



# HAEi Newsletter



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## A Message from the President

Dear HAEi Friends,

Over the past few years HAE physician/scientists have published a number of 'guidelines/recommendations' designed to educate the medical community on how to manage and treat HAE. These documents serve as an invaluable tool for doctors who have little or no experience caring for patients with an extremely rare disease like HAE. In fact, the guidelines/recommendations have proven so effective that one of HAEi's national member organizations decided to distill the principles and concepts into a patient Declaration that the HAE community can use to advocate for better HAE care.

Because the Declaration is derived from published, peer reviewed HAE treatment/management medical journal articles, it can be used confidently as a authoritative source by (1) individual patients as they work with their doctors to design an optimal HAE treatment program, and (2) advocates in our member organizations who are working to convince health ministries and insurers to allow access to and reimbursement for HAE medicines.

The document is simple but articulates the fundamental elements of treatment approach that would lead to a better life for HAE patients.

Every HAE patient has the right to:

- work in partnership with their HAE treating physician to establish an optimal treatment program,

- have their preferences respected when determining an HAE management and treatment plan,
- a treatment that will control their HAE and provide the opportunity to lead a normal life,
- access to at least two standard doses of an FDA-approved therapy for on-demand treatment of acute HAE attacks,
- have all attacks, irrespective of location, considered for treatment as soon as the attack is recognized,
- not be required to fail treatment with anabolic steroids before being prescribed a non-steroidal therapy.

Copies of the Declaration can be found at [www.haea.org/resources/patient-toolbox/patient-bill-of-rights](http://www.haea.org/resources/patient-toolbox/patient-bill-of-rights). HAEi would be happy to help any member organization that might wish to adopt the Declaration (brand it with their home organization's logo) and disseminate it on their web site and/or through printed copies.

I look forward to working with HAE friends in 2015 as we build our patient organizations and energetically advocate for better HAE diagnosis and care! Please remember that HAEi is always available to our member organizations (and patients looking to form an organization) in every aspect of the fight for access to HAE medicines.

Warmest regards to all HAEi Friends

Anthony J. Castaldo  
President, HAEi



## Trials recruiting patients

According to the International Clinical Trials Registry Platform under World Health Organization (WHO) the following trials are recruiting at the moment:



- **Safety of Ruconest in 2-13 Year Old HAE Patients.** Recruiting in Germany, Israel, Italy, Macedonia, Poland, and Romania. <https://clinicaltrials.gov/ct2/show/NCT01359969>
- **Firazyr® Patient Registry Protocol (Icatibant Outcome Survey - IOS).** Recruiting in Austria, Brazil, Denmark, France, Germany, Greece, Ireland, Israel, Italy, Spain, Sweden, and United Kingdom. <https://clinicaltrials.gov/ct2/show/NCT01034969>
- **Screening Protocol for Genetic Diseases of Mast Cell Homeostasis and Activation.** Recruiting in United States. <https://clinicaltrials.gov/ct2/show/NCT00852943>
- **12-Week Safety and Efficacy Study of BCX4161 as an Oral Prophylaxis Against HAE Attacks OPuS-2.** Recruiting in USA. <http://clinicaltrials.gov/show/NCT02303626>
- **Safety and Efficacy Study of CINRYZE for Prevention of Angioedema Attacks in Children Ages 6-11 with HAE.** Recruiting in Argentina, Germany, Italy, Mexico, Romania, United Kingdom, and USA. <http://clinicaltrials.gov/show/NCT02052141>
- **A European Post-Authorisation Observational Study Of Patients With HAE.** Recruiting in France, Germany, Spain, and United Kingdom. <http://clinicaltrials.gov/show/NCT01541423>
- **A Call Center During HAE Attacks (SOS HAE).** Recruiting in France. <http://clinicaltrials.gov/show/NCT01679912>
- **C1 Inhibitor Registry in the Treatment of HAE Attacks.** Recruiting in the Netherlands. <http://clinicaltrials.gov/show/NCT01397864>
- **A Pharmacokinetic, Tolerability and Safety Study of Icatibant in Children and Adolescents With HAE.** Recruiting in Argentina, Australia, Austria, Canada, Colombia, Germany, Hungary, Israel, Italy, Spain, and USA. <http://clinicaltrials.gov/show/NCT01386658>
- **Study to Assess the Tolerability and Safety of Ecallantide in Children and Adolescents With HAE.** Recruiting in USA. <http://clinicaltrials.gov/show/NCT01832896>

- **A Study to Evaluate the Clinical Efficacy and Safety of Subcutaneously Administered C1-esterase Inhibitor in the Prevention of HAE.** Recruiting in Australia, Canada, Czech Republic, Hungary, Israel, Italy, Romania, Spain, United Kingdom, and USA. <http://clinicaltrials.gov/show/NCT01912456>
- **Double-Blind, Multiple Ascending Dose Study to Assess Safety, Tolerability and Pharmacokinetics of DX-2930 in HAE Subjects.** Recruiting in Italy, Jordan, and USA. <http://clinicaltrials.gov/show/NCT02093923>

These three trials are not yet recruiting but will be later this year:

- **A Study to Evaluate the Long-term Clinical Safety and Efficacy of Subcutaneously Administered C1-esterase Inhibitor in the Prevention of HAE.** Recruiting countries presently unknown. <https://clinicaltrials.gov/ct2/show/NCT02316353>
- **HAE, Neurobiology and Psychopathology.** Will be recruiting in Italy. <https://clinicaltrials.gov/ct2/show/NCT02159430>
- **A Phase 2 HAE Prophylaxis Study With Recombinant Human C1 Inhibitor.** Will be recruiting in the Netherlands. <https://clinicaltrials.gov/ct2/show/NCT02247739>

## New and upcoming National Patient Groups

The global family of HAE organizations keeps on growing. In September-October 2014 a National Patient Group (NPG) was established in Kenya as well as in Russia. India was in place in December 2014, and at the moment the first steps to a NPG has been taken in the Philippines.

As mentioned at the HAE Global Conference 2014 HAEi is also working on establishing NPG's - and eventually National Member Organizations (NMO's) - in countries like Venezuela, Chile, South Africa, Thailand, Singapore, Taiwan, and South Korea.

What started with just a good handful of countries in 2004 has now grown into a truly global umbrella organization with NMO's in 27 countries and NPG's in further 13 countries.

No NMO or NPG in *your* country? Please don't hesitate to contact HAEi at [info@haei.org](mailto:info@haei.org) and we will gladly help you through the first steps of establishing a national HAE organization.

# HAE NEWS FROM AROUND THE GLOBE

## From our National Member Organizations

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

**T-shirt competition:** Until the end of January 2015 HAE Australasia is running a design competition: Design a T-Shirt to celebrate **hae day** :-) 2015 and win a Red Balloon voucher for 150 AUD if your entry is chosen. The competition is open to residents of Australia and New Zealand.

**2015 Patient Meeting:** The next annual patient meeting will take place 16 May 2015 in Sydney.

**Canada** ([www.haecanada.org](http://www.haecanada.org))

HAE Canada is inviting the members to a patient information event in Ottawa, Ontario on 31 January 2015. Dr. William Yang, MD, FRCPC, FAAAAI has agreed to be the primary speaker at the event that will be the first with webcast, allowing members from all over Canada to participate.

Information can be found on [www.haecanada.org](http://www.haecanada.org).

Patient events in 2015 are also being planned for Toronto (May), Edmonton (June), and Calgary (September).

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

23 January 2015 Dr. Anette Bygum from the HAE care center Odense Universitetshospital defended her thesis 'Hereditary and Acquired Angioedema in Denmark. Prevalence, Clinical features, molecular genetic aspects and quality of life issues'. Opponents were Professor Markus Magerl from Charité Universitätsmedizin Berlin in Germany, and Professor Werner Aberer from Medizinische Universität Graz in Austria.

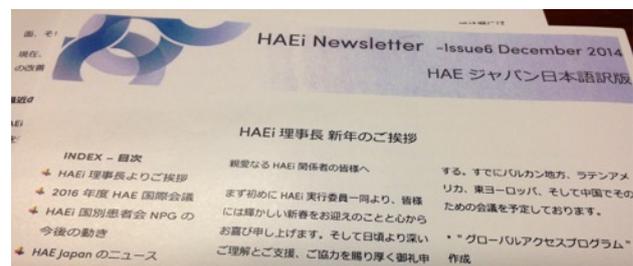
**France** ([www.amsao.fr](http://www.amsao.fr))

The next patient meeting will be held 14 March 2015 at Hôpital Cochin in Paris.

**Hungary** ([www.haenet.hu](http://www.haenet.hu))

The 9th C1-Inhibitor Deficiency Workshop in Budapest is scheduled for 28-31 May 2015. The conference focuses on bradykinin-mediated angioedemas, and particularly on the types resulting from C1-inhibitor deficiency. The topics covered by the four-day long event are, among others, the latest achievements in the diagnostics of the disease, exploration of its hereditary,

pathogenetic, and clinical background as well as the management and follow up of the patients. See more on the conference at [www.haenet2015.hu](http://www.haenet2015.hu).



**Japan** ([www.haej.org](http://www.haej.org))

The HAE Japan President, Beverley Yamamoto, writes:

On 11 January 2015 we held the first HAEJ Scientific Meeting entitled 'Opening-up International Dialogue between HAE Clinicians in Japan and the USA'. We were very honored and delighted by the presence of Dr Bruce Zuraw, HAEA Endowed Chair and Professor of Medicine at the University of California San Diego as our invited speaker. He delivered an exciting and informative talk entitled 'HAE – A Scientific Overview and Prospects for Clinical Practice'.

Two physicians closely involved in HAEJ, Dr Isao Osawa, Associate Professor, and Dr Daisuke Honda, Doctoral Candidate, both affiliated to the School of Medicine, Juntendo University, presented a stimulating paper on 'The Low Opsonization and Immune Complex Solubilization Ability in Sera from HAE Patients'. Dr Hide, another HAEJ affiliation physician, acted as discussant. Dr Hide is Professor and Chief of the Department of Dermatology, Institute of Biomedical and Health Sciences at Hiroshima University. The two papers and the discussant's comments generated a lively discussion and we ended up closing the meeting much later than planned. The meeting was attended not only by a number of key Japanese HAE physicians, but also by HAEi President Anthony J. Castaldo and HAEi Executive Director Henrik Balle Boysen, as well as six HAEJ patient advocates.

At the end of the meeting we discussed possibilities for US-Japan based scientific collaborations and also the need to set up an HAEJ dedicated Medical Advisory Board.

Following the Scientific Meeting, we all adjourned to a beautiful Japanese restaurant on the 42nd floor of a building overlooking the whole of Tokyo. We were joined by other members of HAEJ who were part of the events organizing committee. It was a very special evening.

On 10 January 2015, we held the 2nd HAEJ Patient and Physician's Advocacy Meeting – this is the second major meeting we have held since gaining Non-Profit Organisation status. There were a total of 35 participants, including six from the pharmaceutical industry, our guests from HAEi and Dr Zuraw. The meeting was held at Juntendo University and what had appeared to be a large room when we booked the space, was way over crowded once the meeting started. We were delighted at the high level of participation.

Dr Zuraw gave a fascinating talk entitled 'What Every Patient Should Know About HAE: The Underlying Science, Current Treatments, and Promising Research'. This was then followed by a talk by Anthony J. Castaldo and Henrik Balle Boysen entitled 'Managing HAE: The Patient's Perspective. The importance of early diagnosis, HAE's Impact on the Quality of Life, HAE Management and Treatment in Europe and the United States, Patient Advocacy Organizations can Drive Improvements in Diagnosis and Treatment.'

These sessions were followed by a lively Q&A that included questions about self-administration and home therapy, managing pregnancy, and possible side-effects of HAE therapies. We are so grateful to our interpreters whose skill and warmth allowed us to field questions and offer answers between Japanese and English.

Overall we are indebted to many people for helping making these meetings happen, but especially to our guests Dr Zuraw, Tony J. Castaldo and Henrik Balle Boysen. We are also grateful to Shire, CSL Behring, and BioCryst for helping to financially support these meetings.

Other news is that we have now lodged two petitions to the Ministry of Health, Labour and Welfare to have self-possession, self or home infusion, and short-term prophylactic care of the one available HAE treatment authorized and remunerated under the Specified Disease Law. The revised Specified Disease Law, that provides remuneration for HAE treatment, came into effect from 1 January 2015. We are still waiting to find out how and in what ways patients are affected, but for the time being we remain cautiously positive. We will report back in future editions of this newsletter.

The HAEJ board decided to move ahead with translating key parts of the HEAi newsletter, and the December 2014 edition was made available to participants at the two meetings.

Also, we have had our first inquiry from an overseas visitor coming to Japan and we were able to provide her with details of hospitals that offer HAE treatments and a Japanese language

HAE card, giving basic details of the condition that can be presented at these hospitals.

#### **Macedonia** ([www.haemacedonia.mk](http://www.haemacedonia.mk))

The biannual South Eastern European HAE workshop will be held on 3 April 2015 in Skopje. The organizers have invited participants from Serbia, Croatia, Slovenia, Montenegro, Bosnia, Albania, Kosovo, and Bulgaria as well as prominent international opinion makers in the field of HAE. The aim of the workshop is to establish sustainable and applicable practice for HAE treatment in South Eastern Europe.

#### **New Zealand** ([www.haeaustralasia.org.au](http://www.haeaustralasia.org.au))

Until the end of January 2015 HAE Australasia is running a design competition: Design a T-Shirt to celebrate **hae day :-)** 2015 and win a Red Balloon voucher for 150 AUD if your entry is chosen. The competition is open to residents of Australia and New Zealand.

#### **Spain** ([www.angioedema-aedaf.org](http://www.angioedema-aedaf.org))

AEDAF will hold its 17th annual meeting and general assembly on 18 April 2015 at Hospital Universitario La Paz in Madrid.

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

The 16th HAE Patient Meeting will take place 25 April 2015. In connection with the meeting the participants will have the possibility to visit the Paraplegiker-Zentrum in Nottwil.

#### **United Kingdom** ([www.haeuk.org](http://www.haeuk.org))

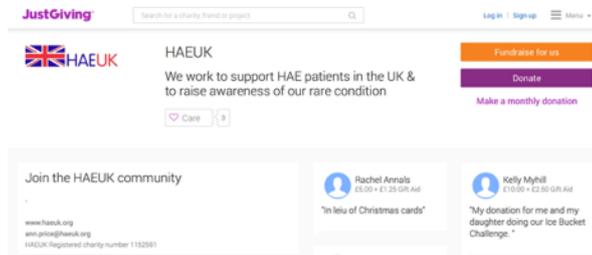
**Database:** The HAE UK membership continues to increase - there are now over 300 members registered. HAE UK encourages any family members, including children, who have HAE to register as this will help the organization to know where HAE patients are and to have a strong(er) voice nationally to continue to improve access to treatment for all HAE patients. To register see [www.haeuk.org/advice-support](http://www.haeuk.org/advice-support).

**Booklet:** HAE UK launched its HAE Patient Information booklet on the patient day in early December 2014. HAE UK hopes that the information booklet will provide first line information for newly diagnosed HAE patients. Also, it might be useful in explaining the rare condition to family, work and school. HAE UK will be making the booklet available in all HAE centres in 2015. It is also available on the HAE UK website and you can request a printed copy to be sent to you by e-mailing [support@haeuk.org](mailto:support@haeuk.org).

**Changes ahead:** HAE UK was set up in October 2010 to support HAE patients and by 2013 it became a registered charity. There is now a need to develop the structure of the organization to meet the present and future needs of the members.

There are presently five trustees: Barrie Hurley (Chair of Trustees), John Price (Treasurer), Ann Price, Ann Harding, and Ed Price. Ann Price has given notice that she will be retiring as a

trustee and volunteer at the end of June 2015 and the Chair of Trustees, Barrie Hurley, will lead the organization in developing HAE UK over the next six months. HAE UK will be looking at establishing voluntary and paid roles that cover the expanding needs of the organization.



**Fundraising:** Over the past four years HAE UK has been run with minimal funding. Now the organization will need to secure sufficient funds to responsibly employ someone to continue to develop the services. The trustees will be looking at all available sources of support in the coming months. HAE UK members have already started to raise funds in various ways. Sponsored cycle rides, sponsored runs, school reunions, gifts in memory of a loved one, raffles. Recently HAE UK was registered with JustGiving, allowing anyone to make a one-off donation, a regular monthly payment, or set up a page to raise funds for a sponsored event. HAE UK has also set up JustTextGiving, so people are able to make a donation to the charity by text. For more information about JustGiving, please see [www.justgiving.com/haeuk](http://www.justgiving.com/haeuk).

**USA** ([www.haea.org](http://www.haea.org))

**Kids with HAE:** Seeing the German youth presentation at the HAE Global Conference 2014 Shari Starr felt that other kids should have a chance to experience the same. She asked a friend, Beth Cottle, to join her in doing a small local meeting for the area HAE kids. Soon after they had the blessing and support from HAEA and on 10 January 2015 they held the first US HAE Youth event. The day featured not only a youth track, but also a separate parent track as well. The parent sessions focused on issues such as how to help a child deal with stress and setting up protocols and emergency plans for a child with HAE - and the youth sessions covered topics such as managing stress and vein care. The venue for the event was the upper level of the children's museum Discovery Place in Charlotte, North Carolina. At the end of the day families were given tickets to enjoy a few hours of fun together at the museum.

**National Patient Summits:** The US HAEA will hold two national patient summits in 2015. The first one takes place 18-20 September 2015 at Renaissance Atlanta Waverly Hotel & Convention Center in Atlanta, Georgia, while the second will be held on 9-11 October 2015 at Denver Marriott Tech Center in Denver, Colorado.

Both summits will be an opportunity to meet new and old HAE friends in a fun, supportive environment, learn about the latest in

HAE research and treatments, have HAE questions answered by expert HAE physicians/scientists, speak to insurance and reimbursement specialists, and participate in research that will be published in medical journals.

**Declaration of rights:** HAE patients have the right to treatment that alleviates suffering and improves quality of life. The HAEA has drawn up a declaration - based on HAE physician treatment recommendations published in a medical journal - that outlines the basic concepts of a sound approach to HAE treatment. It can be shown to emergency room physicians, the doctor who is responsible for the day-to-day care, family members, and anyone else who plays a role in the HAE treatment. You can download the declaration from <http://www.haea.org/resources/patient-toolbox/patient-bill-of-rights/>.



**AAAAI Annual Meeting:** Houston, Texas will be hosting the 2015 AAAAI Annual Meeting 20-24 February 2015. Thousands of allergist/immunologists, health and healthcare professionals will get together for five days with hundreds of educational offerings on a variety of topics such as allergic disease, asthma, immunotherapy, food allergy, skin disease, practice management, new technologies, and health care reform.

**Awareness day 2015:** In 2013, the HAE community in USA pitched in for more than 22 separate **hae day :-)** awareness events and fundraisers. Also, the patient community rallied to support the virtual fundraiser for the HAEA Benevolence Fund, the TransPac Sailing Race. Last year the HAE community created more than 30 separate **hae day :-)** awareness events and fundraisers - and the patient community rallied to support the virtual fundraiser for the HAEA Benevolence Fund, the Kili Care Climb. As for 2015 it is never too early to start planning your **hae day :-)** educational event or fundraiser. You can read about and be inspired by the events held in previous years and see the already growing list of 2015 **hae day :-)** events at [www.haea.org/hae-news/hae-day/about-hae-day-2](http://www.haea.org/hae-news/hae-day/about-hae-day-2).

**Year of the youth:** The US HAEA has declared 2015 the Year of the HAEA Youth and in support of the HAEA younger generations the organization has announced the HAEA Scholarship Fund. This program will provide financial support for young HAE patients seeking to improve their lives through academic achievement. It is available to US citizens with a confirmed HAE diagnosis (letter from a licensed physician) who will be enrolled in an undergraduate educational institution in the fall of 2015. Scholarships will be awarded based on a combination of financial need, academic effort, and individual educational goals. See more at [www.haeascholarship.org](http://www.haeascholarship.org).

## From our National Patient Groups

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

The first patient/physician workshop will take place in Minsk 24-26 April.

### India ([www.haei.org/map/154](http://www.haei.org/map/154))

HAEi is very pleased to announce our most recent National Patient Group. The contact person is Dr. Shaibal Guha in Patna, phone +91 983 506 643 32 and e-mail [shaibal\\_g@yahoo.com](mailto:shaibal_g@yahoo.com). HAE medication is still not available in India and the treatment costs are not yet taken covered by the government.

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

For a couple of years HAE has been one of 24 rare diseases officially included on the list with obligations by the government to treat patients. Presently Firazyr and Danazol is available in Russia - and Ruconest is ready for registration, while Berinerit is registered but not available on the market yet. It is not easy to determine the exact number of Russian care centers and hospitals that are capable in HAE diagnostic and treatment. It is often particular physicians that take care of HAE patients in regions. The leading medical center for HAE is GSC Institute of Immunology of FMBA Russia, located in Moscow.



### United Arab Emirates ([www.haei.org/map/97](http://www.haei.org/map/97))

Mid December 2014 Mr. Rashad Matraji, the HAEi Gulf Region representative, organized a Gulf Region HAE workshop attended by physicians and HAE families from the United Arab Emirates, Saudi Arabia, Kuwait, Qatar, Bahrain, and Oman. The conference was a huge success and focused on raising awareness and increasing diagnosis. A Gulf States HAE Workgroup was established during the workshop, and this group will now work on raising HAE awareness as well as planning new initiatives for the region.

Rashad Matraji worked tirelessly to form a 'cooperative agreement' with the United Arab Emirates Genetic Disease Association (GDA). This relationship has proven to be invaluable as GDA provided HAEi with contact information for Gulf Region physicians who treat HAE, offered administrative support for the meeting, and has promised to work with Rashad Matraji on future Gulf Region HAE activities.

## Patient stories from all over the world

In the last newsletter of 2014 HAEi launched the first three of a series of HAE patient stories from around the globe.

The series started with the stories of Ann Price from the United Kingdom, Rashad Matraji from the United Arab Emirates, and Cindy Hughes from Australia.

"The next three case stories will take us to Brazil, Denmark and Russia as we will meet Renata Martins, Erling Hess-Nielsen and Rada Buhtiyarova - a university teacher born 1980, a retired civil servant born 1940, and a postal operator born 1991", says HAEi Communications Manager Steen Bjerre.

Further case stories are on their way to approval and will be launched within the coming months, bringing the total to at least 12 before **hae day** :- ) 2015. Then more stories will follow and it is the aim to have some 20 patient stories literally covering the globe before the end of the year.

The first three as well as the three new case stories can be downloaded as pdf documents at [www.haeday.org/media/962](http://www.haeday.org/media/962). Feel free to distribute the stories as you see fit and help HAEi raise awareness.



**My courage is  
so much bigger  
than  
my disease**  
*Renata Martins*

**I feel just  
as I want to**  
*Erling Hess-Nielsen*



**Never give up  
- and do not  
pity yourself**  
*Rada Buhtiyarova*

## The HAE situation in Brazil

Renata Martins, 1st Treasurer of the Brazilian HAE organization ABRANGHE, has provided us with an overview of the present situation in her home country.



Brazilian patients have had access to Firazyr since 2011 and Berinert since August 2014 – and both of them will be available for self administration later on in 2015.

While the price of tranexamic acid is 8 USD for a pack of 12 (250 mg), Danazol costs 58 USD for a pack of 50 (100 mg). With tranexamic acid the patient pays for the medicine or gets it for free in (a few) public hospitals. As for Danazol it is registered for HAE treatment and is distributed for free in hospitals provided the patient has a prescription.

Oxandrolone is formulated and a few drugstores make it.

Both Firazyr and Berinert are allowed in Brazil as these medicines are registered with Anvisa, the Brazilian Health Surveillance Agency. However, they don't have clinical protocol for HAE in Brazil yet - and that leads to a pretty special situation: To get the medication the patient must ask his or her doctor to make an individual medical report about the patient and HAE requesting for Firazyr or Berinert. The patient then has to send the medical report and personal documents to a lawyer and provided that the patient pays for the legal assistance the lawyer will make a lawsuit against the state. Only after this bureaucratic and laborious process the patient will receive the medicine.

To make things just a little easier for the HAE patients in Brazil, ABRANGHE has joined forces with an advocacy organization that makes this process free for the patients registered with the Brazilian HAE organization.

Usually there will be some insurance coverage when a patient has an acute attack in a hospital. However, it can be hard to get the proper medicine at that moment. Presently there is only clinical protocol for Danazol, so most acute attacks are treated with painkillers or fresh plasma. For prophylactic treatment the doctors use Danazol, tranexamic acid or Oxandrolone. Some physicians are trying to change to Firazyr and Berinert but they only prescribe these kinds of medicine if the patient is able to pay on his or her own or by filing a lawsuit.

Up until now the patients filing lawsuits against the state have won these lawsuits. Once won, the patient receives a certain amount of medicine, depending on the doctor's prescription and the specific needs of the patient. Whenever the medicine is used the patient will have to turn to the lawyer again.

Particularly the first time it is hard because the patients need to attach a lot of documents and a lengthy medical report. In order to help the members ABRANGHE has developed a model that makes the process easier for patients as well as doctors who haven't dealt with HAE before.

Presently some Brazilian physicians are trying to get Firazyr and Berinert added to the Anvisa's drug list. When that happens there will no longer be any need for individual lawsuits.

### **Organization:**

Brazilian Association of Patients with Hereditary Angioedema (ABRANGHE) - National Member Organization established 2010. [www.abranghe.org.br](http://www.abranghe.org.br)

### **Patients:**

957 registered with ABRANGHE (November 2014)

### **Care centers:**

None.

### **Hospitals:**

27 - São Paulo (14), Rio de Janeiro (5), Rio Grande do Sul, Distrito Federal, Espírito Santo, Paraná, Pernambuco, Bahia, Minas Gerais, and Santa Catarina.

### **Available medication:**

Berinert, Firazyr and Danazol are registered for HAE treatment. Oxandrolone, tranexamic acid and Epsilon amino caproic acid are prescribed off label.

# Global Advocacy Work



## Recent activities

HAEi is invited to participate in a variety of international meetings. This is a brief overview of some of the activities in the recent months:

10-13 January 2015 HAEi participated in the first patient/physician meeting since HAE Japan became a recognized NGO in Japan. The event took place in **Tokyo, Japan**.

At the end of January HAEi along with the partner the Clinigen Group made the first round of presentations of the Global Access Program to several HAE pharmaceutical companies. These meetings took place in **Frankfurt, Germany**.

30 January-2 February HAEi was invited to the long awaited official opening of the US HAEA Angioedema Center in **San Diego, California, USA**. More on this in the next newsletter.

## Future activities

9-11 February HAEi will meet with representatives from the Society for Rare Diseases, the Association of Allergy and Immunology, and Office of Genetics at the National Institutes of Health - all located in **the Philippines**.

In the second half of February 2015 HAEi will be participating at the annual meeting of American Association of Asthma, Allergy and Immunology (AAAAI). This meeting features HAE related presentations by physician/scientists from throughout the world and therefore provides HAEi a unique opportunity to interact the medical community and representatives from industry. This year's meeting will take place in **Houston, Texas, USA**.

In March 2015 HAEi will participate in the annual conference "International Plasma Protein Conference – IPPC 2015". This time the conference is held in **Rome, Italy**.

Early April HAEi will participate in the first regional workshop for the Balkan's taking place in **Skopje, Macedonia**. Dr. Grivcheva-Panovska from Macedonia is coordinating this physician-focused workshop.

Later on in April HAEi will participate in the first patient/physician workshop in **Minsk, Belarus**.

15-17 May HAEi will take part in the national HAE Australasia meeting to be held in **Sydney, Australia**.

At the end of May HAEi will be represented at the 9th C1-inhibitor workshop in **Budapest, Hungary**.

### HAEi Research Grant Program

We will issue a Request for Proposals for HAEi Research grants in the first quarter of 2015. Similar to the 2014 program, HAEi will provide 50,000 USD per year for two years to research project(s) selected by an independent panel of scientists. Two projects were selected for funding in 2014 and we envision the same for 2015.

### HAEi Global Access Program

Together with Clinigen Group, HAEi has created a unique Global Access Program (GAP). It is the first time that a patient group has initiated this type of medication distribution program.

The GAP model includes

- (1) a 'Compassionate Use' Program that offers donated medication to patients in parts of the world where this type of program is allowed,
- (2) an Early Access Program where access to medication will be given in conjunction with a phase III clinical trial, until the medication is commercially available, and
- (3) a Named Patient Program where governments/hospitals order the medicine and provide reimbursement.

Late January HAEi presented the GAP to the pharmaceutical industry. More information will follow in the next newsletter.

### HAE Global Conference 2016

For the 2016 HAE Global Conference we are planning on four tracks – besides the General Sessions: A Patient and Caregiver track, a track for Healthcare Professionals, a Nurses Educational and Networking track, and a HAE Youngsters track. The venue of the 2016 conference will be communicated 16 May 2015.



## NEW PAPERS ON HAE

Here are summaries of some of the HAE related scientific papers published since our last newsletter:

### **HAE Attacks: Local Swelling at Multiple Sites - by Z.L. Hofman et al., University Medical Center Utrecht, the Netherland:**

HAE patients experience recurrent local swelling in various parts of the body including painful swelling of the intestine and life-threatening laryngeal edema. Most HAE literature is about attacks located in one anatomical site, though it is mentioned that HAE attacks may also involve multiple anatomical sites simultaneously. A detailed description of such multi-location attacks is currently lacking. Data of 219 eligible attacks in 119 patients was analyzed. 33 patients had symptoms at multiple locations in anatomically unrelated regions at the same time during their first attack. Up to five simultaneously affected locations were reported. The observation that severe HAE attacks often affect multiple sites in the body suggests that HAE symptoms result from a systemic rather than from a local process as is currently believed.

*(Clin Rev Allergy Immunol., December 2014)*

### **HAE in childhood. Diagnosis and therapeutic challenges - by A. Pagnier, CHU de Grenoble, France:**

In case of laryngeal edema or chronic abdominal pains, diagnosis is difficult in childhood because numerous differential diagnoses possibilities are to be considered. The diagnosis of HAE with normal C1Inh (type III) is also a challenge because it is based only on clinical features. Important school absenteeism can be due to recurrent abdominal attacks. Early diagnosis, specific management, and therapeutic education are necessary for improvement of quality of life. Subcutaneous treatment is not yet available for children. Studies are going on and in the meantime, C1Inh concentrate intravenous administration must be available for children quickly and safely.

*(Presse Med., December 2014)*

### **HAE: Treatment and educational therapeutic program - by I. Boccon-Gibod, CHU de Grenoble, France:**

The treatment of HAE has two main objectives: treat acute attacks and limit their occurrence in the short term and long term. The acute treatment should be administered as soon as possible for better efficiency and patient safety. Self-administration should be encouraged for greater patient autonomy and safety (reducing delay to receive treatment injection). Long-term

prophylaxis treatments should be set up to limit acute attacks occurrences and finally improve patients' quality of life and safety. Short-term prophylaxis treatments are required and should be thoroughly applied in case of exposure to known potential triggers such as surgery and dental care. The HAE National Educational Therapeutic Program "Educreak" is in place to allow the patient and his close family or partners to acquire skills for greater autonomy in day to day disease management.

*(Presse Med., December 2014)*



### **HAE and anxiety in oral surgery: A case series report - by G. Zanette et al.:**

HAE is little known to medical and dental practitioners, but with an increasing hospitalization rate over the years. HAE is an important issue in oral and maxillofacial surgery, otorhinolaryngology, endoscopy, emergency medicine, and anesthesiology because even simple procedures may cause laryngeal edema. Recommendations on the management of HAE include long- and short-term prophylaxis, and treatment for acute attacks, but the importance of controlling anxiety is underestimated.

*(Quintessence Int., December 2014)*

**High-molecular-weight kininogen cleavage correlates with disease states in the bradykinin-mediated angioedema due to hereditary C1-inhibitor deficiency - by C. Suffritti et al., University of Milan, Italy:**

Measuring plasma levels of cleaved high-molecular-weight kininogen may be a sensitive mean of assessing disease severity in HAE-C1-INH patients.

(*Clin Exp Allergy*, December 2014)

**Paediatric HAE: a survey of UK service provision and patient experience - by N. Read et al., Brighton and Sussex Medical School**

To improve knowledge regarding affected children in the UK, we surveyed major providers of care for children with HAE. 16 centres responded, caring for a total of 111 UK children. Seven children had experienced life-threatening crises. One-third of patients were on long-term prophylactic medication, including C1 inhibitor prophylaxis in four children. Eight centres reported patients who were initially misdiagnosed. Broad differences in management were noted, particularly regarding indications for long-term prophylaxis and treatment monitoring. Also, there were substantial variation in the organization of services between centres, including the number of consultants contributing to patient care, the availability of specialist nurses, the availability of home therapy training and the provision of patient information. Ten of 12 patient/carer questionnaires were returned, identifying three common themes: the need to access specialist knowledge, the importance of home therapy and concerns around the direct effect of angioedema on their life. To our knowledge, this study represents the first dedicated survey of paediatric HAE services in the UK and provides useful information to inform the optimization of services.

(*Clin Exp Immunol.*, December 2014)

**Activation of the ficolin-lectin pathway during attacks of HAE - by D. Csuka, Semmelweis University, Hungary, et al.:**

There is a marked heterogeneity of the pathomechanism and development of HAE attacks in different patients. Our results

suggest that the activation of the ficolin-LP may deplete the innately low level of C1-INH and thus, it may contribute to the uncontrolled activation of plasma cascade systems, and thereby to edema formation.

(*J Allergy Clin Immunol.*, December 2014)

**HAE with an estrogen trigger in a 12-year-old - by A.E. Mowat, Greenslopes Gynecology and Obstetrics Group, Australia:**

Although estrogens and progestins have been avoided in the management of HAE in the past, the reasons for this are based only on a small number of case reports. In this case, successful treatment with depot medroxyprogesterone acetate indicates that progestins, as an alternative management for estrogen-triggered HAE, certainly warrants further research.

(*J Pediatr Adolesc Gynecol.*, December 2014)

**Amitriptyline and bromazepam in the treatment of vibratory angioedema: which role for neuroinflammation? - by F. Guarneri et al., University of Messina, Italy:**

Vibratory angioedema is a rare form of physical urticaria, hereditary or acquired, which occurs at body sites exposed to vibrations. Pathogenic mechanisms of disease are not completely clear and, consequently, current pharmacological treatment is sometimes unsatisfactory. We report the case of a horn player affected by acquired vibratory angioedema, relapsing after prolonged use of the instrument and resistant to systemic antihistamines and corticosteroids, which successfully responded to therapy with low doses of amitriptyline and bromazepam. A neuroinflammatory mechanism can be likely implicated in the pathogenesis of vibratory angioedema, in line with many different cutaneous/mucosal diseases involving a complex interplay of homeostatic/allostatic systems. Furthermore, in mucosal diseases, such as vibratory angioedema, physical/psychological stressors have a relevant role. In such cases, because of the complex interplay between nervous and immune system, the pharmacological activity of benzodiazepines and typical antidepressants may downregulate neuroinflammation.



## News from the Industry



**25 December 2014**

The U.S. Food and Drug Administration (FDA) has granted orphan drug designation to **BioCryst Pharmaceuticals'** BCX4161 for the prevention of acute attacks of angioedema in patients with HAE.

Discovered by BioCryst, BCX4161 is a novel, selective inhibitor of plasma kallikrein in development for prevention of attacks in patients with HAE. By inhibiting plasma kallikrein, BCX4161 suppresses bradykinin production. Bradykinin is the mediator of acute swelling attacks in HAE patients.

Orphan drug designation is granted by the FDA Office of Orphan Products Development to novel drugs intended for the safe and effective treatment of a rare disease or condition that affects fewer than 200,000 patients in the U.S. This designation provides certain incentives, including federal grants, tax credits, waiver of PDUFA filing fees and a seven-year marketing exclusivity period against competition, once the product is approved. The approval of an orphan drug designation request does not alter the standard regulatory requirements and processes for obtaining marketing approval of an investigational drug. Sponsors must establish safety and efficacy of a compound in the treatment of a disease through adequate and well-controlled studies.

In May 2014, BioCryst announced positive results from the OPuS-1 (Oral Prophylaxis-1) proof of concept Phase 2a clinical trial of orally-administered BCX4161 in patients with HAE. The trial met the primary efficacy endpoint, several secondary endpoints and all other objectives established for the trial. The primary efficacy endpoint for the trial was the by-subject difference in mean angioedema attack rate on BCX4161 compared to placebo. Treatment with BCX4161 demonstrated a statistically significant mean attack rate reduction of 0.45 attacks per patient-week versus placebo,  $p < 0.001$ . The mean attack rate per patient-week was 0.82 on BCX4161 treatment, compared to 1.27 on placebo.

On 17 December 2014 the first patient was dosed in the OPuS-2 trial, a double-blind, randomized, placebo controlled trial which will evaluate the efficacy and safety of BCX4161 treatment for 12 weeks in patients with HAE.

**PHARMING**



**8 January 2015**

**Pharming Group NV** and **Salix Pharmaceuticals** have treated the first patient in their Phase 2 clinical study of Ruconest for prophylaxis in patients with HAE.

HAE patients deficient in C1 inhibitor and with a history of at least four attacks per month are being enrolled in the randomized, double-blind study, in which 30 patients will receive Ruconest either once or twice weekly, or placebo in each of 3 treatment periods. With the crossover design, all patients will receive each of the dosing regimens. The study will evaluate the safety and efficacy of Ruconest when used for prophylaxis of angioedema attacks in patients with HAE. The study will be conducted at sites in Canada, Europe, Israel, and the United States. The trial is being coordinated by principal investigators, Dr. Marco Cicardi, Professor at the University of Milan, and Dr. Marc Riedl, Associate Professor and Clinical Director of the US HAEA Angioedema Center at the University of California, San Diego.

“We are pleased to have quickly initiated the treatment phase of this important study, and look forward to its completion later in 2015”, said Bruno Giannetti, MD PhD, Chief Operating Officer of Pharming.

Under the terms of the Pharming-Salix license agreement, the companies will equally share the development costs for Ruconest for HAE prophylaxis. Pharming will receive an undisclosed milestone payment from Salix as and when FDA approval for this additional indication is given.



**8 January 2015**

**BioCryst Pharmaceuticals** has appointed Lynne Powell to the role of Senior Vice President and Chief Commercial Officer. Ms. Powell brings 24 years of industry experience to BioCryst, most recently serving as Senior Vice President of North American Commercial Operations at CSL Behring. In this role, she was accountable for the financial performance and general management of CSL Behring's commercial activities within the U.S. and Canada.

“We are very pleased to welcome Lynne to our BioCryst family. Her track record of delivering strong financial results and of

## News from the Industry



building and leading successful commercial organizations focused on rare diseases is exactly what we need at this stage of the Company,” said Jon P. Stonehouse, President and CEO. “As our Commercial Officer, Lynne’s primary responsibility will be to formulate BioCryst’s global commercial strategy and to build the global organization that launches our oral kallikrein inhibitors for the prophylactic treatment of hereditary angioedema.”

Throughout her 17 year career at CSL Behring, Ms. Powell assumed increasing responsibilities within the R&D, and commercial functions of the organization. She has significant global experience gained as Vice President, Global Commercial Development and Head of Business Development & European Marketing. Ms. Powell launched five products globally for rare diseases, including HAE. Prior to CSL, she held positions of increasing responsibility within GlaxoWellcome’s commercial strategy and clinical research organizations.

“I am very excited to be joining the BioCryst team at this point in the Company’s evolution,” said Ms. Powell. “I relish the opportunity to commercialize the portfolio of BioCryst discovered drugs, as we work towards making life better, longer, and easier for people with rare and serious diseases.”



**14 January 2015**

The Committee for Orphan Medicinal Products (COMP) of the European

Medicines Agency (EMA) has issued a positive opinion on the application for orphan drug designation for *BioCryst Pharmaceuticals’* BCX4161 for the treatment of patients with HAE. The European Commission will make a final decision on European Orphan Drug Designation based upon the COMP positive opinion. Orphan drug designation by the EMA provides regulatory and financial incentives for companies to develop and market therapies that treat a life-threatening or chronically debilitating condition affecting no more than five in 10,000 persons in the European Union (EU), and where no satisfactory treatment is available, or where a treatment exists, as with HAE, a new treatment such as BCX4161 may provide a significant benefit to patients affected by the condition.

In addition to a 10-year period of marketing exclusivity in the EU after product approval, orphan drug designation provides incentives for companies seeking protocol assistance from the EMA during the product development phase, and direct access to the centralized authorization procedure. The approval of an

orphan drug designation request does not alter the standard regulatory requirements and processes for obtaining marketing approval of an investigational drug. Sponsors must establish safety and efficacy of a compound in the treatment of a disease through adequate and well-controlled studies.

BioCryst expects to report results from OPuS-2 by the end of 2015.

**22 January 2015**



For the first time *Shire* has been placed in the Global 100 Sustainability Index, ranking 62nd in the index. The Global 100 Index is a global ranking by Canada-based media and investment advisory company, Corporate Knights, of the top sustainability performers and has come to be recognised as the gold standard in corporate sustainability analysis. The Global 100 Index is determined from public data using twelve quantitative sustainability indicators which include leadership diversity, employee compensation, tax paid, innovation capacity, and energy and water use, among others.

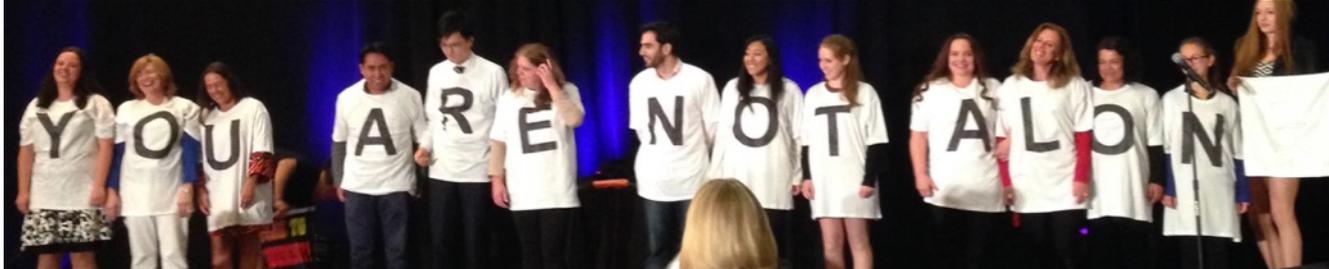
Shire’s CEO, Flemming Ornskov, commented: “We appreciate the recognition for Shire’s approach to being a sustainable, responsible business. Our patients rely on us and our products to live better lives and having an ethical and responsible approach to our daily activities, policies and programs is fundamental for our future, our patients’ future, and the wider global community.”



**26 January 2015**

The U.S. Food and Drug Administration (FDA) has granted Fast Track designation

for BCX4161, an orally administered, selective inhibitor of plasma kallikrein in advanced clinical development for the treatment of HAE from *BioCryst Pharmaceuticals’*. The Fast Track designation process of the FDA is designed to facilitate the development and expedite the review and approval of drugs intended to treat serious or life threatening conditions and that address unmet medical needs. A drug that receives Fast Track designation is usually eligible for more frequent written communication and meetings with the FDA to discuss the drug’s development plan and the collection of appropriate data supporting drug approval. Priority Review and Rolling Review may be granted, if relevant criteria are met. Rolling Review allows a drug company to submit completed sections of its New Drug Application (NDA) for review by FDA on an ongoing basis, rather than wait until the entire NDA is completed and then reviewed.



## HAEi around the globe

HAEi is a global network organization dedicated to raising awareness of C1 inhibitor deficiencies around the world.

Our **National Member Organizations (NMO)** are independent associations working for the benefit of patients in the specific country. Currently we have NMO's in 27 countries:

- **Asia:** Japan
- **Australia:** Australia, New Zealand
- **Europe:** Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Hungary, Israel, Italy, Macedonia, Norway, Poland, Portugal, Spain, Sweden, Switzerland, The Netherlands, United Kingdom
- **North America:** Canada, Mexico, USA
- **South America:** Argentina, Brazil

Our **National Patient Groups (NPG)** are HAE patient representatives in countries where no formal association has yet been founded or where the process of

founding an association is starting up. Presently we have NPG's in 13 countries:

- **Africa:** Kenya
- **Asia:** China, India, Malaysia, Russia, United Arab Emirates
- **Europe:** Belarus, Bulgaria, Croatia, Ireland, Romania, Slovenia, Ukraine

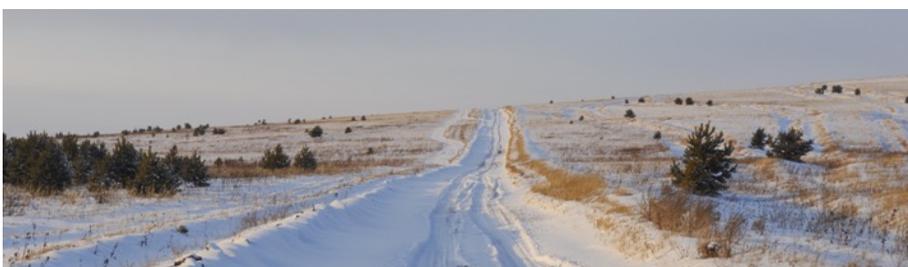
You will find much more information on the HAEi representations around the globe at [www.haei.org](http://www.haei.org). For instance, under each of the countries there is contact data for the national organization/group, information on care centers, hospitals, physicians, trial centers, and pharmaceutical companies as well as a list of available medication in the specific country.

The information on [www.haei.org](http://www.haei.org) is being updated as soon as we receive fresh data from the NMO's or NPG's.

### Your feedback is very welcome

Please let us know what you believe should be included in future newsletters. You can do that by providing feedback to Executive Director [Henrik Balle Boysen](#) or Communications Manager [Steen Bjerre](#). In addition, we invite you to

submit articles on any topics that you believe would be of interest to other readers. We look forward to your comments and working with you on future newsletters.



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

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MANY FACES  
ONE FAMILY