Introduction: Disease activity varies between patients with hereditary angioedema (HAE), but the disease burden may persist. The HELP open-label extension (OLE; NCT02714196) study investigated lanadelumab for long-term prophylaxis (LTP) of HAE attacks. A retrospective post hoc subanalysis by baseline attack rate (≤ 2 attacks/month vs > 2 attacks/month) and prior LTP is presented.

Method: Patients with HAE Type 1/2 aged ≥12 years were newly enrolled to the HELP OLE study (nonrollovers) or entered after completing the HELP study (rollovers). Nonrollovers received lanadelumab 300 mg every two weeks (Q2W) from Day 0; rollovers received a single 300 mg lanadelumab dose until first attack, and 300 mg Q2W thereafter (regular dosing stage). Attack rates during the regular dosing stage were compared with the baseline using data from safety population.

Results: Over a median of 33 months, 212 patients received lanadelumab. Lanadelumab reduced HAE attack rate regardless of baseline HAE attack rate and prior LTP (prior LTP with CI1-INH only: ≤ 2 attacks/month, 70% reduction; > 2 attacks/month, 92% reduction; prior LTP with androgens only: ≤ 2 attacks/month, 93% reduction; > 2 attacks/month, 96% reduction; no prior LTP: ≤ 2 attacks/month, 93% reduction; > 2 attacks/month, 93% reduction) (Figure). Injection site pain was the most frequent related treatment-emergent adverse event (TEAE) regardless of baseline attack rate and prior LTP (CI1-INH only ≤ 2 attacks/month: 333 events in 20 patients; androgens only ≤ 2 attacks/month: 61 events in 4 patients; androgens only > 2 attacks/month: 74 events in 2 patients; no LTP ≤ 2 attacks/month: 322 events in 23 patients; no LTP > 2 attacks/month: 220 events in 13 patients).

Conclusion: In HELP OLE, treatment with lanadelumab showed attack rate reductions regardless of baseline attack rate in patients with prior LTP; the most frequent related TEAE in all analysed subgroups was injection site pain.

Introduction: The GaLEN/EAAACI/WAO Global Guidelines for the management of hereditary angioedema (HAE) support that optimal access to long term prophylaxis (LTP) requires assessment of multiple factors, including disease activity, disease burden and impact on quality of life (QoL).1 There is currently no validated tool that encompasses all of these concepts. To address this, a multifactorial HAE Assessment Tool is being developed.

Method: A panel of six immunologists, two nurses and one patient advocate conducted a literature search, reviewed available existing measurement scales and identified four domains for inclusion in a multifactorial assessment tool. A series of self-report questions was compiled, incorporating custom-designed questions and validated existing tools (HAE-QoL, Questionnaire, Work Productivity and Activity Impairment [WPAI] questionnaire). A scoring grid and algorithm to derive an overall composite HAE impact score have been developed. The proposed HAE Assessment Tool has been piloted by a group of HAE patients, who completed the tool online via Google forms and provided feedback via a hybrid, clinician-facilitated focus group meeting. Focus group outputs included consensus (≥ 75% agreement in the range 7–9 on a scale of 1–9) on the need for the four assessment domains, ranking of their contribution to overall disease burden (11-point visual analogue scale) and weighting of their relative importance to treatment decisions.

Results: The HAE Assessment Tool comprises 36 questions across four domains – attack frequency and location, impact on QoL, work/school productivity, and hospital access. Demographics: The pilot study participants’ (N = 11, all female) ages ranged from 18 to 72 years (mean 43.4, SD 16.3). They had a disease duration of 5 to 58 years (mean 30.0, SD 17.2) and 73% (9/11) were currently on LTP. Participants’ HAE Impact Scores ranged from 0.42% [low impact] to 79.91% [high impact]. Participant feedback: The HAE Assessment Tool took an average of 8 minutes (range 5–20 minutes) to complete. There was a strong consensus agreement that eligibility for LTP should include assessment of QoL (100% consensus, average score 8.8) and productivity (91% consensus, average score 8.0). Agreement on the need for attack frequency/occurrence and hospital access were widely dispersed and did not reach consensus. All domains ranked highly in terms of their contribution to overall disease burden; QoL ranked highest (score 9.1), followed by hospital access (score 8.6), attack frequency/occurrence (score 8.2) and productivity (score 8.0). Overall weighting of relative domain importance was undertaken by 7 participants: QoL (30%), productivity (30%), hospital access (30%) and attack frequency/occurrence (10%). Minor refinements were suggested to the tool and the scoring algorithm.

Conclusion: The HAE Assessment Tool is, to our knowledge, the first multifactorial tool to comprehensively address disease activity and burden to ensure optimal patient access to LTP for the management of HAE. The results of the pilot study provide initial support that the HAE Assessment Tool is fit for purpose. A trial of its use in the clinical setting is warranted.

References
1 Maurer M, et al. The international WAO/EAAACI guideline for the management of hereditary angioedema—The 2021 revision and update. Allergy. 2022 Jan 10.

P92: THYMIC TRANSPLANTATION IN COMPLETE DIGEORGE SYNDROME COMPLICATED BY CYTOMEGALOVIRUS AND COVID-19 INFECTION

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AD is an 8-month-old boy with severe combined immunodeficiency secondary to complete DiGeorge syndrome (DGS). His newborn screen showed absent TREC's. He presented at 6 weeks of age with hypocalcaemic seizures. CMV was acquired postnatally in the period before he presented and at initial workup was detectable in his blood and CSF. He was treated with IV ganciclovir and foscarnet dual therapy. Due to his SCD, he also received replacement IVIG and prophylactic Bactrim and Fluconazole.

Immunological workup confirmed that he had CD3 cell count of 50 x 10^3/L, absent naïve T cells with a restricted repertoire on TCR V-
beta testing. His PHA was significantly reduced. His B cell phenotype showed mostly naive B cells. His CGH microarray confirmed 22q11 deletion. These are all consistent with his diagnosis of SCID due to cDGS.

As AD did not have comorbid cardiac abnormalities and his CMV infection came under control with dual therapy (undetectable in serum and CSF), he became an eligible candidate for a thymic transplant. Prior to his transplant, he was noted to have an erythematous rash which on skin biopsy was consistent with Omenn Syndrome. He was commenced on cyclosporine leading into transplant. AD underwent thymic transplant at Great Ormond Street Hospital, London when he was 4 months old.

Post-transplant, he has had a tumultuous course. He contracted COVID-19 which was treated with sotrovimab and a 10-day course of remdesivir. Post-transplant, he has had a tumultuous course. He contracted COVID-19 which was treated with sotrovimab and a 10-day course of remdesivir. Despite another 6 weeks course of IV foscarnet.

In Australia, omalizumab was listed on the PBS in 2017 for the treatment of severe CSU on the basis of good evidence for efficacy in the pivotal clinical trials. We are a referral centre for chronic spontaneous urticaria patients and have a database of those who have received this treatment since PBS listing.

Method: All patients eligible for omalizumab on PBS were entered into a database. All had UAS7 rating at 28 and met prior treatment criteria before commencement of omalizumab. We examined patterns of use including continuation and discontinuation rates; up and down titration of doses; need for concomitant medications and failure rates.

Results: The cohort consisted of 127 patients; female to male ratio 99:28; age range of 12–92 years. Anti-IgE use was continued in 35 patients. The majority received the standard dose of 300 mg four weekly however a small proportion were escalated to 450–600 mg four weekly to gain control. 91 patients have had a complete cessation of symptoms, 26 have had partial response, 5 have had no response, 1 patient relocated under another specialist, 1 ceased due to pregnancy and 3 have only started in the previous 3 months so response cannot yet be assessed.

Conclusion: In clinical practice omalizumab is highly effective in controlling severe CSU although 27% remain uncontrolled. A small number have needed dose increase to gain complete control.

Results: The majority of individuals have contracted COVID-19, with 67% positive at least once, with 53% experiencing symptoms of long COVID. 72% of individuals are concerned about contracting COVID-19, with 89% concerned about long-term consequences, reflected by the 96% vaccination rate. 48% of individuals experienced moderate stress, while 42% experienced a mental health decline, necessitating coping behaviours to combat this. Numerous behavioural changes were observed, including increased time on the internet (72%) and TV (60%), as well as increases in junk food consumption (56%) and decreases in fruits and vegetables (27%). Certain sociological changes were also observed, with 89% of individuals maintaining safety measures after they have been lifted, and 37% refusing to travel.

Conclusions: The PID/SID community is aware of the health risks and challenges that the COVID-19 pandemic poses, and have adjusted accordingly, demonstrated in the creation of coping behaviours, maintaining safety regulations, and displaying justified levels of caution and hesitancy. However, the impact of the pandemic, physiologically, psychologically, and sociologically is amplified as the PID/SID cohort is of high risk, highlighting the importance of continuous medical care for this population.

P94: THE IMPACT OF COVID-19 ON PATIENTS WITH PRIMARY AND SECONDARY IMMUNODEFICIENCIES: A STUDY INTO THE PHYSIOLOGICAL, PSYCHOLOGICAL AND SOCIOCOLOGICAL EFFECTS
Linda Lin1,2, Ethan Italiano1,2, Carolyn Dewes1

Background: The adverse effects of the COVID-19 pandemic, physiologically, psychologically, and sociologically, on individuals living with primary and secondary immunodeficiencies have not been clearly determined.

Objective: To determine the extent of impact of the COVID-19 pandemic on individuals living with primary and secondary immunodeficiencies.

Method: An online survey was distributed to members of the Immune Deficiencies Foundation Australia (IDFA) with a diagnosis of PID/SID. The survey was designed to observe numerous impacts, including physical and mental health, ability to receive treatment, opinions on vaccines and reintegration into society.

P95: SEBETRALSTAT EFFECTIVENESS IN THE TREATMENT OF HEREDITARY ANGIOEDEMA ATTACKS RATED MILD OR MODERATE AT BASELINE IN THE PHASE 2 TRIAL
Hilary J. Longhurst1, Michael D. Smith2, Christopher Yea3, Paul Audhya4

Introduction: Sebetralstat is an investigational oral plasma kallikrein inhibitor for on-demand treatment of hereditary angioedema (HAE) attacks. A phase 2 trial (NCT04208412) evaluated pharmacokinetics, pharmacodynamics, safety, and efficacy of sebetralstat for treatment of HAE attacks. This post hoc analysis reports effects of sebetralstat on symptom relief or improvement analyzed by baseline attack severity.

Method: Adults with HAE type I or II with 3 or more attacks in the past 93 days participated in a randomised, double-blind, placebo-controlled, phase 2 crossover trial. Attacks were categorised as mild or moderate severity at baseline. Symptom relief was defined as a rating of at least “A Little Better” for 2 consecutive timepoints on Patient Global Impression of Change (PGI-C) or at least 50% reduction from baseline for 3 consecutive timepoints on composite visual analog scale (VAS) scores within 12 hours of study drug. Severity improvement was defined as at least 1 level reduction on Patient Global Impression of Severity (PGI-S) within 12 hours.

Results: Sixty patients completed at least 1 attack treatment (n = 113 attacks). Within 12 hours of sebetralstat administration, symptom relief assessed by PGI-C was achieved for 69.2% and 89.3% of mild and moderate attacks vs 41.9% and 60.9% on placebo (difference vs placebo for mild and moderate attacks: 27.3% and 28.4%). Assessment by VAS achieved symptom relief after sebetralstat for 65.4% and 64.3% of mild and moderate attacks vs 22.6% and 43.5% on placebo (difference vs placebo for mild and moderate attacks: 42.8% and 20.8%). Severity improvement by PGI-S following sebetralstat was achieved for 34.6% and 78.6% of mild and moderate attacks vs. 9.7% and 52.2% on placebo (difference vs placebo for mild and moderate attacks: 24.9% and 26.4%).

Conclusion: These results demonstrate that sebetralstat provides relief of mild and moderate HAE attacks, showing similar treatment effect regardless of baseline attack severity.

P96: NOT FOR PUBLICATION