Humoral immune response against SARS-CoV-2 variants (Omicron BA.1, Beta, Delta and XBB.1.5) of PHH-1V booster vaccine in subjects previously vaccinated with a mRNA vaccine. Results of a randomised controlled trial up to 6 and 12 months.

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Background

There is still a need for broad-spectrum vaccines that may cross protect from new genetic variants of SARS-CoV-2 and provide a long-lasting immune response. PHH-1V (Bimervax®, HIPRA) is a bivalent recombinant protein vaccine based on a heterodimer consisting of the receptor binding domain of two SARS-CoV-2 variants, Beta and Alpha, designed to boost immunogenicity against SARS-CoV-2 in fully vaccinated adult individuals.

Objective

To assess immunogenicity of a booster vaccination with PHH-1V (Bimervax®, HIPRA) compared with BNT162b2 mRNA vaccine (Comirnaty®, Pfizer/BioNTech) in adults fully vaccinated with primary series against COVID-19.

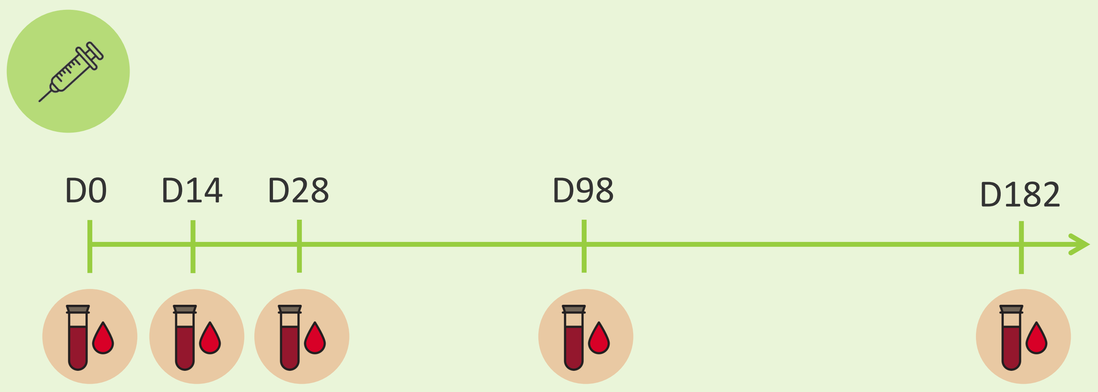
Methods

HIPRA-HH-2 study (NCT05142553) is a Phase IIb, double-blind, randomised, active-controlled, multi-centre clinical trial. 765 participants with a complete prime course against COVID-19 with BNT162b2 were randomised (2:1) to receive a booster dose of PHH-1V or BNT162b2.

Population

≥18 years old (7.3 % ≥65 years old)
Prime vaccination: 2 doses of BNT162b2 (at least 182 days ago)
Naïve subjects at the time of vaccination
White/Caucasian, Hispanic, Asian population included

Procedure



Humoral immunogenicity was measured by changes in levels of neutralising antibodies (PBNA) after PHH-1V (N=513) or BNT162b2 (N=2452) boost at Day 14, 28, 98, 182 against Wuhan-Hu-1, Beta, Delta and Omicron BA.1 variants. The same analysis after PHH-1V (N=101) or BNT162b2 (N=52) boost was performed against Omicron XBB.1.5 at Day 14 , 182 and 365. The number of subjects with SARS-CoV-2 infection after the booster was also assessed up to 12 months.

Results

PHH-1V Booster is superior to BNT162b2 at 6 months

Both PHH-1V and BNT162b2 vaccines elicited a strong neutralising antibody response 14 days after the booster against all variants tested. PHH-1V induced a sustained neutralising antibody response up to 6 months against all variants. When compared to BNT162b2, superiority of PHH-1V was demonstrated against Wuhan, Beta, Delta and Omicron BA.1 variants 6 months after the booster (Day 182) (GMT ratios: 0.62 (p<0.0001), 0.70 (p<0.0001), 0.55 (p<0.0001) and 0.76 (p=0.0028), respectively) (Figure 1).

PHH-1V Booster induces immune response to XBB.1.5

Results show that both BNT162b2 and PHH-1V induce a strong and sustained neutralizing antibodies response against Omicron XBB.1.5, PHH-1V response being numerically higher compared to BNT162b (GMF ratios for PHH-1V and BNT162b2 respectively are: 7.58 and 7.17 at D14; 6 and 5.42 at D182; 5.1 and 4.82 at D365) (Figure 2 and Table 1). Compared to the humoral response induced by PHH-1V vaccination against previous variants[1], the XBB.1.5 neutralizing antibody levels are lower, which is in line with the results obtained with boosters with other vaccines against the XBB.1.5 subvariant[2,3,4].

Neutralizing antibodies titres against different SARS-CoV-2 variants

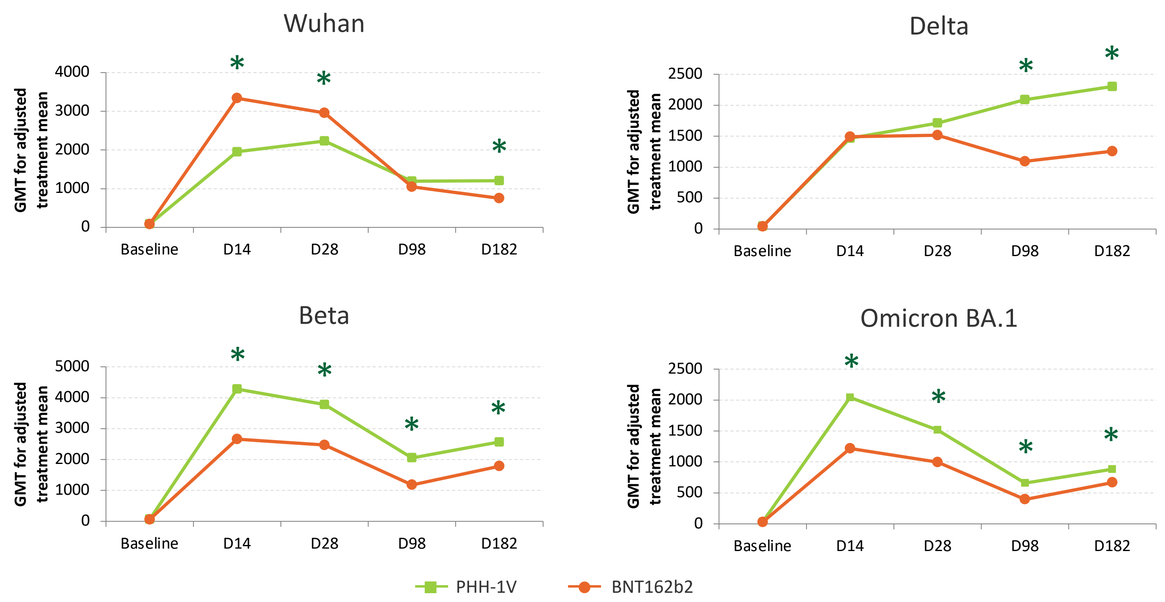


Figure 1. Neutralising antibody titres (GMT for adjusted treatment mean) of PHH-1V and BNT162b2 vaccines against different SARS-CoV-2 variants over time.
Statistically significant differences are shown as * for p<0.05.
Abbreviations: GMT = Geometric Mean Titre.

Neutralizing antibodies titres against Omicron XBB.1.5

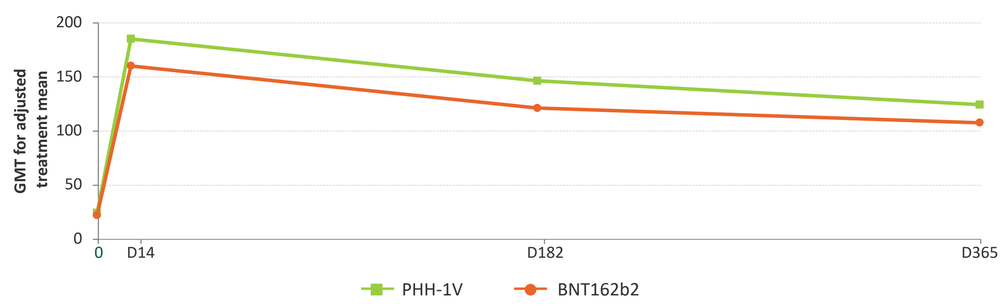


Figure 2. Neutralising antibody titres (GMT for adjusted treatment mean) of PHH-1V and BNT162b2 vaccines against SARS-CoV-2 Omicron XBB.1.5 over time. Statistical analysis is in progress.
Abbreviations: GMT = Geometric Mean Titre. PBNA= Pseudovirus Antiboidies assay.

	Omicron XBB.1.5						
	Baseline	D14		D182		D365	
	GMT	GMT	GMFR	GMT	GMFR	GMT	GMFR
3rth dose PHH-1V (N=101)	24.42	185.21	7.58	146.50	6	124.46	5.1
3rth dose BNT162b (N=51)	22.35	160.23	7.17	121.24	5.42	107.75	4.82

Table 1. Neutralising antibody titres (GMT for adjusted treatment mean) of PHH-1V and BNT162b2 vaccines against SARS-CoV-2 Omicron XBB.1.5 over time.
Abbreviations: GMT = Geometric Mean Titre, GMFR= Geometric Mean Fold Rise calculated from baseline.

During all the study period (12-month follow-up), only non-severe COVID-19 cases were reported (65.1 % and 58.5 % with PHH-1V and BNT162b2, respectively). PHH-1V demonstrates a very good safety profile overall.

Conclusions

PHH-1V (Bimervax®, HIPRA) as a booster elicits a strong and sustained neutralising antibody response against all tested variants in individuals with a complete primary course of mRNA vaccine and protects from severe disease.

Although the increase in antibody titres against XBB.1.5 is lower than those against previous SARS-CoV-2 variants (D614G, Beta, Delta, Omicron BA.1 and BA.4/5)[1], the response generated by the BIMERVAX® booster appears to be sufficient to protect against severe disease.

References

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