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CORRESPONDENCE

Factors associated with long-term antibody response after COVID-19 vaccination in patients treated with systemic treatment for solid tumors

Treatment with chemotherapy and immunotherapy at the time of coronavirus disease 2019 (COVID-19) vaccination may result in inadequate humoral responses.[1,2] We and others have demonstrated that a third vaccination increases serum severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-specific antibody concentration, but little is known about long-term antibody concentrations and breakthrough infections in these patients.[3-5] Here, we report the 18-month data of the prospective multicenter VOICE trial (Supplementary Figure S1, available at https://doi.org/10.1016/j.esmoop.2023.101599, NCT04715438) of COVID-19 vaccination in patients treated for solid tumors with immunotherapy (cohort B), chemotherapy (cohort C), or chemoimmunotherapy (cohort D) compared with controls (cohort A). In the trial, participants received two mRNA-1273 vaccinations (100 μg intramuscularly) 4 weeks apart and a third vaccination if the initial response was inadequate. All participants had access to additional COVID-19 messenger RNA (mRNA) vaccinations in the national vaccination program.

SARS-CoV-2-binding antibody concentrations were measured as previously described.[2] Breakthrough infections were assessed with three-monthly questionnaires and with SARS-CoV-2 nucleoprotein-specific immunoglobulin G (IgG) antibody measurements.

At 18 months, 112, 68, 97, and 36 participants were evaluable in cohorts A, B, C, and D, respectively (Supplementary Figure S2, available at https://doi.org/10.1016/j.esmoop.2023.101599). Participants received up to six vaccinations in total (Supplementary Table S1, available at https://doi.org/10.1016/j.esmoop.2023.101599). The high levels of binding antibody concentrations at 1 year were maintained at 18 months in all cohorts (Supplementary Figure S3, available at https://doi.org/10.1016/j.esmoop.2023.101599), and the geometric mean concentrations even slightly increased by 1.22-, 1.53-, 1.23-, and 1.03-fold in cohorts A, B, C, and D, respectively.

A SARS-CoV-2 infection in the previous 6 months was reported in 16.1% ($n = 18$), 8.8% ($n = 6$), 16.5% ($n = 16$), and 8.3% ($n = 3$) of patients in cohorts A, B, C, and D (Supplementary Table S2, available at https://doi.org/10.1016/j.esmoop.2023.101599) and serological evidence of prior SARS-CoV-2 infection at 18 months was found in 26.8% ($n = 30$), 17.6% ($n = 12$), 21.7% ($n = 21$), and 11.1% ($n = 4$) of patients. Decision tree analysis identified the absence of serological evidence of a prior infection as the most important factor for lower SARS-CoV-2-binding antibody concentrations at 18 months. Other determinants were long interval since last vaccination, no prior infection based on questionnaires, and long interval since infection (Figure 1, Supplementary Figure S4, available at https://doi.org/10.1016/j.esmoop.2023.101599). An increase in antibody concentration compared with previous measurement at 1 year was associated with a prior infection based on serology and time since last vaccination (Supplementary Figure S5, available at https://doi.org/10.1016/j.esmoop.2023.101599).

Based on serology and the questionnaire, 121 participants did not have breakthrough infections nor had received additional vaccines in the past 6 months. The median reduction of SARS-CoV-2-binding antibody concentration from 1 year to 18 months in these 121 participants was 1618.2 binding antibody units (BAU)/ml. The geometric mean concentrations for these participants were 3571.3, 3394.1, 4188.3, and 1607.4 BAU/ml in cohorts A, B, C, and D, respectively at 18 months, compared with 5243, 3373, 6334, and 3055.7, respectively, at 1 year.

Our 18-month data show that patients treated with chemotherapy, immunotherapy, or chemoimmunotherapy for a solid tumor at the time of initial vaccination have sustained high SARS-CoV-2-binding antibody concentrations, similar to controls. Additional vaccinations and infections but not cancer treatment determine antibody response over time. These encouraging results can be used to develop future vaccination strategies for patients with solid tumors, not only for the prevention of infectious diseases but also for the development of cancer vaccines.

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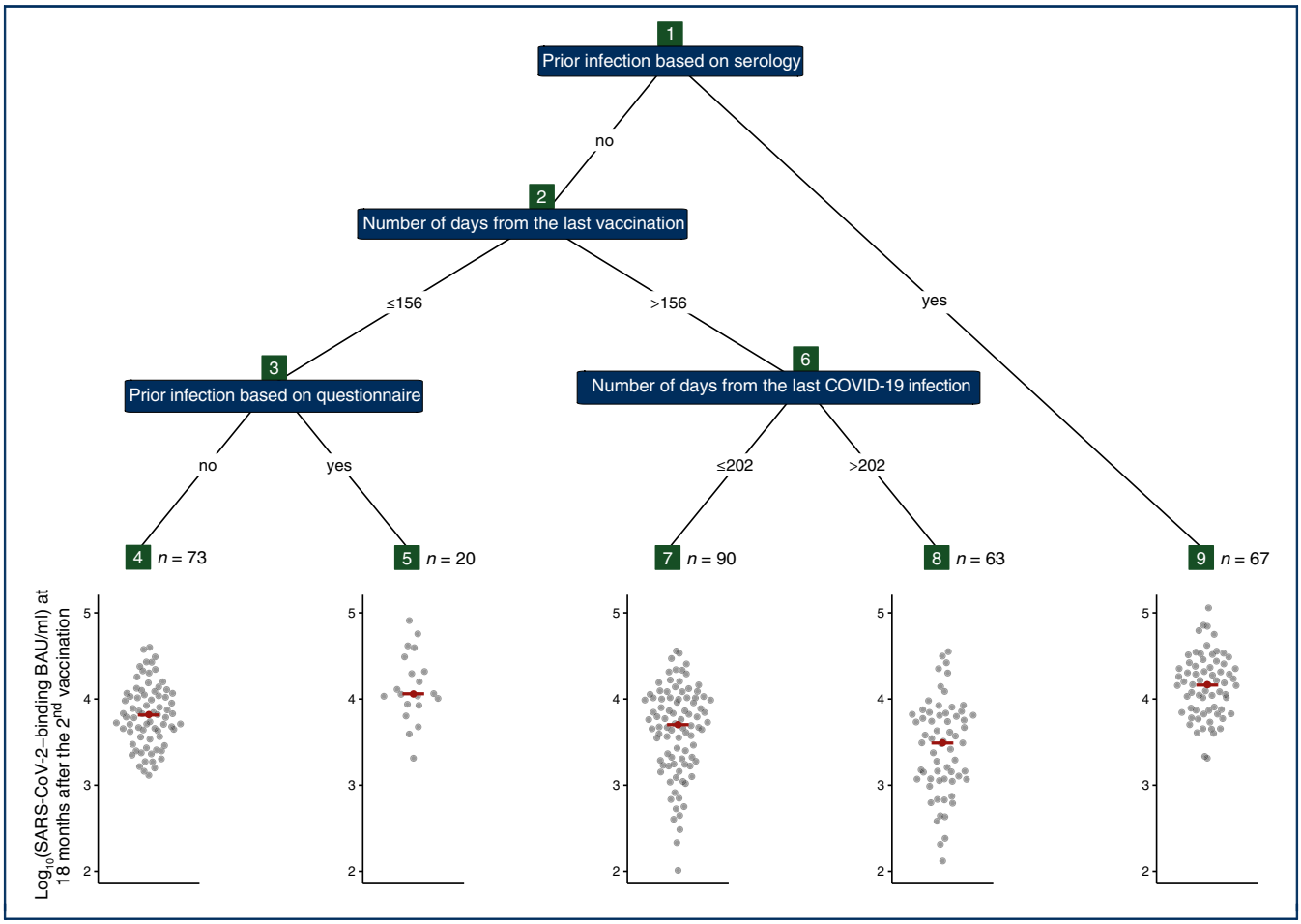

Figure 1. Decision tree demonstrating the five cohorts of participants with significantly different severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-binding antibody concentrations at 18 months after the second vaccination. Each node represents the most significant classifier splitting the corresponding group of patients into two groups with maximum different SARS-CoV-2-binding antibody concentrations (in BAU/ml, log10 transformed) at 18 months after the second vaccination. Significant classifiers are prior infection based on serology, number of days from the last vaccination, prior infection based on the questionnaire, and number of days from the last coronavirus disease 2019 (COVID-19) infection. For each node, the number of participants (*n*) is given. The scatterplots at each node show the distribution of SARS-CoV-2-binding antibody concentrations (in BAU/ml, log10 transformed) with the median in red at 18 months after the second vaccination. For detailed information see Supplementary Figure S4, available at https://doi.org/10.1016/j.esmoop.2023.101599. BAU, binding antibody units.

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S. F. Oosting[1,†], A. A. M. van der Veldt[2,3,*†], R. S. N. Fehrmann[1], A. Bhattacharya[1], R. S. van Binnendijk[4], C. H. GeurtsvanKessel[5], A.-M. C. Dingemans[6], E. F. Smit[7], T. J. N. Hiltermann[8], G. den Hartog[4], M. Jalving[1], T. T. Westphal[9], F. de Wilt[5], S. M. Ernst[6], A. Boerma[10], L. van Zijl[11], G. F. Rimmelzwaan[12], P. Kvistborg[13], C. A. C. M. van Els[14], N. Y. Rots[4], D. van Baarle[10], J. B. A. G. Haanen[11] & E. G. E. de Vries[1]

[1]Department of Medical Oncology, University Medical Centre Groningen, University of Groningen, Groningen; Departments of [2]Medical Oncology and [3]Radiology & Nuclear Medicine, Erasmus Medical Centre, Rotterdam; [4]Centre for Infectious Disease Control, National Institute for Public Health and the Environment, Bilthoven; Departments of [5]Viroscience and [6]Respiratory Medicine, Erasmus Medical Centre, Rotterdam; [7]Department of Thoracic Oncology, Netherlands Cancer Institute, Amsterdam; [8]Department of Pulmonary Diseases, University Medical Centre Groningen, University of Groningen, Groningen;

[9]*The Netherlands Comprehensive Cancer Organization, Utrecht;*
[10]*Department of Medical Microbiology and Infection Prevention University Medical Centre Groningen, University of Groningen, Groningen;*
[11]*Department of Medical Oncology, Netherlands Cancer Institute, Amsterdam, the Netherlands;*
[12]*Research Centre for Emerging Infections and Zoonoses, University of Veterinary Medicine Hannover, Hannover, Germany;*
[13]*Department of Molecular Oncology and Immunology, Netherlands Cancer Institute, Amsterdam;*
[14]*Department of Biomolecular Health Sciences, Faculty of Veterinary Medicine, Utrecht University, Utrecht, the Netherlands*
(*E-mail: a.vanderveldt@erasmusmc.nl).

[†]Contributed equally.

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