European Academy of Allergy and Clinical Immunology (EAACI) 2026 Annual Meeting
Session: Flash Talks session (L-FT04) entitled Immune deficiencies and autoimmunity
Date/Time: Saturday June 13, from 8:45 – 9:45 am TRT
Location: Istanbul Congress Center, Room Glasgow

Title: Onvuzosiran provides deep and sustained reduction of plasma kallikrein levels for the treatment of HAE

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Background
HAE is a devastating genetic disorder resulting in uncontrolled kallikrein activation, leading to unpredictable attacks of swellings that can be painful, debilitating, and life threatening. Small interfering RNA (siRNA) consists of short oligonucleotides that can reduce the production of prekallikrein/kallikrein. Onvuzosiran is an investigational siRNA product designed to reduce plasma kallikrein levels to control HAE attacks. The product is given subcutaneously every 6 months as the primary cohort in the on-going STOP-HAE Phase 3 clinical trial.

Method
A Phase 1, randomized, placebo-controlled, single–ascending-dose trial of subcutaneous (SC) onvuzosiran (0.4 mg/kg to 6 mg/kg) was conducted in healthy adults across 5 doses with an additional group of repeat-dosing every 3 months. An open-label Phase 2 study of 245 mg every 6 months in HAE patients is completing follow-up. Efficacy, safety, and pharmacodynamic measures were collected. A preclinical study with doses increasing to 200mg/kg was conducted in non-human primates (NHP) to assess the safety of higher doses.

Results
In Phase 1, a single SC dose of 300 mg reduced plasma kallikrein levels to over 90% at nadir, with maintenance of 80% reduction through Week 25. In Phase 2, HAE patients experienced plasma kallikrein levels reductions comparable to those seen in Phase 1. Notably, patients who had plasma kallikrein reduction of >80% were attack-free, supporting 300 mg Q6M dosing. Results from the high dose NHP study showed no adverse events, supporting the safety of 300 mg dose (5 mg/kg).

Conclusion
Onvuzosiran was shown to provide deep and sustained reduction of plasma kallikrein in early studies. Phase 1 and 2 studies showed the drug to be well-tolerated. STOP-HAE is a global Phase 3 randomized, double-blind, placebo-controlled study to assess the safety and efficacy of SC onvuzosiran in adults with HAE. The trial is designed to randomize approximately 90 patients to onvuzosiran 300 mg Q6M, 240 mg Q3M, or placebo. The trial is actively recruiting in over 20 countries.