Luncheon Symposium 2

The State of the Art of Hereditary Angioedema

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Hereditary angioedema (HAE) due to C1 inhibitor (C1-INH) deficiency is a rare genetic disease with a prevalence in general population of 1:50.000 The disease is characterized by recurrent episodes of swellings. The reduction in C1-INH function leads to uncontrolled activation of the contact system and generation of bradykinin, the mediator of increased vascular permeability and edema formation. The most common HAE symptoms are cutaneous swellings (usually of the extremities, trunk, genitals or face) without urticaria or pruritus and abdominal pain due to edema of the mucosa of the gastrointestinal tract with consequent bowel subocclusion. Almost all HAE patients (>90%) report cutaneous and abdominal edema episodes. About half of patients experience laryngeal edema; although these episodes occur rarely compared with the frequency of cutaneous and abdominal episodes can lead to asphyxiation. HAE patients typically begin to present angioedema symptoms in childhood and often suffer increased attacks around the time of puberty. Symptoms of angioedema usually last for 3-5 days. Attacks often result in hospitalization, may lead to inappropriate abdominal surgery and can be fatal when involving the airway (if not treated with specific treatments). HAE is a disabling disease and presents a significant psychological, social and economic burden for affected individuals.

Treatment of HAE patients can be addressed to revert attacks (on-demand treatment) or to prevent recurrences (long-term prophylaxis treatment, LTP). Prophylaxis can also be used to prevent symptoms in conditions at high risk as surgical procedures (short-term prophylaxis). In the past, few treatment options were available. Several new therapies with proven efficacy have recently become available to treat and prevent HAE attacks, such as plasma-derived and recombinant C1-INHs that replace the deficient protein, bradykinin receptor antagonist (icatibant) that blocks bradykinin activity and kallikrein inhibitor (ecallantide) that prevents bradykinin release. Self-treatment is recommended, in order to reduce admissions to the Emergency Room and the time between the onset of the attack and the treatment, resulting in a better treatment outcome and an improved quality of life (QoL).

Furthermore the possibilities to control the disease has considerably changed recently with the development of new therapies for LTP: a subcutaneous pdC1-INH and a monoclonal antibody that blocks kallikrein activity and

thus the generation of bradikynin and the edema formation. Other new therapies are under investigation. Such therapies can improve the control of the disease.

Key Words: Hereditary angioedema, Rare disease, Treatment