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COVID-19 vaccination and psoriatic patients under biologics: real-life evidence on safety and effectiveness from Italian vaccinated healthcare workers

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Dear Editor,

COVID-19 outbreak had drastically modified the treatment of chronic inflammatory diseases (i.e. psoriasis) in terms of drug delivery, visits booking and patients' adherence [1,2]. Furthermore, during lockdown several patients modified or even discontinued their anti-psoriatic treatments due to misinformation, COVID-phobia or even cabin fever syndrome experiencing a psoriatic flare and decreasing the overall daily functionality and quality of life [2].

Due to the study heterogeneous methods it is unknown if patients with psoriasis have higher risk of SARS-CoV-2 infection and the potential protective action of target therapy against the most severe COVID-19 clinical manifestations [3,4]. In Italy, two RNA-based vaccine and one viral vector-based anti-COVID-19 vaccines are currently approved (Table 1) and vaccination campaign recently started from healthcare workers and some concerns raised to the concept of "immunosuppressed" because no data are currently available and all vaccine instructions delegate to clinicians the final decision to vaccinate these fragile patients. In particular, patients with psoriasis display higher risk of respiratory comorbidities due to both systemic inflammation [5], high rate of smoking and anti-psoriatic therapies (i.e. conventional and target therapies) [6]. At the same time, National Psoriasis Foundation sustains that vaccines may play a pivotal role in protecting psoriatic patients against SARS-CoV-2 infection and they do not have to discontinue their prescribed anti-psoriatic therapies [7]. Likewise educational campaigns aiming to counteract vaccine-related misconceptions and to improve COVID-19 vaccines knowledge are mandatory [8].

Here we present 4 cases of healthcare workers under biologics that underwent Pfizer mRNABNT162b2 (COMIRNATY) vaccine.

Case 1. A 58-years-old male with body mass index(BMI) of 28.4 kg/m^2 and 16 years psoriasis duration and concurrent hypertension undergoing secukinumab from 2017 obtained a Psoriasis Area Severity Index (PASI) 100 and Dermatology Life Quality Index (DLQI) of 6 starting from PASI 18 and DLQI 22. The patient underwent the two vaccine dose administrations without experiencing any psoriatic flare or even PASI fluctuation. Remarkably, our patient did not modify secukinumab maintenance scheme and underwent the anti-IL-17 four days before the first vaccine dose and two days after the second one.

Case 2. A 67-years-old male with a BMI of 32.9 kg/m^2 presents with concurrent diabetes and hypercholesterolemia treated with metformin and statins. The patient started ixekizumab in 2016

achieving PASI 100 after 4 months without experiencing any flare also during COVID-19 vaccination. Interestingly, he experienced pain in the injection site for 3 days after the first vaccine dose, asthenia and headache that did not appear after the second dose administration. The patient did not discontinue ixekizumab and underwent the drug two days before the first dose of vaccine and five days after the second one.

Case 3. A 28-years-old male with a BMI of 23.1 kg/m^2 recently started risankizumab and achieving PASI 100 starting from PASI 18. During both vaccination doses he complained pain in the injection site for two days with any psoriasis flare or even cutaneous manifestations. The patient did not discontinue or modify risankizumab maintenance phase and underwent the biologic drug 15 days before the first vaccine dose and 20 days after the second one.

Case 4. A 34-years-old female with a BMI of 22.5 kg/m^2 and 6 year psoriasis duration, after failing ciclosporin started secukinumab. From PASI 11 and DLQI 23 in 16 weeks she achieved PASI 2 and DLQI 6 and this results were not perturbated during COVID-19 vaccination. She only complained pain in the vaccine injection sites for three days without any cutaneous manifestation vaccine-related or even a psoriasis flare. Secukinumab was not discontinued and undertaken 12 days before the first vaccine dose and 4 days before the second one.

All patients developed IgG anti- S1- Receptor Binding Domain (RBD) against SARS-CoV-2 and consequently the vaccination was effective.

The four cases described seem to suggest that COVID-19 RNA-based vaccine is safe and effective also for psoriatic patients undergoing target therapies (immunosuppressants) and does not trigger psoriasis flares.

Although these preliminary results are encouraging, they deserve to be validated also in a larger patients cohort and also in patients undergoing small molecules (apremilast and fumaric acid) and conventional therapies (acitretin, methotrexate and ciclosporin). Last but not least, real-life data towards vaccine effectiveness are mandatory in patients undergoing combination therapies and toward the possible minimal erythema dose (MED) modifications due to the vaccine.

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Table Legend:

Table 1. Position statements of vaccines approved in Italy on immunosuppressed patients.

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DRUG AGENCY	DATE OF APPROVAL	LINK	TECHNOLOGY	STATEMENT REGARDING PATIENTS WITH DYSIMMUNITY	APPROVED AGE RANGE (yoa)
Pfizer mRNABNT162b2 (COMIRNATY)					
EMA	21/12/20	https://www.ema.europa.eu/en/news/ema-recommends-first-covid-19-vaccine-authorisation-eu#:~:text=EMA%20recommends%20first%20COVID%2D19%20vaccine%20for%20authorisation%20in%20the%20EU,-Share&text=Comirnaty%20is%20now%20authorised%20across%20the%20EU.&text=EMA%20has%20recommended%20	RNA	**Can immunocompromised people be vaccinated with Comirnaty?** There are limited data on immunocompromised people (people with weakened immune systems). Although immunocompromised people may not respond as well to the vaccine, there are no particular safety concerns. Immunocompromised people can still be vaccinated as they may be at higher risk from COVID-19. (OMISSIS) **What information is still awaited for Comirnaty?** As Comirnaty received a conditional marketing authorisation, the company that markets Comirnaty will continue to provide results from the main trial, which is ongoing for 2 years. This trial and additional studies will provide information on how long protection lasts, how well the vaccine prevents severe COVID-19, how well it protects immunocompromised people, children and pregnant women, and whether it prevents asymptomatic cases.	>16

		granting%20a,from%2016%20years%20of%20age.		[https://www.ema.europa.eu/en/medicines/human/EPAR/comirnaty]	
AIFA	23/12/20	https://www.aifa.gov.it/documents/20142/1281388/DETERMINA_154-2020_COMINRATY.pdf/aa30d61d-32d3-3c56-5c59-27f0b7f004c4	RNA	**Can people with documented immunodeficiency or autoimmune diseases get vaccinated?** No data are yet available on the safety and efficacy of the COVID-19 mRNA BNT162b2 (Comirnaty) vaccine in people with autoimmune diseases, which were however included in the initial trials. During clinical trials, no differences were observed in the appearance of symptoms attributable to autoimmune or inflammatory diseases between vaccinated and placebo-treated subjects. People with autoimmune diseases who have no contraindications can receive the vaccine. The data relating to use in immunocompromised people (whose immune system is weakened) are limited. While these people may not respond as well to the vaccine, there are no particular safety concerns. Immunocompromised people can be vaccinated as they may be	>16

				at high risk for COVID-19. [AIFA press release n. 620. Answers to frequently asked questions]	
FDA	11/12/20	https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccine	RNA	**WHAT SHOULD YOU MENTION TO YOUR VACCINATION PROVIDER BEFORE YOU GET THE PFIZER-BIONTECH COVID-19 VACCINE?** Tell the vaccination provider about all of your medical conditions, including if you: • have any allergies; • have a fever; • have a bleeding disorder or are on a blood thinner • are immunocompromised or are on a medicine that affects your immune system (omissis)	>16
MHRA	02/12/20	Regulatory approval of Pfizer/BioNTech vaccine for COVID-19 - GOV.UK (www.gov.uk)	RNA	**Warnings and precautions** Talk to your doctor, pharmacist or nurse before you are given the vaccine if you have: (omissis) a weakened immune system, such as due to HIV infection, or are on a medicine that affects your immune system (omissis). As with any vaccine, COVID-19 mRNA Vaccine	>16

				BNT162b2 may not fully protect all those who receive it. No data are currently available in individuals with a weakened immune system or who are taking chronic treatment that suppresses or prevents immune responses.	
MODERNA					
EMA	06/01/21	https://www.ema.europa.eu/en/news/ema-recommends-covid-19-vaccine-moderna-authorisation-eu https://www.ema.europa.eu/en/medicines/human/EPAR/covid-19-vaccine-moderna	RNA	There are limited data on immunocompromised people (people with weakened immune systems). Although immunocompromised people may not respond as well to the vaccine, there are no particular safety concerns. Immunocompromised people can still be vaccinated as they may be at higher risk from COVID-19.	> 18
AIFA	07/01/21	https://www.aifa.gov.it/moderna	RNA	Si rivolga al medico, al farmacista o all'infermiere prima di ricevere COVID-19 Vaccine Moderna se: (omissis) - ha un sistema immunitario molto debole o compromesso	> 18
FDA	18/12/20	https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-	RNA	**WARNINGS:** (omissis) Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the Moderna COVID-19 Vaccine. (OMISSIS) 5.2 Altered Immunocompetence	> 18

		19/moderna-covid-19-vaccine		Immunocompromised persons, including individuals receiving immunosuppressive therapy, may have a diminished response to the Moderna COVID-19 Vaccine.	
MHRA	08/01/21	Moderna vaccine becomes third COVID-19 vaccine approved by UK regulator - GOV.UK (www.gov.uk)	RNA	https://www.gov.uk/government/publications/regulatory-approval-of-covid-19-vaccine-moderna/information-for-healthcare-professionals-on-covid-19-vaccine-moderna	> 18
AstraZeneca					
EMA	not yet	https://www.ema.europa.eu/en/news/ema-receives-application-conditional-marketing-authorisation-covid-19-vaccine-astrazeneca	Non-Replicating Viral Vector	(12/01/2021) EMA has received an application for conditional marketing authorisation (CMA) for a COVID-19 vaccine developed by AstraZeneca and Oxford University.	18-55
AIFA	30/01/21	https://www.aifa.gov.it/documents/20142/1289678/Comunicato_AIFA_626.pdf/265e16d3-	Non-Replicating Viral Vect	**Warnings and precautions (DOC. AVAILABLE FROM 02/02/2021):** Talk to your doctor, pharmacist or nurse before you are given COVID-19 Vaccine AstraZeneca: (omitted) if your immune system is not working properly	18-55

		921e-cc38-fdc1-d854c1f18ef8	or	(immunodeficiency) or you are taking medicines that weaken the immune system (such as high corticosteroids). dosage, immunosuppressants or anticancer medicines).	
FDA	not yet	-	Non-Replicating Viral Vector	-	
MHRA	30/12/20	https://www.gov.uk/government/publications/regulatory-approval-of-covid-19-vaccine-astrazeneca	Non-Replicating Viral Vector	**Decision. Information for UK recipients on COVID 19 Vaccine AstraZeneca (Updated 28 January 2021) Warnings and precautions:** Tell your doctor, pharmacist or nurse before vaccination: (OMISSIS) If your immune system does not work properly (immunodeficiency) or you are taking medicines that weaken the immune system (such as high-dose corticosteroids, immunosuppressants or cancer medicines).	18-55

AIFA: Italian Medicines Agency, FDA: Food and Drug Administration, EMA: European Medicines Agency, MHRA: Medicines and Healthcare products Regulatory Agency, RNA: Ribonucleic acid.