

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 spondyloarthritis (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 \pm SD 56.76 \pm 14.88 vs 50.76 \pm 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 \pm SD 132.9 \pm 91.7 vs 218.6 \pm 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 vasculitis, and treatment with GC, MMF, anti-CD20, and abatacept were associated with a reduced likelihood of seropositivity.

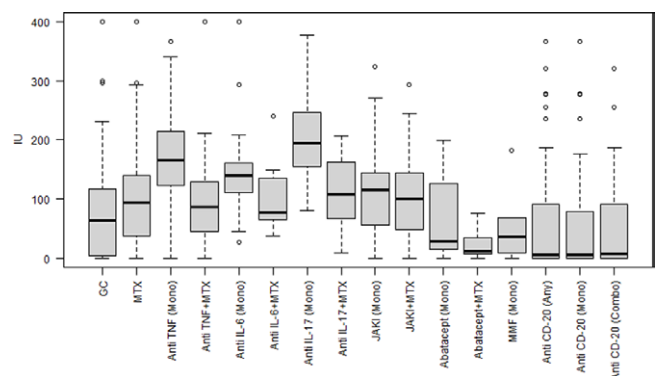


Figure 1. Seropositivity rate by immunosuppressive treatment.

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

of rituximab, when clinically feasible, seems to be reasonable to improve vaccine-induced immunogenicity. Holding treatment with abatacept and MMF may be considered on an individual basis.

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LB0004

EFFICACY AND SAFETY OF SECUKINUMAB IN ENTHESITIS-RELATED ARTHRITIS AND JUVENILE PSORIATIC ARTHRITIS: PRIMARY RESULTS FROM A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, TREATMENT WITHDRAWAL, PHASE 3 STUDY (JUNIPERA)

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Background: Enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA) are two ILAR categories of juvenile idiopathic arthritis (JIA) and represent paediatric correlates of axial spondyloarthritis (axSpA) and adult psoriatic arthritis (PsA), respectively.^{1,2} Secukinumab (SEC) has demonstrated efficacy and safety in adult patients (pts) with PsA, ankylosing spondylitis and non-radiographic axSpA.³⁻⁵

Objectives: Evaluate efficacy and safety of SEC using a flare prevention design in pts with active ERA and JPsA.

Methods: This 2-yr study consisted of an open-label (OL) s.c. SEC (75/150 mg in pts <50/ ≥50 kg) at baseline (BL), and at Weeks (Wk) 1, 2, 3, 4, 8 and 12 in treatment-period (TP) 1. Responder pts who achieved at least JIA ACR 30 response at Wk 12 were randomised into the double-blinded TP2 to continue SEC or placebo (PBO) q4w until a disease flare, or up to Wk 100. Pts (aged 2 to <18 yrs) classified as ERA or JPsA according to ILAR criteria of ≥6 months duration with active disease were included. Primary endpoint was time to flare in TP2 and key secondary endpoints were JIA ACR 30/50/70/90/100, inactive disease, JADAS, enthesitis count and safety. Analysis of time to flare in TP2 included proportion of disease flare, Kaplan-Meier (KM) estimate

of median time to flare in days, hazard ratio (95% CI) from Cox model, and *P*-value for the Stratified log-rank test. KM estimates of the probability to disease flare by treatment groups in TP2 were plotted against days. Observed data were used in all analyses. Post-hoc analyses using non-responder imputation (NRI) were performed for JIA ACR 30/50/70/90/100 responses.

Results: 86/97 (89%) pts were enrolled in the OL period TP1 (mean age, 13.1 yrs; female, 33.7%; ERA, n=52; JPsA, n=34). At BL, mean JADAS-27 score was 15.1 and enthesitis count was 2.6. At the end of TP1, 90.4% (75/83) of pts achieved JIA ACR 30 and 69.9% (58/83) achieved JIA ACR 70. There were 21 and 10 flares in TP2, respectively in PBO and SEC treated pts with a significantly longer time to flare and 72% risk of flare reduction in SEC treatment vs PBO (HR: 0.28; 95% CI: 0.13–0.63; *P*<0.001) (Figure 1). JIA ACR responses, disease activity and enthesitis count are reported in Table 1. NRI analyses showed that 87.2%, 83.7%, 67.4%, 38.4% and 24.4% of pts achieved JIA ACR 30/50/70/90/100, respectively. Rates of adverse events (AEs; 91.7% vs 92.1%) and serious AEs (14.6% vs 10.5%) in SEC and PBO groups were comparable in the entire TP. No new safety signals were observed.

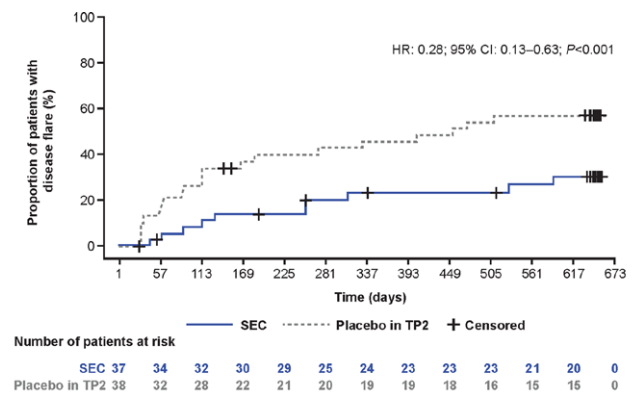


Figure 1. Time to flare in Treatment Period 2 (Primary Endpoint)

Table 1. Efficacy of secukinumab in Treatment Periods 1 and 2 (Key secondary endpoints)

Efficacy Outcomes, %	TP1	TP2 [†]	<i>P</i> -value
	SEC (N=83) [‡]	SEC (N=37) PBO (N=37)	
JIA ACR 30	90.4	89.2	0.014
JIA ACR 50	86.7	78.4	0.152
JIA ACR 70	69.9	67.6	0.042
JIA ACR 90	39.8	51.4	0.431
JIA ACR 100	25.3	43.2	0.745
Inactive disease [§]	36.1	47.2	0.500
JADAS-27, mean (SD)	15.1 (7.2)	14.6 (8.1)	13.3 (5.8) NA
Enthesitis count, mean change from BL (SD)	-1.8 (2.3)	-2.1 (2.0)	-1.9 (1.2) NA

P-values: Cochran-Mantel-Haenszel test, adjusted for analysis factors: JIA category (ERA/JPsA) and MTX use at BL

[†]The N numbers are values at the end of TP2

[‡]Efficacy outcomes (%) in TP1 calculated in patients with evaluable data at Wk 12 (N=83)

[§]Inactive disease: Definition adapted from JIA ACR criteria of Wallace et al., 2011. N=36 for SEC at the end of TP2

JADAS, Juvenile Arthritis Disease Activity Score; N, total number of patients in the treatment group; NA, data not available

Conclusion: In children and adolescents with ERA and JPsA, efficacy of SEC was demonstrated with a significantly longer time to flare vs PBO with sustained improvement of signs and symptoms up to Wk 104 and a favourable safety profile.