

Vaccine developers move to stay ahead of Covid-19 variants



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Though current vaccines show efficacy, work on next-generation iterations against the South Africa variant is under way.

Yesterday's US adcom documents provided the first evidence from a large study that an existing Covid-19 vaccine could provide strong protection against the virus's troublesome South Africa variant. But biopharma is not letting the grass grow under its feet.

Pfizer and Biontech today moved to study a three-dose Comirnaty regimen to tackle variants, as well as mooting a separate variant-specific vaccine, a day after being beaten to the punch by Moderna, which has just shipped the first lots of its next-generation mRNA-1273.351 for clinical trials. At least four other groups are working on similar efforts.

Moderna describes mRNA-1273.351 as a variant-specific booster project designed specifically against the South Africa Covid-19 variant. The first doses have been shipped to the NIH's NIAID, which is to lead a phase I trial, Moderna said yesterday.

Several approaches are planned: just giving mRNA-1273.351, giving it in several combinations with the existing mRNA-1273 vaccine, or giving three doses of mRNA-1273.

In this regard Pfizer/Biontech's approach is similar. A current US phase I trial will offer participants an additional, third dose of Comirnaty to investigate its effect on unspecified circulating and "potential newly emerging" Covid-19 variants. Meanwhile, a separate effort will look at developing a next-generation Comirnaty with a modified sequence against the South Africa variant.

Ahead of the curve

Still, why is there a need for new vaccines if current vaccines are working well? Indeed, before J&J's data yesterday, Moderna and the Pfizer/Biontech group had reported that mRNA-1273 and Comirnaty prompted neutralising antibody production against new variants, in phase I and *in vitro* respectively.

But it is vital to stay ahead of the curve. Moderna yesterday said it was developing mRNA-1273.351 "out of an abundance of caution", while Pfizer/Biontech said they had to be prepared for any future strain changes; next-generation Comirnaty is viewed as a blueprint for the companies' plan to update the current vaccine quickly to address new variants if this need arises.

Earlier this month Glaxosmithkline and Curevac, which have both fallen behind in the Covid-19 vaccine race, teamed up to develop variant-specific, next-generation mRNA vaccines. In January Gritstone said it was working on a second-generation vaccine, and Immunitybio started a South Africa trial of its hAd5 T-cell vaccine, though this does not appear to have been designed specifically against variants.

Selected vaccine work vs South Africa (B.1.351) Covid-19 variant		
Company	Finding	Further work
Pfizer/Biontech	8 Jan: Comirnaty elicits neutralising Abs vs B.1.351 in vitro	25 Feb: ph1 subjects to be offered triple Comirnaty dose; regulatory discussions over clinical trial of next-gen version vs B.1.351
Gritstone	NA	19 Jan: 2nd-gen vaccine against Covid-19 variants to enter ph1 study run by NIAID
Immunitybio/Nantkwest	NA	19 Jan: authorisation to start S Africa ph1 trial of hAd5 T-cell vaccine candidate
Novavax	28 Jan: NVX-CoV2373 is 50% effective in S Africa (90% of cases attributable to B.1.351) vs ~90% in UK trial	28 Jan: next-gen protein vaccine candidate to start clinical trials in Q2
Glaxosmithkline/Curevac	NA	3 Feb: collaboration to develop mRNA vaccines against variants, planning to launch the first in 2022
Astrazeneca	12 Feb: B.1.351 resulted in AZD1222 effectiveness against mild disease falling to 10%; company says it "may still offer protection against severe disease"	No specifics disclosed
Moderna	17 Feb: preliminary report in NEJM that mRNA-1273 produced neutralising Abs against B.1.351, albeit with sixfold reduction in neutralizing titres vs prior variants	24 Feb: next-gen mRNA-1273.351 is shipped for NIAID clinical study vs B.1.351; possible combo with mRNA-1273, which might separately be given as triple dose
Johnson & Johnson	24 Feb: clinical trial shows JNJ-78436735 is 64% protective in S Africa, where 95% of sequenced cases were due to B.1.351	No specifics disclosed

Source: company announcements.

The South Africa variant, known as 20H/501Y.V2 or B.1.351, is thought first to have emerged last October, and now accounts for the vast majority of Covid-19 cases in that country, as well as being detected in others. It is especially worrying because it causes higher viral load and is more transmissible than early strains.

Already there have been some warning signs over existing vaccines. A South Africa study of Novavax's NVX-CoV2373 found efficacy of only 50%, versus almost 90% in its UK trial. A separate South Africa trial of Astrazeneca's AZD1222 found only 10% protection against mild Covid-19, though Astra hopes that the vaccine might still offer protection against severe disease caused by the variant.

A proactive approach by biopharma is warranted.

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