Issue 1 · February 2016

HAEi Newsletter

HAE Camino Walk 2016

For the 2016 version of the global awareness day **hae day :-)** HAEi will be bringing together HAE patients, relatives, care-givers, doctors, nurses, and industry for a mutual experience:

A walk on the pilgrimage route El Camino de Santiago.

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HAEi

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

HAEi Newsletter · Issue 1 · February 2016
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A Message from the President

Dear HAEi Friends,

Welcome to our first newsletter of 2016. It is a very busy time for HAEi as we gear up for the Global Conference and the Camino Walk – both events featured in the following – while continuing to vigorously pursue our global advocacy activities. We have an ambitious agenda for 2016 that features a robust expansion of services offered to our member organizations and a focused plan to encourage new countries to become part of HAEi.

Because HAE patients share a special bond, neither nationality nor language impedes our ability to communicate and learn from each other. The Global Conference and Camino Walk will provide very special opportunities to share our stories, experiences, and dreams for a healthy future.

Indeed, as noted in the theme for our third Global Conference – Creative Advocacy for Expanding Access to Therapy – our community will have a unique opportunity to share ideas and best practices for effective and winning advocacy strategies. I ask every HAEi friend who will participate in the 2016 Global Conference to arrive in Madrid ready to share their challenges and work with colleagues to explore solutions to winning access to life saving HAE medicines.

I am reminded of a quote I saw on a billboard in New York City not too long ago: "An invincible determination can accomplish almost anything…" My dear HAEi friends, let's bring an invincible spirit with us to Madrid! I am certain that, together as a community, we will come up with innovative, action oriented advocacy strategies to help our fellow patients win access to life giving medicine in areas where therapy is not currently available.

With warmest regards to all,

Anthony J. Castaldo
President, HAEi

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HAE GLOBAL CONFERENCE MADRID 19-22 MAY 2016

HAE Global Conference

HAEi cordially invites you to attend the 2016 HAE Global Conference, which will take place in Madrid, Spain 19-22 May 2016.

Already now there are more than 400 delegates registered for the third HAE Global Conference. Patients, care givers, health care professionals, and industry representatives will join to learn more about HAE, share experiences and knowledge in a friendly atmosphere conducted and driven by the patient community through HAEi.

"The theme for the 2016 HAE Global Conference is "Creative Advocacy for Expanding Access to Therapy," where the aim continuously is to find ways to improve time to diagnosis, to secure life saving therapies and get funding for these – allowing HAE friends around the world to lead a safer life and fulfill their life's potential," says HAEi President, Anthony J. Castaldo.

Registration will take place on a first come, first serve basis – and since HAEi again offers some extremely attractive registration rates and conditions, you should not wait too long registering for this exciting conference, expected to gather 550-600 people in Madrid.

Please visit the registration website frequently for the latest information on sessions, exhibitor information and more. HAEi is looking forward to seeing as many of you as possible in May in Madrid.

REGISTRATION IS OPEN

Go to the registration website at

http://www.trippus.net/hae2016-website

REMINDER: Abstract Submission

All participants in the Scientific Track are invited to submit abstracts that pertain to one of the topics listed below for presentation at the Scientific Program session, as part of the 2016 HAE Global Conference.

Deadline for submission of abstracts:

4 March 2016

Abstracts may be submitted to:

scientific@haei.org

General Topics:

1. Improving HAE Diagnosis
2. Improving HAE Care

Guidelines for preparation and submission of abstracts:

- The following structure is requested: Background, Methods, Results, Conclusions.
- The abstract text may not be longer than 2,000 characters, including spaces, excluding title, authors and affiliation.
- All abstracts must be submitted and presented in English.
- Authors should indicate their presentation preference: Oral / poster presentation or poster only.
- The Scientific Program Committee of the 2016 HAE Global Conference reserves the right to decide on the final allocation and presentation method.
- After having submitted your abstract, you will receive an acknowledgement by e-mail, confirming receipt.
- Authors will be notified on acceptance by 28 March 2016 by e-mail. Full instructions concerning the preparation and presentation of their abstract will be given at this time.
- All presenting authors must register to attend the conference. One participant can be the presenting author of maximum two abstracts.

SUBMISSION OF ABSTRACTS

Read more about the submission of abstracts:

http://goo.gl/cwi7DS

Walking the Camino for HAE

For the 2016 version of the global awareness day hae day :-) HAEi and AEDAF will be bringing together HAE patients, relatives, caregivers, doctors, nurses, and industry for a mutual experience: A walk on the pilgrimage route El Camino de Santiago (The Way of St. James) to the shrine of the apostle Santiago (St. James) in the Cathedral of Santiago de Compostela in the northwestern part of Spain.

Over three days (15 to 17 May 2016) the participants will walk three fairly short legs of the Camino (~20, ~15 and ~13 km), allowing everyone interested to take part. And there will be ample time to see things, go places, rest, and just be together.

The aim of **hae day :-)** on 16 May every year is to raise awareness of HAE among the general public and medical community in order to create an environment in which there is better care, earlier and more accurate diagnosis and knowledge that HAE patients can lead a healthy life. Indeed, one of the major reasons to arrange the walk on the Camino is the publicity that can be generated, as an **hae day :-)** event in itself and as a prelude to the HAE Global Conference in Madrid 19-22 May 2016. It will serve as a statement that HAE patients, many of them frequently incapacitated by their attacks, are slowly overcoming the obstacles to leading normal, fulfilling lives and can now feel free to undertake a journey of this nature.

At this moment more than 80 people have signed up for the walk – coming from Argentina, Australia, Brazil, Canada, Denmark, Hungary, Italy, Japan, Mexico, New Zealand, Spain, Sweden, USA, and Venezuela.

Are you interested in taking part in the HAE Camino Walk? There might still be room for one or two more – have a look at the Global Conference website at

http://goo.gl/jWUu02

The British graphic designer Leo Griffin has been so very kind to donate a logo for the HAE Camino Walk:

HAEi/AEDAF CAMINO WALK 2016

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Let HAEi Host Your National Organization's Website

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

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

Also it is worth mentioning, that this services is provided free of charge for the member organizations.

The first national HAE organization to introduce a website under the HAEi umbrella is HAE Spain. Have a look at the new Spanish website at

www.angioedema-aedaf.org.

First HAEi Report on South America

HAEi is delighted to announce the publication of the first report on the 'State of Management of HAE in Latin America'.

The report includes the results of the first survey conducted among representatives of HAE patient associations and groups from 9 Latin American countries reveal that the situation throughout the region is far from acceptable. In only two of the surveyed countries was support for HAE patients gradually approaching the optimal treatment and management model for this disease. The survey also reveals that the quality of diagnosis, patient care and treatment availability varies significantly between the region's countries but that, in all cases, it is clearly deficient and calls for immediate, radical change.

This report is available for download in Spanish:

http://goo.gl/08jAsD

and English:

http://goo.gl/2VgN5I

with Portuguese to follow.

EL ESTADO DEL MANEJO DEL AEH EN LATINO AMERICA

HAEi

Zika Virus and Plasma Protein Therapies

Recent scientific and public press reports have heightened awareness of the Zika virus and its emergence in the Americas. The temporal link between the emergence of the virus in Brazil and the birth of babies with microcephaly is most alarming. HAEi is aware that persons who rely on plasma protein therapies are understandably concerned whether these therapies are safe with respect to the Zika virus.

The following are extracts from statements issued by the Plasma Protein Therapeutics Association (PPTA) and the International Plasma Fractionation Association (IPFA).

PPTA

Zika virus is a Flavivirus that is primarily transmitted by the Aedes mosquitos, however it has been reported that it may be transmitted, even if rarely, from mother to child and also by transfusion of infected blood or by sexual contact.

Practically all Zika infection cases detected in Europe and the USA so far acquired the disease outside of these geographical areas. While the number of cases of travelers to the risk areas showing Zika infection at return may increase, the current situation indicates an almost total absence of Zika infection in the European or USA plasma donor population. In addition, donor-screening procedures make it highly unlikely that any person showing disease symptoms typical of Zika would be accepted for donation.

PPTA is aware that there are recommendations by agencies and blood collection organizations to defer potential donors of blood components who have traveled to areas considered at risk for Zika virus (i.e., Mexico, the Caribbean, and Central and South America). However, based on the practical absence of the virus in areas used for plasma sourcing such as the US and Europe, the low-levels and short-lived viraemia in the blood of infected individuals, as well as the established and very substantial processes with virus inactivation and removal capacity during manufacturing of plasma-derived products, PPTA does not consider that deferral of donors is warranted for donation of plasma for manufacturing use.

IPFA international plasma fractionation association

Zika virus was first identified in Uganda in 1947. Two epidemics were reported in the Yap Isles in 2007 and in French Polynesia in 2013-2014. In April 2015, locally acquired cases of Zika virus infection have been reported in Brazil and in December, the Brazilian Ministry of Health estimated that 440,000–1,300,000 suspected cases of Zika virus infection had occurred in 2015. To date 26 countries and territories in the Americas have confirmed autochthonous circulation of Zika virus with an estimated 1.5 million cases of infection.

A review of available information on this virus and of manufacturing processes of plasma products manufactured by IPFA members supports the view that Zika virus does not represent a risk of transmission through the use of plasma products.

All plasma-derived products manufacturing processes include validated and effective inactivation/removal steps that cover enveloped viruses such as Flaviviridae. Moreover, existing data confirm that a number of purification steps in manufacturing processes also contribute to virus reduction. Since the implementation of these steps in the manufacturing processes of plasma products, there has not been one report of a transmission of an enveloped virus, supporting the conclusion that Zika virus will be inactivated by these measures as well and that no additional measures are required upon collection of plasma specifically destined to the manufacture of plasma products.

It can be concluded that Zika virus does not represent a risk of transmission through the use of plasma-derived medicinal products.

HAE News from Around the Globe

Japan **www.haej.org**

The HAEi newsletter has received this input from Beverley Yamamoto, President of HAE Japan:

On 6 December 2015 we held a Christmas party and talk by Dr Isao Ohsawa at the Hotel New Osaka. There were 25 participants – patients, caregivers, friends, doctors and representatives from industry. Dr Ohsawa's talk covered the basic science around HAE, and available treatments overseas as well as those on the horizon. I could see many participants taking notes! Following on from this, we enjoyed Christmas cake and tea, followed by two breakout discussion sessions. One focused on the health care environment in which each of us experiences HAE as patients. This was apparently a very lively and meaningful discussion that was difficult to bring to an end. The second group focused on HAE with normal C1 inhibitor (type III). Dr Hide, myself and a newly diagnosed patient and her family made up this group. We should have been joined by another patient with HAE with normal C1INH traveling from Okinawa, but for the second time an attack kept her from joining us. The difficulties of confirming diagnosis and the possibilities for treatment were discussed. The evaluation survey that we conducted at the end of the meeting showed a very high rate of satisfaction with the meeting. Nevertheless, without self-administration or ability to carry our own medication, we still have patients who plan or hope to join us, but who are not confident to travel.

On 5 December 2015 Ms. Yukie Imamura, Executive Director of HAEJ, and I held a meeting with Mr. Sato, President of the National Hemophilia Network of Japan, which acts as a national umbrella organization for 25 regional patient groups in Japan. Hemophilia patients have had home therapy and access to self-administration since 1984. We were keen to better understand the hurdles patients had to overcome to be allowed home therapy. It seems that the hurdles were much lower than the ones we continue to face. We heard about the summer camps where doctors and nurses helped even very young hemophilia patients learn how to self-infuse. We were told that the aim is to have all patients able to self-infuse by the age of nine and generally this objective is met. This gave us food for thought as we continue to lobby the Ministry of Health, Labor and Welfare for home therapy and self-infusion to be authorized.

Mr. Sato warned us that the political climate and the condition of the health care system were more conducive to self-infusion being authorized in 1984 than they are today. We do not have the political leverage that hemophilia patients had, sadly, as a result of HIV and contaminated blood products. In addition, there were no co-payments for those insured in 1984. Today, there is a 30 percent co-payment, reflecting the pressures on the health system in the context of Japan's hyper aging society. However, we received valuable advice from Mr. Sato that will help us as we move ahead with our self-administration agenda and we are extremely grateful for the threes hours of his time that he gave us. We are looking forward to continuing the conversation.

Already in the New Year we are busy. We have had many queries from patients wanting to attend the Global Conference in Madrid. The doctors and I are already trying to work out how to ensure that patients can attend safely. Doctors Hide, Ohsawa and Iwamoto, and I are working to create a patient registry. We have completely re-vamped our operations at HAEJ and we expect things to run much more smoothly from here on.

Brazil **www.abranghe.org.br**

According to the most recent survey there are now 1,136 registered patients in Brazil – 812 woman and 324 men. The majority of the patients (393) are in Sao Paulo, while there are 144 in Minas Gerais and 126 in Rio de Janeiro.

Australia **www.haeaustralasia.org.au**

On the list: C1 inhibitor esterase will be included on the national product list. This means that patients who fit the criteria treatment of acute HAE attacks, pre-procedural prophylaxis (for high risk procedures) or routine prophylaxis (for patients who experience eight or more acute attacks per month) will be able to receive subsidized medication in the very near future. The National Blood Authority will work with the Australasian Society of Clinical Immunology and Allergy on clinical guidelines and governance arrangements to reflect funded availability of the treatment.

Managing HAE at School: For parents of children with HAE, there are added concerns about how to approach school. HAE Australasia has put together some materials that may be helpful for you and your school to work together – have a look at

http://goo.gl/BCu0nG

Sydney & Central Coast Meet Up: In December 2015 patients and carers from the Central Coast and Sydney got together for the last meet up of the year. The participants chatted over lunch about their personal experiences, and heard from a couple of the patients who are currently doing clinical trials. It's always great to hear what a difference being part of a trial makes to these patients. By having access to treatment (even if its for a short amount of time) they have an opportunity to feel well and swell free. The group also talked about the upcoming global conference in Madrid – there is a lot of interest for Australasian patients to attend. Each patient and carer received an information pack to take home and the participants discussed ideas on other resources that would be useful.

New Zealand **www.haeaustralasia.org.au**

Special authority listing with Medsafe (the New Zealand Medicines and Medical Devices Safety Authority) has just recently been approved for Icatibant (Firazyr) and it was available from January 1st 2016. As this is a very recent decision, pharmacies may not immediately have stock so there may be short delays while the product is made available.

Austria **www.hae-austria.at**

HAE Austria will be celebrating the 10th anniversary of the national organization 3-4 September 2016.

Serbia **www.haei.org/location/hae-in-serbia**

The global HAE family keeps growing. The newest member is Serbia, where Ivana Golubović has accepted to be the official HAE point of contact for patients in her country. She is located in Belgrade and can be contacted at:

ivana.golubovic@hotmail.com.

Ivana Golubovic – an HAE patient herself – is copy-editor at the Serbian national daily newspaper Politika and together with Dr. Sladjana Andrejevic she is working on the formal founding of a national HAE organization:

"Our primary goal is to pressure healthcare decision makers in our country to provide treatment Serbian patients. There are no available acute attack treatments in Serbia and the same applies to prophylaxis – both androgens and antifibrinolytic drugs. Not less important, we want to raise public awareness on HAE, medical staff included."

The founding assembly of HAE Serbia will be taking place on 27 February 2016 and numerous patients have confirmed their presence. There are 69 diagnosed patients in Serbia.

Continues on next page

United Kingdom www.haeuk.org

New logo: At the Patient Day 2015 HAE UK presented the ideas of a new logo for the organization as the previous one didn't clearly say what HAE UK is all about.

Whilst there was a lot of support for each of the various design proposals, there was also a lot of thinking around "we don't want a heart" or "the blood drop looks a little like a tear and we don't want tears". Based on the discussions at the meeting HAE UK has now decided upon a final design that shows how the members of HAE UK are all together aiming for the same ideals and communicating with the worldwide HAE organizations. The logo, designed by Rachel Annals, emphasizes that HAE UK is an inclusive and dynamic organization. The members who were able to make suggestions of what they wanted the logo to represent have enthusiastically received it.

Fundraising: Members of HAE UK have been busy over the Christmas and New Years holidays. First prize must go to Rick Talbot, who bravely took to the sea on Boxing Day (26 December) to take part in the Annual Boxing Day Sea Dip organized by Llandudno Lions Club in the Irish Sea. Rick Talbot, a fellow sufferer of HAE, along with in excess of 100 hardy souls, the majority of which were in fancy dress and supporting various charities of their choice, joined the annual dash into the sea, swam around for a couple of minutes and then waded back in to the shore. In the process Rick raised a sum in excess of 1,800 GBP for HAE UK. After the swim Rick said that it was in fact not too cold, but this may have been because the rain was pelting down almost horizontally, which made the sea feel quite warm (it is far colder in April after the winter months). Also because of the atmosphere amongst the contestants, everyone was buoyed along, in fact the camaraderie amongst everyone including the 100's of spectator's and members of Rick's family, made it all worthwhile. Rick also said a big thank you to all those who supported him both on the day and financially to make a healthy sum for HAE UK.

A&E cards: HAE UK is starting to get the A&E cards made and sent out. These are credit-card sized plastic cards identifying the patient, his or her immunologist and contact details. The card also contains recommendations as to treatment should the patient present at the emergency department. HAE UK hopes the new card will reduce confusion and delays if there is an emergency admission. The card has been designed in conjunction with the UK Primary Immunodeficiency Network (UK PIN) and bears their logo as well as the new HAE UK logo.

Spain www.angioedema-aedaf.org

HAEi Camino Walk: At the moment some 80 people have signed up the Camino Walk sponsored by HAEi and the Spanish HAE patient organization. If you want to join there might still be room – please have a look at the Global Conference website at www.trippus.net/hae2016-website.

Global Conference: AEDAF is actively involved in the planning leading up to the 2016 HAE Global Conference in Madrid 19-22 May 2016. The Spanish organization was present at the latest meeting with HAEi and ConferenceCare at the newly renovated Madrid Marriott Auditorium Hotel, which no doubt will be a spectacular venue for the conference. AEDAF is looking forward to seeing everyone in Madrid in May.

Website: AEDAF is pleased to announce that it launched its new HAEi-hosted website in December 2015. It is a responsive site adapted to mobile platforms and has a link to the other AEDAF website, which will remain as a database and source of more detailed country-related information. Please visit the new website at

www.angioedema-aedaf.org.

Canada www.haecanada.org

HAE Radio: HAE Canada is proud to announce the release of the second full episode of HAE Radio on 29 January 2016. In this episode, HAE Canada poses the question, "What does HAE mean to you?" to members of the Canadian HAE community. The episode investigates how HAE affects the Quality of Life of patients and caregivers through the unique stories of some of the members.

The episode is available at

www.haecanada.org/hae-radio

as well as on iTunes, Soundcloud and Stitcher. Please subscribe on any of these platforms for up to date notifications and downloads of upcoming episodes.

Current Membership: HAE Canada's membership now stands at 343. This represents a 77 per cent increase in membership since 1 July 2014. Becoming a member is easy and free. Membership is open to Canadians with HAE, their family members, friends and health care providers with treat those with HAE. Please visit www.haecanada.org for more information on how to become an HAE Canada member.

Volunteer Development Program: HAE Canada is excited that the Volunteer Development Program is in the final planning stages and will be implemented shortly. The organization is finalizing the training modules and creating engaging volunteer opportunities. The Volunteer Development program was created so that HAE Canada volunteers could get the most out of their volunteer experience through a positive and fulfilling volunteer experience. Aspiring volunteers who have already contacted the organization will soon be receiving guidance from the Volunteer Development Coordinator as HAE Canada operationalizes the program.

Upcoming Patient Events: Events in the planning stages will be held in Winnipeg and Victoria. Information on precise dates and venues will be posted on the HAE Canada website.

Board Planning Session: The HAE Canada Board of Directors met in January for its annual planning session. The goal of this meeting was – as was the case previous years – to review the organization's goals, objectives and achievements from the past year along with identifying goals for the upcoming year.

Patient Resources: Patient resources are now available to HAE Canada's membership upon request from the website

www.haecanada.org/resource-list.

Macedonia www.haemacedonia.mk

For the past couple of years HAE Macedonia has done its best to inform the general public as well as medical staff in Macedonia about HAE. It has attracted the attention of the government and resulted in HAE patients having both Berinert and Ruconest available in the country. Even though this is great news, there is still a lot to be done. There are distribution gaps, with patients struggling for medications in between, and also the entire supply is centralized. Patients who do not live in the Macedonian capital Skopje are not allowed to have the medications at home and not even in their cities or towns. They need to travel for two or three hours to come to Skopje and have their treatment. For now, HAE patients are also not allowed to take the medications outside Macedonia. Of course, HAE Macedonia will not be stopping here but will continue to push towards improving the conditions for all patients.

Peru
www.facebook.com/AngioedemaHereditarioPeru

There is now one more honorary member of HAE Peru, representing the southern part of the country. The new honorary member is Dr. Harold Manrique Ramiro Rosales who is Head of the Emergency and Intensive Care Unit at Hospital III Yanahuara in Arequipa.

USA www.haea.org

The HAEA Scholarship Program is available to US citizens with a confirmed HAE diagnosis (letter from a licensed physician) who will be enrolled in an undergraduate educational institution or already enrolled in an undergraduate institution in the fall of 2016. The Scholarship Committee, an independent adjudicatory board with no HAEA affiliation, will review applications. Scholarships will be awarded based on a combination of financial need, academic effort, and individual educational goals. Awards will be sent directly to the institution that the student is attending and (depending on the institution's financial aid policies) may be used for tuition, books, and room and board. Applications must be emailed no later than midnight EST on 23 March 2016 to

HAEScholarship@gmail.com.

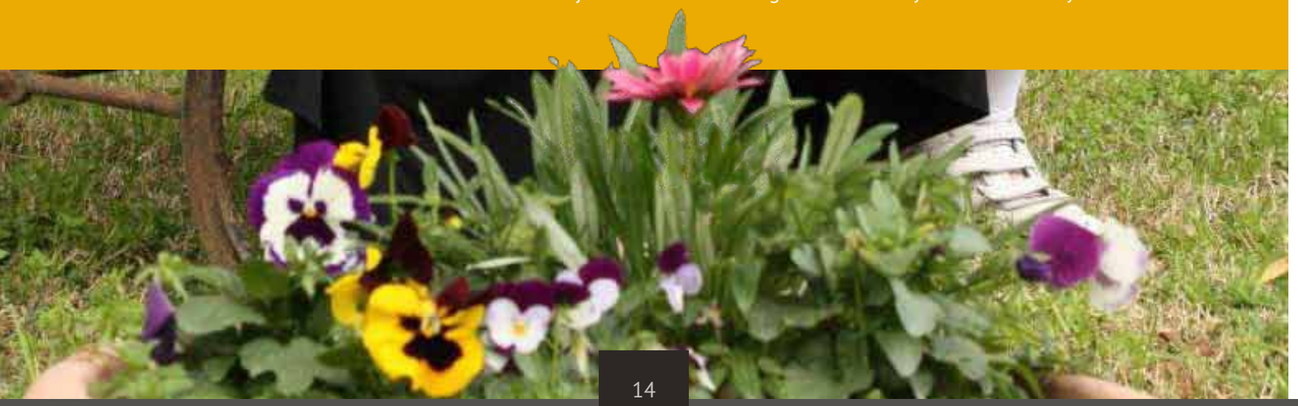
All applicants will be notified after 20 April 2016, regarding the results of the selection process. See much more at

www.haeascholarship.org/application.php.

Bosmat's Story

On the HAEi website at www.haei.org HAE patients from Australia, Belarus, Brazil, Denmark, Hungary, Israel, Norway, Russia, the United Arab Emirates, and the United Kingdom tell their touching and motivating stories. We invite you to read about the HAE lives of a diverse group of fellow patients that include a university lecturer, a truck driver, a retired nurse, an operations manager, a businesswoman, and a cattle farmer.

One of the most recent stories is from Bosmat Friedenreich-Wertzberger, Israel. She is a career woman, presently in a very intensive senior managerial position with 12-hour workdays and 24-7 availability. It is challenging but she loves the action – and since she started to self-inject her life has changed dramatically. This is her story:



I Won't Let the Disease Change my Way of Life

I must have suffered the first attack when I was around 13 and I had a few attacks the following years. However, an actual diagnosis was not made before I was drafted into the Israeli armed forces. At that time I was 18 and I was asked to undergo a blood test in order to detect specific diseases. I am a genetic mutant – the first in my family to have HAE.

How would you describe your years in school – did HAE keep you away from classes or were you able to manage without too much absence?

With only a few attacks between 13 and 18 the disease didn't really affect me in my teens. However, the attacks got worse towards 18 and at that point I was expected to join the armed forces – that is mandatory for young people of both sexes in Israel. That was really a very difficult period of my life since at that point the disease was not at all familiar in my country. On top of that the armed forces is a very rigid institution and it was not easy going through the service with all the attacks.

And later on in life: How did attacks affect your ability to study and to finish an education?

The disease never stopped me from achieving things I wanted. I did in fact fail my first driving test because I had trouble with my right leg due to an attack. That was both disappointing and annoying, but a few years later I finished my BA as well as my MBA successfully as that was a period without attacks.

And today?

Today I am a career woman, in management for 16 years in different positions. I am currently in a very intensive senior managerial position with 12-hour workdays and 24-7 availability. It is challenging. Without a doubt because it is a high stress job but I love the action – and since I started to self-inject the coping and the change in life style is dramatic.

Have your attacks always been the same?

Between 18 and 20 I had multiple attacks followed by a period of almost eight years without any sign of the disease. Then I got pregnant for the first time and the attacks came back full scale. Nowadays I have one to two attacks a week but as I inject myself intravenously with plasma derived C1-inhibitor at the start of an attack I am usually able to control it. I am glad to say that I have experienced no side effects from the medication I am using at the moment.

Frequency of seizures and edema differs from person to person. There are those in whom the seizure evolves and comes to the surface in just minutes. For me, it takes a few hours. Without treatment the edema may remain for two days to a week and gradually it will fade away.

What were your thoughts regarding childbirth, considering the risk of passing HAE on to the next generation?

I have to admit I never had thoughts not having children because of HAE. My daughter Tom was born in 2003 and my son Dor in 2011 – and we know now that I have passed the disease on to Tom. No doubt that being a mother to a child with HAE is more stressful than having the disease yourself but we try to look at it in a rational way and deal with whatever comes.

That seems to be pretty much the way you have managed things in your own case?

Yes, all along it has been my decision not to let the disease change my way of life. I would say that even before there was access to the proper drugs in Israel my life was pretty normal. Whenever I began at a new workplace that was the moment when I would explain to my colleagues about my situation – letting them know that suddenly I could swell and that it was quite okay for them to ask questions. It was my way of raising awareness of the disease. I would consider my life as normal even before I had access to the medications I have now. I learned the rhythm of my attacks and that helped a great deal.

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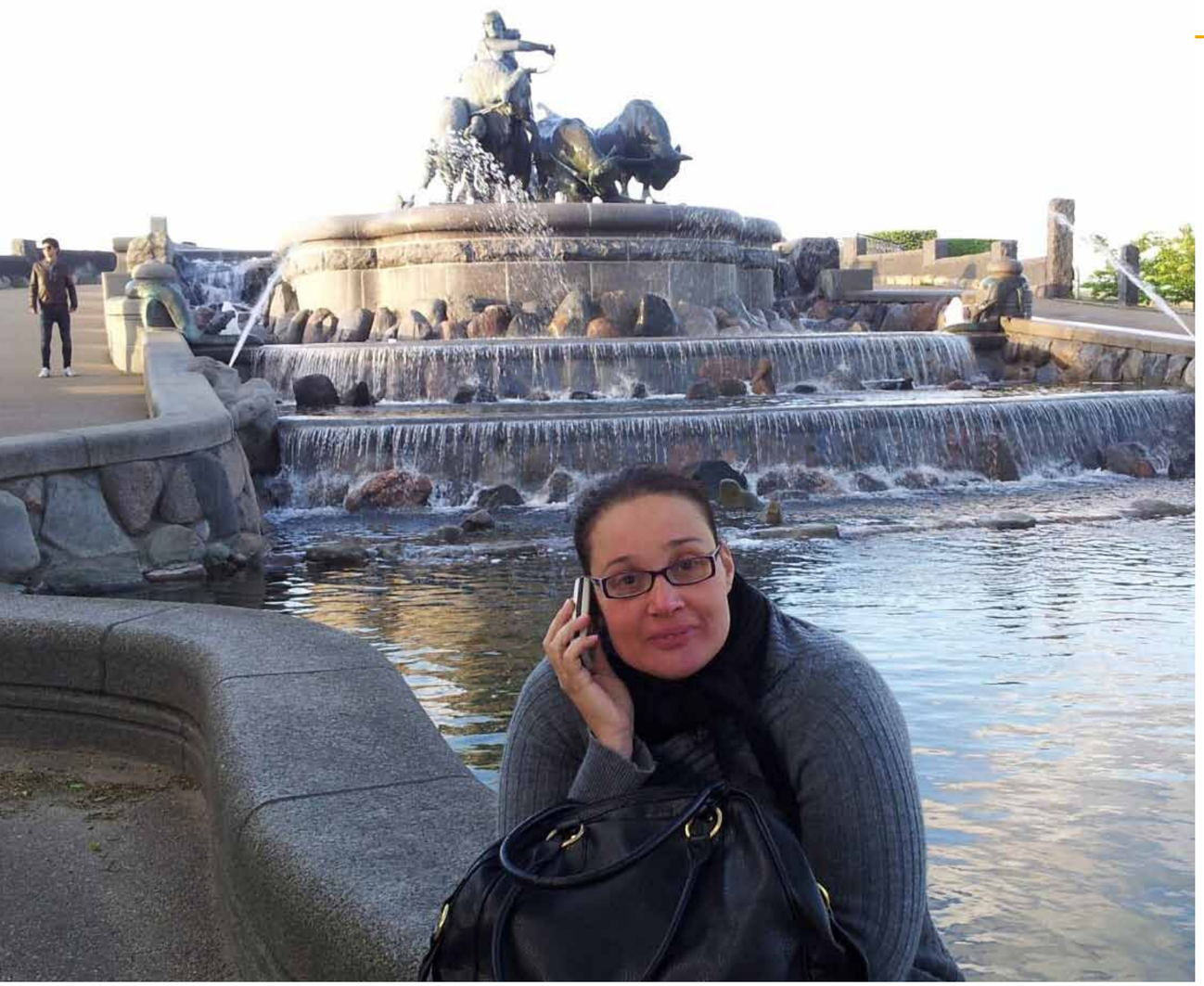

Speaking of drugs – how has things developed in Israel over the years?
When I had my first attack I was given steroids. In retrospect, this did not help and the attack was gone by itself after a few days. Overall, my life is divided in the time before 2009 and the years after. Before that year there was no treatment in Israel except for male hormones – and those were in general not given to women. Then in 2009 Israel received the first proper HAE medicines from Europe. Since I had access to these drugs the quality of my life has changed significantly – beyond recognition, really.

So today HAE patients in Israel have access to the proper medication?
Yes, finally. In Israel, we have a quite bureaucratic procedure regarding the health maintenance organization's approval of the use of drugs for the treatment of rare diseases, as these are often very expensive. This is one of the reasons why I got involved in establishing the national HAE association in my country.

But the right drugs are only one side of the issue.
Indeed. Apart from the HAE centers around Israel this disease is still like Chinese to a great number of people on the medical staff. They haven't got the first idea about what to do should they encounter a patient with HAE. It is all the more important to have organized instructions regarding what to do if such a patient comes to an emergency room. Lack of awareness on the part of a hospital is likely to endanger the patients and more than once our volunteers have helped save a life. For instance it happened when a man arrived at the

hospital with life-threatening edema of the trachea. His wife turned to HAE Israel and we provided the hospital the appropriate medications and that is what saved him. The hospital wanted to open his windpipe but beyond that did not know what to do.

I believe you had a similar experience yourself?
Yes, a few years back I had an episode. As this has happened throughout my life, I didn't really think much of it but as it traveled down my throat I had to go to the emergency room. All the medical staff jumped on me, put me on a respirator, and asked me what I had taken. At that point I was actually able to tell them precisely what was my disease and what should be done but it was very hard to get them to listen to me. In the end my partner had to explain to them that in this case the person suffering from the swelling did in fact know what she was talking about. This was a very unpleasant situation and I can't help thinking that someone that wouldn't have been able to stand up to such questioning could have been in serious trouble. Life-threatening, really.

Can you name a few key factors, which helps you cope with HAE in your daily life?
My way of coping with HAE is to not let it manage me but instead to manage it best I can. I am not allowing my disease to interfere with my daily routines. I try to address it with forgiveness but not complacency. I treat myself immediately when an attack starts. I do my best to fight bureaucracy and to help those HAE patients who have difficulties with bureaucracy mainly in getting the medication.

What is your recommendation to people who suffer – or think that they might be suffering – from this disease?
We need to raise awareness and help patients get diagnosed and treated. Unfortunately, many patients are embarrassed and do not want to have their disease exposed. Most importantly I would say to them that they shouldn't be ashamed to contact the appropriate medical centers so they can get the help and treatment they need. This is really important, you know. If you suspect that you might have HAE it is vital to ask for a blood test that can verify if the enzyme is missing or not. And if you already know that you have HAE – well, then there is absolutely no reason why you should be dealing with that on your own.

Global Advocacy Work

Recent activities

5-8 January: HAEi was in ***Buenos Aires, Argentina*** to discuss and evaluate ways to further enhance patient advocacy for the Latin American region.

14-15 January: HAEi participated in the Plasma User Group (PLUS) Consensus Meeting in ***Estoril, Portugal***.

23-26 January: HAEi met with the Philippine's Rare Disease Organization (PSOD) in ***Manila, Philippines*** to discuss a HAEi Development Grant for disease awareness, patient identification, physician education, and formation of a HAE group under the PSOD umbrella.

27-29 January: HAEi met with the newly established patient association in ***Izmir, Turkey*** in order to give some general guidance on running a patient association and to plan a patient/physician workshop in Turkey.

Future activities

23-26 February: HAEi will meet with rare disease experts (representing the hemophilia, immune deficiency and rare disease groups) in ***Thailand*** to plan expansion in South East Asia.

1-4 March: HAEi will participate in the Healthcare Information and Management Systems Society (HiMSS) in ***Las Vegas, USA***.

4-7 March: HAEi will participate in the 2016 American Academy of Allergy, Asthma and Clinical Immunology (AAAAI) in ***Los Angeles, USA***.

16-20 March: HAEi will participate in and together with our regional representative coordinate the 2nd Gulf Region workshop in ***Doha, Qatar***.

Ask the Doctors

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

What would happen if two people with HAE wanted to have a child together?

Dr. Christiansen: HAE is an autosomal dominant disease – this means that if you get the mutated gene you will have the potential to express the disease and pass it on to your children. HAE due to C1INH deficiency has nearly "full penetrance". This means that if you have the mutated gene, you will express symptoms of the disease. As with all things it is more complicated with HAE-normal-C1INH. This is also an autosomal dominate disease however with variable penetrance. Translating this it means that you could inherit the mutated gene but have no symptomatic expression of the disease – this would be a silent carrier. In general this will be more common for men. We know that with the "50 percent" chance from one parent of passing on one of the mutated genes will now be compounded by the fact that the other parent also has a copy of a mutated gene.

Dr. Riedl: To answer the question, we need to take a look at the basic genetics behind HAE. This has been best worked out for HAE due to C1INH deficiency – what is normally referred to as type 1 and type 2. Every person has two copies of the C1INH gene – one provided by each of their biological parents. Because C1INH gene mutations are rare in the general population, the vast majority of people affected by HAE have one normally functioning C1INH gene and one C1INH gene that does not produce functional C1INH protein due to a mutation. This is called a heterozygous genetic state – one functional and one non-functional gene. HAE is also an autosomal dominant genetic condition, which means that having that one mutated non-functional copy of the gene is enough to cause symptoms of HAE. It also means that for most couples having children, where one parent has HAE and the other does not have HAE, the risk of each child having HAE is 50 per cent because at conception each parent randomly provides one copy of their C1INH gene. The copy from the parent with HAE is a normal gene half the time and a mutated gene the other half. Now, back to our two prospective parents both with HAE: the math changes here because now each parent could randomly contribute a non-functional gene to the child. If we assume each parent is heterozygous for the C1INH mutation – and that is a good bet since this is nearly always the case – the equation works out to a 75 per cent probability that the child will get at least one non-functional C1INH gene and therefore have HAE. The other twist is that there is a 25 per cent chance that a child from these parents could have homozygous HAE – meaning that both copies of the C1INH gene are mutated with one coming from each parent. Homozygous HAE is extraordinarily rare in the medical literature. This may be due to the historically low odds of two unrelated people with a very rare genetic condition meeting and having children, but there is also speculation that homozygosity for C1INH mutations might lead to fetal death early in pregnancy. Interestingly, the very few individuals with homozygous HAE described in the medical literature showed a range of clinical symptom severity from mild to very severe. These homozygous individuals have a 100 per cent chance of passing a C1INH mutation on to their offspring.

Dr. Christiansen: I think that everyone needs to know the odds when making these decisions. Fortunately with the current menu of treatments and more to come we anticipate the ability to normalize the lives of individuals with HAE unlike past years.

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Dr. Zuraw: The risk of inheriting the mutation from each parent is the same as a coin toss. So, the risk of inheriting HAE for a child of two people each with HAE would be the chance of coming up with "heads" at least once when you toss a coin twice. The risk that the child would inherit both mutant genes would be the same as getting "heads" on both tosses. I am aware that some patients have had embryos screened for having HAE-causing mutations. While this is indeed technically possible, I believe that there are risks inherent in doing such a procedure. Similarly, amniocentesis to determine the genetic status of a fetus is not without risk. When we consider how much treatments have improved and especially how much more we expect them to improve in the future, I don't favor genetic screening of embryos or fetuses. Our vision is that the goal of treatment is to give patients a normal life.

HAE Papers

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

Efficacy of on-demand treatment in reducing morbidity in patients with HAE due to C1 inhibitor deficiency – by A. Zanichelli et al., Ospedale Luigi Sacco, Italy:

From January 2009 to August 2014, data on attacks and treatments were collected from 227 patients from the center in Milan. A total of 4,244 attacks were reported; 50 % were treated with approved therapies (pdC1-INH or icatibant), 15 % were with tranexamic acid, and 35 % were not treated. Attack locations were peripheral cutaneous (46 %), abdominal (34 %), multiple (12 %), facial (5 %) and laryngeal (3 %). Most of the treatments were self-administered: 93 % with icatibant and 59 % with pd-C1-INH. Median attack duration with icatibant was 8 and 11.5 h with pd-C1 INH. Median time from onset of symptoms to drug administration was 1 h with icatibant and 2 h with pd-C1INH and median time from drug administration to complete resolution was 5.5 and 8 h, respectively. Second treatment was required in 12.7 % of icatibant-treated attacks and in 1.9 % of pdC1-INH-treated attacks. (Allergy. 2015 Dec)

Swedish children with HAE report good overall health and quality of life despite symptoms – by A. Nygren, Karolinska Institutet and Karolinska University Hospital, Sweden, et al.:

This study explores various aspects of HAE in the Swedish paediatric population. HAE symptoms were experienced by 23 children, including abdominal attacks (96 %), skin swelling (78 %) and swelling in the mouth and, or, upper airways (52 %). Psychological stress was the most common trigger for abdominal attacks and trauma and sports triggered skin swelling. The majority had access to complement-1 esterase inhibitor concentrate at home. Current health and quality of life were generally rated as good. (Acta Paediatr. 2016 Jan)

Type II HAE: The first case report in Taiwan – by Ying-Juang Chen, Taipei Medical University Hospital, Taiwan, et al.:

Type I HAE is a very rare disease in Taiwan (1:1,000,000) and type II HAE is even rarer. We found only one family confirmed with a gene study. The reason for the lower prevalence of HAE may be due to ethnic factors or underdiagnosis. Many patients had a delayed diagnosis and died by laryngeal edema. The physicians in Taiwan must understand this disease to increase the diagnosis rate and decrease mortality. (J Formos Med Assoc. 2016 Jan)

The Janus faces of acquired angioedema: C1-inhibitor deficiency, lymphoproliferation and autoimmunity – by M.A. Wu and R. Castelli:

Several clinical and biological features of lymphoproliferative diseases have been associated with an increased risk of developing autoimmune manifestations. Acquired deficiency of C1-inhibitor (C1-INH) (AAE) is a rare syndrome clinically similar to HAE characterized by local increase in vascular permeability (angioedema) of the skin and the gastrointestinal and oro-pharyngo-laryngeal mucosa. Bradykinin, a potent vasoactive peptide, released from high molecular weight kininogen when it is cleaved by plasma kallikrein (a serine protease controlled by C1-INH), is the mediator of symptoms. In total 46 % of AAE patients carry an underlying hematological disorder including monoclonal gammopathy of uncertain significance (MGUS) or B cell malignancies. However, 74 % of AAE patients have anti-C1-INH autoantibodies without hematological, clinical or instrumental evidence of lymphoproliferative disease. Unlike HAE patients, AAE patients usually have late-onset symptoms, do not have a family history of angioedema and present variable response to treatment due to the hypercatabolism of C1-INH. Experiments show that C1-INH and/or the classical complement pathway were consumed by the neoplastic lymphatic tissues and/or anti-C1-INH neutralizing autoantibodies. Therapy of AAE follows two directions: 1) prevention/reversal of the symptoms of angioedema; and 2) treatment of the associated disease. Different forms of B cell disorders coexist and/or evolve into each other in AAE and seem to be dominated by an altered control of B cell proliferation, thus AAE represents an example of the strict link between autoimmunity and lymphoproliferation. (Clin Chem Lab Med. 2016 Feb)

HAE Attacks: Local Swelling at Multiple Sites – by Z.L. Hofman, University Medical Center Utrecht, the Netherlands, et al.:

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. This study investigated the occurrence, severity and clinical course of HAE attacks with multiple anatomical locations. Data of 219 eligible attacks in 119 patients was analyzed. 28 % 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. 2016 Feb)

Risk of thromboembolism in patients with HAE treated with plasma-derived C1-inhibitor – by H. Farkas, Semmelweis University, Hungary, et al.:

Sporadic reports and a study into the high-dose therapy of neonates with C1-INH concentrate administered in an off-label indication raised concerns that this drug might increase the risk of thromboembolism. A retrospective cohort study of 144 patients with C1-INH-HAE compared the incidence of thromboembolism and its risk factors in patients who received pdC1-INH with those who did not receive pdC1-INH as well as with those treated with danazol or with tranexamic acid. The study did not find any evidence for an increased risk of thromboembolism during treatment with pdC1-INH, despite the presence of multiple predisposing factors. (Allergy Asthma Proc. 2016 Jan)

Difficulties encountered in the emergency department by patients with HAE experiencing acute attacks – by R. Ucar et al., Necmettin Erbakan University, Turkey:

An evaluation of the difficulties experienced by patients with HAE in Turkish emergency departments (ED) shows that inappropriate treatment for HAE attacks was administered to 88.2 % of patients, despite their diagnosis of HAE. The most frequent difficulty was "not knowing how to administer C1 inhibitor concentrate". Other difficulties encountered were ED staff being unaware of HAE, lack of C1 inhibitor concentrate in the ED, and kept waiting for the appropriate treatment in triage despite their having angioedema in the head-and-neck region. (Allergy Asthma Proc. 2016 Jan)

Erythema Marginatum as an Early Symptom of HAE: Case Report of 2 Newborns – by I. Martinez-Saguer, Hemophilia Center Rhine Main GmbH, Germany, and H. Farkas, Semmelweis University, Hungary:

Angioedematous attacks can be fatal in the case of upper airway edema and are often preceded by prodromal symptoms like erythema marginatum. Initial symptoms usually occur in the first decade of life. In two cases of recurrent erythema marginatum in newborns prodromal symptoms could help determine the diagnosis of C1-INH-HAE such that, at a later time, angioedematous attacks could be treated promptly and effectively. Recognition of early symptoms and timely diagnosis of the disease along with adequate education of the pediatrician and parents are a prerequisite for prompt and effective treatment of attacks and the successful management of the disease. (Pediatrics. 2016 Jan)

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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 are recruiting at the moment:

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

Recruiting in United States.

https://clinicaltrials.gov/ct2/show/NCT01832896?term=hereditary+angioedema&recr=Open&rank=1

Open-label, Long-term Safety Study of Avoralstat in Subjects With HAE(OPuS-4).

Recruiting in Belgium and France.

https://clinicaltrials.gov/ct2/show/NCT02670720?term=hereditary+angioedema&recr=Open&rank=2

C1 Inhibitor Registry in the Treatment of HAE Attacks.

Recruiting in the Netherlands.

https://clinicaltrials.gov/ct2/show/NCT01397864?term=hereditary+angioedema&recr=Open&rank=3

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

Recruiting in Czech Republic, Germany, Israel, Italy, Macedonia, Poland, Romania, and Slovakia.

https://clinicaltrials.gov/ct2/show/NCT01359969?term=hereditary+angioedema&recr=Open&rank=4

Safety and Efficacy Study of Cinryze for Prevention of Angioedema Attacks in Children Ages 6-11 with HAE.

Recruiting in Germany, Israel, Mexico, Romania, United Kingdom, and United States.

https://clinicaltrials.gov/ct2/show/NCT02052141?term=hereditary+angioedema&recr=Open&rank=5

Study to Evaluate the Clinical Efficacy and Safety of Subcutaneously Administered C1 Esterase Inhibitor for the Prevention of Angioedema Attacks in Adolescents and Adults With HAE.

Recruiting in United States.

https://clinicaltrials.gov/ct2/show/NCT02584959?term=hereditary+angioedema&recr=Open&rank=6

12-Week Safety and Efficacy Study of BCX4161 as an Oral Prophylaxis Against HAE Attacks OPuS-2.

Recruiting in Belgium, Canada, France, Germany, Hungary, Italy, United Kingdom, and United States.

https://clinicaltrials.gov/ct2/show/NCT02303626?term=hereditary+angioedema&recr=Open&rank=7

A Phase 2 HAE Prophylaxis Study With Recombinant Human C1 Inhibitor.

Recruiting in Canada, Czech Republic, Italy, Macedonia, Romania, and United States.

https://clinicaltrials.gov/ct2/show/NCT02247739?term=hereditary+angioedema&recr=Open&rank=9

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?term=hereditary+angioedema&recr=Open&rank=10

Screening Protocol for Genetic Diseases of Mast Cell Homeostasis and Activation.

Recruiting in United States.

https://clinicaltrials.gov/ct2/show/NCT00852943?term=hereditary+angioedema&recr=Open&rank=13

Pathogenesis of Physical Induced Urticarial Syndromes.

Recruiting in United States.

https://clinicaltrials.gov/ct2/show/NCT00887939?term=hereditary+angioedema&recr=Open&rank=14

These trials are not yet recruiting but are expected to do so soon:

HAE, Neurobiology and Psychopathology.

Will be recruiting in Italy.

https://clinicaltrials.gov/ct2/show/NCT02159430?term=hereditary+angioedema&recr=Open&rank=8

Phase 1 Study to Assess the Safety, Tolerability, and Pharmacokinetics of Recombinant Human C1 Esterase Inhibitor in Healthy Adult Subjects.

Countries not provided yet.

https://clinicaltrials.gov/ct2/show/NCT02663687?term=hereditary+angioedema&recr=Open&rank=11

News from the Industry

PHARMING

21 Dec, 2015

Pharming Group N.V. and its Seoul based South Korean specialty pharma partner Hyupjin have received the marketing authorization for Ruconest in South Korea. Ruconest is approved for the treatment of acute angioedema attacks in adult patients with HAE. Effectiveness was not established in HAE patients with laryngeal and oro-pharyngeal attacks. HyupJin will now seek reimbursement for Ruconest in South Korea.

Sijmen de Vries, CEO of Pharming, commented: "HyupJin is a well-established and experienced company with a proven track record in South Korea. We look forward to them now extending the commercialization of Ruconest by providing HAE patients in South Korea with a new, safe and effective treatment to treat their HAE attacks."

Choon Duk Kim, General Manager of Hyupjin Corporation, said: "Ruconest is the first approved recombinant C1 esterase inhibitor worldwide and this approval of Ruconest will now enable us to provide the Korean HAE patients access to this most innovative way to treat their disease. We fully appreciate all the supports from Pharming Group for the approval of Ruconest in South Korea and we look forward to getting started."

Headquartered in Seoul, Korea, Hyupjin Corporation develops and distributes healthcare products from prominent companies in the USA and Europe since 1975. With 30 years of experience in the medical market, Hyupjin Corporation has tight relationships with healthcare professionals and has built extensive know-how of the medical community. Hyupjin's product portfolio mainly consists of oncology and immunology products, but also OTCs, dietary supplements and medical devices. Hyupjin has made a consistent effort for the treatment of incurable diseases along with improvement of patient's quality of life.

(Source: Pharming)

PHARMING

6 Jan, 2016

Pharming Group N.V. has completed the patient enrolment in the Phase 2 clinical study of Ruconest, (recombinant C1 esterase Inhibitor, 50 IU/kg), for prophylaxis in patients with HAE.

Thirty HAE patients deficient in C1 esterase Inhibitor and with a history of at least four attacks per month have been enrolled in the randomized, double-blind study. The patients receive Ruconest either once or twice weekly, or placebo in each of three four-week 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 recruitment phase of the study was initiated in January 2015 and is being 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, Professor of Medicine and Clinical Director of the US HAEA Angioedema Center at the University of California, San Diego.

"We are pleased with the timely completion of patient enrolment for this double-blind, randomized, placebo-controlled study. We expect the results to be highly informative in determining the safety and efficacy of Ruconest to prevent angioedema attacks in patients with HAE. We expect to have the top-line results of the study around the end of the second quarter. If the results are positive, we intend to meet with the FDA and EMA to discuss next steps for the program, including our plans for a new subcutaneous formulation." said Bruno Giannetti, MD PhD, Chief Operating Officer of Pharming.

Under the terms of the North American licensing agreement with Valeant Pharmaceuticals International, Valeant and Pharming share the development costs for Ruconest for prophylaxis of HAE. Pharming will receive an undisclosed milestone payment from Valeant as and when FDA approval for this additional indication is given. Ruconest has been granted Orphan Drug designation by FDA for the prophylactic treatment of angioedema caused by hereditary or acquired C1 esterase inhibitor deficiency, with data exclusivity until 2026 under the Biologics Price Competition and Innovation Act.

(Source: Pharming)

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Shire Baxalta

11 Jan, 2016

The boards of directors of **Shire plc** and **Baxalta Incorporated** have reached an agreement under which Shire will combine with Baxalta.

Shire CEO Flemming Ornskov, M.D., M.P.H., commented: "This proposed combination allows us to realize our vision of building the leading biotechnology company focused on rare diseases. Together, we will have leadership positions in multiple, high-value franchises and become the clear partner of choice in rare diseases. Our expanded portfolio and presence in more than 100 countries will drive our growth to over $20 billion in anticipated annual revenues by 2020."

Baxalta CEO Ludwig N. Hantson, Ph.D., commented: "The announcement marks a new path forward for our organization and is a testament to the significant progress we have made in achieving our strategic business priorities. We bring to Shire a strong portfolio and pipeline of market-leading products, high-quality manufacturing capabilities and a talented global workforce that places patients at the center of everything we do. The combined organization will be well positioned to accelerate innovation and deliver enhanced value for all stakeholders."

Baxter International Chairman and CEO José E. Almeida commented: "Baxter fully supports the proposed combination of Shire and Baxalta, which will create a major biotechnology company and global leader in rare diseases. Baxter is pleased to support this value enhancing transaction."

The portfolio will include over 20 leading brands and a robust pipeline of expected new product launches with complementary positions across growing multi-billion-dollar franchises. Shire brings HAE leadership through its currently approved prophylactic and acute therapies, Cinryze and Firezyr, respectively, and—pending completion of the Dyax acquisition—a Phase 3, potentially transformative prophylactic therapy.

(Source: Shire)

Shire Dyax

22 Jan, 2016

Shire plc has completed its acquisition of **Dyax Corp.** in an all-cash transaction. Shire's CEO, Flemming Ornskov, MD, MPH, commented:

"We are excited to complete the acquisition of Dyax and look forward to working alongside their very talented and committed team to address significant unmet patient need around the world. The addition of Kalbitor and DX-2930 to our portfolio strengthens our leadership position in HAE and, along with the commercial and research and development expertise at Dyax, is a clear strategic fit for us that advances our position as the global leader in rare diseases. We are confident that our patients, particularly those with HAE, will be served for many years to come."

(Source: Shire)

Continues on next page

1 Febr, 2016

Avalanche Biotechnologies, Inc. and **Annapurna Therapeutics SAS** have entered into a definitive agreement providing for the acquisition of all outstanding shares of Annapurna by Avalanche.

Upon completion of the proposed acquisition, the combined company's pipeline will consist of Avalanche's existing ophthalmic programs and four new gene therapy based programs, which are focused on Alpha1-antitrypsin (A1AT) deficiency, cardiomyopathy associated with Friedreich's ataxia, HAE and severe allergies. The combined company will be headquartered in Menlo Park, California.

Paul B. Cleveland, president and CEO of Avalanche, will serve as the CEO of the combined company, and Amber Salzman, Ph.D., president and CEO of Annapurna, will become president and chief operating officer of the combined company. Both will serve on the combined company's board of directors.

"This transaction creates the opportunity to build a leading gene therapy company with an extensive pipeline and significant scientific, financial and human resources," said Mr. Cleveland. "I have tremendous respect for Annapurna's commitment to high level research and development and we are looking forward to working together to drive our combined current programs forward. At the same time, we are seeking to expand our pipeline further through additional licenses and acquisitions that complement our expertise in vector development and optimization platforms, process development and manufacturing."

"Our businesses are highly complementary, and this transaction enables us to combine the best assets of both companies as we drive toward the development of new gene therapies in multiple disease areas, including rare diseases," said Dr. Salzman. "This transaction provides the capabilities required to bring promising treatments to clinical practice."

ANN-002 is the Annapurna gene therapy product candidate designed for the treatment of patients with HAE. The Annapurna management believes that the one-time ANN-002 gene therapy product, for which the company is planning its clinical trials, can offer meaningful long-term clinical benefit to HAE patients.

(Source: Avalanche and Annapurna)

8 Febr, 2016

BioCryst Pharmaceuticals, Inc. has announced results from OPuS-2 (Oral ProphylaxiS-2), a clinical trial of avoralstat administered three times daily as a liquid-filled soft gel formulation for the prophylactic treatment of HAE attacks.

In the OPuS-2 study, HAE patients with a historical attack frequency of greater than 0.45 attacks per week were randomized to treatment with either 500 mg or 300 mg of avoralstat, or placebo, administered three times daily for 12 weeks. The primary goals of the trial were to characterize the efficacy of avoralstat in reducing the frequency of angioedema attacks, and to evaluate the safety and tolerability of 12 weeks of avoralstat treatment. The primary efficacy endpoint was angioedema attack frequency.

Thirty-eight subjects received avoralstat 500 mg, 36 subjects received avoralstat 300 mg, and 36 subjects received placebo. Treatment with 500 mg and 300 mg of avoralstat three times daily failed to demonstrate a statistically significantly lower mean attack rate versus placebo. The mean (standard deviation) attack rates per week were 0.63 (0.57) on avoralstat 500mg, 0.71 (0.66) on avoralstat 300mg, compared to 0.61 (0.41) on placebo.

"OPuS-2 was a well-designed and executed trial that gave us a clear answer; this dosage form of avoralstat is not a viable formulation to move forward," said Jon P. Stonehouse, President & CEO. "While we are disappointed in the study results, we learned that meaningfully better exposure is needed for avoralstat to succeed. We expect results from a relative bioavailability study testing a novel solid dosage form of avoralstat by mid-year – the primary goals of this study are to achieve much higher exposures and twice daily dosing. Our other opportunity to achieve higher exposure of an oral kallikrein inhibitor is with BCX7353 – we expect results from the BCX7353 APeX-1 dose ranging study in HAE patients by year end."

Secondary efficacy endpoints included measures of quality of life, attack duration and attack severity. Statistically significant improvements in duration of attacks and in the Angioedema Quality of Life total score, and its domains, were observed comparing the 500 mg three times a day avoralstat arm to placebo.

Oral administration of avoralstat in OPuS-2 was generally safe and well tolerated; the adverse event profile was similar to that for placebo; and no safety signals were observed.

(Source: BioCryst)

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9 Febr, 2016

Pharming Group N.V. has extended the exclusive distribution agreement with Cytobioteck S.A.S., a privately owned Bogota, Colombia based specialty healthcare company, for the distribution of Ruconest® (recombinant, non-blood derived human C1 inhibitor) for the treatment of acute attacks of HAE by adding countries in Central and South America.

Pharming entered into the original exclusive distribution agreement with Cytobioteck in May 2015 for the distribution of Ruconest in Colombia and Venezuela. Under the extended agreement, Cytobioteck will also exclusively distribute Recounts in Argentina, Costa Rica, the Dominican Republic and Panama. Cytobioteck will continue to drive all regulatory processes and purchase its commercial supplies of Ruconest from Pharming at a fixed transfer price.

Sijmen de Vries, Pharming's CEO, commented: "We are very pleased that we have been able to extend the agreement with Cytobioteck for the distribution of Ruconest in Central and South America. Over the past year Cytobioteck have made good progress with the regulatory processes in Colombia and Venezuela and several emergency treatments have already been provided to HAE patients in these countries in accordance with local regulations."

Cytobioteck's CEO, Dr. Osvaldo Piñeros, commented: "We look forward to being able to provide HAE patients with Ruconest in Argentina, Costa Rica, the Dominican Republic and Panama, in addition to Colombia and Venezuela. Our role is to deliver the best therapies available for our patients and we believe Ruconest provides a significant treatment option for HAE patients as the one and only recombinant, non-blood derived C1-esterase inhibitor replacement therapy with a proven and consistent efficacy and safety profile."

(Source: Pharming)

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Febr, 2016

To mark the company's founding 30 years ago this year, **Shire plc** is launching a new initiative designed to positively affect the lives of children born with rare diseases, as well as the future of rare disease care.

Shire's Future Generation program, a 5 million USD initiative, launches today with two, global, three-year partnerships: one with SeriousFun Children's Network, the community of camps and programs serving children with serious illnesses and their families; and the other with the ACMG Foundation for Genetic and Genomic Medicine.

"As a company fast-becoming the leading global biotechnology company focused on rare diseases and specialty conditions, we are passionate about making a meaningful – and lasting – difference in the lives of patients," says Shire CEO Flemming Ornskov, MD, MPH. "In this, our 30th year, we want to celebrate our past by making a commitment to the future of the rare disease community. We are very proud to be teaming up with these two great organizations which will help ensure a bright future for the patients and physicians we are privileged to serve."

As a charity founded by actor and philanthropist Paul Newman, SeriousFun Children's Network has earned the respect of caregivers around the world. With its annual gift of 1 million USD for the next three years, Shire will enable nearly 1,000 children, many with rare diseases, to attend these transformational camps. Research has shown the camps to build children's confidence, expand their social network, and develop their capacity for resilience.

"The generous grant from Shire will enable campers coping with rare illnesses to have a life-changing experience at camp, and help their families to bond through Family Weekend programs," says Mary Beth Powers, CEO, SeriousFun Children's Network. "In addition, educational opportunities, made possible thanks to Shire, will strengthen the ability of our camps to serve children living with rare diseases."

Shire's support of the ACMG Foundation for Genetic and Genomic Medicine will fund 10 genetic fellowships, which will begin to address the severe shortage of medical geneticists. In the US alone, there is only one geneticist for every 600,000 individuals, which is less than half of the projected workforce needed. The partnership between Shire and the ACMG Foundation will help foster a future generation of geneticists around the world who will be crucial in the diagnosis and care of patients with rare diseases. Shire's grant to the ACMG Foundation is for 1.65 million USD over the next three years; the remainder of the Future Generation funding comprises other support programming for the initiative.

"We have reached a critical juncture in terms of the integration of medical genetics into health care," says ACMG Foundation Executive Director Michael S. Watson, PhD, FACMG. "Though geneticists are essential to the diagnosis and management of rare diseases and for the care of individuals with genetic conditions, we are faced with a significant deficit in the number of laboratory and clinical geneticists in the United States. Shire's grant supports the ACMG Foundation/Shire Laboratory Geneticist Fellowship Awards and Clinical Genetics Residency Program and will directly help grow the genetics workforce, which will directly benefit patients and their families dealing with rare genetic diseases."

Says Ornskov, "Our grants will open doors to the training of a new generation of practitioners and will make a tremendous difference in the lives of children, their families, and the rare disease community overall for decades to come."

(Source: Shire)

survey

HAEi Newsletter

Newsletter Readers' Survey

In order to make this newsletter still better HAEi would very much like to know your answer to a few questions. It will take you maximum two minutes but never the less be very valuable for the further development of the newsletter.

Please check the survey at

https://www.surveymonkey.com/r/YPMMBS3

HAEi

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

You are not alone

HAEi Worldwide

Currently you will find HAE member organizations in 52 countries:

North America (2): Canada, United States of America

Central America and Caribbean (3): Costa Rica, Mexico, Puerto Rico

South America (8): Argentina, Brazil, Chile, Colombia, Ecuador, Peru, Uruguay, Venezuela

Europe (28): Austria, Belarus, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Macedonia, Norway, Poland, Portugal, Romania, Serbia, Slovenia, Spain, Sweden, Switzerland, The Netherlands, Ukraine, United Kingdom

Middle East (3): Israel, Turkey, United Arab Emirates

Africa (1): Kenya

Central Asia (1): Russia

South Asia (1): India

East & Southeast Asia (3): China, Japan, Malaysia

Australia/Oceania (2): Australia, New Zealand

You will find much more information on the HAE representations around the globe at www.haei.org. On our World Map you will find contact information for our member organizations as well as care centers, hospitals, physicians, available medication, and clinical trials

The information on www.haei.org is being updated as soon as we receive fresh data from the national member organization.

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.

Corporate Information

HAEi is officially registered as a non-profit/ charity organization in the Canton of Vaud in Switzerland. The registered address is:

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