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SUPPLEMENT ARTICLE

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Anti-COVID-19 measurements for hidradenitis suppurativa patients

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Abstract

The reported incidence of COVID-19 among cohorts of patients with inflammatory bowel and skin diseases under treatment with biologicals is low. Treatment may further modify disease severity as some biological modifiers, such as anakinra, are also proposed for the management of COVID-19 patients potentially providing HS patients with an advantage.

The above preliminary evidence suggests that hidradenitis suppurativa (HS) does probably not provide an increased susceptibility for COVID-19 and that any susceptibility is unlikely to be modified negatively by treatment with biologicals.

On the occasion of its 10th International Conference, experts of the European Hidradenitis Suppurativa Foundation e.V. have prepared a consensus statement regarding anti-COVID-19 measurements for HS patients. Based on the available knowledge, patients with HS may be vaccinated against SARS-CoV2 and patients affected by metabolic syndrome constitute a high-risk group for COVID-19 and should be vaccinated at the earliest convenient point in time. HS patients on treatment with adalimumab can be vaccinated with non-living virus anti-SARS-CoV2 vaccines. A possible suboptimal effect of the vaccine may be suspected but might not be expected

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universally. The management of the biological treatment in HS patients is at the discretion of the dermatologist / responsible physician.

KEYWORDS
COVID-19, hidradenitis suppurativa, SARS-CoV2, vaccine

1 | INTRODUCTION

The immunological basis of COVID-19 remains poorly defined.[1] SARS-CoV2 may cause a complex inflammatory disease through hyperstimulation of the immune system[2] and may influence the course of autoimmune and/or autoinflammatory diseases.[3,4] Among them, hidradenitis suppurativa / acne inversa (HS; ICD-11: ED92.0, ORPHANET: 370) is a chronic, inflammatory, immune-mediated skin disease[5,6] with the innate immune system reacting to different triggering factors ending up in the production of skin lesions, such as nodules, abscesses and tunnels. HS comorbidities, such as spondyloarthropathy, inflammatory bowel disease, obesity, metabolic syndrome and concomitant cardiovascular disorders,[7,8] implicate both autoimmune and/or autoinflammatory mechanisms.[9,10] Only few data on the course of COVID-19 in HS patients exist,[11] and the knowledge regarding the proper management of HS patients in the pandemic period is limited.[12]

2 | COVID-19 AND HS

The answer to the crucial question whether patients with HS are more or less prone to infection by the novel coronavirus SARS-CoV-2 (COVID-19) relies on the evidence for the response of the human host to the virus. First data suggest that COVID-19 is mediated by an intense pro-inflammatory reaction of the host, which if unchecked, may lead to severe respiratory failure (SRF). In 25% of patients, progression to SRF is mediated by a hyper-inflammatory reaction of circulating monocytes and tissue macrophages with features of macrophage activation syndrome; serum ferritin is exceeding 4420 ng/ml, hyper-triglyceridemia is pronounced and liver dysfunction predominates. In the remaining 75% of cases progressing into SRF, monocytes lose their ability for antigen presentation leading to lymphopenia and hypoglobulinemia; in parallel, monocytes maintain their potential for hyper-production of pro-inflammatory cytokines.[13] Interestingly, circulating monocytes of HS patients have relative energy for the production of pro-inflammatory cytokines; this is explained as reciprocal feedback to the skin hyper-inflammation.[14] This suggests that in the case of SARS-CoV-2, HS patients are not prone to excessive pro-inflammatory reaction. Furthermore, among 8000 patients with HS from the United States, only 39 developed COVID-19.[15]

The incidence of COVID-19 among cohorts of patients with inflammatory bowel disease[16] and psoriasis[17] under treatment with biologicals was very limited, and the same held true for the two reported cohorts of patients with HS under treatment with adalimumab[12,18] (Table 1). Furthermore, it needs to be considered that biological modifiers used in HS therapy, such as anakinra, are proposed for the management of COVID-19 patients.[19] The above evidence suggests that HS does probably not provide susceptibility for COVID-19 and that any remaining, limited susceptibility seems unmodified after treatment with biologicals.

2.1 | ANTI-SARS-CoV2 IMMUNIZATION AND HS

Anti-SARS-CoV2 vaccines aim to produce specific antibodies against the active viral agents, the spike protein.[20] Such neutralizing

TABLE 1 Published evidence on the risk of COVID-19 among patients under treatment with biologicals

Ref. #	Disease (number)	% anti-TNF intake	Incidence of COVID-19
16	Psoriasis (6501)	32.4	11.7 hospitalizations/100 000 person-months vs 14.4/100 000 person-months in the general population
17	Inflammatory bowel disease (259) Healthy (214)	66.0	PCR(+) for SARS-CoV-2 = 4 (1.5%) vs 0% IgG/IgM for SARS-CoV-2 = 4 (1.5%) vs 0%
18	Cohort 1: HS (75) Cohort 2: HS (35)	100	0% both cohorts

Abbreviations: HS, hidradenitis suppurativa; Ig, immunoglobulin; PCR, polymerase chain reaction; TNF, tumour necrosis factor.

antibodies generate a T-cell response and lead to avoidance of immune-enhanced disease.[21] The B-cell / plasma cell side of the adaptive immunity plays the major role in producing antibodies, and the T-cell side is of great support as well.[22] There is no reliable data-based awareness of possible interactions between the immunological events occurring in HS patients and the immunological effects induced by the anti-SARS-CoV2 vaccine. Taking into consideration the existing initial data,[23] it seems that HS patients can be vaccinated against SARS-Co2 without specific contraindications.

The most frequent cause of death in COVID-19 patients is a severe acute pulmonary syndrome.[1,24] Obesity, diabetes, cardiovascular disorders and pre-existing pulmonary conditions are comorbidities, which may induce an increased risk of severe COVID-19 and lead to increased rates of death.[24,25] Metabolic diseases are increased in HS patients.[26] This patient group should be consequently considered as a priority group for anti-SARS-CoV2 vaccination.[27,28] On the other hand, the main target of biological drugs in HS is to reduce the hyperactivity of the immune system. Therefore, a concomitant vaccination might potentially result in a suboptimal immunization effect. Although the specific targets of biologics are different, the only currently registered biological agent for HS treatment is the tumour necrosis factor (TNF)-α inhibitor adalimumab.[29] TNF-α inhibition acts at different levels on the immune system.

The clinical trials performed for the registration of anti-SARS-Co2 vaccines did not include patients receiving drugs active on the immune system.[28] As a consequence, no specific clinical data on any interference of the biological agents on SARS-CoV2 antibody production and the efficacy of the vaccine in patients under biological treatments are currently available. HS patients must be aware that the effect of a vaccine, while on adalimumab, may be—but must not obligatorily be—suboptimal. On the other hand, the advantages of anti-SARS-CoV2 vaccination overwhelm the risks, if any, and no specific side effects may be expected, despite the fact that evidence is still missing.

It should be pointed out here, however, that no vaccinations containing living microorganisms should be performed in patients treated with biologics. The three currently available vaccines, those of Pfizer-BioNTech, Moderna and Oxford/Astra-Zeneca, are not living virus vaccines. The decision regarding eventual, temporary suspension of biological treatment around the time point of the vaccination should be at the discretion of the dermatologist/responsible physician who knows the clinical situation of the patient at best.

3 | CONSENSUS FOR ANTI-COVID-19 MEASUREMENTS IN HS PATIENTS

Taking into consideration the available data, the participating authors reached unanimously a consensus on behalf of the European Hidradenitis Suppurativa Foundation e.V., which includes the following measures:

- The prevalence of COVID-19 in patients with HS is apparently lower than that of the general population. This may be due to HS patients having been especially careful with social shielding. However, underestimation is also possible.
- HS appears not to be associated with a more severe course of COVID-19.
- Treatment of HS with antibiotics and the TNF-α inhibitor adalimumab seems not to increase the risk for COVID-19 or induce a more severe course.
- Treatment initiation of HS patients with other therapeutic compounds should be carefully evaluated at individual level.
- Even if we do not yet know what effect—if any—vaccination has on HS (and vice versa), anti-SARS-CoV2 vaccination is recommended. Benefits versus risks should be considered at an individual level.
- Treatment with adalimumab appears to be compatible with anti-SARS-CoV2 vaccination and should not be interrupted, especially in moderate-to-severe HS. It might be suspended around the time point of anti-SARS-CoV2 vaccination.
- It is still unclear if biologics may compromise SARS-CoV2 vaccination. Serological confirmation of successful vaccination by ELISA is still not recommended as routine practice.
- National self-protection and hygiene measurements should be adhered to. Self-protection with masks is recommended even despite vaccination.
- This consensus is based on expert opinion and literature evidence, and complements the recommendations already published by other scientific societies.[30]

4 | CONCLUSION

Based on the available knowledge, HS patients may be vaccinated and the group of them, affected with metabolic syndrome, at the soonest possible time. HS patients on adalimumab treatment can be vaccinated with non-living virus anti-SARS-CoV2 vaccines. A possible suboptimal effect of the vaccine may be suspected. The management of the biological treatment in HS patients is at the discretion of the dermatologist / responsible physician.

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CONFLICT OF INTEREST

EJG-B, VB, GBEJ, VdM, AVM, EPP, TT, CCZ declare that none of the mentioned conflicts of interest had any influence to this manuscript.

EJG-B has received honoraria from Abbott, Angelini, bioMérieux, InflaRx, MSD and XBiotech; independent educational grants from AbbVie, Abbott, Astellas, AxisShield, bioMérieux, InflaRx, Thermo Fisher Brahms and XBiotech; and funding from the FrameWork 7 program HemoSpec (granted to the National and Kapodistrian University of Athens), the Horizon2020 Marie-Curie Project European Sepsis Academy (granted to the National and Kapodistrian University of Athens) and the Horizon 2020 European Grant ImmunoSep (granted to the Hellenic Institute for the Study of Sepsis). GBEJ has received honoraria from AbbVie, Chemocentryx, Coloplast, Incyte, Inflarx, Kymera Therapeutics, LEO, Novartis and UCB for participation on advisory boards, and grants from Abbvie, Astra-Zeneca, Inflarx, Janssen-Cilag, LEO, Novartis, Regeneron and Sanofi for participation as an investigator, and received speaker honoraria from AbbVie, Boehringer-Ingelheim, Galderma and Novartis. He has also received unrestricted departmental grants from LEO and Novartis. VdM has received honoraria for advisory board participation from BMS, Leo Pharma, Sanofi. EPP received honoraria from AbbVie, Amgen, Celgene, Galderma, Janssen-Cilag, Novartis and Pfizer for participation as a speaker and serving on advisory boards and investigator-initiated grants (paid to the Erasmus MC) from AbbVie, AstraZeneca, Janssen-Cilag and Pfizer. TT reports fees from AbbVie, UCB and Sanofi (consultancy, speaker honorarium). CCZ has received thematically relevant honoraria from Incyte, Inflarx, Janssen-Cilag, Novartis, Regeneron and UCB as advisor. His departments have received grants from AbbVie, AOTI, Astra Zeneca, Galderma, Inflarx, Naos-Bioderma, Novartis, PPM and UCB for his participation as clinical investigator. AVM declares no conflict of interest.

AUTHOR CONTRIBUTIONS

Evangelos J. Giamarellos-Bourboulis wrote a part of the manuscript, read and approved the final manuscript. Vincenzo Bettoli wrote a part of the manuscript, read and approved the final manuscript. Gregor B.E. Jemec read and approved the final manuscript. Veronique del Marmol read and approved the final manuscript. Angelo V. Marzano read and approved the final manuscript. Errol P. Prens read and approved the final manuscript. Thrasyvoulos Tzellos read and approved the final manuscript. Christos C. Zouboulis wrote a part of the manuscript, read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

EJG-B, VB, GBEJ, VdM, AVM, EPP, TT, CCZ confirm the absence of shared data.

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