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SARS-CoV-2 Immunity in a Cohort of Patients with Head and Neck Carcinoma †

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Abstract: The COVID-19 (coronavirus infectious disease 2019) pandemic caused by SARS-CoV-2 infection (severe acute respiratory coronavirus syndrome 2) forced the implementation of large-scale vaccination worldwide. Numerous studies have investigated the duration of natural and vaccine-induced immunity in the general population but not in specific groups of patients with pathologies, such as cancer patients. The study aimed to monitor the humoral immunity developed upon SARS-CoV-2 infection or vaccination in a group of head and neck cancer (HNC) patients. Peripheral blood was collected from HNC patients (n = 51) recruited at Colțea Hospital (Bucharest) (43 men, 8 women; average age = 65 years; body mass index (BMI): 25 kg/m^2), convalescent (n = 17; mild/moderate symptoms) or vaccinated (n = 34; Pfizer/Moderna RNA vaccine or AstraZeneca/Johnson&Johnson adenoviral vector). The anti-Spike (S1, S2), anti-receptor binding (RBD), and anti-nucleocapsid (NC) IgG antibodies (Abs) were detected in the plasma using MILLIPLEX® (EMD Millipore) technology; the results were expressed by the average fluorescence intensity (MFI) parameter. CD19$^+$CD27$^{+/-}$ B cells producing SARS-CoV-2-specific Abs (IgM, IgG, IgA) were identified by polychromatic flow cytometry analysis of PBMC *ex vivo*, using the SARS-CoV-2 RBD B cells kit (Miltenyi Biotec). Finally, a panel of 25 cytokines was quantified using the MILLIPLEX® technology. The Mann-Whitney test and the Spearman correlation model were used for statistical analysis. Vaccinated and convalescent participants in the Coltea COVID-19 HNC cohort were similar in age, BMI, and time since immunization. S1, S2, and RBD Abs were detected in most HNC participants up to 300 days post-immunization. S2 and NC Abs were significantly higher in convalescent *vs.* vaccinated HNC participants. NC Abs induced only by infection positively correlated with S1, S2, and RBD Abs. SARS-CoV-2 Abs levels did not correlate with the time since infection, age or BMI. RBD-specific B cells were observed at similar frequencies in vaccinated and convalescent HNC individuals and positively correlated with plasma SARS- CoV-2 Abs levels. A predominant memory CD27+ phenotype and IgA isotype were observed within RBD-specific B cells of convalescent *versus* vaccinated individuals. Finally, the frequency of RBD-specific B cells negatively correlated with plasma levels of IL-6, an inflammatory cytokine marker of systemic inflammation. Thus, HNC patients mount efficient humoral

immunity against SARS-CoV-2 upon vaccination or natural infection. Our results highlight the importance of SARS-CoV-2 Abs of an IgA isotype in mucosal immunity and the harmful effect of systemic inflammation on antiviral responses. Longitudinal studies (in progress) will inform us about the duration of SARS-CoV-2 immunity in this group of HNC patients.

Keywords: SARS-CoV-2; immunity.

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Conflicts of Interest

The authors declare no conflict of interest.