rhC1-INH dose of 3075 IU (range, 2100-4200 IU) was administered as prophylaxis, median of 60 minutes prior, for 70 procedures (52.9% [n=37] dental [median, 60 minutes preprocedure]); 30.0% [n=21] surgical [median, 45 minutes preprocedure]; 15.7% [n=11] endoscopy [median, 30 minutes preprocedure, and 1.4% [n=1] stressful life event). Majority (n=48; 68.6%) of 70 cases had rhC1-INH administered 10-65 minutes preprocedure: 25 of 48 (52.1%) dental, 16 (33.3%) surgical, and 7 (14.6%) endoscopy. Nineteen (27.1%) cases involved long-term prophylaxis (danazol/tranexamic acid). Overall, 97.1% (68/70) of cases did not have an HAE attack within 2 days postprocedure; 91.4% (64/70) during >2-7 days postprocedure. For 2 attacks occurring within 2 days, rhC1-INH was administered 230 minutes and ≥24 hours preprocedure, respectively. No adverse events were reported. As a self-control group, 76.9% of 26 cases with no long-term/short-term prophylaxis preprocedure had an attack within 2 days postprocedure.

Conclusions: Short-term prophylaxis with rhC1-INH, administered within several hours preprocedure, was efficacious and safe in adolescents/adults and reduced the risk of an HAE attack postprocedure.

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LANADELUMAB REDUCES HAE ATTACK RATE: INTERIM FINDINGS FROM THE HELP OPEN-LABEL EXTENSION STUDY

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Introduction: Efficacy of lanadelumab in preventing hereditary angioedema (HAE) attacks was demonstrated in the double-blind, phase 3 HELP study (NCT02586805). This analysis reports interim data (26May2017-1September2017) on HAE attack rate with lanadelumab in the ongoing open-label extension (OLE) study (NCT02741596).

Methods: Patients ≥12 years old with HAE type I/II who completed the double-blind study (rollovers), as well as eligible patients who had not previously participated (nonrollovers) were enrolled. Patients received a single 300mg lanadelumab dose at rollover and then received 300mg q2wks starting at the time of their first attack. Nonrollover patients received lanadelumab 300mg q2wks from Day 0. The number of investigator-confirmed HAE attacks during the treatment period was expressed as a monthly HAE attack rate (attacks/4 weeks).

Results: A total of 212 patients were treated (rollover, n=109; nonrollover, n=103); 92.9% remain enrolled. In the overall population (rollover and nonrollover), median age was 42.8 years. Most had HAE type 1 (89.2%); 50% had previously received C1-INH only. At baseline, patients had a median of 2.0 (mean [SD] 3.05 [2.66]) attacks/month. During the treatment period, median and mean (SD) attack rates were 0.0 and 0.30 (0.628), reflecting a median and mean (SD) reduction of 100% and 85.3% (68.4) from baseline in monthly HAE attack rate. On average, subjects were attack-free on most days during the treatment period (median 100%; mean [SD], 97.4% [6.08]), for a median duration of 105.0 days (mean [SD] 125.7 [81.5] days).

Conclusions: Lanadelumab remained highly effective in reducing HAE attacks in the HELP OLE study.

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MARKERS OF TH2 INFLAMMATION IN PATIENTS WITH CHRONIC SPONTANEOUS URTICARIA: A SYSTEMATIC LITERATURE REVIEW

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Introduction: Identifying specific IgE sensitization in patients with chronic spontaneous urticaria (CSU) is not recommended by current guidelines. The objective of this review was to evaluate markers of TH2 inflammation in all patients with CSU undergoing treatment with omalizumab.

Methods: Systematic literature reviews were conducted using the PubMed, Medline and Google Scholar electronic databases for English studies published in peer-reviewed journals between 2010 to 2018 to identify studies of CSU where markers of TH2 inflammation were determined.

Results: A total of 18 studies were identified, involving 1892 patients. Thirteen studies found the mean total IgE levels in the CSU population to be elevated at 211.5 IU/ml (normal 133-570.6 IU/mL, and an absolute range of values of 0-5600 IU/mL. On average, 39% of the CSU population had IgG autoantibody directed to the high-affinity receptor for the Fc region of IgE (FcεRIa) compared to 2.9% in control groups. Patients with CSU were 5.4 times more likely to have IgG autoantibody to FcεRIa (95% CI 2.8-10.6) than the controls ($p < 0.00001$). Mean total blood eosinophil % was elevated at 5.5% (n = 279) (normal ≤ 4%), despite many patients being on systemic corticosteroids.

Conclusions: Elevated levels of total IgE, blood eosinophil counts, and FcεRIa-specific autoantibodies in the CSU population may indicate the importance of TH2 inflammation in the pathogenesis of CSU. Perhaps the role of specific IgE sensitization in CSU should be revisited.

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LANADELUMAB EXPOSURE DURING STEADY STATE: ACHIEVEMENT OF EFFECTIVE CONCENTRATIONS IN PATIENTS IN THE HELP STUDY

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Introduction: In the HELP Study (NCT02586805), treatment with lanadelumab (a monoclonal antibody inhibitor of plasma kallirein) 150 mg q4wks, 300 mg q4wks, or 300 mg q2wks significantly decreased attack rates over 26 weeks. We evaluated the relationship between lanadelumab exposure and efficacy during steady state (days 70-182) among the 3 dose groups.

Methods: Blood samples were collected from patients prior to dosing at weeks 0, 8, 14, and 20 for measurement of lanadelumab concentrations and cleaved high molecular weight kininogen (cHMWK) levels.

Results: Mean observed steady state lanadelumab concentrations in plasma increased and cHMWK levels decreased with dose and dosing frequency. These were associated with decreased attack rates. Attack rates decreased to the greatest extent in patients who received lanadelumab 300 mg q2wks (86.9% reduction vs placebo). The IC90 of lanadelumab (concentration associated with 90% of the maximum inhibitory effect on cHMWK levels) was previously determined to be 18,777 ng/mL. 88.9% of patients in the 300 mg q2wks group attained a maximum concentration at steady state (Cmax,ss) ≥IC90, compared with 65.5% and 0% of patients in the 300 mg q4wks and 150 mg q4wks groups, respectively (Figure). The minimum concentration at steady state (Cmin,ss) and average concentration at steady state (Cavg,ss) was ≥IC90 in 77.8% and 85.2% of patients, respectively, in the 300 mg q2wks group.

Conclusions: Lanadelumab concentrations were maintained ≥IC90 in the majority of patients during steady state in the 300 mg q2wks group, correlating with the high extent of attack reduction observed.

Table. Percentage of patients with lanadelumab exposure ≥IC90

Dosing regimen	% patients		
	Cmax,ss	Cmin,ss	Cavg,ss
150 mg q4wks	0	0	0
300 mg q4wks	65.5	0	20.7
300 mg q2wks	88.9	77.8	85.2