

**CORRESPONDENCE**

**One-year data on immunogenicity and breakthrough infections in patients with solid tumors vaccinated against COVID-19 during systemic cancer treatment**



Patients with cancer have a higher risk of infection and severe coronavirus disease 2019 (COVID-19) despite vaccination.<sup>1</sup> In the prospective multicenter VOICE trial (Supplementary Figure S1, available at <https://doi.org/10.1016/j.esmooop.2023.100785>, NCT04715438), seroconversion rate after two vaccinations with mRNA-1273 was not inferior in patients treated for solid tumors with immunotherapy (cohort B; *n* = 131), chemotherapy (cohort C; *n* = 229), or chemoimmunotherapy (cohort D; *n* = 143) compared with controls (cohort A; *n* = 240).<sup>2</sup> At 6 months, across cohorts, there was a similar decline in binding antibody concentration with limited Omicron BA.1 neutralizing capacity.<sup>3</sup> Thereafter, participants were monitored and could receive additional COVID-19 vaccinations in the national program.

Here, we present 1-year follow-up data on immunogenicity and breakthrough infections. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-binding antibody concentrations, neutralization of wild type (WT) and Omicron BA.5, and T-cell responses were measured as previously described (Supplementary Methods, available at <https://doi.org/10.1016/j.esmooop.2023.100785>).<sup>2,3</sup> Breakthrough infections were assessed with 3-monthly questionnaires and with SARS-CoV-2 nucleoprotein-specific IgG antibody measurements (positive if  $\geq 14.3$  binding antibody units/ml).<sup>4</sup> Since the start of the trial, 24% of patients died, mainly due to cancer progression (Supplementary Figure S2 and Table S1, available at <https://doi.org/10.1016/j.esmooop.2023.100785>), none due to COVID-19. At 1 year, most participants had received three vaccinations, while 0.7%, 27.7%, 38.5%, and 17.9% in cohorts A, B, C, and D, respectively, had received four vaccinations (Supplementary

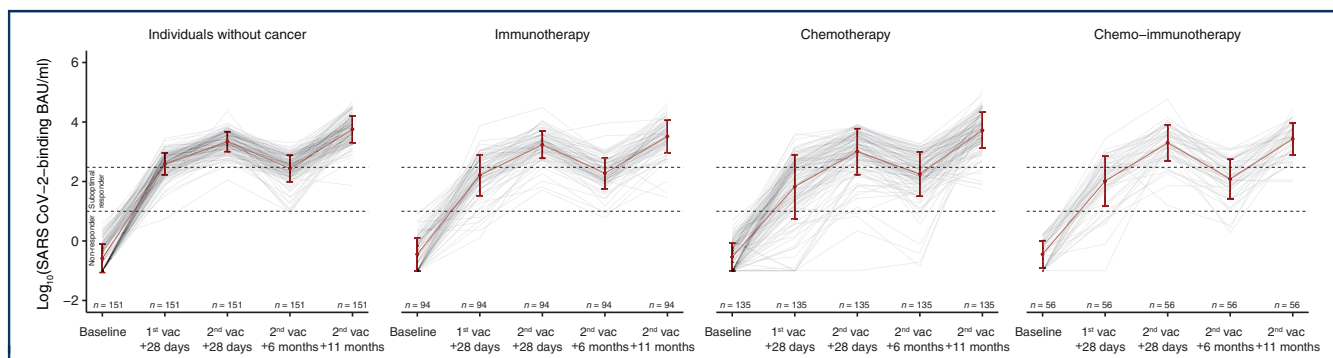
Table S2, available at <https://doi.org/10.1016/j.esmooop.2023.100785>). Across cohorts, there was a strong rise in binding antibody concentration at 1 year compared with the 6-month time point (Figure 1): the geometric mean concentrations increased 21, 17, 30, and 22 times in cohorts A, B, C, and D, respectively.

WT SARS-CoV-2 neutralizing antibody titers were universally high. Most participants in this subgroup analysis had a BA.5 neutralization titer  $>40$ : 100%, 96%, 90%, and 86% in cohorts A, B, C, and D (Supplementary Figure S3, available at <https://doi.org/10.1016/j.esmooop.2023.100785>). Participants who had a SARS-CoV-2 infection had higher WT and BA.5 neutralizing titers than those without a prior infection (Supplementary Figure S3, available at <https://doi.org/10.1016/j.esmooop.2023.100785>). Spike-specific T cells showed no relevant change compared with the 6-month time point (Supplementary Figure S3, available at <https://doi.org/10.1016/j.esmooop.2023.100785>).

Serological evidence of a prior SARS-CoV-2 infection was found in 7.3%, 7.5%, 7.4%, and 5.4% at 1 year in cohorts A, B, C, and D, and 9.9%, 9.6%, 8.1%, and 7.1% reported a SARS-CoV-2 infection (Supplementary Table S3, available at <https://doi.org/10.1016/j.esmooop.2023.100785>).

Decision tree analysis identified risk factors for low binding antibody concentrations at 1 year (Supplementary Methods, available at <https://doi.org/10.1016/j.esmooop.2023.100785>), namely, a longer time since the last vaccination, no prior SARS-CoV-2 infection, and less than three vaccinations in individuals who reported no infection (Supplementary Figure S4, available at <https://doi.org/10.1016/j.esmooop.2023.100785>). Cancer treatment during the first vaccination was not a risk factor.

Our data show that patients treated with chemotherapy, immunotherapy, or chemoimmunotherapy for a solid tumor at the time of the first vaccination have a similar increase in SARS-CoV-2-binding antibody concentration as controls 1 year later. All received at least one additional vaccination after the 6-month time point. Neutralizing capacity against BA.5 indicates cross-reactivity from vaccinations and



**Figure 1. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-binding antibody concentrations over time.** SARS-CoV-2-binding antibody concentrations (log<sub>10</sub> transformed) over time: before and 28 days after the first vaccination and 28 days, 6 months, and 11 months after the second vaccination. The red line connects the geometric mean concentrations, and the bars represent geometric standard deviations. The upper horizontal dashed line indicates the 300 BAU/ml threshold for an adequate response; the lower line represents the 10 BAU/ml threshold for seropositivity. BAU, binding antibody units.

infections. Our results support a booster vaccination before starting immunotherapy, chemotherapy, or chemoimmunotherapy for a solid tumor in patients with no SARS-CoV-2 infection or vaccination in the previous 3 months.

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