can help support the patients with our programs and tools, and how with their collective patient voice we can work towards gaining access to modern treatments.

Dr Shyur is an amazing advocate for patients; he has written many papers on HAE and shared these with media to gain exposure and awareness of HAE throughout Taiwan. Through his tireless work, Dr Shyur has made it so much easier for colleagues to understand HAE, and for patients to find out about their symptoms, and for them to contact him for help.



HONG KONG

Now that the date and venue for the first patient meeting in Hong Kong have been finalized, HAE International is very excited to meet with patients, carers, doctors, industry partners and the Hong Kong Alliance of Rare Disease for this special meeting in August.



SOUTH KOREA

A date has also been set for the first patient “meet and greet” in Seoul. HAEi has previously met with Korean doctors, the Korean Organization for Rare Diseases (KORD), and industry partners in Seoul. We again look forward to visiting Korea in November to meet with patients and their carers.

The patients decided to come together and form HAE Taiwan so the following day Tony, Dr Shyur and I met with pharmaceutical industry partners in Taipei to discuss the need for HAE patients to have access to modern treatments, and how HAE International as a global organization can support the group with our initiatives. HAE International would like to thank Takeda and CSL Behring who both have representatives in Taiwan for meeting with us.

Tony and I then met with Ms Ruth Chen, who is the Executive Director of the Taiwan Foundation for Rare Disorders (TFRD). With 20 years of experience, this umbrella organization for rare disorders has a wonderful support program for individual patient groups, where they help guide them through starting an association and even help with funding sources, and give continued support.

HAE Taiwan and their patients and carers are in great hands with Dr Shyur, industry partners and the Taiwan Foundation for Rare Disorders, and HAE International look forward to continuing our support and working with everyone in Taiwan.

At this stage, the only treatments available for HAE in Taiwan are fresh frozen plasma for acute attacks and Danazol for prophylaxis.



NATASA ANGJELESKA
SOUTH EASTERN EUROPE

GENERAL

Many of the countries in the region celebrated **hae day :-)** 2019 by sharing posts, media interviews, and patients and physicians gathered. As just one example: In the city of Nish, the building of the National Theater was lit in purple as a sign of support.

The patients in the region collaborated on a project for **hae day :-)** with pictures and stories about what entails a silver lining of their HAE cloud. They shared something that empowered them or somebody who inspired them, whether it was something they achieved or the unconditional love they received or something that might be of comfort to patients, especially those newly diagnosed who are still coping and struggling with the fact that they have been diagnosed with a rare disease. The album – containing more than 45 photos – has stories and testimonies from 14 patients from seven countries. The title of the album is “SEE HAE family”, and it was shared through social media on **hae day :-)** 2019.

I would like to share the testimonial we received from Ana-Maria Baltatescu from Romania, who was sponsored by HAEA to visit the US HAEA Center in San Diego in April 2019:

“When I was a child, I remember feeling different than the rest of my friends because of my HAE, and I was hiding for days when I had a facial swell so I wouldn’t scare them. It took me years of pain, scary thoughts, worries and fear of the unknown; to realize that being different is not a bad thing. Being different is a blessing hidden in many challenges that are meant to grow you into the person you are supposed to be. Being different is a gift that you should embrace, both in the good and the bad days. Being different might open you the path for one of the greatest experiences of your life. Because of my HAE, I choose Medical School. Because of my HAE, I became a doctor, and I’ve learned the power of healing through kind words. Because of my HAE, I’ve met a lot of amazing people who made me feel that I am not alone and gave me the courage and support to follow my biggest dreams. Because of HAE, I had the chance to train at the HAEA Angioedema Center in San Diego, working with experts in the field and learning that you can be both an amazing physician and a great person. I feel blessed that my “cloud” turned out to have such a great silver lining.”

Invitations have gone out to the countries of the region for the HAE International South Eastern Europe Workshop to be held 27-29 September 2019. The workshop is entitled “HELP – Helping Empower Lasting Partnerships”. We are pleased to have confirmed Dr Marc Riedl from the US HAEA Angioedema Center in San Diego, and Dr Henriette Farkas from Hungary as key guest speakers.



ALBANIA

In April 2019, I visited Tirana, Albania and met with the HAE patient group – a great reuniting with patients. We discussed the challenges they face due to restricted access to medications and how patients suffer and live under stress when they have limited access to treatment. I will share some resources from North Macedonia for use in emergency rooms and with physicians who are not so familiar with the disease. We talked about HAE International resources like web hosting and shared some of the awareness initiatives that organized in North Macedonia as an example to motivate them in undertaking actions in their country. Patients in Albania are coming up with some great ideas that hopefully can turn into awareness activities to improve quality of life when they get adequate treatments available.

I have also met with Dr Mehmet Hoxha and two other physicians from the department of allergology and immunology at the clinical hospital Nene Teresa in Tirana. The doctors showed interest in getting more information on medications, along with the procedures of delivering medications to patients in North Macedonia. They were also interested in other available therapies for HAE globally and in our region, and they are motivated to collaborate in the proposed suggestions to advocate for the availability of HAE therapies. The doctors are willing to share posters and brochures with basic information on HAE in the Clinical Center and emergency rooms. They confirmed readiness to support patients in any awareness activities that will be organized by them.





JAVIER SANTANA
CENTRAL AMERICA AND THE CARIBBEAN

GENERAL

I have organized meetings with industry partners to discuss issues related to the need for medicines in the Caribbean islands and countries in Central America. Currently, pharmaceutical companies are interested in entering their medicines for HAE in Puerto Rico and nearby islands in the Caribbean and the Virgin Islands. Leaders of patient groups and the medical community that treats HAE patients have received this with great joy. Central America and several countries in the Caribbean region do not yet have treatments to control HAE attacks.

At this time, we have identified patients in the Dominican Republic, Cuba, El Salvador, Guatemala, Costa Rica, Puerto Rico and Panama. Many of them still have no treatment, and for others, access to treatments is very limited.

With this effort, we hope that in the coming months, we can achieve new treatments to these countries and thus continue to help improve the quality of life of HAE patients and those close to them.



PANAMA

As part of the events of **hae day :-)** 2019, Dr Olga M. Barrera (second from left) made an exhibition "The Multiple Faces of HAE" at the San Fernando Hospital in Panama to educate and raise awareness among the hospital's medical community. Dr Barrera attends to 20 patients with HAE in Panama City. During the event, she presented case studies, talked with doctors, and took blood samples from potential patients who have had symptoms similar to those suffering from HAE. Additionally, Dr Barrera conducted interviews with several radio stations and newspapers to raise awareness in Panama City.



FERNANDA DE OLIVEIRA MARTINS
SOUTH AMERICA & MEXICO

GENERAL

27-28 April 2019, I organized a meeting for the leaders of the national HAE patients' associations in South America and Mexico. The gathering took place in Bogota, Colombia and the represented countries were Argentina, Brazil, Chile, Colombia, Ecuador, Mexico, Paraguay, Peru, and Venezuela.



In preparation for the meeting, the leaders of the member associations shared information on the number of registered patients, associated physicians, medicines available and other important information on the situation of each country regarding support to the patient with HAE. The country representatives reported that there are over 2,600 HAE patients registered in the associations, while more than 600 doctors are linked to the associations.

During the meeting, HAE International tools were presented to assist national associations such as HAEi Connect, emergency card, and hosting of websites. On the second working day, each representative worked on the needs of their countries and built a work plan. The aim was for the associations to develop and be able to respond in an increasingly effective way to the needs of HAE patients from their countries.

HAE International was represented by President & Chief Executive Officer Anthony J. Castaldo, Executive Vice President & Chief Operating Officer Henrik Balle Boysen, Chief Regional Patient Advocate Fiona Wardman and myself.



Life-saving medication to South African HAE patients

A 'one-of-a-kind' medication access program from HAE International is now successfully delivering potentially life-saving medication to HAE-patients in South Africa.

"As no modern medications have been commercially available in South Africa until now, HAE patients have been unable to access them. The HAE International Global Access Program offers a regulatory compliant process that allows healthcare professionals to offer treatment for their HAE patients," says Henrik Balle Boysen, Executive Vice President & Chief Operating Officer of HAE International:

"We are delighted to have initiated our Global Access Program in South Africa where patients will now have the option to access an effective therapy to treat painful, debilitating, and potentially life-threatening HAE swellings."

Professor Jonny Peter from Groote Schuur Hospital and the University of Cape Town Lung Institute Allergy and Immunology Unit, Cape Town requested the first shipment of medication to South Africa.

"It is wonderful to finally be able to access a rapid, targeted treatment for our HAE patients. The HAE International Global Access Program provides an access route to much-needed targeted treatments at reasonable costing that is fundamental to HAE patients having the freedom to live their own lives and to be in control of HAE", says Dr Peter:

"The first patient to benefit is severely affected with one to two acute episodes per month without prophylaxis. He has used long-term androgen therapy despite side effects. He has had two episodes of anaphylactoid reactions to fresh frozen plasma, but this has continued to be required for life-threatening acute episodes prior to Ruconest access through the Global Access Program.

We have successfully treated one acute attack with 2100units of Ruconest without adverse event and good efficacy. This patient is an excellent example of both the limited treatment options for HAE patients in low middle income countries, as well as the benefits of the Global Access Program in South Africa."



Professor Jonny Peter from Groote Schuur Hospital and the University of Cape Town Lung Institute Allergy and Immunology Unit, Cape Town

Dr Peter thinks the Global Access Program is "an excellent initiative":

"Provided the pricing can stay as low as possible, numerous HAE patients from low middle income countries stand to benefit."

Until the introduction of the HAE International Global Access Program the only available medications in South Africa have been freeze-dried plasma (available at all hospitals) and Danazol (available on prescription) while no other medication is registered or available in any South African hospitals.



Adrienne de Jongh, President of HAE South Africa

Adrienne de Jongh, President of HAE South Africa, explains:

“After many months of planning the initial rollout of this program is underway. A list of patients has been compiled, applications on a patient named basis processed, and all applicants tested for rabbit allergy. The first orders have been delivered, and some patients are already using the product. Initially, there was a heavy administrative load as all patients had to be put on the system at once, but we anticipate that this process will be fine-tuned over time for repeat orders.”

The Netherlands based company Pharming NV is HAE International’s first Global Access Program pharmaceutical partner. Mischa Boeijen, Senior Product Manager Ruconest of Pharming, says:

“Pharming is extremely privileged to be part of the Global Access Program, a successful collaboration project initiated with HAE International. We are delighted to be able to provide Ruconest, a potentially life-saving therapy to those patients in South Africa who would otherwise not be able to access it. Pharming looks forward to extending our reach to patients across the globe in the future.”

More on the HAE International Global Access Program:
haei.org/resources/global_access_program
 More on HAE South Africa:
haei.org/southafrica

Physician enquiries regarding the HAE International Global Access Program should be directed by email to gap@haei.org.



Mischa Boeijen, Senior Product Manager Ruconest of Pharming



Mark Corbett, Executive Vice-President, Inceptua

According to Adrienne de Jongh research at the Lung Clinic where the HAE unit is based has concluded that one dose of Ruconest more than paid for itself as it reduced the need for many hours of hospital time. For this reason, Ruconest has been approved for use on the patients in the public sector as well as the private sector, which she calls a huge step forward:

“There is at present no modern HAE medication registered in South Africa and these patients would have had to rely on fresh frozen plasma. However delays in time, matching, ordering and getting supplies delivered often resulted in unnecessary delays, which allowed the HAE attacks time to intensify and consequently took longer to resolve.”

The HAE South Africa President says that there still are a number of issues to work through:

“But we are confident that this program is going to make all the difference to the quality of life of our patients. To live a life without disability is something most people take for granted, but HAE patients will most certainly value these new benefits.”

The third partner behind the Global Access Program is the specialist service provider Inceptua Medicines Access. Mark Corbett, Executive Vice-President says:

“Helping to ensure access to treatments for patients in need – where suitable products are not commercially available – is at the very core of what we do. At Inceptua, we are pleased to be supporting HAE International on their critical mission to facilitate access to HAE therapies through the Global Access Program”.

HAE International cannot handle direct patient inquiries. Henrik Balle Boysen explains that if you are an HAE patient and would like to learn more about access to modern HAE medication through the Global Access Program, you should discuss this with your treating physician who should then get in touch with HAE International.



UPDATE OF THE HAE INTERNATIONAL WEBSITE

Over the last few months, the HAE International staff has been working hard on a comprehensive update of the organization's website at haei.org.

"To the not so frequent visitor to the website it will look quite new, but for users visiting on a more steady basis the site will seem refreshed in quite a number of ways", says Enterprise Technology Manager Ole Frolich.

One of the most significant changes to the website is the addition of dedicated pages for all the 75 member countries:

"These pages should not be regarded as national websites – a number of the countries already have that – but merely as our attempt to gather as much information on the specific country as we possibly can. When you click the "75 member countries" button at the top of the front page, you will be taken to a page that presents all the members of HAE International. From there you can click a national flag of your choice. You will then be taken to the page dedicated to the country, and here you will find information on its presence on social media, its national website, the President of National contact of the organization as well as the Regional Patient Advocate if there is one for the country in question", says Communications Director Steen Bjerre.

The dedicated national pages also include points of HAE interest in the country – hospitals, care centers, physicians etc. – as well as news and events.

"We launched the updated website on **hae day :-)** 2019, and it is interesting to see the statistics for the first month. There is no question that the dedicated national pages are by far the most popular", says Ole Frolich.

Like previously the website contains information on topics like "What is HAE?", "What causes HAE?", and "How can HAE be treated?" as well as patient stories, and frequently asked questions.

"You can also find information on clinical trials, emergency cards, the HAE Global Conferences, HAEi Connect, the HAEi Global Access Program, and the HAEi Youngsters. We have also used this opportunity to present the HAEi Regional Patient Advocates and their work in a far better way", says Steen Bjerre.

See the updated website at haei.org.

ANOTHER SUCCESS ON THE ROAD TO SANTIAGO



When planning the HAEi/AEDAF Camino Walk 2019 the organizers hoped for around 30 participants but when the deadline was reached the total was 50 – and the number got even higher as a few people from Spain joined in for a day or two.

“Like the previous years, we ended up with a truly international event, as this time too HAE pilgrims joined in from four continents. Obviously, the most walkers came from Spain, but we also had quite large groups from the United States of America, Italy, and Denmark as well as participants from Hungary, South Africa, Chile, and Norway”, says Steen Bjerre from the 2019 Camino Walk Team.

This time the HAEi/AEDAF Camino Walk took place on part of the *Camino Inglés* or “The English Way”. *Camino Inglés* is a path of some 100 km within Galicia – from Ferrol or A Coruña in northern Spain to Santiago de Compostela. Originally, mainly European pilgrims who arrived by boat from the north used this route. *Camino Inglés* offers a variety of views, from blue coastline to green mountains, and it is often described as a brief, peaceful alternative for a pilgrim experience. The main cities and towns on this route are Ferrol, A Coruña, Bruma, Sigüeiro, and Santiago de Compostela.

The pilgrims met Wednesday 15 May 2019 at the airport in Madrid from where a private bus took them to Ferrol for an overnight stay before the first stage on 16 May. Quite appropriately stage number one coincided with the global HAE awareness **day hae day :-)** 2019, and after walking approximately 14 km from Ferrol to Pontedeume, the pilgrims enjoyed a magnificent reception and lunch at Pazo de Marinãn hosted by the *Presidente de la Diputación* in Galicia, Mr Valentín González Formoso. On Friday the second stage took the

pilgrims from Pontedeume to Betanzos before the third and final stage Saturday from Sigüeiro to Santiago de Compostela. These stages were around 14 and 16 km. Sunday the group visited Monte do Gozo and attended the pilgrims’ mass in Santiago de Compostela before going back to Madrid by bus.

“May tends to bring extremely unpredictable weather patterns in this part of Spain. Temperatures vary greatly, and it can rain for days on end, making some tracks muddy and difficult to walk through. However, for the 2016 Camino Walk, we had three days of sunshine, and the 2017 walk was really good as well. This time we had both sunshine and rain but all in all it was quite agreeable, and it is safe to say that we had another success on the road to Santiago”, says Steen Bjerre:

“It is still too early to say anything solid about a walk in 2020 but since there was one before both the HAE Global Conference in Madrid, Spain in 2016 and the HAE Global Conference in Vienna, Austria in 2018 there just might be a similar event when we meet for the fifth HAE Global Conference in Frankfurt, Germany in May next year.”





2016 HAEi/AEDAF Camino Walk – *Camino Francés*, Spain
2017 HAEi/AEDAF Camino Walk – *Camino Francés*, Spain
2018 HAEi Jakobsweg Walk – Vienna, Austria
2019 HAEi/AEDAF Camino Walk – *Camino Inglés*, Spain





Still more national HAE organizations across the globe are letting HAE International host their websites – for pretty obvious reasons if you ask Enterprise Technology Manager Ole Frölich:

“We have established an advanced system under the HAE International website allowing us to host national websites as well as provide them with templates for an individualized website – naturally all in their native language. And not to forget: This service is for free for all our member organizations. At this point, there are four website templates to choose from – and in the backend, there are powerful editing tools for the website administrator. Furthermore, the HAE International solution supports the organization’s own domain name just as it supports https secure protocol.

We are in contact with quite a few other national organizations and hope to be able to launch at least five more websites during 2019. The next countries we expect to see with websites under the HAE International umbrella are Albania, Bulgaria, Czech Republic, Croatia, India, Ireland, Montenegro, Slovenia, and El Salvador.”

To this date 18 countries have chosen to have HAE International host their website:

- **Australia:** <https://haeausralasia.org.au>
- **Belarus:** <https://by.haei.org>
- **Brazil:** <https://www.abranghe.org.br>
- **Ecuador:** <https://aehecuador.haei.org>
- **Greece:** <https://greece.haei.org>
- **Hungary:** <https://hungary.haei.org>
- **Iceland:** <https://iceland.haei.org>
- **Kenya:** <https://haekenya.haei.org>
- **New Zealand:** <https://haeausralasia.org.au>
- **North Macedonia:** <https://haemacedonia.haei.org>
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- **Romania:** <https://romania.haei.org>
- **Serbia:** <https://rs.haei.org>
- **South Africa:** <https://southafrica.haei.org>
- **Spain:** <https://angioedema-aedaf.haei.org>
- **Turkey:** <https://turkey.haei.org>
- **Uruguay:** <https://uruguay.haei.org>



11TH C1-INH DEFICIENCY & ANGIOEDEMA WORKSHOP

Over four days in the last part of May 2019, an international scientific conference on C1-INH deficiency was held for the 11th time in Budapest, Hungary. This year, another word was added to the title of the event, now reading “11th C1-INH Deficiency & Angioedema Workshop”.

“This designation better reflects the agenda of the conference, because it has become a forum for discussing topics also on other bradykinin-mediated hereditary and acquired angioedemas, in addition to C1-inhibitor deficiency”, says conference chairs Henriette Farkas and Lilian Varga.

Based on the 82 submitted abstracts, the programme included 36 oral and 46 poster presentations. These were supplemented by lectures delivered by Patricia Pozo-Rosich (Spain) on the relationship between migraine and angioedema, as well as by Michael Kirschfink (Germany) on the standardization of the laboratory methods applied for complement testing. Furthermore, Avner Reshef (Israel) summarized the prodromal symptoms of angioedema. By tradition, the agenda of the conference comprised consensus meetings and roundtable discussions intended to facilitate the adoption of international guidelines. This year, Anastasios E. Germeis (Greece) moderated the roundtable session “International consensus

on the use of genetics in the management of HAE”, whereas Teresa Caballero (Spain) led the discussion on “International consensus on the gynecologic and obstetric management of female patients with HAE – updates”. Further, the HAE Global Registry Work Group established to develop an international database on HAE held its meeting during the conference. Also, the delegates of the International Hereditary Angioedema Nursing Organization held a consultative meeting on improving the state-of-the-art care of angioedema patients.

This time some 330 delegates from 39 countries took part in the conference. Researchers, medical professionals, drug development specialists, members of patients’ organizations, and nurses were represented in the audience, which over the past two decades has become an active and creative community.

The 2019 “For HAE Patients” award was presented to Teresa Caballero, who delivered a presentation in the festive session of the first conference day. On the fourth and final conference day, Allen Kaplan (the United States of America) summarized for the audience all the topics and findings discussed at the 11th C1-INH Deficiency & Angioedema Workshop.





SUMMARIES OF PRESENTATIONS

The following are short extracts from some of the more than 80 presentations made at the 11th C1-INH Deficiency & Angioedema Workshop.

Which are the clinical, pathophysiological and therapeutic similarities between migraine and HAE with C1-inhibitor deficiency? – by Patricia Pozo-Rosich, Vall d'Hebron University Hospital, Spain:

Both migraine and C1-INH-HAE are genetically-driven paroxysmal disabling diseases, which are characterized by recurrent unpredictable episodic attacks. In rare cases, C1-INH-HAE is manifested with neurological symptoms, including cephalalgia, which does not respond to conventional treatment. The complement system has important function in the regulation of bradykinin release within the brain. Some of the inflammatory molecules in migraine can be measured indirectly (serum, CSF). This is different from C1-INH-HAE, where conventional laboratory tests are of diagnostic value. The pathophysiology shares the presence of inflammatory molecules, which lead to pain in migraine and angioedema attacks in C1-INH-HAE. Therapeutic options of both diseases are to be personalized and target-driven.

Analysis of C1-inhibitor deficiency: need for standardization and quality control – by Michael Kirschfink, University of Heidelberg, Germany:

In the diagnosis of the various types of angioedema there is considerable need for consensus and standardization of analytical methods. In recent years, laboratories specializing in complement analysis have joined with the International Complement Society and the IUIS to coordinate efforts to standardize and improve complement testing, ongoing efforts show first promising results. Eight rounds of external quality assessment, now covering 18 parameters, also including those to better characterize angioedema patients have been completed. It is recommended to extend this effort to a more comprehensive analysis of parameters of the clotting and kallikrein-kinin systems for better defining the pathophysiological background and to distinguish angioedema with C1-inhibitor deficiency from primary angioedema.

Prodromes of HAE: scientific evidence or delusional perception? – by Avner Reshef, Barzilai University Medical Center, Israel:

Despite consistent patient reports, prodromes remain elusive, and their precise nature and mechanisms are unknown. Prodromes have not been adequately investigated, and systematic tools for their evaluation are missing. Accurate prodrome evaluation is critical for early diagnosis of attacks and timing of medical interventions, particularly in an era when effective drugs are available for self-treatment.

Assessment of C1-INH function – different methods, different results – by Peter J. Späth, University of Bern, Switzerland:

The fundamentally different read-out systems of assay methods provide different result in C1-INH-HAE patients and this comes apparent when C1-INH functions are compared on basis of concentrations. The results of the complex formation read-out fit better to C4 concentrations and the clinical observations. The assay systems compared are those of daily routine diagnostic testing and are based on complement parameters. However, HAE is a pathophysiology of contact activation and the kinin system. Therefore, and because of the introduction of new therapy options, it is an urgent diagnostic need to develop new routine assay methods. Assays on basis of complex formation between C1-INH and target proteases should get particular consideration.

Changes of complement parameters during erythema marginatum in patients with HAE

– by Kinga Viktória Köhalmi, Semmelweis University, Hungary:

Erythema marginatum can be considered as the first phase of the HAE attack, as levels of C3, Factor B, C1-INH concentrations and C4 begin to decrease during the prodromal symptom, and this trend continued during HAE attacks. Nevertheless, more patients and further investigations of the kinin-kallikrein, coagulation and fibrinolytic systems are needed for better understanding of the pathomechanism of erythema marginatum. A new, individualized therapy, administered during erythema marginatum to prevent the development of HAE attacks seems to be thoroughly grounded.

HAE with C1-INH deficiency in 96 Brazilian children

– by Anete S. Grumach, University Center Health ABC, Brazil:

Although more than 80 percent of the patients had family history and several members affected, there was a delay in diagnosis. Abdominal pain and surgical interventions were less frequent than reported in adulthood. Attenuated androgens were prescribed for pediatric patients, probably due to restricted access to on demand therapy. Only recently Icatibant was licensed for use in children, nevertheless it had been previously used in our population. Educational programs should focus on pediatricians, aiming at reducing delayed diagnosis and providing appropriate therapy.

Simultaneous determination of human plasma serine proteases complexed with C1-inhibitor in vivo

– by Erika Kajdácsi, Semmelweis University, Hungary:

The change of the C1-INH concentration, activity or the amount of the measured complex levels cannot totally explain when and why a patient will have an attack. The pathomechanism of the attack formation may have other important factors, which are still unknown. Maybe the local C1-INH production (for example generated by endothelial cells) also take part in the attack formation. The fast changes in the amount of enzyme/C1-INH complexes during the follow up study may reveal that we need a very strict timing if we want to make a good comparison between the amounts of the complexes during attacks.

PHA-022121, the first-in-class orally active bradykinin receptor B2 antagonist for on-demand and prophylactic treatment of HAE

– by Anne S.J. Lesage, Pharvaris, The Netherlands:

Pharvaris is developing PHA-022121 as a first-in-class novel proprietary small-molecule antagonist of the B2 receptor, for oral on-demand treatment of acute HAE attacks and for prophylactic prevention of attacks. Based on experimental data and modeling, Pharvaris expects that a single daily pill of less than 30 mg will provide therapeutic efficacy for at least 24 hours. Pharvaris plans to develop PHA-022121 as an oral on-demand and prophylactic treatment of HAE attacks.

Clinical evaluation of pharmacokinetics, pharmacodynamics, safety, and efficacy dose-response of BCX7353 as an acute treatment for angioedema in patients with HAE

– by Marcin Stobiecki, Jagiellonian University Medical College, Poland:

The observed pharmacokinetic, pharmacodynamic, treatment effects, dose-response, and safety and tolerability profile of oral BCX7353 warrant confirmatory Phase 3 evaluation of the 750mg dose as an acute treatment for angioedema attacks in HAE.

KVD900, a new oral on-demand treatment of HAE attacks achieves complete plasma kallikrein suppression: safety, tolerability, pharmacokinetic and pharmacodynamic results from a phase 1 first-in-human study

– by Andreas Maetzel, KalVista Pharmaceuticals, the United States of America:

A single oral administration of up to 600 mg KVD900 is generally safe and well tolerated without any severe adverse events. KVD900 achieves rapid suppression of plasma kallikrein activity.



Pharmacokinetics, safety, and potency of ATN-249, a novel oral plasma kallikrein inhibitor for HAE

– by Ira Kalfus, Attune Pharmaceuticals, Inc., the United States of America:

ATN-249's pharmacokinetics were dose-linear with low to moderate between-subject variability. Repeat dose trough ATN-249 concentrations were above predicted therapeutic concentrations in ex vivo assays of contact activation. ATN-249 was well-tolerated and no adverse events were drug related. ATN-249 demonstrated potent kallikrein inhibition comparable to lanadelumab in biochemical and ex vivo contact activation assays, including Western blot detection of cleaved kininogen. These results, along with predictable pharmacokinetics, suggest ATN-249 may be a potent, safe, oral plasma kallikrein inhibitor for prophylactic treatment of HAE.

Long-term prophylaxis with C1-inhibitor concentrate in patients with HAE

– by David Loli-Ausejo, Hospital La Paz, Spain:

Long-term prophylaxis with pdhC1INH was more frequently needed by women, proved to be an effective, safe and well-tolerated alternative in patients with contraindications for administration of conventional long-term prophylaxis, including pregnancy and lactation.

HAE with C1-inhibitor deficiency (HAE-C1-INH) in childhood and adolescence

– by Emel Aygören-Pürsün, University Hospital Frankfurt, Germany:

130 patients with HAE-C1-INH aged <18 years were followed at the HAE Comprehensive Care Center at the University Hospital Frankfurt, Germany. The clinical manifestation of HAE-C1-INH begins in childhood mainly, the vast majority occurs already until age 18. Even in childhood and adolescence, HAE-C1-INH is a many faceted disease. All sites of attacks that are involved in manifestation of HAE in adult patients, including the laryngeal region, are represented in the initial manifestation already, although with a tendency towards involvement of extremities. In total, attack frequency increases with age from the onset of disease until the adult age is reached.

Higher annual rate of HAE in HAE-C1-INH patients above the age of 65 compared to patients aged 18 to 64 years

– by Emel Aygören-Pürsün, University Hospital Frankfurt, Germany:

Attack characteristics in 147 adult patients with HAE-C1-INH followed at the HAE Comprehensive Care Center at the University Hospital Frankfurt, Germany, were investigated. Patients with HAE-C1-INH aged 65 years or more had more attacks than younger adults. Apart from more diligence in the documentation of attacks or possible selection of more severe cases in the older patient population, this may be an indication of an individual increase of the attack rate over a lifetime.

Shortage in France of plasma derived C1-INH concentrates: state of play and consequences for patients

– by Laurence Bouillet, Grenoble University Hospital, France:

The shortage of plasma derived C1-INH has impaired patients' quality of life and sometimes put their lives at risk. CREAK (National Reference Center for Angioedema) and ANSM (National Agency for Health and Drugs) had to advocate off-label uses of certain products. Since October 2018, France has obtained the availability of lanadelumab for these severe patients in order to depend less on plasma derived C1-INH. The first encouraging results give new hope to patients and doctors.

Metabolic complications of late diagnosis in HAE

– by Natalia Vélez-Tirado, Instituto Nacional de Pediatría, Mexico:

Metabolic syndrome, obesity and cushing syndrome are serious complications of the excessive use of steroids in patients with type I HAE. As allergologists we must intervene quickly and aggressively seeking to avoid the increased in cardiovascular risk and type 2 diabetes in this group of patients.

hae
day :-)

MANY FACES
ONE FAMILY



90,189,232
steps taken in total

69,376
Kilometers

43,108
Miles

5190
Participants

39
Countries

NEW RECORD IN RAISING AWARENESS STEP BY STEP

HAE International extends a very warm thank you to each and everyone who took part in the HAE Global Walk from 1 April to 31 May 2019 – once more proving that this is a truly worldwide HAE event.

“First launched in 2016 the HAE Global Walk registered more than 12,000,000 steps. In 2017 the number grew to more than 21,000,000. In 2018 we rose to over 54,000,000 steps. And for 2019 we have registered nothing less than a massive increase to 90,189,232 steps”, says HAE International Executive Vice President & Chief Operating Officer Henrik Balle Boysen.

For those interested in the national scores, here you have the first 10 countries walked for:

- North Macedonia (14,000,000+)
- Denmark (13,000,000+)
- Spain (8,000,000+)
- Canada (7,000,000)
- Serbia (6,000,000+)
- USA (6,000,000+)
- United Kingdom (5,000,000+)
- Brazil (5,000,000+)
- Germany (4,000,000+)
- Argentina (3,000,000+)

– followed by Austria, Australia, Netherlands, and Australia (all 2,000,000+) and then Peru, Slovakia, Sweden, Croatia, Mexico, Jordan, Montenegro, Norway, Venezuela, Switzerland, and Belgium.

Furthermore, one or more entries have been made for Bulgaria, China, Colombia, Egypt, France, Hungary, Ireland, Italy, Kenya, New Zealand, Poland, Russian Federation, Turkey, and the United Arab Emirates.

“We will be back with the 2020 version of the HAE Global Walk in the months leading up to the 2020 HAE Global Conference in Frankfurt, Germany. And once again our motto will be: Every step counts”, says Henrik Balle Boysen.



WELCOME TO THE 5TH HAE GLOBAL CONFERENCE

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

As suggested by the conference theme – “Creating the Path to Better Health” – the 2020 HAE Global Conference will be an event nobody will want to miss.

“Frankfurt has been an obvious choice for us as its airport serves as a hub for many destinations worldwide. We have also chosen the Sheraton Frankfurt Airport Hotel as our venue. This hotel is located directly at Terminal 1 at Frankfurt International Airport”, says Executive Vice President & Chief Operating Officer Henrik Balle Boysen, HAE International.

More information about the 2020 HAE Global Conference will follow in the coming months.

NEWS FROM AROUND THE WORLD

POLAND

From President Michal Rutkowski, HAE Poland (Swelling Beautifully Association)

The period of April and May 2019 has been extremely busy for the Polish HAE Patients' Organization with providing educational projects for HAE national community and attending in numerous important events.

With the on-going project called "HAE Regional Workshops" Swelling Beautifully visited and organized another two amazing meetings, this time in the city of Bialystok on 13 April, and in the city of Krakow on 18 May, with the participation of 61 attendees. Additionally, the Krakow's meeting was about to celebrate **hae day :-)** 2019! This year's edition of the workshop has exceeded our wildest expectations, both in terms of the number of attendees, as well as the content of the program that perfectly meets patients' needs and expectations. In the survey conducted by HAE Poland among the participants of the Workshops, 99 percent of the patients rated the workshops as very good or excellent. Taking this opportunity, we would like to thank all participants, especially patients and their relatives, whose emotions and gratitude are the greatest reward for us.

Despite all the successes with educational projects through the years, there is still huge room for improvement in the area of patients' advocacy, awareness, education and guidelines. And that is an extra motivation for the Swelling Beautifully team to keep going for the better future and benefits of HAE patients.

The next HAE Regional Workshop was held 8 June 2019 in the city of Wroclaw, where a large number of participants took part.

On 22-23 May 2019 Swelling Beautifully attended the International Workshop on Surveillance and Screening of Blood-borne Pathogens organized by the International Plasma and Fractionation Association. Just after that – on 23-26 May 2019 – we visited Budapest, Hungary to participate in the 11th edition of C1-INH Workshop organized by Henriette Farkas and Lilian Varga.

All the news and latest information regarding Swelling Beautifully can be found at www.piekniepuchne.org and www.haerw.org.



AUSTRALIA AND NEW ZEALAND

From HAE Australasia CEO Fiona Wardman

During April HAE Australasia held their 2019 HAE Patient & Carers Conference on the Gold Coast, Queensland. This was the first time the conference was held over two days, and also the first time we had separate youngsters sessions.

Day 2 we held a series of workshops on vein management – tips and tricks, being a parent of a child with HAE, patients only and carers only 'hour of power' – techniques to live well with HAE, and how to talk to your child about uncomfortable topics and feelings.



These sessions were very well received and were facilitated by Nurse Kelly from Aesir Health, Dr Chris Bastian and Dr Maria Milic, who are both Clinical Psychologists.

We all had plenty of time to get to know each other during the BBQ dinner, and we had lots of fun during the afternoon Warners Bros. Movie World theme park.

Day 1 opened with an amazing and inspiring keynote speech from Gidon Goodman, who is 16 years of age and has Gaucher's disease. He shared his story of advocacy and persistence through his work as the President of Gaucher Association of Australia and New Zealand.

Patients and carers from Australia and New Zealand attended, and we appreciate the great feedback we received for the conference. The HAE Australasia Board of Directors would like to thank everyone for their participation and for making the conference a great success.

We were very fortunate also to have world-renowned speaker Dr Marc Riedl presenting on how genes play a part in HAE, Dr Connie Katelaris presenting on HAE treatments updates in Australia and New Zealand, and Tricia Mullins spoke about patient and carer advocacy. Furthermore, Henrik Balle Boysen and Anthony J. Castaldo gave an update on HAE International and its initiatives – and we had great questions from patients and carers during the Q&A session.

HAE Australasia took part in the inaugural Australian Patient Organisation Network conference held over two days in Sydney in May. We are excited about the great initiatives, ongoing support, platforms, collaboration and repository of information programs that will be initiated by the Centre for Community Driven Research (CCDR). We look forward to greater outcomes for patients, carers and patient groups.

Meanwhile, in a separate room, the youngsters spent time getting to know each other, they learned about HAE with Dr Katie Frith, how to be an advocate with Tricia, and what the HAE International youngster's community is all about with Henrik and Tony. They also worked on a poster project on what HAE means to them, which they presented to everyone at the end of day 1. A big thank you to Jess Bogoyevitch, who is part of the HAEi youngsters for facilitating and looking after the youngster's group.

The 2019 **hae day :-)** was celebrated with one of our industry partners, CSL Behring. I was invited to share my personal story with HAE and to also speak about HAE Australasia and HAE International and how patients and carers benefit from having a dedicated patient group.



ALBANIA

From HAEi Regional Patient Advocate
Natasa Angjeleska

As part of my annual plan for 2019, I have visited Tirana, Albania, and met with the HAE patient group. We were happy to unite with patients and discuss the challenges they face due to restricted access to medications. Patients suffer and live under stress when they have limited access to treatment. We offered to translate a Macedonian poster and brochures that can be of assistance in emergency rooms and with physicians who are not so familiar with the disease.

I also reminded about the opportunity to have web hosting via haei.org and shared some of the awareness initiatives that we have organized in North Macedonia as an example to motivate them in undertaking actions in their country.

Ideas are coming from patients, and I hope that we can support them in concrete activities in the coming period to improve quality of life when they get adequate treatments available in Albania.



KENYA

From President Patricia Karani, HAE Kenya



hae day :-) 2019 in Kenya was a day to raise media awareness amongst the public on our local television networks that are seen countrywide. I was able to feature in specific TV shows where Dr Priya Bowry, a well-known allergist in Nairobi, got to demystify the differences in types of HAE. I gave a patients perspective to living with HAE and the challenges faced by patients who have rare conditions in Kenya. These where live TV shows were we got a lot of people calling in and seeking advice and clarifications on their angioedema experiences.



UNITED KINGDOM

From CEO Laura Szutowicz and
Executive Officer Rachel Annals, HAE UK

We spend a lot of time sifting through the Facebook posts seeing that people are still tolerating increases in their attack rate and saying 'oh, that is just having HAE'. We cannot emphasize enough that if people suddenly start having more attacks than normal, or they don't seem to respond to treatment this is something they must discuss quickly with their care team. It is very likely that there is some simple reason for this, be it a nasty cold leaving a sinus infection that then triggers more attacks than normal – but it can and must be dealt with. We find that far too many people are content to 'put up with' rather than do something about it.

We all know how emotional stress can affect HAE, and many of you will remember that we sponsored Pippa Adams to carry out her Psychology Masters dissertation. This was recently published in The Bulletin of Health Psychology, a very prestigious publication for Pippa, who has also presented at international meetings on the subject of HAE and how it affects. University Hospital Cardiff Immunology Department is running another project we are sponsoring. It is using 'Fitbits' to see if improving physical fitness helps to reduce HAE attacks, and many of our members are already enrolled in it. This will be run as a clinical trial so that we can look forward to another publication in due course.

The Immunology Department at Salford Royal Hospital ran in the Manchester Half Marathon on 19 May 2019 and raised a phenomenal amount of money for us! We can't thank the team (Lucy Common, Ivonette Jones, Herwadkar Archana and Shuayb Elkalifa) enough for what they did.

We are excited to be holding our first HAE UK Youngsters only event this year. The day is for 12-24-year-olds and will take place at the Drayton Manor Hotel on 31 August 2019. There will be an educational morning with talks from HAE experts and our Youth Ambassadors, followed by a fun afternoon in Drayton Manor Theme Park.



We are planning our 9th National Patient Day, and it is going to be in the Manchester/North West region, so we hope some of the Marathon team will support us! The date is 23 November 2019 at the Renaissance Hotel, Manchester and our theme for this year is 'Advocacy and you; your HAE future'. We will focus on the history of HAE, where we are today and how we can all be good advocates to help raise awareness. We will have presentations from some of the UK's leading HAE experts, and there will be plenty of time to meet and get to know other HAE patients and their family members. As in previous years, we are holding a social event the night before.

The Scottish Patient Day is 2 November 2019 at the DoubleTree Hilton Hotel, Glasgow Central with the theme 'Managing your future with HAE'. Our Scottish events are always well supported, and we hope this one will be too as we have some wonderful presenters coming to educate us. There will be presentations from our Scottish HAE consultants and specialist nurses and time to socialize and make new friends.

Percy the Pufferfish will soon be coming to a book near you! Our wonderful Young HAE group are developing a patient advice book for youngsters, and he will be amongst those invited to the Youngster Event day we have arranged for 31 August 2019 at Drayton Manor Hotel, Staffordshire. This is aimed at HAE UK members aged between 12 and 25 and our fantastic Youth Ambassadors Jack, Alex and Rhiannon will be our presenters there. They will be fresh from having attended the HAEA Summit in Georgia, USA, and we are looking forward to them telling us all about their experience and training more youth advocates for us. We are so lucky in having really keen and proactive young people here in the UK; they are a great bunch.

Ann Harding, one of our Trustees and a very good supporter and advocate for HAE, has kindly organized a 'Family Day' for us at the Railway Inn, West Horndon, Essex on 17 August 2019. There will be bouncy castles, games, a BBQ, ice creams, craft activities and more. This is an event for all of the family, to also raise awareness of HAE.

We are so lucky to have such an involved, and inventive group of people helping us and are always happy to see any of our overseas friends at any event we organize. So if you are going to be in the UK, do contact us and come along to our events!



From Managing Director Michelle Cuevas,
US HAEA

Multiple events: This year's **hae day :-)** generated a lot of excitement in the United States with a large number of HAEA members participating in and/or hosting events, educating others, and raising HAE awareness in their communities! We are very excited that hundreds of the new HAE E.R. Tool Kits have already been ordered, and are being distributed to emergency facilities across the country. Efforts to share this Tool Kit not only help raise HAE awareness in countless local communities but also may help identify people who have swelling symptoms and have not yet received a proper diagnosis.

Meanwhile, HAE patients and family members registered 6,285,500 steps during the US HAEA's first Virtual Walk/Run and as part of our **hae day :-)** celebration. Our energetic teams logged their steps from Rare Disease Day 28 February until **hae day :-)** 16 May 2019 and received a cool participant medal.



Besides the Tool Kit distribution and the Virtual Walk/Run, many HAEA members hosted their own **hae day :-)** events to help educate their community. Through these unique events, important HAE information was presented to hundreds of people and awareness was broadly spread among the general public.

Finally, over 3,000 USD was raised for the HAEA's three key patient programs through the HAEA's Facebook Campaign: 1) the Pam King HAEA Scholarship Program, 2) HAEA Compassion Fund, and 3) HAE Research. We are grateful to everyone who participated, supported, and continue to educate others on **hae day :-)** and beyond to benefit all HAE patients.



Exploring Global Research: US HAEA President and Chief Operating Officer Tony Castaldo, Director of Research Janet Long, and HAEi Executive Vice President and Chief Operating Officer Henrik Balle Boysen, participated in the 11th C1-Inhibitor Deficiency and Angioedema Workshop in Budapest, Hungary, along with the expert scientists from the US HAEA Angioedema Center at UCSD, Drs. Bruce Zuraw, Sandra Christiansen, and Marc Riedl. This series of conferences is organized every other year and is devoted to the presentation and discussion of the latest scientific findings related to bradykinin-mediated angioedemas.

Ready for the US HAEA National Patient Summit – Imagine the Possibilities: We are very excited about the upcoming US HAEA National Patient Summit taking place next month in Atlanta, Georgia. This event will host over 1,000 participants and will commemorate the US HAEA's 20 years serving the HAE patient community in the United States. The Summit in Atlanta will bring together kids, teens, and young adults from around the world for a special three-day Global Youth Advocacy Program developed in collaboration between the US HAEA and HAE International. Participants will learn advocacy skills, participate in group project activities,

develop awareness events, and more. Each participant will receive an Advocacy Certification upon the completion of the program. These attendees will also take part in the US HAEA's Youth Leadership Council's (YLC) Leadership Program, that includes Advocacy and Communication Training, and fun social events.



In addition, to the General and Youth Programs, the Summit will host a Professional-Scientific Track, that offers a comprehensive look at HAE research, and multiple topics of interest that will be presented by the US HAEA leadership, and the experts from the US HAEA Angioedema Center at University of California in San Diego.

Follow the HAE Youth on Instagram: The US HAEA has launched an Instagram account lead and managed by a group of six HAEA social media interns who highlight patient stories, upcoming events, interesting HAE facts, and more! Follow @HAEYouth on Instagram to get updates and announcements about the HAEA youth programs.

The interns will also document the 2019 US HAEA National Patient Summit events, including the Global Youth Advocacy Program that will take place in Atlanta, Georgia. The Summit event will include the participation of kids, teens, and young adults from the United States and around the globe. If you are between

the ages of 12 and 25 and are a registered member of the HAEA YLC or HAE International Youngsters, you'll want to follow us on Instagram to see what's happening in Atlanta!

Symposium with Health Insurers: Marking a "first" for a patient organization, the HAEA organized and conducted a two-day educational symposium for major health insurers on 5-6 June in Chicago, Illinois. The HAEA contingent – CEO Tony Castaldo, Managing Director Michelle Cuevas, Project Manager Christine Selva, and US HAEA Angioedema Center Clinical Director, Dr. Marc Riedl – provided the insurance company attendees with a comprehensive overview of HAE while emphasizing the horrifying physical and psychological burden experienced when the condition is inadequately treated.

The initial part of the meeting focused on educating the insurers about the indications and uses for each of the FDA approved modern HAE medicines. The sessions that followed centered around discussion of the value of HAE therapies in terms of dramatic improvements in the quality of life for all who are affected by HAE – patients, caregivers, and family members. The HAEA emphasized that modern HAE medicines yield a positive economic impact by (1) reducing the need for intensive medical treatment such as ER visits and hospitalizations, and (2) allowing patients to get off disability, pursue educational opportunities, maintain employment, and generally lead a fulfilling life.

The symposium is part of the HAEA's ongoing advocacy strategy, which aims at creating an environment where every patient gets access to and reimbursement for HAE medicines. The insurance company attendees affirmed that they now have a better understanding of HAE as well as the value and overall positive impact of modern therapies. The HAEA continues to apply learnings, like those gathered during the symposium to expand our insurance industry HAE education and awareness outreach activities.



BELGIUM



For **hae day :-)** 2019 in Belgium HAE International Vice President Michal Rutkowski presented the importance of patients' advocacy at a patients' meeting in Brussels, Belgium. The event – gathering 35 attendees – was organized by the Hematology Center of University Hospital Saint-Luc UCL in Brussels and supported by Takeda. The main speakers were Professor Cedric Hermans and Dr Catherine Lambert, who gave fantastic feedback on HAE and the newest treatment options for HAE patients.



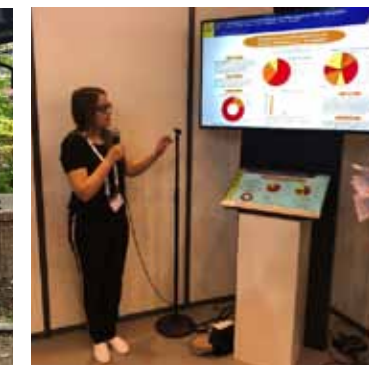
CANADA

From Daphne Dumbrille,
HAE Canada Volunteer Coordinator



HAE Canada has had a busy spring. Things kicked off with the HAE Canada Director at Large, Anne Rowe and Ontario Regional Director, Tina McGrath, attending the Network of Rare Blood Disorder Organizations (NRBDO) Spring Forum in Toronto in April. It was an informative and busy weekend discussing many issues, particularly around the importance of a patient registry.

In April, on behalf of HAE Canada, an enthusiastic member of our Advocacy Committee attended the Canadian Agency for Drugs and Technology and Health (CADTH) conference "Supporting Health System Transformation" in Edmonton, Alberta. It was a valuable three days spent learning about best practices and new ideas from everyone from the pharmaceutical industry to government representatives.



In May, another equally enthusiastic member of our Advocacy Committee, along with Tina McGrath, attended the Canadian Organization for Rare Disorders (CORD) conference titled "A Rare International Dialogue" in Toronto. The three-day conference was jam-packed with dialogue and deliberation on all things rare: from research and policy to action and better outcomes. We appreciated the opportunity to attend this important conference.

hae day :-) 2019 was celebrated by many Canadian footprints making their mark. In Ottawa, CSL Behring hosted a "lunch and learn about HAE" for employees, followed by the staff taking a walk among the historic buildings of downtown Ottawa – adding an impressive 250,000 steps to HAE Global Walk. The learning continued the following week when I attended an additional HAE "lunch and learn" with CSL staff. We all enjoyed an informative HAE presentation from a prominent HAE specialist, touching on subjects from the history of HAE to treatment options. There is always more to learn about HAE, and we appreciate it when people are willing to listen.

In another part of Ontario, to celebrate **hae day :-)** 2019, Tina travelled to Toronto and spent the morning with Takeda staff at Takeda's offices, where she enjoyed lunch, including a wonderful macaroon tree! She shared her patient journey and participated in a question and answer panel discussion to help educate the staff on HAE. After the discussion, a group of 40 walked the streets of downtown Toronto on behalf of HAE – adding to the many other Canadian steps for the HAE Global Walk.

HAE Canada is truly grateful for the time and effort both CSL and Takeda put in marking **hae day :-)** 2019 productively and worthily.

On the other side of our large country, HAE Canada's Pacific Regional Director, Lorraine Coumont, attended the Rare Disease Foundation's Rare Finds Gala in

Vancouver. Money raised at this wonderful event goes toward important and valuable research grants. HAE Canada is proud to attend this event that raised approximately 80,000 CAD.

HAE Canada was lucky to have our Real World Data posters and abstracts presented by Jodi Valois, Clinical Practice Team Lead at Ottawa's Yang Medicine, at the 2019 European Academy of Allergy and Clinical Immunology (EAACI) Congress in Lisbon, Portugal. The posters and abstracts were developed from data collected during HAE Canada's National Report Card. This important global event allows specialists in the field of Allergy and Immunology share discoveries, knowledge and latest trends with colleagues and peers from around the world. HAE Canada wants to thank Jodi for expertly presenting Canadian data at the conference.

Not only have we actively attended relevant conferences and meetings. HAE Canada is also busy preparing a patient submission for the Common Drug Review (CDR) process at the Canadian Agency for Drugs and Technology and Health (CADTH) in support of the new treatment, Takhzyro. We would like to thank our Advocacy Committee from coast to coast for the many hours spent working on this submission. We also want to thank the presidents from the international HAE organizations for their quick responses and contributions to help HAE Canada with this submission. We are blessed to have such a dedicated international HAE team that is willing and able to share their advice and knowledge.

We are truly grateful to all Canadian HAE patients who participated in our survey, which will provide information and data to support this patient submission. We are hoping the valuable perspectives that were gathered will ultimately help ensure this new treatment becomes available to all Canadians.



SPAIN

From President Sarah Smith,
HAE Spain (AEDAF)

HAEi/AEDAF Camino Walk 2019: AEDAF has again this year joined up with HAEi to organize the 3rd Camino Walk on the Camino de Santiago in Galicia (northwest Spain), to commemorate **hae day :-)** 2019. We had more than 50 pilgrims who walked three stages of the English Way on 16, 17 and 18 May. Just as the other years, it was a fantastic experience for all the participants and an excellent way to raise awareness of HAE, along with the HAE Global Walk. Spain was represented by 23 pilgrims, including patients, caregivers, friends and medical professionals, as well as our guide, Rafael Moreno (Rafa) of the Spanish Ministry of Education, Culture and Sports, who has been key to making the three Camino Walks in Spain such a success! Many thanks to him and to our bus driver Javier for all their work guiding us and keeping us on track! Rafa has provided us with the link to the Ministry's Cultural Association blog, where he has posted some pictures of the event: www.asociacionculturalmc.blogspot.com.

On **hae day :-)** 16 May 2019, the pilgrims were welcomed for an official reception at Pazo de Mariñán, a historical Manor House that was bequeathed to the *Diputacion Provincial* [provincial government] de La Coruña in 1936 and is used for socio-cultural purposes. We were received by Valentin Gonzalez Formoso, President of the *Diputacion Provincial*, who applauded and supported our initiative intended to make HAE visible and advocate for more and better research to improve diagnosis and treatment. His address was followed by an excellent lunch and a short tour of the Pazo. Our most sincere thanks to Valentin Gonzalez Formoso and the personnel of the Pazo de Mariñán for such an outstanding show of support and a truly memorable afternoon in Pazo de Mariñán.

And congratulations to an amazing group of pilgrims. Hopefully, our paths will come together again next year in Germany. Buen Camino!

11th C1 Inhibitor Deficiency and Angioedema Workshop: AEDAF member Francisco Sanchez and I represented AEDAF at the workshop that took place 23-26 May 2019 in Budapest, Hungary. We were particularly happy this year for Dr Teresa Caballero, an allergist at La Paz University Hospital in Madrid (the leading HAE center in Spain), coordinator of the Spanish study group for Bradykinin Mediated Angioedema and leading national and international expert in HAE, who was chosen for this year's "For HAE Patients" award. "For HAE Patients"



is awarded at the workshop to a colleague who has made considerable efforts in the interests of HAE patients. Teresa more than meets that criterion thanks to her tireless work, dedication to her patients and many scientific and medical accomplishments. Our most sincere congratulations for a very well-deserved award!

Francisco Sanchez, who is a nurse and doctoral student at the University of Almeria in southern Spain, had a poster accepted in the Budapest workshop scientific program titled "Development and validation of the self-efficacy assessment questionnaire in the management of hereditary angioedema for patients and family caregivers (HAE-SES)". Congratulations to Francisco as well for his early work as a young HAE investigator!



RUSSIA

From Chairman Elena Bezbozhnaya,
HAE Russia (SPHA OPHAE)

On **hae day :-)** 2019, the Interregional Public Organization "Society of Patients with HAE" (SPHA OPHAE) celebrated its third anniversary. Today the organization includes more than 150 people from 40 regions of the Russian Federation, providing administrative and legal support for patients and holding regular specialized scientific conferences, promotion events, seminars and webinars. In spring 2019, the Society organized and participated in several significant events.



In March 2019, we held a webinar for patients with HAE within the "Right to Life" project that we launched in 2017. The event gathered patients from several regions and cities of the country – from Moscow, the Moscow region, Lipetsk, Ulyanovsk, Novosibirsk, and Vladivostok. Coordinated by Vice-Chairman of the governing board Denis Bezhozhnyi and me the webinar focused on the issues concerning the conditions for obtaining official disability status for patients with HAE. PhD Ilya Ushankov, the lawyer of the Society, as the main speaker, presented the criteria and conditions for the assignment of disability.

16 May 2019 we celebrated a public holiday in the Park 50th Anniversary of October in Moscow to raise awareness on the rare disease and inform on ways to recognize the signs and symptoms, sharing brochures and other printed materials. Supported by professional dancers and choreographers, a dance workshop provided a new type of body language experience. The campaign was a great opportunity to support the patients and deliver information that can help save lives. The more people learn about the disease, the higher the chance of survival.

At the end of May 2019, SPHA OPHAE members participated in the 11th C1 Inhibitor Deficiency and Angioedema Workshop in Budapest, Hungary. The event brought together academic researchers, medical practitioners, biochemists, pharmacologists, drug developers, health workers, and patients from around the world. I headed the Russian delegation with five members. During the four days of the forum, the patients and experts raised important details about difficulties diagnosing this disease and treatment prospects and discussed the latest achievements in new drug research and application development.

Following the Budapest workshop, we were busy preparing for the International Scientific and Practical Conference "Strategy and tactics for treating patients with HAE – Life without fear" held in Moscow 19-20 June 2019. The conference invited patients diagnosed with HAE from 40 regions of Russia, specialists in allergy, immunology, genetics, heads of pediatric services, clinical psychologists, and lawyers. Through a range of workshops, panel discussions, round-tables the event focused on the routing of patients with HAE, providing correct diagnosis, effective and accessible treatment, essential medicines, and methods of preventing the disease in Russia and abroad.

Through annual scientific and practical conferences, SPHA OPHAE gathers HAE patients, the best medical specialists from Moscow and regional clinics, and representatives of administrative health care structures. This year, we are delighted to announce the first major international event with the privilege of welcoming the doctors and members of patient organizations from among other countries Belarus, Bulgaria, Hungary, Kazakhstan, and Poland.



URUGUAY

At this point, there are very few registered HAE patients in Uruguay and as they are scattered throughout the country – and due to high travel expenses to come to the capital – there is not much activity. However, HAE Uruguay continues with the formation of the association, accepting that procedures are slow at the moment.



SAUDI ARABIA

One more HAE knowledgeable doctor has been located in the Kingdom of Saudi Arabia. He is Dr Farrukh R. Sheikh, the Program Director for Allergy & Immunology at the King Faisal Specialist Hospital and Research Centre in Riyadh – see his contact information at <https://haei.org/location/physician-saudi-arabia-2>.



BRAZIL

The first half of 2019 has been pretty busy for HAE Brazil (ABRANGHE). The calendar of the three months include signing of an access program in Sao Paulo, meetings on rare diseases in Rio de Janeiro and Sao Paulo, another talk in Bom Despacho, and a presentation for doctors in Brasilia.

ABRANGHE organized a number of events all over the country for **hae day :-)** 2019. In Rio de Janeiro there was a patient reunion on 16 May and on the same date patients got together in Florianópolis. A reunion of doctors took place on **hae day :-)** 2019 in Salvador while the patient reunion in Vitória was scheduled for 17 May. Furthermore, there was an HAE walk in Fortaleza on 19 May 2019.



ALGERIA

The first HAE knowledgeable Algerian doctor has been added to the HAEi world map. Dr Habib Douagui is located at the Centre Hospitalier et Universitaire de Beni Mesous in Algiers.

<https://haei.org/location/physician-algiers-algeria>.



NORTH MACEDONIA

From Natasa Angjeleska, HAE Macedonia

HAE Macedonia marked **hae day :-)** 2019 with a puppet show based on a story written by me about the “Rare boy and the talkative balloon”. The story explains the sorrow of a boy that gets an HAE attack while being at a birthday party. He meets a balloon that started to puff out as the boy’s hand started swelling and he had to leave the birthday party and go to the hospital for an injection. The friendly balloon decided to support him, and they go to the hospital together, although it is very scary for a balloon to be near needles! When the boy was feeling better, they headed home where all his friends were waiting to continue the party. The boy inflated his friendly balloon and continued the joy together with his friends and other balloons!



It was a magical experience for all participants, children and adults who were in a fun and joyful way able to get to know more about the feelings and challenges that HAE patients have in ordinary life events, and indirectly to build empathy and support for HAE patients and families. We had more than 60 visitors in the City Park in Skopje that were able to follow the puppet show. They chatted, played with colorful balloons and took pictures with the actors of the puppet show. At the end of this event, all participants received a colored picture book with the story and several more poems and an HAE rap song.

I am very proud to say that North Macedonia is the country with the most steps recorded (14,000,000+) for the HAE Global Walk. Serbia, Slovenia, Croatia, Montenegro and Bulgaria also contributed to the overall total of more than 90,000,000 steps.





ISRAEL

For **hae day** :-) 2019 HAE Israel had a patient gathering with the medical companies and the doctors from the major hospitals. The theme was HAE the past, present and future – and there were a few lectures of the doctors regarding the innovations, about pregnancy and genetics. There was also a lecture on using the salutogenic model to manage HAE, and there was a Q&A panel with the doctors.



DENMARK, NORWAY & SWEDEN

Leading HAE experts from Scandinavia will be speaking at the third HAE Scandinavia conference taking place in Oslo, Norway 8-10 November 2019. Among the speakers are:

- Christian Jervelund from Copenhagen Economics – speaking on health and socioeconomic topics underlining the importance of access to the right treatment,
- Dr Linn Landrø from Oslo University Hospital, Norway – speaking on how to prepare children for prophylactic treatment,
- Dr Robert Brudevold from Ålesund Hospital, Norway – focusing on how the daily life of HAE patients has changed as still more have gained access to prophylactic treatment,

- Dr Anette Bygum from Odense University Hospital, Denmark – among other topics on the role of the HAE patient in the society and the new possibilities arising,
- The German HAE expert Markus Magerl from the university hospital Charité in Berlin – speaking on the exciting development within new HAE treatments,
- HAE patient Nanna Maria Boysen from Denmark – talking about the work of HAE youngsters globally in order to create a network crossing borders.

Furthermore, the Danish motivational speaker Mark Anthony will inspire the participants and Scandinavian nurses will provide advice and give a mini course in self-administration.

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

HAE – emergency management of attacks by a call center – by N. Javaud, Hôpital Louis Mourier, France, et al.:

Use of emergency departments and hospitalizations are reduced by the use of a coordinated national call center in HAE after therapeutic education program that promoted self-administration of specific treatment and use of call to call center. (Eur J Intern Med., May 2019)

HAE-Associated Acute Pancreatitis in C1-Inhibitor Deficient and Normal C1-Inhibitor Patients: Case Reports and Literature Review – by C.L. Veronez, Universidade Federal de São Paulo, Brazil, et al.:

In rare cases, HAE abdominal attacks can be accompanied by acute pancreatitis. Although rare, severe abdominal HAE attacks could cause pancreatitis; HAE-specific treatments may be efficient for HAE-associated pancreatitis. HAE should be considered as a differential diagnosis of acute idiopathic pancreatitis. (Front Med (Lausanne), April 2019)

Assessment on HAE burden of illness in Brazil: A patient perspective – by A. Abdon Barbosa, Faculdade de Medicina do ABC, Brazil, et al.:

Patients with HAE report understanding how severe their diagnosis represent, but they did not ponder how important their commitment to treatment may decrease the constant fear brought by the disease in its possible swelling crisis. Family data supported this conclusion. (Allergy Asthma Proc., May 2019)

HAE Type 1 with Recurrent Dizziness – by T. Ando, Nagoya University Graduate School of Medicine, Japan, et al.:

Findings indicate that HAE can cause recurrent dizziness, and it should therefore be included in the differential diagnosis in patients with recurrent neurologic symptoms, even in the absence of severe edema. (Intern Med., March 2019)

Recombinant human C1 esterase inhibitor treatment for HAE attacks in children – by A. Reshef, Barzilai University Hospital, Israel, et al.:

Attacks of HAE due to C1 esterase inhibitor deficiency (C1-INH-HAE) usually begin during childhood or adolescence. However, limited data are available regarding indications and modalities of treatment of children. This open-label, phase 2 study included children aged 2-13 years with C1-INH-HAE. Recombinant human C1-INH was efficacious, safe, and well tolerated in children. Data support use of same dosing regimen for HAE attacks in children (50 IU/kg; up to 4200 IU, followed by an additional dose, if needed) as currently recommended for adolescents and adults. (Pediatr Allergy Immunol., April 2019)

A randomized trial of human C1 inhibitor prophylaxis in children with HAE – by E. Aygören-Pürsün, University Hospital Frankfurt, Germany, et al.:

C1-INH prophylaxis was effective, safe, and well tolerated in children aged 6-11 years experiencing recurrent angioedema attacks. A post hoc analysis indicated a meaningful improvement in health related quality of life with C1-INH. (Pediatr Allergy Immunol., April 2019)

The impact of HAE on quality of life and family planning decisions – by Ö. Kuman Tunçel, Ege University Faculty of Medicine, Turkey, et al.:

HAE results in significant impairment in quality of life of the patients and has an impact on family life and life style of the patients. In case of depressive and/or anxiety symptoms, patients should be referred to psychiatrists for better quality of life. Higher levels of C1-inhibitor function and C1q seem to correlate with better quality of life; these needs to be further studied. (Int J Psychiatry Med., March 2019)



CLINICAL TRIALS



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

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, the United Kingdom, the United States of America

A Phase 3, randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy and safety of two dose levels of BCX7353 as an oral treatment for the prevention of attacks in subjects with HAE

– recruiting in Japan

A Long Term Safety Study of BCX7353 in HAE

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

A Study to Investigate CSL312 in Subjects With HAE

– recruiting in Australia, Canada, Germany, Israel, and the United States of America

Biomarker for HAE Type 1 (BioHAE)

– recruiting in Egypt, Georgia, Germany, India

C1 Inhibitor Registry in the Treatment of HAE Attacks

– recruiting in Bulgaria, Croatia, Czech Republic, France, Germany, Hungary, Italy, North Macedonia, Norway, Poland, Slovakia, Slovenia, Sweden

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

– recruiting in France

Epidemiological Analysis for HAE

– recruiting in Germany, Poland, Turkey, the United Kingdom

Firazyr Patient Registry (Icatibant Outcome Survey - IOS)

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

Global Registry to Gather Data on Natural History of Patients With HAE Type I and II

– recruiting in Italy

Pathophysiological study for autoimmune dysregulation of HAE

– recruiting in Japan

Patient Registry to Evaluate the Real-world Safety of Ruconest

– recruiting in the United States of America

Study of BCX7353 as a Treatment for Attacks of HAE

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

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

– recruiting in Japan

Study to Evaluate the Real-world Effectiveness of Lanadelumab in Participants With HAE

– will be recruiting in the United States of America

The Role of the Coagulation Pathways in Recurrent Angioedema

– recruiting in France

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

NEWS FROM THE INDUSTRY

8 May 2019

"In a year with many milestones across our multiple advancing programs of oral medicines for rare diseases, **BioCryst Pharmaceuticals, Inc.** has achieved significant progress in the first quarter and we look forward to reporting data from our APeX-2 trial in the second quarter and filing a new drug application by the end of the year," said Jon Stonehouse, president and CEO at the presentation of the company's financial results for the first quarter ended 31 March 2019.

"We believe that oral BCX7353 could be transformative for many HAE patients and provide them with the opportunity for a normal life without the burden and discomfort of frequent injections and infusions," Stonehouse added.

First Quarter 2019 Developments for HAE Program BCX7353:

- The company dosed the first patients in its APeX-J trial in Japan, designed to support potential Japanese approval of BCX7353 for the prevention of HAE attacks.
- In February 2019, the company announced data from the completed ZENITH-1 trial (including the 250 mg and 500 mg dose cohorts) of BCX7353 for the acute treatment of HAE attacks at the annual meeting of the American Academy of Allergy, Asthma & Immunology. The company plans to commence a Phase 3 trial, ZENITH-2, in the summer of 2019.

Upcoming Key Milestones for HAE Program BCX7353:

- Report 24-week safety and efficacy results from the Phase 3 APeX-2 clinical trial (Q2 2019)
- Begin ZENITH-2, a Phase 3 clinical trial of oral BCX7353 (750 mg) for the acute treatment of HAE (Summer 2019)
- File a new drug application for oral BCX7353 for the prevention of HAE attacks with the U.S. Food and Drug Administration (FDA) (Q4 2019)
- File a marketing authorization application for oral BCX7353 for the prevention of HAE attacks with the European Medicines Agency (EMA) (Q1 2020)

(Source: BioCryst)

**16 May 2019**

On **hæe day** :-)) 2019 **CSL Behring** sent out this article under the heading "Turning an HAE Walk Into a Pilgrimage":

Many of us show support by doing a charity walk or running a 5K – events that usually take the better part of a morning. But is there a cause that you would walk three days for?

For 50 people who will gather in Spain this week, the answer is yes and the cause is the rare disease hereditary angioedema. The group, including a guide, will walk 47 kilometers (about 29 miles) of the Camino de Santiago de Compostela in Spain, part of a thousand-year-old route for Christian pilgrims.

"The Camino Walk is a way to raise awareness and also a way for HAE patients and others to prove that they can overcome their difficulties and experience an event like this one," said Sarah L. Smith, whose husband and three children have HAE.

HAE, a potentially fatal genetic disease, causes sudden and painful attacks of swelling. People who live with the disease often wait a long time for an accurate diagnosis and its unpredictability can disrupt everyday life.

Smith was one of the people who came up with the idea and initiated the first walk in 2016. She serves as president of Spain's advocacy organization for HAE and is on the board of HAE International, which is organizing the 2019 walk. She'll be trekking this year along with people from eight countries, including Chile, Denmark, Hungary, Italy, Norway, South Africa, Spain and the United States. Their walk begins on HAE Day (May 16).

The full Camino is a network of routes to Compostela, which thread into northwest Spain from several parts of Europe and cover more than 1,500 kilometers (900+ miles) in Spain. It was named a World Heritage Site by the United Nations Educational, Scientific and Cultural Organization (UNESCO) because the routes enabled a two-way exchange of cultural advances during the Middle Ages and beyond. In addition to its religious significance for Christians, the well-traveled Camino

gave rise to new cities and features "extraordinary examples of Gothic, Renaissance and Baroque art," according to UNESCO.

More recently, the Camino also has been featured in movies and books, including the 2010 film "The Way" starring Martin Sheen and novels The Pilgrimage and Therapy. What began as a religious pilgrimage continues to draw thousands who find a personal sense of meaning by walking the Camino – through meadows, farms, villages and coastlines. The most popular route runs about 500 miles and all routes end at Santiago de Compostela, where there's a cathedral. That's where the HAE advocates will end their walk later this week.

Like Smith, HAEi's Director of Communications Steen Bjerre has walked the Camino for HAE awareness before. Here's his reflection on that journey:

Up early in the morning, breakfast, bus to the starting point, cold and misty weather but soon sunshine and nice temperature for the walk. Occasional breaks for a bite to eat, a drink and indeed a stamp to prove that we have passed this or that point along the Camino. Surprised by the number of other walkers – some in small groups, some on their own, some on horseback, some on bike, some interested in a talk, some more silent. Always being greeted with a "Buen Camino!" (like "Have a nice walk") from other walkers – even the more silent ones.

Passing through changing landscapes – meadowland, small villages with farms and cattle on the Camino, hills, forests, rivers, fields with wine other kinds of crop. Uphill – a bit hard on the legs. Downhill – a bit hard on the toes. Wondering how people who live here feel about all these pilgrims walking by their homes. Some of them greet – others don't really take any notice of us being here. Sometimes walking close to the highway – at other times walking where nothing but the sound of nature would reach you. Stopping at small monuments or churches along the Camino. Wondering if that thing I can clearly feel under my left foot is a blister.

Finally reaching the endpoint and finding a nice place for

a beer or a glass of wine. Getting back on the bus. Reaching the hotel and getting out of the walking clothes and the boots. Finding some of the others for an evening meal. Going to bed thinking that this was not too bad – and then struggling with the body to get into walking mode the next morning. Eventually finding the pace again and repeating the whole thing from the day before.

Bjerre found the walk to be "a deepening experience." What do Bjerre and other HAE advocates hope participants will gain by the end of this year's Camino walk?

"That they have helped spread HAE awareness, that they have proved something of essence to themselves, and that they will go home with a very special experience in their backpack.

(Source: CSL Behring)

CSL Behring

16 May 2019

On 16 May each year, HAE patient organizations from around the world, led by the HAEi, the international umbrella organization for the world's HAE patient groups, come together to support awareness of HAE. **hae day :-)** aims to raise global awareness to ensure each and every patient receives faster diagnosis and the care they need to lead a better life.

Pharming Group N.V. is proud to support **hae day :-)** 2019. This year, Pharming employees took part in the first **hae day :-)** virtual walk/run, a fundraising event set up by the HAEi to support:

- The Pam King HAEA Scholarship Program, providing financial support for HAE patients seeking to improve their lives through academic achievement
- The HAEA Compassion Fund, which offers financial assistance to patients in need who must travel to see an HAE medical specialist
- The Research Fund, pioneering innovations in HAE science

Sijmen de Vries, Chief Executive Officer of Pharming, commented:

"We are proud to support **hae day :-)** again this year as we renew our commitment to making a positive difference to patients with HAE and their families."

(Source: Pharming)



21 May 2019

The randomized (n=121), double-blind, placebo-controlled, Phase 3 APeX-2 trial of once-daily, oral BCX7353 for the prevention of HAE attacks has achieved its primary endpoint for both dose levels (110 mg and 150 mg), with the 150 mg dose reducing the attack rate in HAE patients by 44 percent (p<0.001) compared to placebo.

Fifty percent of patients receiving 150 mg BCX7353 in APeX-2 had a ≥ 70 percent reduction in their HAE attack rate compared to baseline, compared to 15 percent of placebo patients (p=0.002).

In patients on the 150 mg dose with a baseline attack rate of < 2 attacks per month, BCX7353 reduced the HAE attack rate by 66 percent compared to placebo (p=0.009). In patients with a baseline attack rate of ≥ 2 attacks per month, the attack rate was reduced by 40 percent (p=0.005).

Of 108 patients who completed 24 weeks of study drug treatment, 100 percent continued into the ongoing 48 week extension phase of the trial.

In APeX-2, both the 110 mg and 150 mg dose levels of once-daily oral BCX7353 were generally safe and well-tolerated. No drug-related serious adverse events were reported.

The most common drug-related adverse events reported in at least five percent of patients in APeX-2 were: nausea (9.8% 110 mg, 7.5% 150 mg, 15.4% placebo), dyspepsia (9.8% 110 mg, 7.5% 150 mg, 5.1% placebo) and diarrhea (7.3% 110 mg, 10% 150 mg, 0% placebo).

"HAE patients around the world desperately want access to a cost-effective, convenient, oral therapy to manage their disease. Given the profile of the 150 mg dose of BCX7353 in APeX-2, with half of patients experiencing at least a 70 percent reduction in attack rate, we have a new oral therapy that patients will want to try," said Jon Stonehouse, CEO of **BioCryst Pharmaceuticals, Inc.**

"With successful results from APeX-2, BioCryst is committed to making it easy for HAE patients around the world to access this potentially life-changing oral therapy, and we believe BCX7353 is positioned to become a front-line therapy option," Stonehouse added.

The results from APeX-2 support the submission of a new drug application (NDA) to the U.S. Food and Drug Administration (FDA). BioCryst plans to submit an NDA to the FDA in the fourth quarter of 2019 and a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) in the first quarter of 2020.

"The additional clinical information we now have from APeX-2 confirms that this is an oral kallikrein inhibitor that is effective at preventing HAE attacks in a large segment of the HAE patient population while having a very attractive tolerability profile. Based on this profile, and the consistent observation that real-world efficacy has been higher than clinical trial efficacy with HAE therapies, I expect many patients will want to try this oral option to see how well it works for them," said Bruce Zuraw, M.D., professor of medicine and chief of the Division of Rheumatology, Allergy and Immunology at the University of California School of Medicine, and principal investigator of the APeX-2 trial.

The company plans to submit detailed results from the APeX-2 trial for peer-reviewed publication and presentation.

(Source: BioCryst)



28 May 2019

At the C1 Inhibitor Deficiency and Angioedema Workshop in Budapest, Hungary earlier this month **KalVista Pharmaceuticals, Inc.** presented new data regarding its KVD900 project.

"KVD900 is an oral, novel, potent and selective inhibitor of plasma kallikrein, a validated target in HAE," said Andrew Crockett, CEO of KalVista. "We believe KVD900 represents a new therapeutic opportunity to rapidly halt HAE attacks at their earliest sign and we look forward to seeing the Phase 2 data late this year."

KalVista's oral presentation and poster showed:

- KVD900 rapidly reached high levels of drug exposure and was well tolerated without related gastrointestinal adverse events
- KVD900 successfully interrupts the contact activation system's positive feedback loop between plasma kallikrein, prekallikrein, and FXII
- Within 10 minutes an inhibitory effect on plasma kallikrein activity was detected with KVD900 in undiluted plasma and within 20 minutes it was by greater than 95%. KVD900 provided critical high molecular weight kininogen (HK) cleavage protection for at least 10 hours

(Source: KalVista)



4 June 2019

Takeda Pharmaceutical Company Limited presents new data from an ad-hoc analysis of the Phase 3 HELP Study, designed to evaluate the onset of action for TAKHZYRO (lanadelumab) during days 0-69 of treatment. The analysis suggests that TAKHZYRO starts to prevent HAE attacks during this early treatment phase, with patients experiencing an 80.1% decrease in mean monthly attack rate compared to placebo. The results were presented during the European Academy of Allergy and Clinical Immunology (EAACI) Congress in Lisbon, Portugal.

“The unpredictable nature of HAE attacks makes living with the disease physically and emotionally challenging for patients,” said Professor Marcus Maurer, M.D., Department of Dermatology and Allergy, Allergie-Centrum-Charité, Charité-Universitätsmedizin Berlin, Germany. “HAE requires an individualised approach to treatment, and it is important that a patient’s treatment plan helps reduce the frequency of attacks. These results are exciting as they suggest that lanadelumab begins to prevent HAE attacks during the initial phase of treatment.”

The ad-hoc analysis evaluated the efficacy of TAKHZYRO compared with placebo during days 0-69 of treatment using the same approach that was used to evaluate the primary and secondary endpoints during the complete study period (days 0-182). Results from the analysis showed that in patients receiving the recommended starting dose of TAKHZYRO 300 mg every two weeks, there was a significant reduction in mean monthly attack rate (80.1% decrease) compared to placebo (Adjusted $P < 0.001$). During this initial treatment phase, patients treated with TAKHZYRO 300 mg every two weeks also experienced fewer severe attacks compared to placebo (7.4% vs. 22%) and were more likely to be HAE attack-free compared to those on placebo (48.1% vs. 7.3%).

“Original data from the HELP Study showed that TAKHZYRO was effective in preventing HAE attacks over the entire duration of the study and, according to an exploratory analysis, many patients remained attack-free during the 16-week steady state period,” said Donatello Crocetta, M.D., Franchise Global Medical Unit Head, Rare Immunology and HAE at Takeda. “This new analysis supports previous study findings and builds on our understanding of how quickly TAKHZYRO can begin to help prevent HAE attacks, further supporting its use for appropriate patients as a preventive therapy that can be administered subcutaneously and begins to work rapidly.”

Across all TAKHZYRO treatment arms, (300 mg every two weeks, 300 mg every four weeks, 150 mg every four weeks), there was an improvement in mean monthly attack rate, monthly rate of moderate to severe attacks, monthly rate of attacks requiring acute treatment and the number of attack-free days, versus placebo, during the entire study period.

The most commonly observed adverse reactions (52.4%) associated with TAKHZYRO were injection site reactions. Of these, 97% were of mild intensity. Hypersensitivity reaction (mild and moderate pruritus, discomfort and tingling of tongue) was observed (1.2%).

TAKHZYRO 300 mg is approved in the European Union and Australia for the routine prevention of recurrent attacks of HAE in patients aged 12 years and older. TAKHZYRO 300 mg is approved as prophylaxis to prevent attacks of HAE in patients aged 12 years and older in the United States and for the routine prevention of attacks in patients aged 12 years and older in Canada.

(Source: Takeda)



STILL MORE COUNTRIES ON HAEi CONNECT



In 2018 HAE International presented HAEi Connect – a cloud-based member database for national organizations to manage their members. Due to popular demand, this free-of-charge offer has been updated in February 2019 with a number of highly useful features. Enterprise Technology Manager Ole Frölich explains:

“First and foremost, HAEi Connect includes an easy to use editor for creating emails to members as well as a template for saving and re-using emails. Another addition to the system is the possibility of contacting members via text message. Other updated features are four new sections in the HAEi Connect dashboard to initiate contact to members as well as right-to-left language support.”

To date, HAEi Connect has been implemented in Australia, Bulgaria, Denmark, India, Israel, Kenya, Mexico, New Zealand, North Macedonia, Norway, Peru, Poland, Slovenia, South Africa, Spain, Sweden, and Turkey.

“Furthermore, we are talking to the national organizations in Albania, Belarus, Brazil, Czech Republic, Croatia, Greece, Hungary, Italy, Japan, Montenegro, Romania, Slovakia, Ukraine, United Kingdom, and the United States of America”, says Ole Frölich.



HAEi AROUND THE GLOBE

Currently there are HAE member organizations in 75 countries. You will find much more information on the HAE representations around the globe at 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 haei.org is being updated as soon as HAEi receives fresh data from the national member organizations.

