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COVID-19 vaccination and HIV-1 acquisition

Authors' reply

We appreciate Denis Y Logunov and colleagues' response to our Correspondence,¹ in which we raise concerns about the use of adenovirus type-5 (Ad5) vectors for COVID-19 vaccines in populations at risk for HIV-1 acquisition. They nicely outline some of the hypothetical mechanisms of increased HIV-1 acquisition seen in men in the Step and Phambili trials. Although the exact mechanism has not been determined, the increased HIV-1 acquisition risk seen in both trials, which used an Ad5-vector vaccine without HIV envelope in uncircumcised men, was a robust finding. We believe this increased risk of HIV-1 acquisition is limited to Ad5 vectors and not applicable to all adenoviral vector vaccines as there are many immunological differences between serotypes, including differences in cell receptor usage and both innate and adaptive immune profiles.²⁻⁴ In fact, we have been evaluating adenovirus type-26 (Ad26) vector HIV vaccines in clinical trials,^{5,6} all of which include HIV envelope genes, and have seen no increased HIV-1 acquisition risk in any of these trials.

Logunov and colleagues state that many people have received COVID-19 vaccines using adenoviral vectors globally, and they have not been linked to increased rates of HIV-1 acquisition. However, as far as we are aware, HIV-1 acquisition—an infection that often remains silent for up to a decade⁷—was not measured among recipients of the Ad5-based COVID-19 vaccines, so we would have no way of knowing whether these Ad5-based COVID-19 vaccines are associated with increased HIV-1 acquisition risk. We did not see clinical AIDS in either the Step or Phambili trials and would not have detected this transient increased risk for HIV-1 acquisition had we relied on clinical outcomes to detect infection.

Therefore, it would be prudent both to ensure informed consent is obtained before administering an Ad5 COVID-19 vaccine to populations at risk for HIV-1 acquisition, and to measure HIV seroincidence in these populations as part of post-approval pharmacovigilance before concluding that such a risk does not occur. To be most conservative, all adenoviral vector COVID-19 vaccines could conduct similar pharmacovigilance studies.

We declare no competing interests.

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- 1 Buchbinder SP, McElrath MJ, Dieffenbach C, Corey L. Use of adenovirus type-5 vectored vaccines: a cautionary tale. *Lancet* 2020; **396**:e68–69.
- 2 Barouch DH, Picker LJ. Novel vaccine vectors for HIV-1. *Nat Rev Microbiol* 2014; **12**: 765–71.
- 3 Tan WG, Jin HT, West EE, et al. Comparative analysis of simian immunodeficiency virus gag-specific effector and memory CD8+ T cells induced by different adenovirus vectors. *J Virol* 2013; **87**: 1359–72.
- 4 Teigler JE, Lampietro MJ, Barouch DH. Vaccination with adenovirus serotypes 35, 26, and 48 elicits higher levels of innate cytokine responses than adenovirus serotype 5 in rhesus monkeys. *J Virol* 2012; **86**: 9590–98.
- 5 Baden LR, Stieh DJ, Sarnecki M, et al. Safety and immunogenicity of two heterologous HIV vaccine regimens in healthy, HIV-uninfected adults (TRAVVERSE): a randomised, parallel-group, placebo-controlled, double-blind, phase 1/2a study. *Lancet HIV* 2020; **7**: e688–98.
- 6 Barouch DH, Tomaka FL, Wegmann F, et al. Evaluation of a mosaic HIV-1 vaccine in a multicentre, randomised, double-blind, placebo-controlled, phase 1/2a clinical trial (APPROACH) and in rhesus monkeys (NHP 13-19). *Lancet* 2018; **392**: 232–43.
- 7 Rutherford GW, Lifson AR, Hessel NA, et al. Course of HIV-1 infection in a cohort of homosexual and bisexual men: an 11 year follow up study. *BMJ* 1990; **301**: 1183–88.

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