Seirbhís Sláinte Níos Fearr á Forbairt | Building a Better Health Service

COVID-19 Omicron variant

Board update

24th January 2022

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Introduction

All viruses including SARS-CoV-2, the virus that causes COVID-19, change over time. Most changes have little or no impact on the virus's properties. However, some changes may affect how easily the virus spreads, the associated disease severity, or the effectiveness of vaccines or therapeutic medicines, diagnostic tools or public health or social measures. The SARS-CoV-2 virus continues to evolve and there are constant developments in our understanding of the impact of existing and new variants.

The Omicron variant (B.1.1.529) was first reported to the WHO by South Africa on November 24th 2021. On November 26th, the WHO declared Omicron a Variant of Concern (VOC). To be a designed as a Variant of Concern, a new variant must demonstrate (1) increased transmissibility or detrimental change in COVID-19 epidemiology or (2) increase in virulence of change in clinical disease presentation or (3) decrease in effectiveness of public health or social measures or available diagnostics, vaccines, or therapeutics.

The Omicron variant has marked antigenic drift compared with ancestral strains and previous Variants of Concern. The Omicron variant has over 50 mutations, 26 to 32 of which are in the gene for the spike protein. The spike protein is important as the virus uses it to infect human cells. All the approved COVID-19 vaccines use the spike protein as the target for generating an immune response to protect against the virus, in addition many of the approved therapeutic medicines also use the spike protein as a target. Therefore, significant changes to this spike protein have the potential to cause 'immune evasion' if our immune system can no longer recognise the spike protein after vaccination or previous infection. Our understanding of the significance of all the mutations in the Omicron variant has increased substantially since the variant was first identified.

We now know that Omicron has a substantial growth advantage over Delta, as evidenced by the rapid global spread and displacement of Delta as the dominant variant in many countries. This may be related to a combination of factors including its enhanced ability to attach and enter human cells and/or escape natural or acquired immunity. However, immune escape appears to be only partial as in countries with high primary and booster vaccination rates there has been a decoupling of daily positive cases and ICU and hospital admissions. Compared to previous waves, we are seeing less severe disease per 1000 cases. In addition, numerous population based and laboratory studies, which have been published since the emergence of the new variant, are helping to shed light on the additional characteristics of the variant which may impact public health risks.

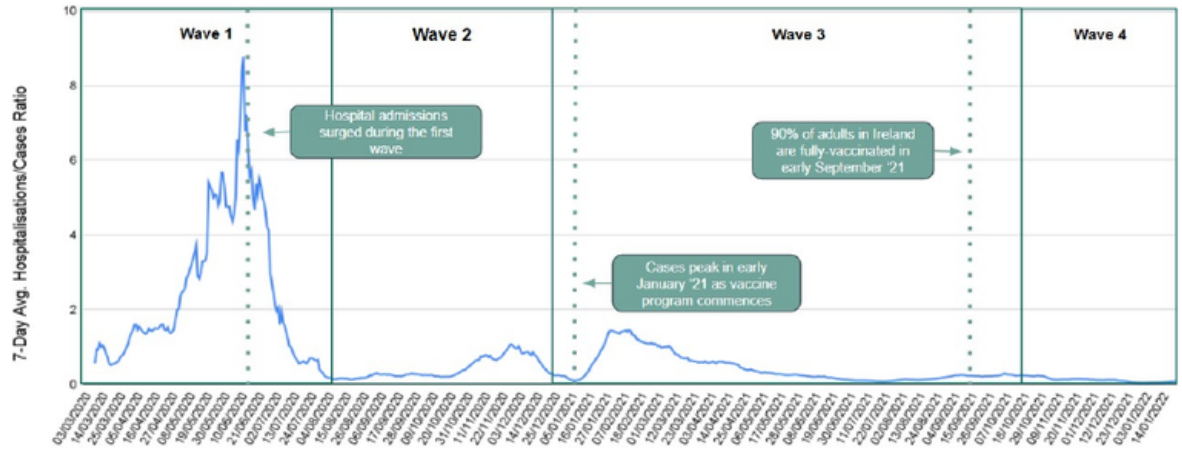
Both the WHO and the ECDC consider that based on the current situation and the available evidence, the overall level of risk to public health associated with the continuing spread of the Omicron variant is very high. Although the conversion rate of cases to severe illness has reduced, the sheer volume of cases combined with high levels of healthcare workers absenteeism due to COVID illness or close contact restriction of movements has the potential to overwhelm healthcare systems. Additionally, high case numbers are likely to exceed the capacity of the testing and tracing capacities of most countries.

Current situation in Ireland

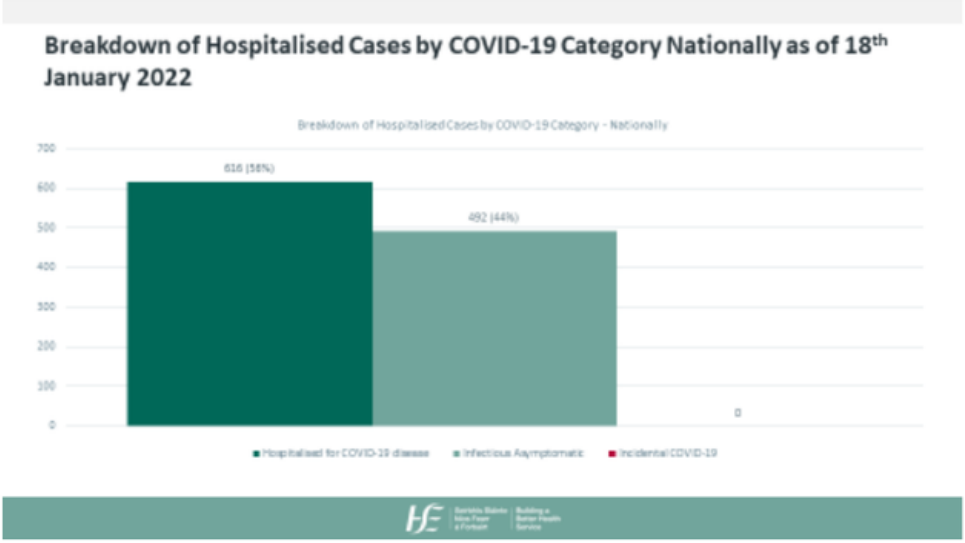
On December 1st, 2021 the first case of Omicron was detected in Ireland. Since then, we have seen a rapid increase in confirmed cases. Omicron is now the dominant variant in the country. As with all respiratory viruses the pace of spread is related to (1) the properties of the virus (2) the level of immunity in the population (3) the extent of social mixing that creates opportunities for viral spread and (4) public compliance with other public health measures. Between January 1st to 23rd there were 399,962 cases reported (both positive PCR and antigen tests) which accounts for 39% of all cases reported in the past 12 months. The 5-day moving average on December 2nd, 2021 when Delta was dominant was 4,477. Since then, as the Omicron variant has displaced Delta, we have seen a 135% increase in the 5-day moving average, which as of January 23rd, 2022 was 10,519. However, the positive case numbers recorded are widely accepted to not be representative of the true incidence of cases in the country. In the past 3 months, it is estimated that over 30% of the population aged between 16 and 40 years have been infected. As such, between primary and booster vaccination and natural infection, substantial immunity may have developed in the population. Notwithstanding the changes made to the national testing strategy, moving from PCR to antigen testing for those aged between 4 and 39 years of age and changes in ascertaining the positive results, the view of the HPSC is that daily case numbers have been falling over the past two weeks.

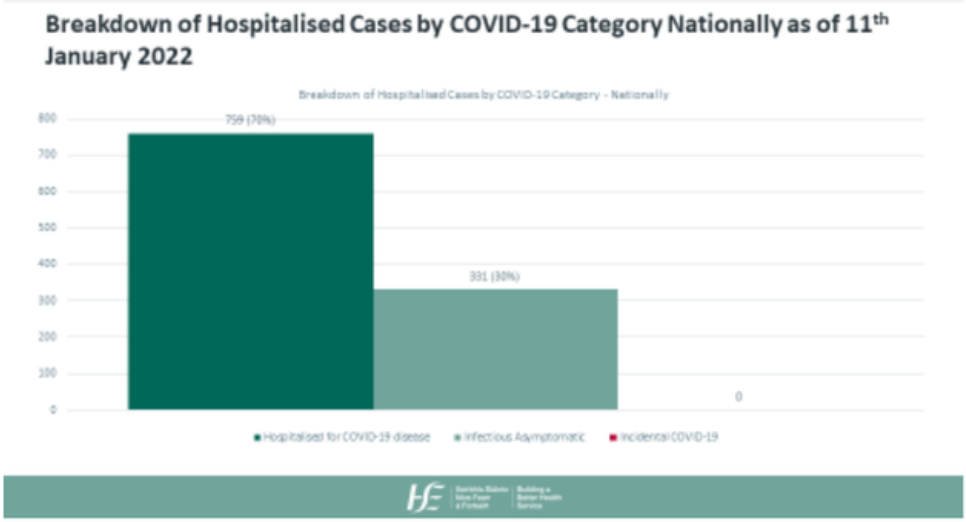
Impact of Omicron on Hospitalisation

However, despite the rapid increase in positive cases, the growth rate of patients in hospital and in ICU has not followed the same trajectory. In recent weeks, the number of patients in ICU has remained relatively stable, as of January 23rd, 2022 there were 79 patients in ICU, compared to 117 patients in ICU on December 2nd, 2021. The number of people in hospital with COVID-19 has been increasing since the end of December. However, current hospital admissions are 50% less than what we experienced during the peak of wave 3.



Category 1 patients are those **admitted to an acute hospital for management of a condition that is attributed to a diagnosis of COVID-19 made before admission** or about the time of admission **OR** those who are **admitted to an acute hospital for a non-COVID-19 related condition but who is now in hospital because of a condition related to a diagnosis of COVID-19 made after hospitalisation** (this will include hospital acquired COVID-19 and community acquired COVID-19 manifesting after admission).





Since the 11th January, the percentage of *category 1 patients* has decreased from 70% (n=759) to 56% (n=616).

Ireland: 7-Day Average Hospitalisation-to-Case Ratio (29/02/2020-23/01/2022)

Impact of Omicron on Healthcare Acquired Infection

In both acute hospital and residential care facilities there has been a sharp increase in healthcare acquired infection associated with widespread community spread of the Omicron variant. As in previous waves, the pattern appears to be one of repeated introduction of the virus into the healthcare setting by infectious people. This results in discrete outbreaks that are rapidly identified and managed followed by subsequent re-introduction of other outbreak(s) elsewhere in the healthcare setting. Essentially, the consistent experience has been that even with rigorous measures, it is not possible to effectively seal off the healthcare environment from infection if infection is widespread in the community which the healthcare setting serves. A HSE team presented Ireland's experience at a WHO meeting on January 12th. The UK, USA, and France reported similar experiences at that meeting.

Impact of Omicron on the Delivery of Healthcare Services

The numbers of healthcare workers who have been absent from work because of infection or because they were contacts of people with infection has proved a huge strain on the healthcare service. Although there are no clear criteria by which to determine with any confidence where a healthcare worker acquired the infection, the clinical impression is that most healthcare worker infections during the Omicron wave are not related to workplace exposure and similar to previous waves a key risk related to the workplace is interaction between colleagues. The healthcare system has also been stressed by loss of bed capacity related to ward closures and other restrictions required to manage outbreaks and control infection risk. There are also serious consequences for patients and service users related to limited access for partners and families who play a key role in supporting patients and service users.

Testing & Public Health Management

Current tests generally work well for the Omicron variant although there have been reports that some antigen test products may not perform quite as well with Omicron as with Delta and previous Variants of Concern. This is not considered to be a major concern with antigen tests in use by the HSE. Although the HSE rapidly increased PCR testing capacity the sheer volume of Omicron cases has overwhelmed testing capacity. This has accelerated a transition to self-care and self-testing of symptomatic people at low risk of severe disease. Other countries have experienced similar trends. Managing the volume of cases and contacts has necessitated an accelerated transition to more automated case and contact management to allow public health to prioritise intervention in higher risk settings including residential care settings.

Current understanding of Omicron variant

Transmissibility
There is consistent evidence that Omicron is highly transmissible and has a **substantial growth advantage** over Delta. Globally, during the week of January 10th to 16th, 2022, the new weekly COVID-19 cases increased by 20% as compared to the previous week. This corresponds to over 18 million new cases. All global regions reported an increase in the incidence of weekly cases with the exception of the African Region, which reported a 27% decrease. The European Region is the current global hotspot for Omicron (2,008 new cases per 100 000 population in week 1 of 2022)
Disease severity
Early evidence suggests a reduced risk of severe disease associated with the Omicron variant compared to the Delta. Several studies from South Africa, the UK, Denmark, and USA reported over the past number of weeks have demonstrated a less severe clinical profile of patients admitted to hospital with Omicron. In addition, we are seeing a decoupling of cases from hospitalisation, ICU, and deaths admission in several countries,

particularly those with high primary vaccination and booster vaccination levels. The decoupling is stronger for ICU and deaths than for hospitalisation. There are some indications that less severe disease may relate to differences in the Omicron variant that result in less efficient replication in the lungs.

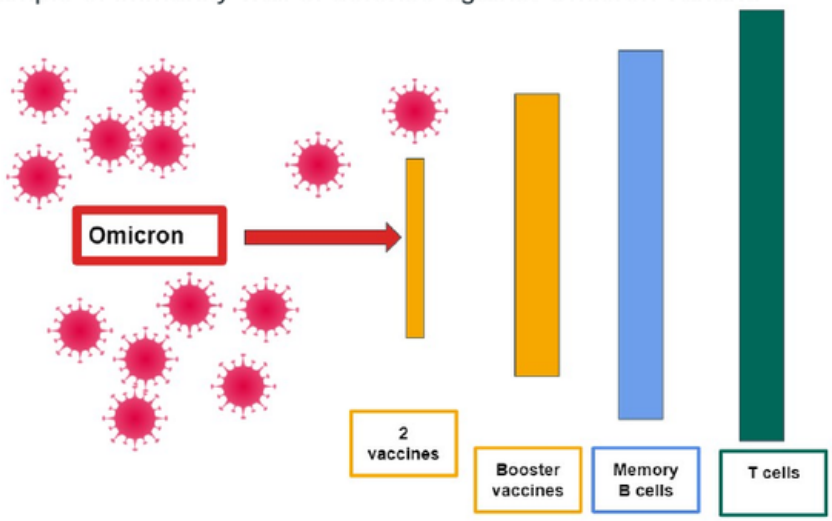
However, hospitalisation only represents one aspect of severity and more data is needed on other clinical markers of severity– such as the use of oxygen, mechanical ventilation, and deaths.

Vaccine effectiveness/ Immune evasion

Neutralising antibodies are just one part of our immune defense against disease, T cells and memory B cells are also important. Preliminary data suggest that there is a reduction in neutralization of Omicron in those who have received a primary vaccination series. Vaccine efficacy is lower for Omicron compared to Delta and immunity wanes quicker. Vaccine efficacy is increased following a booster vaccination although it continues to wane post booster vaccination. However, although vaccine effectiveness against the Omicron variant is reduced, vaccination still strongly protects against severe illness, hospitalisation, and death.

T cells remain effective against Omicron. Six recent studies show that T cell effectiveness against Omicron is well preserved and remains for 6-8 months post primary vaccination schedule (Pfizer, Moderna, AZ, J&J). In addition, memory B cells post booster vaccination have high Omicron reactivity. Therefore, the combination of enhanced antibody response post booster vaccination, B cells and T cells all appear to be protective against severe disease associated with Omicron.

Illustrative example of immunity wall of defense against Omicron variant:



Effectiveness of prior infection

Preliminary evidence suggests a possible increased risk of reinfection.

Impact on diagnostics and testing

The diagnostic accuracy of routinely used PCR and antigen-detection rapid diagnostic tests (Ag-RDT) assays does not appear to be impacted by Omicron. Studies of the

comparative sensitivity of Ag-RDTs are ongoing.
Effectiveness of current treatments
Existing treatments for severe disease such as steroids are expected to remain effective. However preliminary data suggests some of the monoclonal antibodies have decreased neutralisation against Omicron. Several studies have demonstrated that Omicron evades binding and neutralisation by most therapeutic SARS-CoV-2 monoclonal antibodies, with the exception of some broadly neutralising mAbs such as Sotrovimab. Recent laboratory data from Pfizer confirm that PAXLOVID will retain robust antiviral activity against current VOCs, including Omicron as well as other coronaviruses.

Impact on Omicron on the pandemic

The WHO defines pandemics, epidemics and endemics based on a disease's rate of spread. A pandemic spreads across international boundaries, this wide geographical reach means they have the potential to cause sudden widespread morbidity and mortality, as well as social, political, and economic disruption. In contrast, a disease that is endemic has a constant presence in a population but does not affect an alarmingly large number of people or disrupt society, as typically seen in a pandemic. It remains uncertain whether we will transition from a pandemic to an endemic state in 2022. However, because of the high level of primary vaccination uptake and the early role out of the booster vaccination in Ireland, as well as some inherent properties of the omicron variant, there has been a decoupling of population level harm from case numbers. Therefore, the current risk profile for Ireland, based on this variant's epidemiological course, is lower compared to previous waves.

The current levels of infection with Omicron are expected to have a major impact on the level of immunity to SARS-CoV-2 in the population as a whole. Those who have been vaccinated and those infected are likely to have enhanced immunity. Most of those who have not been vaccinated are likely to be infected with Omicron and therefore will no longer be immune naïve.

There is little reason to expect that the virus can be eradicated in the medium term. If the virus persists, it will continue to change and mutate. Other variants will most likely emerge. Some of these variants are likely to represent incremental changes (drift) from Omicron and its predecessors. There may be further waves of infection. However, the fundamental change is the level of acquired immunity that now exists among the population. Based on experience to-date, this provides robust protection for most people against serious disease as a result of infection with variants that represent incremental drift. Emergence of variant that completely escapes this moderating effect of population immunity (a "shift") is much less likely. We are therefore likely to see transitioning from a pandemic phase to an endemic phase of SARS-CoV-2. This means that this virus is likely to become one more respiratory virus in a pre-existing complex landscape of respiratory viruses. These viruses result in fairly frequent infection but cause an illness that is mild for most people although serious for some.

The emergence of therapeutics is expected to mitigate the impact on those most vulnerable to serious disease as a result of infection. A transition to endemic infection will require a fundamental change in approach for our collective response. In an endemic phase the focus will be on preventing, monitoring and managing serious disease and contexts in which serious disease is likely to occur rather than on seeking to confirm every case of infection and aggressively manage the potential for transmission from every case of infection.

Appendix: Evolving evidence from studies

Disease severity
South Africa (December 28th, 2021) The latest report from the Tshwane district, the global epicentre of the Omicron wave, compared the Omicron wave to the previous waves. Finding of study: • 4.5% death rate vs. 21.3% in previous waves • 1% admitted to ICU vs. 4.3% in previous waves • Avg. length of stay in hospital is 4 days vs. 8.8 days in previous waves • 39 years is the average admission age vs. 49.8 in previous waves https://www.samrc.ac.za/news/decreased-severity-disease-during-first-global-omicron-variant-covid-19-outbreak-large-hospital **UKHSA (December 31st, 2021)** University of Cambridge study found a 50% lower risk of hospital admission compared to Delta and the risk of hospital admission from emergency departments with Omicron was approximately one-third of that for Delta. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1045619/Technical-Briefing-31-Dec-2021-Omicron_severity_update.pdf **Scotland (December 22nd, 2021)** Early national data suggest that Omicron is associated with a two-thirds reduction in the risk of COVID-19 hospitalisation when compared to Delta. https://www.research.ed.ac.uk/en/publications/severity-of-omicron-variant-of-concern-and-vaccine-effectiveness- **Denmark (December 27th, 2021)** Omicron is generally 2.7-3.7 times more infectious than the Delta variant among vaccinated individuals. Fully vaccinated and booster-vaccinated individuals are generally less susceptible to infection compared to unvaccinated individuals. Booster vaccinated individuals generally had a reduced transmissibility. The study suggests the virus is mainly spreading more rapidly because it is better at evading immunity obtained from vaccines. https://www.medrxiv.org/content/10.1101/2021.12.27.21268278v1.full.pdf **USA (January 11th, 2022)** A large US analysis of positive cases of Omicron and Delta, during a period when both were in circulation reported:

- 50% less hospitalisations
- 75% less ICU admissions
- 70% reduction in hospital length of stay with Omicron compared to Delta

https://www.medrxiv.org/content/10.1101/2022.01.11.22269045v1

Vaccine effectiveness/ Immune evasion

UK (January 13th, 2022)
VE against symptomatic disease is lower for Omicron compared to Delta for the AstraZeneca (AZ), Pfizer and Moderna vaccines. For AZ VE drops from 45-50% to almost no effect at 20 weeks. For Moderna and Pfizer VE drops from 65-70% down to 10% at 20 weeks. 2-4 weeks post an mRNA booster vaccine VE increases to 65-70% and wanes to 45-50% at 10+ weeks. However, protection against hospitalisation is much greater, post a booster dose VE against hospitalisation is ~85-90%.
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1046431/Vaccine-surveillance-report-week-2-2022.pdf

US (January 7th, 2022)
Vaccine effectiveness of 3 doses of the Moderna vaccine against infection with Delta was high and durable, but VE against Omicron infection was lower and wanes over time (30% protection 3 months post second vaccination). VE of booster vaccine against Omicron is lower than Delta.
https://www.medrxiv.org/content/10.1101/2022.01.07.22268919v1.full.pdf

Denmark (December 22nd, 2021)
VE against the Omicron variant of 55% for the Pfizer vaccine and 37% for the Moderna vaccines, respectively, in the first month after primary vaccination. However, the VE is significantly lower than that against Delta infection and declines rapidly over just a few months. VE is re-established upon revaccination with the Pfizer vaccine (55%)
https://www.medrxiv.org/content/10.1101/2021.12.20.21267966v2

South Africa (December 29th, 2021)
VE against hospitalisation following the primary vaccination schedule with the Pfizer vaccine against Omicron was 70%.
https://www.nejm.org/doi/full/10.1056/NEJMc2119270

Effectiveness of prior infection

UKHSA (January 14th 2022)
There is now a marked increase in overall reinfection rates, this is disproportionate to the increase in first infections. Provisional data for week 2021-52 (beginning December 27th 2021) identified over 100,000 possible reinfections accounting for 9.5% of all infections that week.
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1046623/Technical-Briefing-34-14January2022.pdf

Office for National statistics (January 19th, 2022)

Compared to the Delta variant, the risk of reinfection with the Omicron variant is 16 times higher
https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/coronaviruscovid19infectionsurveycharacteristicsofpeopletestingpositiveforcovid19uk/19january2022#reinfections-with-covid-19-uk

South Africa (January 12th 2022)
The latest South African study found evidence of a substantial and ongoing increase in the

risk of reinfection associated with the Omicron variant illustrating greater immune escape when compared with previous variants. There was a 16% increase in risk of reinfection compared to the Delta wave.
https://www.medrxiv.org/content/10.1101/2021.11.11.21266068v2.full.pdf

Impact on diagnostics and testing

USA (December 28th 2021)
The FDA said early data suggests that while antigen tests do detect the Omicron variant, some may have reduced sensitivity based on preliminary studies by the National Institutes of Health's Rapid Acceleration of Diagnostics (RADx) program which evaluated their performance using patient samples containing live virus.

Switzerland (December 22nd 2021)
The analytical sensitivity to detect the SARS-CoV-2 Omicron variant for Ag-RDTs was lower than that for the other VOCs in most of the tests evaluated.
https://www.medrxiv.org/content/10.1101/2021.12.18.21268018v1.full.pdf

Effectiveness of current treatments

Several studies have demonstrated that Omicron evades binding and neutralisation by most therapeutic SARS-CoV-2 monoclonal antibodies, with the exception of some broadly neutralising mAbs such as Sotrovimab

https://doi.org/10.1038/d41586-021-03796-6
https://doi.org/10.1016/j.cell.2021.12.032
https://doi.org/10.1016/j.cell.2021.12.046
https://doi.org/10.1038/d41586-021-03825-4
https://doi.org/10.1038/d41586-021-03827-2
https://doi.org/10.1038/d41586-021-03826-3

Pfizer: Recent laboratory data from Pfizer confirm that PAXLOVID will retain robust antiviral activity against current VOCs, including Omicron as well as other coronaviruses.

https://www.pfizer.com/news/press-release/press-release-detail/pfizer-announces-additional-phase-23-study-results#:~:text=These%20results%20were%20consistent%20with,three%20days%20of%20symptom%20onset.

https://www.pfizer.com/news/press-release/press-release-detail/pfizer-shares-vitro-efficacy-novel-covid-19-oral-treatment

Mulnupiravir: Data on Molnupiravir's impact against Omicron is not yet available

Sotrovimab: GSK recently announced that Sotrovimab has demonstrated ongoing activity against all tested variants of concern and interest defined by the WHO. The companies are now completing laboratory testing to confirm the neutralising activity of Sotrovimab against the combination of all the Omicron mutations with the intent to provide an update by the end of 2021.
https://www.biorxiv.org/content/10.1101/2021.03.09.434607v