



Open Access

COVID-19 Vaccination in Patients with Pre-Solid-Organ Transplantation

Attapon Cheepsattayakorn^{1,2*}, Ruangrong Cheepsattayakorn³, Porntep Siriwanarangsun¹

¹Faculty of Medicine, Western University, Pathumtani Province, Thailand

²10th Zonal Tuberculosis and Chest Disease Center, Chiang Mai, Thailand

³Department of Pathology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

*Corresponding Author: Attapon Cheepsattayakorn, 10th Zonal Tuberculosis and Chest Disease Center, 143, Sridornchai Road Changklan Muang Chiang Mai, 50100, Thailand; Email: Attapon1958@gmail.com

Received Date: 03-06-2021; Accepted Date: 24-06-2021; Published Date: 01-07-2021

Copyright © 2021 by Cheepsattayakorn A, et al. All rights reserved. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.

Editorial

Vaccine such as influenza vaccine, is administered in stable transplant recipients, although live attenuated virus vaccines are contraindicated, generally due to risk of disseminated infection [1,2]. Neither efficacy, safety, nor durability are well known in transplant recipients due to exclusion of them from recent COVID-19 vaccine trials [1,2]. Currently, there are no SARS-CoV-2 vaccine platforms using attenuated live virus approved in phase III trials. Nevertheless, if they are approved for use, concerns, including potential decrease in efficacy in immunocompromised patients, potential for vaccine-related allograft rejection, unknown durability of the immune response, and long-term safety data still exist. Due to experience with neither the influenza vaccine nor the adjuvant recombinant zoster vaccine having been related to allograft rejection, successful administration of influenza and adjuvanted recombinant zoster vaccines to stable transplant recipients, and unanticipated vaccine-related adverse events to the allograft having not borne out, the influenza and adjuvanted recombinant zoster vaccines are able to be extrapolated to COVID-19 vaccines [2,3]. In immunocompromised host, concerns for adenoviral vector vaccines are focused on a viral infection, but these concerns have no scientific evidence. Although newly approved adenoviral-vector use for vaccination, this vaccine platform has been used for decades for gene therapy for cancer and other rare diseases. Inactivated virus and protein subunit vaccine platforms that have been used in transplant

Cheepsattayakorn A | Volume 2; Issue 2 (2021) | JCIM-2(2)-027 | Editorial

Citation: Cheepsattayakorn A, et al. COVID-19 Vaccination in Patients with Pre-Solid-Organ Transplantation. J Clin Immunol Microbiol. 2021;2(2):1-5.

DOI: <http://dx.doi.org/10.46889/JCIM.2021.2202>

recipients for other infections, such as human papilloma virus, pertussis, and hepatitis A and B, are currently under investigation for SARS-CoV-2 (COVID-19) infection in transplant recipients [2].

A previous prospective-Johns Hopkins University-institutional-review-board's-approval cohort study in the US was conducted among 436 transplant recipients (median age 55.9 years (IQR: 41.3-67.4 years), 61% of women, 89% of Caucasian transplant recipients, 52% received the Pfizer/BioNTech (BNT162b2) vaccine and 48% received the Moderna (mRNA-1273) vaccine, median time since transplant of 6.2 years (QR: 2.7-12.7 years, maintenance immunosuppression regimen: 2% of everolimus, 4% of sirolimus, 9% of azathioprine, 54% of corticosteroids, 66% of mycophenolate, and 83% of tacrolimus, who underwent COVID-19 vaccination from December 16, 2020 to February 5, 2021. The participants underwent either standard venipuncture or the TAPII-blood-collection-device (Seventh Sense Biosystems)-at-home blood sampling [4], using an enzyme immunoassay (EUROIMMUN) for testing for antibodies to the S1 domain of the SARS-CoV-2 spike protein [5], whereas the anti-SARS-CoV-2 enzyme immunoassay (Roche Elecsys) was used to test for antibodies against the receptor-binding domain of the SARS-CoV-2 spike protein in the venipuncture samples [4]. Both EUROIMMUN (sensitivity of 87.1%, specificity of 98.9%) and Roche Elecsys (sensitivity of 84.0%, specificity of 100%) tests are mRNA-vaccine-antigens correspondence and semiquantitative and consistent correlation with neutralizing antibodies [6-8].

These two assays are analogous to the antispikes antibody assays in mRNA vaccine clinical trials that were used during immunogenicity assessments [4]. The study revealed that following the first dose of COVID-19 vaccine at 20 days, a median (IQR : 17-24 days), 76 (of 436) participants (17%, 95% CI : 14%-21%) demonstrated detectable antibody (anti-S1 or anti-receptor-binding domain, 31 in 41 kidney transplant recipients, 28 in 37 liver transplant recipients, 9 in 12 heart transplant recipients, 4 in 5 lung transplant recipients, 1 in 1 pancreas transplant recipient, 2 in 3 multiorgan transplant recipients) [4]. Those participants who received Moderna (mRNA-1273) vaccine developed more antibody response, compared to those receiving Pfizer/BioNTech (BNT162b2) vaccine [4]. Older transplant recipients developed less antibody response (adjusted incidence rate ratio: 0.83 (95% CI: 0.73-0.93) per 10 years; $p = 0.002$), compared to the younger group [4]. Nevertheless, younger transplant recipients not receiving anti-metabolite maintained immunosuppressives and those younger transplant recipients receiving the Moderna (mRNA-1273) vaccine developed more antibody responses, compared to the older recipients [4]. Transplant recipients who receiving anti-metabolite maintained immunosuppressive therapy developed less antibody response than those participants not receiving immunosuppression therapy (37% vs 63%, respective; adjusted IRR: 0.22 (95% CI: 0.15-0.34); $p < 0.001$) that contrast with the early immunogenicity identified in mRNA vaccine trials [4]. These results also include 100% antispikes seroconversion by the day 15 after mRNA-1273 (Moderna) and the day 21 after BNT162b2 (Pfizer/BioNTech) vaccination that contrast with the early immunogenicity identified in mRNA vaccine trials [4,9,10]. Poor antibody-responses-to-spike-protein in transplant

Cheepsattayakorn A | Volume 2; Issue 2 (2021) | JCIM-2(2)-027 | Editorial

Citation: Cheepsattayakorn A, et al. COVID-19 Vaccination in Patients with Pre-Solid-Organ Transplantation. *J Clin Immunol Microbiol.* 2021;2(2):1-5.

DOI: <http://dx.doi.org/10.46889/JCIM.2021.2202>

recipients following the first-dose-mRNA (Moderna and Pfizer/BioNTech) vaccination indicated that despite COVID-19 vaccination, such organ transplant recipients may still be at higher COVID-19-infection-early risk. Characterization of T-cell responses and memory B-cell and advanced-transplant-recipient immunophenotyping following COVID-19 vaccination will be significant in determining immunological responses and vaccination strategies following the COVID-19-second-dose vaccine.

As of December 31, 2020, when focusing on kidney transplant recipients, there is no evidence of mRNA-vaccine-platform (BNT162b2 (Pfizer/BioNTech), mRNA-1273 (Moderna))-induced off-target immune responses in large phase III clinical trials [11,12]. No replicative potential through homologous recombination demonstrated in AdV-vectored vaccine platform (AZD1222 (Oxford/AstraZeneca), JNJ78436735/Ad26.COVS.2.S (Janssen), Convidecia (Ad5-nCoV), Sputnik V (Gamaleya)), does not contain live virus in protein subunit vaccine platform (NVX-CoV2373 (Novavax), SARS-CoV-2 recombinant protein formulation (GSK/Sanofi) (Matrix-M1 contains the same QS21 saponin as the AS01 B adjuvant system contained in the recombinant varicella zoster vaccine) and no association between AS03 exposure and graft rejection (high incidence of anti-HLA antibodies in KTR vaccinated with AS03-adjuvanted influenza vaccines) in protein subunit vaccine platform and does not contain live virus and limited data available in peer-reviewed literature in whole-inactivated (killed) vaccine platform (EpiVacCorona (Vector Institute), BBIBP-CoV (Sinopharm), CoronaVac (SinoVac) [11-16]. Several transplant organizations, such as American Society of Transplantation, The International Society for Heart and Lung Transplantation, American Association for the Study of Liver Diseases, American Society of Transplant Surgeons, International Transplant Nurses Society, The Transplantation Society, NATCO, UNOS, Leading the Way in Organ Transplantation, Canadian Society of Transplantation, Pediatric Infectious Diseases Society, Association of Organ Procurement Organizations, American Society for Histocompatibility and Immunogenetics, International Liver Transplantation Society, The Alliance, Transplant Infectious Disease, International Pediatric Transplant Association, and International Society of Vascularized Composite Allotransplantation established their statement on COVID-19 vaccination in Solid-Organ Transplant (SOT) recipients as the following :

1. Pre-transplant vaccination of all SOT candidates as a priority whenever feasible
2. Continued SOT-recipients-SARS-CoV-2 (COVID-19) vaccination and priority for vaccination of their household members and caregivers to decrease exposure risk for these vulnerable patients
3. Continuation of an at-the-time-of-COVID-19-vaccination-stable-immunosuppression regimen to avoid the organ-rejection risk
4. Continued adherence of all transplant recipients to protect measures, including facial-mask wearing and physical distancing regardless of vaccination status [17].

In conclusion, minimal risk to stable solid-organ-transplant recipients who are more likely to suffer a severe COVID-19 outcome than COVID-19 vaccine will be taken from COVID-19 vaccination.

Conflicts of Interests

The authors declare that have no competing interest and not any conflict of interest.

References

1. Hirzel C, Kumar D. Influenza vaccine strategies for solid organ transplant recipients. *Curr Opin Infect Dis.* 2018;31(4):309-15.
2. Danziger-Isakov L, Kumar D, AST ID community of practice. Vaccination of solid organ transplant candidates and recipients: Guidelines from the American society of transplantation infectious diseases community of practice. *Clin Transplantation.* 2019;33(9):e13563.
3. Dos Santos G, Haguinet F, Cohet C, Webb D, Logie J, Ferreira GL, et al. Risk of solid organ transplant rejection following vaccination with seasonal trivalent inactivated influenza vaccines in England: a self-controlled case-series. *Vaccine.* 2016;34(31):3598-606.
4. Boyarsky BJ, Werbel WA, Avery RK, Tobian AAR, Massie AB, Segev DL, et al. Immunogenicity of a single dose of SARS-CoV-2 messenger RNA vaccine in solid organ transplant recipients. *JAMA.* 2021;325(17):1784-6.
5. Boyarsky BJ, Ou MT, Werbel WA, Avery RK, Clarke WA, Tobian AA, et al. Early development and durability of SARS-CoV-2 antibodies among solid organ transplant recipients: a pilot study. *Transplantation.* 2021;105(5):e52-3.
6. Patel EU, Bloch EM, Clarke W, Hsieh YH, Boon D, Eby Y, et al. Comparative performance of five commercially available serologic assays to detect antibodies to SARS-CoV-2 and identify individuals with high neutralizing titers. *J Clin Microbiol.* 2020;59(2):e02257-20.
7. Higgins V, Fabros A, Kulasingam V. Quantitative measurement of anti-SARS-CoV-2 antibodies: analytical and clinical evaluation. *J Clin Microbiol.* 2021;59(4):e03149-20.
8. Klein SL, Pekosz A, Park HS, Ursin RL, Shapiro JR, Benner SE, et al. Sex, age, and hospitalization drive antibody responses in a COVID-19 convalescent plasma donor population. *The J Clin Invest.* 2020;130(11):6141-50.
9. Jackson LA, Anderson EJ, Roupheal NG, Roberts PC, Makhene M, Coler RN, et al. An mRNA vaccine against SARS-CoV-2-preliminary report. *New Eng J Med.* 2020;383(20):1920-31.
10. Walsh EE, Frenck R, Falsey AR, Kitchin N, Absalon J, Gurtman A, et al. RNA-based COVID-19 vaccine BNT162b2 selected for a pivotal efficacy study. *Medrxiv.* 2020;383 (25):2439-50.
11. American Society of Transplantation: COVID-19 FAQ fact sheet. 2021. [Last accessed on June 30, 2021] <https://www.myast.org/covid-19-vaccine-faq-sheet>
12. Castells MC, Phillips EJ. Maintaining safety with SARS-CoV-2 vaccines. *N Engl J Med.* 2021;384:643-9.
13. Lion T. Adenovirus infections in immunocompetent and immunocompromised patients. *Clin Microbiol Rev.* 2014;27:441-62.
14. Haddadin Z, Krueger K, Thomas LD, Overton ET, Ison M, Halasa N. Alternative strategies of post transplant influenza vaccination in adult solid organ transplant recipients. *Am J Transplant.* 2021;21:938-49.
15. Ahi YS, Bangari DS, Mittal SK. Adenoviral vector immunity: its implications and circumvention strategies. *Curr Gene Ther.* 2011;11:307-20.
16. Heldman MR, Limaye AP. SARS-CoV-2 vaccines in kidney transplant recipients: will they be safe and effective and how will we know? *JASN.* 2021;32:1021-4.

Cheepsattayakorn A | Volume 2; Issue 2 (2021) | JCIM-2(2)-027 | Editorial

Citation: Cheepsattayakorn A, et al. COVID-19 Vaccination in Patients with Pre-Solid-Organ Transplantation. *J Clin Immunol Microbiol.* 2021;2(2):1-5.

DOI: <http://dx.doi.org/10.46889/JCIM.2021.2202>

17. American Society of Transplantation, The International Society for Heart and Lung Transplantation, American Association for the Study of Liver Diseases, American Society of Transplant Surgeons, International Transplant Nurses Society, The Transplantation Society, NATCO, UNOS, Leading the Way in Organ Transplantation, Canadian Society of Transplantation, Pediatric Infectious Diseases Society, Association of Organ Procurement Organizations, American Society for Histocompatibility and Immunogenetics, International Liver Transplantation Society, The Alliance, Transplant Infectious Disease, International Pediatric Transplant Association, and International Society of Vascularized Composite Allograft Transplantation. Statement on COVID-19 vaccination in solid organ transplant recipients. [Last accessed on June 30, 2021] <https://www.myast.org>statement-covid-19-vaccination>

Cheepsattayakorn A | Volume 2; Issue 2 (2021) | JCIM-2(2)-027 | Editorial

Citation: Cheepsattayakorn A, et al. COVID-19 Vaccination in Patients with Pre-Solid-Organ Transplantation. J Clin Immunol Microbiol. 2021;2(2):1-5.

DOI: <http://dx.doi.org/10.46889/JCIM.2021.2202>