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Expert View: Second, Third Wave COVID-19 Vaccines Still Have Much To Vie For

India Could Leverage Polio Experience

by Anju Ghangurde

In a broad-ranging interview with *Scrip*, the ex-CEO of India's Hilleman Laboratories compares the profiles of leading COVID-19 vaccines and urges caution around how far some of the new data now rolling out should be interpreted. The executive also outlines solutions to tackle logistics issues and "vaccine hesitancy" in countries like India.

As mRNA-based COVID-19 vaccines inch closer to the finish line, one industry expert cautions these still have some key milestones to clear and that developers of second- and third-wave candidates should still press on resolutely.

In an wide-ranging interview with *Scrip*, Davinder Gill, ex-CEO of India's *Hilleman Laboratories Pvt. Ltd.*, said the long- term safety profile of vaccines based on mRNA platforms will need to be watched, though there's no denying the promise and hope riding on these. (Hilleman Labs is an equal joint-venture partnership between *Merck & Co., Inc.* and the Wellcome Trust. (Also see "*Hilleman CEO Moving On, Hands Baton To Ex-Takeda Executive*" - Scrip, 28 Jan, 2020.))

Pfizer Inc. and *BioNTech SE* recently disclosed interim Phase III results for their mRNA-based COVID-19 vaccine, BNT162b2, indicating it is 90% effective in preventing infection, while *Moderna, Inc.* took things a notch higher, announcing on 16 November that its candidate, MRNA-1273, met statistical criteria with a vaccine efficacy of 94.5% in the first interim analysis from its Phase III study. (Also see "*The World Celebrates Pfizer's 90% COVID-19 Vaccine Efficacy Data, With Cautious Caveats*" - Pink Sheet, 9 Nov, 2020.)

Anthony Fauci, director of the US National Institutes of Health's National Institute of Allergy and Infectious Diseases, is reported to have described Moderna's early results as "stunningly

impressive."

But full data on these vaccines are still awaited and the potential licensure of an mRNA vaccine for coronavirus would be the first of its type. An Indian firm, Gennova Biopharmaceuticals, in collaboration with US-based HDT Biotech Corporation, is also developing an mRNA vaccine against SARS-CoV-2 and expects to start trials before year-end. (Also see "*Indian Alliance For Pfizer/BioNTech's COVID-19 Vaccine?*" - Scrip, 11 Nov, 2020.)

Moderna Aces COVID-19 Vaccine Results With 94.5% Efficacy

By Andrew McConaghie

16 Nov 2020
Moderna's stunning interim results add to the world's relief brought by Pfizer's first read-out, and also provide the US biotech with the commercial platform it needed

Read the full article here

Gill, whose career spans a stint as vice-president of biotherapeutics at Pfizer, also dissected the comparative profiles of adenovirus vaccine candidates for COVID-19 and the potential implications for countries like India. (Also see "*Experts Skeptical As Russia's COVID-19 Vaccine Outshines Pfizer Results*" - Scrip, 13 Nov, 2020.)

The executive, who has led biotherapeutics laboratories in Ireland and Scotland in collaboration with local governments, also shared his views on post-approval logistics challenges and the need for "inclusive measures" to tackle vaccine hesitancy.

Q **Several COVID-19 vaccines are inching towards the accelerated finish line; India is expected to have access to the *AstraZeneca PLC*/Oxford/*Serum Institute of India Pvt. Ltd.* vaccine and also Russia's Sputnik V, with indigenously developed candidates, including from *Bharat Biotech* and *Zydus Cadila*, also in the pipeline. How would you rate the current comparative profile of the AZ/Oxford vaccine versus Sputnik V? Are the criteria of those who qualify for vaccination identical for both, at least for now?**

A The AZ/Oxford vaccine and the Sputnik V vaccine are very similar in terms of their profile and testing. Both are adenovirus based – AZ/Oxford is based on chimpanzee adenovirus and Sputnik on human adenovirus 26 and adenovirus 5. That said, the AZ/Oxford vaccine is currently in a global clinical trial. Recently, we saw data on efficacy of the AZ vaccine in the elderly which was very positive. The Sputnik V

vaccine, on the other hand, has largely been tested in Russia so far. So that has some implications for India, in terms of a global population profile covered in Phase III clinical trials. In addition, the Sputnik V vaccine is available both as a freeze-dried as well as frozen liquid formulation, whereas AZ/Oxford is only available as a frozen formulation. So that also has implications for India, where a freeze-dried formulation may be preferred to avoid logistics problems associated with cold chain. But in terms of access, as long as both vaccines have been shown to work across diverse age groups including the very young (up to 12 years of age) or the very old (> 65 years), then prioritization between the two vaccines would not be different.

Q **COVID-19 could see the first RNA vaccine emerge, which is exciting but comes with complexities both around the platform itself and the immunity the vaccine can provide. Should we temper exuberance around the Pfizer-BioNTech and Moderna mRNA-based vaccines and others, since final efficacy is yet to be reported and given the uncharted territory we're in?**

A We should be careful in how far we interpret the early Phase III efficacy data reported by Pfizer and Moderna, which looks very promising at 90-95%. These early data suggest most other COVID vaccines will fall within the same efficacy range. Still, we should wait until the full data has been disclosed so that we can examine it carefully with good scientific rigor. Secondly, we have to observe the long-term safety profile of mRNA-based vaccines. Since it is a new platform there is no data available from past vaccines. We should remain open minded on how well the vaccine will perform in people with co-morbidities as well as the very elderly and frail population. Another important point to remember is we do not know the duration of protection of these vaccines. We hope it should be ideally close to one year but that may not be the case. That is another important factor to keep in mind.

Q **Merck CEO Kenneth Frazier has noted there are "different populations that are going to have different needs" as the pandemic ebbs and flows and that there will be an endemic phase after the pandemic phase and the first vaccines may not be ideal. (Also see "*Slow And Steady: Merck Advances COVID-19 Antiviral, Vaccine Programs*" - Scrip, 27 Oct, 2020.) How important is it for vaccines that**

may be trailing the frontrunners to keep going, especially with those like *Johnson & Johnson*'s expected to be single-shot? Do you also anticipate gains for those coming later in terms of cross-trial learnings, clearer regulatory pathways and supply chain preparedness?

A It is extremely important that the second- and third-wave vaccines such as those developed by J&J and *Novavax, Inc.* should continue. It is too early to declare victory as there are still many unknowns despite early promise. A key question that will impact the importance of the second- and third-wave vaccines will be the overall safety of first-wave vaccines across diverse populations that include gender, age, lifestyle, racial or ethnic background etc. Any type of rare side-effect observed in these populations could prove serious if it is life-threatening or otherwise dangerous to the overall health of the individual. Another important question is how long of a protection will be provided by first-wave vaccines. If it is of the order of a few months, that's not so good. If second- or third-wave vaccines can provide longer protection e.g. one year or beyond, that will prove very crucial. Specially, if any of these vaccines can do so using only a single injection, then it becomes a game changer. As the first-wave vaccines gather more data, for sure there is an opportunity for the second- and third-wave vaccines to adapt their clinical testing and licensure accordingly.

Q **A mega logistical challenge awaits once a COVID-19 vaccine is cleared. A paper by DHL, with analytical support from McKinsey & Company, notes that global coverage of COVID-19 vaccines will need up to ~200,000 pallet shipments and ~15 million deliveries in cooling boxes as well as ~15,000 flights across the various supply chain set-ups. Clearly that will require massive co-ordinated effort. Do you believe that the supply chain/warehousing and distribution capacity in developing nations like India is robust enough to meet requirements?**

A I do not believe that warehousing or supply chains and vaccine distribution have been worked out in developing countries. In fact, I would argue this is also true for developed countries because never in their history have they undertaken a

vaccination campaign of this magnitude and complexity. Thus, particularly for low-resource countries like India, it becomes important to keep several things in mind to minimize the impact of logistics failure. First, it is critical to avoid vaccine candidates that require very complex storage and distribution, for example cryopreservation. The country is not ready for it. Second, if India can leverage both its logistics, as well as training and work experience with something like the polio eradication campaign, that could prove very useful. This was successfully done during the early phase of rotavirus vaccination and it proved quite helpful. Similar measures can be adopted for COVID-19 immunization also. In general, though, India will have to invest more in its cold chain infrastructure, manpower training as well as improved logistics, warehousing and supply chain as part of a large strategy for pandemic preparedness.

Q **There are concerns around long-term sequelae from COVID-19 infection; what about any sequelae of vaccination? What is the ideal follow up time for those vaccinated with the current crop of vaccines once they make it over the finish line?**

A Most Phase III protocols being followed by vaccine developers have a two-year follow up post last dose of vaccine administered. I think this is prudent. While any acute effects of vaccine such as hypersensitivity or any autoimmune reaction will be evident soon after vaccination, other effects may take a longer time, especially if they are rare and occur only in certain individuals. Therefore, long-term safety follow up of vaccinated subjects becomes very important.

Q **Finally, what if sections of the population opt out of vaccination – there is considerable skepticism around the fast-tracked vaccines going by some early studies in India. A survey by LocalCircles, a community social media platform, noted that 61% of over 8,000 respondents said that they won't "rush" to take a vaccine in 2021, even if available. How do governments need to tackle this and is compulsory vaccination a grey area, also given that some developers have sought blanket indemnity?**

A I think COVID-19 vaccine hesitancy is inevitable and we are already seeing signs of it.

> If large chunks of the population refuse to get vaccinated, that will be a very unfortunate and dangerous outcome for us. To avoid this, the government should maintain as much transparency in the vaccine development and licensing process. It would not be unusual if stakeholders from diverse groups, including those who maintain vaccine hesitancy, are invited to some of these forums to voice their opinions. These types of inclusive measures will go a long way. In addition, the government can start an information campaign advising people about the merits of COVID-19 vaccination and dispelling some of the myths or rumors associated with it. Once again, the experience from polio eradication will be relevant here. It took an army of approximately 2.5 million volunteers along with free availability of vaccine to uproot polio from every corner of India. Such a vaccine volunteer network that invites community leaders and influencers would assist COVID-19 vaccine implementation in a significant way.