NASDAQ: GOVX

GeoVax®

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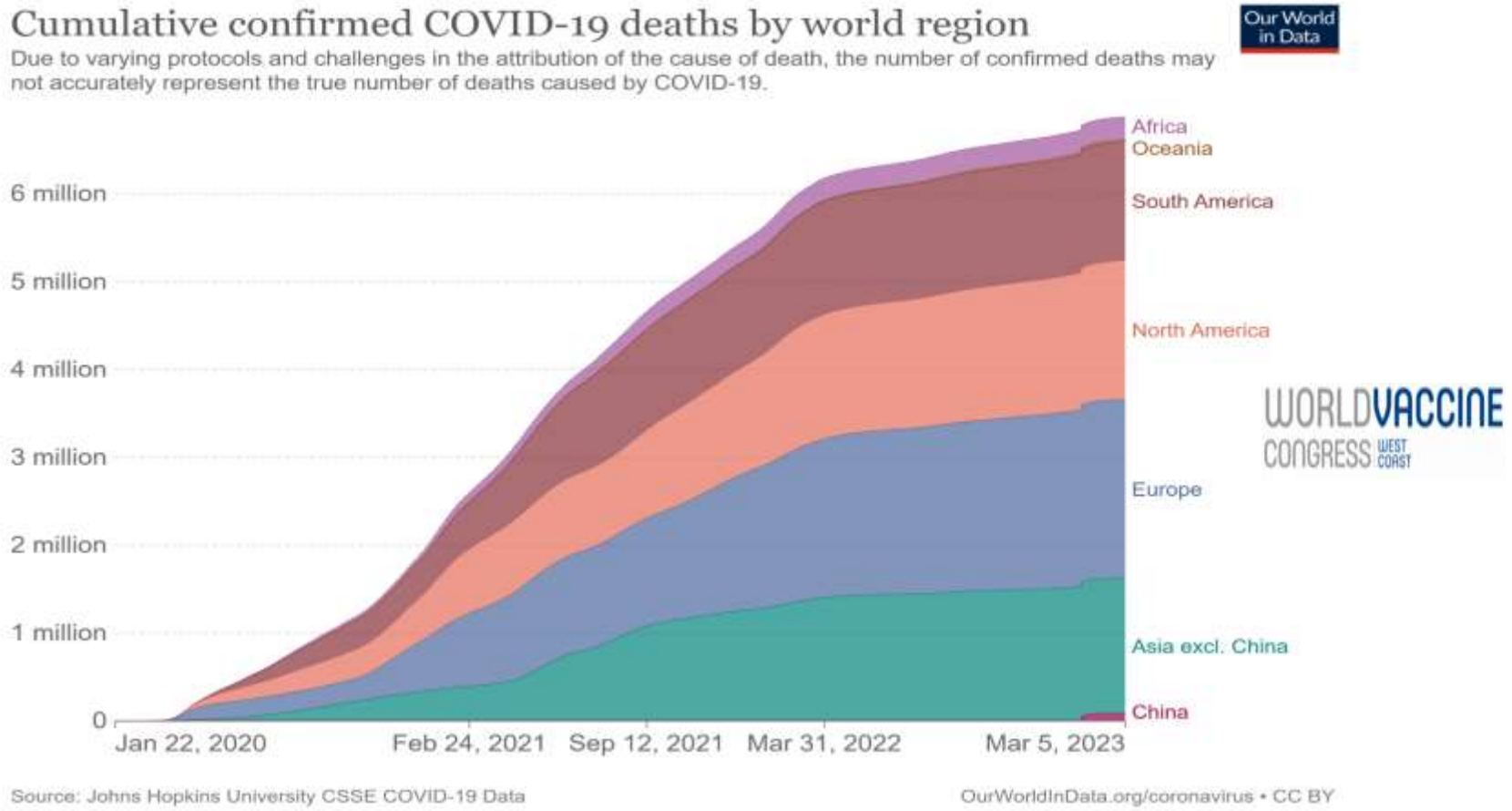
Covid-19 Vaccine GEO-CM04S1: A Superior Viral Platform Alternative for Eliciting Durable T Cell Responses in Immunocompromised Hematologic Malignancy Patients

WORLD VACCINE CONGRESS WEST COAST

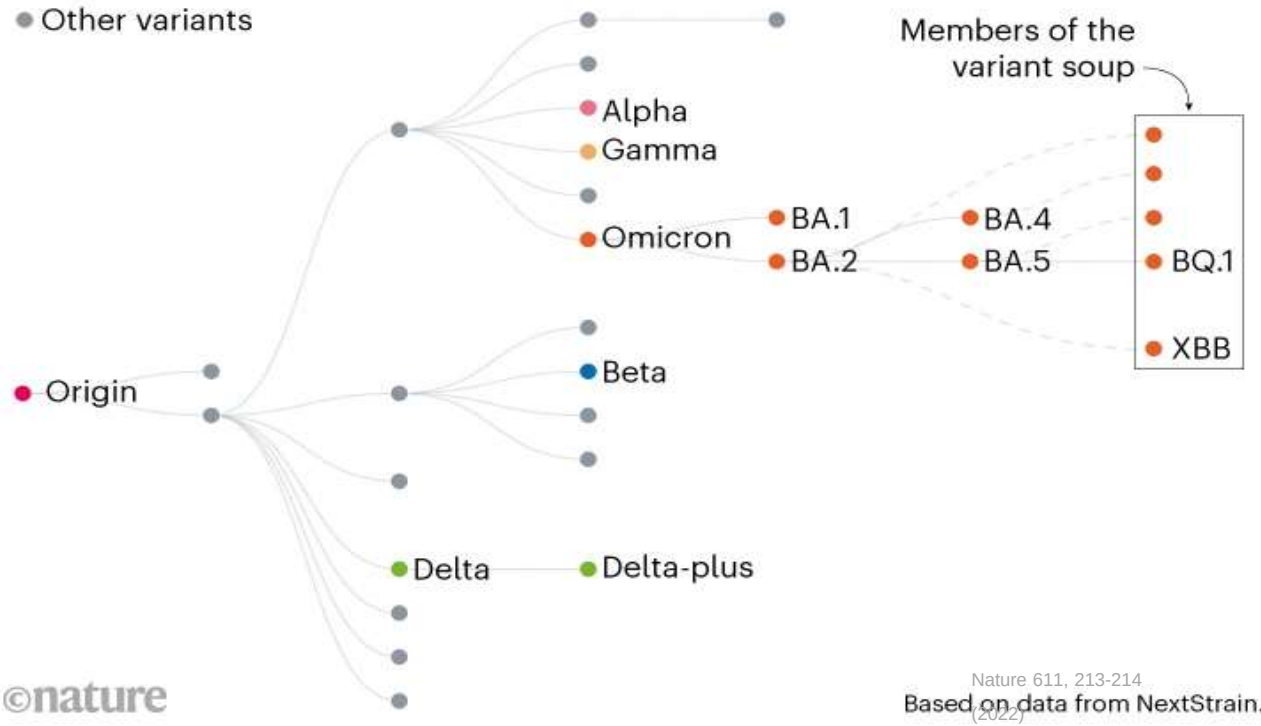
SARS-CoV-2 Pandemic Continues World-Wide



SARS-CoV-2 Evolution

GROWING FAMILY

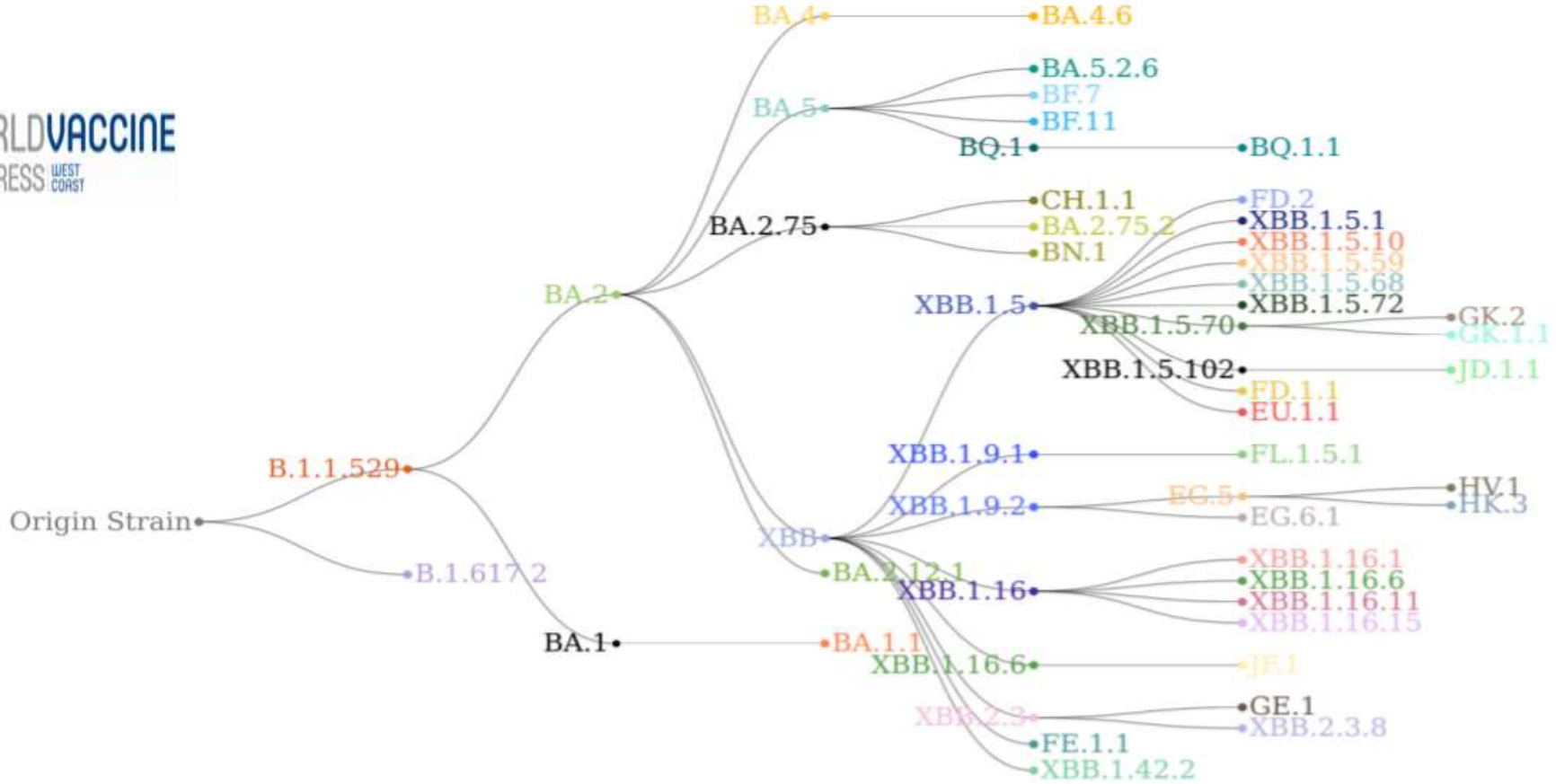
Omicron sublineages come from a single part of the SARS-CoV-2 family tree, unlike earlier variants of concern such as Alpha and Delta.



Nature 611, 213-214 (2022)

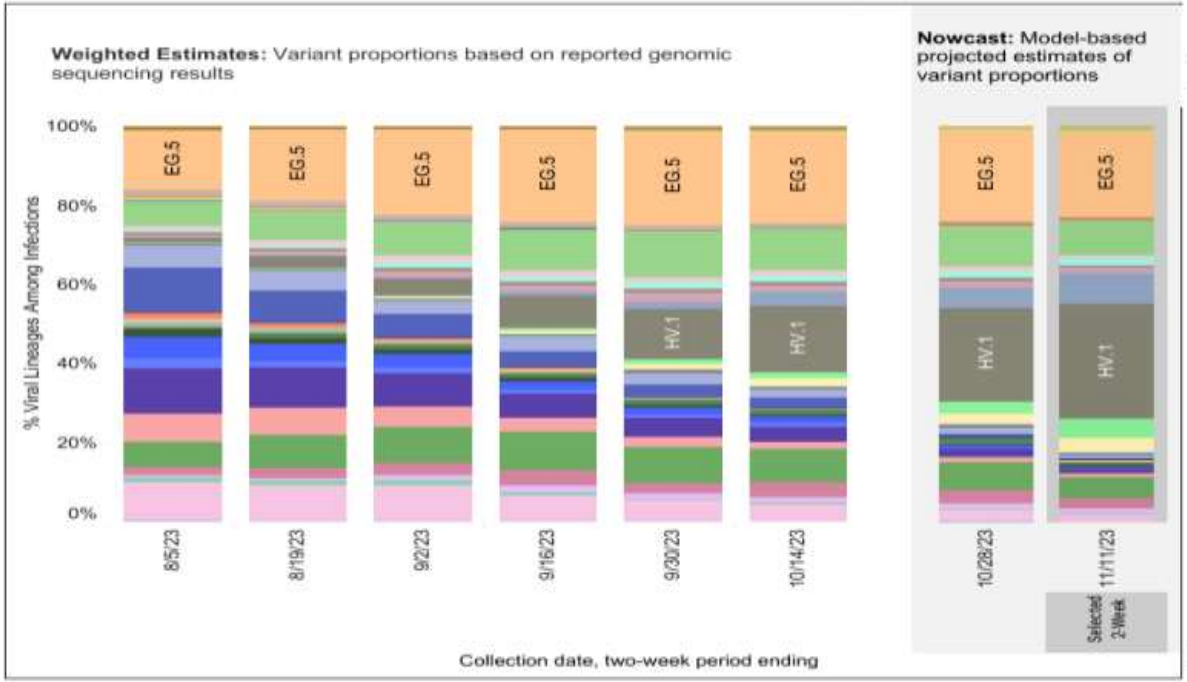
Based on data from NextStrain.

Omicron VOC Evolution



Weighted and Nowcast Estimates in United States for 2-Week Periods in 7/23/2023 – 11/11/2023

Hover over (or tap in mobile) any lineage of interest to see the amount of uncertainty in that lineage's estimate.



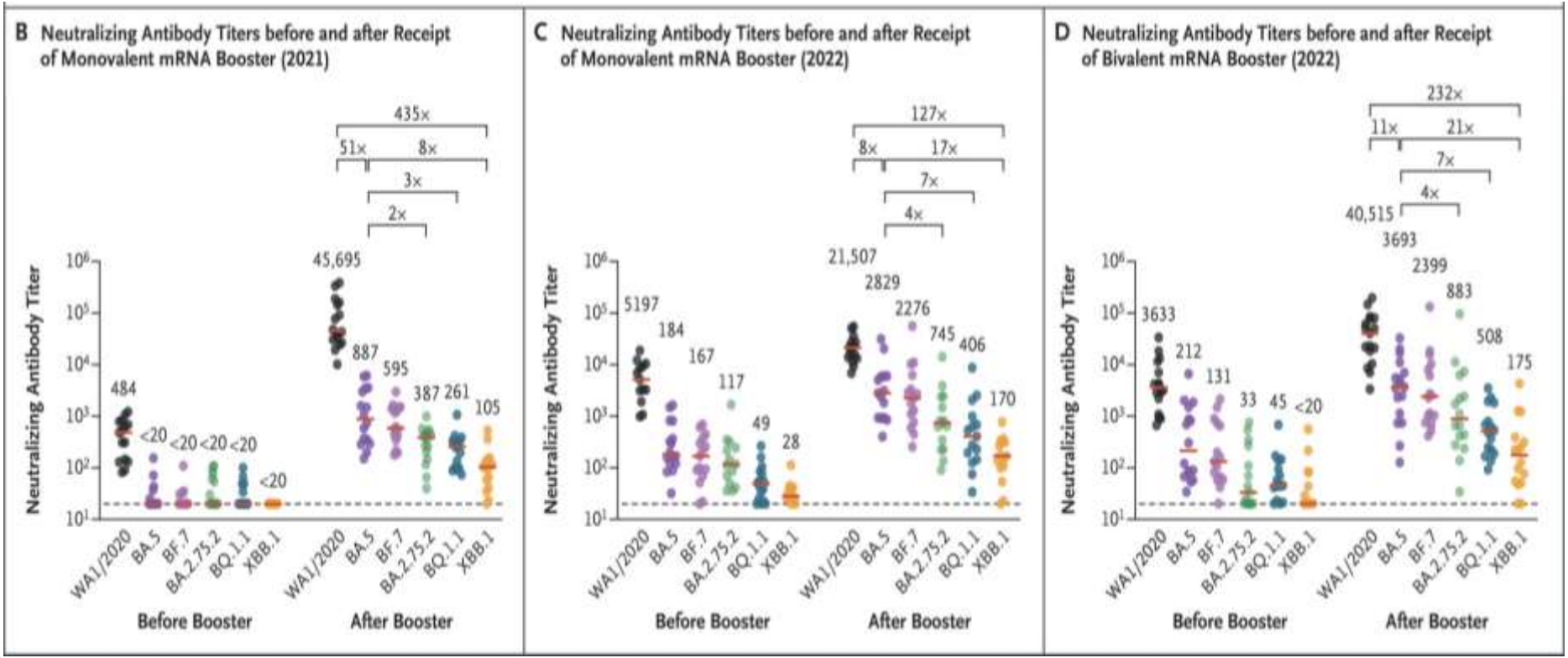
Nowcast Estimates in United States for 10/29/2023 – 11/11/2023

USA

WHO label	Lineage #	%Total	95%PI
Omicron	HV.1	29.0%	26.0-32.1%
	EG.5	21.7%	19.3-24.2%
	FL.1.5.1	9.3%	8.0-10.8%
	HK.3	7.8%	6.2-9.9%
	XBB.1.16.6	5.6%	4.7-6.6%
	JD.1.1	4.6%	3.4-6.1%
	JF.1	3.5%	2.7-4.5%
	XBB.1.16.11	2.5%	2.0-3.2%
	XBB.2.3	1.9%	1.5-2.3%
	GK.1.1	1.6%	1.2-2.3%
	HF.1	1.4%	0.9-2.1%
	XBB.1.16.15	1.4%	1.0-1.9%
	XBB.1.16	1.2%	0.9-1.6%
	XBB.1.5.70	1.2%	0.6-2.2%
	BA.2	1.0%	0.5-2.1%
	GE.1	0.9%	0.6-1.3%
	XBB.1.16.1	0.8%	0.6-1.1%
	XBB	0.8%	0.6-1.0%
	GK.2	0.6%	0.5-0.9%
	EG.6.1	0.5%	0.3-0.7%
	XBB.1.5	0.3%	0.2-0.4%
	XBB.1.9.1	0.3%	0.2-0.4%
	XBB.1.42.2	0.2%	0.1-0.3%
	XBB.1.5.68	0.2%	0.1-0.3%
	XBB.1.9.2	0.2%	0.1-0.2%
	XBB.1.5.72	0.2%	0.1-0.2%
	CH.1.1	0.2%	0.1-0.3%
	XBB.2.3.8	0.1%	0.0-0.2%
	XBB.1.5.10	0.1%	0.0-0.1%
	XBB.1.5.59	0.0%	0.0-0.1%
	FD.1.1	0.0%	0.0-0.0%
	XBB.1.5.1	0.0%	0.0-0.0%
	FE.1.1	0.0%	0.0-0.0%
	EU.1.1	0.0%	0.0-0.0%
Other	Other*	1.1%	0.6-2.0%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one 2-week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all 2-week periods displayed.
# BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. Except BA.2.12.1, BA.2.75, XBB and their sublineages, BA.2 sublineages are aggregated with BA.2. Except BA.2.75.2, CH.1.1 and BN.1, BA.2.75 sublineages are aggregated with BA.2.75. Except BA.4.6, sublineages of BA.4 are aggregated to BA.4. Except BF.7, BF.11, BA.5.2.6, BQ.1 and BQ.1.1, sublineages of BA.5 are aggregated to BA.5. Except the lineages shown and their sublineages, sublineages of XBB are aggregated to XBB. Except XBB.1.5.1,XBB.1.5.10,FD.2,EU.1.1,XBB.1.5.68 and XBB.1.5.70 sublineages of XBB.1.5 are aggregated to XBB.1.5. Except FL.1.5.1, sublineages of XBB.1.9.1 are aggregated to XBB.1.9.1. Except XBB.1.16.1,XBB.1.16.11,XBB.1.16.15 sublineages of XBB.1.16 are aggregated to XBB.1.16, sublineages of XBB.1.42.2 are aggregated to XBB. Except FE.1.1, sublineages of XBB.1.18.1 are aggregated to XBB. For all the other lineages listed, their sublineages are aggregated to the listed parental lineages respectively. Previously, FL.1.5.1, GE.1, EG.6.1 and HV.1, FD.1.1, XBB.2.3.8, HF.1, GK.2, GK.1.1, HK.3, JD.1.1, JF.1 was aggregated to XBB.1.9.1. XBB.2.3.10, XBB.1.9.2, XBB.1.5.15, XBB.2.3, XBB.1.16.13, XBB.1.5.70, XBB.1.9.2.5.1.1, XBB.1.5.102 and XBB.1.16.6 respectively. Lineages BA.2.75.2, XBB, XBB.1.5 , XBB.1.5.1, XBB.1.5.10, FD.2, XBB.1.9.1, XBB.1.9.2, XBB.1.16, XBB.1.16.1, XBB.2.3, BN.1, BA.4.6, BF.7, BF.11, BA.5.2.6 ,BQ.1.1, EU.1.1, XBB.1.5.68, FE.1.1, EG.5, XBB.1.5.72 , FL.1.5.1, GE.1, EG.6.1,XBB.1.16.11, FD.1.1, XBB.1.5.70, XBB.2.3.8, HV.1, XBB.1.42.2, GK.2, HF.1, XBB.1.16.15, GK.1.1, HK.3, JF.1 contain the spike substitution R346T.

SARS-CoV-2 “Variant Soup” and NAb Escape



Miller et al., NEJM 2023

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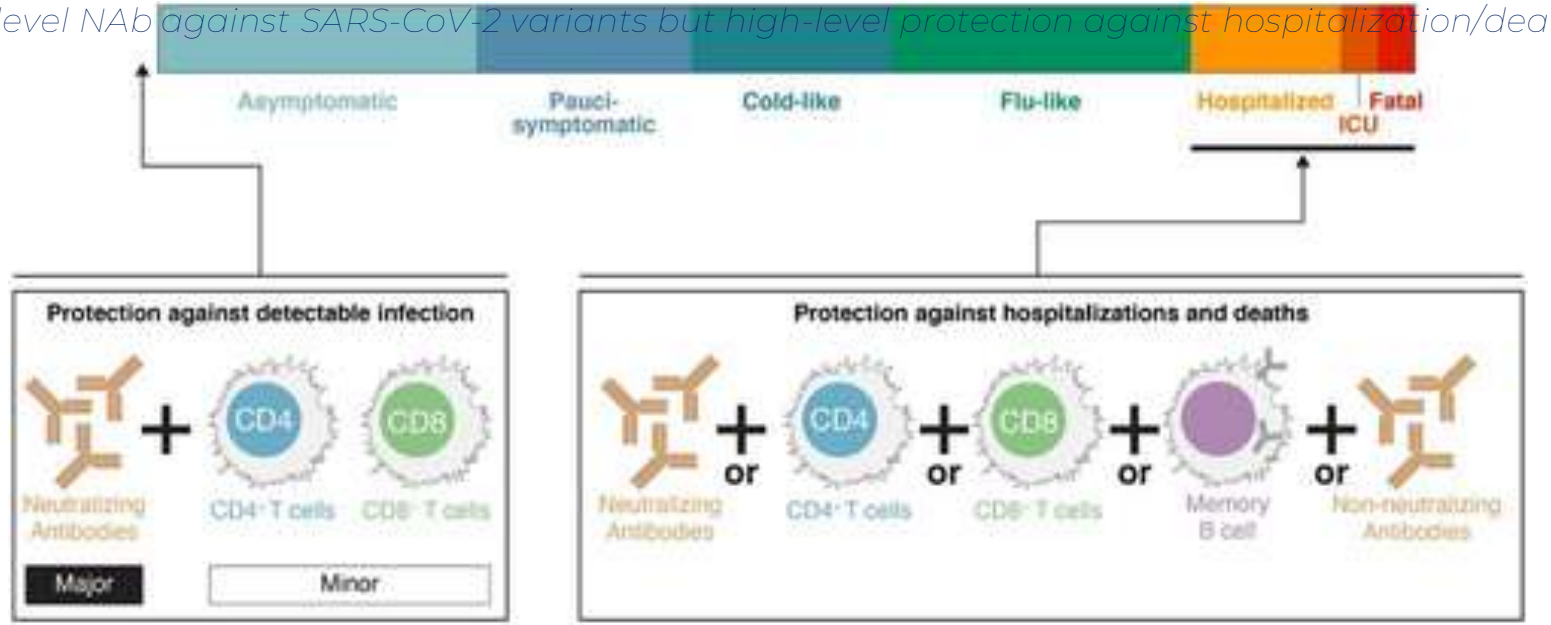
T cells as a Correlate of Protection from Disease

- *Early and/or large T cell responses are associated with faster viral clearance and/or better clinical outcomes*
- *Lower levels of T cells are found in BAL of fatal or severe COVID-19 cases*
- *Agammaglobulinemic individuals have only moderate increased risk of hospitalization post-COVID*
- *Low-level NAb against SARS-CoV-2 variants but high-level protection against hospitalization/death*



Goldblatt et al., 2022. Immun. Rev.

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Modified Vaccinia Ankara (MVA)

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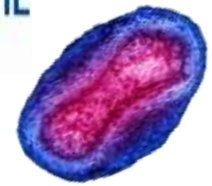
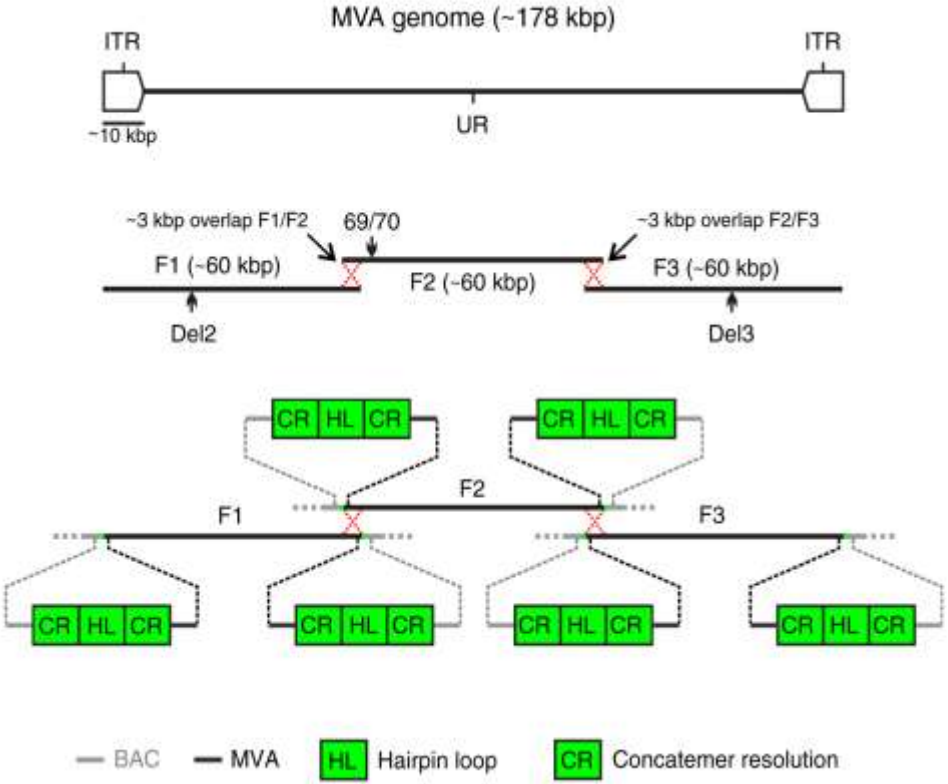
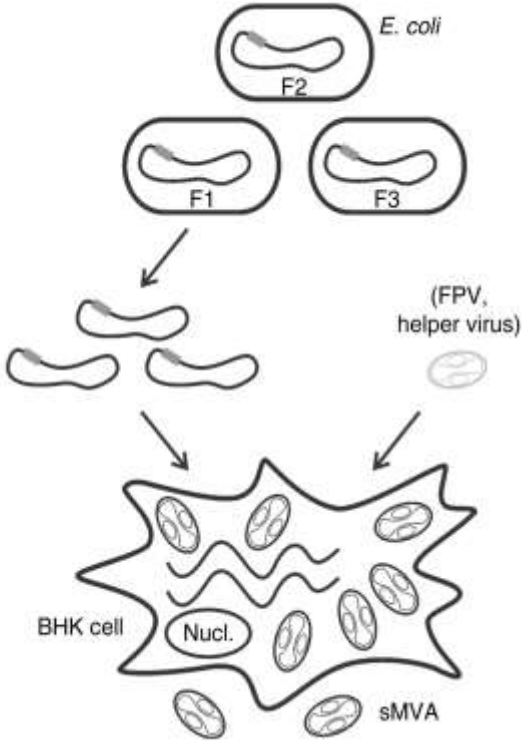


- Safe, highly-attenuated and immunogenic poxvirus-based vaccine vector
- Tested safely in >120,000 young and older individuals in Europe as a smallpox vaccine (70's)
- Reconfirmed safety & properties of eliciting smallpox and mPOX immunity in 1999 at VRC
- Highly restricted host cell tropism with abortive infection in most mammalian cells
- Replicates in cell cytoplasm using own transcription machinery; no chromosome integration
- Large capacity for foreign antigens (~30 kbp) ideal for multiantigen vaccine construction
- Robust stimulation of antigen-specific humoral and cell-mediated immune responses
- Widely used to develop recombinant vaccine vectors for infectious disease and cancer
- Highly thermostable and suitable for large scale vaccine production

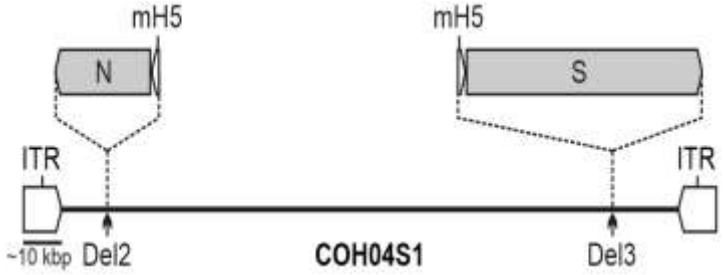
Synthetic MVA (sMVA) Platform





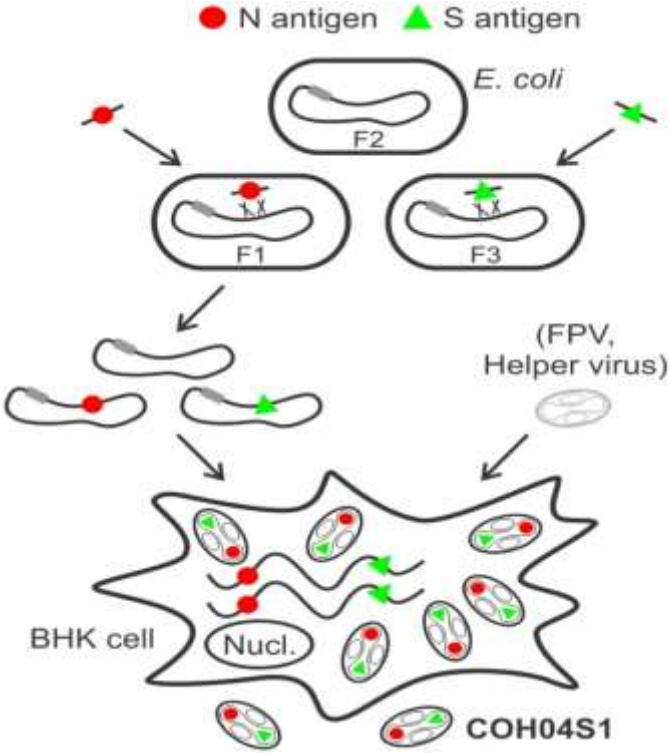
Chiuppesi et al., Nature Comm, 2020[10]

Development of COH04S1 (GEO-CM04S1): A synthetic dual antigen sMVA-based COVID-19 vaccine



- **Spike (S) full-length, Wuhan strain:**
  - **Main target of neutralizing antibodies**
  - **Co-dominant target of cellular immunity**

- **Nucleocapsid (N), Wuhan strain:**
  - **Co-dominant target of cellular immunity**
  - **Less prone to viral escape than S**
  - **Dominant target of ADCC**



Chiuppesi et al., Nature Comm, 2020[11]

Importance of Inclusion of Nucleocapsid (N) in Next Generation Covid Vaccines

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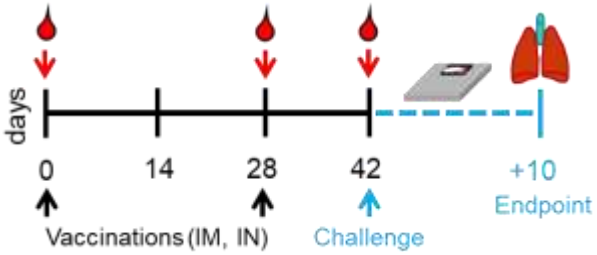
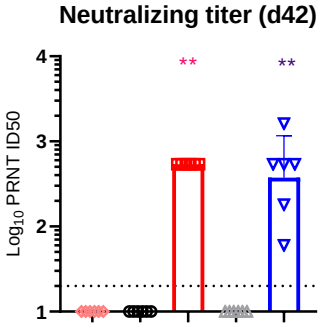
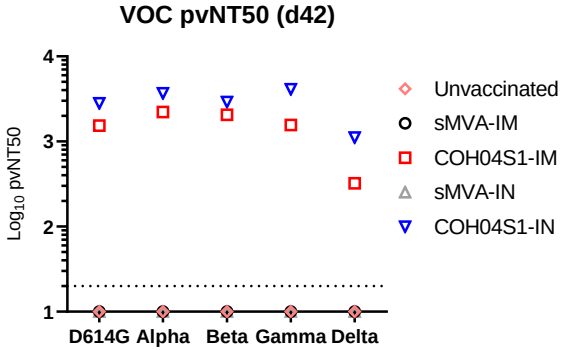
- **N-dependent protective function in animal models:**
  - *N-based vaccination reduced weight loss and viral load in both Syrian hamsters and k18-hACE2 mice*
  - *Combination of spike (S)-based and N-based vaccines confers superior acute protection in mouse lung and brain*
  - *mRNA-N vaccine induces modest control of SARS-CoV-2 in mice and hamsters*
  - *Combination of mRNA-S and mRNA-N conferred enhanced protection compared to mRNA-S alone against variants*

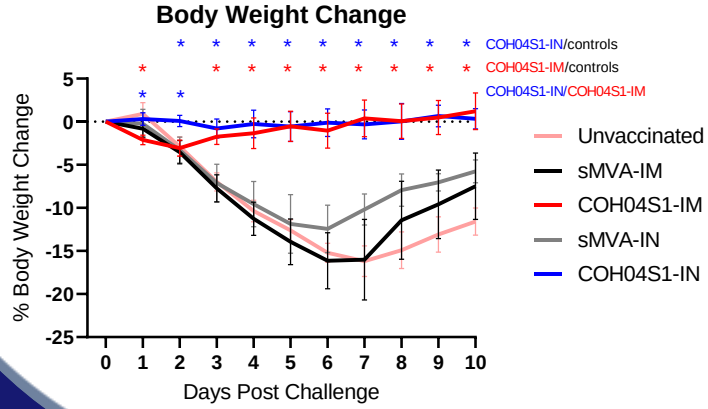
- **Importance of N in clinical studies:**
  - *N is the major target of antibody dependent NK cell activation (ADNKA)*
  - *N is a dominant target in terms of magnitude, breadth and is more sustained than responses to S, M, E*
  - *N-focused immunodominance in COVID-19 disease is associated with improved clinical outcomes*

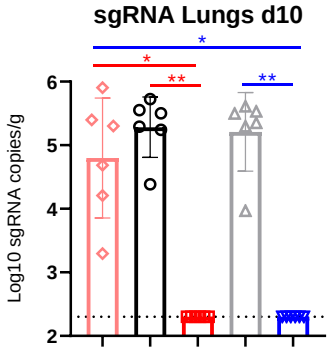
COH04S1 Protective Efficacy in Syrian Hamsters

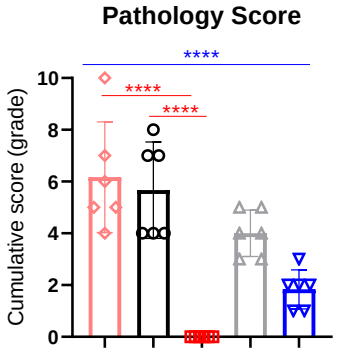












Chiuppesi et al., npj Vaccines 2022

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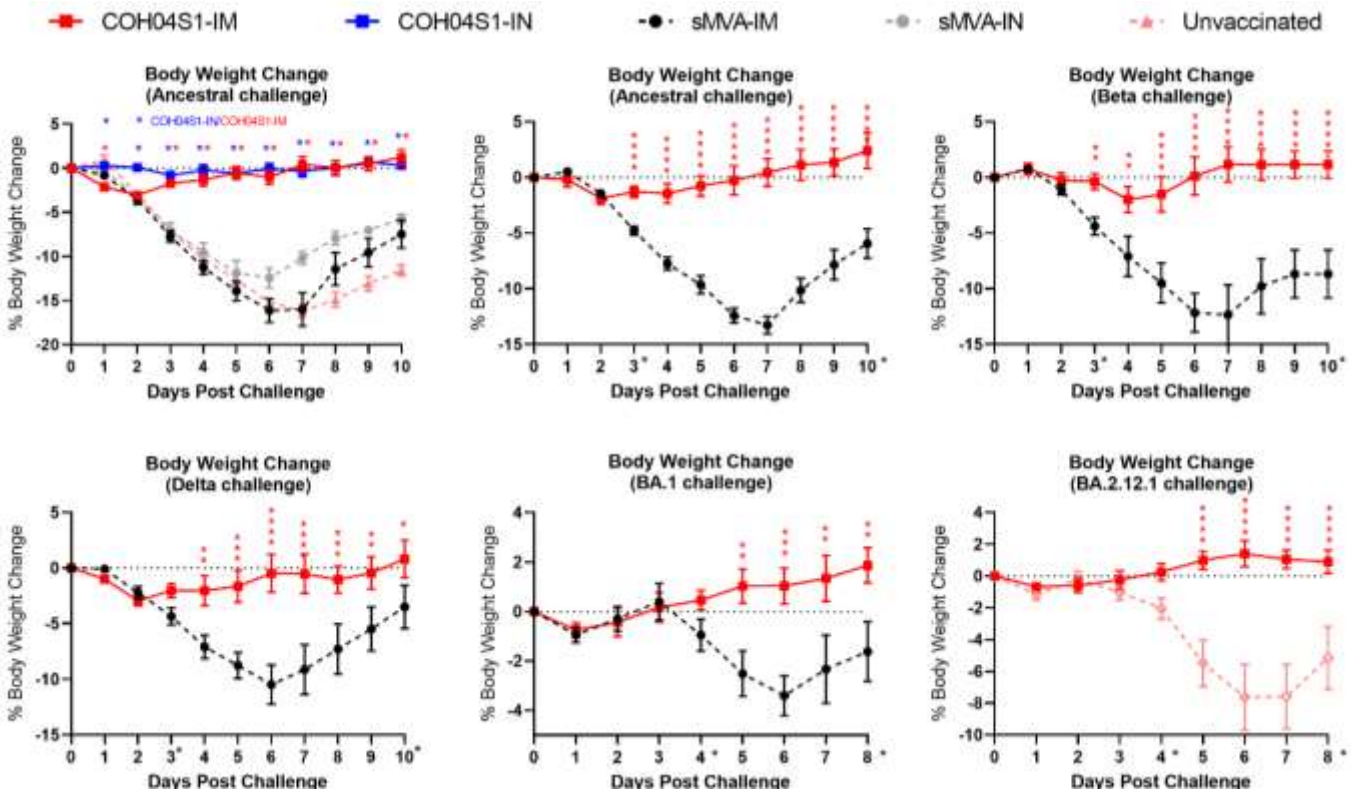
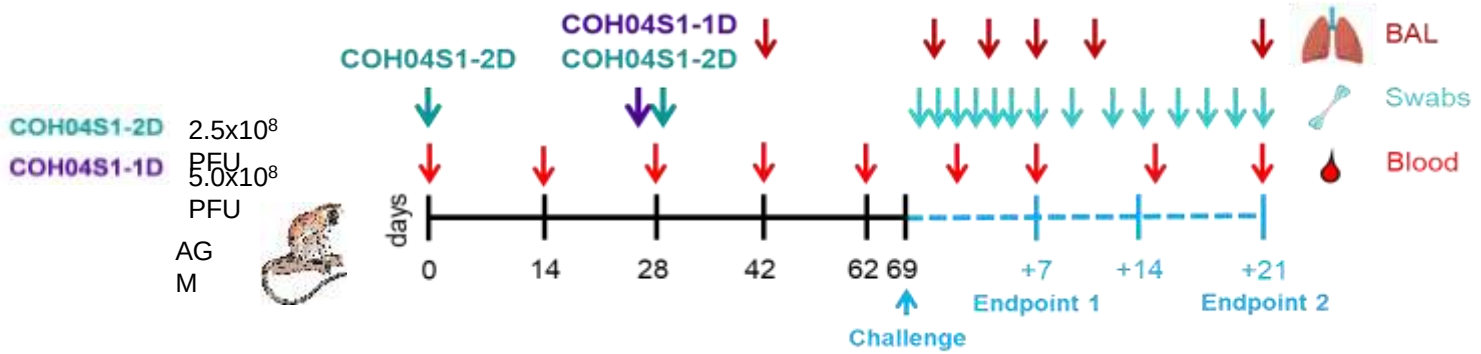
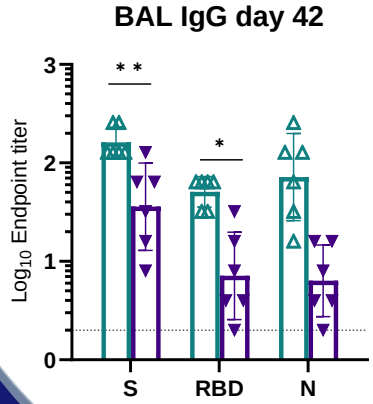
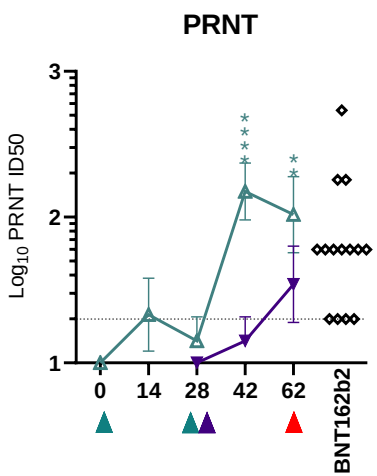
COH04S1 protective efficacy in Syrian hamsters

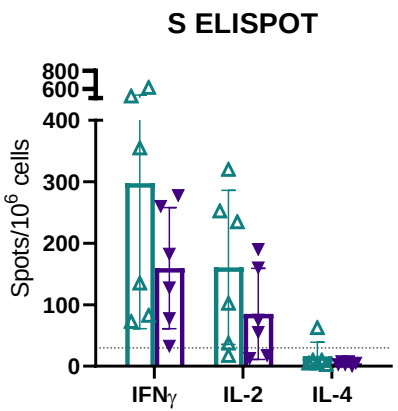


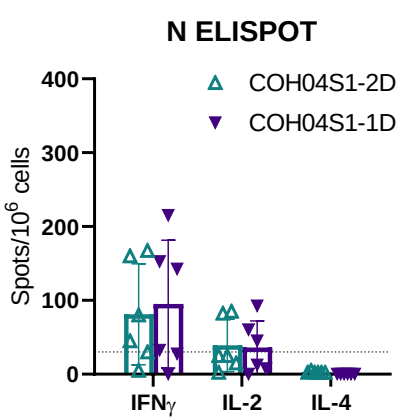
COH04S1 Vaccine Evaluation in NHP











Chiuppesi et al., npj Vaccines 2022

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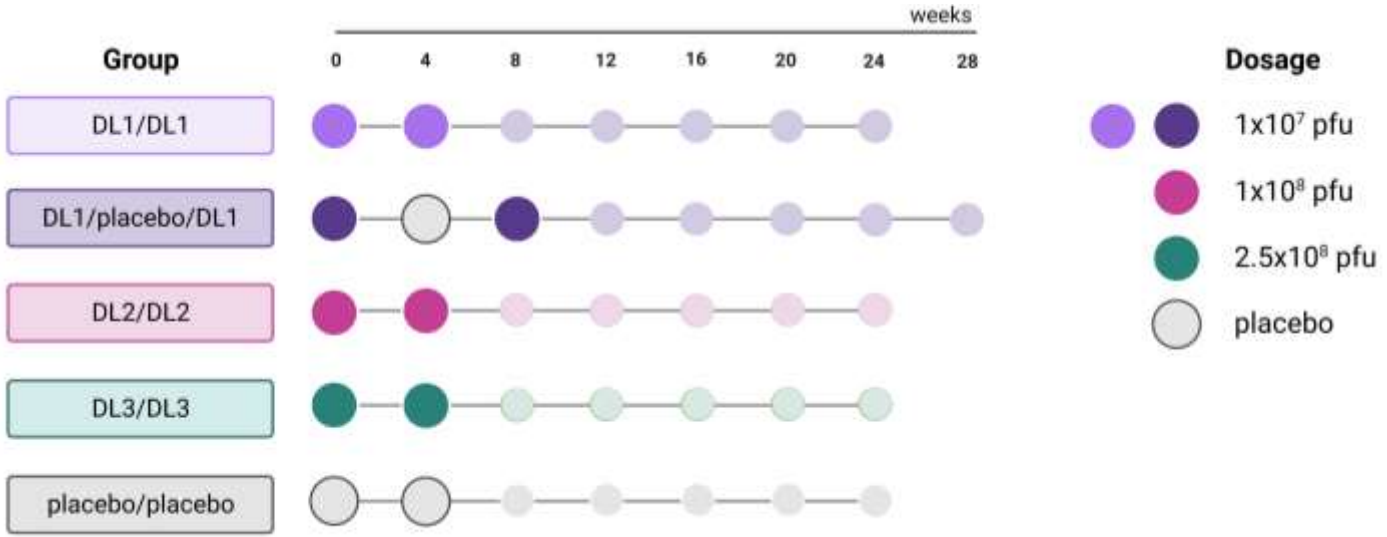
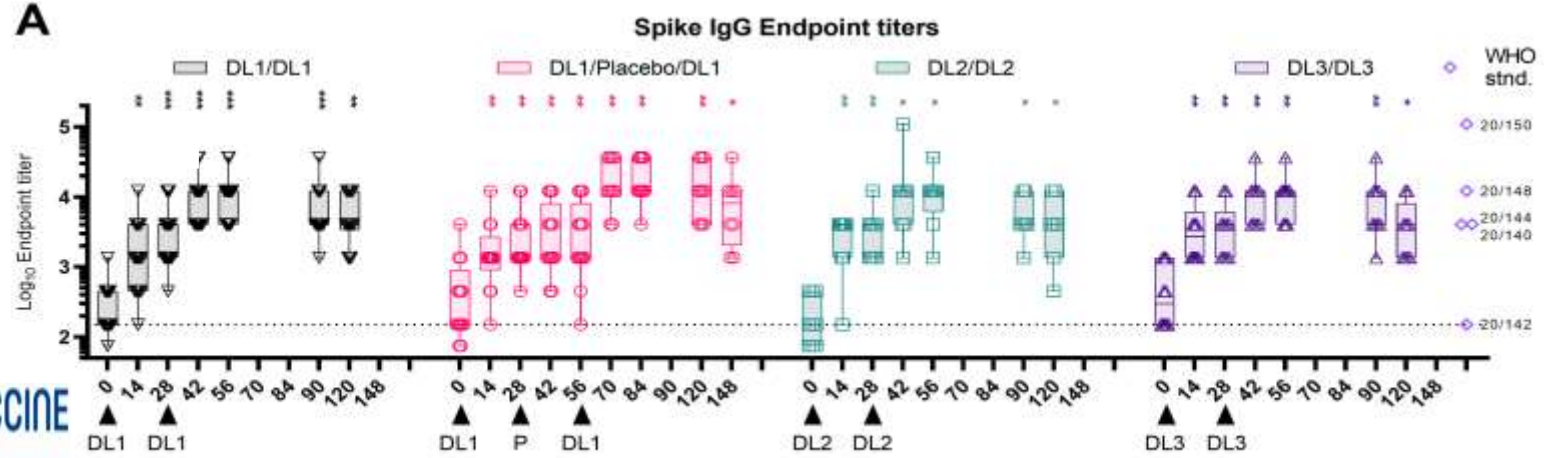
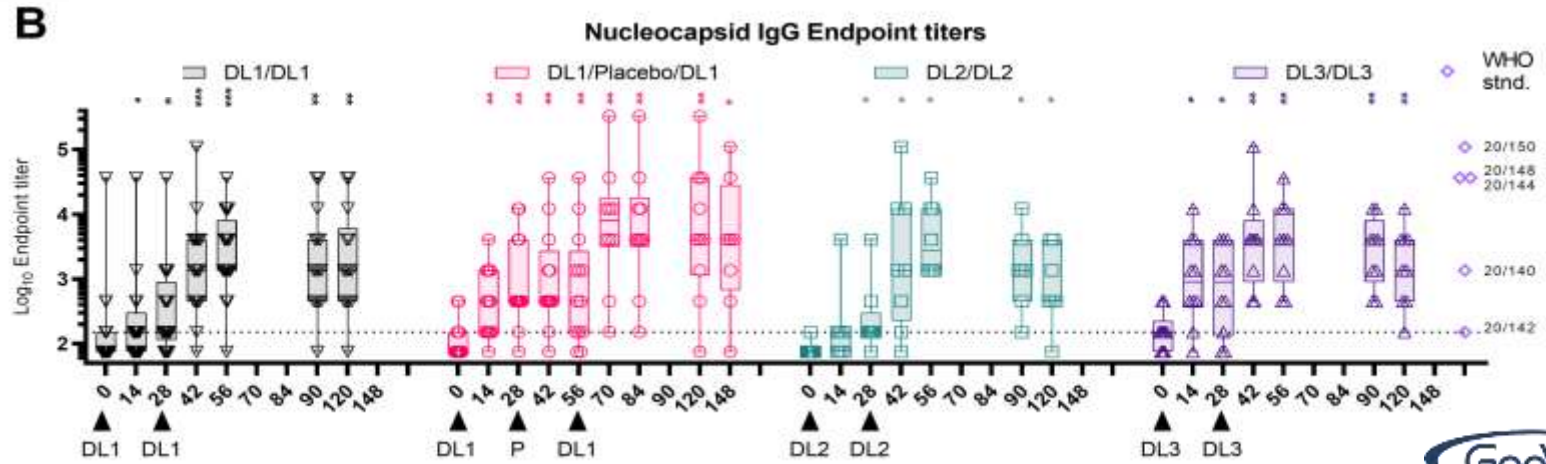
COH04S1 Phase 1 Clinical Trial in Healthy Adults: Design

- NCT04639466 (12/10/2020 started, 06/02/21 closed for accrual)
- 3 dose levels (DL1-3). 4-6 open-label sentinels at each DL. 35 randomized (DL/DL, DL/placebo, placebo/placebo)



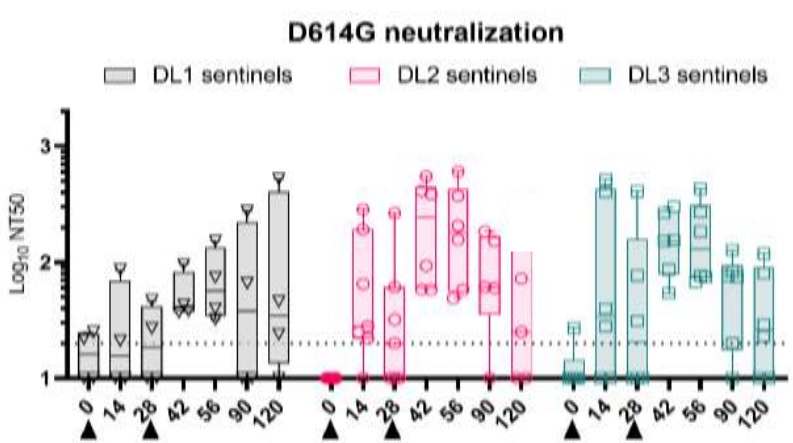
Phase 1 clinical trial: COH04S1-Induced Humoral Immunity



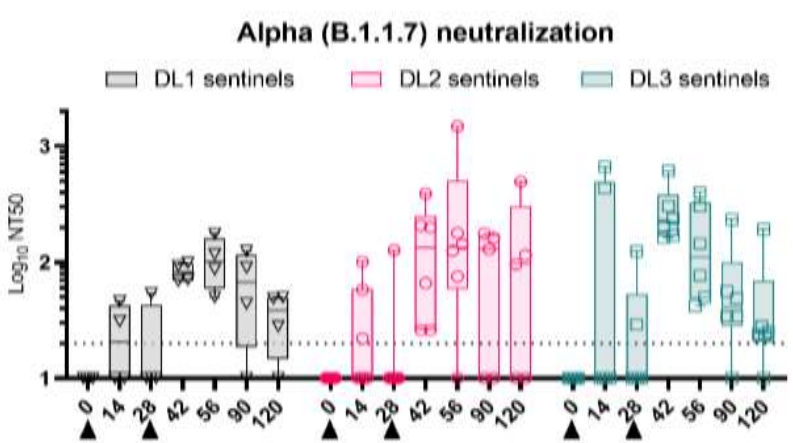


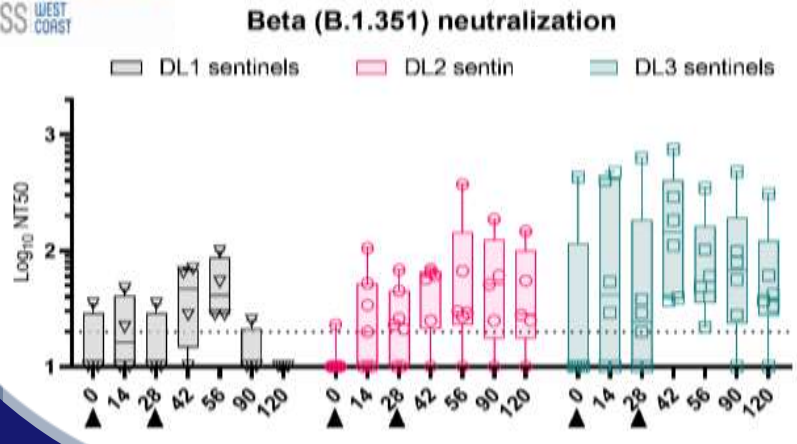
Chiuppesi et al., Lancet Microbe 2022

Phase 1 Clinical Trial: COH04S1 X-NAb Responses



B





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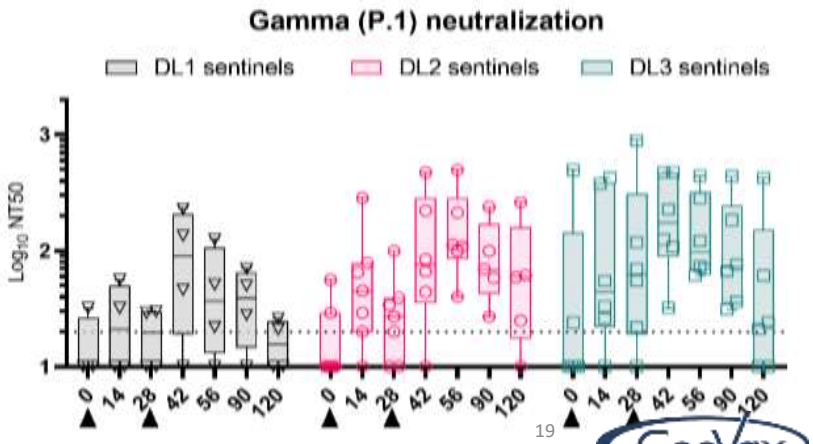

Chiuppesi et al., Lancet Microbe 2022

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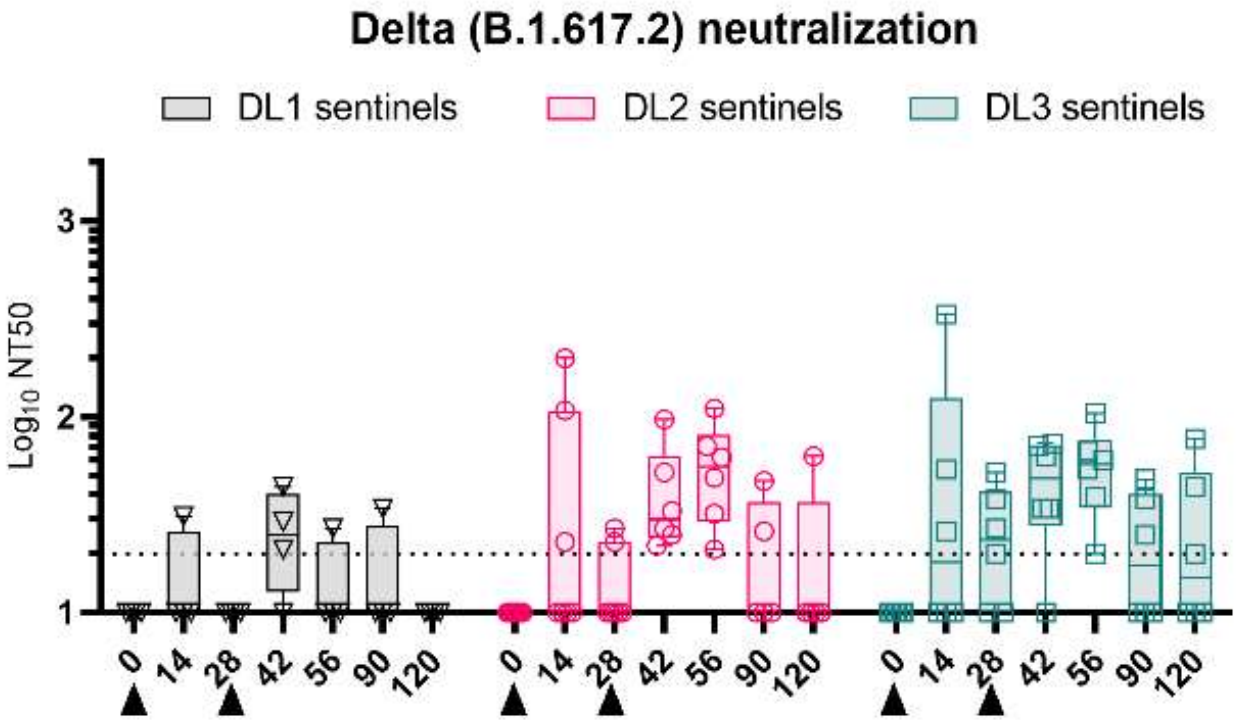
Phase 1 Clinical Trial: COH04S1 X-NAb Responses



Chiuppesi et al., Lancet Microbe 2022

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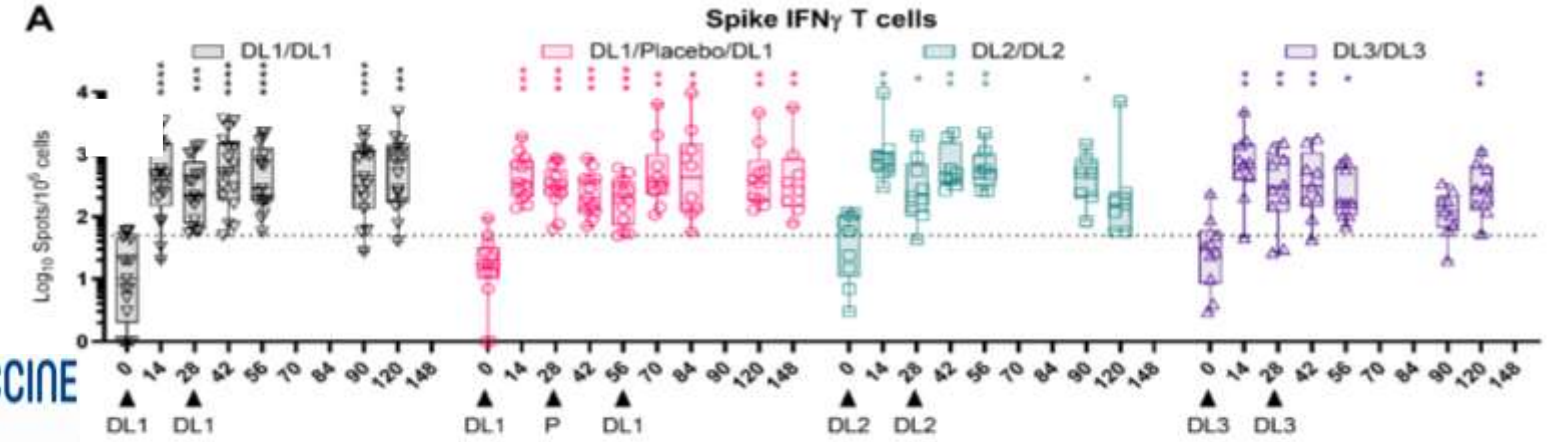
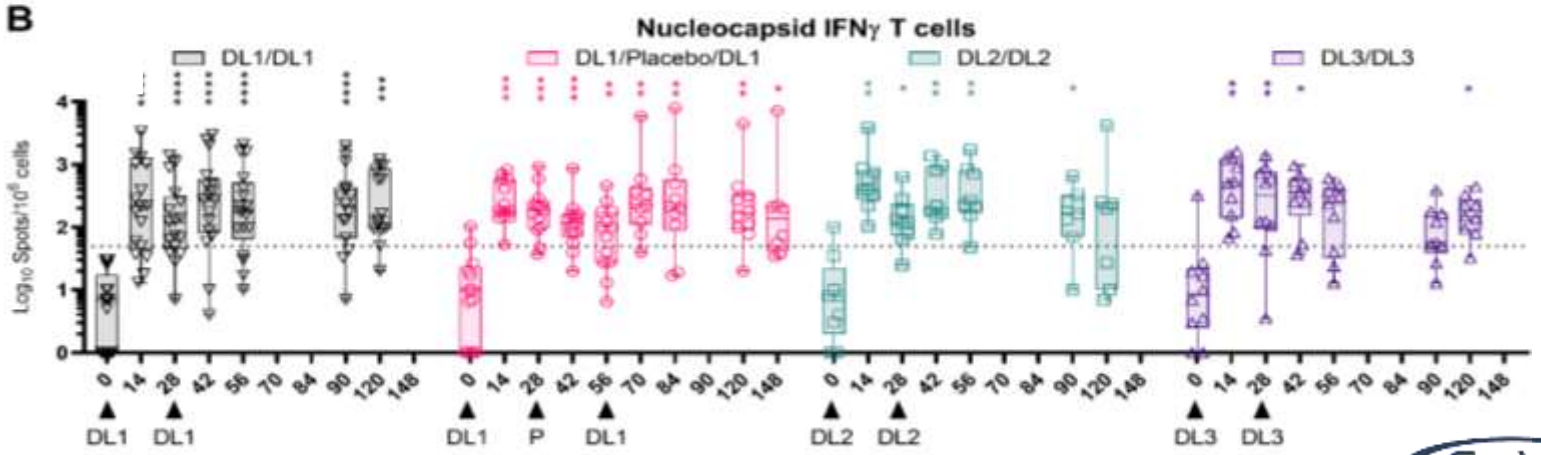
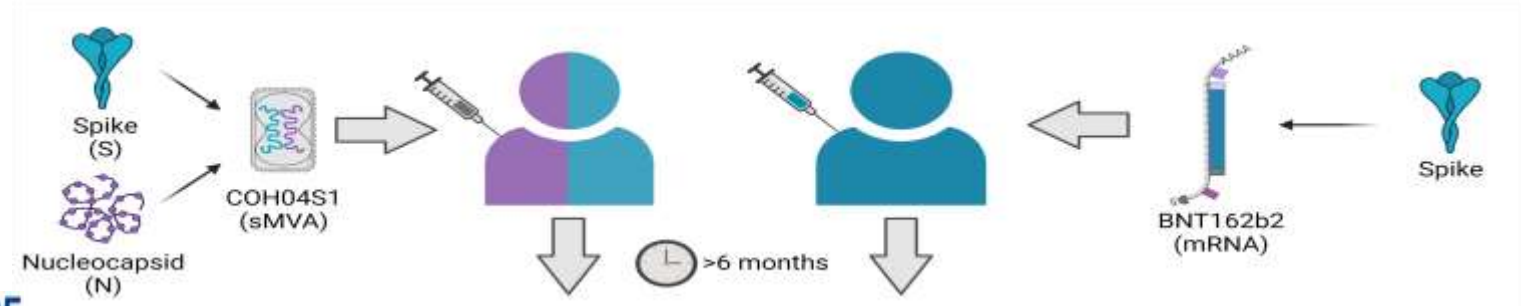
Phase 1 Clinical Trial: COH04S1-induced T Cell Response





Chiuppesi et al., Lancet Microbe 2022

COH04S1 vs. Comirnaty: Long-term Neutralizing Responses



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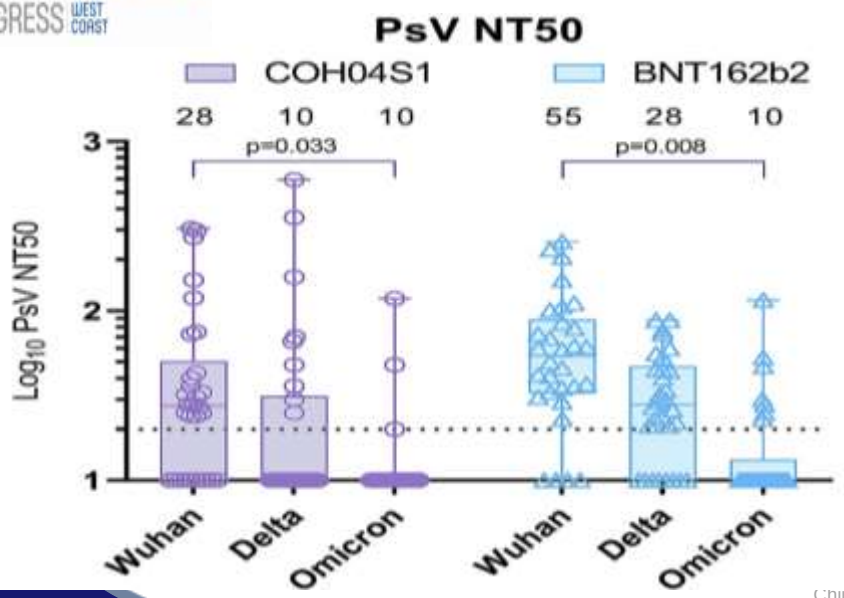

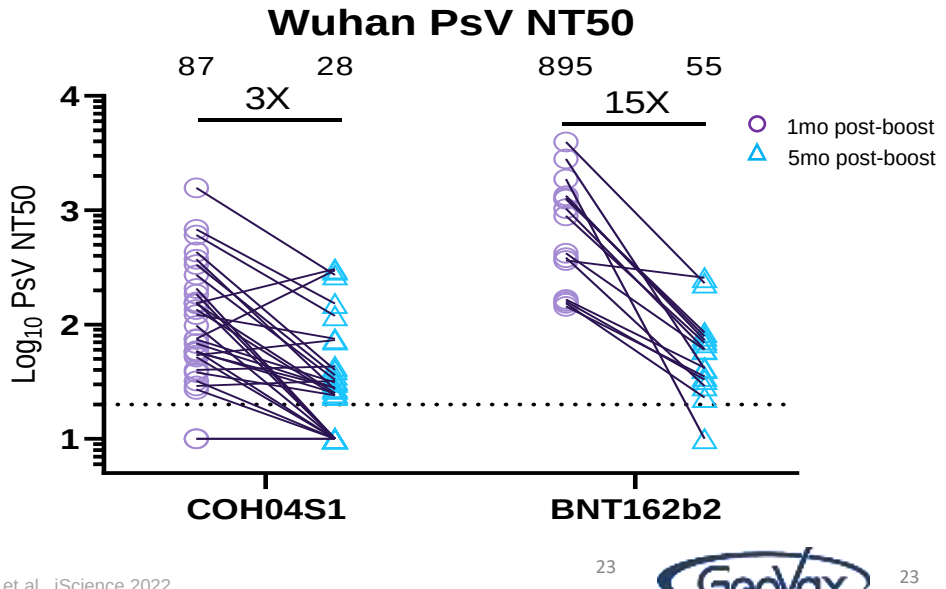

Chiuppesi et al., iScience 2022

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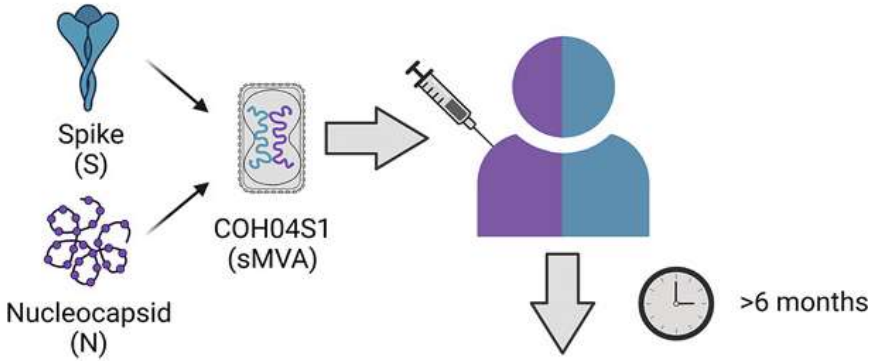
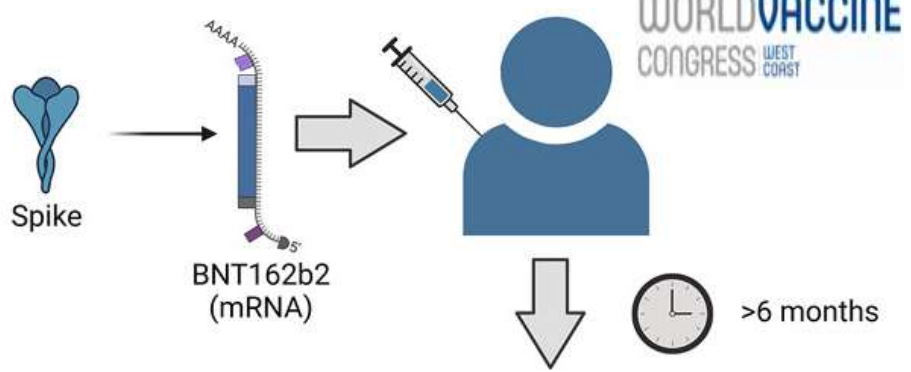
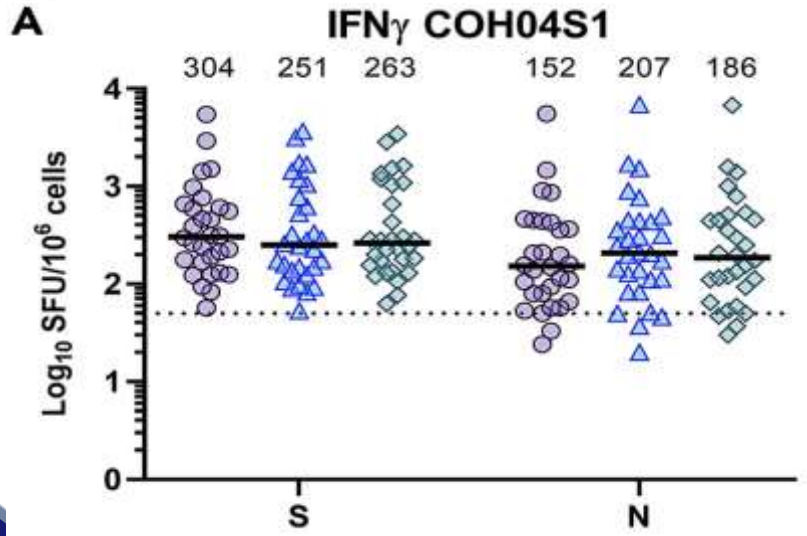
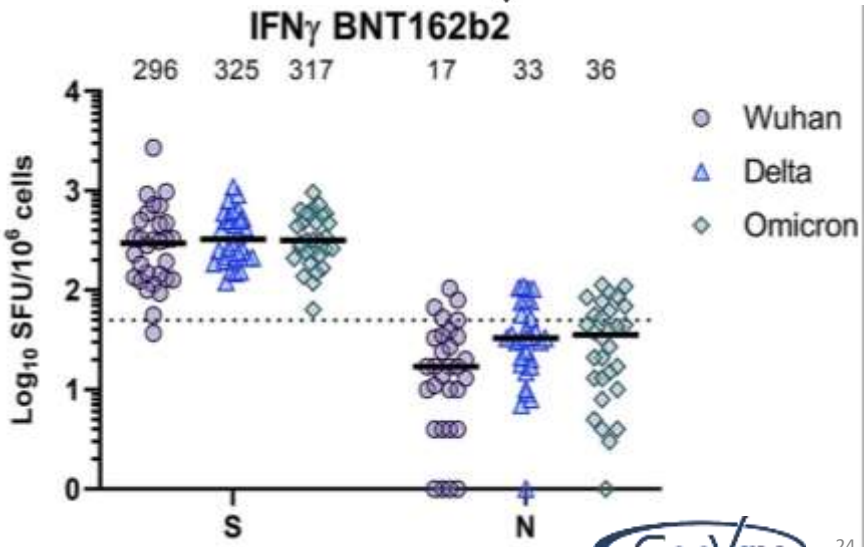
COH04S1 vs. Comirnaty: Long-Term Cellular Responses



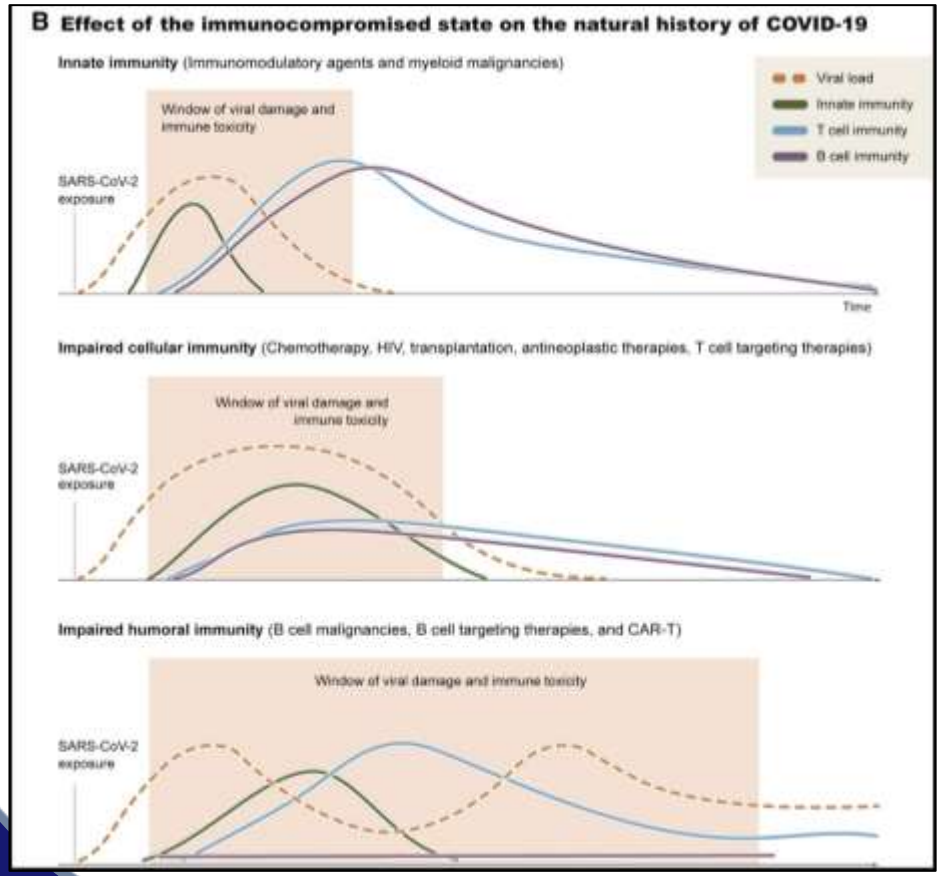






Chiuppesi et al., iScience 2022

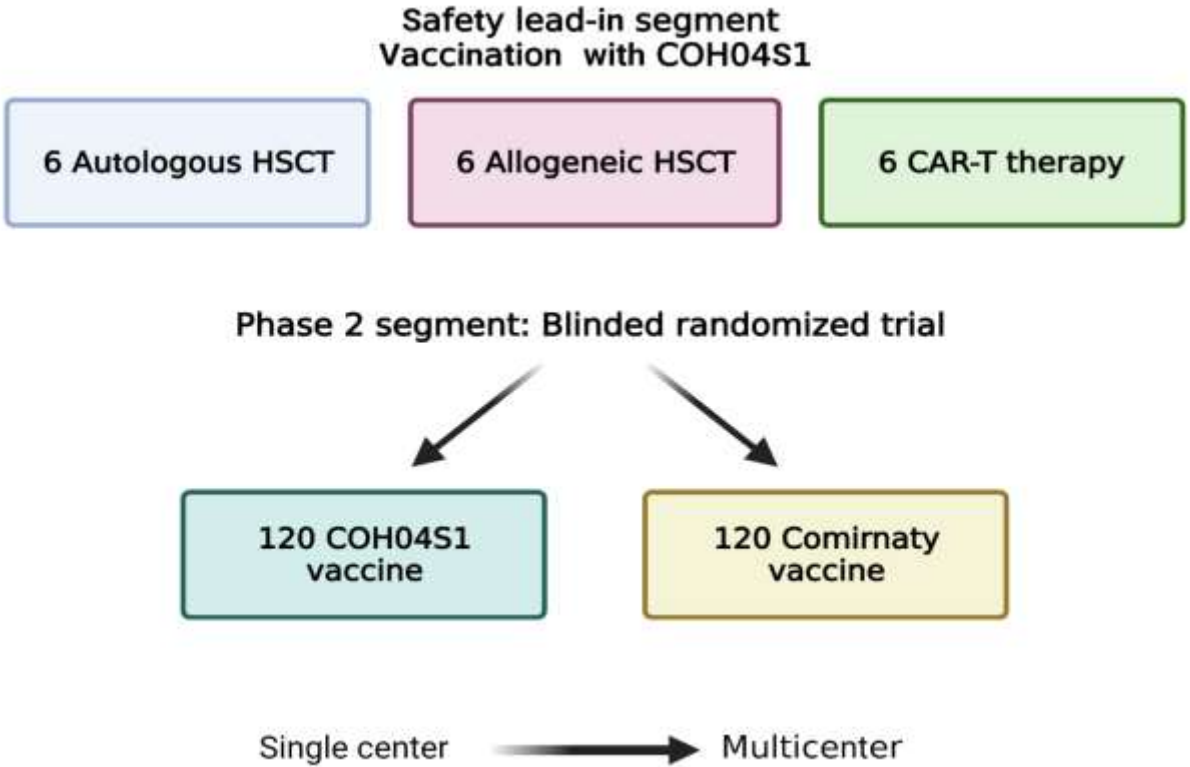
SARS-CoV-2 and Vaccination of the Immunocompromised



- **Immunocompromised individuals are at high risk for SARS-CoV-2 associated morbidity and mortality**
- **Use of Evusheld no longer authorized against new Omicron subvariants**
- **Paxlovid-resistance mutations may arise in the immunocompromised population**
- **Lower vaccine efficacy than in healthy adults**
- **CDC and ASTCT/ASH recommend 3 dose-primary series and one booster**

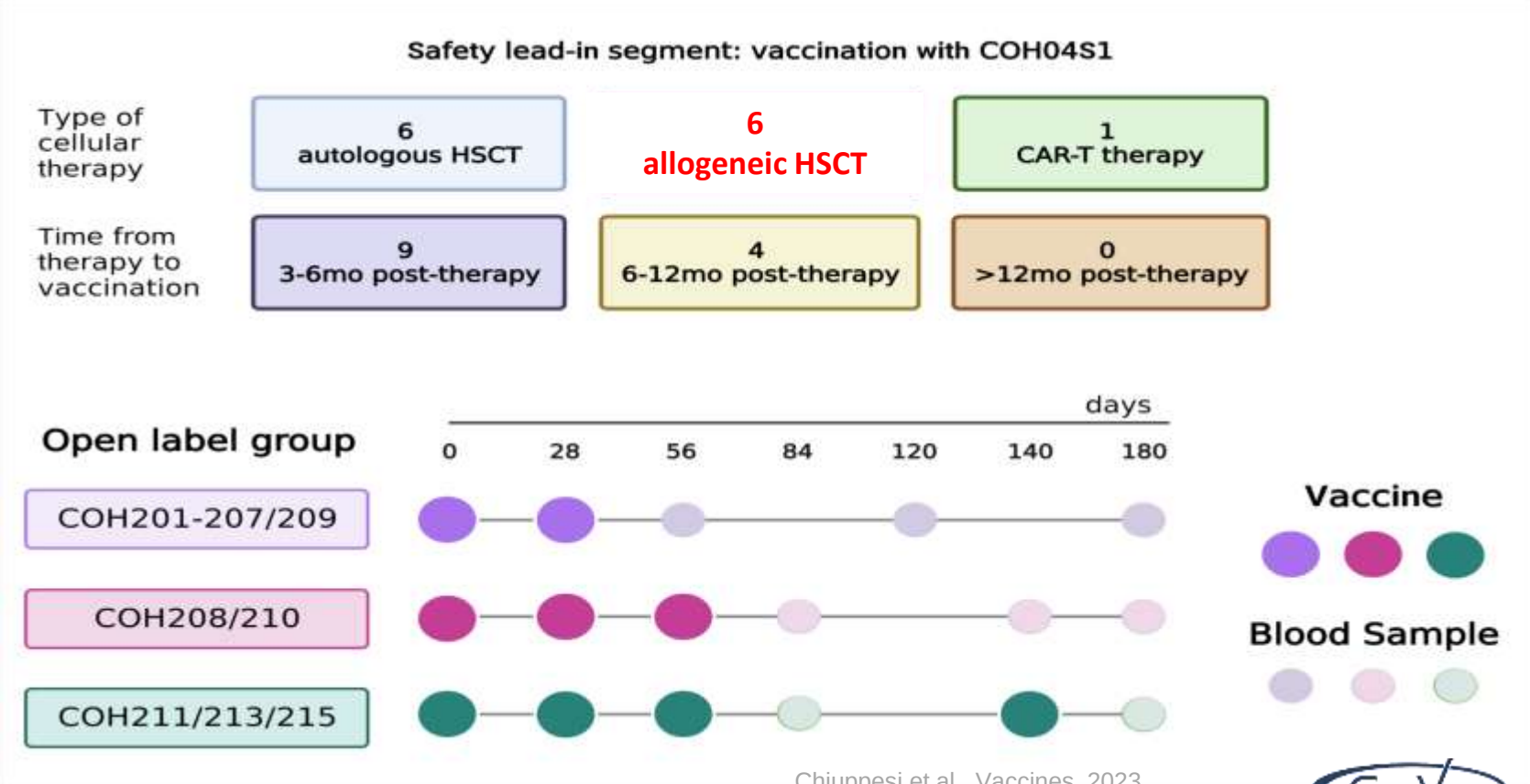
DeWolf et al., 2022 Immunity

COH04S1 in Cancer Patients post-HSCT/CT: Phase 2 Trial



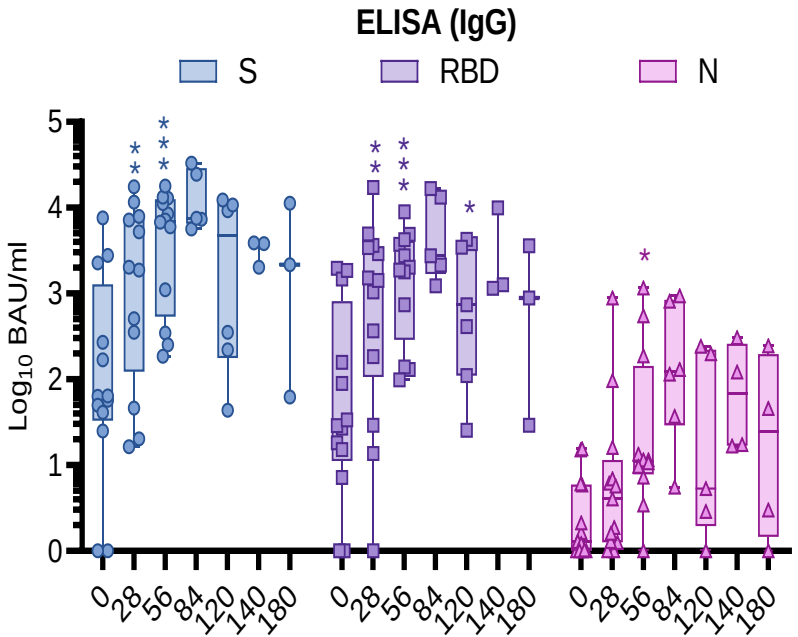
Chiuppesi et al., Vaccines 2023

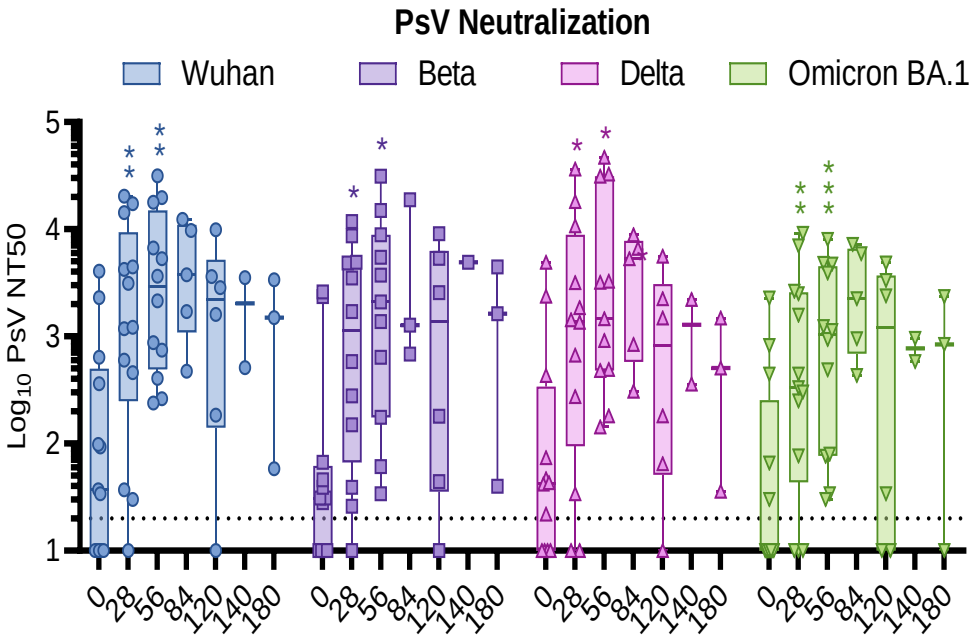
COH04S1 in Hem Malignancy post HSCT/CT: Open Label Portion



Chiuppesi et al., Vaccines, 2023

COH04S1 in Hem Malignancy post HSCT/CT: Humoral Response





Chiuppesi et al., Vaccines, 2023

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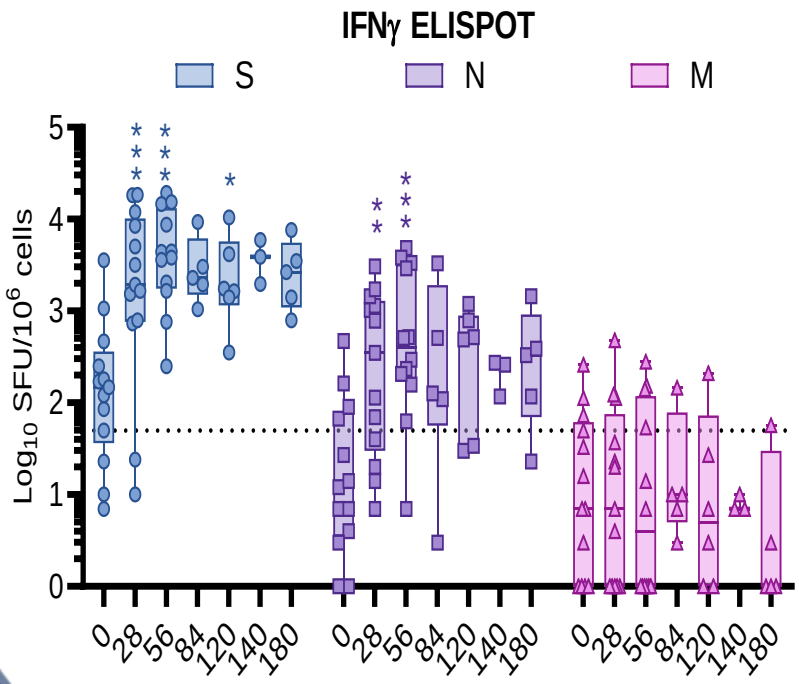
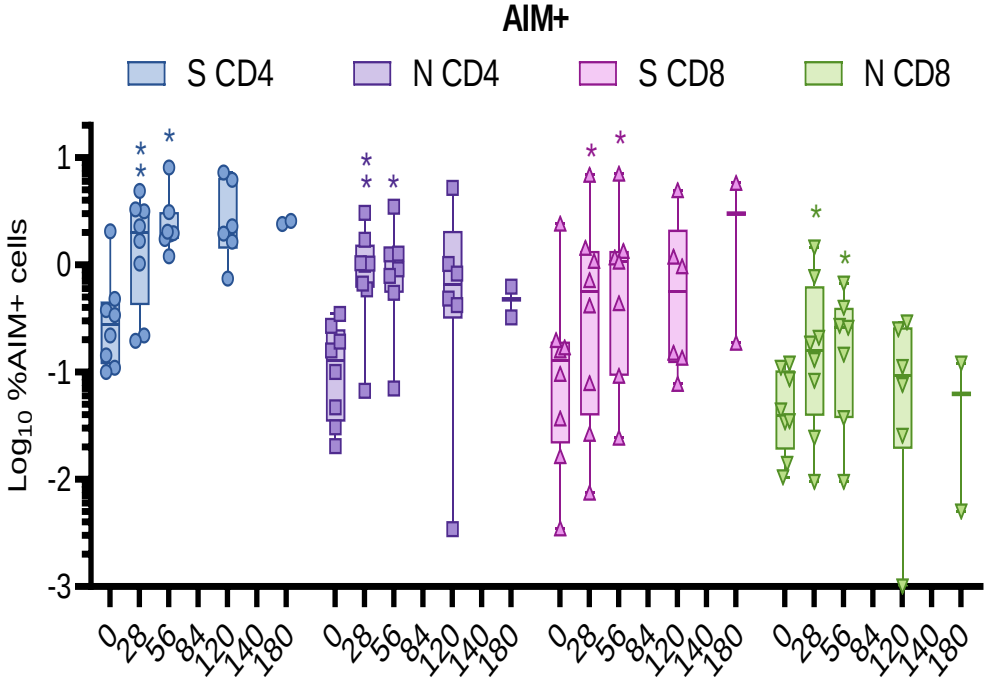
COH04S1 in Cancer Patients post HSCT/CT: T Cell Response





Chiuppesi et al., Vaccines, 2023

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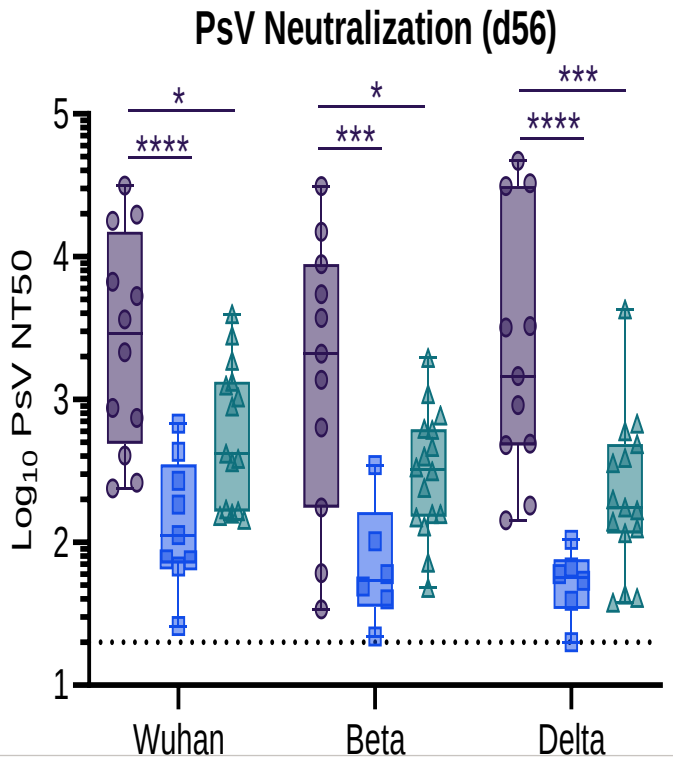
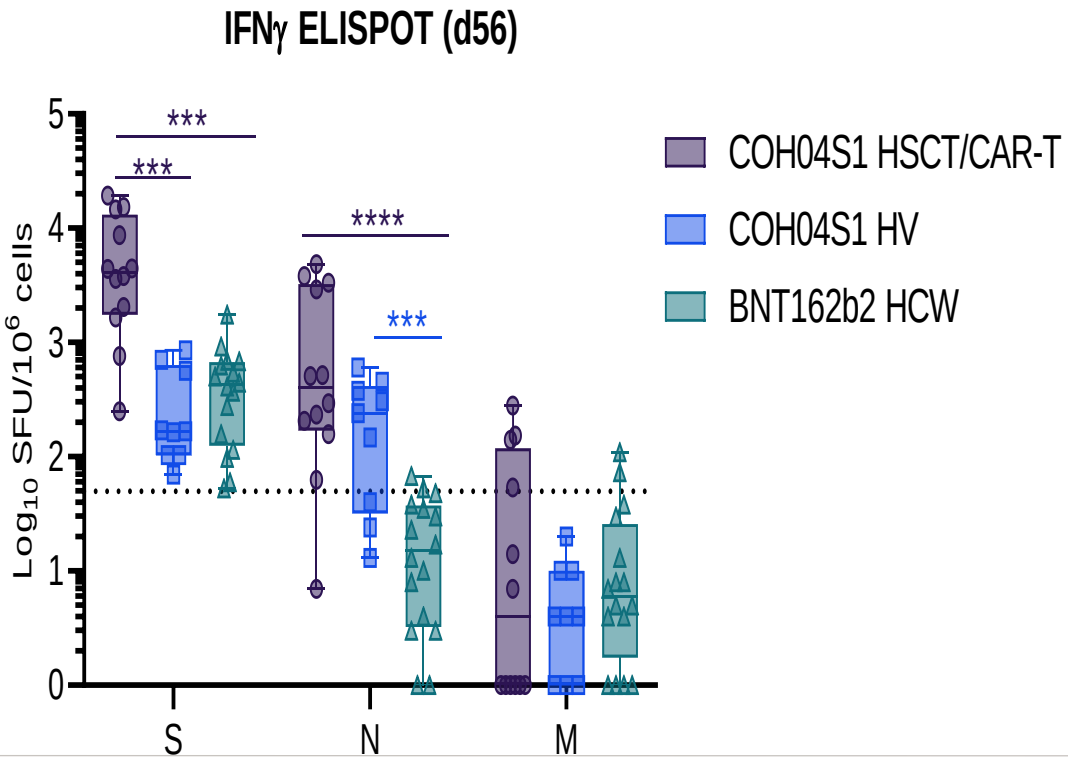
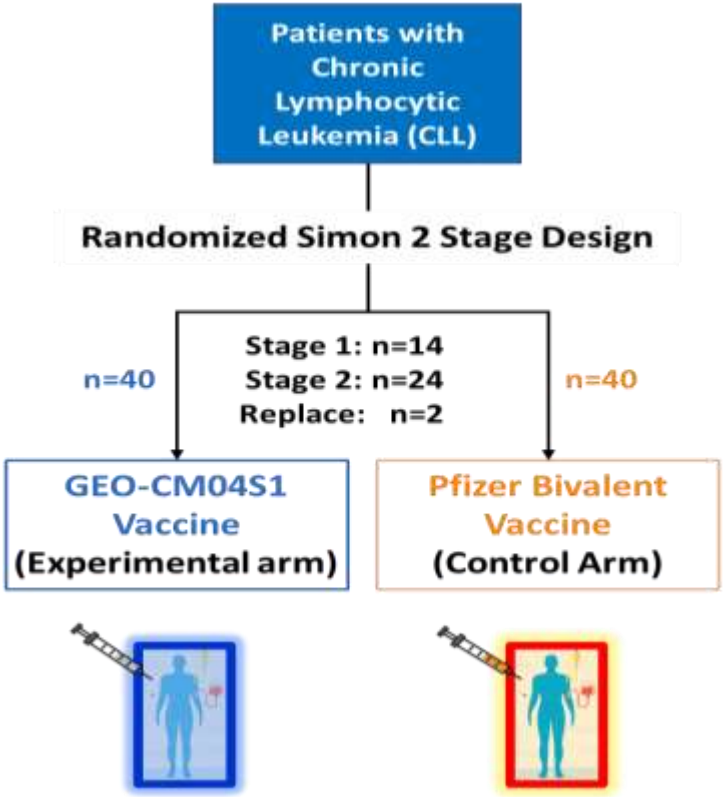
COH04S1 in HSCT/CT Patients and Healthy Volunteers: Comparison with Comirnaty-Vaccinated Healthcare Workers





Chiuppesi et al., Vaccines, 2023

COH04S1 vs Comirnaty in CLL Patients NCT05672355



- Phase 2 randomized, observer-blinded, single-center study
- ~80 pts will be randomized to each arm to receive GEO-CM04S1 or Pfizer Bivalent vaccine
- Simon 2 Stage design
  - **Stage 1:** 14 pts per arm
  - **Interim Analysis:** If ≥4 pts in an arm has a T cell response, proceed to Stage 2
  - **Stage 2:** 24 more pts per arm
  - **Final Analysis:** If ≥12 pts in an arm has a T cell response, the arm is deemed promising. If both arms are promising, employ a Bayesian “pick-the-winner” analysis
- Total Accrual expected to be 80 pts in 1 yr
- Pt follow-up is 1 yr
- Study duration: 2 yrs

Study Rationale

- Chronic lymphocytic leukemia (CLL) is a malignancy of B-lymphocytes. Patients with CLL are immunocompromised, at high risk of severe COVID-19, and respond poorly to mRNA COVID-19 vaccines.
- The GEO-CM04S1 COVID-19 vaccine uses a synthetic form of the Modified Vaccinia Ankara (MVA) viral vector invented at City of Hope (F. Wussow) that is highly immunogenic in post-transplant patients who are also immunocompromised (e.g. CMV-Triplex and GEO-CM04S1)
- The GEO-CM04S1 vaccine targets SARS-CoV-2 Spike and Nucleocapsid
- The GEO-CM04S1 vaccine induces robust T cell immunity in patients post-transplant which is important in patients whose Ab response is diminished

Primary Objective

Estimate the T cell-based immune response rate on day 56 post-injection of GEO-CM04S1 vaccine boost administered at $2.5x10^8$ PFU or Pfizer-BioNTech Bivalent/Monovalent vaccine administered as standard of care.

GEO-CM04S1

Summary

- GEO-CM04S1 was highly immunogenic and protective in animal models
- GEO-CM04S1 induced robust humoral and cellular immunity to Spike and Nucleocapsid in healthy adults
- Spike- and Nucleocapsid-specific T cells maintain cross-reactivity to variants of concern
- GEO-CM04S1 is highly immunogenic in patients post-HSCT
- GEO-CM04S1 is being tested in three phase 2 clinical trials in healthy volunteers and cancer patients post-HSCT
- GEO-CM04S1 is the most clinically advanced MVA-based COVID-19 vaccine

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  - **Quality control**
  - **Regulatory Affairs**
  - **Business Development**
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…and most of all, thanks to our volunteers

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