

COVID-19 vaccination in solid organ transplant candidates and solid organ transplant recipients – an update (Berne, 23.12.2021)

In Switzerland, currently two mRNA based SARS-CoV-2 vaccines (*Spikevax*®, Moderna / *Comirnaty*®, Pfizer/BioNTech) and one vector based vaccine (*COVID-19 Vaccine Janssen*®, Janssen-Cilag) are approved.

The currently approved mRNA based SARS-CoV-2 vaccines are more immunogenic in solid-organ transplant recipients compared to the vector-based vaccine (1). We therefore encourage immunization with an mRNA based vaccine and the following recommendations exclusively relate to mRNA based SARS-CoV-2 vaccines that are presently licensed in Switzerland.

We encourage immunization of patients awaiting solid organ transplantation and of solid organ transplant recipients. In the post transplantation setting, the immune response to SARS-CoV-2 vaccines is reduced (2-6). Current evidence suggest that a third vaccine dose as part of the basic immunization scheme might enhance the immunogenicity of the vaccine in solid organ transplant recipients (7-11). We advise to follow the recommendations published by the Federal Office of Public Health and the “*Eidgenössischen Kommission für Impffragen, EKIF*” (<https://www.bag.admin.ch/dam/bag/en/dokumente/mt/k-und-i/aktuelle-ausbrueche-pandemien/2019-nCoV/merkblatt-impfung-allgemeine-informationen.pdf.download.pdf/General%20information%20on%20the%20COVID-19%20vaccination%20with%20an%20mRNA%20vaccine%20.pdf>) and to administer three doses of an mRNA vaccine with a minimal interval of 4 weeks between each dose as a basic immunization against COVID-19. Vaccine intervals can be extended for logistic reasons (there is no maximal interval). In SARS-CoV-2 infection experienced transplant recipients, two doses of an mRNA vaccine elicit similar antibody responses compared to healthy individuals without previous infection who were vaccinated with two vaccine doses (1). We therefore recommend administering two doses of an mRNA vaccine as a basic immunization if transplant recipients had confirmed COVID-19 before vaccination.

In accordance with the recommendations of the Federal Office of Public Health and the “*Eidgenössischen Kommission für Impffragen, EKIF*”, we recommend to administer a fourth vaccine dose (booster dose) at earliest four months after the third vaccine dose.

The ideal timing of vaccination is uncertain. We recommend delaying vaccination at least one month from transplant surgery and 3 months from use of T-cell or B-cell depleting agents; primarily for reasons of expected reduced efficacy and less for safety concerns. In the pre transplant setting, we recommend vaccination for all patients on the waiting list. In case of urgent listing of severely ill patients (e.g. acute

liver failure) the decision for or against immediate vaccination should be taken on an individual case basis.

Anti-spike antibody concentrations may be measured four weeks after the last vaccine dose. However, we would like to highlight that there are no established cut-offs of anti-spike antibody concentrations for protection. We still recommend to solid organ transplant recipients to continue protective measures after being vaccinated.

We encourage the early use of monoclonal antibody therapy in patients with low or absent antibody titers in case of an infection irrespective of the number of previous vaccinations (12). Details about monoclonal antibody therapies are available at the FOPH homepage (https://www.bag.admin.ch/dam/bag/de/dokumente/biomed/heilmittel/COVID-19/ak-kriterienliste-ssi.pdf.download.pdf/Kriterienliste_CCG-SSI_D.pdf).

Recommendation approved by Dr Cédric Hirzel, President Swisstransplant Working Group of Infectious Diseases, and PD Franz Immer, Medical Director and CEO Swisstransplant

References:

1. Predecki M, Thomson T, Clarke CL, Martin P, Gleeson S, De Aguiar RC, Edwards H, Mortimer P, McIntyre S, Mokrerer D, Cox A, Pickard G, Lightstone L, Thomas D, McAdoo SP, Kelleher P, Willicombe M, Imperial Renal C-vsgicwtOSC. Immunological responses to SARS-CoV-2 vaccines in kidney transplant recipients. *Lancet* 2021; 398: 1482-1484.
2. Grupper A, Rabinowich L, Schwartz D, Schwartz IF, Ben-Yehoyada M, Shashar M, Katchman E, Halperin T, Turner D, Goykhman Y, Shibolet O, Levy S, Houry I, Baruch R, Katchman H. Reduced humoral response to mRNA SARS-CoV-2 BNT162b2 vaccine in kidney transplant recipients without prior exposure to the virus. *Am J Transplant* 2021; 21: 2719-2726.
3. Rincon-Arevalo H, Choi M, Stefanski AL, Halleck F, Weber U, Szelinski F, Jahrsdorfer B, Schrezenmeier H, Ludwig C, Sattler A, Kotsch K, Potekhin A, Chen Y, Burmester GR, Eckardt KU, Guerra GM, Durek P, Heinrich F, Ferreira-Gomes M, Radbruch A, Budde K, Lino AC, Mashreghi MF, Schrezenmeier E, Dorner T. Impaired humoral immunity to SARS-CoV-2 BNT162b2 vaccine in kidney transplant recipients and dialysis patients. *Sci Immunol* 2021; 6.
4. Boyarsky BJ, Werbel WA, Avery RK, Tobian AAR, Massie AB, Segev DL, Garonzik-Wang JM. Antibody Response to 2-Dose SARS-CoV-2 mRNA

Vaccine Series in Solid Organ Transplant Recipients. *JAMA* 2021; 325: 2204-2206.

5. Rabinowich L, Grupper A, Baruch R, Ben-Yehoyada M, Halperin T, Turner D, Katchman E, Levi S, Houry I, Lubezky N, Shibolet O, Katchman H. Low immunogenicity to SARS-CoV-2 vaccination among liver transplant recipients. *J Hepatol* 2021; 75: 435-438.
6. Sattler A, Schrezenmeier E, Weber UA, Potekhin A, Bachmann F, Straub-Hohenbleicher H, Budde K, Storz E, Pross V, Bergmann Y, Thole LM, Tizian C, Holsken O, Diefenbach A, Schrezenmeier H, Jahrsdorfer B, Zemojtel T, Jechow K, Conrad C, Lukassen S, Stauch D, Lachmann N, Choi M, Halleck F, Kotsch K. Impaired humoral and cellular immunity after SARS-CoV-2 BNT162b2 (tozinameran) prime-boost vaccination in kidney transplant recipients. *J Clin Invest* 2021; 131.
7. Werbel WA, Boyarsky BJ, Ou MT, Massie AB, Tobian AAR, Garonzik-Wang JM, Segev DL. Safety and Immunogenicity of a Third Dose of SARS-CoV-2 Vaccine in Solid Organ Transplant Recipients: A Case Series. *Ann Intern Med* 2021; 174: 1330-1332.
8. 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: 661-662.
9. Schrezenmeier E, Rincon-Arevalo H, Stefanski AL, Potekhin A, Staub-Hohenbleicher H, Choi M, Bachmann F, Pross V, Hammett C, Schrezenmeier H, Ludwig C, Jahrsdorfer B, Lino A, Eckardt KU, Kotsch K, Doerner T, Budde K, Sattler A, Halleck F. B and T Cell Responses after a Third Dose of SARS-CoV-2 Vaccine in Kidney Transplant Recipients. *J Am Soc Nephrol* 2021.
10. Peled Y, Ram E, Lavee J, Segev A, Matezki S, Wieder-Finesod A, Halperin R, Mandelboim M, Indenbaum V, Levy I, Sternik L, Raanani E, Afek A, Kreiss Y, Lustig Y, Rahav G. Third dose of the BNT162b2 vaccine in heart transplant recipients: Immunogenicity and clinical experience. *J Heart Lung Transplant* 2021.
11. Hall VG, Ferreira VH, Ku T, Ierullo M, Majchrzak-Kita B, Chaparro C, Selzner N, Schiff J, McDonald M, Tomlinson G, Kulasingam V, Kumar D, Humar A. Randomized Trial of a Third Dose of mRNA-1273 Vaccine in Transplant Recipients. *N Engl J Med* 2021; 385: 1244-1246.
12. Weinreich DM, Sivapalasingam S, Norton T, Ali S, Gao H, Bhore R, Musser BJ, Soo Y, Rofail D, Im J, Perry C, Pan C, Hosain R, Mahmood A, Davis JD, Turner KC, Hooper AT, Hamilton JD, Baum A, Kyratsous CA, Kim Y, Cook A, Kampman W, Kohli A, Sachdeva Y, Graber X, Kowal B, DiCioccio T, Stahl N, Lipsich L, Braunstein N, Herman G, Yancopoulos GD, Trial I. REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with Covid-19. *The New England journal of medicine* 2021; 384: 238-251.

<https://www.bag.admin.ch/dam/bag/en/dokumente/mt/k-und-i/aktuelle-ausbrueche-pandemien/2019-nCoV/merkblatt-impfung-allgemeine-informationen.pdf.download.pdf/General%20information%20on%20the%20COVID-19%20vaccination%20with%20an%20mRNA%20vaccine%20.pdf>