


Global perspectives:

HAEi MAGAZINE · ISSUE 3/2020

 92 Member countries



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– PART OF THE HAEi ACADEMY

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Cover photo

Late August HAEi proudly launched
the first bite of the HAE Academy
– the HAE Trivia Challenge

Read more on page 16

Magazine staff

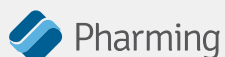
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HAE International is a global non-profit
umbrella organization dedicated to
working with a network of national
HAE member organizations to raise
awareness of HAE

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



DEAR HAE INTERNATIONAL FRIENDS,

We hope that you are staying safe and finding ways to successfully cope with the ongoing restrictions posed by the global COVID-19 pandemic. As evidenced by transforming the canceled 2020 HAE Global Conference into a highly effective virtual event, HAE International has quickly adapted to online delivery of our programs and services. Through it all, we remain dedicated to finding innovative ways to serve the HAE community and are happy to announce two important new initiatives in this edition of *Global Perspectives*.

The first called **HAE Companion** is an exciting new App that provides an easy way to access and store the popular HAE International emergency card that is currently a paper document. The HAE Companion App allows you to download and store the card on your smartphone. When planning a trip, you can download emergency cards in the languages of the countries to be visited. In addition, the App provides contact information and a map giving you directions to the offices of knowledgeable HAE physicians and hospitals with experience treating the condition. HAE Companion is presently awaiting final approval from Apple (iOS) and Google (Android), and HAE International friends should be able to start downloading this important tool by 1 November 2020.

The second new offering is the **HAEi Advocacy Academy**, a free online advocacy training platform that will be rolled out within the next few weeks. The HAEi Advocacy Academy includes a variety of tutorials and other materials that will help you develop the skills necessary to become effective advocates. The platform will also include training on effective use of HAE International's tools such as HAEi Connect and web hosting.

The famous scientist Albert Einstein once said, "In the middle of difficulty lies opportunity."

As you will read in the reports from our member organizations and our Regional Patient Advocates, Einstein's words typify how our incredible global community has continued to move things forward despite the harsh challenges posed by COVID-19. Also, ever inspired by the truly incredible people in our member organizations, HAE International's Board of Directors and leadership remain highly enthusiastic as we, a product and company neutral advocacy organization, lead the fight to achieve our ultimate and collective goal: Access to lifesaving modern therapy for everyone suffering from HAE.

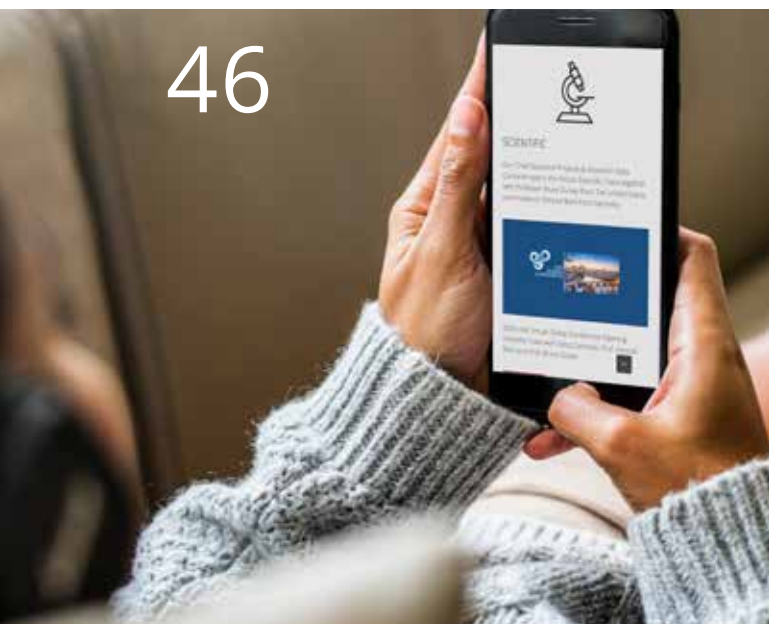
Finally, you will find an added bonus in this third 2020 edition of *Global Perspectives*. We have included a supplement containing the abstracts submitted for the 2020 HAE Virtual Global Conference Scientific Track. The abstracts follow the theme established for the Scientific Track "Determining better pathways to diagnosis and management of HAE" and "Creating a path to normalization of HAE patients' lives".

I wish you good health, please stay safe, and enjoy reading the pages to follow.

Warm Regards,

Anthony J. Castaldo
President & CEO, HAE International

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NEWS FROM THE HAEi REGIONAL PATIENT ADVOCATES

I hope that everyone is keeping as well as possible during the continuing COVID-19 crisis. While COVID-19 has been the main focus for most of our member organizations, the Regional Patient Advocates (RPAs) have continued to:

- Move forward with HAE International projects,
- Expand communication with patient leaders and health care professionals, and
- Participate in virtual meetings.

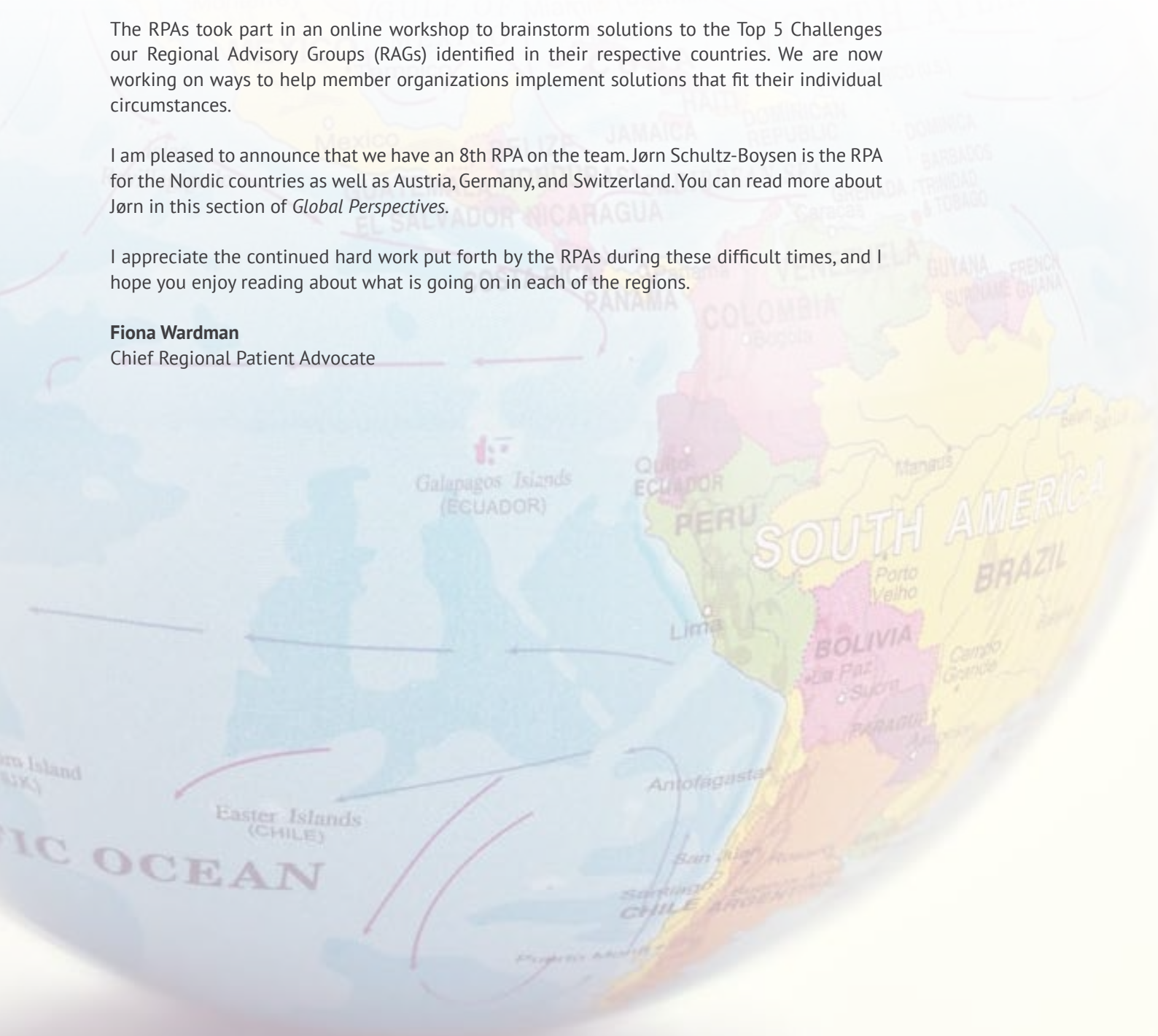
The RPAs took part in an online workshop to brainstorm solutions to the Top 5 Challenges our Regional Advisory Groups (RAGs) identified in their respective countries. We are now working on ways to help member organizations implement solutions that fit their individual circumstances.

I am pleased to announce that we have an 8th RPA on the team. Jørn Schultz-Boysen is the RPA for the Nordic countries as well as Austria, Germany, and Switzerland. You can read more about Jørn in this section of *Global Perspectives*.

I appreciate the continued hard work put forth by the RPAs during these difficult times, and I hope you enjoy reading about what is going on in each of the regions.

Fiona Wardman

Chief Regional Patient Advocate





MICHAL RUTKOWSKI
CENTRAL EASTERN EUROPE,
BENELUX & MIDDLE EAST



I am delighted to report that thanks to the HAE International hosted website tool HAE **Poland** (the Swelling Beautifully Association) has launched a completely new web, containing a number of user-friendly features both for patients and health care professionals. Above all, the site has become a fully digital communication platform, enabling joining the association, the possibility of obtaining the HAE Emergency Card, receiving the necessary educational materials, psychological assistance, as well as detailed information on diagnosis and treatment centers.

Due to reimbursement expiration for on-demand HAE treatments in Poland, on behalf of the Polish HAE patients, I participated in several meetings with decision-makers, emphasizing how important it is to keep access to current treatment options and what lack of access means to patients.

It is with great pleasure that I can inform you that the HAE National Center at the University Hospital in Krakow has become a new member of ACARE and I expect another two centers from Poland to apply for membership soon.

To improve the current state of awareness within members of HAE **Belgium**, I have found a volunteer (an HAE caregiver) with whom we will work on a new website for the Belgian patients. This yet has to be approved by the Chairwoman of HAE Belgium, but we hope to start our work in September. Also, I have successfully contacted Professor Cedric Hermans from the Saint-Luc Hospital in Brussels, who offers a helping hand in reaching HAE patients in **Luxembourg**, and I am looking forward to this very much.

To attract more HAE patients and to help establish new member organizations in the Middle East, I have recently been in contact with health care professionals from **Jordan, Saudi Arabia, Kuwait** and **Oman**.

Furthermore, I am happy to share with you that the HAE **Syria** patient lead, Mr. Mohamad Mechaan, has finalized his university graduation project called "Hereditary Angioedema in Syria".

Together with the HAE International Team, I am currently organizing the 2020 HAEi Central Eastern Europe & Benelux Workshop that will be held in the fourth quarter of this year. Due to the global pandemic situation and after communication with member organizations from my regions, the 2020 Workshop will be organized in virtual form. To attract as many patients as possible and increase the efficacy of the meeting, HAE International plans to use multiply languages translation service.

Stay tuned and stay healthy!



MARIA FERRON
MEDITERRANEAN, NORTH AFRICA & BRITISH ISLES



The ACARE Center initiative has been presented to all the countries in the region, and it has been well received. We already have ACARE Centers set up in the **United Kingdom, France, Spain, and Portugal** and I am expecting that more will be settled by the end of the year.

Both **Ireland** and **Libya** are collecting information to set up a formal HAE association in these countries.

HAE **Portugal** (ADAH) is now in both Facebook and Instagram – you can stay tuned at www.facebook.com/associacao.adah and www.instagram.com/hae_portugal. The Portuguese organization has requested

to have its website hosted under the HAE International umbrella – we will start working on this during the next months. Also, I have set up a call with HAE Portugal to establish an action plan for the coming months.

HAE **Spain** (AEDAF) will have their annual virtual meeting on 19 September 2020 after having to cancel the one scheduled for April due to COVID-19.

Both HAE **Morocco** and HAE **Ireland** now have a website hosted by HAE International – have a look at <https://haemorocco.haei.org> and <https://haeireland.haei.org>.



JAVIER SANTANA
CARIBBEAN AND CENTRAL AMERICA

Like many countries around the world, the Central American and Caribbean region has also been affected by the COVID-19 pandemic. This has allowed many governments to enact lockdown and establish new regulations to avoid contagion. We have not received information on HAE patients in the region who have been reported infected. Our group leaders and HAE International continue to work together in the effort to achieve a better quality of life for HAE patients in the region in the future.

As part of the efforts made, I held a Zoom meeting with all the member organizations in my region so that they could meet, maybe see each other's faces for the first time, and share ideas and strategies that they have used in their respective countries. For several hours, the participants were able to talk about their experiences with HAE, their experiences with the lack of medicines, what efforts they have made in their respective countries, and how they could support each other as neighboring countries. As a representative of HAE International, I made a commitment with them to continue holding Zoom meetings in order to offer them workshops and guidance on how to work in their countries.



JØRN SCHULTZ-BOYSEN
NORDICS & DACH



My name is Jørn Schultz-Boysen, and I am extremely happy to be appointed as the Regional Patient Advocate for the Nordics (covering **Denmark, the Faroe Islands, Finland, Greenland, Iceland, Norway, and Sweden**) as well as **Austria, Germany, and Switzerland** (also referred to as DACH).

I look very much forward to cooperating with the great member organizations in these countries. I will hopefully soon meet with representatives from Austria, Germany, and Switzerland to discuss further opportunities for cooperation and amongst other things, the utilization of the HAE International tools available.

Apart from being RPA, I also serve on the Board of Directors of HAE International and as a Project Manager for HAE International's event management system EventZoo. In addition, I hold the position as Treasurer of HAE Scandinavia. I have a professional background from a number of large Danish corporations including Bang & Olufsen and Grundfos, and I now serve as Business Development Director for the company adcobio ApS. I am an HAE patient myself as is one of my two children. I live in Struer, Denmark.



PATRICIA KARANI
SUB-SAHARA AFRICA



HAE International was able to make collaborations with the Sudanese Society of Clinical Immunology and Allergy (SSCI&A) to conduct the first doctor training seminar on HAE amongst health care professionals in **Sudan**. The online seminar was hosted by Dr. Rayan Goda, a clinical immunology and allergy specialist, and Dr. Nahla Erwa, a clinical immunology consultant and Assistant Professor at the Soba University Hospital, Faculty of Medicine, University of Khartoum, who is also the President for the African Society for Immunodeficiency (ASID).

The seminar took place over two days, with two sessions each day. The first one was conducted by the HAE International President & CEO Anthony J. Castaldo, and Fiona Wardman, Chief Regional Patient Advocate for HAE International. They elaborated on the important role that global organization plays around the world as well as the tools that doctors could utilize

in improving the situation in their country. I shared my detailed journey towards diagnosis in an African setup.

The second session was the scientific one which was done by Dr. Priya Bowry, an allergist and general physician from **Kenya**, in partnership with Professor Jonathan Peters who specializes in allergology and clinical immunology at the University of Cape Town Lung Institute, **South Africa**. They focused on the pathophysiology of HAE and the differential diagnosis between allergic angioedema and HAE. Professor Peters also highlighted his journey in realizing a patient group in South Africa as well as how they were able to get the first modern medication available for his patients.

The sessions were very interactive with a good question and answer session that highlighted the interest of doctors in Sudan.



NATASA ANGJELESKA
SOUTH EASTERN EUROPE



I have had continuous communication with patient organizations, pharma and physicians in the past period. Most frequently the newly established patient organization from **Croatia** informed me and consulted about their plan for activities in the next couple of months, including children's gathering and activities for the youngest members of HAE community in this country, accompanied by their parents. The meet-and-greet would be organized in the following way: lectures from a physician and an immunologist, workshop for children and parents, distribution of children's books, a picnic, and a visit to the Tuheljske Toplice museum where the event is to be held. Sixty people are planned to participate: Twenty-five children, as many parents accompanying those children, five physicians, three representatives from the pharmaceutical industry, and three organizers. At the moment, the event has been scheduled for November, but it will depend on the situation with COVID-19.

I have had consultations and information sharing with the physician in **Bosnia & Herzegovina** regarding the establishment of a Rare Disease Patient Alliance as well as the development in identifying new patients in the country. So far, to the best of my knowledge, there might be around ten new potential HAE patients. About eight have been diagnosed with either angioedema or HAE, and they are still waiting for three more to be diagnosed.

An interesting thing happened with a couple of potential patients contacting the President of HAE Croatia who was able to refer those patients to the physician in Bosnia & Herzegovina, which wouldn't have been the case if we hadn't established our network previously due to their participation at the South Eastern Europe regional workshops.

Verche Jovanovska Jankovska, the Vice-President of HAE **Macedonia**, participated in the meeting between the National Alliance of Rare Diseases in Macedonia (NARBM) and the Association of Citizens for Rare Diseases in Children (LIFE) from **Serbia** regarding the signing of a memorandum on collaboration between the two associations. The memorandum is signed to improve the position of patients suffering from rare diseases and members of their families through the exchange of knowledge and information on the retkebolesti.com portal, HAE included. This will enable patients, physicians, pharma representatives etc. to have general information about many rare diseases translated into languages spoken in our region. It is envisaged that with typing the keyword at the portal, for example "Swelling", will take you to a possible diagnosis that has this symptom and hopefully guide the patient and physician to run tests. Ivana Golubovic, the former President of HAE Serbia, is now coordinating the project for LIFE.

I started preparations for this year's virtual 2020 HAEi Regional Workshop South Eastern Europe by sending all patient representatives an invitation for their presentation and receiving an answer from some of them. I invited Dr. Marcus Margerl and Dr. Marc Riedl to present as experts at the regional workshop, and both cordially accepted it. There will be lots of work regarding the recording of different sessions following the initial agenda I have planned. All sessions are to be translated in the languages spoken in our region and videos to be subtitled to be accessible and available to as many viewers as possible who are not fluent in English. I have communicated with a group of youngsters from the countries in my region and received feedback from Erini Giannakidi from **Greece** with the aim to prepare the youngsters' track for the virtual regional conference.



FERNANDA DE OLIVEIRA MARTINS
SOUTH AMERICA & MEXICO



COVID-19 has hit Latin America very hard. Unfortunately, many lives have been lost, including that of family members of people linked to HAE patient associations.

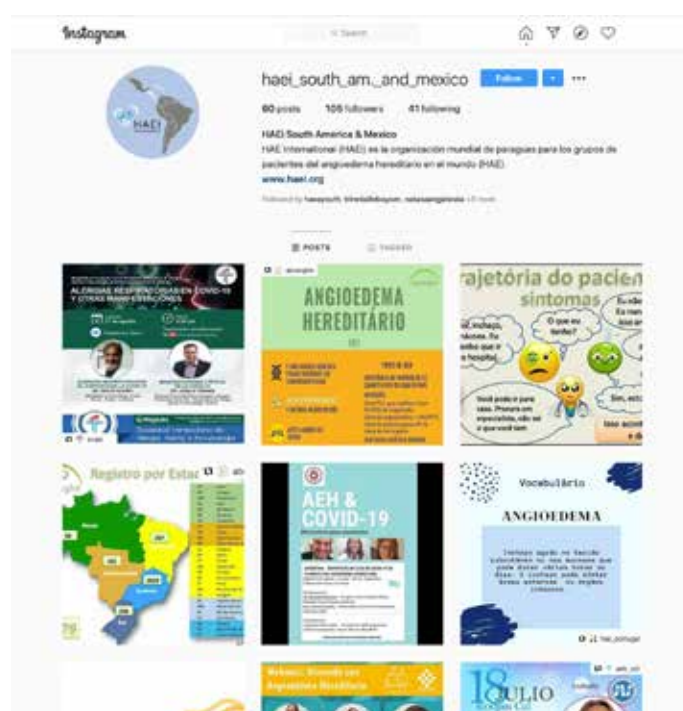
In **Mexico**, more than 187,000 people lost their lives to COVID-19. In **Brazil**, the number is more than 120,000. In **Peru**, there have been more than 28,000 deaths. In **Colombia**, more than 19,000, in **Chile** more than 11,000, in **Argentina** there over 8,000, and in **Ecuador** more than 6,000 losses. This is very sad.

Several associations in my region focused on supporting patients in these uncertain times. The many uncertainties about the virus, the crowding of health services and the lack of reliable information offered by some of the governments, generated panic among the population. Fear of exposure to the virus has caused some HAE patients to avoid medical consultations and to avoid seeking help during crises. After all, what would be more dangerous, an HAE crisis or the possibility of infection with the coronavirus?

Fortunately, COVID-19 does not appear to aggravate HAE conditions, and this has actually been the subject of some webinars promoted by the member organizations.

At this moment that we live in, in which many countries are still with strong guidelines of social distancing, social media are even more important to maintain communication. That is why in the last two months we

have worked on updating the website of HAE Ecuador and on creating a page for HAE Colombia. Also, we are in the process to have countries like Brazil, Peru, and Colombia fully operating on HAEi Connect.



Besides, the HAE South America and Mexico Instagram channel has been used to share information about HAE, member organization activities and news from HAE International.



FIONA WARDMAN
ASIA PACIFIC



The Asia Pacific region is diverse in terms of how the member organizations are structured. The region has well-established groups and some in their infancy, the others, somewhere in between. Despite the COVID-19 crisis continuing in so many countries, some good work is still being done to continue to create awareness in the region.

HAE **India** currently has a survey running for patients to answer a set of questions that will give a good understanding of the burden of illness and quality of life in India. There have been many patients taking part who are members of the HAE India patient group, and we hope to have more patients complete the survey who are not currently in the group but are made aware of the study via their doctors.

India now has two ACARE Centers – one in Mumbai and the most recent one in Chandigarh in Northern India.

The outcome of the first round of Regional Advisory Group answers and challenges was shared with the member organizations in each country. Having access to this information will go a long way to understand the region, and we will be working together to overcome these challenges.

Together with HAE **Taiwan**, a patient brochure was created. The flyer can be handed to HAE patients in hospitals to let them know about the patient group and some necessary information on HAE.

Introductions have been made between HAE **Singapore** and the Rare Disorders Society Singapore (RDSS). The patient lead is working on her own story to share on the RDSS website and social media platforms to help raise awareness of HAE. The patient leader is now also in contact with the President of the Clinical Immunology Society of Singapore.

HAE **Hong Kong** has a multilingual emergency card which can be downloaded from their website.

HAE **South Korea** has a new website at <http://haek.or.kr>.

I took part in the CSL Behring webinar on “Suffering in Silence: Assessing Rare Disease Awareness and Management in Asia Pacific”. The link to the webinar was shared in the translated languages to the region’s patient groups.

MAKE YOUR MEMBER ORGANIZATION VISIBLE – get started on haei.org/resources/haei-hosted-websites

- Freedom to add content and additional pages
- Choose from five templates as starting points
- Supports right-to-left (RTL) text direction
- Always updated
- Daily backup
- Training for editors
- Your domain name
- Secure https://
- **And it is free**

HAE INTERNATIONAL CAN HELP YOU WITH WEBSITE HOSTING

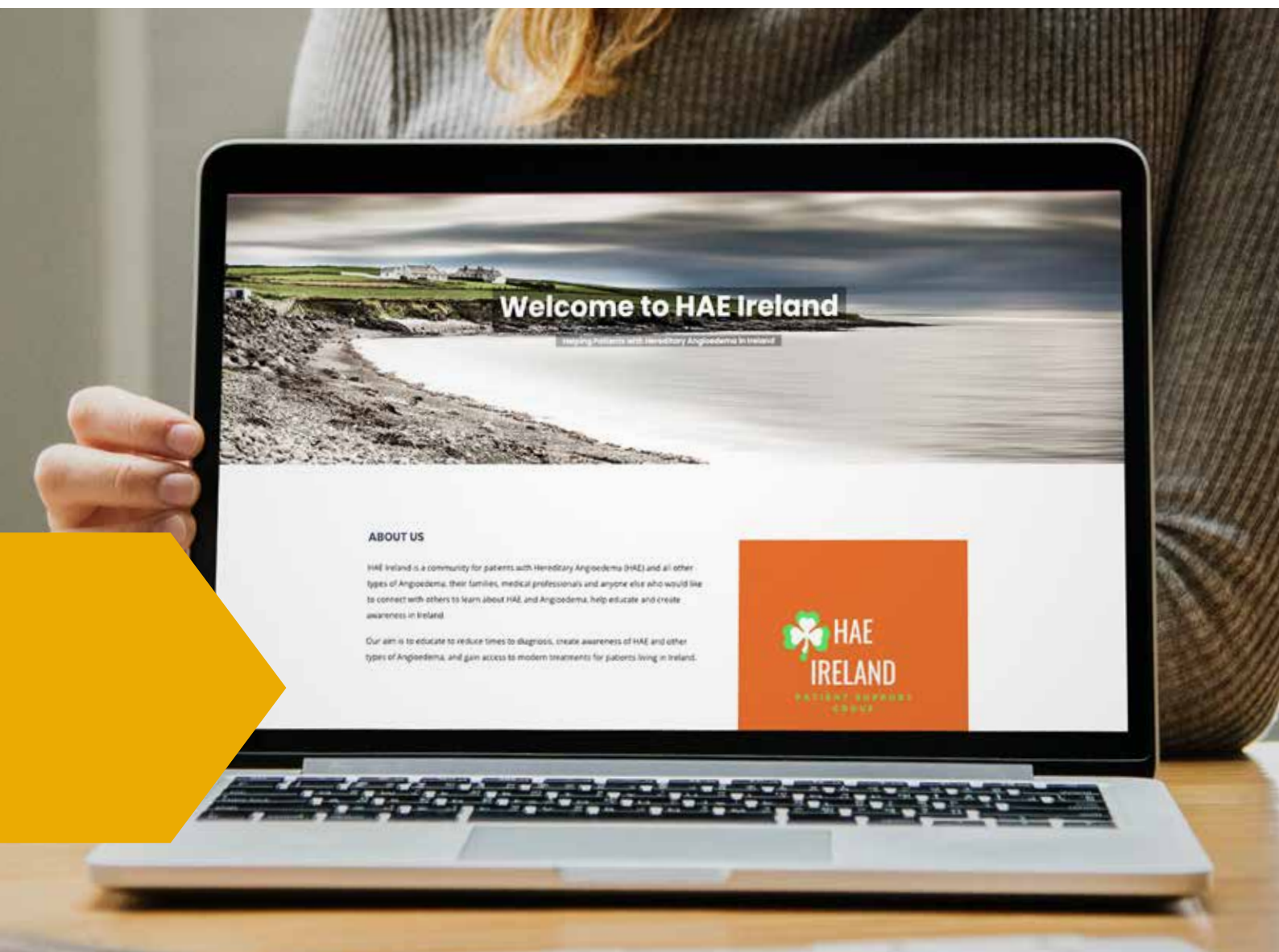
When it comes to website design, editing and hosting, it doesn't get much easier than what HAE International has to offer.

"For quite some time now, we have provided those member countries that would like it a full-scale national website, and many of them have chosen our solution. However, some organizations with, for instance, a limited number of members or in other ways reduced needs have been asking for a somewhat simpler solution. That is why we introduced a 2Go system that can be up and running within a few days", says Enterprise Technology Manager Ole Frølich.

At the other end of the spectrum, you will find countries that have had a good website for some years but are now facing a required update of content and design – and perhaps both. On that topic, Ole Frølich says:

"By nature, it takes more to move such a website under the wings of HAE International, but it is by no means an impossible task. In fact, it is quite a nice challenge that we gladly take on. Recently, we have done just that for the national organization in Canada with Belarus, Hungary, and Spain as other examples."

To this date, around 50 countries have chosen to have HAE International host their website.



GLOBAL NETWORK OF ACCREDITED ANGIOEDEMA CARE CENTERS GROWS RAPIDLY

Ten months ago, HAE International and the non-profit organization of leading clinical and research facilities in the field of allergy and asthma GA2LEN established GA2LEN/HAEi Angioedema Centers of Reference and Excellence – or in short ACARE.

“The joint venture with GA2LEN fulfills our longstanding goal of establishing a worldwide network of accredited angioedema care centers. Together we work on developing ACARE, ensuring that it is an attractive partner for HAE treating physicians all over the world”, says HAE International President & CEO Anthony J. Castaldo.

Establishing ACARE through cooperation with GA2LEN has given HAE International the certified accreditation program that the organization has been looking for as well as an inclusive solution where nobody will be left out as ACARE aims to be a worldwide network of specialized treatment centers.

“GA2LEN/HAEi ACARE is based on 32 requirements that must be met for a hospital to become accredited. Among these requirements are multidisciplinary approach, structured and valid protocols of diagnosis and management, assessment of patient satisfaction and unmet needs, support of the ACARE network, a “Never give up” attitude, knowledge and use of current nomenclature as well as classification of angioedema, family screening, scientific and educational activities as well as a cooperation with the patient organization in their country”, says Anthony J. Castaldo:

“If you wish to become an ACARE Center, you reach

out to the ACARE office and apply. It’s a very simple process: The office will assign an auditor to you – that’s the head or the deputy of another ACARE – and they then come to you or set up a virtual meeting to go over the criteria to make sure that all of them are met. Once this is done the recommendation for the decision goes to the Steering Committee, and then you are accredited and receive a certificate valid for two years. It is then followed by a re-audit to make sure that the high standards are being met over time. By this process we grow as a network because each audit and re-audit is a nice opportunity for one ACARE center to talk to another ACARE center, to learn from each other, and to work together on projects and other initiatives.”

Interacting with patient organizations is within the criteria: You must have a link to a patient organization in order to be accredited. But ACARE is the evolution of this because this is not just being linked to a patient organization – you must have true partnering with the organization.





Please see www.acare-network.com for an updated list of ACARE Centers across the globe.

If you would like to become an ACARE Center, please use this link for further information: www.acare-network.com/index.php/become-an-acare-center.



The new global network of specialized treatment centers has grown at high speed. At this point, there are ACARE centers in Argentina, Brazil, Bulgaria, China, Denmark, France, Georgia, Germany, India, Japan, Kuwait, Oman, Peru, Poland, Portugal, Russia, Slovenia, Saudi Arabia, South Africa, Spain, Thailand, Turkey, and the United Kingdom.

HAEi ADVOCACY ACADEMY



HAEi ADVOCACY ACADEMY IS YOUR FIRST STEP TO SUCCESSFUL ADVOCACY

HAE International remains dedicated to finding innovative ways to serve the HAE community and are happy to announce the new initiative HAEi Advocacy Academy.

“HAEi Advocacy Academy – a free online advocacy training platform that will be rolled out within the next few weeks – includes a variety of tutorials and other materials that will help HAE friends around the globe develop the skills necessary to become effective HAE advocates. The platform will also include training on effective use of our free tools such as HAEi Connect and web hosting”, says Anthony J. Castaldo, President & CEO of HAE International:

“If you believe that advocacy is a force to change the world, then this is the place for you: The free online learning platform HAEi Advocacy Academy is designed to help anyone interested in becoming a better advocate.”

“We are very excited to finally present the HAEi Advocacy Academy to our global community”, says Nevena Tsutsumanova, HAE International’s Operations Manager. And her colleague, the HAE International Executive Vice President & COO Henrik Balle Boysen says:

“HAE International’s main focus has always been on creating awareness and advocating for HAE patients no matter where they are located. That is what inspired us to look into an online learning platform that is free and easy to access from anywhere at any time. We want to share all our experience and help not only young HAE patients, but anyone interested in advocacy take their first steps towards becoming a successful HAE advocate.”

While HAE International is getting ready for the official launch everyone is encouraged to join the HAE Trivia Challenge and test their knowledge in the field of HAE.

THE RULES ARE SIMPLE:

- You can be in a team with your family and friends or go through the trivia by yourself
- If you are in doubt about an answer, you can always use the hints
- Remember to have fun – and happy quizzing everyone :-)

Once you are done, make sure to share your score with HAE International on social media using the hashtag #haetriviachallenge. Don’t forget to tag your friends and challenge them too.

MAKE SURE TO SIGN UP ...

Make sure to sign up at academy.haei.org to hear from HAE International as soon as the HAEi Advocacy Academy goes live.



JOSÉ EGIDIO FABIANI IN MEMORIAM



Dr. José Egidio Fabiani, who distinguished himself within HAE in his native Argentina as well as in Latin America, passed away earlier this year.

In a eulogy Alejandra Menendez, President of HAE Argentina, writes:

“Dr. José Egidio Fabiani was the initial engine for the development of the study and treatment of HAE in Argentina. Those of us who have had the pleasure of meeting him know of his constant struggle and dedication throughout his life for the knowledge of this disease. When many still disbelieved the disease, with his perseverance and tenacity, Dr. Fabiani gradually managed to transcend borders to the rest of Latin America. The lives of many of us would not have been the same if we had not had the fortune to cross his path and get the diagnosis of HAE.

It is very difficult personally to find the words for a goodbye after so many years of shared work, talks, discussions, and projects. I have enormous, sincere gratitude and appreciation for the man who started the fight for HAE in our country. I witnessed his great satisfaction at seeing the incredible advances in the field of HAE in recent years and his passion for continuing collaborating on the cause to which he dedicated his life.

Dr. Fabiani always expressed his enormous pride in having been the first to describe HAE in Argentina and Latin America. The photo of the newspaper article is a testimony of his lifetime commitment as it marks his beginnings with HAE. Far away and a long time ago; what a great achievement. How not to be grateful?!

We will miss him, and we will always remember him with great affection, admiration and respect. People only die the day they are forgotten, and you, Dr. Fabiani, will hardly be forgotten.”



As Dr. Fabiani stated (in Spanish) on his LinkedIn profile regarding the HAE situation in South America: “Unfortunately there is a lack of knowledgeable doctors, lack of laboratories for diagnosis and almost all countries have Danazol as the only treatment. Governments must take an interest; patients must act and defend their rights in each country, they must not allow themselves to be discriminated against. Indeed, HAE is a disease with the lowest cost of treatment within rare diseases.”

Dr. Fabiani was MD (Allergy and Immunology) from Universidad Nacional de La Plata, Argentina 1963-1969, and from 1970 onwards he worked tirelessly as a consultant on HAE in Argentina and Latin America. From 1972 to 1976 he worked at Hospital Finochietto in Argentina (Allergy and Immunology), followed by Hospital Italiano Buenos Aires, Argentina (Allergy and Immunology) until 1979. From then and until 2014 Dr. Fabiani worked at Instituto Argentino de Alergia Inmunologia Buenos Aires where he diagnosed the first HAE patients in 1979. He was the co-founder of Instituto Argentino de Alergia in the 1970ies, and from 2014 he was the President and founder of Asociacion Latinoamericana de Angioedema Hereditario (ALAeh).



Many member organizations will undoubtedly be able to recognize the challenge of maintaining a membership system. It applies whether it is based on a spreadsheet or some kind of technological solution.

“For many, there is a need for a degree of spring cleaning – regardless of the season. This is where HAE International’s free solution HAEi Connect can be of great value because in connection with the implementation you review and update the data of the individual member and subsequently you have all information in an efficient and easy to understand system”, says HAE International’s Enterprise Technology Manager Ole Frølich.

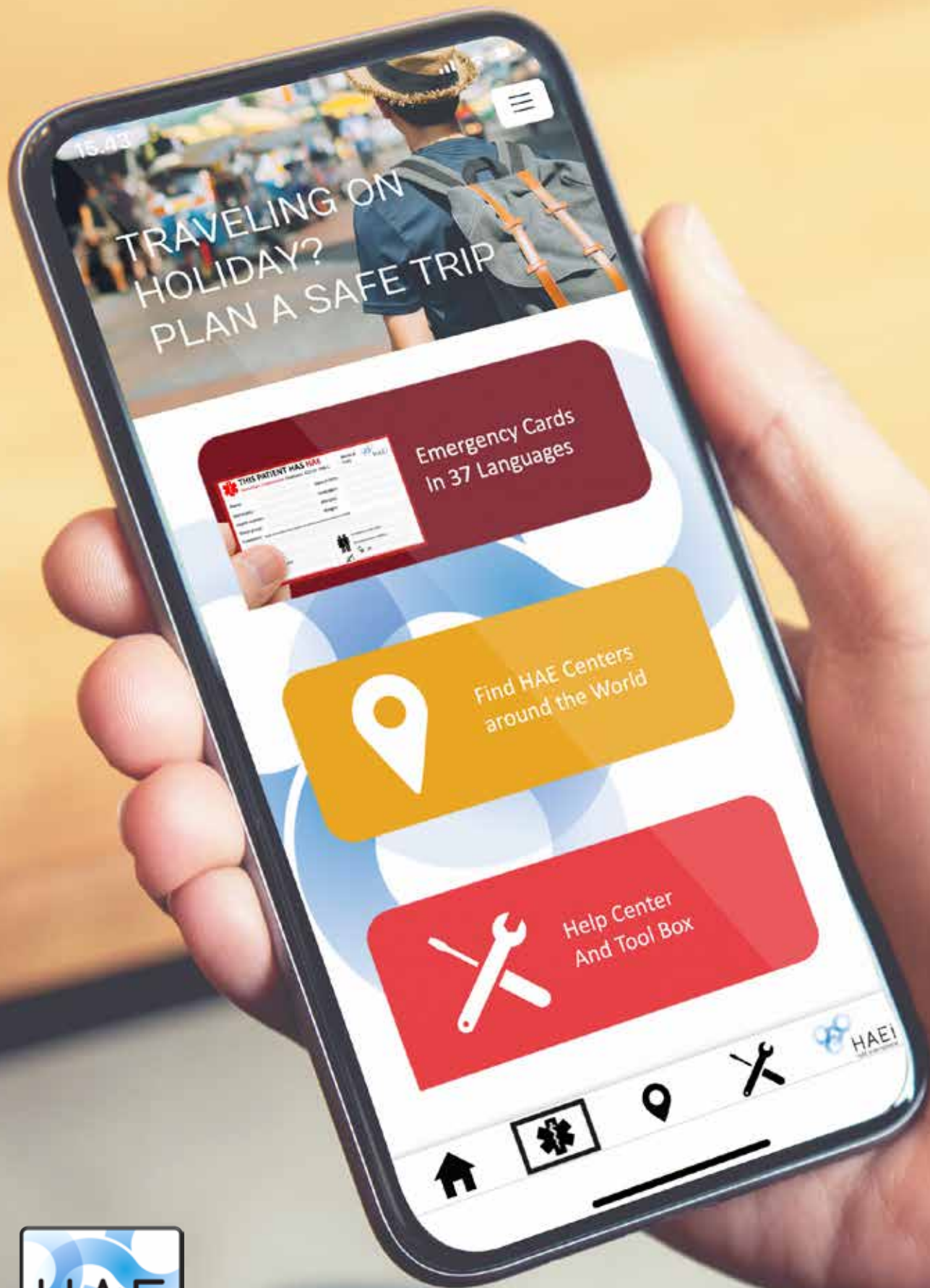
HAEi Connect – a cloud-based member database for national organizations to manage their members – is being rolled out to still more countries.

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

To date, HAEi Connect has been implemented in Australia, Brazil, Bulgaria, Denmark, Egypt, Hong Kong, Hungary, India, Iraq, Israel, Kenya, Lebanon, Mexico, New Zealand, North Macedonia, Norway, Peru, Poland, Qatar, Saudi Arabia, Slovenia, South Africa, Spain, Syria, Sweden, Turkey, the United Arab Emirates, and the United Kingdom.

“Furthermore, we are talking to a handful of national organizations so I expect that we will within the coming months be able to add countries like Japan, Czech Republic, Canada, China, Croatia, Lithuania and the United States of America”, says Ole Frølich.







New App from HAEi will be Your Loyal Companion

HAEi has developed HAE Companion an exciting new App that provides an easy way to access and store the popular HAE International emergency card that is currently a paper document. This App will become available on both Apple's App Store and Google Play for the Android platform.

"One of the key elements for the new App is the excellent emergency card project that our Regional Patient Advocates have undertaken over the last couple of years. People may, however, find it cumbersome having to complete, download, and print the emergency cards – and that is why we introduce the HAE International App "HAE Companion". The App will feature our full range of emergency cards and will allow smartphone users to download emergency cards to their device", says Henrik Balle Boysen, HAE International Executive Vice President & COO.

On Apple's platform, the emergency cards will be stored in Apple Wallet, and on the Android platform, the cards will be stored in the App PassBook with similar functionality.

"The new App allows the user to store as many emergency cards as needed. When planning a trip, the user can download relevant languages for the locations he or she is going to visit. The emergency cards are very easily added to Apple Wallet and PassBook – and can be removed just as easily", says Henrik Balle Boysen.

Should the user accept that HAE Companion knows the user's location, the App also offers so-called geofencing. This means that the App can send push messages to the user when he or she is on the move – for instance, "We can see that you are near an Italian speaking country. Do you want to download the HAE Emergency Card in Italian?"

The HAE Companion App also links to the HAE International database with contact information on ACARE Centers as well as HAE knowledgeable hospitals and physicians. Therefore, the user can always ask the App to show the nearest HAE knowledgeable center, hospital or physician. Using GoogleMaps or Apple Map, the App also indicates directions and distance to the nearest place.

"Initially, the HAE Companion App will focus on the mentioned main features, but we expect to add new functionality to the App moving forward", says Henrik Balle Boysen.

HAE Companion is presently awaiting final approval from Apple and Google. Provided this goes smoothly the App should be available around 1 November 2020.

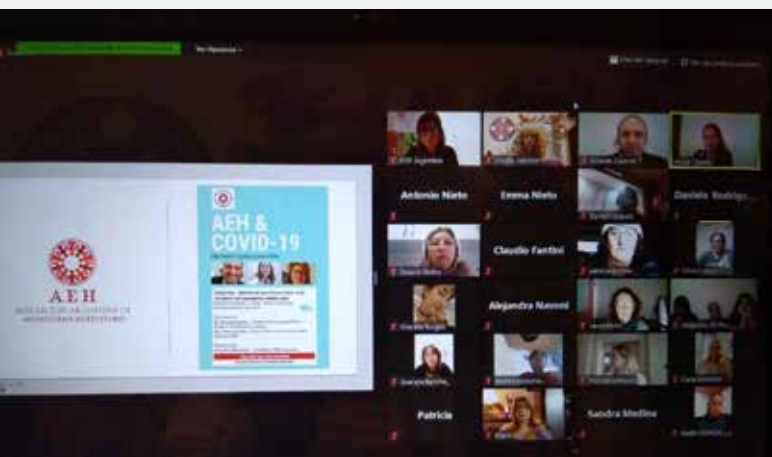
NEWS FROM MEMBER ORGANIZATIONS AROUND THE GLOBE



ARGENTINA

From President Alejandra Menendez:

Considering the ongoing pandemic situation and the importance of experience sharing on 8 August 2020, HAE Argentina held a patient webinar to present the first reported case of COVID-19 in an HAE patient in our country. The meeting was co-hosted by Dr. Ricardo Zweiner, Dr. Jesica Cepeda and myself as the meeting moderator.



Dr. Zweiner (Allergy and Clinical Immunology, Hospital Universitario Austral; member of the HAE Scientific Committee at Asociacion Argentina de Alergia e Inmunologia Clinica (AAAeIC); member of Sociedad Latinoamericana de Alergia, Asma e Inmunologia (SLAAI)) gave an excellent overview of HAE as well as of the SARS-COV-2 coronavirus and the current situation in Argentina. He moved on to specifically consider COVID-19 in HAE patients and provided some useful general recommendations. He then particularly referred to the case of the HAE patient he treated during the course of her COVID-19 infection.

Following Dr. Zweiner's presentation, patients were moved to hear Jesica Cepeda's personal life story with HAE and her struggle to get a correct diagnosis and how she achieved her freedom once she learnt how to self-inject and treat her condition at home. Jesica Cepeda, who is a medical doctor specializing in Gastroenterology at Hospital Italiano de Buenos Aires, retold her experience during the days she suffered

from COVID-19 and the successful outcome of her treatment.

The presentations were followed by a Q&A session which resulted in an extremely enriching discussion for all the attendees; many doctors from our country who had also joined the meeting were able to provide their comments and suggestions.

Needless to say, the webinar provided a wonderful opportunity for experience sharing and for venting out fears and concerns regarding the effects of COVID-19 in HAE patients. We thank all the participants from the HAE community in Argentina and our friends from several Latin American countries – Brazil, Mexico, Uruguay, Colombia, Peru, and Ecuador – who also attended the meeting.



IRAQ

Still more national organizations choose to have their website hosted with HAE International. One of the most recent is Iraq – please have a look at <https://haeiraq.haei.org>.



PERU

From HAE Peru (Asociación de Pacientes con Angioedema Hereditario del Perú):

From Peru we want to inform you a brief summary of the most significant advances in favor of patients with HAE:

- In June of this year, after more than two years of having obtained the sanitary registration granted by the General Directorate of Medicines, Supplies and Drugs (DIGEMID), it was possible to apply, for the first time in Peru, Ecallantide (Kalbitor) for an acute HAE crisis.

- Since July of this year we have two ACARE reference centers, the only Peruvian specialized centers internationally recognized by the HAE International and Global Allergy and Asthma European Network (GA²LEN) to treat patients with HAE. You will find their contact information at <https://haei.org/hae-member-countries/peru>.
- Currently, the Peruvian Society of Allergy, Asthma and Immunology (SPAAI) has prepared a guide for the management of HAE, which is in the process of being published.



We leave you the links in which we share the news at the respective moment: <https://bit.ly/2Z3PcGn> and <https://bit.ly/3l00LLC>.

You can also follow HAE Peru via www.instagram.com/aeperu and <https://twitter.com/aeperu>.



USA

*From Patient Advocate/Social Media Manager
Janice Viel, US HAEA:*



US HAEA Programs Transition During COVID-19

Pandemic: The COVID-19 pandemic has dramatically altered the way we communicate and connect with one another. At the US HAEA, we understand how vital it is for our HAE community to feel connected despite COVID-19 restrictions. Our commitment to our HAE family is heartfelt, so we have rapidly adapted to offer uninterrupted access to the HAEA Team, as well as our services and programs.

This spring, over 300 people celebrated **hae day :-)** through a very successful HAEA Virtual Walk that enabled our community to raise awareness and funds via online mediums while keeping active and counting steps at home.

Our annual HAE IN-MOTION® events are popular because they bring friends and family together to raise awareness while engaging in fun, physical activity. This year, we opted to hold our HAE IN-MOTION® event virtually, and in turn, we are now able to not only reach the individual cities of the original events, but to do it simultaneously across the entire United States. The events will be divided into four regions, and we are looking forward to some friendly competition among these, as we have added weekly challenges for them to go head to head to keep things exciting. The 2020 HAE IN-MOTION® Virtual Challenge began on 24 August 2020 with lots of participation and enthusiasm.

We have also transitioned our in-person HAEA Meet & Greet events to an online format. We have already held 15 virtual Meet & Greets, which are wonderful venues to meet members of the HAE community in their area and learn more about HAEA programs and services.

All of our HAEA youth programs are now online, including our advocacy training program and group workshops. We have also introduced new and interactive Brady Club activities and even produced an e-book version in English and Spanish of our children's book, Nico's Lunchbox.



HAE Research – Understanding HAE community challenges in times of COVID-19: As part of our response to understand the impact COVID-19 has had on our community, the US HAEA has prepared and shared two separate important surveys with patients to help us understand and identify: 1) access to therapies, and 2) the interaction between COVID-19 and HAE. The survey results will provide valuable insight to allow us to better respond to our community's needs.

With respect to the first survey, the HAEA will use this information to 1) identify patterns in insurance denials, and 2) develop strategies and education materials that the community and prescribing physicians can use to overcome insurance coverage obstacles. The second survey focuses more specifically on COVID-19 and seeks to examine whether people with HAE are more vulnerable to the virus. It also evaluates if HAE or HAE therapies affect the duration and/or severity of a COVID-19 infection. The data gathered for the study will provide valuable insights that could guide treatment decisions for anyone with HAE who may contract COVID-19.

HAE Speaks Podcast – Showcasing HAE Life Experiences: In our continued outreach to the community, we heard many requests for more opportunities to share the HAE journey. In response to our members' input, we recently launched a new podcast series: HAE Speaks. The podcast

series seeks to tell the stories and life experiences of individuals affected by HAE using a popular platform that enables us to reach a wider audience. HAE Speaks focuses on relevant topics, explained simply through friendly and open conversations. It is our hope that the HAE Speaks podcast becomes a regular addition to our community's playlists and that we are able to convey meaningful stories and information that enrich daily lives. Find the HAE Speaks podcast on iTunes or Spotify, or access <https://anchor.fm/haespeaks>.



- Episode 1: Life as a Caregiver
- Episode 2: Tips for navigating life through the COVID-19 pandemic
- Episode 3: Ongoing Research for New HAE treatments (Tony Castaldo, HAEA CEO)
- Episode 4: Life before and after an HAE diagnosis of a child



US HAEA Webinar Briefs provide useful and timely information: The US HAEA developed a series of educational webinar briefs, hosted by our CEO Tony Castaldo, that presents information on issues that are important to our HAEA community. All webinar briefs

provide timely and concise information to the HAE community, and all are offered by professionals who understand HAE. They are easily accessible through the US HAEA webpage and social media outlets. The webinar briefs cover a wide array of topics and are a great way to stay updated with the latest developments affecting the HAE community, including COVID-19. Following is a list of all webinars available to date:

- HAEA Webinar Brief: COVID-19 and HAE, with Dr. Marc Riedl, Clinical Director at the US HAEA Angioedema Center at University of California San Diego
- HAEA Webinar Brief: COVID-19 and Insurance, with HAEA Health Advocate, Troyce Venturella, MPH, RN, CCM
- HAEA Webinar Brief: COVID-19 recovered HAE Patient Scott McCoy
- HAEA Webinar Brief: HAEA Scholarships Support Education for our Youth, with HAEA Patient Advocate, Lisa Facciolla
- HAEA Webinar Brief: Why People with HAE Should Not Fear the Dentist, with Dr. Jonathan Bernstein

All webinar briefs are available through the US HAEA YouTube Channel ([ushaea](https://www.youtube.com/channel/UCshaea)).



ALGERIA

One more country to choose HAE International's offer regarding free website hosting is Algeria. You will find the new website of HAE Algeria at <https://haealgeria.haei.org>.



SYRIA

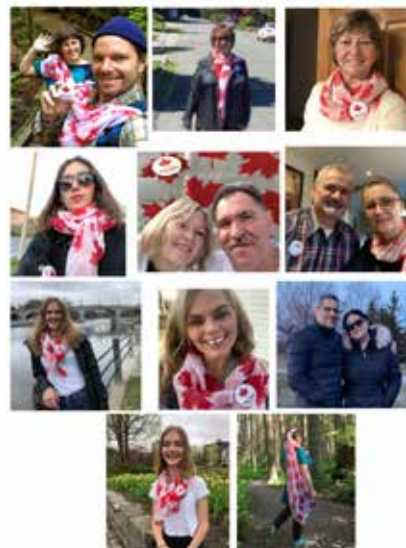
If you go to <https://haesyria.haei.org> you will find the new website of HAE Syria. The website is hosted with HAE International.



CANADA

From President Jacquie Badiou and COO Daphne Dumbrille, HAE Canada:

You wouldn't know it based on the temperatures outside, but summer is quickly wrapping up. Seems like ages ago we were venturing outside to go on much-needed walks (and runs, bike rides, swims etc.), then logging our steps into HAE International's 2020 Virtual Global Walk website. We know many Canadians put their walking shoes on and participated in this amazing awareness campaign because Canada logged the most steps; allowing Canada to win the Global Walk! Canada logged impressive 7,748,272 steps because of participation from many across the country.



Thank you to all our members who not only added their steps but went one step further and asked their friends and families also to get involved. Not only did our membership add steps, but also our extended HAE community enthusiastically participated. Teams from our two major sponsors, CSL Behring and Takeda, added many steps on a regular basis, as did healthcare providers who work with HAE patients. Thank you for the time and energy all Canadians put into the Virtual Global Walk. We are so proud of our engaged HAE community here in Canada.

In the spring, HAE Canada realized many Canadians needed current information regarding accessing new HAE treatments in Canada. We decided the best way to share reliable information was to host a virtual Patient

Information Update. On 29 June, four panelists came together: Dr. Sylvain Grenier (Director, Plasma Protein Products Formulary, Canadian Blood Services (CBS)) and Dr. Bruce Ritchie (MD, FCPC, Professor, Division of Hematology, Dept. of Medicine at University of Alberta) and the two of us from HAE Canada. Dr. Grenier and Dr. Ritchie each provided interesting presentations to educate and inform our membership on different topics related to accessing HAE treatments, and they also graciously answered pre-submitted questions from the members. Jackie's presentation updated participants on the latest news and the great initiatives that HAE Canada has been working on, while Daphne's moderating kept the meeting on track and moving along. It was a wonderful, interactive event, and we want to thank our panelists for providing their perspectives and expertise to our members. Their time was greatly appreciated. A recording of the Patient Update is available for viewing on our website's "Past Events" page: <https://haecanada.org/past-events/>. We are already looking forward to our next planned Patient Information Updates in Manitoba, Saskatchewan and Ontario, which will be scheduled once we are safe to gather in person.

We were excited and honoured to participate in two virtual conferences in June. HAE Canada submitted a slide show presentation to the 2020 HAE Global Conference titled: "Fear of Attacks Reduces Quality of Life for Canadian HAE Patients" and to EAACI's Digital Congress titled: "Real-world data of Canadians living with HAE: Need for Innovative, Newer Prophylactic and Subcutaneous Treatments". We want to thank everyone who worked on creating and developing these documents, specifically, Dr. Suzanne Kelly at Red Maple Trials and members of our dedicated Advocacy Committee who always step up to the plate to help with these documents. We appreciate all the help we receive to ensure each project is a success. We are proud to report that Dr. Marcus Maurer awarded our poster a Five Star Rating at the EAACI Digital Congress. Please feel free to view both submissions on our website's Abstracts and Posters page: <https://haecanada.org/national-report-card-abstracts-posters/>.

In June, HAE Canada's Governance Committee completed the necessary and important task of updating our bylaws. A huge thank you to our Board members, Anne Rowe (chair) and Tina McGrath, who worked extremely hard to ensure the bylaws remain accurate and follow all required standards. The Governance Committee also attended multiple webinars held by the Canadian Organization for Rare Disorders (CORD) to remain up

to date on the current situation with the Patented Medicine Prices Review Board (PMPRB). We are grateful for the work CORD is doing to prevent the PMPRB from introducing new guidelines which will prevent treatments for rare disorders from coming to Canada.

Over the summer months, HAE Canada had a fantastic team working on our next major survey, which will gather essential data to create our second National Report Card. This team included Bob Bick, policy consultant, Maggie Dow, our summer student, as well as Dr. Suzanne Kelly from Red Maple Trials (RMT). Jackie regularly provided the team with guidance and feedback to ensure this survey will be a success. Thank you to the HAE specialists, CADTH staff and others who reviewed the questionnaire to reflect our Canadian Healthcare System. We look forward to gaining valuable insight and perspectives from HAE patients and their caregivers from across Canada. The National Report Card will be a vital tool used to help bring new treatments to HAE patients in Canada.

HAE Canada collaborated with the Canadian HAE Network (CHAEN) on two Quality of Life abstracts, titled "Assessment of HAE-specific quality of life and proximity to acute therapy" and "Prodromes and attack triggers in Canadian HAE patients". We are happy to report these two abstracts have been accepted by the World Allergy Organization's online JSA/WAO Joint Congress 2020. Congratulations to CHAEN, HAEC's Regional Directors and all who worked on these important abstracts.

Recently we learned encouraging news that INESSS (Institut national d'excellence en santé et en services sociaux) has reevaluated lanadelumab (Takhzyro) and soon HAE patients in Quebec will have access to Takhzyro through Héma-Québec. To help INESSS make an informed decision, in December 2019, HAE Canada submitted Patient Input for Lanadelumab (Takhzyro): Drug Evaluation Questionnaire for Patient and Caregiver Associations and Groups. This document references HAE Canada's submission to the Canadian Agency for Drugs and Technologies in Health (CADTH) Common Drug Review (CDR) Pharmacoeconomic review report – Lanadelumab (Takhzyro). All documents can be found at <https://haecanada.org/hae-canada-patient-submissions/>. Thank you to our Advocacy Committee, consultants, Bob and Suzanne, staff member Daphne and Jackie, who diligently worked on this important patient submission.

To help keep the drug prices affordable, the pan-

Canadian Pharmaceutical Alliance (pCPA) conducts joint negotiations with the provinces, territories and the federal government for brand name and generic drugs in Canada. Jacquie and our VP, Tina McGrath, have been working with Takeda regarding access to Takhzyro and we are anxiously awaiting pCPA's decision on when and how lanadelumab (Takhzyro) will be available to HAE patients outside of Quebec.

Over the summer, Jacquie regularly met with CBS and CSL Behring to discuss when and how patients outside Quebec will access HAEGARDA, a subQ prophylaxis treatment. We can report that we expect the treatment to be available through CBS this fall.

Finally, we would like to thank our diligent and dedicated treasurer, Richard Badiou. Over the past year, Richard has been leading the development of the Canadian Angioedema Scholarship Program (CASP) Foundation, and we are confident the research funded by CASP will contribute to positive changes in the HAE community.

We hope all re well and staying safe.



RUSSIA

From Chairman Elena Bezbozhnaya, HAE Russia:

In the summer of 2020, Russia adopted legislative changes in the area of health care, which also affected patients with HAE. Therefore, HAE Russia held several events with legal presentations for the members of our organization to better navigate when making important decisions on the treatment and prevention of the disease. In addition, in 2020, we provided a statistical study and presented the results during remote and in-person meetings.

- **In May, we released an animated information film** with an illustration of all stages of routing patients with HAE and recommendations to patients with a confirmed diagnosis of HAE regarding preferential medicine provision.
- **In June, we organized an online webinar “Clinical research and generics: what a patient needs to know”**, which gathered patients with HAE from 10 Russian regions.



During the meeting, the speakers – our lawyer Ilya Ushankov, Ph.D., and myself – delivered speeches on clinical researches, clinical trials and generics system. Ilya Ushankov also introduced the webinar participants with foreign experience in this area. The webinar then proceeded to new generation medicines for patients with HAE. The lawyer considered new developments of three large foreign companies. Summing up the results of the online meeting, I expressed my hope that advanced medicines of a new generation will appear in Russia in the near future: “We really count on it, although it is not yet clear when this will happen, whether they will be available to us. Long-term prevention, which we still lack, would make our life much easier”.

• **In July, HAE Russia held a webinar “Medical Commission – New Opportunities for Patients.”**

Patients with HAE from 13 Russian regions participated in the event. As main speaker, Ilya Ushankov presented major legislative documents regulating the activities of the Medical Commission.

The speaker elaborated on the features of the medical commission and the requirements of the protocol of the medical commission. Ilya Ushankov also noted that often the meetings of the medical commission are held in the absence of the patient – moreover, the patient is not even informed about it – and gave recommendations on how to act in such cases.

In the final part of the presentation, Ilya Ushankov focused on changes in Russian legislation that entered into force on 14 July 2020. According to a decree, patient’s attending physicians shall follow the tactics and treatment regimen chosen by the medical board during the patient’s stay in hospital. At the end of the webinar, project coordinator Denis Bezbozhny considered the nearest plans of HAE Russia: “The results of our electronic survey showed that most patients are not satisfied with the level of knowledge among medical specialists. In this regard, we decided to host a series of webinars for the medical community. These webinars shall contribute to raising awareness on and clinical suspicion of the rare disease, its symptoms, therapy and prevention methods.”

• **In August, in St. Petersburg, we provided a face-to-face lesson at the School of Patients with HAE,** which included an interactive workshop “Clinical Guidelines”. The workshop gathered patients with HAE from St. Petersburg and the Leningrad Region.

In the first part of the meeting, I introduced the participants to the statistical data obtained from the results of an electronic survey of patients with HAE, conducted in the spring of 2020. The survey revealed that the disease has a negative impact on patients’ personal life (“significantly” 41.2%, “rather affects than not” 37.1%), on their education (32% and 27.8% respectively), professional activities (49.5% and 28.9%), and on daily activities such as the ability to travel and exercise (60.8% and 28.9%). Commenting on the survey results, Elena Viktorovna noted that almost two-thirds of patients (64.9%) feel insecure because of their disease. To a large extent, this feeling is due to objective factors insufficient provision of medicines. The survey also indicated another problem: Low awareness of doctors about the disease, therapeutic methods and prevention of HAE. I reminded that now the law gives the patient the right to choose a doctor himself.

Elena Latysheva, researcher at the Russian Institute of Immunology, Doctor of Medical Sciences, allergist and immunologist, joined the second part of the meeting as a speaker. The doctor informed the patients on the specifics of the disease and clinical recommendations on the treatment and prevention of HAE. Ilya Ushankov presented “Patient’s legal ABC”, devoted to the legal substantiation of patients’ actions and their rights.

The final part of the Patient School was held in an interactive format. The speakers introduced the participants to the main news from the 2020 HAE Global (Virtual) Conference. During the meeting, patients with HAE were offered medical and legal advice.

• **In August 2020, based on the results of the international audit and considering the recommendations given by the management of the Institute of Immunology of Russia, the GA2LEN center for patients with HAE was established.** GA2LEN (Global Allergy and Asthma European Network) is a consortium of more than 90 leading European research centers specializing in the treatment of allergic and immunological diseases. The Institute of Immunology is the second medical institution in Russia to receive this status. Prior to that, only the Allergology and Immunology Department of Moscow City Clinical Hospital No. 52 received a similar certificate.

• **In spring and autumn of 2020, the lawyers of HAR Russia provided assistance to our members in the issues of medical supply.** In many regions of Russia, patients with HAE still experience difficulties in receiving modern medicines, although the law grants them this right. But in practice, this right has to be regained, including in the courts. Not only do regional ministries and health departments not help patients to obtain the necessary medicines, but they often prevent them from doing so. HAE Russia has prepared and published several articles on this issue in the Russian media to shape public opinion and change the situation. We continue to provide legal, social and psychological support to our members.



BAHRAIN

HAE Bahrain is yet another national organization to have HAE International host its website – please have a look at <https://haebahrain.haei.org>.



HONG KONG

In July, HAE HK introduced a bilingual emergency card tailored for Hong Kong residents' different language needs. With the introduction of this emergency card, Hong Kong medical staff is now in a better position to understand this rare illness so that HAE patients can receive proper treatment as soon as possible in the event of an emergency.

On 15 August 2020, HAE HK celebrated its 1st anniversary of establishment. Due to the COVID-19 restrictions, the members were not able to gather and celebrate this day in person. However, they still managed to mark this occasion with a slide show to show the progress that the organization has made since the establishment and the activities and promotions it has participated in to raise awareness of HAE in Hong Kong. HAE HK aims to continue with the efforts in raising awareness of HAE in Hong Kong in the coming year.



With the help of new student volunteers, and increasing interests to support the organization, HAE HK trusts the coming year will bring even more progress for HAE in Hong Kong.

Thank you to all HAE HK supporters over the past year. Wishing everyone good health. Stay safe and strong!



PORTUGAL

HAE Portugal (ADAH) is now present on both Facebook and Instagram – please have a look at www.facebook.com/associacao.adah and www.instagram.com/hae_portugal.



UNITED KINGDOM

From Laura Szutowicz, CEO of HAE UK:

Normally at this time of year, we are in overdrive planning for the Patient Days which we hold in October and November, with the Scottish one first and then the National one in November.

We were very excited about this year as it was going to be our 10th Anniversary! HAE UK was started as an autonomous organization in 2010 following on from ending of the PIA, which had represented HAE patients as well as Primary Immune deficient patients. The PIA left an enormous vacuum, and the representation of HAE patients and families was taken on by Ann Price, who with her husband John started HAE UK with advice from Anthony J. Castaldo, Henrik Balle Boysen, and HAE International.

How things have moved on from small beginnings! We now have some 650 members and, following on from Ann's great work, HAE UK is growing all the time.

But sadly, the COVID-19 outbreak has made us reassess our plans. Obviously, it is not going to be possible to hold a large meeting with the social event we had also planned. But we have become quite expert with Zoom and other forms of 'virtual' meetings, and so we are going to have a virtual Patient Day! We will combine the Scottish day with the National one, as no travelling will be involved, but the format will be very much the same. We will have the wonderful, informative presentations from our clinicians as well as the inspirational patient stories – all done to the camera. We hope that this will not only 'fill the gap' for this year but will be a useful addition to our website as a resource for years to come.

We also intend having a virtual cocktail party to take the place of our usual pre-meeting social evening! So, we will be expecting everyone to dress up in their finery and raise a glass to the screen. More details about this and the Patient Event will follow once we have finalized the details.

We have run many more Zoom meetings over the summer, with a selection of our clinicians presenting and available for 'Q&A'. We have also run some very successful fun quizzes with Rachel Annals as quiz mistress extraordinaire. These have been a very good way of keeping in touch with members, and it has been great to see old faces and some new ones too.

We are losing one of our medical advisory panel to New Zealand! Dr. Longhurst and her husband are fulfilling a long-held desire to live there. They are looking forward to indulging in their favourite pastimes of trekking in the beautiful New Zealand National Parks, as well as swimming and skiing. They are also hoping to get a small boat. However, Dr. Longhurst is not giving up medicine but will be working in Auckland General Hospital and Greenlanes Health Centre with Dr. Karen Lindsay. There are 53 adult patients in New Zealand and their families, so she is hoping to help with an audit that Dr. Lindsay is setting up and also clinical trials there. She will also be looking after primary immune-deficient patients and working in the labs. She is looking forward to working with Fiona Wardman, who is in charge of Australasia and continuing her work with them. Dr. Longhurst intends to return to UCLH twice a year to the HAE clinic there once a vaccine for COVID-19 is available. We are hoping she will also still be available for us to consult as a member of our medical advisory panel, which at least we can do remotely!

We are delighted that the UK has been given the opportunity to participate in the HAE International socio-economic study, run on similar lines to the Nordic and USA ones. We have already had quite a good uptake with about 150 respondees, and the HAE network clinicians are also recruiting patients into it. We hope this will be a useful tool to reinforce our arguments for the various new products coming for HAE patients, the next one to be considered for use in the UK is oral prophylaxis, and there are of course several other products in clinical trials which are now able to restart.

Things in the UK are gradually returning to some sort of normal, with shops, pubs and restaurants opening. Schools will have reopened by the time you read this, and most hospitals are running face to face – or mask to mask? – clinics again. Clinicians have generally been very good about keeping in touch with patients even when they were only able to be consulted by phone, and at the height of the pandemic in the UK, many of our immunologists were drafted into the COVID-19 wards. At least two of them contracted COVID-19 because of this but thankfully did not have too severe illness. We are so lucky to have these wonderful people look after us!

I hope that the other members of HAE International have remained well and that we can now all look forward.



SAUDI ARABIA

Like a great many national organizations HAE Saudi Arabia has decided to use the free HAE International hosting service for websites. You will find the recently launched website at <https://haesaudiarabia.haei.org>.



IRELAND

In conjunction with HAE International HAE Ireland has launched an official website at <https://haeireland.haei.org>. Patients and caregivers in Ireland are encouraged to register on the site.



BRAZIL

Raquel de Oliveira Martins, President of HAE Brazil (ABRAGHE) writes that the pandemic has caused the cancellation of several scheduled activities. Therefore, the organization has taken the opportunity to produce some statistical tables on the HAE situation in Brazil.

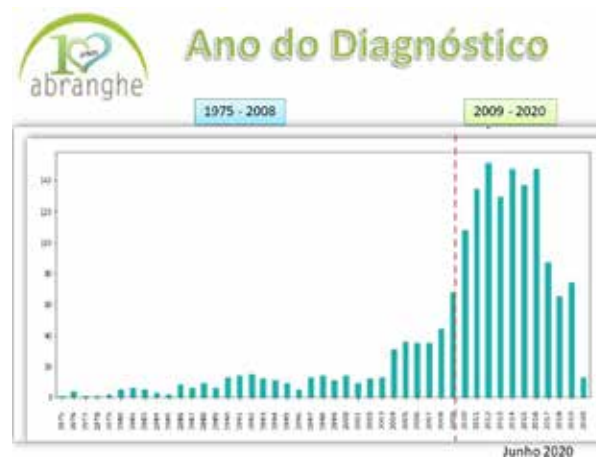




Junho 2020



Junho 2020



Junho 2020



AUSTRALIA AND NEW ZEALAND

From Director Fiona Wardman, HAE Australasia:

HAE Australasia recorded a Q&A video with Prof. Connie Katelaris in June. The questions and answers related to COVID-19, existing and new treatment options, clinical trials, and a new support service was announced for patients in Australia and New Zealand. The video has been uploaded on to our HAE Australasia YouTube channel and is accessible at <https://youtu.be/FgO-8f96iqg>.

The Pharmaceutical Benefits Advisory Committee (PBAC), the independent expert body to recommend medicines on the Pharmaceuticals Benefits Scheme (PBS), released its decision on the outcome of the latest submission to fund one of the new HAE treatments in Australia. The decision was to defer for further information. This deferral means that while the PBAC can see the treatment's value and benefit, they require some extra information. A panel of stakeholders will be called upon to give their views, and we hope there will be a positive outcome for HAE patients in Australia. This same treatment has been registered recently in New Zealand. Our organization will be working on patients gaining access to New Zealand.

Plans are currently underway for the 2021 HAE Australasia Patient and Carers Conference in Sydney, Australia. We are looking at venues and will provide our members with more information as soon as plans are finalized.

HAE Australasia is presently working on a video project for our website. Our concept is to bring information, education, support, and awareness of HAE with various topics such as patient stories, mental health tools and tips, and general information on HAE.





POLAND

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

Apart from the global pandemic situation, 2020 itself has been a challenging time for HAE Poland. This year, all three HAE treatments reimbursed in Poland (C1-INH, rec C1-INH, icatibant) lose reimbursement approvals and the goal no. 1 for us was effective activities enabling the extension of the current treatments' reimbursement. As 2020 is our jubilee year, on the occasion of the 15th anniversary, we wanted to organize 15 events: workshops and conferences in which, apart from patients and HCP's, healthcare system representatives and decision-makers would attend. However, the reality is writing its history, and the COVID-19 coronavirus has changed our plans entirely and forced us to adapt to virtual reality – which opens up totally new possibilities.

Thanks to the HAE International hosting service we were able to launch an entirely new website, containing a number of user-friendly features both for patients and HCP's. Above all, the site has become a fully digital communication platform, enabling joining the association, possibility of obtaining the HAE Emergency Card, receiving the necessary educational materials, psychological assistance, as well as detailed information on diagnosis and treatment centers. What is equally important, we are doing our best to develop the US HAEA Brady Club in Poland to convey knowledge to our youngest patients most gently and understandably. In the coming months, we will focus significantly on helping pediatric patients.

Very soon, we start a series of 11 virtual workshops for HAE patients and caregivers. From September to December 2020, we plan to be virtually present in different locations, sharing knowledge and the latest news from around the HAE world.

In August this year, a scientific book on angioedema (HAE included) has been published, and the Swelling Beautifully Association is its co-author. In the book, we focus on the importance of patients' advocacy and the role of patient organizations in rare diseases.

Also, currently, we work on the first-ever Polish HAE Report. It will be a first of its kind report with a focus on the current state of management of HAE in Poland and unmet needs of Polish HAE patients. The basis for

the preparation of materials for the report has been a study conducted by HAE Poland with over half of the diagnosed Polish HAE patients. This study is being developed in collaboration with the HAE National Center at the University Hospital in Krakow.

One of the greatest achievements of the most recent period has been the implementation of the ACARE network in Poland. The HAE National Center at the University Hospital in Krakow has been the first in Poland to pass a complete audit and become an accredited angioedema center. We hope that thanks to the cooperation with the Swelling Beautifully Association, other Polish centers will soon join ACARE.

In recent months, we have launched the campaign "Fight for breath, withstand pain", which aims to raise awareness about the disease, as well as ensure reimbursement for on-demand and long-term prophylaxis HAE treatments. I have participated in numerous virtual events regarding healthcare system and rare diseases. Furthermore, I was invited as a key-note speaker to take part in a session called "Rare Diseases in Poland" at the 2020 Virtual Health Challenges Congress, a prestigious and opinion-forming event devoted to health care. I presented the most urgent responses to Polish HAE patients: maintenance of drugs' reimbursement for on-demand treatment, as well as ensuring access to innovative, preventative treatment.

It should be emphasized that the summer period has been an extremely stressful time for HAE Poland and our representatives, who have participated in several meeting with decision-makers, emphasizing how important it is for patients to have access and reimbursement for HAE therapies.



SOUTH KOREA

HAE South Korea has moved its website to a new address – please see <http://haek.or.kr>. The website is still hosted with HAE International.



SOUTH AFRICA

From President Adrienne de Jongh, HAE South Africa:

This year we have used the lockdown time to consolidate our admin and legal positions. We have formally established a non-profit company and thereafter concentrated on finalizing the legal infrastructure to be able to accept donations.

We have regular Zoom meetings and are adding an additional board member.

We have formulated a presentation that will be used to interact with patients in their teens as we view this as the entry point for patients becoming consciously responsible for their own treatment and HAE control. This project has since been incorporated into the youth sector who will expand and develop it further as they see fit. We are very proud of this initiation and plan to expand it sector by sector in the future so that all ages will eventually be covered.

We have also established links with pharmaceutical companies presently supplying our medications and plan to extend this outreach to companies who are planning to market the new medications.



MOROCCO

The website of HAE Morocco (Association Marocaine des Malades d'Angio-Oedeme) is now live at <https://haemorocco.haei.org>.



SINGAPORE

From HAE Singapore:

HAE Singapore is currently working on growing the patient and carer member base while also establishing contact with HAE physicians. We are working towards this by creating a patient brochure for physicians to hand out to existing and new patients to let patients and family members know they are not alone, and patient to patient support is available.

HAE Singapore is in touch with the Rare Disorders Society Singapore and working on a patient story that is to be shared on their website and social media further to create awareness of HAE to the broader community.



DENMARK, NORWAY AND SWEDEN

From HAE Scandinavia:

In previous years, HAE Scandinavia has had the pleasure of inviting all members to information and network meetings – in Norway and Sweden in the autumn and in Denmark during summer.

We had looked forward to inviting the members to meetings again this year, but due to the COVID-19 pandemic, we are forced not to have any physical meetings. However, that should not stop us from getting new and interesting information out to the members and therefore we are right now in the process of producing exciting videos which we expect will be ready later this fall.

We would like to give members the opportunity to ask questions to the doctors and to the association. Therefore, HAE-related questions can be submitted until October 1, 2020 at info@haescan.org.

We look forward to addressing members' questions and to being able to meet virtually as an alternative to the physical meetings. And then, of course, we look forward to meeting face to face with everyone again at some point.

Due to COVID-19, the 2020 Annual General Meeting of HAE Scandinavia will take place as a Zoom Webinar on 8 October 2020.

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

Antisense Inhibition of Prekallikrein to Control HAE – by Danny M. Cohn, University of Amsterdam, the Netherlands, et al.:

In a compassionate-use pilot study, two patients with severe bradykinin-mediated angioedema were initially administered weekly subcutaneous injections of the unconjugated parent drug, IONIS-PKKRx, for 12 to 16 weeks, after which they received IONIS-PKK-LRx at a dose of 80 mg every 3 to 4 weeks for 7 to 8 months. The treatment led to a reduction in the angioedema attack rate.

(N Engl J Med, September 2020)

A Germany-wide survey study on the patient journey of patients with HAE – by Markus Magerl, Charité – Universitätsmedizin Berlin, Germany, et al.:

The self-perceived status of health for patients is much better once the final correct diagnosis has been made and specific treatment is available. Future challenges will be to increase awareness for HAE especially in settings which are normally approached by patients at occurrence of first symptoms to assure early referral to specialists and therefore increase the likelihood of receiving an early diagnosis.

(Orphanet J Rare Dis, August 2020)

Does HAE make COVID-19 worse? – by Yingyang Xu, Peking Union Medical College Hospital, China, et al.:

We explore the potential interactions between COVID-19 and HAE in terms of the contact system, the complement system, cytokine release, increased T helper 17 cells, and hematologic abnormalities. We conclude with the hypothesis that comorbidity with HAE might favor COVID-19 progression and may worsen its outcomes, while COVID-19 might in turn aggravate pre-existing HAE and prompt the onset of HAE in asymptomatic carriers of HAE-related mutations. We suggest that long-term prophylaxis should be considered in patients with HAE at risk of SARS-CoV-2 infection, especially the prophylactic use of C1 inhibitor and lanadelumab, and that HAE patients must have medications for acute attacks of angioedema. Therapeutic strategies employed in HAE should be considered for the treatment of COVID-19, and clinical trials should be performed.

(World Allergy Organ J, September 2020)

Association Between Self-Reported Dental Hygiene Practices and Dental Procedure-Related Recurrent Angioedema Attacks in HAE Subjects: A Multicenter Survey – by Umesh Singh, University of Cincinnati College of Medicine, the United States of America, et al.:

Data support the hypothesis that patients with HAE who are predisposed to having episodes in response to medical or physical trauma visit the dentist less and engage in specific oral hygiene practices more frequently than matched control patients and patients with HAE who reported that they were less likely to swell after a dental procedure

(J Allergy Clin Immunol Pract, June 2020)



HAE in children and adolescents – A consensus update on therapeutic strategies for German-speaking countries – *by Volker Wahn, Charité Universitätsmedizin, Berlin, Germany, et al.:*

Currently, plasma-derived C1 inhibitor concentrates have the broadest approval status and are considered the best available option for on-demand treatment of HAE-C1-INH attacks and for short- and long-term prophylaxis across all pediatric age-groups in German-speaking countries. For on-demand treatment of children aged two years and older, recombinant C1-INH and bradykinin-receptor antagonist icatibant are alternatives. For long-term prophylaxis in adolescents, the parenteral kallikrein inhibitor lanadelumab can be recommended due to proven efficacy and safety.

(Pediatr Allergy Immunol, June 2020)

Co-occurrence between C1 esterase inhibitor deficiency and autoimmune disease: a systematic literature review – *by Donald Levy, University of California, the United States of America, et al.:*

Based on literature reports, systemic lupus erythematosus is the most common autoimmune disease co-occurring with HAE Type I and II. Cause and effect for co-occurring HAE and autoimmune diseases has not been clinically established but could be related to lack of sufficient C1-INH function.

(Allergy Asthma Clin Immunol, May 2020)

Long-term safety and efficacy of subcutaneous C1-inhibitor in older patients with HAE – *by Jonathan A. Bernstein, University of Cincinnati College of Medicine, the United States of America, et al.:*

Subcutaneous C1-INH was well-tolerated and effective in the management of HAE in patients aged 65 years and older with multiple comorbid conditions and polypharmacy.

(Ann Allergy Asthma Immunol., September 2020)

Real-world cohort study of adult and pediatric patients treated for HAE in the United States – *by Raffi Tachdjian, University of California, the United States of America, et al.:*

In a large U.S. cohort of adult and pediatric patients who received treatments indicated or used for HAE, common comorbidities and trends in resource use denoted the substantial burden of attacks. This reflects a continued need that recently approved long-term prophylactic treatments may help to address.

(Allergy Asthma Proc, May 2020)

Characteristics of patients with C1 esterase inhibitor deficiency: a single center study – *by E.S. Aytekin, Hacettepe University Medical School, Turkey, et al.:*

In Mediterranean countries, patients with abdominal attacks may be misdiagnosed with familial Mediterranean fever. Thus, health-care professionals should be alert, and put HAE in the first line of differential diagnoses when the disease symptoms are present. Consequently, morbidity/mortality will decrease with effective treatment options.

(Eur Ann Allergy Clin Immunol, April 2020)

Life-threatening laryngeal attacks in HAE patients – *by Katarzyna Piotrowicz-Wójcik and Grzegorz Porebski, Uniwersytet Jagielloński Collegium Medicum w Krakowie, Poland:*

HAE-C1INH patients with laryngeal attacks require particular attention. Proper training regarding the identification of these patients, adequate management, access to emergency services and emergency drugs are essential to ensure the safety of subjects with this localization of HAE-C1INH attacks.

(Otolaryngol Pol, March 2020)

HAE: the challenges of cross-border family investigation and treatment – *by Anna Trier Heiberg Brix, University of Southern Denmark, Denmark, et al.:*

We present a Syrian refugee family with HAE who have lived in Denmark since 2014. The index patient is an 8-year-old girl diagnosed after being hospitalized in Denmark with an angioedema attack. Her younger sister and father were diagnosed later, following investigation of the family. Exploring the family history, deaths due to suffocation were described in previous generations and other family members based in Sweden, Germany, Turkey, Saudi Arabia, the United States of America, and Syria could also be affected. This highlights the need for a cross-border effort to diagnose and treat HAE.

(BMJ Case Rep, April 2020)

Advances in HAE: The Prevention of Angioedema Attacks with Subcutaneous C1-Inhibitor Replacement Therapy – *by William Lumry, AARA Research Center, the United States of America, et al.:*

C1-INH replacement is highly effective for preventing HAE attacks and can improve health-related quality of life. C1-INH now available as a subcutaneous formulation for self-administration is shown to provide sustained plasma levels of C1-INH and reducing the monthly median HAE attack rate by 95%. Subcutaneously administered C1-INH satisfies multiple unmet needs in the management of patients with HAE.

(J Infus Nurs, May-June 2020)

Experience with Intravenous Plasma-Derived C1-Inhibitor in Pregnant Women with HAE: A Systematic Literature Review – *by Joel P. Brooks, Yale University School of Medicine, the United States of America, et al.:*

The use of plasma-derived C1-INH in women with HAE during pregnancy has been widely reported in the scientific literature and has a favorable safety profile, supporting treatment guideline recommendations.

(J Allergy Clin Immunol Pract, June 2020)

Clinical Characteristics and Safety of Plasma-Derived C1-Inhibitor Therapy in Children and Adolescents with HAE – A Long-Term Survey – *by Henriette Farkas, Semmelweis University, Hungary, et al.:*

Studying the clinical characteristics and safety of treatment with plasma-derived C1-inhibitor in Children and Adolescents with HAE we confirm that the clinical manifestations and the use of plasma-derived C1-inhibitor are different in the various age groups of pediatric patients with C1-INH-HAE. Our long-term survey shows that the use of plasma-derived C1-inhibitor is safe in this patient population.

(J Allergy Clin Immunol Pract, July-August 2020)

Perioperative Management of Patients with HAE With Special Considerations for Cardiopulmonary Bypass – *by Kenichi A. Tanaka, University of Maryland School of Medicine, the United States of America, et al.:*

Recent clinical developments of biological and pharmacological agents have immensely improved acute and long-term care of patients with moderate-to-severe HAE. The therapies are given as on-demand and/or prophylaxis, and self-administration is highly recommended and performed with some agents via intravenous or subcutaneous route. Perioperative clinicians need to be familiar with the symptoms and diagnosis of HAE as well as available therapies because of the potential need for airway management, sedation, or anesthesia for various medical and surgical procedures and postoperative care.

(Anesth Analg, July 2020)

Changes of coagulation parameters during erythema marginatum in patients with HAE

– by Kinga Viktória Kőhalmi, Semmelweis University, Hungary, et al.:

HAE with C1-inhibitor deficiency is characterized by recurrent episodes of subcutaneous/submucosal edema, which may be preceded by erythema marginatum as a prodromal symptom. We have analyzed the changes occurring in the parameters of the coagulation system during the development of erythema marginatum and HAE attacks. D-dimer levels were elevated during erythema marginatum and this suggests that it may be part of the HAE attack. However, further research into the complement and kinin-kallikrein systems is needed in more patients for a better understanding of the pathomechanism of erythema marginatum.

(Int Immunopharmacol, April 2020)

Anaesthetic Approach for Patient with HAE

– by Maize Cordeiro Melo, Federal University of Minas Gerais, Brazil, et al.:

Surgical trauma may spur the HAE crisis, leading to complications such as swelling of the respiratory tracts and hemodynamic instability. Thus, the pre-surgical approach to HAE patients requires a specific plan that ensures short term prophylaxis, careful intra-operative management, rescue therapy and intensive post-surgery care.

(Turk J Anaesthesiol Reanim, February 2020)

Biological therapy in HAE: transformation of a rare disease

– by Hilary Longhurst, Addenbrooke's Hospital, the United Kingdom, and Henriette Farkas, Semmelweis University, Hungary:

Over the past ten years, several evidence-based parenteral treatments have been licensed, including two plasma-derived C1 inhibitor replacement therapies and one recombinant C1 inhibitor replacement for acute treatment of angioedema attacks and synthetic peptides for inhibition of kallikrein or bradykinin B2 receptors, with oral small molecule treatments currently in clinical trial. Moreover, recent advances in prophylaxis by subcutaneous C1 inhibitor to restore near-normal plasma function or by humanized antibody inhibition of kallikrein have resulted in freedom from symptoms for a high proportion of those treated. This plethora of treatment possibilities has come about as a result of recent scientific advances. Collaboration between patient groups, basic and clinical scientists, physicians, nurses, and the pharmaceutical industry has underpinned this translation of basic science into treatments and protocols. These in their turn have brought huge improvements in prognosis, quality of life and economic productivity to patients, their families, and the societies in which they live.

(Expert Opin Biol Ther, May 2020)

Evaluation of the efficacy and safety of home treatment with the recombinant human C1-inhibitor in HAE resulting from C1-inhibitor deficiency

– by Noémi András, Semmelweis University, Hungary, et al.:

Treatment with Conestat alpha, a C1-inhibitor produced by recombinant technology (rhC1-INH) is effective and safe both for acute management, and for short-term prophylaxis. Following the onset of an HAE attack, early administration of rhC1-INH may reduce time to the improvement and to the complete resolution of symptoms. Repeated administration of rhC1-INH does not impair its efficacy.

(Int Immunopharmacol, March 2020)

CLINICAL TRIALS

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

A Long-Term Safety Study of BCX7353 in HAE

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

A Phase II, Cross-over Clinical Trial Evaluating the Efficacy and Safety of KVD900 in the On-demand Treatment of Angioedema Attacks in Adult Subjects with HAE Type I or II

– recruiting in Austria, Czech Republic, Germany, Hungary, Italy, the Netherlands, North Macedonia, Poland, the United Kingdom, and the United States of America

A Study to Assess the Clinical Efficacy of IONIS-PKK-LRx in Participants with HAE

– recruiting in the Netherlands, and the United States of America

An Extension Study of IONIS-PKK-LRx in Participants with HAE

– recruiting in the United States of America

Biomarker for HAE Disease

– recruiting in Armenia, Georgia, and Romania

C1 Inhibitor Registry in the Treatment of HAE Attacks

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

Cloud-R HAE Registry

– recruiting in France

Contrast-Enhanced Ultrasound for the Evaluation of Changes in Tumor Blood Flow Surrounding HAE

– recruiting in the United States of America

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

– recruiting in France

Efficacy and Safety of Lanadelumab (SHP643) in Japanese Participants with HAE

– recruiting in Japan

Epidemiological Analysis for HAE Disease

– recruiting in Germany, Italy, Japan, Poland, Turkey, and the United Kingdom

Firazyr General Drug Use-Results Survey (Japan)

– recruiting in Japan

Firazyr Patient Registry (Icatibant Outcome Survey - IOS)

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

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

– recruiting in Italy



National Institutes of Health
Turning Discovery Into Health

HAE Kininogen Assay

– recruiting in Germany

Oral Berotralstat Expanded Access Program

Patient Registry to Evaluate the Real-world Safety of Ruconest

– recruiting in the United States of America

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

– recruiting in Canada, Puerto Rico, and the United States of America

Study to Evaluate the Real-World Long-Term Effectiveness of Lanadelumab in Participants with HAE

– recruiting in Austria, Germany, Switzerland, and the United Kingdom

The Role of the Coagulation Pathways in Recurrent Angioedema

– recruiting in France

Read more about these and other clinical trials at clinicaltrials.gov and apps.who.int/trialsearch.

NEWS FROM THE INDUSTRY

1 July 2020

At the presentation of the financial results for the fiscal year ended 30 April 2020 CEO Andrew Crockett of **KalVista Pharmaceuticals, Inc.** said:

“We have two oral candidates in clinical trials that have the potential to provide HAE patients with a complete set of options to treat their disease. We are pleased with our progress with the formulation work for KVD824 to deliver a twice-daily treatment for prevention of HAE attacks. Subjects have begun dosing with these new formulations to obtain additional pharmacokinetic and pharmacodynamic data, and we look forward to providing these data later this year in advance of starting a Phase 2 clinical trial. Patients also continue to be treated in our Phase 2 clinical trial for KVD900 as an on-demand therapy, and we expect data from that trial in the second half of this year.”

Fiscal 2020 and Recent Business Highlights:

- Opened an Investigational New Drug (IND) Application for KVD900 with the U.S. Food and Drug Administration (FDA) to enable clinical development in the United States.
- Presented at The International Symposium on Ocular Pharmacology and Therapeutics (ISOPT). KalVista's Chief Scientific Officer, Edward P. Feener, PhD, spoke on “Kallikrein-Kinin System in Diabetic Retinopathy – Novel Target.”
- Received Fast Track designation for KVD900 from the FDA, supporting KalVista's belief in the high level of unmet need in HAE for oral therapy and providing a potentially expedited path to drug approval.
- Selected KVD824 for development as a twice-daily oral prophylactic treatment for HAE. KVD824 is a highly potent and selective plasma kallikrein inhibitor which achieved high exposures and a favorable safety and tolerability profile in a first-in-human study. Additional formulation work on KVD824 is ongoing, and the Company expects to provide this and other data before initiating a Phase 2 clinical trial, which is anticipated to be in the second half of 2020.
- Adjusted expectations for KVD900 data to the second half of 2020 due to the impact of COVID-19, and revised financial guidance that activities are funded into at least early 2022.

(Source: KalVista)



7 July 2020

CSL Behring has enrolled the first patient in its Phase 2 study to assess the safety and efficacy of CSL312 (garadacimab, Factor XIIa antagonist monoclonal antibody) to treat patients suffering from severe respiratory distress, a leading cause of death in patients with COVID-19 related pneumonia.

In this multicenter, double-blind, placebo-controlled study, approximately 124 adult patients testing positive for the SARS CoV-2 infection will be randomized to receive either CSL312 or placebo, in addition to standard of care (SOC) treatment. The primary endpoint being the incidence of tracheal intubation or death.

“The greatest clinical challenge in treating patients with severe COVID-19 and improving outcomes has been our ability to manage the serious respiratory complications associated with the disease,” said Lars Groenke, R&D Lead, Respiratory Therapeutic Area, CSL Behring. “Our hope with CSL312 is to be able to prevent the progression of COVID-19, improve patient outcomes, and provide physicians with an effective tool in the fight against this deadly virus.”

Currently, CSL Behring is evaluating five approaches across its plasma fractionation and recombinant and antibody strategic scientific platforms to preventing and treating COVID-19.

In addition to the study of CSL312, CSL Behring:

- Has entered into a partnering agreement with the Coalition for Epidemic Preparedness Innovations (CEPI), and The University of Queensland (UQ) to accelerate the development, manufacture and distribution of a COVID-19 vaccine candidate that has been pioneered by researchers at UQ.
- Is one of the founding members of the CoVlg-19 Plasma Alliance, an unprecedented industry partnership to develop CoVlg-19, a potential plasma-derived therapy for treating COVID-19. The CoVlg-19 Plasma Alliance will work toward developing the unbranded anti-SARS-CoV-2 polyclonal hyperimmune immunoglobulin medicine with the potential to treat individuals with serious complications from COVID-19, and to support national governments in their efforts to fight the current pandemic. The

collaboration will leverage leading-edge expertise and work that the companies already have underway.

- Is developing an anti-SARS-CoV-2 plasma product for the Australian market with the potential to treat people with serious complications of COVID-19, particularly those whose illness is progressing towards the need for ventilation. The investigational product, to be known as COVID-19 Immunoglobulin, is under development at the company's advanced manufacturing facility located in Broadmeadows, Victoria.
- Has also formed a partnership with SAB Biotherapeutics, a clinical-stage biopharmaceutical company, to advance and deliver a novel immunotherapy targeting COVID-19. The potential therapy would be produced without the need for blood plasma donations from recovered COVID-19 patients. Clinical trials could begin this summer in North America.

"When it comes to COVID-19, we have gone all in on the battle and are in the fight together with many external partners," said Bill Mezzanotte, MD, MPH, Executive Vice President, Head of Research and Development, and Chief Medical Officer for CSL Behring. "Whether it is preventative with vaccines, or preventing progression with a hyperimmune, or using our monoclonal antibodies, like CSL312, to help people who are experiencing severe respiratory complications, CSL has taken on projects we think make sense both scientifically and that fit our capabilities. In this way we are most likely to deliver on our promise to patients by helping find solutions to stop this virus and to treat the damage it inflicts on people."

Garadacimab is a novel Factor XIIa-inhibitory monoclonal antibody (FXIIa mAb) that CSL Behring is currently investigating for indications where FXIIa inhibition may be a factor in improving clinical outcomes. These include a recently initiated study to assess garadacimab for prevention of respiratory failure in adult patients with the COVID-19 virus. Garadacimab is also currently in clinical development as a new type of once-monthly subcutaneous prophylactic treatment for attacks related to HAE. Results from this Phase 2 study showed that garadacimab was well tolerated and met the primary endpoint of reduction in attacks in HAE patients. Garadacimab inhibits the plasma protein, FXIIa. When FXIIa is activated, it initiates the cascade of events leading to edema formation. By targeting FXIIa, garadacimab can prevent the initiation of this cascade. The U.S. Food and Drug Administration (FDA)

has granted orphan-drug designation to garadacimab as an investigational therapy for the prevention of bradykinin-mediated angioedema.

(Source: CSL Behring)

CSL Behring

15 July 2020

Cipla Limited has received final approval for its Abbreviated New Drug Application (ANDA) for Icatibant Injectable 30mg/3mL from the United States Food and Drug Administration (US FDA).

Cipla's Icatibant Injectable Pre-Filled Syringe 30mg/3mL is AP-rated generic version of Shire's Firazyr. Icatibant injection is indicated for the treatment of acute attacks of HAE in adults 18 years of age and older.

(Source: Cipla)

Cipla

5 August 2020

Together with the COVID R&D Alliance partners AbbVie, Inc. and Amgen Inc., Takeda Pharmaceutical Co. Ltd. has enrolled the first patients in the I-SPY COVID Trial (Investigation of Serial Studies to Predict Your COVID Therapeutic Response with Biomarker Integration and Adaptive Learning) clinical trial. The trial will evaluate the efficacy of a chemokine dual-receptor antagonist, a PDE4 inhibitor, and Firazyr, a bradykinin B2 receptor antagonist used for the treatment of HAE.

The trial utilizes Quantum Leap Healthcare Collaborative's adaptive platform trial design, which is intended to increase trial efficiency by minimizing the number of participants and time required to evaluate potential treatments.

"Collaborative research efforts leveraging adaptive platform trials enable faster and more complete learning about what works for patients, and they are especially critical for addressing urgent public health threats like COVID-19", says Dr. Mark McClellan, Director of the Robert J. Margolis Center for Health Policy at

Duke University and former commissioner of the U.S. FDA and administrator of the Centers for Medicare and Medicaid Services: “Platform trials bring down the cost and increase the ease of executing well-powered, high quality studies, especially when multiple, potential therapies need to be evaluated quickly. The I-SPY COVID Trial is expanding a timely and effective platform trial strategy to evaluate promising treatments while maintaining an appropriate level of safety and statistical rigor necessary for regulatory evaluation.”

The study is a collaboration between members of the COVID R&D Alliance, Quantum Leap, and the U.S. Food and Drug Administration (FDA). AbbVie, Amgen, and Takeda are members of the COVID R&D Alliance (COVID R&D), a group of more than 20 of the world’s leading biopharmaceutical and life science companies working to speed the development of potential therapies, novel antibodies, and anti-viral therapies for COVID-19 and its related symptoms.

“Sick patients in hospitals cannot wait; options are urgently needed. I’m proud to partner with AbbVie and Amgen and the dozens of other companies who have joined the COVID R&D Alliance, to initiate critical platform trials like I-SPY COVID”, says Andy Plump, President of R&D at Takeda Pharmaceuticals and co-founder of the COVID R&D Alliance. “The world learned of COVID-19 only six months ago, and the speed at which the scientific community has joined forces to address the critically high unmet need is inspiring. Together, experts across our companies and industry can accelerate trials with promising, well-understood therapies that upon investigation, may show efficacy in this devastating disease.”

The therapies under investigation were selected based on their potential to impact the immune system response of COVID-19 patients who need respiratory support. Approximately 10-15 percent of patients afflicted by COVID-19 develop acute respiratory distress syndrome (ARDS), and up to 60 percent of those patients admitted to an ICU require ventilation for an average of two weeks. It is estimated that half of those patients will not survive. Based on the respective mechanisms of action, Firazyr may ameliorate bradykinin-driven pulmonary edema.

(Source: Takeda)



6 August 2020

“We are currently in an exciting transformation from a company primarily focused on R&D to one that is about to launch its first oral drug to patients with HAE (ORLADEYO) this year. We expect to end the year with ORLADEYO approved in the U.S. and Japan”, says President and CEO Jon Stonehouse, BioCryst Pharmaceuticals, Inc., at the presentation of the financial results for the second quarter of 2020.

HAE Program – ORLADEYO: Oral, once-daily treatment for prevention of HAE attacks

- BioCryst expects three regulatory approvals for ORLADEYO in Q4 2020 and early 2021. The U.S. Food and Drug Administration (FDA) is reviewing a new drug application for ORLADEYO and has set an action date of 3 December 2020, under the Prescription Drug User Fee Act (PDUFA).
- In Japan, ORLADEYO is being reviewed under Sakigake designation. The Pharmaceutical and Medical Devices Agency (PMDA) has confirmed their regulatory review schedule and the company expects an approval decision in December 2020.
- On 30 March 2020, the company announced that the European Medicines Agency (EMA) had validated its marketing authorization application (MAA) submission for ORLADEYO and begun its formal review of the MAA under the centralized procedure. The company expects an opinion from the Committee for Medicinal Products for Human Use (CHMP) within approximately 12 months from MAA validation.
- BioCryst has completed significant preparations to support the launch of ORLADEYO in the U.S.
- The company has attracted an accomplished U.S. rare disease sales team, which averages 20 years in pharmaceutical sales and nearly a decade of rare disease experience.
- The company is well-positioned in terms of product supply and inventory on-hand to support the launch and anticipated global demand for ORLADEYO.
- On 9 June 2020, the company announced that it had established an expanded access program with ORLADEYO for patients with HAE in the United States. Through this program, physicians may be able to request ORLADEYO for HAE patients who do not have access to the product through a clinical trial.
- On 6 June 2020, at the European Academy of Allergy and Clinical Immunology (EAACI) Digital Congress, the company presented new data highlighting

the burden of therapy faced by HAE patients taking currently available injectable prophylactic medication. Patients taking oral, once daily ORLADEYO experienced sustained decreases in their attack frequency and improvements in quality of life scores over 48 weeks. ORLADEYO was also safe and generally well-tolerated over 48 weeks in both the APeX-2 and APeX-S clinical trials.

“Our ongoing dialogue and research with HAE patients and physicians continue to reinforce their strong demand for an oral, once-daily medicine that is safe and provides the significant and sustained attack reduction we are seeing with ORLADEYO in our clinical program. Nearly half of patients in our APeX-2 and APeX-S trials have prior experience with injectable or infused therapies and most have chosen to remain on ORLADEYO,” said Charlie Gayer, chief commercial officer of BioCryst.

(Source: BioCryst)



6 August 2020

From Intellia Therapeutics, Inc.'s presentation of the financial results for the second quarter of 2020:

NTLA-2002 is a wholly owned, in vivo development candidate for the treatment of HAE. Building on Intellia's modular lipid nanoparticle (LNP) delivery system, NTLA-2002 is designed to knock out the prekallikrein B1 (KLKB1) gene in the liver after a single course of treatment, which is expected to prevent improperly regulated bradykinin production and therefore, reduce HAE attacks.

In a non-human primate (NHP) study of its lead LNP formulation for NTLA-2002, the knockout of KLKB1 resulted in a therapeutically relevant reduction of serum kallikrein levels and activity following a single dose. Consistent with the durability achieved in earlier NHP studies for its lead in vivo program, Intellia has now demonstrated sustained kallikrein activity reduction for 10 months in an ongoing study. Based on these results, Intellia believes NTLA-2002 could be efficacious and durable in preventing HAE attacks following a single course of treatment.

Intellia continues to progress IND-enabling (Investigational New Drug) activities and is on track to submit an IND or IND-equivalent for NTLA-2002 in the second half of 2021.

(Source: Intellia)



10 august 2020

The first patient has been enrolled in a randomized, controlled, investigator-initiated clinical trial in up to 150 patients for the treatment with Ruconest (recombinant human C1 inhibitor) of patients with confirmed COVID-19 (SARS-CoV-2) infections hospitalised with related severe pneumonia at the University Hospital Basel in Basel, Switzerland.

In April 2020, Pharming Group N.V. reported encouraging results from a compassionate use programme at the University Hospital Basel, in which four male patients and one female patient (between 53-82 years of age) with COVID-19, suffering from related severe pneumonia, who did not improve despite standard treatment, including hydroxychloroquine and lopinavir/ritonavir, had been administered Ruconest. Following treatment, fever resolved in four of the five patients within 48 hours, and laboratory markers of inflammation decreased significantly (CRP, IL-6). Soon thereafter, four of the five patients were discharged from the hospital as fully recovered. One patient had increased oxygen requirement and was eventually transferred to the ICU for intubation but has also since made a full recovery.

Following these encouraging results, the Company, in partnership with treating physician Dr Michael Osthoff from the University Hospital of Basel, saw potential for a larger investigator-initiated, multinational, multicentre study to investigate the full extent of the role of Ruconest in the treatment of severe pneumonia related to a COVID-19 infection. If successful, the clinical trial could also lead to additional studies in patients suffering from other diseases with severe respiratory or other organ failure complications driven by activation of the complement system as part of a systemic hyperinflammatory syndrome, also known as a 'cytokine storm'.

Ruconest is a recombinant C1 esterase inhibitor (C1INH) approved for the treatment of HAE in the EU and US. C1INH is a protein that naturally occurs in the human body. It regulates several inflammatory pathways in the body by inhibiting certain proteins that are part of the

human immune system. Systemic hyperinflammation is a hallmark of more severe stages of COVID-19 leading to acute respiratory distress syndrome, mechanical ventilation and ultimately death. Treatment with Ruconest may; 1) dampen uncontrolled complement activation and collateral lung damage and 2) reduce capillary leakage and subsequent pulmonary edema by direct inhibition of the kallikrein-kinin system and 3) reduce the generation of microthrombi by inhibiting MASP-1 induced clot formation and factor XII amplified thrombo-inflammation.

C1 inhibitor is an acute phase reactant, meaning that the body naturally increases production during inflammatory conditions, such as infections. Despite this, a relative deficiency may occur and complement activation continues unchecked, often leading to a cytokine storm, a dangerous biochemical process that worsens the complications of COVID-19 infection, such as organ failure and death.

This clinical study in hospitalised patients with COVID-19 seeks to identify if the administration of additional C1 INH can control or stop the systemic hyperinflammation syndrome or cytokine storm. Once results from either an interim analysis or after all patients have been treated, headline data will be made publicly available.

Prof. Bruno Giannetti, Pharming's Chief Medical Officer comments:

"COVID-19 has proven that there is a significant need for better understanding of how the immune system fights infections. We have learned that cytokine storms caused by complement system activation cannot be controlled by targeted anti-inflammatory therapies. Instead, broad anti-inflammatory agents are required to stop the activation of multiple inflammation pathways. Ruconest's multiple interactions with key inflammation pathways therefore make it a promising candidate to prevent the severe complications observed in COVID-19 patients. This investigator-initiated clinical trial in partnership with Dr Michael Osthoff, will be important not only for the treatment of pneumonia as a result of COVID-19 infection, but will also provide

key insight into the future treatment of complement system influenced diseases."

Dr Michael Osthoff, University Hospital Basel and the treating physician, says:

"After the encouraging results observed in five patients treated with Ruconest in our clinic, it is justified to investigate this drug and its unique mode of action of targeting several inflammatory cascades in a clinical trial with a large number of patients. We will gather precious information about efficacy, safety and appropriate dosing of the drug in the treatment and prevention of the severe complications of COVID-19. After a short period of remission, we observe a worrisome increase of new COVID-19 cases in Europe, whilst in a number of other countries the disease still spreads almost uninhibited. The need for a treatment of COVID-19 associated complications is more urgent than ever."

(Source: Pharming)



17 August 2020

Pharming Group N.V. announces the publication of data in the peer-reviewed journal, *Frontiers in Immunology*, from a compassionate use programme of five patients with confirmed COVID-19 (SARS-CoV-2) infections hospitalized with related severe pneumonia that were treated with Ruconest (recombinant human C1 inhibitor, conestat alfa) at the University Hospital Basel, Switzerland.

As reported on 21 April 2020, following treatment with Ruconest, fever resolved in four of the five patients within 48 hours, and laboratory markers of inflammation decreased significantly (CRP, IL-6). Soon thereafter, four of the five patients were discharged from the hospital as fully recovered. One patient had increased oxygen requirement and was temporarily transferred to the ICU for intubation but over the subsequent days made a full recovery.

Given this was a small case series, the outcomes were retrospectively compared to a matched control population of 15 patients. Baseline characteristics, admission laboratory parameters and treatments

administered were similar in both groups. Both groups received standard of care as well as experimental therapies including antiviral and anti-cytokine directed medications. However, 8/15 (53%) patients in the control population required mechanical ventilation and four of these patients died, compared to only one (20%) requiring mechanical ventilation and no deaths in the Ruconest group. Overall, treatment with, in total five normal dose equivalents of Ruconest over 48h was well-tolerated.

(Source: Pharming)



4 September 2020

Ionis Pharmaceuticals, Inc. announces the publication of the results from a compassionate-use study evaluating IONIS-PKKRx and IONIS-PKK-LRx in patients living with severe bradykinin-mediated angioedema in The New England Journal of Medicine (NEJM). IONIS-PKKRx and IONIS-PKK-LRx are investigational antisense medicines designed to reduce the production of prekallikrein (PKK), which plays a key role in the activation of inflammatory mediators associated with acute attacks of HAE. In the study, researchers found that the drugs reduced plasma prekallikrein activity levels and showed evidence of clinical efficacy in reducing the number of breakthrough attacks per month in patients over the course of the treatment, including complete resolution in a patient with Type 1 HAE.

"The results of this study are encouraging and support continued development of IONIS-PKK-LRx as a potential treatment in patients with severe HAE for whom current therapies offer limited therapeutic benefit. The study also highlights the progress we continue to make advancing investigational medicines that are wholly owned by Ionis", says Richard S. Geary, Ph.D., Executive Vice-President of Development and a co-author on the paper.

In the study, two patients – Patient 1 with Type 1 HAE and Patient 2 with Type 3 HAE – were first treated with IONIS-PKKRx for a period of 12 to 16 weeks, after which they received IONIS-PKK-LRx at a dose of 80 mg every three to four weeks for seven to eight months at the time of data analysis. During treatment

with the ligand-conjugated IONIS-PKK-LRx and the unconjugated parent drug, IONIS-PKKRx, there was a clinically meaningful reduction in HAE attack rates in both patients. Plasma prekallikrein activity levels decreased substantially following treatment.

Physicians have long prescribed prophylactic treatment approaches, including C1-INH replacement therapies and more recently inhibitors of plasma kallikrein, to prevent and reduce the severity of HAE attacks. IONIS-PKK-LRx is an investigational antisense medicine that is being developed because it has the potential to provide significant efficacy with the convenience of once per month low volume subcutaneous injections.

(Source: Ionis)



14 September 2020

At the presentation of the operational update and released financial results for the first fiscal quarter ended 31 July 2020 KalVista Pharmaceuticals, Inc. CEO Andrew Crockett says:

"We are pleased that our KVD900 Phase 2 trial has met its enrollment target and data is expected before the end of this year. We believe KVD900 can bring the first effective and well-tolerated oral on-demand treatment option to patients suffering from HAE attacks. Our portfolio of oral options intended to treat HAE also includes prophylactic treatment candidate KVD824, for which we are completing our formulation studies which include dosing in subjects. We look forward to providing additional pharmacokinetic and pharmacodynamic data for KVD824 later this year in advance of starting a Phase 2 clinical trial. Similar to KVD900, our goal with KVD824 is to conduct a robust Phase 2 trial to provide proof-of-concept and potentially an expedited development pathway. We will provide further details on our plans as we prepare to initiate the trial."

(Source: KalVista)



– SUPPLEMENT –

SCIENTIFIC TRACK OF THE 2020 HAE VIRTUAL GLOBAL CONFERENCE



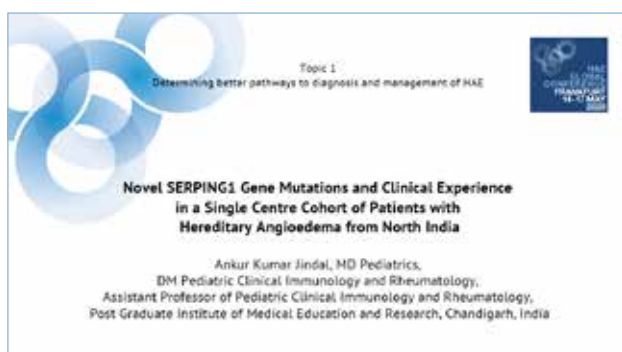
**HAE
GLOBAL
CONFERENCE
FRANKFURT
14-17 MAY
2020**

PRESENTATIONS FROM THE 2020 HAE VIRTUAL GLOBAL CONFERENCE



While the coronavirus COVID-19 pandemic prevented the planned version of the 2020 HAE Global Conference in Frankfurt, Germany, the “can-do” spirit of the HAE global community inspired transforming the widely anticipated bi-annual conference into an exciting virtual event.

At <https://haei.org/gc2020/#scientific> you will find video presentations from the Scientific Track under the topics “Determining better pathways to diagnosis and management of HAE” and “Creating a path to normalization of HAE patients’ lives”. The following are summaries of the presentations for the Scientific Track.



Novel SERPING1 Gene Mutations and Clinical Experience in a Single Centre Cohort of Patients with HAE from North India

Ankur Kumar Jindal^{1*}, Anit Kaur¹, Amit Rawat¹, Dhrubajyoti Sharma¹, Himanshi Chaudhary¹, Anjani Gummadi¹, Sunil Dogra², Deepti Suri¹, Anju Gupta¹, Vikas Suri³, Dipankar De², Vinay K², Varun Dhir³, Surjit Singh¹

1) Pediatric Allergy Immunology Unit, Department of Pediatrics, Post Graduate Institute of Medical Education and Research, Chandigarh, India. 2) Department of Dermatology, Post Graduate Institute of Medical Education and Research, Chandigarh, India. 3) Department of Medicine, Post Graduate Institute of Medical Education and Research, Chandigarh, India. *Corresponding author.

BACKGROUND

There is a lack of information about the genetic profile and follow-up of people with HAE from developing countries. A group of clinicians in India examined the medical records of 52 HAE patients from 26 families, to understand more about the genetics of the condition and its management.

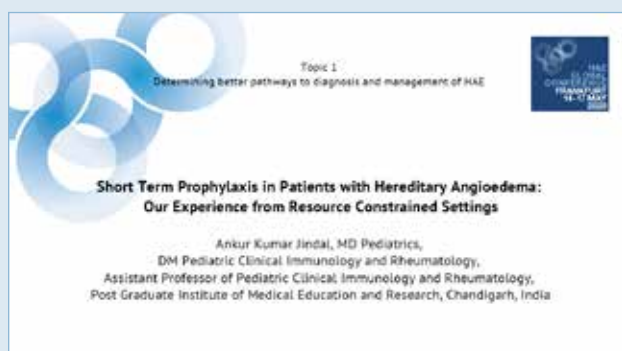
RESULTS

The authors found that the average time between onset of symptoms and a patient receiving a diagnosis was 11 years. In families where genetic sequencing had been conducted, just over half (11/21) had a mutation in the SERPING1 gene, which has been associated with the majority of cases of HAE.

In the management of their HAE, all patients received stanazolol or tranexamic acid, while acute, life-threatening attacks were treated with plasma infusion. There was an average of over four-years of medical records per patient and none of the 52 patients died as a result of HAE.

WHAT DOES THIS MEAN FOR PATIENTS?

The study doctors conclude that this offers hope for people with HAE who live in resource-limited settings where C1-INH therapy is not available. The authors also question if the genetic background of patients with HAE in India may be different to other countries.



Short Term Prophylaxis in Patients with HAE: Our Experience from Resource Constrained Settings

Ankur Kumar Jindal^{1*}, Ankita Singh¹, Himanshi Chaudhary¹, Anjani Gummadi¹, Anit Kaur¹, Manoj Jaiswal², Pooja Sikka³, Amit Rawat¹, Deepti Suri¹, Anju Gupta¹, Surjit Singh¹

1) Pediatric Allergy Immunology Unit, Department of Pediatrics, Post Graduate Institute of Medical Education and Research, Chandigarh, India. 2) Department of Oral Health Sciences, Post Graduate Institute of Medical Education and Research, Chandigarh, India. 3) Department of Obstetrics and Gynaecology, Post Graduate Institute of Medical Education and Research, Chandigarh, India. *Corresponding author.

BACKGROUND

Use of short-term medication to prevent attacks is necessary when patients with HAE are undergoing operations, as the surgical trauma could lead to an attack. A group of clinicians in India looked at options for short-term medication to prevent attacks of HAE in patients undergoing surgical procedures, when C1-INH therapy is not available.

RESULTS

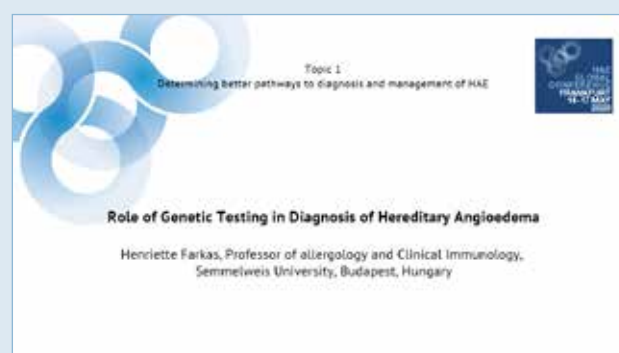
The authors report two case studies. The first was a nine-year old girl with HAE type 1, who was previously managed on tranexamic acid and stanozolol. Prior to dental surgery, the dose of stanozolol was doubled (0.5mg per day to 0.5mg twice a day). The patient also received infusions of fresh frozen plasma twice a day for two days before the surgery, and one dose during her operation. The authors report that the patient had a general anesthetic and a breathing tube inserted during an uneventful operation, and she suffered no HAE attacks.

The second patient case study was a 29-year old woman with HAE, previously treated with stanozolol

and tranexamic acid. In two previous pregnancies, she took the medication and continued to experience attacks. These two pregnancies ended in the first three months and as a result she stopped taking medication. She became pregnant again and decided on a caesarean section. During the pregnancy she experienced no attacks. In preparation for the birth, she was given three units of fresh frozen plasma before the operation, along with 2mg stanozolol in the day before. Further units of fresh frozen plasma were given during the caesarean, and the stanozolol was continued for five days post operation. The operation was a success – she had an uneventful delivery and she had no episodes of angioedema.

WHAT DOES THIS MEAN FOR PATIENTS?

The study doctors conclude that short-term preventative treatment with fresh frozen plasma and stanozolol may be considered in patients with HAE undergoing operations, when C1-INH therapy is not available.



Role of Genetic Testing in Diagnosis of Hereditary Angioedema

Henriette Farkas¹, Edina Szabó¹, Anna Dóczy¹, Kinga Viktória Kohalmi¹, Lilian Varga¹, Anastasios E. Germentis², Dorottya Csuka¹

1) Hungarian Angioedema Reference Center, Department of Internal Medicine and Haematology, Semmelweis University, Budapest, Hungary. 2) Department of Immunology & Histocompatibility, University of Thessaly, School of Health Sciences, Faculty of Medicine, Larissa, Greece.

BACKGROUND

Establishing a correct diagnosis of HAE could be crucial for a patient's prognosis and quality-of-life. Different types of testing can identify different types of HAE; complement testing can identify HAE with

C1-inhibitor deficiency whereas genetic testing is essential to accurately diagnose HAE with normal C1-inhibitor function. Genetic tests for SERPING1, factor XII (F12) and plasminogen (PLG) genes are available at the Hungarian Angioedema Reference Centre (HARC). Clinicians from specialist centers in Hungary and Greece used HARC to map the genetic mutation present in a group of HAE patients to help establish a correct diagnosis.

RESULTS

198 patients were followed-up at HARC. Following the genetic testing the authors found that 194 patients had hereditary C1-inhibitor deficiency (HC1-INH-def), two patients had factor XII (F12) gene mutation, whilst another two had a plasminogen (PLG) mutation. When patients were considered in family groups, 70 families were HC1-INH-def; one family with F12 and one family with PLG.

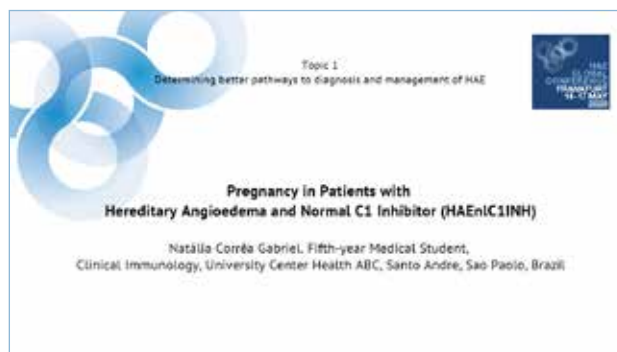
Of these family groups the authors saw from the genetic testing that;

- From the 70 HC1-INH def families, SERPING1 gene mutations were identified in 61 families
- In eight families with HC1-INH-def, mutation was not detected
- In a family with nC1-INH-HAE, F12 gene mutation was described which was a novel mutation
- A family with PLG-HAE was diagnosed

The authors also report that in five patients with C1-INH deficiency, genetic testing helped to establish a diagnosis (results from the complement testing was not clear) and in four patients they were able to diagnose HC1-INH-def using blood taken from the umbilical cord of newborns.

WHAT DOES THIS MEAN FOR PATIENTS?

The increased use of genetic testing in cases of HAE will help distinguish between different types of the condition, especially in more complex cases where complement testing results aren't clear, or in infants where the immune system isn't yet fully formed.



Pregnancy in patients with HAE and Normal C1 Inhibitor (HAE-nC1INH)

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1) Clinical Immunology, University Center Health ABC, Santo André, SP, Brazil. 2) Brazilian Association of HAE patients (ABRANGHE). 3) Post-graduation student, University Center Health ABC, Santo André, SP, Brazil. 4) Federal University of Bahia, BA, Brazil. 5) Private Clinica, Belo Horizonte, MG, Brazil. 6) State University of Campinas (UNICAMP), SP, Brazil. 7) Private clinic in Brasília, DF, Brazil.

BACKGROUND

Estrogen has been described as a trigger of attacks in patients with HAE with normal C1 inhibitor (HAE-nC1-INH). Women are more likely to have symptoms, so there is concern that pregnancy may trigger the disease or lead to a worsening of the condition. There is a lack of information in this area and the authors present data from following the course of pregnancies in a number of women with HAE-nC1-INH.

RESULTS

The study authors looked at the medical records of 26 Brazilian women with confirmed HAE-nC1-INH. The average of the women now was 42.5 years and at the time of pregnancy, the average age of the women was 27.4 years.

These women had a total of 37 pregnancies. In 18 out of the 26 women, their first attacks were reported prior to being pregnant. In two out of the 26 women their first attack occurred during pregnancy, whilst in six out of the 26, the first attack was on average 2.5 years after a pregnancy.

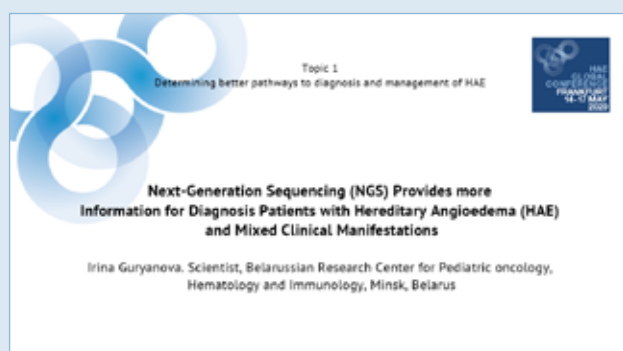
When attacks did occur during pregnancy, they were most common in the 1st third of pregnancy (41.7%). 12.5% of attacks happened in the 2nd trimester, while 20.8% were in the 3rd trimester.

Fifteen women reported attacks before or during their pregnancy, with nine saying their condition got worse, and four reporting an improvement. One suggested no change and another one didn't respond.

Overall the authors found no difference in rates of miscarriage between women with HAE-nC1-INH and those without the condition.

WHAT DOES THIS MEAN FOR PATIENTS?

Although data is limited, the authors conclude that pregnancy does not cause the onset of HAE-nC1-INH, and that the impact of pregnancy on HAE attacks was temporary. Where patients may be concerned about long-term changes in their HAE due to or following pregnancy, the authors found that any change in attack rate – whether better or worse during pregnancy – did not continue long-term.



Next-Generation Sequencing (NGS) Provides More Information for Diagnosis Patients with HAE and Mixed Clinical Manifestations

Irina E. Guryanova^{1}, Valeria V. Pugacheva¹, Chiara Suffritti², Ekaterina A. Polyakova¹, Salivonchik Andrei³, Mikhail V. Belevtsev¹, Sonia Caccia⁴, Natalia E. Konoplya¹*

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BACKGROUND

It is important to diagnose the acquired and hereditary forms of HAE accurately, as they are managed differently. The authors used the latest DNA sequencing technology (called next-generation sequencing or NGS) to investigate whether this technique could help establish an accurate diagnosis.

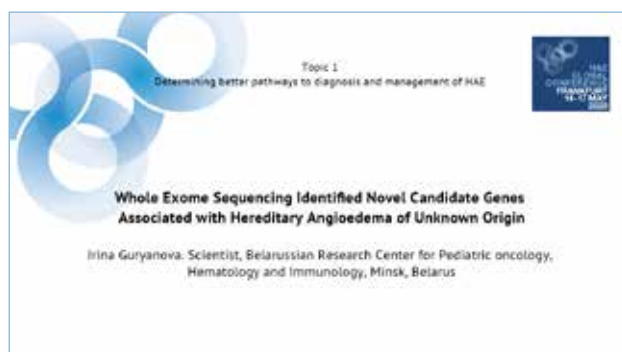
RESULTS

The authors investigated 257 patients who had angioedema without rash (urticaria), using a wide range of different tests using blood; C1-INH, C3c, C4, C1q, immunoglobulin E (IgE), high molecular weight kininogen (HMWK) and antinuclear antibodies (ANA). In addition, the authors used NGS to sequence the SERPING1 gene, as well as more traditional Sanger sequencing.

Of all patients tested, 68 (26.5%) had genetically confirmed C1-INH-HAE, while 11 (4.3%) were found to have an acquired form of angioedema (IH-AAE). There were 39 patients (15.2%) where a specific trigger factor for their acquired angioedema could be identified, such as food, medication or environmental allergen. The authors also report on a family – not included in the numbers above – where an interesting and specific change was observed in the SERPING1 gene and had resulted in various forms of acquired angioedema being seen in family members.

WHAT DOES THIS MEAN FOR PATIENTS?

The authors have provided a view on how NGS can be used in a clinical setting to help accurately diagnose a disease. Ultimately, accurate diagnosis ensures patients receive appropriate therapy which can improve quality of life.



Whole Exome Sequencing Identified Novel Candidate Genes Associated with HAE of Unknown Origin

Irina E. Guryanova^{1*}, Vladislav R. Vertelco¹, Silvia Berra², Chiara Suffritti³, Alexandr A. Migas¹, Ekaterina A. Polyakova⁴, Andrei S. Babenka⁴, Anastasiya V. Punko⁴, Elena I. Lebedeva⁵, Debora Parolin², Mikhail V. Belevtsev⁴, Natalia E. Konoplya⁴, Sonia Caccia²

1) *Belarussian Research Center For Pediatric Oncology, Hematology And Immunology, Minsk, Belarus.* 2) *Department of Biomedical and Clinical Sciences Luigi Sacco, Università degli Studi di Milano, Milan, Italy.* 3) *General Medicine Department, ASST-Fatebenefratelli-Sacco, Milan, Italy.* 4) *Department of Bioorganic chemistry, Belarussian State Medical University, Minsk, Belarus.* 5) *Department of Histology, Cytology and Embryology, State Medical University, Vitebsk, Belarus.* *Corresponding author.

BACKGROUND

Little is known about HAE of unknown origin (U-HAE), a condition which accounts for approximately 1% of all cases of HAE. By using the latest DNA sequencing technology, called next-generation sequencing (NGS) the authors hoped to better understand U-HAE.

RESULTS

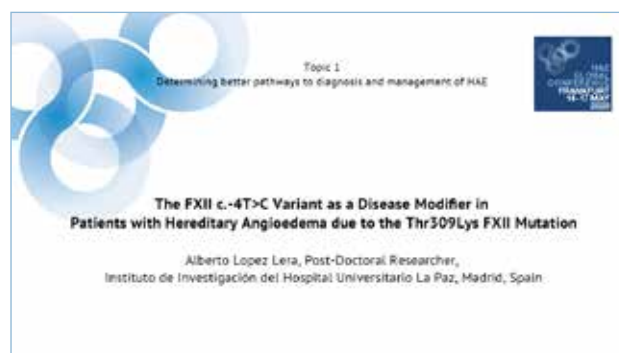
The authors identified five individuals from two unrelated families who clinical and laboratory testing had shown signs of normal C1-INH-HAE. These patients were tested for 18 genes known to be associated with HAE, including FXII, PLG, ANGPT1 and KNG1, using NGS, but this sequencing didn't provide definitive results.

The authors then used a different form of genetic testing, called whole exome sequencing (WES), that is focused only on genes which allow the body to build proteins. Using this technique, a change on gene CPA3 was identified, which has never been described

in relation to HAE. In the other family a variant of the ANGPT1 gene was identified, although this has already been associated with normal C1-INH-HAE.

WHAT DOES THIS MEAN FOR PATIENTS?

The identification of a potential new genetic change in patients with U-HAE may help with accurate diagnosis and treatment. However, this is early research in small numbers of patients. The authors will continue with this line of research and test all other members of the two families (both those with and without symptoms) to see if they share the genetic change or not. This would ensure that the genetic change can be confirmed as associated with HAE.



The FXII c.-4T>C Variant as a Disease Modifier in Patients with HAE due to the Thr309Lys FXII Mutation

Corvillo F^{1,2}, de la Morena-Barrio ME³, López-Trascasa M^{2,4}, Marcos-Bravo C⁵, Vicente V³, Emsley J⁶, Caballero T^{1,2,7}, Corral J³, López-Lera A^{1,2}

1) *Centre for Biomedical Network Research on Rare Diseases (CIBERER) U-754, Hospital Universitario La Paz, Madrid, Spain.* 2) *Hospital La Paz Institute for Health Research (IdiPaz), Madrid, Spain.* 3) *Servicio de Hematología y Oncología Médica, Hospital Universitario Morales Meseguer, Centro Regional de Hemodonación, Universidad de Murcia, IMIB-Arrixaca, CIBERER, Murcia, Spain.* 4) *Facultad de Medicina, Universidad Autónoma de Madrid, Spain.* 5) *Sección Alergología, Complejo Hospitalario Universitario de Vigo Hospital Meixoeiro, Vigo, Spain.* 6) *Centre for Biomolecular Sciences, School of Pharmacy, University of Nottingham, Nottingham NG72RD, England.* 7) *Allergy Department, La Paz University Hospital, Madrid, Spain.*

BACKGROUND

HAE due to mutations in the FXII gene can be complex to diagnose and manage, as the clinical symptoms can vary, and some people may have the mutated gene but not show symptoms of the condition. HAE due to the Thr309Lys mutation in FXII (HAE-FXII) mainly affects women, and in these patients, the symptoms can be greatly dependent on estrogen levels. The authors worked to better understand links between the c.-4T>C polymorphism – which has been recognized as influencing the variability of FXII plasma levels – and the severity of HAE symptoms.

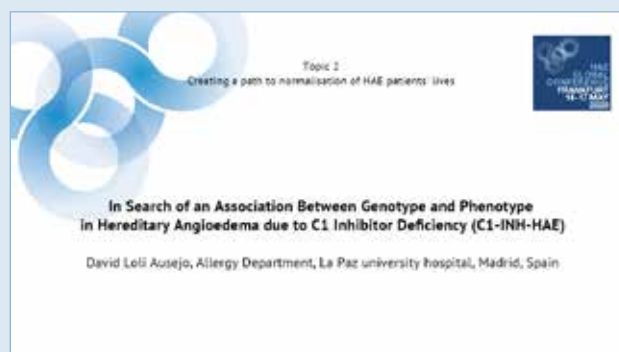
RESULTS

Thirty-nine non-related Spanish patients with HAE-FXII were investigated. The frequency that the c.-4T>C polymorphism occurred in the patients, along with their symptom severity, was assessed. In the patients, the authors report that the CC-homozygous (c.-4CC) was most common, with 71% having this form of the studied genotype. The patients with c.-4CC had significantly higher scores for severity of their HAE.

The authors also looked for evidence of association between the c.-4T>C polymorphism and the impact of estrogen levels or time to resolution of attacks but did not find any links.

WHAT DOES THIS MEAN FOR PATIENTS?

The authors conclude that the c.-4T>C polymorphism can act as a genetic disease modifier which influenced the severity of symptoms of HAE-FXII in patients with the Thr309Lys mutation. They also conclude that due to its clinical impact and presence in many of the studied patients, c.-4T>C could be important for diagnosis.



In Search of an Association Between Genotype and Phenotype in HAE due to C1 Inhibitor Deficiency (C1-INH-HAE)

David Loli-Ausejo¹, Alberto López-Lera^{2,3}, Marina Lluncor⁴, Elsa Phillips-Anglés¹, Rosario Cabañas^{1,2}, Teresa Caballero^{1,2,3}

1) Allergy Department, La Paz University Hospital, Madrid, Spain. 2) Hospital La Paz Institute for Health Research (IdiPaz), Madrid, Spain. 3) Center for Biomedical Network Research on Rare Diseases (CIBERER U754), Madrid, Spain. 4) Allergy Department, Juan Ramón Jiménez Hospital, Huelva, Spain.

BACKGROUND

HAE due to C1-inhibitor deficiency (C1-INH-HAE) is caused by mutations affecting the SERPING1 gene. Bos et al have proposed a classification system for the mutations; class 0, class 1, class 2, class 2. These classes are not exclusive, so patients could have a mutation that belongs to more than one class. The authors wanted to investigate whether the observable characteristics of C1-INH-HAE could be simply aligned to or described by the classification system.

RESULTS

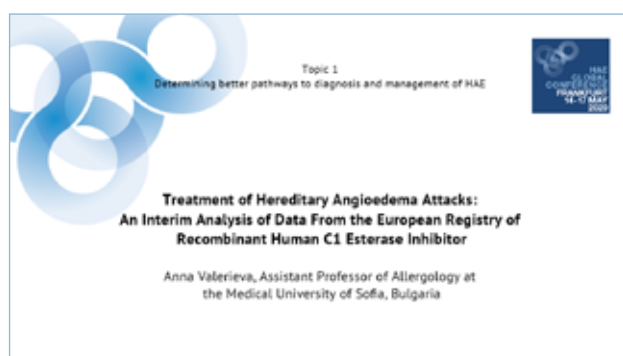
Eighty-eight adult patients were included in the analysis, of which 67 patients had mutations that could be classifiable according to the Bos et al system. Sixty-six patients corresponded to HAE type 1 and 1 patient to HAE type 2.

The authors found that there were variations in the characteristics and the mutation classifications. The mean age at onset of symptoms and at diagnosis were lower in patients with class 2 mutations. The highest average number of angioedema attacks was observed for patients with class 1 mutations. Similar C4 levels were found in patients in all mutation

classes. C1 inhibitor levels were higher in patients with class 1 mutations, and functional C1 inhibitor levels were higher in patients with class 2 mutations. A higher score for the HAE-Activity Score (HAE-AS) questionnaire (scale 0-30) was seen in patients with class 1 mutations.

WHAT DOES THIS MEAN FOR PATIENTS?

The authors conclude that the results indicate that there are differences between the observable characteristics and the classes of SERPING1 gene mutations, but that much larger studies would be needed to confirm this.



Treatment of HAE Attacks: An Interim Analysis of Data from the European Registry of Recombinant Human C1 Esterase Inhibitor

Anna Valerieva¹, Maria T. Staevska¹, Vesna Grivcheva-Panovska², Milos Jesenak³, Kinga Viktória Kóhalmi⁴, Katarina Hrubiskova⁵, Andrea Zanichelli⁶, Luca Bellizzi⁷, Anurag Relan⁸, Roman Hakl⁹, Henriette Farkas⁴

1) Medical University of Sofia, Sofia, Bulgaria. 2) PHI University Clinic of Dermatology, School of Medicine, University Saints Cyril and Methodius, Skopje, North Macedonia. 3) University Hospital in Martin, Martin, Slovakia. 4) Hungarian Angioedema Reference Center, Semmelweis University, and Hospital of Hospitaller Brothers of St. John of God, Department of Rheumatology, Budapest, Hungary. 5) Comenius University in Bratislava and Bratislava University Hospital, Bratislava, Slovakia. 6) ASST Fatebenefratelli Sacco University of Milan, Milan, Italy. 7) Pharming Technologies BV, Leiden, the Netherlands. 8) Pharming Healthcare Inc., Bridgewater, New Jersey, USA. 9) St. Anne's University Hospital, and Masaryk University, Brno, Czech Republic.

BACKGROUND

An ongoing study, called a Registry, is following patients using recombinant human C1 esterase inhibitor (rhC1-

INH) as a therapy for HAE. This study looks at attacks that patients have had, how well the therapy works for patients in their everyday lives, as well as any side effects of using this therapeutic option.

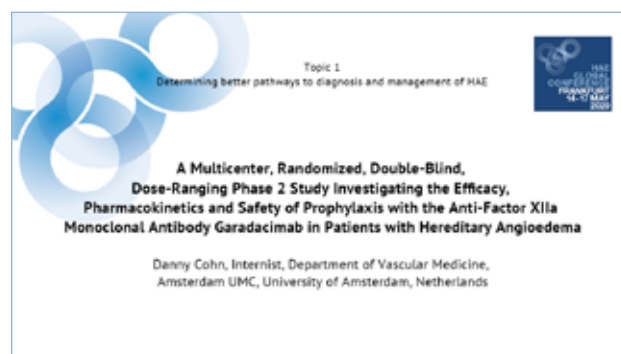
RESULTS

At the point that the authors analyzed the data, 85 patients with C1-inhibitor deficiency HAE (C1-INH-HAE) were enrolled in the Registry. Over an 8.5-year period, these patients experienced an average of 30 HAE attacks every year, totally 2,543 attacks and all the attacks were treated with rhC1-INH. Patients reported 96.9% of attacks were resolved by the use of rhC1-INH within four hours. Most HAE attacks (99.8%) only required one dose of rhC1-INH, with five HAE attacks being treated with a second dose.

The authors report that no hypersensitivity or blood clotting problems were reported, nor did patients report any serious drug-related adverse events.

WHAT DOES THIS MEAN FOR PATIENTS?

The authors conclude that the data from 2,543 HAE attacks treated with rhC1-INH in everyday life, supports the safety and effectiveness of this form of therapy for HAE.



A Multicenter, Randomized, Double-Blind, Dose-Ranging Phase 2 Study Investigating the Efficacy, Pharmacokinetics (PK) and Safety of Prophylaxis with the Anti-Factor XIIa Monoclonal Antibody Garadacimab (CSL312) in Patients with HAE

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BACKGROUND

A potential new preventative therapy for HAE is being trialed in patients in a phase 2 study. This new therapy, which is not yet available for use, is called garadacimab. It works by inhibiting Factor XIIa, to prevent HAE attacks. This study looked at how garadacimab is processed in the body, as well as the optimal dose to maximize safety and efficacy in preventing attacks.

RESULTS

Thirty-two patients with C1-inhibitor deficiency HAE took part in this study. In order to be eligible, patients had to have had four or more HAE attacks in a consecutive two-month period (during the three months prior to joining the study), and at least two HAE attacks in any consecutive four-week period during the run-in period. Eligible adult patients were randomly assigned to receive 75mg, 200mg, or 600mg of garadacimab, or a dummy treatment (placebo) every four weeks during the first phase of treatment. After 13 weeks, a second treatment period saw all patients randomly receive either 200mg or 600mg of garadacimab for a further 44 weeks. Injections were given under the skin (subcutaneously) every four weeks.

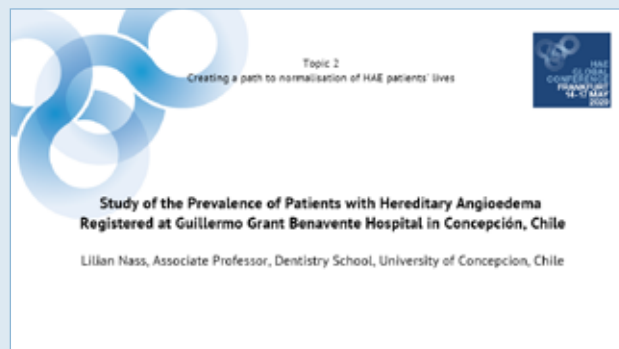
Overall all doses of garadacimab reduced the mean number of HAE attacks; however, the 200mg and 600mg doses reduced the mean number of attacks by 98.94% and 90.50% respectively, which was not the result of chance (statistically significant, $P < 0.001$).

All patients taking 200mg or 600mg of garadacimab reported side effects, however none were considered serious and none led to patients stopping the medication. The most common side effect of treatment was a mild to moderate reaction around the area of the injection.

WHAT DOES THIS MEAN FOR PATIENTS?

The authors conclude that garadacimab is well-tolerated, and at the 200mg and 600mg doses was effective in reducing HAE attacks compared to placebo. This study provides the first clinical evidence of the role of Factor XIIa in C1-INH-HAE. The study is ongoing,

and the results will inform the phase 3 study design to further evaluate the role of garadacimab in preventing attacks.



Study of the prevalence of patients with HAE registered at Guillermo Grant Benavente Hospital in Concepción, Chile

Dr. Lilian Nass, Dr. Gonzalo Espinoza, Dr. Matías Cisterna, Dra. María Nass, EU Caprice Sanhueza

Guillermo Grant Benavente Regional Hospital, Bronchopulmonary Department, Concepción, Chile. University of Concepción, Dentistry School, Department of Restorative Dentistry, Concepción, Chile.

BACKGROUND

Little is currently known about the prevalence and impact of HAE in the Bío – Bío and Nuble regions in Chile. The authors conducted a study of patients with Hereditary Angioedema at the Guillermo Grant Benavente Hospital – a Regional Hospital – in Concepcion, Chile to try and understand more.

RESULTS

Data was collected via review of clinical records of patients with HAE registered at the Regional Hospital. Patient consent was obtained for the review.

The preliminary results are for 17 HAE patients; of whom 11 are women and six are men. The patients have an average age of 39 years. The authors found patients had an average of 13 attacks over just under a year and a half (17 months); the highest number of attacks seen was 53, and the lowest number of attacks was one. One patient died as a result of an attack, which corresponded to 6% of the total number of patients.

WHAT DOES THIS MEAN FOR PATIENTS?

Thanks to the work of the authors, there is now a

better understanding of the prevalence and disease characteristics of the HAE patients in the Bío – Bío and Nuble regions in Chile. This information should support patients in terms of managing their attacks and increasing their quality of life.



Psychological Impact of HAE led to the Creation of the BITTEN Model of Trauma Informed Healthcare

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2) Institution: University of North Carolina Charlotte, Department: Psychological Science and Health Psychology, Charlotte, NC, United States of America.

BACKGROUND

People with HAE experience psychological impacts as a result of factors other than HAE. One possible cause for these impacts is institutional betrayal (IB). IB occurs when an individual's trust in an institution – such as healthcare providers – is betrayed through negative care or when expected care isn't delivered. HAE patients may experience healthcare system IB in different ways, for example:

1. having their symptoms of HAE dismissed or misdiagnosed
2. insurance denials
3. barriers accessing medication (for example due to an unfamiliarity with prescribing a particular rare medication, or the medication not being stocked) or
4. hospital system and structure failures due to unfamiliarity with HAE.

HAE patients are already at risk of experiencing medical trauma due to the severity and unpredictability of HAE

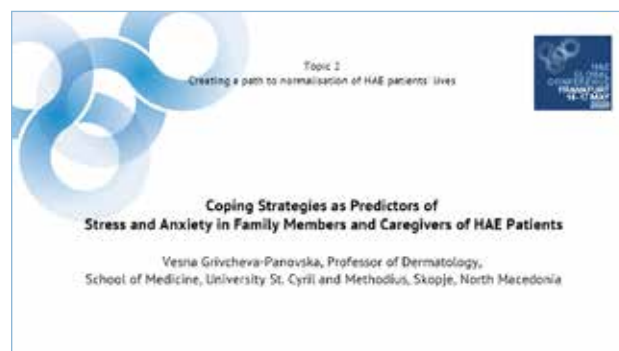
attacks, and the authors identified that healthcare providers may not be prepared to address the impact of HAE attacks when combined with the psychological impact of any pre-existing IB. As a result, the authors developed a new model of care to help identify and appropriately address these challenges.

RESULTS

The authors were part of the team that created the BITTEN (Betrayal, Indicator for healthcare, Trauma history, Trust in provider, patient Expectations and Needs) Model of trauma informed care to provide a best practice framework for healthcare professionals. The BITTEN model helps healthcare professionals to look at past experiences to identify what the patient expectations of their current healthcare provision could be, and how patient needs for their healthcare experiences in the future can be addressed.

WHAT DOES THIS MEAN FOR PATIENTS?

The BITTEN Model helps healthcare professionals to understand that previous experiences may impact patient expectations of their current care, identify where these expectations are having a negative psychological impact and to respond appropriately with the ultimate aim of avoiding further negative healthcare experiences for the patient.



Coping strategies as predictors of stress and anxiety in family members and caregivers of HAE patients

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BACKGROUND

It is known that the unpredictability and fear of potentially life-threatening HAE attacks causes anxiety for patients, however patients' family members and caregivers (FM&C) can also experience anxiety as a result of fear of their loved ones having these attacks. It is also known that anxiety limits psychosocial functioning and has a strong impact on quality of life (QoL), however little is known about the coping strategies chosen by FM&C and their association with levels of anxiety experienced.

RESULTS

The authors report results from 178 FM&C of patients split into four groups:

- A1- 17 FM&C of HAE patients diagnosed less than (<) six months before the study start
- A2- 67 FM&C of HAE patients diagnosed more than (>) six months before the study start
- B1- 12 FM&C of patients with a severe food allergy which include angioedema symptoms diagnosed less than (<) six months before the study start
- B2- 82 FM&C of patients with a severe food allergy which include angioedema symptoms, diagnosed more than (>) six months before the study start

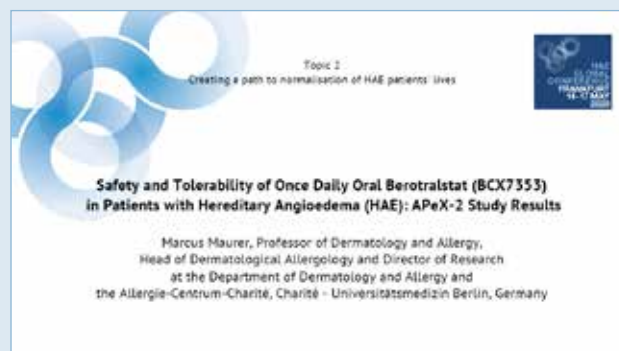
Group B was included in the study as a control group, and the authors explained that six months was chosen as the time frame to assess before and after, as studies have shown that this is the time needed to establish and build coping strategies. All participants underwent semi-structured interviews specialized for the purpose of the study using the Ways of Coping Questionnaire and the Hamilton Anxiety Rating Scale (HAM-A).

The authors found similarities in the groups where they were of similar timescales. In group A1 the coping strategy of confrontation was more pronounced (53%), and in group B1 confrontation was 42%. A high level of anxiety was diagnosed in group A1, where it was found that the coping strategies adopted, and high levels of anxiety, interfere QoL.

The most common strategies used post six months of diagnosis were planned problem solving (A2 & B2), seeking social support (A2), attitude (B2) and positive evaluation of the state (A2 & B2). Where these functional, positive and proactive coping styles were used, participants were found to have reduced levels of stress and anxiety related to the disease and its therapy.

WHAT DOES THIS STUDY MEAN FOR PATIENTS?

Using positive and proactive coping strategies can help reduce levels of anxiety and stress. This can lead to an increased following of healthcare professional advice and a positive effect on the overall health and QoL for the patient.



Safety and Tolerability of Once Daily Oral Berotralstat (BCX7353) in Patients with HAE: APeX-2 Study Results

Marcus Maurer¹, Jonathan Bernstein², Douglas Johnston³, Aleena Banerji⁴, Marc Riedl⁵, Bruce Zuraw⁵, Emel Aygören-Pürsün⁶, Sandra C. Christiansen⁵, Sylvia Dobo⁷, Heather Iocca⁷, Sharon Murray⁷, Phil Collis⁷, William R. Lumry⁸ on behalf of the APeX-2 Investigators

1) Charité - Universitätsmedizin Berlin, Germany. 2) UC Health, Cincinnati, USA. 3) Asthma & Allergy Specialists, Charlotte, USA. 4) Harvard Medical School, Boston, USA. 5) UC San Diego Health, San Diego, USA. 6) Goethe University Hospital Frankfurt, Germany. 7) BioCryst Pharmaceuticals, Durham, USA. 8) Allergy & Asthma Specialists of Dallas, USA.

BACKGROUND

A potential new preventative therapy for HAE is being trialed in patients in a phase 3 study. This new therapy, which is not yet available for use, is called berotralstat and is a once a day oral pill. This phase 3 study investigates the safety and tolerability of this potential HAE therapy.

RESULTS

A total of 121 patients with HAE type 1 or 2, who had at least two confirmed attacks in the 56 days before treatment started, received either 110mg berotralstat or 150mg berotralstat, or a dummy pill for a period of 24 weeks. The number of side effects reported by

patients were collected, along with their severity and the likelihood that they were due to the new medication. In particular, the study examined any gastrointestinal side effects in detail.

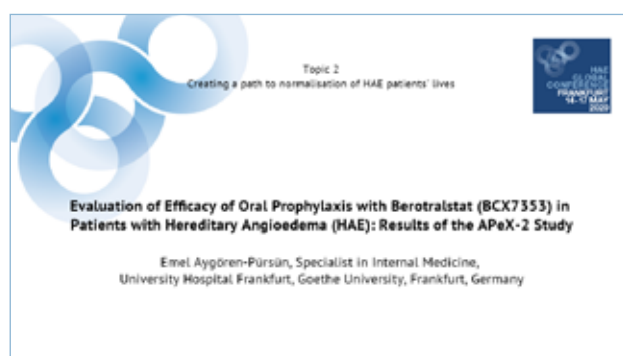
82.9% of patients taking 110mg berotralstat reported side effects. The proportion of patients taking 150mg berotralstat who reported side effects was 85.0%. In the placebo group (those taking the dummy pill) 76.9% of patients reported side effects.

The rate of side effects considered to be directly related to berotralstat were 41.5% in the 110mg group; 37.5% in the 150mg group and 33.3% in the placebo group. Four patients reported serious side effects; one from the group taking 110mg berotralstat and three taking placebo. Overall five patients stopped taking the therapy; three in the 110mg group, and one each in the 150mg group and placebo group.

The most common drug-related side effects were vomiting, diarrhea, abdominal pain and back pain. Gastrointestinal side effects were mostly mild, generally resolved without the need for medication and only led to one patient stopping treatment (one patient in 110mg group).

WHAT DOES THIS MEAN FOR PATIENTS?

Overall authors conclude that the study shows berotralstat is safe and generally well-tolerated at both 110mg and 150mg doses, with no serious drug-related side effects. The most common side effects were mild gastrointestinal problems. This study provides the largest in-patient clinical evidence for berotralstat to date, and results will inform applications to medicines approvers/ regulators in the future.



Evaluation of Efficacy of Oral Prophylaxis with Berotralstat (BCX7353) in Patients with HAE: Results of the APeX-2 Study

Emel Aygören-Pürsün¹, Sandra C. Christiansen², Marc Riedl², Bruce Zuraw², William R. Lumry³, Douglas Johnston⁴, Jonathan Bernstein⁵, Marcus Maurer⁶, Melanie Cornpropst⁷, Sharon Murray⁷, Eniko Nagy⁷, William P. Sheridan⁷, and Aleena Banerji⁸ on behalf of the APeX-2 Investigators

1) Goethe University Hospital Frankfurt, Germany. 2) UC San Diego Health, San Diego, USA. 3) Allergy & Asthma Specialists of Dallas, USA. 4) Asthma & Allergy Specialists, Charlotte, USA. 5) UC Health, Cincinnati, USA. 6) Charité - Universitätsmedizin Berlin, Germany. 7) BioCryst Pharmaceuticals, Durham, USA. 8) Harvard Medical School, Boston, USA.

BACKGROUND

A potential new preventative therapy for HAE is being trialed in patients in a phase 3 study. This new therapy, which is not yet available for use, is called berotralstat and is a once a day oral pill. This study investigates how effective this potential HAE therapy is in patients.

RESULTS

A total of 121 patients with HAE type 1 or 2, who had at least two confirmed attacks in the 56 days before treatment started, received either 110mg berotralstat or 150mg berotralstat, or a dummy pill for a period of 24 weeks. Patients recorded HAE attacks in a diary and were asked to treat any attacks in accordance with their usual treatment plan. The authors were primarily examining the rate of confirmed HAE attacks during the 24 weeks of treatment, but also looked at the use of on-demand medication and the reduction in the number of confirmed HAE attacks compared to the rate before the trial started.

Presenting results from the 150mg group, the authors observed that patients taking 150mg berotralstat experienced 44.2% fewer attacks per month compared to the placebo group (those taking the dummy pill). In this group, more than half of patients (57.5%) experienced at least a 50% reduction in rates of HAE attacks, and half of patients (50%) experienced at least a 70% reduction in their rates of HAE attacks, both compared to HAE attack rates before the start of the trial.

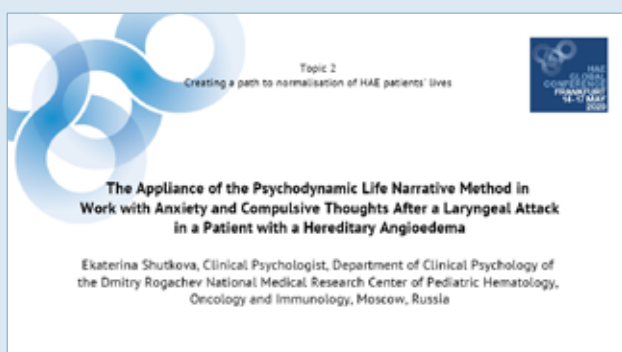
All patients taking berotralstat used less on-demand medication to manage HAE attacks. In the 150mg group this meant 1.5 fewer doses of on-demand medication per month.

Overall treatment with 150mg berotralstat led to a 44.2% reduction in the rate of HAE attacks; a 49.2% decrease in the rate of HAE attacks requiring treatment; and a 53.6% reduction in the use of on-demand medication, all when compared to placebo.

The authors report that the most common side effects of treatment were nasal congestion, nausea and vomiting.

WHAT DOES THIS MEAN FOR PATIENTS?

The authors conclude that HAE patients receiving berotralstat had fewer attacks, needed to treat fewer attacks and used less on-demand medication than those on placebo. This study provides the largest in-patient clinical evidence for berotralstat to date, and results will inform applications to medicines approvers/regulators in the future.



The Appliance of the Psychodynamic Life Narrative Method in Work with Anxiety and Compulsive Thoughts after a Laryngeal Attack in a Patient with a HAE

Ekaterina S. Shutkova, Dmitry Rogachev National Medical Research Center of Pediatric Hematology, Oncology and Immunology, Department of clinical psychology, Moscow, Russia.

BACKGROUND

There is a link between mental health and the severity of HAE, with swellings of the upper airways being potentially life-threatening and therefore associated with high levels of patient anxiety. Psychological impact can also be a trigger for attacks. Methods to help patients deal with anxiety could be very valuable in improving management of HAE and lead to better quality of life for patients.

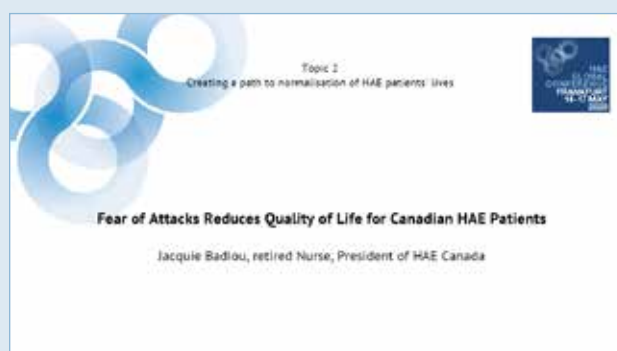
RESULTS

The authors report the case of a 37 woman with HAE, who had high levels of anxiety and compulsive thoughts related to having another HAE attack in her larynx (voice box in the throat). Her concerns were related to anxiety about death, a lack of control over her life, dependence on physicians and concern about being able to access medical help.

Using the psychodynamic life narrative method during three online consultations, psychologists helped the patient to place her anxieties in context of her current life circumstances. This helped reduce the amount of compulsive thoughts the patient had, and greatly reduced her anxiety.

WHAT DOES THIS MEAN FOR PATIENTS?

The author concludes that psychodynamic life narrative may be a promising way for HAE patients to lessen anxiety and reinforce a feeling of control. Further research on the psychodynamic life narrative could be promising to positively help anxiety and depression in HAE patients.



Fear of Attacks Reduces Quality of Life for Canadian HAE Patients

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BACKGROUND

Assessing the day-to-day experiences of HAE patients is important to understanding the impact of HAE on daily life. New prophylactic therapies offer the potential for a great reduction in HAE attacks, and the impact on daily life. HAE Canada wanted to assess the

challenges faced by HAE patients and caregivers as well as understand the impact that the availability of the newest prophylactic therapies has had for patients.

RESULTS

The authors report results from the first six questions, asked in two online surveys conducted in 2019.

The first survey looked at the challenges in daily life for HAE patients and included respondents who were treated with lanadelumab. In this survey, there were 73 respondents, 68 (92%) who were HAE patients and 6 (8%) caregivers. Respondents were asked how often that had attacks, and around one in three patients (29%) experienced attacks more than once a month and one in six patients experienced attacks more than once a week. Attacks most commonly occurred in the GI tract, the face and in the upper airway for patients. Three in four patients indicated that they feared having unpredictable and debilitating attacks. This resulted in more than half of respondents reporting generalized anxiety and also a desire for control of swelling and treatment plans.

Of the first survey respondent, eight had been treated with lanadelumab via participation in a clinical trial. Five patients considered it “extremely effective” in preventing attacks.

The second survey had 19 respondents and was designed to gather information about subcutaneous C1 inhibitor. Three respondents had received subcutaneous C1 inhibitor and all reported this to be “extremely effective”.

In both surveys, reported side effects from patients taking lanadelumab or subcutaneous C1 inhibitor were “tolerable” to “very tolerable”.

WHAT DOES THIS MEAN FOR PATIENTS?

The authors conclude that the fear of unpredictable, painful or life-threatening HAE attacks can lead to negative feelings and generalized anxiety. Patients report that the newest medications are effective in reducing attacks which could reduce the fear of attacks and so improve the quality of life of Canadian HAE patients.



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

