Efficacy and tolerance of vaccination against COVID-19 in patients with systemic lupus erythematosus: the international VACOLUP study

Renaud FELTEN[1] (MD), Lou KAWKA[1] (MD), Maxime DUBOIS[1] (MD), Manuel UGARTE-GIL[2] (MD), Yurilis FUENTES-SILVA[3] (MD), Matteo PIGA (MD)[4], Laurent ARNAUD[1] (MD, PhD).

[1]Service de rhumatologie, Centre National de Référence des Maladies Auto-immunes Systémiques Rares Est Sud-Ouest (RESO), Hôpitaux Universitaires de Strasbourg, Strasbourg, France.

[2]School of Medicine. Universidad Cientifica del Sur, Lima, Peru. Rheumatology Department. Hospital Nacional Guillermo Almenara Irigoyen. EsSalud, Lima, Peru.

[3]Division of Rheumatology, Complejo Hospitalario Universitario Ruiz y Páez, Universidad de Oriente, Ciudad Bolívar, Centro Nacional de Enfermedades Reumáticas, Venezuela

[4]Department of Medical Science and Public Health, University of Cagliari, Cagliari, Italy

***Corresponding author:**
Pr. Laurent ARNAUD, Service de rhumatologie, Centre National de Référence des Maladies Autoimmunes et Systémiques Rares, Hôpital de Hautepierre, 1 Avenue Molière BP 83049, 67098 Strasbourg Cedex, France. Phone: 03 88 12 84 74 | Fax: 03 88 12 82 90
Email: Laurent.arnaud@chru-strasbourg.fr

Keywords: COVID-19; systemic lupus erythematosus; vaccination

Acknowledgements: We wish to acknowledge the crucial role of the following patient associations: LupusEurope (tweeter: @LupusEurope), Agrupacion Lupus Chile (@Lupus_Chile), Lupus UK, Lupus France, AFL+, Gruppo LES Italiano (https://www.lupus-italy.org/), in the dissemination of the survey. We are indebted to Gonzalo Tobar Carrizo (@pinkycito) for the Spanish translation of the survey and all patients for their kind participation in our study. We wish to thank Ms. Sylvie Thuong for her invaluable assistance in the preparation of the manuscript.

Commentato [MP1]: Please also add Gruppo LES Italiano

Contributors:

Conceptualization: RF, LK, MD, LA

Data curation: RF, LA

Investigation: RF, LK, MD, MP, MUG, YFS, LA

Methodology: RF, LK, MD, LA

Writing - original draft: RF, LA

Writing - review & editing: RF, LK, MD, MP, MUG, YFS, LA

Declaration of interest:

Renaud FELTEN has received consultancy fees from Pfizer and Janssen (unrelated to the VACOLUP study). Matteo PIGA has received consultancy fees from GSK and Pfizer (unrelated to the VACOLUP study). Manuel F. Ugarte-Gil reports grants from Janssen and Pfizer (unrelated to the VACOLUP study). Laurent ARNAUD has received consultancy fees from Pfizer and Astra-Zeneca (unrelated to the VACOLUP study). Other authors have nothing to disclose.

ABSTRACT (348 words)

Introduction

Both efficacy and safety data regarding COVID vaccines in systemic lupus erythematosus (SLE) are lacking. We conducted the international Vaccination Against COvid in systemic LUPus study (VACOLUP) to evaluate the efficacy and tolerance of the vaccination against SARS-CoV-2 (COVID-19) in SLE. Our main objective was to describe the tolerance of SARS-CoV-2 vaccination in SLE patients, and to assess the risk of post-vaccination flare.

Methods

VACOLUP was designed as a cross-sectional study which consisted of 43 web-based questions. The study took place from March 22, 2021 to May 17, 2021. Main study outcomes included: demographical characteristics; history of COVID-19; history of vaccination against SARS-CoV-2 and tolerance. Self-reported side-effects, medically-confirmed lupus flare or COVID-19 after vaccination were analyzed.

Results

The study included 696 participants (669 [96.1%] women and 27 [3.9%] men), with a median age of 42 years [IQR: 34-51]), from 29 countries. Side-effects were reported by 316 patients (45.4%) after the first dose of COVID-19 vaccine and 181 (52.8%) of those who received a second dose of vaccine. There was no difference in the occurrence of side effects according to gender (p=0.11), age (p=0.08) or by mechanism of action (mRNA vaccines versus others, p=0.69). The type and intensity of side effects were minor or moderate in intensity (i.e., with no consequence on the ability to perform daily tasks) in more than 80% of cases. A total of 21 patients (3.0%) reported a medically-confirmed SLE flare, typically with predominant musculoskeletal symptoms (90.5%) and fatigue (85.7%). Of note these symptoms were reported to occur after a median delay of 0 day (IQR: 0-1) following COVID-19 vaccination. This led to a change in lupus treatment in 15/21 cases.

Conclusion

Side effects are common but minor or moderate in 80% of the cases. Only 21 (3.0%) self-reported a medically confirmed SLE flare. These flares were mainly represented by musculoskeletal symptoms and fatigue and occurred very early after COVID-19 vaccination, suggesting it might be difficult to distinguish between lupus flares and common side-effects of vaccination in SLE patients. Disseminating these reassuring data should therefore help clinicians to increase vaccine coverage in SLE patients.

Introduction

Vaccination is an important and effective tool to prevent infections in the general population as well as in patients with autoimmune diseases (AIDs). Regarding SARS-CoV-2, 120 vaccine candidates have been evaluated in more than 350 trials, eventually leading to 16 vaccine approvals[1] and more than one billion people vaccinated worldwide as of May 1. Importantly, we are lacking data regarding both the efficacy and safety of COVID-19 vaccines in AIDs such as Systemic Lupus Erythematosus (SLE), because SLE patients have largely been excluded from trials[2–4]. Also, the use of RNA vaccines has raised significant concerns about the tolerance of these new vaccine technologies in SLE, as Toll-Like Receptor stimulation by nucleic acids might increase the risk of lupus flare. These uncertainties have been shown to be major determinants of reduced vaccine willingness in AIDs[5]. The main objective of the international Vaccination Against COvid in systemic LUPus (VACOLUP) study was therefore to assess the efficacy and tolerance of SARS-CoV-2 vaccines in SLE, including the risk of incident lupus flare from the patients' perspective.

Methods

Study design

VACOLUP was designed as a cross-sectional study based upon a 43-question web-based survey which took place from March 22, 2021 to May 17, 2021. Dissemination of the study was facilitated by main national and international patients' associations through their websites as well as by the following social media: Twitter, Facebook, Instagram (see acknowledgements). The study was approved by the ethic review board of Strasbourg medical faculty (#CE-2020-29) and respondents gave their consent to participate to this research via a dedicated question at the beginning of the online questionnaire. The data which support the findings of this study are available from the authors upon reasonable request.

Study participants and main study outcomes

The study targeted patients with a self-reported medically-confirmed diagnosis of SLE. Patients reporting purely cutaneous lupus, non-medically confirmed SLE, or any other diagnosis instead of SLE were excluded. Main study outcomes included: demographic characteristics (sex, age, country of residence); prior medical conditions and treatments; previous infection by SARS-CoV-2, if any; date and type of SARS-CoV-2 vaccine which was administered. We assessed the occurrence of side-effects, of a lupus flare or incident COVID-19 after vaccination, according to the patients' perspective. Participants were asked to rate the intensity of side-effects as absent, minor, moderate or severe (the latter being defined as symptoms affecting the ability to do daily activities). The VACOLUP questionnaire is shown in the appendix.

Commentato [MP2]: Are these the study variables or patients characteristics?

Commentato [MP3]: These look as the study outcomes

Statistics

Qualitative variables were described using numbers and percentages and quantitative variables as medians and the 25th-75th percentile interquartile range (IQR). The association between side effects and other study parameters was assessed using the relative risk (RR) and its 95% confidence interval (95%CI) when appropriate. Comparisons between groups were performed using the Chi-squared test, exact Fisher's test or logistic regression when appropriate. A p-value < 0.05 was considered as statistically significant and all tests were 2-sided. Statistical analysis was performed using JMP 13 (SAS institute, Cary, USA).

Results

Study participants

The study included 696 participants (669 [96.1%] women and 27 [3.9%] men) from 29 countries, with a median age of 42 years (IQR: 34-51). The detailed patient characteristics are shown in Table 1. The type of COVID-19 vaccines administered and the occurrence of side-effects following vaccination (as self-reported by patients) are summarized in table 2. All patients received at least one dose of vaccine and 343 (49.3%) received a second dose (figure 1). The most common vaccines were those from Pfizer-BioNTech (57.3% of participants), Sinovac (22.4%), Astra-Zeneca (10.5%) and Moderna (8.2%).

Frequency of side-effects, as reported by SLE patients

Side-effects were reported by 316 patients (45.4%) after the first dose and by 181 (52.8%) after the second dose, with no difference according to gender (p=0.11), age (p=0.08) or vaccine type (mRNA vaccines versus other modes of action, p=0.69). Patients who reported side-effects after the first dose were more likely to report side-effects after the second dose (RR=2.30 [IC95%: 1.88-2.82], p<0.0001). The occurrence of side-effects by country and vaccine brand is shown in the supplementary table.

Type and severity of side effects, as reported by SLE patients

The type and intensity of side effects reported by SLE patients are shown in figure 2. The symptoms were minor or moderate in intensity (i.e., without consequence on the ability to perform daily tasks) in more than 80% of cases. Taking into account all vaccine doses (n=1039), side-effects led to a medical consultation in 81 cases (7.8%), to an Emergency Room consultation in 14 cases (1.3%) and to a hospitalization in 5 cases (0.5%, including 4 for a SLE flare).

A total of 21 patients (3.0%) reported a medically-confirmed SLE flare (table 2), typically with predominant musculoskeletal symptoms (90.5%) and fatigue (85.7%), after a median delay of 0 day (IQR: 0-1) following COVID-19 vaccination. Those flares led to change in lupus treatment in 15/21 cases

Commentato [MP4]: Any difference between 1st and 2nd dose?

and to a hospitalization in 4 cases. Having experienced a flare in the year prior to vaccination was associated with an increased risk of SLE flare following COVID vaccination (RR=5.52 [2.17-14.03], p<0.0001). Also, patients with a confirmed history of COVID-19 were more likely to report a lupus flare following vaccination (RR=4.72 [1.68-13.24], p=0.002).

Discussion

The VACOLUP study about the safety and efficacy of anti-SARS-CoV-2 vaccines in SLE patients has included 696 participants with SLE from 29 countries and represents the first large-scale data in this population. One of the main findings of the VACOLUP study is that side-effects following SARS-CoV-2 vaccination in SLE are common but do not impair daily functioning in a vast majority of cases. Also, there was no difference in the occurrence of side effects following mRNA vaccines versus other modes of action (RR: 0.96 [95%CI: 0.81-1.14], p=0.69), which is another important and reassuring finding. Finally, the number of medically-confirmed flares reported following SARS-CoV-2 vaccination was low (3.0%) while the very short median delay between vaccination and flare onset suggests that it might be difficult to distinguish actual lupus flares from common and expected post-vaccine side-effects and therefore that the 3% figure is likely an overestimation. Nevertheless, having experienced a SLE flare during the year prior to vaccination was associated with an increased risk of reported flare following COVID vaccination (RR=5.52 (2.17-14.03], p<0.0001). This should encourage clinicians to recommend vaccination only in quiescent patients. In terms of efficacy, it is interesting to note that no patient has reported COVID-19 following vaccination, whereas the majority of our patients were treated with immunosuppressants. This finding should however be interpreted with caution due to the study design. The main limitation of our study is obviously the self-reported nature of the data. However, we tried control for this by asking patients to report only medically-confirmed flares.

Conclusion

Altogether, the VACOLUP study suggests that the benefit-risk ratio of COVID-19 vaccination appears largely favorable in SLE, with only a minimal risk of flare, if any, including following the use of mRNA vaccines. As previously highlighted, the willingness to get vaccinated against COVID-19 in patients with autoimmune diseases is limited by the fear of side effects and the lack of available data[5]. Disseminating these reassuring data may therefore prove crucial to increase vaccine coverage in SLE patients.

REFERENCES

1. Vaccines – COVID19 Vaccine Tracker [Internet]. [cited 2021 May 27]. Available from: https://covid19.trackvaccines.org/vaccines/

2. Ramasamy MN, Minassian AM, Ewer KJ, Flaxman AL, Folegatti PM, Owens DR, et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. Lancet Lond Engl. 2021 Dec 19;396(10267):1979–93.

3. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med. 2020 Dec 31;383(27):2603–15.

4. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. N Engl J Med. 2021 Feb 4;384(5):403–16.

5. Felten R, Dubois M, Ugarte-Gil MF, Chaudier A, Kawka L, Bergier H, et al. Cluster analysis reveals 3 main patterns of behavior towards SARS-CoV-2 vaccination in patients with autoimmune and inflammatory diseases. Rheumatol Oxf Engl. 2021 May 13;

Figure 1. Flow chart

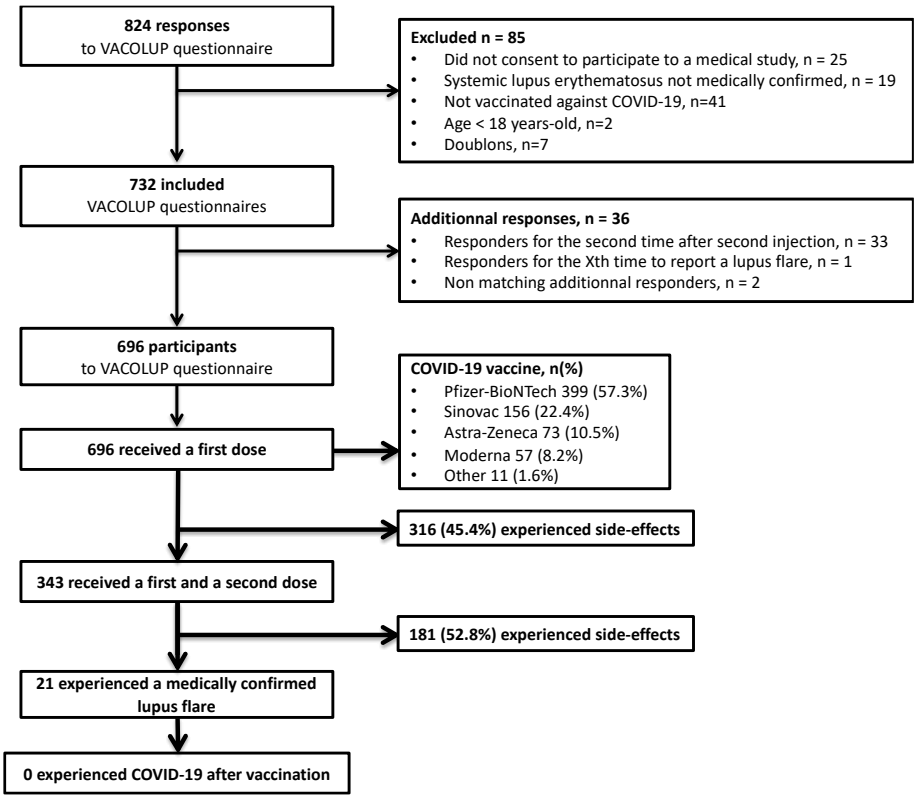


Table 1. Patient characteristics

	Patients
N	696
Age (years), median [IQR25-75]	42 [34-51]
Female, n (%)	669 (96.1%)
Male, n (%)	27 (3.9%)
Country, n (%)	
Italy	247 (35.5%)
Chile	190 (27.3%)
France	88 (12.6%)
USA	60 (8.6%)
UK	31 (4.5%)
Uruguay	14 (2.0%)
Other*	66 (9.5%)
Prior SLE manifestations, n (%)	n=695
Malar skin rash	301 (43.3%)
Discoid skin rash	134 (19.3%)
Photosensitivity	489 (70.4%)
Oral ulcers attributed to lupus	237 (47.1%)
Inflammatory joint pain / Arthritis	630 (90.7%)
Pleuritis or Pericarditis	188 (27.1%)
Lupus nephritis (renal involvement due to lupus)	240 (34.5%)
Lupus seizure or psychosis	61 (8.8%)
Lupus treatments, n(%)	
Oral glucocorticoids	373 (53.6%)
Hydroxychloroquine / Chloroquine	542 (77.9%)
Immunosuppressive agents: Methotrexate / Leflunomide / Mycophenolate / Azathioprine / Cyclophosphamide	347(49.9%)
Belimumab (intravenous or subcutaneous)	76 (10.9%)
Rituximab	22 (3.2%)
Lupus flare during the past year, Yes, n (%)	217 (31.2%)
Lupus flare at the time of COVID vaccination, n (%)	49 (7.0%)
COVID-19 since the beginning of the pandemic before vaccination, Yes, n (%)	33 (4.7%)

* Other countries: Spain n=12, Canada n=9, Mexico n=7, Australia n=5, Belgium n=5, Argentina n=3, Finland n=3, Austria n=2, United Arab Emirates n=2, Germany n=2, Peru n=2, Venezuela n=2, Bolivia n=1, Colombia n=1, Denmark n=1, Dominican Republic n=1, El Salvador n=1, Guatemala n=1, Ireland n=1, Israel n=1, Netherlands n=1, Nigeria n=1, Philippines n=1, Poland n=1.

Table 2. COVID-19 vaccination and consequences

	Patients
Vaccination, n (%)	
First dose	696 (100%)
First and second dose	343 (49.3%)
COVID vaccine, n (%)	
Pfizer-BioNTech	399 (57.3%)
Sinovac	156 (22.4%)
Astra-Zeneca	73 (10.5%)
Moderna	57 (8.2%)
Other*	11 (1.6%)
Side effects after first COVID vaccine dose, n (%)	316 (45.4%)
Timing of onset of side effects after first dose, in days, median [IQR25-75]	0 [0-1]
Side effects after second COVID vaccine dose, n (%)	181 (52.8%)
Timing of onset of side effects after second dose, in days, median [IQR25-75]	0 [0-1]
Consultations/hospitalizations for side-effects (1st and 2nd doses together), n (%)	1039
Medical consultation	81 (7.8%)
Emergency consultation	14 (1.3%)
Hospitalization	5 (0.5%)
Lupus flare following vaccination, n (%)	21 (3.0%)
Lupus flare manifestations, n (%)	21
Fever (Temperature > 38°C / 100.4°F)	10 (47.6%)
Cutaneous (skin) flare (medically confirmed)	12 (57.1%)
Musculoskeletal symptoms (joint, arthritis, arthralgia, myalgia) (medically confirmed)	19 (90.5%)
Pleuritis / pleurisy (medically confirmed)	1 (4.8%)
Pericarditis (medically confirmed)	1 (4.8%)
Renal involvement (medically confirmed)	2 (9.5%)
Neuro-psychiatric manifestations (medically confirmed)	0
Cytopenia (anemia, thrombopenia, leucocytopenia) (medically confirmed)	8 (38.1%)
Low complement (medically confirmed)	5 (23.8%)
Increase in anti-dsDNA antibody titer (medically confirmed)	7 (33.3%)
Fatigue	18 (85.7%)
Lupus flare consequences, n (%)	21
Lupus treatment modification	15 (71.4%)
Medical consultation	21 (100%)
Hospitalization	4 (19.1%)
COVID-19 after vaccination	0

*Other vaccines: Cansino (n=1), Curevac (n=1), Janssen (n=5), Sinopharm (n=2), Sputnik V (n=1), Unknown (n=1).

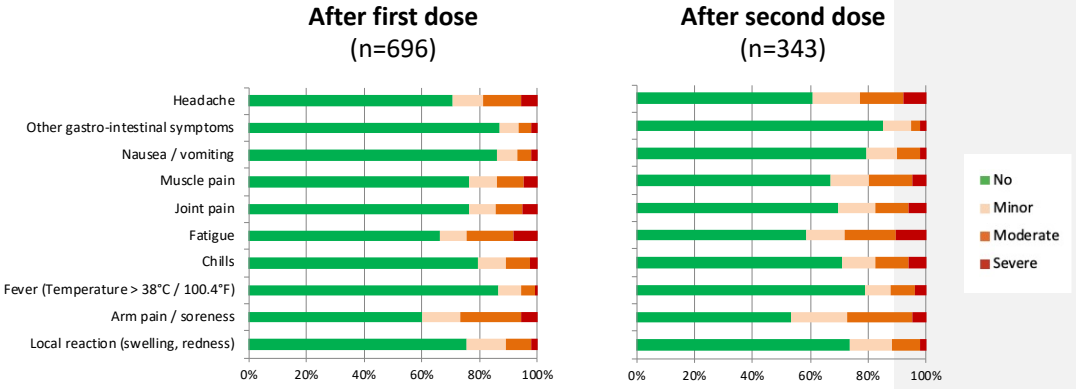
Supplementary Table. Side effects and SLE flare according to countries and COVID vaccines

	Side effects after first dose of vaccine	Side effects after second dose of vaccine	SLE flare
Country*, n (%)			
Italy (n=247)	96 (38.9%)	76 (56.7%)	1 (0.4%)
Chile (n=190)	81 (42.6%)	39 (40.6%)	5 (2.6%)
France (n=88)	28 (31.8%)	17 (48.6%)	1 (1.1%)
USA (n=60)	40 (66.7%)	30 (76.9%)	7 (11.7%)
UK (n=31)	26 (83.9%)	6 (75%)	2 (6.5%)
Uruguay (n=14)	3 (21.4%)	1 (11.1%)	0
Spain (n=12)	7 (58.3%)	5 (83.3%)	1 (8.3%)
Canada (n=9)	6 (66.7%)	0	0
Mexico (n=7)	5 (71.4%)	0	2 (28.6%)
Australia (n=5)	4 (80.0%)	1 (100%)	1 (20.0%)
Belgium (n=5)	4 (80.0%)	0	0
COVID vaccine, n (%)			
Pfizer-BioNTech	169 (42.4%)	127 (57.2%)	8 (5.5%)
Sinovac	59 (37.8%)	27 (33.8%)	4 (2.6%)
Astra-Zeneca	47 (64.4%)	1 (20.0%)	4 (5.5%)
Moderna	35 (61.4%)	24 (80.0%)	5 (8.8%)
Janssen (n=5)	3 (60%)	-	0
Sinopharm (n=2)	0	1 (100%)	0
Cansino (n=1)	1 (100%)	0	0
Curevac (n=1)	0	0	0
Sputnik V (n=1)	1 (100%)	1 (100%)	0
Unknown (n=1)	1 (100%)	0	0

* Countries with at least 5 participants

Figure 2. Type and intensity of side effects after COVID-19 vaccination

Cumulative plot showing the proportion of minor, moderate and severe reaction for each adverse event (As self-reported by patients, with severe manifestations defined as affecting the ability to do daily activity)



Appendix (VACOLUP questionnaire)

VACOLUP (Tolerance and consequences of VAccination against COVID-19 in LUPus patients)

Thank you for your participation in this study, which aims to assess the tolerance and consequences of vaccination against COVID-19 in SLE (systemic lupus erythematosus) patients.

The purpose of this questionnaire is to identify the potential side effects of the COVID vaccination in lupus patients and to provide all lupus patients throughout the world with a regularly updated summary.

Participation in this survey is anonymous and takes approximately 10 minutes.

The information collected in the questionnaire is anonymous and recorded in a computerized file by Renaud FELTEN and Laurent ARNAUD for the Rheumatology Department of Strasbourg & the National Reference Center for Rare Systemic Autoimmune Diseases (RESO). The legal basis of the treatment is the consent.

The data collected will be communicated to the following recipients only: Renaud FELTEN and Laurent ARNAUD for the Rheumatology Department of Strasbourg & the National Reference Center for Rare Systemic Autoimmune Diseases (RESO). They are kept for the duration of the study.

You can access your data, rectify them, request their deletion or exercise your right to limit the processing of your data. You may withdraw your consent to the processing of your data at any time.

Consult the cnil.fr website for more information on your rights.

To exercise these rights or if you have any questions about the processing of your data in this device, you can contact:

Dr Renaud FELTEN

Rheumatology Department of Strasbourg

1 avenue Molière

67098 STRASBOURG Cedex

1. **I am answering this 'VACOLUP' survey...***

for the first time

for the second time AFTER second INJECTION of COVID-vaccine

for the Xth time to report a lupus flare which occured since I filled-in the questionnaire for the first time

to report a medically confirmed COVID-19 after vaccination

2. **I am***

a man

a woman

non-binary

Other…

3. **How old are you? (e.g 34)***

4. **In which country do you live?***

5. **When did you get the FIRST INJECTION of the vaccination against COVID-19? (this question will be asked again later in the questionnaire for verification purposes)**

Day, month, year

6. **How did you hear about this survey?**

via Internet / Twitter

via a patient association

via my doctor

via a relative / family member / friend

Other…

7. **Do you agree to the use of your data for medical research purposes?***

Yes

No

8. **DO YOU HAVE A MEDICALLY-CONFIRMED DIAGNOSIS OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)? (excluding Cutaneous Lupus Erythematosus (CLE), lupus-like disease, incomplete lupus, drug-induced lupus, SLE suspicion only).***

Yes

No

9. **Since the beginning of the pandemic, have you contracted the SARS-CoV-2 / COVID (medically confirmed infection)?**

Yes

No

I am not sure

10. **Did you get the vaccination against COVID-19?***

Yes

No

11. **Which of the following symptoms have you ever experienced during the follow-up of your LUPUS?***

	Yes	No	I am not sure
Malar skin rash			
Discoid skin rash			
Photosensitivity			
Oral ulcers attributed to lupus			
Inflammatory joint pain / Arthritis			
Pleuritis or Pericarditis			
Lupus nephritis (renal involvment due to lupus)			
Lupus seizure or psychosis			
Hematologic Disorder due to lupus (Anemia OR Leukopenia OR Lymphopenia OR Thrombocytopenia			
Positive Anti-dsDNA and/or Anti-Sm and/or antiphospholipid antibodies			
Positive Antinuclear Antibody			

12. **Which of the following treatments were you taking for your lupus at the time of your COVID-19 vaccination?***

Yes No

Oral glucocorticoids (prednisone / prednisolone)?

Hydroxychloroquine PLAQUENIL / Chloroquine NIVAQUINE

IMMUNOSUPPRESSIVE AGENTS: Methotrexate / Leflunomide / Mycophénolate (e.g Cellcept) / Azathioprine (Imuran)

Cyclophosphamide (intravenous)

Belimumab BENLYSTA (intravenous or subcutaneous)

Rituximab

13. **Did you have a MEDICALLY CONFIRMED lupus flare during the past 12 months?**

Yes

No

I am not sure

14. **Did you have a medically confirmed lupus flare at the time of your vaccination against COVID-19?**

Yes

No

I am not sure

15. **Which vaccine did you get?***

Pfizer–BioNTech COVID-19 vaccine

Moderna COVID-19 vaccine

Oxford–AstraZeneca COVID-19 vaccine

Gam-COVID-Vac (Sputnik V)

BBIBP-CorV (Sinopharm)

CoronaVac (Sinovac)

Ad5-nCoV (Convidicea)

EpiVacCorona [ru]

BBV152 (Covaxin)

Ad26.COV2.S (Janssen Pharmaceutica [Johnson & Johnson])

NVX-CoV2373 (Novavax)

ZF2001 (RBD-Dimer)

Zorecimeran (CVnCoV) (CureVac)

ZyCoV-D (Cadila Healthcare)

I do not know

Other…

16. **When did you get the FIRST INJECTION of the COVID vaccine?***

Day, month, year

17. **Did you experiment any side effects after FIRST INJECTION injection of the COVID vaccine?***

Yes

No

Side effects after the FIRST INJECTION of the vaccination against COVID-19?

18. **What kind of side effects did you experiment after the FIRST INJECTION of the vaccination against COVID-19? (Which intensity?)***

No Minor Moderate Severe (= affecting your ability to do daily activities)

Local reaction (swelling, redness)

Arm pain / soreness

Fever (Temperature > 38°C / 100.4°F)

Chills

Fatigue

Joint pain

Global muscle pain

Nausea / vomiting

Other gastro-intestinal symptoms (pain, diarrhea,...)

Headache

19. **Did you experiment other symptoms after the FIRST INJECTION of the vaccination against COVID-19?**

When did the side effects begin?

Day, month, year

20. **Did you consult a doctor because of any of those symptoms?***

Yes

No

21. **Did you go to the emergency because of any of those symptoms?***

Yes

No

22. **Were you hospitalized because of any of those symptoms?***

Yes

No

23. **Did you also get the SECOND INJECTION of the COVID vaccine?***

Yes

No

24. **If yes, when did you get the SECOND INJECTION of the COVID vaccine?**

Day, month, year

25. **Did you experiment any side effects after the SECOND INJECTION of the COVID vaccine?***

Yes

No

26. **What kind of side effects did you experiment after the SECOND INJECTION of the vaccination against COVID-19? (Which intensity?)***

No Minor Moderate Severe (= affecting your ability to do daily activities)

Local reaction (swelling, redness)

Arm pain / soreness

Fever (Temperature > 38°C / 100.4°F)

Chills

Fatigue

Joint pain

Global muscle pain

Nausea / vomiting

Other gastro-intestinal symptoms (pain, diarrhea,...)

Headache

27. **Did you experiment other symptoms after the SECOND INJECTION of the vaccination against COVID-19?**

When did the side effects begin?

Day, month, year

28. **Did you consult a doctor because of any of those symptoms?***

Yes

No

29. Did you go to the emergency because of any of those symptoms?*

Yes

No

30. Were you hospitalized because of any of those symptoms?*

Yes

No

31. Did you experience a MEDICALLY CONFIRMED LUPUS FLARE following the vaccination?*

Yes

No

Yes but not medically confirmed

I don't know

32. Date of the beginning of your lupus flare following the COVID-19 vaccination*

Day, month, year

33. What kind of symptoms of lupus flare did you experiment AFTER COVID-19 vaccination?*

No I am not sure Yes

Fever (Temperature > 38°C / 100.4°F)

Cutaneous (skin) flare (medically confirmed)

Muskuloskeletal symptoms (joint, arthritis, arthralgia, myalgia) (medically confirmed)

Pleuritis / pleurisy (medically confirmed)

Pericarditis (medically confirmed)

Renal involvement (medically confirmed)

Neuro-psychiatric manifestations (medically confirmed)

Cytopenia (anemia, thrombopenia, leucocytopenia) (medically confirmed)

Low complement (medically confirmed)

Increase in anti-dsDNA antibody titer (medically confirmed)

Fatigue

Other symptoms

34. Did you consult your doctor because of your LUPUS flare?*

Yes

No

35. Did you modify your treatment because of your LUPUS flare?*

Yes by myself

Yes after a medical consultation

No

36. Were you hospitalized because of your LUPUS flare?*

Yes

No

37. How was your COVID-19 AFTER COVID vaccine confirmed?

By RT-PCR nasopharyngeal test

By rapid COVID-19 nasopharyngeal test

By salivary test

I am not sure

38. Which vaccine did you get?*

Pfizer–BioNTech COVID-19 vaccine

Moderna COVID-19 vaccine

Oxford–AstraZeneca COVID-19 vaccine

Gam-COVID-Vac (Sputnik V)

BBIBP-CorV (Sinopharm)

CoronaVac (Sinovac)

Ad5-nCoV (Convidicea)

EpiVacCorona [ru]

BBV152 (Covaxin)

Ad26.COV2.S (Janssen Pharmaceutica [Johnson & Johnson])

NVX-CoV2373 (Novavax)

ZF2001 (RBD-Dimer)

Zorecimeran (CVnCoV) (CureVac)

ZyCoV-D (Cadila Healthcare)

I do not know

Other…

39. When did you get the FIRST INJECTION of the COVID vaccine?*

Day, month, year

40. Did you get a SECOND INJECTION of the COVID vaccine?*

Yes

No

41. If yes, when did you get the SECOND INJECTION of the COVID vaccine?

Day, month, year

42. When did you infected by the COVID?

Day, month, year

43. How was your COVID-19 medically managed?

At home

Hospitalization in standard care with no need for oxygen

Hospitalization in standard care with a need for oxygen

Hospitalization in ICU

End of the survey...

Thank you very much for your kind participation.

As specified at the beginning, the purpose of this questionnaire is to identify the potential side effects of the COVID vaccination in lupus patients and to provide all lupus patients throughout the world with a regularly updated summary.

You can therefore access a brief summary of previous participations by following this link:

www.maladie-autoimmune.fr/vacolup/ (this data will be updated regularly).

Should you have a lupus outbreak as a result of your vaccination, even though you have already completed this questionnaire, we will give you the opportunity to answer again. To do so, you will have to answer the first question: "I am answering this survey to report a lupus flare which occured since I filled-in the questionnaire for the first time". Then all you have to do is re-enter your gender, age and country and fill in the description of your lupus flare.

Renaud FELTEN and Laurent ARNAUD for the Rheumatology Department of Strasbourg & the National Reference Center for Rare Systemic Autoimmune Diseases (RESO)