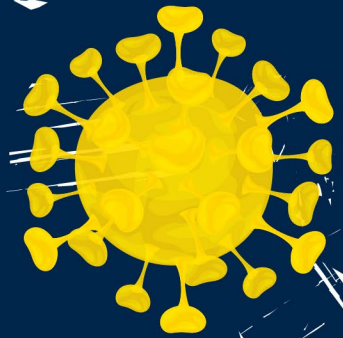
CROI ICAR AWARDS 2024

CROI Affiliated Event for
Italian Young Investigators



CHAIRS:
F. Kirchhoff
(Ulm, Germany, EU)
D. Margolis
(Chapel Hill, North Carolina, USA)

Denver, Colorado
March 4th, 2024
h 06.00 - 07.30 pm

CROI 31st CONFERENCE ON
Retroviruses and **Opportunistic Infections**
MARCH 3-6 2024 DENVER, COLORADO

ICAR 16th NATIONAL CONGRESS
Italian Conference on **AIDS** and **Antiviral Research**
JUNE 19-21 ROME, ITALY

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CHAIRS: F. Kirchhoff (Ulm, Germany, EU), D. Margolis (Chapel Hill, North Carolina, USA)

Immune responses to an original–BA.4/5 booster of SARS-CoV-2 mRNA vaccine in people living with HIV on antiretroviral therapy

Matteo Augello, M.D.
Clinic of Infectious Diseases and Tropical Medicine,
San Paolo Hospital, ASST Santi Paolo e Carlo,
Department of Health Sciences, University of Milan

Mentor: Prof. Giulia Marchetti

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Background

- Variant-adapted bivalent mRNA vaccines have been recommended especially in vulnerable populations to address the waning immunity and the emergence of immune-escaping SARS-CoV-2 variants.
- Unexpectedly, several studies reported that neutralizing antibody levels against omicron BA.4/5 and subsequent variants were lower than neutralizing antibody responses against the wild-type (WT) strain after a bivalent booster, and not discernibly better than after a monovalent original one, suggesting *immunologic imprinting* to the ancestral virus.
- However, data on immune responses to such vaccines in people living with HIV (PLWH) are limited.

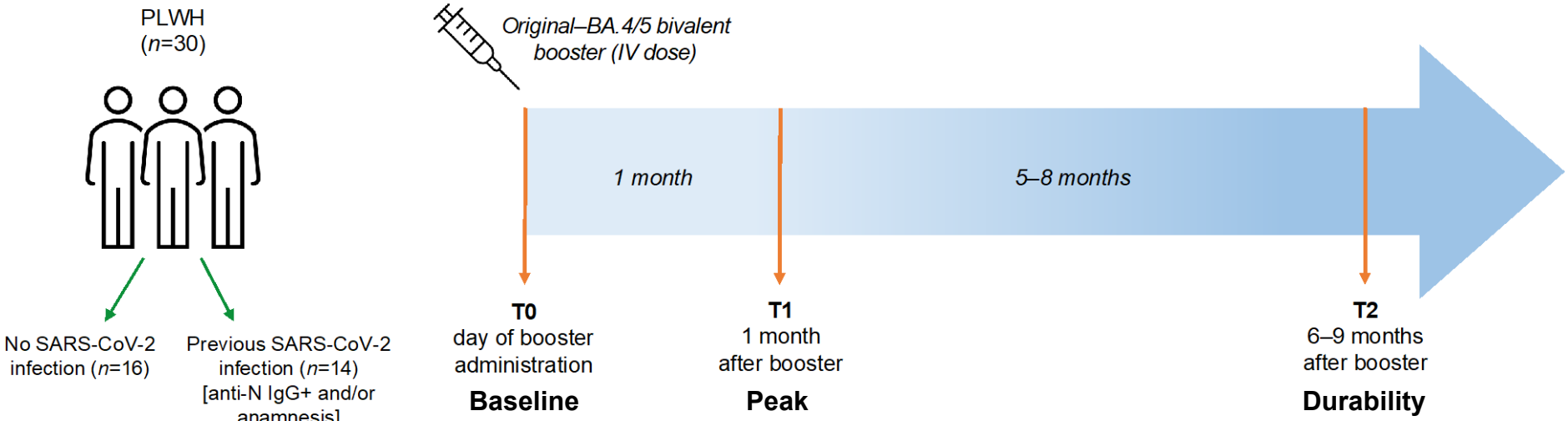
Collier A, et al. NEJM 2023
Wang Q, et al. NEJM 2023
Davis-Gardner, et al. NEJM 2023

Study aims

1. To assess *peak* and *durability* of cellular and humoral responses to an original–BA.4/5 bivalent mRNA booster in PLWH on effective antiretroviral therapy (ART)

2. To evaluate the role of previous SARS-CoV-2 infection in modulating vaccine-induced immune responses

Methods



Immune parameters
SARS-CoV-2–specific T cells → flow cytometry
SARS-CoV-2–specific B cells → flow cytometry
RBD-binding antibodies → ELISA
RBD-blocking antibodies → RBD-ACE2 binding inhibition assay

Statistical analyses → Kruskall-Wallis with Dunn's multiple comparisons test and Wilcoxon test

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Study population

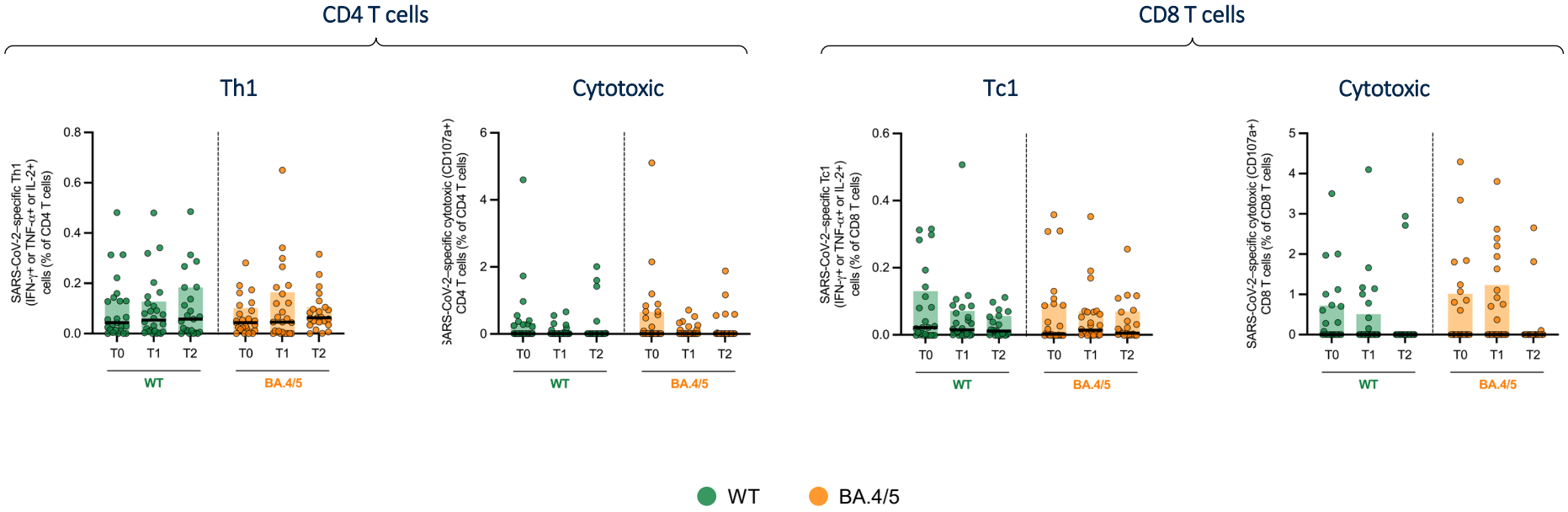
Characteristics	PLWH (*n*=30)
Age, years, median (IQR)	51 (42–55)
Sex, *n* (%)	
Male	27 (90)
Female	3 (10)
Ethnicity, *n* (%)	
Caucasian	26 (86.7)
Latin	2 (6.7)
African	1 (3.3)
Asian	1 (3.3)
Epidemiology	
MSM	16 (53.3)
MSW	6 (20)
WSM	3 (10)
IDU	3 (10)
Unknown	2 (6.7)
Comorbidities, *n* (%)	
None	6 (20)
Hypertension	10 (33.3)
Ischemic heart disease	1 (3.3)
Non-ischemic heart disease	1 (3.3)
Peripheral vascular disease	1 (3.3)
Chronic kidney disease	1 (3.3)
Liver disease	5 (16.7)
Previous viral hepatitis (HBV/HCV)	11 (36.7)
Asthma	1 (3.3)
Neurologic disease	4 (13.3)
Gastrointestinal disease	6 (20)

Original–BA.4/5 bivalent booster administered as fourth vaccine dose at a median time of 15 months from third (monovalent) vaccine dose

Viro-immunologic parameters, median (IQR)	
CD4 *nadir*, cells/μL	277 (115–558)
Current %CD4	34 (28–39)
Current CD4, cells/μL	790 (598–929)
Current %CD8	42 (36–48)
Current CD8, cells/μL	952 (771–1151)
Current CD4/CD8 ratio	0.78 (0.59–1.1)
Current HIV-RNA, copies/mL	<20
Previous AIDS diagnosis, *n* (%)	7 (23.3)
Time from HIV diagnosis, months, median (IQR)	160 (85–259)
Current cART regimen, *n* (%)	
INSTI-based triple	16 (53.3)
INSTI-based dual	11 (36.7)
NNRTI-based triple	3 (10)
Duration of cART, months, median (IQR)	134 (65–187)

Legend: IQR, interquartile range; MSM, men who have sex with men; MSW, men who have sex with women; WSM, women who have sex with men; IDU, injective drug use; INSTI, integrase strand-transfer inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor

The original–BA.4/5 booster does not increase the frequency of SARS-CoV-2–specific Th1/Tc1 and cytotoxic CD4/CD8 T cells against WT and BA.4/5, which are similar at all time-points and stable for 9 months



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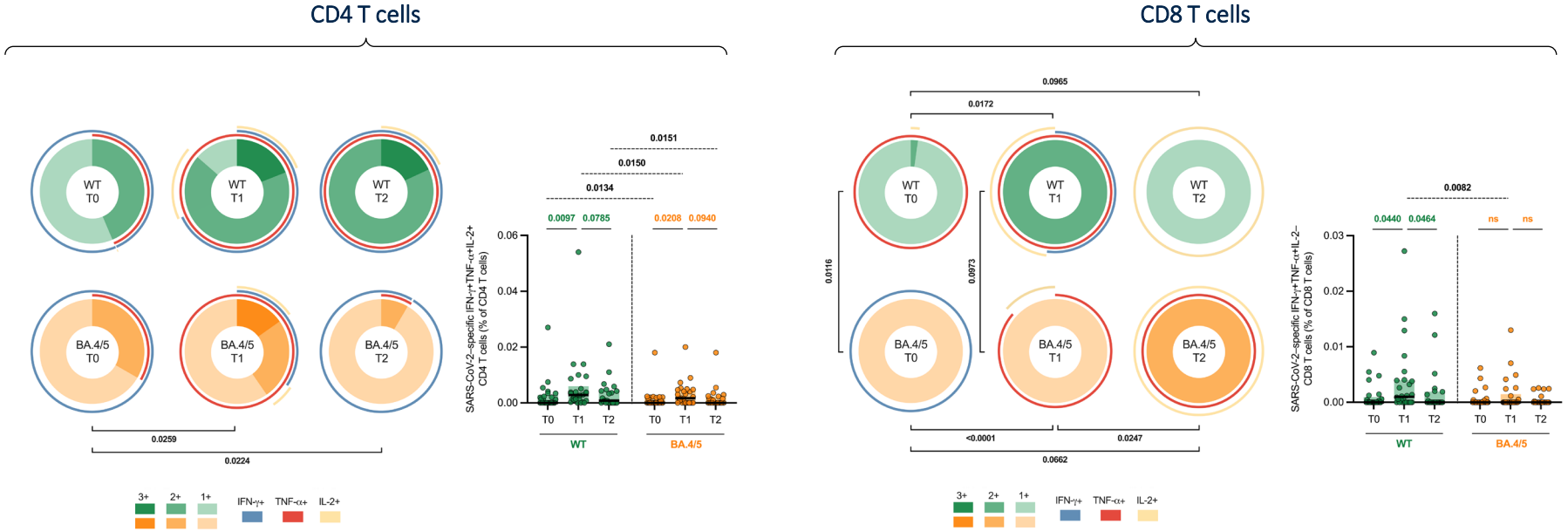
The original–BA.4/5 booster transiently increases polyfunctionality of Th1/Tc1 cells reactive against both WT and BA.4/5; however, polyfunctional Th1/Tc1 cells are higher against WT than BA.4/5



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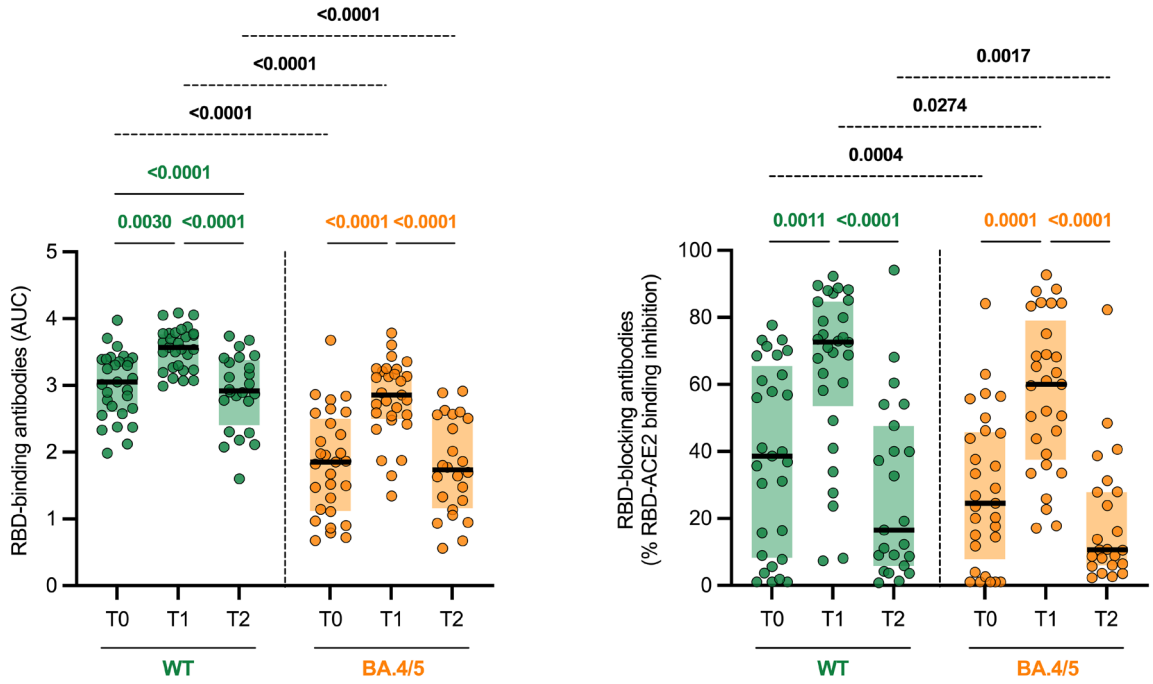
The original–BA.4/5 booster transiently increases levels of RBD-binding and RBD-blocking antibodies against both WT and BA.4/5; WT-reactive antibodies are higher than BA.4/5-reactive ones



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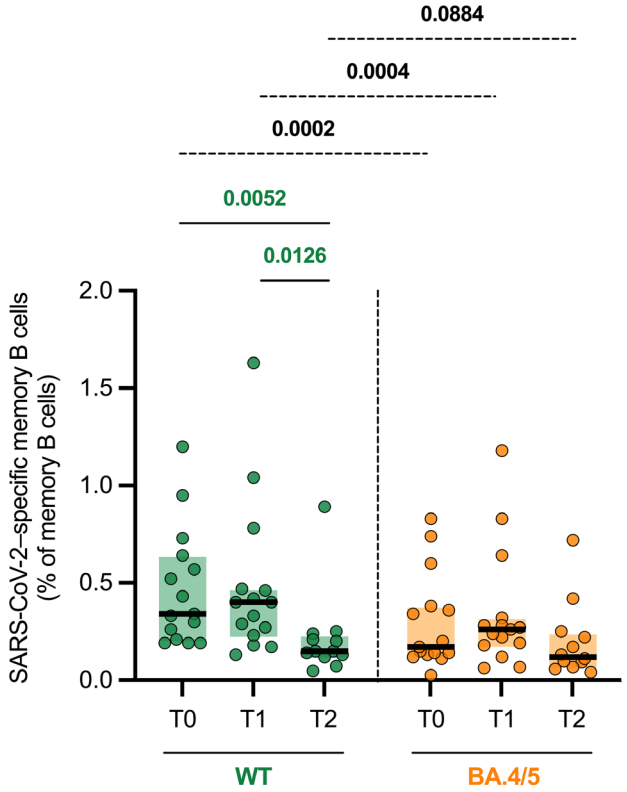
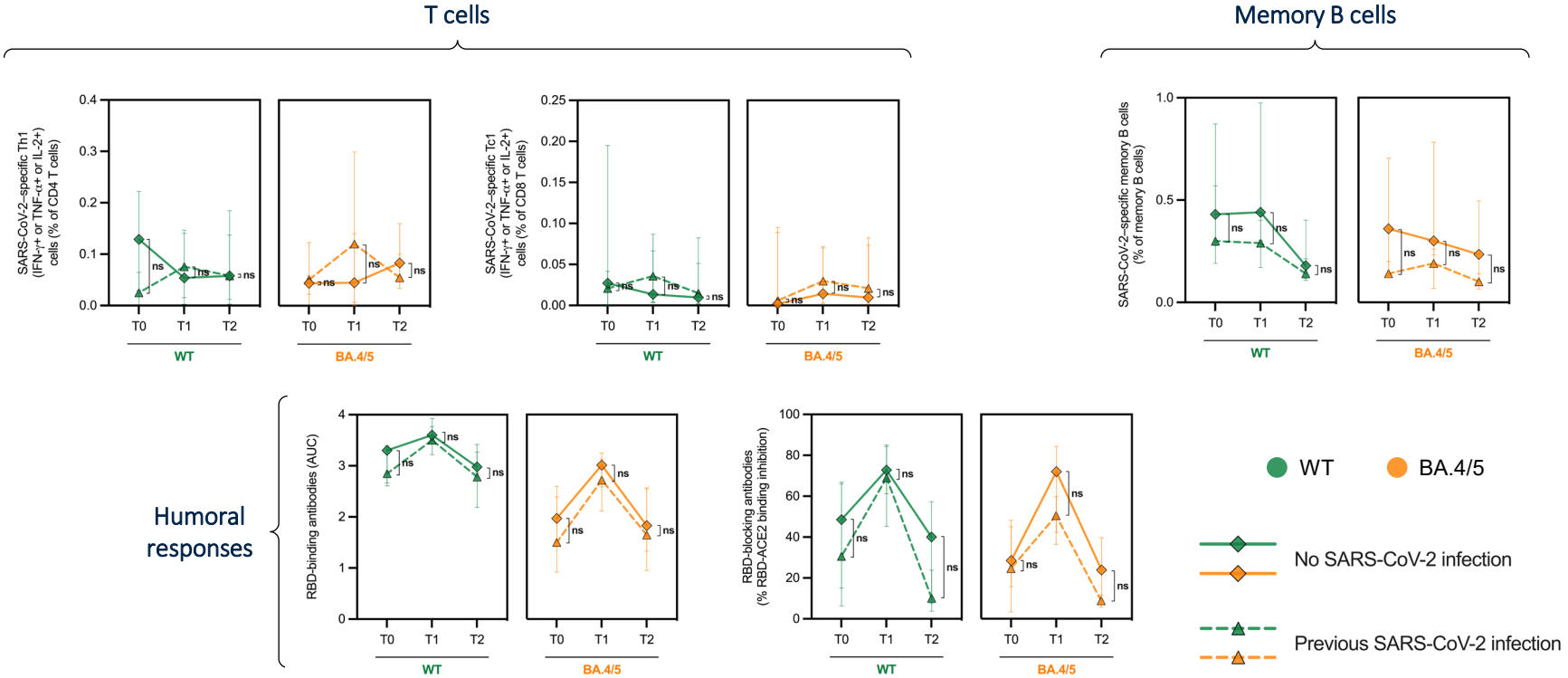
The original–BA.4/5 booster does not increase the frequency of SARS-CoV-2–specific memory B cells reactive against WT and BA.4/5; WT-reactive memory B cells are higher than BA.4/5-reactive ones



WT BA.4/5

SARS-CoV-2–specific cellular and humoral responses to bivalent booster does not significantly differ according to previous SARS-CoV-2 infection



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Conclusions

- The original–BA.4/5 bivalent mRNA booster is able to transiently increase humoral and polyfunctional T cell responses towards both wild type and omicron BA.4/5 virus in PLWH on effective ART, irrespective of previous SARS-CoV-2 infection, thus providing additional protection against both infection and severe disease.

- While T cell responses are cross-reactive against viral variants and stable over time, hence ensuring long-lasting protection from severe disease, humoral responses are strikingly imprinted to the ancestral virus and wane quickly, pointing to less durable protection against infection.

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**Infectious Diseases Lab,
Department of Health Sciences,
University of Milan,
Milan, Italy**

Valeria Bono
Roberta Rovito
Sabrina Marozin
Camilla Tincati
Giulia Marchetti

**ICONA Foundation,
Milan, Italy**

Alessandro Tavelli
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Antonella d'Arminio Monforte

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