fewer attacks/month compared with those receiving placebo (0.31–0.48 vs 2.46 attacks/month, respectively).
Conclusions: Lanadelumab resulted in a marked suppression of kallikrein activity at drug levels approximately equimolar to the amount of protease, resulting in sufficient inhibition for effective HAE prophylaxis.

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Efficacy of lanadelumab in the Phase 3 HELP study: Exploratory analyses based on prior disease activity and prior use of C1-INH long term prophylaxis therapy

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Background: The HELP Study evaluated the efficacy and safety of lanadelumab for long-term prophylaxis (LTP) in patients ≥ 12 years old with HAE type I/II (NCT02586805). Here, we report lanadelumab efficacy based on a patient's prior disease activity and prior use of C1-INH LTP.
Methods: The HELP study is a phase 3, randomized, double-blind, placebo-controlled study. We performed two exploratory efficacy analyses: (1) a responder analysis comparing normalized HAE attack rates over 26 weeks of treatment to a 4–8 week run-in period prior to treatment with lanadelumab and (2) a Poisson regression model to compare the mean HAE attack rate in the lanadelumab groups to placebo by patient prior C1-INH LTP use.
Results: Over the 26-week treatment period, the percentage of patients with a ≥ 50%, ≥ 70%, and ≥ 90% reduction in investigator-confirmed HAE attacks from the run-in period, respectively, was 89.3%, 78.6% and 64.3%, [lanadelumab 150 mg q4wks (n = 28)]; 100%, 75.9%, 55.2% [lanadelumab 300 mg q4wks (n = 29)]; 100%, 88.9% and 66.7% [lanadelumab 300 mg q2wks (n = 27)] and 31.7%, 9.8% 4.9% [placebo (n = 41)], respectively. In C1-INH LTP patients (n = 60), the attack rate was significantly reduced in all lanadelumab groups versus placebo (P < 0.001); the reduction was similar in magnitude to those who did not receive prior LTP (n = 55). For the lanadelumab 150 mg q4wks, 300 mg q4wks, 300 mg q2wks and placebo groups, respectively, C1-INH LTP users reported mean monthly attack rates (3 months prior to the study) of 3.0, 2.7, 2.6 and 4.0; during run-in 3.3, 3.7, 4.6 and 4.6; and during the treatment period 0.5, 0.7, 0.5 and 2.9.
Conclusions: Treatment with lanadelumab for 26 weeks resulted in a high rate of patients who experienced a clinically meaningful reduction in investigator-confirmed HAE attacks compared to baseline run-in. Furthermore, all lanadelumab doses significantly reduced attack rates versus placebo, regardless of whether patients had received prior C1-INH LTP.

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Alterations in cord blood hemopoietic progenitor cell surface receptor expression precede atopy and poor lung function at 1- and 3-years in the Canadian Healthy Infant Longitudinal Development Study

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Background: Hemopoietic progenitor cells (HPC), both in the bone marrow and in peripheral tissues, differentiate towards inflammatory effector cells and, thus, can modulate central and peripheral inflammation. There is growing evidence for the involvement of hemopoietic processes in the pathogenesis of atopy and asthma from pre-conception and birth. This is the basis for the "bone marrow" hypothesis of allergic disease, arguing that a perinatal environmental challenge leads to the skewed production and mobilization of HPC, regulating central and peripheral production of cell types that perpetuate allergic responses. The objective of this study was to assess the association of cell surface receptor profiles of cord blood (CB) HPC with atopy development and lung function at 1- and 3-years in the Canadian Healthy Infant Longitudinal Development (CHILD) Study
Methods: We used six-colour flow cytometry to assess cytokine and toll-like receptor expression levels in CB HPC from infants with atopy data (defined as positive skin prick test and atopic dermatitis and wheeze) and lung function data (by lung clearance index (LCI)) at 1- and 3-years of age in CHILD.
Results: We found a significant increase in IL5R and IL17RB-expressing HPC populations in the CB of children atopic at 1-year. Conversely, GM-CSFR and ST2-expressing CB HPC were decreased in atopic children both at 1- and 3-years. The expression levels of IL17RB on the surface of CB-HPC were higher in atopics at 3-years. Finally, infants with poor lung function at 3-years exhibited higher IL5R expression on the surface of CB HPC.
Conclusion: This study provides evidence of pre-existing cellular alteration in the infants' CB progenitors at birth, which antedate development of atopy/allergic disease and potentially future asthma. Our results can contribute to novel strategies for atopic/allergic disease interception in infants before onset, and hence participate in the health and well-being of Canadian children.

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Efficacy and safety of lanadelumab for prevention of hereditary angioedema attacks: results from the phase 3 HELP Study

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