



HED therapy

Potential treatment would address rare genodermatosis

By Lisa B. Samaloni
Staff Correspondent

Cambridge, Mass. — A novel potential treatment is on the horizon for hypohidrotic ectodermal dysplasia (HED), according to the director of research at a patient advocacy foundation.

“One of the most exciting developments in the current state of research for therapy is a new novel approach called EDI200,” says Mary Fete, R.N., M.S.N., C.C.M., director of research, National Foundation for Ectodermal Dysplasias (NFED).

The therapy is a form of ectodysplasin-A1 (EDA-A1) being developed by Edimer Pharmaceuticals as a treatment for certain patients with X-linked hypohidrotic ectodermal dysplasia (XLHED). EDI200 is produced by using recombinant DNA technology.

HED diagnosis

HED results in the abnormal development of structures including the skin, hair, nails, teeth and sweat glands. The condition is characterized by hypotrichosis, hypohidrosis and hypodontia. Physical growth and psychomotor development are otherwise within normal limits.

HED is the most common form of ectodermal dysplasia in humans, affecting approximately one in 17,000 people worldwide.

Managing HED includes optimizing psychosocial development, establishing optimal oral function and preventing hyperthermia. Dermatologic concerns include eczema, rashes and dry skin associated with certain outdoor exposures.

Potential therapy

EDA-A1 is a protein occurring naturally in healthy people, involved in the formation and development of skin and teeth.



Ms. Fete

“This protein is missing in patients with X-linked HED,” Ms. Fete says.

Researchers in Lausanne, Switzerland, first developed a synthetic version of EDA-A1 that has shown promising results in animals with a disease similar to XLHED, she says.

“This research has led to the development of EDI200. The rationale for the use of EDI200 in XLHED patients is based on the lack of functional EDA-A1 protein in these patients, which affects the formation of ectodermal struc-

she says. “This novel therapy offers hope for treatment of the symptoms. As with any research that is in the beginning phases, we are cautiously optimistic that this therapy will be successful in treating the manifestations of the condition.”

Recent research

A recent study systematically studied the three disease-causing genes for both autosomal dominant and recessive forms on hypohidrotic and anhidrotic ectodermal dysplasia (HED/EDA): EDA1 accounting for X-linked forms; EDAR; and EDARADD. Also analyzed was the WNT10A gene, the gene identified as responsible for various autosomal recessive forms of ectodermal dysplasias, including onycho-odonto-dermal dysplasia and Schöpf-Schulz-Passarge syndrome.

The study included a cohort of 65 unrelated patients, of which 61

quick read

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Mascoutah, Ill.

tures,” she says. “EDI200 has been shown to substitute for this protein during development in mice and dogs.”

Edimer plans to conduct clinical trials at the end of 2011, Ms. Fete says.

“The NFED is excited about EDI200 as a potential therapy for individuals affected by XLHED,”

presented with HED/EDA. The four genes accounted for 92 percent of HED/EDA cases, with the EDA1 gene the most common disease-causing gene (58 percent of cases). WNT10A and EDAR were each responsible for 16 percent of cases.

“Although no clinical differences between patients carrying **Genodermatosis** see page 51



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EDA1, EDAR or EDARADD mutations could be identified, patients harboring WNT10A mutations displayed distinctive clinical features (marked dental phenotype, no facial dysmorphism), helping to decide which gene should be first investigated in HED/EDA," the researchers reported.

Early detection

A recent Austrian cross-sectional postal survey among parents of 100 children with ectodermal dysplasia looked at the prevalence and prevention of severe complications of HED in infancy. The study aimed to re-evaluate the mortality of HED and the prevalence of hyperpyrexia and possible neurological sequelae in affected infants.



Children with HED have abnormal development of structures including the skin, hair, nails, teeth and sweat glands.

(Photo: Mary Fete, R.N., M.S.N., C.C.M.)

The researchers concluded that the mortality of HED and the risk of hyperthermic brain damage

are still increased, but lower than reported previously. They also noted that the individual's prognosis depended on the type of genetic defect and the time point of diagnosis. Early recognition of the disease was aided by neonatal care and consulting a dermatologist or geneticist, according to the study. Adequate instruction to parents and networking with patient support groups also reduced the risks associated with HED.

Ms. Fete says the recent developments concerning EDI200 and other research is critical.

"It is really important to get this information out to doctors about potential treatments and therapies, so they can be aware of it for their patients, because early diagnosis is crucial for treatments," she says. **DT**

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birthmark that's located on the face will definitely put someone at a much higher likelihood of having to deal with the effects of social stigma," Dr. Frieden says. "Since we can't completely cure most patients of their port wine stains, we need to work with families to help them feel more comfortable and to create strategies to deal with public comments, teasing or bullying. If they are unusually self-conscious about their birthmark, we need help them find resources — such as parent support groups or counseling — to aid in this process."

Follow-up care is important, even if laser treatment has reached its potential, Dr. Frieden says.

"Even if we have reached the maximum benefit from laser therapy, I always try to balance the limitations of our current therapies with the hope that new treatments may come along," she says. "For this reason, we ask families to check in or come for a return visit periodically to discuss whether they should get further treatments."

Honesty with parents about the benefits and the limitations of various therapies is also crucial, Dr. Frieden says.

"If there's one thing I've learned after doing this work for more than 20 years, it's the importance of frankly discussing up front both the benefits and the potential limitations of the current therapies,"

she says. "It can be frustrating to get to a treatment plateau and then not be able to get any further. Whether the future holds improvements by using combinations of lasers or lasers plus some sort of medication that inhibit regrowth remains to be seen. These are the unanswered questions that young investigators should be working on right now."

"Until we have more answers, we also need to look at our patients holistically, not just as the birthmark they have, but as a whole child, keeping their social and emotional selves in mind, as well." **DT**

Disclosures: Dr. Frieden reports no relevant financial interests.

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Lesion removal

Melanomas are easier to spot on these smaller lesions, he says, because they are a flat, single color, and parents are told to watch for focal area color change, such as a brown/black mole developing a focal area of gray, blue, red or white elevated papules.

The location of congenital nevi also plays a role in the risk of pediatric melanoma, Dr. Hansen says. If they

occur over the extremities, the risk is lower. But nevi occurring on the back, especially over the spine, carry a higher risk.

"If I saw an intermediate-sized nevus over the spine, I might elect to have them removed, because there could be some prevention in doing that," he says.

The only treatment for childhood melanoma is early diagnosis and removal. Prophylactic removal of congenital nevi of all sizes is controversial, but the only curative treat-

ment is surgical removal.

"Although promising new treatments for metastatic melanoma are being studied for adults, they haven't been tried in children yet," Dr. Hansen says. "The only time chemotherapy or radiation is used, is if cancer has spread to the lymph nodes. These treatments don't work very well, so if the melanoma is metastatic, chances of survival are very low." **DT**

Disclosures: Dr. Hansen reports no relevant financial interests.