SUPPLEMENTARY MATERIAL

Hydroxychloroquine is associated with lower seroconversion upon 17DD-Yellow Fever primovaccination in patients with primary Sjögren's Syndrome

Ketty Lysie Libardi Lira Machado^{*}, Ismael Artur da Costa-Rocha^{*}, Laura Gonçalves Rodrigues Aguiar, Isac Ribeiro Moulaz, Samira Tatiyama Miyamoto, Priscila Costa Martins, Erica Vieira Serrano, Ana Paula Espíndula Gianordoli, Maria da Penha Gomes Gouvea, Maria de Fatima Bissoli, Sheila Maria Barbosa de Lima, Waleska Dias Schwarcz, Adriana de Souza Azevedo, Juliana Fernandes Amorim da Silva, Renata Tourinho Santos, Joaquim Pedro Brito-de-Sousa, Jordana Grazziela Coelho-dos-Reis, Ana Carolina Campi-Azevedo, Andréa Teixeira-Carvalho, Vanessa Peruhype-Magalhães, Francieli Fontana Sutile Tardetti Fantinato, Licia Maria Henrique da Mota, Olindo Assis Martins-Filho^{#§} and Valéria Valim^{#§}

* These authors contributed equally to this study.

[#] These authors share the senior authorship.

[§] Corresponding authors

Supplementary Table S1. Adverse events post 17DD-YF primovaccination in patients with primary Sjögren's Syndrome categorized according to the use of HCQ immunotherapy

	pSS subgroups		
Adverse Events	Non-HCQ (n=18)	HCQ (n=16)	p value
Local % (n)	33 (6)	31 (5)	>0.9999
Pain	28 (5)	25 (4)	>0.9999
Node	0 (0)	б (1)	0.4706
Edema	11 (2)	0 (0)	0.4866
Warmth	0 (0)	6 (1)	0.4706
Systemic % (n)	44 (8)	50 (8)	>0.9999
Fever	6 (1)	6 (1)	>0.9999
Malaise	17 (3)	31 (5)	0.4290
Headache	22 (4)	13 (2)	0.6602
Myalgia	28 (5)	6 (1)	0.1801
<u>Arthralgia</u>	<u>33 (6)</u>	<u>0 (0)</u>	<u>0.0198</u>
Back pain	17 (3)	0 (0)	0.2299
Diarrhea	6 (1)	0 (0)	>0.9999
Abdominal pain	6 (1)	6 (1)	>0.9999
Nausea	11 (2)	6 (1)	>0.9999
Emesis	6 (1)	0 (0)	>0.9999
Pruritus	6 (1)	13 (2)	0.5909
Dyspnea	0 (0)	6 (1)	0.4706
Cough	б (1)	6 (1)	>0.9999
Weakness	22 (4)	0 (0)	0.1052

pSS = patients with primary Sjögren's Syndrome; Non-HCQ = pSS not using hydroxychloroquine; HCQ = pSS using hydroxychloroquine. Comparative analysis was carried out by Chi-square test. In all cases, significant difference was considered at $p \le 0.05$ and underscored by bold underlined format.

	pSS subgroups			
Parameters	Non-HCQ (n=18) Median (IR)	HCQ (n=16) Median (IR)	p value	
CXCL8	3.5 (2.3-11.3)	8.6 (3.3-56.5)	0.1989	
CCL11	20.8 (16.3-53.3)	28.3 (10.3-68.8)	0.6588	
CCL3	1.8 (1.1-2.9)	2.0 (1.4-2.7)	0.6083	
CCL4	61.6 (15.9-118.0)	95.9 (12.4-307.4)	0.4221	
CCL2	14.7 (9.5-21.9)	<u>31.1 (14.1-53.3)</u>	<u>0.0510</u>	
CCL5	188.4 (180.8-402.9)	251.4 (87.2-368.2)	0.9809	
CXCL10	55.6 (33.4-88.4)	104.3 (51.1-232.4)	<u>0.0314</u>	
IL-1β	0.3 (0.2-0.6)	0.3 (0.2-0.3)	0.4146	
<u>IL-6</u>	0.1 (0.1-0.3)	0.4 (0.2-0.4)	<u>0.0378</u>	
TNF-α	3.3 (1.7-4.9)	7.3 (1.0-8.9)	0.3661	
IL-12	0.3 (0.2-0.4)	0.3 (0.2-0.5)	0.8953	
<u>ΙFN-γ</u>	0.6 (0.3-1.1)	1.1 (0.8-2.0)	<u>0.0208</u>	
IL-15	44.9 (29.1-68.8)	29.1 (27.8-79.2)	0.7500	
IL-17	3.7 (2.4-6.2)	3.3 (2.2-16.9)	0.7398	
IL-1Ra	44.8 (24.0-66.8)	<u>107.1 (58.2-295.6)</u>	<u>0.0058</u>	
IL-4	0.8 (0.5-1.2)	1.2 (0.5-1.6)	0.4172	
IL-5	6.7 (2.3-10.0)	6.9 (4.0-7.5)	0.9932	
<u>IL-9</u>	<u>2.8 (2.1-5.3)</u>	<u>6.5 (4.0-12.5)</u>	<u>0.0302</u>	
<u>IL-10</u>	<u>1.7 (1.1-2.2)</u>	2.2 (1.5-5.7)	<u>0.0509</u>	
IL-13	0.3 (0.2-0.5)	0.4 (0.2-0.6)	0.5105	
FGF-basic	4.3 (2.9-5.5)	5.1 (2.3-8.6)	0.3293	
PDGF	92.6 (42.1-187.1)	74.4 (24.5-265.2)	0.8592	
VEGF	20.4 (16.3-27.4)	18.7 (8.1-33.1)	0.7941	
G-CSF	11.7 (7.0-31.9)	21.3 (12.8-28.7)	0.8063	
GM-CSF	0.4 (0.2-0.7)	0.5 (0.2-0.9)	09144	
<u>IL-2</u>	0.7 (0.5-1.1)	<u>1.3 (0.9-7.3)</u>	0.0225	
IL-7	3.5 (1.3-4.7)	2.6 (1.9-3.6)	0.5728	

Supplementary Table S2. Serum soluble mediators in patients with primary Sjögren's Syndrome categorized according to the use of HCQ immunotherapy

Serum soluble mediators are expressed in median with interquartile range (IR); pSS = patients with primary Sjögren's Syndrome; Non-HCQ = pSS not using hydroxychloroquine; HCQ = pSS using hydroxychloroquine. Comparative analysis was carried out by Mann-Whitney test. In all cases, significant difference was considered at $p \le 0.05$ and underscored by bold underlined format.



Supplementary Figure S1. Neutralizing antibody titers and viremia according to age in patients with primary Sjögren's Syndrome Upon 17DD-YF Primovaccination categorized according to the use of HCQ immunotherapy. The YF-specific neutralizing antibodies titers and viremia levels were determined in serum samples from patients with primary Sjögren's Syndrome (pSS), categorized according to the use HCQ immunotherapy, referred as: Non-HCQ (\blacklozenge , n = 18) or HCQ (\blacktriangle , n = 16). Correlations analysis between PRNT titers and viremia levels with age was carried out by Spearman rank test and data shown as scattering of individual values. Analysis of cumulative RNAnemia for individual samples along the kinetic timeline according to age was performed by Kolmogorov-Smirnov (KS) test and data shown in line charts. In all cases, significant differences were considered at p < 0.05. Correlation indices (r score) as well as AUC, X and Y Peaks values are provided in the figure.