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A tabulated summary of the evidence on humoral and cellular responses to the SARS-CoV-2 Omicron VOC, as well as vaccine efficacy against this variant.

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SUMMARY

Introduction: SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) is the virus responsible for COVID-19. It is one of the most mutating viruses in the world. These mutations are responsible for the appearance of new variants, most recently the Omicron variant (line B.1.1.529). This new variant was first identified in South Africa in November 2021. The main fear with this variant is that of an immune escape and ineffectiveness of vaccines currently available.

Objective: We studied the response of our immune system and the effectiveness of current vaccines against SARS-CoV-2 Omicron VOC.

Methods: We carried out a narrative review from 32 scientific articles from databases: MEDLINE (PubMed), Embase, BioRxiv and MedRxiv.

Results: Faced with SARS-CoV-2 Omicron VOC: The humoral immune response decreased, while the cellular immune response was preserved. The booster vaccine provided protection against symptomatic or non-symptomatic infections, transmission, and serious forms.

Conclusion: In the end, according to these data, the 3rd dose appears to be the solution to be able to defeat SARS-CoV-2 Omicron VOC. But the health authorities must not forget to insist on the primary vaccination of individuals not yet vaccinated, as well as on an “equal” distribution of vaccines against COVID-19 throughout the world.

1. Introduction

SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) is the virus responsible for COVID-19. It is one of the most mutating viruses in the world. These mutations mainly concern the Spike protein domain, which has given rise to several variants of concern (VOC) which have had a special designation by the World Health Organization (WHO): Alpha (line B.1.1.7), Beta (line B.1.351), Gamma (line P.1), Delta (line B.1.617.2) and more recently Omicron (line B.1.1.529). [1]

This new variant of SARS-CoV-2 was first identified in South Africa. On 24 November 2021, B.1.1.529 named Omicron was designated as a monitored variant (VUM) by the World Health Organization (WHO).

Two days later, the Omicron variant was classified as a variant of concern (VOC). [2,3]

The SARS-CoV-2 Omicron VOC is a variant with 32 mutations in the spike protein compared to the wild-type strain of SARS-CoV-2. [4,5]

Very quickly, this variant spread to several European countries, Africa, Asia and even the United States. This therefore suggests a rapid increase in cases and therefore a high transmissibility. [6] As of 23 December 2021, the SARS-CoV-2 Omicron VOC had been confirmed in 110 countries. From an experimental model, on SARS-CoV-2, Chen et al. revealed that: SARS-CoV-2 Omicron VOC can be more than ten times more contagious than the original virus or about twice as infectious as the SARS-CoV-2 Delta VOC. [7] SARS-CoV-2 Omicron VOC is expected to replace SARS-CoV-2 Delta VOC and become the dominant variant in a number of countries in the European region in early 2022 [8] In the United States of America, SARS-CoV-2 Omicron VOC became the dominant variant the week ending 18 December, accounting for approximately 73% of cases [9].

The main vaccines against COVID-19 currently available: Pfizer-BioNTech (BNT162b2), Moderna (mRNA-1273), Janssen of Johnson & Johnson (Ad26.COV2.S), AstraZeneca (ChAdOx1 nCoV-19) and Novavax (NVX-CoV2373), have been shown to be effective against SARS-CoV-2 (the ancestral strain, Alpha, Beta, Gamma, Delta). [10]

Due to the high number of mutations in the spike protein of the SARS-CoV-2 Omicron VOC, we feared viral invasion, immune evasion and therefore insufficient efficacy of current vaccines. With this study, we studied the response of our immune system and the effectiveness of current vaccines against SARS-CoV-2 Omicron VOC.

2. Materials and methods

We made a narrative review. To do this, we conducted electronic searches of scientific articles using several databases from November 01, 2021 to January 1, 2022.

The databases consulted were: MEDLINE (PubMed), Embase, BioRxiv and MedRxiv.

The terms used for the search were: "Omicron", "vaccine", "efficacy", "effectiveness", "humoral response", "cellular response".

We considered the four vaccines against COVID-19 currently approved by health authorities: the European Medicines Agency (EMA) and the US Federal Food and Drug Administration (FDA). These were...
### Table 1
Humoral immune response to SARS-CoV-2 Omicron VOC.

| Studies | Study sample | Vaccines against COVID-19 | Key results |
|---------|--------------|---------------------------|-------------|
| [11] Planas et al. (France, Belgium) | Sera from people vaccinated or infected with COVID-19. (In vitro data) | Pfizer, AstraZeneca | Omicron was totally or partially resistant to neutralization by all monoclonal antibodies tested. Booster vaccination with Pfizer and vaccination of individuals with a history of SARS-CoV-2 infection generated a neutralizing response against Omicron but with antibody titers 6 to 23 times lower than those against Delta. |
| [12] Nemet et al. (Israel) | Sera of vaccinated health care workers: 2 doses Vs 3 doses. (In vitro data) | Pfizer | No neutralization of Omicron after 2 doses of Pfizer. 100-fold increase in the neutralization effectiveness of Omicron after 3 doses of Pfizer but reduced by 4 times compared to Delta. With 2 doses of Pfizer: limited ability to neutralize Omicron. With 3 doses, antibody titers were boosted but were reduced 4-fold for Omicron compared to lineage A.2.2 SARS-CoV-2. |
| [13] Basile et al. (Australia) | Sera collected 1, 3 and 6 months after two doses of Pfizer. (In vitro data) | Pfizer | The vaccine booster with mRNA vaccines resulted in a potent neutralization of Omicron, but 4 to 6 times lower than that of the ancestral strain. |
| [14] Garcia-Beltran et al. (USA) | People vaccinated in the last 3 months, 6 to 12 months. People vaccinated in the last 6 to 12 months who have already been infected. People who have received a booster in the last 3 months. | Moderna, Pfizer, Janssen | The neutralizing activity of convalescent or vaccinated sera was low against Omicron. The neutralizing activity of boosted mRNA sera, doubly vaccinated and boosted convalescents, was maintained against Omicron, although reduced by 4 times compared to Delta. |
| [15] Hoffmann et al. (Germany) | Sera of convalescents or vaccinated individuals. (In vitro data) | AstraZeneca, Pfizer | The vaccine booster with mRNA vaccines resulted in a potent neutralization of Omicron, but 4 to 6 times lower than that of the ancestral strain. |
| [16] Carreño et al. (USA) | Sera of convalescents, doubly vaccinated mRNA, boosted mRNA, doubly vaccinated convalescents and boosted convalescents. (In vitro data) | Pfizer, Moderna | The neutralizing activity of convalescent or vaccinated sera was low against Omicron. The neutralizing activity of boosted mRNA sera, doubly vaccinated and boosted convalescents, was maintained against Omicron, although reduced by 4 times compared to Delta. |

### Table 1 (continued)

| Studies | Study sample | Vaccines against COVID-19 | Key results |
|---------|--------------|---------------------------|-------------|
| [17] Cele et al. (South Africa) | Sera of infected participants and vaccinated or not vaccinated without any evidence of previous infection. (In vitro data) | Pfizer | In all participants, decrease in the mean neutralizing antibody titers by a factor of 22 with the Omicron variant. However, in the previously infected and vaccinated group, the level of residual neutralization of Omicron was similar to the level of neutralization of ancestral virus observed in the vaccination only group. |
| [18] Gruell et al. (Germany) | People vaccinated with two doses of Pfizer and convalescent people. | Pfizer | In those who received 2 doses of vaccine or convalescents: lack of neutralizing activity against Omicron. The vaccine booster resulted in a significant increase in neutralizing activity against Omicron. |
| [19] Zou et al. (USA) | Sera from patients collected 1 or 6 months after SARS-CoV-2 infection. (In vitro data) | Pfizer | 1 and 6 months after SARS-CoV-2 infection, the neutralization titers against Omicron were 15.8 and 4.4 times lower than those of the ancestral strain, respectively. With 2 doses of mRNA vaccines: minimal neutralization against Omicron. The vaccine booster allowed a strong neutralization against Omicron. |
| [20] Zeng et al. (USA) | Sera of vaccinated health care workers. (In vitro data) | Pfizer, Moderna | With 2 doses of mRNA vaccine, the Delta and Omicron variants showed a 4.2-fold and 21.3-fold reduction in neutralizing activity. |
| [21] Zeng et al. (USA) | Vaccinated solid tumor patients. (In vitro data) | Pfizer, Moderna | With 2 doses of mRNA vaccine, the Delta and Omicron variants showed a 4.2-fold and 21.3-fold reduction in neutralizing activity. (continued on next page) |
| Studies                                                                 | Study sample                                                                 | Vaccines against COVID-19                                                                 | Key results                                                                                                                                 |
|------------------------------------------------------------------------|------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| [22] Schmidt et al. (USA)                                              | Plasmas of convalescents, convalescent vaccinated, (in vitro data)           | Vaccins à ARNm, Janssen                                                                | Deactivated, Moderna After 2 doses of Pfizer.                                                                                             |
| [23] Dejirattisai et al. (United Kingdom)                              | Participants vaccinated with 2 doses of AstraZeneca or Pfizer.               | pfizer, astraZeneca                                                                     | Titrations on sera from participants who had received homologous astraZeneca: reduced by 29.4 fold from 1609 (the ancestral strain) to 54 (Omicron variant), with one participant dropping below the detection threshold. |
| [24] Khan et al. (South Africa)                                        | Previously vaccinated and unvaccinated patients who were infected with SARS-CoV-2 during the Omicron wave in South Africa. |                                                                                            |                                                                                                                                             |
| [25] Doria-Rose et al. (USA)                                           | Sera samples from Moderna vaccine recipients. (In vitro data)                | Moderna                                                                                  |                                                                                                                                             |
|                                                                         |                                                                              |                                                                                          |                                                                                                                                             |

**Pfizer-BioNTech (BNT162b2), Moderna (mRNA-1273), Janssen of Johnson & Johnson (Ad26.COV2.S) and AstraZeneca (ChAdOx1 nCoV-19). We also considered in a single study a vaccine against COVID-19 already authorized by the European Medicines Agency (EMA) but in the process of authorization by the US Federal Food and Drug Administration (FDA), it was the Novavax vaccine (NVX-CoV2373).**

The humoral response corresponds to:

- The quantification of the neutralizing antibody titers or the geometric mean neutralization titers of the reciprocal plasma dilution resulting from a 50% reduction in the foci of infection. The values of these titers were determined for each combination of sera (infected or vaccinated) and virus of SARS-CoV-2 (the ancestral strain, Alpha, Beta, Delta, Omicron).

- The antibodies binding to the RBD (Receptor Binding Domain) and NTD (N-Terminal Domain) of SARS-CoV-2 (the ancestral strain, Alpha, Beta, Delta, Omicron) in infected or vaccinated individuals.

The cellular response corresponds to the quantification of the level of CD4 and CD8 (cytotoxic) T cells specific for the Spike protein of SARS-CoV-2 (the ancestral strain or the variants of concern) in vaccinated or infected patients.

Efficacy refers to the ability to prevent symptomatic or non-symptomatic infection, transmission, hospitalization or death.

To meet our objective: we first analyzed the humoral response to the SARS-CoV-2 Omicron VOC, then the cellular response to the SARS-CoV-2 Omicron VOC, then the effectiveness of the main vaccines against this variant.
3. Results

Humoral immune evasion after vaccination or infection plays an important role in the progression of Omicron cases, whether breakthrough infections or re-infections. Table 1

Ferguson et al., in their report published on December 16, 2021, showed that: the risk of reinfection is 5.41 (95% CI: 4.87–6.00) times higher for Omicron than for Delta. [28]

UK Health Security Agency, in its December 23 report found that: 5.9% of confirmed cases between November 1 and December 13 resulted from reinfection, estimating the risk of reinfection with Omicron at 3.3 (95% CI: 2.8 to 3.8) compared to the other variants [29].

In Denmark, 5233 reinfections were reported on 15.12.21. Most people recorded with a reinfection have only been infected once [30].

Similar results were made in Israel [31]

In South Africa, Pulliam et al., found that: The recent spread of the Omicron variant has been associated with a decrease in the hazard coefficient for primary infection and an increase in reinfection hazard coefficient. The estimated hazard ratio for reinfection versus primary infection for the period from 1 November 2021 to 27 November 2021 versus wave 1 (March 2020 to September 2020) was 2.39 (95% CI: 1.88–3.11) [32] Table 2

Omicron does not escape cellular immunity, which provides protection against serious forms. Many studies in the literature have shown that Omicron is associated with less clinical severity.

Ferguson et al., in their report published on December 22, 2021 showed that: In England, cases infected with Omicron were 15% less likely to be hospitalized and 40% less likely to spend a night or more in the hospital, compared to cases infected with Delta [36].

In Denmark, in the report on the Omicron variant from the Statens Serum Institut on December 13, 2021: 98.9% of Omicron cases have not been hospitalized [37].

According to Jassat et al., in South Africa, Omicron is associated with lower hospitalization rate and in-hospital mortality compared to other waves (Beta, Delta) [38].

Unlike the other waves, the characteristics of the patients hospitalized during the Omicron wave were as follows: young (median age, 36 years), more often women, few comorbidities, few acute respiratory failure, mostly unvaccinated, low proportion of patients on oxygen therapy or mechanical ventilation, low proportion of ICU (intensive care unit) admissions, shorter hospital stay of 3 days, lower mortality. [39]

A study led by researchers from the LKS Faculty of Medicine at The University of Hong Kong found that: Omicron SARS-CoV-2 infects and multiplies 70 times faster than the Delta variant and original SARS-CoV-
2 in human bronchus, which may explain why Omicron may transmit faster between humans than previous variants. Their study also showed that the Omicron infection in the lung is significantly lower than the original SARS-CoV-2, which may be an indicator of lower disease severity. This research is currently under peer review for publication.

Table 3 (continued)

| Studies | Vaccine Efficacy against Omicron (VE) | Infections | Hospitalizations | Death |
|---------|---------------------------------------|------------|-----------------|-------|
| (47) Buchan et al. (USA) | with Pfizer and 36.7% with Moderna. With the vaccine booster: VE against Omicron was restored to 54.6% with Pfizer, no data for Moderna. Receiving 2 doses of mRNA vaccine was not protective against Omicron. VE against Omicron was 37% ≥7 days after receiving an mRNA vaccine for the third dose. |

4. Discussion

This study showed that in the face of SARS-CoV-2 Omicron VOC, the humoral response was reduced while the cellular response was preserved. The vaccine booster provided protection against Omicron-related infections, transmissions, hospitalizations and deaths.

The statistics on the deployment of COVID-19 vaccines in Africa are appalling. While in Europe, on average, 60% of the population received vaccines against COVID-19, in Africa, only 5–10% (24% in South Africa) of the population received the first dose. Vaccine acceptance rates have also been low in some African countries [48,49].

Unlike other viral strains (ancestral, Alpha, Beta, Delta), SARS-CoV-2 Omicron VOC appeared much more contagious but generates few severe forms [36–40]. This sharp increase in cases can lead to short-term consequences: saturation of health systems, high rate of absenteeism secondary to the obligation of isolation in case of infection in Omicron (multiple work stoppages with risk of repercussions on the economic system) and social isolation with the risk of psychological distress, without forgetting the risk of ‘long covid’.

The main strength of this study is that it is the first narrative review on the subject.

The main limitations of this study: First, it is a narrative review that deserves to be supplemented by a systematic review of the literature or even a meta-analysis. Second: as Omicron is a new variant of concern, most of the articles included in this analysis were pre-printed articles being published. Thirdly: many results from small samples, which may have altered the power of our study. Fourth: We limited ourselves to vaccines currently recommended in Europe and the United States (Pfizer, Moderna, AstraZeneca and Janssen), only 1 study focused on Novavax which is currently authorized in Europe and in the process of authorization in the United States. Fifth, some studies have used in vitro data. Sixth: there is a lack of data on the impact of Omicron on children. Even if it is clear that the main vaccines currently available on the market remain effective against the new SARS-CoV-2 Omicron VOC, pharmaceutical companies are currently working on a vaccine specifically targeting the SARS-CoV-2 Omicron VOC [50] We can also consider a vaccine with a versatile formulation such as seasonal influenza.

5. Conclusion

In the end, according to these data, the 3rd dose appears to be the solution to be able to defeat SARS-CoV-2 Omicron VOC. But the health authorities must not forget to insist on the primary vaccination of individuals not yet vaccinated, as well as on an "equal" distribution of vaccines against COVID-19 throughout the world.

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Declaration of Competing Interest

No conflict of interest

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