Open Forum Infectious Diseases

BRIEF REPORT

Antibody Response After Third Vaccination With mRNA-1273 or BNT162b2: Extension of a Randomized Controlled SARS-CoV-2 Noninferiority Vaccine Trial in Patients With Different Levels of Immunosuppression (COVERALL-2)

Alexandra Griessbach,[1] Frédérique Chammartin,[1] Irene A. Abela,[2,3] Patrizia Amico,[4] Marcel P. Stoeckle,[5] Anna L. Eichenberger,[6] Barbara Hasse,[3] Dominique L. Braun,[2,3] Macé M. Schuurmans,[7] Thomas F. Müller,[8] Michael Tamm,[9] Annette Audigé,[2] Nicolas J. Mueller,[3] Andri Rauch,[6] Huldrych F. Günthard,[2,3] Michael T. Koller,[4] Alexandra Trkola,[2] Selina Epp,[2] Alain Amstutz,[1] Christof M. Schönenberger,[1] Ala Taji Heravi,[1] Katharina Kusejko,[2,3] Heiner C. Bucher,[1] Matthias Briel,[1,10] and Benjamin Speich,[1] the Swiss HIV Cohort Study and the Swiss Transplant Cohort Study

[1]Division of Clinical Epidemiology, Department of Clinical Research, University Hospital Basel and University of Basel, Basel, Switzerland, [2]Institute of Medical Virology, University of Zurich, Zurich, Switzerland, [3]Department of Infectious Diseases and Hospital Epidemiology, University Hospital Zurich, Zurich, Switzerland, [4]Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Basel, Switzerland, [5]Division of Infectious Diseases and Hospital Epidemiology, University Hospital Basel, University of Basel, Basel, Switzerland, [6]Department of Infectious Diseases, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, [7]Division of Pulmonology, University Hospital Zurich, Zurich, Switzerland, [8]Nephrology Clinic, University Hospital Zurich, Zurich, Switzerland, [9]Clinic of Respiratory Medicine and Pulmonary Cell Research, University Hospital Basel, Basel, Switzerland, and [10]Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Canada

Extension of the COVERALL (COrona VaccinE tRiAL pLatform) randomized trial showed noninferiority in antibody response of the third dose of Moderna mRNA-1273 vaccine (95.3% [95% confidence interval {CI}, 91.9%–98.7%]) compared to Pfizer-BioNTech BNT162b2 vaccine (98.1% [95% CI, 95.9%–100.0%]) in individuals with different levels of immunosuppression (difference, −2.8% [95% CI, −6.8% to 1.3%]).

Keywords. SARS-CoV-2; HIV; Organ transplant; Vaccine; randomized trial.

Received 14 November 2022; editorial decision 06 March 2023; accepted 16 March 2023; published online 30 March 2023

Correspondence: Alexandra Griessbach, MSc, Division of Clinical Epidemiology, Department of Clinical Research, University Hospital Basel, Totengässlein 3 CH-4051, Basel, Switzerland (alexandranatacha.griessbach@usb.ch); Benjamin Speich, PhD, Division of Clinical Epidemiology, Department of Clinical Research, University Hospital Basel, Totengässlein 3 CH-4051, Basel, Switzerland (benjamin.speich@usb.ch).

Open Forum Infectious Diseases®

https://doi.org/10.1093/ofid/ofad150

The COrona VaccinE tRiAL pLatform (COVERALL) [1] is a randomized trial nested into 2 national cohort studies, the Swiss HIV Cohort Study (SHCS) [2] and the Swiss Transplant Cohort Study (STCS) [1, 3]. The first COVERALL study (COVERALL-1) determined the noninferiority of the Moderna mRNA-1273 vaccine to the Pfizer-BioNTech BNT162b2 vaccine in terms of antibody response after basic immunization, with 2 vaccine doses in patients with different levels of immunosuppression [4]. While people with human immunodeficiency virus (PWH) showed adequate antibody response, solid organ transplant (SOT) recipients showed insufficient antibody responses [4] as also shown in other studies [4–6]. A third vaccine dose was recommended for this population in winter 2021/2022 by the Swiss Federal Office of Public Health to ensure basic immunization and to accommodate for genetic drift, prevent the emergence of new variants, and provide prolonged protection of patients [7].

We invited all participants from COVERALL-1 to an extension of the COVERALL study (COVERALL-2) to investigate the noninferiority of antibody response of Moderna mRNA-1273 compared to Pfizer-BioNTech BNT162b2 after the third vaccine dose.

METHODS

The methods are explained in detail in the protocols (master protocol, protocol COVERALL-1, protocol COVERALL-2) and were approved by the ethical committee of Northwestern and Central Switzerland (BASEC [Business Administration System for Ethics Committees] number 2021-000593). These documents are publicly available on the trial registration site (https://clinicaltrials.gov/ct2/show/NCT04805125). In short, we included participants from the SHCS and STCS who received a third dose of Moderna vaccine (Spikevax; 50 µg [SHCS] or 100 µg [STCS] of mRNA-1273 in 0.5 mL) or Pfizer-BioNTech vaccine (Comirnaty; 30 µg of BNT162b2 in 0.3 mL) as part of their clinical routine following national recommendations in Switzerland [7]. Only patients who were previously randomized into COVERALL-1 (see Supplementary Material for detailed inclusion and exclusion criteria and flowchart) were included. Blood samples (ethylenediaminetetraacetic acid tubes; 2 × 7.5 mL) were collected at baseline (up to 2 weeks prior to the third vaccination) and 8 weeks (±2 weeks) after receiving the third vaccination. Patients were recruited from December 2021 to March 2022.

The primary outcome was the proportion of patients with a positive antibody response to SARS-CoV-2 spike (S1) protein receptor-binding domain (RBD) in human serum or plasma, assessed by the commercial immunoassay Elecsys

Anti-SARS-CoV-2 S from Roche Diagnostics at the follow-up visit 8 weeks after the third vaccination [8]. The primary outcome was binary and was considered positive if a threshold ≥100 units/mL was reached. This threshold has been shown to be predictive of 50% protective neutralization [9, 10]. We calculated the difference in antibody response between the 2 vaccines with a 2-sided 95% Wald confidence interval (CI). We chose a noninferiority design, assessing if the vaccines have a similar efficacy (in terms of antibody response) as the storage and handling of Moderna mRNA-1273 was supposed to be easier [1]. As previously described [4], we assumed noninferiority if the lower limit of the 95% 2-sided CI was above −10% in the intention-to-treat (ITT) and the per-protocol (PP) populations. The ITT population included all randomized patients who agreed to participate in the study extension and provided follow-up data at any time point. The PP population was restricted to participants who received the 3 vaccine doses in line with their randomized allocation (ie, 3 doses of Moderna vs 3 doses of Pfizer) and provided follow-up data within the prespecified time at 8 ± 2 weeks after the third vaccine dose. Secondary outcomes (see detailed definition in Supplementary Material) included (1) using a threshold of ≥0.8 units/mL for the primary outcome (Elecsys); (2) the proportion of patients with a positive antibody response using the Antibody CORonavirus Assay (ABCORA) 2 [11]; (3) the proportion of patients with neutralization activity against the vaccine strain Wuhan-Hu-1 in sera, defined as having an ABCORA sum S1 >17 [11]; (4) mean pan-immunoglobulin antibodies against the RBD in the S1 subunit of the spike protein (pan-immunoglobulin anti-S1-RBD) of SARS-CoV-2; (5) mean immune response of immunoglobulin M (IgM), immunoglobulin A (IgA), and immunoglobulin G (IgG) to the subunit S1 using ABCORA 2; (6) newly polymerase chain reaction (PCR)–confirmed SARS-CoV-2 infection; (7) newly PCR-confirmed asymptomatic SARS-CoV-2 infection; (8) newly PCR-confirmed symptomatic SARS-CoV-2 infection; (9) severe COVID-19 infection; (10) SARS-CoV-2 infection of a household member; (11) local symptoms limiting normal daily activities during the first 7 days after vaccination; (12) symptoms limiting normal daily activities during the first 7 days after vaccination; (13) any symptoms leading to contacting a physician during the first 7 days after vaccination; and (14) serious adverse events (SAEs). All analyses were additionally stratified by cohort (SHCS and STCS; Supplementary Table S4). Detailed information on statistical analyses are presented in the Supplementary Material.

RESULTS

A total of 312 of 430 (72.6%) participants from the previous COVERALL study agreed to participate in the extension study (154 received Moderna mRNA-1273 and 158 Pfizer-BioNTech BNT162b2; Supplementary Figure 1). We included 303 patients (277 SHCS and 26 STCS) in the ITT analysis and 234 patients (228 SHCS and 6 STCS) in the PP analysis. In the ITT dataset, 5 patients who were originally allocated to Moderna mRNA-1273 received Pfizer-BioNTech BNT162b2 and 17 who were originally allocated to Pfizer-BNT162b2 received Moderna mRNA-1273 as a third vaccine.

The majority of the patients were male (234/312 [75.0%]), had a median age of 54 years (interquartile range, 44–60 years), and were PWH (283/312 [90.7%]); Supplementary Tables 1 and 2). PWH generally had CD4 cell counts >350 cells/μL (262/312 [84.0%]) and a suppressed HIV RNA load (269/312 [95.1%]). Baseline characteristics were similar among COVERALL participants enrolled in COVERALL-2 and those who were not participating (Supplementary Table 1).

For patients randomized to Moderna mRNA-1273, 142 of 149 (95.3% [95% CI, 91.9%–98.7%]) had a sufficient antibody response (ie, Elecsys S test ≥100 units/mL) after the third SARS-CoV-2 vaccination. For patients randomized to Pfizer-BioNTech BNT162b, 151 of 154 (98.1% [95% CI, 95.9%–100.0%]) had an adequate antibody response (difference, −2.8% [95% CI, −6.8% to 1.3%]), fulfilling the noninferiority of Moderna mRNA-1273 (based on the ITT dataset; Table 1). According to the ABCORA 2 test, 143 of 149 (96.0% [95% CI, 92.8%–99.1%]) patients randomized to Moderna mRNA-1273 and 149 of 152 (98.0% [95% CI, 95.8%–100.0%]) randomized to Pfizer-BioNTech BNT162b2 showed a seroconversion (based on the ITT dataset; Table 1). Mean immunoglobulin values were comparable between groups (Table 1). Based on the Elecsys S test, 276 of 277 (99.6% [95% CI, 98.9%–100.0%]) PWH showed an adequate antibody response (Supplementary Table 4), whereas only 17 of 26 (65.4% [95% CI, 47.1%–83.7%]) SOT recipients had antibody levels above the Elecsys S test ≥100 units/mL cutoff (Supplementary Table 4). Further prespecified immunological outcomes are listed in Table 1. The PP results are in line with the ITT analysis (Supplementary Table 3).

Eight weeks after receiving the third vaccine, 24 of 307 (7.8%) patients reported that they had tested positive for SARS-CoV-2 (mRNA-1273: 14/151 [9.3%]; BNT162b2: 10/156 [6.4%]) (Table 1). No patients had severe COVID-19 infections leading to hospitalization. Furthermore, 15 of 307 (4.9%) patients reported household members who tested positive for SARS-CoV-2 (mRNA-1273: 7/151 [4.6%]; BNT162b2: 8/156 [5.1%]; Table 1). After receiving the third vaccine, 31 patients (10.1%) had reported systemic symptoms (13.3%; [20 of 150 patients] after receiving the third dose of Moderna mRNA-1273 and 7.1% [11 of 156 patients] after receiving the Pfizer-BioNTech BNT162b2 vaccine (Table 1). Two patients had at least 1 SAE, requiring hospitalization for (1) worsening of general condition, fever, and dyspnea and (2) simultaneous viral pulmonary and gastrointestinal infection (both SARS-CoV-2 negative), but no deaths occurred. None of the SAEs were classified as related to vaccines received (see SAE classification and reasons for hospitalization in Supplementary Table 5).

Table 1. Outcomes Based on the Intention-to-Treat Dataset

Outcomes	mRNA-1273 (Moderna)	BNT162b2 (Pfizer-BioNTech)	Total	Difference
Immune response (Elecsys S, cutoff ≥100 units/mL)	95.3% (91.9%–98.7%); 142/149	98.1% (95.9%–100.0%); 151/154	96.7% (94.7%–98.7%); 293/303	−2.8% (−6.8% to 1.3%)
Immune response (Elecsys S, cutoff ≥0.8 units/mL)	96.6% (93.8%–99.5%); 144/149	98.7% (96.9%–100.0%); 152/154	97.7% (96.0%–99.4%); 296/303	−2.1% (−5.5% to 1.3%)
Immune response (ABCORA 2) [11]	96.0% (92.8%–99.1%); 143/149	98.0% (95.8%–100.0%); 149/152	97.0% (95.1%–98.9%); 292/301	−2.1% (−5.9% to 1.8%)
Neutralization (ABCORA 2) [11], cutoff 17	92.6% (88.4%–96.8%); 138/149	96.7% (93.9%–99.6%); 147/152	94.7% (92.2%–97.2%); 285/301	−4.1% (−9.2% to 1.0%)
Immunoglobulins, mean (95% CI)				
IgG RBD	208.4 (195.7–221.1)	202.4 (192.9–212.0)	205.5 (197.5–213.5)	…
IgG S1	230.5 (214.7–246.3)	220.2 (207.2–233.1)	225.5 (215.2–235.7)	…
IgA S1	5.3 (4.8–5.8)	5.765 (5.4–6.3)	5.5 (5.2–5.9)	…
IgM S1	0.2 (.1–.2)	0.2 (.1–.3)	0.2 (.1–.2)	…
Clinical outcomes[a]				
Confirmed SARS-CoV-2 infection	9.3% (4.6%–13.9%); 14/151	6.4% (2.6%–10.3%); 10/156	7.8% (4.8%–10.8%); 24/307	…
Asymptomatic SARS-CoV-2 infection	0.7% (0.0–2.0%); 1/151	0.6% (0.0–1.9%); 1/156	0.7% (0.0–1.6%); 2/307	…
Symptomatic SARS-CoV-2 infection	8.6% (4.1%–13.1%); 13/151	5.8% (2.1%–9.4%); 9/156	7.2% (4.3%–10.1%); 22/307	…
Severe COVID-19 infection[b]	0.0% (0.0–0.0); 0/151	0.0% (0.0–0.0); 0/156	0.0% (0.0–0.0); 0/307	…
Confirmed SARS-CoV-2 infection of household members	4.6% (1.3%–8.0%); 7/151	5.1% (1.7%–8.6%); 8/156	4.9% (2.5%–7.3%); 15/307	…
Serious adverse events	0.7% (0.0–2.0%); 1/151	0.6% (0.0–1.9%); 1/156	0.7% (0.0–1.6%); 2/307	…
Death	0.0% (0.0–0.0); 0/151	0.0% (0.0–0.0); 0/156	0.0% (0.0–0.0); 0/307	…
Safety outcomes[c]				
Any symptoms at injection site limiting continuation of normal daily activities during the first 7 d following third vaccination	7.3% (3.2%–11.5%); 11/150	5.8% (2.1%–9.4%); 9/156	6.5% (3.8%–9.3%); 20/306	…
Any systemic symptoms (e.g. fever, muscle pain, joint pain) limiting continuation of normal daily activities during the first 7 d following third vaccination	13.3% (7.9%–18.8%); 20/150	7.1% (3.0%–11.7%); 11/156	10.1% (6.7%–13.5%); 31/306	…
Any vaccine-related symptoms leading to consultation 7 d following third vaccination	1.3% (0.0–3.2%); 2/150	0.0% (0.0–0.0); 0/156	0.7% (0.0–1.6%); 2/306	…

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M; RBD, receptor-binding domain; S1, S1 subunit of the spike protein; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a]Clinical outcomes: 5 missing.

[b]Safety outcomes: 9 missing.

[c]Symptoms leading to hospitalization.

DISCUSSION

In this extension of the randomized COVERALL study, we confirmed noninferiority of the Moderna mRNA-1273 vaccine to the Pfizer-BioNTech BNT162b2 vaccine in patients with different levels of immunosuppression, as assessed by the antibody response 8 weeks after receiving a third vaccine dose. Whereas almost all PWH showed an adequate antibody response, this response was still insufficient for 35% of SOT recipients.

Our results are in line with the findings from our previous study where almost all PWH had an adequate antibody response after 2 SARS-CoV-2 vaccinations [4]. It should be noted that the vast majority of PWH in our population had high CD4 cell counts (>350 cells/μL) and had a suppressed HIV RNA load (<50 copies/mL; Supplementary Table 2). For SOT recipients we noticed an improvement in the proportion of patients with antibody response, from 23.9% (17/71) in the first substudy (COVERALL-1) to 65.4% (17/26) in this extension (COVERALL-2). Due to the small number of participating SOT recipients (ie, only 26 in the ITT and 6 in the PP analysis), these findings need to be interpreted with caution.

The number of SARS-CoV-2 infections increased compared to the previous COVERALL-1 study [4], which is likely due to the emergence of new variants with higher transmissibility, such as Omicron [12]. Continued protection will require new or adapted vaccines such as the bivalent vaccines currently being approved or in the process of approval by Moderna and Pfizer-BioNTech, respectively [12].

Our extension study has the following limitations: First, many SOT recipients were vaccinated with a third dose before national guidelines recommended the third dose for the entire population and before this study could be initiated. Consequently, many SOT recipients who were randomized into COVERALL-1 could not be included in the COVERALL-2 extension study. Second, the event rates for the clinically relevant outcomes were strongly dependent on the progression of the pandemic, which was hard to predict. Hence, we chose a serological primary outcome (ie, antibody response). These 2 limitations also highlight the difficulties of conducting clinical trials in a pandemic setting. Third, since the vaccines were applied during clinical routine and not in the frame of the study, we had several participants who switched the vaccine product after the second vaccination (22/303 [6.7%]; Supplementary Figure 1). Nevertheless, ITT results are consistent with PP analyses.

In conclusion, the antibody response of Moderna mRNA-1273 compared to Pfizer-BioNTech BNT162b2 after third vaccination was noninferior in patients with different levels of immunosuppression. Additional strategies (eg, new vaccines, monoclonal antibodies) need to be investigated for nonresponders such as SOT recipients.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Members of the Swiss HIV Cohort Study (SHCS). Irene Abela, Karoline Aebi-Popp, Alexia Anagnostopoulos, Manuel Battegay, Enos Bernasconi, Dominique Laurent Braun, Heiner Bucher, Alexandra Calmy, Matthias Cavassini, Angela Ciuffi, Günter Dollenmaier, Matthias Egger, Luigia Elzi, Jan Fehr, Jacques Fellay, Hansjakob Furrer, Christoph Fux, Huldrych Günthard (President of the SHCS), Anna Hachfeld, David Haerry (deputy of "Positive Council"), Barbara Hasse, Hans Hirsch, Matthias Hoffmann, Irene Hösli, Michael Huber, David Jackson-Perry (patient representatives), Christian Kahlert (Chairman of the Mother and Child Substudy), Laurent Kaiser, Olivia Keiser, Thomas Klimkait, Roger Dimitri Kouyos, Helen Kovari, Katharina Kusejko (Head of data center), Niklaus Labhardt, Karoline Leuzinger, Begona Martinez de Tejada, Catia Marzolini, Karin J Metzner, Nicolas Müller, Johannes Nemeth, Dunja Nicca, Julia Notter, Paolo Paioni, Giuseppe Pantaleo, Matthieu Perreau, Andri Rauch (Chairman of the Scientific Board), Luisa Salazar-Vizcaya, Patrick Schmid, Roberto Speck, Marcel Stöckle (Chairman of the Clinical and Laboratory Committee), Philip Tarr, Alexandra Trkola, Gilles Wandeler, Maja Weisser, Sabine Yerly.

Members of the Swiss Transplant Cohort Study (STCS). Patrizia Amico, John-David Aubert, Vanessa Banz, Sonja Beckmann, Guido Beldi, Christoph Berger, Ekaterine Berishvili, Annalisa Berzigotti, Isabelle Binet, Pierre-Yves Bochud, Sanda Branca, Heiner Bucher, Emmanuelle Catana, Anne Cairoli, Yves Chalandon, Sabina De Geest, Olivier De Rougemont, Sophie De Seigneux, Michael Dickenmann, Joëlle Lynn Dreifuss, Michel Duchosal, Thomas Fehr, Sylvie Ferrari-Lacraz, Christian Garzoni, Déla Golshayan, Nicolas Goossens, Fadi Haidar, Jörg Halter, Dominik Heim, Christoph Hess, Sven Hillinger, Hans H. Hirsch, Patricia Hirt, Linard Hoessly, Günther Hofbauer, Uyen Huynh-Do, Franz Immer, Michael Koller, Bettina Laesser, Frédéric Lamoth, Roger Lehmann, Alexander Leichtle, Oriol Manuel, Hans-Peter Marti, Michele Martinelli, Valérie McLin, Katell Mellac, Aurélia Merçay, Karin Mettler, Nicolas J. Mueller, Ulrike Müller-Arndt, Beat Müllhaupt, Mirjam Nägeli, Graziano Oldani, Manuel Pascual, Jakob Passweg, Rosemarie Pazeller, Klara Posfay-Barbe, Juliane Rick, Anne Rosselet, Simona Rossi, Silvia Rothlin, Frank Ruschitzka, Thomas Schachtner, Stefan Schaub, Alexandra Scherrer, Aurelia Schnyder, Macé Schuurmans, Simon Schwab, Thierry Sengstag, Federico Simonetta, Susanne Stampf, Jürg Steiger, Guido Stirnimann, Ueli Stürzinger, Christian Van Delden, Jean-Pierre Venetz, Jean Villard, Julien Vionnet, Madeleine Wick, Markus Wilhelm, Patrick Yerly.

Author contributions. H. C. B., B. S., F. C., H. F. G., A. R., M. T. K., I. A. A., M. B., and K. K. designed the study. K. K. was responsible for managing the data platform. F. C. conducted the statistical analyses and was responsible for monitoring. B. S., A. G., C. M. S., A. T. H., A. Am., and M. B. coordinated the study. H. C. B., P. A., M. P. S., A. L. E., B. H., D. L. B., M. M. S., T. F. M., M. T., A. R., H. F. G., M. T., and N. J. M. were responsible for patient recruitment and follow-up at local centers. I. A. A., A. T., S. E., and A. Au. conducted all laboratory analyses. A. G., B. S., M. B., F. C., A. Am., and C. M. S. interpreted the data, A. G. and B. S. wrote the first draft of the manuscript; all authors read and approved the final version of the manuscript.

Acknowledgments. We thank all cohort patients who voluntarily participated in this study. We further thank the members of the data and safety monitoring board (Pietro Vernazza, Andreas F. Widmer, and Tracy Glass). We are grateful for all work conducted at the local centers in Basel (Erol Cetinkaya, Patricia Francois, Diana Grauwiler, Maria Pascarella, Rebekka Platter, Louise Seiler), Zurich (Daniela Gsell, Eliane Benz, Herbert Kuster, Laura Tschuor, Rosita Nujic, Christina Grube, Flurina Brunschweiler, Rheliana Katzensteiner, Christine Schneider, Claudia Schmidt, Dominik Damm, René Hage), Bern (Daniela Hirter, Manuela Correia da Silva Saúde, Pia Scherler, Anna Rehbock), and the Institute of Medical Virology, University of Zurich. Furthermore, we would like to thank the ethical committee Nordwest- and Zentralschweiz, Switzerland for their fast feedback.

Patient consent. Written informed consent was obtained from all participants. The study conforms to local and international standards (International Conference on Harmonisation Good Clinical Practice).

Disclaimer. The study design was discussed with the funder (Moderna) before funding was granted. The funders had no role in study, data collection and analysis, decision to publish, or preparation of the manuscript. Before submission, Moderna had the right to read and suggest

revision to the manuscript; however, no changes were proposed by Moderna.

Financial support. This substudy-2 (ie, COVERALL-2) was funded by Moderna. The set-up of the trial platform and COVERALL-1 were funded by the Schweizer nationalfond zur Förderung der Wissenschaft (grant number 31CA30_196245). The SHCS and STCS are funded by the Swiss National Science Foundation (SHCS: grant numbers 177499 and 201369; STCS: grant number 33CS30_177522). The virus diagnostic work was supported by a grant of the Pandemiefonds of the UZH Foundation (to A. T. I.). A. A. is supported by a research grant of the Promedica Stiftung (grant number 14851M). B. S. was supported by a grant from the Research Foundation of the University of Basel.

Potential conflicts of interest. B. S. and M. B. received a research grant from Moderna for the conduct of this study. H. C. B. has received in the 36 months prior to the submission of this manuscript grants, support for traveling, consultancy fees and honorarium from Gilead, BMS, ViiV Healthcare, Roche, and Pfizer that were not related to this project. He served as the president of the Association contre le HIV et autres infections transmissibles until June 2022. In this function he has received support for the SHCS from ViiV Healthcare, Gilead, BMS, and MSD. I. A. A. has received honoraria from MSD, Sanofi, and travel grant from Gilead Sciences and is supported by a research grant from the Promedica Foundation (all not related to this study). A. T. received a consultant fee from Roche and has received unrestricted research funding from Gilead and Roche not related to this study. D. L. B. received honoraria for advisory boards from the companies Gilead, MSD, and ViiV outside of the study. H. F. G., outside of this study, reports grants from the Swiss National Science Foundation, National Institutes of Health (NIH), and the SHCS; unrestricted research grants from Gilead Sciences, Roche, and Yvonne Jacob Foundation; and personal fees from consulting or advisory boards or data and safety monitoring boards for Merck, Gilead Sciences, ViiV Healthcare, Mepha, and Sandoz. H. F. G.'s institution received money for participation in the following clinical COVID-19 studies: 540-7773/5774 (Gilead), TICO (ACTIV-3, INSIGHT/NIH), and the Morningsky study (Roche). N. J. M. received honoraria for advisory boards from the companies Pfizer and Takeda outside of the study. A. R. reports support to his institution for advisory boards and/or travel grants from MSD, Gilead Sciences, Pfizer, and Moderna, and an investigator-initiated trial grant from Gilead Sciences. All remuneration went to his home institution and not to A. R. personally, and all remuneration was provided outside the submitted work. All other authors report no potential conflicts.

References

1. Speich B, Chammartin F, Smith D, et al. A trial platform to assess approved SARS-CoV-2 vaccines in immunocompromised patients: first sub-protocol for a pilot trial comparing the mRNA vaccines Comirnaty and COVID-19 mRNA vaccine Moderna. Trials **2021**; 22:724.
2. Scherrer AU, Traytel A, Braun DL, et al. Cohort profile update: the Swiss HIV Cohort Study (SHCS). Int J Epidemiol **2022**; 51:33–34j.
3. Koller MT, van Delden C, Müller NJ, et al. Design and methodology of the Swiss Transplant Cohort Study (STCS): a comprehensive prospective nationwide long-term follow-up cohort. Eur J Epidemiol **2013**; 28:347–55.
4. Speich B, Chammartin F, Abela IA, et al. Antibody response in immunocompromised patients after the administration of SARS-CoV-2 vaccine BNT162b2 or mRNA-1273: a randomised controlled trial. Clin Infect Dis **2022**; 75:e585–93.
5. Schietzel S, Anderegg M, Limacher A, et al. Humoral and cellular immune responses on SARS-CoV-2 vaccines in patients with anti-CD20 therapies: a systematic review and meta-analysis of 1342 patients. RMD Open **2022**; 8:e002036.
6. Galmiche S, Luong Nguyen LB, Tartour E, et al. Immunological and clinical efficacy of COVID-19 vaccines in immunocompromised populations: a systematic review. Clin Microbiol Infect **2022**; 28:163–77.
7. Swiss Federal Office of Public Health. Empfehlung einer Auffrischimpfung gegen Covid-19 mit einem mRNA-Impfstoff (Stand 13.04.22). Accessed 12 December 2022.
8. Roche Diagnostics. Elecsys Anti-SARS-CoV-2 S. Available at: https://diagnostics.roche.com/global/en/products/params/elecsys-anti-sars-cov-2-s.html. Accessed 9 August 2022.
9. Hall VG, Ferreira VH, Ku T, et al. Randomized trial of a third dose of mRNA-1273 vaccine in transplant recipients. N Engl J Med **2021**; 385:1244–6.
10. Khoury DS, Cromer D, Reynaldi A, et al. Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. Nat Med **2021**; 27:1205–11.
11. Abela IA, Pasin C, Schwarzmüller M, et al. Multifactorial seroprofiling dissects the contribution of pre-existing human coronaviruses responses to SARS-CoV-2 immunity. Nat Commun **2021**; 12:6703.
12. Callaway E. Fast-evolving COVID variants complicate vaccine updates. Nature **2022**; 607:18–9.