



Response to Tozinameran vaccination in renal transplant recipients is associated with a distinct initial profile of immunity cells and with certain alterations in their subpopulations

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## Background

- Immune status profile can predict response to vaccination
- Alterations in the concentrations and proportions of immune cells can be representative of vaccination effectiveness
- We evaluated the above parameters in renal transplant recipients (RTRs), with regards to Tozinameran (BNT162b2) vaccination



## Materials and Methods (I)

### Inclusion Criteria

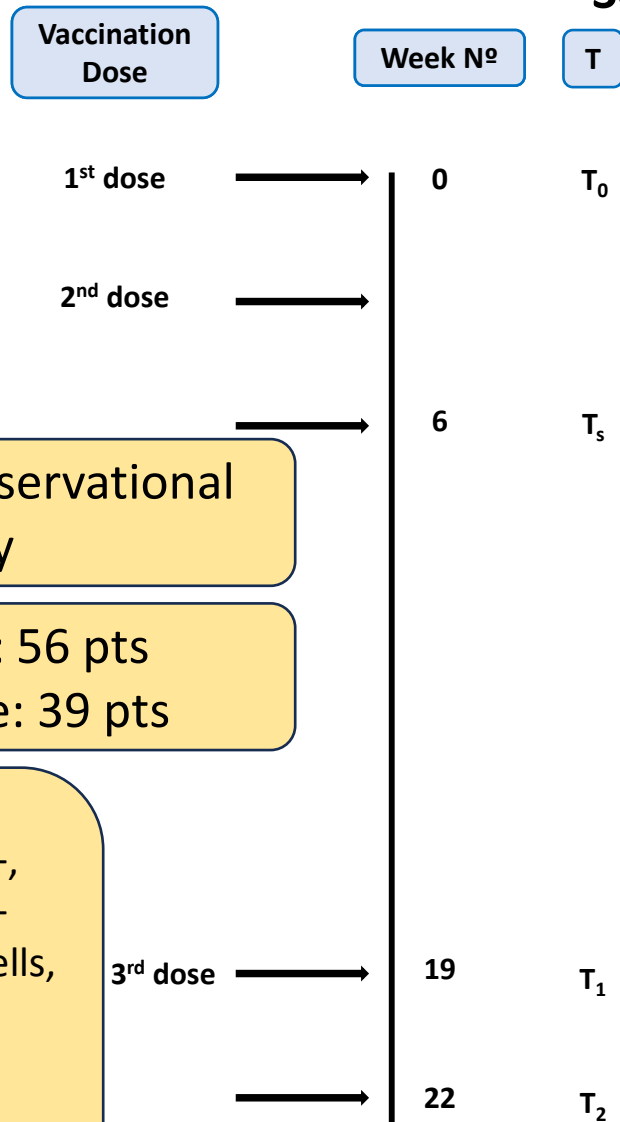
- Age  $\geq$  18 y.o.
- Kidney transplantation  $\geq$  3 mo before
- Stable dosages of IST (CS+CNI+MMF)
- No previous COVID-19 disease (negative anti-SARS-CoV-2 Abs at recruitment)

### Exclusion Criteria

- Comorbidities
- Chemo or RTX during the last 2 mo
- Rejection events during the last 6 mo
- Viral or microbial infection during the last 3 mo

# Materials and Methods (II)

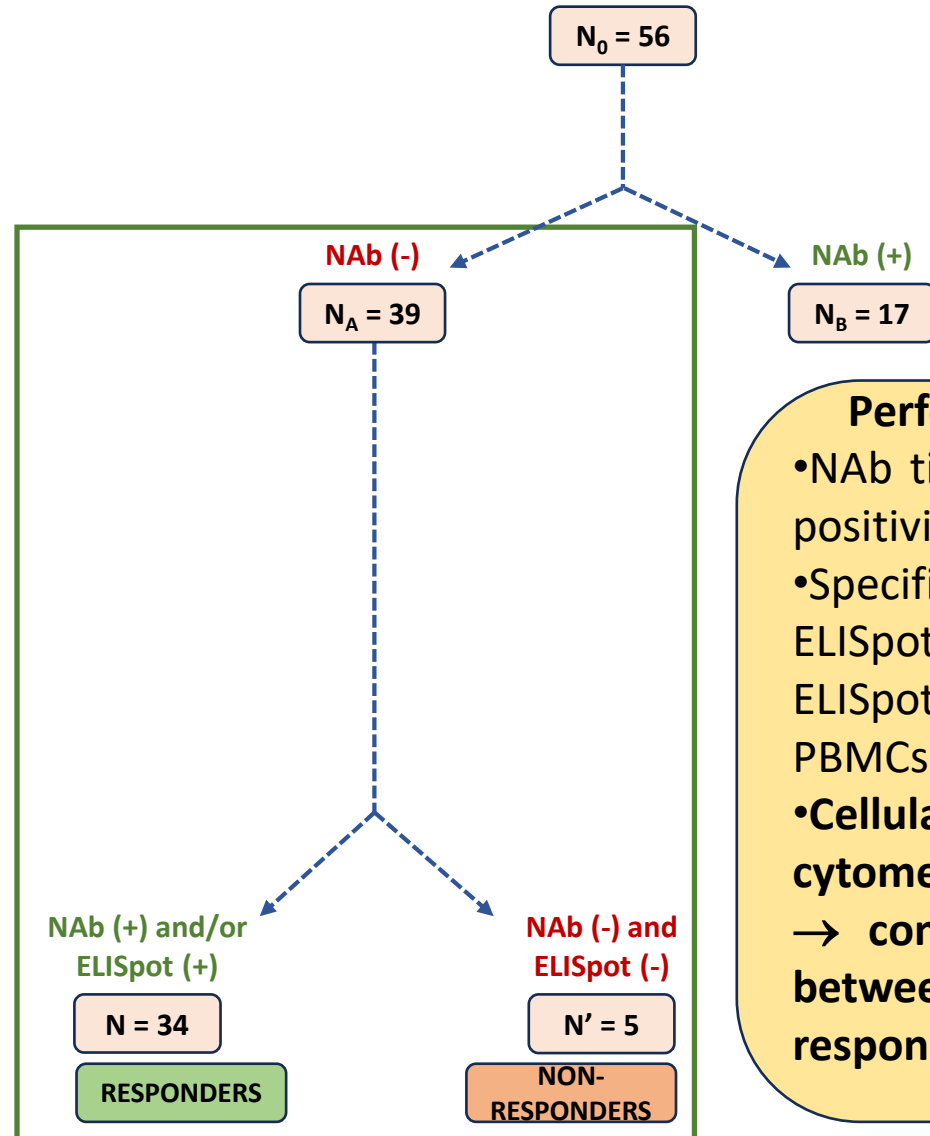
## Schedule of the study



Prospective observational study

Initial pool: 56 pts  
Final sample: 39 pts

**At T<sub>1</sub> and T<sub>2</sub>**  
CD4+, activated CD4+,  
CD8+, activated CD8+  
NKT, activated NKT cells,  
NK- cells,  
CD45+CD19+:  
Naïve, Marginal,  
Transitional, Memory B-  
cells, Plasmablasts



**Performed Measurements**

- NAb titers - CLIA at T<sub>0</sub>, T<sub>s</sub>, T<sub>2</sub> – positivity: NAb>0.3AU/ml
- Specific T-cell immunity - ELISpot at T<sub>2</sub> – positivity: ELISpot value ≥ 30 SFC/5×10<sup>5</sup> PBMCs
- Cellular subpopulations - flow cytometry at T<sub>0</sub>, T<sub>1</sub>, T<sub>2</sub>

→ comparison of the results between responders and non-responders

## Results (I)

Responders vs. non-responders: at  $T_0$ : higher total and transitional B-lymphocyte count

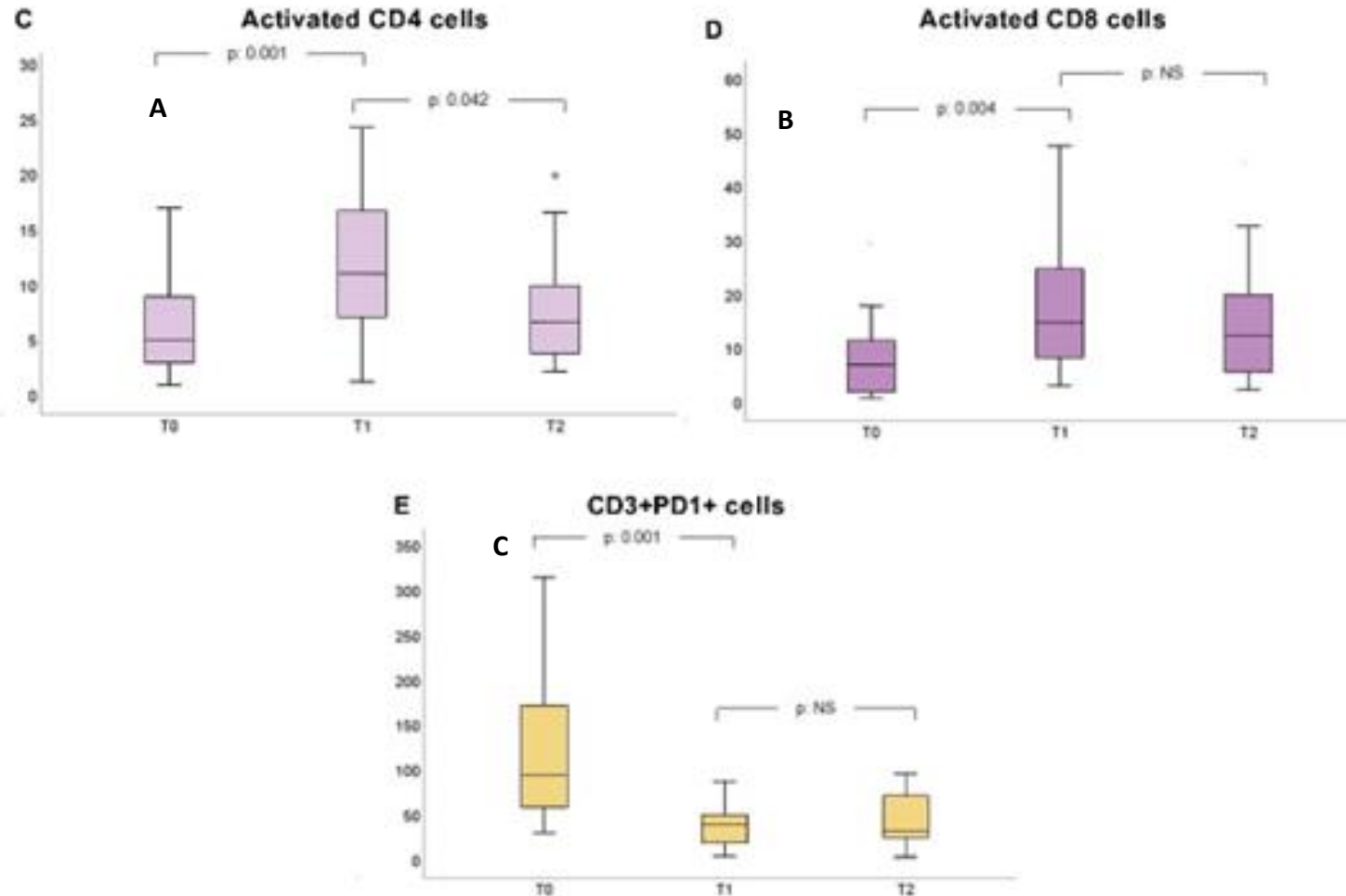
Cell Subpopulation	Responders	Non-responders	p
Total B-cells	96.5(93) cells/ $\mu$ L	51(52) cells/ $\mu$ L	0.045
Transitional B-cells	9(17) cells/ $\mu$ L	1(2) cells/ $\mu$ L	0.031

Among responders:

- From  $T_0$  to  $T_1$ :  $\uparrow$  in activated CD4+ and CD8+ numbers  $\downarrow$  in CD3+PD1+ T-cell numbers

Cell subpopulation	$T_0$	$T_1$	p
Activated CD4+ T-cells	6.5(4) cells/ $\mu$ L	10.08(11) cells/ $\mu$ L	0.001
Activated CD8+ T-cells	8(19) cells/ $\mu$ L	14.76(16) cells/ $\mu$ L	0.004
CD3+PD1+ T-cells	130(121) cells/ $\mu$ L	30.44(25) cells/ $\mu$ L	0.001

## Results (II)



Concentrations of activated CD4+ (A), activated CD8+ (B) and CD3+PD1+ T-cells (C) at T<sub>0</sub>, T<sub>1</sub> and T<sub>2</sub> in the responders' group

## Results (III)

- From  $T_0$  to  $T_1$ :  $\uparrow$  in percentages of memory and marginal zone B-lymphocytes, activated CD4+, CD8+ and natural killer (NK) T-cells  $\downarrow$  in percentages of naïve B-cells and CD3+PD1+ T-cells

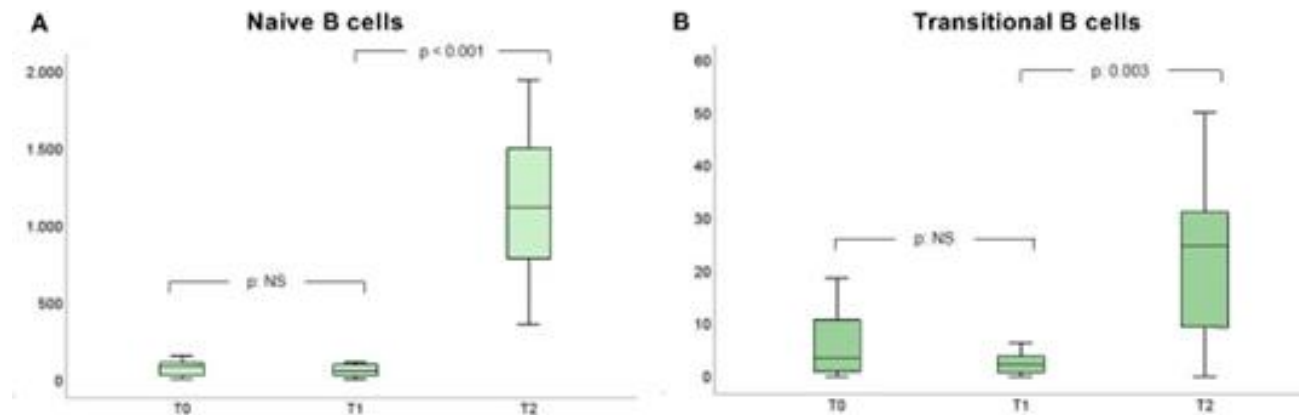
Cell subpopulation	$T_0$	$T_1$	p
Memory B-cells	25.6(23.9)%	32(26)%	0.001
Marginal zone B-cells	10.7(12.4)%	14(12.4)%	0.031
Naïve B-cells	74.4(23.7)%	69.7(25.7)%	0.002
Activated CD4+ T-cells	0.9(0.9)%	1.2(1.1)%	0.001
Activated CD8+ T-cells	1.9(3.7)%	3.2(2)%	0.017
Activated NKT-cells	1.4(3)%	2.6(2.8)%	0.001
CD3+PD1+ T-cells	7.3(4.7)%	1.8(1.4)%	<0.001

*Memory, marginal zone and naïve B-cells are estimated as percentages of B-lymphocytes, activated CD4+ and CD8+ T-cells as percentages of CD3+CD4+ and CD3+CD8+ T-cells respectively, activated NKT-cells as a percentage of CD3-CD56+ NK cells and CD3+PD1+ T-cells as a percentage of total lymphocytes*

## Results (IV)

- From  $T_1$  to  $T_2$ :  $\uparrow$  in the numbers of naïve and transitional B-cells

Cell subpopulation	$T_1$	$T_2$	p
Naïve B-cells	57.55(66) cells/ $\mu$ L	1149.3(680) cells/ $\mu$ L	<0.001
Transitional B-cells	1.4(3) cells/ $\mu$ L	17.5(21) cells/ $\mu$ L	0.003



Concentrations of naïve (A) and transitional B-cells (B) at  $T_0$ ,  $T_1$  and  $T_2$  in the responders' group





## Conclusions

- Baseline immune cell profile (according to our findings mostly with regards to the B-lymphocyte compartment) can determine response to vaccination with Tozinameran among RTRs
- Response to vaccination is correlated to several alterations in cellular subpopulations' composition (more specifically to an increase of activated forms and to a drop of naïve and exhausted forms)

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**Thank you for your attention!**