



**IPIC** 5<sup>TH</sup> EDITION  
INTERNATIONAL PRIMARY  
IMMUNODEFICIENCIES  
CONGRESS

APRIL 27-29, 2022  
VILAMOURA - PORTUGAL



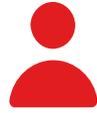
# ANTIBODY AND T-CELL RESPONSES FOLLOWING SARS-COV-2 VACCINATION IN PATIENTS WITH INBORN ERRORS OF IMMUNITY



Trinidad Alba-Cano  
Division of Immunology



# Cohorts of study



115

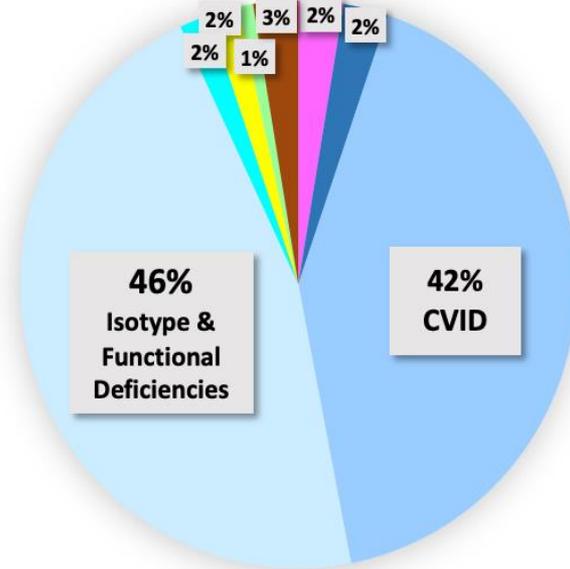
Patients  
(IEI)



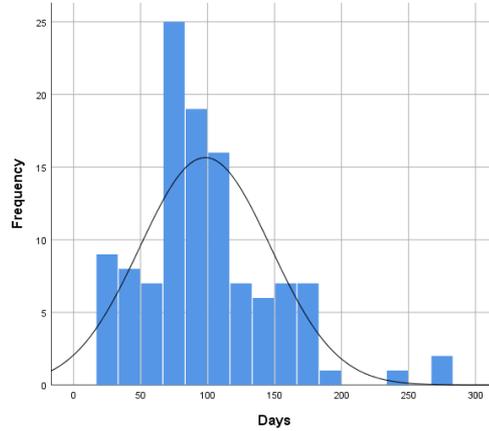
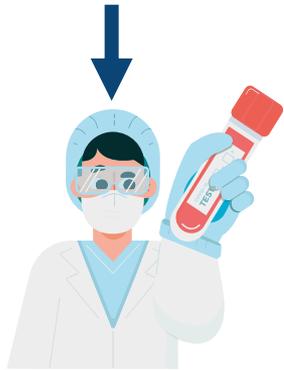
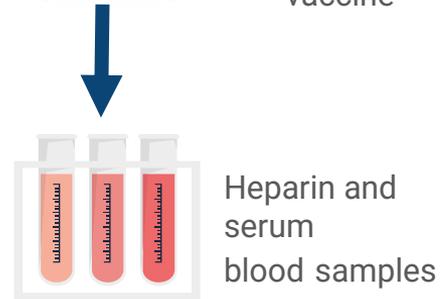
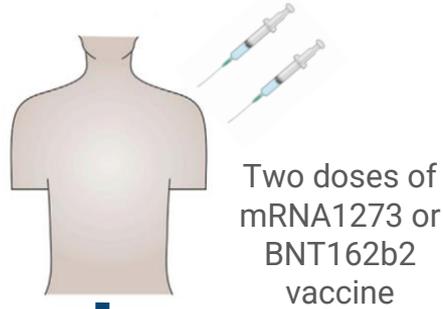
38

Healthy Controls  
(HC)

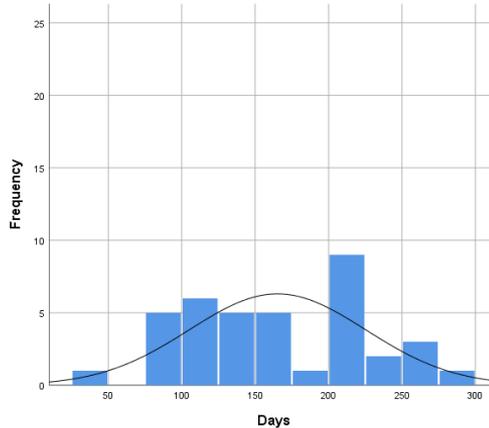
| IEI classification  | IEI classification  | Patients |
|---|---|----------|
| <b>2. CID with associated or syndromic features</b>                 | 2. CID with associated or syndromic features (CID syndromic features) | 3        |
| <b>3. Predominantly antibody deficiencies (PAD)</b>                 | 3a. Agammaglobulinemia  | 3        |
|   | 3b. Common variable immunodeficiency (CVID)                           | 48       |
|   | 3c. Isotype, Light Chain, or Functional Deficiencies                  | 53       |
|   | 3d. Hyper IgM Syndromes   | 2        |
| <b>4. Diseases of immune dysregulation</b>                          | 4. Diseases of immune dysregulation                                   | 2        |
| <b>5. Congenital defects of phagocyte number, function, or both</b> | 5. Congenital defects of phagocyte number, function, or both          | 1        |
| <b>8. Complement deficiencies</b>                                   | 8. Complement deficiencies  | 3        |



# Timing of study after complete vaccination anti SARS-CoV-2

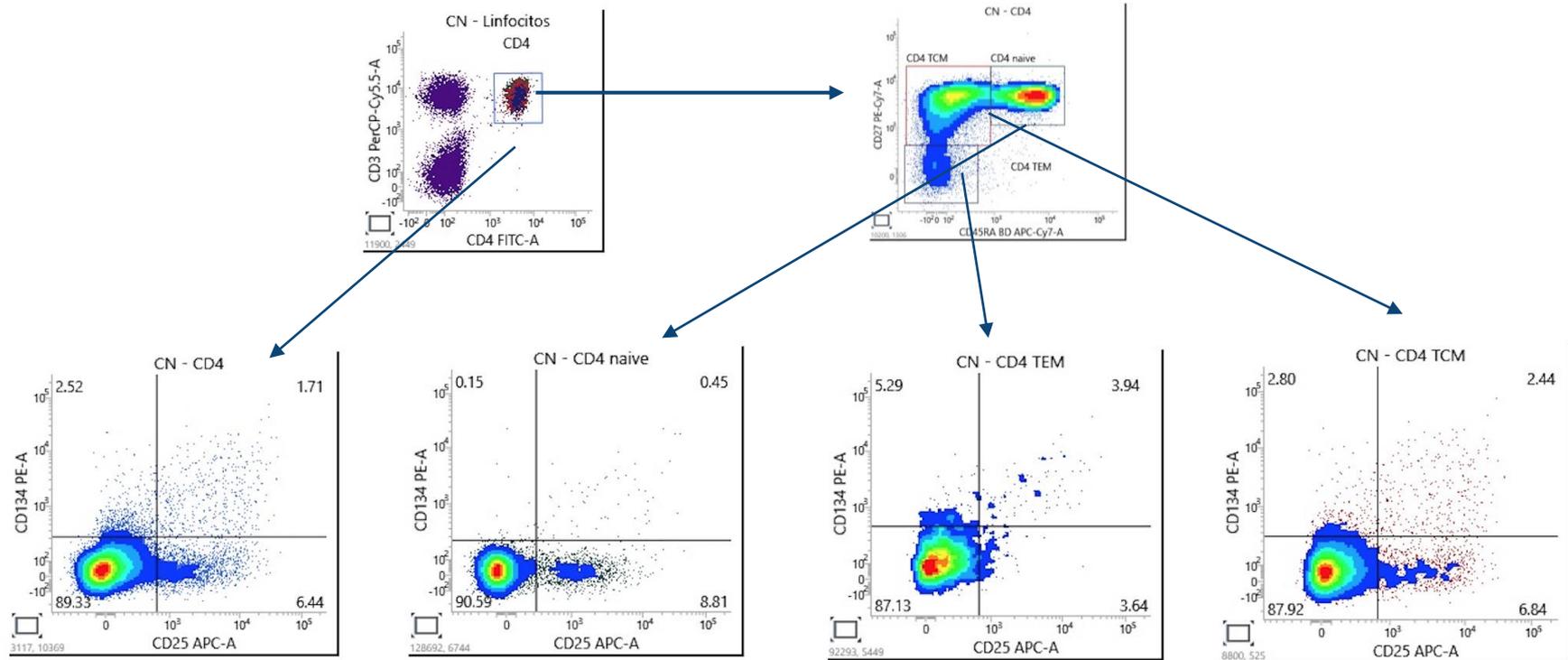


IEI  
 $89 \pm [72-120]$  days after the second dose (~ 3 months).



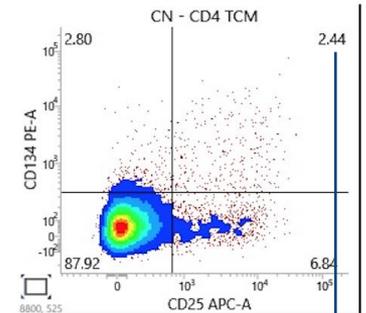
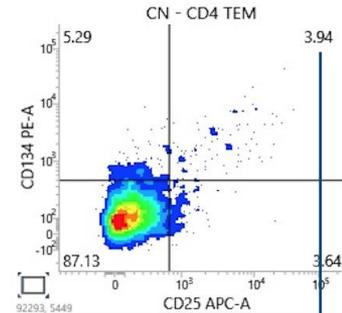
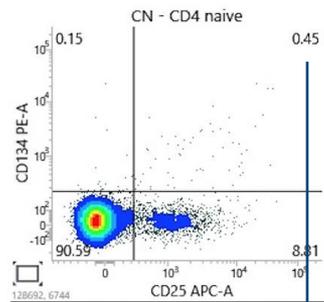
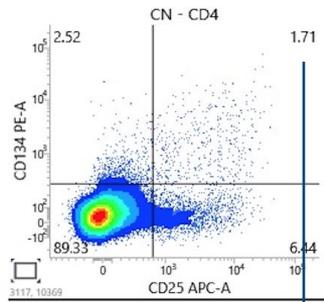
HC (health care workers)  
 $158,5 \pm [118-216]$  days after the second dose (~5 months).

# Antigen-specific T-cell response: Activation Induced Marker (AIM) assay

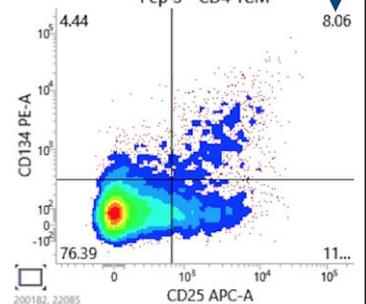
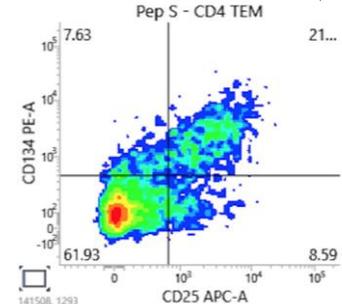
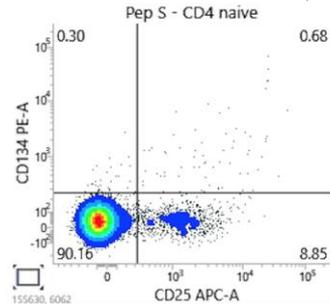
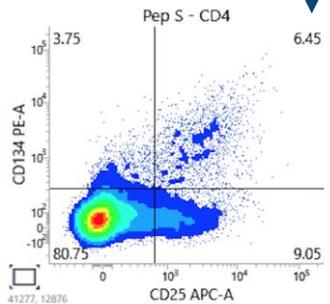


# AIM assay: CD134 (OX40) and CD25 coexpression

Negative Control  
(non-stimulated)



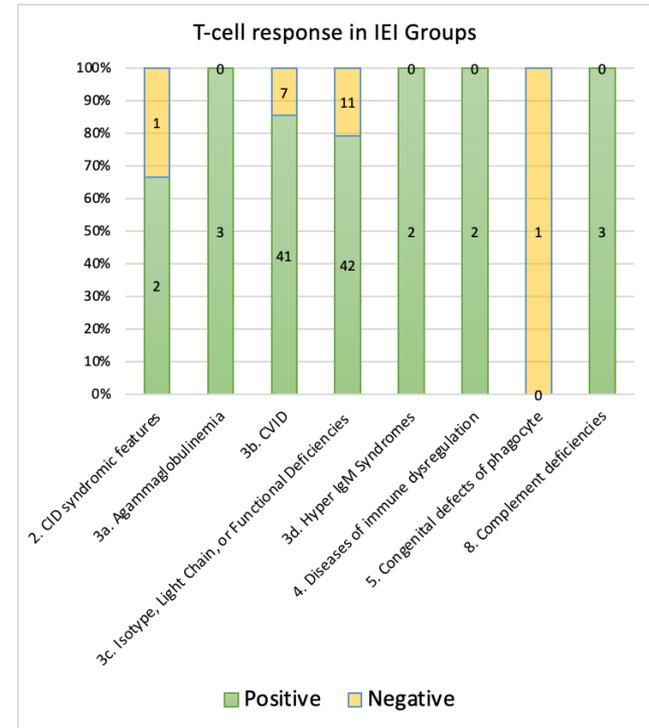
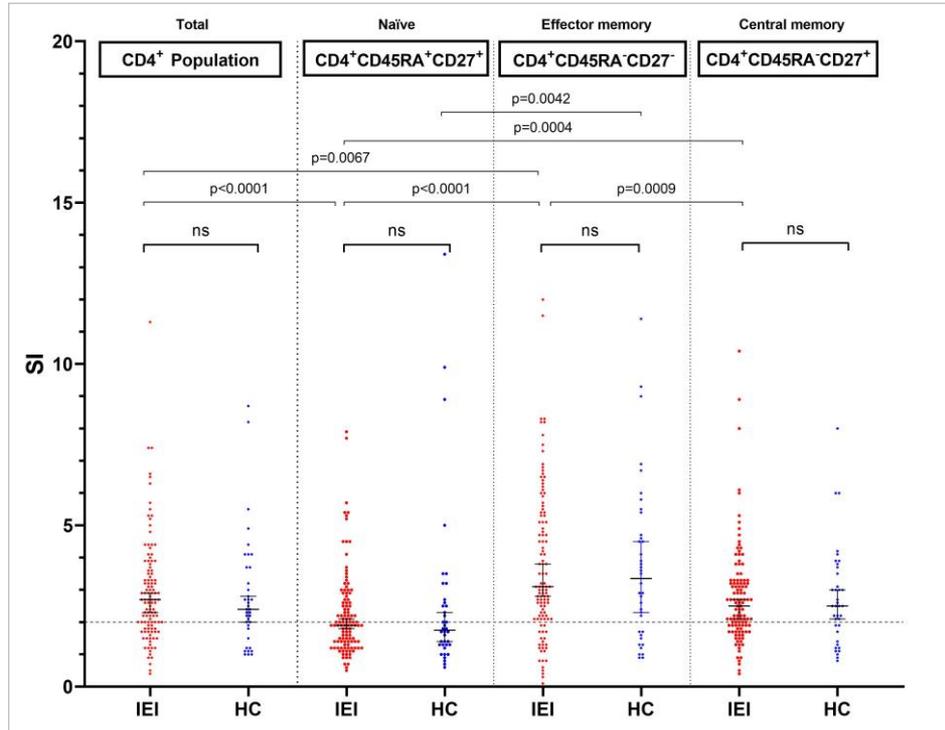
SARS-CoV-2  
Spike peptide pools  
stimulation



$$SI = \frac{\% CD134 + + CD25 + \text{ cells after the antigen stimulation}}{\% CD134 + + CD25 + \text{ cells in the unstimulated condition}}$$

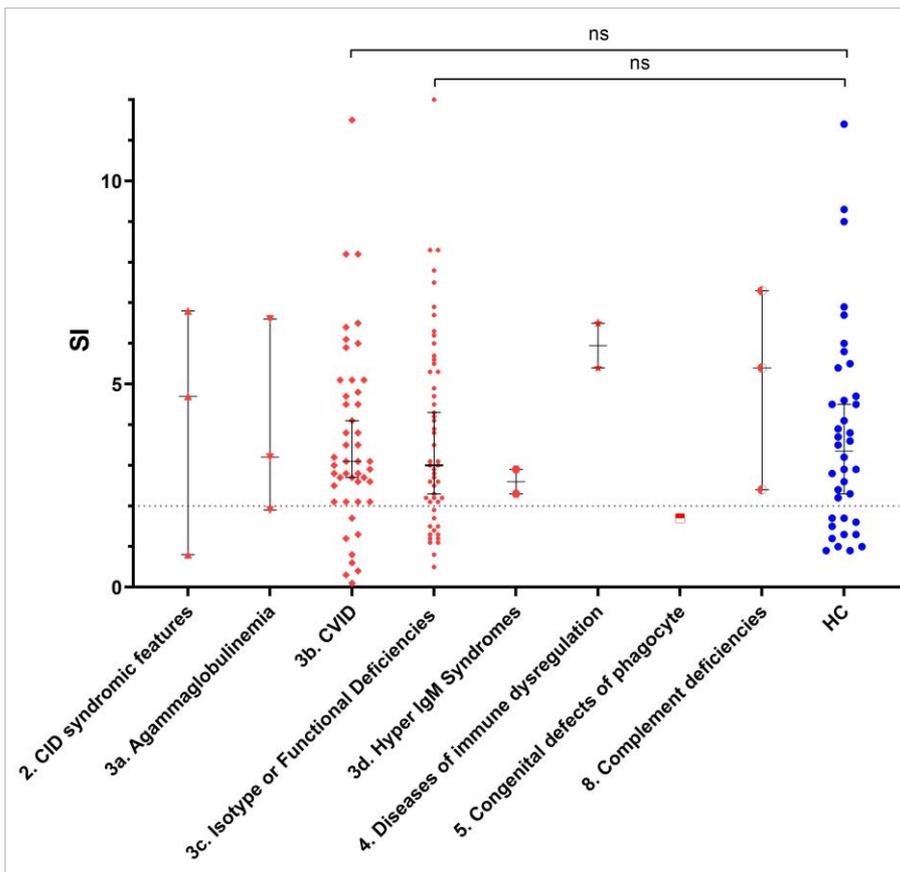
SI ≥ 2 positive

# SARS-CoV-2 Spike-specific CD4+ T-cell responses



Spike-specific CD4+ T-cell responses detected in 95 out of 115 (**82.6%**) IEI patients.  
No differences in SI as compared to HC.

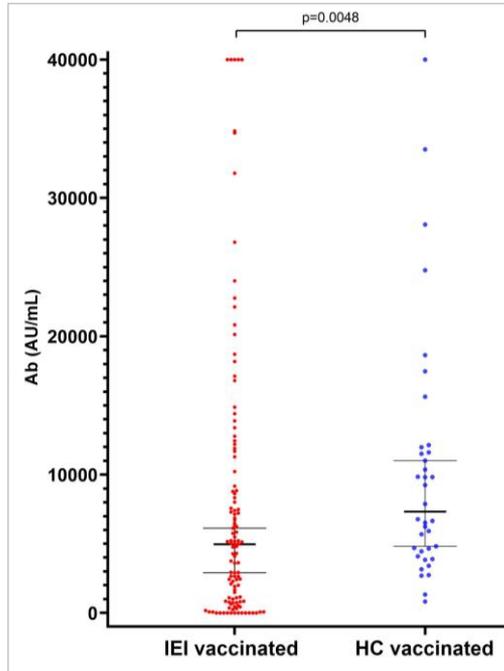
## SARS-CoV-2 Spike-specific TEM CD4+ T-cell response in different IEI groups



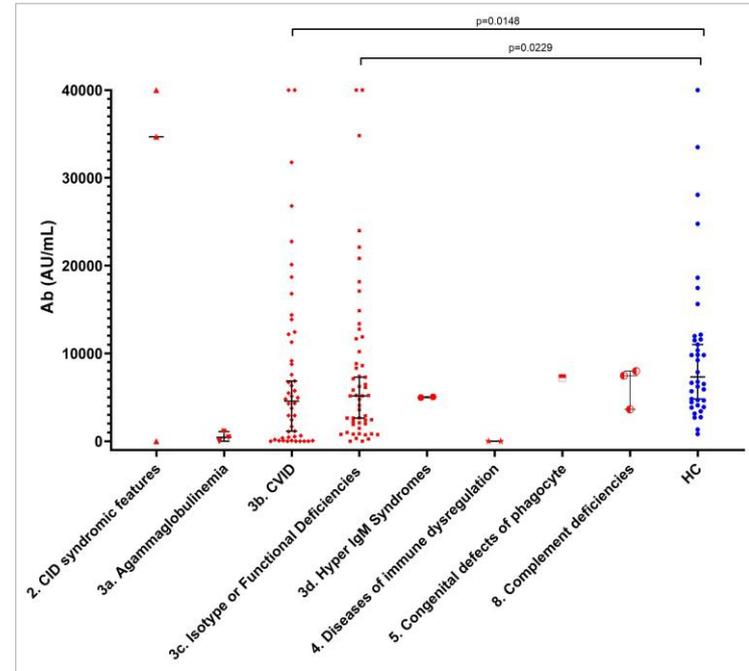
No statistically significant differences were found in anti-S SARS-CoV-2 cellular responses in IEI patients further stratified by any category and HC.

Due to the low number of patients in the others groups (no PAD) we can not draw conclusions about the significant differences between groups in IEI.

# Antibody response against SARS-Cov-2 Spike protein

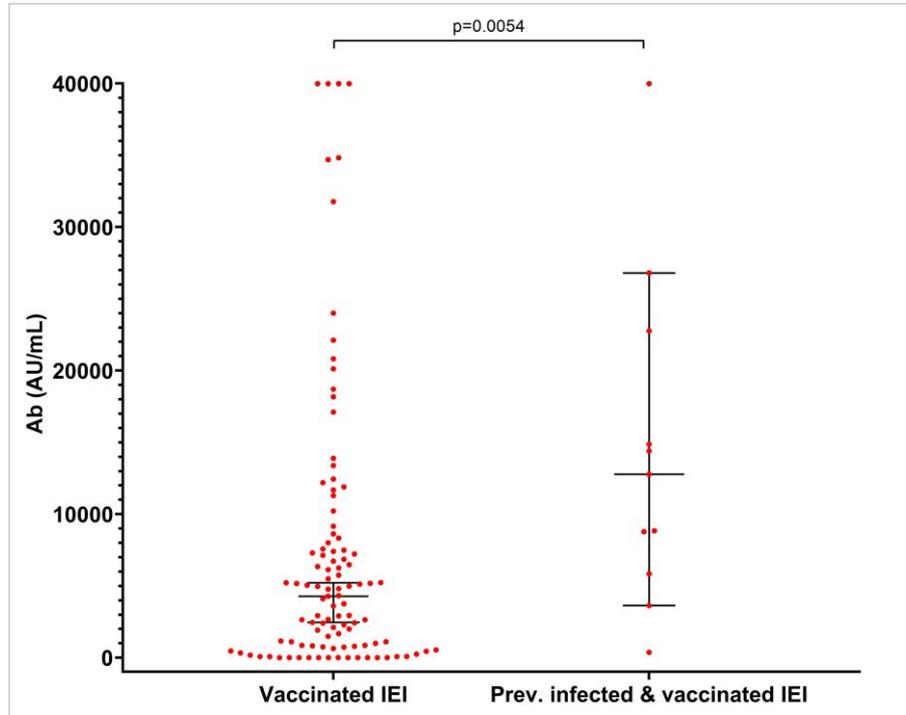


Post-vaccination serum anti-S protein IgG levels were significantly lower in the group of IEI patients than in HC.  
4953 AU/mL [840,9-10215] vs 7324 AU/mL [4362-12016],  $p=0.0048$  (median  $\pm$  [interquartile range]).



Within the IEI patients, the subgroup of CVID and the isotype and functional antibody deficiencies showed a significant decrease in specific anti-S IgG as compared with HC.  
4557 AU/mL [387,3-11961] vs 7324 AU/mL [4362-12016],  $p=0.0148$  and 5170 AU/mL [1950-10946] vs 7324 AU/mL [4362-12016],  $p=0.0229$  (median  $\pm$  [interquartile range]).

# IgG antibodies anti-SARS-CoV-2 in IEI patients recovered of COVID-19



Patients who were previously infected with SARS-CoV-2 (n=11) raised higher anti-S IgG levels than those IEI vaccinated patients naïve to the infection.

12767 AU/mL [5834 - 22757] vs 4271 AU/mL [782,3-8001],  $p= 0.0054$ .

(median  $\pm$  [interquartile range]).

## Conclusions

- In our study -performed with a median of 3 months after the second dose of mRNA SARS-CoV-2 vaccines- we have been able to detect spike specific CD4+ T-cells responses with mainly effector memory phenotype in IEI patients with PAD (agammaglobulinemia, CVID, isotype and functional deficiencies, hyper IgM syndromes). These responses are comparable to the T-cell-mediated specific responses found in vaccinated HC.
- After vaccination, IEI patients had a significant decrease in IgG anti-spike protein antibody responses as compared to vaccinated HC, which is in accordance with the predominance of antibody deficiency in 92% of our IEI patients
- IEI patients previously infected with SARS-CoV-2 showed a higher levels of IgG anti-spike protein responses compared to uninfected IEI patients.
- In patients with IEI and PAD, although induction of specific antibody responses are impaired, SARS-CoV-2 vaccination can induce strong and long-lasting specific cell-mediated T CD4+ responses, which might confer protection against viral infection and/or development of severe COVID-19 disease. A follow-up study in our IEI patients after receiving the third dose of SARS-CoV-2 vaccination is ongoing.
- The need of subsequent boosters of COVID-19 vaccination requires an individualized approach in IEI patients with PAD , which should include the evaluation of memory specific T-cell induced immunity.

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# THANK YOU!

All the participants, patients and healthy individuals