

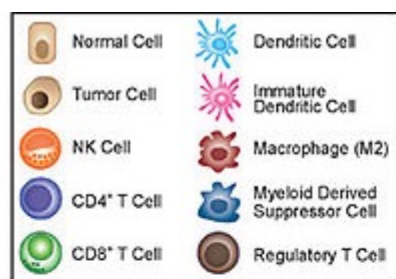
# Lymphocyte subpopulation in oncological diseases: an assessment tool to verify the immune system and the efficacy of integrated therapies

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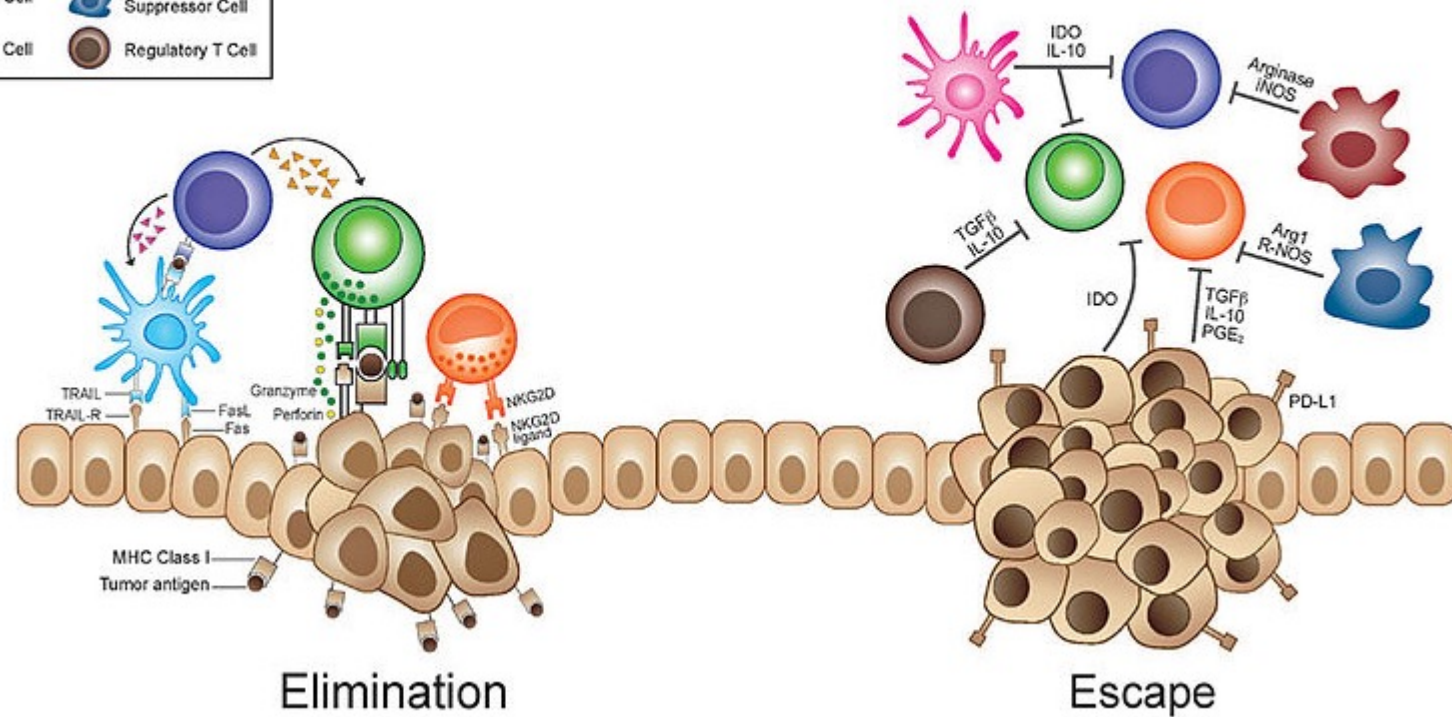
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## Tumor Microenvironment

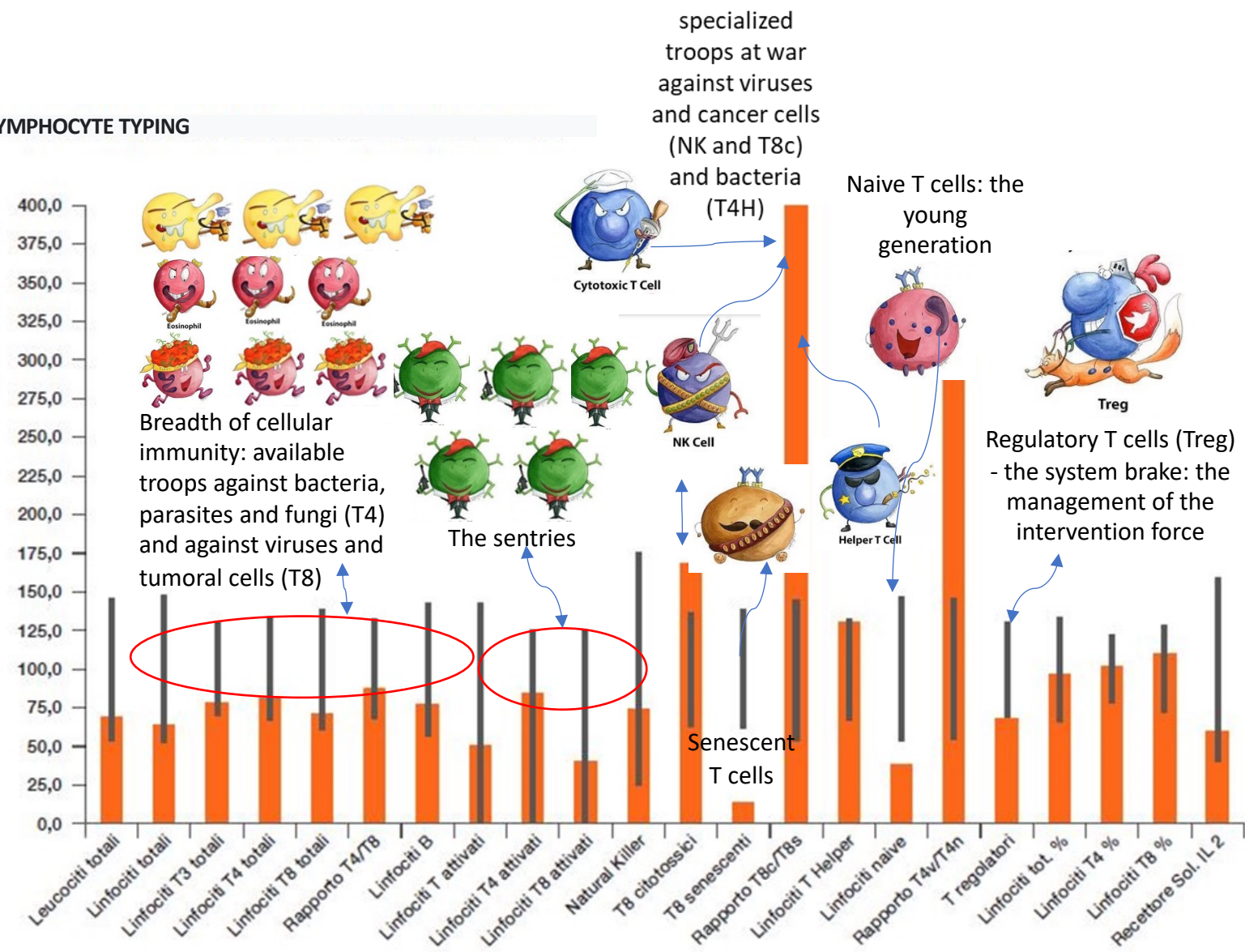




# HOW TO READ THE IMMUNE PANEL



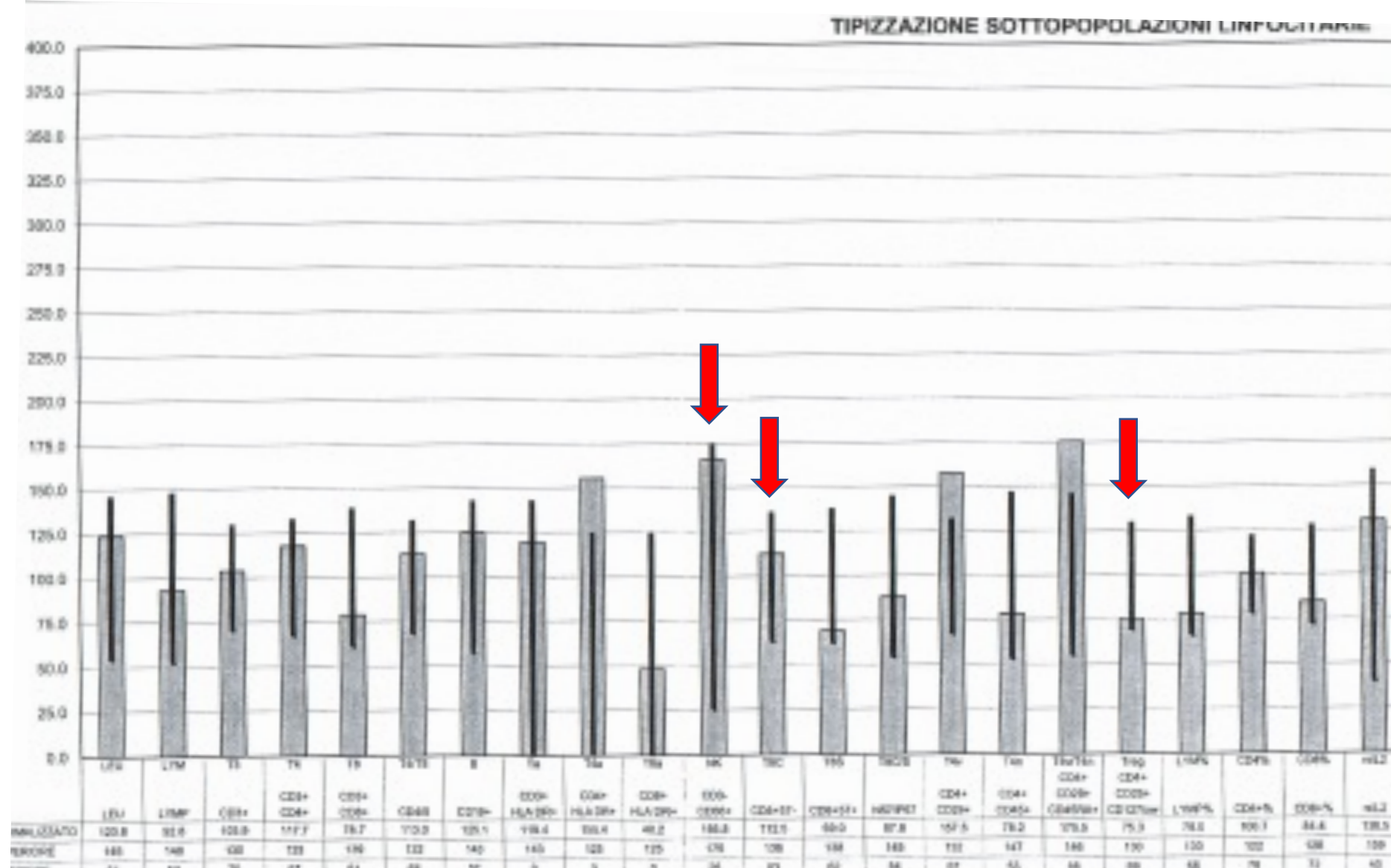
LYMPHOCYTE TYPING



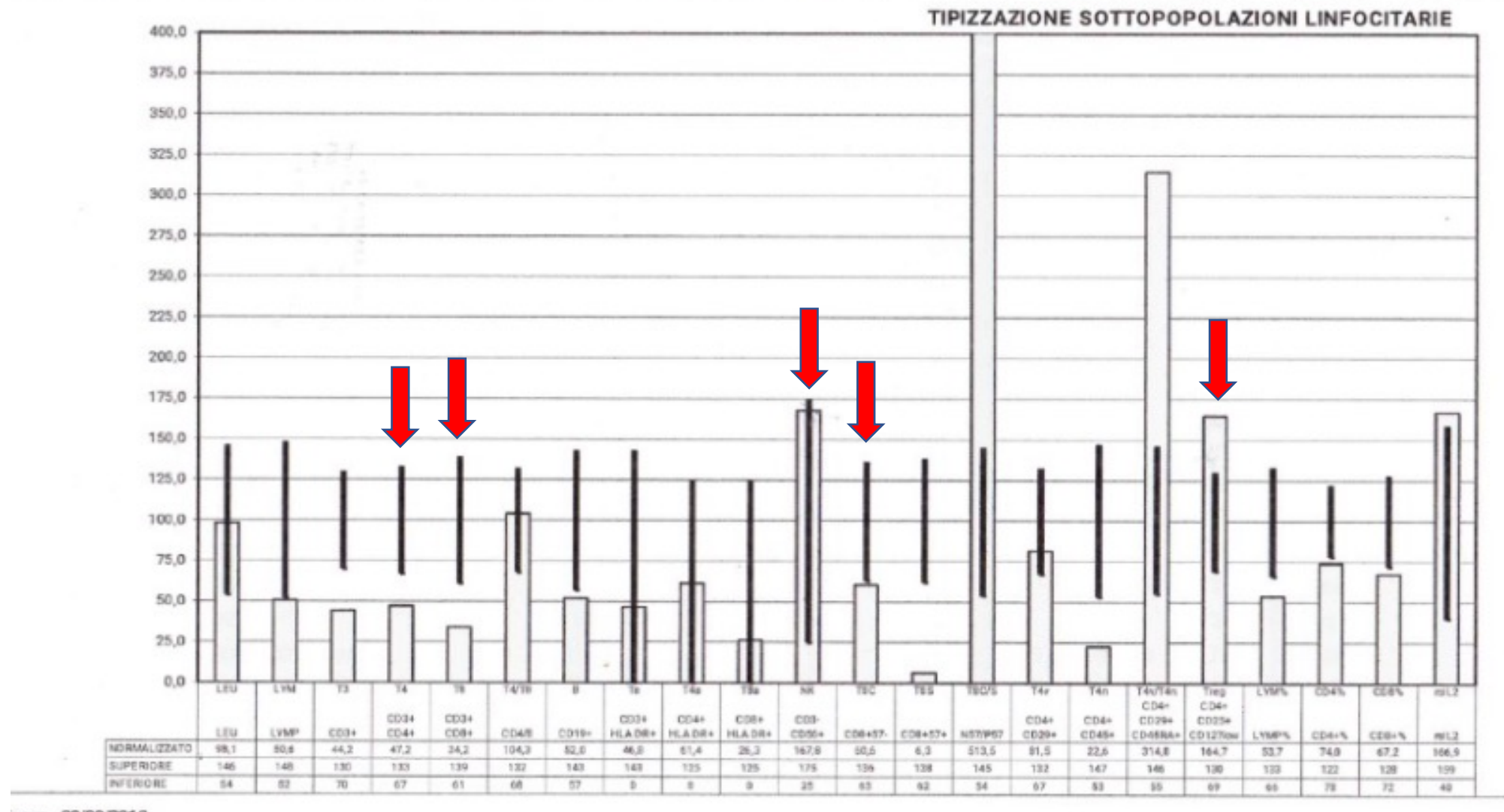








59-year-old patient with a history of prostate cancer treated with radiotherapy and rectum sigmoid carcinoma. Adequate immune system is observed with good NK, T8c and low Treg response.

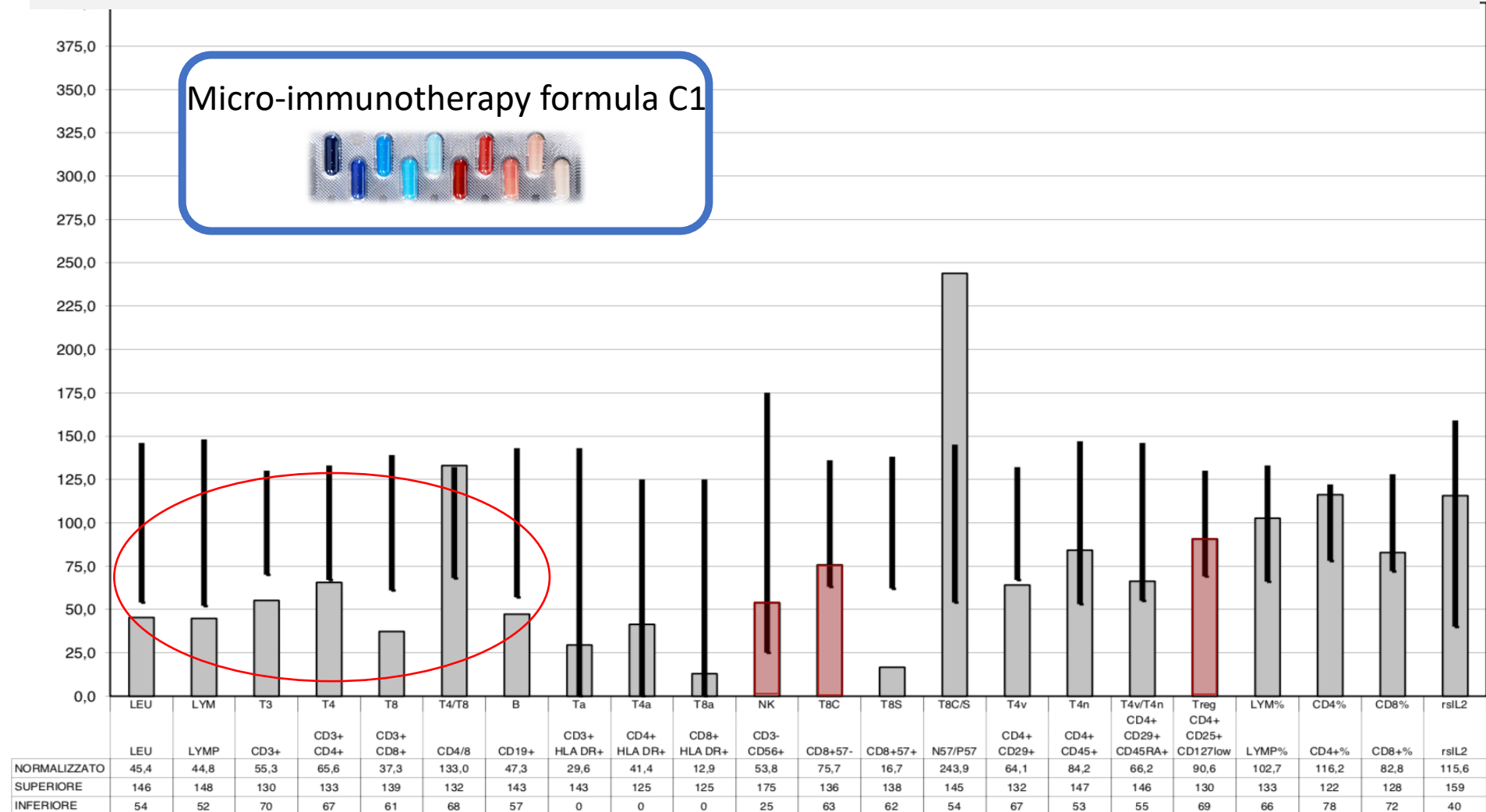


56-year-old woman with breast cancer. An inadequate immune system is observed (reduction of T4, T8, T8c, normal NK but with high Treg)



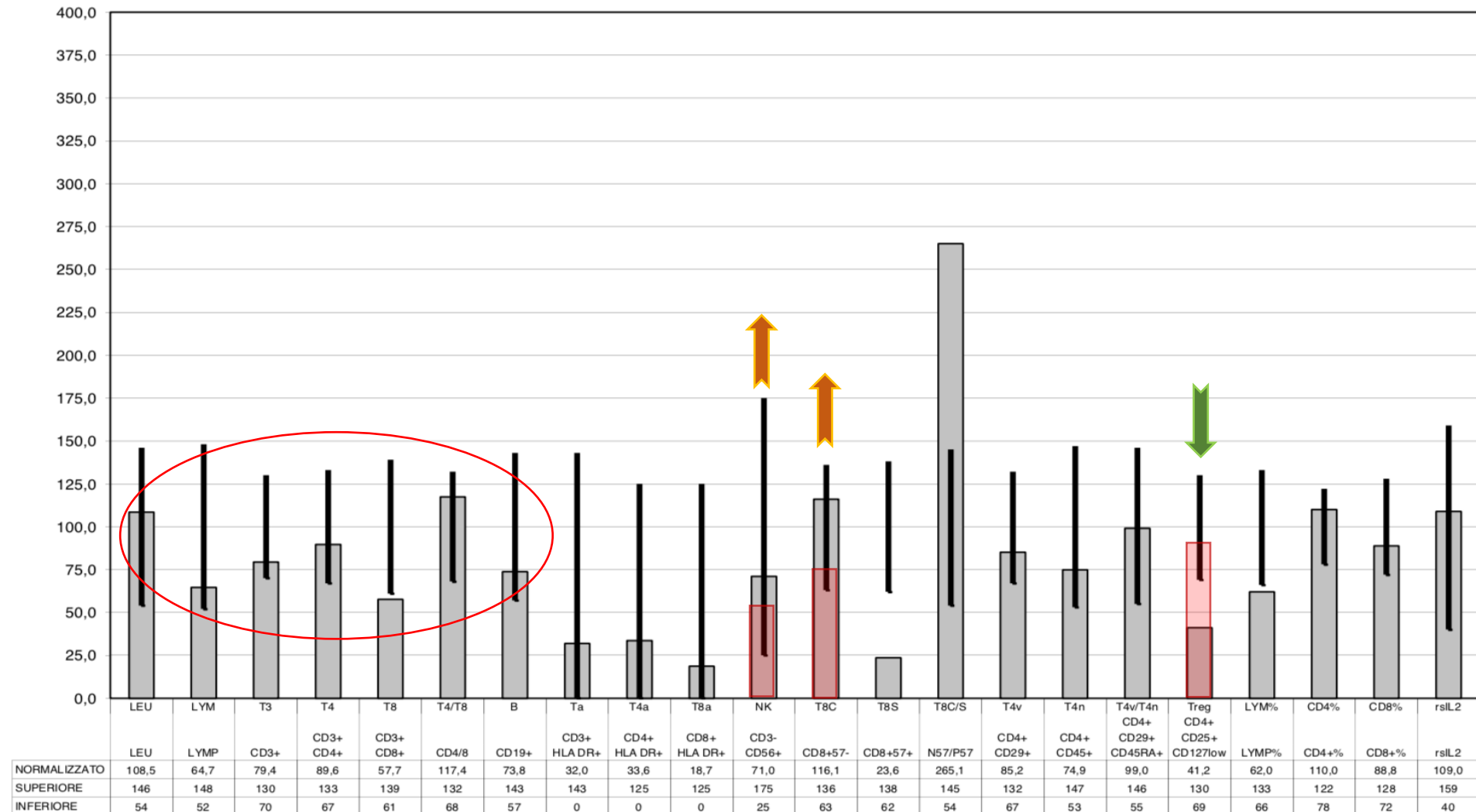
# CASE REPORT 1

Patient with breast cancer. Lymphocyte typing performed 1 year after the end of chemotherapy. Patient in good general condition, complete tumor response, disease free interval 1 year and 6 months. TH1 arm at the lower limits (NK and T8c), high Treg, normal sIL-2R



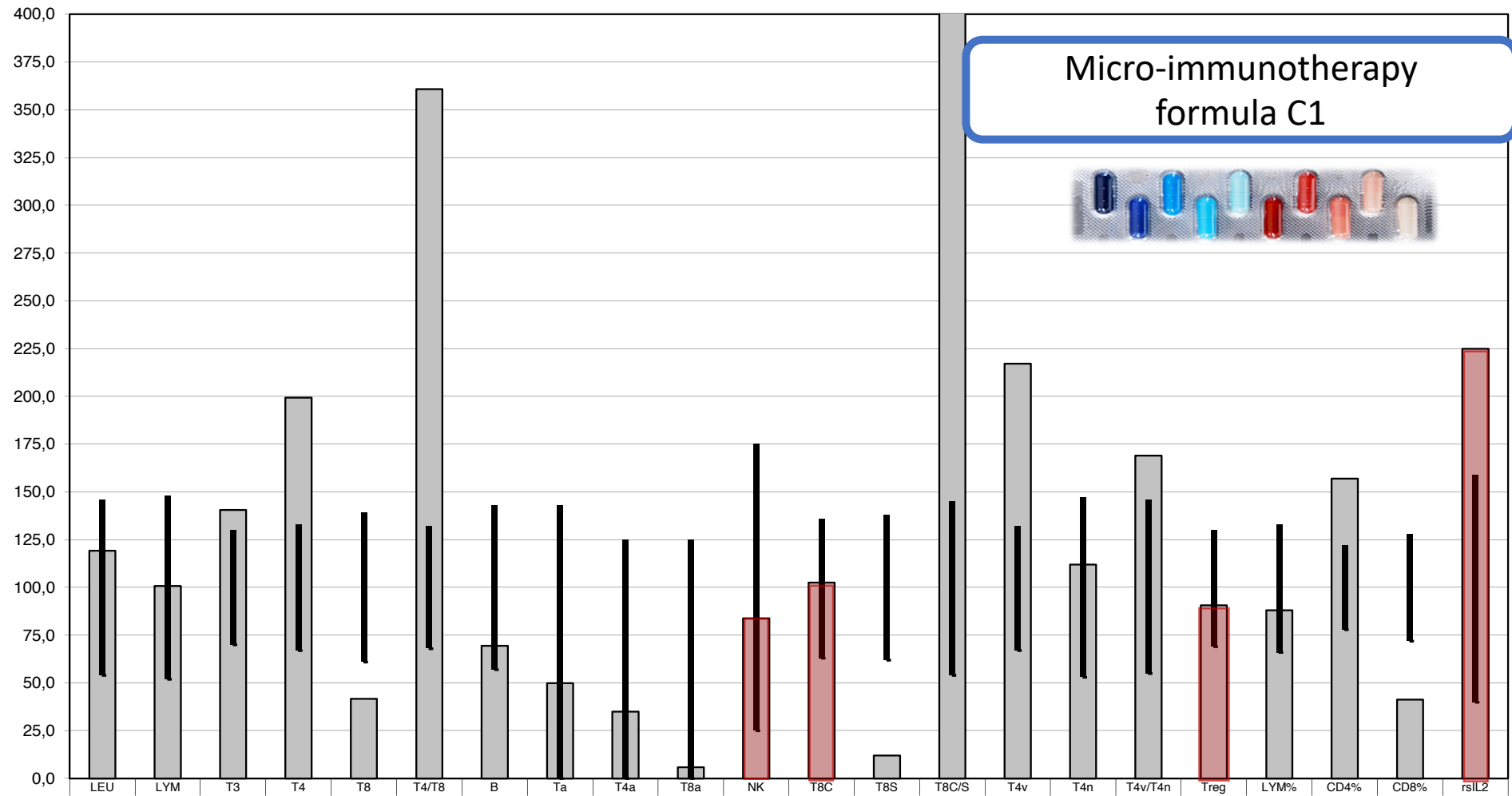
# CASE REPORT 1, AFTER SIX MONTHS

Lymphocyte typing performed after 6 months of treatment with the micro-immunotherapy formula C1. Complete tumor response, disease free interval 1 year and 6 months. Increase of cellular immunity. Increase of cytotoxic arm (NK and T8c). Decrease of Treg.



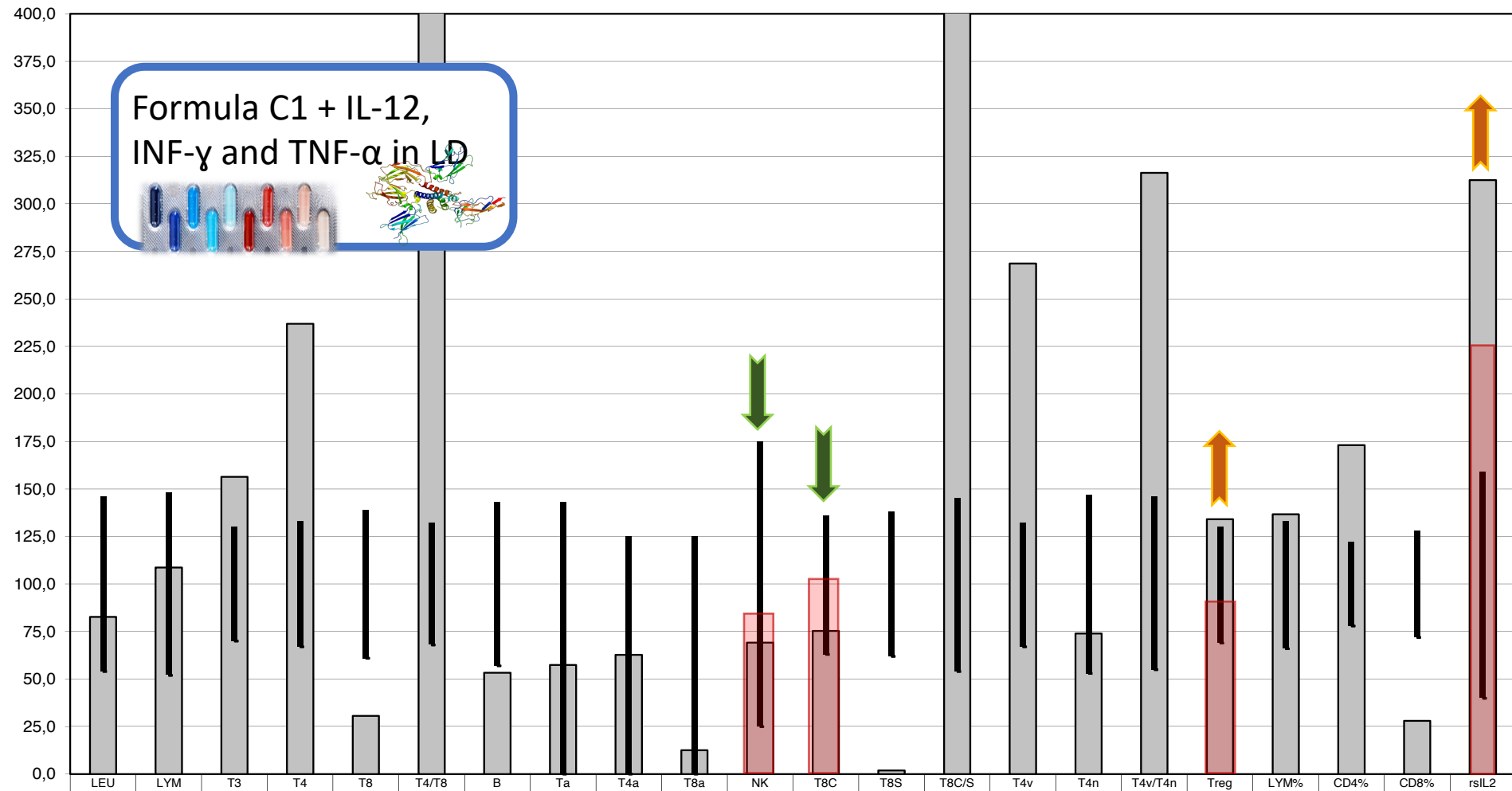
## CASE REPORT 2

Patient with colon cancer pT4, N0, M0. Complete tumor response, disease free interval 6 months, does not perform CT. Low TH1 arm, high sIL-2R. Begins treatment with micro-immunotherapy formula C1.



## CASE REPORT 2, AFTER 10 MONTHS

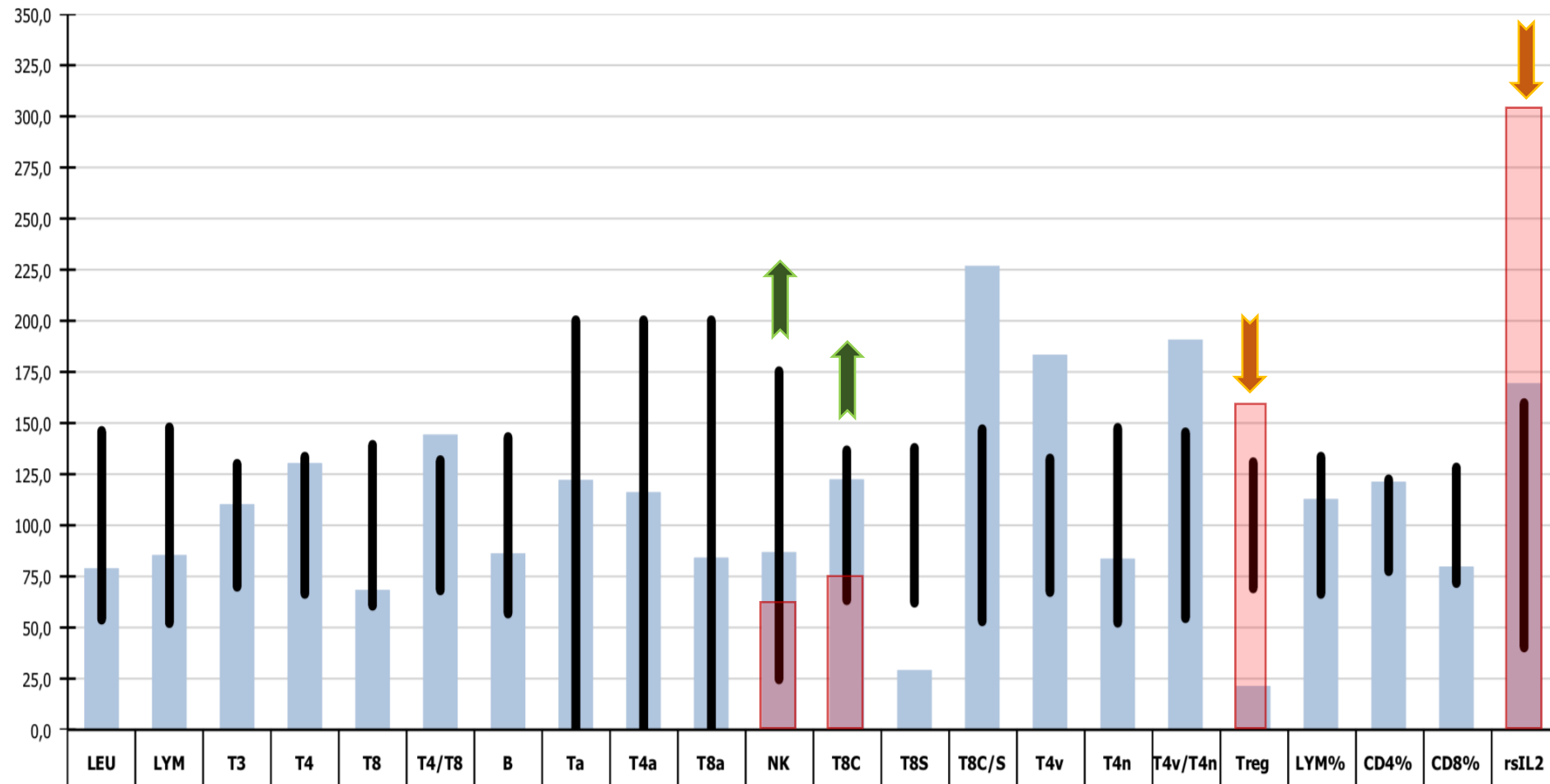
4 months of treatment with the micro-immunotherapy formula C1. Diagnosis of peritoneal carcinosis, good general condition. Reduction of NK and T8c, increase in Treg and sIL-2R. The formula C1 is maintained and IL-12 – INF- $\gamma$  – TNF- $\alpha$  in low doses (LD) 4CH are added.





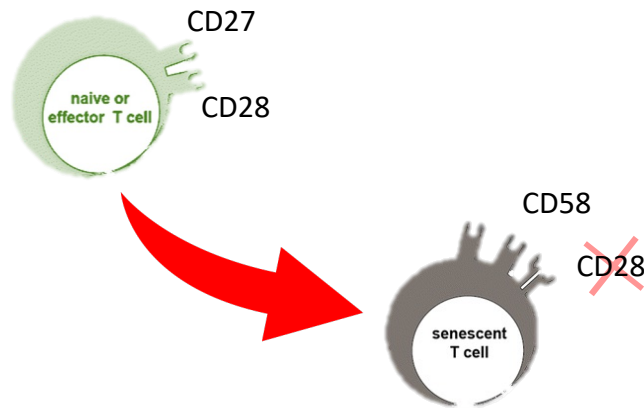
## CASE REPORT 2, AFTER 14 MONTHS

8 months of therapy with formula C1 + 4 months of IL-12 – INF- $\gamma$  – TNF- $\alpha$  in low doses (LD) 4CH. Stability of disease, good general condition. Increase of NK and T8c, collapse of Treg and sIL-2R



# SENESCENT T LYMPHOCYTES: WHAT KIND OF CELLS ARE THEY EXACTLY?

**Cytotoxic T8 lymphocytes are TH1 immune defense effectors (viruses and tumors)**



Senescent cells are CD8 T cells that have replicated many times and are terminal differentiated due to:



age of the patient



Stimulation from chronic infection



Tumors in long surviving

The loss of CD28, which is an important costimulation molecule for the activation of cytotoxic CD8 T cells, and the acquisition of CD58 are considered to be the markers of the senescence of cytotoxic T8 cells.

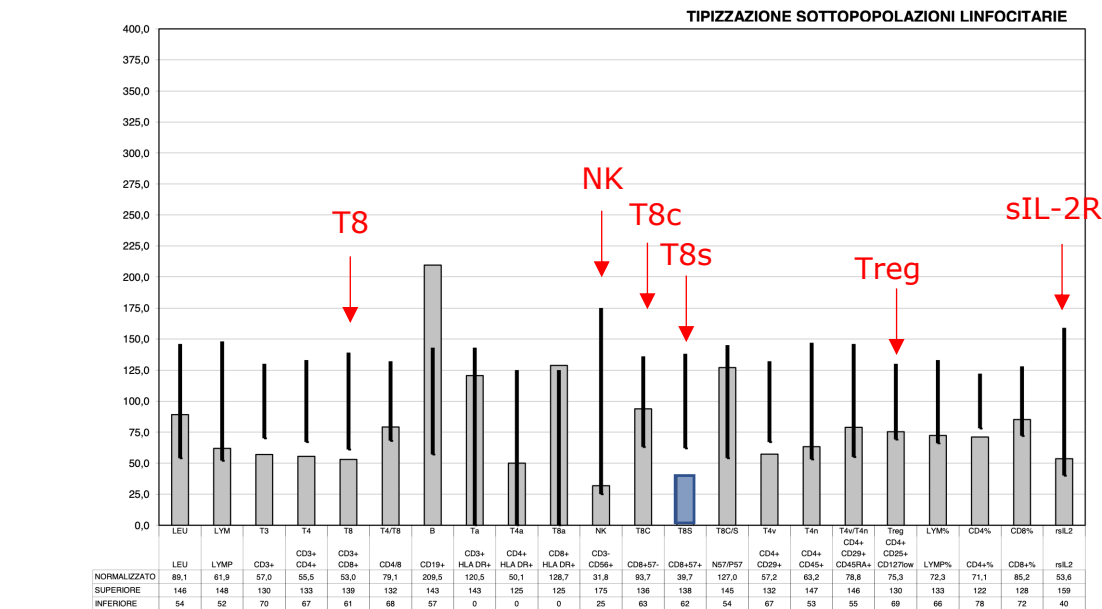
**Senescent T (Ts) are CD8+ CD28- CD58+ cells**

Patient with IV degree cerebral astrocytoma.  
Lymphocyte typing at the time of diagnosis.  
Ab anti-CMV: 147, anti-EBV EBNA: 262, anti-EBV VCA: 62.  
Starts temozolamide therapy by mouth in association with micro-immunotherapy formula C1, mistletoe derivatives and IL-12 + INF- $\gamma$  in low doses 4CH.

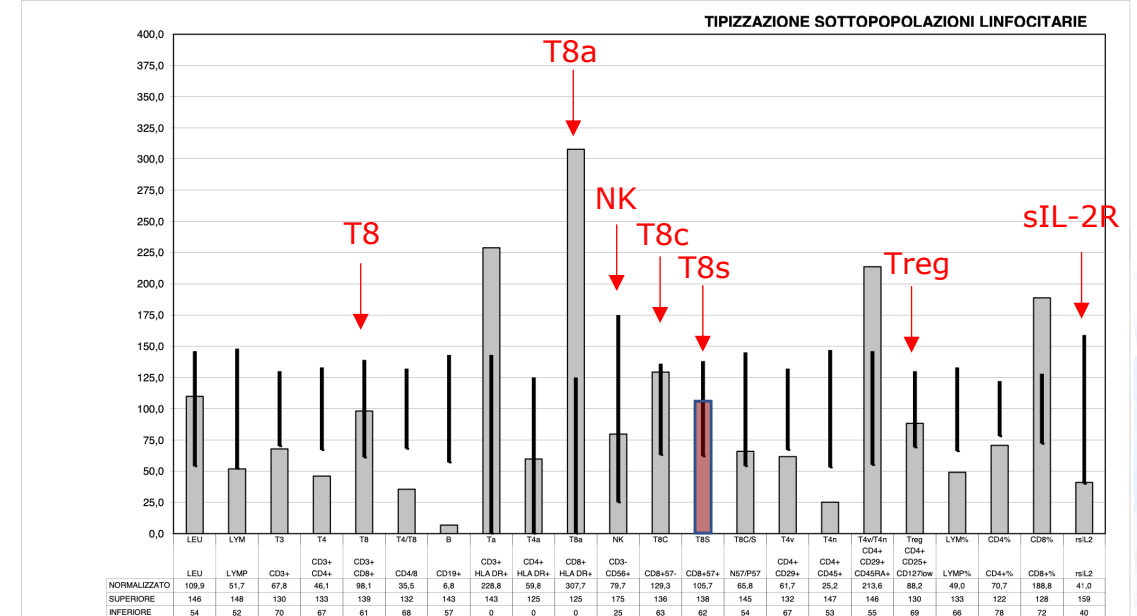
The arrows show the values of total T8 cells, NK cells, cytotoxic and senescent T8 cells, Treg and sIL-2R

Panel 9 months after the start of temozolamide therapy.  
Decrease in cellular immunity (chemotherapy), increase in total T8 cells, cytotoxic T8 and NK cells, collapse of sIL-2R.

Concomitant increase in senescent T8 cells (CMV reactivation, Ab anti-CMV: >180).  
Elevated activated T8 cells (T8a) precedes a herpes zoster reactivation after a few days.

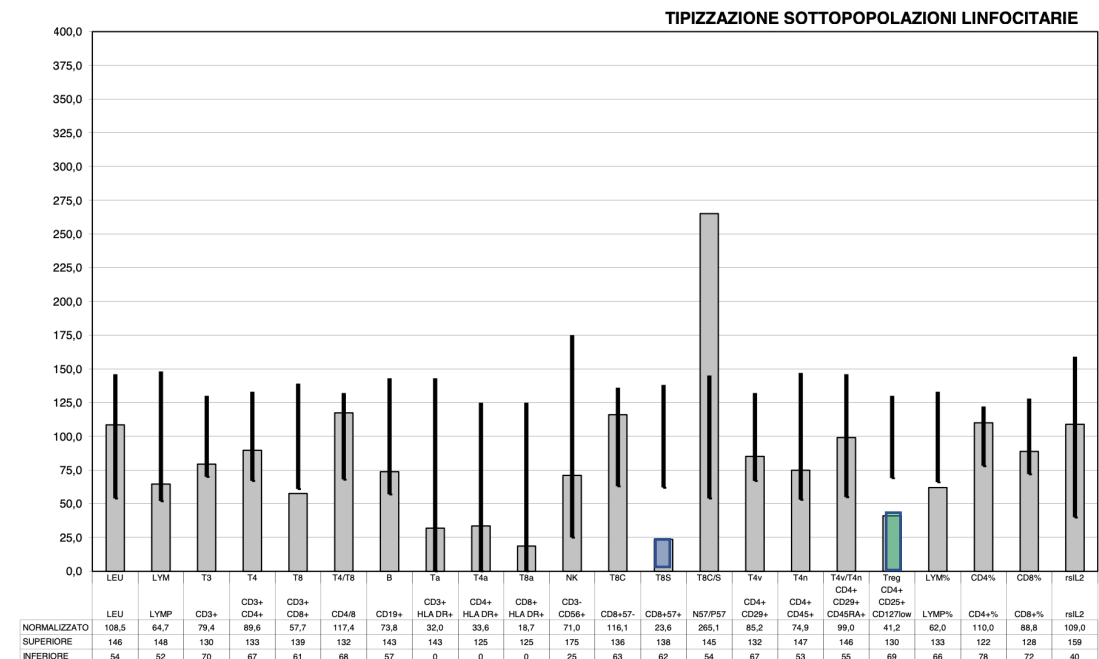
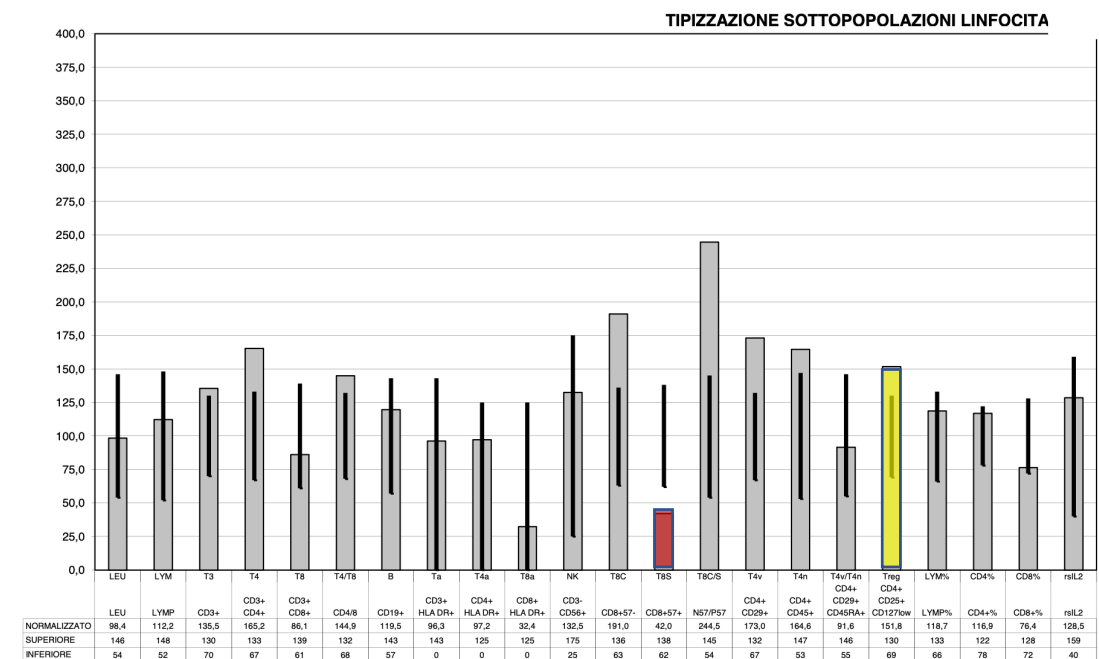


Monza, 18/07/2017



Monza, 13/04/2018

In the first panel: immune system status in patient with ovarian cancer.  
In the second panel: the same patient one year after surgery + complete remission of the disease after 4 months of chemotherapy in combination with microimmunotherapy.  
Good cellular immunity after chemotherapy, good TH1/TH3 (T8/Treg) ratio, normal sIL-2R, decrease in senescent T8 cells (red and blue column), decrease in Treg (yellow and green column).

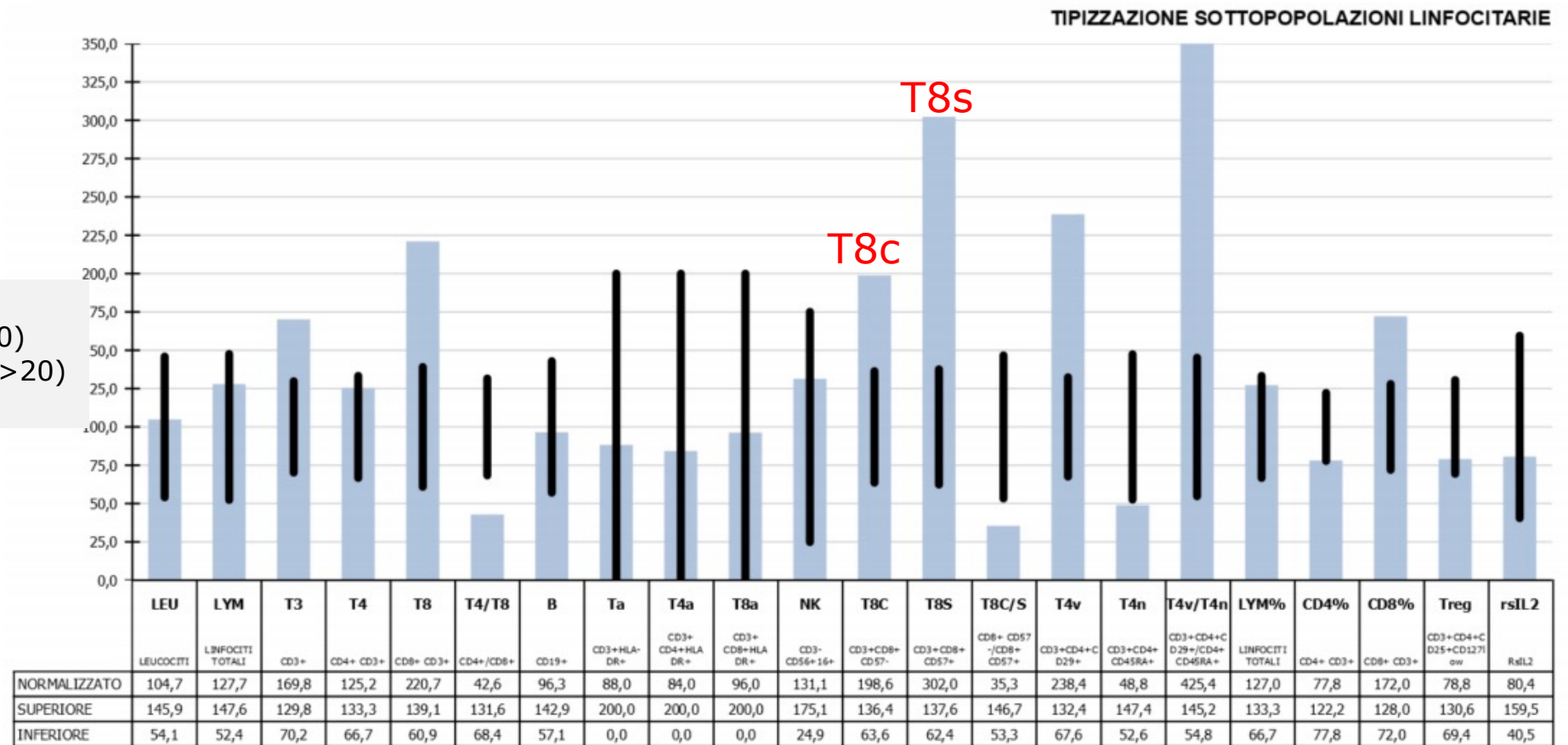




# An aging immune system

47-year-old patient with Long COVID and EBV / CMV reactivation.  
Could the herpesvirus reactivation with the increase in senescent T8 cells lead to a lower efficacy of anticancer immunosurveillance?

Ab anti-CMV IgG: 122 (Pos. >14)  
Ab anti-EBV VCA IgG: 698 (Pos. >20)  
Ab anti-EBV EBNA IgG: >600 (Pos. >20)  
Ab anti EBV EA IgG: 5



# 'If you cannot measure it, then it is not science'

- When you can measure what you are speaking about, and express it in numbers, you know something about it; but when you cannot measure it, when you cannot express it in numbers, your knowledge is of a meagre and unsatisfactory kind: it may be the beginning of knowledge, but you have scarcely, in your thoughts, advanced to the stage of *science*, whatever the matter may be.

*Popular Lectures and Addresses* vol. 1 (1889) 'Electrical Units of Measurement', delivered 3 May 1883

William Thomson, Lord Kelvin (1824-1907)



Thank you for your attention!

Grazie!

Dr. Tiziana Semplici

