P93: REAL LIFE EXPERIENCE WITH OMALIZUMAB IN THE TREATMENT OF CHRONIC SPONTANEOUS URTICARIA (CSU) IN A METROPOLITAN SPECIALIST CLINIC
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Introduction: 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 ≥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. Antihistamine 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.

P94: THE IMPACT OF COVID-19 ON PATIENTS WITH PRIMARY AND SECONDARY IMMUNODEFICIENCIES: A STUDY INTO THE PHYSIOLOGICAL, PSYCHOLOGICAL AND SOCIOCOLOGICAL EFFECTS
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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.

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.

Conclusion: 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.

P95: SEBETRALSTAT EFFECTIVENESS IN THE TREATMENT OF HEREDITARY ANGIOEDEMA ATTACKS RATED MILD OR MODERATE AT BASELINE IN THE PHASE 2 TRIAL
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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 54.6% 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

P97: MEMORY RESPONSES TO SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 VACCINATION IN PATIENTS WITH HYPER-IMMUNOGLOBULIN E SYNDROMES
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Introduction: Pathogenic variants in genes encoding components of the Signal Transducer and Activator of Transcription 3 (STAT3) signalling pathway cause diverse systemic and immunologic manifestations. In particular, recurrent infections and defects in both cellular and humoral memory have been described in individuals with Hyper IgE Syndrome (HIES) due to dominant negative mutations in STAT3 or ILAST, or recessive mutations in DQCK5 or ZNF341. We examined the adaptive immune response to vaccination against SARS-CoV-2 in patients with HIES.

Method: Serial (baseline and post-vaccine doses 1, 2 and 3) blood and serum samples were collected from 36 HIES patients and 24 healthy donors receiving SARS-CoV-2 mRNA vaccination. A flow cytometric assay was optimized to assess Spike and Receptor-Binding-Domain specific B cells. An activation-induced-marker assay enabled quantification and characterization of CD4 and CD8 T cell responses to Spike and Nucleocapsid antigens. Serological assays were used to measure SARS-CoV-2 specific antibodies and SARS-CoV-2 pseudovirus neutralizing titres.

Results: Consistent with previous findings from our lab, experiments to date have demonstrated a reduction in CD27+ memory B cells (MBCs) as a proportion of total B cells in HIES patients compared with controls (4% vs. 20%, p < 0.01). Furthermore, while Spike-binding B cells were detected in HIES patients, they had a phenotype characteristic of atypical (CD27-IgG+) MBCs. In contrast, most MBCs specific for Spike and RBDB detected in healthy donors were CD27-IgG+, consistent with commitment to and selection into the classic MBC pool. Spike-binding B cells increase markedly following a 3rd vaccine dose in HIES, as well as in combination with a history of infection in both healthy donors and HIES.

Conclusion: HIES patients can develop a humoral response to SARS-CoV-2 vaccination. However, this response differs quantitatively, qualitatively and functionally from that observed in healthy donors. Experiments to further characterize vaccination responses in this cohort are ongoing.

P99: IMMUNODEFICIENT PAEDIATRIC PATIENTS TRANSITIONED TO SCIG BY TELEHEALTH DURING THE COVID19 PANDEMIC

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Introduction: Immunoglobulin replacement therapy is used for prophylactic treatment of patients with primary or secondary antibody deficiency1. At the beginning of the COVID-19 pandemic, anxiety driven by the unknown impact of this vulnerable cohort of patients led to the question “How do we limit the time spent in hospital to protect these patients and their families?”

Overview of initiative: Subcutaneous immunoglobulin (SCIG) infusions are given with a spring-loaded pump that is well tolerated, easy to use and safe to be administered at home replacing the need for monthly hospital admissions and intravenous cannulations. At the beginning of the pandemic the service developed to encourage transition patients deemed medically and socially appropriate to SCIG. Due to the large geographical area covered by the service some families were not willing to travel to the tertiary centre due to safety concerns. Arrangements were made with local, regional hospitals to facilitate initial infusions via telehealth with the paediatric specialist nurse. Once competence was achieved, telehealth via Microsoft Teams and telephone support was provided with the family in their home.

Results: During 2020 approximately 10 patients were transitioned to SCIG. A total of 48 patients are currently receiving SCIG and 15 receive IVlg. No family has since requested to go back to monthly intravenous immunoglobulin (IVlg) infusions. The clinical nursing service continues to support families as needed through telehealth from their homes reducing the need for attendance at hospital.

Conclusion: This initiative has allowed for greater patient centred care, allowing patients and families to choose when they receive their infusion and telehealth appointments. The use of telehealth has led to a reduction in the financial burden of travel costs to the patients and their families, and the healthcare system.

References

1 Abolhassani, H, et al. J Clin Immunol, 2012;32;1180–92

P99: ANTI-SARS-COV-2 ANTIBODIES IN IMMUNOGLOBULIN PRODUCTS (COVIG)

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Introduction: Intravenous and subcutaneous immunoglobulin (IVlg and SCIG) are plasma products derived from thousands of donors and cover a large spectrum of antimicrobial antibodies which are present in the general population. Previously published literature suggested anti-SARS-CoV-2 antibodies in therapeutic IVlg products may mirror the immunogenic status of the source population, however no data for local products exist. This investigation aimed to determine the presence of anti-SARS-CoV-2 antibodies in available IVlg products to assist interpretation of serological testing of patients receiving these products.

Method: Residual liquid from discarded bottles were diluted to 10 g/L (1%) prior to testing using the standard clinical PathWest SARS-CoV-2 serology assays for anti-spike (anti-S) and anti-nucleocapsid (anti-N) IgG. Products tested included in-house, Intragram, and EU/US IgG products: Flebogamma, Privigen,Octagam, Cuvitru, and Evogam. The expiry date and shelf-life of Ig products were used to estimate the manufacturing date. Measured anti-S IgG was plotted together with SARS-CoV-2 vaccination data for Australia, United States and Europe, while anti-N IgG was assessed against both vaccination and infection data.

Results: Anti-S IgG results from IVlg products based on assumed date of manufacture aligned well with the changes in vaccination coverage over time from the source population(s). Anti-N IgG was low in all products with no specific pattern identified when compared to either vaccination or infection rates of the source population(s).

Conclusion: This investigation provides further data to show a correlation of anti-S IgG within IgG products and vaccination rates within a source population, suggesting the date of manufacture could be used to predict their presence within any particular batch. While anti-N IgG levels were low, they were sufficient in some samples to provide a positive result. These results assist with interpretation of serological assays in patients receiving IgG products, while the clinical implication of these antibodies remains to be determined.

P100: CSL BEHRING CARES: SUPPORTING PATIENTS WITH PRIMARY IMMUNODEFICIENCY (PID) TO USE SUBCUTANEOUS IMMUNOGLOBULIN (HIZENTRA®) IN THE HOME

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Objectives: Treatment for primary immunodeficiency (PID) includes intravenous immunoglobulin (IVlg) and subcutaneous immunoglobulin (SCIG), which have both traditionally been administered in hospital. In 2018, the CSL Behring CARES patient support program (PSP) for Hizentra® was established to help educate patients and their carers to provide SCIG treatment in their home environment. CARES is managed by an independent provider, Aesir Health, and offers in-home education and support services using qualified registered nurses. Through the CARES PSP, patients can receive in-home educational visits from a nurse trained in the administration of SCIG. An analysis of PID patients enrolled in CARES is presented here.

Method: Patient competence in SCIG self-administration was assessed on completion of each nurse home visit using a standardised form. Patient’s skills and knowledge were rated in relation to the preparation, infusion and post-infusion care.

Results: At the time of writing, 251 patients with PID had been enrolled in CARES, ranging from age 2 to 92 years. The average weekly dose of Hizentra® was 14.7 g and average weekly volume was 55.6 mL. Prior to enrolling in the PSP, 63% of patients were receiving IVlg, 18% were receiving SCIG, 18% were treatment naive and 1% had received both IVlg and SCIG. For patients who were receiving SCIG, 31% had received self-administration training in the hospital. Competency was achieved by...