Global Trials Focus

March 2022

The ISN-ACT (Advancing Clinical Trials) team presents this monthly round up of randomized trials in nephrology. Trials are selected not just for impact, but also to showcase the diversity of research produced by the global nephrology community. Each trial is reviewed in context and has a risk of bias assessment. We hope to drive improvement in trial quality and promote greater engagement in trial activity.

Key to risk of bias assessment

- (R) Random sequence generation
- (A) Allocation concealment
- (BP) Blinding of participants/personnel
- (BO) Blinding of outcome assessment
- (CD) Complete outcome data
- (CR) Complete outcome reporting
- (B) No other sources of bias

High risk
Uncertain risk / not stated
Low risk

Do you agree with our trial of the month? Tell us what you think!

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Want to run your own trial?
ISN-ACT Clinical Trials Toolkit
www.theisn.org/isn-act-toolkit

Would you like to write your own reviews?
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Contact us at research@theisn.org

ISN Academy: ***Transplant***

Boost or bust? Homologous vs heterologous third SARS-CoV-2 vaccine dose among transplant recipients

Comparison of SARS-CoV-2 antibody response 4 weeks after homologous vs heterologous third vaccine dose in kidney transplant recipients: a randomized clinical trial

Reindl-Schwaighofer et al. JAMA Intern Med. 2021.

(R) (A) (BP) (BO) (CD) (CR) (B)

Reviewed by DV O'Hara

Summary: The study recruited 201 kidney transplant recipients who had previously received two doses of an mRNA SARS-CoV-2 vaccination without developing spike protein antibodies, and who had not had COVID-19 disease. Participants were randomised to homologous vaccination, i.e. receiving a further mRNA vaccine (BNT162b2 [PfizerBioNTech] or mRNA-1273 [Moderna]), or to have a heterologous third dose by receiving a viral vector vaccine (Ad26COVS1 [Janssen]). Among the 197 patients who completed the study, 39% responded to the third vaccine by producing SARS-CoV-2 antibodies after 4 weeks, however only 22% of these responders developed sufficient levels to have virus neutralizing capacity. There was no statistically significant difference between the two vaccination strategies, with 35% seroconversion with the mRNA vaccines and 42% with the vector vaccine. Higher response rates were seen among those not on triple immunosuppression, among those with a greater amount of time since kidney transplantation, and among those with lower levels of the ubiquitous and non-pathogenic torque teno virus (TTV), which is used as a surrogate marker to indicate immune system integrity, with lower viral levels suggesting better immune system function, which was expected to result in improved response to the vaccine. Rates of local injection site pain were higher with the mRNA vaccine, but no other safety concerns were seen.

Comment: Prior studies have demonstrated that for recipients of kidney transplants, two doses of SARS-CoV-2 vaccination provide an insufficient vaccine response, with up to half of patients not developing antibodies. Risk factors for poor response identified in other studies include treatment with mycophenolate, calcineurin inhibitors, or belatacept, and with lymphocyte-depleting induction therapy. The lack of response confers a major risk in the context of a global pandemic. In the present study of patients who had not responded to 2 prior SARS-CoV-2 vaccinations, either a heterologous or a homologous third dose appeared safe but only provoked seroconversion among a minority. Serological response may not correlate clearly with clinical outcomes, however, with other studies suggesting an ~80% reduction in symptomatic COVID-19 infection among solid organ transplant recipients who have been vaccinated. Further research is needed to clarify the relative impact of vaccine type on clinical outcomes for transplant recipients, and to evaluate the response to four-dose vaccination strategies.

Edited by A Gallagher, DV O'Hara, M Provenzano, and A. Zykova