Poster 1954

Immunogenicity against SARS CoV-2 ancestral strain and variants of two new COVID-19 recombinant adjuvanted vaccines compared to BNT162b2 as a third dose following two doses of BNT162b2: a single-blinded multicenter randomized controlled trial

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❖ ABSTRACT

BACKGROUND

New recombinant adjuvanted protein vaccines against coronavirus disease 2019 (COVID-19) could be of interest as heterologous boosters to maximize the benefits of vaccination against SARS CoV-2 including the ancestral strain and new variants, such as Omicron.

METHODS

In a randomized, single-blinded, multicenter trial across 11 centers in France, adults with no history of SARS-CoV-2 infection, who had received two doses of Pfizer-BioNTech mRNA vaccine (BNT162b2) 3–7 months before, were randomly assigned in a 1:1:1 ratio to receive a boost of BNT162b2, or Sanofi/GSK SARS-CoV-2 recombinant adjuvanted protein MV D614 (monovalent parental formulation) or SARS-CoV-2 recombinant adjuvanted protein MV B.1.351 vaccine (monovalent Beta formulation).
The primary endpoint was the proportion of subjects with a ≥10-fold increase rate in neutralizing antibody titers for the Wuhan (D614) and B.1.351 (Beta) SARS-CoV-2 viral strains between D0 and D15.

RESULTS

Of the 247 randomized participants, 223 were included in the per-protocol analysis (mean age, 40.6 years): 76 in Sanofi/GSK MV(D614) group, 71 in Sanofi/GSK MV(Beta) group and 76 in BNT162b2 group. The proportion of participants whose neutralizing antibody titers against the Wuhan (D614) SARS-CoV-2 strain increased by a factor ≥10 between Day 0 and Day 15 was 55.3% (95% CI 43.4–66.7) in Sanofi/GSK MV(D614) group, 76.1% (64.5–85.4) in Sanofi/GSK MV(Beta) group and 63.2% (51.3–73.9) in BNT162b2 group (p=0.03). These rates were 44.7% (33.3–56.6), 84.5% (74.0–92.0) and 51.3% (39.6–63.0) for the B.1.351 (Beta) viral strain, respectively (p<0.0001). The three vaccines also elicited neutralizing antibodies against Delta and Omicron BA.1 variants with higher neutralizing titers after Sanofi/GSK MV(Beta) vaccine compared to the other vaccines in the study.

CONCLUSION

All the three vaccines boosted antibodies and neutralizing response after a BNT162b2 initial course.
Heterologous boosting with the Sanofi/GSK SARS-CoV-2 recombinant adjuvanted protein vaccine B.1.351 (Beta formulation) provided higher rates of neutralizing antibodies against variants, including Omicron BA.1, compared with the mRNA BNT162b2 vaccine.

❖ INTRODUCTION

Some vaccines developed more recently such as Sanofi vaccines based on recombinant SARS-CoV-2 spike proteins adjuvanted with GSK AS03, the first targeting the S protein of the Wuhan (D614) strain and the second targeting the B.1.351 variant (Beta) might offer an interesting alternative for boost in terms of accessibility, cost, reactogenicity, thermostability and acceptability and could be more immunogenic.
These vaccines could be of interest as heterologous booster to increase both the intensity and duration of immune response against the new variants SARS CoV-2. They may also increase the breadth of protection against other variants, such as Omicron, and the formulation including the B.1.351 variant (Beta) spike protein is of specific interest since it has the potential to provide a different spectrum of cross-protection.

❖METHODS

- A randomized, single-blinded, multicenter trial across 11 centers in France
- Adults aged 18 years and older in good health or with stable health, no history of SARS-CoV-2 infection, who had received two doses of Pfizer-BioNTech mRNA vaccine (BNT162b2) 3–7 months prior to the administration of the study booster dose.

- Randomly assigned in a 1:1:1 ratio to receive:
  - one dose of BNT162b2
  - or one dose of Sanofi/GSK SARS-CoV-2 recombinant adjuvanted protein MV D614 (monovalent parental formulation) or MV B.1.351 vaccine (monovalent Beta formulation).

  Randomization was stratified on center and age group (18–64 years or ≥ 65 years)

- Main exclusion criteria were pregnancy or breastfeeding, acute febrile infection within the previous 72 h and/or presenting symptoms suggestive of COVID-19 within the previous 28 days or having been in contact with an infected individual for the last 14 days before the inclusion visit, virologically documented history of COVID-19 (PCR or serology),

- Safety assesment: Injection-site and systemic solicited adverse events were collected for 7 days and unsolicited adverse events through 28 days after vaccination using diary cards provided to each participant

- **The primary endpoint was the proportion of subjects with at least 10-fold increase rate in neutralizing antibody titers for the Wuhan (D614) and B.1.351 (Beta) SARS-CoV-2 viral strains between day 0 (before boost) and day 15 after the boost.**

❖LABORATORY ASSAY

Neutralizing antibodies against the Wuhan (D614) SARS-CoV-2 viral strains and B.1.351 (Beta), Delta and Omicron BA.1 variants were assessed with a microneutralization test. The test uses clinical strains of SARS-CoV-2 (100 TCID50/well), TMPRSS2-expressing VeroE6 cells and counts the number of cytopathic effect (CPE) at 5 days post-infection

Anti-SARS-CoV-2 IgG antibodies directed against the S1 domain of the virus Spike protein were assessed using the QuantiVac ELISA kit

Neutralizing antibody titers increased by a factor ≥ 10 between Day 0 and Day 15:

- Against the Wuhan (D614) SARS-CoV-2 strain :
  - MV(D614) group (n=76), 55.3% (95% CI 43.4-66.7)
  - MV(Beta) group (n=71) : 76.1% (64.5-85.4)
  - BNT162b2 group (n=76): 63.2% (51.3-73.9)

- These percentages were 44.7% (33.3-56.6), 84.5% (74.0-92.0) and 51.3% (39.6-63.0) for the B.1.351 (Beta) viral strain, respectively.

- Higher neutralizing antibodies rates against Delta and Omicron BA.1 variants were also elicited after Sanofi/GSK MV(Beta) vaccine compared to the other vaccines.

❖RESULTS

Table 1. Characteristics of patients at inclusion (per-protocol population).

	Total population (n=223)	Sanofi/GSK-D614 (n=76)	Sanofi/GSK-B.1.351 (n=71)	Pfizer BNT162b2 (n=76)
Age, y				
Mean (SD)	40.6 (13.0)	40.2 (13.5)	41.4 (11.3)	40.4 (13.9)
Range	18–73	18–73	22–68	20–69
Female gender, n (%)	90 (40.4)	29 (38.2)	23 (35.2)	36 (47.4)
Body mass index, kg/m²				
Mean (SD)	25.0 (4.5)	25.2 (4.5)	25.4 (4.5)	24.4 (4.6)
Range	15.2–40.8	16.8–35.6	18.5–40.8	15.2–40.4
Current smoker, n (%)	49 (22.1)	16 (21.3)	17 (23.9)	16 (21.1)
Comorbidity, n (%)				
Obesity [a]	27 (12.1)	13 (17.1)	8 (11.3)	6 (7.9)
Hypertension	11 (4.9)	6 (7.9)	2 (2.8)	3 (3.9)
Dyslipidemia)	6 (2.7)	4 (5.3)	1 (1.4)	1 (1.3)
Diabetes	2 (0.9)	2 (2.6)	0	0
Time between 1st and 2nd dose, days				
Median (IQR)	39 (31; 42)	39 (30: 42)	39 (33; 42)	38 (32; 40)
Range	21–49	21–49	21–44	21–42
Time between 2nd and 3rd dose, days				
Median (IQR)	174 (164; 187)	176 (167.5; 188)	171 (164; 184)	174.5 (160; 188)
Range	121–223	121–211	148–223	141–212

[a] Body mass index > 30 kg/m²

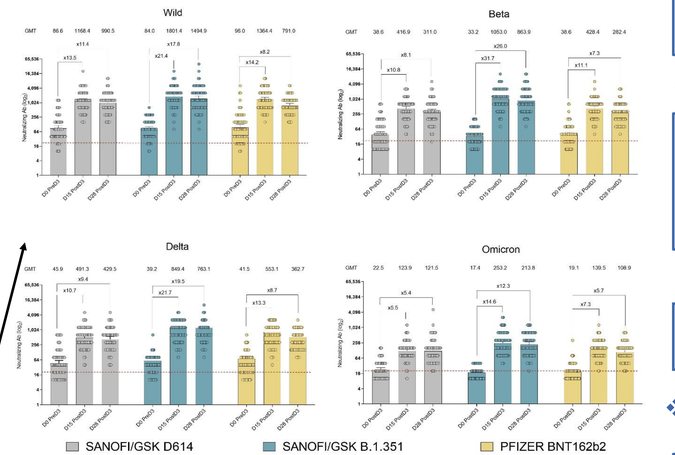

Figure 1. Neutralizing antibodies against D614 (wild-type; Wuhan) SARS-CoV-2 and variants Beta, Delta and Omicron at D0 and D15 after the boost dose with Sanofi/GSK-D614, Sanofi/GSK-B.1.351 or BNT162b2 (per-protocol population); dotted line represents the positivity threshold,

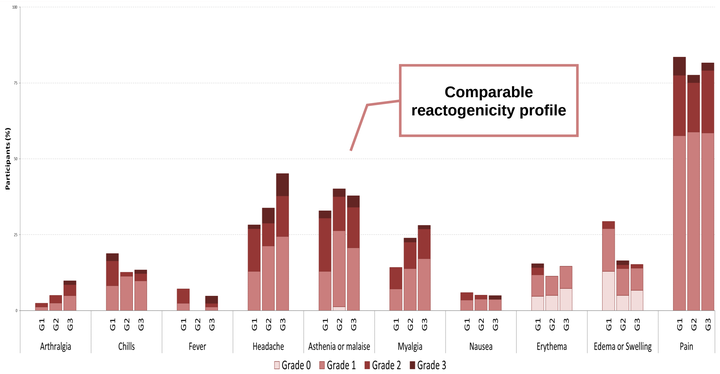

Figure 2. Rates and grades of severity of solicited adverse events reported from D0 to D7 by participants from the three randomized groups of the safety population (G1, Sanofi/GSK-D614; G2, Sanofi/GSK-B.1.351; G3, BNT162b2). according to the Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials (Modified FDA scale/September 2007).

❖LIMITATIONS

- The study population was younger and included a smaller percentage of people ≥65 years than previously planned.

- Another limitation is the priming with a unique vaccine. The primary endpoint was based on an increase in neutralizing antibodies against the Wuhan (D614) and B.1.351 (Beta) strains, which are variants of SARS-CoV-2 that no longer circulate.

❖CONCLUSION

- All three vaccines boosted neutralizing antibodies after BNT162b2 initial course with no safety concerns.
- Due to the waves with the new variants, neutralizing antibodies against them were also assessed.

- Heterologous boosting with the Sanofi/GSK recombinant adjuvanted beta formulation provided higher rates of neutralizing antibodies against the ancestral strain, but also against Beta, Delta and Omicron BA.1 variants compared to the homologous boost with mRNA BNT162b2 vaccine.

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