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Neutralizing antibody response to the highly divergent BA.2.86 SARS-CoV-2 lineages in vaccinated health care workers with or without subsequent infection

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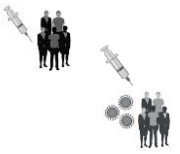
INTRODUCTION

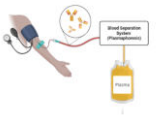
- Since the emergence of the Omicron variant, SARS-CoV-2 has been evolving into a constellation of related lineages.
- A highly mutated Omicron variant BA.2.86 emerged in the late 2023 with over 30 amino acid changes in Spike protein.
- One key issue is whether past natural and/or vaccine induced immunity remains effective against latest lineages.
- Aim of this work was to investigate in a live virus in vitro assay, the neutralizing antibody (NtAb) response against BA.2.86 and ancestral B.1 SARS-CoV-2 in a cohort of previously vaccinated health care workers (HCWs) with or without following infection, enrolled in the EuCare consortium.

STUDY POPULATION



- 68 HCWs (49±11 years, male 12%) were selected from the EuCare cohort participated in the study including 47 (51±10 years) SARS-CoV-2 vaccinated with 4-5 doses but never infected (**V**) and 21 (44±10 years) vaccinated with 3-5 doses and then infected during the early Omicron waves (**VI**).

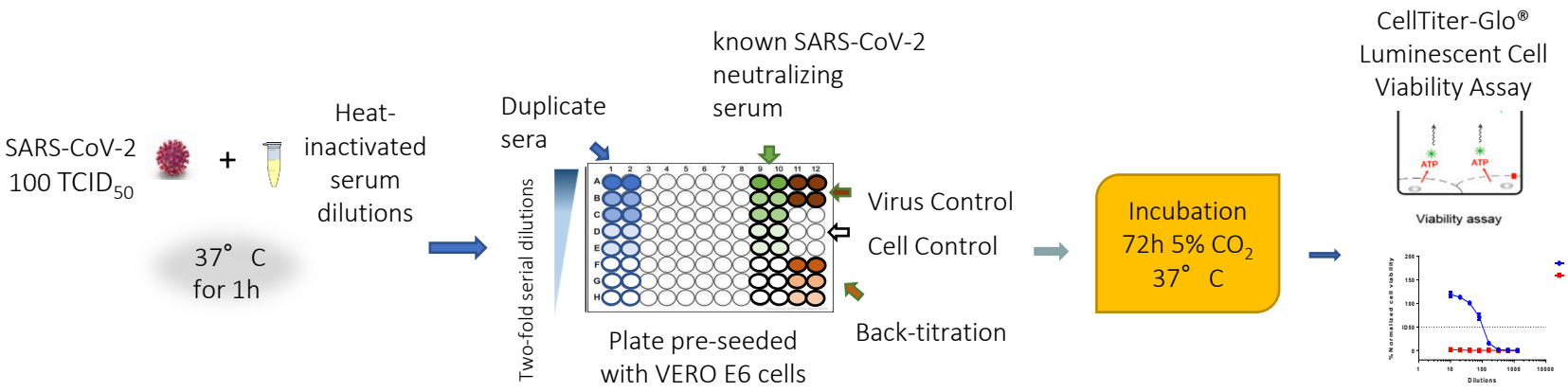
- 77% HCWs received mRNA vaccines and 24% received the bivalent (BiV) vaccination.



- Sera were collected at median 119 [17-137] days since the last immunization event: **167** [18-229] days for **VI** vs. **114** [16-129] days for **V** p = 0.012

METHODS

- NtAb titers against ancestral strain (B.1) and BA.2.86 were expressed as the reciprocal value of the sera dilution showing 50% protection of virus-induced cytopatic effects (ID_{50}).
- Sera with ID_{50} titers ≥10 were defined as SARS-CoV-2 positive and neutralizing.



RESULTS (I)

- Overall, NtAb titres to **B.1** were significantly higher than to **BA.2.86** (**1201** [572-2518] vs.**164** [56-437]; p<0.001) (Fig.1)
- NtAbs titers vs. **B.1** and **BA.2.86** were not measurable in **1** subject
- NtAbs titers were not measurable only vs. **BA.2.86** in **3** subjects
- Overall, no significant correlation between days since last immunization and NtAb levels to **B.1** (rho = -0.096; p = 0.437) and **BA.2.86** (rho = -0.169; p = 0.169) were observed.

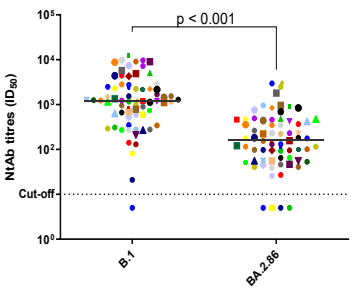
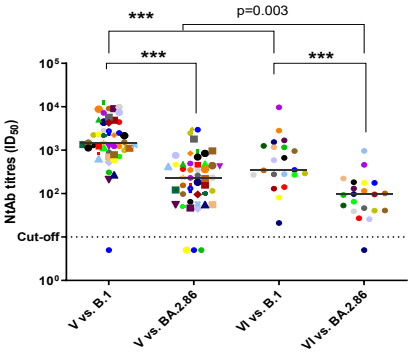


Figure 1. Neutralizing antibodies titres against the wild type B.1 lineage (D614G) and BA.2.86 lineage.

RESULTS (II)

- The uninfected group (**V**) had significantly higher NtAb titres compared with the infected group(**VI**), both against **B.1** (**1440** [906-4415] vs. **349** [271-1162] p<0.001) and against **BA.2.86** (**231** [96-470] vs. **93** [40-176] p=0.003) (Fig.2)



- NtAbs titres were comparable between HCWs receiving monovalent vs. BiV vaccination against **B.1** (**1179** [591-2740] vs. **1228** [404-2422]; p=0.795) and **BA.2.86** (**135** [47-320] vs. **174** [56-486]; p=0,301).

Figure 2. Neutralizing antibodies titres against the wild type B.1 lineage (D614G) and the highly divergent BA.2.86 lineage in vaccinated HCWs with and without natural infection as their last immunisation event. The same symbols indicate the individual ID_{50} values for the same subjects: *** p < 0.001.

CONCLUSIONS

Almost 1-log reduction in NtAbs titres to the highly divergent BA.2.86 virus vs. the ancestral B.1 was observed in HCWs vaccinated or vaccinated and infected. Ongoing analyses on a larger number of samples associated with studies of cell-mediated immunity will enrich the data on NtAb response clarifying the breadth and duration of immunity to SARS-CoV-2 variants.