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Background: Patients with autoimmune systemic diseases (ASDs) can be counted among frail populations as regards the predisposition to COVID-19 due to the frequent visceral organ involvement and comorbidities, as well as the ongoing immunomodulating treatments.

Objectives: Our long-term multicenter telephone survey prospectively investigated the prevalence, prognostic factors, and outcomes of COVID-19 in Italian ASD patients during the first 3 pandemic waves.

Methods: A large series of 3,918 ASD patients (815 M, 3103 F; mean age 59±12SD years) was consecutively recruited at the 36 referral centers of COVID-19 & ASD Italian Study Group. In particular, ASD series encompassed the following conditions: rheumatoid arthritis (n: 981), psoriatic arthritis (n: 471), ankylosing spondylitis (n: 159), systemic sclerosis (n: 1,738), systemic lupus (172), systemic vasculitis (n: 219), and a miscellany of other ASDs (n: 178). The development of COVID-19 was recorded by means of telephone survey using standardized symptom-assessment questionnaire (1).

Results: A significantly increased prevalence of COVID-19 (8.37% vs 6.49%; p<0.0001) was observed in our ASD patients, while the cumulative death rate revealed statistically comparable to the Italian general population (3.65% vs 2.95%; p: ns). In particular, among the 328 ASD patients complicated by COVID-19, 57 (17%) needed hospitalization, while mild-moderate manifestations were observed in the large majority of individuals (83%). In addition, 12/57 hospitalized patients died due to severe interstitial pneumonia and/or cardiovascular manifestations.

Interestingly, a significantly higher COVID-19-related death rate was observed in systemic sclerosis patients compared to the Italian general population (6.29% vs 2.95%; p=0.018). Other adverse prognostic factors to develop COVID-19 were the patients' older age, male gender, pre-existing ASD-related interstitial lung involvement, and chronic steroid treatment. Conversely, patients treated with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) showed a significantly lower prevalence of COVID-19 compared to those without (3.58% vs 46.99%; p=0.000), as well as the chronic administration of low dose aspirin in a subgroup of SSc patients (with 5.57% vs without 27.84%; p=0.000).

Conclusion: The cumulative impact of COVID-19 on ASD patients after the first 3 pandemic waves revealed less severe than that observed during the first phase of pandemic (1), especially with regards to the death rate that was comparable to the Italian general population in spite of the increased prevalence of complicating COVID-19 in the same ASD series.

Ongoing long-term treatments, mainly csDMARDs, might usefully contribute to generally positive outcomes of in this frail patients' population.

Of note, a significantly increased COVID-19-related mortality was recorded in only SSc patients' subgroup, possibly favored by pre-existing lung fibrosis. Among different ASD, SSc deserves special attention, since it shares the main pathological alterations with COVID-19, namely the interstitial lung involvement and the endothelial injury responsible for diffuse microangiopathy.

Besides SSc, the patients' subgroups characterized by older age, chronic steroid treatment, pre-existing interstitial lung disease, and/or impaired COVID-19 vaccine response (1-3), may deserve well-designed prevention and management strategies.

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POS1268 PHASE II TRIAL OF ENPATORAN IN PATIENTS HOSPITALIZED WITH COVID-19 PNEUMONIA

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Background: Enpatoran is a selective and potent dual toll-like receptor (TLR) 7/8 inhibitor in development for the treatment of cutaneous and systemic lupus erythematosus (CLE/SLE). Enpatoran inhibits TLR7/8 activation *in vitro* and suppresses disease activity in lupus mouse models.[1] Enpatoran was well tolerated and had linear pharmacokinetic (PK) parameters in healthy volunteers.[2] As TLR7/8 mediate immune responses to single-stranded RNA viruses, including SARS-CoV-2, it was postulated that enpatoran may prevent hyperinflammation and cytokine storm in COVID-19.

Objectives: In response to the COVID-19 pandemic, we conducted an exploratory Phase II trial to assess safety and determine whether enpatoran prevents clinical deterioration in patients (pts) hospitalized with COVID-19 pneumonia. PK and pharmacodynamics (PD) of enpatoran were also evaluated.

Methods: ANEMONE was a randomized, double-blind, placebo (PBO)-controlled study conducted in Brazil, the Philippines, and the USA (NCT04448756). Pts aged 18–75 years, hospitalized with COVID-19 pneumonia (WHO 9-point scale score =4) but not mechanically ventilated, with SpO_2 <94% and PaO_2/FiO_2 ≥150 (FiO_2 maximum 0.4) were eligible. Those with a history of uncontrolled illness, active/unstable cardiovascular disease and SARS-CoV-2 vaccination were excluded. Pts received PBO or enpatoran (50 or 100 mg twice daily [BID]) for 14 days, with monitoring to Day 28 and safety follow-up to Day 60. Primary outcomes were safety and time to recovery (WHO 9-point scale ≤3). Clinical deterioration (time to clinical status >4, WHO 9-point scale) was a secondary outcome. Exploratory endpoints were enpatoran and biomarker concentrations (cytokines, C-reactive protein [CRP], D-dimer and interferon gene signature [IFN-GS] scores) assessed over time.

Results: 149 pts received either PBO (n=49), or enpatoran 50 mg (n=54) or 100 mg (n=46) BID; 88% completed treatment and 86% received concomitant steroids. Median age was 50 years (77% <60 years old), 66% were male, and 50% had ≥1 comorbidity (40% hypertension, 24% diabetes). Overall, 59% pts reported a treatment-emergent adverse event (TEAE) with three non-treatment-related deaths; 11% reported a treatment-related TEAE. The proportion of pts in the enpatoran group reporting serious TEAEs was low (50 mg BID 9%; 100 mg BID 2%) vs PBO (18%). Gastrointestinal disorders were most common (PBO 8%; 50 mg BID 28%; 100 mg BID 9%). The primary outcome of time to recovery with enpatoran vs PBO was not met; medians were 3.4–3.9 days. A positive signal in time to clinical deterioration from Day 1 through Day 28 was observed; hazard ratios [95% CI] for enpatoran vs PBO were 0.39 [0.13, 1.15] (50 mg BID) and 0.30 [0.08, 1.08] (100 mg BID). Mean enpatoran exposure was dose-proportional, and PK properties were within expectations. The median (quartile [Q]1– Q3) interleukin 6 (IL-6), CRP and D-dimer baseline concentration across the groups were 5.7 (4.0–13.5) pg/mL, 30.04 (11.40–98.02) and 0.62 (0.39–1.01) mg/L, respectively. Baseline IFN-GS scores were similar across groups.

Conclusion: The ANEMONE trial was the first to evaluate the safety and efficacy of a TLR7/8 inhibitor in an infectious disease for preventing cytokine storm. Enpatoran up to 100 mg BID for 14 days was well tolerated by patients acutely ill with COVID-19 pneumonia. Time to recovery was not improved with enpatoran, perhaps due to the younger age of patients who had fewer comorbidities compared to those in similar COVID-19 trials. However, there was less likelihood for clinical deterioration with enpatoran than placebo. This trial provides important safety, tolerability, PK and PD data supporting continued development of enpatoran in SLE and CLE (NCT04647708, NCT05162586).

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POS1269 CLINICAL COURSE AND OUTCOMES OF COVID-19 INFECTION IN PATIENTS WITH SJOGREN'S SYNDROME TREATED WITH RITUXIMAB.

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Background: Data from multiple rheumatological cohorts have shown that treatment with rituximab (RTM) is associated with higher COVID-19 morbidity and mortality. Information about the course of COVID-19 in patients (pts) with Sjogren's syndrome (SjS) is still lacking.
Objectives: To compare clinical course of COVID-19 in pts with SjS treated with anti-CD20 monoclonal antibody (RTM) and treated with synthetic disease-modifying antirheumatic drugs and low doses of glucocorticoids.
Methods: Single center observational study. Pts with SjS were screened for SARS-CoV-2 infection anamnesis via telephone interview. Diagnosis of SjS was based on ECR/EULAR 2016 criteria. COVID-19 diagnosis was based on positive PCR test and typical clinical features (CT signs, fever and anosmia). RTM was administered as two infusions of 1000 mg each 2 weeks apart, and then 500 mg every 6 months.
Results: 387 pts with SjS were interviewed, 142 of them with confirmed SARS-CoV-2 were included in the study and divided into 2 groups. The first group (gr) consisted of 86 pts (79 women and 7 men) receiving RTM (gr R), median age was 56 years (33-66,5 years), and median rituximab treatment duration was 36 months (12-42 months). Pts in the control gr (gr C), 56 pts did not receive RTM (55 women and 1 man), their median age was 50 years (35-69 years). Median time from last RTM administration to COVID-19 symptoms onset was 4 months (2-6 months). Ten pts had concomitant RA, 4 pts - SLE, 5 pts - Systemic sclerosis. Fifteen pts had MALT-lymphoma anamnesis. Additionally, 15 pts (10.5%) had pulmonary involvement secondary to rheumatic disease. In total 37 pts had chronic ischemic heart disease and/or severe arterial hypertension, diabetes mellitus type 2.
In gr R 31 pts (36%), and in gr C 13 (23%) required hospitalization due to marked shortness of breath and long febrile period (p=0,1). Anti-IL6 treatment or/and Jak inhibitors were prescribed to 17 of 31 pts (54.8%) in gr R and to 5 of 13 (38%) in gr C (p=0,1). The risk of hospitalization was slightly higher in pts with comorbidity (p=0.06) and with a history of lymphoma (p=0.056) and didn't correlate with the following parameters: age, the duration of RTM therapy, lung damage. A high rate of hospitalization correlated with a shorter period between the administration of the RTM and the development of COVID-19 (R=0,387, Spearman`s Rank Correlation). Anti-SARS-CoV-2 IgG were measured in 66 pts, 47 (71%) of them were positive. Positive Anti-SARS-CoV-2 IgG were significantly more often detected in gr C (84% vs. 57,6%). No correlation was found between the formation of antibodies and the duration of RTM therapy or the time from the last RTM administration.
Conclusion: According to our data anti-CD20 therapy doesn't predispose SjS pts to severe course of COVID-19. Lymphoma anamnesis, cardiovascular diseases and diabetes have greater impact on COVID-19 severity. Obviously, anti-CD20 therapy negatively affected the formation of specific anti-SARS-CoV-2 humoral immunity.
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POS1270 COVID19 VACCINATION IN PATIENTS WITH AXIAL AND PERIPHERAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS: ADVERSE EVENTS AND IMPACT ON DISEASE ACTIVITY

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Background: There is scarce evidence on the rate of adverse events and the consequences on disease activity after vaccination against covid19
Objectives: To evaluate adverse events to vaccination and disease flares after vaccination in patients with axial spondyloarthritis (axSpA), peripheral spondyloarthritis (pSpA) and psoriatic arthritis (PsA) and to evaluate factors associated with adverse event.
Methods: Cross-sectional, observational, descriptive study. Consecutive patients with diagnosis of ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA) according to ASAS 2009 criteria; pSpA according to ASAS 2011 criteria and PsA according to CASPAR criteria were included. Demographic data, disease clinimetry, treatments, vaccination received and post-vaccination adverse events were recorded. We evaluated, according to medical criteria, whether the patient presented a flare disease after vaccination and whether it was mild, moderate or severe. We also evaluated the factors associated with the presence of at least one mild adverse event. Statistical analysis: descriptive statistics were performed, qualitative variables were expressed as frequency and percentage (%), numerical variables as mean and standard deviation (SD) or median and percentile25-75. Binary logistic regression was performed using the presence of at least one mild adverse event to vaccination as the dependent variable.
Results: 210 patients were included with a mean age of 45 (SD 15) years. The diagnoses were: AS 50 (23.8%), nr-axSpA 10 (4.8), pSpA 9 (4.3%), PsA 141 (67%) and time of disease evolution in months 109 (SD 96). Regarding comorbidities, the following frequencies were reported: arterial hypertension 60 (30%), diabetes mellitus 25 (12%), heart failure 4 (2%), asthma/EPOC 15 (7%), inflammatory bowel disease 2 (1%), acute anterior uveitis 20 (9.5%), psoriasis 128 (61%). Sixteen percent (n=33) of the patients had SARS-CoV-2 infection prior to vaccination. Regarding treatments, those used were: antiTNF 88 (42%), Tofacitinib 6 (2.9%), Ustekinumab 2 (1%), Secukinumab 35 (17%), Ixekizumab 2 (1%), methotrexate 98 (47%), leflunomide 7 (3. 3), sulfasalazine 7 (3.3), apremilast 1 (0.5%), continuous NSAIDs 26 (12.4%) and NSAIDs on demand 103 (49%). Vaccines received were: Sputnik V 109 (51.9%), Oxford Vaccine, AstraZeneca 63 (30%), Janssen 1 (0.5%), BioNTech Vaccine, Pfizer 1 (0.5%), Sinopharm 33 (15.7%), Moderna 0%, Novavax 0% and others; 3 (1.4%). Thirty-eight percent (n=80) of patients reported having mild post-vaccination symptoms, of which 3.75% did not resolve, 41% resolved with medication and 39% resolved ad integrum without medication. The presence of mild adverse event to the vaccine was associated with lower use of methotrexate (31% vs 56 %, p<0.001), and lower age (54 (SD 14) vs 47 (SD 12), p<0.001), and lower BMI (25 (24-30.5) vs 28 (25-31), p<0.001); while no association was found with sex, diagnosis, comorbidities, treatments, desease activity or vaccines. In the logistic regression analysis all the variables remained independently associated with a lower probability of presenting a mild adverse event: methotrexate: OR: 0.30, 95%CI 0.15-0.58, p<0.001, age: OR: 0.97, 95%CI 0.95-0.99, p: 0.03, BMI: OR: 0.92, 95%CI 0.95-0.99, p: 0.02. Sixty-one percent (n=129) of patients received the 2nd dose of vaccination, which 27% (n=35) presented mild adverse event and only 1 (0.8%) patient suffered post vaccination disease flare.
Conclusion: Vaccination against COVID19 appears to be safe in this population, with only mild adverse events and low frequency of flare disease. Mild adverse events were associated with less use of methotrexate, younger age and lower BMI.
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POS1271 THE COURSE AND OUTCOMES OF COVID-19 IN PATIENTS WITH TAKAYASU ARTERITIS: CASE SERIES OF 15 PATIENTS FROM A TERTIARY SINGLE CENTER

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Background: The Coronavirus disease 2019 (COVID-19) has affected more than two hundred million individuals and many risk factors for increased mortality and morbidity in COVID-19 have defined. There are many studies evaluating the effect of immunosuppressants used in inflammatory rheumatic diseases in the course of COVID-19. (1,2) However, fewer data are available on the course of COVID-19 in patients with Takayasu arteritis (TAK).
Objectives: In this study, we aimed to evaluate the characteristics and outcomes of TAK patients with COVID-19.
Methods: A phone survey was conducted among TAK patients that are followed up in our clinic between February 2021 and March 2021. All patients were asked whether they were diagnosed as COVID-19 during the pandemic. The patients who had a history of confirmed COVID-19 were asked about the symptoms, hospitalization status and the treatment received for COVID-19. Information about their chronic diseases were obtained from the patient files.
Results: Among 118 TAK patients, 15 had COVID-19 infection during the first year of pandemic, 13 of them were female and mean age was 42,5 ± 12,0 years. None of the patients had been vaccinated before the diagnosis of COVID-19. Nine of the patients were taking prednisone therapy and 3 of them were taking moderate to high doses of glucocorticoids during the infection period. Twelve patients were taking conventionally synthetic disease-modifying antirheumatic drugs (csDMARDs), 7 patients were taking biological disease-modifying antirheumatic drugs (bDMARDs), and 5 patients were taking a combination of csDMARD and bDMARD therapy when they were diagnosed with COVID-19. Two patients were hospitalized; one of them required nasal oxygen support and discharged after 5 days. The other patient was 61 years old and had multipl comorbidities and had admitted to intensive care unit for 5 days. One patient who had a mild COVID-19 disease had pulmonary thromboembolism 2 weeks after the infection and his symptoms resolved after starting anticoagulation therapy. All of the patients fully recovered and had no mortality related to COVID-19.