Towards a Pan-Sarbecovirus Vaccine: Progress and Anticipated Challenges

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COVID-19

- Considering the performance of almost all available vaccine and their efficacy / effectiveness against the variants, it seems logical to have a vaccine which offers something beyond RBD

- Coronavirus known for not generating long lasting immune response as seen in 'Common Cold'

- COVID-19 has something unique in delaying the Interferon response

- In order to encompass all present and future Coronaviruses, reactive vaccination campaigns may not be a complete solution

All these facts put together pose huge challenge in getting a Pan-Sarbecovirus Vaccine

Points to Consider

- Logical is to generate a response mimicking the infection
- Breakthrough cases show significant rise in Neutralizing Antibodies and IgA response

COVID-19

- Within the scope of available information, the first step to evaluate the development of Pan-Sarbecovirus vaccine is to look at response to multiple antigen and mimic the site / mode of infection
- Immunizing the population with most conserved part of the virus (broader antigenic composition) and continuing the immunization right from infant stage may be one of the strategies to block the transmission
- Immunizing infants routinely will introduce the children with memory to Coronavirus
- Generating memory pools from the young age and boosting it at regular intervals may reduce the impact of mass spread
- Prime and Boost strategy with Live Attenuated vaccines, alongwith Inactivated vaccines, may be the best alternative

Probable Solution

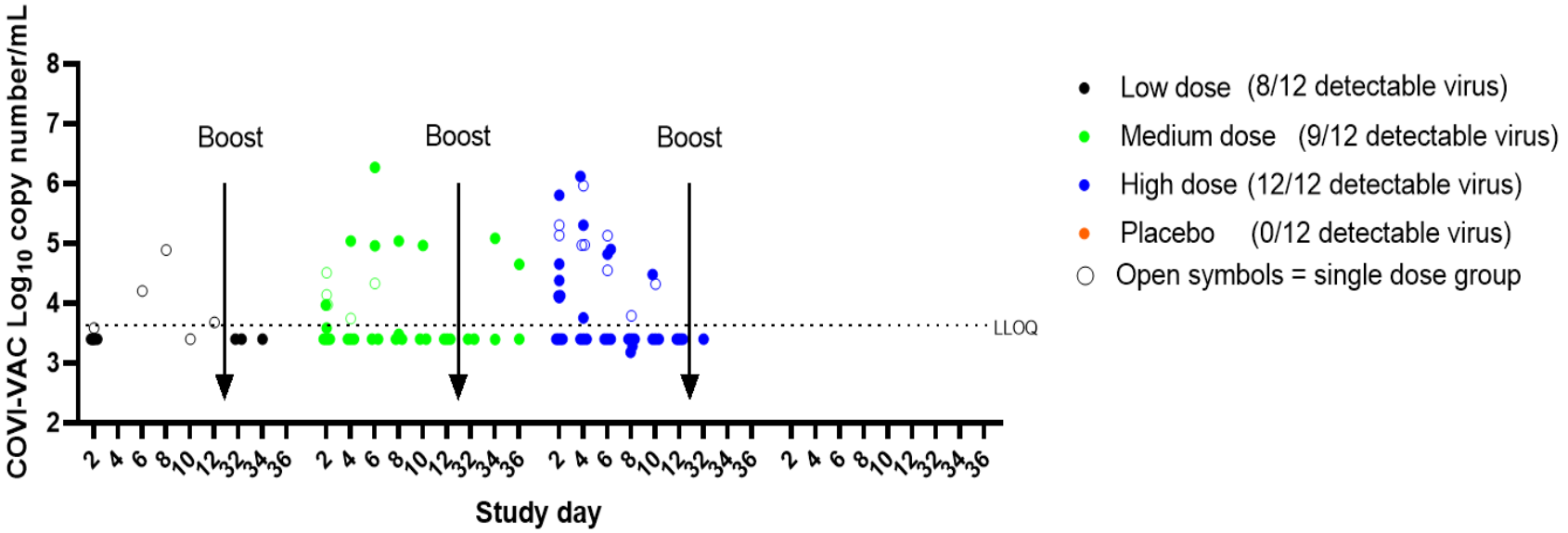
- One can address these issues (to an extent) by assessing a live-attenuated vaccine delivered intranasally and/or injectable and look for:
  - *Neutralizing Antibodies*
  - *Local IgA*
  - *CMI (T Cell response)*

Available Platform

Live Attenuated COVID-19 Vaccine

- Codon-Pair Deoptimization (CPD) - replace preferred codons with synonymous codons that are translated more slowly
- Virus is identical at the amino acid level but attenuated
- Large number of silent mutations insurmountably high to back mutate

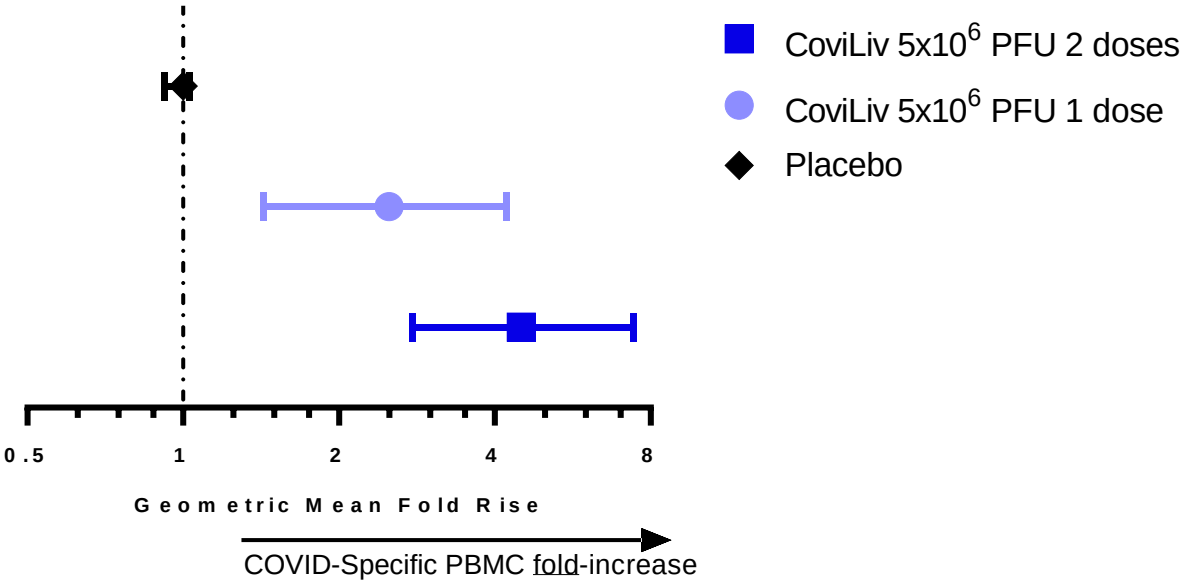
Prevents Challenge Vaccine Shedding, Blocks Surrogate Re-infection



- Peak shedding was equivalent to ~ 100 PFU, which poses a low risk of onward transmission
- 1st dose of vaccine blocked quasi-challenge with 2nd vaccine dose in the high dose group
- Potential predictor of efficacy

Cell Mediated Immunity - ELISpot

Assay performed with commercially available SARS-CoV-2 peptide pools against SARS-CoV-2 SMNO (4 viral proteins including spike)



Data for the day 36 time-point (1 week post second dose) plotted for individuals who received placebo and participant who received 2 doses of the vaccine

Challenges

- Biggest hurdle is the design of Clinical Trial when the comparator is an Injectable preparation

- Difficult to match Serum Antibody response for proving non-inferiority

There is a need for initial evaluation based on CMI, IgA & IgG Response and then a trial design which compares the immunological effect / "vaccine take" by combining all the responses mentioned above

Namaskar !!