Evaluate Vantage

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Covid-19 developments over the Christmas period

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Drug makers and regulators take aim at Omicron.

Despite suggestions that the Omicron variant might produce milder disease than Delta and other strains, biopharma groups are working hard on vaccines and treatments for the newest iteration of the coronavirus.

Though many of the developments are positive, supply constraints and, in some cases, disappointing clinical findings suggest that 2022 could be yet another difficult year. Here is *Evaluate Vantage*'s summary of these important events.

December 31:

Having approved one Covid-19 antiviral at the start of November, the UK regulator has now approved a rather better one. **Pfizer**'s Paxlovid is now available as a five-day oral course for patients with mild to moderate Covid-19 who are at an increased risk of developing severe disease.

This is of course good news, though there are two concerns. First, the MHRA said that it is too early to know whether the Omicron variant has any impact on Paxlovid's effectiveness, though this is of course under investigation. Secondly, supplies are short: Pfizer said before Christmas that it was able to supply a total of 2.75 million doses to the UK throughout 2022. With new infections in the country running at nearly 200,000 per day, this might not stretch too far.

On the prevention rather than treatment side, a study suggested that two doses of **Sinovac**'s Covid-19 vaccine followed by a Pfizer-BioNTech booster showed a lower immune response against the Omicron variant compared with other strains.

The study, conducted in the Dominican Republic and published as a preprint, showed that the Sinovac regimen plus the Comirnaty shot produced an antibody response similar to a two-dose mRNA vaccine. Antibody levels against Omicron were 6.3-fold lower compared with the original variant and 2.7-fold lower when compared with Delta.

The two-dose Sinovac vaccine alone did not show any detectable neutralization against Omicron.

December 30:

More hope might come from **Johnson & Johnson**. Two doses of J&J's Covid-19 vaccine cut the risk of

hospitalisation by up to 85%, according to the Phase 3b Sisonke study, conducted in South Africa at a time when the Omicron strain was dominant.

The trial enrolled more than 69,000 healthcare workers and assessed the efficacy of a booster shot of the vaccine administered six to nine months after primary vaccination. It should be noted that J&J did not definitively state that some or all of the patients had Omicron, only that during the period of the trial Omicron frequency increased from 82% to 98%.

J&J also reported a separate analysis of 65 people who received primary vaccination with Pfizer/Biontech's Compirnaty, followed by either a homologous booster shot or a J&J booster.

The J&J booster increased anti-Omicron neutralising antibody titres by 41-fold at four weeks post-boost. Comirnaty increased antibody titres to a higher level at week two post-boost, before declining to represent a 17-fold increase at week four post-boost. The J&J jab prompted a 5.5-fold increase of Omicron-reactive CD8+ T cells, versus a 1.4-fold increase with Comirnaty.

Though it has been largely scorned by the West, the J&J jab is widely used in South Africa and elsewhere.

December 22:

Before Christmas **Novavax** reported initial data indicating that its Covid-19 vaccine, NVX-CoV2373, now branded Nuvaxovid, was effective against Omicron.

The data demonstrate broad cross-reactivity against the variant, with a 9.3-fold boost in anti-spike IgG titres following the booster compared with peak IgG levels after the initial two doses. Two days before this data was released, the EMA had recommended Nuvaxovid for authorisation in the EU.

Despite this, Novavax said it was working on an Omicron-specific vaccine, with manufacturing set to begin in early January. Both Moderna and Astrazeneca are also pursuing Omicron-specific vaccines.

Elsewhere, a phase 1b/2 clinical trial evaluating **Mereo Biopharma**'s alvelestat found the oral neutrophil elastase inhibitor to speed recovery of hospitalised Covid-19 patients. Five of the eight patients in the alvelestat arm of the Costa study, had a two-point decrease in the WHO disease severity score by day five, compared to two of the seven patients in the placebo arm. By day seven this improvement in WHO severity score had increased to seven out of eight in the alvelestat arm and four out of seven in the placebo arm. the drug was safe and well-tolerated, Mereo said.