In brief

Emerging variants

13 May 2022

Summary

- The World Health Organization is monitoring BA.1, BA.2, BA.3, BA.4, BA.5 and descendent lineages and BA.1/BA.2 circulating recombinant forms such as XE under Omicron; however, the World Health Organization advises that public health authorities should monitor descendent lineages as distinct lineages.1
- Variants under monitoring listed by the World Health Organization include B.1.640 and XD recombinant (Delta AY.4 and Omicron BA.1).1
- Three Omicron sublineages BA.4, BA.5 and BA.2.12.1 have acquired additional mutations that may impact their characteristics (BA.4 and BA.5 have the del69/70, L452R and F486V mutations; BA.2.12.1 has the L452Q and S704L mutations).2

BA.2.12.1

- In the week ending 30 April 2022, BA.2.12.1 made up 36.5% of all newly sequenced positive COVID-19 tests in the United States.3
- Preliminary data suggests that BA.2.12.1 exhibits increased ACE2-binding affinities compared to BA.1.4
- Early data suggests use of pOGTF as a proxy for BA.2.12.1 provides faster tracking than whole genome sequencing.5
- Early reports of a growth advantage for BA.2.12 over BA.2.6
- There are evaluations on the sensitivity of BA.2.12.1 to eight therapeutic monoclonal antibodies. Findings from two studies suggest several antibodies are less effective against BA.2.12.1.7, 8

BA.4 and BA.5

- In a risk assessment published by the United Kingdom Health Security Agency on 28 April 2022 on BA.4 and BA.5 sublineages there was:
  - evidence of an overall growth advantage (red status with low level confidence) compared to BA.2 in the context of South Africa
  - insufficient data to report on transmissibility
  - evidence of some antigenic change (red status with moderate level confidence) compared to BA.2 based on structural modelling and pseudovirus neutralisation data
  - insufficient data to report on infection severity.9
- The European Centre for Disease Prevention and Control reported no current evidence for impact on transmissibility or on severity for BA.4 and BA.5 on 5 May 2022. However, early data suggests increased impact on immunity.
- Mutation profiles:
BA.4 shares all mutations and deletions with the BA.2 lineage except the following:

- S: 69/70 deletion, R408 (WT), L452R, F486V, Q493 (WT)
- ORF 7b: L11F
- N: P151S
- synonymous SNP G12160A.

BA.5 shares all mutations and deletions with the BA.2 lineage except the following:

- S: 69/70 deletion, R408 (WT), L452R, F486V, Q493 (WT)
- ORF6: D61 (wild type)
- M: D3N
- synonymous SNPs: G12160A, A27038G, and C27889T.

- Preliminary data suggests BA.4 and BA.5 sequences have the 69-70 deletion responsible for S gene target failure (SGTF).²
- Early reports suggest the observed escape of BA.4 and BA.5 from BA.1 elicited immunity is more moderate than the escape of BA.1 from previous immunity.⁴, ¹⁰ One study showed that the BA.1 infection elicited neutralising capacity against BA.4 and BA.5 was five-fold higher in vaccinated individuals (Comirnaty and Johnson & Johnson) than unvaccinated individuals.¹⁰
- BA.4 and BA.5 have rapidly replaced BA.2, reaching more than 50% of sequenced cases in South Africa.¹¹ Estimated growth advantages for BA.4 and BA.5 are 0.08 and 0.12 per day respectively over BA.2 in South Africa.¹¹
- According to the National Institute for Communicable Disease from South Africa, as of 4 May 2022, there was no indication that the BA.4 and BA.5 will increase the risk of developing severe disease in South Africa. However, the situation will continue to be monitored.¹²
- A preliminary comparative analysis and modelling study projected that the BA.4 and BA.5 are about 36% more infectious than BA.2 and will likely to become the new dominant variant.¹³
- Evaluations on the sensitivity of BA.2,¹².¹ and BA.4/5 to eight therapeutic monoclonal antibodies (bamlanivimab, bebtelovimab, casirivimab, cilgavimab, etesevimab, imdevimab, sotrovimab and tixagevimab) showed that bebtelovimab had two-fold more neutralising activity against BA.2 and other Omicron subvariants than against the parental virus (B.1.1). Sotrovimab had a 20-fold reduced neutralising activity against BA.2 than against the parental virus, however, it had more neutralising activity against BA.2.11 and BA.4/5 than against BA.2. Cilgavimab was active against BA.2, however, in comparison had 2-5-fold reduction in neutralising activity against BA.2.12.¹ and 30-fold reduction against BA.4/5.⁷

Recombinant lineages

- There are reports of three recombinant lineages: XD, XE and XF.¹⁴ The United Kingdom Health Security Agency identified two different combinations of Delta and BA.1 (XD and XF).¹⁴
- XD and XF are combinations of Delta AY.4 and BA.1. XD has the Omicron S gene incorporated into a Delta genome. XE is a combination of BA.1 and BA.2, with most of the genome including the S gene belonging to BA.2.¹⁴
- The XD recombinant is a variant under monitoring by the World Health Organisations and XE is monitored as Omicron.¹⁵
COVID-19 Critical Intelligence Unit: Emerging variants

- It is estimated that XE has a growth rate 12.6% above that of BA.2.16
- There are reports that XF is no longer detected in the European Union and European Economic Area.17
- Early data suggests Delta-Omicron recombinant infections are rare and there is no evidence of increased transmissibility compared to other Omicron lineages.18
- Early reports suggest there is no current evidence that XD is associated with higher transmissibility or more severe outcomes.19

References

7. Yamasoba D, Kosugi Y, Kimura I, et al. Sensitivity of novel SARS-CoV-2 Omicron subvariants, BA.2.11, BA.2.12.1, BA.4 and BA.5 to therapeutic monoclonal antibodies. bioRxiv. 2022:2022.05.03.490409. DOI: 10.1101/2022.05.03.490409


