HCWAX Study: cellular and humoral immune-responses evaluation at different times after SARS-COV-2 vaccination in health care workers cohort

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Poster Board Number: 1949

IDWeek™ 2022; Washington, Oct. 19-23, 2022

Background

The duration and effectiveness of immunity from infection with and vaccination against SARS-CoV-2 are relevant to health policy interventions, including the timing of vaccine boosters, specially for health care workers (HCW). Immune memory against SARS-CoV-2 infection is associated with cellular and humoral adaptive immunity. The generation and clinical importance of T cell responses following SARS-CoV-2 vaccination is also discussed, with particular focus on protection against viral variants. Evidence thus far indicates that T cells play a critical role in protection against SARS-CoV-2 .

In this prospective cohort analysis, we aimed to determine the level and durability of the cellular and humoral immune-responses against SARS-CoV-2 infection after two doses of vaccine in HCW cohort at our Infectious Disease Unit, in University Hospital in Genoa, Italy (HCWAX study).

Materials and Methods

We enrolled prospectively HCW without (group A) and with previous infection (group B). We collected peripheral blood at baseline (before the BNT162b2 vaccine), T1 (before the 2nd dose), T2 and T6 (after 1 and 6 months after of 2nd dose). The activation induced cell marker assay (AIM) was performed with CD4 and CD8 Spike peptide megapools (MPs). We evaluated the Stimulation Index (SI) as AIM+ stimulated cells/negative control (positive response SI >= 2). Quantitative antibodies (Abs) to Spike-1 protein (S) and to nucleocapside protein (N) were detected with an electrochemiluminescence immunoassay. We tested at T6 the responses to alpha, beta, gamma, delta and epsilon variants MPs. We used the linear mixed model with random intercept adjusted for age and sex to compare specific times to T0. To assess differences over time between groups the interaction with time was tested.

Results 1

The subjects were enrolled from December 2020 to October 2021. In group A (HCW without previous infection), 13/22 (59%) were female, compared to 5/7 (71%) in group B (previously infected). The mean age was 39.9 years (SD 13.1) versus 37.7 years (SD 13.2), respectively. Only two subjects (one for each group) had comorbidities (hypertension, under treatment). No significant differences were observed between the two groups. The subjects in group B were vaccinated with the first dose of BNT162b2 vaccine at a mean of 8.6 months (SD 2.9) after SARS-CoV-2 infection.

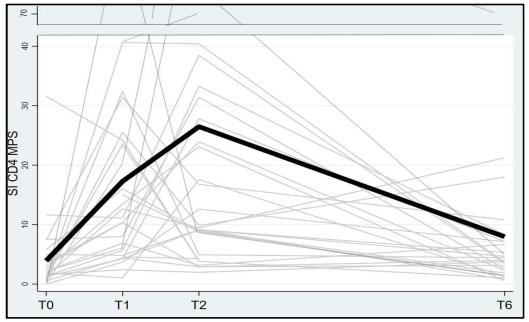
Results 2

For CD4+ Spike the overall rate of change over time was significant at T1 (p=0.038) and at T2 (p< 0.001) vs T0 with a decreasing at T6 (p not significant) [Figure 1] with a trend of higher response in group A. CD8+ Spike reactivity showed a significant overall time group interaction (p = 0.0265) and also retained significance at each timepoint. Significant differences were also observed at the baseline (p = 0.0030) with higher SI in previously infected subjects, as expected.

For overall, the anti-S Abs significantly increased from T1 to T6 compared to T0. The group B at T6 retained a higher anti S (p< 0.001) [Figure2].

At T6 in both groups we found a high CD4+ T cells response to epsilon variant, even if not circulating virus.

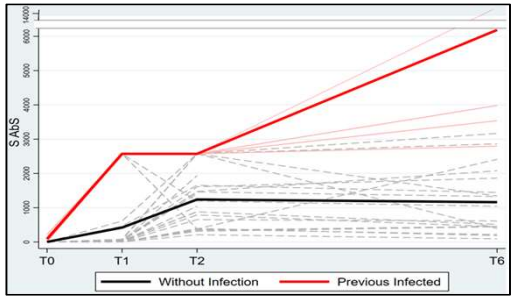
Figure 1 The overall rate of change over time for CD4+ T cell response to Spike megapools (MPS).



The bolded line indicates the overall rate of change over time among the entire cohort of health workers

	T0	T1	T2	T6
Mean (SD)	3.91(6.41)	17.28(19.87)	26.48(41.67)	7.96(13.62)
Median (IQR)	1.88(1;3.51)	10.74(4.70; 23.83)	9.66(4.61; 29.62)	4.00(2.29;7.14)
N	25	28	28	25
p-value	ref	0.038	<0.001	0.551

Figure 2. The quantitative antibodies to Spike-1 protein (S AbS) in the two groups.



	T0	T1	T2	T6
W/o infection (A)				
Mean (SD)	1.45(6.51)	420.59(888.13)	1240.20(810.61)	1161.32(964.00)
Median (IQR)	0(0; 0)	33.13(9.26; 79.53)	1117.80 (392.59; 1653.29)	828.19 (442.70; 1864.20)
N	21	22	22	18
Prev infected (B)				
Mean (SD)	85.87(81. 25)	2572.02(0.00)	2572.02(0.00)	6187.5(5517.49)
Median (IQR)	61.06 (24.90; 143.72)	2572.02 (2572.02; 2572.02)	2572.02 (2572.02; 2572.02)	3761.32 (3167.70; 9207.31)
N	6	6	6	4
p-value	<0.001	<0.001	0.001	0.001
p-value interaction	---	0.003	0.076	<0.001

Quantitative anti-S antibodies (S Abs) are expressed using Binding Antibody Unit (BAU). P-value between the two groups is analyzed at each timepoint with Mann–Whitney test

Conclusion

The humoral response was persistent and increased over time in HCW previously infected by SARS-CoV-2 when compared to uninfected individuals, up to 9 months of follow-up. The CD4+T cell response after vaccination was retained in both groups, while the CD8+ response was only maintained in previously infected individuals. At 6 months post-vaccination, CD4 + T cells were stable and able to cross-recognize circulating and non-circulating variants. Overall, SARS-CoV-2-specific responses after full vaccination are still able to recognize the virus and cross-recognize its variants but showed a progressive decline 6 months post-vaccination, which was more pronounced in uninfected individuals, suggesting the need for a booster dose.

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