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Contact: Jo Ann Faber at (847) 427-1200
joannfaber@acaai.org

Novel Therapies May At Last Bring Relief for U.S. Hereditary Angioedema Patients

DALLAS – Although there is currently no treatment approved by the Federal Drug Administration (FDA) for acute attacks of hereditary angioedema (HAE) – a genetic disease causing swelling of extremities, face and internal organs that can be life-threatening – hope is on the horizon according to a team of experts presenting the latest research at the annual meeting of the American College of Allergy, Asthma and Immunology (ACAAI) in Dallas.

HAE is a rare but serious problem with the immune system that is passed down through families. There are an estimated 10,000 people with HAE in the United States. HAE is caused by low levels or improper function of a protein called C1-inhibitor. The disease affects the blood vessels and causes attacks of swelling lasting hours to days, most often in the arms and legs. Many patients also have swelling of the bowel wall, causing severe abdominal pain; disfiguring facial swelling; genital swelling; and, swelling of the larynx that can cause difficulty breathing and can be fatal.

“Diagnosis of HAE is sometimes difficult because there are other diseases that have similar signs and symptoms,” said Michael M. Frank, M.D., Samuel L. Katz Professor of pediatrics, medicine and immunology at Duke University Medical Center, Durham, N.C. “The patient may not report a family history because up to 25 percent of new HAE cases result from *de novo* (new) mutations.”

Mark Gompels, M.D., consultant immunologist, Southmead Hospital, Bristol, U.K., said diagnosing hereditary C1-inhibitor deficiency may be compared to looking for a needle in a haystack. “The rarity of the diagnosis means that even the most specific of tests may be wrong,” he said. “C4 may be a helpful screening test, but not under all circumstances. Interpretation of the test results needs to be done by an expert in HAE.”

Because there is no currently approved treatment for acute HAE attacks currently available in the U.S., allergists-immunologists are limited to providing symptomatic relief and supportive care, such as pain medications for severe abdominal swelling or intubation to prevent patients from asphyxiating in episodes of laryngeal swelling. HAE does not respond to treatment with epinephrine, antihistamines, or corticosteroids.

Chronic treatment with high dose androgen therapy (danazol, an anabolic steroid) can prevent HAE attacks but will not stop them when they occur. These hormones cannot be given to children and have virilizing side effects (masculinisation) in women. Fresh frozen plasma infusions to prevent or treat acute attacks is available but its use is controversial. Side effects may include allergic reactions and transmission of blood-borne illnesses.

“Replacement therapy with C1-inhibitor has been available since the 1970’s in Europe and some other countries for treatment of this life-threatening disorder,” said William R. Lumry, M.D., clinical professor of internal medicine at the University of Texas Health Science Center and in private practice in Dallas. “Some patients have imported this purified C1 Inhibitor from other countries to treat their acute attacks, but it has not been available to the majority of our patients. Hopefully the FDA will approve one or all of the therapies in the near future.”

Once approved by the FDA, new drugs in the pipeline will be the first emergency treatments available to patients in the United States with this difficult disease. Companies conducting clinical trials for effective therapy for HAE include:

- Dyax Corporation (Cambridge, Mass.) is now conducting its second Phase III trial of its subcutaneously administered drug ecallantide, which blocks the generation of bradykinin the vasodilating chemical responsible for swelling in HAE.
- Jerini AG (Berlin, Germany) recently completed both of its Phase III clinical trials of Icatibant, a subcutaneous therapy which blocks receptors on blood vessels for bradykinin.
- Lev Pharmaceuticals (New York, N.Y.) completed its acute attack and preventive treatment portions of its Phase III clinical trial with C1 Inhibitor. Its brand of C1-inhibitor intravenous replacement therapy has been used safely and effectively in the Netherlands for more than 30 years.
- Pharming Group (Leiden, The Netherlands) is testing a recombinant C1-inhibitor concentrate product that is derived from genetically altered rabbits that produce human C1-inhibitor in their milk.
- ZLB Behring (Melbourne, Australia) is conducting a Phase III clinical trial of their C1-Inhibitor concentrate product, Berinet, which also has decades-long record of safely and effectively treating HAE patients in Europe and other parts of the world.

For more information, visit the U.S. Hereditary Angioedema Association (HAEA) Web site at www.haea.org. The HAEA, a non-profit patient advocacy organization, provides a wide range of services for patients and physicians, including education, clinical trial placement, physician referrals and individualized patient case management.

The American College of Allergy, Asthma and Immunology (ACAAI) is a professional medical organization headquartered in Arlington Heights, Ill., that promotes excellence in the practice of the subspecialty of allergy and immunology. The College, comprising more than 5,000 allergists-immunologists and related health care professionals, fosters a culture of collaboration and congeniality in which its members work together and with others toward the common goals of patient care, education, advocacy and research.

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