HAEi Newsletter

IN THIS NEWSLETTER

A Message from the President

Dear HAEi Friends,

The HAEi Executive Committee is very excited that, at last count, 33 countries will be represented at the HAE Global Conference that will take place May 15 – 18 in Washington, DC. This meeting will provide HAE friends with a perfect opportunity to interact, share information with fellow patients from all corners of the earth, and establish working relationships that lead to meaningful ongoing post conference communication.

The world's foremost HAE expert physician/scientists will be on hand to answer all of your HAE-related questions. In addition, attendees will learn about

- the latest advances in HAE treatments,
- strategies for engaging fellow patients, physicians, and pharmaceutical companies to help start or expand patient organizations,
- tangible steps for improving the HAE diagnosis in your country, and
- how to develop and implement an action plan for convincing health ministries and insurance authorities to getting access to and reimbursement for HAE medicines.

I look forward to personally welcoming each and every HAEi friend to Washington, DC.

Warm regards,

Anthony J. Castaldo
President, HAEi

2014 HAE Global Conference

More than 300 people have by now signed up for the HAE Global Conference taking place in Washington D.C. Metro Area around **hae day :-)** 2014.

The attendees are representing more than 30 countries as we will be having people coming in from Argentina, Australia, Austria, Belarus, Brazil, Canada, China, Czech Republic, Denmark, Finland, France, Germany, Hungary, Ireland, Israel, Japan, Macedonia, Malaysia, Mexico, Netherlands, New Zealand, Norway, Pakistan, Poland, Portugal, Russia, Spain, Sweden, Switzerland, United Arab Emirates, United Kingdom, Venezuela, and obviously United States of America.

HAE GLOBAL CONFERENCE WASHINGTON DC 15-18 MAY 2014

Preparations for the 2014 HAE Global Conference are ongoing.

Although we do not have any more travel grants available, there are still possibilities to register for this important HAE event.

For more information and registration please visit our registration website

Grants to support research

A primary aim of HAEi is to make a significant contribution to efforts that will ultimately result in improving the lives of the global HAE community. To implement this goal, HAEi's Executive Committee has decided to provide grants to support research that may lead to curing or better controlling HAE symptoms.

The grants are being offered to encourage the development of new information that contributes to the understanding of the basic etiology and pathogenesis of HAE.

Preference will be given to research projects that provide a prominent role for junior researchers, and can be carried out in the period of time and with the resources provided by the grant. The awards are meant to help individuals interested in careers related to HAE research, and will hopefully lead to submission to other agencies that fund medical research.

The project period covers two years and applicants may submit a budget for direct costs of up to 50,000 USD per year.

We have received 16 grant proposals, which are now being reviewed by a panel of independent expert physicians/scientists who will choose the proposal to be funded. The HAEi Executive Committee will have no involvement, nor influence over the independent Panel's deliberations and decision.

We expect to announce the grant recipient in late April 2014.

HAEi on social media

The HAEi group page on Facebook was opened a couple of years ago and by now we have 890 members coming from literally all over the world.

Last year we introduced a company page on LinkedIn as well, and here we have some 60 followers.

You can find HAEi on Twitter where we have around 100 followers at the moment. Also, there is a special Facebook page for the **haeday :-**) event with close to 15,000 followers.

HAEi on Facebook:
https://www.facebook.com/groups/172320032283/
hae day :-) on Facebook:
https://www.facebook.com/haeday
HAEi on LinkedIn:
http://www.linkedin.com/company/3363107?trk=tyah&trkInfo=tas%3AHAEi%2Cidx%3A1-1-1

Second DACH meeting

In November 2013 HAEi conducted the second DACH meeting in Munich, Germany. The aim of the meeting was to improve treatment options and guidelines in the German speaking countries Germany (D), Austria (A), and Switzerland (CH). Again this time ViroPharma funded the activity.

The DACH group is currently in the process of capturing input for the practical clinical recommendation for treating HAE in the three German-speaking countries.

NEWS FROM OUR NATIONAL MEMBER ORGANIZATIONS AROUND THE GLOBE

Australasia (www.haeaustralasia.org.au)

Meet Up: Just before Christmas 2013 HAE Australasia President Fiona Wardman joined patients in Brisbane for a MEET UP lunch. Six patients, including one patient who was meeting others with HAE outside of her own family for the first time, as well as three carers attended the lunch. As with all MEET UPs, the discussions focus on treatments, medications and sharing experiences and information within the HAE family.

Patient Meeting: HAE Australasia will be holding the third patient meeting on 29 March 2014 in Adelaide. The event will provide the participants with an opportunity to hear from HAE experts and to meet others who may share similar HAE experiences. It will also be a good opportunity to meet with the HAE Australasia board members and discuss how to help spread awareness of HAE in Australia & New Zealand. A limited number of travel grants are available to assist participants from interstate or New Zealand.

Brazil (www.abranghe.org.br)

The very good news at the start of 2014 is that C1 Esterase Inhibitor - Berinert P has been approved for the treatment of HAE in Brazil. The medication is expected to be for sale in a few months. Up until now only Firazyr (Icatibant) has been registered/licensed.

Canada (www.haecanada.org)

The Canadian patient organization was formed in 2010 to work with physicians, nurses, and other healthcare professionals to create a better life for HAE patients living in Canada. Most recently the organization has issued a brochure on HAE, both in English (wildnetworks.biz/hae/wp-content/uploads/2013/11/HAEC-general-info-brochure-13-10-09.pdf) and French (wildnetworks.biz/hae/wp-content/uploads/2013/11/HAEC-general-info-brochure-13-10-09.pdf).

Germany (www.angiooedem.de)

During 2014 the German HAE organization will be presenting a short film and a brochure on patient stories. The production of the film is supported by ViroPharma. Other material from HAE Germany include a book for children to be issued later this year – and most recently the organization has published brochures on veins care as well as primary HAE diagnosis, both supported by CSL Behring.

Israel (www.edema.co.il)

Ruconest® (recombinant human C1 inhibitor) has been approved for marketing in Israel and at the same time it has been approved by the reimbursement committee to be added on the Israel Health basket with no extra costs. The number of HAE patients in Israel is estimated at approximately 250 and they are expected to have access to the new medication already during the first quarter of this year.

Mexico (www.haei.org/map/96)

We have just been informed that the second Latin American congress on HAE will take place in Veracruz, Mexico 28 May 2014. We expect to have more information in the next newsletter.

Netherlands (www.hae-qe.nl)

The Dutch Patients' Federation has launched a campaign for safer care. One of the spearheads of the campaign is hygiene. Do you want to know whether there but test your knowledge in this area, click on the link below. Further information on the subject can be found here (zorgzine.npcf.nl/hygiene) .

Poland (www.hae.org.pl)

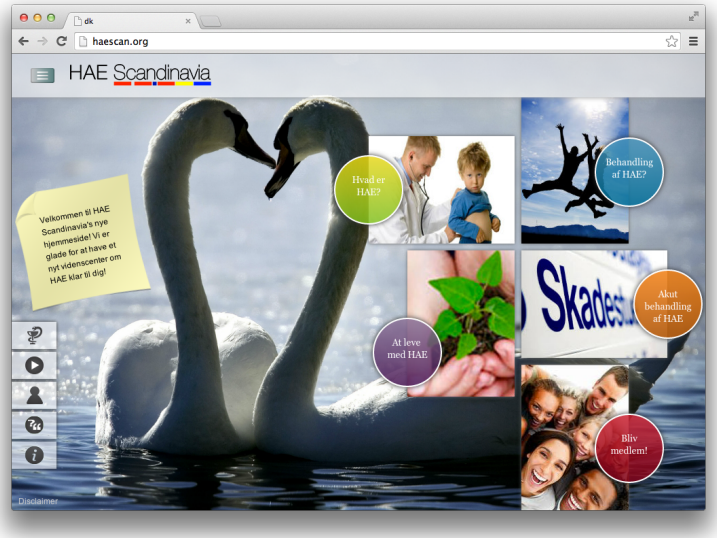
The Polish Association of Hereditary Angioedema consists of more than 200 patients/members in the age of 4 to 86. However, the number of patients in Poland suffering from lack of

C1 inhibitor is being estimated as 1,000-1,300. For more than 20 years Professor Krystyna Obtulowicz from Allergology Clinic in Krakow has been taking care of the patients with this disease and is involved in diagnosis, treatment and educational initiatives. Due to her efforts supported by other physicians, patients with HAE and CSL Behring it was possible to obtain the reimbursement for Berinert in Poland recently.

The product will be reimbursed in treatment of severe attacks of HAE as well as in pre-procedure prevention of acute episodes (short term prophylaxis). It will be available for the patients free of charge in open pharmacies on prescription.

Scandinavia (www.haescan.org)

Danes, Norwegians and Swedes joined forces at the end on 2013, forming HAE Scandinavia. The new organization has been established in order to work for patients and relatives in the three



Northern European countries and to form a strong network of Scandinavian doctors. At the moment there are some 330 diagnosed patients in Scandinavia – with an expected total of around 640 patients. HAE Scandinavia will launch its new website in all three Scandinavian languages (Danish, Norwegian and Swedish) later this month.

Spain (www.angioedema-aedaf.org)

The next General Assembly Meeting of the AEDAF will be held in Madrid on 5 April 2014.

Among the speakers are Dr. Margarita López Trascasa from Hospital Universitario La Paz ("Commitment of patients in the study of angioedema"), Dr. Teresa Caballero Molina ("New classification of angioedema – Additional Study Results of Burden of Ilness", Dr. Nieves Prior ("Survey of Quality of Life in HAE"), and Dr. Maria Pedrosa ("HAE in children").

Switzerland (www.hae-vereinigung.ch)

The 15th Patient Meeting will take place 24 May 2014 in Berne. Apart from a number of HAE related topics the program will include a visit to the soccer stadium Stade de Suisse in Berne.

United Kingdom (www.haeuk.org)

Registered Charity: Recently HAE UK has become a Registered Charity and a Company Limited by Guarantee. The organization has established a clear structure for the team. The HAE UK Trustees are Ann Price (Chair of Trustees and patient contact), John Price (treasurer), and Barrie Hurley (business and fund raising advisor), while the HAE UK Executive Officer is Rachel Annals (website and confidential database manager, events organizer/planner and general administrator).

Raising awareness: During 2013 the HAE UK organization has been out and about meeting patients and immunology staff in an effort to raise the profile of HAE across the country. Among other activities they hosted a day for patients from the West Midlands, hosted an informal social meeting for patients from The London Hospital, manned a HAE stand at a conference for immunologists and specialist nurses, and presented a patient perception of HAE to an Oral Medicines Symposium.

Patient Day: Over 100 patients, family members, doctors, nurses and members of the pharmaceutical industry met for the HAE UK Patient Day in November 2013. It was a very busy day with lots of presentations, such as The New Clinical Commissioning Policy, The HAE Patient Care Pathway and Home Therapy Treatments. Tony Castaldo, President of HAEi, and Henrik Balle Boysen, HAEi Executive Director, gave an international perspective on HAE management and the HAE UK immunologists and specialist nurses gave up their free time to come and talk to the many people present at the Patient Day.

Updated website: HAE UK is in the process of updating the website. If you have any information from your own personal experiences regarding either travel insurance, recommended holiday destinations for HAE patients, experience of employment regulations and/or successful applications for claiming benefits, and experiences of HAE management in children and schools, HAE UK would much appreciate if you would share this information with the organization. Please e-mail to ann.price@haeuk.org.

Booklet and passport: HAE UK will be producing a small patient information booklet, hopefully to be endorsed by UKPIN (the UK Primary Immunodeficiency Network, a multidisciplinary organization of those caring for patients with primary immunodeficiencies) for use in all HAE centers. Also, HAE UK will be working on a HAE passport to be available for the **hae day :-**) 2014. These will be cards that patients can use in A&E departments to hopefully fast track then to the appropriate treatment.

USA (www.haea.org)

In December 2013 the US HAEA presented a webinar on the new US health care law's effect on insurance coverage for HAE patients. For those who were not able to join the webinar online, the organization has provided a recording on its website. The featured speaker is Eric Gascho, Director of Government Affairs of the National Health Council.

This non-profit organization provides a united voice for the more than 133 million people in USA with chronic diseases and disabilities and their family caregivers. The webinar lasts about 30 minutes and can be found here (https://attendee.gotowebinar.com/recording/8856944748778214658).

NEW PAPERS ON HAE

Internationally quite a number of scientific papers on HAE research are issued every month. In every newsletter we will try to keep you updated on the most recent and most interesting papers made public since the last issue:

"Feasibility of Home Infusion and Self-Administration of Nanofiltered C1 Esterase Inhibitor for Routine Prophylaxis in Patients with Hereditary Angioedema and Characterization of a Training and Support Program" – ***by C. Gregory, L.M. Landmesser, L. Corrigan, D. Mariano; Specialty Pharmacy Nursing Network, Inc, Florida, USA, and ViroPharma Incorporated, Pennsylvania, USA):***
Study researchers evaluated the prevalence of home and self-administration of nanofiltered, human-derived C1 esterase inhibitor infusions and the implementation of a nursing training and support program. Home administration rate increased from 49.0% to 75.8%. The percentage that self-administered increased from 20.3% to 43.9%. Doses per week averaged 1.85 at home compared with 1.40 in infusion centers and physicians' offices. Patients required an average of five visits to be trained. Self-administration is a viable, feasible option in the management of HAE, which is facilitated by a nurse-managed training and support program. (J Infus Nurs., January/February 2014)

"Pediatric hereditary angioedema" – ***by A.J. Macginnitie; Boston Children's Hospital, Boston and Harvard Medical School, Massachusetts, USA:***
In addition to the physical symptoms, HAE patients experience significant decrements in vocational and school achievement as well as in overall quality of life. Symptoms often begin in childhood and occur by age 20 in most patients, but life-threatening attacks are uncommon in the pediatric population. The availability of new therapies has transformed the management of HAE. (Pediatr Allergy Immunol., 9 December 2013)

"C1-esterase inhibitor deficiency in pediatric heart transplant recipients: incidence and findings on ultrasound" – *by S. Pabst et al.; University Hospital Giessen, Germany):*

Acquired angioedema (AAE) of the bowel caused by a deficiency of C1-esterase inhibitor can lead to severe abdominal pain with sudden onset, mimicking an acute surgical abdomen. In contrast to HAE, which usually manifests in childhood, AAE is broadly recognized to affect people older than 40 years. A cohort of 207 children and adolescents who had undergone heart transplantation was assessed at regular follow-up examinations for incidence of AAE. AAE was diagnosed in 3/207 patients, presented with sudden onset of severe abdominal pain. Single episodes of AAE were encountered in 1.4% of our series of pediatric heart transplant recipients. Radiologists should be familiar with this disease so they can diagnose it on US imaging. (Pediatr Radiol., 21 December 2013)

"Ultrasound assessment of acute abdominal pain in hereditary angioedema" – *by S. Montoro, A. Palacios, M.C. Gallego, O. Ordóñez; Hospital Universitario 12 de Octubre, Madrid, Spain:*

Article only in Spanish ("Valoración ecográfica del dolor abdominal agudo en el angioedema hereditario") – can be downloaded from http://www.elsevier.es/eop/S1695-4033(13)00403-7.pdf (An Pediatr (Barc)., 28 November 2013)

"Angiotensin Converting Enzyme-induced Angioedema - A Dangerous New Epidemic" – *by E.R. Rasmussen, K. Mey, A. Bygum; Koege Hospital, Denmark:*

In the last decades the incidence of severe angioedema involving the upper airways and even fatal outcome due to asphyxia has increased. This is mainly due to pharmaceuticals such as angiotensin converting enzyme-inhibitors, which are extensively used worldwide. Some aspects of the pathophysiology have been elucidated and the vasoactive molecule bradykinin is shown to be one of the main causative agents. The diagnosis is often delayed and traditional treatment usually ineffective. Complement C1 inhibitor concentrate and bradykinin receptor antagonists, normally used to treat patients with HAE, have shown good results when used in patients with bradykinin-mediated angioedema. (Acta Derm Venereol. 21 November 2013)

"Cost-utility analysis of Ruconest® (conestat alfa) compared to Berinert® P (human C1 esterase inhibitor) in the treatment of acute, life-threatening angioedema attacks in patients with hereditary angioedema" – *by P. Kawalec, P. Holko, A. Paszulewicz; Jagiellonian University, Krakow, Poland:*

Administration of human C1 esterase inhibitor (Berinert® P) from target import is the most widespread treatment strategy for patients with HAE. However, a therapeutic health program including Ruconest® (conestat alfa) could shorten a patient's expectancy for a life-saving treatment. The cost-utility analysis from the Polish healthcare payer's perspective was performed for one year (2012). The costs and health outcomes were simulated for three pairs of eligible HAE patient groups (active treatment and corresponding placebo). The incremental cost-utility ratios (ICURs) for the evaluated interventions compared with placebo were EUR 15,226 per QALY (Ruconest®) and EUR 27,786 per QALY (Berinert® P). The probability of cost-utility (ICUR < EUR 24,279 per QALY) assessed for Ruconest® administered in the case of acute angioedema attack was 61% and 41% for Berinert® P. The administration of Ruconest® in acute life-threatening angioedema attacks is economically justified from the Polish healthcare payer's perspective, results in lower costs and is characterized by higher cost-utility probability compared with Berinert® P. (Postepy Dermatol Alergol., 30 June 2013)

"Nanofiltered C1 esterase inhibitor for treatment of laryngeal attacks in patients with hereditary angioedema" – *by M.A. Riedl et al.; University of California-Los Angeles, USA:*

Laryngeal edema is a life-threatening manifestation of HAE. The preparation of nanofiltered C1 INH (C1 INH-nf) used in this study is indicated for routine prophylaxis against angioedema attacks in USA and for treatment, preprocedure prevention, and routine prevention of HAE in Europe. The objective was to evaluate the effectiveness and tolerability of C1 INH-nf when used for the treatment of laryngeal attacks. In the open-label treatment study, 60 (50/84) and 77% (65/84) of attacks achieved unequivocal relief within one and four hours, respectively, after treatment. Time to unequivocal relief was shorter with prompt treatment. When C1 INH-nf was administered within four hours of symptom onset, clinical relief was achieved in 94% (45/48) of attacks within four hours after treatment. Of 265 attacks from the four studies, 62% received two 1,000-U doses of C1 INH-nf. No serious adverse events occurring within seven days after treatment were attributed to study drug, and only one patient required intubation after receiving C1 INH-nf (14.5 hours after symptom onset). This analysis supports that C1 INH-nf is an effective and well-tolerated therapy for laryngeal angioedema attacks. (Am J Rhinol Allergy, 27 November 2013)

"Hereditary disorders presenting with urticaria" – *by N. Kanazawa; Wakayama Medical University, Japan:*

The latest clinical guideline includes three major hereditary disorders presenting with urticaria: urticaria pigmentosa (mastocytosis), HAE, and cryopyrin-associated periodic syndromes. Understanding the genetic cause and the consequent pathogenesis of such disorders helps in providing disease-specific essential therapeutic regimens. In recent years, distinct hereditary autoinflammatory syndromes with cold urticaria have been reported: NLRP12-associated periodic syndrome, and PLCG2-associated antibody deficiency and immune dysregulation. Rapid progress in genetic analysis and further insights into undefined hereditary urticaria promise the development of novel therapeutics in the near future. (Immunol Allergy Clin North Am., February 2014)

"The humanistic burden of hereditary angioedema: Results from the Burden of Illness Study in Europe" – *by T. Caballero et al.*

The broad range of consequences of HAE on patients' lives is not well understood. The study objective was to comprehensively characterize the burden of illness and impact of HAE types I and II from the patient perspective. The HAE Burden of Illness Study in Europe was conducted in Spain, Germany, and Denmark to assess the real-world experience of HAE from the patient perspective via a one-time survey. 186 patients participated; 59% reported having an attack at least once a month, 67% reported moderate-to-severe pain during their last attack, and 74% reported moderate-to-severe swelling. The most common sites of the last attack were the abdomen and extremities; 24% experienced an attack in more than one site. The impact of HAE on daily activities was high during attacks and did not vary significantly by body site affected; patients also reported that HAE impacted their daily activities between attacks. Patients reported substantial anxiety about future attacks, traveling, and passing HAE to their children. Based on Hospital Anxiety and Depression Scale scores, 38 and 14% had clinically meaningful anxiety and depression, respectively. Despite standard of care, HAE patients still have frequent and painful attacks. Patients experience substantial impairment physically and emotionally both during and between attacks. A better understanding of these effects may help in the clinical management of HAE patients. (Allergy Asthma Proc., 22 November 2013)

"Pharmacokinetics of plasma-derived C1-esterase inhibitor after subcutaneous versus intravenous administration in subjects with mild or moderate hereditary angioedema: the PASSION study" – *by I. Martinez-Saguer et al.; Hemophilia Center Rhine Main GmbH, Mörfelden-Walldorf, Germany:*

Human C1-INH concentrate given intravenously (IV) is effective and safe, but venous access may be difficult. We compared subcutaneous (SC) and IV administration of human pasteurized C1-INH concentrate with respect to pharmacokinetics, pharmacodynamics, and safety. 24 subjects with mild or moderate HAE were randomly assigned during an attack-free interval to receive 1,000 units of human pasteurized C1-INH concentrate IV or SC. The mean relative bioavailability of functional C1-INH after SC administration was 39.7%. Maximum C1-INH activity after SC administration occurred within 48 hours and persisted longer than after IV administration. C4 antigen levels increased and clHK levels decreased after IV and SC administration, indicating the pharmacodynamic action of C1-INH. The mean half-life of functional C1-INH was 62 hours after IV administration and 120 hours after SC administration ($p = 0.0595$). C1-INH concentrate was safe and well tolerated when administered via both routes. As expected, SC administration resulted in a higher incidence of injection site reactions, all of which were mild. With a relative bioavailability of 39.7%, SC administration of human pasteurized C1-INH yields potentially clinically relevant and sustained plasma levels of C1-INH and is safe and well tolerated. (Transfusion, 24 November 2013)

"Antihistamine-resistant Angioedema in Women with Negative Family History: Estrogens and F12 Gene Mutations" – *by K. Bork et al.; Johannes Gutenberg University, Mainz, Germany:*

In women with sporadic recurrent angioedema with an unknown cause who are unresponsive to antihistamines and have normal C1 inhibitor activity and a negative family history of angioedema, it is unclear whether they have idiopathic angioedema or HAE with normal C1 inhibitor, and what impact exogenous estrogens have on their angioedema. 147 women were analyzed for F12 exon 9 mutations and for the influence of oral contraceptives, hormonal replacement therapy, and pregnancy on their angioedema. 142 women had idiopathic angioedema unresponsive to antihistamines. Five women had an F12 mutation and thereby HAE with F12 mutations. Among these women angioedema symptoms occurred during four pregnancies, whereas no symptoms occurred during any of the 58 pregnancies in women with idiopathic angioedema. Women with recurrent angioedema unresponsive to antihistamines may have idiopathic angioedema or, more rarely, HAE with F12 mutations. Both conditions may be provoked or aggravated by exogenous estrogens. In idiopathic angioedema, treatment with progestins may be helpful. (Am J Med., December 2013)

"Algorithm for diagnosis and treatment of hereditary angioedema as a tool for management" – *by A. Navarro Ruiz et al.; Hospital General Universitario, Elche, Spain:*

HAE is a disease with low prevalence and high heterogeneity with regards to the severity of the clinical picture, which makes the diagnosis difficult and requires the need for early start of specific treatment in order to prevent complications. Four decision algorithms have been developed for HAE; diagnosis of bradikinin-mediated angioedema, treatment of acute attacks and short and long-term prophylaxis for HAE due to C1 inhibitor deficiency. The application of a decision algorithm based on the clinical variables helps to select the most efficient therapeutic option at each time and may be a useful tool for the therapeutic approach. (Farm Hosp., November-December 2013)

"Repeat treatment with icatibant for multiple hereditary angioedema attacks: FAST-2 open-label study" – *by M. Baş et al.; Technische Universität München, Munich, Germany:*

54 patients received icatibant for 374 attacks (176 cutaneous, 168 abdominal, and 30 laryngeal). For cutaneous and/or abdominal attacks, the median times to onset of symptom relief ranged between 2.0 and 2.5 h. For all laryngeal attacks, the median times to regression (start of improvement) of symptoms ranged between 0.3 and 4.0 h. Post hoc analyses showed that the overall median time to onset of symptom relief was 2.0 h. Overall, 89.8% of attacks resolved with a single icatibant injection. No drug-related serious adverse events were reported. These findings have demonstrated the efficacy and safety of repeated icatibant treatment for HAE attacks. (Allergy, November 2013)

"A UK national audit of hereditary and acquired angioedema" – *by S. Jolles et al.; University Hospital of Wales, Cardiff, United Kingdom:*
There are limited UK data on HAE and acquired angioedema (AAE) patients to help improve practice and understand more clearly the burden of disease. An audit tool was designed, informed by the published UK consensus document and clinical practice, and sent to clinicians involved in the care of HAE patients. Data sets on 376 patients were received from 14 centers in England, Scotland and Wales. There were 55 deaths from HAE in 33 families, emphasizing the potentially lethal nature of this disease. These data also show that there is a significant diagnostic delay of on average 10 years for type I HAE, 18 years for type II HAE and five years for AAE. For HAE the average annual frequency of swellings per patient affecting the periphery was 8, abdomen 5 and airway 0·5, with wide individual variation. The impact on quality of life was rated as moderate or severe by 37% of adult patients. The audit has helped to define the burden of disease in the UK and has aided planning new treatments for UK patients. (Clin Exp Immunol., January 2014)

News from the industry

CSL Behring has enrolled the first patient in COMPACT, an international phase III study of a volume-reduced, subcutaneous formulation of C1-esterase inhibitor (C1-INH) concentrate in patients with frequent HAE attacks.

This phase of the COMPACT program will assess the efficacy and safety of a new formulation of the CSL Behring C1-INH concentrate in preventing HAE attacks when the therapy is administered twice weekly subcutaneously of patients diagnosed with HAE.

"To date, COMPACT has shown that various doses of this volume-reduced formulation of C1-INH concentrate are well tolerated when administered at a single infusion site twice weekly," said Bruce Zuraw, MD, Professor of Medicine at the University of California, San Diego, USA, and Chairman of the Steering Committee for the COMPACT program. "We also observed a dose-dependent, physiologically relevant increase in functional C1-INH plasma levels. From a clinical perspective, these results are intriguing and could lead to a more convenient option for people with HAE."

CSL Behring
Biotherapies for Life™

Dyax Corp. has announced positive results from the first-in-human clinical study of their investigational product, DX-2930. The Phase 1a study met all objectives of assessing safety, tolerability and pharmacokinetics of DX-2930, a fully human monoclonal antibody inhibitor of plasma kallikrein being developed for the prevention of HAE attacks.

"We are very excited by the study results," said Burt Adelman, M.D., Executive Vice President and Chief Medical Officer at Dyax. "With these results we continue to be impressed by DX-2930 and are encouraged that our scientific hypotheses are on track. We look forward to initiating our Phase 1b study of DX-2930 in HAE patients in mid-2014."

Dyax

The Food and Drug Administration (FDA) has extended the Prescription Drug User Fee Act (PDUFA) Action Date to July 16, 2014 for the Biologics License Application (BLA) for the investigational drug Ruconest® (recombinant human C1 esterase inhibitor) 50 IU/kg. **Salix Pharmaceuticals, Ltd.** and **Pharming Group NV** are seeking U.S. marketing approval of Ruconest for the treatment of acute angioedema attacks in patients with HAE.

PHARMING

Swedish Orphan Biovitrum AB (Sobi) has been awarded the EURORDIS Company Award 2014, presented by the largest European Patient Organization in the field of rare diseases. The award recognizes pioneering companies developing treatments for rare diseases. Sobi was honored based on the treatments in the company's commercial and development portfolio, on the company's policy and track record on access to drugs, and on its

sobi
SWEDISH ORPHAN BIOVITRUM

collaboration with patient organizations.

At the presentation of the company's Full Year 2013 Financial Results, Gustav Christensen, President and CEO of **Dyax Corp.**, said: "Dyax achieved a number of milestones during 2013, including the advancement of DX-2930 into human clinical trials, profitability of the Kalbitor business, and a significant strengthening of our balance sheet. Looking forward to 2014, Dyax will continue to serve the HAE community and is on track to begin by mid-year the Phase 1b clinical study of DX-2930 in HAE patients."

Findings announced by **CSL Behring** show that current HAE treatment options, such as C1 Esterase Inhibitor (C1-INH) concentrate, are allowing for greater patient satisfaction, higher rates of home treatment and a decrease in the number of hospitalizations and visits to the emergency room.

"The previously conducted survey revealed wide variability in HAE management, leaving questions about the impact of newer treatment options and changes in HAE care," said Marc A. Riedl, MD, MS, Associate Professor of Medicine and Section Head of Clinical Immunology and Allergy at the UCLA David Geffen School of Medicine, and one of the study's investigators. "As our results have shown, current treatment practices now align more closely with current HAE treatment guidelines, with patients demonstrating an increase in satisfaction and physicians noticing improved patient outcomes."

A few weeks ago **BioCryst Pharmaceuticals, Inc.** presented the phase 1 clinical trial results for its potent and selective oral kallikrein inhibitor, BCX4161, together with details of the company's plasma kallikrein inhibition assay. BCX4161 is currently being evaluated in a Phase 2 clinical trial, OPuS-1, as a potential treatment for the prevention of HAE attacks.

BCX4161 was generally safe and well tolerated in the Phase 1 clinical trial, and there were no serious or dose limiting adverse events reported. Plasma levels of BCX4161 showed dose-related exposure consistent with saturable absorption, and plasma kallikrein inhibition correlated with BCX4161 levels.

Plasma concentrations of BCX4161 met or exceeded the target range (25-40 ng/mL) predicted for efficacy in preventing HAE attacks for 80-90 percent of the dosing interval. The safety, pharmacokinetic (PK) and PD results of this phase 1 clinical trial supported the selection of the 400 mg TID regimen being tested in the ongoing OPuS-1 clinical trial.
"The research expands our understanding of kallikrein inhibition and the activity of BCX4161. The PD assay results have provided a solid foundation for testing '4161's treatment effect in HAE patients," said Dr. William P. Sheridan, Chief Medical Officer at BioCryst. "We look forward to sharing results from OPuS-1 by the end of the second quarter."

BIOCRYST PHARMACEUTICALS, INC.

Your feedback is very welcome

Please let us know what you believe should be included in future newsletters. You can do that by providing feedback to Executive Director Henrik Balle Boysen or Communications Manager Steen Bjerre. In addition, we invite you to submit articles on any topics that you believe would be of interest to other readers. We look forward to your comments and working with you on future newsletters.

2014 HAE Global Conference

We would like to thank our industry supporters for making the 2014 HAE Global Conference. A warm thank you to: **Shire** and **ViroPharma**, who both signed up as *Diamond Sponsors*, to **CSL Behring** as *Gold Sponsor*, to **Dyax Corp.** as *Silver Sponsor* and finally to **BioCryst Pharmaceuticals, Inc.** as *Basic Sponsor.*

We are looking forward to welcoming patients, relatives, health care professionals and the pharmaceutical industry in Washington in May.

If you still haven't registered for the conference, you can do so here: http://eventus.trippus.se/hae-2014

HAEi is a global umbrella organization dedicated to raising awareness of C1 inhibitor deficiencies around the world. It is a non-profit network of national HAE patient organizations.

NEWSLETTER STAFF

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