17º CONGRESO BARCELONA
SCT BCN
22-24 marzo 2023
SOCIETAT CATALANA DE TRASPLANTAMENT

T-CELL EXHAUSTION-INDUCED BY IS IMPACT SARS-COV-2-SPECIFIC ADAPTIVE RESPONSES AFTER MRNA VACCINATION IN SOLID ORGAN TRANSPLANT PATIENTS

L. Donadeu[1], S. Gomez-Olles[1], E. Crespo[1], M. Lopez-Meseguer[1], L. Lladó[2], J. Gonzalez-Costello[2], I. Campos-Varela[1], A. Favà[2], M. Muñoz[1], J. Quintero[1], MF. Cortese[1], A. Torija[1], M. Meneghini[1], D. Kervella[1], F. Moreso[1], O. Bestard[1]

[1] Vall d'Hebron Research Institute, Vall d'Hebron University Hospital
[2] Bellvitge University Hospital

Vall d'Hebron Institut de Recerca

Vall d'Hebron

Bellvitge Hospital Universitari

BACKGROUND

- Coronavirus disease 2019 was declared a pandemic by the World Health Organization on March 11, 2020 and has had devastating consequences.

Polack FP, et al. N Engl J Med 2020.

- Due to their immunocompromised status, solid organ transplant recipients are at higher risk for developing fatal forms of COVID-19.

Marinaki S, et al. Transplant Proc 2022.

- T-cells with a dysfunctional phenotype, characterized for the expression of exhaustion markers, have been identified in CMV infection.

Kaminski H, et al. J Am Soc Nephrol 2022.

- Exhausted T cells have been described during prolonged COVID-19 associated with PD-1 on cell surface, particularly in those patients overtly symptomatic or requiring ICU.

Diao B, et al. Front Immunol 2020.

- Increased proportion of exhausted T cells were observed in cancer patients without response to three doses of SARS-CoV-2 mRNA vaccine.

Benitez JD, et al. Front Oncol 2022.

HYPOTHESIS AND OBJECTIVES

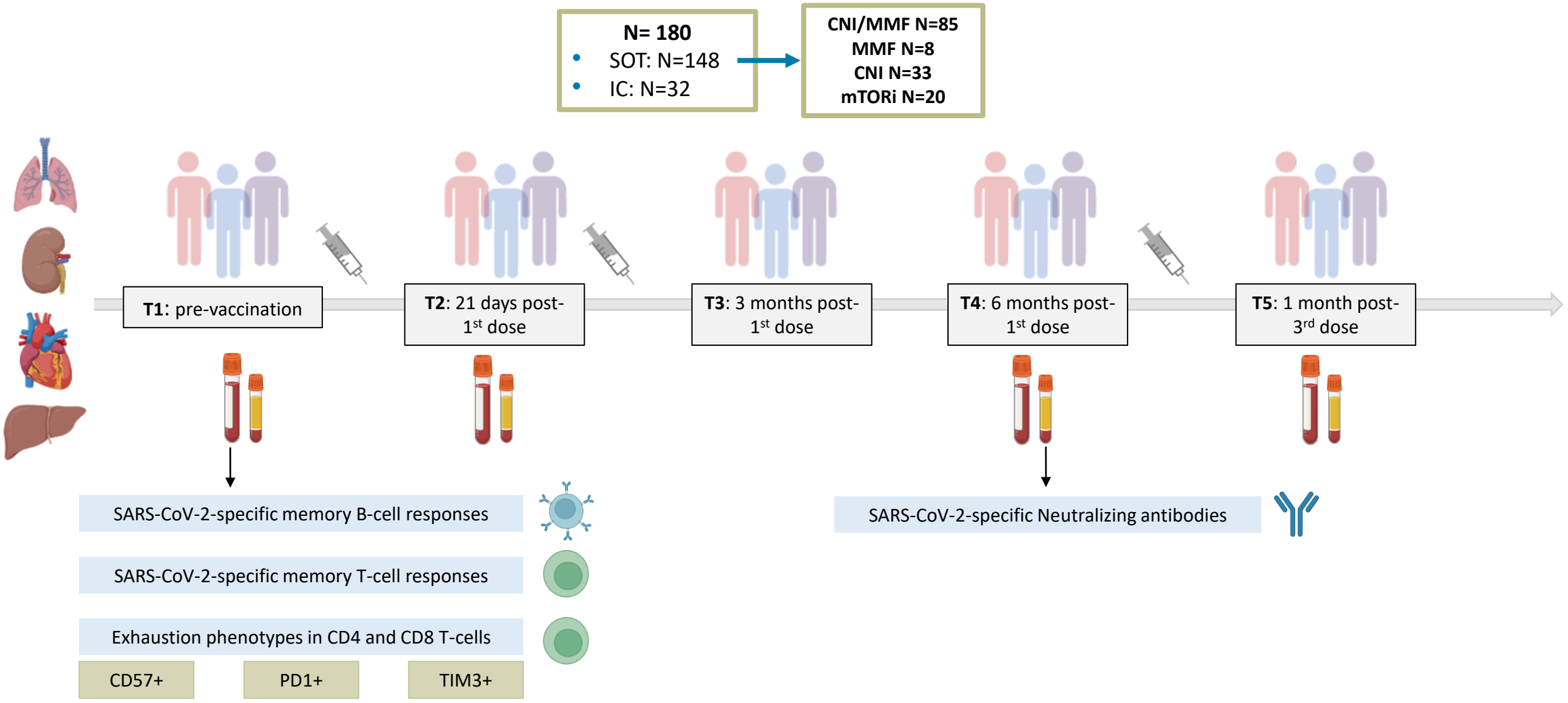
Exhausted T-cells can impact the adaptive functional response after subsequent **SARS-CoV-2 mRNA vaccine** boosters in **Solid Organ Transplant patients** and the **immunosuppressive treatment** has an important role in the proportion of these dysfunctional T-cells.

OBJECTIVES:

1. To characterize different exhaustion **T-cell phenotypes** that could identify patients more likely to respond to booster vaccination.

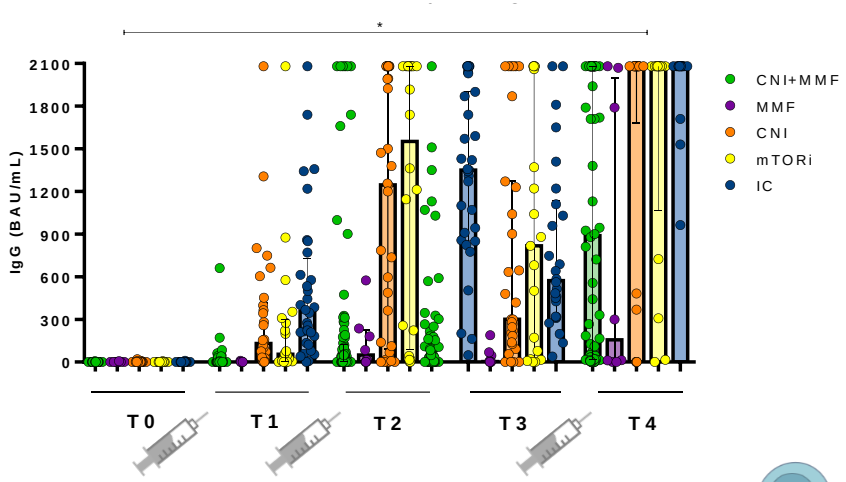
2. To evaluate how **Immunosupressive Treatment** impacts the strength and duration of the immune responses and their impact on T-cell exhaustion.

STUDY DESIGN AND METHODS

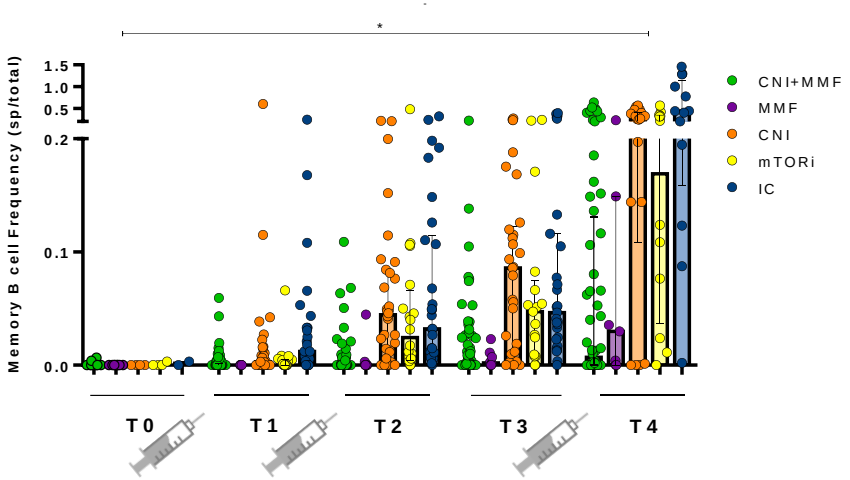


EFFECT OF IMMUNOSUPRESSION IN THE HUMORAL RESPONSE

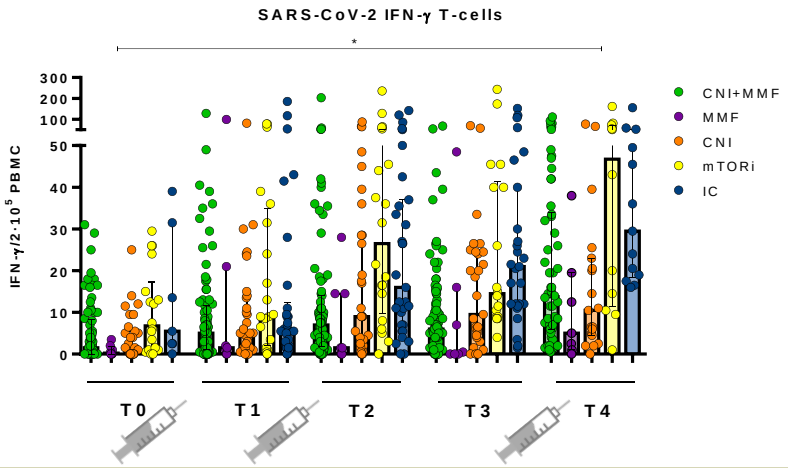
Serological memory

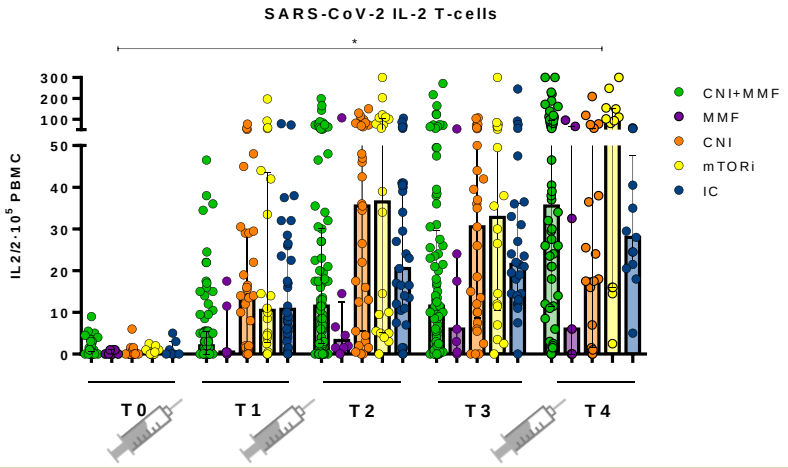


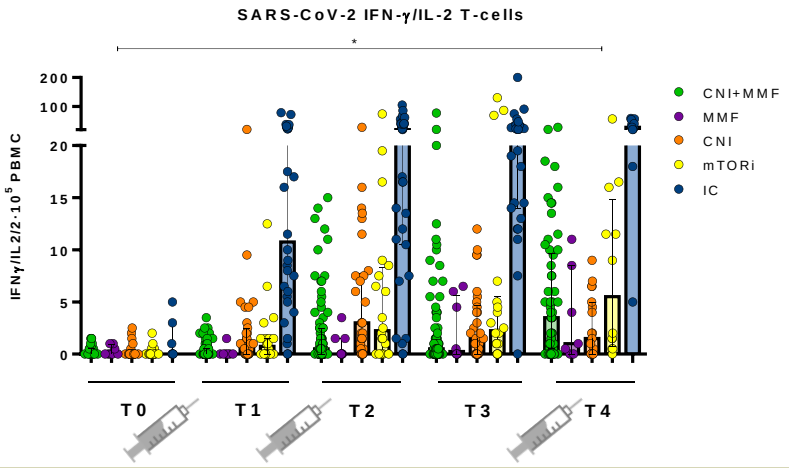
B cell memory



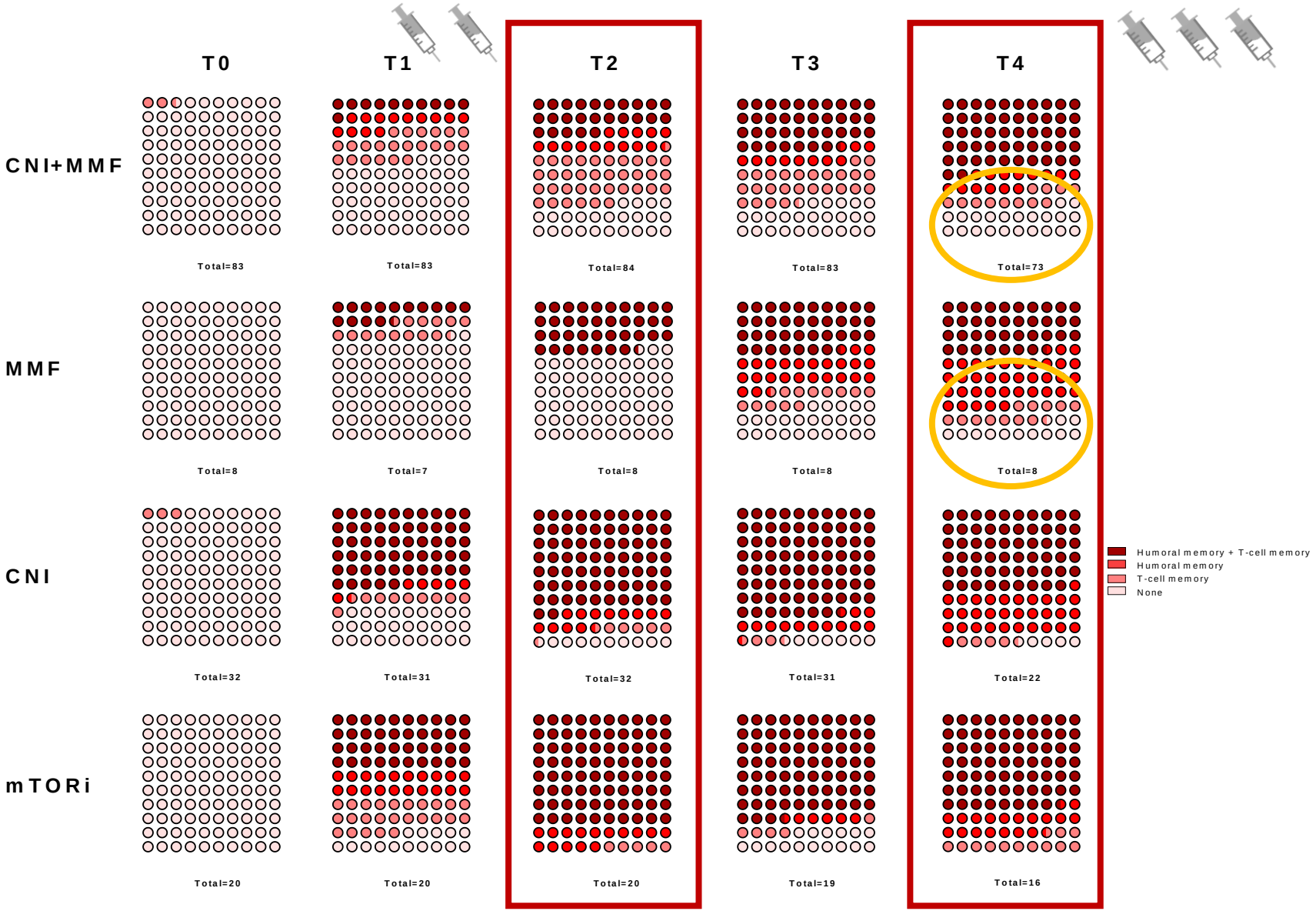
Th1 T cell frequencies







EFFECT OF IMMUNOSUPRESSION IN THE IMMUNE RESPONSES

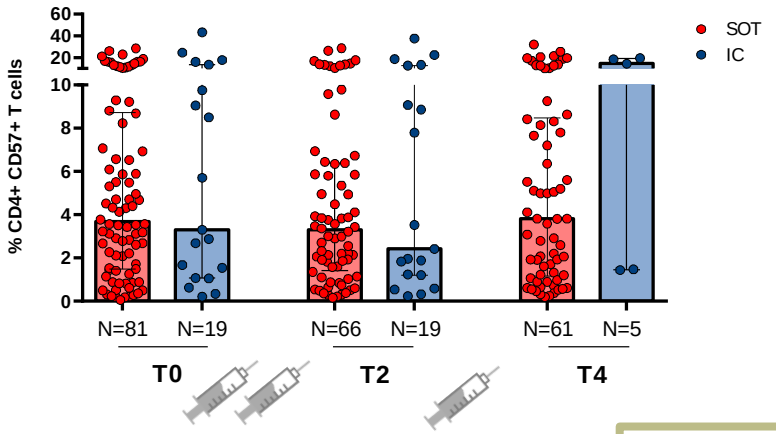


Are T-cells from those patients not responding to booster vaccination **more exhausted**?

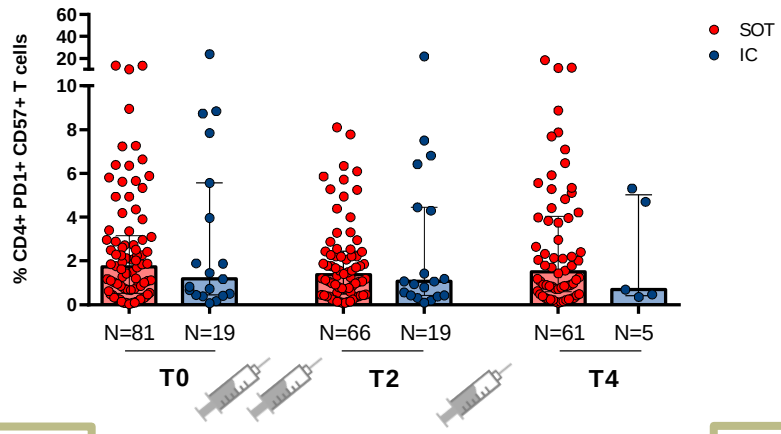
EVOLUTION OF CD4 T-CELL EXHAUSTION

CD4 T cells

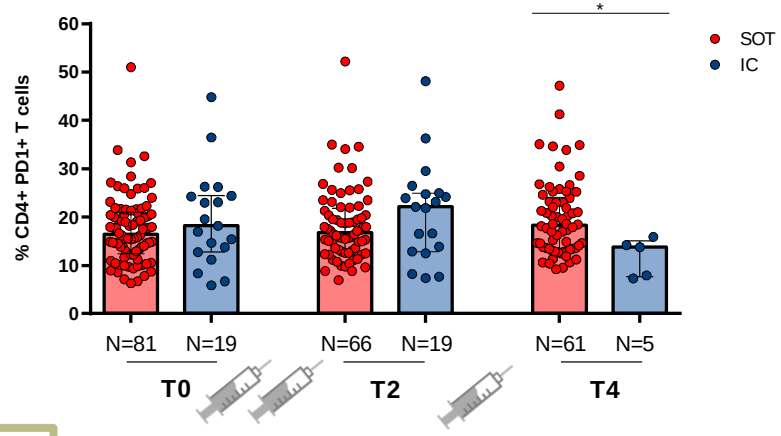
CD57+



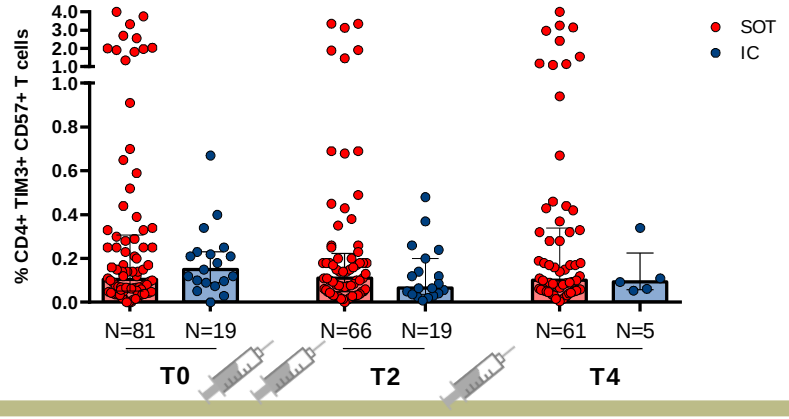
CD57+ PD1+



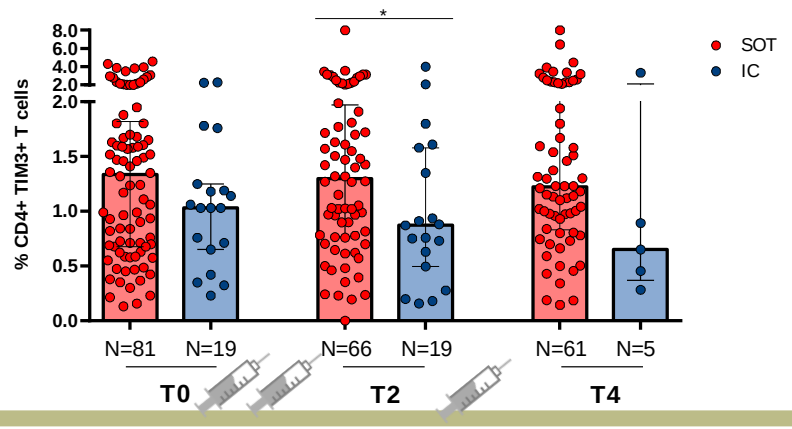
PD1+



CD57+TIM3+



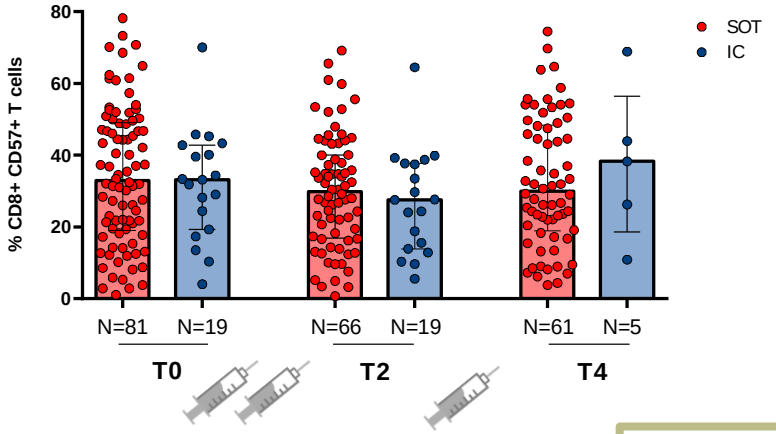
TIM3+



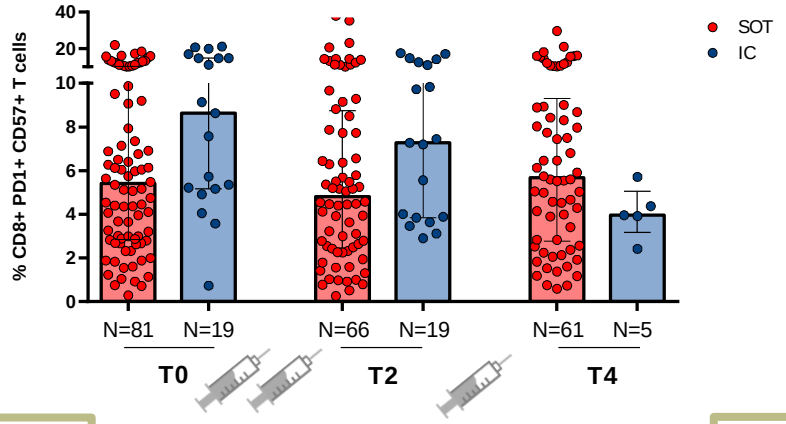
EVOLUTION OF CD8 T-CELL EXHAUSTION

CD8 T cells

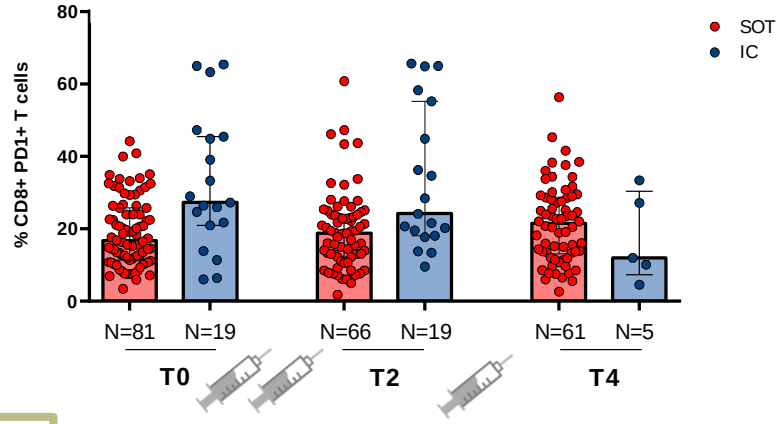
CD57+



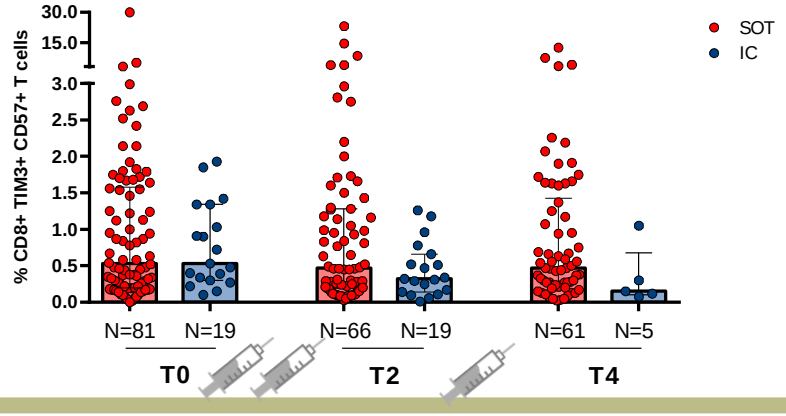
CD57+ PD1+



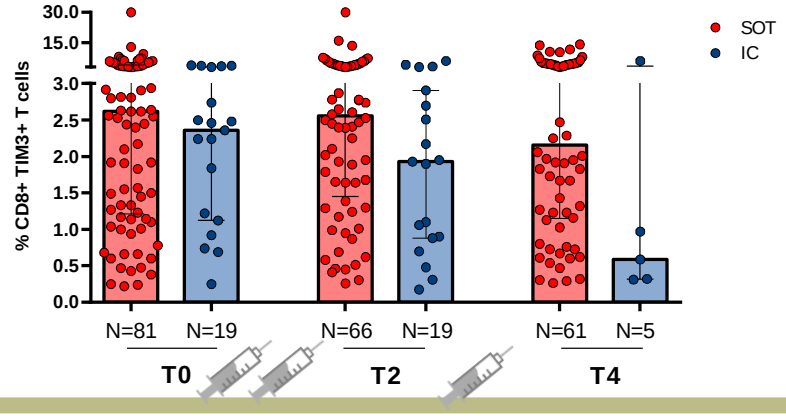
PD1+



CD57+TIM3+



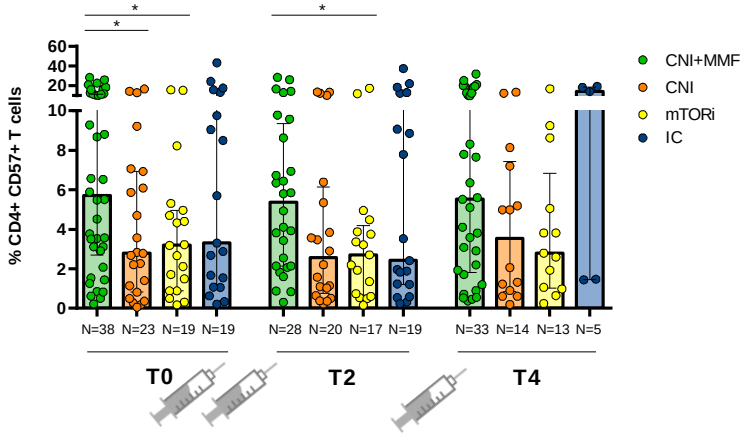
TIM3+



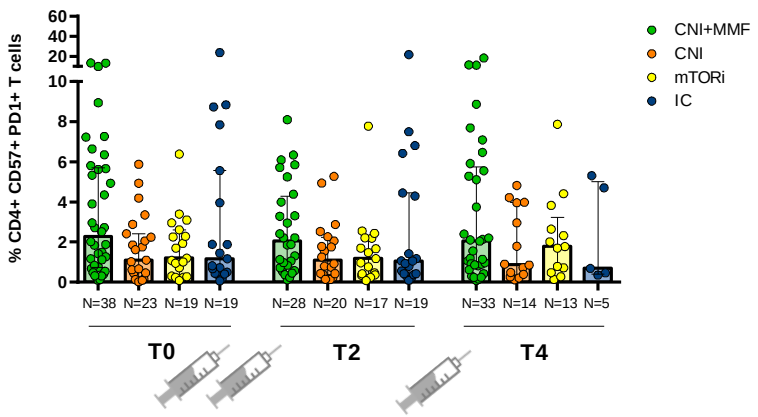
EFFECT OF IMMUNOSUPRESSION IN T-CELL EXHAUSTION

CD4 T cells

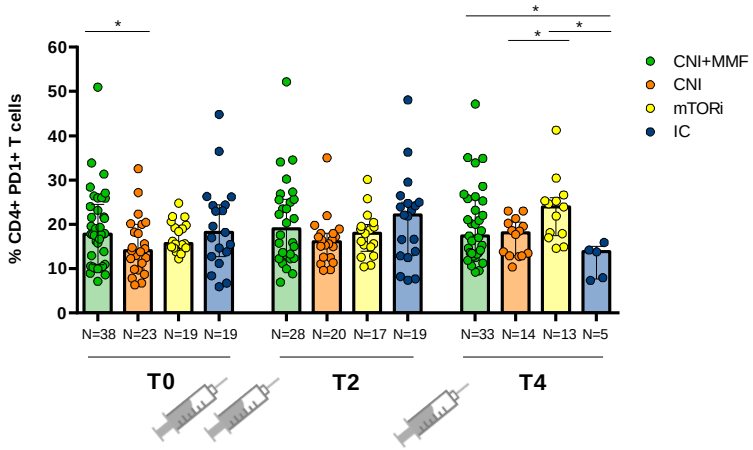
CD57+



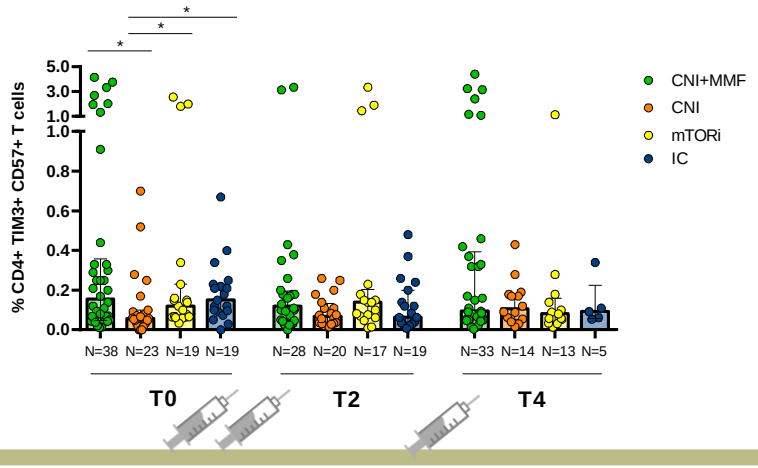
CD57+ PD1+



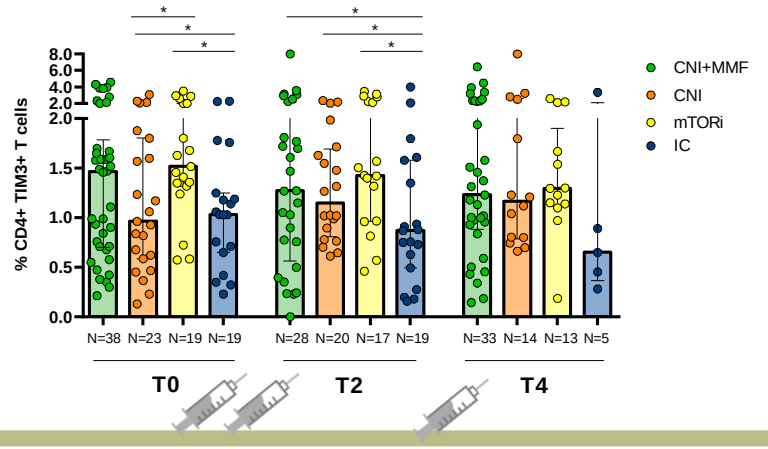
PD1+



CD57+TIM3+



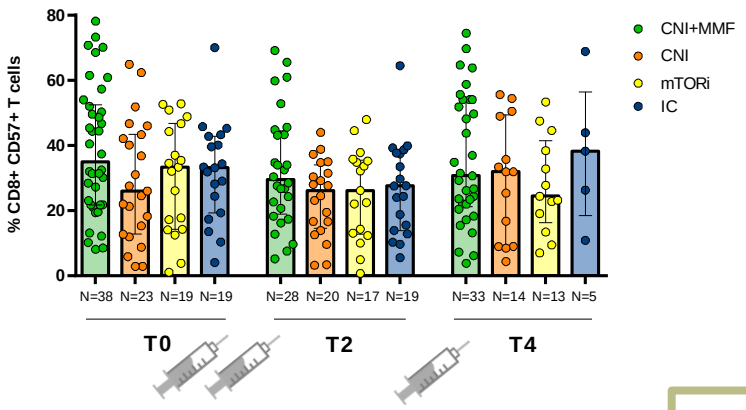
TIM3+



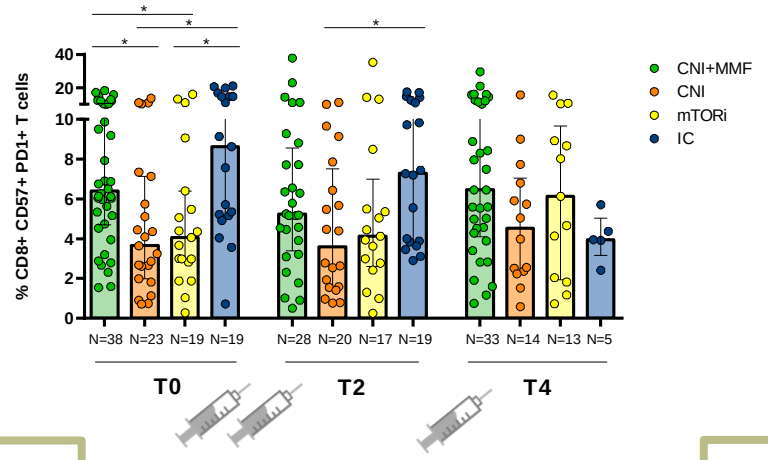
EFFECT OF IMMUNOSUPRESSION IN T-CELL EXHAUSTION

CD8 T cells

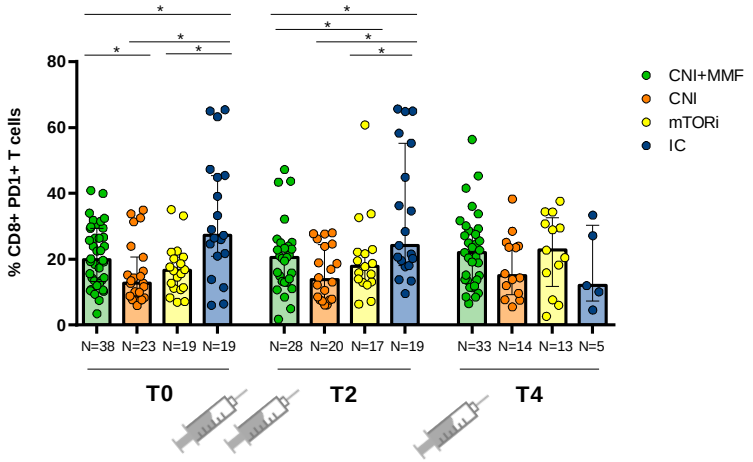
CD57+



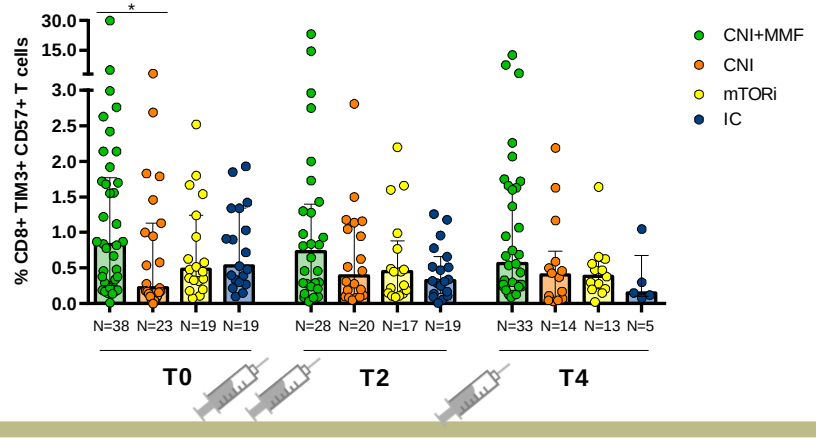
CD57+ PD1+



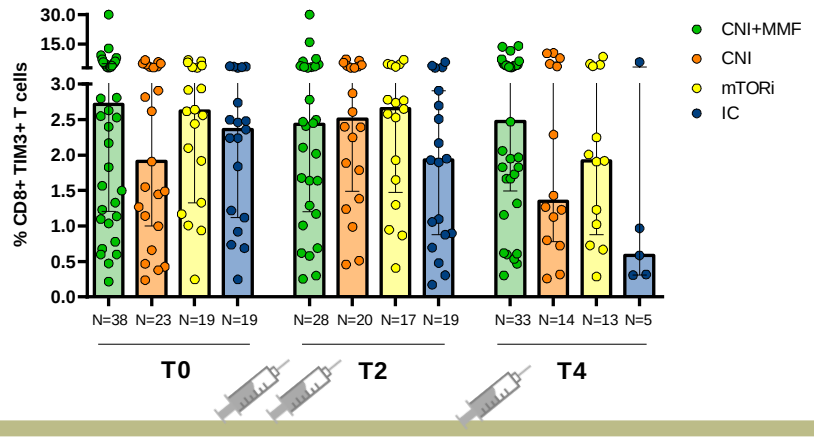
PD1+



CD57+TIM3+



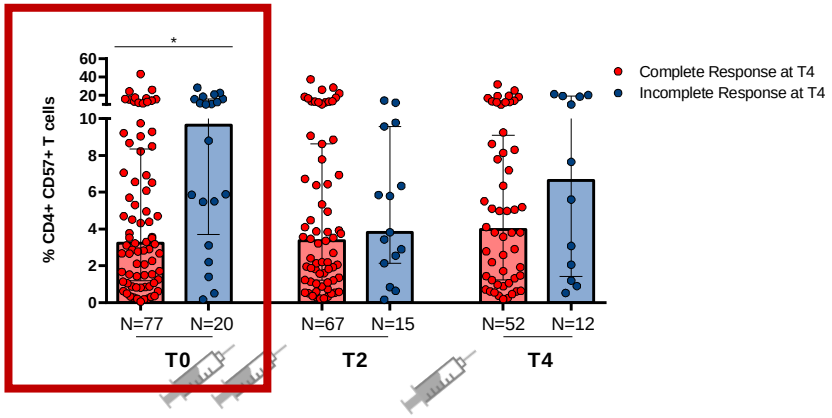
TIM3+



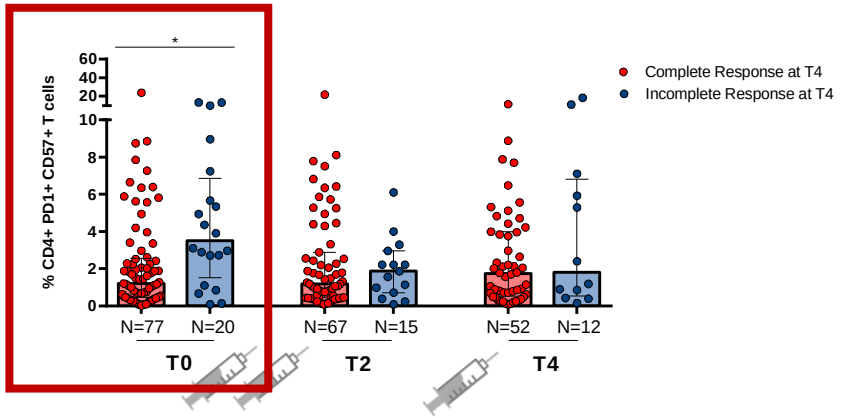
T-CELL EXHAUSTION ACCORDING TO IMMUNOLOGICAL RESPONSE

CD4 T cells

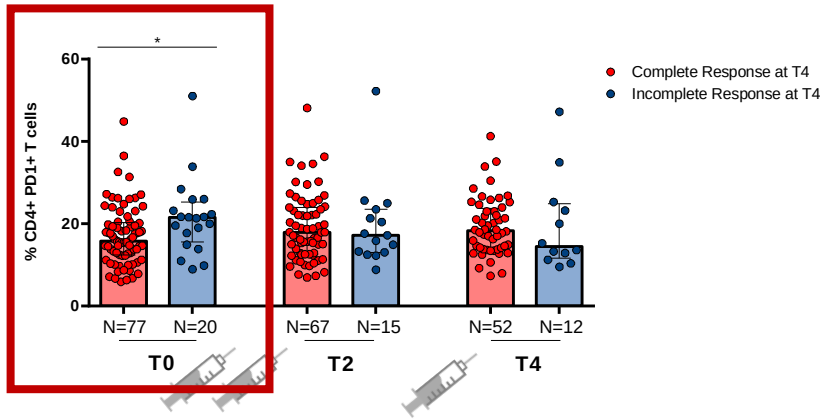
CD57+



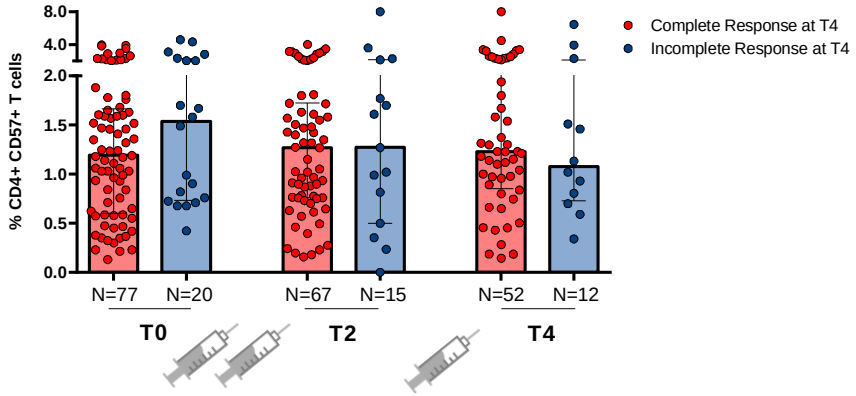
CD57+ PD1+



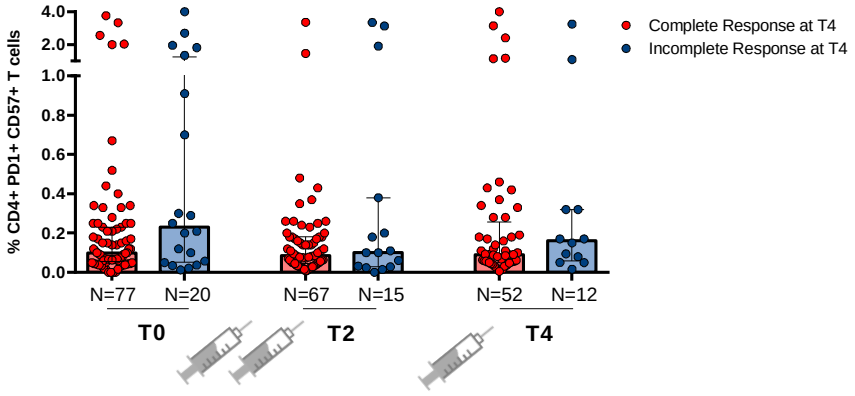
PD1+



CD57+TIM3+



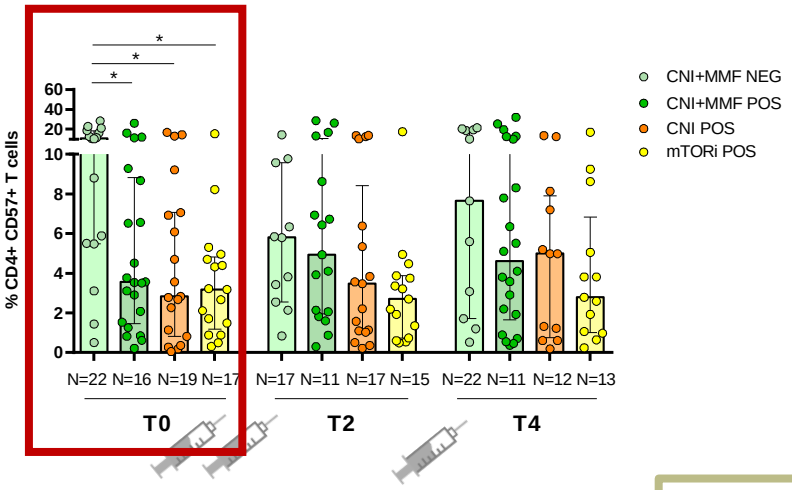
TIM3+



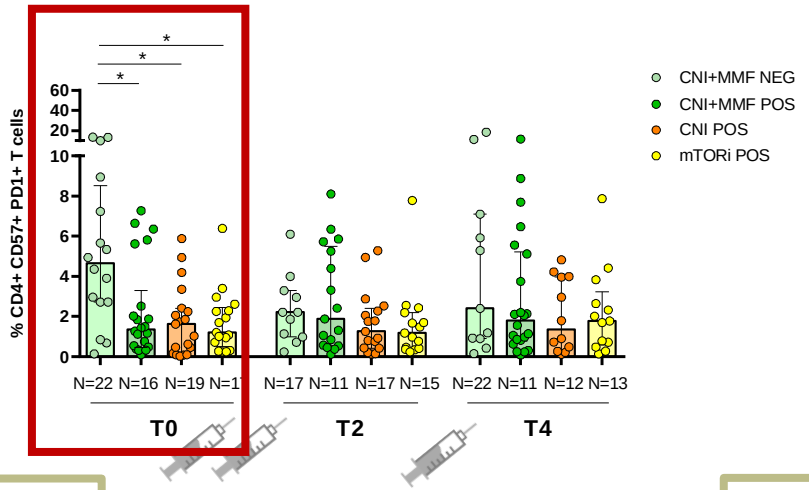
T-CELL EXHAUSTION ACCORDING TO IMMUNOLOGICAL RESPONSE

CD4 T cells

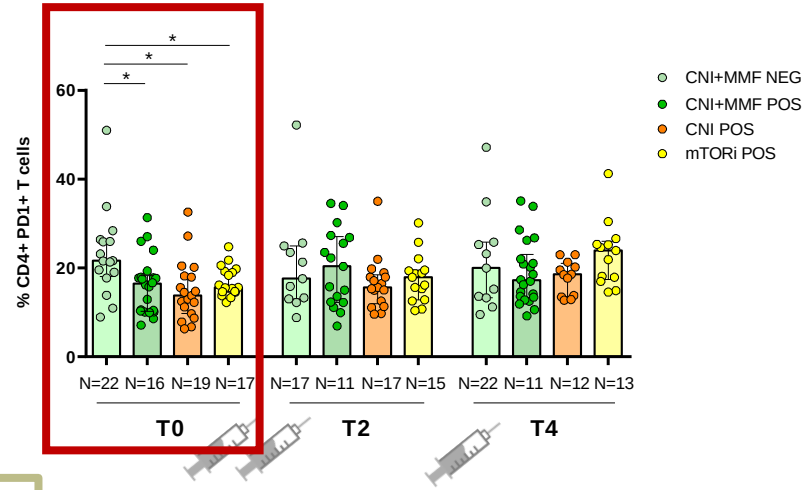
CD57+



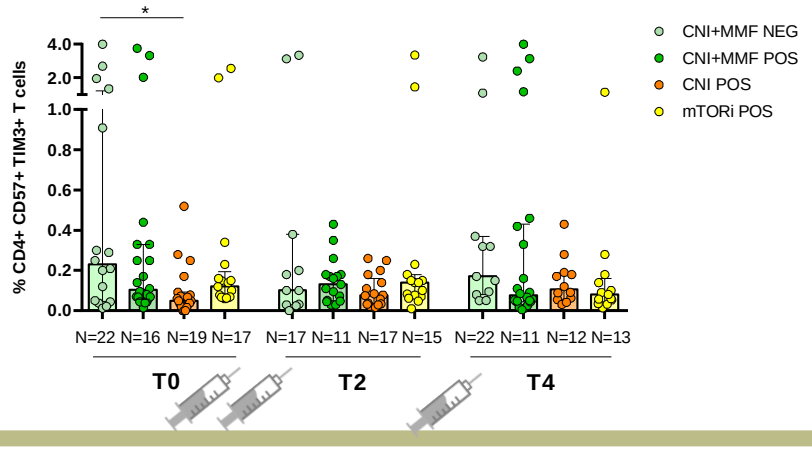
CD57+ PD1+



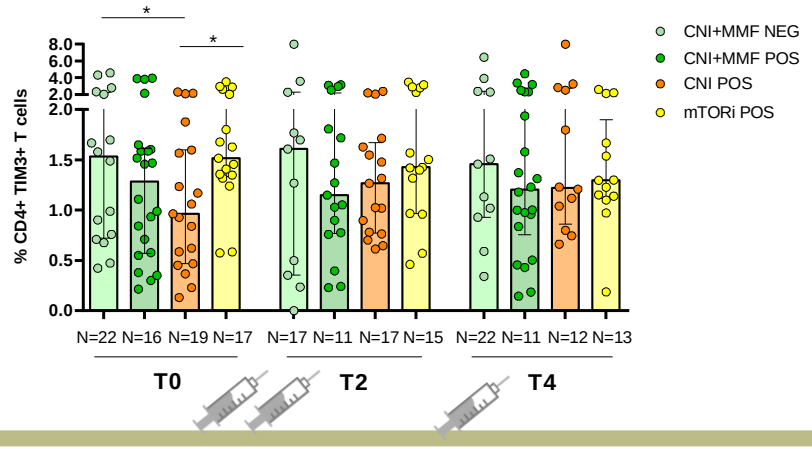
PD1+



CD57+TIM3+

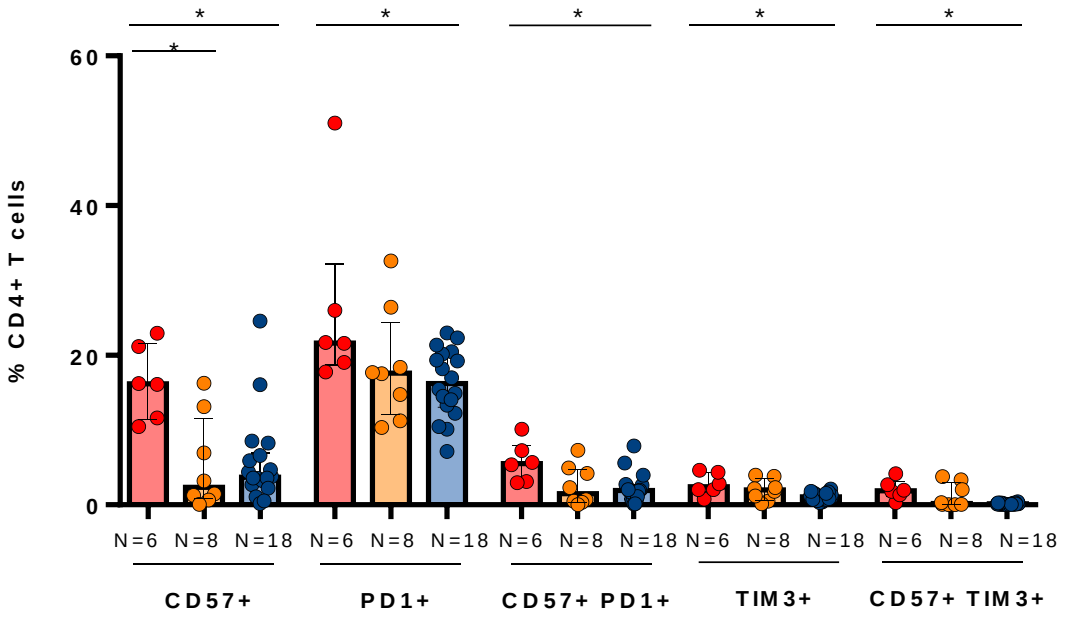


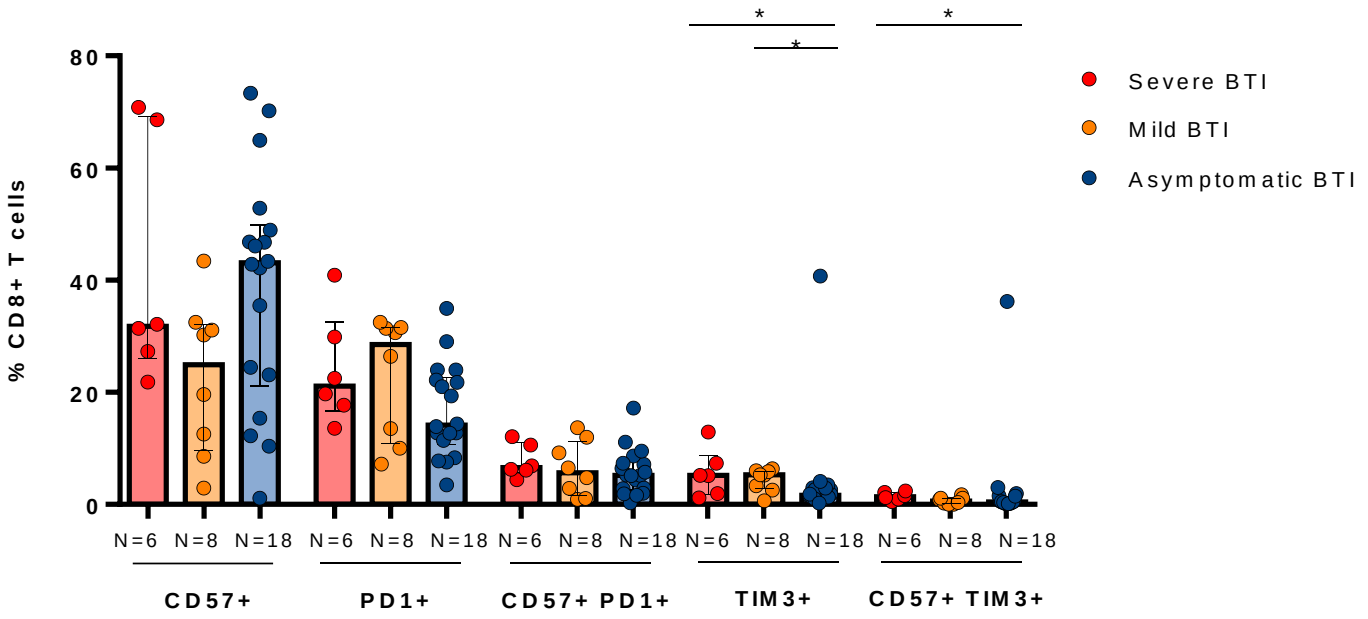
TIM3+



T-CELL EXHAUSTION IMPACTS SEVERITY OF BTI

Pre-vaccination





SUMMARY

- After vaccination there is a progressive appearance of adaptive immunity (humoral and T cell) amount SOT which strength and duration seems to be mostly driven by the type and burden of immunosuppression.

- Patients receiving CNI MMF-free and mTORi-based treatments display significantly higher capacity to respond to mRNA-based SARS-CoV-2 vaccines as compared to patients on standard of care therapy based on CNI/MMF.

- T-cell exhaustion phenotypes seem to drive poor antiviral immune responses after SARS-CoV-2 booster vaccination, mainly for CD4+ T cells.

- Patients not developing a complete (humoral and T-cell) memory immune response exhibited a significantly more exhausted phenotype prior to vaccination.

- CD4+ exhausted T cells seem to favour severe BTI if infected.

ACKNOWLEDGEMENTS

Vall d'Hebron Research Institute:

- Elena Crespo
- Alba Torija
- Delphine Kervella
- Mariona Juvé
- Núria Bolaños
- Susana Gomez
- Meritxell Boada
- Victòria Ruiz
- Cristina Font
- Candela Fernandez

Bellvitge University Hospital:

- Alexandre Favà
- Laura Lladó
- José Gonzalez
- Isabel Campos

Vall d'Hebron University Hospital:

- Francesc Moreso
- Manuel Lopez
- Marina Muñoz
- Jesús Quintero
- Oriol Bestard
- Maria Meneghini
- Juliana Esperalba

Vall d'Hebron
Institut de Recerca

Bellvitge
Hospital Universitari

Vall
d'Hebron