A LONGITUDINAL STUDY OF HUMORAL IMMUNE RESPONSE TO CORONAVIRUS SARS-COV-2

03.2020 – 04.2022

Pierre Gumowski

INRAAIC -ADR.AC *Meyrin*

Immunologie Clinique Hôpital de la Tour Meyrin

3rd ADR-AC Symposium
Bern, May 12th 2022

INRAAIC
Institute de Recherche Appliquée en allergologie & Immunologie Clinique

First year : 1st and 2nd Wave

AIM OF STUDY March 2020 – April 2021

Evaluate the lasting immune protection, clinical effects and laboratory strategies after **SARS-CoV-2 first wave infection** in healthy individuals and in patients with immune disease.

- 54 convalescent COVID patients from the 1st wave epidemic and 12 COVID negative relatives accepted after informed consent to participate.
  - 29% had an auto-immune disease,
  - 31% allergies
  - 13% had immune deficiencies.

RESULTS: Along the 12 months of the study, over 90% of patients maintained significant antibodies and effective % of neutralising ab (peak: 3rd to 5th month). The persistence of this immunity was corroborated by the demonstration of circulating memory T $CD4^+$, $CD8^+$ and B $CD19^+$ towards various SARS.CoV-2 antigens in patients 10 to 12 months after their COVID infection.

First year : 1st and 2nd Wave

Early phase:

- Trying and selecting the best assays
- Use of external sera from reference COVID centres
- Repeatability and stability
- Submitting our samples to external controls
- UKNEQUAS submission

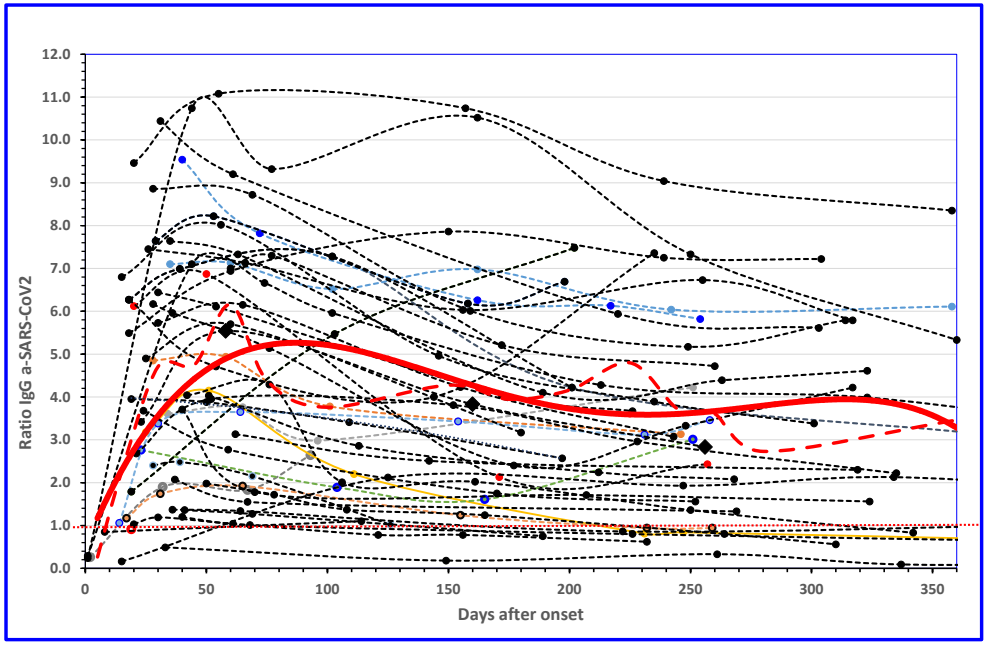
- Recruitment and follow-up of patients
  - § 8-10 RDV for blood samples for serological assays
  - § at 10months: memoryLTT (Daniel & Lester at ADR.AC)

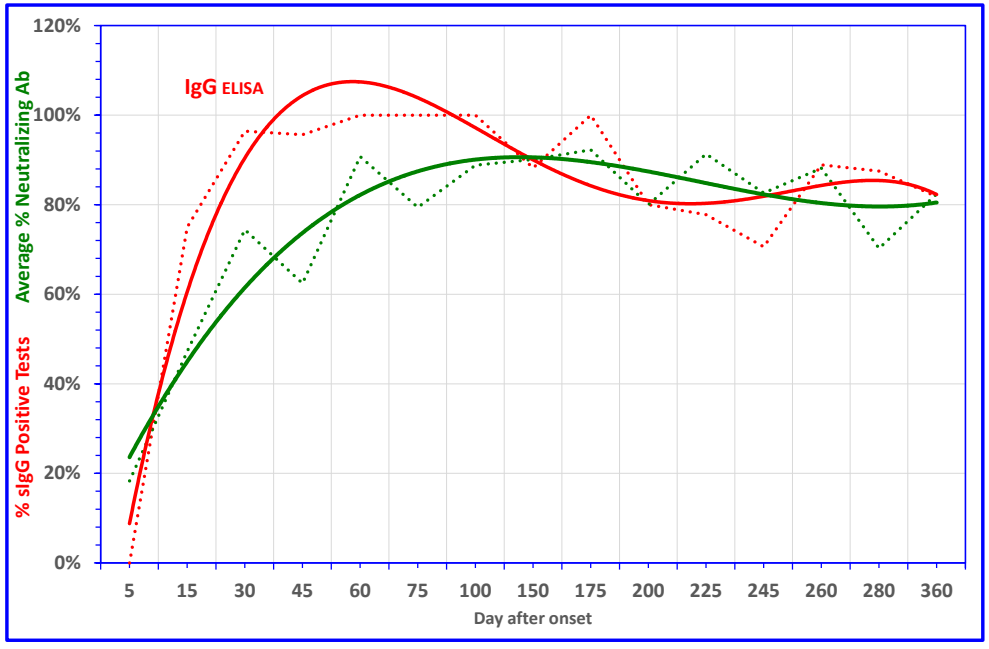
Selected IgG ELISA

- Sugentec™
- Euroimmun®

Ab anti-Sp1
Neutralising Ab

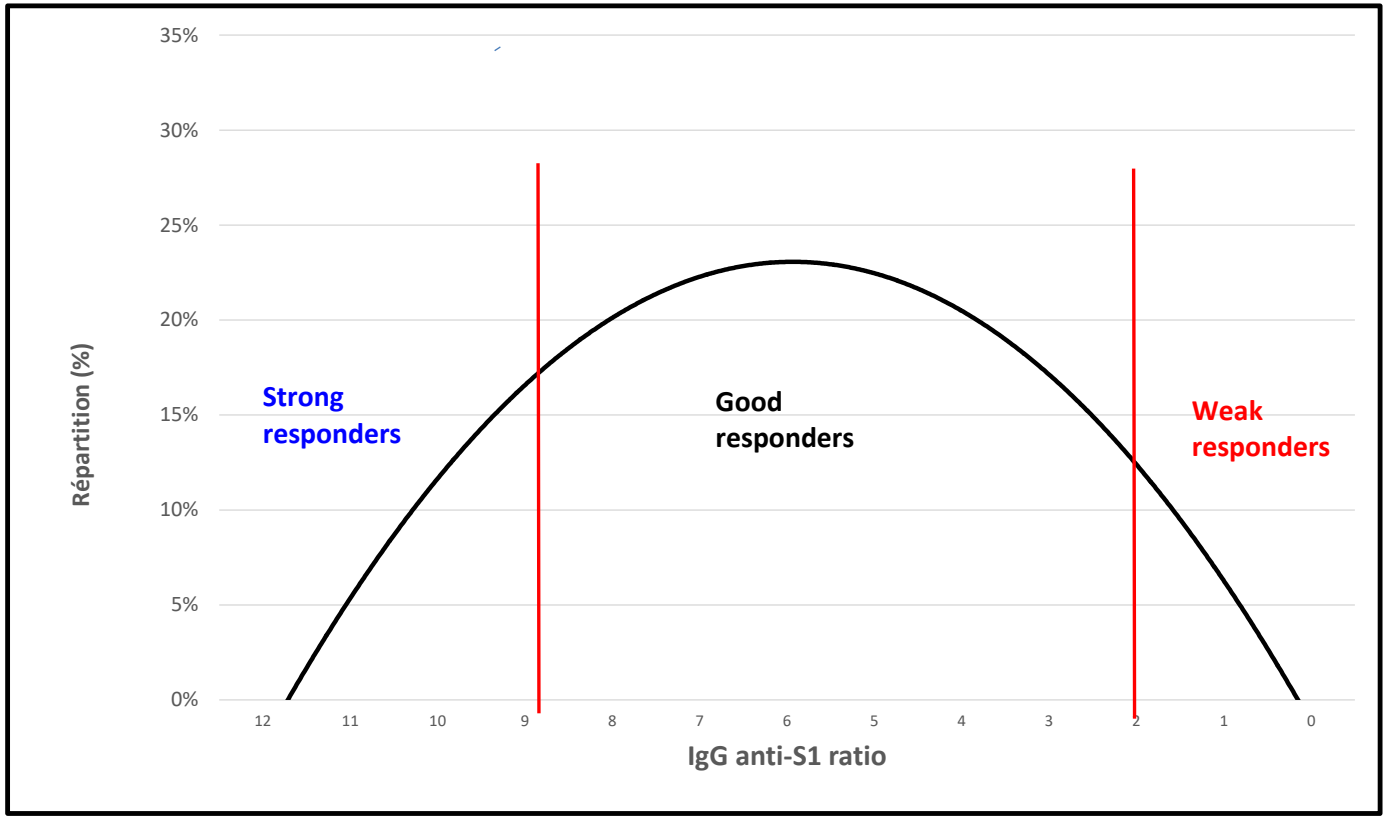
First year : 1st and 2nd Wave





P. Gumowski May 12th 2022

1st and 2nd wave allows the establishment of Cut-off and serological infection response



2022 : OMICRON Wave

- **End of December: Coronavirus SARS-CoV-2 OMICRON appears in Geneva**

- Gradually the Delta strain diseapears (*from the front scene ?*):
  Less and less identified by PCR (but since end of January, all attributed federal fonds are ***discontinued***).
  Clinic manifestation is different and symptoms limited to upper part of the body

- Vaccination with RNA and viral vaccines developed from the original Beta and Delta strain do not appear to prevent an infection.

  - Does vaccination or previous infection attenuates clinical manifestations ?

  - No statistical differences in clinical symptoms severity or duration between naïve COVID patients and those that received 1, 2 or 3 vaccines*

** data from the Covid Centre Hôpital de la Tour*
P. Diaz-Badal personal communication

2022 : OMICRON Serum antibody detection

Observations in 4 subgroups of patients that contracted Omicon COVID

1. Naïve COVID Patients prior to Omicron infection
2. “NEIN SAGER” or children which hat both Delta and Omicron strain infections
3. Vaccinated patients with no previuous Delta infection prior to Omicron infection
4. Patients vaccinated after a previous Wuhan strain infection

2022 : OMICRON Serum antibody detection

- Results with an “Anti-S1 Coronavirus-SARS-CoV-2 Wuhan strain detection kit*”

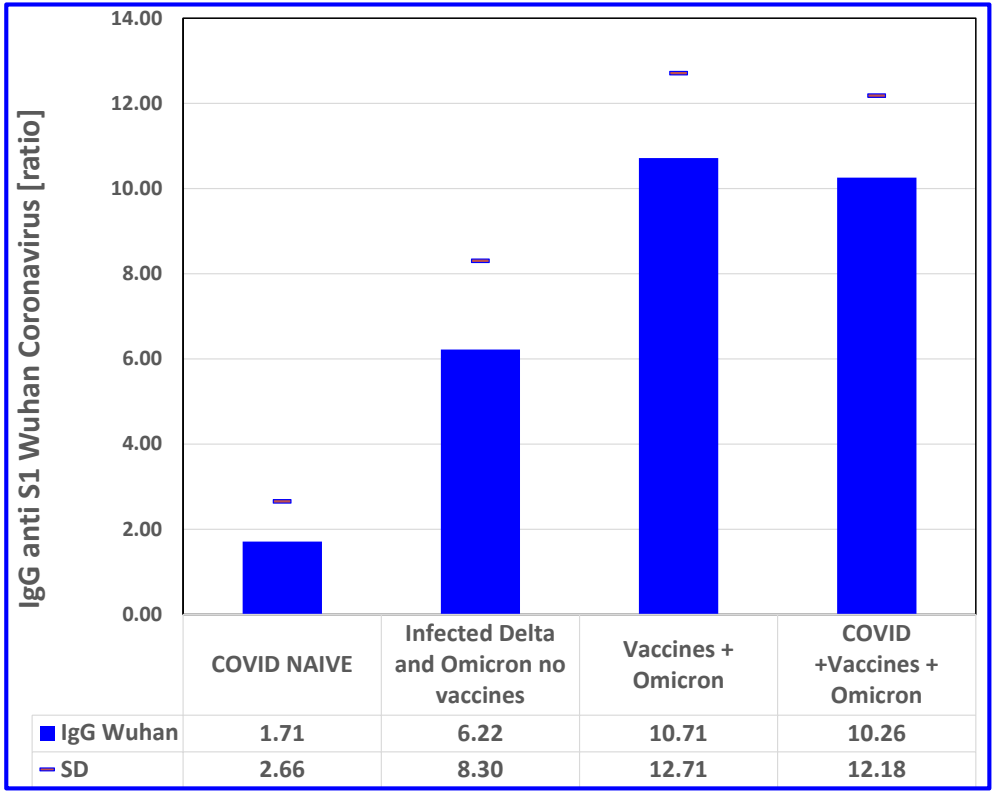
I. COVID Naïve n= 21
Mean days after onset: 54± 26

II. “Nein Sager” and children, no vaccines
n=19 Mean days after onset: 55± 23

III. Vaccinated no prior COVID n= 36
Mean days after onset: 40± 21

IV. Prior COVID + vaccines n=11
Mean days after onset: 51± 23

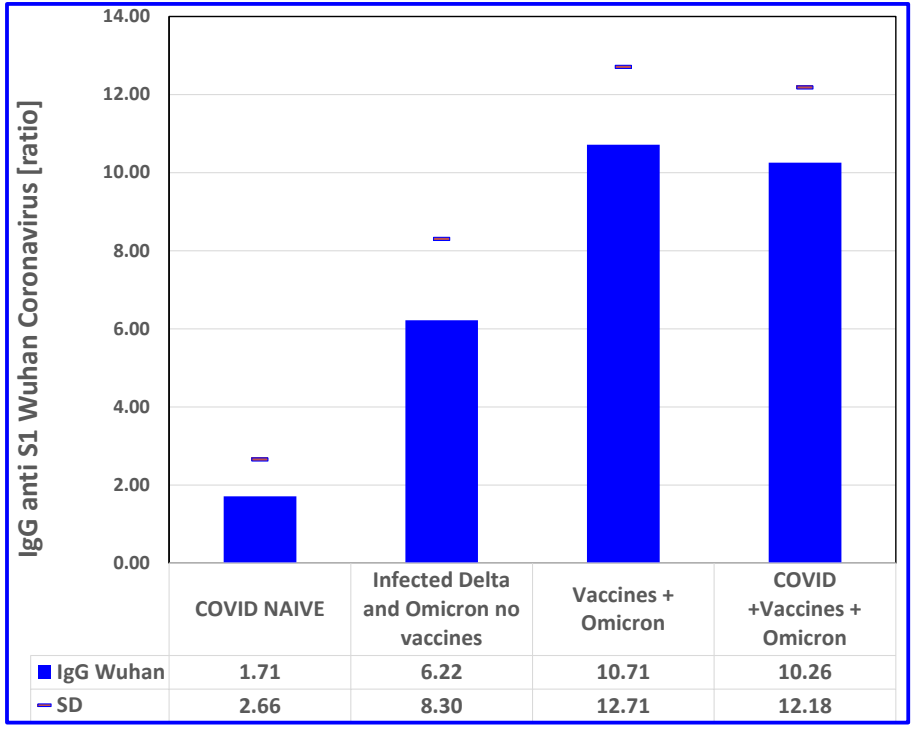
**Material: Euroimmun® IgG kit*

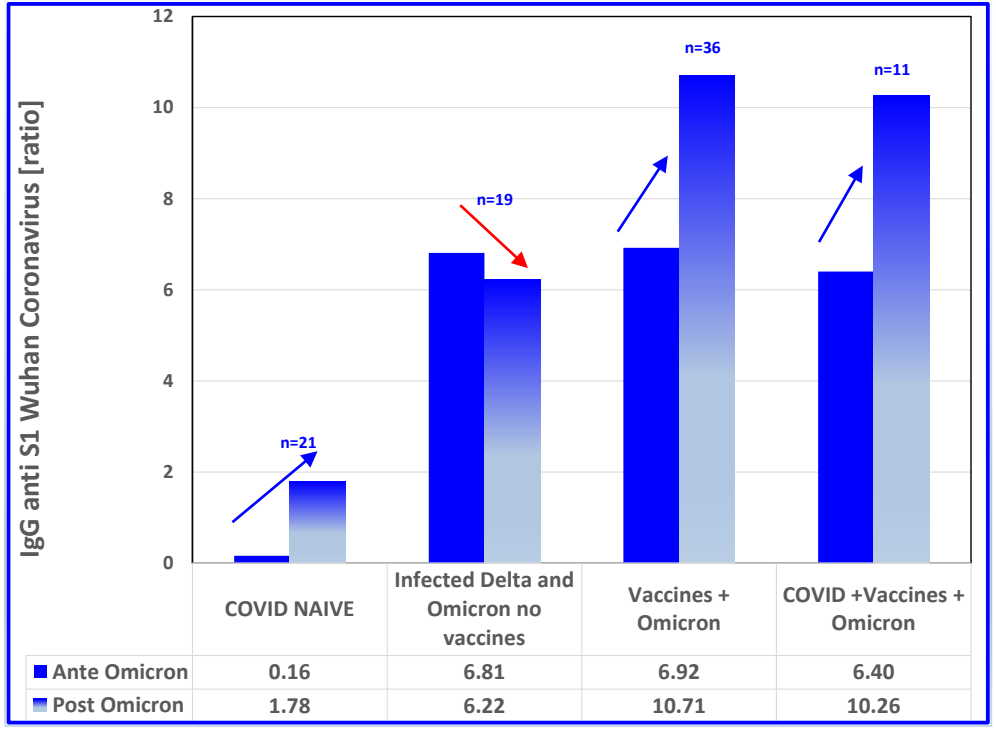


P. Gumowski May 12th 2022

2022 : OMICRON Serum antibody detection

➢ Results with an “Anti-S1 Coronavirus-SARS-CoV-2 Wuhan strain detection kit*”





P. Gumowski May 12th 2022

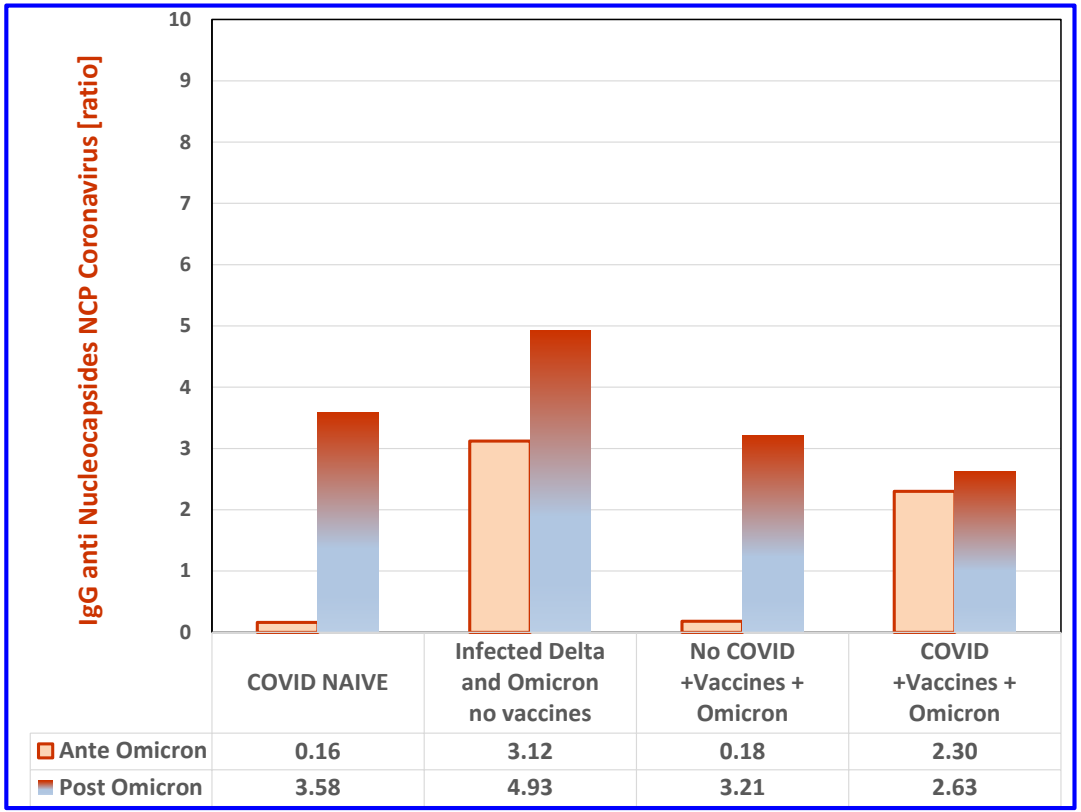
*Material: Euroimmun® IgG kit

2022 : OMICRON Serum antibody detection

➢ Use of an“Anti-Coronavirus-SARS-CoV-2 Nucleocapsides Ab detection kit*”

- At 30 days after infection, all patients with a PCR+ have a significant anti NCD response.
- Time curve response is slower than anti-Sp1 IgA/IgM and IgG

- **Lab ratio cut-off:**
  > 0.46 weak
  > 1.1 positive



	COVID NAIVE	Infected Delta and Omicron no vaccines	No COVID +Vaccines + Omicron	COVID +Vaccines + Omicron
Ante Omicron	0.16	3.12	0.18	2.30
Post Omicron	3.58	4.93	3.21	2.63

P. Gumowski May 12th 2022

*Material: Euroimmun® IgG kit

2022 : OMICRON Serum antibody detection

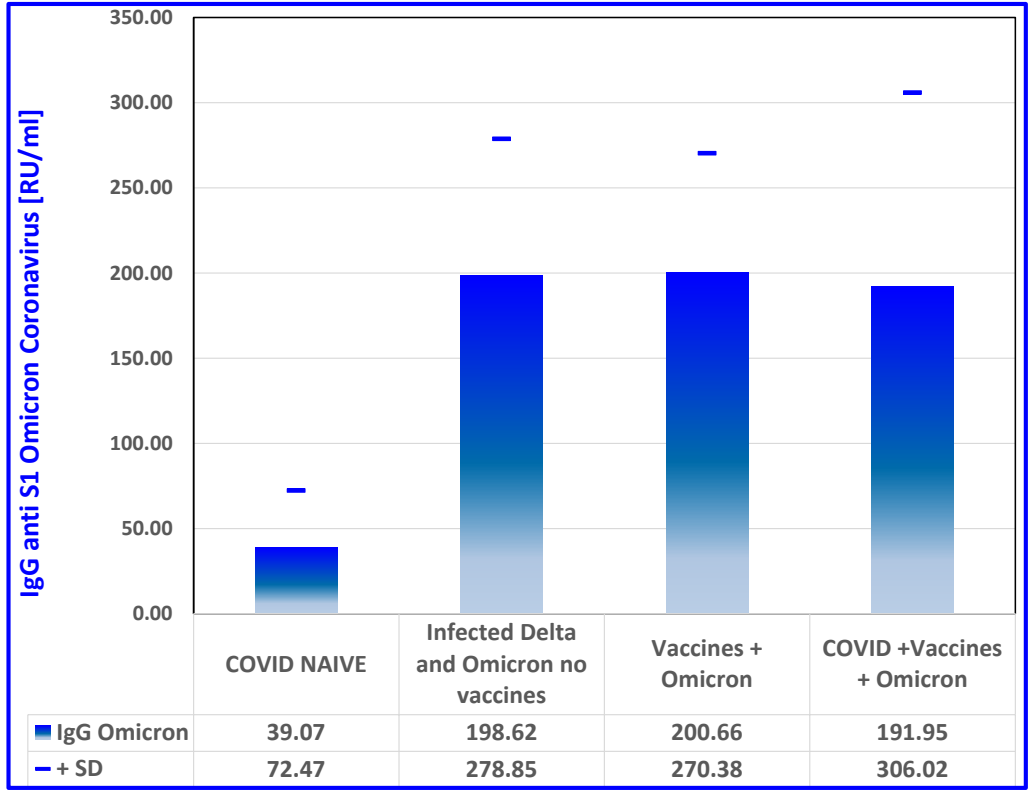
➢ Results with an “Anti-S1 Omicron Coronavirus-SARS-CoV-2 detection kit**”

I. COVID Naïve n= 21
Mean days after onset: 54± 26

II. “Nein Sager” and children, no vaccines
n=19 Mean days after onset: 55± 23

III. Vaccinated no prior COVID n= 36
Mean days after onset: 40± 21

IV. Prior COVID + vaccines n=11
Mean days after onset: 51± 23



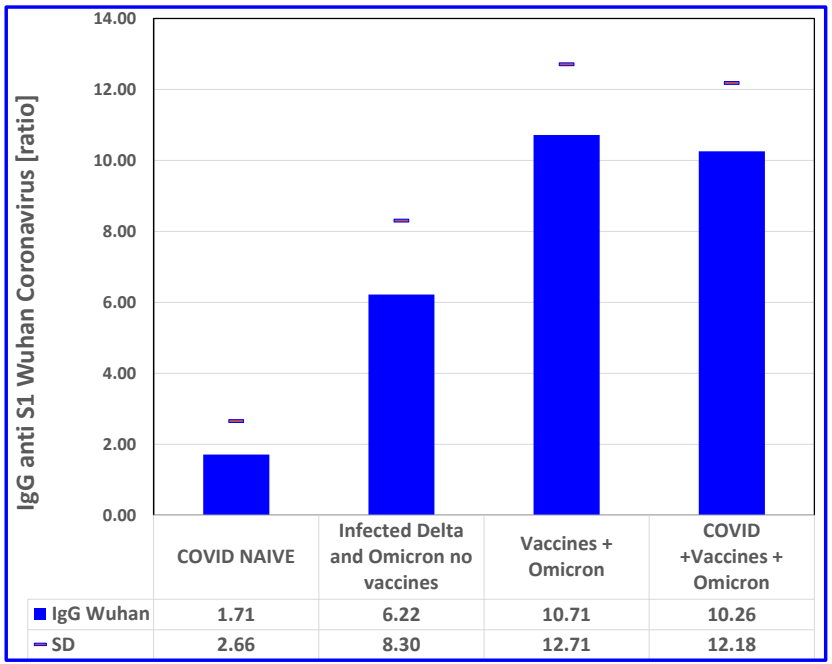
	COVID NAIVE	Infected Delta and Omicron no vaccines	Vaccines + Omicron	COVID +Vaccines + Omicron
IgG Omicron	39.07	198.62	200.66	191.95
+ SD	72.47	278.85	270.38	306.02

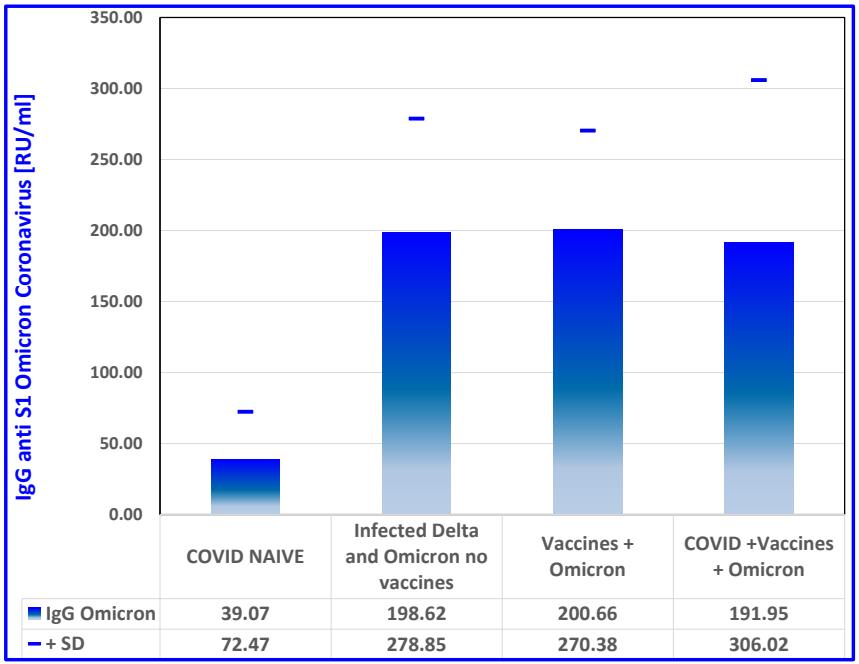
** *Research ELISA IgG anti Spike 1 from Omicron B strain kindly provided by Dr Katia Steinhagen, Euroimmun R&D, Lübeck, Germany*

P. Gumowski May 12th 2022

2022 : OMICRON Serum antibody detection

Prior infection and/or vaccination is associated with a stronger IgG response to S1 Omicron antigens than natural infection only.



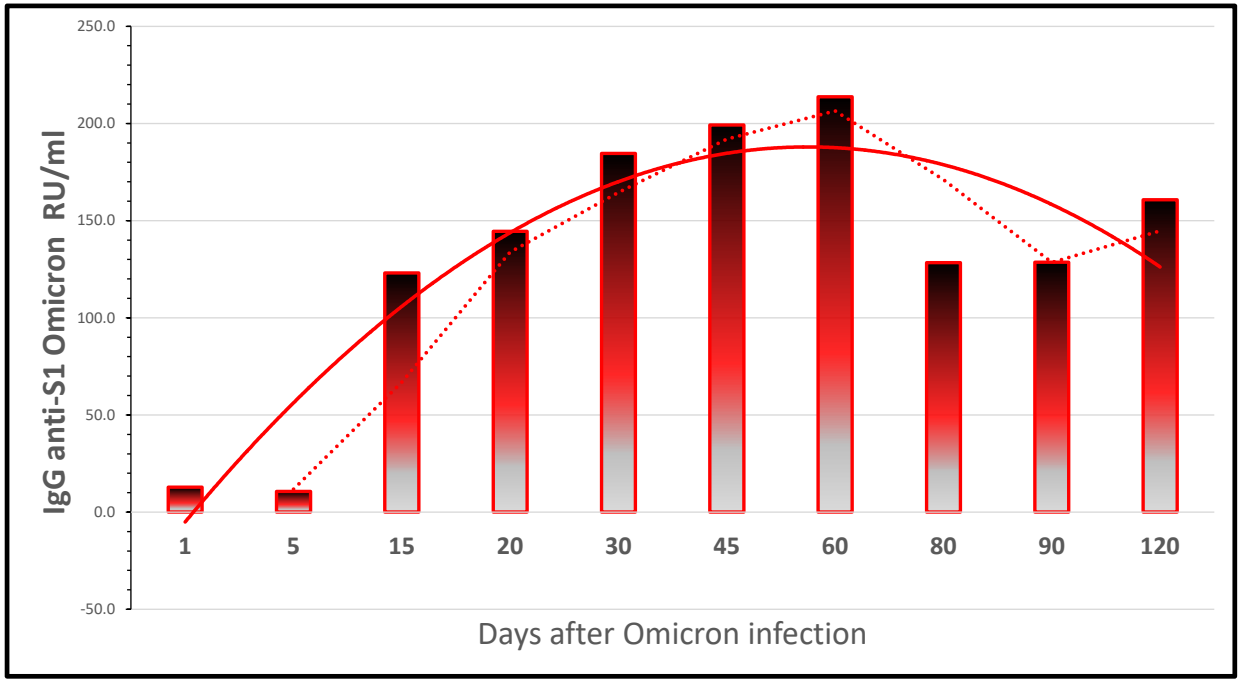


P. Gumowski May 12th 2022

2022 : OMICRON Serum antibody kinetics

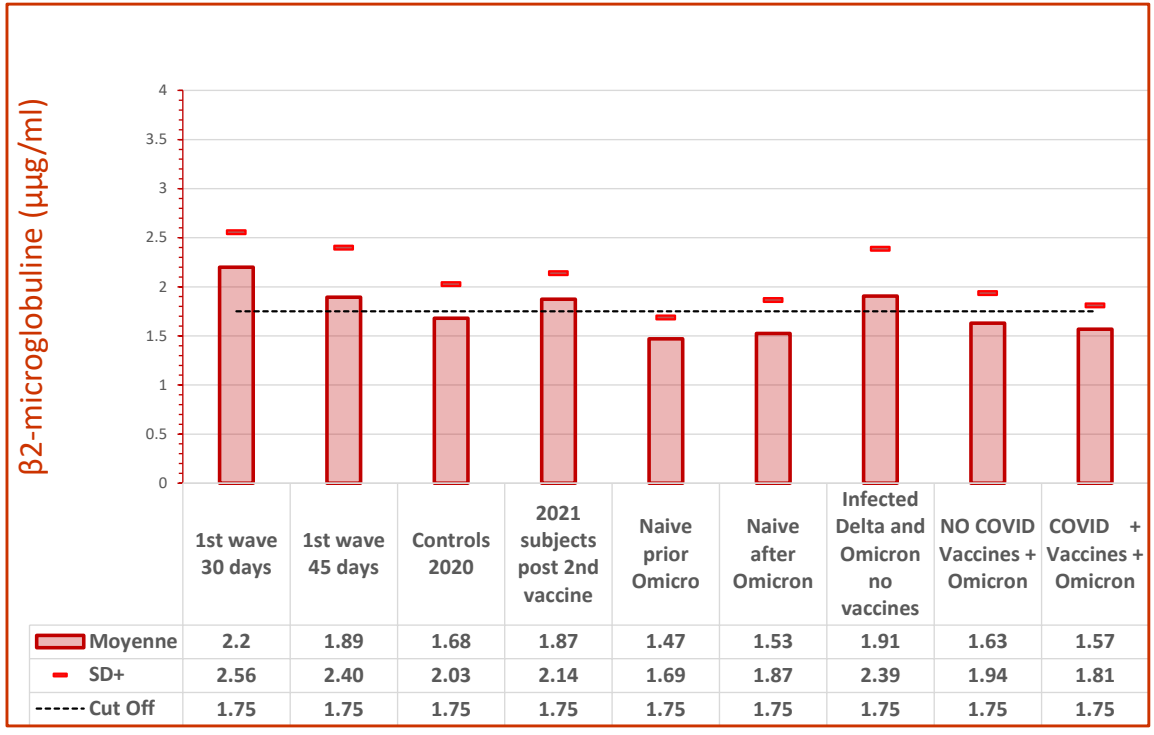
- Mean of
  IgG anti-S1 Omicron titre**

**Research *ELISA IgG anti Spike 1 from Omicron B strain* kindly provided by Dr Katia Steinhagen, Euroimmun R&D, Lübeck, Germany*



2022 : OMICRON Humoral markers of cellular activity

- β2-microglobuline in serum can be considered as a reflect of CD8+ cells involvement.
- Patients with bone marrow involvement and/or auto-immune diseases with increased basal β2-microglobuline were excluded for this assay.
- All measures at 30 days post infection; evolution at 45 days in 1st wave infected shows a transient evolution with time.
- Omicron infected do not show to have an increase in CD8+ cell activation.



	1st wave 30 days	1st wave 45 days	Controls 2020	2021 subjects post 2nd vaccine	Naive prior Omicro	Naive after Omicron	Infected Delta and Omicron no vaccines	NO COVID Vaccines + Omicron	COVID + Vaccines + Omicron
Moyenne	2.2	1.89	1.68	1.87	1.47	1.53	1.91	1.63	1.57
SD+	2.56	2.40	2.03	2.14	1.69	1.87	2.39	1.94	1.81
Cut Off	1.75	1.75	1.75	1.75	1.75	1.75	1.75	1.75	1.75

P. Gumowski May 12th 2022

2022 : OMICRON Wave

Essentials I:

- Coronavirus SARS CoV 2 Omicron behaves differently clinically but also immunologically than the previous Wuhan derived strains Beta and Delta.

- The kinetics of the IgG humoral response to S1 Omicron does not differ in the first 4 months studied from what has been observed with the previous Delta mutant. It peaks between 45 to 60 days after infection.

- Detection of **anti-NCP ab** at 1 month confirms an immune response to infection and correlates with positive PCR. The detection is negative in non infected patients be them vaccinated or not.
  It could thus be **an appropriate surrogate for the confirmation a past COVID** when conditions did not allow a proper PCR or antigenic tests.

2022 : OMICRON Wave

Essentials II:

- **The specific anti-S1 Omicron tested can help in giving an information on Omicron immunity.**
- **Prior infection and/or vaccination is associated with a strong IgG response to previously present anti-S1 Wuhan as well as to S1 Omicron antigens. This response is 2-3 fold stronger than the effect of natural infection only.**
  A kind of "booster" effect on the observed specific humoral immunity.
- **However, previous infection and/or vaccination did not protect against an infection to the Omicron mutant.**
  Will this combined "immune sensitization" help for another new Coronavirus SAR-CoV-2 mutant?
- **A QUESTION: is this observed immune booster effect of the Omicron infection only limited to Coronavirus ?**
- **Another QUESTION: how long will this booster effect persist?**

INRAAIC
CLINCAL IMMUNOLOGY
ADR AC
Adverse Drug Reactions
Analysis & Consulting

INRAAIC's team in Meyrin

Maud Echenard
Frédérique van Eck
Ciro Ceresa
Lecticia Da Costa R

Collaborations

Dr Lucien Gamba

FMH Allergologie-Immunologie

Dr Pablo Diaz Badal

Head Covid Centre, Hôpital de la Tour Meyrin