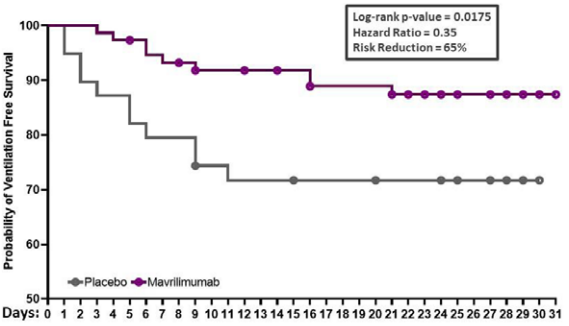
ventilation (to maintain SpO_2 ≥92%) and Cohort 2 patients requiring mechanical ventilation, initiated ≤48 hours before randomization. Here, we report results for Phase 2, Cohort 1: 116 patients with severe COVID- 19 pneumonia and hyperinflammation from USA, Brazil, Chile, Peru, and South Africa; randomized 1:1:1 to receive a single intravenous administration of mavrilimumab (10 or 6 mg/kg) or placebo. The primary efficacy endpoint was proportion of patients alive and free of mechanical ventilation at Day 29. Secondary endpoints included [1] time to 2-point clinical improvement (National Institute of Allergy and Infectious Diseases COVID-19 ordinal scale), [2] time to return to room air, and [3] mortality, all measured through Day 29. The prespecified evidentiary standard was a 2-sided α of 0.2 (not adjusted for multiplicity).

Results: Baseline demographics were balanced among the intervention groups; patients were racially diverse (43% non-white), had a mean age of 57 years, and 49% were obese (BMI ≥ 30). All patients received the local standard of care: 96% received corticosteroids (including dexamethasone) and 29% received remdesivir. No differences in outcomes were observed between the 10 mg/kg and 6 mg/kg mavrilimumab arms. Results for these groups are presented together. Mavrilimumab recipients had a reduced requirement for mechanical ventilation and improved survival: at day 29, the proportion of patients alive and free of mechanical ventilation was 12.3 percentage points higher with mavrilimumab (86.7% of patients) than placebo (74.4% of patients) (Primary endpoint; p=0.1224). Mavrilimumab recipients experienced a 65% reduction in the risk of mechanical ventilation or death through Day 29 (Hazard Ratio (HR) = 0.35; p=0.0175). Day 29 mortality was 12.5 percentage points lower in mavrilimumab recipients (8%) compared to placebo (20.5%) (p=0.0718). Mavrilimumab recipients had a 61% reduction in the risk of death through Day 29 (HR= 0.39; p=0.0726). Adverse events occurred less frequently in mavrilimumab recipients compared to placebo, including secondary infections and thrombotic events (known complications of COVID-19). Thrombotic events occurred only in the placebo arm (5/40 [12.5%]).

Mavrilimumab Reduced the Risk of Mechanical Ventilation or Death by 65% Versus Placebo



Conclusion: In a global, diverse population of patients with severe COVID-19 pneumonia and hyperinflammation receiving supplemental oxygen therapy, corticosteroids, and remdesivir, a single infusion of mavrilimumab reduced progression to mechanical ventilation and improved survival. Results indicate mavrilimumab, a potent inhibitor of GM-CSF signaling, may have added clinical benefit on top of the current standard therapy for COVID-19. Of potential importance is that this treatment strategy is mechanistically independent of the specific virus or viral variant.

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LB0002

COVID-19 VACCINE SAFETY IN PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASE

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Background: The consequences of the COVID-19 outbreak are unprecedented and have been felt by everyone around the world, including people with rheumatic and musculoskeletal diseases (RMDs). With the development of vaccines, the future is becoming brighter. Vaccines are a key pillar of public health and have been proven to prevent many serious diseases. However, vaccination also raises questions, especially for patients with inflammatory RMDs and/or treated with drugs that influence their immune system.

Objectives: Our aim was to collect safety data among RMD patients receiving COVID-19 vaccines.

Methods: The EULAR COVID-19 Vaccination (COVAX) Registry is an observational registry launched on 5 February 2021. Data are entered voluntarily by clinicians or associated healthcare staff; patients are eligible for inclusion if they have an RMD and have been vaccinated against SARS-CoV-2. Descriptive statistics are presented.

Results: As of 27 April 2021, 1519 patients were reported to the registry. The majority were female (68%) and above the age of 60 (57%). Mean age was 63 years (SD 16), ranging from 15 to 97 years. A total of 28 countries contributed to the registry, with France (60%) and Italy (13%) as the highest contributors. The majority (91%) had inflammatory RMDs. Inflammatory joint diseases accounted for 51% of cases, connective tissue diseases 19%, vasculitis 16%, other immune mediated inflammatory diseases 4%, and non-inflammatory/mechanical RMDs 9%. The most frequent individual diagnoses were rheumatoid arthritis (30%), axial spondyloarthritis (8%), psoriatic arthritis (8%), systemic lupus erythematosus (SLE, 7%) and polymyalgia rheumatica (6%). At the time of vaccination, 45% were taking conventional synthetic DMARDs, 36% biological DMARDs, 31% systemic glucocorticoids, 6% other immunosuppressants (azathioprine; mycophenolate; cyclosporine; cyclophosphamide; tacrolimus), and 3% targeted synthetic DMARDs. The most frequent individual DMARDs were methotrexate (29%), TNF-inhibitors (18%), antimalarials (10%) and rituximab (6%). The vaccines administered were: 78% Pfizer, 16% AstraZeneca, 5% Moderna and 1% other/unknown; 66% of cases received two doses and 34% one dose. Mean time from 1st and 2nd dose to case report was 41 days (SD 26) and 26 days (SD 23), respectively. COVID-19 diagnosis after vaccination was reported in 1% (18/1519) of cases. Mean time from first vaccination until COVID-19 diagnosis was 24 days (SD 17). Disease flares were reported by 5% (73/1375) of patients with inflammatory RMDs, with 1.2% (17/1375) classified as severe flares. Mean time from closest vaccination date to inflammatory RMD flare was 5 days (SD 5). The most common flare types were arthritis (35/1375=2.5%), arthralgia (29/1375=2.1%), cutaneous flare (11/1375=0.8%) and increase in fatigue (11/1375=0.8%). Potential vaccine side effects were reported by 31% of patients (467/1519). The majority were typical early adverse events within 7 days of vaccination, namely pain at the site of injection (281/1519=19%), fatigue (171/1519=11%) and headache (103/1519=7%). Organ/system adverse events were reported by 2% (33/1519) but only 0.1% (2/1519) reported

severe adverse events, namely a case of hemiparesis in a patient with systemic sclerosis/SLE overlap syndrome (ongoing at the time of reporting), and a case of giant cell arteritis in a patient with osteoarthritis (recovered/resolved without sequelae).

Conclusion: The safety profiles for COVID-19 vaccines in RMD patients was reassuring. Most adverse events were the same as in the general population, they were non-serious and involved short term local and systemic symptoms. The overwhelming majority of patients tolerated their vaccination well with rare reports of inflammatory RMD flare (5%; 1.2% severe) and very rare reports of severe adverse events (0.1%). These initial findings should provide reassurance to rheumatologists and vaccine recipients, and promote confidence in COVID-19 vaccine safety in RMD patients, namely those with inflammatory RMDs and/or taking treatments that influence their immune system.

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LB0003

IMMUNOGENICITY AND SAFETY OF THE BNT162B2 MRNA COVID-19 VACCINE IN ADULT PATIENTS WITH AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES AND GENERAL POPULATION: A MULTICENTER STUDY

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Background: Vaccination represents a cornerstone in mastering the COVID-19 pandemic. Data on immunogenicity, efficacy, and safety of the novel BNT162b2 mRNA vaccine in patients with autoimmune inflammatory rheumatic diseases (AIIRD) are limited.

Objectives: To investigate the immunogenicity, efficacy, and safety of the BNT162b2 mRNA vaccine in patients with AIIRD compared to the general population.

Methods: A prospective multicenter study investigated immunogenicity, efficacy, and safety of the two-dose regimen BNT162b2 mRNA vaccine in adult patients with AIIRD including rheumatoid arthritis (RA), psoriatic arthritis (PsA), axial spondyloarthropathy (axSpA), systemic lupus erythematosus (SLE), connective tissues diseases (CTD), systemic vasculitides, and idiopathic inflammatory myositis (IIM), compared to control subjects without rheumatic diseases or immunosuppressive therapies. Serum IgG antibody levels against SARS-CoV-2 spike S1/S2 proteins were measured 2 - 6 weeks after the second vaccine dose. Seropositivity was defined as IgG ≥15 binding antibody units (BAU)/ml. Post-vaccination efficacy defined as post-vaccination COVID-19 infection and safety were assessed. Pre- and post- vaccination disease activity indices were assessed as appropriate for each disease.

Results: A total of 686 AIIRD patients and 121 controls participated into the study. AIIRD patients were significantly older than controls, mean age±SD 56.76±14.88 vs 50.76±14.68, respectively, p<0.0001. A total of 95.2% (n=653) AIIRD patients were treated with immunomodulatory medications.

The seropositivity rate was 86% (n=590) in patients with AIIRD compared to 100% in controls (p <0.0001) The level of the S1/S2 antibodies was significantly reduced in AIIRD patients compared to controls (mean± SD 132.9±91.7 vs 218.6±82.06, P<0.0001). In patients with PsA, AxSpA, SLE, and LVV, the seropositive rate was above 90%. In RA, the seropositive rate was 82.1% and the lowest seropositive rate (<40%) was observed in patients with AAV and IIM.

Anti-CD20 significantly impaired the vaccine's immunogenicity, with the lowest seropositivity rate of 39%. The use of GC, mycophenolate mofetil (MMF), and abatacept was associated with a significantly lower rate of seropositivity (Figure 1). MTX significantly reduced the seropositivity in patients treated with MTX monotherapy and in combinations with other treatments (92% and 84%, respectively), although at a lesser magnitude than anti-CD20, MMF, and abatacept. More than 97% of patients treated with anti-cytokine therapies including TNFi, interleukin-17 and interleukin-6 inhibitors had an appropriate immunogenic response when used as monotherapy. The combination of TNFi with MTX significantly reduced the rate of seropositivity to 93%, p=0.04. Age over 65 years, a diagnosis of RA, IIM, ANCA-associated vascilitis, and treatment with GC, MMF, anti-CD20, and abatacept were associated with a reduced likelihood of seropositivity.

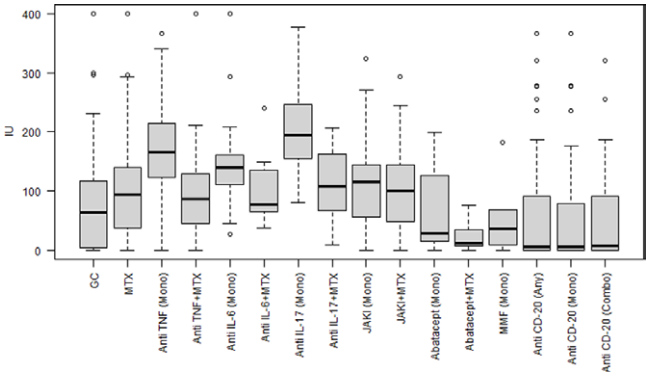

Figure 1. Seropositivity rate by immunosuppressive treatment.

There were no post-vaccination symptomatic cases of COVID-19 among AIIRD patients and one mild case in the control group. Major adverse events in AIIRD patients included death (n=2) several weeks after the second vaccine dose, non-disseminated herpes zoster (n=6), uveitis (n=2), and pericarditis (n=1). Post-vaccination disease activity remained stable in the majority of patients.

Conclusion: Vaccination with the BNTb262 vaccine resulted in an adequate immunogenic response with an acceptable safety profile in the majority of patients with AIIRD. Treatment with GC, rituximab, MMF, and abatacept may impair BNT162b2-induced immunogenicity. Postponing administration