Team A - Daily Summary
Wednesday, 27 January 2021

Highlights
1. HIV vaccine research paved the way for COVID-19 vaccine development.
2. The VRC01 monoclonal broadly neutralizing antibody did not prevent HIV infection overall in the AMP trials, but HIV strain sensitivity determined its protection efficacy.

Summary
The first-ever virtual HIVR4P conference began with Dr Anthony S. Fauci (PL01.01) elucidating how decades of multi-disciplinary HIV vaccine research paved the way for prompt and adept development of COVID-19 vaccines. Expertise in HIV structure-based vaccine design was then galvanized into designing the stable pre-fusion spike immunogen of SARS-CoV2. Capability developed by NIAID trial networks and their global HIV clinical trial sites allowed for COVID-19 vaccines to be tested with proficiency. Key lessons across the two infectious diseases include (i) the exacerbation of societal disparities by disease, (ii) the need for community engagement in research, (iii) the power of treatment to serve as prevention and (iv) the ill effects of “denialism” by some people who refute not only the disease, but our duty to be responsive.

Findings on the first ever efficacy trial of an HIV antibody were shared by Dr Lawrence Corey (HY01.01LB) on behalf of the Antibody Mediated Prevention (AMP) trial teams. AMP had evaluated VRC01, a broadly neutralizing antibody, in two Phase 2b proof-of-concept trials: one among women at risk (HVTN 703/HPTN 081) and the other among men and transgender persons who have sex with men (HVTN 704/HPTN 085). Overall, VRC01 was safe and tolerable, but did not significantly reduce HIV acquisition. However, there was lower HIV-1 incidence for in vitro VRC01-sensitive (IC80<1 µg/ml) isolates in VRC01 recipients compared to placebo recipients. A further discovery from the study was the neutralization assays to be used to calibrate similar studies in future. The AMP findings suggest that administration of multiple antibodies combined in a “cocktail” could be used to prevent HIV-1 acquisition.

Implications of the AMP findings were discussed through the day. In the panel (HY01.03) and amongst attendee comments and questions (RT01, OA03), it was discussed that the administration format may need to be subcutaneous injections for user acceptability and implementation ease, there were affirmations about having more prevention choices but also thoughts about whether proof of the prevention efficacy of long-acting cabotegravir (HY01.02) made bnAb development less urgent.

Two further studies with AMP data were presented. In a study of viral populations following infection in AMP, there was evidence of infection with viruses of mixed neutralisation phenotypes, as well as probable VRC01 pressure resulting in low frequency resistance mutations (OA03.04LB). In a study of neutralization profiles of HIV-1 subtype C breakthrough viruses in AMP, it was shown that all breakthrough viruses were of the tier 2 phenotype, most could be neutralized by VRC07-523LS, and all could be neutralized by bNAb combinations. This provided further rationale to test combination bNAbs to improve coverage of subtype C viruses. There was the possibility that the phenotype of some of the breakthrough viruses were altered by exposure to VRC01 (OA03.05).
The pipeline for more HIV bnAbs was said to be robust (RT01) with technological advances to increase bnAb potency, lower the required dose, permit administration subcutaneously and allow longer intervals between administration.

Early-phase results of clinical trials evaluating novel bNAb approaches were presented (OA03). No safety or tolerability issues were found amongst HIV-1 exposed infants given VRC07-523 LS and there were preferable pharmacokinetic measures to VRC01 (OA03.02). VRC07-523LS administered to adults at various doses and routes of administration (including intravenous and subcutaneous) was safe and well-tolerated, with a half-life of approximately 40 days and peak concentrations increasing linearly by dose (OA03.02).

Through moments of silence, multiple sessions honoured colleagues, family and friends who have died during the COVID-19 pandemic.