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GFEV | GROUPE FRANÇAIS
D'ÉTUDE DES
VASCULARITES

Sévérité de la Covid-19 et efficacité vaccinale au cours des vascularites

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Médecine interne Cochin
Journée du GFEV
21/10/2021

Trois principales questions

- **Quelle sévérité de l'infection chez les patients atteints de vascularites?**
- **Quelle réponse vaccinale en fonction des traitements?**
- **Quelle tolérance du vaccin dans cette population de patients?**

Population à risque de formes sévères d'infection

CLINICAL SCIENCE

Severity of COVID-19 and survival in patients with rheumatic and inflammatory diseases: data from the French RMD COVID-19 cohort of 694 patients

FAI²R /SFR/SNFM/ISOFREMIP/CRI/IMIDIATE consortium and contributors

7-8% de patients atteints de vascularites

24% à 46% d'hospitalisation

9 à 13% de formes sévères

CLINICAL SCIENCE

Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry

Milena Gianfrancesco,¹ Kimme L Hyrich,^{2,3} Sarah Al-Adely,^{2,3} Loreto Carmona,⁴

Table 2 Association between demographic and clinical characteristics and severity of COVID-19

	All patients (n=694)	Patients with mild infection (n=438)	Patients with moderate infection (n=169)	Patients with severe infection (n=87)	OR (95% CI)*	P value	aOR (95% CI)*†	P value†
Disease history§						<0.001		0.023
Chronic inflammatory arthritis	464 (66.9)	325 (74.2)	97 (57.4)	42 (48.3)	1.00 (ref.)	—	1.00 (ref.)	—
Autoinflammatory diseases	12 (1.7)	5 (1.1)	4 (2.4)	3 (3.4)	3.66 (0.89–12.07)	0.053	7.88 (1.39–37.05)	0.014
Vasculitis	65 (9.4)	21 (4.8)	22 (13.0)	22 (25.3)	5.14 (2.80–9.32)	<0.001	2.25 (1.13–4.41)	0.020
Systemic autoimmune diseases	122 (17.6)	73 (16.7)	35 (20.7)	14 (16.1)	1.33 (0.69–2.45)	0.38	1.64 (0.80–3.25)	0.17

Population à risque de formes sévères d'infection

Table 4 Multivariable analyses for disease severity

Variable	Imputed analysis* (n=694)			Available case analysis (n=601)		
	n/N	OR (95% CI)	P value	n/N	OR (95% CI)	P value
Age (years)	87/694	1.08 (1.05–1.10)	<0.001	73/601	1.08 (1.05–1.10)	<0.001
Female gender	44/462	0.45 (0.25–0.80)	0.007	37/395	0.43 (0.24–0.78)	0.005
BMI	87/694	1.07 (1.02–1.12)	0.006	73/601	1.07 (1.02–1.12)	0.007
Hypertension	51/182	1.86 (1.01–3.42)	0.047	42/162	1.83 (0.99–3.37)	0.054
Corticosteroids	51/216	1.97 (1.09–3.54)	0.024	45/188	2.04 (1.13–3.67)	0.018
Mycophenolate mofetil/mycophenolic acid	3/16	6.60 (1.47–29.62)	0.014	3/14	6.51 (1.45–29.23)	0.015
Rituximab	11/34	4.21 (1.61–10.98)	0.003	10/32	4.60 (1.75–12.11)	0.002

French RMD Cohort, ARD, 2020

Table 3 Unadjusted and adjusted logistic regression models examining the association between demographic and clinical characteristics and COVID-19 hospitalisation status

Rheumatic disease medication prior to COVID-19 diagnosis§				
No DMARD	52/97 (54)	Ref	Ref	--
csDMARD only	249/272 (55)	1.05 (0.66 to 1.67)	1.23 (0.70 to 2.17)	0.48
b/tsDMARDs only	31/107 (29)	0.35 (0.20 to 0.63)	0.46 (0.22 to 0.93)	0.03
csDMARD+b/tsDMARD combination therapy	45/124 (36)	0.49 (0.29 to 0.85)	0.74 (0.37 to 1.46)	0.38
NSAIDs	39/111 (35)	0.55 (0.35 to 0.84)	0.64 (0.39 to 1.06)	0.08
Prednisone-equivalent glucocorticoids				
None	162/403 (40)	Ref	Ref	--
1–9 mg/day	67/125 (54)	1.72 (1.15 to 2.57)	1.03 (0.64 to 1.66)	0.91
≥10 mg/day	43/64 (67)	3.05 (1.74 to 5.32)	2.05 (1.06 to 3.96)	0.03

Global Rheumatology Alliance, ARD, 2020

Population à risque augmenté de décès

EPIDEMIOLOGICAL SCIENCE

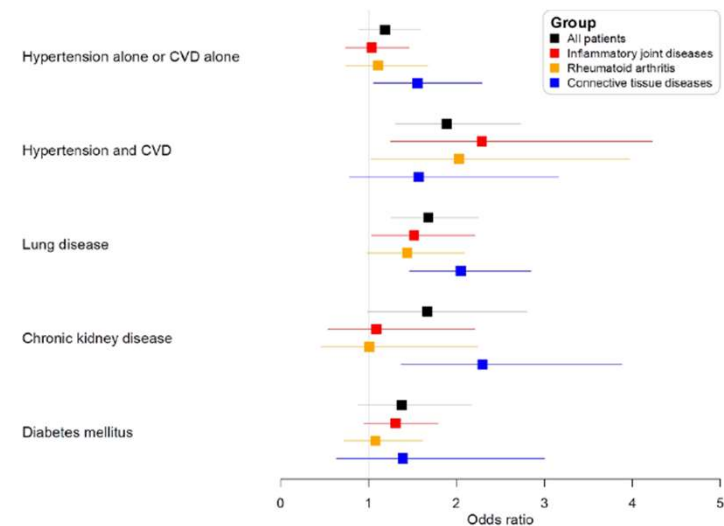
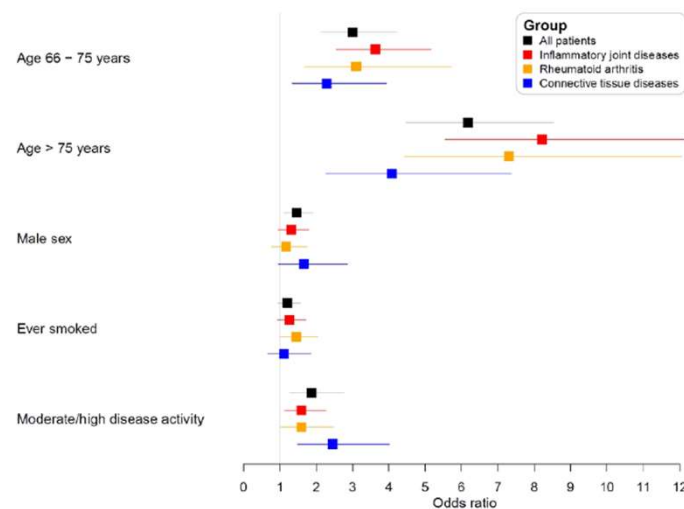
Factors associated with COVID-19-related death in people with rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance physician-reported registry

3729 patients

8,7% de patients atteints de vascularites

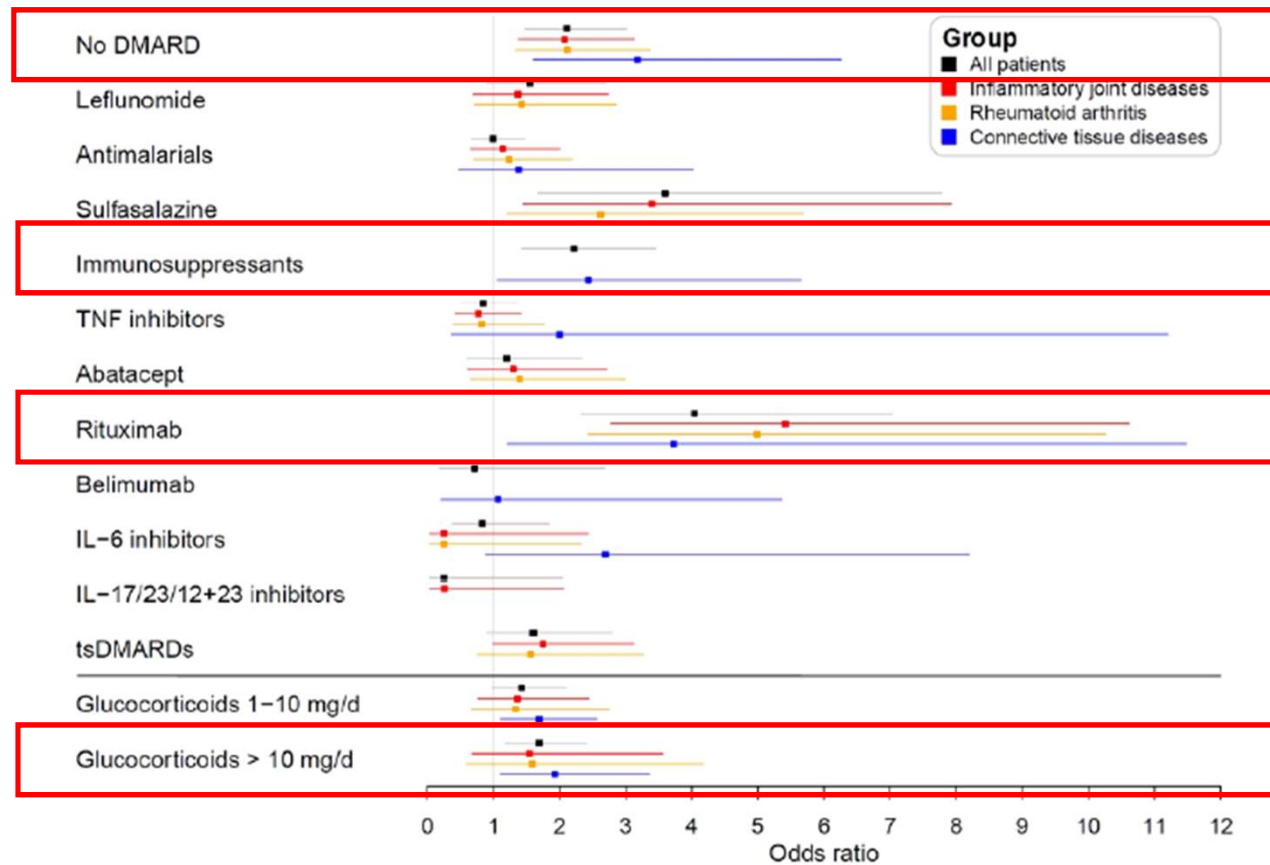
10,5% de mortalité globale

20% de mortalité parmi les patients avec vascularite

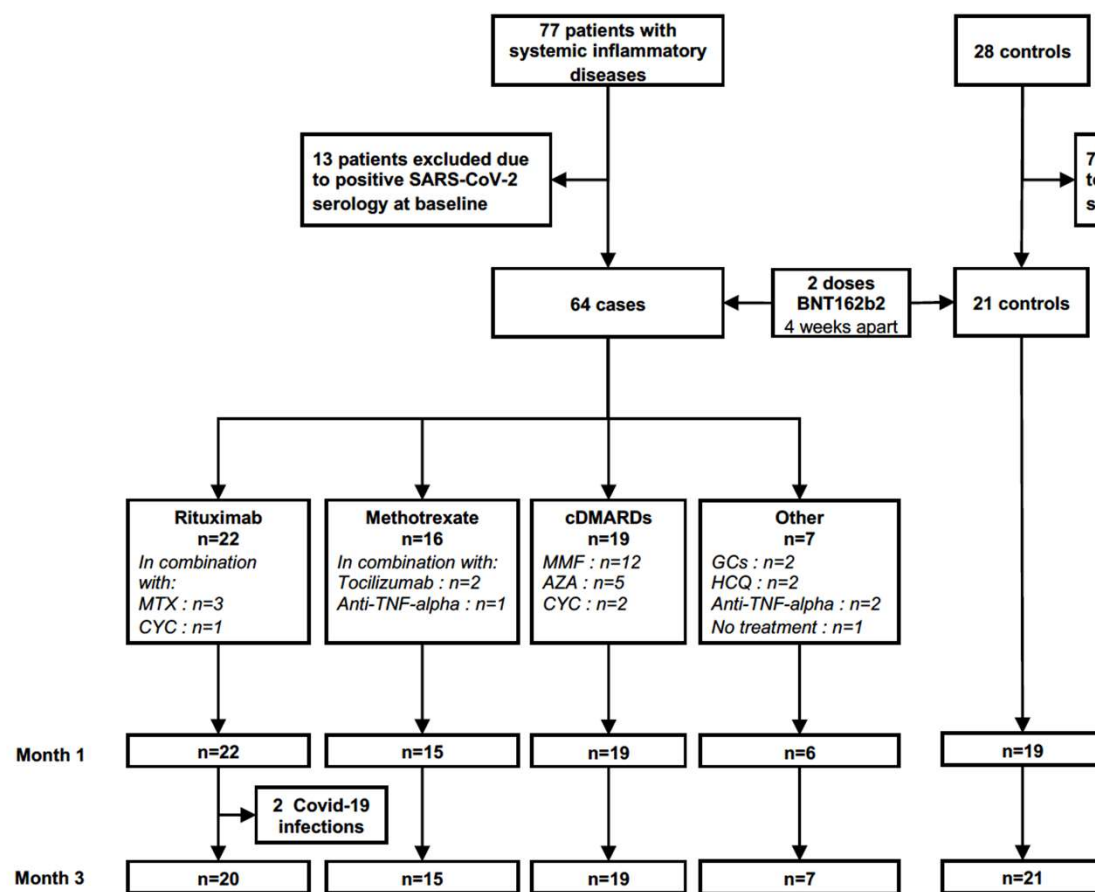


Population à risque augmenté de décès

Comparaison avec MTX seul



Réponse vaccinale chez la patients avec vascularites : étude COVADIS

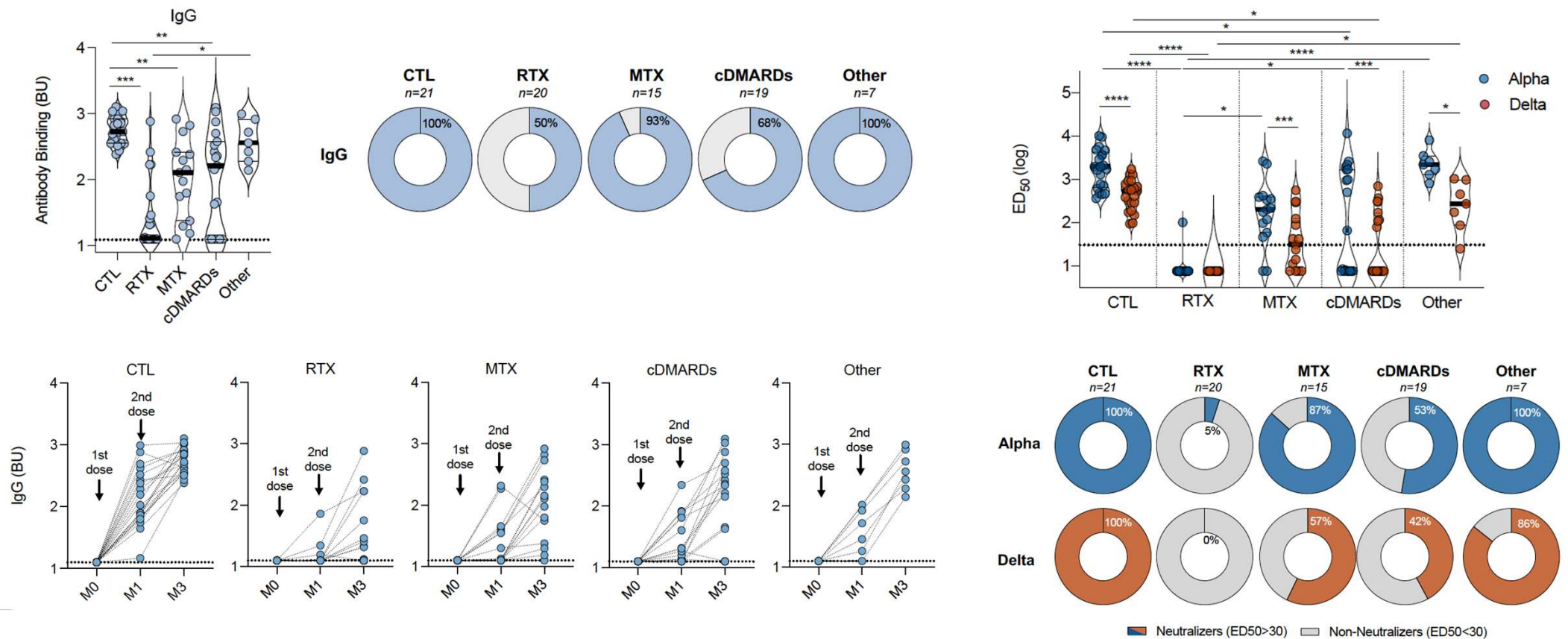


40% de patients avec vascularite

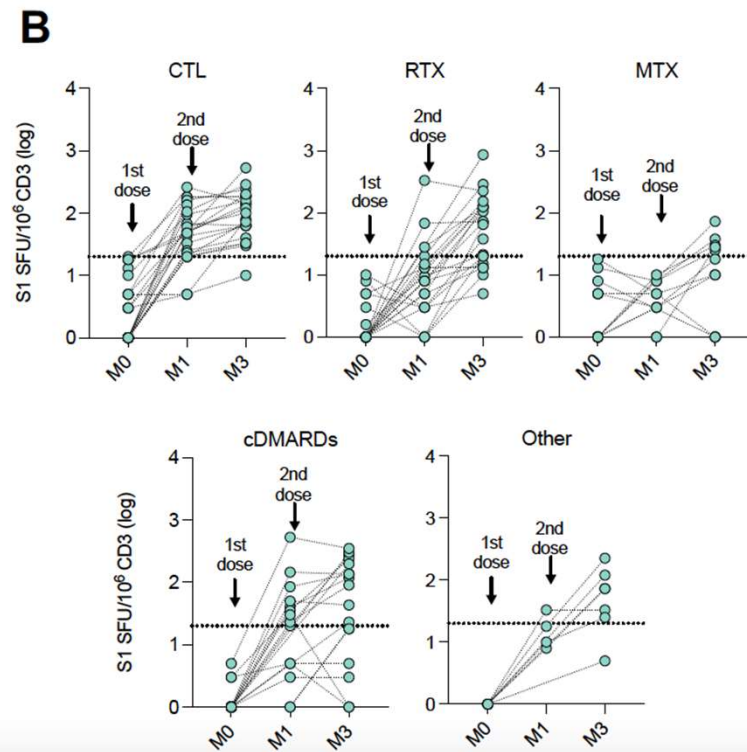
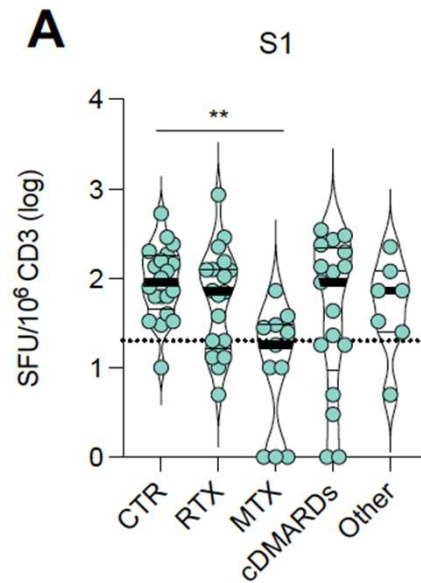
Analyse de la réponse humorale :
Production d'anticorps anti-Spike
Neutralisation des virus Alpha et Delta

Analyse de la réponse cellulaire :
Elispot IFNgamma

Le rituximab impact sévèrement la réponse humorale



Le méthotrexate impact sévèrement la réponse cellulaire

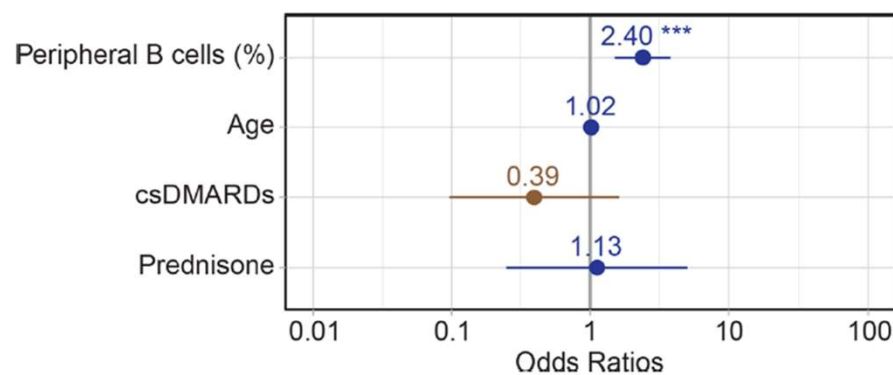
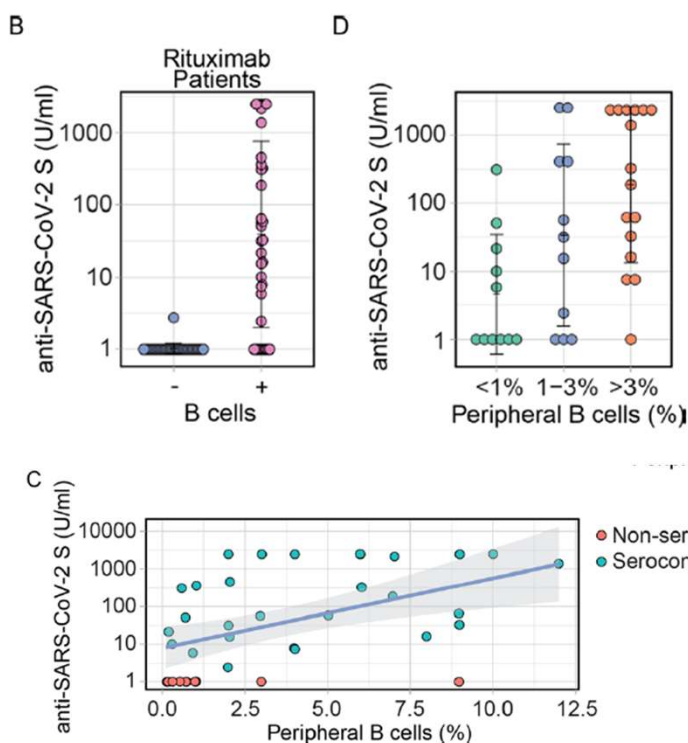


Facteurs associés avec une seroconversion chez les patients sous Rituximab

CLINICAL SCIENCE

SARS-CoV-2 vaccination in rituximab-treated patients: B cells promote humoral immune responses in the presence of T-cell-mediated immunity

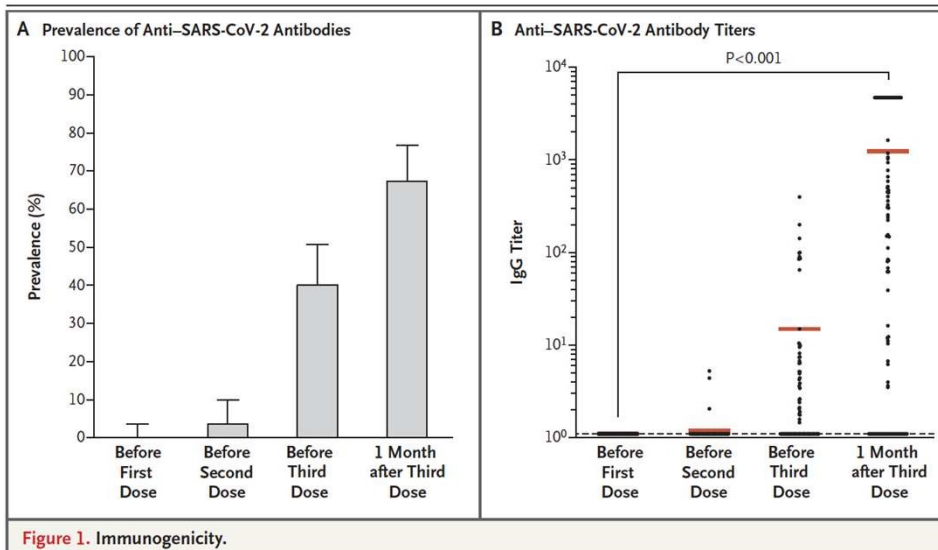
Daniel Mrak ¹, Selma Tobudic ², Maximilian Koblichke ³, Marianne Graninger ³, Helga Radner ¹, Daniela Sieghart ¹, Philipp Hofer ⁴, Thomas Perkmann ⁵, Helmuth Haslacher ⁵, Renate Thalhammer ⁵, Stefan Winkler ², Stephan Blüml ¹, Karin Stiasny ³, Judith H Aberle ³, Josef S Smolen ¹, Leonhard X Heinz ¹, Daniel Aletaha ¹, Michael Bonelli ¹



Quelles solutions pour améliorer la protection?

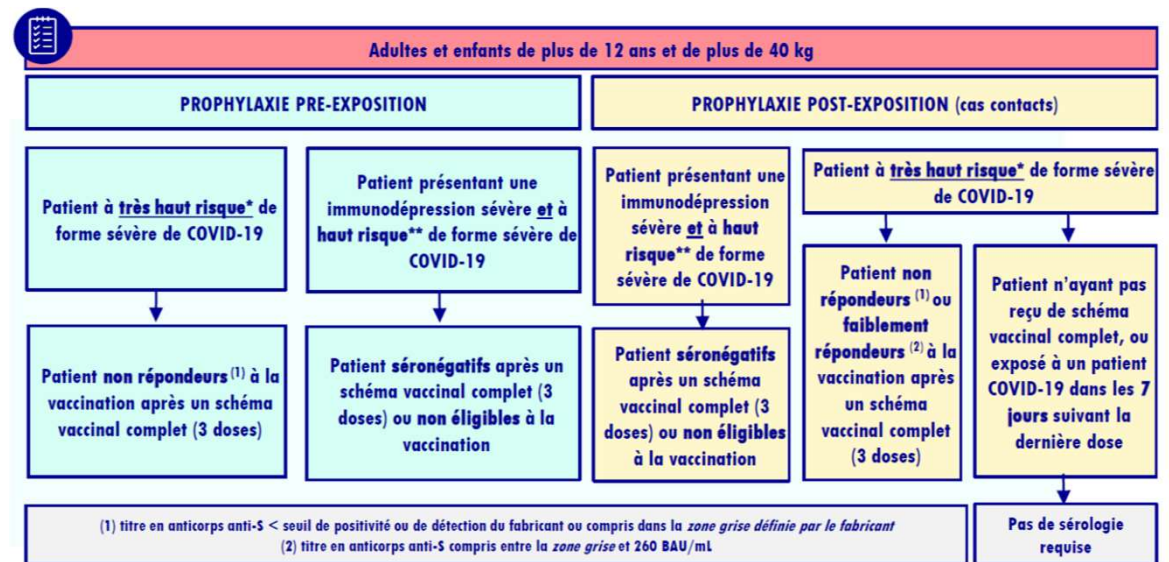
1) Le boost

Intérêt démontrer chez les transplantés d'organe



Kamar et al., NEJM, 2021

2) Anticorps monoclonaux prophylactiques



Quelle tolerance des vaccins?

Etude Covadis : 4 patients (6,3%) ont eu une poussée de la maladie dans les 3 mois post vaccination

Adverse event	After the first vaccine dose		After the second vaccine dose				
	Controls n=121	AIIRD n=673	Controls n=121	AIIRD n=670			
Local reactions, n (%)							
Pain	69 (57.02)	377 (56.02)	51 (42.5)	314 (46.87)			
Erythema	4 (3.31)	12 (1.78)	6 (5)	10 (1.49)*			
Swelling	6 (4.69)	18 (2.68)	6 (5)	15 (2.24)			
Pruritus	3 (2.48)	8 (1.19)	2 (1.67)	4 (0.6)			
Tingling	7 (5.79)	3 (0.45)**	1 (0.83)	0			
Systemic reactions, n (%)							
Fever $\geq 38.0^{\circ}\text{C}$	1 (0.83)	8 (1.19)	6 (4.96)	35 (5.24)			
Nausea	0	7 (1.04)	2 (1.67)	14 (2.09)			
Vomiting	1 (0.83)	3 (0.45)	0	1 (0.15)			
Rhinorrhea	3 (2.48)	0 *	0	1 (0.15)			
Cough	1 (0.83)	2 (0.3)	0	1 (0.15)			
Myalgia	5 (4.13)	25 (3.71)	21 (17.36)	63 (9.4)*			
Arthralgia	1 (0.83)	23 (3.42)	6 (4.96)	49 (7.32)			
Chills	2 (1.65)	13 (1.93)	21 (17.36)	60 (8.96)*			
Malaise	1 (0.83)	13 (1.93)	21 (17.36)	53 (7.91)*			
Headache	7 (5.97)	47 (6.98)	18 (14.88)	85 (12.69)			
Allergic reaction	0	0	0	1 (0.15)			
Lethargy	6 (4.96)	36 (5.35)	10 (8.26)	96 (13.49)			
Worsening of rheumatological symptoms	NA	17 (2.53)	NA	12 (1.79)			
Other symptoms, n							
Dizziness	2	Throat pain	5	Weakness	5	Weakness	10
Numbness	1	Arm numbness	5	Dizziness	1	Dizziness	11
Throat pain	1	Dizziness	4	Numbness	3	Throat pain	6
Chest pain	1	Weakness	4	Facial pain	1	Excessive sweating	3
		Rash	2	Chest pain	2	Pericarditis	1
		Flu-like	2			Chest pain	1
		Diarrhoea	2			Local lymphadenopathy	2
		Pruritus	2			Vaginal bleeding	2
		Palpitations	2			Lack of appetite	2
		Uveitis	1			Diarrhoea	2
		Herpes Labialis	1			High blood pressure	2
		Other	3			Herpes zoster	6
						Uveitis	2
						Other	7
Death	0	0	0	2 (0.3)			

* $p < 0.05$; ** $p < 0.0001$



ORIGINAL RESEARCH

Early experience of COVID-19 vaccination in adults with systemic rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance Vaccine Survey

2860 patients

6% de patients avec vascularites

Questionnaire online, données rapportées par les patients

Fréquence d'effets indésirables similaire à la population générale

Arrêt temporaire des traitements : inquiétude++

4,6% de poussée de la maladie de fond nécessitant un changement de traitement

Furer V, et al. Ann Rheum Dis 2021;0:1–9.

Conclusions

- **Patients avec vascularite à risque de formes sévères et de décès :**
 - Facteurs de risques communs avec la population générale
 - Activité de la maladie
 - Corticoïdes >10mg/jour, Rituximab et immunosuppresseurs conventionnels
- **Réponse vaccinale altérée sous immunosuppresseurs, impact différent selon les traitements**
- **Bonne tolérance la vaccination**
- **Perspectives : données M6 avec 3^{ème} dose**