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EFFICACY OF COVID-19 VACCINATION IN PATIENTS WITH IMMUNE SYSTEM DISORDERS AND CANCER

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On December 31st, 2019, the first official cases of Coronavirus Disease 2019 (COVID-19) were registered in Wuhan, China. From that day onward the pandemic caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection started to spread all over the world, affecting millions of people and changing their lives. The COVID-19 is responsible of a complex set of symptoms, primarily affecting the respiratory tract, but also targeting multiple organs, leading to life-threatening conditions and even death. To date more than 616 million of cumulative cases and 6.5 million cumulative deaths have been reported worldwide by the World Health Organization (WHO)[1]. During the first wave we were totally unarmed, and COVID-19 pandemic overwhelmed us. The hospitals were full. The health advocates were on the brink and the first to suffer the major losses. We were on the verge of collapse and to prevent further disasters we had to stop, but so did not the research. To end this dark chapter in world history, we needed answers. Until vaccines' commercialization, we were mere spectators of the pandemic, only able to act on the prevention and on the identification of patients at increased risk, also assisting to the lack of effect on in-hospital mortality of the drugs used[2-6]. Leading pharmaceutical companies managed to develop and evaluate the effectiveness of new vaccines in less than a year. Soon after, Food and Drug Administration (FDA) and European Medicines Agency (EMA) approved them for emergency use. At the beginning only few data were available from approval trials. A recent meta-analysis, enrolling over one million individuals from seven studies, reported that COVID-19 vaccination was able to significantly reduce the disease severity and mortality in COVID-19 patients. Moreover, the authors also found that regardless of the vaccine brand, there is a statistically significance difference in the number of patients hospitalized for severe COVID-19 disease between the vaccinated and non-vaccinated groups[7]. Although the benefit-risk ratio of these vaccines has been proven to be largely favourable in the general population, we had no evidence in special cohorts as they were initially excluded from the pivotal trials, such as pregnant and breastfeeding women, children/adolescents, frail people (firstly malignancies), and people with a history of allergy or previous SARS-CoV-2 infection[8]. With vaccines administration, careful pharmacovigilance, and with the approval of international drug agencies and international scientific societies, most of these taboos have lapsed, and we have also assisted to an extend of indications[8,9]. However, not all that glitters is gold. In fact, a major issue in evaluating vaccine efficacy is one's immune response. It has been reported that hyperglycaemia may induce specific dysfunction of both the virus-neutralizing antibodies and adaptive immune response in diabetic patients (including T cells)[10]. Nevertheless, it seems that a strict glycaemic control during the vaccination period (through the emerging role of telemedicine, newer screening tools and therapies) improves type 2 diabetic patients' immune response[11,12]. Moreover,

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TABLE 1. COVID-19 vaccines authorized by Food and Drug Administration (FDA) and/or European Medicines Agency (EMA).

COVID-19 vaccines	*FDA authorization*	*EMA authorization*	*Type*
Comirnaty-Pfizer-BioNTech	Yes	Yes	mRNA
Comirnaty-Pfizer-BioNTech bivalent	Yes	Yes	mRNA
Spikevax-Moderna	Yes	Yes	mRNA
Spikevax-Moderna bivalent	Yes	Yes	mRNA
Vaxzevria (previously AstraZeneca)	No	Yes	viral vector
Jcovden (previously Janssen)	Yes	Yes	viral vector
Nuvaxovid-Novavax	Yes	Yes	recombinant, adjuvanted
Vulneva	No	Yes	inactivated, adjuvanted

in patients affected with immunosuppressive diseases or patients on immunosuppressive medications, vaccines' efficacy is still debated as they present an impaired immunogenicity response[13]. A recent systematic review has reported a wide variation in vaccination non-response rate, which is higher in solid organ transplant recipients (in particular in lung and renal transplant recipients), in patients with haematological malignancy (especially in patients affected with chronic lymphocytic leukaemia), and is lower in cancer patients, dialytic patients and with varying levels across different immune-mediated diseases (most of all in patients with multiple sclerosis)[14]. In patients on immunosuppressive medications, a case-by-case evaluation is crucial to assess whether delaying immunosuppressive therapy to improve immune response[13,15]. This evidence is further enhanced by the fact that immunocompromised patients present an increased incidence of persistent SARS-CoV-2 infection, representing an important reservoir for the emergence of novel viral variants[16].

In cancer patients, who were receiving active systemic therapy, several studies have reported a positive seroconversion rate (78-90%). Lower seroconversion rates were associated with haematological malignancies (59-77%), in contrast to solid ones (85%-98%)[17-20]. Moreover, in this subgroup of patients, the lower seroconversion rate was also associated to the combination of chemotherapy plus immunotherapy[19].

Real-world observational studies demonstrated that vaccination of the most vulnerable immunosuppressed and cancer population is not fully protective. Due to this, in some countries, an additional dose of vaccine has become available to further stimulate the immune to produce antibodies. In this subset of patients there may be no safety issue, as for now no attenuated vaccine has been approved (Table 1)[14]. However, both the FDA and EMA do not recommend antibody testing for SARS-CoV-2 to determine immunity or protection from COVID-19[18].

COVID-19 vaccines have largely proven both their safety and efficacy. Up to now, WHO have reported that more than 12 billion doses of the vaccine have been administered[1]. However, there are still individuals who neglect vaccination and/or cannot be vaccinated for several reasons (aged less than 5, history of recent pericarditis, allergies…). Indeed, we do believe that the achievement of herd immunity may protect these populations as well.

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REFERENCES

1. https://covid19.who.int/ (accessed October 05, 2022)
2. Huang YZ, Kuan CC. Vaccination to reduce severe COVID-19 and mortality in COVID-19 patients: a systematic review and meta-analysis. Eur Rev Med Pharmacol Sci 2022; 26: 1770-1776.
3. Galiero R, Pafundi PC, Simeon V, Rinaldi L, Perrella A, Vetrano E, Caturano A, Alfano M, Beccia D, Nevola R, Marfella R, Sardu C, Coppola C, Scarano F, Maggi P, De Lucia Sposito P, Vocciante L, Rescigno C, Sbreglia C, Fraganza F, Parrella R, Romano A, Calabria G, Polverino B, Pagano A, Bologna C, Amitrano M, Esposito V, Coppola N, Maturo N, Adinolfi LE, Chiodini P, Sasso FC; COVOCA Study Group. Impact of chronic liver disease upon admission on COVID-19 in-hospital mortality: Findings from COVOCA study. PLoS One 2020; 15: e0243700.
4. Pafundi PC, Galiero R, Simeon V, Rinaldi L, Perrella A, Vetrano E, Caturano A, Alfano M, Beccia D, Nevola R, Marfella R, Sardu C, Coppola C, Scarano F, Maggi P, De Lucia Sposito P, Vocciante L, Rescigno C, Sbreglia C, Fraganza F, Parrella R, Romano A, Calabria G, Polverino B, Pagano A, Bologna C, Amitrano M, Esposito V, Cop-

pola N, Maturo N, Adinolfi LE, Chiodini P, Sasso FC; COVOCA Study Group. Lack of effect on in-hospital mortality of drugs used during COVID-19 pandemic: Findings of the retrospective multicenter COVOCA study. PLoS One 2021; 16: e0256903.
5. Valdenassi L, Franzini M, Ricevuti G, Rinaldi L, Galoforo AC, Tirelli U. Potential mechanisms by which the oxygen-ozone (O2-O3) therapy could contribute to the treatment against the coronavirus COVID-19. Eur Rev Med Pharmacol Sci 2020; 24: 4059-4061.
6. Carta MG, Scano A, Lindert J, Bonanno S, Rinaldi L, Fais S, Orrù G. Association between the spread of COVID-19 and weather-climatic parameters. Eur Rev Med Pharmacol Sci 2020; 24: 8226-8231.
7. Luxi N, Giovanazzi A, Capuano A, Crisafulli S, Cutroneo PM, Fantini MP, Ferrajolo C, Moretti U, Poluzzi E, Raschi E, Ravaldi C, Reno C, Tuccori M, Vannacci A, Zanoni G, Trifirò G; Ilmiovaccino COVID19 collaborating group. COVID-19 Vaccination in Pregnancy, Paediatrics, Immunocompromised Patients, and Persons with History of Allergy or Prior SARS-CoV-2 Infection: Overview of Current Recommendations and Pre- and Post-Marketing Evidence for Vaccine Efficacy and Safety. Drug Saf 2021; 44: 1247-1269.
8. Hause AM, Gee J, Baggs J, Abara WE, Marquez P, Thompson D, Su JR, Licata C, Rosenblum HG, Myers TR, Shimabukuro TT, Shay DK. COVID-19 Vaccine Safety in Adolescents Aged 12-17 Years - United States, December 14, 2020-July 16, 2021. Morb Mortal Wkly Rep 2021; 70: 1053-1058.
9. Caturano A, Pafundi PC, Sasso FC, Dendramis G, Brugada P, Russo V. Brugada syndrome and COVID-19 vaccines. Europace 2021; 23: 1871-1872.
10. Marfella R, D'Onofrio N, Sardu C, Scisciola L, Maggi P, Coppola N, Romano C, Messina V, Turriziani F, Siniscalchi M, Maniscalco M, Boccalatte M, Napolitano G, Salemme L, Marfella LV, Basile E, Montemurro MV, Papa C, Frascaria F, Papa A, Russo F, Tirino V, Papaccio G, Galdiero M, Sasso FC, Barbieri M, Rizzo MR, Balestrieri ML, Angelillo IF, Napoli C, Paolisso G. Does poor glycaemic control affect the immunogenicity of the COVID-19 vaccination in patients with type 2 diabetes: The CAVEAT study. Diabetes Obes Metab 2022; 24: 160-165.
11. Galiero R, Pafundi PC, Nevola R, Rinaldi L, Acierno C, Caturano A, Salvatore T, Adinolfi LE, Costagliola C, Sasso FC. The Importance of Telemedicine during COVID-19 Pandemic: A Focus on Diabetic Retinopathy. J Diabetes Res 2020; 2020: 9036847.
12. Guarneri C, Rullo EV, Pavone P, Berretta M, Ceccarelli M, Natale A, Nunnari G. Silent COVID-19: what your skin can reveal. Lancet Infect Dis 2021; 21: 24-25.
13. Negahdaripour M, Shafiekhani M, Moezzi SMI, Amiri S, Rasekh S, Bagheri A, Mosaddeghi P, Vazin A. Administration of COVID-19 vaccines in immunocompromised patients. Int Immunopharmacol 2021; 99: 108021.
14. Galmiche S, Luong Nguyen LB, Tartour E, de Lamballerie X, Wittkop L, Loubet P, Launay O. Immunological and clinical efficacy of COVID-19 vaccines in immunocompromised populations: a systematic review. Clin Microbiol Infect 2022; 28: 163-177.
15. Valente G, Rinaldi L, Sgambato M, Piai G. Conversion from twice-daily to once-daily tacrolimus in stable liver transplant patients: effectiveness in a real-world setting. Transplant Proc 2013; 45: 1273-5.
16. Marra AR, Kobayashi T, Suzuki H, Alsuhaibani M, Tofaneto BM, Bariani LM, Auler MA, Salinas JL, Edmond MB, Doll M, Kutner JM, Pinho JRR, Rizzo LV, Miraglia JL, Schweizer ML. Short-term effectiveness of COVID-19 vaccines in immunocompromised patients: A systematic literature review and meta-analysis. J Infect 2022; 84: 297-310.
17. Massarweh A, Eliakim-Raz N, Stemmer A, Levy-Barda A, Yust-Katz S, Zer A, Benouaich-Amiel A, Ben-Zvi H, Moskovits N, Brenner B, Bishara J, Yahav D, Tadmor B, Zaks T, Stemmer SM. Evaluation of Seropositivity Following BNT162b2 Messenger RNA Vaccination for SARS-CoV-2 in Patients Undergoing Treatment for Cancer. JAMA Oncol 2021; 7: 1133-1140.
18. Addeo A, Shah PK, Bordry N, Hudson RD, Albracht B, Di Marco M, Kaklamani V, Dietrich PY, Taylor BS, Simand PF, Patel D, Wang J, Labidi-Galy I, Fertani S, Leach RJ, Sandoval J, Mesa R, Lathrop K, Mach N, Shah DP. Immunogenicity of SARS-CoV-2 messenger RNA vaccines in patients with cancer. Cancer Cell 2021; 39: 1091-1098.e2.
19. Thakkar A, Pradhan K, Jindal S, Cui Z, Rockwell B, Shah AP, Packer S, Sica RA, Sparano J, Goldstein DY, Verma A, Goel S, Halmos B. Patterns of seroconversion for SARS-CoV2-IgG in patients with malignant disease and association with anticancer therapy. Nat Cancer 2021; 2: 392-399.
20. Greenberger LM, Saltzman LA, Senefeld JW, Johnson PW, DeGennaro LJ, Nichols GL. Antibody response to SARS-CoV-2 vaccines in patients with hematologic malignancies. Cancer Cell 2021; 39: 1031-1033.