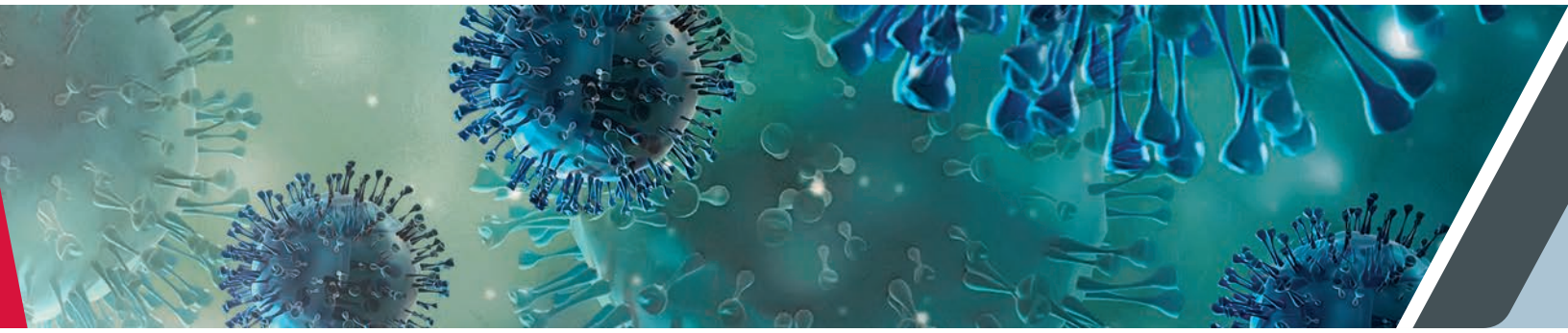
Ortho's Call to Action

Maximizing the Benefits of COVID-19 Vaccines With the Right Serological Tests

Lily Li, MD, PhD,[a] **Ivan Salgo, MD**[b]
[a]Director of Medical and Scientific Affairs, [b]Global Head of Medical, Clinical and Scientific Affairs, Ortho Clinical Diagnostics



Background

Since the end of 2019, the world has been fighting the unprecedented global COVID-19 pandemic caused by SARS-CoV-2.[1] This pandemic inspired significant efforts for the development of diagnostic tests, therapeutics and vaccines.[2,3,4] As a result, multiple efficacious COVID-19 vaccines have been developed and authorized in record speed[5] and are playing a critical role to provide protection against SARS-CoV-2 infection and to eventually put the pandemic under control.[6–10]

There is a critical and urgent need to identify surrogate markers, e.g., antibody levels or titers, that correlate with immune protection from SARS-CoV-2 breakthrough infection or reinfection to maximize the benefits of COVID-19 vaccines.

With more than 200 million people infected with SARS-CoV-2 and about 4.8 billion vaccine doses administered,[11,12] there is a critical and urgent need to identify surrogate markers, e.g., antibody levels or titers, that correlate with immune protection from SARS-CoV-2 breakthrough infection or reinfection to maximize the benefits of COVID-19 vaccines.[13,14] In regions and countries where vaccines are in short supply, correlates of protection may allow prioritizing vaccine administration and optimizing dosing schedules to achieve broader population protection.[15,16] For people who received vaccines, correlates of protection can help to evaluate if individuals have developed optimal immune responses, especially in high-risk populations such as elderly individuals and immunocompromised patients,[17] or may need additional booster(s). In addition, since immune responses wane over time, correlates of protection will indicate who and when people may need to be revaccinated or receive a booster to maintain immune protection.[18]

Circulating antibody levels or titers are used to indicate vaccination or immune protection in infectious diseases.[19] An antibody threshold is used to determine protection with the hepatitis B vaccine[20] and a correlation of hemagglutination-inhibition (HAI) antibody titer with 50%, 80% or 90% protection can be established for influenza vaccines.[21,22] Serological antibody levels or titers may serve as a promising biomarker to assess the immune protection of the COVID-19 vaccine to help maximize the benefits of these vaccines globally.

Neutralizing antibodies are a key mechanism of immune protection

Adaptive immunity is a combined outcome of both cellular and humoral (antibody) immune responses,[23] and antibodies serving as the frontline of protection are the hallmark of the humoral immune response.[24] Neutralizing antibodies are a subset of antibodies often against the viral surface proteins.[25] SARS-CoV-2 infects human cells using the Spike (S) protein, which consists of S1 and

S2 subunits.[26] The S1 subunit contains a receptor-binding domain (RBD) that can specifically bind to angiotensin-converting enzyme 2 (ACE2) on host cells and trigger the infection.[26] Neutralizing antibodies, particularly long-lasting Immunoglobulin G (IgG), that inhibit the binding of S1/RBD to ACE2 and block viral infection and replication represent a key mechanism of immune protection.[24,27]

Monoclonal antibodies to the S1 protein that exhibit neutralizing activities have been developed and proved to be effective therapeutics for COVID-19 patients.[28,29] Neutralizing antibodies to the S protein are the key active ingredients of convalescent plasma used to treat severe COVID-19 patients.[30] Almost all COVID-19 vaccines target the S protein with the goal to induce neutralizing antibodies to prevent SARS-CoV-2 infection.[31] In addition, several clinical studies showed that neutralizing antibody levels or titers correlated with immune protection.[27] All these observations suggest that anti-S neutralizing antibodies represent a key mechanism of vaccine-induced immune protection.

Anti-S neutralizing antibodies represent a key mechanism of vaccine-induced immune protection.

Neutralizing antibodies are typically measured by biological assays mimicking viral infection in cultured cells.[32] The plaque reduction neutralization test (PRNT) is the classical test for measuring neutralizing antibody titers[33] and pseudo viral neutralization tests are also commonly used.[34] However, neutralization tests are time-consuming, labor-intensive and not suitable for scaled-up routine testing in large populations.[33,34] Studies have shown that some serological tests targeting the S1 subunit or the RBD of the SARS-CoV-2 S protein exhibited good correlation with neutralizing titers, and thus may be used as surrogate tests to assess neutralizing antibody and immune protection in large patient populations.[35]

The suitable serological test to measure antibody level and evaluate immune protection by vaccines

Since the beginning of the pandemic, hundreds of serological tests have been developed including more than 80 tests that received U.S. Food and Drug Administration Emergency Use Authorization.[36] These tests represent different formats including Lateral Flow Rapid tests, lab-developed enzyme-linked immunosorbent assay (ELISA) and automated high throughput chemiluminescent tests.[37] Different tests target different viral antigens including nucleocapsid (N) protein, S protein, S1 subunit and RBD.[35] The tests also detect different antibody isotypes including IgM, IgG, IgA or Total (all isotypes) and report qualitative or semi-quantitative or quantitative test results.[36]

It is challenging to compare study results across a large variety of COVID-19 serological tests, and standardization of serological tests is critically needed for the next phase of pandemic control.

Lastly, clinical performance may vary significantly among the tests regarding clinical sensitivity and specificity.[36] Therefore, it is challenging to compare study results across a large variety of COVID-19 serological tests, and standardization of serological tests is critically needed for the next phase of pandemic control.[38]

To address this challenge, the World Health Organization (WHO) generated an International Standard for SARS-CoV-2 antibodies.[39] The standard material was developed from a pool of convalescent plasma and can be used for the calibration and harmonization of serological assays detecting SARS-CoV-2 neutralizing antibodies or binding antibodies. The availability of an International Standard for antibodies would facilitate the standardization of SARS-CoV-2 serological methods and allow for comparison and harmonization of datasets across laboratories, and most importantly, this will help determine the antibody levels that are needed to assess vaccine efficacy and therapeutics and improve our understanding of virus epidemiology.[40]

Quantitative assays calibrated to the WHO International Standard are critical for the measurement of antibody levels, allowing for the evaluation of immune protection of COVID-19 vaccines over time and data comparison across studies.

Therefore, quantitative assays calibrated to the WHO International Standard are critical to measure antibody levels and evaluate immune protection of COVID-19 vaccines over time and data comparison across studies. In addition, the tests need to measure the long-lasting IgG antibodies targeting the S protein, S1 subunit or the RBD that include neutralizing antibodies that mediate immune protection. The tests need to demonstrate good correlation with a neutralized assay (preferably a PRNT). The tests should run on fully automated, high-throughput platforms to handle a high volume of samples, and must show excellent clinical sensitivity and specificity.

Antibody measurement post-vaccination can provide a multitude of clinical benefits, especially in immunocompromised individuals

Due to individual variations, completion of a full course of vaccination does not necessarily mean successful induction of immune response nor immune protection.[14] Reports have shown that a small percentage of people did not seroconvert after a full course of the vaccine[41] and immune response was lower in elderly individuals.[42] In immunocompromised patients, such as solid organ transplant recipients,[43] autoimmune patients receiving high-dose corticosteroids, anti-inflammatory biologics or immunomodulatory treatments, a large portion of these patients either did not have detectable antibody production after vaccination or with significantly lower antibody levels.[44,45] Studies showed that for some of the solid organ recipients, antibodies were not detected even after a third vaccine booster.[46] Management of at-risk individuals remains a major challenge for the health care system. Therefore, it would be helpful to assess antibody response related to vaccination in order to identify individuals who may not produce antibodies or may not have an "optimal" antibody response to ensure appropriate behavior for self-protection.

It would be helpful to assess antibody response related to vaccination in order to identify individuals who may not produce antibodies.

For the population at large, longitudinal measurement of antibody levels can monitor the waning of the immune response and thus determine the need for revaccination or a booster.[47] For individuals who have an elevated risk of adverse reaction to vaccines, testing can help to determine the timing of a booster only if it is needed.[48] In addition, for countries/regions where there is a shortage of vaccines, testing may help to prioritize dispensation of vaccines to seronegative patients and to optimize dosing schedules to cover larger populations.[14]

Establishing antibody level threshold or correlation with immune protection

Approximately 4.8 billion vaccine doses have been administered globally, a correlate of protection for SARS-CoV-2 vaccines is urgently needed, as stated in a recent commentary article in *Nature Medicine.*[13] Recent studies suggest that antibody could serve as a marker for correlate of protection for vaccines against SARS-CoV-2,[49,50] the optimal goal is to establish a universal or transferable antibody threshold or correlate for immune protection with standardized quantitative assays.

The optimal goal is to establish a universal or transferrable antibody threshold or correlate for immune protection with standardized quantitative assays.

The threshold or correlations of protection were often established via longitudinal follow-up studies in large and diverse populations.[27] Correlation of protection against symptomatic SARS-CoV-2 infection of the AstraZeneca (AZD1222) vaccine was reported in a recent study.[50] In this study, four different assays (anti-spike and anti-RBD IgG immunoassays and two neutralization assays) were used to measure antibody levels or neutralizing titers and different threshold was established for each of these assays for 80% protection.[50] Another study reported immune correlates of the Moderna (mRNA-1273) vaccine in the efficacy trial.[49] Anti-Spike IgG and anti-RBD IgG immunoassays and a pseudo viral neutralization test were used, antibody levels or neutralizing titers were each inversely correlated with risk of SARS-CoV-2 infection hazard ratios, and not surprisingly, the antibody levels or titers mediated vaccine efficacy differ among different assays.[49]

Because different antibody binding assays or neutralization assays were used in these studies, and the assays were not standardized, antibody thresholds or level of correlation with protection were not transferable to other assays, which largely limited the use of the identified thresholds or correlates of protection. In an effort to address the challenge, a study published in *Nature Medicine* from May 2021 established a correlation of neutralizing antibody levels with immune protection from symptomatic COVID-19 patients by modeling the data from seven vaccine clinical trials. The study "standardized" the neutralization tests based on convalescent plasma titers and developed a predictive model for immune protection based on neutralization level.[49] However, the authors did point out one of the caveats of the study was aggregation of data collected from diverse neutralization assays and clinical trial designs. The author hoped that in the future a standardized neutralization assay would be developed and utilized, which will allow direct comparison of neutralization titers and further refinement of these analyses.[49]

The establishment of correlation with immune protection with a standardized assay is urgently needed to offer better patient management and to plan the next steps in the COVID-19 vaccine program.

Therefore, the establishment of correlates of protection with standardized assays is urgently needed to offer better patient management and to plan the next steps in the COVID-19 vaccine program. As stated in the *Nature Medicine* article: "… swift data sharing and collaboration to establish an absolute correlate of protection should be the number one priority for vaccine producers, academic researchers and regulatory agencies."[13] It takes a village to achieve this goal, and this is the most urgent goal for all of us, the global villagers.

Summary

As of mid-August, over 4.8 billion vaccine doses have been administered yet supply continues to be a challenge for many countries, and the number of infected individuals continues to rise. To help stop the transmission of SARS-CoV-2, there is a critical and urgent need to identify reliable, scalable surrogate markers to assess immune protection to SARS-CoV-2 and to guide clinical actions. Clinical studies with COVID-19 vaccines have demonstrated a correlation between antibody levels or titers and immune protection; however, these studies were conducted using different serological or neutralization tests, and the results, therefore, cannot be easily compared or transferrable across tests.

To address this, the WHO has developed a standard for quantitative IgG tests targeting the S1 or RBD of SARS-CoV-2 with good correlation to neutralization assays. These tests can help evaluate an antibody response to vaccination, especially after vaccination booster administration. Additionally, they can help give perspective on the correlation of protection to breakthrough infection post-vaccination. More large population studies are underway to better understand the correlate of protection with different vaccines, in different patient populations and against SARS-CoV-2 variants.

A correlate of protection established by the standardized serological tests will be a valuable tool in evaluating immune protection, especially for the immune-compromised patient as well as other high-risk populations, and to identify the patients who need additional booster(s). Antibody tests can potentially help patients with a high risk of adverse reaction to the vaccine to avoid unnecessary booster(s). In regions with vaccine scarcity, antibody testing may help prioritize vaccine administration and optimize dosing strategy. There is little doubt that a correlate of protection established using the right serological test can help to maximize the benefits of vaccines at the individual level as well as in global population scales.

Key takeaways:

- A correlate of protection for COVID-19 vaccines is urgently needed for patient care as well as for vaccine strategies
- The right tests to establish the correlate of protection are quantitative IgG assays targeting S/S1/RBD and are standardized to the WHO International Standard
- High-risk individuals, such as the elderly, or immunocompromised patients or those who do not have an optimal immune response to vaccines need to be identified by antibody testing for additional management

REFERENCES

1. World Health Organization. Coronavirus disease (COVID-19) pandemic. Accessed August 19, 2021. https://www.who.int/emergencies/diseases/novel-coronavirus-2019

2. Gitman MR, Shaban MV, Paniz-Mondolfi AE, Sordillo EM. Laboratory diagnosis of SARS-CoV-2 pneumonia. *Diagnostics (Basel).* 2021;11(7):1270. doi:10.3390/diagnostics11071270

3. Marei HE, Althani A, Afifi N, et al. Pandemic COVID-19 caused by SARS-CoV-2: genetic structure, vaccination, and therapeutic approaches. *Mol Biol Rep.* 2021. doi:10.1007/s11033-021-06630-4

4. National Institutes for Health. Therapeutic management of hospitalized adults with COVID-19. Accessed August 19, 2021. https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/hospitalized-adults--therapeutic-management/

5. Heinz FX, Stiasny K. Distinguishing features of current COVID-19 vaccines: knowns and unknowns of antigen presentation and modes of action. *NPJ Vaccines.* 2021;6(1):104. doi:10.1038/s41541-021-00369-6

6. Thompson MG, Burgess JL, Naleway AL, et al. Prevention and attenuation of COVID-19 with the BNT162b2 and mRNA-1273 vaccines. *N Engl J Med.* 2021;385:320-329. doi:10.1056/NEJMoa2107058

7. Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med.* 2021;384:403-416. doi:10.1056/NEJMoa2035389

8. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. *N Engl J Med.* 2020;383:2603-2615. doi:10.1056/NEJMoa2034577

9. Kumar S, Saurabh MK, Maharshi V. Efficacy and safety of potential vaccine candidates against coronavirus disease 2019: A systematic review. *J Adv Pharm Technol Res.* 2021;12(3):215-221. doi:10.4103/japtr.JAPTR_229_20

10. Puranik A, Lenehan PJ, Silvert E, et al. Comparison of two highly-effective mRNA vaccines for COVID-19 during periods of Alpha and Delta variant prevalence. *medRxiv.* [Preprint]. 2021:2021.08.06.21261707. doi:10.1101/2021.08.06.21261707

11. World Health Organization. WHO Coronavirus (COVID-19) dashboard. Accessed August 19, 2021. https://covid19.who.int/

12. Johns Hopkins University & Medicine. COVID-19 dashboard. Accessed August 19, 2021. https://coronavirus.jhu.edu/map.html

13. Krammer F. A correlate of protection for SARS-CoV-2 vaccines is urgently needed. *Nat Med.* 2021;27:1145-1153. doi:10.1038/s41591-021-01432-4

14. Lippi G, Henry BM, Plebani M. Anti-SARS-CoV-2 antibodies testing in recipients of COVID-19 vaccination: why, when, and how? *Diagnostics (Basel).* 2021;11(6):941. doi:10.3390/diagnostics11060941

15. Kow CS, Hasan SS. Real-world effectiveness of BNT162b2 mRNA vaccine: a meta-analysis of large observational studies. *Inflammopharmacology.* 2021;29(4):1075-1090. doi:10.1007/s10787-021-00839-2

16. Zollner A, Watschinger C, Rössler A, et al. B and T cell response to SARS-CoV-2 vaccination in health care professionals with and without previous COVID-19. *EBioMedicine.* 2021;70:103539. doi:10.1016/j.ebiom.2021.103539

17. Kamar N, Abravanel F, Marion O, Couat C, Izopet J, Del Bello A. Three doses of an mRNA COVID-19 vaccine in solid-organ transplant recipients. *N Engl J Med.* 2021;385(7):661-662. doi:10.1056/NEJMc2108861

18. Pegu A, O'Connell S, Schmidt SD, et al. Durability of mRNA-1273 vaccine-induced antibodies against SARS-CoV-2 variants. *Science.* 2021:eabj4176. doi:10.1126/science.abj4176

19. Plotkin SA, Gilbert PB. Nomenclature for immune correlates of protection after vaccination. *Clin Infect Dis.* 2012;54(11):1615-1617. doi:10.1093/cid/cis238

20. Poorolajal J, Hooshmand E. Booster dose vaccination for preventing hepatitis B. *Cochrane Database Syst Rev.* 2016;2016(6):CD008256. doi:10.1002/14651858.CD008256.pub3

21. Coudeville L, Bailleux F, Riche B, et al. Relationship between haemagglutination-inhibiting antibody titres and clinical protection against influenza: development and application of a bayesian random-effects model. *BMC Med Res Methodol.* 2010;10:18. doi:10.1186/1471-2288-10-18

22. Dunning AJ, DiazGranados CA, Voloshen T, Hu B, Landolfi VA, Talbot HK. Correlates of protection against influenza in the elderly: results from an influenza vaccine efficacy trial. *Clin Vac Immuno.* 2016;23(3):228-235. doi:10.1128/CVI.00604-15

23. Manners C, Larios Bautista E, Sidoti H, Lopez OJ. Protective adaptive immunity against severe acute respiratory syndrome Coronaviruses 2 (SARS-CoV-2) and implications for vaccines. *Cureus.* 2020;12(6):e8399. doi:10.7759/cureus.8399

24. Castro Dopico X, Ols S, Lore K, Karlsson Hedestam GB. Immunity to SARS-CoV-2 induced by infection or vaccination. *J Intern Med.* 2021;0:1-19. doi:10.1111/joim.13372

25. Dispinseri S, Secchi M, Pirillo MF, et al. Neutralizing antibody responses to SARS-CoV-2 in symptomatic COVID-19 is persistent and critical for survival. *Nat Commun.* 2021;12(1):2670. doi:10.1038/s41467-021-22958-8

26. Almehdi AM, Khoder G, Alchakee AS, Alsayyid AT, Sarg NH, Soliman SSM. SARS-CoV-2 spike protein: pathogenesis, vaccines, and potential therapies. *Infection.* 2021:1-22. doi:10.1007/s15010-021-01677-8

27. Khoury D, Cromer D, Reynaldi A, et al. Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. *Nat Med.* 2011;27:1205-1211. doi:10.1038/s41591-021-01377-8

28. Baral PK, Yin J, James MNG. Treatment and prevention strategies for the COVID 19 pandemic: a review of immunotherapeutic approaches for neutralizing SARS-CoV-2 [published online ahead of print, 2021 Jul 5]. *Int J Biol Macromol.* 2021;186:490-500. doi:10.1016/j.ijbiomac.2021.07.013

29. Taylor PC, Adams AC, Hufford MM, et al. Neutralizing monoclonal antibodies for treatment of COVID-19. *Nat Rev Immunol.* 2021;21:382-393. doi:10.1038/s41577-021-00542-x

30. Rojas M, Rodríguez Y, Monsalve DM, et al. Convalescent plasma in COVID-19: Possible mechanisms of action. *Autoimmun Rev.* 2020;19(7):102554. doi:10.1016/j.autrev.2020.102554

31. Malik YS, Kumar P, Ansari MI, et al. SARS-CoV-2 Spike protein extrapolation for COVID diagnosis and vaccine development. *Front Mol Biosci.* 2021;8:607886. doi:10.3389/fmolb.2021.607886

32. Larsen SE, Berube BJ, Pecor T, et al. Qualification of ELISA and neutralization methodologies to measure SARS-CoV-2 humoral immunity using human clinical samples. [Preprint] *bioRxiv*. 2021:2021.07.02.450915. doi:10.1101/2021.07.02.450915

33. Bewley KR, Coombes NS, Gagnon L, et al. Quantification of SARS-CoV-2 neutralizing antibody by wild-type plaque reduction neutralization, microneutralization and pseudotyped virus neutralization assays. *Nat Protoc.* 2021;16:3114-3140. doi:10.1038/s41596-021-00536-y

34. Crawford KHD, Eguia R, Dingens AS, et al. Protocol and reagents for pseudotyping lentiviral particles with SARS-CoV-2 Spike protein for neutralization assays. *Viruses.* 2020;12(5):513. doi:10.3390/v12050513

35. Luchsinger LL, Ransegnola BP, Jin DK, et al. Serological assays estimate highly variable SARS-CoV-2 neutralizing antibody activity in recovered COVID-19 patients. *J Clin Microbiol.* 2020;58(12):e02005-e02020. doi:10.1128/JCM.02005-20

36. U.S. Food and Drug Administration. EUA authorized serology test performance. Accessed August 18, 2021. https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/eua-authorized-serology-test-performance

37. Shi AC, Ren P. SARS-CoV-2 serology testing: Progress and challenges. *J Immunol Methods.* 2021;494:113060. doi:10.1016/j.jim.2021.113060

38. Gundlapalli AV, Salerno RM, Brooks JT, et al. SARS-CoV-2 serologic assay needs for the next phase of the US COVID-19 pandemic response. *Open Forum Infect Dis.* 2020;8(1):ofaa555. doi:10.1093/ofid/ofaa555

39. NIBSC. Coronavirus (COVID-19)-related research reagents available from the NIBSC. Accessed August 18, 2021. https://www.nibsc.org/science_and_research/idd/cfar/covid-19_reagents.aspx

40. World Health Organization. WHO/BS.2020.2403 establishment of the WHO International Standard and reference panel for anti-SARS-CoV-2 antibody. Accessed August 18, 2021. https://www.who.int/publications/m/item/WHO-BS-2020.2403

41. Lustig Y, Sapir E, Regev-Yochay G, et al. BNT162b2 COVID-19 vaccine and correlates of humoral immune responses and dynamics: a prospective, single-centre, longitudinal cohort study in health-care workers. *Lancet.* doi:10.1016/S2213-2600(21)00220-4

42. Parry HM, Tut G, Faustini S, et al. BNT162b2 vaccination in people over 80 years of age induces strong humoral immune responses with cross neutralisation of P.1 Brazilian variant. *Lancet.* 2021. doi:10.2139/ssrn.3816840

43. Del Bello A, Abravanel F, Marion O, et al. Efficiency of a boost with a third dose of anti-SARS-CoV-2 messenger RNA-based vaccines in solid organ transplant recipients. *Am J Transplant.* 2021. doi:10.1111/ajt.16775

44. Ammitzbøll C, Bartels LE, Bøgh Andersen J, et al. Impaired antibody response to the BNT162b2 messenger RNA Coronavirus disease 2019 vaccine in patients with systemic Lupus Erythematosus and Rheumatoid Arthritis. *ACR Open Rheumatol.* 2021. doi:10.1002/acr2.11299

45. Drulovic J, Ivanovic J, Martinovic V, et al. Humoral response to SARS-CoV-2 and COVID-19 vaccines in patients with multiple sclerosis treated with immune reconstitution therapies. *Mult Scler Rel Dis.* 2021;54:103150. doi:10.1016/j.msard.2021.103150

46. 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. doi:10.1056/NEJMc2111462

47. Hamady A, Lee J, Loboda ZA. Waning antibody responses in COVID-19: what can we learn from the analysis of other coronaviruses? [Epub ahead of print]. *Infection.* 2021:1-15. doi:10.1007/s15010-021-01664-z

48. Mungmunpuntipantip R, Wiwanitkit V. Letter to the Editor: Antibody response to SARS-Cov-2 vaccination, previous SARS-CoV-2 infection, and change to single-dose vaccination. *J Med Virolo.* 2021. doi:10.1002/jmv.27263

49. Gilbert PB, Montefiori DC, McDermott A, et al. Immune correlates analysis of the mRNA-1273 COVID-19 vaccine efficacy trial [Preprint]. *medRxiv.* 2021:2021.08.09.21261290. doi:10.1101/2021.08.09.21261290

50. Feng S, Phillips DJ, White T, et al. Correlates of protection against symptomatic and asymptomatic SARS-CoV-2 infection. *medRxiv.* 2021. doi:10.1101/2021.06.21.21258528

© Ortho Clinical Diagnostics 2021. "Because Every Test Is A Life" is a trademark of Ortho Clinical Diagnostics. PR-11784

Ortho Clinical Diagnostics is a global leader of in vitro diagnostics dedicated to improving and saving lives through innovative laboratory testing and blood-typing solutions. We never stop innovating to offer streamlined, sustainable laboratory solutions that deliver fast, accurate, reliable test results to support exceptional patient care. **OrthoClinicalDiagnostics.com**

Ortho Clinical Diagnostics

Because Every Test Is A Life™