PRESS RELEASE

Effective therapy for genetic disease

Hereditary angioedema (HAE) is a disease resulting in swelling of one or more parts of the body in the absence of a specific trigger. If the condition occurs in the upper respiratory tract, a so-called HAE attack ensues which can be life threatening. To date, the therapies to treat HAE are in form of injections and infusions. In a Phase 2 study involving the Universitätsklinikum Frankfurt, Charité – Universitätsmedizin Berlin and the Fraunhofer ITMP, it has now been shown for the first time that an orally administered drug can also treat HAE. This therapy has the potential to overcome the issues relating the complicated route of administration for injections as well reduced cost.

Berlin. Patients with hereditary angioedema (HAE) have a genetic disorder which manifests itself predominantly in childhood and adolescence and remains symptomatic in most affected individuals throughout their lives. It can manifest itself in severe, localized swelling of the skin and mucous membranes, which can occur in various parts of the body. The face, gastrointestinal tract, extremities and urogenital system are often affected. If the upper respiratory airways are involved, an HAE attack can be life threatening. If, for example, oedema develops in the larynx as a result, this is one of the most frequent causes of death in HAE patients. "Treatment guidelines therefore recommend addressing these attacks as early as possible", explains Prof. Marcus Maurer, head of Fraunhofer ITMP Immunology and Allergology IA in Berlin. "Studies have shown that treating patients quickly reduces the time to symptom relief and the overall duration of the attack significantly."

Development of an HAE attack

The plasma kallikrein concentration is the key factor in the disease caused by hereditary angioedema. In healthy people, the activity of this enzyme is regulated by the C1 inhibitor protein. In HAE, a genetic defect causes the C1 inhibitor concentration to be too low and the kallikrein-kinin system to be over-activated. As a result, there is increased permeability of the blood vessel walls. Fluid then migrates from the vessels into the tissues and the typical HAE swelling, also referred to as the oedema can develop. Oedema attacks are unpredictable and can develop over several hours or very suddenly. In addition, their frequency and duration can also vary, with some people have the attacks several times a week, while others have them once a year or less. The swelling can endure from a few hours up to several days. In most cases, there are no direct triggers of the attacks, although potential causes include infections, stress, complications from medication and operations, trauma and changes in hormone balance. It is also difficult to predict when and on which part of the body the next attack will occur.

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However, with timely intervention, HAE can be readily treated, allowing the rapid recovery of patients experiencing an unexpected HAE attack.
"Acute HAE attacks can currently only be treated with intravenous or subcutaneously administered agents", explains Dr. Emel Aygören-Pürsün, a specialist in internal medicine at the Angioedema Outpatient Clinic of the Department of Paediatrics and Adolescent Medicine at Universitätsklinikum Frankfurt. "The interventional clinical Phase 2 study has shown that an effective oral therapy for acute angioedema attacks in HAE has been identified". In addition to the Universitätsklinikum Frankfurt, the Charité – Universitätsmedizin Berlin and the Fraunhofer ITMP, scientists from several European countries, the USA, New Zealand and Canada were involved in the study. The first peer-reviewed publication relating to an oral therapeutic to treat HAE attacks has been published in The Lancet, which is one of the most reputable medical publications on February 11, 2023.

Oral on-demand therapy with sebetralstat

Currently approved therapies for HAE consist of on-demand and prophylactic drugs, for acute treatment or prevention of attacks. However, their administration has been cumbersome to date as patients receive the drugs via infusion or injection. These methods require training, can cause delays in treatment and can lead to undesirable side effects such as pain and hypersensitivity reactions at the infusion or injection site. "With the new orally administered drug that we tested in our Phase 2 study, these adverse side effects can now be avoided. Sebetralstat is a plasma kallikrein inhibitor that makes it easier to treat HAE patients at home", explains Prof. Maurer. "Sebetralstat proved to be well tolerated in the study and achieved improved symptom relief compared to placebo, reduced the severity of attacks and reduced recovery time compared to the conventional treatment", adds Dr Emel Aygören-Pürsün. Sebetralstat is rapidly absorbed and reaches maximum plasma concentration within one hour, which is essential for rapid symptom relief.
Based on the positive results of the study, a Phase 3 clinical study using Sebetralstat is currently being conducted, in which the drug will be further studied.

Publication:

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