BNT162b2 mRNA vaccination did not prevent an outbreak of SARS COV-2 variant 501Y.V2 in an elderly nursing home but reduced transmission and disease severity

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Abstract

We report an outbreak of SARS-CoV-2 501Y.V2 in a nursing home. All non-vaccinated residents (5/5) *versus* half of those vaccinated with BNT162b2 (13/26) were infected. Two of 13 vaccinated *versus* 4 of 5 non-vaccinated residents presented severe disease. BNT162b2 did not prevent the outbreak, but reduced transmission and disease severity.

keywords: SARS CoV-2, outbreak, variant, BNT162b2 vaccine, nursing home

Introduction

On December 27th, 2020, France started its vaccination campaign in nursing homes using the BNT162b2 mRNA vaccine (Pfizer). At approximately the same time, the emergence of SARS-CoV-2 variant 501Y.V2 has been reported in South Africa and the virus quickly spread throughout Europe (1). We describe here an outbreak related to SARS-CoV-2 variant 501Y.V2 occurring in an elderly nursing home in France after a vaccination campaign with the BNT162b2 mRNA vaccine.

Methods

The study included 31 residents and 59 staff members from a nursing home unit located in Jura, East of France, prospectively followed for 3 weeks after a resident had been diagnosed with COVID-19. All residents and staff members were systematically tested at baseline by RT-qPCR. The tests were repeated in case of symptoms occurring during the following days, and every 7 days until no further cases were found to be positive in the nursing home. All SARS CoV-2 RNA-positive samples were sequenced (full-length genome sequence analysis by means of next-generation sequencing) by the national SARS CoV-2 sequencing platform located at the Henri Mondor virology laboratory, one of the 4 platforms involved in the French national SARS-CoV-2 genomic surveillance program. Antibodies targeting both the nucleoprotein and the RBD domain of the spike protein were sought by means of enzyme immmunoassay at the time of COVID-19 diagnosis in all of the vaccinated individuals. Our study protocol followed the ethical guidelines of the declaration of Helsinki and was approved by our institutional review board (N° IRB 00011558-2021-107). No additional tests were performed outside routine care in agreement with the “Agence Régionale de Santé” (ARS) and the medical support team. Data collection was performed as part of routine care

by the medical staff. Antibody assays were performed at the request of the ARS in order to evaluate vaccine efficacy.

Results

On March 8th, 2021, a fully vaccinated 92-years old resident presented with abdominal pain, fever and diarrhea. SARS CoV-2 RNA was detected in a nasopharyngeal swab (NPS) sampled on the same day. Full-length viral genome sequence analysis identified a 501Y.V2 variant. From March 8th to March 29th, 17 additional residents were tested SARS CoV-2 RNA-positive in their NPSs. Full-length genome sequence analysis was performed in 10 of them and all were infected with SARS CoV-2 variant 501Y.V2. Phylogenetic analysis showed that their genome sequences were all closely related (Supplementary Figure 1), carrying the same amino acid pattern, including spike mutations L18F, D80A, D215G, Del-L242, Del-A243, Del-L244, K417N, E484K, N501Y, D614G, A701V. All sequences were submitted to GISAID database.

At the time of the study, 26 out of the 31 residents (83.9%), mean age: 87.0±8.2 years, 64.5% of females, had been fully vaccinated with 2 successive doses of the BNT162b2 mRNA vaccine 19 days apart. The second dose was administered to all of them between the 4th and the 26th of February 2021 (Table 1). The 5 remaining residents had not been vaccinated. Thirteen of the 26 fully vaccinated residents (50.0%) *versus* all of the 5 non-vaccinated residents (100%) were infected during the outbreak (p=0.058, Fisher's exact test). Thus, vaccination efficacy against SARS-CoV-2 infection was 50.0% (95% confidence interval: 34% to 73%). Among the 13 fully vaccinated residents who were infected, 2 (15.4%) presented with an asymptomatic disease, 9 (69.2%) developed mild to moderate symptoms, and 2 (15.4%) progressed to severe disease with fatal evolution secondary to acute respiratory distress syndrome (ARDS). The 2 latter patients had chest CT scans showing bilateral patchy peripheral ground glass opacities. The group of vaccinated residents had varying

levels of anti-S antibodies at diagnosis (median: 1169 AU/mL, range: <6.8-8188 AU/mL, Table 1), with no relationship with disease severity. Among the 5 non-vaccinated residents, 4 (80%) progressed to severe disease, including a resident with a recent history of COVID-19. One of them died. Overall, the proportion of residents with severe disease in the non-vaccinated group (4/5) was higher than that in the vaccinated group (2/13). The SARS CoV-2 viral load, estimated by the mean cycle threshold (Ct) value, was significantly higher in non-vaccinated residents (mean Ct: 15, range 12-17) than in vaccinated residents (mean Ct: 21, range: 13-32; $p<0.05$, Student t test).

Among the 59 staff members tested, 19 (32.2%) had been vaccinated with 2 doses of the BNT162b2 mRNA vaccine, while 4 (6.8%) had a history of prior COVID-19 confirmed by RT-qPCR. Only 1 vaccinated staff member (5.2%) *versus* 10 non-vaccinated staff members (25.0%) were ultimately infected ($p=0.085$, Fisher's exact test). No infected staff member developed severe disease.

Discussion

We report here the first description of an outbreak related to SARS-CoV-2 variant 501Y.V2 in an elderly nursing home in which more than 80% of residents had received two injections of the BNT162b2 mRNA vaccine. All but one of the vaccinated residents had received the second vaccine dose more than one month before the outbreak. The remaining one had received the second dose 11 days before. All but one of the infected residents who had been vaccinated had detectable anti-S antibodies at the time of diagnosis, at levels ranging from 79 to 8188 UA/mL. According to the nationwide vaccination survey performed in Israel after BNT162b2 vaccination has been massively administered to their population, the efficacy of the vaccine after the second dose was 92% and 94% against documented infection and symptomatic disease, respectively (2). Subgroup analysis showed

that vaccine efficacy was similar for adults more than 70 years of age. However, circulation of SARS CoV-2 variant 501Y.V2 is low in Israel. Thus, the effect of vaccination on this variant could not be evaluated. In another study, Benenson *et al.* reported high efficacy of vaccination with BNT162b2 in a population of healthcare workers predominantly infected with SARS-CoV-2 variant B.1.1.7/501Y.V1 (but not 501Y.V2) (3).

Preliminary reports from clinical trial efficacy suggested reduced protection of the vaccines against variant 501Y.V2 as compared to other variants. AZD1222 efficacy was only 22% according to preliminary data from South Africa (4). In a South-African study, the efficacy of NVX-CoV237 was 49% (5) and that of Ad26.COV2-S was 57% (6). Thus far, there is limited data regarding the clinical efficacy of BNT162b2 vaccination against variant 501Y.V2. Kustin *et al*. observed an increased incidence of 501Y.V2 among vaccine breakthrough infections in individuals fully vaccinated with BNT162b2 after mass vaccination in Israel (7)**.** An outbreak with a SARS-CoV2 R.1 lineage harboring the Spike E484K substitution has been reported in a nursing home after vaccination with BNT162b2. In this study, the estimated vaccination efficacy against SARS-CoV2 infection among residents was 66.2% (8), similar to that observed against SARS CoV-2 501Y.V2 in our study (50.0%). Our study also suggests that vaccination is associated with reduced SARS CoV-2 viral loads in the upper respiratory tract in case of infection by 501Y.V2, thus possibly with reduced contagiousness. Our study is thus the first to confirm partial effectiveness of BNT162b2 vaccination against 501Y.V2 variant infection an elderly population. These results remain to be confirmed as our study is observational with a limited sample size.

In vitro studies have documented escape of the 501Y.V2 variant from serum neutralizing antibody responses acquired after BNT162b2 vaccination. Reduced sensitivity to neutralization was mainly due to the acquisition of amino-acid substitutions in the spike RBD domain, including K417N, E484K and N501Y (9,10). In contrast, adaptive T-cell responses, which play a role in the modulation of COVID-19 severity, do not seem to be affected by these mutations. This could explain the small

number of severe cases in the vaccinated resident group. In our cohort, the case fatality rate of fully vaccinated residents was similar to the fatality rate observed in nursing homes before the vaccination campaign (11), although severity was greater in unvaccinated compared to vaccinated residents. Larger observational studies are urgently needed to confirm these results.

The low COVID-19 vaccination coverage of staff members in this study (32.2%) was similar to the national rate of vaccination coverage in healthcare workers during the same period (25%) (12). In France, non-compulsory vaccination adhesion is usually low among healthcare workers (13,14). SARS-CoV-2 vaccination of visitors and healthcare workers is now being actively promoted, as recommended by the French National Academy of Medicine in all healthcare workers

Several studies reported a major impact of social isolation on mental health in nursing homes, where restrictive measures can increase depression, anxiety and worsen dementia (15,16). In this context, some of these restrictions were removed after vaccination. Our study shows that vaccination of residents in nursing homes may not be sufficient to prevent outbreaks with emerging variants, such as 501Y.V2, that may escape the action of neutralizing antibodies induced by currently available vaccines. Weekly symptom screening and viral testing of residents, visitors, and staff members should be maintained even after vaccination campaigns to preempt and identify outbreaks of emerging variants.

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Conflict of interest disclosures

S.F. has served as a speaker for MSD, Abbvie and Abbott diagnostics. J.-M.P. has served as an advisor, and/or speaker for Abbvie, Gilead, GlaxoSmithKline, Merck, Regulus, and Siemens Healthcare. N.D. The remaining authors have no conflict of interest to disclose.

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Table 1. Clinical and biological characteristics of vaccinated and non-vaccinated residents infected with SARS-CoV-2 variant 501Y.V2.

	Age	Underlying conditions*	Date of the last dose of BNT162b2	Date of RT-PCR +	RT-PCR (Ct value)	Onset symptom	Anti-S antibodies (Architect, Abbott UA/mL)	Anti-N antibodies (Architect, Abbott, index)	Illness Severity
Vaccinated residents									
Resident 1	92	DM HC	02 February	08 March	13	04 march	139	<1,4	Death
Resident 2	95	HC Hypertension	02 February	09 March	19	11 march	79	<1,4	mild to moderate
Resident 3	69	CD Cancer NC	02 February	09 March	20		3364	<1,4	Asymptomatic
Resident 4	88	Obesity T2DM HC Hypertension NC	02 February	09 March	17	11 march	643	<1,4	Death
Resident 5	89	T2DM HC Hypertension COPD NC	02 February	09 March	32	11 march	3298	<1,4	mild to moderate
Resident 6	99	HC NC	02 February	09 March	19	12 march	<6.8	<1,4	mild to moderate

Resident 7	89	HC Hypertension	02 February	09 March	14	09 march	2683	<1,4	mild to moderate
Resident 8	95	HC cancer	02 February	09 March	29	12 march	599	<1,4	mild to moderate
Resident 9	97	Hypertension NC	02 February	09 March	32		867	<1,4	Asymptomatic
Resident 10	80	T2DM	02 February	11 March	29	11 march	4903	<1,4	mild to moderate
Resident 11	87	NC	02 February	15 March	18	11 march	8188	<1,4	mild to moderate
Resident 12	83	HC NC	02 February	15 March	15	12 march	1471	<1,4	mild to moderate
Resident 13	93	Hypertension	26 February	22 march	17	15 march	550	<1,4	mild to moderate
Unvaccinated resident									
Resident 14	77	NC COPD	-	09 march	17	09 march	-	-	Severe
Resident 15	88	NC HC hypertension	-	09 march	13	09 march	-	-	Death
Resident 16	83	NC	-	09 march	12	10 march	-	-	mild to moderate
Resident 17	81	Obesity hypertension	-	09 march	16	10 march	-	-	Severe
Resident 18	92	NC CD	-	09 march	17	10 march	-	-	Severe

* Underlying conditions increased risk for severe illness according CDC.HC : heart condition such as heart failure, coronary artery disease, or cardiomyopathies. T2DM: Type 2 T2DM. CD: Cerebral disease (affects blood vessels and blood supply to the brain). NC : Neurologic conditions, such as dementia