1203 STING/TYPE I INTERFERON PATHWAY ACTIVATION IN PATIENTS WITH PERNIOSIS DURING THE COVID–19 PANDEMIC

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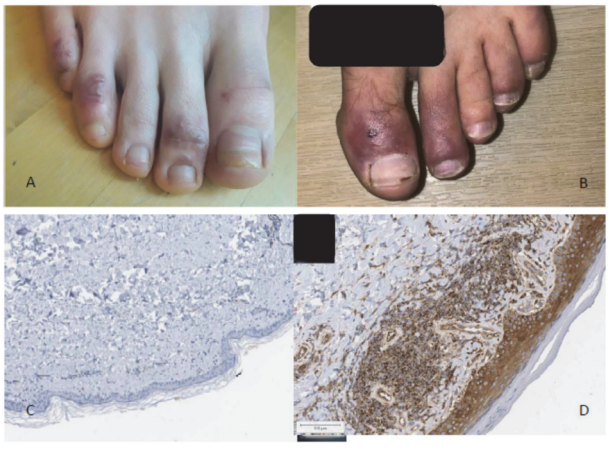
Background During the COVID-19 pandemic, a high incidence of patients with perniosis was observed worldwide. Classically, perniosis is secondary to cold exposure, hemoproliferative and autoimmune diseases. Although the pathomechanism of perniosis is incompletely characterized, lupus pernio is associated with a Type I interferon (IFN-I) signature. Therefore we explored the role of IFN in patients with perniosis.
Methods Antibodies to SARS-COV-2 were tested by protein microarray. Expression of IFN-I, IFN stimulated genes (ISGs) and other inflammatory cytokines in peripheral blood were determined by qPCR. Inflammatory cytokine proteins in serum were quantified by Biolegend LegendPlex. Immunohistochemistry was used to detect expression of the IFN-induced protein, Myxovirus resistance protein A (MxA) in lesional skin. STING protein phosphorylation in CD14 monocytes was determined by flow cytometry. The effect of patient sera on microvessels-on-a-chip was determined by Von Willebrand Factor (vWF) protein release to the vessel lumen. Statistical significance was determined by Student's t-test.
Results Between April-September 2020, 7 patients (3M;4F age 31-56) with pernio of the toes and/or fingers were studied (figure 1A and B). Two patients had previous Raynaud's phenomenon but none had prior or co-existent autoimmune disease. 1/5 patients tested was ANA+. 4/7 patients reported suspected COVID-19 symptoms prior to onset of perniosis. Antibodies to COVID antigens were negative in all patients.



Abstract 1203 Figure 1 Clinical appearance of perniosis in study patients showing red and purple papules over several toes some with near blisters (A and B). MxA staining of skin from perniosis lesion (D) showing lymphocytic inflammation in the dermis with perivascular and periadenexal inflammation. There is prominent MxA staining in the epidermis, dermal inflammatory infiltrate and in the superficial endothelial cells indicating interferon activation in skin. This is compared to no MxA staining in normal skin (C).

Blood studies showed an increase in TNF gene expression in perniosis patients compared to healthy matched controls (p=0.02). While there was a trend toward increased mRNA expression of IFNb (p=0.07) and the ISG CXCL10 (p=0.07), the results did not reach statistical significance. Phosphorylation of STING in CD14+ monocytes was higher in perniosis than healthy controls (n=3 per group), with borderline statistical significance (p=0.05). Lesional skin biopsies in perniosis (n=2) showed striking expression of MxA in tissue (Fig1. C&D). 4 patient sera induced high vWF release into the lumen on the microvessel 3D chip.
Conclusions The frequency of perniosis during the COVID pandemic, suggests a relationship between these two conditions although direct evidence of COVID-19 infection has been limited. We observed a trend toward higher IFN-b gene expression in PBMC as well as higher phospho-STING protein expression in CD14 monocytes and, most significantly, strong expression of MxA in skin. While the small number of patients preclude a definitive explanation, our data suggest that COVID associated perniosis is an interferonopathy. We propose that acute, transient COVID infection led to monocyte activation, IFN-I production and damage to the small vessels, likely aggravated by cold exposure.

1204 CHARACTERISTICS AND FACTORS ASSOCIATED WITH VACCINE HESITANCY IN A PREDOMINANTLY BLACK SYSTEMIC LUPUS ERYTHEMATOSUS COHORT

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Background Communities of color are disproportionately impacted by COVID-19 and systemic lupus erythematosus (SLE). We explored factors associated with vaccine hesitancy (VH) in a SLE cohort.
Methods The Georgians Organized Against Lupus Cohort is a population-based cohort of adult, validated lupus patients in Atlanta, Georgia. Participants were surveyed by internet, mail, phone or in person beginning in April 2020 covering sociodemographics, medications, and psychosocial factors. An additional survey beginning January 2021 assessed vaccination perceptions. Frequency of responses through June 2021 were reported overall and by vaccine hesitancy status. Differences were evaluated using t-tests and P-values. Multivariate logistic regression analyses were conducted to explore factors associated with VH.
Results Excluding those with severe reactions to previous vaccinations (n=71), religious exemptions (n=33), or diagnoses of primary cutaneous lupus (n=74), 598 individuals (details in table 1) with SLE were predominantly female (93.3%) and Black (78.4%) with a mean age at survey of 51.4 years. Many lived in poverty (25.5%), were unemployed (35.6%), and had Medicare and/or Medicaid (51.6%). Those endorsing VH (42.1%) were younger, more often Black, less married, poorer, less educated, and had more Medicare and/or Medicaid compared to those who were vaccine receptive (57.9%). They were significantly younger at diagnosis but with shorter disease duration. There were no differences in disease activity, damage, or medication use, except for more glucocorticoid use in the VH group. The VH group had less trust in the government, news, doctors, and lupus advocacy or support groups

Abstract 1204 Table 1 Factors Associated with COVID-19 Vaccine Perception in SLE Patients from the Georgians Organized Against Lupus Cohort

Category	Sub-Category		Overall (n=598)	COVID-19 Vaccination Perception		
				Receptive (n=342)	Hesitant (n=252)	P-Value
Socio- demographics	Age at Survey Completion (year)	18-34	85 (14.2)	30 (8.8)	55 (21.8)	**<0.0001**
		34-54	264 (44.1)	132 (38.6)	131 (52.0)	
		55+	249 (41.6)	180 (52.6)	66 (26.2)	
	Gender	male	40 (6.7)	24 (7.0)	15 (6.0)	0.6
		female	558 (93.3)	318 (93.0)	237 (94.0)	
	Race	Non-Black	129 (21.6)	105 (30.7)	23 (9.1)	**<0.0001**
		Black	469 (78.4)	237 (69.3)	229 (90.9)	
	Marital Status	Never married	203 (34.0)	95 (27.8)	107 (42.6)	**0.0001**
		Married	201 (33.7)	140 (40.9)	59 (23.5)	
		Separated	24 (4.0)	14 (4.1)	9 (3.6)	
		Divorced	104 (17.4)	57 (16.7)	47 (18.7)	
		Widowed	22 (3.7)	15 (4.4)	7 (2.8)	
		Living with Partner	43 (7.2)	21 (6.1)	22 (8.8)	
	Living in Poverty	Yes	147 (25.5)	52 (15.8)	94 (38.5)	**<0.0001**
	Current Work Status	Employed	248 (42.8)	150 (45.6)	97 (39.4)	**<0.0001**
		Off work force	125 (21.6)	92 (28.0)	31 (12.6)	
		Unemployed	206 (35.6)	87 (26.4)	118 (48.0)	
	Educational Attainment	≤ High School	159 (27.0)	73 (21.7)	85 (34.3)	**<0.0001**
		Some College	186 (31.6)	97 (28.8)	87 (35.1)	
		≥ College	243 (41.3)	167 (49.6)	76 (30.6)	
	Insurance type	Medicare and/or Medicaid	307 (51.6)	160 (46.9)	144 (57.6)	**<0.0001**
		Private	233 (39.2)	166 (48.7)	66 (26.4)	
		Under or uninsured	55 (9.2)	15 (4.4)	40 (16.0)	
Health Care Provider	Primary Care Physician visit in past 12 months	Yes	505 (84.4)	298 (87.1)	203 (80.6)	**0.03**
	Rheumatologist visit in past 12 months	Yes	516 (86.3)	294 (86.0)	220 (87.3)	0.6
Lupus Characteristics	Disease Duration (year)	Mean ± SD	18.7 ± 10.4	20.4 ± 10.4	16.2 ± 9.7	**<0.0001**
	Age at Lupus Diagnosis (year)	Mean ± SD	32.7 ± 11.9	34.4 ± 12.3	30.3 ± 11.1	**<0.0001**
	Disease Activity: Systemic Lupus Activity Questionnaire (SLAQ) score	Mean ± SD	12.6 ± 8.2	12.2 ± 7.7	13.3 ± 8.8	0.1
	Organ Damage: Self-Administered Brief Index Damage (BILD) score	Mean ± SD	3.3 ± 3.0	3.4 ± 3.2	3.2 ± 2.6	0.4
	Organ Damage Group	No Damage (BILD=0)	73 (12.2)	41 (12.0)	32 (12.7)	0.9
		Mild damage (BILD=1 or 2)	199 (33.3)	116 (33.9)	82 (32.5)	
		Severe damage (BILD≥3)	326 (54.5)	185 (54.1)	138 (54.8)	
Medications - current	glucocorticoids		247 (42.3)	127 (38.1)	120 (48.4)	**0.01**
	methotrexate		35 (6.2)	16 (4.9)	19 (7.9)	0.1
	cyclosporine		1 (0.2)	1 (0.3)		0.4
	dapsone		8 (1.4)	4 (1.2)	4 (1.7)	0.7
	belimumab		29 (5.1)	17 (5.2)	11 (4.5)	0.7
	anti-TNF agents		9 (1.6)	5 (1.5)	4 (1.6)	0.9
	hydroxychloroquine		415 (70.6)	236 (70.4)	177 (70.8)	0.9
	cyclophosphamide		11 (1.9)	7 (2.2)	4 (1.7)	0.8
	mycophenolate mofetil		116 (20.2)	59 (18.1)	57 (23.4)	0.1
	azathioprine		73 (12.7)	35 (10.7)	38 (15.7)	0.1
	rituximab		13 (2.3)	4 (1.2)	9 (3.7)	0.1
	Highest Steroid Dose in the past 12 months (mg/day)	Mean ± SD	18.7 ± 21.8	17.2 ± 22.5	20.3 ± 21.2	0.3
Sources of trusted COVID-19 information	Government		298 (49.8)	202 (59.1)	94 (37.3)	**<0.0001**
	News		289 (48.3)	182 (53.2)	103 (40.9)	**0.003**
	Social Media		44 (7.4)	24 (7.0)	20 (7.9)	0.7
	Doctors		445 (74.4)	276 (80.7)	165 (65.5)	**<0.0001**
	Lupus Advocacy or Support Groups		333 (55.7)	203 (59.4)	128 (50.8)	**0.04**

COVID-19 Well-Being	Concern for COVID-19 in general	Not at all concerned	9 (1.5)	2 (0.6)	7 (2.8)	**0.049**
		A little concerned	34 (5.7)	14 (4.1)	20 (8.0)	
		Moderately concerned	77 (13.0)	42 (12.4)	34 (13.6)	
		Very concerned	200 (33.7)	119 (35.0)	79 (31.6)	
		Extremely concerned	274 (46.1)	163 (47.9)	110 (44.0)	
	Concern lupus will worsen	0 (not concerned)	63 (10.8)	39 (11.6)	22 (9.1)	0.5
		1	21 (3.6)	15 (4.5)	6 (2.5)	
		2	18 (3.1)	11 (3.3)	7 (2.9)	
		3	22 (3.8)	12 (3.6)	10 (4.1)	
		4	10 (1.7)	6 (1.8)	3 (1.2)	
		5	57 (9.8)	24 (7.1)	32 (13.2)	
		6	35 (6.0)	19 (5.6)	16 (6.6)	
		7	40 (6.8)	24 (7.1)	16 (6.6)	
		8	63 (10.8)	41 (12.2)	22 (9.1)	
		9	46 (7.9)	27 (8.0)	19 (7.8)	
		10 (extremely concerned)	209 (35.8)	119 (35.3)	90 (37.0)	
	Concern for getting infected with COVID-19	0 (not concerned)	43 (7.4)	22 (6.5)	20 (8.3)	0.4
		1	15 (2.6)	6 (1.8)	9 (3.8)	
		2	24 (4.1)	15 (4.5)	9 (3.8)	
		3	18 (3.1)	10 (3.0)	7 (2.9)	
		4	17 (2.9)	9 (2.7)	8 (3.3)	
		5	69 (11.9)	32 (9.5)	37 (15.4)	
		6	30 (5.2)	20 (5.9)	9 (3.8)	
		7	39 (6.7)	25 (7.4)	14 (5.8)	
		8	62 (10.7)	41 (12.2)	21 (8.8)	
		9	54 (9.3)	31 (9.2)	23 (9.6)	
		10 (extremely concerned)	209 (36.0)	126 (37.4)	83 (34.6)	
	Concern for someone in family getting infected	0 (not concerned)	37 (6.4)	20 (6.0)	16 (6.6)	0.2
		1	14 (2.4)	6 (1.8)	8 (3.3)	
		2	13 (2.2)	5 (1.5)	8 (3.3)	
		3	10 (1.7)	5 (1.5)	5 (2.1)	
		4	12 (2.1)	8 (2.4)	4 (1.7)	
		5	61 (10.5)	28 (8.4)	33 (13.6)	
		6	24 (4.1)	14 (4.2)	10 (4.1)	
		7	30 (5.2)	17 (5.1)	12 (5.0)	
		8	63 (10.9)	44 (13.2)	19 (7.9)	
		9	61 (10.5)	41 (12.3)	20 (8.3)	
		10 (extremely concerned)	254 (43.9)	146 (43.7)	107 (44.2)	
Vaccination Attitudes	Mistrust (do not feel safe, cannot rely to stop serious infection, do not feel protected)	Mean ± SD	3.2 ± 1.6	2.4 ± 1.2	4.2 ± 1.5	**<0.0001**
Examination (VAX) scale	Unseen Effect (problems yet to be discovered, unforeseen problems in children, worry about unknown future effects)	Mean ± SD	4.1 ± 1.3	3.9 ± 1.2	4.4 ± 1.4	**<0.0001**
	Profiteering (Pharma profits, authorities profit, vaccination programs are a big con)	Mean ± SD	2.8 ± 1.5	2.4 ± 1.3	3.4 ± 1.4	**<0.0001**
	Natural Immunity (natural immunity lasts longer, natural exposure gives safest protection, natural exposure is safer)	Mean ± SD	2.6 ± 1.3	2.3 ± 1.2	3.0 ± 1.3	**<0.0001**
	VAX score	Mean ± SD	3.2 ± 1.0	2.8 ± 0.9	3.8 ± 0.9	**<0.0001**
Vaccine Beliefs	People with lupus have more vaccine side effects	Strongly disagree	37 (6.3)	30 (8.8)	6 (2.4)	**<0.0001**
		Disagree	81 (13.7)	67 (19.7)	12 (4.8)	
		Neither agree nor disagree	367 (62.0)	209 (61.5)	157 (63.3)	
		Agree	73 (12.3)	26 (7.6)	47 (19.0)	
		Strongly agree	34 (5.7)	8 (2.4)	26 (10.5)	
	Vaccine will flare lupus	Strongly disagree	48 (8.1)	41 (12.1)	6 (2.4)	**<0.0001**
		Disagree	83 (14.0)	71 (20.9)	10 (4.0)	
		Neither agree nor disagree	382 (64.5)	209 (61.5)	172 (69.4)	
		Agree	54 (9.1)	12 (3.5)	42 (16.9)	
		Strongly agree	25 (4.2)	7 (2.1)	18 (7.3)	
	Vaccine is not as effective in lupus	Strongly disagree	71 (12.0)	56 (16.6)	13 (5.2)	**<0.0001**
		Disagree	117 (19.8)	90 (26.6)	26 (10.5)	
		Neither agree nor disagree	347 (58.8)	169 (50.0)	177 (71.4)	
		Agree	39 (6.6)	18 (5.3)	21 (8.5)	
		Strongly agree	16 (2.7)	5 (1.5)	11 (4.4)	

Vaccination Behavior	Number of flu shots in the past 3 seasons	0	118 (19.9)	33 (9.7)	85 (33.9)	**<0.0001**
		1	86 (14.5)	41 (12.0)	45 (17.9)	
		2	71 (12.0)	39 (11.4)	32 (12.7)	
		3	319 (53.7)	228 (66.9)	89 (35.5)	
Psychosocial	Perceived Stress	Mean ± SD	15.8 ± 7.0	15.6 ± 7.1	16.1 ± 6.9	0.4
	Healthcare Discrimination: Better care if different race/ethnic group	Yes	86 (20.1)	53 (20.2)	33 (20.0)	0.9
	PROMIS Self-efficacy: manage medication and treatment (T-score)	Mean ± SD	49.2 ± 9.4	49.7 ± 9.2	48.5 ± 9.6	0.1
	Brief Resilience Scale	Mean ± SD	3.6 ± 0.8	3.7 ± 0.8	3.5 ± 0.8	**0.02**
	PROMIS Depression (T-Score)	Mean ± SD	49.3 ± 9.3	48.3 ± 8.7	50.5 ± 10.0	**0.004**
	Everyday Discrimination	Mean ± SD	1.4 ± 0.6	1.4 ± 0.6	1.5 ± 0.6	0.2

PROMIS=Patient-Reported Outcomes Measurement Information System

Abstract 1204 Table 2 Factors associated with COVID-19 vaccine perception in sle patients from the georgians organized against lupus cohort, multivariate analyses

	Model 1		Model 2		Model 3		Model 4		Model 5		Model 6	
Factor	**OR (95%CI)**	**P-Value**	**OR (95%CI)**	**P-Value**	**OR (95%CI)**	**P-Value**	**OR (95%CI)**	**P-Value**	**OR (95%CI)**	**P-Value**	**OR (95%CI)**	**P-Value**
Age at survey (per 5 years↓)	**1.3 (1.2-1.4)**	**<0.0001**	**1.3 (1.2-1.4)**	**<0.0001**	**1.3 (1.2-1.4)**	**<0.0001**	**1.3 (1.2-1.4)**	**<0.0001**	**1.3 (1.2-1.4)**	**<0.0001**	**1.3 (1.2-1.4)**	**<0.0001**
Disease duration (per 5 years↓)	1.0 (0.9-1.2)	0.5	1.0 (0.9-1.2)	0.7	1.0 (0.9-1.2)	0.7	1.0 (0.9-1.2)	0.7	1.0 (0.9-1.2)	0.7	1.0 (0.9-1.1)	0.8
Education (per 3 years↓)	**1.5 (1.2-1.8)**	**0.0003**	**1.5 (1.2-1.8)**	**0.0003**	**1.5 (1.2-1.8)**	**0.0002**	**1.5 (1.2-1.8)**	**0.0004**	**1.5 (1.2-1.9)**	**0.0001**	**1.5 (1.2-1.8)**	**0.0002**
Black race	**4.7 (2.7-8.3)**	**<0.0001**	**4.8 (2.7-8.4)**	**<0.0001**	**4.7 (2.7-8.4)**	**<0.0001**	**4.8 (2.7-8.5)**	**<0.0001**	**5.0 (2.8-8.9)**	**<0.0001**	**4.7 (2.7-8.4)**	**<0.0001**
Female gender	1.4 (0.7-3.0)	0.4	1.4 (0.7-3.0)	0.4	1.4 (0.7-3.1)	0.4	1.4 (0.7-3.0)	0.4	1.5 (0.7-3.3)	0.3	1.4 (0.7-3.0)	0.4
Unemployed vs Employed	1.5 (1.0-2.3)	0.1	1.6 (1.0-2.6)	0.1	1.6 (1.0-2.5)	0.1	1.5 (1.0-2.5)	0.1	1.5 (0.9-2.5)	0.1	1.6 (1.0-2.5)	0.1
Not Married or With Partner	1.2 (0.8-1.8)	0.4	1.2 (0.8-1.8)	0.4	1.2 (0.8-1.8)	0.4	1.2 (0.8-1.8)	0.4	1.2 (0.8-1.8)	0.3	1.2 (0.8-1.8)	0.4
No primary care visit in past year			1.2 (0.7-2.1)	0.4	1.3 (0.7-2.1)	0.4	1.3 (0.8-2.2)	0.4	1.3 (0.8-2.2)	0.4	1.2 (0.7-2.1)	0.4
Disease activity (Systemic Lupus Activity Questionnaire, per 3 units ↑)			1.0 (0.9-1.1)	0.9	1.0 (0.9-1.1)	0.9	1.0 (0.9-1.1)	0.9	1.0 (0.9-1.04)	0.3	1.0 (0.9-1.1)	0.98
Organ damage (Self-Administered Brief Index Damage, per 1 unit↑)			1.0 (0.9-1.04)	0.3	1.0 (0.9-1.04)	0.4	1.0 (0.9-1.04)	0.4	1.0 (0.9-1.04)	0.4	1.0 (0.9-1.04)	0.3
PROMIS Self-efficacy: manage medication and treatment (per 5 units ↓)					1.0 (0.9-1.2)	0.5						
Brief Resilience Scale (per 1 unit ↓)							1.2 (0.9-1.5)	0.3				
PROMIS Depression (per 5 units ↑)									**1.2 (1.0-1.3)**	**0.01**		
Everyday Discrimination (per 1 unit ↑)											1.1 (0.8-1.6)	0.5

OR=odds ratio; CI=confidence interval; PROMIS=Patient-Reported Outcomes Measurement Information System; VAX=Vaccination Attitudes Examination.

and less general concern for COVID-19. Their vaccination attitudes were strongly towards mistrust, concern about unseen effects, and natural immunity. Their vaccine beliefs favored more lupus-related side effects, more potential to flare lupus, and decreased efficacy in lupus. They also had fewer flu vaccinations in previous seasons, less resilience, and higher depression but no differences in healthcare or everyday discrimination. Multivariable logistic regression showed higher odds of VH in younger, less educated, Black, and depressed participants (table 2).

Conclusions Very high levels (42.1%) of VH persist in a predominantly Black SLE population. Despite lower vaccine uptake, 66.1% with COVID-19 VH had a recent flu vaccine, indicating potential vaccine receptivity. With less trust in the government, news, doctors, and lupus groups, community leaders and peers should lead outreach. Focus should include those who are younger, Black, and from lower socioeconomic groups, particularly with depression.

1205 COVID-19 VACCINE BELIEFS AMONGST INDIVIDUALS LIVING WITH LUPUS

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Background Patients with systemic lupus erythematosus (SLE) are known to be at higher risk for severe COVID-19. However, some individuals with SLE are hesitant to receive the COVID-19 vaccine. This study assessed the basis for COVID-19 vaccine hesitancy in individuals with SLE.

Methods A survey was distributed electronically, through the Lupus Foundation of America (LFA) e-newsletters and social media channels, March through April of 2021. The survey was based on an adaptation of the Vaccine Hesitancy Scale (VHS), with additional questions specific to COVID-19 vaccines and detailed demographics.

Results A total of 415 people responded to the survey, of whom 91% indicated that SLE was their primary rheumatologic diagnosis. Mean respondent age was 48, and 27.5% had less than a college education, whereas 31.3% had a graduate degree. When asked about race and ethnicity, 68.7% identified as non-Hispanic White, 15.2% as Black, 9.6% as Latinx, 4.6% as Asian, and 1.2% as Native American. At the time of the survey, 59.6% of respondents had received at least one COVID-19 vaccine dose; of these, 44.5% had spent less than 1 hour scheduling the vaccine, with 30.7% having spent 1-4 hours and 24.8% having spent over 4 hours. Another 20.2% of respondents wanted the COVID-19 vaccine but had not yet received it, and 20.2% did not want the vaccine. The prior year, 76% of respondents received the flu shot;16.1% of respondents indicated they don't trust the industry that creates vaccines. When asked about their beliefs regarding the COVID-19 vaccines, 66.6% were concerned the vaccine could flare their SLE, 27.1% were worried the vaccine could interact with their medications, 23.5% were concerned due to a history of allergies to foods and/or medications, and 12.2% were afraid they could get COVID-19 from the vaccine. Hesitant respondents were asked what would make them more likely to get the vaccine, and they cited evidence of safety in lupus as most important factor, with recommendations from the American College of Rheumatology (ACR), the LFA, or 'a trusted doctor' as more influential than vaccine mandates (figure 1).

Conclusions These results indicate an opportunity for healthcare professionals and patient advocacy organizations to assuage unfounded patient concerns, such as vaccine interactions with medications or food allergies being a contraindication to COVID-19 vaccination, while reassuring patients that vaccine-triggered flares are rare.

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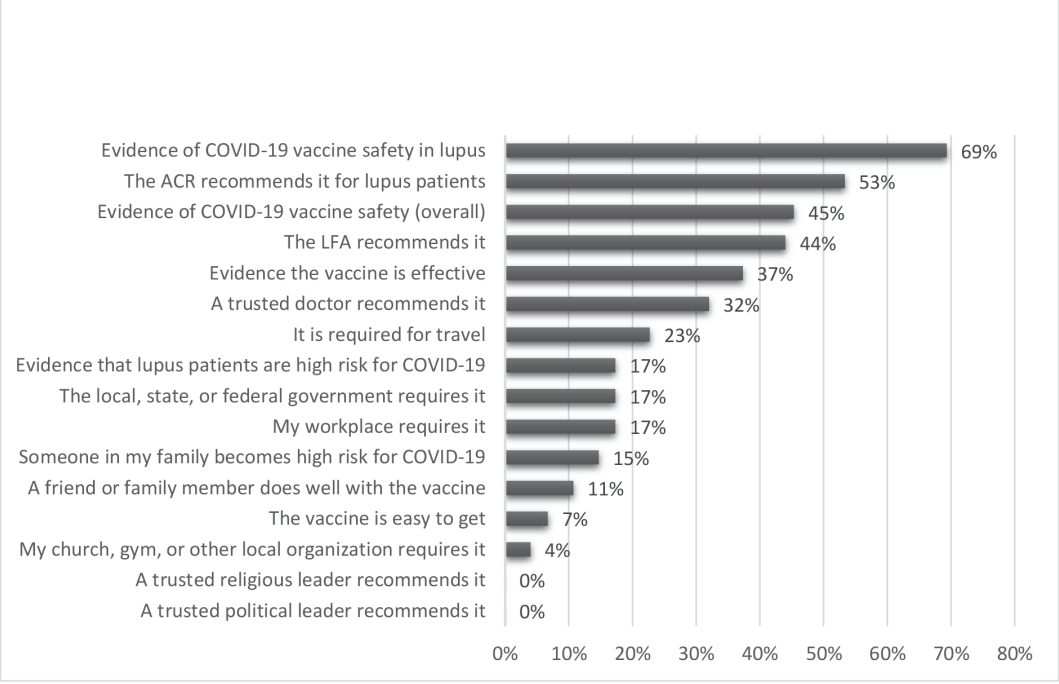

Abstract 1205 Figure 1 Respondents indicated which factors would have a positive influence on their likelihood of getting vaccinated against COVID-19; more than two-thirds of respondents indicated they would be more likely to pursue vaccination if they were presented with evidence of COVID-19 vaccine safety in lupus.