In brief

Omicron BA.2 sub-lineage

18 March 2022

Summary

- Omicron (B.1.1.529) was designated a variant of concern by the World Health Organization (WHO) on 26 November 2021. It has 50 mutations, including 26-32 mutations on its spike protein.[1, 2]
- Omicron includes four Pango lineages: the parental B.1.1.529 and the descendent lineages BA.1, BA.2 and BA.3. WHO is monitoring all variants under Omicron.[2, 3]
- The spike profile of BA.2 contains 28 mutations and a deletion at 25-27.[4]
- WHO recommends that investigations into the characteristics of BA.2, including immune escape properties and virulence, should be prioritised independently (and comparatively) to BA.1.[5]
- While BA.1 has previously been the most dominant strain, BA.2 is increasing and is dominant in several countries.[2]
- WHO released interim guidance on contact tracing and quarantine for Omicron.[6]

Transmissibility

- The United Kingdom Health Security Agency (UKHSA) Variant Technical Group designated BA.2 as a ‘variant under investigation’ on 19 January 2022.[2, 4] A risk assessment updated by the agency on 23 February 2022 reported moderate confidence level risk for overall growth advantage, low confidence level risk for transmissibility, and moderate confidence risk for immune evasion and infection severity.[7] The WHO used the UKHSA framework to conduct a risk assessment which reported moderate confidence level risk for transmissibility, low confidence risk for disease severity, moderate for immune escape and low for impact on detection capacity. There was insufficient data on differences in effectiveness of current treatments between BA.2 and other lineages. [8]
- Early reports suggest BA.2 has an increased growth rate compared to BA.1. Preliminary data from Denmark suggests BA.2 may be 1.5 times more transmissible than BA.1.[9, 10]
- BA.2 appears to be more infectious than BA.1 (higher viral loads and longer infectious periods).[11]
- One study suggests the within-round reproduction number (R) is 0.94. The R additive advantage for BA.2 (vs BA.1 or BA.1.1) was estimated to be 0.40.[12] Other estimates suggests the reproduction number of BA.2 is 1.4-fold higher than BA.1,[13] and that the reproductive number of BA.1 is 1.99 times and that of BA.2 is 2.51 times larger than the effective reproduction number of Delta.[14]
- Preliminary analysis suggests a mean serial interval of 3.27 days compared to 3.72 days for BA.1. Both are shorter than the mean serial interval for Delta of 4.09 days.[13]
- Preliminary analysis from the UKHSA suggests a 13.4% secondary attack rate for BA.2 compared to 10.3% for other Omicron cases.[9] Estimates from Denmark are 29% and 39% in households with BA.1 and BA.2, respectively, and data suggests increased transmissibility from unvaccinated primary cases in BA.2 households.[15]

Severity

- Early data from Denmark suggests there is no difference in the risk of hospital admissions between BA.1 and BA.2.[16]

- One study assessed the severity of BA.2 infections compared to BA.1 in South Africa. Findings suggest that while BA.2 may have a competitive advantage over BA.1 in some settings, the clinical profile of the illness remains similar.[17]

COVID-19 vaccines

- Early assessments do not suggest a difference in vaccine effectiveness against symptomatic disease for BA.2 compared to BA.1. Preliminary unpublished data from the University of Oxford found BA.1 and BA.2 pseudoviruses did not differ substantially in neutralisation by sera from vaccinated individuals. Another study suggests vaccine effectiveness against symptomatic disease is similar for BA.1 and BA.2; reporting that 25 plus weeks after two doses vaccine effectiveness was 9% and 13% respectively for BA.1 and BA.2. At two weeks following a booster vaccine, effectiveness was 63% for BA.1 and 70% for BA.2.[9, 18]
- Estimated vaccine effectiveness of Comirnaty against symptomatic infection for BA.1 is 46.6% and for BA.2 is 51.7% in the first three months, both with a decline to approximately 10% thereafter.[19]
- Reports suggest vaccine-induced humoral immunity fails to function against BA.2 like BA.1, and notably, the antigenicity of BA.2 is different from BA.1. Infection experiments using hamsters show that BA.2 is more pathogenic than BA.1.[13]

Reinfection

- Early evidence suggests BA.2 reinfections occur shortly after BA.1 infections, however reinfection is rare. Findings from a study in Denmark identified 47 instances of BA.2 reinfection after a BA.1 infection, mostly in unvaccinated individuals with mild disease not resulting in hospitalisation or death.[20] Another study suggests the protective effectiveness of BA.1 infection against reinfection with BA.2 is estimated at 94.9%.[21]
- Reports of co-infections and infection by Delta-Omicron recombinant virus in several countries.[22]

Monoclonal antibodies

- Preliminary studies suggest BA.2 exhibits marked resistance to monoclonal antibodies, including sotrovimab, which retained neutralising activity against BA.1.[23, 24]
- One study, comparing the sensitivity of BA.1 and BA.2 to neutralisation by nine monoclonal antibodies, suggests BA.2 was sensitive to cilgavimab, partly inhibited by imdevimab and resistant to adintrevimab and sotrovimab. Anti-Omicron activity of Ronapreve, and to a lesser extent that of Evusheld, is reduced in patients' sera, which is associated with decreased clinical efficacy.[25]
- The United States Food and Drug Administration issued an emergency use authorisation for bebtelovimab on 11 February 2022. Laboratory testing suggests the monoclonal antibody retained activity against BA.2.[26, 27]

Diagnosis

- BA.2 does not contain the deletion at S:69-70 and is S-gene target positive on polymerase chain reaction (PCR) diagnostic assays. UKHSA suggests that S-gene target failure is no longer sufficient to assess the spread of Omicron as a whole.[4, 9] N-gene target failure can detect BA.2.[28]
- Results for rapid testing are conflicting, with some studies showing a reduced detection rate of Omicron infections, however a study from the United States showed comparable sensitivity between Omicron and Delta.[29, 30] It is difficult to predict the test performance specific to BA.2.[31]

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