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Background: Low immunoglobulin (Ig) levels can occur after rituximab treatment, but the clinical significance is not completely understood. Not all patients (pts) who develop low Ig levels after rituximab are at an increased risk of serious infection (SI), but factors such as pre-existing low Ig levels, prior biologic therapies, history of SI and other disease and age-related factors may increase the risk.

Objectives: To assess the risk of SI in pediatric pts with prolonged low IgG or IgM serum concentrations following rituximab treatment for GPA or MPA in a global clinical trial.

Methods: In the Phase 2a PePRS study (WA25615), pts aged ≥ 2 to ≤ 18 yrs with GPA or MPA received 4 weekly intravenous rituximab infusions of 375 mg/m² body surface area and concomitant oral glucocorticoid taper. After 6 months, pts could receive further rituximab and/or other immunosuppressants at the investigator's discretion during a minimum 12-month follow-up phase. Pts with IgG/IgM levels below age-specific reference ranges at baseline were excluded. Ig levels were measured every 4-12 wks. SI occurrence was assessed during/after low IgG or IgM. Prolonged low Ig was defined as IgG or IgM levels < lower limit of normal (LLN) reference range for age for a ≥ 4 -month period.

Results: All 25 pts completed 4 weekly rituximab infusions and the 6-month Remission Induction Phase; 24/25 pts completed ≥ 18 months of follow-up. 17 pts received additional rituximab treatment on or after Month 6. 11 pts received concomitant immunosuppressants (cyclophosphamide, azathioprine, mycophenolate mofetil) during the study. All pts had a decrease in IgG and IgM mostly after the first rituximab infusion. There was no consistent trend in IgG or IgM levels over time and no clear relationship between low IgG or IgM levels and the number of follow-up rituximab treatments. 18 pts (72%) had prolonged low IgG ≥ 4 months, of whom 5 had IgG levels < LLN at screening and/or baseline; in 7 pts, IgG levels returned to within normal range by study end. During or after prolonged low IgG, 6/18 pts experienced a total of 7 SIs. Three pts received treatment with intravenous Ig. 19 pts (76%) had prolonged low IgM, of whom 5 had IgM levels < LLN at screening and/or baseline. During or after prolonged low IgM levels, 6/19 pts experienced a total of 8 SIs. There were no deaths or study discontinuation due to SI. All pts with prolonged low IgG or IgM had past and/or concomitant treatment with steroids and/or immunosuppressants as potential contributory factors. Analysis of SI onset in relation to timing of low Ig was limited due to protocol-defined time points for Ig assessments.

Conclusion: In pediatric pts with GPA/MPA treated with rituximab, there was no consistent pattern in IgG or IgM levels over time. The majority of pts with prolonged low IgG or IgM did not experience any SIs; no increase in the number of SIs was observed over time or with multiple rituximab treatments. While no firm conclusions can be made on a possible relationship between prolonged low IgG or IgM and risk of SI following rituximab due to study limitations (low pt numbers, lack of placebo comparator), these observations are consistent with the known rituximab safety profile in adult pts with GPA/MPA.

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SAT0504

STING-ASSOCIATED VASCULOPATHY WITH ONSET IN INFANCY (SAVI SYNDROME) CAN MIMIC JUVENILE IDIOPATHIC ARTHRITIS.

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Background: STING-associated vasculopathy with onset in infancy (SAVI syndrome) can mimic Juvenile Idiopathic Arthritis.

Objectives: The aim of this study is to describe a detailed cohort of patients with SAVI syndrome and highlight the similarity, in some cases, of the phenotype of this disease with Juvenile Idiopathic Arthritis.

Methods: 3 patients diagnosed with SAVI syndrome from the institution Hospital Universitari Vall d'Hebron were recruited. Written informed parental consent was obtained for the use of clinical data and pictures reported. Demographic, clinical, analytical, lung function and previous and current treatment are described.

Results: Patient 1, a 11-year-old boy, was identified to carry a de novo p.V155M mutation in TMEM173. He presented at first month of life with recurrent bronchial infection and skin vasculitis lesions in nose, cheeks and toes. Arthritis affected hands, toes and knees but no erosions were found at X-Ray. Fever was not reported. High-resolution computed tomography (HRCT) of the lungs identified a nonspecific interstitial pneumonia (NSIP) and a lung biopsy showed lymphoid hyperplasia. Elevated inflammatory markers were reported and rheumatoid factor (RF), ACPA antibodies and antinuclear antibodies (ANA) were also positive. At the age of 6 years Ruxolitinib (RX) was introduced at the initial dose of 5 mg twice daily with an improvement of skin disease and lung function. Arthritis was well controlled and RX was well tolerated.

Patient 2, a 17-year-old girl, was identified to carry a de novo p.V155 mutation in TMEM173. She presented at the age of 3 with a severe polyarthritis of large and small joints. No fever, skin or respiratory symptoms were reported at the beginning of the disease. Laboratory tests were positive for RF and ACPA antibodies. She was diagnosed with Polyarticular JIA and was treated with steroids and Methotrexate without improvement. Few months later she reported dyspnoea with recurrent bronchial infections. HRCT showed NSIP and lymphoid interstitial pneumopathy was found at the lung biopsy. RX was initiated at the age of 17 years but at this time lung fibrosis was established. Moreover, RX was not well tolerated due to headache. She requires continuous domiciliary oxygen and has been included to lung transplant.

Finally, patient 3, a 29-year-old man, was recently diagnosed with a de novo p.V155 mutation in TMEM173. He presented at the age of 7 years with symmetrical polyarticular arthritis after a bronchial infection that course with fever. No skin manifestations were objectified. Autoimmune lab test was positive for RF, ACPA, and ANA. With the diagnosis of Polyarticular JIA he received different treatments with no response. Due to recurrent bronchial infections a HRCT was performed showing an ILD at bases and follicular bronchiolitis with NSIP pattern in a lung biopsy. Functional tests were worsening without any response to different treatments. SAVI syndrome was suspected, and genetic test was performed with positive result. RX was initiated but compliance was not good.

Conclusion: SAVI syndrome is a rare monogenic autoinflammatory disease with few cases reported in the literature. Disease phenotype could be different in every patient, with no presence of skin vasculitis lesions or fever. Patient 2 and 3, in contrast with patient 1, had severe articular and lung manifestations with no skin involvement. Furthermore, lab tests were positive for RF and ACPA and were misdiagnosed as JIA so genetic test was performed later in the follow-up. Being aware of the distinct phenotype of the disease could help the clinicians to make a PRONTO diagnostic and reassess the patients with these presentations that not respond well to conventional treatments.

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SAT0505

PLUTO TRIAL OF INTRAVENOUS BELIMUMAB IN PAEDIATRIC PATIENTS WITH CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS (CSLE): PATIENT RESPONSES OVER TIME

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Background: Belimumab (BEL) is a human monoclonal antibody that specifically inhibits B-cell activating factor (BAFF). PLUTO is an ongoing trial evaluating efficacy and safety of intravenous (IV) BEL in children ≥ 5 years of age with cSLE. Efficacy, and safety endpoints of PLUTO have been reported;¹ briefly, numerically more BEL vs PBO pts met the primary and major secondary efficacy endpoints. We present patient (pt) response to BEL over time.

Objectives: To evaluate changes in SLE Responder Index (SRI) 4 and SRI6 responses, and disease activity over 52 weeks, in paediatric pts receiving BEL, or placebo (PBO), plus standard SLE therapy (SST).