Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Immunology Letters 243 (2022) 38–43

Contents lists available at ScienceDirect

Immunology Letters

journal homepage: www.elsevier.com/locate/immlet

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.

ARTICLE INFO

Keywords
Omicron
SRAS-CoV-2
Vaccine against COVID-19
Humoral response
Cellular response
Neutralizing antibodies

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 virus in the world. These mutations are responsible for the appearance of new variants, the most recent of which is Omicron (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 virus 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, Bêta, 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

https://doi.org/10.1016/j.imlet.2022.02.002
Received 7 January 2022; Received in revised form 23 January 2022; Accepted 3 February 2022
Available online 4 February 2022

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 at 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.
[13] Basile et al. (Australia)	Sera collected 1, 3 and 6 months after two doses of Pfizer. (In vitro data)	Pfizer	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.
[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 vaccine booster with mRNA vaccines resulted in a potent neutralization of Omicron, but 4 to 6 times lower than that of the ancestral strain.
[15] Hoffmann et al. (Germany)	Sera of convalescents or vaccinated individuals. (In vitro data)	AstraZeneca, Pfizer	Astrazeneca & Pfizer together with homologous immunization (3 doses of Pfizer) provided potent neutralization against Omicron.
[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 doubly vaccinated sera was low against Omicron. The neutralizing activity of boosted mRNA sera, doubly vaccinated and boosted convalescents, was maintained against Omicron, although at lower levels compared to the ancestral strain and Bêta. Binding to the B.1.1.529 receptor binding domain (RBD) and N-terminal domain (NTD) was reduced in convalescent not vaccinated individuals, but was mostly retained in vaccinated individuals.
[17] Cele et al. (South Africa)	Sera of infected participants and vaccinated or 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)		1 and 6 months after SRAS-CoV-2 infection, the neutralization titers against Omicron were 15.8 and 4.4 times lower than those of the ancestral strain, respectively.
[20] Zeng et al. (USA)	Sera of vaccinated health care workers. (In vitro data)	Pfizer, Moderna	With 2 doses of mRNA vaccines: minimal neutralization against Omicron. The vaccine booster allowed a strong neutralization against Omicron.
[21] Zeng et al. (USA)	Vaccinated solid tumor patients.	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

(*continued on next page*)

Table 1 (*continued*)

Studies	Study sample	Vaccines against COVID-19	Key results
			antibody titers, respectively, compared to the ancestral strain. Overall, with the vaccine booster, stronger neutralization.
[22] Schmidt et al. (USA)	Plasmas of convalescents, convalescent vaccinated, vaccinated. (In vitro data)	Vaccins à ARNm, Janssen	In convalescent those, or those who received 2 doses of mRNA vaccines or 1 dose of Janssen, neutralizing activity against Omicron was low compared to that of the ancestral strain. Vaccination of people who had recovered from COVID-19 or booster vaccination with mRNA vaccine resulted in greater neutralization against Omicron.
[23] Dejnirattisai et al. (United Kingdom)	Participants vaccinated with 2 doses of Astrazeneca or Pfizer.	pfizer, astrazeneca	neutralizing titres on sera from participants who had received homologous astrazeneca dropped to below the detectable threshold in all but one participant. median neutralizing titres on sera from participants who had received homologous pfizer reduced by 29•8 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 SRAS-CoV-2 during the Omicron wave in South Africa.		In patients infected with Delta: improvement in omicron neutralization, which has been multiplied by 14.4. In patients infected with Omicron: improved neutralization of the Delta virus, which has increased 4.4-fold.
[25] Doria-Rose et al. (USA)	Sera samples from Moderna vaccine recipients. (In vitro data)	Moderna	After 2 doses of Moderna at 100 µg: low neutralizing activity against Omicron, compared to the ancestral strain and Bêta. A 50 µg boost increased neutralization titers against Omicron.
[26] Edara et al. (USA)	Patients doubly vaccinated, convalescents vaccinated, and boosted.	Pfizer, Moderna	2 to 4 weeks after the 2nd dose of vaccine: 30-fold reduction in neutralizing activity against Omicron. 6 months after the 2nd dose: no neutralizing activity against Omicron. In vaccinated convalescents: 22-fold reduction in neutralizing activity against Omicron. With the vaccine booster: 14-fold reduction in neutralizing activity against Omicron and more than 90% of boosted subjects showed neutralizing activity against Omicron.
[27] Lusvarghi et al. (USA)	Sera of vaccinated participants, unvaccinated convalescents, therapeutic antibodies. (In vitro data)	Pfizer	After 2 doses of vaccine, or convalescents sera or therapeutic antibodies: low neutralizing activity against Omicron. With vaccine booster, significant increase in neutralizing activity against Omicron.

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, Bêta, Delta, Omicron).
- The antibodies binding to the RBD (Receptor Binding Domain) and NTD (N-Terminal Domain) of SARS-CoV-2 (the ancestral strain, Alpha, Bêta, 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.

Table 2
Cellular immune response to SARS-CoV-2 Omicron VOC.

Studies	Study sample	Vaccines against COVID-19	Key Results
[33] Keeton et al. (South Africa)	Vaccinated or convalescents participants.	Pfizer, Janssen	Faced to Omicron: 70 to 80% of the T cell response was maintained in all participants.
[34] Tarke et al. (USA)	Vaccinated adults.	Pfizer, Moderna, Janssen, Novavax	Faced to Omicron: T cell responses were largely conserved, regardless of the vaccine used.
[35] GeurtsvanKessel et al. (Netherlands)	Vaccinated health workers.	Pfizer, Moderna, Janssen, AstraZeneca	CD4+ T-cell responses were detected up to 6 months after all vaccination regimens.

In the end, we retained 32 scientific articles in our narrative review.

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 recorded 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 (Bêta, 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-

Table 3
Vaccine efficacy against symptomatic and non-symptomatic infection, transmission, hospitalization, and death related to SARS-CoV-2 Omicron VOC.

Studies	Vaccine Efficacy against Omicron (VE)		
	Infections	Hospitalizations	Death
[41] Andrews et al. (United Kingdom)	No protection after 2 doses of AstraZeneca. Less than 40% protection after 2 doses of Pfizer. VE of booster with Pfizer: −71% after 2 doses of AstraZeneca −76% after 2 doses of Pfizer		
[29] UK Health Security Agency. Report of 23 December 2021 (United Kingdom)	After primary vaccination with Astrazeneca, VE against symptomatic infection was approximately 60% 2 to 4 weeks after a Pfizer or Moderna booster, then dropped within 10 weeks to 35% with a Pfizer booster and to 45% with a Moderna booster. After primary vaccination with Pfizer, VE against symptomatic infection was approximately 70% after a Pfizer booster, falling to 45% after more than 10 weeks. This VE remained around 70–75% after a Moderna booster for up to 9 weeks after the booster.		
[42] UK Health Security Agency. Report of 31 December 2021 (United Kingdom)		After 2 doses of vaccine, 65% reduction in the risk of admission to hospital. After 3 doses of vaccine, 81% reduction in the risk of admission to hospital.	
[43] Collie et al. (South Africa)		The efficacy of 2 doses of Pfizer against hospitalization decreased from 93% for Delta to 70% for Omicron.	
[44] Sheikh et al. (Scotland)	Risk of reinfection: 10 times higher with Omicron than with Delta (7.6% with Omicron versus 0.7% with Delta). With vaccine booster: 57% reduction in the risk of symptomatic Omicron infection and an 88% reduction in the risk of symptomatic Delta infection, compared to 2 doses of vaccine.	With Omicron: 2/3 reduction in the risk of hospitalization compared to Delta.	
[45] Lyngse et al. (Denmark)	Vaccine booster reduces transmission of Omicron and Delta.		
[46] Hansen et al. (Denmark)	1 month after primary vaccination, VE against Omicron was: 55.2%		

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Table 3 (*continued*)

Studies	Vaccine Efficacy against Omicron (VE) Infections	Hospitalizations	Death
	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.		
[47] Buchan et al. (USA)	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.		

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. [40] Table 3

Primary vaccination led to less effective protection against symptomatic or non-symptomatic Omicron infections. On the other hand, it remains effective against severe forms.

The booster vaccine restored this efficacy against Omicron infections, reduced transmission and reinforced protection against severe forms.

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, Bêta, 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.

No funding

Declaration of Competing Interest

No conflict of interest

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